# INTRODUCTION TO BIOTECHNOLOGY

Dr. Sunita Rao
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# CONTENTS

# CHAPTER 1

# A COMPREHENSIVESTUDY ONCAUSES, TRANSMISSION AND TREATMENT OF ELEPHANTIASIS

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**ABSTRACT:**

An infection known as filariasis, which affects the lymphatic system, is the root cause of the condition known as elephantiasis. This condition is both excruciating and difficult to treat. Resulting from the transmission of a nematode parasite belonging to the family filariodidea by the bite of an infected mosquito. This parasite falls under the category of nematode. The illness is spread by mosquitoes, which also spread Wuchereria bancrofti, B. timori, and Brugia malayi all over the globe. The disease is very much still widespread and is associated with a lengthy period of disability that includes both mental and physical impairments. This study includesan illustration of elephantiasis, which is also known by its alternative name, filariasis. This study presents a concise overview of parasites, the lifecycle of lymphatic filarial, related symptoms, as well as approaches that may be used for the diagnosis and detection of the condition. With the following strategies for disease management and additional information regarding the subject. The comprehensive study review may help in effectively eliminating the disease from the areas that are at risk, and it will also contribute to the advancement of diagnostic tools that are currently in use.

**KEYWORDS:**

Disease, Elephantiasis, Filariasis, Filarioidea, Parasitic Worms, Wuchereria bancrofti.

## 1. INTRODUCTION

Parasitic worms termed filariae are responsible for causing the condition known as filariasis. Filariae are microscopic roundworms that may be found in the body's tissues and blood.Lymphatic filariasis occurs when adult worms make their habitat in the lymphatic system, which is the most significant filarial disorder for humans. The lymphatic filariasis subtype. When referring to lymph, the term "elephantiasis" is occasionally used. Clinically speaking, elephantiasis is the most severe manifestation of filariasis[1]. In tropical and subtropical regions, elephantiasis is a significant public health issue due to the thickness of the skin and associated subcutaneous tissues, most especially in the legs, sexual organs, and female breasts. This is due to parasitic worms or toxic metals [2].

Human roundworm parasites belonging to the subfamily Filarioidea are responsible for the devastating illness known as filariasis. *Brugia* ***malayi*** ,*Wuchereria bancrofti, Dirofilaria spp.*,*Loa loa*, *Onchocerca volvulus*, are the agents responsible for majority of the filariasis in human

beings. One of the most serious forms of filariasis is lymphatic filariasis (LF), often called elephantiasisconsidering that mature worms reside in the lymphatic system. Mosquitoes of the genera Culex, Mansonia, and Anopheles are responsible for the transmission of filarial parasite from one host to another.[3].

Lymphedema (acute dermatolymphangioadenitis (ADLA) and elephantiasis) and male urogenital illness are two of the most painful and disfiguring chronic forms of LF morbidity (hydrocele and lymph scrotum). ADLA bacterial infections are very painful, feverish, and progressive. Lymphedema of the breast, vulvar swelling, and rheumatic and pulmonary issues are other possible but less often documented clinical manifestations [4].

**Figure 1: Bilateral Swelling characteristic as Podoconiosis** [5]**.**

Ernest Price developed the name "podoconiosis,"a term derives from the Greek for "foot" (podos) and "dust" (konos), implying that the condition is caused by the patient's feet coming into repeated exposure to sensitive clay soil. Barefoot subsistence farmers in places with red volcanic soil are particularly at risk for podoconiosis, a non-filarial type of elephantiasis. Alkaline volcanic rock has transformed into red clay soil causing a persistent and devastating geochemical illness. Disabling swelling of both lower legs, accompanied by mossy and nodular skin alterations, characterizes this condition seen in Figure 1 [6].In the chronic stage of lymphatic filariasis, elephantiasis manifests as a result of the blockage of lymphatic channels by the parasites. A mature in the lymphatic system, particularly in and around the genitourinary system, after they invade lymph vessels. By using ultrasonography, found actively swimming adult worms in enlarged and twisted lymphatic channels. Lymphedema affects the legs, arms, mammae, and other extremities if lymphatic vessels are blocked. Connective tissues in the subcutis become too developed as a result of this condition. Rough skin on the legs, trunk, and other body parts gives the impression of elephant hide because of secondary and recurring bacterial or fungus infections [7].

The helminths *B. malayi*and *W. bancrofti*are responsible for the spread of filariasis in India. There are places around the globe where macaques and leaf monkeys serve as reservoirs.

Microfilariae, the larval forms delivered by mosquitoes, are responsible for acute infection. Adult worms induce chronic lymphoedema by depositing in and blocking lymphatic vessels. It seems from experimental research that simple lymphatic blockage may not result in lymphoedema unless there is concurrent inflammation. Blockages in the lymphatic system considerably increase the likelihood of lymphangitis attacks, which may then lead to swelling [8].

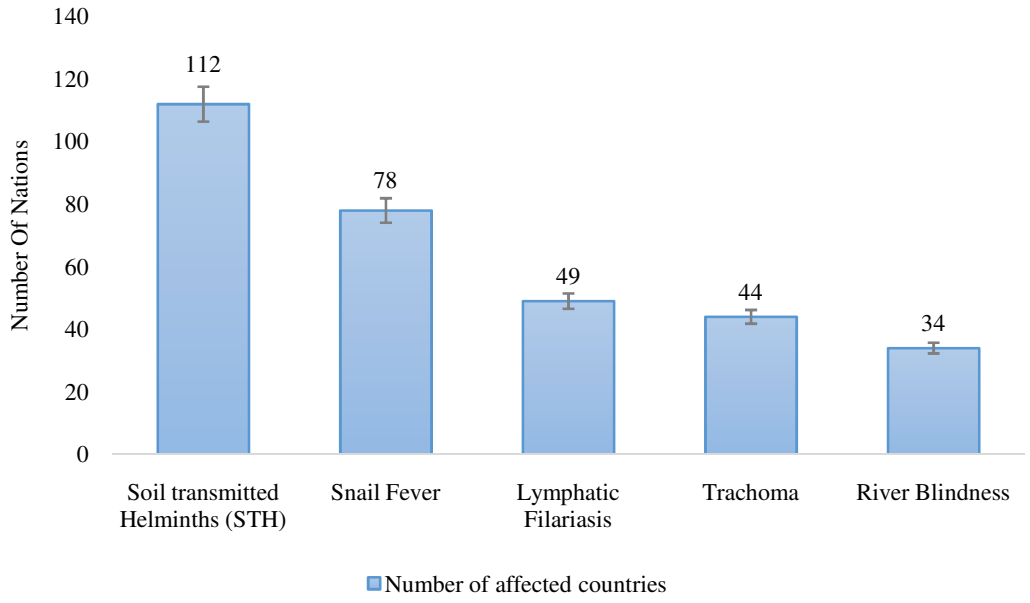


**Figure 2: Number of Nations Globally Impacted by Neglected Tropical Diseases.**

By the year 2020, this map will show the number of countries all over the world that are battling with a few distinct tropical diseases that have been neglected. The disease known as lymphatic filariasis, which is also known by the name elephantiasis, has caused damage to the people of around 49 countries as of today. Elephantiasis is characterized by the severe expansion of some bodily parts, as depicted in Figure 2. This condition is caused by parasitic worms.

## 2. LITERATURE REVIEW

Zulma M. Medeiros *et al.* stated in their study the "Global Program to End Lymphatic Filariasis" (GPELF) is to eliminate the disease by the year 2030. The GPELF method centers on MDA ("mass drug administration") and morbidity prevention.The author reviewed filarial morbidity literature. In the Americas, systematic morbidity aid programs were limited, according to the author. The author reviewed the pathophysiology, epidemiology, consequences, and management of filarial mortality in endemic areas in the Americas.The author searched PubMed, LILACS, Scopus, and the Web of Science for as long as the author could and in as many languages. Information from 2150 studies was culled by three reviewers, who then assigned quality ratings. The author stated that a knowledge vacuum exists, thus health providers and researchers must deploy and improve GPELF morbidity methods [9].

Negar Bizhani *et al.* discussedin their study that the Authors used a systematic review and meta-analysis to evaluate Lymphatic filariasis (LF) prevalence in Asia.Together, the terms were searched throughout all 48 Asian nations. For this study's statistical consideration, 41,742 unique

instances were found. It was determined that overallnearly 3% of the Asian population had LF (95% CI [1.7, 5.2]). After looking at the data, the author concluded that the overall prevalence of LF showed no discernible change over time [10].There are 119 million individuals infected with lymphatic filariasis throughout73 nations; 40% of global incidence is found in India. Lymphatic filariasis is a neglected disease despite the severe impairment it causes. The lack of data on the financial impact of the condition is a contributing factor. Recent research conducted in rural regions of south India has demonstrated that the disease's treatments and associated productivity losses are substantial. Therefore, Kapa Ramaiah *et al.* utilize these research findings to estimate India's yearly economic loss due to lymphatic filariasis and then explore the significance of these results [11].Elizabeth Acromwell *et al.* evaluated in their study that73 countries are either currently or historically endemic to lymphatic filariasis, and this study utilized a global database of georeferenced survey locations to project the annual incidence of the disease from 2000 through 2018.To develop spatially continuous estimates of global all-age 2000-18 lymphatic filariasis diseases with a 5 km2 accuracy, the researcher utilized Bayesian model-based geostatistics and time series techniques. There were 14,927 data points included in the geospatial algorithms. From 3.1 million in the Americas to 107 million in South and East Asia, about 199 million persons were affected by lymphatic filariasis in 2000 (95% uncertain band 174-234 million). As of the year 2018, an estimated 43–63 million persons were afflicted. Prevalence is decreasing worldwide, while it is less likely that Africa and Southeast Asia have achieved eradication levels. The author argues that more data gathering or action may be required before MDA activities can come to a close and that such places may be identified using mapping estimates[12].

## 3. DISCUSSION

When blood levels of the parasite microfilariae are at their peak is called their "periodicity." This is consistent with how diverse mosquito species eat. Except for the W. virus vector *Aedes polynesiensis*, most animals that spread lymphatic filariasis eat only at night. Currently, no animal hosts for lymphatic filariasis. *W. bancrofti* is narrower than Brugian microfilaria and has a curved front end.Authentic elephantiasis is a parasitic ailment brought on by one of three different types of roundworms.

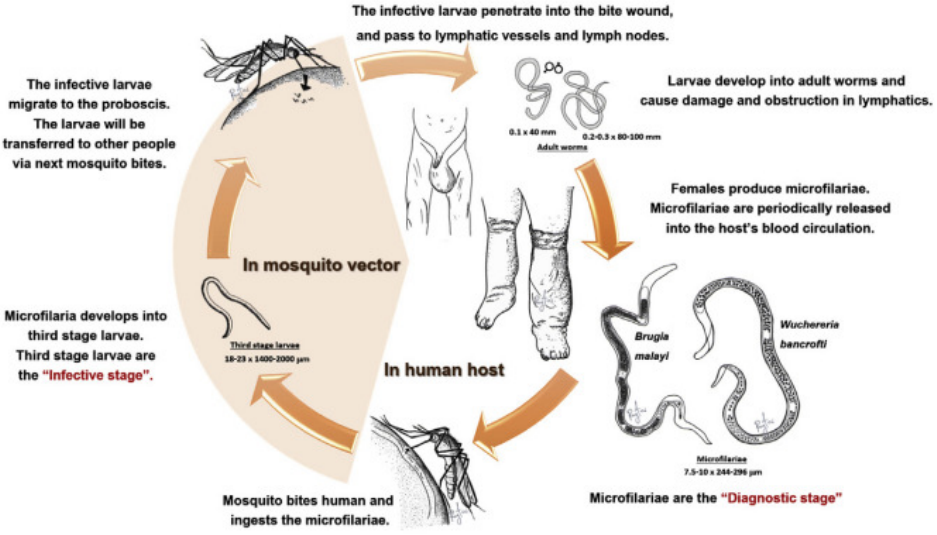


**Figure 3: Stages in life cycle of lymphatic filariasis**[13].

Lymph is drained from the body through a network of lymphatic arteries, lymph nodes, and lymphoid organs from tissues into circulation to assist the body to regulate its fluid levels. The long, threadlike worms obstruct this drainage system. A condition known as lymphedema may develop when lymph fluid cannot drain from the tissues, causing swelling. Extreme limb swelling may cause them to seem like the front leg of an elephant, both in size and appearance. This is elephantiasis, a debilitating and disfiguring illness [7].

Third-stage larvae (L3s) feed on blood and travel from the bite site to the lymphatic system. The lymph nodes, which is where the worms mature into adults. About 50,000 microfilariae may be produced by the female worm every day after mating. The parasite's species dictates the timing at which millions of microfilariae are discharged from the lymphatics into the host's blood circulation. Microfilariae may survive for 6–12 months, whereas adult lymphatic filarial infections live for 5–10 years [14].Microfilariae are eaten by infected people when mosquitoes bite them; once inside, they lose their sheath, breach the stomach wall, and eventually make their way to the thoracic muscles. They undergo a metamorphosis into immature infective larvae after the first stage of development. This is contagiousas seen in Figure 3, Mosquitoes' proboscises are where the larvae ultimately end up, from whence they are spread to additional hosts by further mosquito bites.

### *3.1.Contributing Factors and Transmission Mechanisms:*

*Culex quinquefasciatus*, a common mosquito-like insect, is responsible for transmitting the illness *Wuchereria bancrofti* over most of mainland India (96.4 percent). This illness may be found in both cities and countries. Due to the vector's unusual breeding habits, which include floating plants, *Brugia malayi* infection is often relegated to rural locations.*Mansonia annulifera* (Mansonioides) is the primary vector, while *M. uniformis* is the secondary vector. *M. Indiana* has such a low population density that it plays little more than a supporting role in any vectorial calculations. Microfilaraemia caused by *W. bancrofti* and *B. malayi* in mainland China occurs mostly at night. Native people living on the Nicobar Islands in the Andaman and Nicobar Islands were the first to have diurnal subperiodic *W. bancrofti* infections detected in 1974–75. Mosquitoes belonging to the genus *Aedes (Finlaya) niveus* were blamed as the source of the disease [15].

### *3.2.Lymphatic filariasis clinical manifestations:*

Depending on the prevalence of endemicity, the clinical presentation of LF may change. Hydrocele is the most prevalent symptom, whereas lymphedema and elephantiasis are less common complications. Lymphedema and hydrocele are both frequent in India and the surrounding regions. Less common manifestations of the illness include chyluria and tropical pulmonary eosinophilia. Places, where *Brugian filariasis* is common, do not have cases of hydrocele. The most important finding concerns chronic diseases, where the central function of acute bouts and the progression of the disease have been linked to pathogenic bacteria [16].Lymphatic filariasis is notoriously difficult to diagnose since the microfilariae must be found in nighttime blood samples. It's still the gold standard for making a conclusive diagnosis of lymphatic filariasis. Microfilariae are most easily detected by seeing their movement in a microscope and fresh blood smear obtained from a finger prick. However, the parasite species cannot be determined using this approach.Giemsa staining of both thin and thick blood slides is the standard method for detecting microfilariae in samples. However, the sensitivity of the fresh blood smears and the Giemsa staining methods is low.

*3.3.Disease prevention and control face significant obstacles:*

Even though there is more support for eradicating lymphatic filariasis internationally today, the illness still hasn't been eradicated in India because of a few key concerns. There is a lack of knowledge about the relationship between endemicity and vector/parasite complexes, as well as the eradication goal's coverage and yearly treatment length. Tools, techniques, and criteria are needed immediately to track the progress of eradication efforts and assess their success. Predicting and demonstratingpublic health and economic effects of eradication efforts especially in hard-to-reach places is becoming more critical. Significant restrictions exist in the current therapeutic options.

However, present medication distribution techniques fall short of stopping transmission only 40-60% are treated if mass therapy is conducted by the usual health services, which is the fundamental difficulty with existing treatments. Thus, there is an urgent need for more efficient methods of medicine distribution for the elimination of lymphatic filariasis that are adapted to regional circumstances and variations in health sector development[17].

*3.4.Lymphatic filariasis treatment:*

Parasite typically microfilariae detection in human blood or skin samples was required for the diagnosis of filarial infection until recently. This required very laborious procedures and consideration of the microfilariae in the blood cycle whether it be nocturnal or diurnal. Identification of antibodies through immunodiagnostic tests was attempted as an alternative, but this approach was not successful because the tests were not able to differentiate between current and past infections, and because they showed cross-reactivity with prevalent gastrointestinal parasites as well as other organisms.

1. *Drug Treatment:*

More than 70 nations have widespread problems with filarial illness. Although their death rate is modest, they may suffer significant morbidity from complications including secondary infections or blindness. Ivermectin's efficacy in destroying microfilariae has been investigated for some years, and its application to treat onchocerciasis has led to several studies in this area as well as lymphatic filariasis. Amocarzine and other new medications provide the possibility of macrofilaricidal substances that are less difficult to deliver than older treatments like suramin sodium. Having access to medicines that work against adult worms is a crucial long-term objective.

SemisyntheticStreptomyces avermitilis antinematodal principle derivatives, such as ivermectin and suramin, are particularly effective. Ivermectin and suramin cause tonic paralysis in nematodes. To its credit, it only functions as a particular subset of glutamate-gated CI channels in invertebrates. Flukes and tapeworms, which are resistant to ivermectin, do not use these channels for motor control. Evidence of the potentiation worm has been spotted. Humans may not exhibit any GABA-related behaviors since the neurotransmitter is excluded from the brain owing as a result of its low affinity for GABA receptors in mammals and consequent rejection from the BBB (most likely due to poly protein-mediated efflux) [18].

Nematodes' glycogen stores are depleted and their ability to produce the ATP they need for life is stunted when they are treated with mebendazole or flubendazole. This results in the eventual death or immobilization of the parasites, which are then expelled from the digestive tract. Human

blood glucose levels are unaffected by this substance. Maximum plasma concentrations of benbenazonium are obtained within 2 to 4 hours.Albendazole, an anthelmintic taken twice daily for two weeks, has been demonstrated to kill adult filarial worms at dosages of 400 mg. Since bancroftian filariasis adult worms often lodge in the scrotum,[12] the death of the adult worm causes severe scrotal responses. Albendazole has no direct effect on microfilaria and does not quickly diminish microfilaria levels. Microfilaria is killed off more effectively by DEC and ivermectin when both are administered in a single 400 mg dosage. The elimination program advocatesalbendazole in combination with doxorubicin (DEC) or ivermectin.

Adenolymphangitis (ADL) is a complication of acute or chronic filariasis that may be treated with antibiotics. Referral centers need to be established since the vast majority of acute attacks seem to be of bacterial origin. To allow lymphoedema to be reversed, it is necessary to adopt rigorous local hygiene measures to avoid ADL, which may include the use of local antibiotics and antifungal drugs. Preventing additional lymphatic injury and kidney failure in my carriers requires prompt treatment with regular 12-day treatment.

2. *Surgical Treatment:*

Common surgical treatments, such as excision/eversion, are used to treat hydroceles. Elephantiasis often necessitates the removal of the skin on top of the condition. Due to the high prevalence of infections, it is advised that thorough skin cleansing be combined with perioperative antibiotic coverage.There are two primary categories of limb lymphoedema surgery: drainage treatments and excisional procedures.Creating new lymphatic pathways (as in omental transposition) or rerouting existing ones (through lymph venous anastomosis) are the primary goals of drainage treatments. Excisional techniques reduce the size of an abnormally big limb by removing excess tissue. Incisions, skin closure methods, and surgical sequences might vary greatly across surgeries. Homan's surgery involves 2–4 phases to clean the full leg circumference, although other surgeries have attempted to combine the two.Assuming that DEC is effective against the adult parasite, giving it to a patient who already has microfilaria in his blood early on may kill the worms before they can reproduce and cause lymphoedema. Since lymphoedema and its development are both caused by recurring infections, protecting these individuals against ADL attacks is crucial.

3. *Thermal Treatment:*

It has been discovered that the Chinese have developed a novel therapy forreducing swelling caused by lymphedema by alternating hot and cold treatments for the affected limb kitchen equipment consisting of an oven. According to reports, however, this strategy is very successful and cumbersome. Evidence suggests that cooking using a microwave oven may be better.Acute outbreaks of ADL are the most unpleasant symptom of lymphatic filariasis because they hinder the patient from doing his regular daily tasks. For the afflicted people, this means a significant hit to their wallets and a decline in quality of life. As a result, it is crucial to treat ADLs as away to prevent them from happening in the first [19].

## 4. CONCLUSION

Despite the World Health Organization's (WHO) attempts to reduce microfilaremia through mass medication administration, filariasiscontinues to be one of the most devastating diseases ever recorded. Once substantial lymphatic damage has been established in lymphatic filariasis, the

disease state seems to be permanent, according to the available evidence.The elimination of lymphatic filariasis is a secondary goal of such integrated approaches but as well as exploring new possible regimens, vector control, and involvement in MDA programs. A more hopeful future in the fight against this potentially eradicable illness is on the horizon, thanks to the recent availability of medications to prevent transmission of the disease and simple, low-cost treatment techniques which bring relief to those with obvious sickness. To stop the spread of filariasis in India, it is suggested that everyone get a single dosage of albendazole 400 mg once a year, in addition to a dose of DEC calculated according to their body weight. This also helps get rid of helminths in the community's digestive tracts, which is a benefit.Because of this, there is a pressing need for improved medicine delivery methods that take into account variations in India's many regions.

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# CHAPTER 2

# A PROSPECTIVE STUDY ON THE DEVELOPMENT OF A QUANTUM DOT-BASED DETECTING SYSTEM FOR BREAST CANCER

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**ABSTRACT:**

Breast cancer is more likely to develop in women than any other kind of cancer. The prognosis for cancer improves with early diagnosis. More people are being diagnosed with breast cancer, which has sparked worries about over-treating individuals who already have a confirmed diagnosis. The best indicator of needless therapy in individuals with a clinical diagnosis is the subject of recent investigations. Study on the peculiar optical and electrical properties of biological and medicinal applications. Semiconductor quantum dots (QDs), a particular kind of nanoparticle, have gained popularity recently. The present usage of QDs in cancer therapies is the main emphasis of this study, which includes early detection of primary tumors such as pancreatic cancer, ovarian cancer, breast cancer, and prostate cancer, as well as distant metastases or local lymph nodes. The production and modification of QDs would boost their impact on the study of tumor metastasis. In addition to examining the remaining difficulties and promise, this research also examines the application of QD-based nanotechnology in the detection of malignant cells and tumor microenvironment studies in vitro and in vivo models.

**KEYWORDS:**

Breast Cancer, Cancer cells, Human Epidermal Growth Factor Receptor-2 (HER2) Nanotechnology, Quantum dots (QD'S), Tumor.

## 1. INTRODUCTION

The development of nanotechnology has made it possible to manufacture the smallest possible particles, which may then be put to use in illness diagnostics and the development of more effective treatment methods. It does this by capitalizing on the one-of-a-kind optical, structural, electric, and magnetic features that nanoparticles possess. Imaging at the microscopic level is becoming more important in modern medical practice. Therefore, neither the spatial nor the high temporal is very high [1].The main signaling route, receptor-ligand interactions, or protease–substrate interactions, for example,have not yet been identified as the limiting steps in the genesis and spread of cancer.Cancer invasion is now seen as an adaptive and diversified process that includes a tumor microenvironment.The ongoing interactions between the tumor and also its microenvironment, which includes tumor stromal components, host cells, and surrounding supporting tissues, ensure that the tumor will continue to grow and advance [2].

There is now technology availableto detect breast cancer. The availability of therapeutic medicines, both natural and synthetic, that truly can prevent or control critical molecular receptors has recently increased, and this has helped to enhance breast cancer patients' chances of

surviving the disease. Despite this, mortality rates continue to climb, which is why researchers never stop seeking innovative therapies for breast cancer [3].These are easy to measure, reliable, and reasonably priced because of their excellent sensitivity and selectivity. In addition to monitoring and identifying recurrences, this assists not just in monitoring but also in predicting and predicting disease progression. There are several ways to discover novel biomarkers for a wide range of disorders. There are several ways to find and understand signs of biological processes, like invasions, metastases, or proliferating. Biological information indexes or libraries are one of these strategies.

In comparison to other cancers, the incidence and mortality rates for female breast cancer are astronomically high. An increase in breast cancer incidence has resulted in a decrease in death rates, which have been steadily decreasing over time. According to Figure 1,the term 'incidence' refers to the number of those females who have been told they have breast cancer for the first time in that given year. In India, a total of 162,468 women were found to have breast cancer for the first time in the year 2018. In addition, breast cancer was responsible for 27.7 percent of all newly discovered cases of cancer in female patients. That works up to almost one out of every four newly diagnosed cases of cancer in women in India being breast cancer.

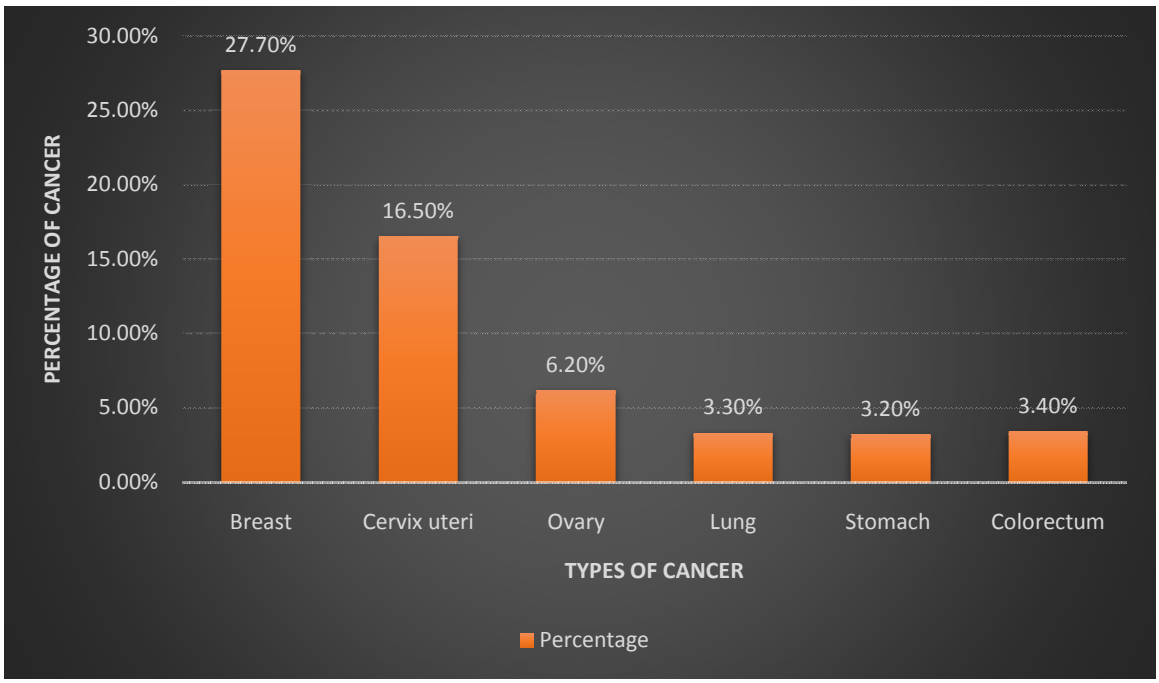


**Figure 1: Shows the Number of female cases in India that are expected to be diagnosed in 2018.**

Breast cancer is a phenotypically complicated disease: infiltrating ductal carcinomas, carcinoma in situ, and invasive carcinoma may coexist as mixed histological forms of invasive carcinoma. There is a morphological heterogeneity that mimics molecular heterogeneity, and also physically comparable tumors may vary in genetics and metabolic functions, and unique genetic anomalies may impact clinical outcomes [4].

Due to the effects of quantum mechanics, the optical and electrical characteristics of quantum dots, also known as QDs, are distinct from those of bulk materials. Quantum dots are semiconductor Nanocrystals in the nano dimensions. Because of the QDs' narrow spectral peaks,

size-dependent emission spectrum, or wide excitation range, they are suitablefor severaluses in diagnostics, biosensing, and imaging applications, and also other biomedical fields. In the realm of biomedical application, QDs, nanoparticles with intriguing optical and electrical characteristics, are of particular interest. For molecular and cellular imaging, they are an obvious option because of their high degree of brightness and photostability. Combinatorial optical encoding using QDs is made possible by their wide excitation and limited emission spectra [5].

## 2. LITERATURE REVIEW

Goro Kutomi et al. discussed in a study that Breast cancer biomarkers could improve patients' quality of life during treatment and disability. With increasingly detailed genetic investigations, breast cancer's molecular pathways have become clear. To clarify breast cancer, biochemical parameters, diagnosis, prognostic, or therapeutic response were researched between 2009 and 2014 for biomarker information. The final analysis found 16 breast indicator studies. Cancer growth. Seven biomarkers in 9 studies were reliable survival predictors, while seven others were inaccurate. These prognostic factors may increase therapeutic options [6].

G Peng et al. stated in the study that, the author tested a nanosensor array's capacity to distinguish between healthy and cancerous breath volatile organic compounds (VOCs).177, 20–75-year-old participants exhaled alveolar breath (prostate cancer patients, healthy controls, lung, colon, and breast). Patients' breath was collected before treatment. Patient data showed a healthy population. A network of cross-reactive biosensors built on naturallythe breath of participants was examined utilizing functionalizedcombined techniques of mass spectrometry and gas chromatography on gold nanoparticles (GC-MS).According to the findings achieved, the nanosensor array could distinguish among both ‘healthy,’ and noncancerous, breath, as well as between patients with various types of cancer. Because of this, a low-cost and user-friendly foldable noninvasive instrument that helps to overcome several of the shortcomings of the existing diagnostic techniques for cancer [7].

Aristarchos Papagiannaros et al. conducted a study that thin-layer PEG-PE quantum dot micelles including 5% para-nitro phenol were synthesized for imaging techniques.When the 2C5 antibody was hydrated, it was coupled to PEG-PE micelles, and the QD micelles were separated from the rest by filtration. When compared to the poorly targeted QD-micelles, the signal strength of the contrast material at the tumor was increased by a factor of 2. Dorsal images of an animal may disclose organs like the kidneys and liver, but lateral images can only reveal malignancies. After 24 hours, the agent can identify melanoma nodes in a lung pseudo metastatic model ex vivo, but at 1 hour, only a homogeneous signal is obtained. The author concluded that passively targeted medicines at the same low dose and speed as the targeted agent creates ultra-bright tumor pictures and double fluorescence intensity. It might improve early metastasis detection [8].

## 3. DISCUSSION

It is generally accepted that cancers, such as breast cancer, originate from a unicellular organism in which errors and epigenetic alterations have changed the transcriptional activity that codes for cellular growth regulators. After such occurrences, the subsequent molecular pathways might lead to the creation of malignant sub-clones with increased proliferation or the advancement of tumors.The use of nanotechnology as a platform for cancer molecular imaging has a lot of potential. Because of the one-of-a-kind optical and electrical properties that quantum dots (QDs) possess, they are now the subject of extensive research as a potentialnovel biomedical imaging probe for in vitro and in vivo applications. To discover solutions to the problems that QDs

provide for biomedical imaging, researchers have looked closely at their physicochemical properties, such dimensions as shape, content, and surface texture [9].

QD-based probes could be used to recognize cancer compounds with great specificity and selectivity when paired with biomolecule agents like antibodies, peptides, or even other small molecules. This process is known as bimolecular targeting. Therefore, QD-based multiplexed molecular imaging may provide light on the temporal-spatial interaction between molecules by concurrently staining many different tumor indicators. This strategy has been proven in some studies to be helpful in the investigation of the tumor microenvironment both the molecular mechanism of cancer invasion, which is essential to understanding, and cancer itself [10].

*3.1.Quantum Dot Biomedical Applications:*

Semiconductor quantum dots (QDs) have sizes between 2 and 10 nm and are made up of elements in either Periodic Table Classes II through VI or III through V. QDs are among the most promising Nanocrystals because of their one-of-a-kind optical and chemical capabilities. Their particular size and surface effect make them stand out from other Nanocrystals.Spectroscopy is an ideal application for the numerous benefits quantum dots (QDs) have over traditional organic fluorescent dyes.These advantages include high fluorescence intensity, a long lifetime, and great photo-bleaching tolerance.The luminosity of multifunctional probes based on QDs makes it possible to achieve great sensitivity in cancer molecular imaging and targeted treatment at the same time. When applied in spectrum applications, the sensitivities of quantum dots-based molecular diagnostics maybe that is two to three orders of magnitude larger than that of conventional fluorescent dyes [11].

*3.2.Quantum Dots: Their Characteristics and Possible Applications:*

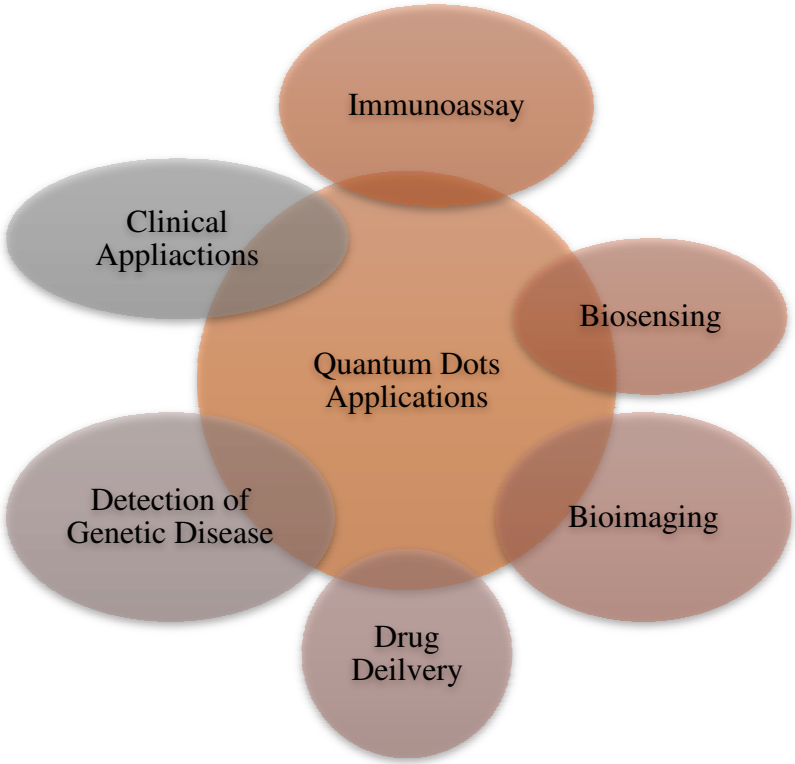


**Figure 2: Displays The Quantum Dots In Their Many Applications.**

The inner Cadmium selenide (CdSe) semiconductor core covered with Zinc Sulfide (ZnS) outermost casing is the most widely utilized QD system. The CdSe core's chemical or optical durability is ensured by the ZnS shell. Changing the size of QDs allows them to generate fluorescent light in the ultraviolet to infrared range. Depending on the QD's size, the QD's fluorescence wavelengths are dictated byits potential energy discrepancy (i.e.,what sets its aroused state different from its ground state).A broad variety of absorption coefficients over a wide spectrum range, great photostability, and the ability to be multiplexed are just a few of the advantages of quantum dots (QDs). Advanced molecular imaging, drug delivery, and high-sensitivity bioassays may all benefit from their brilliant and stable in vivo characteristics. QD bio conjugates have allowedReal-time imaging with better resolution and monitoring of single receptor molecules on the surface of live cells is now possible.Biological systems make use of a variety of imaging methods, including optical, magnetic resonance, and nuclear imaging, all of which complement one another. There are several downsides to using these procedures including expensive prices, lengthy imaging times, and poor prognosis at early stages. This necessitates the development of a probe that can overcome all of these obstacles. QDs are ideal candidates for multimodal imaging probes in both the medical and industrial fields, and their use is rising rapidly.

Biological species that are conjugated with organic dye in traditional bio-imaging suffer tremendously from the drawbacks of high photosensitivity, wide emission bands, limited absorbance, and medium condition sensitivity in traditional cell imaging whereas on the other hand, QDs are promising prospects since they can be tuned to emit and absorb at desired wavelengths from the ultraviolet to the near-infrared luminous region by varying their sizes, composition, and covering. Figure 2 depicts a variety of quantum dot uses.Several methods have been used to successfully produce QDs of high quality. Moreover, they are often made in the presence of a surfactant in organic solvents like toluene or chloroform, and at higher temperatures. However, particles coated with surfactants are insoluble in water because of the hydrophobic strand which extends into the extraction solvent and also the polar surfactant head group that is connected to the inorganic core of the QD [12].

### *3.3.Research on Cancer Using Nanotechnology Based on Quantum Dots:*

#### *3.3.1. In vitro detection of a primary tumor:*

Cancer-specific ligands and antibodies have been coupled with QD-based sensors for in vitro imaging and detection of cancer since biocompatible QDs were available in 1998 [13].At low expression levels, QD-IHC is more accurate and precise than traditional Immunohistochemistry (IHC) as well astherefore can accomplish quantitative detection, which could give considerably more information for individualized therapy compared to IHC. QD-based scanning is now one of the most promising techniques for early cancer detection because of its remarkable biomedical imaging capabilities.When detecting lower levels of protein expression, QD-IHC is more reliable and precise than standard immunohistochemistry (IHC) and also can accomplish quantitative detection, which would give considerably more information for individualized therapy compared to IHC. Because of its exceptional medical and biological performance, one of the most useful methods for diagnosing cancer now is imaging based on quantum dots [14].

Wu et al. investigated HER2 (human epidermal growth factor receptor 2), a protein found on the membranes of breast cancer cells. The Humanized epidermal growth factor receptor 2 (HER2) is overexpressed in around 25%-30% of invasive and metastatic breast cancers. When it comes to

predicting outcomes and tailoring treatments for breast cancer, HER2 is crucial [15]. To perform a comprehensive, quantitative analysis of many biomarkers in a single experiment using viable breast tumor cells and clinical samples. Researchers Yezhelyev et al. used quantum dots of varying colors (QD). Then, they compared their findings to those found by utilizing more conventional techniques like western blotting and fluorescence in situ hybridization (FISH) [16].Using QD-based probes, Chen et al. were able to successfully identify BC, showing that QD-IHC could distinguish between low and high levels of HER2 expression and that multiplexed QD-based detection was possible at the same time. The study found that there are five distinct kinds of breast cancer, each with a different five-year survival rate. Because of this, the individual tumor events, tailored diagnostic, prediction, and therapy would all benefit from QD-based multiplexed imagery [17].

*3.3.2. Tumor imaging In vivo:*

Using in vivo imaging, it is possible to see the development of tumors in real-time. In vivo tumor imaging provides more conclusive data than molecular imaging in vitro.To improve the quality of in vivo tumor imaging while minimizing the animals' physiologic stress, however, the author urgently needs sensitive and targeted imaging agents. Targeted molecular imaging or "Enhanced Permeability and Retention" (EPR) are two approaches that QD-based imaging agents may use to address this need.Tumor blood arteries are notoriously leaky, which is why EPR-based tumor imaging relies on this fact. It's vital to note that, in comparison to normal tissues, tumor vasculature is substantial, but it's also irregular and leaking, dilated and badly coordinated. Macromolecules and nanocarriers from the circulatory system are more likely to seep into tumor tissue because of the EPR effect.The identification of the Sentinel Lymph Node (SLN) is a critical step in the process of removing cancerous tissue using surgical means. Lymph flow is responsible for transporting cancer cells to lymph nodes after they have disseminated from the primary tumor.Sentinel lymph node (SLN) excision is most effective when cancer cells in the SLN near the tumor site are discovered with high sensitivity. Commonly used in breast cancer therapy, SLN imaging entails watching the lymph node closest to the organ being attacked for signs of regionally dispersed malignant cells. It has been demonstrated thatNear Infrared (NIR) QDs, which emit at 850 nm, perform better than other types of quantum dots in this procedure. Recent experiments have also demonstratedNIR light and invisible fluorescent QDs were used to map the gastrointestinal system's SLNs. This method is exceedingly sensitive and may be performed in real-time intraoperative [18].

*3.4.Detection of Cancer Metastasis Through the Use of QDs:*

Initially, tumor cells infiltrate neighboring tissue, enter the circulation (intravasate), and make their way through to the parenchyma surrounding the target organ (vasculature).The vast majority of breast cancer patients have advanced or metastatic disease, making surgery impractical.There has been much research into what causes carcinoma cells to acquire their invasive and metastatic characteristics, however, this has highlighted the need for a new way of viewing cancer metastasis. The QDs-based technique has benefits for metastatic detection.

*3.5.Targeting Cancer with a Quantum Dot Delivery System*:

An impermeable polymer coating was added to the original CdSe QD by Shuming Nie et al.Molecular binding of tumor-targeting molecules and drug delivery activities were affixed to the QD conjugate by this coating, preventing extremely hazardous cadmium ions from escaping. In addition, the coating managed to prevent the leakages of highly toxic cadmium ions. The team

is now focusing its efforts on the creation of a medication delivery system that is specific to cancerous cells [19].The company is working on QDs that are attached to peptides or antibodies and are being used to attack tumor cells in mice. To avoid tissue harm, QDs would be adjusted to emit energy in the infrared range. These QDs would release the medicine only when they were struck by laser light, which would be a peptide or antibody specific to the cancer marker on cancer cells. This would enable the poison to be targeted to specific cells, reducing the risk of adverse effects. QDs' fluorescence wavelengths are also being extended over 900 nm since few biomolecules emit above this wavelength.

*3.6.Quantum Dots Have the Capability to Recognize the Breast Cancer Cells:*

The study's authors employed QDs manufactured by Quantum Dot Corporation and Genentech to isolate breast cancer cells in real time and determine which ones would react best to chemotherapy. As a preliminary step, they used QDs in combination with Immunoglobin G (IgG) and streptavidin to identify the tumor marker Her2, which is expressed by actively dividing breast cancer cells. Researchers also studied QD technologies for simultaneously labeling Her2 on the surface of the cell and nucleus.Multiplex target detection was achieved by the scientists by allowing them to identify two different biological targets with a single wavelength of stimulation. This proved the viability of multiplex quantitative approaches by showing that QDs of varying colors and sizes manufactured of the same materialmay be combined for use in identifying cellular components.

The fact that biomarkers play an increasingly crucial role in the therapy and management of cancer is now well-acknowledged throughout the cancer community. Biomarkers are cellular indicators of not only the state of physiology but also of changes that occur throughout the progression of the illness. A common side effect of carcinogenic transformation is an increase in the concentration of aberrant molecules, also known as biomarkers that are secreted into the fluids of body. These biomarkers may give information on the onset and development of the illness. A wide range of malignancies has been linked to some proteins that have been identified as particular indicators. Analytes that may be detected by biosensors for cancer detection include antigens, proteins, H2O2, cancer-related byproducts, nucleic acids, proteins on the surface of epithelial cells, and pH variations. In the last several years, several new ways of detecting carcinomas using GQDs as sensor nanoplatforms have emerged.

According to their specific nature, these biomarkers may be beneficial for risk assessment, early identification, and prognosis as well as for the progression of the disease and recurrent prognosis and therapy response. It is critical to employ biomarkers after cancer has been found to classify it into distinct subtypes since all of these subtypes come with a significantly varied prognosis and therapeutic preference.

Cancer's progression is tied to more than just cellular behavior. This process of carcinogenesis is controlled by intrinsic genetic alterations in both cancer cells and stromal cells. As a result of its extended life span, human cancer is particularly difficult to study since it displays a wide range of genetic, cellular, and architectural diversity.The co-evolution of a tumor microenvironment is not well understood by investigations at the molecular and cellular levels, and also clinical studies. For a long time, this co-evolution of the tumor microenvironment was overlooked owing to a lack of suitable technological platforms to highlight the dynamical spatiotemporal processes involved. Due to the high surface area of nanocarriers (QDs), a wide variety of ligands may be attached to them, including new tumor-specific antibody fragments, growth regulators, tiny

chemicals, and peptides, may be attached to them, which could be used to assess the appropriateness of therapies and predict response to treatment.When many biomarkers are simultaneously detected and measured, this nanoplatforms technique may provideincreased signal contrast compared to QDs treated with just one type of targeted ligand. When it comes to researching the causes of cancer growth and devising more precise treatment methods, these features are crucial for understanding the interplay between cancer cells and their microenvironment.

## 4. CONCLUSION

Researchers have just begun exploring QDs during the last two decades. The unusual optical and electrical features of QDs have fascinated scientists and engineers despite the immaturity of the sector. Quantum dots have transformed molecular imaging.QDs are technical wonders with properties that have the potential totransform cancer screening and treatment.QDs have several currents in vitro applications, including molecular pathology cancer biomarker detection; tumor invasion; tumor microenvironment;in addition to a fresh strategy for learning about the diversity of tumors; classification, analysis, and therapy.Nanomedicine's future rests on multifunctional nanoplatforms that integrate therapeutic components with many imaging modalities. The ultimate objective of nanoplatforms-based medicines is to enable the delivery of drugs in vivo to be efficient and selective, with minimal systemic side effects, and the dose and treatment benefits can be carefully assessed noninvasively throughout time. Clinical translation of QDs is hindered by poor distribution, possible toxicity, and the lack of measurement.The author should expect to see a wide range of applications for QDs and QD bio complexes as they become more biocompatible, and the transport of QD/QD bio complexes is significantly influenced by the cell type used. The creation of new QDs has improved several approaches related to QDs, yet key difficulties must be addressed soon.

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# CHAPTER 3

# A COHERENT STUDY ON RECENT DEVELOPMENTS IN REGENERATIVE MEDICINE AND TISSUE ENGINEERING

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**ABSTRACT:**

Printing tissues in has lately come under consideration as a rapid and easy way to create tissue scaffolds. They may be able to meet the rising need for organ transplants in the future. It is an excellent substitute which is biocompatible, mechanically resilient, and readily moldable 3D printed tissue is required for its use in 3D printing. As a result of 3D printing's capacity to create implants that are tailored to the specific needs of each patient, it has revolutionized the medical industry. This study explored tissue engineering technologies like the classic strategy of employing scaffolds to grow cells and modern 3D printing technology may help address these organ needs. For the bio-fabrication of various organs, bio-ink is employed in conjunction with inkjet bio printers. The extracellular matrix (ECM) is employed as a bio-ink in non-vascularized organs, although its application is restricted to a small number of tissues. One of the most recent developments in this subject is the use of vascular organ-generating bio-inks, such as those for the Decellularized (dECM). Tissue engineering has a bright future, but there are still several difficulties to be resolved, such as ethics, regulatory permission, and the exorbitant expense of the technique.

**KEYWORDS:**

Bioink, Extracellular matrix (ECM), Tissue Engineering, Three dimensional (3-D), Regenerative Medicine.

## 1. INTRODUCTION

Age-related tissue degeneration, diseased tissue, trauma, and congenital abnormalities may all cause organs and tissues to decrease their function and structural integrity. The use of regenerative techniques makes it possible to either replace or repair damaged organs or tissues with ones that have normal structure and function. There are two distinct channels through which regeneration can be influenced: the external environment, which can be influenced by parameters such as chemical changes, pressure, temperature, gravity, and light also the internal environment, which could be influenced by factors like structure, material constitution, polarity, as well as orientation. Investigation into regenerative medicine focuses on a variety of clinical and biological contexts, including transplantation, cytology, chromosomes, and epigenetics, among others [1].

The area of medical study known as tissue engineering enables the reconstruction and repair of damaged tissues located inside the body.Integrating cell biology, engineering, and medicine, among others, seeks to find ways to promote the body's natural ability to generate new cells and

tissues. Almost every kind of human cell has been studied using these methods, from bone and cartilage to the many cells that make up the eye.As an example, tissue engineering of bone, it has been shown that polymeric scaffolds are a feasible alternative to the more traditional grafts that are used. These constructions, both those that include cells and those that do not include cells, can promote the necessary processes that are involved in bone tissue regeneration [2].It is possible for all species, particularly humans, to regenerate via molecular processes, which are controlled by the gene-expression program that governs regeneration. Complex tissue architectures may be generated using the mammalian body's inherent ability to regenerate. In situ tissue regeneration is a technique that makes use of the body's inherent regenerating mechanisms in conjunction with synthetic biomaterials.

Tissue damage may be repaired and replaced by the body's natural ability to heal itself. Regeneration, on the other hand, is restricted by a variety of variables (e.g., tissue type, or growth hormones). External assistance or organ transplantation is required for any substantial tissue injury or damage over a particular size. The availability of organ and tissue donors is critical in light of the aging population and the hazards of a rising number of accidents or illnesses that result in the loss of organs or tissues. Autologous and allogeneic transplants of tissues have been made possible because of substantial advances in scientific research [3].

Additive manufacturing (AM) is another name for three-dimensional printing, generally known as 3D printing. It is a method through which a three-dimensional solid model of any form may be built using digital data. This method is known as solid modeling. For a good number of years, the idea of using 3D printing technology in the medical field has been a pipe dream. In the 1980s, Hull CW was the first company to submit a patent application for 3D printing [4]. To generate a 3D print of any item, Hull CW came up with the concept of stacking consecutive layers of base material on top of one another in successive order. Since that time, 3D printing has had an influence not just on the medical profession but also on various other disciplines, like engineering, manufacturing, and medicine.

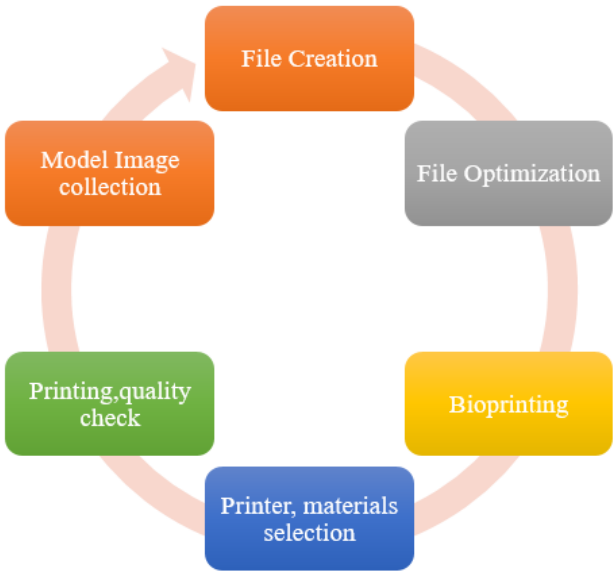


**Figure 1: Description An overview of the procedure for organ 3D bioprinting.**

Powder, polymers, metals, liquids, or even cells may be used in 3D printing. Using these materials, the method may be tailored to suit the specific needs of the application. As a result of

the method's accuracy, efficiency, and reproducibility, it may facilitate the manufacturing of customized tissues with confidence. This also gives physicians, engineers, and researchers a chance to work together to create a real product from a digital file that was transferred and downloaded over the internet.Therefore, 3D bioprinting is crucial in the medical field for the production of a broad range of human and animal organs and tissues surgical implants, and anatomical modeling for diagnostics and training. The objective of this study was to present a synopsis of the potential medical applications of 3D printing. The presentation also covered recent developments in research as well as the consequences such developments have for the medical industry.

A printed model requires a total of five technical processes to be completed. The initial step is to figure out what part of the body you're trying to reach.The structure is then 3D modeled using a Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) scan. As a result, the resulting file is well-suited for printing on paper. Then, the right 3D printer and materials are chosen to meet the needs. To build layered slices of the model, further processing is performed on the data file. To print, these portions are supplied to the printer. Some layers are printed (or constructed) on top of each other until the full object is created. Figure 1, shows a flowchart for the 3D bioprinting procedure [5].To begin 3D bioprinting, researchers must determine the anatomy of the target location they want to print. Created and subsequently optimized for physical printing, the 3D geometry file. Then, the right 3D printer and materials are chosen to meet your needs. As an output, the printer creates a scaffold.

## 2. LITERATURE REVIEW

Using pluronic (P123), butyl diisocyanate (BDI), and collagen, Yin et al. developed a thermosensitive hydrogel with the intention of tissue engineering tendon (BC hydrogel). Tendon stem/progenitor cells were then implanted into the hydrogel. At a temperature of 25 degrees Celsius, the hydrogel underwent a sol-gel transition. Collagen has been demonstrated to greatly increase BDI hydrogel's ability to support cellular proliferation in some different cell lines (pure BDI hydrogels do not promote cell proliferation in any of these cell lines) [6].

Jennifer L Olson et al. conducted a study that presently, research into regenerative medicine is being conducted on practically every kind of human tissue and organ.Due to its incorporation of tissue engineering, cell biology, nuclear transfer, and materials science, regenerative medicine necessitates personnel skilled in cell harvesting, culture, expansion, transplantation, and polymer design to successfully apply these innovations to prolong human life. At various stages of development, different tissues are in diverse stages of clinical studies and pre-clinical trials,whereas some are still in the research phase. In the future, engineered tissues could find larger clinical use and may be a successful treatment alternative for patients who might advantage from tissue regeneration or repair [7].

Gia Saini et al. stated in a study that regenerative medicine concentrates on restoring or regenerating damaged tissue's functional components. Tissue engineering strives to generate completely functional tissue components or organs. 3D printing may replicate real tissue using biomaterials and living cells. Regenerative medicine just began using 3D bio-printing to produce very specialized tissue models. Their research paper focuses on the application of 3D bio-printing to the field of tissue engineering and describes its advantages over other methods. Bio-printing materials, processes, clinical applications, difficulties, and field directions are explored [8].

Andrea De Pieri et al. discussed in a study that since it was initially described in the early 1980s, the process of in vitro organogenesis without the use of a scaffold has gone a long way since then. Despite the considerable advances that have been madeseveral concepts have been taken from in vitro, preclinical, and clinical environments to become clinically and economically viable products. For this innovative and game-changing idea to gain widespread acceptance, some issues relating to the requisite amount of functional cells, dimensions of space, production timeline, mechanization, expandability (which influences reimbursement), and regulatory standards and categorization need to be resolved [9].

## 3. DISCUSSION

There are millions of people throughout the world who need organ transplants, and this situation is made more difficult by the rising number of those awaiting a transplant and the consequent increase in the mortality rate due to organ failure. Finding a healthy organ donor for transplants is a difficult and time-consuming procedure, and storing it for a prolonged period after it has been kept might cause issues following transplantation.In 2019, there are already over 100,000 patients waiting for an organ transplant, according to a study from the United States government regarding organ donation and transplantation. Both organ transplantation and the shortage of organ donors are at their worst at this point [10].

The positioning of cells in scaffolds is one of the most difficult aspects of this process. 3D bioprinting has transformed the use of scaffolds and cells in grafts and constructions by allowing for the production of structures with a degree of material and cell placement control. Among the most popular techniques utilized today include inkjet printing, micro extrusion, and laser-assisted 3D bioprinting. Micro extrusion delivers a stream of ink or scaffolding-containing cells onto a stage, while inkjet bioprinting employs droplets of scaffolding or hydrogel-containing cells [11].cartilage, aortic valves, and blood vessels are just a few of the many 3D tissues in the body, that have been created using these 3D bioprinting technologies, with implanted cells capable of producing ECM proteins like collagens and fibronectin being used to create these tissues. There are a variety of bioprinting devices on the market, each with its unique characteristics [59, 110]. However, there are still several issues that need to be addressed. Cell viability is a big issue with 3D bioprinting [12].

### *3.1.Inkjet Bioprinting:*

One of the first forms of AM to be developed was the inkjet printing technique. To put it another way, the ink travels through a chamber where it is compressed and then squeezed to force the droplets out of a pore. At the moment, the squeezing of inkjet droplets is accomplished using one of three primary methods: thermal, piezoelectric, or electrostatic. The thermal and piezoelectric approaches are the ones that are used for structure creation the most often. Due to the high pressure of the air bubbles created by the localized heating, ink droplets are ejected from the nozzles in thermal inkjet printers shown in Figure 2 [13].Inkjet printers (sometimes called "drop-on-demand printers") may be used for both biological and non-biological purposes. Commercially accessible inkjet printers were essentially transformed into biological material printers. High-speed and precise application of volumes of biological material in liquid form to designated surfaces is achieved. It is common for the printer to spew liquid onto a scaffold (or substrate) that will be used to support the graft after it has been implanted into the patient's body [14].

There are three primary benefits of inkjet printing: speed, availability, and affordability. However, the key drawbacks include the inability to precisely locate and size droplets, as well as the need for bioink with a low viscosity. Thermal inkjet printers, on the other hand, are prone to clogging, making them less reliable.Heated print heads in thermal inkjet printers dispense biological material onto a support structure to print. The biological substance is not harmed in any way by the heating process. The cheapest and most extensively used bioprinting method is the thermal inkjet printer. Many biological materials are also suitable with inkjet printers. A piezoelectric crystal creates acoustic waves in acoustic printers.

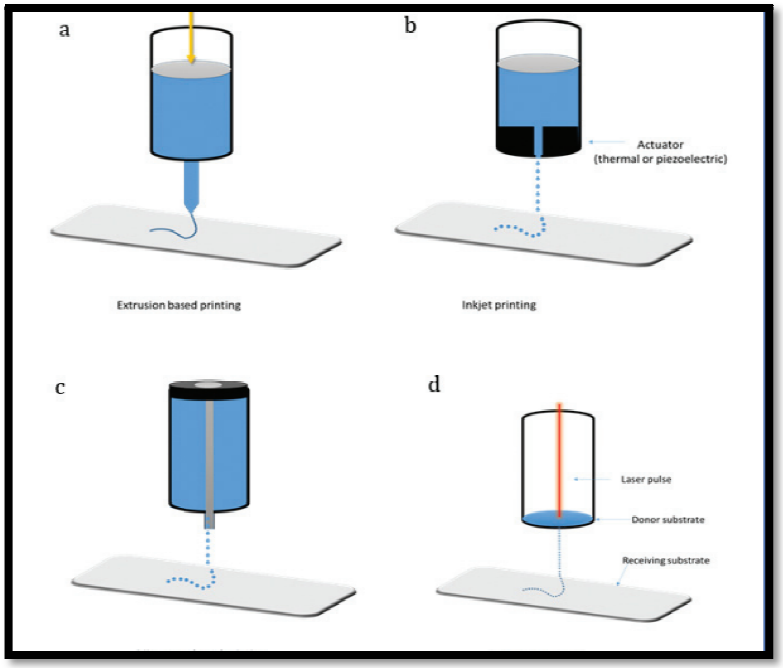


**Figure 2: Many different bioprinting processes are shown schematically. A) Extrusion printing, (b) Inkjet printing, (c) Microwave printing, and (d) Laser-aided bioprinting** [15]**.**

A disadvantage of employing inkjet printers is the need that biological material being printed to be kept at a certain viscosity. The printer head might get clogged if the ink reaches a specific viscosity. As a result, the number of cells that are printed is frequently reduced to keep biological materials as liquids. Droplet creation may be hampered by high cell densities, and printer head clogging is more likely. Skin and cartilage may be regenerated via inkjet bioprinting.

### *3.1.1. Extrusion bioprinting:*

The creation of three-dimensional structures may be accomplished by a method of bioprinting called extrusion-based bioprinting. This method includes forcing bioinks through nozzles. The bioinks are composed of living organisms that have biological significance for upcoming technologies like organs-on-a-chip, tissue scaffolds, tissue regeneration, and delivery systems for drugs.Physical, mechanical, biological, and rheological characteristics are only some of how bioinks, which are mixtures of biomaterials and living cells, impact the quality of printed structures. The capacity of bioinks to produce structures with well-defined boundaries is referred to as their "printability". The rheological qualities of the material and the printing settings are the key aspects that determine the quality of bioprinted constructions, among all of the contributing

components. Extrusion bioprinting is becoming more and more common, and as a result, a variety of strategies for managing the features and parameters of printed objects have arisen [16].

### *3.1.2. Micro valve-based Droplet Ejection:*

In general, a microvalve-based bioprinting system will have a moveable robotic platform as well as several electromechanical microvalve print heads. Every print head has its connection to a gas regulator, which supplies the pressure necessary to keep the valve open for a certain amount of time. With the help of the solenoid coil and plunger, one could adjust the open time of the valve. Solenoid coils produce a magnetic field when an electric current is sent through them, which ultimately results in the opening of the nozzle. After some time, the pneumatic pressure will eventually be greater than the resistive force in the nozzle orifice (the viscosity of the fluid and the surface tension of the fluid), which will result in the deposition of the bio-ink. The material deposition process is heavily influenced by a wide variety of parameters, including the diameter of the nozzle,the hydraulic pressure, the release time of the valves, the bio-surface ink's tension and viscosity, and so on.

### *3.1.3. Laser-Assisted Printing:*

Bioprinting machines are based on the laser-direct writing process. A photopolymerization approach, which is used in laser-assisted bioprinting, is the most common technique. This approach allows for the printing of a wide variety of cells while also preserving the cells' vitality. This focusing tool guides the laser beam from the pulsed laser source to a metallic ribbon film that absorbs the laser energy, as well as the receiving substrate. To print, a nano-thick gold and titanium coating is applied to the ribbon's top glass layer using a laser beam. The laser evaporates the film, causing bubbles to develop at the bottom of the layer and ejecting the bio-ink contained inside them as droplets onto the receptive surface [17].

Contrasted with inkjet and microextrusion bioprinting, this method sees far less utilization. Under pressure, laser pulses are used to create bubbles, which are subsequently sprayed onto the scaffolding or substrate. Because there is no nozzle involved in this process, there is no risk of the printer head being clogged. Additionally, the approach is adaptable to a wide variety of different viscosities.This study indicates it may be possible to achieve cell densities similar to those observed in physiological tissue with no interference with the cells' capacity to survive and function. The finished 3D printed material sometimes contains metallic leftovers from the printing process, which is a major drawback of the technology. This approach is expensive, although expenses may drop with time. Laser-assisted bioprinting can create animal and human tissues.

### *3.1.4. Decellularized extracellular matrix-based bio-ink (DECM) bioink:*

By combining decellularized organs with bio inkjet printing organs, a novel method has been developed to address their drawbacks. First, organs are decellularized, and then their ECM is employed as bioink for the bioprinter in this process. Decellularized matrix is being hailed as the next-generation bioink. While this approach was being developed in 2014, Pati et al. 2015 created soft tissue from decellularized fat. Up to ten times as many layers may be printed using this technology, each one measuring 400-300m in thickness. The hybrid technique, which employs re-absorbable polymer scaffolds, has so far been discovered to be beneficial in the production of the complete organ and in improving the mechanical properties of decolorized organs [18].

*3.2.Innovative Aspects of Regenerative Medicine and Tissue Engineering:*

Several factors, such as the biomaterial to be used and the biological source, must be taken into account before tissue or graft production can begin. Optimal cell-cell and cell-biomaterial (cell-matrix) connections would be enabled by such parameters, which will improve the scaffold's effectiveness. Tissue that has been regenerated for transplantation must have the same cell types and functions as normal tissue. It is much like in real tissues and organs, where various cells have varied functions, such as endothelial cells, which perform structurally and supporting tasks. As a consequence, the 3D bioprinted graft or scaffold's functionality will be determined by the cells employed in the printing process.

Integration into the host requires self-renewal and homeostasis from the transplanted graft or scaffold. Autologous cells are the preferred source of cells to prevent the host's immune system from reacting. Before 3D bioprinting or transplanting, cells from the patient may be grown and induced in vitro to become the desired cells. The use of autologous cells has several downsides to be aware of. These include the inability of primordial cells to regenerate, as well as technological limitations on cell cultivation in vitro.Cellular printing, which would need seeding cells after printing, is regarded as more difficult to control than 3D bioprinting. Grafts must be properly integrated into the patient's vasculature to be accepted by the body. The body's cells are located near blood arteries so that nutrients and oxygen may be exchanged [19].

Cells utilized in 3D bioprinting have several difficulties that need to be addressed. 3D bioprinting requires that cells, such as stem cells, be able to proliferate, stay resilient, and undergo differentiation throughout the printing process. There is a requirement for cells with the same cellular function as normal cells after a scaffold or graft has been implanted.The ability of the cells used in 3D bioprinting to interact directly or through the release of biomolecules like growth factors and cytokines is the last need. Self-renewing cells, like embryonic and adult stem cells may create a large number of new cells hence intriguing. Since adult stem cells can be 3D printed, they are regarded as the safest cells to utilize for transplantation.Encapsulating cells with hydrogel may avoid rejection and extend their stay in the transplanted tissue. By covering transplanted cells with antibodies and peptides, they may target particular tissues and organs. The immune system rejects transplants or new tissues, but it also promotes tissue regeneration and engraftment. Technological advances may reduce graft rejection and increase graft tolerance by changing scaffold properties [20].

*3.3.Tissue 3D Bioprinting:*

Cartilage in the joints gives animals as well as humans the capacity to move without experiencing any discomfort. Other species also have cartilage in their joints. Accidents and pathological disorders such as osteoarthritis are two examples of things that may contribute to a loss of cartilage in humans, which can then cause uncomfortable movement.Because joints are protected by a layer of cartilage, which not only acts as a lubricant but also "cushions" the weight of the body during movement.Type II collagen and aggrecan are examples of ECM proteins, that make up the majority of cartilage. These proteins, in conjunction with synovial fluids, are responsible for the lubricating and weight-bearing capabilities of cartilage [21].Most notably, the regeneration process has been improved by incorporating cells into biomaterials, which is superior to using cells and biomaterials separately. Several translational research is examining the effects of combining stem cells with biomaterials. The differentiation of stem cells into chondrogenic tissue may be supported by sturdy soft materials. The healing of cartilage defects

is being investigated using a variety of Polyethylene glycol (PEG) hydrogels in combination with other polymers. High biocompatibility and a boost in chondrocyte proliferation were seen in 3D-printed complex cartilage structures made from alginate, gellan, and type II collagen.

## 4. CONCLUSION

As is the case with the introduction of any new technology, the 3D printing process has opened up an infinite number of doors for the field of medicine; nevertheless, this will also contain a provision for variety, given that the requirements of each patient will be clinically distinct. The age of personalized medicine will undoubtedly begin when this occurs. Nevertheless, to prevent inappropriate use of the technology, this should be carefully controlled by a regulatory agency.The microbiome affects practically all body cellular functions, therefore understanding its involvement in constructionor graft acceptance is essential. To further the field of regenerative medicine, 3D-bioprinted human models of diseases and conditions are required. Scientists and doctors' abilities to "imitate nature" or "work with nature" are crucial to organ transplants and tissue regeneration" to develop breakthrough biomaterials and technologies like nanotechnology.Advances in tissue engineering research and technique led to bioprinter scaffolds and decellularized organs. More research is improving prior approaches. Improving understanding of regenerative biology, microelectronics, and 3D printing assist overcome barriers. Organ production is no longer far off. FDA rules, expense, and ethical considerations may delay the technique, but research predicts organ shortage will be decreased soon.

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# CHAPTER 4

# AN ANALYSIS OF THE POTENTIAL APPLICATIONS OF ARTIFICIAL INTELLIGENCE AND MACHINE LEARNING IN THE FOOD INDUSTRY

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**ABSTRACT:**

The widespread usage of artificial intelligence (AI) is rapidly turning the world into a global car and gently reducing the amount of human dialogue that occurs between individuals. These improvements are focused on quick mass manufacturing, a precise but organized supply chain, and on-time delivery to please every client. This research will show how artificial intelligence (AI) is used in many areas of the food sector. These options significantly reduce costs while also making the best use of resources and reducing human error. By increasing production with the use of different fitting methodologies for sales estimates, combining artificial intelligence and data science can improve food quality in facilities such as eateries, cafés, delivery service chain restaurants, hotels, and food stores. By extending the shelf life of packaging, including meal replacements into AI algorithms, and creating a more user-friendly supply chain monitoring system, AI may enhance packaging while also enhancing food safety. The future of the food business is smart farming, robotic agriculture, and drone agriculture, all of which will be made possible by machine learning and artificial intelligence.

**KEYWORDS:**

Artificial Intelligence (AI), Agriculture, Deep Learning, Food Industry, Machine Learning (ML).

## 1. INTRODUCTION

Agriculture, forestry, and fisheries all have the potential to provide the globe with wholesome food. The expansion of the food business on a worldwide scale remains consistent. (Coronavirus is having an effect on the food business throughout the world.) The rising number of people around the world is contributing to a widening gap between the availability and demand of food. The current population of the world is more than seven billion. Technology is the only way to satisfy the ever-increasing demand for food throughout the world. It is also necessary to establish solid commercial partnerships with farmers and agronomic specialists located in many places around the globe.

Many aspects of the food industry are resistant to technological change yet continue to thrive despite this. However, as rivalry increases within the agricultural food-producingand processing industries,the technology aids in the refinement of distribution, packaging, and testing more swiftly and faultlessly within a limited budget. This is made possible by technology. There is a reduction in the use of human workers and an increase in the use of robotic mechanisms and data processing procedures. This practically assures that there will be no faults or harm to the food quality and provides reassurance to its clients about the safety of the food [1].

When it comes to embracing new technology, the food industry is always at the forefront. Increasingly, the food sector is relying on AI, or computer algorithms that can learn from past experiences. In the food business, artificial intelligence (AI) has the potential to bring about significant change. Artificial intelligence (AI)is a new technology that can significantly revolutionize agriculture in the next years. In the food supply chain, artificial intelligence (AI) may be used at any point, which will lead to a huge boost in productivity.ML and deep learning are the two most prevalent artificial intelligence (AI) approaches today, which may be used to forecast global demand and offer safe food supplies [2].

Humans need food, and it is widely accepted that the optimal result of farming is a ration of diverse commodities that farmers distribute.Food products are vital to the development of every country. Furthermore, it has a tremendous impact on both domestic and global economic growth. Therefore, food sector goods must be of high quality and distributed safely to ensure their long-term viability. Recent advancements in artificial intelligence (AI) have been able to accomplish the expected outcomes in recent decades.

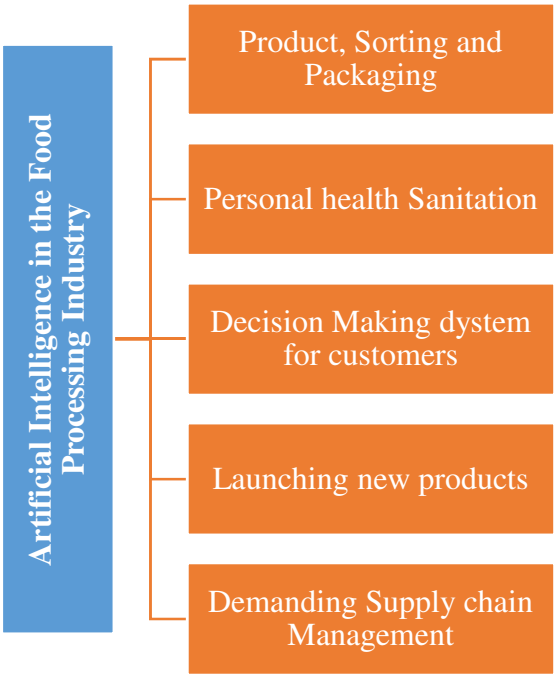


**Figure 1: Displays the in the food processing and handling business, important applications have been adopted.**

Pattern classification, data science, deep learning, machine learning, and robotics are just a few of the many areas of AI that have applications in the food processing business. The food handling industry is just as important as the food production industry, and AI plays a crucial role in overseeing the many tasks associated with the food processing system as a whole. As can be seen in Figure 1, the food processing and handling sector are responsible for the development of some significant applications.All corners of the IT business make heavy use of AI-based or autonomous technologies. It paves the way for the global optimization of issues, the automation of the food business, and the modification of food products. The food industry may conduct an analysis and guarantee optimal conditions, like the production of seeds, crop management,

irrigation, and temperature sensors, which could be enhanced by employing a computerized system, resulting in excellence in food industry product quality[3].

## 2. LITERATURE REVIEW

Varsha Sahni et al. stated in a study that it is possible to extend the life of agricultural operations by using artificial intelligence techniques. Farming uses AI to make the process easier and more efficient.This computerized system gives comparable results across periods ranging from hours to months, enabling the construction of period-specific cycle simulations. These frameworks may be used immediately hence the inferred intelligent algorithms in business settings can be easily transferred to a commercial context where they can be refined over time [4].

H. H Aldhyani et al. conducted a study that powerful AI systems predict Water Quality Index (WQI) or categorization (WQC). Artificial neural network models used to forecast WQI (NARNET and LSTM) have been created. WQC forecasting also uses SVM,Machine learning algorithms such as K-NN and Naive Bayes.The findings showed that the suggested models predicted WQI and categorized water quality properly. The NARNET model predicted WQI valuesmarginally superior to the LSTM model, whereas the SVM technique predicted WQC with the highest accuracy (97.01%). The NARNET and LSTM systems performed equally well in testing, with just a slight difference in regression coefficient, and this work has the potential to enhance water infrastructure [5].

Vijay Kakani conducted a study that discusses the use of the 4.0 industrial revolution technology in agricultural and food production.The evaluation is centered on topics including agricultural software,future farming, analyzing plant data, using smart irrigation, and more. The report also focuses on using sustainable 4 IR technologies to provide a sustainable food supply by 2050. With appropriate sources and use cases, the author explored the Agri Tech sector and AI and vision investments. AI and computer vision companies in the agricultural food market have been analyzed and categorized. This article mentions future-generation farms and animal data businesses in addition to the food sector and agricultural startups. This study is a one-stop shop for AI and vision-related food and agriculture materials [6].

## 3. DISCUSSION

When it comes to making difficult judgments that are either beyond the capabilities of conventional programming or would require a large amount of human labor and expense, artificial intelligence proves to be very useful. For example, artificial intelligence may be used to execute data and workforce analytics, both of which are vital components for organizations to work with to remain competitive and be in a better position. Artificial intelligence can also be used to execute other types of analytics.These are just a few examples of how AI may be put to use. Processing, storing, and delivering food may all benefit from it. Robotics and intelligent drones, for example, may play a big role in reducing the cost of packaging. Other benefits include making it easier to transport goods in risky conditions and also delivering high-quality items.The use of artificial intelligence (AI) has the potential to significantly improve food safety and quality management. Each category has its own space.This research provides an overview of the literature on machine learning and AI in food items, taking into account all elements of AI in the food sector.

In the last several years, advances in computer power, data storage, and learning algorithms have given artificial intelligence a new lease of life. The food business may benefit from this approach

even though it is not a new one. Without machine learning, artificial intelligence will be of little service to these people. To deal with industrial challenges during food processing, such as Autoregressive Moving Average (ARMA) and ARIMA Industry, both artificial intelligence and machine learning are being applied nowadays.Accurate time prediction that anticipates food sales by employing radicalization algorithms and powerful vector machines makes manufacturing more systematic and modular in these businesses [7].

*3.1.Smart Farming:*

AI has various important applications in the food industry, like soil monitoring, robot farming, and predictive analysis. The most cutting-edge uses of AI in the food business are shown in Figure 2. The next part will describe each application that has been submitted.

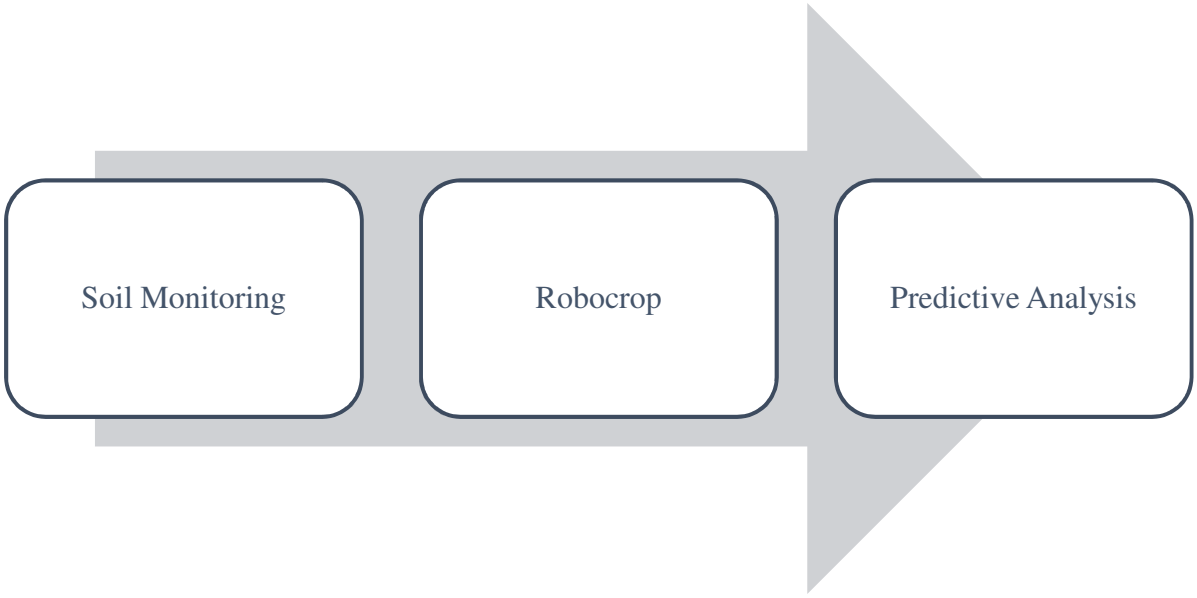


**Figure 2: Displays The Uses Of Artificial Intelligence That Are Now Hot In The Food Sector.**

*3.1.1. Monitoring of Soil:*

AI-based robots can monitor the advancement of soil and crop condition by studying the sequence of data or information they receive by utilizing machine vision and deep learning methods.To educate clients about the strengths and limits of their soil, computerized technologies are used. The primary goal of developing this system is to locate crops with faults and decide on the most effective strategy for optimal crop growth [8].If a farmer sends in a sample of the soil from his or her agricultural field, the monitoring system will give the customer a comprehensive report on the soil's characteristics. A suitable choice has been made for the advancement of bacteria, fungi, and other microorganisms as a consequence of the derived findings. In Japan, crop dusting was the first use of an AI-based drone in 1980 [9].The majority of firms are already using aerial technology and farm AI to check crop performance. The path of the drone is preprogrammed by the user, and the gadget is then integrated. When the computer vision is done, it will take a series of images that will be utilized for further investigation.

Internet of things (IoT) -based Soil monitoring (SM) aids farmers and food producers in maximizing their economics, reducing the risk of illness, and maximizing their available

resources. The temperature of the soil is measured, as well as the quantity of NPK (nitrogen, phosphorus, and potassium), as well as how much water is present, the potential in the soil, and how much photosynthesis radiation is absorbed by the soil.Soil trends must be identified, and a careful selection of conditions must be made,to achieve optimal crop yield and high-quality goods Agriculture-based IoT is known as smart farming. It is referred to as the "smart food sector" because of its use relating to the Internet of Things (IoT). With the IoT, farmers can monitor soil conditions, weather patterns, and crop health from afar. IoT-based agriculture relies heavily on weather and irrigation, as is well known. Good air quality and well-maintained irrigation systems are included in the explanations of smart agriculture.

### *3.1.2. Robo Crop:*

The food business is making use of technological advancements to enhance output. Researchers have created a technology called Robo crop as a result of their work.An artificial intelligence-powered robot system that improves the production process by increasing utility and consistency. Crop tools are lined up precisely and quickly using this machine. An accurate and high-resolution system monitors theovergrown bushes in the food industry's workflow. The captured image is processed on a high-powered workstation, with a special focus on the green band of pixels at the crop line. Thanks to the extensive data acquired by input devices and the many processing lines, a superior level of crop center-line tracking are obtained [10].Several authors have done outstanding work on harvest robotics in robocropping or agriculture mechanization, which has considerably increased productivity in recent decades. Because of innovations and extra benefits such as improved productivity and reduced demand for labor, these systems have grown in popularity. For robotic weed management, an image-processing-based system was developed to recognize agricultural plants at different development stages. Adaptive Robotic Chassis (ARC)is a technology created specifically for strawberry blooms among many already in existence[11].

The performance of robotic cropping is reliant on the quality of the image with which it is utilized. Exceptional outcomes are seen when the image's main characteristics are present. Crops must have more shrubbery thanevery input photo has wildflowers in it,and also the ideal color for crop shrubbery is somewhere in the middle of the RGB color range. An ADC adapter, several detectors and cameras, a three-point linkage framework, a hydraulic-based shaft, a high-definition camera, and other components are common in robocop systems.

### *3.1.3. Predictive Analysis:*

It is possible to predict the impact of weather variations on agricultural yields using learning algorithms. Machine Learning (ML) algorithms play a crucial part in this. Crop sustainability, weather forecasts, and the presence of pests and diseases may all be determined using ML algorithms in conjunction with satellites. Using this strategy, you can get high-quality data or information that is constantly updated. Customers may access more than a billion agronomic data stacks every day from the company, which is confident in the quality of the data it supplies. Precipitation, wind speed, solar radiation, and temperature data, as well as historical data, are critical for predictive analysis. The results of the study are crucial in determining the best time and crop to plant on a given plot of land [12].

*3.2.Artificial Intelligence Applications in the Food Industry:*

The most significant uses of AI in the food sector, other than the aforementioned study, are the following: production, development, and design of customized products; marketing; manufacturing; robotics; and the processing of food goods. AI can enhance the hospitality industry which comprises restaurants, hotels, and cafes.

1. *Agriculture:*

Artificial intelligence (AI) is increasingly seen as a potential answer to the significant issues that agriculture is now experiencing. There is without a doubt a trend toward the increased use of artificial intelligence in agricultural settings, and this trend is rising. When it comes to agricultural operations, making the proper judgments is less than half the battle required to win to get the outcomes you want. Intelligent agents putting measures into effect are increasingly being seen as viable answers for the problems that will exist in the future. The mechanization and computerization of agricultural processes should be every nation's top priority.It has benefited from a variety of automation methods, incorporating neural networks, machine learning, the IoT, deep learning as well as wireless technology. Despite this, the use of technology in agricultural settings is yet in its infancy [13].

2. *Food Processing:*

In many locations, the processing of food is not entirely mechanized. The food processing business is reaping the benefits of artificial intelligence, which is assisting with a variety of tasks, including the sorting of foods, the maintenance of health and safety compliances, the development of new goods, and the improvement of supply chain efficiency. Essentially, the technology is assisting in the process of streamlining work procedures, which is simplifying the job that people do and making operations more effective. By automating as many of their operations as they possibly can, the food processing sector can ensure both absolute cleanliness and a high level of product quality.

3. *Manufacturing of Food:*

In the food production process, AI may be used by food corporations. Vast-scale manufacture of commodities necessitates the use of mechanisms that are not only large and complex but also developed in a sophisticated manner. The use of AI in the food production industry helps monitor each step of the process and generates predictions for the management of costs and stock.Machine learning enables the identification of variables that impact product quality and cause flows in the manufacturing process. It also tracks the journey that things travel from where they are manufactured to where buyers eventually receive them, ensuring openness.

4. *Production of food:*

The production of food is made more productive, secure, and lucrative by the use of AI in increasingly complex applications. It has a huge potential to improve production efficiency and identify the optimal operating areas in industrial facilities. It can make production changeovers go more quickly and help discover bottlenecks in the manufacturing process before they become an issue. Artificial intelligence can improve the production, productivity, and efficiency of the facility.

*5. Food Supply Chain and Food Packaging :*

To meet customer expectations, the food sector must offer markets high-quality food items at a fair cost. Supply networks in the food business are becoming more complex.The use of artificial intelligence (AI) to enhance food safety across the supply chain is a promising area of research. Using this new technology, food safety items may be tested and monitored throughout the supply chain. The whole supply chain may be monitored and controlled by AI-powered supply chain management solutions. Artificial intelligence (AI) can keep a tight eye on every step of the supply chain, reducing delays and increasing profit margins.Equipment that is driven by AI is capable of doing difficult human activities such as packing with high accuracy. Robots can fulfill the increased demand for picking and packaging caused by the expectations of customers. The nature of the process, which is complicated and requires a lot of manual effort, presents a unique opportunity for intelligent automation.

*3.3.The Role of Artificial Intelligence in Preventing Foodborne Illness:*

Because of their sterility, robots are widely recognized in the food processing business. As a result, the frequency of food-related illnesses is greatly reduced. For the whole supply chain, the Food Safety Modernization Act (FSMA) has written higher sanitary requirements. Cereals, spices, and other foods that don't need refrigeration are to blame since they are located in the region most likely to be contaminated. Until recently, such foods were not at risk of contamination, but that is no longer the case. AI-based technologies can certainly assist with these kinds of issues. They can't spread diseases as humans can. Furthermore, maintaining an AI-based system is cheap and straightforward.Technavio predicts a 30% increase in the use of robots in food processing facilities in the next years. Some new revolutionary concepts employ artificial intelligence in food standards procedures that are predicted to gain widespread acceptance shortly. Their major purpose is to minimize the spread of foodborne illnesses[14].

*3.3.1. Electric Noses and Next-Generation Sequencing:*

The food business has seen some of the most exciting new technologies emerge recently in the form of next-generation sequencing (NGS) and electronic noses (ENs).NGS is quickly replacing the DNA method in the field of food security. Artificial intelligence-based automated tools and procedures have made data collecting and laboratory experiments more efficient and accurate than ever before. The NGS is capable of promptly and accurately detecting dangerous inclinations. The spread of infectious diseases can be stopped before large numbers of people are harmed by them.These sensors simply detect the odors surrounding them, and the data they gather is transferred to a data center for analysis by machine learning algorithms. The ML-based system made this decision. The production units get an alert signal. EN, on the other hand, might be the future of food safety [15].

*3.3.2. Food Waste Management:*

By 2030, AI, according to McKinsey, will be able to tackle these kinds of problems and remove massive amounts of food waste. Launching additional regenerative leisure farming strategies may achieve such astonishing numbers. It demonstrates that people are not making the most of their given resources. Rather than relying on old-fashioned agricultural practices, other techniques may be used. The information is gathered by deploying a variety of sensors. After the data is gathered and analyzed using ML algorithms, the right choices may be made. Farmers may

quickly and accurately make judgments with them. Using AI, here are some ideas for reducing food waste [16].

It's easier for food and beverage companies to reduce human mistakes and product waste thanks to the use of artificial intelligence (AI). This results in lower operating expenses, more satisfied consumers, and a more customized shopping experience. In comparison to human labor, machines powered by artificial intelligence (AI) provide solutions that are more precise, faster, and more consistent. The primary effect on food safety is cleanliness and cleaning, and AI technologies show considerable promise in this area.Businesses may utilize creative techniques to enhance the value of their goods and services to best represent their customers. Artificial Intelligence (AI) has the potential to develop our food crops at a quicker rate than ever before. Companies may become digital pioneers by using AI.There are both advantages and disadvantages to adopting AI in the food sector. As long as there aren't enough AI professionals to go around, this technology will remain a niche.Because of the substantial costs associated with large-scale adoption in this industry, the market's potential for expansion is limited. Introducing new technology, such as AI in the food industry, might be difficult. Many countries outside the United States and Europe have yet to fully embrace AI. Humans will never be able to fully substitute AI in the food business because of the necessity for human oversight, repair, and maintenance of aging technology. To improve operational efficiency, the technology may operate alongside people [17].

## 4. CONCLUSION

AI's benefits and applications in the food industry were clearly outlined in this study, which included a wide range of data. Food processing now makes use of low-level artificial intelligence. Businesses in the food, manufacturing, and processing plants, as well as businesses like restaurants and bakeries, which had previously considered artificial intelligence and machine learning technologies to be an unnecessary investment, quickly recognized the importance of these technologies in making their businesses better in terms of growth and strategic plan. They were aware that the only way for them to stay in business was to maintain their position in the highly competitive market since the only people whose services are sought after are those who guarantee both high quality and a rapid response time.AI and ML are already being used in food manufacturing and restaurant operations to ensure food safety. Human mistakes in food production and, to a lesser degree, waste due to underutilized items have been reduced thanks to artificial intelligence. Customers are more satisfied, service is quicker, voice search is available, and purchases are more personalized with reduced shipping costs. In the long term, large food corporations may reap the benefits of these commercial advantages.

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# CHAPTER 5

# A PROSPECTIVE STUDY ON THE DIAGNOSIS OF CANCER BY USING ARTIFICIAL INTELLIGENCE

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**ABSTRACT:**

The ability of computers and other devices to think logically and learn on their own is referred to as "artificial intelligence" (AI). As a result, AI can imitate how the human brain functions. The traditional approach to cancer drug development has the potential to be greatly enhanced by AI technologies like machine learning. There are hundreds of potential genetic and epigenetic variations for cancer, making it a disease with numerous dimensions and complexity. Algorithms based on artificial intelligence hold great potential for the early detection of genetic flaws and abnormal protein interactions. In this study, the author describes a potentially game-changing method that will be used in clinics in the future: how AI-based support might help oncologists offer more accurate therapy by fusing biology and AI. The results demonstrate that more concentrated efforts are being made to introduce AI technology into clinical use and alter how cancer treatment is carried out in the future, although most of the research on AI applications in oncology hasn't yet been thoroughly tested for accuracy, reliability, and generalizability.

**KEYWORDS:**

Artificial Intelligence (AI), Cancer, Computer-Assisted Diagnostics (CADe), Machine Learning (ML).

## 1. INTRODUCTION

Despite extensive studies on cancer's basic foundations, patients, researchers, and physicians continue to be frustrated by the disease since it is a self-sustaining and adaptable disease that interacts constantly with its surroundings. Given this complexity, problems arise at every phase of diagnosis and management, from precise early detection to distinguishing preneoplastic from malignant tumors, detecting infiltrative tumor margins throughout surgery, tracking tumor growth and potential future developed resistance to alternative treatments over time, and forecasting tumor aggressiveness, cancer progression patterns, and occurrence.Considering that there are billions of cells in the human body, cancer is a real possibility at any time, in any location. Cancer is predicted to be at the top of the list of main causes of death in every nation, and Non-communicable diseases (NCDs) in general have become a significant cause of mortality worldwide[1].

One of the most crucial factors in the battle against cancer is the timely and precise detection of the illness in its earliest stages. Mammography, ultrasound, and thermography are the three imaging procedures that are considered to be the most reliable when it comes to diagnosing and detecting cancer. However, there are many more imaging modalities that are also

accessible.Mammography is a crucial tool in the fight against breast cancer, but it is not very useful for women who have heavy breasts. Because of this, the use of ultrasonography or other diagnostic sonographic methods is strongly suggested [2].

Gradually but steadily, Machine Learning (ML)and Artificial Intelligence (AI) are expanding their effect in many facets of modern life, and it is expected that they will play a defining role in the future of digital health care, particularly in the management and therapy of illness. AI and ML have opened the way for autonomous illness diagnostic tools by using massivedata sets to answer the future difficulties of early human illness detection, notably in cancer. One subfield of AI is machine learning (ML) focused on creating a neural network–based algorithms with the ability to learn and solve problems in the same way that a human brain does [3].

Cancer is a disease wherein the body cells multiply in an uncontrolled manner, leading to the disease known as cancer. It begins to form without obvious signs, but over time it may become unusually large, posing a threat to life. It is usual for malignancies other than leukemia to grow into tumors, however, leukemia is an exception to this rule. Cancerous tumors may form in the oral cavity, the nasal cavity, the throat, the stomach, the esophagus, the intestines, the liver, the lungs, the cervix, the testicles, the brain, and the blood. Cancer of the skin is not an exception. A malignant tumor not only impacts the organ that it is located, but it also impacts the functioning of other organs in the body and also the way the body works as a whole during the day [4].

Recent studies have shown that microwave imaging (MI) methods may be used to detect breast cancer at a fraction of the cost of mammography without compromising on safety. Scientists have focused a lot of time and energy over the last several years on perfecting the theory behind MI and creating effective systems for use in controlled laboratory settings. There are a variety of MI approaches that have been successfully tested both numerically and experimentally.High-sensitivity radio-frequency (RF) sensors and sensor arrays may need to be a focus of future research on MI ideas for therapeutic settings, according to the results of several recent medical examinations [5].Breast biopsies are often conducted in addition to screening methods to differentiate between malignant and benign cells,therefore, hiring seasoned professionals is necessary and may be rather pricey. In addition, biomarker-based methods including radioimmunoassay, immunohistochemistry, enzyme-linked immunosorbent assay (ELISA), and fluoroimmunoassay may be able to meet the requirements of breast cancer diagnostics.

While the use of biomarkers has the potential to greatly improve the accuracy and specificity of diagnostic tests, these methods also have some drawbacks [6].Post-treatment monitoring is a commonly recommended part of cancer therapy that provides patients with continuous assistance for treatment-related adverse effects, reassurance, and co-morbidity management. Increased monitoring intensity based on risk might allow for earlier recurrence therapy or increase early detection of second primary tumors, particularly if common risk factors exist. Furthermore, stratified monitoring may allow effective resource allocation and result in large cost savings. ML was capable of predicting recurrent bladder cancer at 1, 3, and 5 years post-cystectomy with higher than 70% sensitivity and specificity using commonly available clinical data (patient, tumor, and treatment characteristics). In a tumor that lacks well-recognized biomarkers, these models offer a valuable prognostic standard.

## 2. LITERATURE REVIEW

In their discussion of methods for detecting cancer tumors, Khan et al. delved into the use of machine learning. Improvements in healthcare have resulted from a wide range of artificial

intelligence-reported strategies during the last several years. Today, difficult issues like cancer may be tackled with the aid of machine learning methods that may be used in several ways throughout the therapy process (from assessment to labeling [7].

To locate cancer tumors, He et al. developed an algorithm forComputer-Assisted Diagnostics (CADe) and a computer-aided detection methodology. It is vital to provide a clear explanation of the imaging procedures to identify malignant tumors using conventional medical practices. They accomplished this by using computer-assisted detecting techniques. The many different outcome stages that are produced as a direct consequence of these kinds of applications make it simpler for physicians to make the appropriate judgments [8].

Yaqub et al. reviewed the most recent advancements in CNN optimizer technology as they relate to brain tumor images. Now, the vast majority of individuals have made advancements to the system of the brain's skills and machine learning. If this were improved, it may lead to more certain judgments concerning the categorization of brain tumors. They never stopped investigating the continuously advancing technical possibilities [9].

The calculation of tumors was made much more straightforward by Kong et al. calculating and identifying different types of cancers is becoming progressively less difficult as new technologies emerge. In addition, the proliferation of the Internet of Things-based accomplishments has given birth to a significant industrial revolution in the present day and age, which has further contributed to the singularity of the series of health structures [10].

A strategy for classifying lung cancers that are based on a hybrid algorithm that was elegantly built has been created by Prabukumar et al. using this technique, several kinds of blocks of complicated tumor were studied to differentiate between their constituent parts. They did this by using a technique of measurement known as the fuzzy C-means (FCM). This allowed for a precise calculation of the geometric structure of the tumor as well as the complicated features of the tumor's location. It had a precision of 98.5 percent [4].

A hybrid fuzzy brain-storm optimization technique was created by Narmatha et al. Following the development of this method, the MRI scan pictures were categorized according to the kind of brain tumor present. The new techniques used to determine the accurate findings were obtained for tumor localization and shape analysis using functional brain imaging and other brain assessment techniques. There is a 94.21% degree of accuracy in the tumor [11].

## 3. DISCUSSION

Multiple advancements, including AI, have been put into practice out of a desire to improve clinical care's efficiency and effectiveness. The streamlining and optimization of clinical pathways are of rising importance due to the ever-increasing demand for healthcare services and also the massive amounts of data produced every day from parallel sources. Artificial intelligence's prowess in spotting intricate patterns in photos presents a unique chance to make what was formerly an entirely subjective and qualitative process into one that is objective, quantitative, and easily repeatable.

Furthermore, AI may evaluate data from visuals that individuals cannot identify and so supplement clinical decision-making. AI may also be used to combine different data sources into sophisticated integrative medical diagnostics that encompass radiography imaging, genetics, pathology, electronic medical records, and social networks [12].The benefits and drawbacks of each approach are compared and summarized in Table 1. At the present, technologies that

incorporate digital image processing are routinely utilized to tackle machine visual issues, and they have achieved good benefits.

**Table 1: Comparison of breast cancer imaging modalities and their benefits and drawbacks.**

| Imaging Method | Application | Advantages | Disadvantages |
|---|---|---|---|
| **Mammography** | Early-stage breast cancer imaging and diagnosis using the gold standard | • It employs low-level X-ray imaging.<br>• This technique is effective for identifying DCIS and calcifications. | • Dangers posed by radiation and other sources<br>• Low contrast in mammography makes it hard for radiologists to read the data. |
| **Ultrasound** | For both hard and soft tissues. | • Accessible and Widely Available<br>• Quick<br>• Highly Sensitive | • Image quality and interpretation are heavily dependent on the competence of the individual doing the scan. |
| **Thermography** | Adaptable to the needs of muscle | Non-invasive | The original generation of medical infrared imaging cameras produced poor quality and inadequate-resolution pictures, making it difficult for doctors to analyze them. |

Artificial intelligence (AI) allows computers and robots to simulate human intellectual activity, generate medication formulations, help with diagnostic techniques and robotic technology, create clinical analytical databases, and analyze the cellular structure of human illnesses like cancer. AI's effects on medicine extend beyond the digital realm into the real world. The virtual part uses DL information management capabilities, which allow it to evaluate the data set from EHRs and direct the doctor toward more informed decisions. Learning in DL is boosted by a mathematical strategy. Furthermore, the AI's physical system could assist in robotic-assisted surgery and nano-robotic technologies for directed medicine delivery [13].DL and Logistic data mining are used in

clinical diagnostics to give ML the ability to reason and aid doctors in making informed treatment recommendations.On May 11, 1997, IBM's Big-Blue AI program shocked the chess world by defeating world champion "Gary Kasparov", the concept gained widespread acceptance in the scientific community. Robotic heart valve replacement, hysterectomy, and vasectomy procedures are just a few examples of how AI is already being employed in the medical field, it is predicted to play a critical role in the future fight against cancer [14].

Computational aid enables the systematic collection and management of vast amounts of data in radiology, genetics, and microbiology for tailored therapy. Artificial intelligence (AI) supervised and unsupervised technologies are still in their infancy, and additional work is needed to eliminate the predicted error. To accurately determine infection-related carcinogenesis, the use of theIt has been suggested that the support vector machine approach and generative probability network tools be used.Examining a patient's symptoms often relies on the clinician's background and expertise. Diseases may be detected with the use of this clinical information and data, but there is no way to ensure a 100% accurate diagnosis or prevent any misdiagnoses from happening. One might infer from this that the human brain has a finite capacity for integrating massive volumes of sample data. The models used in AI, however, are experts at processing massive volumes of information. As a result of the efficacy of education and training on big datasets, integrative analysis and extracting may enable more precise illness detection.

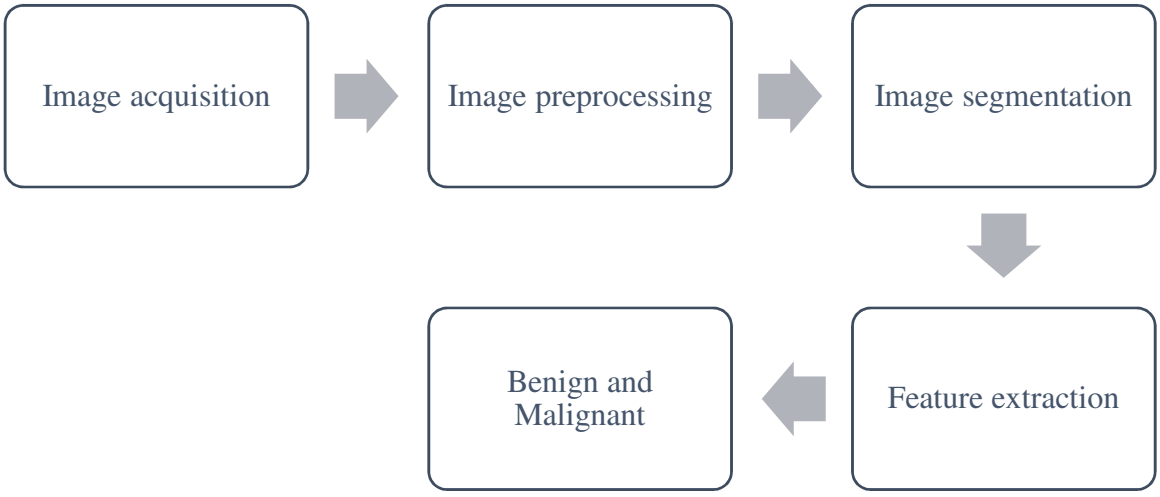


**Figure 1: This shows that Image processing may identify various stages of cancer in its early stages.**

In the domain of detection, the initial step is the collection of medical pictures, followed by preprocessing, segmentation, the extraction of features, and finally classification. The steps required are shown in Figure 1 [15].Mathematical formulations utilizing statistical and biomechanical modeling work aimed at solving computer vision-based image analysis problems form the basis of low-level transformation methods used to incorporate the categorization of images in the first stage of image processing alongside segmentation and registration.

1. *Image Acquisition:*

The first thing that needs to be done to process photos is to capture one. During this stage of the process, Digital photos are used to collect data. Pictures are not lost when compressed because the image format is generally a portable gray map with a fixed format [16].

2. *Image Preprocessing:*

The following phase is called "preprocessing," and its purpose is to enhance the quality of the input photos by removing noise. Before being presented, the photographs are preprocessed with the middle filter. In addition to getting rid of or lowering the amount of noise in a picture, preprocessing may enhance image quality by increasing contrast [17].

3. *Image Segmentation:*

The process of chopping apart a picture and separating it into its component pieces is referred to as segmentation. The process of fragmenting a picture is the most significant stage in both the analysis and processing of images. A picture is segmented when it is physically cut up into smaller portions that, depending on the characteristics of the image, might be identical or distinctive. The precision with which the measurements of the characteristics were taken has a major influence on the outcome's quality [18].

4. *Feature extraction:*

Feature extraction is the process of transforming raw data into a set of meaningful characteristics. There are a lot of different approaches to extracting features. The following are some of the approaches that are used most frequently: 1) qualities about space, 2) features about transformation, 3) features about edges and boundaries, 4) features about color, 5) features of shape, and 6) features of texture. Techniques for the extraction of features are used extensively throughout the diagnostic process of various conditions. The characteristics of the tissue may be quite helpful in distinguishing the tumor from the normal tissue of the breast. These groups of characteristics can differentiate between normal and pathological lesions of the masses or microcalcifications.

Using AI to execute cancer imaging gives a high degree of application and flexibility, which improves three important areas of biomedical work: the sensing, categorization, and therapeutic targets of tumors. The process of using a computer to assist in the identification of objects in radiographs is referred to as computer-aided detection or CADe. CADe has been employed as companion assistance in discovering concealed tumors in circumstances of low-quantity CT screenings and detecting brain tumor growth in MRI images with remarkable sensitivity throughout detection. These applications have been successful.Recent research has shown that CADe is effective in lowering a few diagnostic restrictions, such as inter-rater bias, irregular regeneration reports by biomedical specialists, time consumption, and labor. The use of AI-based applications brings a high level of efficiency to the process of successfully recreating the nature of tumors through automated segmentation. Artificial intelligence algorithms can analyze images of the full body to accomplish tasks related to segmentation. It is possible to improve its performance in the detection of organ structures, which are often not identified by the majority of employees outside of a pathological experience [19].

Automated tumor segmentation and a simulation of the tumor's original characteristics are made much more efficient by an AI-based application. Segmentation tasks may be performed on whole-body images using AI algorithms. Improvements may be made in its ability to identify organ structures that are often missed by all but the most trained professionals. The radiological data are being utilized to teach AI to diagnose suspicious tumors and categorize them as malignant or benign. Tumor extension and multi-modality in breast MRI have been the focus of recent studies.Gene expression has been measured using a variety of high-throughput

approaches. Although microarray technology is widely used for this purpose, it has certain drawbacks: it is costly, requires skilled management, and interprets genetic information by using a massive data set. Therefore, cancer molecular signature was developed by oncologists to identify the overexpression of rogue genes. Patients' responses to medications were tracked, and new approaches to illness treatment were developed. Today, ML may be used practically in computer-aided design. With the help of AI, the collective knowledge of the world's medical professionals in the fields of diagnosis and treatment may be automatically archived (cloud scaling). Because of this, Tumor Atlas was created [20].

To surpass human intellect, AI primarily employs two methods: neural networks and fuzzy logic. While neural networks are almost impossible to decipher (black box), fuzzy logic is straightforward. The two methods may seem contradictory, yet they are both utilized by doctors to identify breast cancer. Pancreatic and stomach cancers, among others, are often not detected until they have progressed significantly. Screening for lung cancer is also a challenging endeavor. To test for cancer, doctors often employ low-dose CT scans, which is an unsatisfactory technique compared to blood profiling, where artificial intelligence-based systems assessplasma ctDNA and microRNA profiles.The primary demand in modern medical care is for ML models that can properly forecastimaging-guided needle biopsies of high-risk cancer lesions, with updated pathology results to prevent needless surgical excisions.

Researchers from a variety of institutions have created randomized forest ML models to predict cancer patients' chances of surviving the disease and how their brains would age over time. Based on the results of a clinical trial including 335 high-risk cancer patients, it was shown that the random forest ML model has the potential to reduce the number of unnecessary surgical procedures by about a third. Several research in recent years has shown evidence in favor of ML since cancer is the most common malignancy in females globally.With a combination of neural networks, extreme boost, decision trees, and support vector machine approaches, these researchers were able to accurately analyze survival data by detecting and retrieving visual cancer signs.

Recently, it has become clear that surgical operations benefit fromthe CSC, or Collective Surgical Consciousness, which is a data analysis tool with applications in both individual and societal settings. Analyzing digital images with an artificial neural network has been employed in a select number of clinical situations to determine a pre-operative complete risk assessment using the computational approach. Additionally, ML can be used to improve surgical outcomes by analyzing data from surveillance cameras and real-time video images to provide ANN-based clinical decisions and predictions based on whole-population results extracted from the appropriate genetic pool (patient age, gender, and other body biological parameters).

## 4. CONCLUSION

Artificial intelligence (AI) is the most potent yet smart tool in the war against cancer, and it is going to change cancer therapy. However, AI has yet to be used in poor nations due to a lack of computational methods and the understanding of IT among doctors and physicians. AI-based DL technologies have several drawbacks at the macro and micro levels for the healthcare industry, despite their popularity in scientific circles that focus on technological advancements.Problems with the learning data set approach, unsupervised learning implementations, patient data security, data set size, and cancer classification based on more than a hundred distinct forms of cancer all call for a heavy emphasis on the human-computer interface (HCI) and also the usage of AI. It

takes many years to bring a viable formulation to the market after clinical research, making the repeatability of clinical experiments among the most critical challenges in molecular drug development. With increased specificity and cheap cost, repeatable computational drug design has been a potential approach for future medication discovery. As a result, more medical and technological improvements are needed to aid in the early detection and improved treatment of cancer, which is causing an increasing number of cases and deaths each year. The field of medicine is only one of several that is benefiting from the widespread use of machine learning and artificial intelligence. Extensive research shows that AI is a reliable supplement to human medical professionals, with the ability to significantly improve detection and treatment.

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# CHAPTER 6

# ANALYZING HEART DISEASES PREDICTION BASED ON MACHINE LEARNING ALGORITHM

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**ABSTRACT:**

Heart diseases of various kinds are referred to as "heart disease" the most typical cardiac condition. The World Health Organization (WHO) describes coronary artery disease (CAD) as a condition that reduces blood flow to the heart. A heart attack can result from decreased blood flow. The worst illness and one of the main causes of mortality worldwide is heart disease. The medical field is heavily reliant on machine learning. In this study, machine learning algorithm techniques are utilized to improve the accuracy of heart disease prediction. Heart conditions have a significant influence in the current day. Accurate outcomes are crucial for doctors since they work with priceless human lives. As a consequence, a program was created that analyses fundamental symptoms such as pulse rate, resting blood pressure, age, gender, fasting blood, glucose, cholesterol, resting electrocardiographic findings, exercise-induced angina, and depression to determine one's sensitivity to heart disease. Our heart disease prediction project's objective is to assess whether a patient should receive a heart disease diagnosis or not. There are two possible outcomes: a successful result and a negative result; in both cases, the patient will receive a heart disease diagnosis. The future potential of this system includes providing more advanced extracting features tools, risk calculation tools, and prediction models for additional clinical problems. The author will work on directed machine learning-based categorization for the diagnosis of heart disease.

**KEYWORDS:**

Blood, Disease, Heart, Medical, Machine learning algorithms, Support Vector Machine.

## 1. INTRODUCTION

There is a lot of active research into the use of machine learning techniques in the medical area, which mostly focuses on modeling certain human activities or thought processes and identifying illnesses from a range of input sources. Knowledge discovery and biological systems, which include genetics and DNA analysis, are further application domains. In addition to the performance overall, the intended success on one or more different classes of the issue may also have an impact on the design [1]. This is typical in most medical jobs since the system's success in each class may demand a varied Degree of importance. The employment of computer

programs or machine learning techniques can decrease mortality rates, increase illness detection accuracy, and, most importantly, shorten diagnosis times. Health care professionals are more likely to utilize the Internet or healthcare due to advancements in communication and computer technologies [2].

What is required in a medical diagnosis problem is a group of instances or characteristics that are indicative of all the different illness manifestations. If the system is to operate consistently and effectively, the examples must be chosen with great care [3]. One significant benefit of using machine learning approaches to solve these kinds of challenges is the lack of requirement for a specific methodology on how to detect the sickness. However, creating artificial intelligence systems to solve issues with medical decision-making is not a simple undertaking. The acquisition, gathering, and arrangement of the data that will be utilized to train the system present challenges.

This becomes a significant issue, particularly when the system calls for extensive data sets collected over extended periods, which are frequently unavailable owing to the absence of an effective recording method [4]. The medical task's current methods or the aforementioned issues may not be the sole elements influencing the design of a decision support system (DSS). In addition to the overall performance, the intended performance on one or more distinct classes of the issue may also have an impact on the design [5]. This is typical in most medical jobs since the system's performance in each class may require a varied level of importance. For instance, in a task to diagnose heart disease, the accuracy on healthy individuals must be as high as feasible, as a mistake in this category might lead to a healthy patient receiving treatment without a need [6].

The distribution of the system's performance across the various groups might change and depends mainly on the nature of the underlying medical condition and the data gathered [7]. Additionally, the mortality of patients with various ailments has grown in the majority of countries due to a shortage of medical specialists. In both urban and rural settings, heart disease has become the leading cause of death in the majority of the world's nations [8].

### *1.1 Heart Disease Diagnosis*

A expressing the importance that pumping blood to the lungs and a left heart that pumps blood through the body's various organs make up the heart, which is illustrated in Figure 1. Each of these hearts, which consists of an atrium and a ventricle, is a due to cardiac two-chamber pump. Each atrium functions as a flimsy priming pump for the ventricle, assisting in the flow of blood there. Then, the ventricles provide the primary pumping power that drives the blood through either the left ventricle's bloodstream or the right ventricle's bloodstream [9].

The cardiac cycle refers to the cardiac events that take place from the start of one pulse to the start of the next [10]. A period of relaxing known as diastolic pressure, during which the heart is filled with blood, is followed by a period of contractions known as systole in the cardiac cycle. Normally, blood flows continuously into the right atrium from the great veins; roughly 80% of the blood passes right through the atria and into the ventricular even before the atria compress. The ventricles then typically fill an additional 20% as a result of atrial contraction [11].

Therefore, the atria only serve as priming pumps that up the efficiency of ventricular pumping by 20%. Unless a person exercises, it is unlikely that they will notice a change when the atria stop working; at that point, acute heart failure symptoms, including shortness of breath, may appear [12].

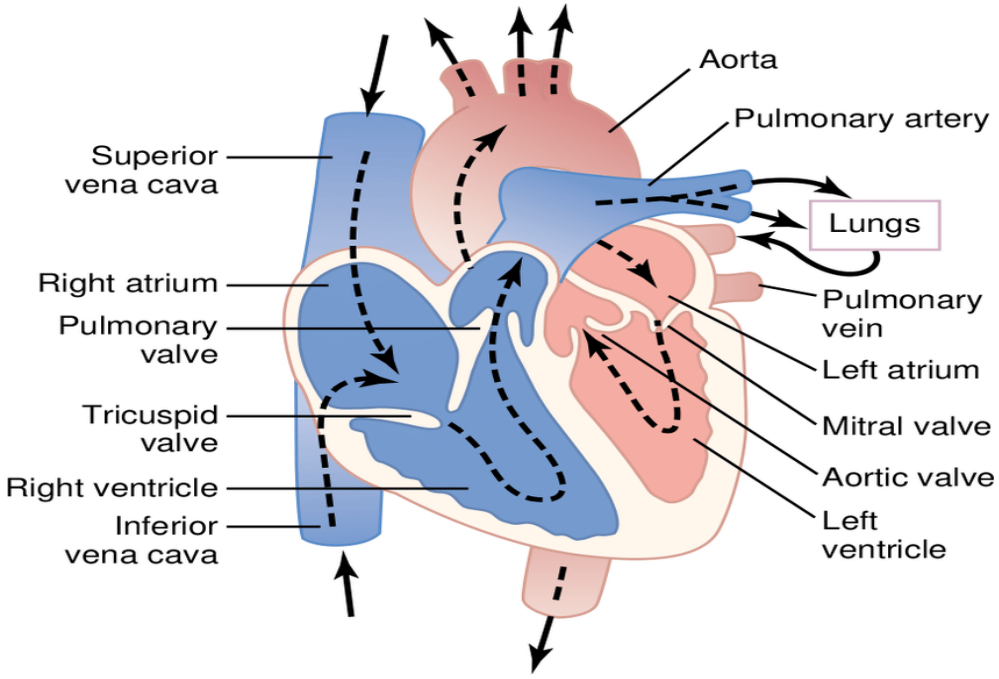


**Figure 1: Structure of the heart. The heart valves and chambers both have blood flow.**

Symptoms of cardiovascular issues that may be brought on by routine exercise include: excessive weariness Palpitations are the feeling that the heart is beating excessively quickly or missing beats. Breathing that is laborious or uncomfortable, Chest discomfort brought on by increasing exertion is angina [13]. A thorough medical history review, physical examination, electrocardiogram (ECG) to look for any abnormalities brought on by heart injury, and occasionally a blood test to look for abnormal levels of certain enzymes in the bloodstream are used by the doctor to identify a heart attack [14].Blood tests corroborate (or disprove) theories put out during the preliminary phases of examination that may take place in an emergency department, critical care unit, or urgent care setting. These examinations are also known as cardiac enzymes or heart damage indicators [15].

## 2. LITERATURE REVIEW

Tabreer T. Hasan et al will study this paperthe diagnosis system is suggested in this work to help physicians by transforming medical elements of the patients into numeric values to diagnose the cardiac problem. When the efficiency of this classifier was assessed using gathered information, simulation results demonstrate that the suggested Multi-layer Perceptron classifier MLP classifier has 98 percent accuracy in two heart illnesses categorization. While the SVM classifier's performance for support vector machines has reached 96%. Additionally, MLP has surpassed the SVM classifier when categorizing four types of heart disease in addition to the norm for efficiency to reach 81 percent. The MLP and SVM are thought to be the best classifiers

for classifying heart disease, based on the unique client identification UCI database. Additionally, a fair comparison is made between the two recommended systems and the best previous work systems under comparable circumstances. The comparison clearly showed that when compared to the best recognizer of earlier studies under a comparable learning and testing database partition, the two best-proposed recognizers (MLP and SVM) offer superior grouping correctness [16].

Tausifa Jan Saleem and Mohammad Ahsan Chishti The belief that intelligent machines can help health professionals make better decisions and speed up the judicial process in healthcare systems has been ingrained although healthcare organizations are not convinced to have complete reliance on machine intelligence despite the field's rapid advancement in big data and machine intelligence. Researchers now have the chance to apply machine learning algorithms to healthcare datasets thanks to the expanding availability of healthcare data, rapid improvements in computer power, and emerging paradigms for data analysis. The deployment of machine learning for healthcare applications is the subject of a thorough evaluation of research projects in this publication.

The following categories provide a breakdown of the research investigations that were carried out: The presented literature shows that machine learning approaches are highly efficient in determining the medical complications an individual is suffering from, predicting the risk of the illness a patient is likely to develop shortly, examining and recovering the individual, optimizing the clinical judgment process, premature pregnancy detection, and other healthcare-related discoveries [17].

Gao Xiao-Yan The suggested approach to predict cardiac disease was created in this research. To enhance the performance of heart disease prediction, ensemble approaches (boosting and bagging) are used with feature extraction algorithms (PCA and LDA). The Cleveland heart disease dataset is used to extract key characteristics using feature extraction methods. Selected features are used to compare the performance of ensemble techniques (boosting and bagging) and five classifiers (SVM, NB, DT, and RF). According to the experimental findings, the bagging ensemble learning algorithm using DT and PCA feature extraction approach had the greatest performance [18].

Shashikant U. Ghumbre and Ashok A. Ghatol will discuss the technological progress that has recently been greatly credited with improving medical diagnostics. The application of medical practices has also been greatly enhanced by computer and communication systems. Although the Artificial Neural Network Ensemble is a potent learning technique that could help significantly improve the generalization ability of neural learning systems, it's less lucid than a single Artificial Neural Network, which prevents it from receiving widespread acceptance among medical professionals. By using a radial base function network model and a support vector machine, the author of this study has proposed a decision-making support system for the detection of heart disease. As a consequence, different data samples from various individuals are used to diagnose heart disease, and the findings show that SVM with Sequence Minimize Optimization is just as effective as ANN and other models in this regard. The SVM has been

proven to have excellent classification accuracy, sensitivities, and specificity, which makes it a suitable candidate for diagnosis [19].

Abdul Matin and Hafsa Binte Kibria in this paper will study that Machine learning is essential right now, especially in the health industry. The goal of this study is to more accurately forecast people with heart disease using machine learning algorithms. To categorize cardiac disease presence and absence, two fusion models have been created. To determine whether the model performed better, comparisons were made. Here, three algorithms have been employed. Fusion models may be created using more than two algorithms and classifiers for various datasets that can be used for future medical diagnostics [20].

*Research Question*

1. Why Use Machine Learning in Heart Diseases?
2. How does heart disease happen and why?
3. What are the benefits of using machine learning in heart disease?

## 3. METHODOLOGY

*The Proposed Heart Disease Prediction System:*

The provided system method aims to leverage ensemble techniques to boost the accuracy of heart disease prediction. The suggested system's architecture is shown in Figure 2. It is divided into six stages: data gathering, data preprocessing, and extraction of features, data splitting, model training, and model evaluation. The following provides a detailed explanation of each phase of the suggested strategy.

*i. Design:*

Heart Flow is a unique imaging technique that makes it easier for doctors to decide if a patient requires an invasive operation to open clogged arteries or if a non-invasive therapy, like medication, will work.

*ii. Data collection:*

The Models are trained and tested using data related to heart disease. It has 1025 records, several attributes, and a single target patient. This essay lists both heart disorders and others that are not heart diseases. Features and specifics are all described.

*iii. Data analysis*

The following three algorithms were used in the approach for predicting heart diseases, and the findings are detailed below. Explains the architectural schematic used to forecast heart and blood vessel problems is shown in figure 3.

- Support Vector Machin (SVM)
- Decision tree (DT)
- Multilayer Perceptron (MLP)

One of the most serious issues affecting human safety today is heart illness. Recently, research that has garnered significant attention in the global medical system made recommendations for the treatment of cardiac diseases. One of the leading causes of mortality globally is the cardiac illness. According to the World Health Organization, heart disease will cause 17.7 million deaths worldwide in 2019, accounting for nearly 31% of all fatalities (WHO).

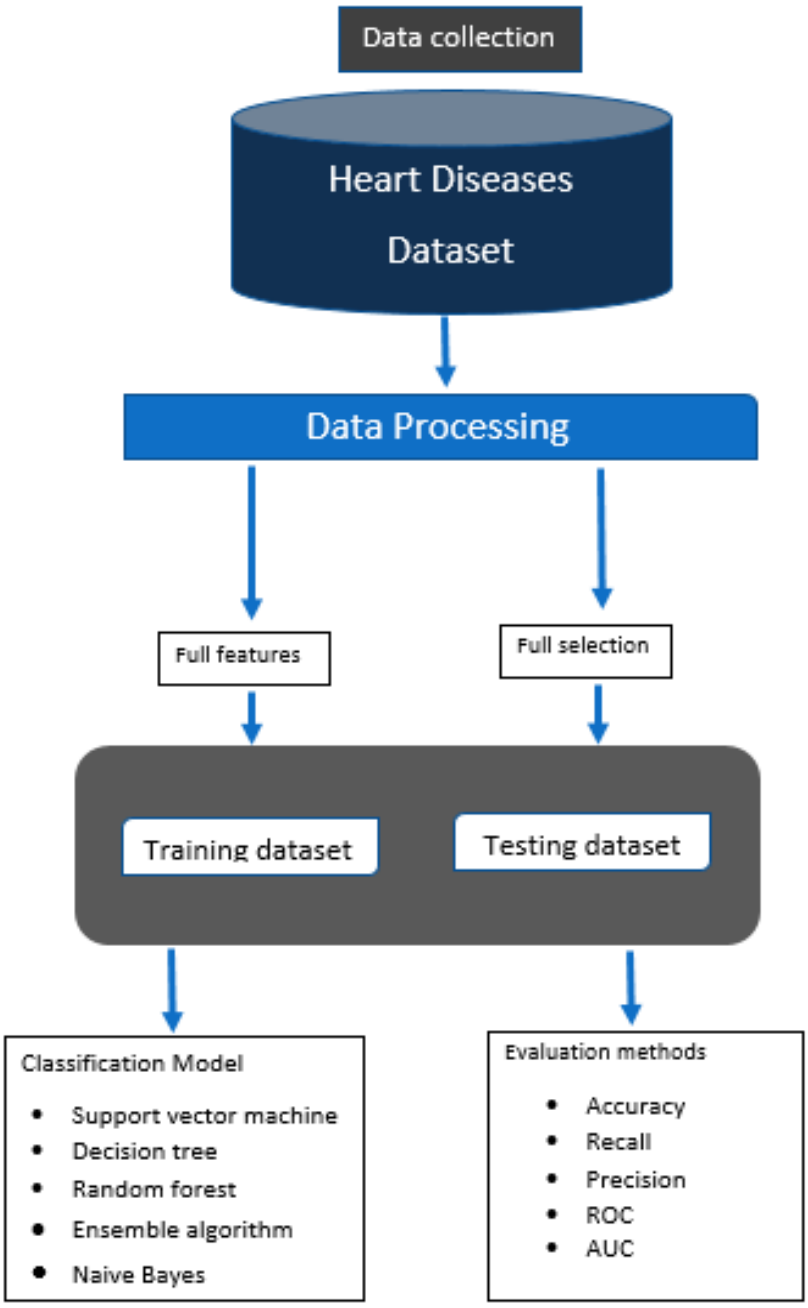

**Figure 2: This structure represents the system for the prediction of heart disease.**

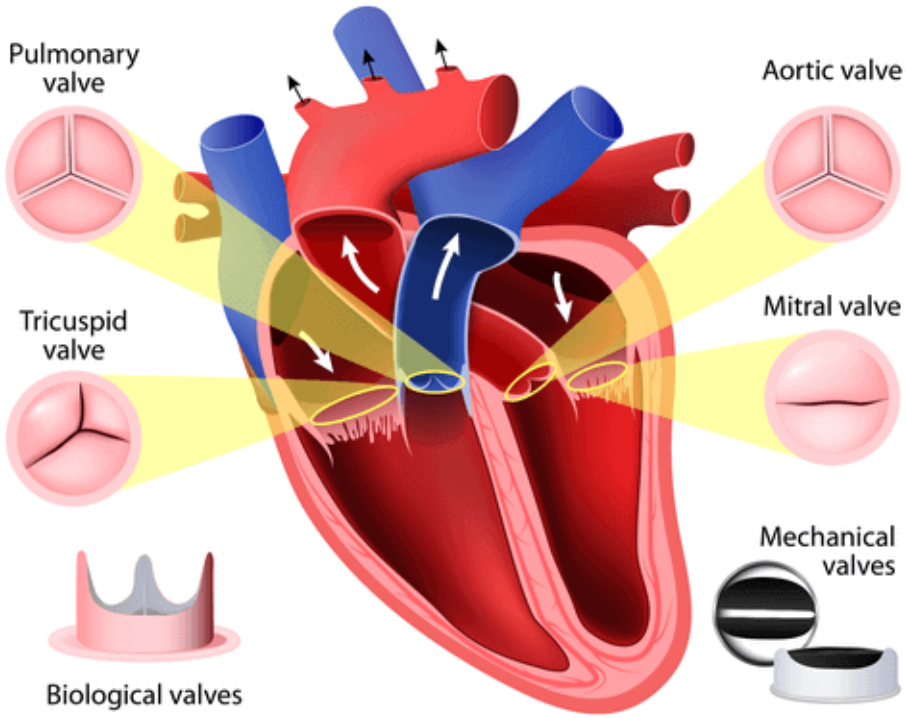


**Figure 3: Represent the sample of heart disease.**

The number of cardiac cases is the study's main topic. Indicates that low- and middle-income nations account for 82% of instances, 17 million individuals are under 70 and at risk for non-infectious illnesses, 6.7 million experience strokes, and 7.4 million have heart disease (WHO, 2019). Heart disease is responsible for almost half of all fatalities in the US and other industrialized nations, as well as for one-third of all fatalities globally. Heart disease impacts not only the health of individuals but also the economics and expenses of nations.

## 4. RESULT AND DISCUSSION

*4.1 The multilayer perceptron (MLP)*

A fully connected kind of feedforward artificial neural network is called a multilayer perceptron (MLP) (ANN). The term "multiple layer perceptron (MLP) is used ambiguously; sometimes it is used broadly to refer to any feedforward ANN, and other times it is used specifically to describe networks made up of several layers of perceptron (with threshold activation); see Terminology. MLP, which is a kind of supervised neural network, is one of the most widely used neural network designs in medical decision support systems (MDSS). A typical MLP network has at least three layers of processing nodes, including an input layer for receiving external inputs, one or more hidden layers, and an output layer for producing classification results. Figure 4.

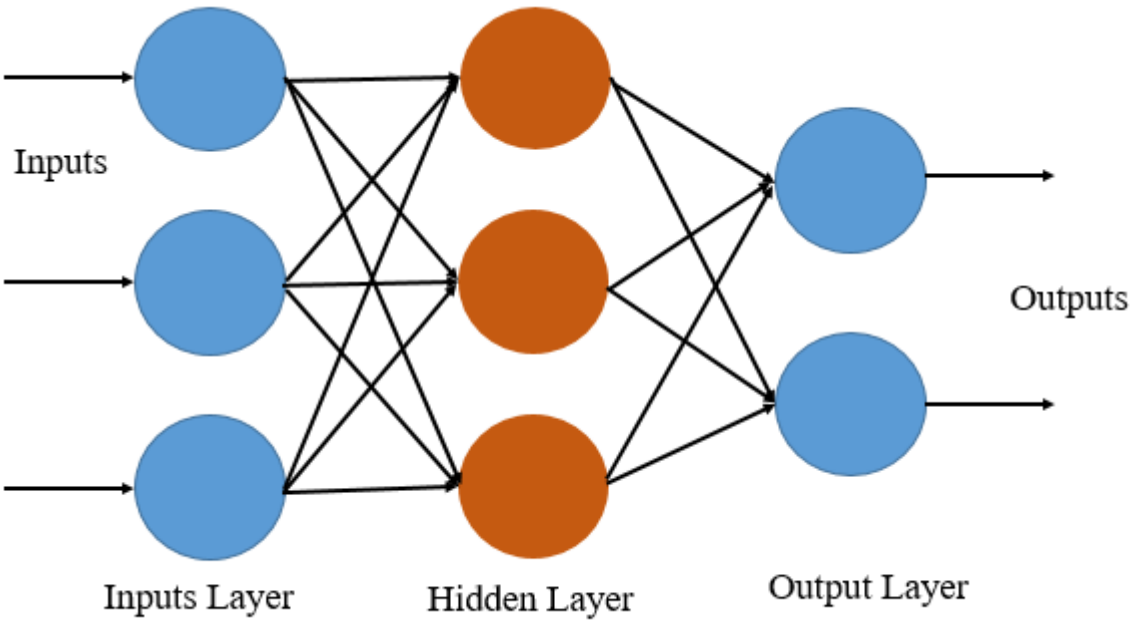


**Figure 4: Represent the multilayer perception MLP.**

*4.2 Support Vector Machine (SVM)*

Support Vector Machine (SVM), developed by Vapnik, is a subcategory of universal feed-forward networks, similar to circular function networks. SVM may be applied to nonlinear regression and pattern categorization. The support vector machine, to be more specific, is a rough implementation of the structural risk reduction approach. This theory is based on the observation that the sum of the learning rate and term that depends on the Vapnik Chervonenkis (VC) dimension limits the error rate of a learning machine on test data. On the subject of pattern classification, the support vector machine may do well in terms of generalization.

*4.3 Decision tree*

A decision tree is a branching, nodal, and leaf nodal structure that resembles a tree. It is a branching graph that behaves for each unique property like a splitting rule. Every characteristic is viewed as a node in a branching tree. These nodes construct a rule, and values are categorized into several classes following the rule. In a decision tree, the leaf makes some judgments towards the end, while the root, which is at the top, divides the tree into sections depending on attribute values. A DT is simple to construct and more effective in predicting outcomes. Overfitting is vulnerable to DT. It occurs when a model performs poorly on test data despite being highly effective at recognizing learned data. By having very little impurity in the leaf node, it becomes excessively skillful for training data. Pre-pruning is therefore required to reduce the number of leaf nodes that are unnecessary for the construction of models. It provides improved forecast accuracy. Another crucial factor is information gain, and the qualities with the biggest information gains are divided first. The lowest entropy characteristics are chosen for splitting in that strategy. In the suggested design, the Gini criteria were applied, and the maximum tree depth

and minimum leaf size were both set at 8. To get the ideal parameters, pre-pruning was carried out.

Heart diseases have suffered significantly in the contemporary era. Since they are dealing with a precious human life, doctors must take great care to ensure their conclusions are accurate. A program was developed as a result that can determine a person's risk of developing heart disease based on common symptoms like age, gender, pulse rate, relaxing heart rate, cholesterol, fasting glucose levels, exercise-induced angina, ST depression, St - segment elevation slope, the number of major vessels highlighted by microscopy, and the highest heart rate attained. This may be used by doctors to confirm and verify that their patients are healthy. The classification of cardiovascular disease is also compared and contrasted in this work utilizing machine learning techniques including multilayer perceptron (MLP), Support Vector Machine (SVM), and Decision tree. The most accurate and reliable machine learning algorithm, multilayer perceptron, is used in the recommended system since similar evaluations have demonstrated it to be such. This strategy also provides information on the association between diabetes and the degree to which it influences heart disease.

## 5. CONCLUSION

You may run out of oxygen as a result of blood flow being restricted by heart muscle thickening. That may result in issues including shortness of breath, dizziness, and fainting. Additionally, your heart may go out of sync and begin to flutter, pound, or competition. The Support Vector Machine (SVN), the multilayer perceptron (MLP), and the decision tree are three machine learning techniques that have been employed in this study (DT). Two fusion models (MLP+DT) model-1 and mode-2 were created by individually combining the decision tree and the multilayer perceptron (MLP) using machine learning. Accuracy, recall accuracy, and four other performance metrics have been used to compare model performance. After combining the methods in this study, performance parameters showed a considerable increase. By combining the decision scores from two algorithms, the fusion was achieved at the decision level. The primary goal is to improve classification accuracy by fusing the decisions of the various models to improve the performance of the fused model.

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# CHAPTER 7

# CONTROL, PREVENTION OF *MYCOBACTERIUM* INFECTION AMONG VARIOUS ANIMALS

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**ABSTRACT:**

All animal species are susceptible to tuberculosis, an infectious, local or widespread, chronic or acute, granulomatous disease brought on by mycobacteria. In cattle, the disease is mostly transmitted by inhalation, but also by obligate pathogenic or opportunistic species of mycobacteria. An initial investigation of the mycobacteria that infect tuberculosis cattle from two distinct management systems. Mycobacterium tuberculosis was isolated from an animal in about 27.00% of cases, but in cattle raised in intensive production methods, M. Bovis was the only infection. One possible method of M. tuberculosis transmission from people to cattle is the local farmers' custom of feeding chewing tobacco into the mouths of grazing animals. This paper's author discussed mycobacterium infection and its prevention among various animals. The main objective of this paper is to learn more about the Control, and prevention, of Mycobacterium Infection in Various Animals. In the future, this paper will aware people of mycobacterium infection in animals.

**KEYWORDS:**

Bovis Infection, Bacteria, Diseases, Mycobacterium, Tuberculosis.

## 1. INTRODUCTION

The Mycobacterium tuberculosis complex (MTBC) is the cause of diseases that can spread to people, animals, and wild animals. Although the MTBC bacteria may live on a variety of hosts, there are distinctions in host vulnerability and the unique pathophysiology of the illness that is now manifesting. Human tuberculosis (TB) is mostly brought on by “Mycobacterium tuberculosis” (Mtb), but bovine TB in cattle, other animals, or wildlife is primarily brought on by Mycobacterium Bovis (M. Bovis). Mycobacterium Bovis (Mb), a zoonotic bacterial agent that is particularly dangerous in sub-Saharan Africa, is once more on the rise. In April 2016, the “World Health Organization” (WHO), the “International Union against Tuberculosis”, and the Lung Disease gathered in response to the public's growing awareness of the importance of zoonotic TB as a crucial strategy for battling the disease zoonotic TB. Health released a multisectoral plan in 2017 outlining their major goals for battling zoonotic bacteria-caused human or animal TB [1]. They gave top priority to the need to increase intersectoral or collaborative methods, limit transmission only at the animal-human interface, as well as to increase the scientific evidence foundation. It is essential to consider the disease burden in animal reservoirs or the risk factors that contribute to transmission if zoonotic TB is to be successfully treated [2].

The Mycobacterium TB complex contains several closely related microorganisms that cause tuberculosis in animals. Every organism has an ancestral host, yet it may also infect and affect different species. M. Bovis, which causes bovine TB, and M. Capre, which is suited for goats but may also spread to some cow herds, are the two agents that are most usually found in domestic animals. Both result in declining profitability for the animal industry due to growing mortality, illness, subpar productivity, and trade restrictions. Animals in zoos, pets, or untamed animals can all be affected. According to reports, M. Bovis poses a major threat to various animals, including endangered Iberian lynx and lions (Panthera leo) in Africa (Lynx pardinus). Mycobacterium origin, Mycobacterium pinniped, or Mycobacterium microti, three microorganisms that are present in nature, are sporadically detected in animals, companion animals, or people [3].

M. Bovis was a significant global contributor to TB in humans in the past. It was particularly prevalent in kids who consumed raw milk. Clinical cases are now rare in many nations as a result of the introduction of pasteurization and the subsequent implementation of control measures in cattle. However, this illness continues to be a problem since it is still a significant zoonosis in certain underdeveloped countries and because animal reservoirs can hinder its total elimination in wealthy nations. In some places, M. caprae has also become a problem. In several European nations where M. Bovis has been controlled, a sizable portion of human TB cases are now caused by this bacterium. Its recent discovery in China or North Africa suggests that its distribution likely extends beyond Europe [4].

### *1.1. Animals Affected:*

#### *1.1.1. Bovis Mycobacteria:*

Cattle are M. Bovis' primary hosts, however, it is likely infectious to most animals including marsupials. Variations in illness susceptibility may exist. Clinical instances have been reported in a variety of hosts, including pigs, horses, camels, South American camelids, other canids, cats, and dogs, such as different wild felids, numerous more wild ruminants or elephants, cervids, rhinoceroses (“Diceros bicornis, Ceratotherium simum”), or giraffes (Giraffa). Given that M. Bovis has been found in grey seals (Halichoerus grypus), marine animals are likely also vulnerable to it. This is still true even if the majority of organisms previously described in the sea lions and seals have been reclassified as M. pinnipeds [5].

Although it may also be kept alive in goats, restricted cervids, as well as other free-living animals, M. Bovis is mainly maintained in cattle. Depending on its population density or other transmission-facilitating variables, a species may serve as a maintenance host in one place and an overflow host in another. Although elk (Cervus Canadensis) perform the primary function, white-tailed deer (Odocoileus virginianus) are also considered to act as maintenance hosts adjacent to Canada's Riding Mountain National Park. However, when white-tailed deer is necessary to maintain M. Bovis's survival in Michigan, function as backup hosts. In other regions of the United States or Canada, neither species currently seems to be impacted by this pathogen. Wild boar are believed to be significant maintenance hosts on the Iberian Peninsula in Europe, despite seeming to be overflow hosts in Atlantic Spain and other parts of Europe [6].

M. avium, a strain that is not a part of the M. TB complex, is typically the cause of tuberculosis in birds. However, a few examples of birds with M have been reported. A black swan, a parrot, as well as an ostrich, have all contracted the Bovis virus (Cygnus atratus). M. Following oral as well as intratracheal injection, Bovis multiplied in pigeons (Columba livia), or subsequently in budgerigars following intramuscular inoculation (Melopsittacus undulatus). Despite the lack of

clinical signs, some pigeons occasionally passed the bacteria in their feces. Budgerigars did not exhibit any clinical symptoms. American starlings (Sturnus vulgaris), Mallard ducks (Anas platyrhynchos), crows (Corvus brachyrhynchos), or wild turkeys appear to be less affected by the experimental virus (Meleagris gallopavo).

*1.1.2. Mycobacterium caprae:*

Goat TB is largely caused by M. caprae. Numerous zoo animals have also been proven to exhibit clinically significant immune responses, including Siberian tigers (Panthera tigris altaica), Borneo elephants (Elephas maximus borneensis), dromedary camels (Camelus dromedarius), and American bison. Red foxes, wild boars, red deer, pigs, lambs, and pigs (Vulpe) (Bison bison). M. caprae has been discovered in cow herds that don't appear to have any interaction with small ruminants, even though goats are the typical maintenance hosts. It appears to be retained in red deer that live in the wild and probably in wild boar in Europe.

Studies on the dissemination of M. Bovis have provided a wealth of knowledge on the transmission of zoonotic mycobacteria. Depending on where it is found, this organism may be found in respiratory droplets, wound exudate, draining lymph nodes, other skin lesions, feces, urine, vaginal fluids, or semen. There are several different types of intermittent shedding. Transmission of M. Bovis is more likely when the respiratory tract is affected, the disease progresses, and the lesions are more severe. Proximity in cramped areas encourages its spread. In addition, it has been grown from the mouth secretions of some animals, such as ferrets, which may make it easier for a bite to spread. Animals can get an infection by direct contact with broken skin or mucous membranes, inhalation, or ingestion. In general, more organisms are required to cause infection by ingestion than by inhalation. Depending on the host species, different transmission pathways have varying degrees of relevance. During close touch, aerosols frequently infect cattle [7].

Except for calves who nurse from diseased cows, ingestion is less significant in this species. Transmission through the skin, genitalia (sexually), and congenitally is conceivable in cattle but appears to be rare. It is also believed that respiratory transmission predominates in a few additional hosts, including nonhuman primates, badgers, or camels. The most frequent route, nevertheless, is believed to be ingestion in cats, ferrets, deer, or horses. Cats but also badgers are two examples of animals that frequently hunt or engage in combat and exhibit percutaneous transmission. When they wash off food after eating, cats may potentially ingest bacteria on their mucous membranes. It was believed that dogs with kidney lesions had spread M. Bovis through kennel urine. In at least two small animal veterinary practices, nosocomial transmission has been documented. In one case, healthy feline surgery patients contracted an infection from an ill cat through contact with their hands or clothing.

*1.1.3. Embryonic Stage:*

Clinical indications of tuberculosis sometimes take several months or longer to appear and typically have a delayed start. It's also possible for infections to go dormant for years before reactivating. Rarely, exceptionally quick incubation times have been seen, notably in the case of two cats that unknowingly got the illness through surgical incisions and showed symptoms after 14 and 42 days.

*1.2. Clinical Symptoms:*

*1.2.1. Tuberculosis in cattle (Mycobacterium Bovis):*

Although there are instances of acute and quickly progressing tuberculosis in cattle, the disease is typically chronic and crippling. The onset is often gradual, with little to no outward symptoms at first. Weight loss, severe emaciation, impotence, fluctuating temperature, low-grade lymphadenopathy, or respiratory activity with an intermittent, wet cough that is worse in the morning, in cold weather, or after exercise are all clinical signs typical to this species. Involvement of the gastrointestinal tract may cause dyspnea or tachypnea, in addition to irregular bowel movements and constipation. Sometimes the superficial lymph nodes might burst or protrude and seem significantly inflated. In this species, the retropharyngeal lymph node is commonly affected. Deep lymph node enlargement can sometimes obstruct the digestive tract, airways, or blood vessels. Various syndromes, recurrent miscarriage, uterine lesions, or ocular disease (including choroidal infiltration, anterior uveitis, and subretinal exudates) have been reported. In cattle, skin lesions are rare.

Other species may have different main symptoms or illness courses, but tuberculosis is essentially comparable in all of them. In equids and certain other hosts, the respiratory system is more frequently afflicted than the abdominal organs, but elephants typically show little symptoms until the lesions are substantial. There are several recorded pathologies in farmed cervids, ranging from cases that take years to manifest and have unexplained abscesses in discrete lymph nodes to widespread illnesses that manifest suddenly and become fulminant. Skin lesions can infrequently be seen in the cervids. Pigs are prone to subclinical illnesses, but it is also possible to find widespread diseases, especially in young animals. According to accounts, this species is prone to osteomyelitis or meningeal involvement. Both badgers but also brush-tailed opossums are susceptible to respiratory disease, a type of tuberculosis, but badgers are more likely to survive for years after contracting it, whereas opossums frequently pass away within a few months. When wildlife exhibits odd behavior, it occasionally turns out that they have advanced TB (e.g., Opossums scurrying about throughout the day).

### *1.2.2. Other Germs Cause Tuberculosis:*

Clinical cases brought on by other organisms are sometimes difficult to identify from those brought on by M. Bovis in terrestrial animals. Nevertheless, whether or not other organs are also affected, cats infected with M. microti commonly appear with a clinical picture that includes hard, elevated skin lesions or submandibular lymphadenopathy. Other symptoms, such as lung illness, arthritis, ocular signs, and widespread disease, can also be brought on by M. microti in cats. When pinnipeds have M. pinniped infection, lethargy, anorexia, weight loss, and respiratory symptoms are frequently seen.

### *1.2.3. Birds:*

Instead of the typically encapsulated tubercles that Mycobacterium sp. produces in birds, the internal organs typically have granulomatous infiltration or white, pale yellow, or tan nodules. Larger nodules might well be caseous but seldom mineralize, while small nodules are often not caseated. Some mycobacterial-infected birds have no obvious lesions.

### *1.2.4. Diagnostic Tests:*

Either the pathogenic organisms or the immunological responses to these organisms can be used to diagnose tuberculosis. Animals who respond to either kind of test are often considered as having an illness that is actively spreading. To see internal organ anomalies in some animals, diagnostic examinations may be enhanced by x-rays or other imaging methods.

### *1.2.5. Test for tuberculin:*

The tuberculin skin test, which looks for cell-mediated immune responses, is the main screening procedure for cattle and several other animals (CMI). Following intradermal injection of the bacterial protein cocktail tuberculin, the area is checked for acute inflammatory swelling 48–96 hours later. The test's sensitivity and specificity are impacted by the passage of time. M. Bovis antigens can also be used to identify infections with other M. TB complex members, although they are often utilized in testing animals. To decrease false positive results, a comparison test that assesses relative reactivity to "M. Bovis or environmental mycobacteria (M. avium)" may be utilized [8].

### *1.3. Economic Effects:*

Over US $3 billion in economic losses are attributed to cattle TB each year, according to estimates globally. Since losses in many developing nations have not been thoroughly or even at all evaluated, this may represent an underestimate. Reductions in meat output, milk yields, and fertility are all examples of productivity losses inflicted upon infected animals. Milk output in dairy cattle may fall by between 4 and 18%. Mortality, infertility, calf deaths, extra processing for diseased animals, and condemnation of corpses at slaughterhouses are some more direct losses. Export market limits are non-tariff trade obstacles. Inspection of meat, testing, and killing of positive animals, pasteurization of milk, and farmer compensation programs all contribute to the expense of control. Treatment costs, death, lost earnings and livelihoods, food poverty, stigmatization, and additional working hours for those caring for ill people are all included in the cost of public health. In 2016, it was predicted that there were 147,000 new cases of zoonotic TB in humans worldwide, including 12,500 fatalities. The continent of Africa had the most instances, followed by South-East Asia [9].

## 2. LITERATURE REVIEW

C.J.CPhillips et al. studied Cattle infection via Mycobacterium bovis transmission. Since the chances of coming into contact with infected individuals or their excreta while cattle are grazing on farm boundaries are rather small, this puts them at greater risk. The presence of single reactors in several herds meant that transmission within the herd was uncommon. The spreading slurry is a dangerous issue in herds of sick cattle; it may be reduced by storing the slurry for an extended period, spreading it in pastures not utilized for grazing, or injecting it into the soil. M. Bovis may also reside in water or can enter the respiratory system by drinking. There are several ways that M. Bovis infection in cattle can spread, some of which can be stopped by practicing good husbandry [10].

W. Yayo Ayele et al. studied the spread of TB and its effects on domestic animals.in this paper, the author discussed the spread of M. paratuberculosis among animals and the significance of the condition for animal production. The majority of infected animals do not show clinical symptoms, although they may expel the germs. Emaciation or, in certain species, diarrhea are symptoms of clinical illness in animals, which eventually lead to death. M. paratuberculosis is excreted in feces and milk throughout the illness, and it spreads to several internal organs of affected animals through their blood and lymphatic systems. The male or female reproductive systems are affected by the illness. Although it is unknown if M. paratuberculosis affects humans, human-transmissible cattle illnesses are presently having a greater impact on consumer trust than ever before [11].

Robert M.M. Smith et al. studied Mycobacterium Bovis Infection. Since the disease's comeback in cattle in the nation, they report the first known case of bovine TB spreading from animals to humans in the United Kingdom. This study raises the possibility that there is a tiny danger of human transmission, necessitating further caution. Due to the existence of M. Bovis in the cattle's respiratory system and the fact that this incident marks the first known probable animal-to-human spillover since the disease's resurgence in cattle, it is possible that humans could still be at low risk of transmission even after the bovine case is declared closed [12].

Bugwesa Z. Katale et al. studied the approach to mycobacterial infection treatment and prevention. Due to the increasing proximity of people, livestock, and animals as well as its relevance in the dynamics of mycobacterial infections, an OH approach is necessary for the surveillance of zoonotic diseases. The chance of infectious illnesses spreading between species, particularly drug-resistant mycobacteria, is raised by intimate contact between people and animals. When HIV co-infection is also widespread, opportunistic infection by atmospheric "non-tuberculosis mycobacteria" (NTM), also known as mycobacteria other than TB, may exacerbate the consequences of treatment resistance. The hazards to public health presented by mycobacterial diseases, particularly the proliferation of drug-resistant strains, might be resolved with the support of a coordinated multidisciplinary approach among specialists [13].

## 3. DISCUSSION

Mammals, fish, and birds are all susceptible to tuberculosis, an infectious, either chronic or acute, localized as well as a disseminated granulomatous illness that is brought on by bacteria from the genus Mycobacterium. Only pathogenic tuberculosis (TB) may cause the disease, which is brought on by mycobacteria of the Mycobacterium tuberculosis complex in a range of mammalian hosts but with diverse host tropisms. The Mycobacterium tuberculosis complex of mycobacteria causes tuberculosis (TB) in several mammalian hosts, although they each have unique host tropisms. The nucleotide sequences of the 16S rDNA genes of the different bacterial species in the complex are 99.8% or more similar to one another. The principal pathogenic species in the complex include M. tuberculosis and M. Bovis, which cause TB in humans or cattle, respectively. There have been infrequent reports of M. tuberculosis infections in both domestic and wild animal species, most commonly in those that have frequent, intimate interactions with humans. M. Bovis, on the other hand, is a widely recognized zoonotic. Cattle or opportunistic mycobacterial species in cattle are the domestic animals where M. tuberculosis infection is most commonly seen. When a sickness spreads among animals, they become emaciated and finally perish. The disease's zoonosis as well as the resulting financial losses are what makes it important.

### *3.1. Treatment:*

Some animals with TB have been treated with antibiotics, particularly pets or zoo animals. Therefore, it is important to consider the potential for clinical improvement without the need for a bacteriological cure. Some animals that at first showed signs of improvement eventually reverted, especially when given insufficient care. Treatment is debatable because of the possibility of shedding organisms, risks to people (especially if there are draining lesions or an infection of the respiratory system), as well as the potential for the emergence of drug resistance. Some nations do not allow for treatment. Members of the M. tuberculosis complex can only be treated with a few tuberculocidal drugs since they are not responsive to several conventional antibiotics. The simultaneous delivery of two or more drugs over a lengthy period is a common

feature of effective human treatment protocols used on animals. It should be kept in mind while selecting medications since, barring exceptionally unusual conditions, M. Bovis is naturally resistant to pyrazinamide, a standard "first line" therapy for TB. However, animals with M. caprae infections can use this medication. One therapy strategy for cats includes rifampicin, a fourth-generation fluoroquinolone comparable to pradofloxacin, clarithromycin, or azithromycin, due to cats' special sensitivity to some of the often administered tuberculocidal medications. When tiny masses, ocular TB (including such enucleation), or amputating an infected joint are involved, surgery may be performed in conjunction with tuberculocidal medications to treat such conditions. Drug treatment alone typically produces subpar outcomes in cats with significant osteomyelitis or joint involvement.

### *3.2. Reporting on disease control:*

Following local or national disease reporting requirements is advised when a veterinarian has reason to believe that an animal is infected with a member of the M. tuberculosis complex. Although the majority of rules are written for M. Bovis or M. caprae in cattle, numerous countries insist that sick dogs or other members of this complex be reported (for example, cats with TB in the UK). State authorities in the US must be contacted regarding regulations.

### *3.3. Prevention:*

To prevent the transmission of TB within a herd, sanitation and disinfection, open-air living as opposed to confinement, and avoiding crowding may all be implemented. Controlling rodent populations reduces the likelihood that these animals may spread the disease. In locations where M. caprae, M. Bovis, or M. microti are endemic, keeping cats indoors can assist to protect them. When animals exhibit symptoms suggestive of TB in endemic locations, veterinary facilities should take into account barrier nursing precautions and tuberculocidal disinfectants.

Bovine TB in cattle is the typical target of control efforts, while M. caprae may also be included in some of them. The tuberculin skin test or other tests are often used to screen the animals in these programs. If it is found that a herd is polluted, the reactors are removed, and the herd is segregated until every animal tests negative. Only a small percentage of herds include infected animals in places where testing is often conducted. Even if reactors are frequently destroyed, some countries may adopt test-and-segregation practices at first before converting to test-and-slaughter practices. Although infrequent, depopulation of whole herds is also a possibility. When eradication is almost complete, slaughter surveillance with animal infection tracking may be a better use of resources. It's indeed, however, not very sensitive and can overlook sick animals with minimal or no obvious lesions. Other species might occasionally be included in screening procedures (farmed deer, for example), although these animals are typically only discovered through passive monitoring or epidemiological research on sick cattle.

The presence of M makes eradication efforts more challenging. M. or Bovis caprae in reservoirs for wildlife. Biosecurity measures like wildlife barriers around feed storage facilities or strong metal barriers and gates to keep badgers out of cow pens can lessen the risk of transmission from these animals to livestock. Additionally, a few nations have put control mechanisms in place that are directed at the primary maintenance host (s). Their population density may fall below what is required to maintain transmission as a result of culling. Additionally, each situation must be assessed independently since culling may have unforeseen implications if it encourages the spread of ill animals. With the release of healthy animals, capture and testing operations have occasionally been employed on African buffalo and badgers. Bans on feeding deer and elk are

part of some control efforts to lessen transmission between hordes of animals and prevent transmission on food sources. It is impractical to eradicate species like M. origins, M. pinnipedii, or M. microtia, which are mostly found in animals.

### *3.4. Morbidity and Mortality*

Following exposure to a member of the M. tuberculosis complex, several outcomes are possible. These include immune system-mediated clearance of the organism, persistent asymptomatic infection with or without limiting lesions, or the beginning of a chronic and ultimately deadly illness. Some animals don't show indications of subclinical illness until they are very old, fragile, or under stress. In experimentally infected animals, M. Bovis-caused lesions have also been reported to heal, either with or without the removal of the organism, but this is regarded to be a rare case. The kind of animal, the Mycobacterium, the number of organisms, the injection location, and the individual's overall health are some factors that might affect the result of an infection. The severity of clinical cases in young animals also seems to be higher. Some hosts, including cattle, domesticated red deer, and African buffalo, are genetically resistant to M. Bovis. Bos indicus, or Zebu, cattle have greater levels of TB resistance than Ankole or Holstein Bos taurus cattle, according to research.

### *3.5. Bovis Mycobacteria:*

A tuberculin test reaction occurred in 0–40% of susceptible contacts in two investigations on the transmission of M. Bovis in naturally infected cattle, and macroscopic lesions appeared in 0–10% of contacts. Although it is believed that sheep are more resistant to M. Bovis than goats or cattle, given the rise in reports of the disease in these animals, underdiagnosis may still be a problem. Sheep can be kept from being exposed through management ("such as less rigorous rearing") or behavior. Rabbits also seem to be somewhat resistant; it has been shown that animals living in highly contaminated environments tend to develop the bulk of their clinical cases.

Infected cattle with significant lesions were more prevalent in the early half of the 20th century, but tuberculosis was also often found in pigs, cats, dogs, and horses. Only a few occurrences have recently been documented in dogs or horses. In one recent epidemic, 8 of the 14 infected dogs fell sick, infecting around 8% of the dogs in a functioning English foxhound kennel. The M. Bovis virus appears to be relatively contagious in ferrets, cats, or guinea pigs. Infections were formerly thought to affect 7.00% of cats in Switzerland or 50% of cats in Pennsylvania who were exposed to sick cow herds. A Swiss investigation conducted later, in the 1970s, discovered TB in 0.3% of feline necropsies [14].

According to the OIE Terrestrial Animal Health Code, bovine TB is prohibited. Reduced prevalence in animals must be the goal of control measures to stop transmission to humans. The continual identification and killing of sick animals is the suggested technique of control in cattle. Pasteurization of milk and postmortem meat inspection are two efficient ways to keep contaminated animal products out of the food supply. Meat inspection enables the ability to identify the original herd, which may then be tested or eradicated. Cattle can be individually tested to reduce prevalence, infected animals can be removed, or animal mobility can be restricted. However, due to a lack of financial resources, a pastoral production technique that involves unregulated animal movement, inadequate veterinary organizations, and unstable political environments, testing and killing may not be feasible in underdeveloped nations.

Additionally, sheep and goats are farmed alongside cattle in poor nations, particularly in Africa. These animals serve as reservoirs so are not used for testing or slaughter.

## 4. CONCLUSION

This study emphasizes the potential danger of M. tuberculosis transmission from humans to cattle through the method of mouth-to-mouth feeding of tobacco juice or in environments where animals dwell close to tuberculous humans. The effects of feeding tobacco juice to cattle as well as the possibility of M. tuberculosis transmission to cattle are the subject of current epidemiological investigations. The author of this paper talked about mycobacterium infections in animals and how to prevent them. The major goal of this study is to get more knowledge about the prevention and control of mycobacterium infection in various animals. This paper will educate readers about mycobacterium infections in animals in the future.

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# CHAPTER 8

# POSSIBLE HEAT STRESS MITIGATION MEASURES AND THEIR EFFECTS ON POULTRY HEALTH

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**ABSTRACT:**

In the poultry industry, heat stress is well acknowledged as a significant environmental stressor, and it has been associated with significant economic loss. Higher mortality decreased feed effectiveness, body mass, feed consumption, and changed meat and egg production and quality, are all results of the physiological changes caused by heat stress, including oxidative stress, acid-base imbalance, or reduced immune function. Heat stress is an important environmental element that reduces poultry output worldwide. This study discusses the consequences of heat stress on chicken production, fertility, and development, as well as how these effects may be mitigated by genetic manipulation also this study discussed how broiler chickens and laying hens perform when exposed to high temperatures, and how these animals' health and productivity suffer as a result. Therefore, appropriate management and a nutritional strategy, in addition to the development of heat-tolerant breed lines, should be examined as options for addressing this problem.

**KEYWORDS:**

Egg Production, Heat Stress, Poultry Production, Reactive Oxygen Species (ROS).

## 1. INTRODUCTION

To meet the rising demand for chicken meat and eggs, the poultry business is expanding globally.Chicken and poultry are excellent sources of protein, vitamins, and minerals, and they contain relatively little saturated fats. Because of this, chickenwhen it comes to the price per gram of protein from animals, and eggs is unequaled. Eggs are a great source of nutrients for the body as a whole, but they also include antioxidants like lutein and zeaxanthin, which are beneficial to eye health. Considering these numbers, it's clear that demand for chicken and eggs throughout the world has skyrocketed in the previous decade and is expected to almost quadruple by 2050 [1].

One of the most important climatic challenges is presently heat stress, significantly affecting the productivity, reproduction, and specific growth rate of several poultry and livestock species.When an organism's heat energy production exceeds the quantity of energy lost to the environment, the organism experiences heat stress. Changes in both external (such as solar and thermal) and internal (such as air temperature, humidity, and motion) elements might contribute to this discord (rate of metabolism, species, and thermoregulatory systems). Heat stress is an

example of an environmental stressor that may have a devastating effect on animal husbandry [2].

The body's reaction to stress is a strategy it has developed to cope with adversity. Definition: the process through which a chicken flock adjusts to an atypical situation in response to any external demand or challenge[3]. The birds' physiological homeostasis (state of being in a state of relative calm) is disrupted by stress. Proper environmental factors for the formation, maturation, preservation, and generation of healthy chickens are essential for optimal performance in poultry farming.When an animal's metabolic rate exceeds its ability to dissipate heat into the external environment, the species experiences heat stress. Sunlight, thermal irradiation, weather conditions, humidity, the animal's species, metabolic rate, and thermoregulatory processes might all have a role in causing this difference [3].

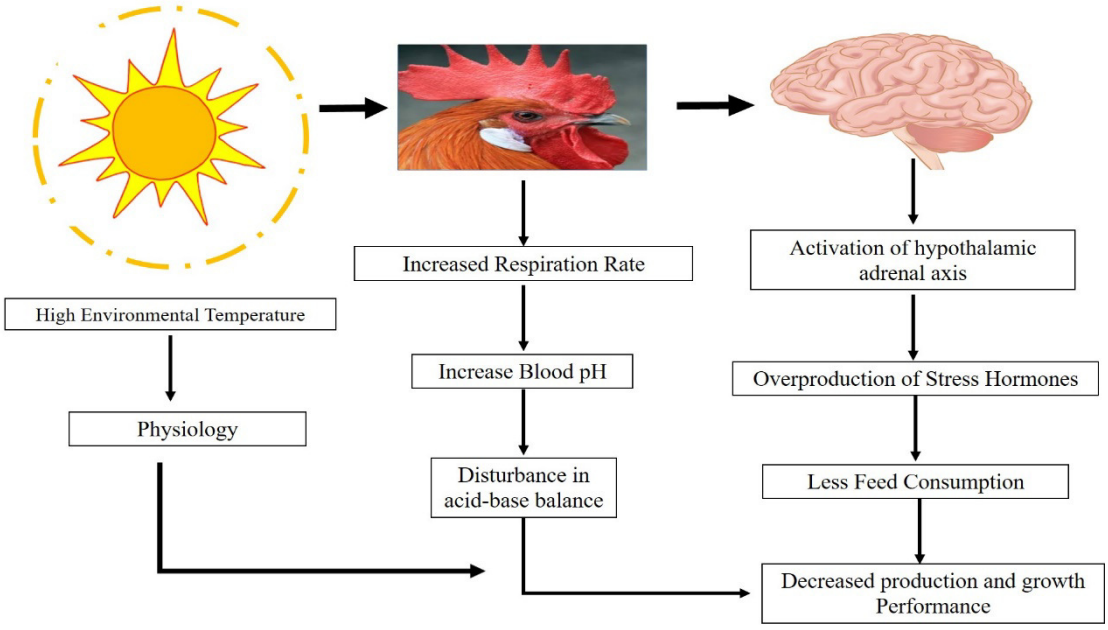


**Figure 1: Flow Diagram Illustrating the Underlying Process of Heat Stress and the Numerous Reactions Shown By Poultry.**

Increasing the supply of whole, healthy, high-quality eggs is a primary goal in the chicken business. However, heat stress affects chicken performance, manifesting first as lower feed intake, then increased panting, and finally lowered plasma protein and calcium levels. It causes an overall drop in egg output and quality from hens.In addition, commercial turkey hens have a decrease in productivity due to an increase in blood corticosterone levels brought on by heat stress. Egg production, freshness, and the proportion of saleable eggs all dropped in poultry when ambient temperatures were raised to 36 °C from the more optimal 21 °C. In addition to high temperatures, high winds have also been linked to decreased productivity in Japanese quail [4].

In addition, the uterus receives less of the calcium it needs from the blood to make the eggshell while the bird is panting, which leads to the formation of fractured eggs owing to the weakness of the eggshell. In poultry, this has a negative reciprocal effect on feed consumption and metabolic activity, ultimately resulting in lower performance overall see Figure 1. This is because the stress hormone levels cortisol, corticosterone, catecholamine, glucocorticoids, and

adrenocorticotropic are all produced as a result of activation of the hypothalamic-pituitary-adrenal axis [5].

All animals, regardless of species, need to learn to adapt to their surroundings. Poultry, in particular, seems to be very vulnerable to heat stress and other environmental stresses associated with high temperatures. It has been hypothesized that the higher metabolic activity in today's chicken breeds accounts for the increased body heat production in these birds. When raising healthy, happy chickens, it's essential to know and manage the surroundings in which they live. The goal of this project is to compile current scientific (peer-reviewed) literature on Broilers and laying hens are the primary targets of research into the effects of heat stress in the chicken production industry [6].

## 2. LITERATURE REVIEW

Lindonne Glasgow et al. stated in their study thatevidence to support the control of antibiotics in chicken farming is typically insufficient in low-income nations. There are risks to human health from the widespread use of antibiotics in livestock agriculture that go unchecked.In August-September 2016, 30 poultry producers with 500 or more commercial birds were surveyed. The findings revealed that 18 farms (60%) had above 1000 birds.The vast majority of farms (25, or 83.3%) utilized antibiotics. The majority of responders (21, or 70%) were unable to explain antibiotic resistance, and more than half (19, or 63.3%), were only hazily aware of antibiotic difficulties. The vast majority (83.3%) of farms utilized antibiotics. More than two-thirds of respondents (19, or 63.3%), were only somewhat familiar with antibiotic concerns, and 21 (70.0%), couldn't explain resistance to antibiotics. The authors concluded that farmers' awareness and conduct were contrary to World Health Organization (WHO) antimicrobial stewardship standards. This study underscores the necessity for quick methods of treatment, such as educating farmers and tracking antibiotic acquisition and usage, to prevent a threat to public health in low-income nations like Grenada [7].

Oladeji Bamidele et al. discussed in their study in five Nigerian agroecologies, that 350 farmers were given standardized questionnaires for cross-sectional research. Most farmers (39%) used EVM.Almost two-thirds of agriculturalists reported using some kind of medication, either alone (25%) or in combination with EVM (35%).Infection treatment and prevention accounted for over 82% of all antibiotic usage. Semi-intensive (37%) and scavenge (14%) methods have the most antimicrobial use. Gender (2 = 9.30, = 0.01) and locality (2 = 216.86, 0.001) affected farmers' bird-treatment choices.Reduced antibiotic use was related to greater levels of education (3.06, 95% CI 2.10-4.44), income (1.99, 95% CI 1.10-3.59), and system management (1.97, CI% 1.1-3.45). 40% of farmers used antibiotics with a low to moderate resistance risk. These results demonstrated farmers' indiscriminate use of antimicrobial drugs and also the possibility of resistant bacteria in Nigeria'sSmallholder Poultry Production Systems (SPPS).

Egg production, egg weight, and eggshell thicknesses were all shown to be reduced in laying hens that had been treated with heat stress, according to Mack et al. Egg production was subjected to an intriguing and informative set of tests, which indicated the increasingly damaging impact that persistent heat stress produces. In the aforementioned series of tests, the egg production of laying hens that were treated to heat stress for 8 to14 days, 30 to 42 days, or 43 to 56 days resulted in a decrease of 13.2%, 26.4%, or 57%, correspondingly [8].

## 3. DISCUSSION

As with any business, poultry farming has the same day-to-day challenges faced by other businesses. Notable among them are management competence, feed availability, rivalry with imported poultry products, severe weather, illness, and inadequate government policies, all of which are particularly problematic in developing countries situated in hot, tropical climes.However, it has been shown that when it comes to environmental challenges, high ambient temperature (HAT) ranks high in the development of tropical chickens, particularly in developing nations where poultry farmers cannot afford the prohibitive cost of contemporary artificial regulation of ambient temperature in hen houses [9].

When faced with high outside temperatures, animals use several strategies for thermoregulation and equilibrium, including increased radiative, convective, and evaporation heat loss through vasodilation and sweat [10]. The air sacs on a bird's body are another mechanism that aids in the transfer of heat to and from the outside world. During panting, air sacs are helpful because they increase the surface area exposed to air, which in turn increases the rate of gas interactions with the atmosphere and the rate at which heat is lost by evaporation.There are several ways in which a bird's reproductive capabilities might be impacted by heat stress. Reproductive hormones in women may be negatively impacted by heat stress, both locally in the hypothalamus and systemically.The dangers of heat stress in men have been shown in several research. When men were put under heat stress, their sperm quantity, concentrations, number of viable cells, and mobility all dropped [11].

### *3.1.Heat Stress and Its Impact on the Body's Defenses:*

A great deal of study has been conducted on how stress affects the immune system in animals. The Central Neurological System's (CNS) ability to modulate the immune response is mediated by a complex network of linked pathways which includes the nervous system, the endocrine system, and also the immune system. It is possible to modify the immune response largely via the hypothalamic-pituitary-adrenal (HPA) and sympathetic-adrenal-medullar (SAM) axis [12].Felver-Gant et al. [13]discovered that laying chickens subjected to severe heat stress had noticeably diminished liver pigmentation. Bartlett and Smith [15] found that heat-stressed broilers had lower levels of total specific antibodies and plasma antibodies of certain immunoglobulin(Ig) (IgM) and immunoglobulin(Ig) (IgG) subclasses, suggesting that these birds had impaired secondary and primary humoral responses (IgG). Weights of the thymus, bursa, spleen, and liver were all drastically decreased as well. Aengwanich [14] showed that heat-stressed broilers had fewer lymphocytes in their bursa medulla and cortex and that the bursa themselves were smaller in mass.

It has been shown by others that heat-stressed broilers have a diminished antibody response and a weakened capacity of their macrophages to ingest foreign particles. In addition, heat-stressed broilers showed a decrease in both basal and provoked oxidative bursts in macrophages. Heat stress has been shown in recent years to affect cellular counts in the blood. Heat stress has been found to raise the heterophils:decrease the ratio of lymphocytes to heterophils by increasing the number of heterophils in circulation.The bird's body produces more reactive oxygen species (ROS) as it attempts to keep its thermal homeostasis in a hostile environment. The body responds by entering an oxidative stress state, during which heat shock proteins (HSP) are made and secreted to counteract the harmful effects of reactive oxygen species (ROS) on cells [15].

### *3.2.Heat Stress's Effect on Poultry Production:*

The quality of meat produced by broilers and the effects of fat deposition are adversely impacted by prolonged exposure to high temperatures, but the effect varies by breed. Recent research has shown that excessive heat decreases the chemical composition and quality of meat in broilers. The percentage of breast muscle in broilers was found to be reduced by chronic heat stress, while the percentage of thigh musclewas also shown to have risen in the same study. Heat-stressed birds also had larger fat deposits and lower protein levels, the research found [16].During travel from the farms to the processing facilities, broilers could be subjected to some stressors, such as the temperature fluctuations of the transportation microenvironment, acceleration, vibrations, movement, impacts, dehydration, separation from peers, and social disturbance, and noise. Thermal stress, and in particular heat stress, is an important component of this multifaceted set of elements. The birds' behavioral and physiological thermoregulatory processes are impaired by the constrained environment within the transit containers.

Furthermore, the research demonstrated a significant rise in broiler mortality when the ambient temperature rose. A correlation was found between the percentage of bruises and the time of year, the length of the trip, and the temperature outside in a detailed look at what factors influence theincreased broiler mortality and morbidity at harvest; these parameters also correlate with body weight and stocking density, transportation, and the length of time between hatching and harvest. It has also been shown that the size of the bird is correlated with its likelihood of dying during transport from the farm to the processing plant.Environmental stress (like heat stress) is likely among the most commonly recurring difficulties in many agricultural systems across the globe, and it could have a substantial influence on the productivity of laying hen flocks.Reducing feed intake is the first step in mitigating the negative impacts of heat stress on production, which include lower body weight, higher feed efficiency, higher egg output, and better egg quality. However, it has been shown that heat stress may reduce feed intake while simultaneously decreasing plasma protein and calcium levels, hence lowering nutritional digestion [17].

*3.3.Heat stress and genetics:*

The most pressing issue now is the breeding of birds that can survive in very hot climates. The foundation of this method is the isolation and selective breeding of heat- and disease-resistant genes. Broiler hens and turkeys have significant difficulty responding to heat stressas a direct effect of deliberate breeding for high growth rates.Because of a negative relationship between rapid development and heat stress, they were not able to reach their genetic makeup for fast development when the ambient temperature was high. Another issue is that heat stress causes mitochondrial damage and oxidative stress in chickens, and this is exacerbated by the selection of birds for production qualities.

Supplementation with epigallocatechin-3-gallate (EGCG) during heat stress resulted in a 42% suppression of NF-kappaB activity in quail hepatic cells, as reported by Sahin et al. Additionally, “Nrf2 (Nuclear factor-erythroid 2-related factor 2)” is a known participant in the cellular defense system towards oxidative stress in heat-stressed chickens [18].

The heat's toll on hens' nutrient-carrying mechanisms, free radical-fighting antioxidants, and inflammatory immunological responses.Most nutrient transporters' expression was downregulated in response to heat stress. Due to an increase in ROS generation, antioxidant enzyme synthesis has been ramped up. Heat stress induced an up-regulation of inflammatory cytokines and toll-like receptors in chickens.The hens succumbed to the heat's effects. Chickens

raised in warmer conditions take in fewer nutrients because their metabolism is slowed by the increased formation of reactive oxygen species and immunological activation shown in Figure 2.As the temperature rises outside, animals become less interested in eating, and their digestive systems become less healthy. The function of nutrient absorption may be better understood via the study of nutrient transporter genes,this might be used to determine how heat stress affects the digestive system. Another drawback of tinkering with the temperature is a decrease in immune function. Interleukins (ILs), tumor necrosis factors (TNFs)" and "toll-like receptors (TLRs)", are only a few examples of immunological marker genes that have been shown to change in expression in the spleen and intestines of chicks exposed to high temperatures [19]. Climate change poses risks to the poultry sector. Recent developments in biotechnology have made it possible to study the genetic changes brought on by the long-term exposure of birds to high temperatures.

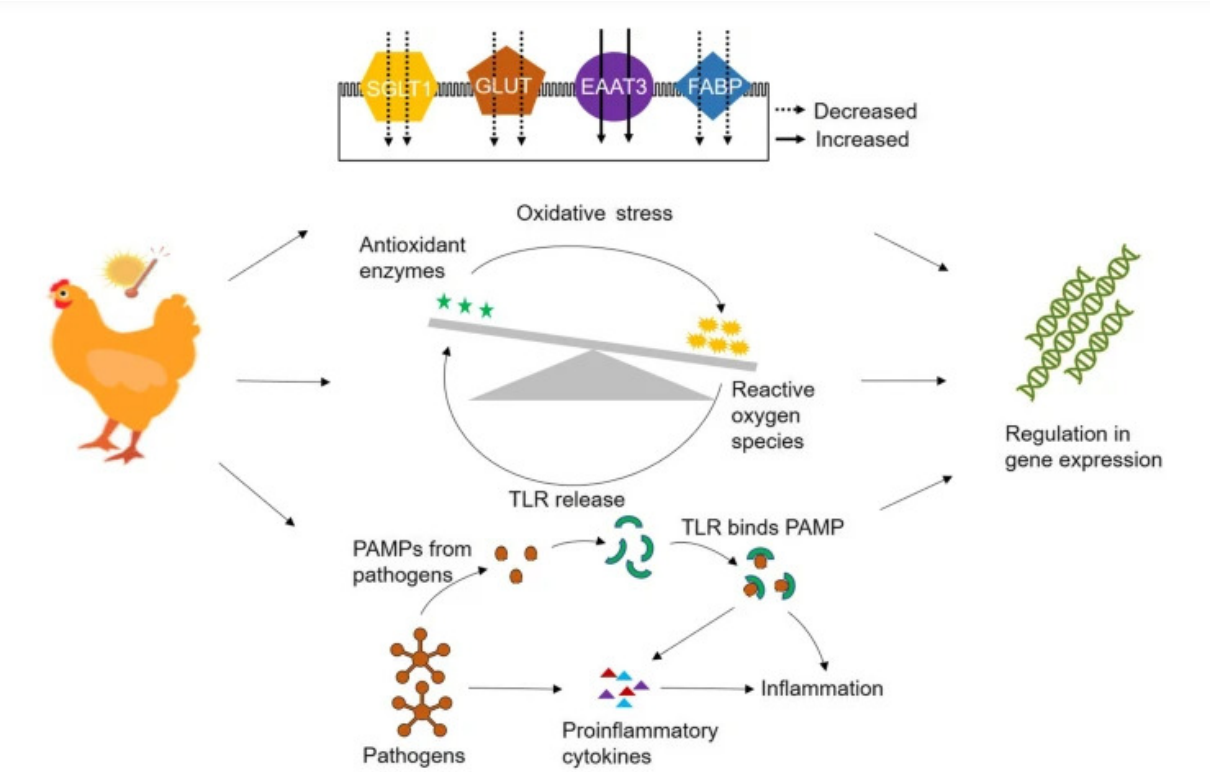


**Figure 2: High ambient temperature increases reactive oxygen species generation, immunological inflammation, and nutritional absorption in hens** [20]**.**

*3.4.Potential Heat Stress Management Strategies for Poultry:*

*3.4.1. Feeding Strategies:*

To keep chickens healthy and productive, it is standard practice to limit their access to food during the hottest part of the day. In this method, birds' metabolic rates are lowered by withholding nutrition for a specific period (often between 8 a.m. and 5 p.m.). In heat-stressed broilers, feed limitation is reported to lower rectal temperature, reduce mortality, and decrease abdomen fat. To test fearfulness, birds are put on their backs and their righting reflex is observed. Uzum et al.[21] reported thatrestricted feed availability to 8 hours per day in broilers

during hot seasons increased feed efficiency and reduced tonic immobility. Restricting feed for broiler chickens was also observed to result in a 23percentage decrease in their metabolic heat output. Although this method is sometimes used, it is not as common as it should be since it slows the birds' development and makes them too old to sell at a younger age.

### *3.4.2. Wet Feeding:*

Birds lose a lot of water via their respiratory systems under heat stress, so they have to drink more to get their body temperature back to normal. By diluting the feed with water, you may boost the animal's water consumption and speed up its transit through the digestive tract. Wet feeding promotes pre-digestion, enhances gastrointestinal nutrient absorption, and quickens the digestive enzyme's reaction to the meal.Feed intake, body weight, and GI tract weight in broilers all increased when they were fed a moist diet. Feeding laying hens moist feed at a high temperature enhanced their crude protein intake, egg production, and the number of chickens that laid eggs. Heat-stressed birds benefited from this method, but poultry producers don't use it as often since there's a chance that the feed may get contaminated with mold and the birds would become sick [22].

### *3.4.3. Including Fat in Your Diet:*

Heat stress's detrimental effects on hens may be mitigated to some degree by feeding the animals a diet rich in fat and protein. When compared to protein and carbs, fat has a smaller heat rise during metabolism. Because of this, it is common practice in hot climates to add extra fat to the diet to boost energy and lessen heat stress's negative implications. Fat supplementation in the chicken diet has several benefits, including enhanced nutritional utilization in the GI tract (through slower food transit) and increased power value of the other feed elements.In a similar vein, a 5% fat diet was shown to significantly enhance the performance of broilers. Performance of broilers, meat lipids, and immunological and physiological characteristics was all negatively affected by prolonged heat stress, however, Attia et al. [23]Oil addition in diets with greater protein amounts was shown to mitigate these effects. Despite these advantages, raising broilers with added fat greatly increased their belly fat.

The development of defective intestinal permeability begins with oxidative stress. Increased intestinal permeability under heat-stress circumstances allows for the easy movement of germs across the intestinal mucosa. This is because of the elevated levels of reactive oxygen species (ROS). It has been found that heat-stressed broilers exhibit elevated levels of the pathogen "*Salmonella Enteritidis*" in their spleens due to an increase in inflammation and transmission of the bacteria.Salmonella and Campylobacter colonization of birds is a major public health and economic issue in the poultry and egg industries, and also the consequent transmission of these infections down the food chain to humans. Among the most prevalent causes of food poisoning is contact with raw or undercooked chicken [24].

## 4. CONCLUSION

Global warming and climate change have a major impact on the environment, particularly on heat stress, and both have an impact on poultry output across the world. When birds are exposed to it, substantial unfavorable impacts on productivity, reproduction, and growth are triggered. Performance as a consequence of the production of immunological reactions, physiological, and behavioral. It results in significant financial losses for the poultry industry.One of the most significant challenges to the chicken industry's growth is the consequences of heat stress,

especially in light of global warming.The consequences of heat stress on chickens have been the subject of many studies, and many methods have been implemented to alleviate the problem. However, its use is restricted inside the poultry sector. Heat stress may produce a wide range of physiological, neuroendocrine, and behavioral disorders in poultry due to a combination of conditions, including but not limited to high external temperature, humidity, radiant heat, and airspeed.Prenatal heat acclimation and also the selection of genetically predisposed breeds have both been studied for their potential to improve animals' chances of survival in warmer climes (i.e., increased heat tolerance). Despite the promise, further study and improvement are needed to fully make use of these possibilities (especially for poultry farming in hot climatic locations).More studies are needed to compare the effectiveness and cost-benefit of various heat-stress mitigation strategies in poultry production.

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# CHAPTER 9

# COMPREHENSIVE STUDY OF SOLAR ENERGY EFFECTS ON THE EARTH'S ATMOSPHERE WITH SUBSTANTIATE EVIDENCE

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**ABSTRACT:**

The radiant heat and light from the Sun are collected by a wide range of technologies, such as solar architecture, solar thermal energy, and solar energy that helps generate electricity. To safeguard humans, animals, and the ecosystem from harm because of solar energy, it's also imperative to reduce greenhouse gas emissions and avoid climate change. Solar energy is a sustainable resource that contributes suggestively to these efforts. Furthermore, using solar energy may lower water usage and improve air quality. This study also includes environmental drawbacks of solar energy, and these contain habitat loss, land use changes, pressure on water supplies, exposure to toxic products, and contamination of air, soil, and water resources. Advances in technology will make solar energy even more affordable which also explain in this study with the help of different literature studies. It is possible that by 2030 solar power will be the primary source of energy for electricity generation in a significant part of the planet. Additionally, it will benefit the ecology and combat climate change which helps in future understanding of solar energy.

**KEYWORDS:**

Atmosphere, Earth, Environment, Photovoltaic, Solar Energy.

## 1. INTRODUCTION

During use, solar energy equipment and facilities don't pollute the atmosphere or produce any greenhouse gases. Solar energy replaces or reduces the use of further energy sources with larger environmental consequences, there may be beneficial, indirect effects on the environment. However, when solar energy technology develops and is used, environmental hazards do occur. Metals and glass are among the energy-intensive materials used to build solar energy devices [1]. Solar power systems may be associated to the environmental problems associated to the manufacturing of these elements if a life-cycle or cradle-to-grave environmental study is done. Photovoltaic (PV) systems may create as much energy as was used in their construction in one to four years, according to studies conducted by several companies and academic institutions [2].

Photovoltaic (PV) panels and cells are made using hazardous chemicals, which require careful handling to avert environmental discharges. Heavy metal are used in many PV cell technologies, and after their beneficial life is over, these panels and PV cells may essential to be handled contrarily [3]. Solar thermal system employs potentially dangerous fluids to transferal heat, and if these fluids leak, the environment might be harmed. In the US, environmental rules control

how hazardous materials are used and disposed. The US Department of Energy is supporting many innovations, along with the recycling and recovery of the components used to create panels and PV cells, to solve the challenges associated with solar power technology's end-of-life. State laws in various countries support the recycling of PV panels [4].

Large solar power plants can have an impact on the environment like any other type of power plant depending on where they are located or nearby. The local plant and animal habitats may be harmed over the long term by land clearing and the siting of the power station. However, putting up solar energy systems can benefit farmers financially and environmentally, especially if they live in agriculturally-deficient areas or farms [5]. In certain solar generating installations, water may be needed to cool turbine engines or clean solar collectors and concentrators. Cleaning collectors with a lot of surface or groundwater in certain desert areas may be harmful to the ecosystems that depend on water supplies. Moreover, the solar power tower's concentrated sunlight beam has the potential to harm birds and flying insects [6].

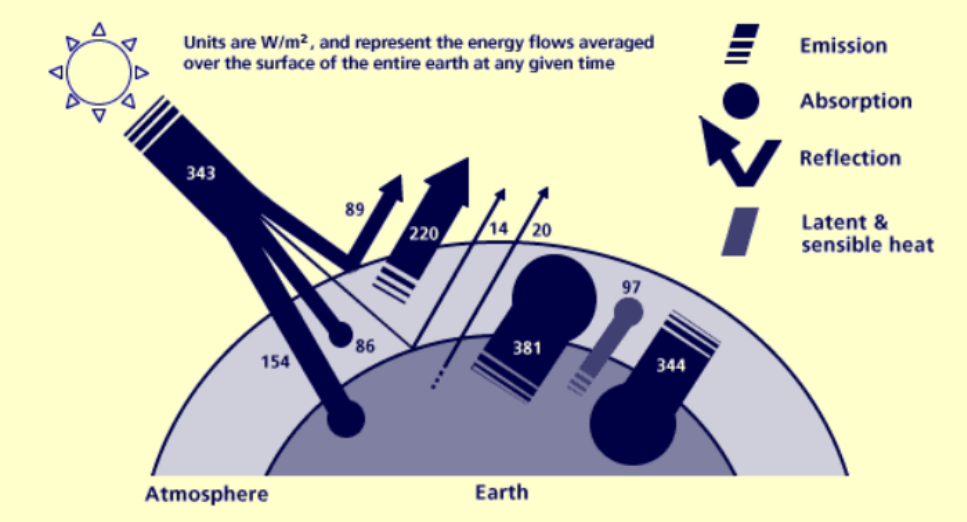


**Figure 1: Illustrate the relation of the earth's atmosphere with sunlight for solar energy.**

About 1.1 × 10 E20 kilowatt-hours of energy is produced per second by the Sun. A 100-watt bulb requires one kilowatt-hour of electricity to run for ten hours. About 1,500 quadrillion (1.5 × 10 E18) kilowatt-hours per year, energy produced by the Sun, and by Earth's outer atmosphere. But, only 47% of this, or around 700 quadrillion (7 × 10 E17) kilowatt-hours, get to the surface of the Earth due to the atmosphere's gases and particles reflecting, dispersing, and absorbing it seen in Figure 1. Fossil fuels are used extensively in almost all human undertakings, which has led to several negative outcomes, including air and environmental pollution that has never been observed previously in recorded human history. In the literature, terminology like climate change, global warming, greenhouse effect, depletion of the ozone layer, and acid rain started to appear often [7]. Due to the production of greenhouse gases like carbon dioxide ($CO_2$) and methane ($CH_4$), which emit long-wave terrestrial radiation, fossil fuel usage has been linked to these occurrences since tests and studies began in the 1970s. Exit into space and warm the Earth's troposphere as a consequence. Increasing the quality of fossil fuels by lowering their harmful emanations into the atmosphere or, more crucially, being as clean, green, and dependent on fossil fuels as feasible, are the two main alternatives for averting additional effects of these catastrophes. using renewable energy sources instead of fossil fuels [8].

In comparison to other renewable energy sources like wind, hydro, wave, geothermal, and tidal energy, solar energy is more widespread and uniformly dispersed in nature. The advancement of solar energy technologies is essential for the creation of a sustainable energy future. Despite assertions that there is a plentiful supply of petroleum and different fossil fuels that they are inexpensive and easy to get, these fuels are scarce and a substantial source of greenhouse gas emissions [9]. Energy production and its harmful effects on the environment increase with increasing energy needs. Thus, environmental pollution became a threat globally. As a result, clean energy sources such as solar power have become more important in recent years. However, solar energy technologies themselves have contributed to the environment in some way or the other. In this paper, these effects will be examined, along with the prerequisites that must be present to prevent them [10].

An important energy source that has recently been used is the Sun. It offers a plentiful supply of resources that may be utilized to generate electricity that is sustainable, clean, and pollution-free without causing any related greenhouse gas emissions. In recent years, it has been shown that solar energy can be harnessed and stored for use on a global scale as a potential replacement for conventional energy sources. The relevance of solar energy has increased tremendously as the world has shifted its attention to green forms of energy [11]. Compared with the conventional energy resources, solar power systems have substantial environmental benefits. As a result, they significantly support the sustainable development of human activities. Large-scale deployment of such devices sometimes, nevertheless, necessitates handling possibly negative environmental effects. These possible problems might, for certain users, represent a substantial barrier to the development of these technologies.

Along with the tremendous increase in global warming and air pollution, the increasing demand for energy around the world has also contributed to the reduction of fossil fuels used in the generation of electricity. The difficulties arising from the excessive combustion of the fossil fuels for electricity generation are best solved by the use of clean solar energy, which is widely accessible. Solar power conversion has been a top focus, and there are now many uses for this technology, both in space and on Earth. In order to transform solar energy directly into electricity, photovoltaic cells use couples of semiconductors to interact with light. Low photovoltaic efficiency is what prevents solar cells from being used more often. The fact that photovoltaic cells use only a small portion of the energy in the Sun's spectrum is the main reason for their poor efficiency. In this study explain about the Solar Energy Effects on the Earth’s Atmosphere with different evidence by studying the different literature reviews. In this paper also discussed about the impacts of the solar energy and what are the process which is used for the making the solar energies and how it will be utilized.

## 2. DISCUSSION

The use of renewable energy is increasing, mostly to reduce reliance on limited fossil fuel supplies and mitigate the effect of climate changes. Over the past ten years, the world has seen a rapid increase in the production of electricity from solar energy, both direct (photovoltaic) and indirect concentrating solar energy. This is not unexpected given that solar power technologies are no longer prohibitively expensive and that the Sun can produce more than 2500 terawatts (TW) of technically usable energy over a significant portion of Earth's surface. Other renewable energy sources, such wind and biomass-derived energy, have far smaller potential than solar power technologies [12]. Additionally, solar energy's numerous advantages which include decreased greenhouse gas emissions, stabilization of the degraded land, increased employment

opportunities, accelerated rural electrification, increased the energy independence, and improved superiority of life in emerging nations make it appealing in many parts of the world.

With the exponential growth in the global population, energy production is seen as a major impediment to industrial development. Communities are growing, moving to formerly uninhabited areas, and creating new technologies, and this has an impact on both the overall energy demand and especially the electrical energy load [13]. Therefore, a sustainable and healthy society today needs a safe, ecologically friendly and effective energy supply more than ever before. Crude oil, natural gas and coal, accounted for more than 81% of the primary energy supply in 2018, demonstrating the dominance of fossil fuels and conventional energy production methods. People were unaware that the widespread usage of these fossil fuels had a detrimental influence on the ecology and is a double-edged sword. Many dangerous environmental issues, such as land droughts, heat waves, wildfires, sea level rise, floods and other serious climate events have resulted from excessive reliance on fossil fuels and their widespread misuse in almost all regions of society.

Given their limited supply and negative impacts on the environment, research has been conducted to identify several ecologically acceptable and effective substitutes to the conventional energy markets. The efficacy of existing energy conversion system has been greatly improved by developing effective energy conversion systems based on renewable energy resources, like solar thermal energy, wind power, solar PV energy, geothermal energy, hydropower, and biomass energy. These initiatives have been essential in advancing renewable energy systems to the point that industrialized nations are now striving to include more renewable energy sources into their energy mix and are advocating for a reduction in carbon emissions worldwide. Reductions in global carbon emissions are mandated by important geopolitical agreements, notably the Paris Agreement (UNFCC, 2015), but, according to the IRENA's 2017 Climate Safe Energy Solutions reports, complete de-carbonization of energy use to effectively accomplish Must be in less than 50 years. Such lofty objectives substantially mitigate the adverse effects of climate change [14]. When examining renewable technologies and their most current development figures closely [15].

Given the immense interest in solar technology in particular and renewable energy systems in general, it is imperative to take necessary environmental safeguards. Researching the sustainability levels likes renewable technologies, the environmental assessment of every technology, and the mitigation of any possible environmental implications are crucial in order to prevent any future environmental difficulties caused by newly announced energy supply systems. Compared to other energy producing methods, solar energy is fairly affordable [16]. They are numerous and appropriate for a variety of purposes. Furthermore, solar power system maintenance costs are minimal. The biggest drawback is that they depend on unpredictable weather, requiring an energy storage system and increasing the cost of the entire equipment.

Between 1992 and 2020, the development of solar energy expanded dramatically. It has progressed from modest use to a common source of power. Since the progress of solar cells in the 1950s, many nations have shifted to the production of solar power. Even though the United States, Germany and Japan were the first, China remnants the world's leading producer of solar energy. The solar energy used, whether for the direct production of electricity in solar PV, photo-assisted fuel cells, concentrated solar PV systems or the reduction of CO2 from fuels like hydrocarbons or hydrogen. Concentrated solar power plants use indirect sun radiation as a source of electricity [17].

If global warming and other issues caused by fossil fuels are to be stopped then the world must convert to renewable energy resources such as sunlight, biomass and wind. As with the generation of conventional energy and environmental concerns must also be taken into account [18]. This report highlights the main environmental impacts of renewable technology. Solar, wind, biomass, geothermal and hydropower are examples of renewable energy sources that can significantly impact sustainable development. Their current level of commercial market exploitation is limited because external costs and benefits are not rewarded, intermittent supply, and other technical and institutional factors. While renewable energy has site-specific implications, generalizations are still achievable. When it comes to air pollutants, renewable energy is often more ecologically friendly than other energy sources.

*2.1 Wind Energy:*

It does not contain any poisonous or hazardous material other than those often contained in large equipment, polluting the air or water, or endangering public safety. Public resistance, however, expressed concern about the wind turbine's sight, noise and impact on wilderness areas, a significant obstacle to the wind sector [19]. Commercial wind turbine noise pollution can sometimes be associated with the small jet engine. Although wind power generating has very low life cycle emissions, there are a number of environmental repercussions that might restrict its potential. The most important environmental consequences are:

i. *Noise:* Both aerodynamic noise from wind blowing over the mechanical noise and blades from the rotating sections of the turbine, particularly the gearbox, are produced by wind turbines. Research continues, and better designs have reduced noise. By definition, wind farms built outside densely populated areas are less objectionable.
ii. *Electromagnetic interference:* Electromagnetic signals from wind turbines may be scattered, interfering with communication networks. Choosing an appropriate location away from military bases or airports might lessen this effect.
iii. *Bird safety:* When the birds run into the rotating blades of the turbine, they are killed. Compared to permanent species, tropical species are far more fragile. By maintaining the turbines far from the migratory pathways, the effect is reduced.
iv. *Visual effects:* Wind turbines should be located in open spaces, making them quite noticeable. Some people find them unattractive, and concerns have risen as the new generation of turbines gets bigger.

Wind power production on a big scale may be influenced by decreased wind speed and ecological stress. Lakes near windmills may warm up as a result of less water evaporating from their surface. An increase in soil moisture is also possible. These effects may not be very significant, except in a few sensitive places. Land use is another component of wind energy. Most studies assume that wind farms will be dispersed separately and that the entire area in between should be considered populated.

*2.2 Solar Energy:*

Since solar power systems don't emit any air pollution while in use, their production, installation, and eventual disposal pose the most environmental, health, and safety concerns. Certain solar system components might be hazardous to the health and safety of workers as well as anybody else who comes into contact with them. Particularly, the manufacture of solar cells often requires the use of hazardous materials like arsenic and cadmium. Even generally safe silicon, a critical element of solar cells, poses a danger to workers if they breathe it in as dust. According to

estimates, central photovoltaic systems need unusual inputs, some of which, like cadmium sulphide, are explosive and hazardous. Both kinds of solar energy systems, including rust inhibitors, antifreeze, and heavy metals leaked from the system, will produce significant amounts of harmful water contaminants, and claims [20]. The use of herbicides to prevent excessive plant development around the collectors will also result in the indirect creation of water contaminants. The production of non-recyclable materials during plant shutdowns, such as fibre glass, coolant, glass, and insulations in PV-based systems, would cause additional disposal problems due to cadmium and arsenic, pose a risk to eye health due to reflectors, pose a risk from toxicants in coolant fluids, cause soil erosion and compaction, and possibly result in a decrease in crop yield are additional negative effects of central solar systems. An additional danger of harming firefighters exists from hazardous gases released by solar modules attached to burning homes or buildings, however, it is highly unlikely.

*2.3 Geothermal Energy:*

The heat permeates the Earth's crust and is known as geothermal energy. Hydrothermal energy, which results from the trapping of hot water or steam, is the only kind of geothermal energy that has been thoroughly explored. To extract magma, geo-pressurized resources, pressurised brine containing methane, and hot dry rock that may be reached by drilling deeply into the rock, new techniques are being developed. The physical consequences of geothermal energy sources, including surface disturbances, fluid evacuation, thermal pollution, noise, and subsidence due to chemical reliefs, are all potentially negative environmental impacts of geothermal energy resources. The many geothermal resource types vary significantly from one another, yet they all raise comparable environmental issues. The correct disposal of hazardous waste, ground subsidence, water and air pollution are major problems. Instable species including boron, mercury, arsenic, as well as gases, leak into liquids when geothermal steam or hot water travels through rocks, minerals, and metals. People who live and work nearby may be at risk when geothermal fields are undesirable for commercial use, producing large amounts of chemicals. Most geothermal power facilities will need a lot of water for cooling or other uses. This demand can lead to disputes with other water users in areas where water is scarce.

*2.4 Biomass:*

The only other renewable energy source other than hydroelectricity that presents more significant environmental concerns than biomass power is biomass. There are anxieties about the impact of land use for the cultivation of energy crops in addition to air pollution as a result of the combustion of biomass and the fuel generated from biomass. How well the resource is handled will determine how severe these effects are. Further complicating matters is the lack of a single biomass technology and the existence of a broad variety of production and conversion methods, each having a different environmental effect.

It is unknown how much pressure such a large plantation would exert on soil moisture, but it would undoubtedly be substantial due to both water intake and evaporation. Other significant impacts on the microclimate, biodiversity and soil productivity will have serious implications for the region's ecosystem. Groundwater pollution hazards would be high and it would be difficult to stop sewage from such large ponds from leaking into subsurface aquifers from aquatic weed farms. Other issues such as the threat of mosquitoes and the spread of the virus will need to be addressed. Additionally, disposing of the used hyacinth once the energy is taken will be a significant issue.

Removal of biomass from land and water for energy generation schemes can lead to flooding, loss of nutrients and soil and water erosion. Natural biota and fauna could potentially be affected. These and other environmental risks associated with biomass production seem to have not received much attention. Projects that produce biomass energy can make soil erosion issues worse. In addition to slowing groundwater recharge, soil erosion also accelerates water runoff, which can get to rivers, lakes and estuaries by producing eutrophication may reduce the quality of the collection of agricultural waste for biomass energy would result in significant nutritional loss. The habitat and food sources of animals and another biota will change as a consequence of the conversion of natural ecosystems into plantations for energy crops. Many of the preferred habitats and breeding grounds for various animals, birds, and another biota would be diminished if forests and wetlands are replaced.

Changes in employment and increased workplace health and safety issues will have a significant social impact. If biomass resources are used to meet the country's energy demands, total employment is predicted to increase. Agriculture and forestry industries will need labourers to harvest, cut and transport biomass resources, as well as to run conversion plants. At the Sun's core, fusion happens when two hydrogen atoms' protons violently collide and join together to generate helium atoms. The huge amount of energy produced by this mechanism is due to a proton-proton (PP) chain reaction. The centre of the sun burns 620 million tonnes of hydrogen per second. The PP chain reaction generates heat and energy for other stars that are similar in size to our sun, supplying them with a steady supply. At roughly 4 million degrees Kelvin, these stars are rather hot (about 4 million degrees Celsius, 7 million degrees Fahrenheit). Stars with a mass of 1.3 times that of the sun generate energy via the CNO cycle. Carbon, nitrogen, and oxygen are burned during the CNO cycle, a process that turns hydrogen into helium (C, N and O). Less than 2% of solar energy presently comes from the CNO cycle. In nuclear fusion, massive amounts of energy are released as waves and particles via the PP chain reaction or CNO cycle. Throughout the solar system, solar energy is continually being emitted from the sun.

Electromagnetic radiation (EMR) is the method by which the Sun's heat, light and energy are transmitted far EMR. Electromagnetic spectrum consists of waves of dissimilar frequencies and the wavelengths. The number of times a wave repeats in a given amount of time is indicated by its frequency. High-frequency waves are ones that recur often over a certain time period and have very small wavelengths. The Sun's highest frequency waves contain X-rays, gamma rays, and ultraviolet light (UV rays). The most harmful UV radiation is nearly entirely absorbed by the atmosphere of Earth. Sunburns may be caused by less intensity UV rays that travel through the atmosphere. The Sun also emits infrared radiation, which consists of very low-frequency waves. The majority of the heat produced by the Sun is infrared radiation. The region between infrared and ultraviolet light is known as the visible spectrum and contains all the colours we perceive on Earth.

The wavelength of violet is the shortest, while the wavelength of red, which is closest to infrared, is the longest. As soon as the sun rises, the earth's components and things start to warm. Those materials continuously absorb heat from the sun's beams. The chemical distributes its heat back into the environment as the sun goes down and the nighttime temperature drops. Passive solar energy is used to effectively and economically transport heat in homes and other structures. An example of this is calculating the "thermal mass" of a structure. Most of the material heated during the day forms the thermal mass of the building. The thermal mass of a building can be represented by materials such as wood, metal, concrete, clay, stone or clay. Thermal mass returns

its heat to space at night. A moderate, constant internal temperature is maintained through efficient ventilation systems that circulate hot air through rooms' corridors, windows, and air ducts.

Passive solar technology is often included in building design. For e.g, the engineer or architect might position the building such that it faces the sun's path during the planning phase of construction to guarantee that it gets the optimal amount of sunlight. This process takes into consideration the local latitude, elevation, and typical clouds cover. Additionally, while building or retrofitting buildings, extra shade, thermal insulation, or thermal mass may be added. Other instances of the passive solar structure include the usage of cool roofs, green roofs and radiant barriers. Cool roofs with white paint deflect sunlight rather than absorb it. Due to the white surface of the building, the inside gets less heat, which minimizes the energy needed to chill the facility. Cool roofs and radiant barriers both functions similarly. They use highly thoughtful materials, like aluminum foil, to provide insulation. The foil may save cooling expenses by up to 10% and reflects heat rather than absorbing it.

To sustain the plants, they need a waterproof cover underneath, as well as soil and irrigation. Green roofs provide vegetation in addition to reducing the amount of heat absorbed or lost. Vegetation on green roofs produces oxygen and absorbs carbon dioxide through photosynthesis. They reduce some of the negative consequences of energy use in that area by filtering out pollutants from the wind and rain. In recent years, green roofs have gained popularity in Australia, Canada, Western Europe and United States. They have long been a tradition in Scandinavia. For example, Ford Motor Company planted saplings on the roofs of its assembly facility in Dearborn, Michigan, which is 42,000 square meters (450,000 sq ft) in size.

Roofs absorb several millimeters of precipitation, reducing storm water runoff in addition to greenhouse gas emission. The effect of "urban heat island" can also be reduced by the use of cool and green roofs. Temperatures can often be higher in crowded cities than in surrounding areas. Several factors play a role in this, including the use of heat-absorbing materials like concrete and asphalt in city construction, the blocking of air by tall buildings and its cooling effects, and the large amount of waste heat produced by traffic, industry, and densely populated. Urban spaces can reduce the increase in local temperatures to some extent by planting trees in the available roof space or reflecting heat with white roofs.

## 3. CONCLUSION

An increasingly significant alternative source of energy is solar energy. Being a renewable and unlimited source of energy, it has now become important. However, there are some environmental impacts of solar power systems. In this paper discussed about the solar energy and utilization of the solar energy with the help of the different literature studies. The harmful effects of solar power systems can be minimized with the right precautions. Before applying, the venue must first be carefully selected. The biggest usable surface is on the rooftops of small buildings, and solar cell modules are an excellent substitute for covering the glass on the sides of huge structures like skyscrapers. Solar modules should be utilized as a building material and completely integrated with the structures in order to avoid the aesthetic load. There are many steps that may be taken to lessen the environmental effect of solar power systems. Due to the hazardous elements used in solar cell modules, promoting module efficiency and lifetime will be crucial which also effects on the future growth of the solar energy.

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# CHAPTER 10

# CRYOPRESERVATION: AN IMPORTANT TECHNOLOGY FOR PRESERVATION AND ITS APPLICATION

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**ABSTRACT:**

The process of keeping living cells, tissues, or biological samples in deep freezers at extremely low temperatures for storage as well as preservation is known as cryopreservation. The sample is typically stored at 196 °C or less. All the biological processes of a cell come to an end at such a low temperature, and the cell dies. Cryopreservation makes it possible for cells to resist freezing and thawing. The breakdown of cell membranes can occur as a result of the accumulation of ice inside the cells. This can be prevented by carefully selecting the cooling medium and managing the rate of solidification. In this paper, the author talks about cryopreservation, the process of cryopreservation, the use of preservation for the storage of biological material, and the application of cryopreservation. The main objective of this paper uses the cryopreservation technique. In the future through this paper people will be aware of cryopreservation and its various application.

**KEYWORDS:**

Cryopreservation, Freezing, Preservation, Stem Cells, Temperature.

## 1. INTRODUCTION

Cryopreservation is based on the capacity of particular tiny molecules to penetrate cells and stop dehydration or intracellular ice crystal creation, which can result in cell death as well as organelle destruction even during the freezing process [1]. The two substances that are usually employed as cryoprotectants are glycerol and dimethyl sulfoxide (DMSO). Red blood cells are largely protected from freezing by glycerol, whereas other organs and tissues are primarily protected from freezing by DMSO. Cryopreservation methods like freeze-drying employ trehalose, a sugar present in organisms that can withstand extremely low levels of moisture. Trehalose is particularly helpful for maintaining sperm, stem cells, or blood cells because it stabilizes cell membranes [2]. A controlled-rate freezer is used in the vast majority of cryopreservation procedures. The cell suspension is placed in a container that is tightly sealed. The cooling system then disperses the liquid nitrogen [3]. Careful observation of the freezing rate helps to avoid ice crystal production or rapid cellular dehydration. The cells are typically heated in a controlled-rate freezer from room temperature to about 90 °C (130 °F). Liquid-nitrogen freezers, which can contain either liquid as well as vaporized nitrogen, but are maintained at extremely low temperatures, are then used to store frozen cell suspensions. On a freeze-drying basis, cryopreservation does not require a liquid-nitrogen freezer [4], [5].

An important use of cryopreservation is the freezing or storage of hematopoietic stem cells that develop in the bone marrow or peripheral blood. In the case of autologous bone-marrow rescue, hematopoietic stem cells are extracted from the patient's bone marrow prior to high-dose chemotherapy [6], [7]. After treatment, cryopreserved cells from the patient are thawed or reinserted into the body. The significant bone marrow toxicity of high-dose chemotherapy necessitates this procedure.

The prognosis for the treatment of several solid tumors and lymphoma malignancies has been significantly improved because of cryopreserved hematopoietic stem cells. Since the blood cells of leukemia patients are cancerous, they cannot undergo autologous bone marrow transplantation.

Therefore, these patients rely on cryopreserved blood and cryopreserved hematopoietic stem cell obtained from the umbilical cord of newborns [8], [9]. Hematopoietic stem cells, also known as mesenchymal stem cells, have been known to develop from embryonic connective tissue, skeletal or cardiac muscle tissue, as well as nerve tissue that may fuse into a bone since the late 1990s. The growth of these cells in tissue culture systems or their cryopreservation as future treatments for a variety of diseases, including those affecting the neurological or muscular systems, such as the liver or heart, are both now of significant interest [10], [11].

This process involves the preservation of biological materials such as cells, oocytes, tissues, pre-implantation embryos, spermatozoa, ovary tissues, organs, etc., at extremely low temperatures without compromising the viability of the cells. Typically, this approach uses dry ice and liquid nitrogen.

### *1.1. Steps of Cryopreservation:*

The following are all of the actions required to preserve the biological samples that were gathered, as shown in Figure 1:

#### *1.1.1. Material Selected:*

The correct plant material must be chosen for cryopreservation. It is dependent on nature or density, two significant aspects. Any tissue, including embryos, meristems, seeds, ovules, etc., could be chosen for this use.

#### *1.1.2. Addition of Cryoprotectant:*

The chemical component is crucial because it guards against cryo degradation. Alcohol and certain amino acids like proline, or dimethyl sulfoxide are a few examples of cryoprotectants. Generally speaking, two cryoprotectants should be employed in conjunction rather than just one since they are thought to be more effective, which is shown in Figure 2.

- *Freezing:* Various plant species exhibit varying degrees of sensitivity to cold temperatures.
- *Slow Freezing Method:* The tissue and plant material are gently frozen using this method, which also uses a gradual cooling rate. The primary benefit is that the plant cells are partly hydrated and function more effectively.

- *Method for Rapid Freezing:* Liquid nitrogen is injected into the vials. The temperature rapidly drops throughout this procedure from -300 -1000 degrees.
- *Dry Freezing Method:* Dry freezing is a technique used to preserve seeds and hydrated cells.

Liquid nitrogen storage is essential for keeping goods or materials at a particular temperature. The temperature is often maintained between 70 and 196°C. Liquid nitrogen is used for long-term storage when the temperature is -196 °C. Nitrogen must be continuously available to prevent harm.

- *Thawing:* The vials are often placed into a warm water bath and vigorously swirled to begin the thawing process. Additionally, it results in the vials being moved to a different bath that is 0 °C.
- *Washing and Reculturing:* To get rid of the cryoprotectant, the preserved material is cleaned. The material is also recultured in new media.
- *Viability Measurement:* Cell death is a potential result of storage stress. In the majority of instances, viability is present.
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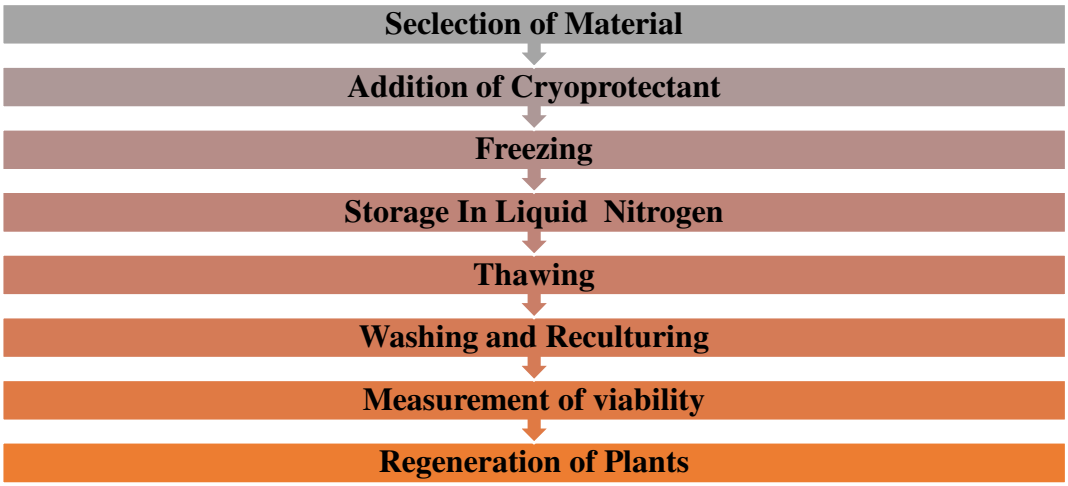


**Figure 1: Illustrate the mechanism of Cryopreservation.**

Human embryos or sperm are also frozen and stored via cryopreservation. It is particularly useful for freezing excess embryos produced by in vitro fertilization (IVF). In this procedure, biological materials such as cells, oocytes, pre-implantation embryos, organs, tissues, spermatozoa, ovarian tissues, etc. are preserved at incredibly low temperatures without compromising the viability of the cells. Usually, liquid nitrogen or dry ice is used in this method. Children born from frozen embryos are at a slightly but significantly increased risk of developing childhood cancer following frozen embryo transfer [12], [13].

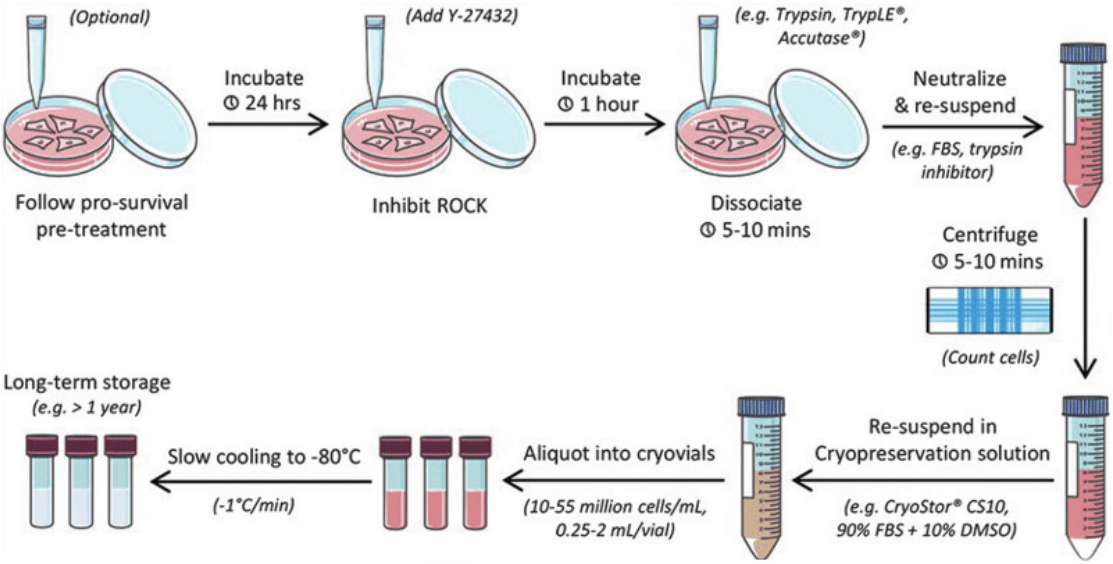


**Figure 2: Illustrate the General Procedure of the Cryopreservation Process** [14]**.**

There are many uses for deep hypothermia, a moderate type of cryopreservation used on human patients. Excessive hypothermia is often induced before difficult cardiovascular surgery. Blood flows through a cooling chamber after the patient is placed on complete cardiopulmonary bypass to use a heart-lung machine. Temperatures as low as 10-14 °C (50-57 °F) may be attained while the patient is being gently chilled. All brain activity is effectively stopped by this level of chilling, which also protects all the critical organs. After achieving this severe cooling, the heart-lung machine may be turned off, allowing the surgeon to do exceedingly difficult aortic and cardiac repairs while the patient is in circulatory arrest. No blood is flowing through the patient at this moment [15], [16]. The blood is gradually reheated using the same heat exchanger that was used to chill it. When the body gradually reaches normal body temperatures, regular brain and organ functions resume. However, compared to freezing or long-term cryopreservation, this acute hypothermia is considerably different. Cells can live for more than 10 years if they are properly frozen. Aorta tissue, heart valves, veins, or parathyroid glands are among the other tissues that can be successfully cryopreserved. Furthermore, freezing keeps early ova (eggs), sperm or human embryos, viable for a long time. These tissues could be frozen using tried-and-true methods and remained frozen for a long period at a temperature of 14 °C (6.8 °F) in the existence of cryoprotective chemicals.

## 2. LITERATURE REVIEW

Takao Niino et al. studied Utilizing cryopreservation to protect potato genetic resources. In contrast to sustaining through vegetative development in gene banks, practical ways created using in vitro tissue culture could be a quick and efficient conservation alternative for potato genetic resources due to their uniform character. For long-term preservation against plant germplasm loss during field collection, cryoprotected material is given. Genetic diversity in tissue culture cells in extended subcultures may be decreased using proper cryopreservation procedures that guarantee sufficient regrowth, opening the door to methodical and purposeful cryo-banking of plant genetic resources. The shown method of potato cryopreservation can significantly improve farm or in vitro conservation efforts, enabling the preservation of genotypes utilising different approaches, wild types, and even other species designated as priority collection [17]. Toshikazu Matsumoto studied cryopreserving genetic resources from

plants. Cryopreservation is a crucial in vitro preservation method for the long-term storage of PGR. The methods of vitrification or dehydration/encapsulation are often utilized in this process. High rates of regeneration after cryopreservation and easy handling even during surgery are advantages of using cryo-plate technology. Researching genetic stability in long-term tissue-cultured or cryopreserved plants is essential for the long-term conservation of plant germplasm. In this paper, current cryopreservation techniques are evaluated. When carried out under ideal conditions, the examinations to far have demonstrated little to no differences between cryopreserved or non-cryopreserved materials through morphological, chemical, but also genetic analysis [18].

B. Panis and M. Lambardi studied plant cryopreservation techniques that have advanced rapidly in recent years, allowing potentially long-term storage of the invaluable genetic resources of many agricultural and forest species. Research has progressed from the first slow-cooling method to simpler, more repeatable methods that enable complete vitrification of extracellular and intracellular fluids by immediate immersion in liquid nitrogen. The majority of techniques for the cryopreservation of different tissues and organs, including such cell suspensions, embryogenic callus, pollen, embryonic axes, meristematic tissue, or seeds, have been developed throughout time and are briefly summarised in this article. Also given are the most notable accomplishments in the cryopreservation of grassland, hardwood, and softwood species [19]. S. Tsai and C. Lin studied about use of cryopreservation for fisheries science. The paternal and maternal gametes may be stored and preserved, providing a dependable source of fish genetic information for research, aquaculture, and biodiversity preservation. More than 200 fish species have successfully had their sperm cryopreserved, and a large number of fish species are suitable for cryobanking. Fish embryo cryopreservation is not feasible, mostly due to the same restrictions that apply to fish oocytes, namely, high chilling sensitivity and poor membrane permeability. However, another choice for retaining both paternal and maternal DNA is the cryopreservation of separate embryonic cells. This essay begins with a summary of the situation of aquatic animals and then moves on to a description of sperm, embryos, oocytes, and embryonic cells, or blastomeres [20].

M. E. González-Benito et al. studied cryopreservation is used to protect the genetic material of vegetative propagated plants. For the long-term preservation of the biological resources of vegetative growing plants, cryopreservation is a practical and affordable technique. A number of methods have been developed to ensure high propagation recovery and reduce harm from aridity or frost. The plant material that is frequently utilized for the cryopreservation of plant leaves and roots is apis from in vitro-grown shoots. The verification of internal liquids or freeze-induced dehydration are the foundations of cryopreservation techniques [21].

## 3. DISCUSSION

Cryopreservation is the process of permanently preserving cells by putting an end to their metabolism at extremely low temperatures. All cells or tissues are under stress during the freeze-thaw process. As a result, efficient methods for avoiding cell damage and death were created. One typical cryopreservation method entails switching from a culture medium containing a cryopreservation chemical, such as dimethyl sulfoxide, to media used for cell maintenance (DMSO). A substance, like dimethyl sulfoxide (DMSO). Subsequently, cells are transferred to a dedicated cooling container and chilled at a rate of -1°C/min (for mammalian cells). Cells are moved to an ultralow temp. Storage at or below -135°C after cooling to -80°C. Liquid nitrogen,

either in liquid or vapor form, is the most typical ultralow temperature storage. Cells are kept frozen as working stock or original seed assets.

### *3.1. Cryopreservation's Application:*

The long-term storage method of cryopreservation is primarily used to preserve and sustain the viability of biological samples for an extended period. Numerous fields, including cryosurgery, food science, molecular biology, ecology, and plant physiology, including numerous medicinal applications, utilize this preservation technique extensively. Cryopreservation is also used for other purposes, which is shown in Figure 3:

#### *3.1.1. Embryo cryopreservation:*

Hormones are utilized in the treatment of infertility to promote the production of eggs. After that, the eggs are removed and fertilized in a lab. It is feasible to create more embryos and place them in the woman's uterus at the same time. Cryopreserved versions of these embryos can be used in the future. By doing this, the woman can receive another embryo transfer in the future without having to pay for another In vitro fertilizer (IVF) treatment.

#### *3.1.2. Cryopreservation of Oocytes:*

The eggs freeze quickly during the verification process, which leaves less time for ice crystal formation. Products with anti-freeze properties are employed in high concentrations along with novel cryoprotectants. The cryoprotectant, which acts as an anti-freeze, is first dissolved in low concentrations in the bath with the oocyte. Some sucrose is added to the egg to help remove some of the water. Eggs are rapidly transferred to liquid nitrogen after spending very little time in high-concentration anti-freeze cryoprotectants. When the woman's body receives the defrosted, implanted frozen egg.

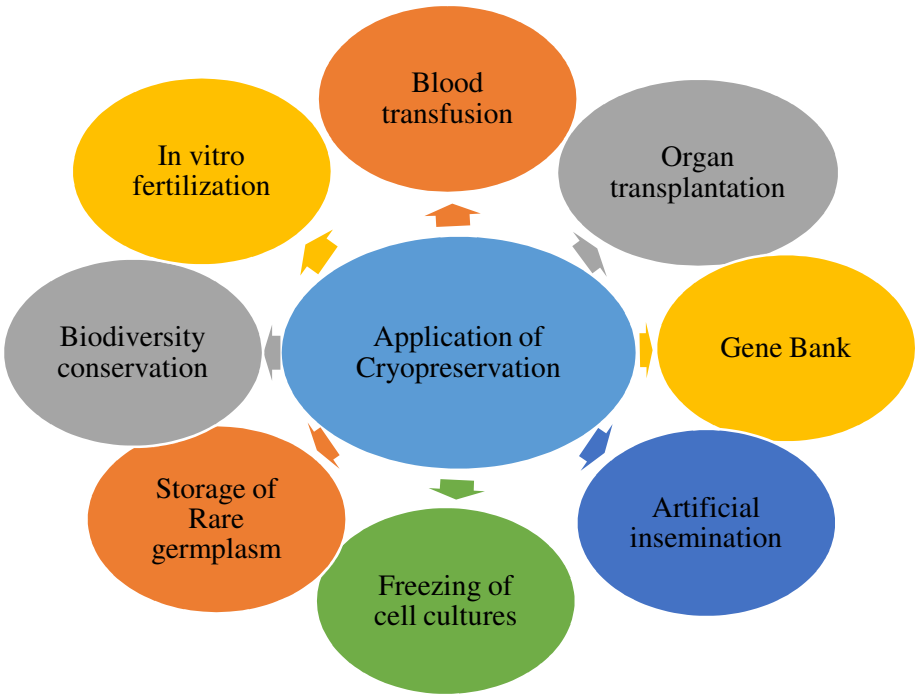


**Figure 3: Illustrate the Some Major Application of Cryopreservation.**

### *3.1.3. Sperm Cryopreservation:*

A solution is added to the semen sample to preserve it from freezing and thawing. After that, the sample is transferred to polypropylene vials and maintained in liquid nitrogen to freeze. The possibilities of conception in the future are secured by this process. Also possible is the deposit, freezing, and short-term storage of the sperm in cryobanks. Later, this sperm may be employed in certain infertility therapies.

## *3.2. Uses*

### *3.2.1. Therapeutics:*

After being used to treat infertility, cryopreservation gained favor in human medicine. Since then, a method of treating infertility called gamete cryopreservation has been created. The spermatozoa were the first successfully frozen reproductive cell and continue to be the easiest to freeze due to their tiny cytoplasm and therefore low water content. The sperm's nuclear content is also contained and safeguarded. These reasons have led to the widespread use of sperm cell cryopreservation in contemporary human medicine. Live newborns have been seen in recent years after assisted reproductive cycles utilizing frozen eggs or sperm. Human ovarian tissue and oocytes are also cryopreserved. Immune system memory for bone banking, aortic root allografts, lymphoid cells, or osteoblasts are still being researched. Cryopreservation of corneal, umbilical, but also hematopoietic cells is now routinely performed with sperm banking in human medicine. Bull semen has been cryopreserved for use in breeding endangered and uncommon species. With frozen-thawed bull sperm, more than 25 million bovine calves are artificially impregnated each year. Now, cryogenic banks can also store serum samples, Deoxyribose Nucleic Acid (DNA), cell lines, tissues, or cell lines.

### *3.2.2. In Biological Sciences:*

Cryopreservation is one of the best techniques for the long-term preservation of plant genetic resources. Cryopreservation of germplasm improves domestic cultivars' genetic make-up and environmental adaptability. While the practice of preserving plant germplasm at cryogenic temperatures is still relatively new, scientists have been working on ways to preserve plant cells and tissues for more than 40 years. Now, these methods can also help with plant genotypes. Recently, two new cryolite-based cryogenic techniques have been created. These technologies offer benefits including simple application and fantastic rates of regeneration following cryopreservation. Cryopreservation of embryos, gametes, or embryonic cells is essential to aquatic biotechnologies' ability to reproduce commercially important species, protect endangered species, or preserve genetic diversity. According to research, marine fish sperm can be preserved more successfully than freshwater fish, and their rates of fertilization are comparable to those of the human species.

## *3.3. Advantages:*

All removed and/or fertilized cells may be preserved for use in the future thanks to cryopreservation, which increases the effectiveness of assisted reproductive techniques. By storing embryos in between cycles, ovarian stimulation is not necessary every time, or implantation may be delayed without wasting recovered oocytes if the woman's ovaries are overstimulated. Cryopreservation allows couples who become pregnant during their first treatment cycle to donate their unused frozen embryos to research. Currently, just one or two

embryos are typically implanted, with any surplus being cryopreserved for use in upcoming treatment cycles. Cryopreservation allows people who are losing their fertility to save their reproductive cells if they are unable to conceive naturally in the future. Women who want to delay having children or who have a family history of early menopause may use it. An effective method for conserving the genetic material of threatened species is cryopreservation. The technology of cryopreservation has several advantages. Infertility treatments are among them.

i. Little labor and space are needed.
ii. Protection against genetic contamination.
iii. Preserves the genetic integrity of priceless stains.
iv. Preserves the genetic material of threatened species.
v. It is possible to keep biological samples for a longer period.
vi. Prevents microbiological contamination or illness from affecting the samples.
vii. Prevents genetic drift by freezing gametes, embryos, and other biological materials.

### *3.4. Major Issues with Tissue and Organ Cryopreservation:*

Tissue- and organ-based cryopreservation is far more complicated than is the case with individual cell cryopreservation. Firstly, there are numerous main issues with organ cryopreservation, including the intracellular ice formation (IIF)-induced cell cryoinjury or solution effects mentioned above.

Blood vessel damage/rupture leading to vascular injury Water from dehydrated cells enters blood arteries and forms ice or expands. A better comprehension or prediction of the underlying processes causing ice formation as well as cell dehydration in biological tissues/organs are required to lessen this cryo-destructive impact. Although these biophysical phenomena in single cells have been widely studied using cryomicroscopy methods, there is a serious paucity of experimental data for whole tissues. The heat tension that develops during the warming process might cause frozen tissue or organs to break. One sort of mechanical stress known as thermal stress is brought on by no uniform warmth in a solid or frozen substance. For instance, glass can break when a surface is suddenly heated or chilled. The necessity for consistent heating is necessary to decrease thermal stress.

## 4. CONCLUSION

Farm animals have been used for cryopreservation of oocytes, embryos, and semen with varying degrees of success; nevertheless, this method still has to be improved, and more study into the underlying principles is necessary to achieve greater performance and higher efficiency. Since cellular characteristics fluctuate across and within species, as well as at different stages of development within a species, different cryopreservation procedures are designed with distinct goals in mind. Oocyte or embryo cryopreservation is a widespread process in the animal production sector. For example, additional research using higher hydrostatic pressure with more validation solutions and perhaps cytoplasm delipidation for cryopreservation of pig oocytes or embryos has the potential to yield more accurate and reliable findings. To find out if the incidence of cryodamage in this species is a possible obstacle to efficient verification, more investigation should be conducted. It may be possible to remove the developmental restrictions that exist in this species by conducting more studies into how verification impacts transcription factors in ovine oocytes. In this paper, the author discusses cryopreservation, the process of doing it, how it is used to store living cells, and its applications. The cryopreservation approach

is the primary goal of this paper. Through this paper, readers will learn about cryopreservation and its potential applications in the future.

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# CHAPTER 11

# A STUDY ON THE UTILIZATION OF GENE THERAPY TO TREAT CANCER

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**ABSTRACT**:

Gene therapy studies have historically centered on the potential for treating cancer. Recent advances in identifyingtargeting potentials, and progress in non-viral and viral gene delivery methods have been encouraging, but no commercially accessible cancer gene therapy medicines are yet available. Potential targets fornumerous genes have been investigated so far in cancer gene therapy. This study aims to summarize cancer gene therapy and also highlighting some of the most important outcomes from clinical trials and describing the most widely utilized non-viral and viral vectors and procedures.When new genes areinjected into a cancer cell or the tissue around it, it may either cause the cell to die or slow its development, making gene therapy a revolutionary treatment method. Multiple genes andclinical studies with vectors on humans have proven effective and demonstrated the adaptability of this therapeutic approach. These drugs have the potential to be used either alone or in combination with current therapies to make cancer therapy more tolerable in the future.

**KEYWORDS:**

Cancer, DNA, Gene therapy,Genome editing, Non-viral Vectors, Plasmid DNA, Viral Vectors.

## 1. INTRODUCTION

The purpose of gene therapy is to alter the use of human cell expression of a gene or even other biological features for therapeutic effects. Gene therapy is a procedure or cure in which a person's genes are modified [1].Gene therapies may function in several ways, including:

i. Correction of genetic illness by inserting a normal copy of the mutant gene.

ii. An improperly functioning gene that causes the illness may be turned off.

iii. Diseases may be treated by inserting new or altered genes into the body.

The hereditary unit, or gene, is a string of bases that contains the blueprint for a protein. Proteins may not receive the same amount of credit as genes, yet they are responsible for almost every cellular process. Genetic disorders arise when genes are changed in ways that render the encoded proteins dysfunctional. Therefore, gene therapy aims (the therapeutic use of genes) to repair the faulty genes that cause hereditary diseases.Several hematologic illnesses, both congenital and acquired, show great promise for treatment using gene therapy.In gene therapy, a therapeutic gene is introduced into an organism tonormalize protein function, or a gene sequence is given to replace a mutant gene. Blood cells are sometimes harvested from a patient so that certain cells,

like hematopoietic stem cells (HSCs), may be engineered. Gene therapy involves inserting the genetic materials into a vector and then delivering the vector to the cells in need of treatment. When these specific, genetically edited cells are ready, they are reintroduced into the patient. This technique is known as ex vivo gene therapeutic intervention because it modifies cells in a laboratory rather than in a living patient [2].

A broad variety of laboratory development has been undertaken to evaluate the efficacy of gene transfer in achieving substantial benefit in experimental animals with varying degrees of pain severity. These studies serve to assess the relative advantages of viral vector-based techniques for pain reduction by simulating the nociceptive mechanism that underpins pain genesis and transmission. Although some of the animal pain paradigms were not created to examine cancer-related nociception or to give a thorough recapitulation of human settings, they are useful for developing possible cancer pain treatments. As previously said, cancer patients might suffer a wide range of discomfort. Understanding these findings, on the other hand, aids in establishing scientific justification for using these techniques in cancer pain treatment.

Cancer, hereditary illnesses, and viral diseases are all being examined as potential targets foritems derived from gene therapy, or their use. Product categories that fall under the umbrella of gene therapy include:

i. *Plasmid DNA*:

DNA from a plasmid is a circular, double-stranded form found in bacterial cytoplasm that replicates separately from the bacterial chromosome.Modified circular DNA molecules might be used to improve the therapeutic genes in human cells.The DNA contained in plasmids is essential to the organism's continued existence. It defends itself by creating a tolerance to the invading organism or by directly destroying it, and it uses harmful proteins to kill other host cells.Plasmid DNA plays a crucial role in maintaining the organism. It employs damaging proteins to kill other host cells and may develop a resistance to the invading organism or eliminate it outright.Plasmids have several purposes. For instance, genes encoding proteins involved in cell death or host defense systems like toxin synthesis might improve an organism's chances of survival. It's also possible that certain plasmids facilitate the multiplication of bacteria. Small in size, the genes located on plasmids often perform a specific task (in contrast to an abundant amount of noncoding DNA). Multiple plasmids, each with its specialty, may co-exist in a single cell [3].

*ii. Viral Vectors:*

Some gene therapy products are generated from viruses because of their inherent capacity to transport genetic material into cells. By altering viruses such that they can no longer spread illness, these modified viruses may be employed as vectors (vehicles) to transport genetic materials into human cells.There is a wide variety of viral vectors, with some designed for temporary short-term expression and others for stable long-term expression. Also, there is a wide variety of vectors, including those that carry RNA and those that carry DNA, with either a single- or double-stranded genome.Tumor antigens (proteins expressed by tumor cells) might be manufactured via viral vectors to elicit an anticancer immune response. Likewise, genes that may convert cancerous cells back to healthy ones might be delivered by viral vectors [4].

iii. *Bacterial Vectors:*

To prevent them from spreading illness, bacteria may be engineered to carry genetic materials instead of pathogens. Bactofection, in which bacteria are employed to transplant eukaryotic host cells, is one method of employing bacteria in gene therapy. Another method, known as non-host-genome altering gene therapy, employs the prokaryotic expression vector and may be regulated or terminated exogenously.Using bacteria to transport treatments has been around for a while, and there are several benefits to doing so compared to using alternative gene delivery methods. Even though bacteria are studied as part of the safer 'non-viral' category of delivery technologies, many of the inherent benefits of viral vectors are still present because of the biological nature of bacterial vectors [5].

*iv. Human Gene Editing Technology:*

The two primary aims of gene editing are the removal of defective genes and the correction of dangerous mutations. Genome editing, also known as gene"editing" is shorthand for the collection of techniques used by scientists to make changes to the DNA of living creatures. These methods make it possible to insert, delete, or modify DNA in specific places. Numerous methods of genome editing have been established.

*v. "Patient-derived cellular gene therapy products":*

Surgery involves removing tumor cells, altering their DNA (usually using a viral vector), and then re-injecting them into the patient. A brief overview of hematopoietic, adult, and embryonic stem cells (ESCs) are all examples of cellular therapy products, or other autologous or allogeneic cellular components for particular therapeutic signs.

*1.1.Advantages of Gene Therapy:*

vi. Hereditary diseases include alpha-1 antitrypsin deficiency, cystic fibrosis, sickle cell condition, hemophilia, and beta-thalassemia. Genetic treatment may one future be used to prevent, treat, or cure diseases. They have the potential to combat diseases like cancer and infections like HIV. When a gene is put to "silence." If someone had HIV but it hadn't progressed into AIDS yet, doctors might use gene therapy to' silence' the virus and save them from the agony of the illness.

vii. Cystic fibrosis, cardiovascular disease, HIV/AIDS, and cancer are just a few of the disorders that might one day be cured through gene therapy.

*1.2.Disadvantages of Gene therapy:*

i. While genetic treatments show promise in alleviating symptoms of a wide variety of disorders, they are still novel forms of therapy that carry some degree of risk. Some forms of cancer, allergic reactions, and organ or tissue damage are possible side effects of injections.

ii. The safety of genetic therapy has improved greatly thanks to recent developments. The Food and Drug Administration has given its OK to the clinical use of several gene transfer medicines because of their improved safety. Genome editing is a novel technique that has just recently been tested in humans. Scientists have yet to fully investigate the potential consequences.

iii. Toxicity, immunological, and inflammatory reactions may all be introduced through viral vectors.

iv. The potential for iatrogenic (medically caused) tumor development in humans and the transient nature of gene therapy are also drawbacks [6].

## 2. LITERATURE REVIEW

Samantha L. Ginn et al. stated in their study analyses that clinical studies have been or are being conducted internationally. The November 2017 update includes 2597 tests in 38 countries. The authors studied the geographic range of trials, illness indications (or other causes), vector types employed, and transmitted genes.The author also discusses major changes since the last assessment, which include the advances in genome editing technology and also the potential game-changing utilization of antigen receptor T cells in cancer therapy [7].

V. Scaiewicz et al. discussed in their study thatthe death rate from pancreatic cancer ranks sixth among all cancers worldwide, as reported by the "American Cancer Society" and therapeutic therapies have significant side effects.The author discovered that a 65percent of pancreatic tumors displayed moderate to high H19 gene expression. In vivo pancreatic cancer models showed tumor growth stops. In the heterotopic model (P=.035), tumor size differences between the untreated and treated groups were 75percentage points and 50 percent, respectively. The orthotropic model treatment group had no apparent metastases. These data suggest the potential of DTA-H19 as a breakthrough treatment for pancreatic cancer [8].

Bohan Fan et al. evaluated in their study that since prostate cancer (PCa) is so common in males, the author is seeking to create a gene profile linked to angiogenesis to predictbiochemical relapse (BCR) in individuals with PCa who have had radical treatment. "The Cancer Genome Atlas (TCGA)" and Gene Expression Omnibus were mined for gene expression patterns and clinical and pathological information (GEO). An angiogenesis-related gene profile was analyzed using machine learning and Cox modeling to determine prognostic genes.Subjects diagnosed with squamous cell carcinomaof the prostate (PCa) were found to have an increased risk of biochemical recurrence (BCR) if they had angiogenesis A unique predictive fingerprint based on 3 genes (NRP1, JAG2, and VCAN) was created during the training phase (HR = 1.58, 95% CI: 1.38-1.81) and confirmed in three independent cohort studies. To better evaluate risk and provide customized care for patients with PCa after radical therapy, the three-gene profile linked with angiogenesis may serve as a predictive factor for BCR.

## 3. DISCUSSION

Several prerequisites need to be completed before a gene therapy program may be launched to treat cancer. Among them includes having several genes expressed enough in the cells to be addressed, havingan ideal gene to delete or alter, as well as a vehicle to transport the target gene to the cell, and having precision targeting of the vector. The treatment's effectiveness depends not only on its therapeutic efficacy but also on its safety.Among the pioneers in this field was the research group led by Rogers et al., who presented the first convincing evidence for the viability of virus-mediated gene transfer. They also demonstrated that viruses may be used to transmit foreign genetic material to target cells. Authors were encouraged by the findings and decided to do human trials [9].

### *3.1.A Review of Gene Transfer Techniques and Vectors for Therapeutic Applications in Humans:*

Cancer's origins have long been speculated to be in a single cell's transformation under the impact of environmental stimuli such as physical stresses, chemical exposures, and viral

infection. Mutations in various genes are what turn a healthy cell malignant. Turning on oncogenes or turning off tumor suppressor genes are the two most common ways in which cells undergo functional alterations that lead to transformation.Malignant transformation is often triggered bycancer development caused by unchecked gene expression and defective tumor suppressors. These alterations are essential for tumor cell growth to continue.It is common for a changed cell to acquire critical biological features necessary for the development of a malignant illness. In a recent study, Hanahan and Weinberg describe in depth the features of cancer, which include unregulated growth, avoidance of death, immortality by replication, angiogenesis, proliferative signaling, invasion, and metastasis[10].

The two biggest obstacles in gene therapy are getting enough DNA into the right cells and keeping it there for long enough. There are a variety of ways that genetic material may be delivered to cells or tissues. It may, in theory, categorize them as either a bacterial or yeast infection, a fungal infection, a physical injury, or a virus infection. Physical examples of methods include electroporation, ultrasonography, and genetic gun delivery. The term "viral vector" refers to the use of a biological (i.e. viral)vector for the transfer of genetic material to cells, whereas the term "non-viral gene transfer" refers to the use of synthetic carriers (liposomes or nanoparticles). Transduction efficiency and the ability to effectively express inserted genes vary across vectors. They also vary in terms of the length of time a transgene is expressed and the degree of risk involved. Various vectors may be utilized for various therapeutic goals, based on the specifics of each instance.

### *3.1.1. Viral Vectors:*

The nucleic acids included inside a virus's genome may be sent to certain cell types, especially cancer cells, as part of the virus's innate biology. These qualities make such gene-delivery vehicles appealing and widely used. Cancer gene therapy vectors often include modified forms ofviruses including “retroviruses”, “adenoviruses”, “adeno-associated viruses (AAV)”, “herpes simplex viruses (HSVs)”, “poxviruses”, and baculoviruses. Therefore, chimeric viral-vector systems that combine two or more virus types' best features are created.

Viral vectors may also be classified as either integrating or non-integrating, depending on their mode of transmission. There are other non-integrating vectors, such as adeno- and baculoviruses. They are incapable of incorporating their genome (and the transgenic it contains) into the host genome. However, some vectors do incorporate into the host genome, such as lentils- and retroviruses, and AAVs.Adenoviruses are the most often used viral vectors.To activate the target gene's short-term episomal transcription in plenty of host cells, naked adenoviruses may be utilized due to their capacity to transport a maximum of 7.500 kb of alien (foreign) DNA. When it comes to immunological responses, first-generation adenovirus vectors are unmatched, and subsequent-generation vectors with mutations (so-called "gutted" vectors) have been demonstrated to elicit less immune responses [11].

The long-term transgenic expression provided by chromosomal integration is what gives AAV its positive reputation for minimal virulence and toxicity. The recurrent delivery of AAV might cause an immunological response, which is a drawback of the technology. To solve this issue, researchers have begun to use a new AAV serotype each time the virus is reintroduced. The difficulty in enclosing foreign DNA in recombinant AAV particles is another problem. The development of two AAV vectors has allowed this limitation to be corrected [12].Engineering vector constructs where the damaging viral genomes have been substituted with nucleic acid

sequences encoding promoters to drive gene expression and an analgesic transgene is required for the use of viral vectors in chronic pain treatment. This strategy takes use of the virus's innate capabilities, which enable it to enter cells and undergo transduction.

### *3.1.2. Non-Viral Vectors:*

Large-scale production and minimal host immunogenicity are two areas where non-viral technologies excel over viral ones. The early therapeutic efficacy of non-viral techniques was lower because they resulted in lower transfected and levels of gene expression. With the development of more precise methods of cell-specific targeting and subcellular transport management, modern technologies have shown potential in addressing these issues.It is now well-established that viruses may be used as effective vectors for the transmission of genetic material. However, limitations such as the speed with which viral vectors are cleared from the circulation after systemic injection, and novel synthetic gene delivery vectors have now been developed despite their immunogenic and inflammatory properties.This fact drives the widespread investigation of non-viral gene delivery technologies as potential substitutes for viruses. Naked plasmid DNA is the simplest kind of non-viral system. Naked plasmid seems to have the advantage of being the safest and generating the fewest adverse effects. It's also cheap to make and simple to formulate. Therefore, in comparison to viral-mediated gene transfer, its poor transfection efficiency is a major drawback [13].

### *3.2.Cancer gene therapy utilizing gene targeting:*

Changes to the regular cycle of cell division and death (apoptosis) are at the root of cancer. The development of more effective cancer treatments requires the discovery of a new therapeutic drug with an unexplored method of action, multiple cell death mechanisms destruction, and interaction with standard care. All of these characteristics can be seen in gene treatments.There are many different types of gene therapy for treating cancer that has been developed. Gene therapies include anti-angiogenic, suicide, immunotherapeutic, pro-apoptotic, oncolytic viro-therapeutic, and gene-directed enzyme prodrug medicinal.

### *3.2.1. Physical Targeting:*

The first is the use of purely physical techniques, like localized injection, catheter, gene guns, and electrodeposition, to address a specific area. Most cancer victims, who may have cancer that has spread throughout their bodies, are not good candidates for this technique since it is often employed for the local distribution of regenerative medicine vectors. After intradermal injection, supercoiled DNA molecules and oligonucleotides reach skin cells and are taken up by the immune system to attack the tumor deposits that localized injections may reach. Physically treating the tumor accumulation in the peritoneum, pleura, meninges, and subcutaneous tissues in the clinical setting has great potential for the utilization of gene therapy carriers [14].

### *3.2.2. Biological Targeting:*

Another method involves tailoring the viral or non-viral vectors carrying the genes so that they connect specifically to tumor cells and not healthy ones. However, the poor transduction effectiveness of existing vectors for gene therapy in remote locations when used systemically means that the chance to achieve adequate anticancer activity may lie in the particular transgenic activation or viral multiplication in target tissues. This objective has been met via the creation of vectors that are specific for transcription and transduction.

Replication-deficient vector systems are often ineffective for treatinglarge, solid tumors because of poor transport and gene transfer capacity. Because of this, replicating vectors may not only transmit genes effectively but also boost the efficacy of therapies to their oncolytic impact. These vectors may be designed to specifically target tumor cells, where they would proliferate without harming any healthy tissue.Vector delivery limitations and limited treatment of big solid tumors using replication-deficient vectors are not advised due to their limited gene transfer capability. Furthermore, replicating vectors may transfer genes effectively and boost treatment efficacy through an oncolytic impact. These vectors might be designed to multiply just in tumor cells, sparing healthy tissue and organs from any potential harm.

*3.2.3. Transcriptional Targeting:*

The therapeutic index would determine the malignancy gene therapy program's potential for actual clinical use. The therapeutic index might be increased by limiting the transcription of therapeutic genes to the intended organs or tissues..Gene therapy vectors may be able to transfer genomic information to the intended cancer cells while preserving normal organs due to their high specificity. Possibilities for lower toxicity and lower dosages delivered by vectors rise. Therapeutic toxicity may be reduced and specificity improved by the use of transcriptional targeting, which involves the manipulation of transgene expression through the manipulation of DNA regulatory (promoter/enhancer) regions. These transgenes might be driven in viral or non-viral vectors by tumor-selective, inducible, or cell cycle-regulated controllers in cancer treatment. Cancers tend to have high levels of expression for some genes, including “L-plastin”, “surviving”, “telomerase”, and “midkine” [15].

*3.2.4. “Transductional Targeting”:*

Altering viral or nonviral vectors is another biological targeting strategy to ensure that they are exclusively acquired by tumor cells and expressed there. The vectors have been the subject of various efforts to increase specificity for tumor cells and lowering toxicity by being modified with tumor cell-specific receptors. Thus, it is appealing to direct DNA complexes toward the receptors expressed only on tumor cells.Coating the compounds with transferrin, a plasma protein that binds iron, is common practice.In constantly dividing cells, like cancer cells, their production is typically boosted. Systemic viral vector delivery and cell-specific translation of transgenes both need precise cell targeting. If there is no use for those vectors to address the natural receptors on inflammatory and immune cell surface membrane, immunity and inflammation as a result. Replication-capable retroviral vectors generated from murine leukemia virus (MLV) are appealing as a gene delivery strategy because of their capacity to reproduce and to offer long-term gene transcription in rapidly proliferating cells [16].

*3.3.Gene Therapy Is Safe:*

The safety results gathered from many human gene therapy experiments with adenoviral vectors have been universally encouraging.The viral vectors used in gene therapy, nevertheless, have several serious drawbacks primarily human infections, and this means there may be antibodies that were already present against the viral vector that might cause a harmful immune response. In general, there is a lack of long-term safety evidence for the use of viral vectors in people. However, multiple meta-analyses show that adenoviruses are safe for human usage. Mild to moderate side effects have been reported from gene therapy using adenoviral vectors, however, no important negative events have been reported [17].A science devoted to improving the creation of gene transfer vectors may lead to a higher degree of safety for these tools (i.e., the

establishment of production cell lines, production procedures, and purifying stages). For instance, gutless adenoviral vectors are vectors in which the desired gene is controlled by an appropriate promoter while all other genes save those required for virus generation have been deleted.

The transport of vector gene mutations or their metabolites to the targeted malignant cells and their vasculature is the biggest challenge facing clinical gene therapy research in humans. The proliferation of poisons is a further concern. Increases in the efficiency and precision of gene therapy vectors over the last several years have raised hopes that these studies could provide positive results soon. Efforts to employ vectors to stimulate the immune system to attack tumor tissue fall under this category. It is possible that further clinical trial testing of these tactics may open up new doors for people fighting cancer on a personal level.Furthermore, the character of the disease's remote spread is a primary reason why traditional treatment techniques fail, and it is also one of the key limitations of cancer gene therapy.

## 4. CONCLUSION

As a unique approach, gene therapy offers hope for the treatment of incurable illnesses. There has been a significant advancement inthroughout the past 30 years, cancer has been treated by gene therapy, with a small number of licensed medications and many more in the testing phase. Compared to chemotherapy, the side effects of gene therapy for cancer treatment are more manageable and less severe. It will be easier in the future to choose the right patient for gene therapy because of advances inevaluating host humoral and cell-mediated immunity based on tumor genomics. Future genome editing as a novel therapy technique for incurable illnesses like cancer is made possible bymodern advancements in nuclease activity research and the development of safe vectors for gene transfer.Improvements in the delivery and selectivity of gene therapy vectors over the last several years have raised hopes that these studies could provide positive results shortly. Efforts to employ vectors to stimulate the immune system to attack tumor tissue fall under this category. It is possible that further clinical trial testing of these tactics may open up new doors for people fighting cancer on a personal level.

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# CHAPTER 12

# AN EVALUATION STUDY ON BENEFITS OF GENETICALLY MODIFIED CROPS AND THEIR ASSOCIATED CONCERNS

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**ABSTRACT:**

As conventional crops are not able to fulfill the need of the growing population and high demand which makes a significant portion of undernourished individuals, genetically modified crops are there to address these issues by increasing nutritional value, and imparting resistance to herbicides, insects, and diseases. Genetically modified (GM) crops are plants whose DNA has been transformed using genetic engineering procedures to develop desired traits. There are several discussions concerning the utility, effectiveness, benefits, and downsides of GMcrops. Each side is presenting its arguments in a deterministic manner. Therefore, this review study aims to provide highlight the need for GM crops in the present world with special emphasis on reviewing studies on the benefits of GM crops. In addition to that, a critical discussion on the downsides of GM crops is also provided which provides future recommendations for stakeholders involved in crop improvement. However, the present need is also there to change consumer attitudes which can be done by educating them.

**KEYWORDS:**

Genetically Modified Foods, Genetic Engineering, Genetically Modified Crops, Insect resistance, Pesticides.

## 1. INTRODUCTION

The use of genetic engineering in agriculture, foods and feed dependent on them, has been hailed as a biological breakthrough since the early 1980s. Numerous technological challenges related to the genetic manipulation of economically significant species of plants have been addressed after twenty years of expensive development and research in the private and public sectors. Genetically modified food and agricultural products eventually made it to the market in the middle of the 1990s [1].

Genetically modified (GM) foods have become a part of life in the United States. GM crops account for more than half of all crops farmed in the U. S., notably 70% of corn[2]. Whereas the European Union has mostly opposed GM crops, biotechnology companies like Monsanto are expanding in regions such as India and Africa. GM crops provide a lot of advantages for farmers and consumers both. GM crops have made it possible for farmers for using fewer pesticides on their crops since they can produce their inherent toxins to combat pests. According to one research, the usage of 965 million pounds of pesticide has been saved because of GM crops. GM crops have also been predicted to save on fuel since farmers require fuel to run equipment for applying pesticides [3]. According to one estimation, GM crops cut emissions of carbon dioxide

by the same amount as 8.6 million cars. Since they have been altered to target specific particular pests, like rootworms, GM crops are also advantageous. In the United States, only a small number of different types of GMO crops are planted, yet certain of them account for a sizable portion of the total agricultural production (e.g., corn, canola, sugar beets, soybeans, and cotton) [4].A total of 94% of the soybeans, 96% of the cotton, and 92% of the maize grown in 2020 were genetically modified organisms (GMOs). In 2013, there was a 95% increase in the amount of GMO canola planted and a 99.9% increase in the amount of GMO sugar beets harvested.

However, Growing research into genetically modified foods has uncovered two harsh realities in recent years: genetically modified foods are more common than we believed, and they are more hazardous than we anticipated. Furthermore, the great majority of Americans have already been consuming genetically modified foods even without realizing it for decades. Genetically modified foods, popularly known as GM foods or bioengineered foods, are food products derived from organisms whose genomic material has undergone genetic modifications and alterations to generate a unique characteristic to increase product quantity or quality. While GM foods can refer to products derived from organisms as well as genetic engineering, genetically modified organisms (GMOs) particularly relate to animals genetically engineered to make consumable products with unique or enhanced features. The development of genetically modified foods commenced in 1994 with the introduction of the Flavr Savr tomato, which received FDA clearance in 1992. However, the exact and real-time origins of GM food production could well be traced back to 10,500 to 10,100 BC, when producers forced selective breeding by crossing across between crops having genes that carry desirable characteristics and features and by artificial selection [5]. Later discoveries of DNA molecules and genetic material enabled the direct engineering of diverse varieties of plants to achieve the desired trait. The process of genetic engineering in crops is illustrated in Figure 1 below [6].

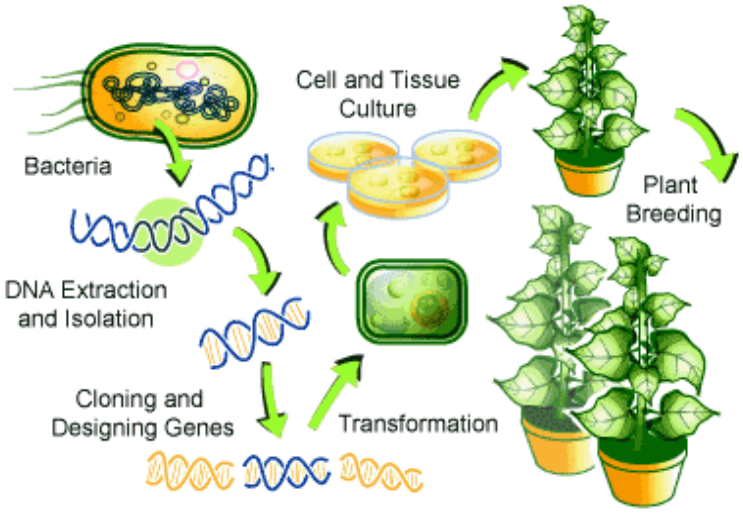


Figure 1: Genetic Engineering Process of Crops for Imparting Desired Trait.

Conversely, pesticides frequently kill a wide variety of insects without determining which are damaging to the crop. Finally, increased agricultural yields are frequently a byproduct of GM crops. Corn crop yields are reportedly Thirty one million tonnes more abundant than they would be without the use of GM crops, while soybean crop yields are fourteen million tonnes more abundant. The estimated $14 billion increase in farmer revenue resulted from this. With the

world's population expanding, this improvement in food yields is extremely crucial. Scientists predict that more food will need to be produced globally than at any other time in history.

## 2. LITERATURE REVIEW

### *2.1.1. Lack of Arable Land for Agriculture*

The problems we encounter are exacerbated by several complicating variables, the most significant of which is the limited amount of agricultural farmland accessible for farming. According to the FAO baseline scenario, by 2050, the world will have around 0.18 hectares of agricultural land accessible for agricultural production for each person on the earth, up from the present 0.242-hectare value [7]. According to the FAO research, the worldwide yield increases necessary to fulfill future needs must be obtained using the same land area which is presently under cultivation [8]. Without such ability to farm more area, output gains must originate from genetic transformation or increased agricultural inputs (water, fertilizer, and pest/weed control) [9], [10].

### *2.1.2. Rapidly growing Population*

According to a United Nations report released in June 2019, there will be 9.7 billion people on earth in 2050, an increase of 2 billion above the current 7.7 billion. Furthermore, according to a recent World Resources Institute (WRI) study, global food production techniques would have to evolve to feed a planet with around 10 billion people in 2050. This will need increasing public investment in innovations like genetic engineering. Tim Searchinger, the principal author, stated: "We must boost yields considerably, at an even faster pace than we have done previously. It must be accomplished by becoming smarter" [11].

Global hunger continues to be a major issue even without taking into consideration the significant population rise during the following 30 years. The number of individuals who experience hunger worldwide has marginally grown over the previous five years, according to a 2019 UN report. And over 2 billion individuals do not presently possess access to safe, adequate, and nutritional food, according to the research, which estimated that more than 800 million people are suffering from starvation.

GM food use is not without its challenges and debates, but these issues pale in comparison to the root of the problem. All of the food needed to feed the world's population is already present. Thus, hunger is caused by inequity rather than a shortage of food. Today's world hunger is mostly caused by the uneven distribution of nutritious food among impoverished groups, not by wealth or the size of food stocks. Access to healthy food for malnourished people is impacted by a variety of political, environmental, and social factors, most significantly armed conflict and natural calamities. While seen in this context, GM crops may contribute a role in decreasing world poverty; nevertheless, just boosting agricultural production or nutrient benefits (by any technology) would not solve the bigger issue of food disparity.

## *3. Benefits of GM Crops*

Below are some of the characteristics as illustrated in Figure 2, which favor the use of genetically modified crops which primarily include imparting, editing, or inserting a resistance gene in the genome of crops from making resistance to several stressors which can be both biotic and abiotic stressors. The figure below illustrates some of the major benefits of GM crops.

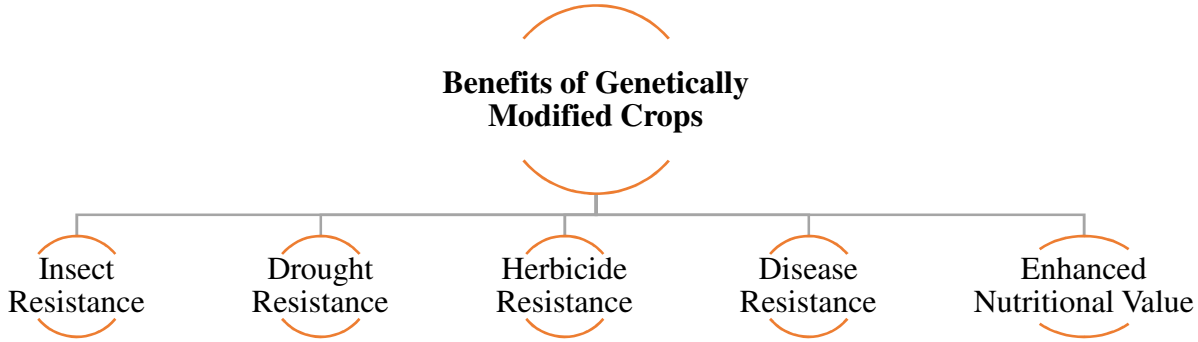


**Figure 2: Multiple Benefits of Genetically Modified Crops including Crop resistance and Improved Nutritional Profile.**

*3.1. Insect Resistance*

Insect-resistant transgenic crops were initially marketed in the mid-1990s with the advent of GM cotton, potato, and corn (maize) plants encoding genes for *Bacillus thuringiensis* entomocidal -endotoxin (Bt; also referred to as Cry proteins). The adoption of insect-resistant varieties minimizes the need for insecticides. Because harmful chemicals found in pesticides will not be introduced to the soil, soil fertility will be maintained for a longer length of time. Since mid-1990, a lot of studies are getting published on the development of transgenic insect-resistant crops or plant varieties [12], [13].

Singh *et al.* reported Cry2Aa expression in transgenic pigeon peas as well as its efficiency against *H. armigera* using an Agrobacterium-mediated planta transformation method. In their study, they identified 0.8% of T1 lines as putative transformants. Cutting-edge generations based on the bioefficacy of transgenes and their integration and expression were used to analyze further promising events. The results of their study revealed that the T3 line demonstrated 80-100% of the larval mortality and further prevent damage that was caused by larvae, therefore, demonstrating the potential of using the study for the improvement of pigeon peas [14].

Karthik *et al.* used two BtICPs, cry1AcF and cry2Aa in transgenic cotton cv. Pusa 8-6 against *H. armigera*. H. armigera-resistant individuals were identified by employing a stringent trait efficacy-based selective screening of T2 and T1 generational transgenic plants following purposeful exposure. Nine excellent transgene events with both genes were discovered after the evaluation of nominated occurrences in the T3 generation (three with cry2Aa and six with cry1AcF). The "*H. armigera"* larval mortality was 80–100% and the plants had 10–30% leaf damage [15].

*3.2.Drought Resistance*

Drought is the leading cause of agricultural loss worldwide, and it poses a significant danger to food security. Plant biotechnology is now one of the most potential disciplines for generating crops capable of producing large yields in water-stressed circumstances. The key response pathways to drought stress have been revealed via research on Arabidopsis thaliana in entire plants, and numerous drought-resistance genes have been put into crops.

Li *et al.* investigated the negative parts played by "Strigolactone-related SMXL6, 7, and 8" in drought tolerance. Physiological studies revealed that the mutant plants had lower cuticle permeability, greater leaf surface temperature, and lower drought-induced water loss & cytoplasmic membrane disruption as compared to wild-type plants. Furthermore, cotyledon opening and growth inhibition experiments showed an increase in anthocyanin production under drought, improved detoxifying ability, and increased susceptibility to abscisic acid in mutant plants demonstrating the negative regulatory activity of the SMXL6, 7, and 8. Therefore disruption of these genes can provide novel ways for improving drought tolerance in plants [16].

### *3.3.Herbicide Resistance*

Since agricultural plants were domesticated, weeds have continuously interfered with them, causing a greater yield loss than pests and diseases, which has made the use of weed management methods essential. To ensure that there is enough food for a population that is expanding quickly, weed management is essential. The most reliable and efficient way to implement weed management programs may combine herbicide with integrated weed management (IWM) approaches. The need for developing herbicide-resistant (HR) crops is urgent given the widespread use of herbicides for weed management. Recent advancements in genome editing technology, especially with "CRISPR-Cas9", have opened up new opportunities for sustainable agriculture in the modern agriculture sector. However, other publications are making use of other genetic engineering techniques for making crops herbicide-resistant.

In a study by Liu *et al.* a rolled and spotted leaf (sprl1) mutant in *rice.* In their study, they found that that rolled leaf phenotype was ins4nsitive and the "spotted leaf" phenotype was sensitive to that low temperature and high light intensity, and the phenotypes were confirmed that they were caused by a substitution of single nucleotide in gene *"OsPPO1"*. The results of their study revealed that transgenic plants with OsPPO1-overexpression were resistant to the herbicides acifluorfen and oxyfluorfen, but had no impact on plant development or yield components. The findings of their research suggested that the gene could be used to develop herbicide resistance in rice.

### *3.4.Disease Resistance*

Despite the best attempts to tackle them, plant diseases continue to pose a serious issue in agriculture. Using genetic modification (GM) and genetic manipulation to control plant diseases is one of the most effective and sustainable means of increasing the breeder's toolset. These solutions must be effective in the field, have no detrimental impact on plant agronomy, and be applied with caution.

Zhou *et al.* generated a null mutation in "OsSWEET13" to further study "PthXo2-dependent disease" susceptibility, and the result mutants were immune to "bacterial blight". The next stage in achieving bacterial blight resistance will involve other genome editing techniques for "multiplex recessive resistance" using a combination of other R genes and important effectors [17].

In another study carried out by Zheng et al., a snapshot of the central role of Phytomelatonin in plant disease resistance was provided. They outlined the established mechanisms through which melatonin mediates pathogenicity by inhibiting the gene expression involved in cell survival and virulence. The many processes that underlie melatonin's effects on both crop immunology and

pathogenesis support the hypothesis that the hormone is vital in relationships between plants and pathogens, emphasizing phytomelatonin as a key player in plant immune responses [18].

### *3.5. Nutritional Profile*

The number of “minerals”, “vitamins”, or “fatty acids” contained in the modified crop can be altered by the gene that was chosen for modification. A category of wheat that is without gluten, a nutrient that induces many food allergies, fruits and vegetables with elevated amounts of vitamin E composition to protect the heart, and "golden rice" that has been a genetic alteration to contain “vitamin A” and “iron” to prevent popular nutritional deficits in underdeveloped nations are just a few of the "nutritionally enhanced" GM crops which are currently under development. Products developed in the US from GM corn include high-fructose corn syrup, which is used as a sweetener in soda and bakery items, tortillas, snacks, and cornmeal.

## 3. METHODOLOGY

The information of this review study is obtained from an electronic database search strategy using a variety of narrow keywords. Electronic databases, like “PubMed”, “Scopus”, “Google Scholar”, and “Science Direct” were used to search out and sort out relevant records. The keywords “Insect resistance”, Drought Resistance”, Genetic Engineering”, Genetically Modified Crops”, “Disease Resistance”, “Herbicide Resistance”, “and Genome Editing” were used. The methodology of the present review study is provided in Figure 3 below.

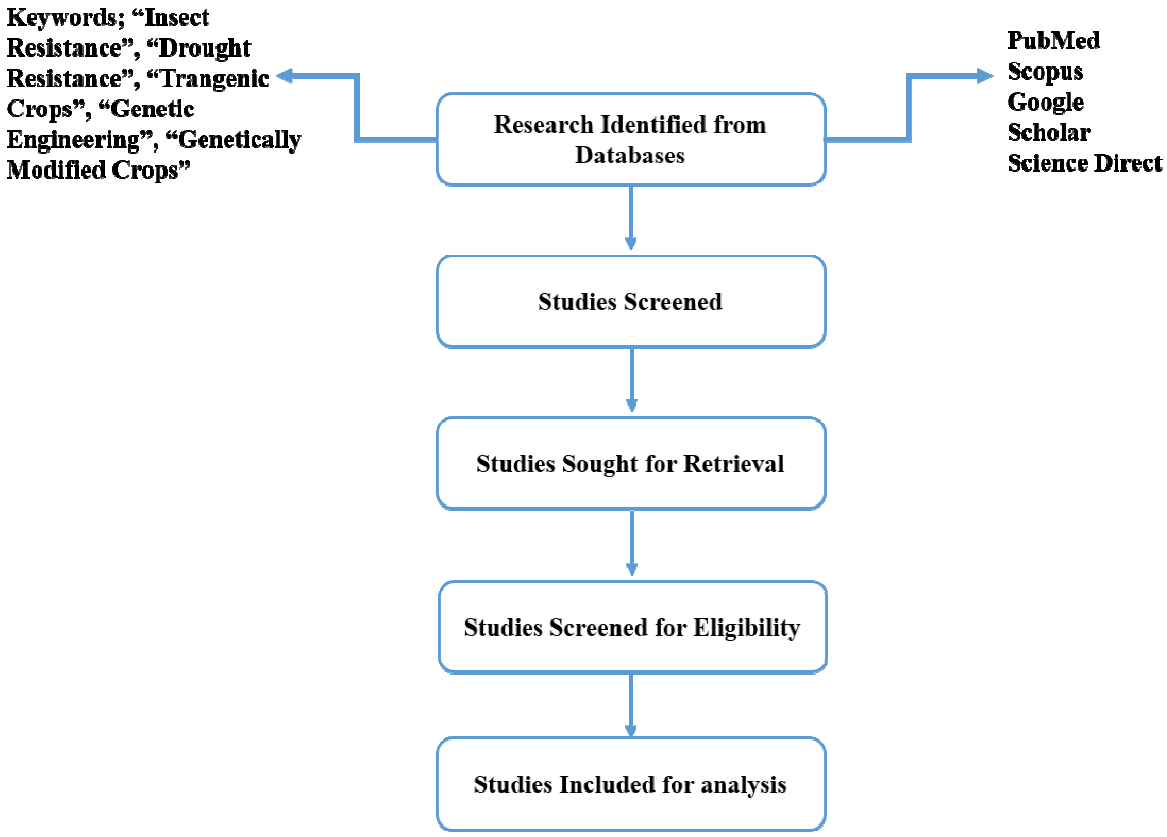


**Figure 3: Methodology used for Carrying out the Present Review Study.**

## 4. DISCUSSION

GM crops have the potential to address a number of the hunger and nutrition challenges of the world while increasing production and reducing dependency on chemical pesticides and herbicides, which will assist to protect and maintain the environment. The actual challenges are labeling laws, rules, and safety checks. Many people argue that genetic engineering is an unavoidable future trend and that, given its huge potential advantages, we cannot afford to ignore it.

Many people feel that there is a dearth of information about the potential health impacts of genetically engineered foods, even though they should have been investigated and eliminated before being introduced. Even though some claim that minor differences between GM and non-GM crops have minimal biological significance, the majority of GM and parent line products are thought to not meet the stringent equivalence requirements. If we are to put these advanced technologies on a truly scientific foundation and allay public concerns, innovative methods and strategies are almost always required to examine the toxicity, nutrient, composition, and metabolic distinctions between GM and conventional crops, in addition to the safety of the genetic strategies used during GM crop design.

Among the concerns concerning GMOs, which are widely utilized and consumed across the world, the most pressing concern is the potential health risks posed by GMOs consumed as food. As genetically modified crops become more common, concerns over their effects on the environment and health become more common. In general, specialists on the subject support the continuation of investigations, while consumers oppose them because they lack sufficient understanding. El-Shamei *et al.* reported histopathological changes in experimental rats when fed corn that is genetically modified. In their study, they used treatment and control groups. The results of their study revealed a desquamation of spermatogonial germ cells with some extent of necrosis. Kidneys in experimental rats also demonstrated congestion of renal blood vessels. In this regard, GM products should be allowed to the market only after extensive scientific research has been completed and a legal framework has been established, and consumers should be educated about the matter. Critics of GM crops have expressed concerns regarding their possible negative ecological effects alongside potential threats to food safety.

- Firstly, foreign transgenes might "contaminate" the natural environment if GM crops interbreed with wild relatives. For instance, Bt-corn pollen has been seen to fertilize non-Bt plants. Some American trading partners as well as certified organic produce growers may have issues as a result of genetic contamination.
- Secondly, some environmentalists have expressed concern about the negative impacts of BT corn on non-target species, such as “Monarch butterflies” who eat the wild milkweed that grows next to cornfields and is therefore not the intended target. These concerns have not come true as of yet. However, a more extensive investigation is required.

## 5. CONCLUSION

In conclusion, crop improvement has greatly benefited from plant transformation and genetic engineering, which introduce beneficial foreign genes or suppress the function of indigenous genes in agricultural plants. “Abiotic stress tolerance” “disease resistance”, “Insect resistance”, “herbicide tolerance”, and “nutritional enhancement” are all features of GM crops that are

reviewed here in the present study. As there are also a large number of risks associated with crops having genetic modification, it is becoming important to have stringent laws for consuming and manufacturing GMOs.

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# CHAPTER 13

# AN EVALUATION OF FERMENTED FOODS AND BEVERAGES FOR HUMAN HEALTH BENEFITS

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**ABSTRACT:**

A majority of fermented foods and beverages are more common in daily human diet because of their good nutritional qualities, sensory taste, and prolonged shelf life. The first concern, the presence of nutrients that is more accessible due to fermentation, such as minerals, bioactive compounds, vitamins, and other substances. Numerous studies have been done to prove that beverages and foods that have undergone fermentation are healthy, but still, there is an urgent need for a more thorough approach to include fermented foods in daily diet. Therefore, the present work aims to provide a comprehensive review of the health benefits of various fermented food products and beverages with their proposed mechanism of action with a new perspective on limitations. In the upcoming years, it is expected that developments in molecular microbial ecology and characterization methods, along with an in-depth understanding of the microbial community during fermentation processes and the interplay between fermentation as well as other processing techniques, will raise the market of fermented products to new heights. To assist in addressing the growing public health problems, more effort should be put into producing healthy microorganisms and fermented foods. Foods with fermentation characteristics should be sustainable and tailored for different demographics and cultural groups to accomplish this goal.

**KEYWORDS:**

Fermentation, Fermented Milk, Fermented Foods, Microbes, Nutrition, Healthy Diet, Yogurt.

## 1. INTRODUCTION

Fermentation, which is defined as a technology that leverages the metabolic activities and growth of microbial organisms for the preservation of food, is one of the most cost-effective and oldest techniques of food preparation. It is the primary method of producing food in several civilizations since it is a cheap process that uses relatively little energy. Aerobic fermentation, which includes fungal and alkaline processes, and anaerobic fermentation, which includes lactic acid and alcoholic processes, are the two main types of food fermentation [1]. Microorganisms use fermentation to convert fermentable carbohydrates into final products like carbon dioxide, organic acid, and alcohol as well as antimicrobial metabolite compounds like bacteriocins that improve safety by eliminating or by inhibiting pathogens that are responsible for foodborne disease [2], [3].

There are a variety of fermented beverages and foods due to the wide variety of food-microbe interactions. Almost every culture on the planet uses one of these products if not all of them. The variety of fermented foods has decreased during the past century, especially in the West, despite

their long history, widespread use, and culinary significance [4]. However, in recent years, Western diets that prioritize artisanal practices have given fermented foods a resurgence of interest. The possibility for them to promote health is one factor in this increase in interest. Fermented foods ought to be included in national dietary recommendations, according to recent suggestions from several organizations.

In addition to improving the organoleptic qualities of food, protein and carbohydrate digestion, and mineral and vitamin bioavailability, fermentation extends the lifespan of foods, particularly those that are very perishable. Because of their positive effects, fermented beverages and foods have served as an essential component of human diets since old times and continue to be significant in many developing nations wherein they are ingrained in regional cultures and customs. By boosting the immune system, lowering the levels of blood cholesterol, and diabetes, fending off infections, and allergies, combating obesity, and atherosclerosis, and relieving lactose intolerance symptoms, fermented foods have positive health effects [5]–[8].

Food is said to as fermented when its sugars and carbohydrates have been converted into alcohol or beneficial acids. Foods that have undergone fermentation are more nutrient-dense, simpler to digest, and rich in probiotics and enzymes. They are essential to a diet high in conventional, nutritious foods [9]. Consuming fermented foods regularly has various advantages. A microbial fermentation could be homo-fermentative, producing a single major product, or hetero-fermentative, producing a variety of products [10]–[13].

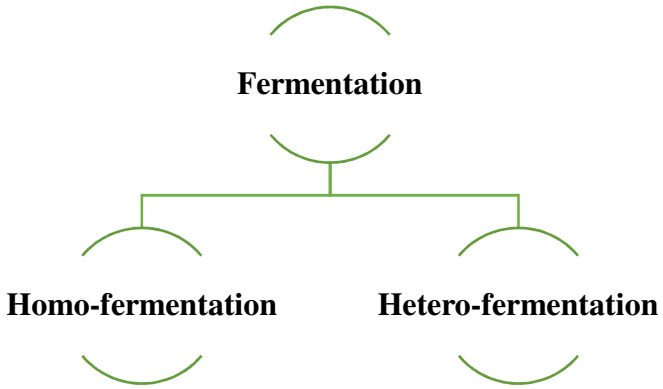


Figure 1: Illustrating the two types of Fermentation; i) Homo-Fermentation, ii) Hetero-Fermentation.

The majority of important staple foods are or were fermented in various societies and historical periods. For instance, approximately all of the calories consumed in medieval monasteries in Europe came from cheese (fermented with various communities) wine (fermented with yeasts), and bread (fermented with sourdough starters). Fermentation is less prevalent in other cultures. However, whether it is for ancient, historical, or current times, this pattern, like others linked to fermented food, has gone largely unquantified.

The term "fermented foods" refers to foods that have undergone microbial or enzymatic action to produce desired biochemical changes that significantly change the food. Rather, "fermentation" refers to a kind of energy-producing metabolism of microorganisms that occurs when an “organic substrate”, for example, carbohydrates, is incompletely oxidized and an “organic

carbohydrate" serves as the "electron acceptor" to produce energy [14], [15]. Food products that have been exposed to the action of lactic acid microorganisms are referred to as fermented foods. It is crucial to incorporate fermented foods because they provide probiotic bacteria in their best possible form. The different types of fermented foods and beverages are given in Figure 2 below.

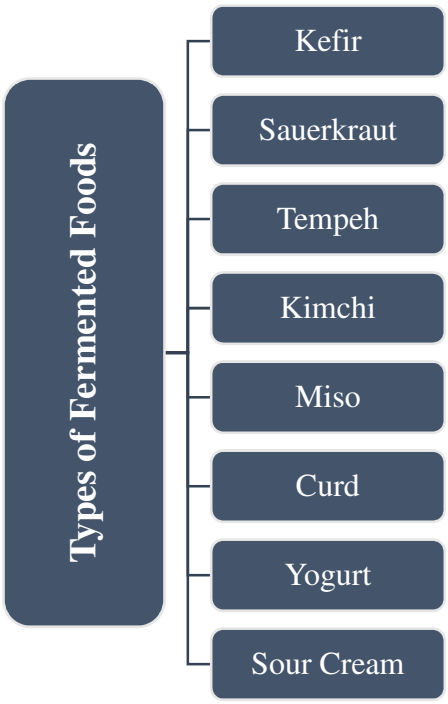


Figure 2: Illustrating the Different Types of Fermented Foods and Beverages.

Different cultures and geographical areas have different levels of diversity in the various types of fermented foods. Meats are the only foods that are fermented in some cultures and regions, whereas other cultures and regions ferment other proteins, carbohydrates, and lipids as well. Additionally, different types of fermented foods come in different numbers of variants. Naturally, there are further geographic and cultural trends related to fermented foods that deserve an explanation, but we won't get into them in this paper. For instance, different regions of the world consume differing amounts of foods that have undergone fermentation.

## 2. METHODOLOGY

The information presented in this paper is obtained from an electronic database search strategy. The search was carried out in databases; Research gate, Google Scholar, Science Direct, PubMed, and Scopus. Narrow keywords and their combinations were used to obtain the relevant records including "Fermented Foods", "Fermented Food products", "Fermented Milk", "Fermented Raw Milk, Curd", "Yogurt", "Kefir", and "Idli". A manual screening was also employed in google scholar for obtaining the important relevant records. Duplicate studies and records with languages were included in the exclusion criteria. The whole methodology of the review study is presented in Figure 3 below.

### *2.1.Fermented Milk Products*

Due to the high bioavailability of calcium concentration in milk products, these foods have been recognized as essential dietary supplements for bone health. In an animal model of "postmenopausal osteoporosis", bone resorption can be inhibited by "milk basic protein (MBP)", which is defined as an active whey protein that has been shown to prevent bone loss. Bu *et al.* study the effects of milk protein, the peptides present in milk for their protective effects on bone health. Their study served as a primer or foundation which can emphasize the use of milk proteins and peptides as a potential treatment for osteoporosis [16]. Fermented milk products (FMPs) can also benefit bone health in addition to MBP. In addition to improving bone health, new studies have shown that dairy products with lactobacillus also reduce the risk of diabetes, hyperlipidemia, and pathogen infection.

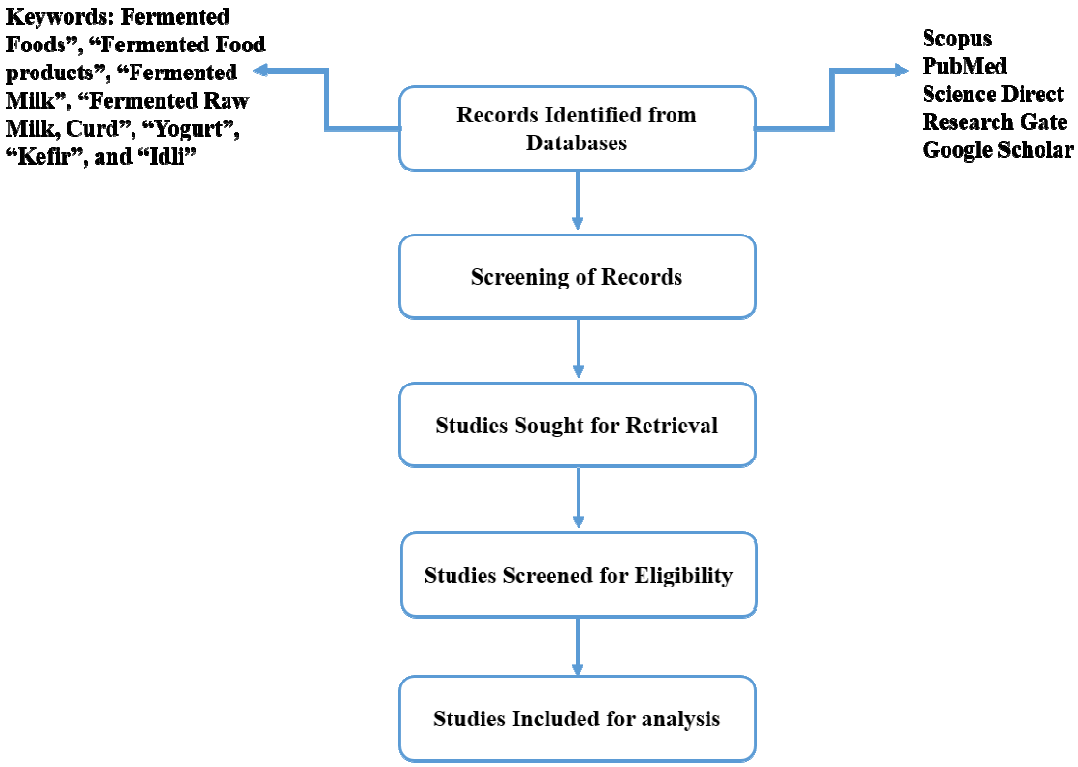


Figure 3: Illustrating the Methodology used for Carrying out the Review Study.

In a separate study by Lee *et al.*, an investigation on the anti-osteoporotic effects was carried out for "*Lactobacillus plantarum* B719-fermented milk product (FMP-B719)". When treated MC3T2-E1 mouse with "FMP-B719", high proliferation and mineralization was observed. In addition to that, normal phosphorous, and normalized serum alkaline phosphatase were also revealed in postmenopausal osteoporosis in an ovariectomy-induced rat model [17].

Fernandez and Marette provided a new perspective on the mechanistic evidence as well as the observational evidence on the benefits of fermented milk production on metabolism. The health benefits to metabolism are attributed to the instrumental mechanism of microbial balance in the gastrointestinal tract which was further supported by the role of peptides derived from LAB present in fermented milk [18].

### *2.1.1. Kefir*

New studies on the health advantages of kefir are making it more and more popular. It is a Russian fermented milk drink that originated in the Caucasus Mountains. "Kefir" is made by inoculating milk using kefir grains that are a mix of yeasts and bacteria in a symbiosis environment. According to a paper published on Lactobacillus taxonomy by Salvetti *et al.*, Lactobacillus species in kefir belong to several subgroups, with at least one strain belonging to *the "Lactobacillus delbrueckii", "L. reuteri," "L. casei", "L. buchneri", and "L. plantarum"* groups, as well as other strains belonging to the "Lactococcus" and "Leuconostoc" genus. The preponderance of the kefir-derived strains from Lactobacillus, though, belonged to the "*Lb. buchneri" and "Lb. delbrueckii"* groups, due to "*L. kefiranofaciens"* and "*L. kefiri*" species. These specific *Lactobacillus species* constitute an important fraction of the *Lactobacillus species* identified in kefir. "*Lb. plantarum*" has also been thoroughly examined and is known to be found in significant amounts in kefir [19].

Bola *et al.* conducted an *in vivo* investigation utilizing "*Mesocricetus auratus*" due to their significance as an important model for human infections by "*C. difficile*". "*Lb. plantarum CIDCA 83114"* was included in a microbial mixture (MM) comprising multiple yeasts as well as the bacteria species that were given to hamsters in drinkable water (at varying dilution rates of "1:100" and "1:1000") before infection with "*C. difficile"*. Administration with the "1:1000 MM" considerably decreased the number of animals with mortality and diarrhea. In addition to that, the "1:100 MM" dilution resulted in no relief in symptoms, implying that a high concentration of microorganisms can be harmful, probably increasing any kind of inflammatory responses to "*C. difficile*" [20].

In a randomized, placebo-controlled, single-blind study, Cheng Wang *et al.* isolated the putative probiotic strains from Kefir that have been found to have positive effects on the improvement of gastrointestinal health and the parameters linked to it. The findings of their study revealed that the daily consumption of the kefir which contains several probiotic strains resulted in reduced events of bloating, appetite, and abdominal pain in the male subjects. The positive effects of the kefir were attributed to the total anaerobic bacteria and total bacterial populations [21].

Another study carried out by Baars *et al.*, investigated after conditions when starting to consume raw fermented milk. In their study, they rated immune status, 1-item immunity score, bowel, mood, and skin conditions before and at least 60 days after consumption of fermented milk using data from 390 participants for analysis. The results of their study revealed that the highest intake of raw fermented milk was from kefir and the individuals consumed 1 glass of kefir per day. In addition to that, the highest improvement in health conditions was observed in the people in poor health which was evident in improved immunity, mood, and bowel scores. Apart from that women have also reported significant improvements in health suggesting the positive effects of raw fermented milk products [22].

### *2.1.2. Curd*

Curd is recognized as a whole, natural food. It is a milk byproduct that has a white color and was produced by bacterial activity. Because it includes nutrients and probiotic microorganisms, eating fresh curd regularly aids in the prevention of various diseases which is supported by multiple research studies. It is a functional food that increases both natural and acquired

immunity and improves stamina. Curd, which has the highest concentration of probiotics, provides the digestive system with beneficial as well as wholesome microflora.

Manoharan *et al.* enrolled a total of 30 school children in randomized controlled trials with treatment and control groups. The treatment group received the freshly prepared curd at home for 30 days which was then followed by the evaluation at baseline. The results of their study revealed a significant reduction in several *S. mutans* which was confirmed by various other studies with potential and proposed mechanical inferences. Therefore, the results of their study revealed that there are potential probiotic effects of curd on the elimination of anaerobic organisms responsible for developing dental plaque [23].

#### *2.1.3. Yogurt*

"Yogurt" is one of the fermented milk products that has been investigated a lot for its health benefits for a variety of organ systems in both healthy and diseased objects. Schmid *et al.* conducted a study to investigate the link between the regular consumption of yogurt and cause-specific, risk of all-cause mortality in women and men in the U.S. using 40,278 men and 82,348 women. The results of their years of follow-up revealed that low mortality was associated with regular consumption of yogurt [24].

Savaiano & Hutkins also established a crucial relationship between regular consumption of yogurt with proper digestion and tolerance of lactose and low risk of developing type 2 diabetes and breast cancer. In addition to that, their review study also revealed the well-established and researched roles of yogurt in improving cardiovascular health, good weight, and bone health maintenance [25].

Wade & Elias demonstrated that the higher intake of Yogurt is associated with low BP in individuals that suffer from hypertension with their findings from cross-sectional studies taking a total of 915 community-dwelling adult individuals. The habitual consumption of Yogurt was then assessed using a "food frequency questionnaire". The results of their study demonstrated an inverse relationship between systolic blood pressure and the consumption of yogurt in individuals having hypertension issues [26].

There has been a lot of attention from the scientific community in developing yogurt with more and more nutritional qualities. El-Fattah & Hany Elkashef prepared a novel yogurt from Sikkim milk which was fortified with whey protein concentrate. Their study demonstrated that partial proteolysis and proteolytic starter can be used as a tool for the development and preparation of functional yogurt enriched with bioactive peptides having positive effects on cardiovascular health [27].

### *2.2. Other Fermented Food Products*

In a study carried out by Sadishkumar *et al.*, a total of eight lactic acid bacteria were selected to screen for biofilm-forming ability and antioxidant potential which was further followed by in Vitro probiotic properties screening. The results of their study revealed 5 out of 8 isolates that were capable of inhibiting biofilm-forming *Staphylococcus aureus.* In addition to that significant properties like gastrointestinal juice tolerance, bile tolerance, acid tolerance, co-aggregation, and resistance to other antibiotics, therefore, suggesting the use of tested probiotic strains for the formulation of functional foods [28].

## 3. DISCUSSION

Fermented beverages and foods have long been regarded to provide health advantages and have been a vital element of the human diet. Carvalho *et al.* suggested one of the most proposed mechanisms of action of fermented food products and beverages is attributed to the maintenance of the microbiome of the gut with the intake of these fermented products which further leads to good health in terms of physical as well as mental health (Figure 4) [29]–[32].

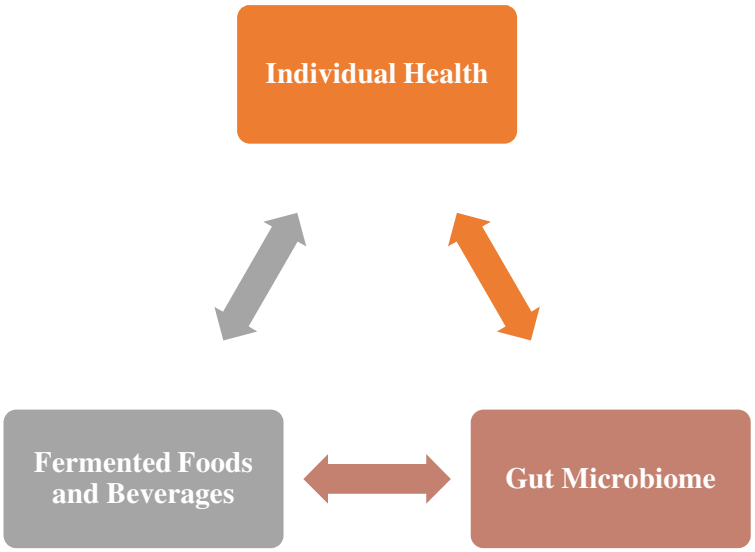


Figure 4: Illustrating the Interplay between Fermented foods, Gut Microbiome and Health.

Fermented foods can lower diabetes, high cholesterol, obesity, risk of hypertension, thrombosis, diarrhea, and other diseases. The bioactive compounds generated during fermentation are one reason for the nutritional advantages provided by foods that have undergone fermentation. Fermentation raises the amounts of many vitamins in foods, including "vitamin B9 (folate)", "vitamin B12", "vitamin B2 (riboflavin)", and "vitamin K". Melatonin, as well as GABA, which controls blood pressure & defends against cancer and CVD, are synthesized. However, to make them evident for their health benefits for health as well as diseased patients, the following areas need to be addressed:

### ***3.1.****Lack of Quantitative Nutritional Measures*

There aren't enough quantitative nutritional measures available to calculate the recommended daily intake of fermented foods. Prebiotics, Probiotics, and biogenic are present in fermented foods, but their amounts are often not specified. Even "colony forming units (CFU)", a measurement of the live probiotic bacterial counts, could probably vary based on the food, preparation techniques, and storage settings at the time it was consumed. It is difficult to compare products because of this. More study is needed to determine the viable probiotic populations present in fermented food products currently on the market. Physicians and registered dietitians require this information to recommend fermented food products to patients as an adjuvant treatment technique for different pathophysiological conditions.

### *3.2. Drawbacks and Further Research*

The amount of research examining the efficacy of interventions employing fermented foods for treating the nervous system has limitations, notably wide heterogeneity driven by different study parameters and a lack of studies demonstrating solid methodologies for measuring mental health results. In addition, several of the studies used tiny sample sizes and weren't designed to answer the therapeutic question about whether or not fermented foods could be an effective treatment for depression or anxiety. Additionally, the fermented foods utilized in previous research varied greatly in terms of their constituent ingredients and physical attributes; hence, there is inadequate evidence to draw any conclusions concerning either one food, either individually or collectively. Finally, there aren't enough safety data available to adequately counsel patients about risk. Since we know of this, no detailed studies have been conducted to evaluate the safety of fermented foods, especially for special populations like the pharmacologically ill pregnant women, children, and elderly. Even though fermented foods have been available for consumption all across Asia for thousands of years, they have not been thoroughly studied.

The microbiology of fermented food products is a fantastic model which is closely related to the forces that shape the human microbiome at various body locations. The understanding interplay of the microbial community, that are crucial for preventing the threat of worldwide anti-microbial resistance, will aid in revealing, via a comprehensive strategy, the undiscovered mysteries of the human microbiome as well as the interactions that have a significant impact on a variety of public health, nutrition, and well-being problems.

Future clinical research will determine the significance and promise of fermented beverages and foods with contradictory and ambiguous findings, and advocacy for their incorporation in nutritional recommendations. Because of the limitations and contradictions in the current body of information, no clear conclusions on the possible health advantages of fermented food can be reached at this time.

## 4. CONCLUSION

To conclude, Fermented foods include a variety of compounds, including health-promoting nutrients, bio-actives, and enzyme bacteria, as well as some undesirable components. These substances may have beneficial or negative effects on the health of specific communities and people, and their effectiveness and safety must be evaluated in a case-by-case situation. Furthermore, microorganisms in fermented foods are thought of as "micro-factories" that generate and enrich minerals and bio-actives with specialized nutritional and physiological functions as supported by the large body of literature available online.

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# CHAPTER 14

# AN EXPLORATIVE STUDY ON THE HISTORY OF ROBOTS AND THEIR APPLICATION IN FOOD INDUSTRY AUTOMATION

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**ABSTRACT:**

The impacts of climate change, shifting consumer preferences, and escalating regulatory pressure from the government enforce several problems for the global food industry and have led to several fronts for change. It is becoming more apparent that the big, inflexible production systems in use today cannot sustain the minimum requirements necessary to put such changes into reality. In recent years, automation by Robots has attracted a lot of attention from researchers and scientists from multidiscipline for addressing the above issues using robots. However, this is still a lack of studies documenting the use of robots in the food industry with a comprehensive approach. Therefore, this paper aims to provide a clear view into the history of robot development and its application in meat processing, food packaging, stacking pallets, and other food-related services. In addition, this study also discussed about the advantages of robotics and automation for the food industries with a critical analysis of the review studies and recommendations for future research.

**KEYWORDS:**

Automation, Food Industry, Food Packaging, Palletizing, Robots.

## 1. INTRODUCTION

Over the past 20 years, developments in several technology fields have made previously fictional robots a reality. Industrial automation is a category that includes robotics. The use of robots to automate operations has become necessary due to pressing demands for increased productivity. Robots are now seen as a necessary component of many industries. Industrial robot populations have historically increased, with sales surpassing records as 2015 saw the sale of 240,000 units mark a first and an 8% global year-over-year gain [1]–[4].

The development and use of robots, notably in food production, ha**ve** advanced dramatically as a result of informatics advancements. Robots are now much smarter and more effective due to drastically increasing computational power and associated software solutions. Not only that, though. They can now "see" various scenarios and respond to them due to sophisticated optical devices designed to record and analy**z**e pictures. Nowadays, automation is frequently employed for activities that were formerly handled by people. The procedure can run without help from or intervention from humans when it is automated. In reality, the majority of automated systems are capable of carrying out their duties faster, more accurately, and with higher precision than people. A large number of manufacturing sectors with clearly defined processes and products have effectively applied robots and automation.

Automation is a type of technology that mechani**z**es a repetitive operation, minimi**z**ing the necessity for human help. Automation may refer to anything from self-checkout queues at the

supermarket to automated teller machines (ATMs) at banks. It is critical to investigate the influence of automation in the workplace and how this technological revolution can disrupt the core production processes of industries.

According to the report, the industries that employ the most robots are those that have labor that can be readily mechanized and the financial means to get around the adoption costs of robotic systems. Automobile and other transportation-related industries, metals, electrical and electronic devices, beverage, chemicals, food production, and wood and paper commodities are some of these areas. There has been an increase in automation worldwide, even though some industries have been quite slow to adopt robots. The number of industrial robotic deployments in the US increased at a compound annual growth rate (CAGR) of 10.28% during the previous ten years, from 15,170 in 2008 to 40,373 in 2018. The great majority of automation in the United States is in manufacturing, which accounted for 82.3 % of all industrial robot installations in the United States in 2018 as Illustrated in Figure 1 [5].

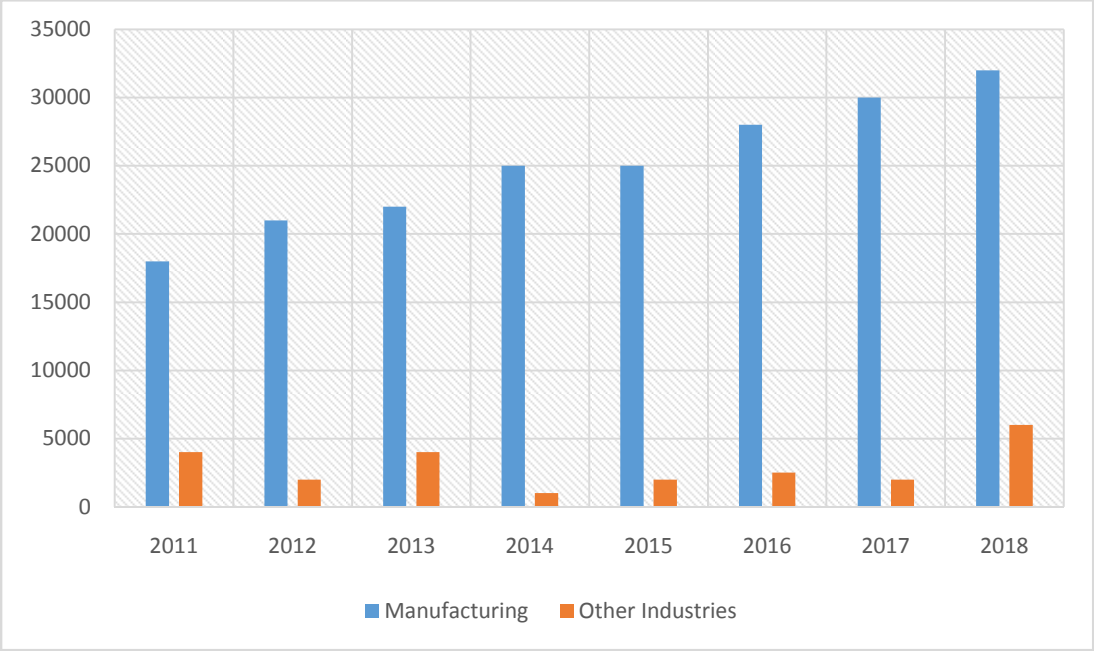


**Figure 1: Illustrating the number of Industrial Robot Installations From 2011 to 2018 in the U.S. by Sector.**

Out of several manufacturing industries, the food industry is the one that is increasingly choosing robots for automating processes and services. However, there are very limited studies defining and documenting the robotization of the food industry. Therefore, this paper aims as providing the significance of deploying robots in the food industry by highlighting the course of history.

## 2. LITERATURE REVIEW

### *2.1. History of Robots*

Industrial robots are frequently brought up while talking about 21st-century developments. Their origins, however, go a long way back, to the 1950s, when George Devol built the very first industrial robot—a two-ton device that used hydraulic actuators to independently move products from one location to the other. Since then, the functionalities of robotic systems have

significantly increased to also include complex operations like painting, assembly, palletizing, inspecting, welding, packaging, and testing all accomplished with precision, speed, and repeatability. This is attributable to breakthroughs in electronics, sensors, and software applications. The whole history of Robot development is illustrated in Figure 3 below [6], [7].

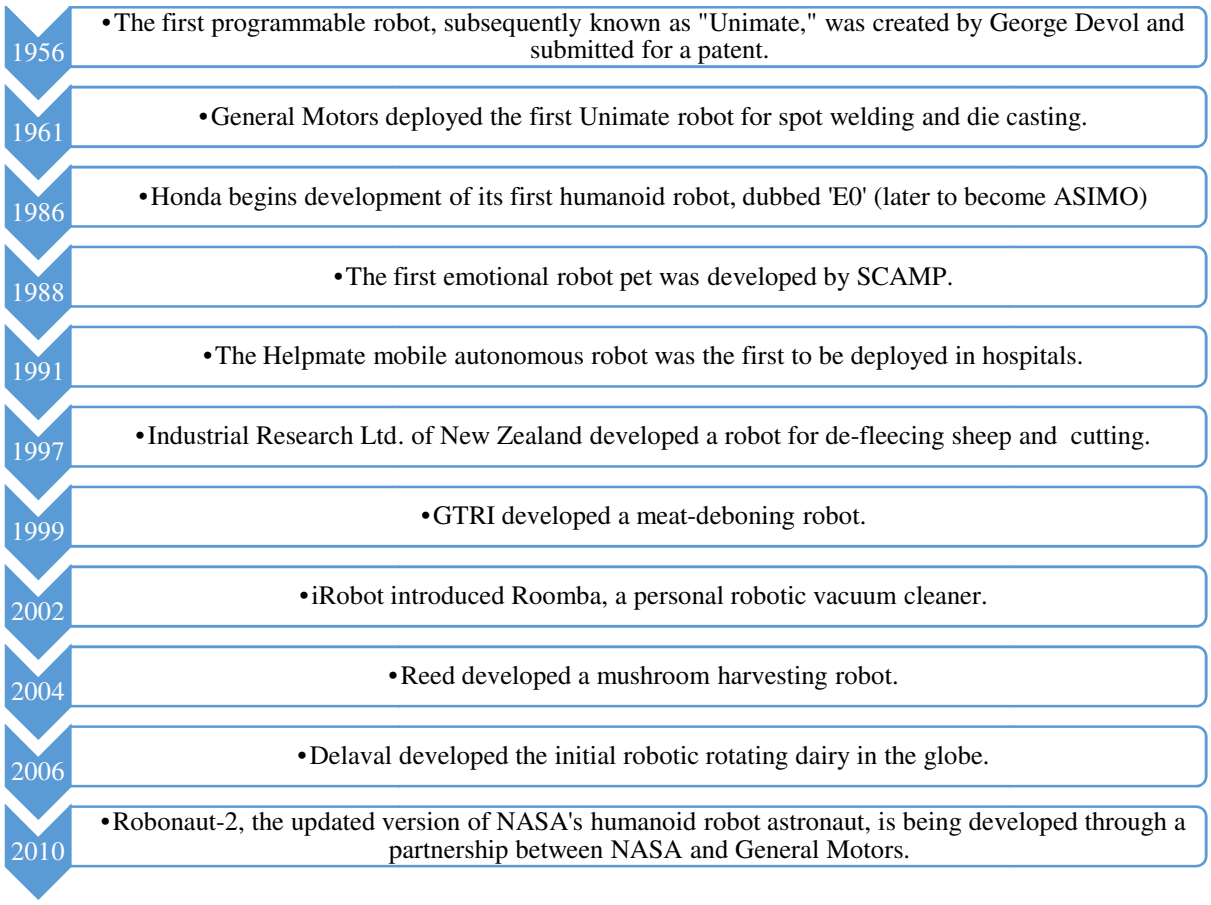


**Figure 2: Illustrating the History behind the Robots and their development.**

In the early 1960s, robotics was initially employed commercially in assembly operations. Most have been made for heavy lifting and had pneumatic or hydraulic arms. Despite being simple, sensor-less, and having limited programmability, the devices were extremely useful for increasing output in industrial facilities and helped pave the way for a protracted era of robotics development.

The focus of robot technology changed from heavy lifting toward materials handling and accuracy operations in the late 1960s and early 1970s as the demand for automation of labor-intensive manufacturing, tasks increased. As a result, smaller electric robots with complex controllers, gyros, miniature motors, microprocessors, and servos were created, making them perfect for simpler assembly tasks like tightening bolts and nuts**.**

By the late 1970s, robots were able to do painting, arc welding, and material transferring, among other activities. Additionally, they started performing hazardous activities in factories. Robots, for example, were utilized in steel mills to transport components and materials in hostile to human high-temperature settings. This led to greater workforce productivity and a considerable

improvement in facility safety by allowing experienced workers to concentrate on more crucial industrial processes.

### *2.2. Use of Robots in the Food Industry*

In the food industry, robots are used for a variety of tasks, including packaging and food processing. Bisello et al. investigated a total of 20 case reports for the recent changes in a task in manufacturing occupations such as meat processing. The finding of their study revealed that due to automation, physical activities in manufacturing are typically decreasing; yet, computer-controlled machinery is used more often and quality standards are taken more seriously. However, there are an increasing number of intellectual activities that manual industrial workers must do to reap the benefits of robots in manufacturing industries like the food sector [8]. Below are some of the

#### *2.2.1. Food Packaging and Palletizing*

The two most common uses of food-handling robots nowadays are packaging and palletizing. In packaging materials, which is the stage of the manufacturing line when food is put into its vacuum-sealed bag, container, or wrapper, food robots are used. Robots are extensively used in secondary packaging, another industry. Another important application of robots in the beverage and food industry is palletizing.

To solve the limited multi-objective optimization problems, Szczepanski et al. developed four alternative goal functions relating to potential needs in a factory setting. An algorithm enabled by Deb's principles called the Artificial Bee Colony has been used to address this issue. According to their study's findings, the suggested method greatly boosts production rate and meets specific criteria, such as an energy-to-palletized-item ratio of no more than one and an even distribution of filling amongst containers.

Wang et al. for the establishment of a palletizing robot system, used B-spline trajectory planning algorithm. In their testing of palletizing function, they found that the system can reduce trajectory planning time since the average evolutionary algebra for each layer varies from 32.49 to 45.66 and the single-step code packet time is steady at about 5.8 s, which further stresses the practical significance of the study [9].

A separate study carried out by Dang et al. developed a soft robotic gripper with four actuators that use pneumatic systems to work and are constructed of a hyperelastic material. The finite element approach in the ABAQUS software was used to simulate the gripper dynamics and deformation problems. According to their research, the proposed gripper can grip things of different shapes and sizes with a geometrical constraint of up to 8 cm and a gripping mass of up to 300 grams. Further testing demonstrated that the gripper could perform with an efficiency of 3 components per minute, demonstrating that it could meet the real requirement of the currently-used product packing line [10].

In a study by Noorden et al. stabilization of Delta Robot motion for flexibility in packaging viscous fluid products in a bag is investigated. The approach known as input shaping was developed for canceling out oscillations from a construction crane load. The parameters are determined from measurements performed on a test setup given by BPA, which includes a Spider DPR01 delta robot. The performance of input shaping is evaluated in simulations and

practice using the generated parameters. Their findings show that input shaping can successfully minimize the oscillatory behavior of the gripper-product system in this application [11].

### *2.2.2. Meat Processing*

For many years, experts have been researching how robots may be used in the meat processing sector. The major objective of utilizing an industrial robot is to increase process efficiency and cleanliness while decreasing production costs and occupational hazards. Robotics' advantage comes in their capacity to do repeated jobs more effectively and reliably than is now achievable, especially in boning rooms where labour costs are already high.

A study by Liu & Ji proposed a cost-effective robotic processing cycle for meat dissection. In their study, they implemented a single manipulator for a series of dissection tasks, such as butterfly harvesting, cone-fixture, and off-Shackle. The proposed framework was then tested and validated. They found that the butterfly obtained from their proposed system after harvesting demonstrated smoothness quality which was much higher than that of manually performed separation. In addition to that, they also found higher satisfaction with the proposed system in terms of the current demand of the industry.

### *2.2.3. Food Service*

The food service industry is likewise being shaken by robots. From mixing to cutting, robots are capable of a wide range of culinary activities. More than a dozen robots are being used by Chinese restaurants to prepare and serve meals to customers. Customers are greeted, dishes are placed on tables, and the meal is prepared by robots.

Seyitoğlu and Ivanov developed a framework for the development of delivery of service for the hospitality industry using a variety of theoretical strategies such as, “PESTEL analysis”, “value chain analysis”, “resource-based view”, “positioning strategy”, “stakeholder theory”, and system design for system delivery. They also defined three service delivery system designs and analyzed their needs, benefits, drawbacks, and prospective target markets. The suggested model advised hospitality businesses to first investigate the expectations of customers and clients before analyzing how they may differentiate themselves from their counterparts, which might or might not require using robotic technologies for automation, cleanliness, and safety purposes [12].

In a study by Chiang & Trimi. Investigated the effects of service robots on the quality of service. In their study, 201 sampled customers provided feedback on the level of service they expected from robots as well as their overall output experience after the service. They used Technique for Order Preference by Similarity to an Ideal Solution (TOPSIS) and important performance analysis (IPA) to investigate this relationship. The findings of their study revealed reliability and assurance [13].

In a study carried out by Singh et al., They attentively reviewed and analyzed the research on robotic and automated kitchen appliances. The primary factors used to classify things are their function, the technology they employ, and the type of food they serve. In addition to that they also developed a 3D simulated model to address the current limitations and flagged issues, however, there is still a need to further validate the same [14].

All the above studies have evaluated the studies concerning the use of robots in the food industry involving food service, meat processing, food packaging, and palletizing. However, this review

is carried out to put all of them in one frame to address the current limitations that are now faced in the path to their adoption.

## 3. METHODOLOGY

The information provided in this paper is reviewed from high-quality records obtained from electronic databases such as Scopus, PubMed, Google Scholar, Science Direct, and Research Gate. Relevant records were obtained by using a variety of keywords; such as "Meat Processing", "Food Industry", "Automation", "Robots", "Industrial Robots", and Manufacturing Industry" as Illustrated in Figure 2.

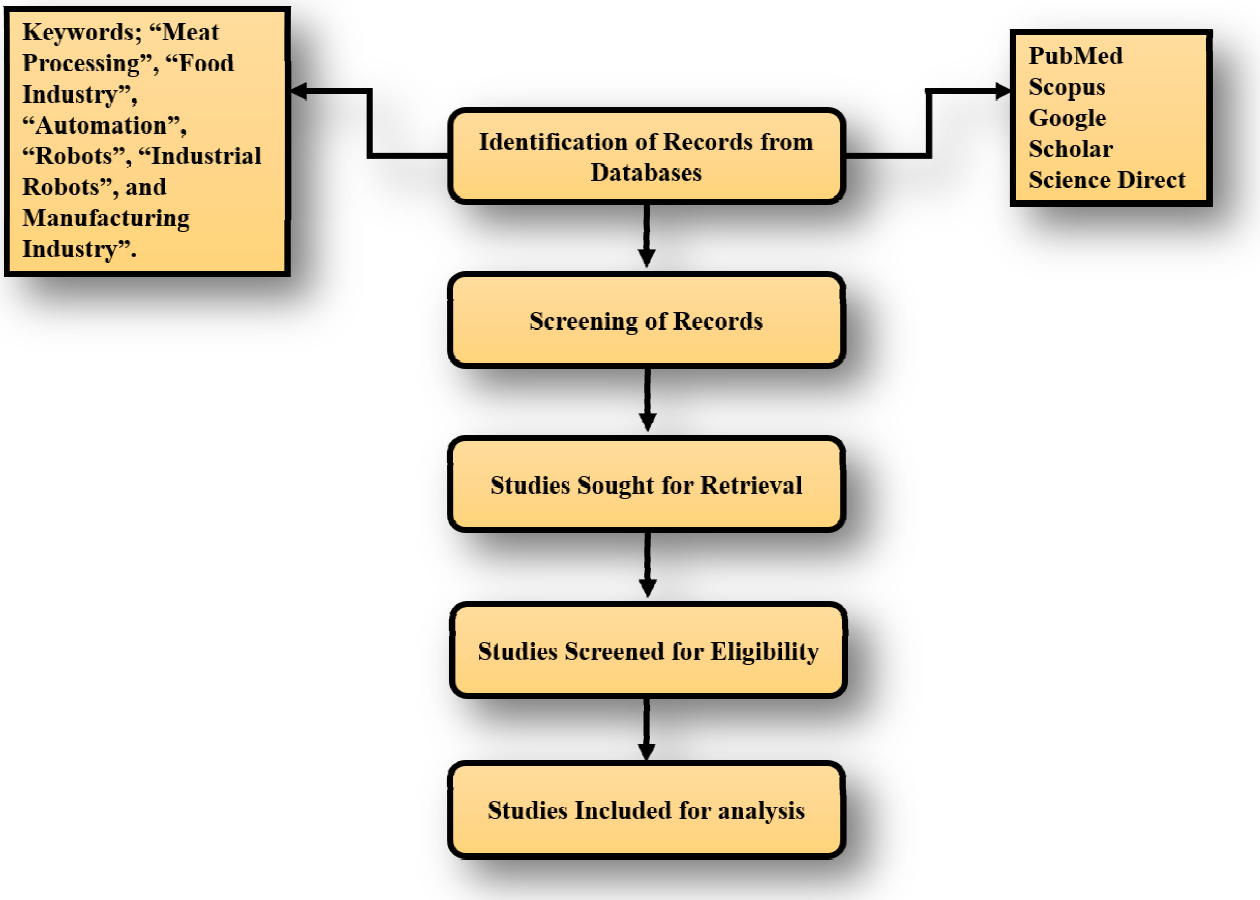


**Figure 3: Illustrating the Methodology Used for Carrying out the Review Study.**

## 4. DISCUSSION

It should come as no surprise that in the food and beverage industry, robots are still mostly utilized for "hard labor," such as packaging, repacking, and stacking pallets. Typically, the products under question are packaged foods. Handling them is typically simple and may be accomplished with a conventional model selected from a wide range of robot designs. However, before robots could undertake activities in the actual manufacturing of food, and thus come into direct contact with food, major obstacles had to be addressed, necessitating a rethink among robot manufacturers.

Food products, after all, are produced with naturally occurring substances that cannot be standardized, have unique rheological behavior, and are sometimes extremely susceptible to mechanical interference. Additionally, strict hygiene methods that satisfy the pertinent disinfection and cleaning criteria are necessary for the needed level of product safety and storage stability, and this also holds for robots. Environmental factors that affect food production are frequently complex. For example, corrosive substances like acid, water, and salt can come from both food and machinery, while the outside temperatures can fluctuate from very hot to well below freezing. But it was particularly these conditions that made robot deployment in the food and beverage industry appealing and logical.

The main causes behind this argument were the humanization of the workplace and the improvement of food safety through increased attempts to establish sanitary procedures in manufacturing. Then there was the constant problem of increasing efficiency while lowering expenses. Who desires to spend eight hours a day doing the same thing over and over at a temperature of 8 °C? Who wants to spend most of their day operating in a freezer? And how are scientists going to exclude the risk of microbiological pathogens from contact with human skin indefinitely? How can a standardized production line be maintained for more than eight hours, much alone 24 hours?The food industry is mostly composed of small and medium-sized businesses with diversified product offerings. This, together with the concomitant requirement for flexibility at many levels, implies that it demands the technical solutions that robots can provide. One unarguable element about the employment of robots in manufacturing is that if they are to work directly on and with food, they must be able to be cleaned correctly and using standard means and processes, as well as disinfected if necessary. As illustrated in Figure 4, below are some of the main advantages of automation achieved by employing robots:

- **Traceability:** One of the most important advantages of automation is traceability. Automation may enhance the traceability of raw resources and foods from the fields all the way to order fulfillment, especially when combined with analytics.
- **Standardizes Quality Control**: Automation can make the numerous moving parts of a food industry function more effectively as a whole. The supply, production, and distribution processes include several distinct touchpoints, and each one requires sufficient quality control. Since quality is the main method by that food firms set themselves apart from their competitors, this problem is very important. The reputation of a company's brand might be permanently damaged by a significant error, such as permitting tainted food to reach the final customer.


**Figure 4: Illustrating the Advantages of Using Robotic Automation in the Food Industry.**

With the appropriate automated systems and food processing equipment, issues in the distribution or production processes may be more easily identified earlier. Early problem detection helps companies prevent later, more significant problems.

Automation also makes it feasible to precisely pinpoint the origin of a given issue. Once the weak point is identified, you can determine how to address the situation and stop it from happening again. It is simple to standardize the food manufacturing process while using automated equipment. Each product undergoes the same processes from beginning to end.

Because machines are exact, everything is kept uniform in a way that humans find challenging to accomplish. Automation makes quality repeatable from one sample to the next, and effective quality control becomes a realistic objective.

- **Workplace Safety:** Automation can increase workplace safety, but it cannot take the place of competent personnel and safety training. One-way automated systems and equipment may reduce worker risks is by performing, supervising, or controlling hazardous operations. Workers can stay away from parts of the production process that could cause harm. A continuously running dicer and slicer, for instance, may tackle cutting duties that would be challenging for a human to accomplish precisely at such a high output. While many businesses aim to create a safe working environment, the added security offered by automated systems can assist drive down total expenses by reducing the frequency.
- **Increased Efficiency:** Probably one of the most obvious advantages of automation in the food industry is increased productivity.

Automation can speed up and improve the performance of the operations of companies when it is designed and implemented properly. In the food industry, timing is crucial, and more effective operations may boost quality, reduce waste, and boost profitability by cutting expenses. Industrial ovens with built-in belt systems make it possible to process food on a bigger scale in a smaller space with less supervision from humans or interaction with the food itself. There are fewer direct points of contact and possibilities for delay, unpredictability, or downtime the more automation business use.

## 3. CONCLUSION

Over the next 20 years, a lot of tasks that people today perform while processing, packaging, and distributing food will be fully automated. Robotics will be used in situations when doing so is both economically and technologically sensible. Automating challenging jobs will be feasible, and collaborative robots will assist people in tough tasks. Intelligent robots will be better able to communicate with one another. In much the same way as computers and mobile phones did in recent years, robots will likely take over the food industry and daily life of humans.

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# CHAPTER 15

# A STUDY OF THE PATHOPHYSIOLOGY OF POLYCYSTIC OVARY SYNDROME AND ITS IMPLICATIONS FOR WOMEN'S REPRODUCTIVE HEALTH

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**ABSTRACT:**

Polycystic Ovarian Syndrome (PCOS) is an endocrine and gynecological condition that affects a large population of women of childbearing age. The specific origin and pathophysiology of PCOS remain unknown, although a component of the process that is involved in the formation of PCOS has been found. Women's reproductive and metabolic health is affected by a combination of endocrine abnormalities (such as hyperandrogenism, abnormal menstrual cycles, and obesity) and metabolic alterations. The author of this study investigated the pathophysiology of PCOS in addition to its therapy, and also the author places a particular emphasis on medications that have been repurposed. The pathophysiology of polycystic ovary syndrome, which would be characterized by ovarian and metabolic issues, is also discussed in this study. Therapeutic considerations for the treatment of PCOS and also the interaction between PCOS's reproductive and metabolic features are also explored.

**KEYWORDS:**

Follicle-Stimulating Hormone (FSH), Insulin Resistance (IR), luteinizing hormone (LH), Gonadotropin-Releasing Hormone (GnRH), Polycystic Ovary Syndrome (PCOS).

## 1. INTRODUCTION

Complex in nature, polycystic ovarian syndrome (PCOS) manifests itself in many ways, including increased androgen levels, menstruation abnormalities, and/or smaller cysts on one or both ovaries. Both morphological causes (polycystic ovaries) and primarily biochemical causes (unbalanced hormones) have been identified for the condition (hyperandrogenemia) [1]. Clinical features of polycystic ovary syndrome (PCOS) include hyperandrogenism, which may lead to follicular development suppression, micro cysts in the ovaries, anovulation, and menstruation abnormalities [2].At least 7 percent of all adult women are affected with polycystic ovary syndrome (PCOS) [3], a diverse illness with a variety of causes.About 5 million American women of childbearing age have polycystic ovary syndrome, according to the NIH's Office of Disease Prevention. Polycystic ovary syndrome diagnosis and therapy cost the American healthcare system over $4 billion annually [4].

“Polycystic ovarian syndrome”, is complicated many women of childbearing age suffer from an endocrine disease [5]. Ovarian enlargement and dysfunction, high testosterone levels, insulin resistance, etc., are common symptoms of this condition. Before menopause, PCOS affects around one in ten women, causing some difficulties[6].Although the fundamental factors of PCOS are recognized to bea high “*Luteinizing Hormone* (LH)” to “*Follicle-Stimulating*

*Hormone* (FSH)" proportion and a higher proportion of "*Gonadotropin-Releasing Hormone* (GnRH)", the specific etiology and pathophysiology are not well understood [7]. Statistics show that several both external and internal variables, such as insulin resistance (IR), hyperandrogenism (HA), external conditions, genetics, and epigenetic changes, have a role. Moreover, PCOS increases the danger of developing comorbidities including cardiovascular disease, diabetes, metabolic disturbances, depression, and anxiety [8].

The intrinsic features of PCOS including its clinical heterogeneity, symptom variability across age ranges, and consensus on clinical recommendations are difficult to achieve because of the overlap between instrumental and laboratory clinical standards and physiological conditions, and also the resulting absence of a common and useful threshold for clinical settings.Blood metabolomics, hormone concentrations, and the makeup of the gut microbiomeare all emerging as novel indicators in the study of PCOS phenotypes [9]. Clinical phenotypes may coexist in a single patient and can evolve as the person gains or loses weight. Even while individualized care is still the norm, it may be clinically appropriate to classify phenotypes and then implement therapeutic suggestions.Endometrial and ovarian cancers are more common in women with PCOS, making it all the more essential that precise guidelines be put into place well before these difficulties arise.According to the findings of a large-scale study done across India in 2020, over 16% of women respondents aged 20-29 years had symptoms of polycystic ovarian syndrome. Rising rates of polycystic ovarian syndrome have been linked to changes in diet and physical activity, as seen in Figure 1.

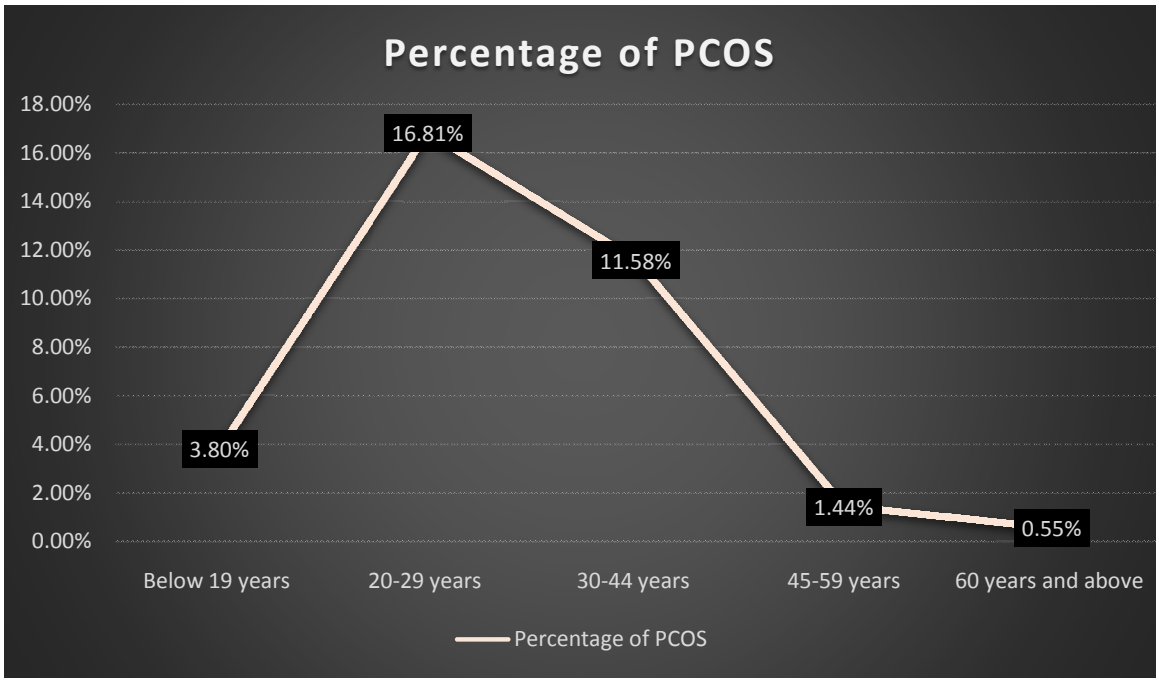


**Figure 1: Polycystic ovarian syndrome concerns among women in India by age group in 2020.**

PCOS is linked to being overweight, having early signs of cardiometabolic disorders like insulin resistance and hyperinsulinemia, and also having a host ofdifficulties in mental health. The frequency of PCOS in women of reproductive age is high reported between 9 and 18 percent,

with the greatest rates seen in Western nations [10]. There has been some variation in these rates, although this is generally because various diagnostic criteria have been used. Anovulation is common in people with PCOS, although PCOS is a normal-gonadotropic, normal-estrogenic syndrome [11]. Clinically or biochemical hyperandrogenism, abnormal menstrual periods, and therefore polycystic ovarian morphology areRotterdam 2003 PCOS diagnostic criteria. Many of the signs used to diagnose PCOS in adult women, like acne, irregular menstruation, and polycystic ovarian morphology (PCOM), might be typical physiological aspects of puberty, making the clinical definition for PCOS in adolescents controversial [12].

## 2. LITERATURE REVIEW

Subeka Abraham Gnanadass et al. stated in their study that to describe PCOS inflammatory markers.A search was conducted using Google Scholar, PubMed, and Science Direct, for articles relating to inflammation and PCOS. Inflammatory cytokines and PCOS were analyzed utilizing original studies, evaluations, and systematic meta-analysis.Inflammatory indicators control ovarian functioning. Ovarian dysfunction may result from hormone imbalances. PCOS pathophysiology involves inflammatory markers. Interactions between inflammatory cytokines in PCOS ovaries suggest inflammation is a major risk factor. Inflammatory indicators regulate the ovary, the study concluded. This study stresses metabolic and inflammatory PCOS indicators. Although PCOS is a metabolic illness, researchers may concentrate on the inflammatory indicators in PCOS to enhance women's health [13].

Shaimaa Aboeldalyl et al. conducted a study to identify whether PCOS-related inflammation is linked to obesity or PCOS itself.The author looked at studies comparing women with PCOS to healthy controls for CRP and other inflammatory indicators by searching the databases, Dynamed Plus, TRIP, Science Direct, PubMed, Embase, Medline, Scopus, and the Cochrane Library. The original study quality and potential bias were assessed using a slightly different version of the Newcastle-Ottawa scale by the author.RevMan was used to determine the 95percent CI and standard deviation (SD) for C-reactive protein (CRP) values.The meta-analysis includes 63 of the 85 studies that were qualified. C-reactive protein levels in the blood were significantly greater in PCOS (n = 4086) women compared to the controls (n = 3120), [SMD] 1.26 and 95% CI 0.99 to 1.53).Evidenced by a meta-analysis of 35 high-quality studies on women who are not overweight, women with PCOS had substantially greater CRP than control (SMD 1.80 and 95% confidence interval [CI] 1.36 to 2.25). Low-grade inflammation is indicated by the fact that PCOS women, regardless of their weight, have considerably higher levels of CRP[14].

M. Rondanelli et al. discussed in their study that PCOS is treated with synthetic hormones and lifestyle adjustments, but they can't be taken continually, particularly by women who want to conceive. Nutraceuticals were studied as PCOS treatments. Berberine reduces insulin resistance and visceral fat tissue (VAT). Due to its qualities, research suggests Berberine might cure PCOS.This study assessed berberine's utility in PCOS control. 5 suitable studies were reviewed. Despite a few investigations, 1078 women were investigated, and the findings are noteworthy. Two authors found that Berberine redistributed adipose tissue, lowered VAT without weight loss, and enhanced insulin sensitivity like metformin. Berberine increased lipid patterns, according to one study. Three scientists showed that Berberine reduced insulin sensitivity in theca cells and ovulation rate each cycle, hence it boosts fertility and lives fertility rates.Premenopausal women who want to become pregnant shouldn't worry about using berberine since it has minimal side effects. In conclusion, Berberine for PCOS is acceptable and

effective, but further research is required to determine a long-term dose [15].Vanessa Machado et al. Updated and assessed all data associating PCOS and PD, as well as a bidirectional connection. SORT was used to assess the evidence's strength and quality. Twelve case controls (876 with PCOS and 48170 healthy controls) met inclusion criteria and had a minimal bias. The incidence of periodontitis (PD) was 28% greaterin women suffering from PCOS, Women with Parkinson's disease had a 46% greater incidence of PCOS.Gum bleeding, pocket depth, and clinical attachment loss were all worse in PCOS women with PD. Underestimation is caused by an undefined periodontal condition. The discovery reveals a bidirectional link between PCOS and Parkinson's disease. PCOS increases the chance of Parkinson's disease by 28%, while PD raises PCOS risk by 46%. PCOS was linked to increasing PD symptoms and inflammation. PCOS and PD may be connected. Additional observational and clinical study investigations with nonsurgical periodontal treatment are needed to establish the incidence of PCOS in PD patients and conversely [16].

## 3. DISCUSSION

Women of childbearing age are disproportionately affected by polycystic ovarian syndrome (PCOS), an endocrine condition. When Stein and Leventhal finally characterized it in 1935 [1], it was a major step forward. According to the recommended revision of diagnostic criteria put out by the PCOS Consensus Workshop Group, PCOS is defined as the co-occurrence of two or moreof these indications and symptoms:

i. Oligo-anovulation.

ii. A clinically or biochemically observable form of hyperandrogenism.

iii. Signs of polycystic ovary syndrome on ultrasound.

To correctly diagnose polycystic ovary syndrome (PCOS), it is necessary to rule out other conditions that have clinical manifestations that are identical to that of PCOS.Among these diseases and disorders areCushing's disease, congenital adrenal hyperplasia, and androgen-secreting cancers.

### *3.1.Physiological Basis:*

The following are the four primary factors that contribute to the physiological basis of PCOS:

i. Abnormalities in the production of gonadotropin-related hormones;

ii. Evidence of insulin resistance developing;

iii. The effects of carrying around excess fat that is already present; and ultimately;

iv. Insulin synthesis and action, steroidogenetic encoding, and other metabolic and hormonal processes shown in Figure 2 are all thought to have a role in polycystic ovarian syndrome (PCOS) [17].

Ovarian follicle formation and subsequent ovulation are dependent on the healthy operation of three organs: the hypothalamus, the pituitary gland, and the ovaries. These three organs work together to regulate reproductive function. Hormone synthesis and release are regulated by the hypothalamic-pituitary-ovarian axis, which employs negative responses. Neurotransmitters in the suprachiasmatic nucleus of the hypothalamus createGnRH is subsequently released into the pituitary portal circulation through to the posterior end of the pituitary gland. A set of neurons working together controls GnRH secretion.

Gonadoliberin is a pulsatile hormone, and the kind of gonadotropin emitted is determined by the rhythmicity of its secretion.In reaction to low-frequency Gonadoliberin pulses, the anterior lobe ofthe pituitary gland promotes the production of follicle-stimulating hormone (FSH), and to high-frequency Gonadoliberin pulses, it produces luteinizing hormone (LH). Corpus luteum luteinization, or the differentiation of granulosa cells into progesterone-producing theca lutein cells, is triggered by LH.

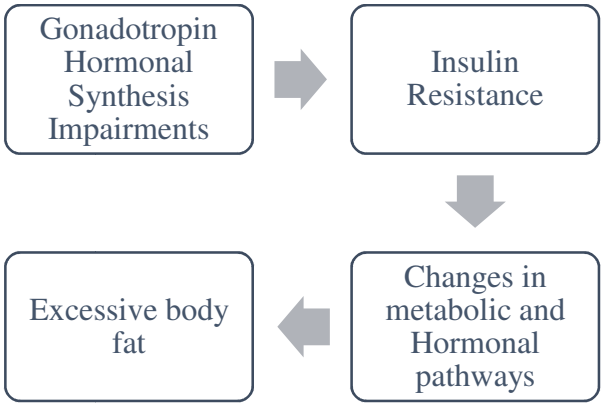


**Figure 2: Displays the Primary pathophysiological mechanisms behind polycystic ovary syndrome (PCOS)-related diseases.**

The granulosa cells in the ovaries respond to FSH by increasing their production of estrogen and maturing into follicles. And it stimulates aromatase, the enzyme that changes the male hormones testosterone and androstenedione into the female hormones estrogen. Abnormally high levels of androgens are produced when luteinizing hormone levels are elevated compared to FSH, as is more often the case in PCOS-afflicted females [18].

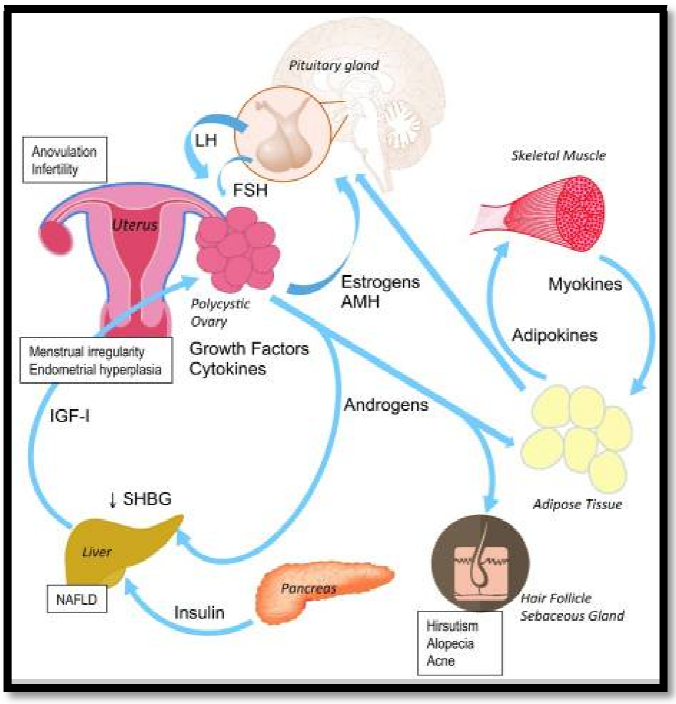


**Figure 3:The diagram below depicts, schematically, several of the pathophysiological mechanisms that are involved in polycystic ovary syndrome**[19]**.**

Because of the lack of progesterone opposition, continuous estrogen synthesisby the ovaries and also subcutaneous fat causes menstrual cycle disruption and raises the probability of endometrial hyperplasia, while androgens are involved in dermatology manifestations. The condition is characterized by metabolic changes, which could be contributed to by adipokines and myokines.Major factors in the development of type 2 diabetes include the contribution of insulin resistance and also the compensatory hyperinsulinemia it causes to the maintenance of anovulation and the development of metabolic disorders. Insulin-like growth factor I, non-alcoholic fatty liver disease,anti-Mullerian hormone, "luteinizing hormone", "follicle-stimulating hormone", and "sex hormone-binding globulin". Recent advances in our understanding of the pathophysiology mechanisms represented in Figure 3 have had a considerable influence on both the therapy of PCOS and the diagnosis of the condition.

*3.2.Risk Factors and Etiology:*

The diverse, symptomatic, and biochemical pattern in PCOS is determined by the interplay of several genetic and environmental variables. Having a relative with PCOS is comparatively rare, the exact nature of the genetic connection between PCOS and its familial history is unclear since its etiology is still a mystery. However, a proper segregation analysis is now impossible due to a lack of phenotypic data. However, recent studies reveal that PCOS runs in families with an autosomal dominant pattern [20].

*3.2.1. External Factors:*

*i. Epigenetic Mechanism:*

Epigenetic modifications to the genome and expression and activity are heritable but do not affect the DNA sequence. These variants result from the incorporation or removal of chemical modifications to DNA or histone. Women with PCOS often have elevated LH activity. Possible connection to PCOS-related issues with follicle growth and hyperandrogenism (HA). The process of steroidogenesis in theca cells is regulated by the LH/chorionic gonadotropin receptor (LHCGR). Increased gene expression and susceptibility to LH result from hypo methylation of these receptors [21].Overexpression of LHCGR on the surface of theca cells has been linked to hypo methylated regions, according to research conducted on individuals with polycystic ovary syndrome (PCOS). Epoxide hydrolase 1 (EPHX1), meanwhile, is a busy enzyme in the process of breaking down aromatic molecules. Enzyme expression is boosted by the hypo methylation of its gene promoter.Another factor in ovarian function is "*Peroxisome Proliferator-Activated Receptor Gamma"* (PPAR-γ).

*ii. Toxicants in the Environment:*

The binding mode of Endocrine-Disrupting chemicals (EDCs) to hormone receptors is not well understood. Nearly all of the things people use daily have electronic display components (EDCs). They mimic the effects of steroid hormones because their molecules include phenols or halogens such as chlorine and bromine. Women with polycystic ovary syndrome have been shown to have a higher serum concentration of EDCs. Susceptibility to polycystic ovary syndrome (PCOS) may be increased by prenatal and ongoing exposure to environmental hormone disruptors (EDCs).Additionally, "Bisphenol A" "(BPA)" is a potent receptor for "Sex Hormone-Binding Globulin" (SHBG), and it could serve as a hold for testosterone, leading to an increase in free testosterone concentration. High levels of androgen have been linked to decreased BPA clearances in the liver since this hormone blocks the enzyme responsible for

breaking down the chemical in the first place, uridine diphosphate-glucuronosyl transferase. The harmful effects of free BPA on the ovaries are exacerbated by this procedure, which leads to a high concentration of dissolved BPA in the blood [22].

*iii. Stress, both physical and emotional:*

There is some evidence that stress contributes to polycystic ovary syndrome, although research is limited. PCOS is associated with negative changes in self-image and psychological well-being, but the exact mechanisms are not well understood. Adipocytes enlarge and multiply in response to prolonged stress. The influence of glucocorticoids on the development of pre-adipocytes is responsible for this phenomenon. Secretion of adipokines, recruitment of immune cells to the stroma, and their subsequent activation are all linked to prolonged psychological stress [23].Under conditions of psychological strain, the "hypothalamic-pituitary-adrenal (HPA)"stress hormone cortisol is produced by the axis. Increases in cortisol cause IR by promoting the formation of visceral fat, glucose production, and the breakdown of fat in the liver and muscle. Plus, cortisol stimulates the liver to produce glucose. Similarly, stress contributes to already elevated insulin levels.Polycystic ovarian syndrome (PCOS) may be influenced by stress in several ways, including changes in anti-mullerian hormone (AMH) and sex hormonal changes.

*3.2.2. Internal factors:*

*iv. Insulin Resistance (IR):*

IR refers to cells not responding adequately to insulin. Patients' levels of adiposity, body fat topography, and androgens did not affect their susceptibility to IR, and vice versa. It is important to note that PCOS women have tissue-selective IR, meaning that although their skeletal muscles, adipose tissue, and liver may become insulin-resistant, their adrenal glands and ovaries will continue to respond normally to insulin.Ovarian theca cells respond to insulin by producing androgens. Activating its receptors on the follicular membrane cells, insulin efficiently increases ovarian follicle development and hormone release. Chorionic gonadotropin has a synergistic impact on ovarian P450c17 and P450scc enzymatic activities, increasing ovarian steroidogenesis.

Furthermore, PCOS is made worse by hyperinsulinemia, which also affects the pituitary gland. When insulin levels are consistently high, the pituitary gland responds by stimulating LH secretion via specific receptors.Enhanced insulin levels cause the size and length of GnRH and LH pulses to expand. Polycystic ovarian syndrome may be affected indirectly by hyperinsulinemia due to the increased activation of GnRH neurons.In addition, the BMI does not affect the degree to which IR lowers omentin levels in a patient (BMI). Furthermore, mononuclear cells secreting TNF- in response to hyperglycemia might contribute to the inflammatory cascade (MNCs)[24].

*v. Hyperandrogenism:*

Hyperandrogenism (HA) often causes a decrease in SHBG, which then increases free testosterone. Higher plasma testosterone levels, which may bePCOS women have been shown to have elevated levels of androgens, which may produce estrone when stored fat is broken down. When follicle-stimulating hormone (FSH) levels are low compared to LH levels, ovulatory dysfunction can develop. Raise in anti-mullerian hormone (AMH) are another way in which HA might interfere with ovulation and follicle growth. Moreover, HA decreases IGF-II in follicular fluid, which is inversely correlated with androgen levels. Follicle diameters and estradiol levels in follicular fluid are strongly correlated with insulin-like growth factor II [25].It's also worth

noting that research on PCOS women has shown that their adipose tissue is similar to men's, suggesting that HA may ameliorate adipose tissue malfunction. In addition, adipocyte enlargement and subsequent harm to adipokine secretion are both caused by HA.

*vi. Obesity:*

Three-to-six percent of women with PCOS have a BMI of 30 or above. Even here, though, the cut-off point might be debated and revised in light of regional and societal factors. It is common for women who are obese and have PCOS to have a waist-hip ratio (WHR) over the normal range of 0.82 to 0.85, indicating that they are viscerally obese [26].Obesity is associated with a worsening of the clinical picture in women with PCOS, both metabolically and reproductively.Recent studies have connected PCOS patients' dysregulation of lipolysis to an increase in visceral fat lipolysis, which in turn increasesfats that aren't attached to anything and are instead discharged into the portal vein. Hepatic gluconeogenesis is controlled by free fatty acid levels in the portal vein. An increase in lipolysis in visceral fat has been suggested as the process through which glucose intolerance occurs.Inflammation and endoplasmic reticulum (ER) oxidative stress is also triggered by the buildup of lipids in non-adipose tissues, a process known as lipotoxicity. Insulin receptor serine phosphorylation by diacylglycerol is the mechanism bywherein elevated levels of muscle and liver fat create insulin resistance. Lipid buildup in the liver also lowers HNF-4 levels, which in turn decreases sex hormone-binding globulin (SHBG) synthesis.

*vii. Hirsutism:*

Symptoms of hyperandrogenism include this. Factors like culture and ethnicity influence how seriously people take the occurrence of hirsutism. The Ferriman–Gallwey score is widely used inclinical assessment, and a score of 8 or higher is regarded as diagnostic. The reality remains, nevertheless, that evaluations are very arbitrary. There is a much higher rate of hirsutism in Caucasian women (60-70%) than in Japanese women (30%). Furthermore, hyperinsulinism in PCOS patientsincreases the body's sensitivity to the hormone ACTH, which in turn causes more adrenal androgens to be secreted.

viii. *Infertility:*

Women with PCOS often struggle to conceive because of this condition, which is mostly caused by persistent anovulation. The incidence of polycystic ovarian syndrome (PCO) on ultrasound was found to be greater in individuals who were normal-ovulatory but subfertile and had several miscarriages. Although the an exact cause-and-effect relationshipthere is no known link between polycystic ovarian syndrome (PCOS) and miscarriage, it is believed to entail processes related to steroidogenesis, folliculogenesis, oocyte maturation, and decreased endometrial receptivity.Consistently high estrogen levels and the inability to ovulate may lead tothe onset of endometrial hyperplasia and cancer and also endometrial hyperplasia.Women who suffer from polycystic ovary syndrome have an increased likelihood of getting endometrial hyperplasia in addition to endometrial cancer, and this is well established. Endometrial cancer is more common in women who are overweight or who have type 2 diabetes;there is an elevated risk of this condition in women who have polycystic ovary syndrome.

*3.3.Pharmacological Treatments:*

All women, regardless of weight, complaints, or anything else, should be provided healthy lifestyle recommendations after a PCOS diagnosis. This is because diet and exercise alone may

effectively treat mild to moderate instances in most women.To a large extent, however, the therapy would depend on the patient's preferences and the state of those around them. Patients who do not want to get pregnant and who have irregular menstrual cycles may benefit from combination oral contraceptives (COCs) or progestins.Orally contraceptives like Yasmin®, and Yaz®, as well as other medicines may exhibit anti-androgenic influences and on the other side, potential outcomes in a drop in testosterone production, so the doctor can choose the appropriate contraceptive pill by considering factors other than monthly irregularities.

Due to its insulin-sensitizing properties, the biguanide metformin is often used in concert withCOCs for PCOS women to get their ovulation cycles back to normal. Short-term use of metformin has also been associated with decreased androgenic activity in men. Persons who are just concerned with the dermatological symptoms of hyperandrogenism may benefit more from including 5-alpha reductases and aldosterone receptor antagonists (like spironolactone) (such as finasteride). Drugs like clomiphene citrate and aromatase inhibitors, which induce ovulation, are now among the many alternatives accessible to infertile individuals [27].Metformin's side effects of vomiting and diarrhea in the early stages of treatment are another reason why some patients stop taking the drug. Hyperkalemia can occur in patients taking spironolactone, a commonly prescribed medication for androgen-related side effects. Furthermore, it is recommended to research the possibility of adverse reactions or restrictions in reputable medication research or to inquire about the patient's condition or responses before medication.

## 4. CONCLUSION

Indicators of polycystic ovarian syndrome (PCOS) phenotype and their association to extra ovarian variables including obesity, insulin resistance, and the environment are the focus of the ongoing scientific investigation. The pathogenesis of polycystic ovarian syndrome (PCOS) from the polycystic ovary (PCO) is poorly understood. A true evaluation of PCOS requires knowledge of its etiology and natural course.Examining the causes and consequences of polycystic ovary syndrome, longitudinal studies are necessary.In terms of repurposing, other licensed medications might have positive benefits on polycystic ovary syndrome (PCOS). Since these drugs' full profiles are accessible and their effectiveness and safety have been extensively explored, the road to discovering new therapies is smoother. Though much has been learned and studied, there is still a great deal left to learn about the pathophysiology and, therefore, the mechanism that has to be targeted by the right medicine.

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# CHAPTER 16

# POTENTIAL IMPACT OF VERTICAL FARMING SYSTEMS ON THE ENVIRONMENT

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**ABSTRACT:**

Vertical Farming Systems (VFS) are engineering solutions that have been created to boost crop output per acre of land by relocating agricultural activities vertically. Even while there is promising research showing that VFS may increase crop yields, it is also quite energy-intensive due to the requirement to regulate the lighting, heating/cooling, and ventilation systems. In this study, the author explores the issues of integrating renewable energy into VFS, stressing how light spectrum, intensity, and day length may be modified to affect crop quality. In addition, the author also highlights how the difficulties of integrating renewable energy into VFS could be overcome. The hypothesis is that the knowledge gained from studying the photobiology of plants might be put to use to improve the overall energy efficiency of this rapidly developing industry. Vertical farms have a bright future because of recent developments in greenhouse technology including hydroponics, aeroponics, and aquaponics.

**KEYWORDS:**

Agriculture, Environment, Vertical Farming Systems (VFS).

## 1. INTRODUCTION

Plants are grown at vertical levels in what is called "Vertical Farming." The method of raising plants inside is known as indoor farming in soilless soil and controlled environments (including but not limited to light and temperature) outside of the natural environment. It employs soil-less techniques including Aquaponics, Aeroponics, and Hydroponics to maximize output in confined settings. Water and pesticide use may be reduced with vertical farming. The indoor growing environment protects the crops from the vagaries of weather and allows for consistent harvests throughout the year. This method may be used to cultivate lettuce, tomatoes, and other greens [1].

Japan is not just one of the first adopters of vertical farming but also now dominates the international industry. For example, every day, Spread, a Japanese corporation, produces 30,000 heads of lettuce.By 2050, the world's population is predicted to reach 9 billion, with a sizable percentage living in urban areas. This will need a 70% increase in agricultural production. Migration from rural areas toward urban centers is expected to hasten the development of urban areas and the abandonment of agricultural land in suburban and inner-city settings [2].As a result of intensified agricultural land, land use, and climate change is degrading and losing fertility at an alarming rate, making it both a limited resource and a risk to biodiversity. For these reasons, it's crucial that develop new strategies to maximize farmland output [3].

Producing food vertically has the potential to improve water and energy efficiency, boost the economy, lessen pollution, create jobs, revitalize ecosystems, and increase the availability of nutritious food. In a well-managed environment, pests, the nitrogen cycle, crop rotation, polluted water runoff, pesticides, and dust are all mitigated, protecting crops from damage [4].By proactively tackling the issue of hunger among the world's growing urban population, vertical farming has the potential to safeguard the long-term viability of modern cities.Advanced technology and intense agricultural techniques are also used in vertical farms, which together allow for tenfold greater yields.Many parameters, Light intensity, light hue, space temperatures, crop and root, CO2 levels, soil, water, and even air humidity are all factors to consider, were the subject of fine-tuning and modification by researchers seeking to improve the art of indoor farming. Furthermore, the use of vertical farming may help stimulate regional economies. Converting vacant urban buildings into vertical farms is a viable solution to the lack of access to nutritious food in food deserts [5].The ever-increasing need for food is placing further pressure on the resources of the Earth; therefore, businesspeople are reevaluatingthe principles of agriculture to establish a new, sustainable food system. As can be shown in Figure 1, several novel approaches have acknowledged indoor farming in cities as a viable alternative to conventional farming to perhaps alter global food systems.

**Figure 1: Shows the Creating Pesticide-Free Indoor Farms in Cities for Year-Round Food [6].**

Specifically, the research on the topic distinguishes between three distinct vertical farming methods. The first method includes the construction of massive, multi-story towers outfitted with many layers of planters and, most often, a series of artificial lights. This kind of urban farm, often of modest size, is proliferating in cities all over the world. Across the country, this method has been used in both new and repurposed buildings, particularly former warehouses put to use in the agricultural sector. Rooftop farming is the second kind of vertical farming, and it may be found on the top of both new and ancient buildings, homes and businesses, eateries, and grocery stores. Creative multi-story skyscrapers are the third type of vertical farmer [7].

## 2. LITERATURE REVIEW

Solomon Tibebu et al. stated in their study the pathogen-removal capacity of progressive hydroponics using Duranta erecta. Series-connected experimental and control devices. Each cascaded unit has three bioreactors. Two experimental units utilized plants and medium to treat wastewater, whereas two control units just used media.The experiment ran continuously for 1, 3, 5, and 7 days. Input and effluent quality was used to assess the hydroponic system's effectiveness. At optimal hydraulic retention time (7 days), experimental units 1 and 2 removed 98.7% of heterotrophic bacteria, 96.2% of total coliform, and 92.9% of fecal coliform, correspondingly.The author concluded that the hydroponic treatment method cultivated with Duranta erecta may remove pathogens from residential wastewater in impoverished nations like Ethiopia.

Cagri Tolga et al. discussed in their study Author used MCDM techniques to assess the viability of three different vertical farming models. Although there are now commercial vertical farms up and running in several different nations, this field is still relatively new, and obtaining reliable data is challenging. To resolve the resulting uncertainties, we relied primarily on fuzzy logic. Both the MACBETH (Measuring Attractiveness by a Categorical Based Evaluation Technique) and the Weighted Euclidean Distance Based Approximation (WEDBA) are used for this purpose [8].

G W Michael et al. conducted a study on automated vertical hydroponics cultivation monitoring is proposed. This study intends to build an automated method to monitor vertical farming nutrient levels. The rectangular PVC's nutrition solution's EC, pH, liquid level, and water temperature are monitored. Bok Choy was grown hydroponically instead of in dirt. The Arduino Mega will send and analyze the data, and also the ESP8266 NodeMCU would upload it to Ubidots Cloud. The mechanism controls nutrient levels and solution flow into each vegetable layer. The deployed technology is anticipated to cut water and energy usage and monitor plant development without a human [9].

Reynabel Ladigohon et al. evaluated in their study that the use of aquaponics has quickly become a staple in today's agricultural industry. There have been reports in the past that certain farmers regularly construct an artificial ecosystem consisting ofland, sea, vegetation, and aquatic life.However, in recent times, aquaponics has emerged as a way to connect aquaculture with hydroponic systems, enhancing hydroponics and aquaculture via the use of android graphs to track temperatures, turbidity, and pH. The researcher here created an Android app to monitor plant growth and water use. A servo motor is being utilized for the fish feeder while three sensors (temperature, turbidity, and ph) obtain information. The study's functionality, reliability, and usefulness are evaluated using a waterfall model or a survey-style research technique [10].

## 3. DISCUSSION

A wide range of individuals from all walks of life has been taking part in this grassroots uprising to preserve mankind from a food-depleted, ultra-urbanized future. Recent years have seen significant development in the areas of robotics, aeroponics, aquaponics, and hydroponics, all of which have found great success due to the popular acceptance of the notion of vertical farming. Groups dedicated to social and environmental justice have come out in support of the vertical farm. The need for locally grown food has also garnered the backing of for-profit businesses. Furthermore, governments have begun sponsoring these initiatives as a means to improve domestic food security.Countries as diverse as South Korea, Japan, China, Germany, the United

Arab Emirates, China, France, India, Sweden, Singapore, and the United States (U.S.) are all working together to learn more about vertical farming. They have often said that they believe this idea is crucial to the continued success of their towns[11].

*3.1.Types of Vertical Farming:*

*3.1.1. Building Based Farms:*

Vertical farming is a method that often makes use of repurposed abandoned structures, such as "The Facility," a farm in Chicago that was once a meatpacking plant before it transformed. On the other hand, there are occasions when new buildings are created to accommodate vertical farming systems.

*3.1.2. Shipping-container vertical farms:*

Vertical farms made out of shipping containers are becoming an increasingly popular choice. These vertical farms make use of shipping containers that are 40 feet in length and are often used in the transport of commodities all over the globe. Several businesses are now in the process of transforming old shipping containers into self-contained vertical farms. These farms will be equipped with LED lighting, drip-irrigation devices, and vertically stacked shelves for beginning and nurturing a range of plants. Users can monitor all of the systems in these self-contained units remotely using a computer or a smartphone since the development management systems inside these units are computer-managed [12].

*3.1.3. Deep farms:*

An underground or "deep" farm is a kind of vertical farm that makes use of abandoned mine shafts or tunnels. These structures were formerly used for mining. Because the humidity and temperature beneath are often moderate and stable, deep farms have a lower need for the amount of energy used for heating. The exploitation of adjacent groundwater by deep farms is another method for lowering the cost of the provision of water.Saffa Riffat, who works as the Sustainable Energy Professor at the University of Nottingham, claims that a deeper farm may yield seven to nine times as much food as a conventional farm on the same amount of land, even though the expenses of operating a deep farm are lower. These subsurface farms, when combined with automatic cropping systems, have the potential to be completely self-sufficient.

*3.2.High-Tech Indoor Farming:*

*3.2.1. Hydroponics:*

Hydroponics refers to the technique of growing plants in a liquid nutrient solution, which may be used with or without a growth medium. Expansive clay, coir, perlite, vermiculite, broken bricks, polystyrene packing peanuts, and wood fiber are all examples of common media. Hydroponics is now widely acknowledged as a practical technique for cultivating a wide variety of plants, including edible ones like tomatoes, lettuce, cucumber, and pepper, and also decorative ones like herbs, roses, freesia, and foliage plants.

Hydroponics is a way of producing food that does not need the use of soil by instead growing it in mineral fertilizer solutions in water. Hydroponically grown plants can be cultivated in nutrient-rich water with or without the aid of mechanically maintained inert material like gravel or sand. The English term "water performing labor" or "water works" is derived from the Greek phrases hydro and ponos, which mean "water doing work" or "water works." Plants grown in

water as a growing medium are not a novel concept; however, the use of hydroponics in the agriculture-based economy is a relatively new development [13].

There has been a rise in the usage of hydroponics in commercial farming. This method offers some benefits over the more conventional method of growing plants in soil. One of the most significant benefits of using this approach is that it has the potential to eradicate or, at the least, significantly cut down on issues with cultivation that is connected to the soil (that is, soil organisms like insects, fungi, and bacteria). The hydroponic technique eliminates the need for laborious tasks such as weeding, kneeling, tilling, and cleaning up soil. This results in much-reduced upkeep requirements. Hydroponics also enables a less labor-intensive approach to handle bigger regions of production, which is another advantage of using this technology [14].

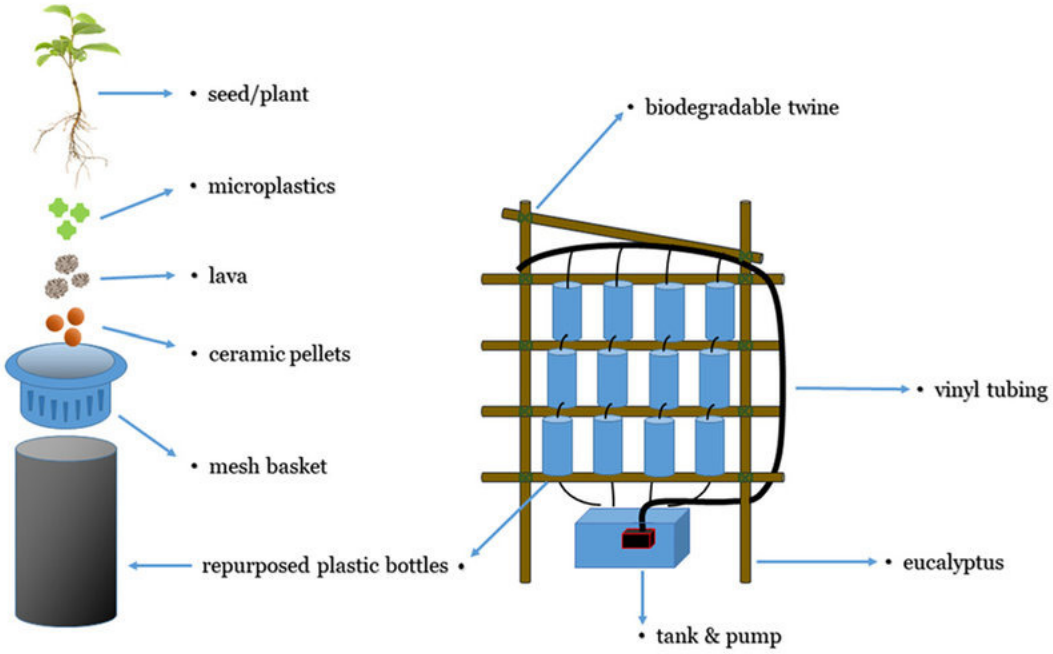


**Figure 1:Diagrammatic representation and enlarged view of the vertical hydroponic system** [15]**.**

Since no animal waste is required for this method, it might also be more hygienic. In addition, hydroponic technology makes it simpler to regulate the concentration of nutrients and the acidity of the medium.Soil-fixed micronutrients are only available to plants under certain conditions, as described by Ebba Hedenblad and Marika Olsson: "In soil, diverse parameters, like temperatures, oxygen concentration, moisture, and microbes." This is because, through processes like erosion and mineralization, nutrients are being washed away into the water. Hydroponics allows for the provision of the optimal mix of nutrients to all plants, which may lead to more uniformity and higher yields [16].

### *3.2.2. Ultrasonic Foggers:*

Researchers have developed ultrasonic foggers to save costs and improve efficiency. They want to use them in a variety of horticultural applications, mainly hydroponics, to give several advantages such as [17]:

i. By providing the top roots with nutrient-rich fogs and allowing them to permeate deeply into the root tissues, we may prevent the roots from drying up, becoming malnourished, and rotting.

ii. Growing tiny root hairs significantly increases a plant's ability to absorb water, nutrients, and exchange carbon dioxide for oxygen.

iii. Up to a fifty percent reduction in the amount of water and fertilizers used.

iv. Minimizing the need for cumbersome and expensive growth media.

v. Minimal footprint due to the reservoir's separation from the units.

vi. When ultrasonic foggers are included in hydroponic systems, they become quite similar to aeroponics systems.

There are some reservations about the hydroponic approach since all of the plant nutrients are dissolved within the water and the system depends significantly on chemical inputs. A hydroponic system uses chemical formulations to deliver mineral element concentrations.Non-circulating water culture is essential to the Nutrient Film Technique (NFT) and other parts of liquid hydroponic systems, while innovative recirculation technologies could be incorporated into NFT approaches. Additionally, there are concerns that the lack of oxygen in the plant's roots makes the final product tasteless. The aeroponic approach helps to mitigate some of these drawbacks [18].

### *3.2.3. Aeroponics:*

As of right now, the Aeroponics System is at the cutting edge of hydroponic gardening. A timer controls the operation of the food pump. A short cycle timer that runs the pump for a few seconds every few minutes is essential for the aeroponics system. Because aeroponics doesn't need soil or other growth media, no special pots or other containers are needed. Water is not utilized in this system, but rather as a mist or nutritional solution.The term "aeroponics" refers to a method of cultivating plants in which the roots are continually or intermittently misted with a nutrient solution; this method may be thought of as a variation on hydroponics, in which the roots of plants are cultured in a nutrient solution [19].

The plant containers are stacked in such a way that the tops and bottoms are heldin the open air, where the plant's top may expand upward and its roots can extend out horizontally. An ultrafine spray of nutrient-rich water is used to water and nourish plants. The system's closed nature allows for complete recycling of the nutrient mix, resulting in substantial water savings. Therefore, areas with a water shortage will benefit greatly from this technique. The absence of the need for fertilizers or pesticides is another perk of the aeroponics approach. In addition, studies have shown that this technique of high-density planting facilitates harvesting and produces greater yields.Despite its obvious benefits, aeroponics has not been widely adopted due to a lack of understanding of the system's operation conditions and also the complexity of keeping the system running.

### *3.2.4. Aquaponics:*

In a closed-loop recirculating system called aquaponics, both hydroponics (developing plants in water without soil) and aquaculture are combined (fish farming). In aquaponics, the waste

products of aquatic organisms are used to fertilize plants in a mutually beneficial cycle. In exchange, the fish are provided with clean water thanks to the vegetables. Some of the most important sources of nutrition for plants are microbes and fish waste. These beneficial bacteria cluster in the cracks between plant roots, where they process fish waste and sediments into nutrients the plants can use. The result is a harmonious union between aquaculture and farming.

Aquaponics is a bio-system that combines hydroponic cultivation of plants with recirculating aquaculture (also called fish farming). The goal of aquaponics is to establish mutually beneficial connections between the fish and also the plants. This symbiosis is achieved by the process of "fertigating" hydroponic production platforms with the nutrient-rich waste that is collected from fish tanks. In a reversal of roles, the hydroponic beds may also perform the role of biofilters, removing gases, acids, and chemicals from the water. Some examples of these contaminants are ammonia, nitrates, and phosphates. Concurrently, the gravel beds serve as homes for nitrification, which not only filters water but also contributes to the cycle of nutrients in the environment. This means that the water in the fish tanks may be reused once it has been filtered. Wetland pools stocked with fish like perch and tilapia, whose waste was used to fertilize nearby plants, were the basis of the novel aquaponics systems and remedied the factors that motivated hydroponics as well as aquaculture, as discussed above and shown in Figure 2.

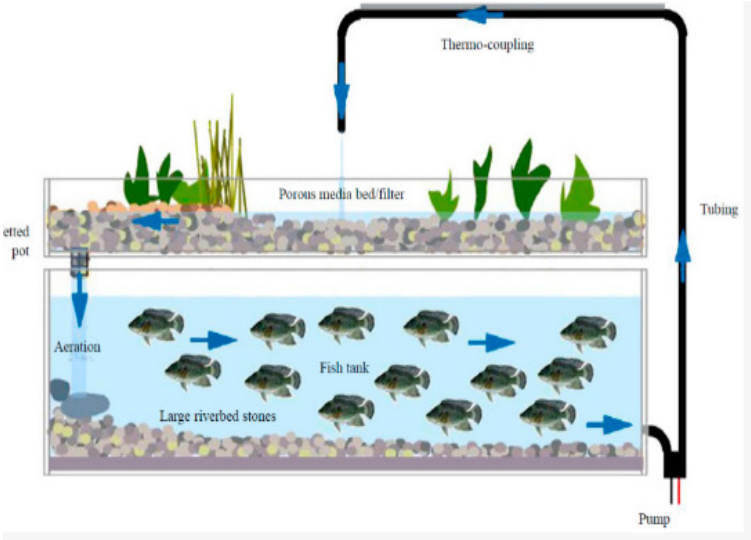


**Figure 2: Shows The Fundamentals of An Aquaponic Setup** [20]**.**

Life cycle assessment (LCA) is a strong tool for assessing the environmental implications of agricultural production systems. Water usage, chemical pollution, and global warming GHGs are all instances of environmental impacts. The author will concentrate on electrical energy use, which is normally evaluated and regulated using a "carbon accounting" approach.An activity's carbon effect is calculated and added up throughout a product's life cycle (in a unit such as kilograms of carbon dioxide equivalent) before being normalized to a system output (for example, kg of sellable lettuce). These might be used to provide a common measure for a vertical farm, such as CO2eq per kilogram of marketable output.By using the same inputs and outputs, several complex systems may have their effects compared to using a life cycle assessment (LCA). This covers a broad variety of indoor farming techniques that have a comparable

influence on the natural environment despite their varied input materials, methods, results, and modes of sale and transportation.

By tackling the problem of food insecurity, vertical farming is an example of a forward-thinking strategy that may help cities remain habitable for the long term. The rising price of oil, water scarcity, and the loss of other natural crops are driving up food prices, which are already a problem for the urban population. Current food distribution systems in metropolitan areas have economic and environmental impacts, like the wasteful habit of carrying food across long distances.Changes in temperature, water availability, and light intensity may negatively impact harvests in traditional farming, but these elements are less of a concern in controlled indoor environments. Produce yields are typically reduced by these conditions; for example, droughts devastate crops throughout the globe every year. Because of the dangers posed by climate change to our urban areas, the vertical farm will be crucial to our ability to ensure food safety.

### *3.3.Breeding through Selection Offers Opportunities to Optimize Crops for VFS:*

Selective breeding has been used in many cases of plant domestication throughout history to enhance the prevalence of desirable characteristics including larger fruit/seed size and decreased levels of bitter-tasting compounds. In addition to these gastronomic enhancements, breeding frequently helps to farm by promoting a reduction of seed dormancy, synchronizing blooming time, and decreasing susceptibility to photoperiod. This latter quality is especially important when cultivating crops at different latitudes from where they were originally developed [21].

Both light and temperature change seasonally in the natural world. These frequent environmental cues have prompted the creation of intricate sensory networks that allow plants to react to both daily and seasonal variations. Communities are better equipped to adapt to changing weather systems and climate when there is a healthy amount of natural variety throughout the population. During domestication, the gene encoding circadian function was selected in soybeans, tomatoes, sugar beets, rice, and barley since these plants assess the photoperiod by relating signals originating from the circadian system to the duration of the day [22].

## 4. CONCLUSION

In terms of urban food security, the vertical farm might play a crucial role.Hydroponics, aeroponics, and aquaponics are examples of new high-tech production techniques, that are posing a threat to soil-based farming. The development of greenhouse and auxiliary technologies includes automated multi-racking systems, recycling systems, and hydroponics.Environmental, social, and economic sustainability all point to the many ways in which vertical farming outperforms traditional agricultural methods. Eventually, completely automated vertical farms may be a possibility. Theoretically, the city's inhabitants might be fed by incorporating vertical farms into the urban landscape. Still, innovations that boost project size are required to provide optimal commercial viability and return on investment (ROI).Moreover, future studies should investigate the problem of modern equipment for vertical farming being too expensive for underdeveloped nations. To make vertical farm projects possible in these nations, researchers should create, improve, and further expand indigenous agricultural practices.

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# CHAPTER 17

# A STUDY ON ADVANCED TISSUE ENGINEERING USING 3D PRINTING

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**ABSTRACT:**

The concept of employing engineering methods to replace or repair tissue is referred to as "Tissue Engineering" for bodily tissues and organs that have been injured. Tissue engineers utilize Three-Dimensional (3D) matrices to grow cells into tissues that look and function like those found in the body normally. The inability to promote cell development and build new tissue is attributable in large part to the fact that in conventional scaffold construction the scaffold's architecture, pore geometry, porosity, or interconnectivity cannot be manipulated using these procedures. Traditional manufacturing processes have their drawbacks, but they may be surmounted by 3D printing technology. In this study, the author takes a look at how various strategies have helped push 3D printing forward by coming up with exciting new ways to fabricate tissue engineering scaffolds. The study will also cover the use of both man-made and organic substances in 3D printing-enabled tissue creation. Future 3D nano scaffold development must concentrate on enhancing manufacturing accuracy, discovering novel biomaterials, and studying the impact of biomolecules on cell attachment, growth, and differentiation.

**KEYWORDS:**

Three-Dimensional (3D), Tissue Engineering, Printing, Scaffolds.

## 1. INTRODUCTION

Using 3D printing to rapidly and reliably build functional tissue in vitro is an exciting prospect for the field of tissue engineering. Specific micro-architectures must be in place to give the mechanical and structural supports, enough nutrition, the appropriate cell types, and also the capacity for active remodeling when an implanted macro-tissue has been established. Biomaterials, printing processes, and a cell delivery strategy are all proposed and all of these necessary parts may be easily made using 3D printing [1].When combined with cell transport methods, biomaterials, and printing techniques, 3D printing offers a practical method for fabricating all of these critical parts. Scaffold-based designs or scaffold-less designs strive to eliminate stages and provide structure and cells concurrently, while earlier solutions entailed printing complicated scaffolds accompanied by a cell seeding procedure [2].

Tissue engineering involves the replacement of damaged tissue or organs with newly grown ones via the use of various engineering techniques to restore the original function of the tissue. Cells, biomolecules, and scaffolds are the three main building blocks of tissue engineering. Scaffolds provide a synthetic framework for tissue development in three dimensions (3D).Biomolecules in the growth media stimulate the proliferation and differentiation of cells planted onto the scaffold. Success in tissue regeneration requires the correct combination of these three

factors.Biocompatibility, in addition to the right porous structure, interconnectedness, and mechanical qualities, is essential for scaffolds that are intended to promote tissue regeneration. Ideally, the body would absorb the scaffold, eliminating the need for removal surgery.

The ideal 3D printed construct for tissue engineering should be a structure that guides cell development, allowing cells to move and multiply to build a functioning tissue. Although genetics may influence the directions a cell takes, studying this phenomenon has been time-consuming and difficult.Tissue engineering for regenerative treatments ultimately aims to create functioning tissue and organs and to substitute organs entirely. Seeding cells onto scaffolds, which could subsequently drive cellular proliferation into 3D functional tissue, is the most frequent tissue engineering approach [3].Developments in 3D printing in recent years may be traced back to the human body's remarkable capacity for regeneration. About 31 million Americans reportedly have some kind of physical defect. Injuries and degeneration procedures of varying etiology account for a growing fraction of the world's population each year [4]. To repair severe flaws, cells need help growing [5].

Several factors, including growth hormone availability and the defective tissue's capacity to function, restrict the extent to which the human body can regenerate itself. Conventional medical treatment included eitherfor a long time, the only options for treating such cases were either autologous transplantation (less frequently, autologous transplantation) or the implantation of an endoprosthesis which replicated the functioning of the damaged organ.The area of tissue engineering is one of the more recent human endeavors. Conceptually, it bridges the gaps between the fields of biology, medicine, materials science, and mechanics.Tissue engineers work to find ways to repair injured organs and tissues, particularly those that were previously thought to be irreparable. Everyday clinical practice serves as instances of these kinds of tissue and organ damage. Most often, they are severe breakdowns in the skin, bones, or nerves.

There are many different kinds of 3D printing techniques available today, technology including selective laser sintering, inkjet printing, electrospinning, and Stereolithography [6]. These methods have been extensively employed in investigations of tissue regeneration, including nerve cells, muscles, skin, tendons, ligaments, bones, and cartilage, and also organ regeneration, including the trachea, liver, kidney, and heart. Submicron accuracy may be achieved usingTwo-photon polymerization (2PP) and electrospinning. As a result, this study would discuss the current state of scaffold manufacturing utilizing various 3D printing methods.

## 2. LITERATURE REVIEW

Koroleva et al. stated in their study created 3D fibrin scaffolds with precisely adjustable pore diameters and connectivity using a mixture of 2PP and micro molding. The authors created master structures using 2PP and then regenerated them with a two-step replication procedure. The fibrin scaffolds that were created were very porous and linked. Endothelial cells cultured on scaffolds exhibited directed lining and cell expansion inside while endothelial cells contained in fibrin gel blocks exhibited disordered and unequal dispersion despite the repeated pore network. These results demonstrate that micro molding may be an effective complement to 2PP and may produce sophisticated 3D structures for tissue regeneration [7].

Hong Song et al. conducted a study that Breast lesion diagnosis and quantitative analysis benefit from tissue segmentation and visualization. In this study, the author presents a 3D segmentation technique for breast MR images using Kernel-based Fuzzy C-Means (KFCM). Furthermore, a novel model of the transfer function is used in combination with an enhanced volume rendering

technique to bring about the desired 3D breast image. There seems to be a fair amount of consistency in the visual displays of experimental data [8].

Kanchan Maji et al. discussed in their study that Sol-gel produced 20–30 nm bioactive glass nanoparticles (58S). Bioglass scaffolds with Freeze-dried chitosan and gelatin matrices with 10-30% bioglass at 40% solids loading. Cross-linking samples using glutaraldehyde increased their mechanical strength. The scaffolds have >80percent porosity and 100-300 micron pores. The scaffold's expansion and breakdown investigations indicated hydrophilic nature and biodegradability. MTT experiment and RUNX-2 expression showed that GCB 30 scaffold promoted mesenchymal stem cell adhesion, growth, and development. 58S bioglass nanoparticles improved cell adhesion, growth, and differentiatingcompared to GCB 0 in the GCB 30 scaffold. The research demonstrated that composite scaffolds can regenerate bone cells [9].

Qi Zhang et al. evaluated in their study, that strontium (Sr)-containing electrospun nanofibers may considerably stimulate bone regeneration and repair by mediating osteolysis and osteogenesis, making them a potential bioactive material for BTERM. Here, the author provides a brief overview of the study on Sr-containing electrospun nanofibers' effects on stem cells, osteoblasts, and osteoclasts in bone tissue engineering and regeneration models. The issues that need to be resolved and the opportunities that lie ahead for Sr-containing electrospun nanofibers in BTERM are also mentioned. The goal of this study was to provide a comprehensive look at Sr-containing nanofibers for BTERM in the hopes that it would motivate readers to go further into the topic and speed up their translation from the lab to the clinic [10].

## 3. DISCUSSION

Humans now live in a technologically and digitally advanced age. There is almost no way that technology and software won't continue to develop and improve. In today's rapidly evolving world, the healthcare industry is making great strides to incorporate cutting-edge technology for the benefit of patients and to explore new, complex terrain. Constant technology innovation provides us with useful tools that improve upon or replace older methods while also making them more user-friendly. Incredibly, this cutting-edge technology can be used to increase industrial output [11].The technology is a marvel because it combines the fabrication science field with different building procedures to sequentially produce different materials of interest (inks) in a wide variety of shapes and forms. It is a basic layout based on fast prototyping and Additive Manufacturing (AM).

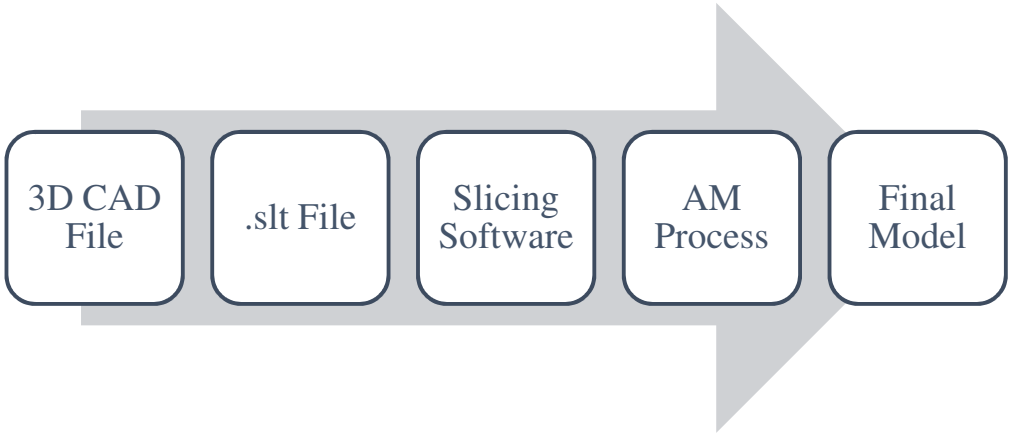


**Figure 1: Displays the Additive Manufacturing's (AM) Conceptual Blueprint.**

The development of contemporary civilization may be traced back to the industrial revolution triggered by traditional production methods. However, these methods have serious weaknesses that must be addressed by adopting new strategies.The term "additive manufacturing" (AM) describes a set of relatively new techniques for creating physical things by layering their cross sections. This action initiates the use of Computer-Aided Design (CAD) software, short for computer-aided design, to generate a three-dimensional model of the required component. The submitted model is sliced into many films using cutting-edge scientific software, which then generates the file readable by AM machines. This is how the machine creates the focus of attention in Figure 1: it imbricates the inks to make the shape [12].

*3.1.The Role of 3D Nanoprinting in Tissue Engineering:*

*3.1.1. 3D Printing Using Two-Photon Absorption, or 2PA:*

It wasn't until the 1980s that Kodama et al. came up with the idea for Stereolithography (SL3D Systems, Incorporated introduced the world to the first SL system for general sale. Laser sintering (SL) entailsUV lasers being used to harden liquid photopolymers by irradiating their surfaces with ultraviolet light.Overlapping UV laser lines that were scanned together hardened the area between them. Subsequently, these cross-sectional areas are added together to make the final 3D shape. Similar to Stereolithography (SL), Microstereolithography (MSTL) uses a laser to create three-dimensional models, however, the laser beam in MSTL is much narrower (only a few micrometers in width to optical elements) [13].Automation of both the design and production processes via the use of computers allows for exact regulation of the building's internal architecture.Based on these features, when it comes to the development of efficient scaffolds for tissue engineering, 2PP is a material with a lot of untapped promise. The advent of photodegradable polymers has made the use of a two-photon corrosion process and an ablation method possible with submicron accuracy has been achieved by the manipulation of a two-photon pulse laser.

*3.1.2. Using Scaffolds in Tissue Engineering:*

Daily, 13 individuals lose their lives because of the lack of availability of a donor organ [14]. Furthermore, there is the troublesome issue of tissue incompatibility. In this case, tissue engineering may provide some novel scaffold construction approaches in which the problem of tissue incompatibility may be readily circumvented. The plan is to use the patient's cells to create an organ that will work in the recipient. However, due to the various aspects involved in the organism's physiology, such as the need to culture a wide variety of cells, this may be an extremely difficult procedure.Scaffolds made of TE provide a foundation for cell proliferation, differentiation, and the development of new tissue during tissue regeneration. Therefore, the design and morphology of the materials, together with their chemical and physical characteristics, are essential for cell survival and proliferation. In certain cases, reconstructing many kinds of neighboring tissue including bone, gland, muscle, artery, ligament, nerve, and cartilage is necessary for a successful restoration of the abnormalities [15].

i. *Strategies for Tissue Engineering (TE):*

In TE, tissue scaffolds are employed in two main ways to correct tissue deficiencies. Each procedure involves first seeding the manufacturedcells added to scaffolding (this occurs when cells are included in the scaffold matrix), then cultivating the cells in a bioreactor, and then

implanting the scaffold, which is now filled with freshly produced tissue, at the defect location. The timing of the implantation is the defining factor.

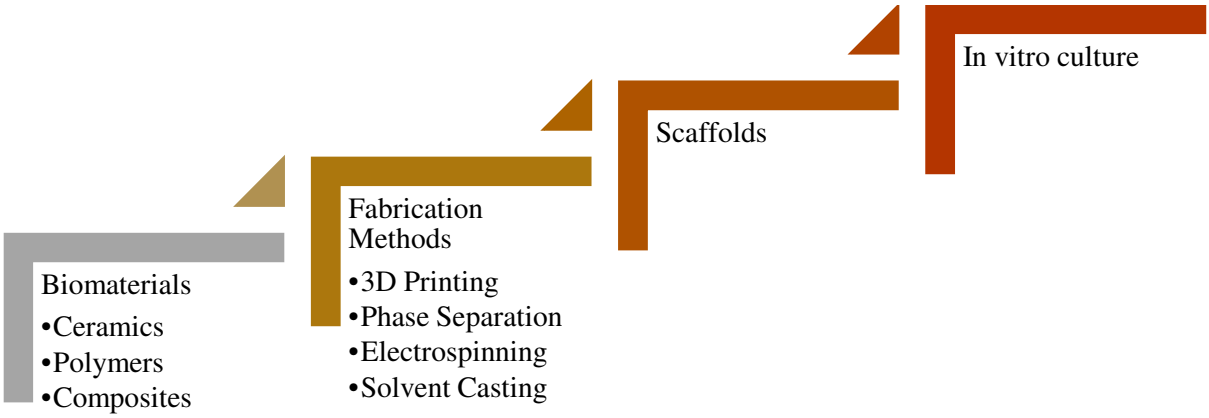


**Figure 2: Displays the process of Tissue Engineering (TE).**

Before the time of implantation, the scaffold needs to have undergone comprehensive degradation and metabolization.

The second technique involves implanting a scaffold that has been filled with tissue that has not yet been completely developed.Different rates of deterioration (erosion) of the implanted scaffold must be identified, but these should vary according to the method that was selected.

In most cases, the manufacturing of TE scaffolds is followed by surface alterations that are suitable to obtain the necessary structure and characteristics when seen from the viewpoint of the cells. During the process of cell culture, a variety of hormones and growth agents are often administered. The procedure for the creation of the tissue engineering product is shown in Figure 2 [16].

*ii. Comparison of Traditional TE Scaffold Fabrication Methods to Novel 3D Printing Approaches:*

There are many different ways that scaffolds may be formed, which enables them to fulfill the needs of a wide variety of different applications. In addition, numerous biomaterials are continuously being enhanced so that they may be used in tissue engineering more effectively. Figure 3, presents a diagrammatic representation of the example. Some of these processes include self-assembly, solution casting, foaming, electrospinning, additive manufacturing, extrusion, and phase separation are some of the most common scaffold production processes. To mitigate the negative impacts of some aspects of the methodologies, it is common practice to combine them, which may result in results that are both extremely intriguing and potentially quite productive [17].

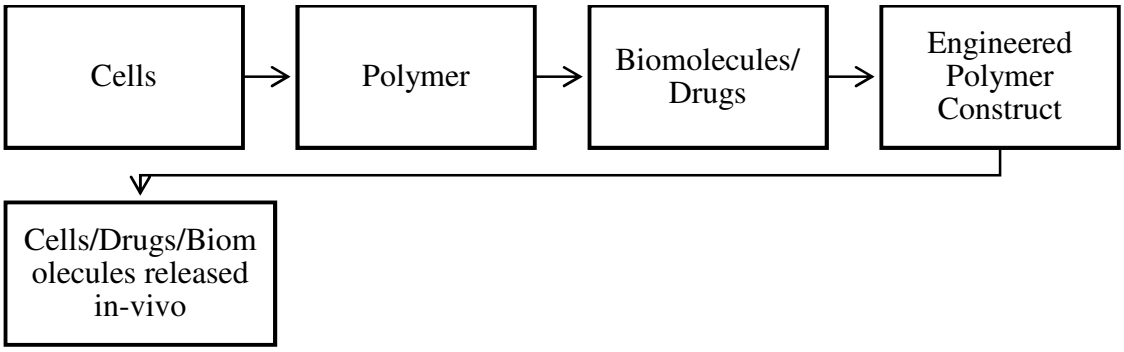


**Figure 3: A diagrammatic representation of the scaffold including the development of cells, medicines, or biomolecules.**

Following the removal of the precursor material by dissolution and the evaporation of the solvent, the remaining structure is porous. Because endothelial cells are dispersed in a consistent manner across solvent scaffolds, these materials have potential uses in the field of cardiac tissue engineering, for example. Utilizing this method, it is possible to build structures that have a consistent porosity yet have only a very restricted thickness. Table 1 provides an overview of these different approaches.

**Table 1: Applications and advantages/disadvantages of the most prominent scaffold construction methods**.

| Methods | Applications | Advantages | Disadvantages |
|---|---|---|---|
| Phase separation | Potential uses in protein delivery and medication release | High porosity allows for the incorporation of bioactive substances | Problems with leftover solvents and a restricted pore size range |
| Solvent Casting | Technologies for vascular tissue engineering | Easy to use, with regulated porosity | Small pores, low thickness, and weak mechanical strength |
| Electrospinning | Cardiac tissue engineering, Bone, nerve, and skin | Features a large amount of exposed surface area relative to its volume, a high level of porosity, and a straightforward production method. | Insufficient variety of polymers |

Tissue engineering requires a comprehensive familiarity with human biology, from cellular proliferation and differentiation through the immune system. The requirements of TE scaffolds (including 3D-printed ones) are, in a nutshell, highly difficult and varied. Scaffolds should be easily sterilized to avoid infections, and the material used to make them must be biocompatible (i.e., they must not trigger a cytotoxic or immunological response). Additionally, the mechanical qualities should be adequate for the patient's daily life and activities [18].

*3.2.Electrospinning-Based Controlled 3D Printing:*

Electrospinning is based on ejecting a viscoelastic polymer solution onto collectors while applying an electric charge to create fibers. The output of a polymer solution is subjected to a high voltage as it is guided to a collector creating a powerful electric field that directs the route of the charged polymer solution as it moves through the system.This method can produce ultrafine fibers with diameters ranging from a few micrometers to a few nanometers by adjusting the solution conditions (pH, concentration, and solvent), device conditions (lengths between tip and plate, strength of electric field, and measurement systems of nozzle), and collection methods (plate versus rotating mandrel and collection speed). Electrospun nanofibers, on the other hand, are whipped, therefore the result is often a nonwoven mat with fibers in random orientations. Due to this property, the fabrication of patient-specific structures for use in tissue repair has been hampered by this approach. Furthermore, electrospinning technology is field-tested and has been utilized in tissue engineering due to the development of several strategies to coordinate and place the nanofibers.

Bellan and Craighead [19] used electric fields to contain and guide an electrospun polymer jet for precise deposition of biomaterials, and they interposed electrodes between the electrospinning tip and also the rooted specimens to suppress the jet's chaotic whipping mode and so shrink the spot's radius. Through adjustments to the electrode configuration, scientists were able to rapidly terminate electrospun fibers and deposit isolated fibers in precise locations. Their findings would make it possible to create more intricate shapes using electrospun nanofibers.Electro conductive collectors were employed by Zhang and Chang [20], to create poly (lactic acid) (PLA) electrospun matting with a variety of patterns. The scientists developed an electroconductive template that allows them to regulate the layouts and structures, as well as the factors that govern the production of the structures, of the fibrous materials.They demonstrated that the collector protrusions are essential in generating patternsin the electrospun mat, and that woven nanostructures can be produced by varying the collector protrusion pattern with time. These impacts of protrusion organization and planned patterns might be used to provide fiber mats for use in biomedical settings.

Tissue engineering might benefit greatly from 3D printing technology with nanoscale precision. Compared to conventional scaffold manufacturing techniques, 3D printing allows for much moremanagement of pore size, permeability, and connection. The ability to manufacture a 3D scaffold exactly as specified makes 3D printing a viable option for creating uniform scaffolds.Several subfields of tissue engineering have taken an interest in the 3D printing techniques of nanofabrication using two-photon lasers and electrospinning under precise control are promising owing to the ability of each to produce structures with a large surface area to volume ratio as well as a porous, interconnected network structure on a sub-micron scale.

## 4. CONCLUSION

The potential of bioprinting applications in tissue engineering to provide unique answers to the medical world's numerous issues makes it an appealing topic. Though existing fabrication methods are insufficient to create sophisticated complete organs, they are adequate to create organs and tissues with basic structures.To create functioning tissue, tissue engineers mix engineering principles with tissue biology. Significant obstacles to the field of tissue engineering might be solved with the use of 3D printing, a quick prototyping technique with the inherent capability for manufacturing on an industrial scale.Some evidence suggests that the

aforementioned design considerations may help 3D printed tissue engineering constructs integrate better with cells, hosts, and blood vessels.The absence of a well-defined regulatory framework and uniform criteria for the certification of tissue-engineered products is a significant challenge for researchers, physicians, and engineers working in this field. It is well knowledge that current legal constraints make it more difficult to transfer laboratory results to a commercial setting. From the perspective of existing standards, the attesting of patient-specific TE devices is challenging as well. The danger associated with moving from animal studies to human trials may be mitigated by expanding our understanding of how to print human tissues in 3D. To sum up, 3D printing may be a potent tool for assembling functional tissue in vitro, which can speed up the application of tissue engineering principles in regenerative medicine and drug testing.

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# CHAPTER 18

# AN ANALYSIS OF THE CURRENT AND POSSIBLE FUTURE USE OF NANOTECHNOLOGY IN HIV/AIDS PREVENTION AND THERAPY

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**ABSTRACT:**

Nanotechnology has several applications in different disciplines of research. When it comes to the fundamentals of nanotechnology, nanoparticles are very crucial. Recent advances in nanotechnology have shown promising therapeutic applications of nanoparticles. Combining Nanoparticles (NP's) with therapeutic compounds solves difficulties with traditional medicine, but their use in living systems is still controversial due to concerns regarding toxicity and other negative effects. In this study, the author presents a review of the special characteristics of nanoparticles in living organisms. The author of this study also explores the current state of treatment and prevention methods for human immunodeficiency virus (HIV) and Acquired Immune Deficiency Syndrome (AIDS), including antiretroviral therapy, gene therapy, immunotherapy, and microbicides, and highlights the tremendous potential of nanotechnology in these areas. There is currently no HIV/AIDS vaccine or therapy available. Even though combined antiretroviral therapy has significantly improved outcomes, it must be taken indefinitely, may have serious adverse effects, and is no longer useful in people whose viruses have become resistant.

**KEYWORDS:**

Acquired Immune Deficiency Syndrome (AIDS), Antiretroviral Drugs (ART), Highly Active Antiretroviral Treatment (HAART), Human immunodeficiency virus (HIV), Nanotechnology, Nanoparticles (NP's).

## 1. INTRODUCTION

A new field called nanomedicine is developing around the idea of using nanotechnological systems for clinical purposes. In this subfield of nanotechnology, we may broadly divide the field into two classes: nanodevices and nanomaterials [1]. Microarrays and certain types of machine intelligence, such as respirocytes, are examples of nanodevices. At least one of the nanoparticles in a nanomaterial is 100 nm or less in size [2].The creation of therapeutic agents used in the treatment of illness has been greatly improved thanks to recent research in biomedical science. However, the transport of therapeutic substances to the target location is a significant barrier to the efficacy of treating numerous illnesses. Non-selectivity, unfavorable side effects, ineffectiveness, and poor biodistribution are only some of the problems with using traditional medicinal medicines. As a result, researchers are concentrating on developing systems that are both highly precise and versatile [3].

The "Human Immunodeficiency Virus", often known as HIV, is the virus that leads to "Acquired Immune Deficiency Syndrome (AIDS)", and is one of the world's most significant public health

issues. HIV/AIDS is still very hard to cure at this point in the 21st century. However, the current scenario benefits from the presence of various antiretroviral drugs, which have turned HIV into a chronic condition rather than a life-threatening one [4].As a result of HIV's invasion of the mucosal barrier and subsequent destruction of the host's immune system making it is vulnerable to infection by a broad range of microorganisms, including bacteria, viruses, fungi, and protozoa. HIV spreads when infected blood, organs, or sexual fluids are passed from an infected parent to a susceptible child. Sexual transmission is a major route of entrance via the mucosal membranes.

Among heterosexual partners, the female vaginal canal is the most common site of HIV transmission [5]. Rectal route sexual transmission of HIV is also a serious problem because of how the virus is physiologically transmitted.Figure 1 indicates that immune cells, particularly the primary targets of HIV infection are macrophages and dendritic cells, which may be located in the sub-epithelial layers of the vaginal or cervical mucosa [6].

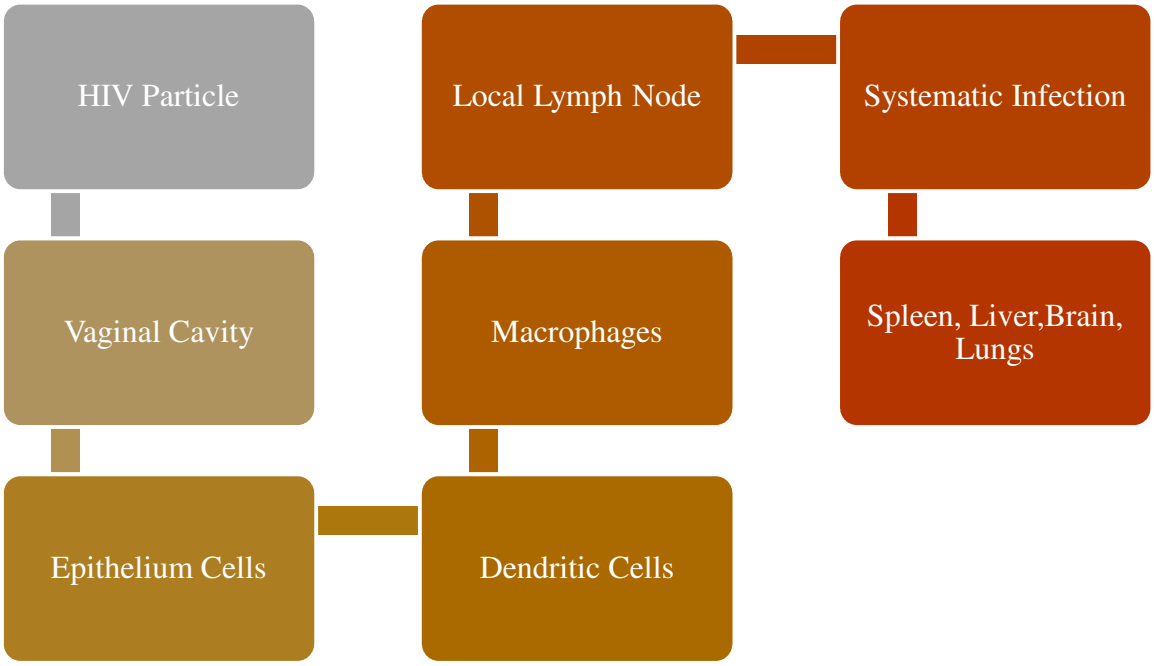


**Figure 1: A Pictorial Depiction of the Infection Caused By HIV Particles.**

The emphasis is on HIV, which causes AIDS. It focuses on Nanotechnology in healthcare research (Acquired Immune Deficiency Syndrome). Patient tolerance to HIV treatment may be enhanced, medication administration simplified, and the pharmacological characteristics of many antiretroviral medicines might be optimized with the use of nanotechnology. Despite over 30 years of study, a cure for HIV/AIDS remain unclear. Antiretroviral medicines, the primary focus of early therapy, were only partially successful. It wasn't until the mid-1990s that triple-drug therapy and a new class of medications called protease inhibitors changed the face of HIV/AIDS care forever. That marked the beginning of the era of Highly Active Antiretroviral Treatment (HAART), in which three or more medication classes are used in tandem to treat HIV/AIDS [7].

## 2. LITERATURE REVIEW

Christian A. Engell et al. investigated the effectiveness of lamivudine monotherapy followed by combination treatment with tenofovir and emtricitabine or lamivudine. The author examined the medical records of 31 people who were co-infected with HIV and HBV. 12 individuals who had

never been exposed to 3TC naïve were given the combination of tenofovir and emtricitabine. Treatment with tenofovir and emtricitabine was tried on patients diagnosed who had previously been unsuccessful with epivir.Median HBV DNA was identical in Epivir-nave and expert groups (P =.65). In the naive group, HBV suppression took 466 days, and in the expert group, 877 days (P =.0101). The author found that treatment-naive individuals had lower median HBV DNA reduction times. At 24 months, more naive individuals had suppressed HBV DNA. Findings reinforce dual treatment for HIV/HBV co-infection [8].

Omoladun O. Odediran et al. stated in their study thatNigerian women may be discouraged from seeking HIV treatment due to cultural and economic factors.This research is focused on HIV-positive women's retention in care following the Test and Treat program at a big hospital in Lagos, Nigeria. Between April 1 and October 31, 2021, twenty-four HIV-positive women were interviewed at the "AIDS Prevention Initiative in Nigeria (APIN)" Centers in Lagos, Nigeria. The mean respondent age was 37.4+/-9.27 years. Three overarching themes emerged: familiarity with HIV status in the home, benefits of antiretroviral treatment, and community engagement. The author discovered that Test and Treat has not changed the prevalence of clinical obstacles, insufficient social support, or status-based confidentiality agreements. It is crucial to overcome these hurdles and apply facilitators for improved health outcomes among HIV-positive women to achieve "treatment as preventive" for HIV/AIDS, particularly in Sub-Saharan Africa.

Karl Peltzer et al. discussed in their study that this study seeks to examine HIV and AIDS communication programs' impact on information, perceptions, and HIV risk behaviors in South Africa's overall population.This cross-sectional poll comprised 13234 15–55-year-olds. The survey indicated a high level of exposure to 18 HIV communication programs (median 6, 14 above 30%) across age categories. Most programs were seen by 15-24-year-Higher rates of HIV knowledge, condom usage, and testing in the prior year were seen in areas with more exposure to HIV mass communication programs, and fewer stigmatization attitudes toward People living with HIV/AIDS (PLWHA) [9].

## 3. DISCUSSION

Nanotechnology techniques may improve upon present treatment and progress novel therapeutic options, such as gene therapy and immunotherapy, according to studies conducted over the previous several years. In addition, certain nanomaterials may be used as a standalone treatment. Prevention measures like vaccination and microbicide development may also benefit greatly from nanotechnology. Although there are a variety of Highly Active Antiretroviral Treatment (HAART) regimens available, all of them need daily medication and, in some instances, severe adverse effects, and must be taken indefinitely. In addition, treatment failure may occur when a patient has developed resistance to a particular medicine or therapeutic combination. The fact that HIV/AIDS cannot be cured using the methods now in use emphasizes how important it is to keep looking for new methods of therapy.Nanosystems used to treat HIV have some unique benefits, like making Antiretroviral drug (ARV) drugs more bioavailable, water-soluble, stable, and able to target specific cells. Figure 2 shows that liposomes, nanoparticles, liposomes, polymeric micelles, and dendrimers are the major nanotechnology-based systems that are being looked into for HIV treatments.

### *3.1.Using Nanotechnology To Transport Antiretroviral Drugs:*

Highly active antiretroviral treatment (HAART) often entails the use of three or more antiretroviral medications in tandem. Alternative names for HAART include antiretroviral

treatment (ART) and combined ART (cART). A central tenet of HAART is the simultaneous administration of two or more antiretroviral medications that work by separate methods to prevent viral reproduction, hence preventing the spread of a virus that is resistant to one of the treatments. Treatment with a "Highly Active Antiretroviral Therapy (HAART)" is recommended by the "Infectious Diseases Society of America (IDSA)" prescription be carried out by, or in conjunction with, a clinician with adequate training. This strategy is essential for enhancing patient care since research has shown a favorable correlation between provider experience and improved outcomes for patients[10].

Different classes of antiretroviral medications exist for treating retroviral infections like HIV dependent on which point inthey are interested in the HIV life cycle. Reverse transcriptase inhibitors impede viralinhibiting reverse transcriptase (RT) enzyme activity and therefore DNA synthesis.Since certain viral strains have developed resistance to existing antiviral medications, antiretroviral treatment (ART) based on a single medication class has not proven successful in halting the spread of infection or slowing the course of illness. Highly effective antiretroviral treatment includes the administration of three or more drugs together to combat the virus more effectively and reduce the likelihood of drug resistance. As a result of HAART, people with HIV may expect to live longer than they did before and the number of deaths caused by the virus has dropped substantially [11].

Drug resistance, inaccessible viral reservoirs, latent cells harboring incorporated HIV DNA that can be activated in vivo at a later time, decreased treatment adherence because of increased adverse effects, and toxicity from the high and regular dosages embroiled all contribute to the difficulty of managing the disease. The expensive expense of HAART is also a major problem, particularly in underdeveloped countries with a high HIV prevalence rate [12].Multiple enzymes and metabolic pathways control HIV replication at the cellular and molecular levels. Effective anti-HIV medications need significant extra- and intracellular dispersion to provide appropriate time-on-target at the target locations. In terms of how drugs are administered, there are three main lines of inquiry: antiretroviral therapy (ART) for infection prevention (such as sexual transmission), antiretroviral therapy (ART) for virus eradication from circulation, and antiretroviral therapy (ART) for virus separation from safe zone sites.

Active targeting strategies have been used in the administration of ART medications, with a focus on macrophages, the major reservoirs of HIV. They contain several surface receptors that may be utilized to bring mediated receptors into the cell, including mannose, Fc receptor, formyl peptide, and galactose. Liposomes attached with galactose and mannose improved cellular absorption of stavudine (a water-soluble medication) and produced a significant drug level in the spleen, liver, and lungs compared to simple liposomes.As shown above, these findings strengthen the case for using nanoparticles to improve antiretroviral medication delivery and provide credence to the kind of cutting-edge study that will ultimately lead to clinical trials. Although clinical trials based on these preliminary results have not yet ended, the studies far make assertions that encourage theoptimism that some preclinical innovations may reach clinical trials in the future.

HAART programs are necessary to enhance outcomes for patients and limit HIV transmission, but drug administration is a fluid process that necessitates expert oversight. Utilization and persistence of a HAART protocol are crucial for achieving therapeutic efficacy and preventing viral resistance. Before beginning a regimen, health professionals must acquire a complete history and screening and consider variables like comorbid conditions. The desire for pregnancy,

accountability to contraceptive method usage, birth control financial pressure of the treatment plan, financial impact, previous HAART usage, and drug-drug interactions; cardiovascular problems; psychiatric conditions; tuberculosis; drug abuse, osteoporosis; renal dysfunction; hepatitis B; hepatitis C. Patients with a history of drug abuse or mental disease who reside in a setting with minimal resources are at significant risk of noncompliance. Administrators of healthcare must be cautious to achieve optimum health results.

*3.2.Using Nanobiotechnology For Drug Delivery:*

Applying Nanotechnology in the distribution of antiretroviral medications shows promise as a treatment for HIV/AIDS, and could be useful in that regard by Increasing the half-life of medications and storing them in an anatomical reservoir[13].Due to nanotechnology, researchers can improve drug distribution even for those that aren't water-soluble, target drug delivery to particular cells or tissues, and enable macromolecules to communicate inside of cells.

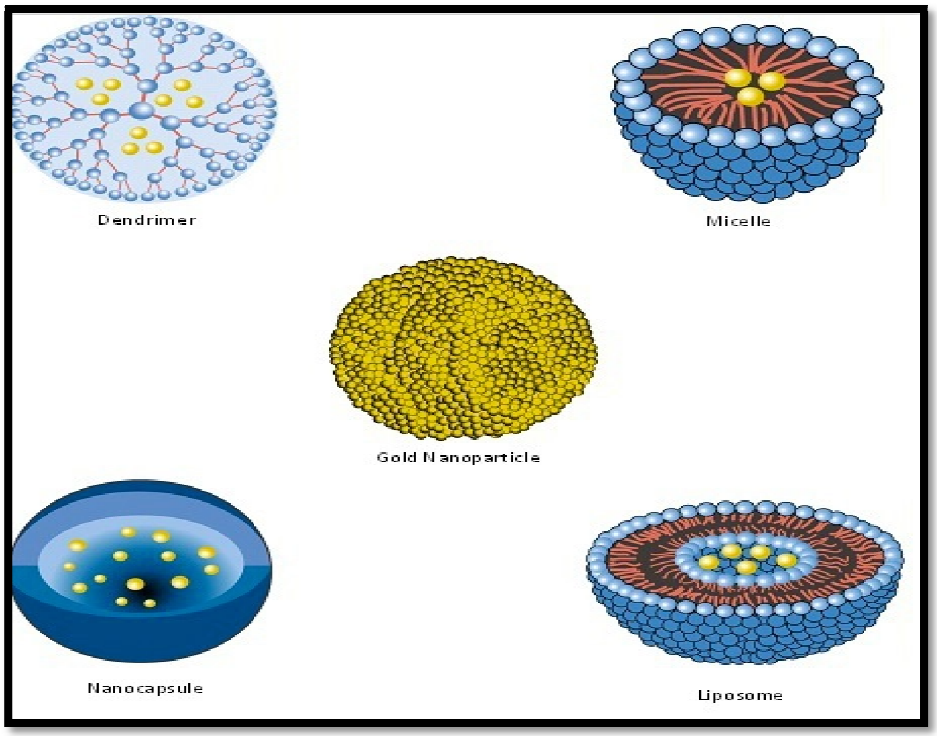


**Figure 2:Displays The Nanopharmaceuticals Applications And Examples In HIV Infection.**

i. *Liposomes:*

Microscopic vesicles, or liposomes, are made up of one or even more phospholipid bilayers, and they often include an aqueous center. Between 25 nm and many microns, liposomes span a wide range of sizes. Liposomes are a kind of foreign body that is quickly and efficiently ingested by the body's mononuclear phagocytic cells. Since the sick person's mononuclear phagocytic cells harbor HIV, liposomes are promising transporters for delivering anti-HIV medications to the diseased tissue. As a result, liposomes may boost the potency of anti-HIV medications while decreasing their potential for harm [14].

It has an aqueous shape in its center and is composed of a bilayer of phospholipids. The phospholipid bilayer and also the aqueous core cavity may be loaded with hydrophilic and lipophilic medicines, respectively. Liposomes' distinctive benefits come from their adaptability

to a broad variety of compositions, and their capacity to encapsulate and shield a wide variety of biomolecules, including their biodegradability and biocompatibility. Since liposomal compositions may act as immunological adjuvants, they are the subject of many studies in vaccinology [15].

*ii. Nanoparticles:*

The size range of nanoparticles is from 10 to 1000 nm, and they are solid colloidal particles. Their colloidal size and polymeric composition determine their ability to target medication to specific locations within the body and also its prolonged release. The majority of anti-HIV therapies use one of three kinds of nanoparticles: polymeric nanoparticles,nanostructured lipid carriers, and inorganic nanoparticle carriers are both solid lipid nanoparticles.Improved effectiveness, lower drug resistance, decreased dose, fewer toxicities, negative impacts, and enhanced patient compliance may all result from encapsulation into these systems[16].For zidovudine administration, Lobenberg et al. synthesized poly-hexyl -cyanoacrylate nanoparticles. After orally administered, the encapsulating medication resulted in greater zidovudine levels throughout the body in rodent trials than the free drug solution. When radioluminography was employed to evaluate oral and intravenous injection of the nanoparticles, it was observed that a substantially larger proportion of the orally supplied nanoparticles remained in the gastrointestinal system [17].

iii. *Niosomes:*

When used as a drug delivery method, niosomes (vesicles made of nonionic surfactant) may increase the stability and solubility of naturally occurring medicinal compounds. The purpose of these systems is to allow for the precise administration of biopharmaceutical substances. Nonionic surfactant vesicles, or niosomes, have another name. They may entrap many different medications, and they develop by themonomers of man-made nonionic surfactants that assemble themselves when exposed to water. Alternatives to liposomes, such as niosomes, have been explored [18].

*iv. Polymeric micelles:*

Increases in water solubility have been achieved by using polymeric micelles, nanostructures having a diameter of less than 100 nm, intestinal absorption, and site-specific illness treatment of some different therapeutic compounds. In the same way, as micelles made from surfactants have a core (hydrophobic block) as well as a shell (hydrophilic block),having a core-shell structure and being composed of block polymers, polymeric micelles have been studied for their potential applications. Micelles have a diameter between 10 and 100 nm. They have a water-hating compound on the inside and a water-loving polymer on the outside. Polymeric micelles, for example, have attracted interest as drug-delivery agents with promising therapeutic applications [12].One fascinating element of nanotechnologies that may increase water stability and solubility of unstable medications is the encapsulation of pharmaceuticals with polymeric micelles. Micelles have a decreased dissociation rate, which prolongs drug storage and increases drug accumulation at the target site [19].

v. *Dendrimers:*

In chemistry, a dendrimer is a nanoscale (100 nm) polymeric structure with a core unit. Dendrimer development, sizing, and local conditions are defined by the layered arrangement of the branching units surrounding the core units. Each dendrimer is made up of several smaller

pieces called dendrons. Once the central units have been removed, the resulting dendron may be sectioned into a (nonexistent) core, an interior composed of branching units, and an exterior composed of rim units (end groups).Dendron's interior cavities show promise as a site for the trapping of pharmaceutical compounds for uses like solubilization and controlled medication release, targeting, and defense against degradation [20].

Many types of illness therapy are benefiting greatly from the use of nanotechnology frameworks for medication delivery. With the use of nanotechnology, we may now improve the dispersion of drugs that aren't water-soluble, target drug delivery to specific cells or tissues, and even provide macromolecules intracellularly [21].People infected with HIV type 1 are the primary target population for this combo medication. The combination of two nucleoside reverse transcriptase inhibitors (often tenofovir-emtricitabine) and one non-nucleoside reverse transcription blocker or integrative strand transfer inhibition is the foundation of treatment for most treatment-naive individuals[22].

### *3.3.The Application of Nanoparticles as Therapeutic Agents:*

Evidence suggests that nanoparticles may have curative effects on themselves. The HIV capsid has been shown in studies to be a potential beginning for the structure-based creation of medications to interrupt the virus's replication process. Researchers have so reported chemicals that hinder HIV capsid assembly. Different nanoparticles have been demonstrated to inhibit in vitro virus reproduction, which is indicative of structural interference with the viral agent's assembly.Several different types of fullerenes (C-60)-based nanostructures, inorganic nanoparticles, and dendrimers have all been shown to possess anti-HIV activity in vitro. Even though these results have not yet been confirmed in vivo, they do demonstrate the therapeutic effects of nanoparticles in inhibiting HIV replication [23].Treatment nanoparticles aim to enhance therapeutic effectiveness and minimize the occurrence and severity of side effects by restricting the distribution of pharmacologically active compounds to non-targeted healthy tissue.

The "targeted delivery" occurs when a medicinal drug is successfully guided to and accumulates mostly at a preferred location. The agent-loaded system has to stay put in the body for as long as possible, avoid being attacked by the immune system, home in on the desired cell or tissue, and then release the therapeutic agent [24].There is now extensive investigation on the potential of nanoparticles for targeted delivery in the treatment of cancer. 20 percent or more of the therapeutic nanoparticles currently in use or being evaluated in human clinical trials were created specifically to treat cancer. Additionally, studies in this area have concentrated on the use of nanoparticles as a mediumuse in the treatment of neurodegenerative disorders and autoimmune disorders.

## 4. CONCLUSION

The global spread of HIV/AIDS has become an urgent matter of public health. Although it is evident from this that study the use of NPs to treat and prevent HIV infection has acquired momentum in recent years, more research is required to address barriers to NPs achieving their target sites, especially in macrophagesas well as the brain and spinal cord, two areas where antiretroviral medicines have a limited ability to reach, leaving a slow and continuous the virus's replication intracellular.To present, the substantial body of research on nanocarrier's antiretroviral medication delivery systems has focused on the administration of a single antiretroviral agent. Studies using nanocarriers to combine delivery techniques are warranted in light of the evidence that combining medications might improve treatment efficacy and lower

resistance profiles. We need further research into the nanocarriers for antiretroviral, particularly into their safety and effectiveness. The short- and long-term toxicities of nanocarriers are mostly unknown at this time. Furthermore, to make the nanocarrier treatment method practical, it is necessary to take into account scale-up issues for the production of nanocarrier systems.

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# CHAPTER 19

# AN EXPLORATION OF POSSIBLE CURRENT AND POTENTIAL FUTURE THERAPIES FOR ALZHEIMER'S DISEASE

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**ABSTRACT:**

One of the leading causes of mortality worldwide, Alzheimer's disease (AD) is a kind of neurological illness that mostly affects older individuals. The care and financial expenditures associated with Alzheimer's disease are a significant strain on families, communities, and society as a whole. Alzheimer's disease (AD) disease-modifying therapy methods are currently being researched extensively. There are currently only symptomatic therapies for this condition, all of which attempt to counteract the neurotransmitter disruption: Memantine and three cholinesterase inhibitors. Possible disease-modifying treatments under study, along with personalized therapy approaches that have shown promise for AD patients, are discussed in this study. The authors of this study focus on the present symptomatic therapies and also the novel perspective of Alzheimer's disease disease-modifying medicines that are presently being explored in clinical trial phases I-III. It is possible that soon, different specific agents will be used for each patient in a "precision medicine" perspective, in which abnormal biomarkers and a certain sequence of neuropsychological and neuroimaging study results would then evaluate a unique treatment plan within a specialized therapeutic structure.

**KEYWORDS:**

Alzheimer's disease (AD), Dementia, Memory Loss, Memantine, Neurodegenerative.

## 1. INTRODUCTION

The most typical kind of dementia, The deposition of amyloid-beta peptide (A) is a characteristic of “Alzheimer's condition (AD; termed after German psychiatrist Alois Alzheimer)”, within the middle temporal forebrain and neocortical structures seen in Figure 1, leading to the formation of neurotic tangles and plaques [1].One kind of brain disorder is Alzheimer's disease (AD) which may lead to a gradual decline in mental capacity; other conditions, such as dietary deficiencies, vitamin B12 inadequacy, malignancies, and illnesses, can have a similar effect [2].Recent developments in molecular genetics, techniques including positional cloning, “genome-wide association studies (GWAS)”, and genetic association studies have generated an explosion of research in the search for the genes responsible for Alzheimer's disease, in both its autosomal dominant and sporadic forms[3].

Millions of individuals worldwide are afflicted withamong the several clinical forms of dementia,the most common kind of sickness is by far Alzheimer's.A deterioration in mental capabilities is one of the hallmarks of dementia, especially memory. Memory loss, reasoning and judgment issues, disorientation, inability to learn, language impairment, and other cognitive declines are all symptoms that often manifest themselves gradually.As the most pressing unmet

clinical need in neurology, Alzheimer's disease (AD) therapy has lagged far behind other neurological conditions. Alterations in the metabolism of amyloid precursor proteins and tau proteins, as well as oxidative stress, insufficient energy production, mitochondrial dysfunction, inflammatory, dysregulation of membrane lipids, and interference of neurotransmitter pathways, all, play contribute to the development of Alzheimer's disease [4].

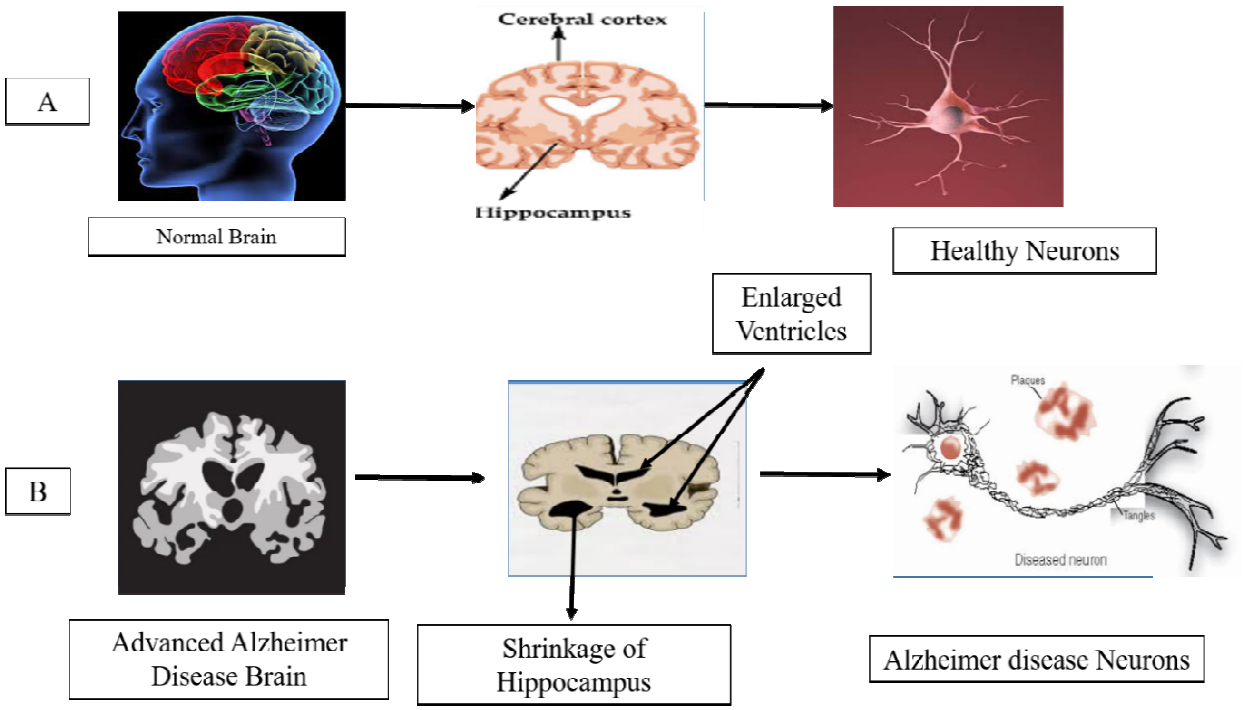


**Figure 1: Comparing The Neuronal and Brain Anatomy of a Healthy Brain (A) And (B)Alzheimer's disease affects the brain.**

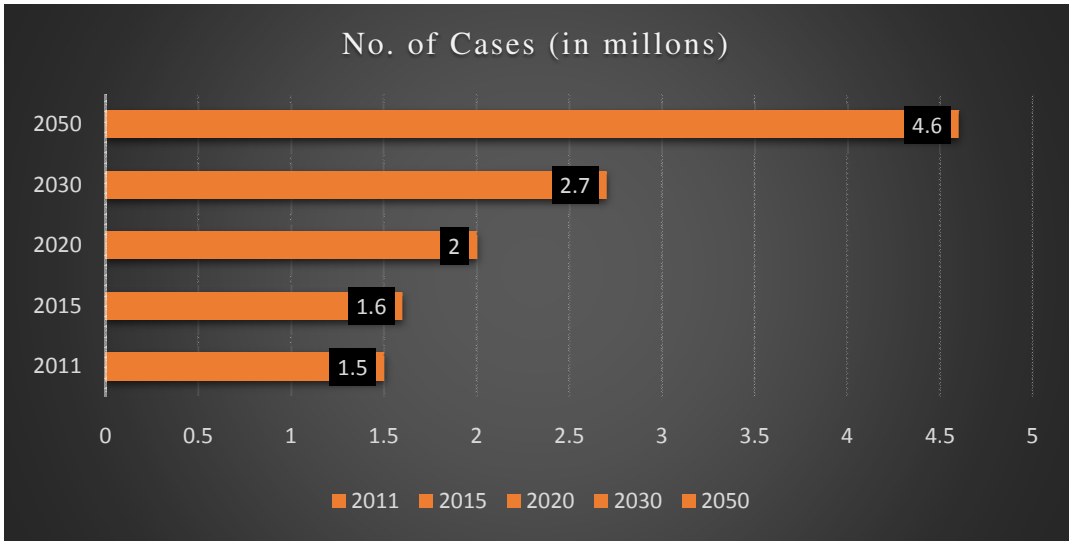


**Figure 2: Alzheimer's disease prevalence among Indian seniors, 2011–2050.**

Data from 2011 to 2050 are shown in figure 2 to show the prevalence of Alzheimer's disease among India's older folks. In 2050, it was predicted that there will be around 4.6 million instances ofAlzheimer's illness among India's senior citizens.This study's goal is to offer a basic overview of the screening options for Alzheimer's disease (AD), its pathophysiology, causes, and treatments currently in use while also highlighting recent advancementsof substances that could treat or prevent AD by targeting numerous pathological processes, including Aβ as well asoxidative stress, inflammation, tau misfolding, aggregation, and other tau-related pathologies.

## 2. LITERATURE REVIEW

Jing Xia et al. stated in their study Comparing gene expression in afflicted areas to detect biological process variations may provide light on AD etiology and early symptoms. The author found that Genes that are differentially expressed (DE) in many brain regions, including the "entorhinal cortex (EC)", "hippocampus (HIP)", "posterior cingulate cortex (PCC)", and "medial temporal gyrus (MTG)" are the four brain areas affected by Alzheimer's disease. The author created region-specific gene co-expression pathways from DE genes in four regions of the brain.Increased oxidative stress and lipid metabolism changes in neurons may represent early AD symptoms. The author found that low expression of genes in two interacting protein networks is linked to cancer, diabetes, renal disorders, and coronary heart disease [5].

Chao Ke et al. evaluated in their study that analyzes current animal studies on acupuncture for Alzheimer's disease (AD) patients. From their creation through November 2021, the author used electronic libraries. Journals, publication records, animal models, intervention strategies, acupuncture point preferences, diagnostic techniques, and diagnostic markers were evaluated.75 studies were chosen for further analysis. APP/PS1 transgenic male SAMP8 mice. Experimentally, a 20-minute retention period was optimum, and 14 treatments were the most prevalent therapy. The author concluded that by compiling high-quality research data, It was shown that acupuncture is an effective treatment for AD in mice models.

Yahan Wang et al. discussed in their study the treatment of oral liquid Shen Zhi Ling for Alzheimer's illness (Tiao Xin preparation) (AD). Exclusion and inclusion criteria were used to explore CNKI, Wanfang, and VIP. Extracted data were analyzed descriptively. Twenty-four "Tiao Xin preparing" articles have been included. AD models numbered seven.The oral liquid form of Shen Zhi Ling reduces amyloid-beta (a) deposition and tau hyper-phosphorylation, controls a plethora of neurotransmitters, boosts energy metabolism, and upregulatesproteins linked to learning memory and autophagy. AD is a multifactorial illness, according to the author. Shen Zhi Ling's oral liquid showed multi-target impacts and AD treatment potential. Molecular biology and associated fields would better understand Shen Zhi Ling's AD process [6].

Anmu Xie et al. conducted a study has been suggested by research that noradrenergic neurons in the lateral geniculate nucleus (LC) die out at an early stagerelated to the progression of dementia and Parkinson's.Researchers have found a link between the "Cys-loop" "superfamily of pentameric ligand-gated ion channels known as nicotinic acetylcholine receptors (nAChRs)", and neurodegenerative illnesses such as "Alzheimer's disease (AD)" and "Parkinson's disease (PD)". The data from these clinical and experimental research may provide the groundwork for understanding the shared processes underlying AD and PD.Some studies have shown that degeneration of noradrenergic neurons in the Locus Coeruleus (LC) precedes the development ofThis body of research, both experimental and clinical could serve as the groundwork for understanding the same underlying processes of AD and PD [7].

## 3. DISCUSSION

The incidence of dementia increases from 1% at age 60 to at least 35percent at age 90, making it one of the most significant medical concernsbetween the generations.One of the most prevalent dementiamore often than not, those individuals above the age of 65 years old are identified with Alzheimer's illness (AD). Increasing memory and orientation loss, as well assome of the clinical features of this illness, include a poor ability to judge and make decisions, apraxia, and language difficulties. The neuropsychiatric symptoms that accompany these conditions tend to be somewhat varied (i.e. delusions, hallucinations, depression, apathy, anxiety, and agitation) [8].The global population is living longer than ever before, and this has led to a rise in cases of dementia, and Alzheimer's disease, in particular,is rapidly increasing. This has prompted a surge in efforts to find treatments for dementia. No pharmacotherapeutic approaches for the prevention and therapy of AD exist at this time, despite extensive research [9].

### *3.1.Diagnostic Standards for Alzheimer's Disease (AD):*

Tests such as an MRI of the brain's neurons, biochemical analyses (including vitamin B12 levels), and more should be performed on anybody suspected of having Alzheimer's disease. B12 deficiency has been associated in some research with cognitive decline and even an increased chance of developing Alzheimer's disease. Increased levels of homocysteine are a reliable sign of vitamin B12 deficiency and have been associated with neuron death and cell death through apoptosis, oxidative stress, and calcium infiltration in the brain.Vitamin B12 deficiency may be detected using a variety of tests, including serum homocysteine concentrations and a full blood count [11].The diagnostic criteria for Alzheimer's disease were not established until 1984 when a joint effort between the “National Institute of Neurological and Communicative Disorders” and Stroke (NINCDS) and the “Alzheimer's disease and Related Disorders Association (ADRDA)” was undertaken:

i. Alzheimer's disease is probable when neuropsychological testing demonstrates dementia, memory loss occurs gradually, everyday tasks become difficult, and other symptoms such as language impairment, motor skill problems, and a lack of knowledge are present (a loss of perception). Symptoms like this may arise at any moment between the ages of 40 and 90 if there are no underlying systemic or neurological illnesses.

ii. Potential Dementia is not caused by Alzheimer's disease alone, but rather by a combination of factors including age, genetics, and lifestyle.

iii. The histopathological confirmation of Alzheimer's disease in the setting of a biopsied or autopsied specimen [10].

Potential and likely Alzheimer's disease dementia are advocated for use in healthcare situations, whereas probable and potential Alzheimer's disease dementia supported by pathophysiological data are suggested for use in laboratory settings. The biomarkers for Alzheimer's disease may be broken down into two groups:

i. “Cerebrospinal fluid (CSF)” and “Positron emission tomography (PET)” scan analysisare both signs of amyloid accumulation in the brain.

ii. The presence of tau in cerebrospinal fluid (CSF), the use of fluorodeoxyglucose (FDG) to identify metabolic rate, and magnetic resonance imaging is used (MRI) to evaluate the degree of atrophy are all markers of neuronal damage [11].

*3.2.Alzheimer's Disease Progresses Through Its Stages:*

Alzheimer's disease progresses through distinct clinical stages: (1) the long-lasting pre-clinical, or asymptomatic, phase. This stage is characterized by mild cognitive impairment, early degenerative anomalies in the hippocampus and cortex, and a lack of symptoms and signs of AD [12].(2), some signs of Alzheimer's disease begin to appear in the moderate or early stage, including difficulty with everyday activities due to a decline in focus and memory, confusion about where and when they are, a shift in mood, and also the onset of depression.

Increased memory loss, difficulties recognizing familiar faces, impaired impulse control, and language impairment characterize the third, moderate stage of AD, which occurs when the illness has advanced to the cerebral cortex. (4) Late-stage AD, in which the disease has spread throughout the entire cortex and is characterized by a massive buildup of neurons in the plaques and neurofibrillary causing progressive cognitive and behavioral disorder to the point where patients no longer recognize their loved ones and could progress to bedridden with swallowing and urinary incontinence difficulties, and ultimately resulting in death [13].

The illness worsens and worsens, causing a wide range of symptoms. Alzheimer's and Related Diseases Society of India and other medical professionals should be consulted. There are several potential causes for these signs and symptoms, including but not limited to depression, medication interactions, and infections.Independence is compromised over time as patients lose the ability to carry out even the most fundamental of everyday tasks as the disease progresses.

The inability to retain vocabulary that contributes to frequent inaccurate word replacements is a major contributor to the onset of speech issues (paraphasias). The ability to read and write is also being lost. The risk of falling increaseswhen Alzheimer's disease advances, and coordination in complicated motor sequences deteriorates, making movement more difficult. In this stage, memory loss becomes more severe, and the affected individual may lose the ability to recognize even close family members.

*3.3.Current Alzheimer's disease symptomatic approaches:*

*3.3.1. "Cholinesterase (Cls) inhibitors":*

In the initial stages of Alzheimer's disease (AD), memory loss and a decrease in other non-cognitive and cognitive functions, like clinical symptoms, appear because of a reduction in acetylcholine neurons and also the enzymatic function for the break - down and synthesis of acetylcholine, as postulated by the cholinergic hypothesis [16]. Donepezil (Pfizer; New York, NY, USA), rivastigmine (Novartis; Basel, Switzerland), and galantamine (Janssen; Beerse, Belgium) are the three CIs currently approved for the treatment options for moderate to serious Alzheimer's disease [14].The use of these medications is routinely the first line of defense against Alzheimer's disease and represents the current medical standard of care. Positive benefits on cognitive, ADL, and global functioning have been shown across many RCTs of these threeAlzheimer's disease CIs in those with mild to severe cases, and there was no statistically significant distinction in effectiveness across individual CIs, as determined by published studies.

The frequency with which gastrointestinal symptoms including sickness, throwing up, diarrhea, and stomach discomfort occur was shown to be reduced with donepezil compared to rivastigmine and galantamine in related systematic studies. Higher therapeutic doses were linked with a greater frequency of side events. If a cautious and slow titration procedure lasting more than 3 months is adopted, however, galantamine and rivastigmine can be as well tolerated as

donepezil. Some medical professionals favored the dermal formulation of rivastigmine because it was more convenient for them to administer the drug and had fewer side effects without sacrificing effectiveness. Syncope, bradycardia, and the need for a pacemaker have all been linked to CI use. These side effects are a potential downside of the medications that should be evaluated against their positive effects [15].

*3.3.2. "N-Methyl-D-Aspartate Antagonist":*

For people who have Alzheimer's disease ranging from mild to severe memantine may be used as an adjunctive treatment. The neuroprotective effects of this medication, an NMDA antagonist with moderate affinity and no competitive binding, have been hypothesized. Patients with moderate to serious AD who took Memantine for 6 months had improvements in cognition, ADL, and behavior, according to a thorough examination of randomized controlled trials (RCTs) using a double-blind design and a control group with similar characteristics. In studies with Memantine, dizziness, headaches, and disorientation were the most often reported negative side effects. The possibility exists that some patients may become restless [16].

*3.3.3. Combination therapy:*

Alzheimer's patients with moderate to severe symptoms who used Memantine and donepezil managed better than those who took either drug alone in randomized controlled trials (RCTs), compared to those who took neither drug (Memantine and placebo). However, those diagnosed with moderate to severe AD did not benefit from this [17].

*3.4.Factors That Raise Alzheimer's Risk And Potential Causes*:

AD has been deemed a complex illness related to various risk factors illustrated in Figure 3, like growing age, hereditary factors, brain traumas, vascular disorders, infections, and environmental variables. Figure 3: Factors that increase your risk of Alzheimer's disease (components such as heavy metals, trace metals, and many others). Just what exactly is causing these pathological alterations, such as amyloid beta, that are characteristic of Alzheimer's disease remains unknown, as neurofibrillary tangles, and synapse loss.

An injury in the cholinergic function is suspected and believed by some to be a change in the production and manufacturing of amyloid beta protein is the key factor that causes Alzheimer's disease, while others believe that a change in the development and manufacturing of amyloid beta protein is the major factor that causes the illness.Multiple hypotheses have been put out to explain Alzheimer's disease, but only two of them are suspected to be the primary cause. However, no commonly accepted theory exists to explain the underlying pathophysiology of Alzheimer's disease [18].

Recent developments in brain imaging have made it possible to see, in near-real-time, changes in brain structure and function, as well as the emergence and spread of aberrant amyloid and tau proteins. To put it simply, alpha-amyloid is a subunit of the bigger beta-amyloid protein. Clusters of these pieces have a deleterious impact on neurons and interfere with the cell-to-cell transmission when they form. By expanding in size, these deposits, known as amyloid plaques, become more widespread. Tau proteins function as a kind of internal transport system that supplies neurons with food and other necessities. Neurofibrillary tangles are a result of the abnormal organization of tau proteins, which are caused by the illness. The tangles are harmful to cells and impair the transport mechanism [19].

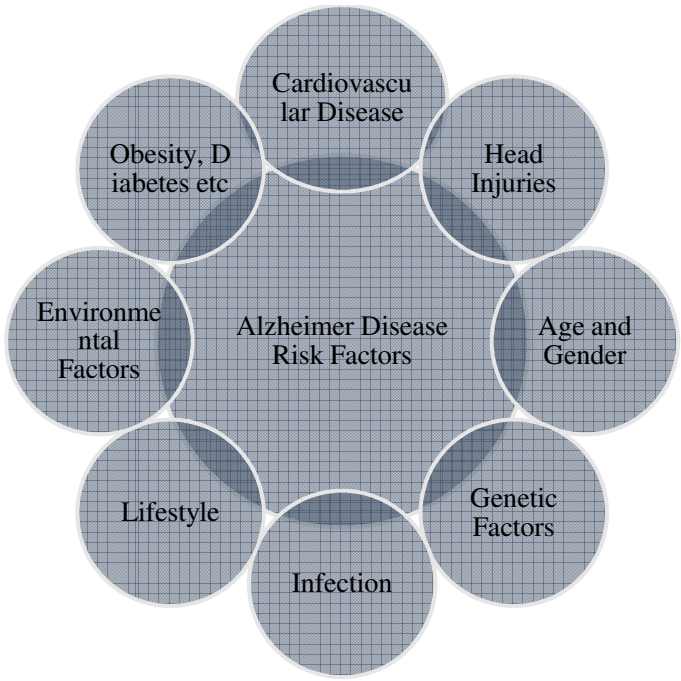


**Figure 3:The factors that increase or decrease a person's likelihood of developing Alzheimer's disease.**

*3.5.Current Landscape in Treatment Research for AD:*

There are currently no approved DMTs for Alzheimer's disease (AD), althoughNo new AD medication has been approved by the FDA since 2003. In the previous decade, almost 200 research projects have been deemed unsuccessful or scrapped. But there are still several medicines in the AD therapeutic pipeline with disease-modifying or symptomatic MOAs. It is generally agreed that insufficient knowledge of the biology of AD is mostly to blame for the continued failure of clinical studies with DMT medicines for the illness, along with other factors like delayed treatment initiation, incorrect drug dosing, and misdirected treatment focus [20].

Some anti-amyloid medicines, including semagacestat,29 bapineuzumab, and solanezumab, as well as the Beta -secretase inhibitors (BACE) lanabecestate, verubecestat, and atabecestat, have recently failed in phase 3 clinical studies in individuals with initial, mild, or moderately severe AD.It appears that the novel approach to the problem is more technological and numerical than biological, suggesting that the diagnostic endpoint of the identified tests could be premature. Furthermore, the variance in diagnostic biomarkers and endpoints could lead to an incorrect diagnostic test of patients' disease state, an endpoint is, ultimately, a definitive cause of the error.Contrarily, risk factors for AD that can be modified, such as cardiovascular disease and unhealthy lifestyle choices, may often be avoided even without the use of preventative medicine.Cognitive abilities in the elderly have been proven to improve with regular exercise due to its effects on vascularization, plasticity, and neurogenesis of the brain, as well as it is anti-inflammatory and endorphin-releasing properties.

There may be fewer cases of AD if people do this. Alzheimer's disease (AD) may be slowed, memory boosted, and other cognitive capacities enhanced by the Mediterranean diet (MD), mental engagement, and higher education. Numerous studies have shown that improving or preserving cognitive function and avoiding Alzheimer's disease from developing in the elderly

can be achieved by simultaneously addressing multiple aspects of aging, including nutrition, exercise, and cognitive change, in addition to lowering AD symptoms and managing cardiovascular risk factors. The current therapies for AD, as well as the drugs and concepts that are being investigated to enhance these treatments.

#### *3.5.1. Treatment of Alzheimer's Disease Symptoms:*

*i. Donepezil:*

The best-known medication for treating Alzheimer's disease is donepezil, a second-generation Acetylcholinesterase Inhibitor (AChEI) and derivative of indanone-benzyl piperidine. Donepezil blocks the release of acetylcholine (ACh) from nerve terminals, reducing the amount of Acetylcholine (ACh) at the synapse byinhibiting the degradation of acetylcholinesterase by reversibly binding to the enzyme. The medicine has few and short-lived cholinergic adverse effects that mostly affect the digestive and neurological systems, hence it is easily tolerated. Donepezil is used to treat AD symptoms including improving behavior and cognition, but it does not stop or reverse the progression of AD itself [21].

*ii. "Rivastigmine":*

Pseudo-irreversible inhibitor of acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) is rivastigmine. Involvement in acetylcholinesterase (AChE) metabolism through interaction with the enzyme's anionic and stearic active sites.The enzyme benzoylcholinesterase (BChE) is found predominantly in glial cells and is responsible for only 10% of AChE activity in a healthy brain, suggesting that BuChE activity may result in mild to severe dementia but its function increases to 40%-90% in an AD brain, while ACh activities concurrently decline. In the synaptic space, AChE and BuChE are responsible for the metabolism of the pseudo-irreversible rivastigmine, where its dissociation is slower than that of AChE. The medicine is prescribed for patients with moderate to severe AD. It's a boon to one's mental health and general ability to go about one's day.

*iii. Galantamine (GAL):*

Oftentimes, galantamine is used as first-line therapy forAlzheimer's disease ranging from mild to severe. GAL functions as a competitive inhibitor of acetylcholinesterase because it is a particular tertiary isoquinoline alkaloid that interacts allosterically with the -subunit of the nicotinic receptor for acetylcholine and activates it. Like other AChE inhibitors, GAL may effectively reduce behavioral symptoms while having little to no negative impact on quality of life or tolerance.

## 4. CONCLUSION

Alzheimer's disease has a disproportionately negative impact on the older population (ADThere is still a lack of clarity on what causes this sickness. The cause of this disease is still poorly understood. There are progressive, irreversible stages of the illness in which cognitive (memory, thinking, and reasoning) and behavioral skills deteriorate to the point that patients are wholly reliant on others for even the most fundamental of everyday tasks.Several studies have demonstrated that making changes to one's diet and exercise routine may enhance brain health and lessen AD without the need for medication, and as such, these changes are now recommended as the first line of defense for all individuals with AD. Recent studies have aimed to eliminate A and p-tau, two pathogenic hallmarks of AD.Disease-modifying therapies of the futurecould be able to slow or stop the development of AD by blocking the A pathway. Several

such treatments have entered clinical trials but so far have failed to demonstrate any efficacy; these include AN-1792, solanezumab, bapineuzumab, semagacestat, avagastat, and tarenflurbil.

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# CHAPTER 20

# AN ANALYSIS OF THE FUNCTION OF GENETIC ENGINEERING IN THE PROCESS OF ANIMAL BREEDING

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**ABSTRACT:**

"Genetic engineering (GE)" is a critical component in the development of innovative medical diagnostics, drugs for animals and human disorders, human health diets, and cell and tissue production for xenotransplantation. By changing nutritional components or introducing health-providing proteins, peptides, or other components, vaccine components for the management of the disease and nutraceuticals for human health could become a vital element of human living in the future. Animals that have been genetically engineered might give significant benefits to human welfare and health. This study looks at genetic engineering and how it's being used in animal breeding, including topics like its fundamental concepts, methods, varieties, relevance, and boundaries. Cattle, sheep, pigs, and poultry have all benefited from genetic modification. It has a variety of biomedical applications in addition to boosting agricultural production (meat, milk, wool) and enhancing resistance to illness (vaccine production). The novel, high-value cow populations might be developed by studying the impact of individual genes and gene combinations on desirable features.

**KEYWORDS:**

Animal Breeding, DNA, Genetic Engineering (GE), Genetic Improvement, Marker Assisted Selection (MAS).

## 1. INTRODUCTION

The term "Genetic Engineering" (GE)" means a methodical approach that includes the recombination of DNA to directly alter the genetic makeup of an organism or a population of organisms. These methods help locate, duplicate, modify, and transplant genetic material across cells, tissues, or species [1].Numerous real-world applications are emerging for genetic engineering in livestock breeding, including the creation of disease-resistant transgenic animals, the enhancement of livestock productivity, the remediation of genetic abnormalities, and also the manufacture of vaccinations. The medical field would benefit from this technology in some ways that would be difficult or impossible without it [2].

To control the expression of certain genes, most methods involve the direct alteration of DNA. Incorporating DNA-based selection indicators "marker-assisted selection" (MAS)" is a sort of genetic engineering that has the potential to vastly improve the effectiveness of so-called "conventional" breeding techniques based on phenotypic data. The direct modification of DNA sequences is generally considered the primary goal of genetic engineering. Specific DNA fragments belonging to individual genes may be isolated, cut, and moved using these methods [3].

Mammal genomes are bigger and more intricately organized than those of viruses, bacteria, or plants. Therefore, molecular genetic engineering and recombinant DNA technology for genetic alteration in animals are more challenging and expensive than in simpler species. Strategies for manipulating gametes and embryos are commonly important parts of these methods in mammals, including generating artificial reproduction techniques such as in vitro fertilization, embryo transfer, and artificial insemination (AI), cloning, the creation of a new organism from an existing one's differentiated cells [4].

Numerous terms, such as genetically modified, genetically transformed, genetically manipulated, transgenic, and biotechnology-derived, are used to refer to animals that have been created via genetic engineering. Transferring genes from one organism to another, or transgenesis, was the major technique used in the early stages of genetic engineering. Additionally, alternative applications emerged without the requirement for transgenesis as technology progressed: Using modern techniques, genetically altered animals may be created by insertion or deletion of new genes.There have been many distinctmethods of breeding animals to improve their genetic qualities. The majority of breeding operations have sought to increase the genetic value of animals via the use of traditional, phenotype-based selection approaches [5]. The success of such an approach depends on several variables, such as the efficiency with which high-quality individuals can be identified, the vigor with which selection is applied, the length of time over which the strategy is implemented, and the degree to which genetic diversity is maintained and, ultimately, translated into short- and long-term genetic gains [6].

Recent advances in genotyping and sequencing have enabled us to examine the cow genome, significantly contributing to our present knowledge of genomic selection. It was in the 1940s when the best linear unbiased prediction was made[7], and since then, there have been several developments that have likely had a major impact on animal breeding. Gene editing is a potent tool to change the genome, and its recent breakthroughs have sparked excitement among animal breeders who want to use the technology to speed up the process of improving animal populations' genetics [8].The possibility of using genetic engineering of mammalian cells in the future to treat genetic disorders like the prevention of cystic fibrosis by replacing faulty genes in developing fetuses and infants with healthy ones (gene therapy) is what has sparked the field's current attention [9]. Therefore, the purpose of this is to examine the techniques, certain applications, and ethical concerns surrounding genetic engineering in animal breeding.

## 2. LITERATURE REVIEW

Ismail Mansouri et al. stated in their study that European turtle doves' migratory patterns, reproductive performance, and breeding phenology were analyzed at the region's highest breeding habitats in Midelt, Morocco (1400–1600 m). The Common Bird Census technique was used to collect the data, which was collected from March to October 2015-2018.The findings indicated that As of March 28.25±2.05, turtle doves arrived and departed on 28.00.±1.47 September at high-altitude nesting locales (n = 20). However, the first day of nesting was April 26.5 ±0.64, whereas the first day of laying was April 28, barelywithin a day and a half of constructing the nest. The earliest fledge date was 17.50 ±2.72 May, while the earliest day that chicks began to fly was 3.50± 2.33 June. The author concludes that the turtle dove may be able to escape the adverse effects of the harsh environment found in the mountains by choosing to nest in breeding seasons that are shorter and later in high-altitude habitats [10].

Ashutosh Das et al. conducted a study in which the phenotypic performance and genetic determinants for body mass and egg production at sexual maturity were studied by breeding the egg-type light chicken breed Fayoumi with the Bangladeshi regionally adapted chicken type Hilly. Hilly Fayoumi (HF) hatchlings averaged 350.1 g. At 20 weeks, HF crossbred chickens weighed more thanvariations among Bangladesh's native chicken breeds. 8-10 weeks had the most weight increase. HF cross-bred chickens reached sexual maturity at 147.51.6 days and 135016.8 g/bird. The average weight of a fully developed egg was 33, 70.5. The normal range of variation in body weight is 0.15 to 0.26. Researchers discovered a correlation between WSM and EWSM, suggesting that hens with more WSM also laid larger eggs [11].

The goal of the research, as stated by Duguma Dibbisa Itana, and Ararsa Duguma is to investigate the part growth hormone plays in achieving maximum yields in livestock. Proteins called growth hormones may be produced either naturally or artificially to stimulate growth. There are plant-based hormones, such as phytoestrogens, phytoprogestrons, and phenolic substances. Medicines derived from cow placenta and colostrum include the hormones progesterone, estrogen, gonadotropin, and prostaglandins. Popular uses of growth factors include the development of fat-free meat (produced by injecting somatotropin into pigs), nutritionally and medicinal purpose beneficial milk (created with Bovine Somatotropin and cows), and fodder crops that are both tasty and resistant to disease and insect pests. As a result of their work with oestrus synchronization and superovulation, particularly in the context of embryo transfer (ET) and artificial insemination (AI), they have also made significant contributions to the maximization of livestock output. These hormones are controversial because of the vast range of effects they have on humans, animals, the ecosystem, and other organisms. Hormones excreted by animals pollute the groundwater, which has been linked to health problems including cancer, infertility, and mineral imbalances in the soil and water[12].

## 3. DISCUSSION

Animals are being genetically engineered for potential use in healthcare, agriculture, and other fields. There is also a need to learn more about the fundamentals of mammalian genetics and physiology, such as how many different genes contribute to the complex features that cause so many different illnesses in both humans and other animals. The potential of gene therapy to cure a wide variety of diseases has sparked an interest in genetically altering mammalian cells in congenital disorders like cystic fibrosis in newborns and children by replacing defective copies of the gene with healthy ones (gene therapy)[13].

Genomic selection has been met with so much excitement that several breeding businesses are considering reworking their breeding strategies. Genomic selection may be used to forecast the breeding qualities of a candidate’s birth with a higher degree of accuracy than the traditional pedigree index. As a result, animals may be chosen for desirable traits at a younger age, which has the potential to increase the pace of genetic progress by a factor of two every year. The use of genomic data in animal breeding offers promising potential, since it may play a pivotal role in shaping breeding strategies to optimize long-term genetic benefits. There is mounting evidence that more of genetic information's advantages might be reaped if it were used in individual breeding programs [14].Conventional livestock improvement programs aim to increase the genetic diversity of domestic animal populations by selecting men and females that are expected to produce children when fertilized with improved performance above the average of the latest generation. When evaluating performance, it is common to look at some different attributes many of which tend to be numerical.Quantitative traits such as an animal's milk production, fat

production, and protein production in the case ofanimal development, fattening, and feed intake in the case of production of meat; and dairy production, are examples of traits that are regulated by multiple genes (potentially hundreds or thousands) and are subject to environmental influences.

The knockout mouse is only one example of how genetically modified animals may be used to study human genetic illness and uncover the role of certain regions of the genome. It's likely that xenotransplantation, in which human organs are harvested from genetically engineered animals, may one day include pigs. Uses for genetically engineered milking animals include producing human medicinal proteins like insulin in the mammary gland (transgenic animals, bioreactors) [14].Increasing the frequency of beneficial alleles in food-producing populations, these methods may be used to boost resistance to disease and production in the agricultural production of essential animals. To achieve this goal, it is possible to transfer alleles, and allele combinations, or to overexpress or silence certain genes.

Selection intensity, or the degree to whichfuture parents diverge from their peers' average breeding value, determines how quickly genetic progress occurs or how quickly a population responds to selection. The shortened the generation interval, the faster genetic progress occurs. Increases in genetic variety (the molecular substrates of breeding programs), improvements in the precision of selection, shorter generation intervals, and greater selection intensities are four ways in which biotechnology is being used to hasten genetic advancement[15].In the field of biotechnology application to livestock genetic improvement, three primary themes may be differentiated: techniques for artificial insemination, genetic modification, transgenic animals, and marker-assisted selection (MAS) for livestock [16].

### *3.1. Modern Different Ways in Which Genetic Engineering Is Used in Animal Production:*

Ethical considerations, practical applications, and an outline of the procedures involved in using genetic engineering in animal breeding are all covered in this study.The phrase "genetic engineering" refers to a wide variety of practices used to extract, replicate, modify, and then transfer the DNA of specific cells, tissues, or species. The following are some of the most significant uses of genetic engineering in animal breeding:

#### *3.1.1. Using Genetic Markers as a Breeding Tool in "MAS (Marker Assisted Selection)":*

Rapid progress in genetic technology has provided a pool of genes for animal breeding that were previously unavailable via more traditional means. As a result, many individuals are fascinated by MAS (Marker Assisted Selection), which stands for "marker-assisted selection". In the future, molecular genetic technology will allow for earlier (even embryonic) selection of breeding animals, allowing for the selection of a wider range of desirable features [17].By integrating data on DNA markers with phenotypic and family trees, this approach aims to improveeconomically relevant animals' disease resistance, productivity, and output quality.

The genetic markers that researchers rely on are still being established. The transmission of these markers in animal populations may provide light on the impact of genes on phenotype by revealing whether or not genetic inheritance is linked to enhanced performance. Marker-assisted selection refers to the practice of using knowledge of genetic markers to guide future breeding programs, guaranteeing that offspring carrying the marker will also possess the beneficial trait associated with it (MAS)[18].Increasing the efficiency of the selection process is the goal of MAS [4]. The identification of individual polymorphisms which have been responsible for the

detected impact is necessary for the proper deployment of suchQuantitative traits loci (QTL) inside selection procedures. Recombination between both the marker and the actual QTL and mutations in other parts of the genome may reduce the efficiency of MAS [19].

When genome mapping and quantitative trait loci (QTL) analyses advance, the recombination issue will be solved as the genes as well as the particular polymorphic alleles that cause QTL are pinpointed. Based on the size of the QTL, MAS may increase genetic benefits by 10% to 20%. In contrast to traditional selection based on “best linear unbiased prediction (BLUP)”, the frequency of the beneficial QTL allele in a population swiftly increases when MAS is utilized BLUP. The QTL and marker locus connection should be considered while choosing an animal for genotyping. Using the discovered QTL in the selection process necessitates the creation of selection criteria that link this genetic information with phenotypic data [20].Genetic illness, disease resistance, and high-quality product genes may all be identified by marker-assisted selection. Marker-assisted selection for enhancing animal traits including hardiness, pecking ability, and stress tolerance [21].

### *3.1.2. Assisted Reproductive Technology (ART) in Animal Breeding:*

Infertility may be remedied with the use of ART. It involves reproductive therapies that manage both eggs and sperm. Eggs are extracted from the ovaries, which leads to their efficacy. The eggs are subsequently combined with sperm to produce embryos. The embryos are then implanted back in the parent's body [22]. “Aided reproductive technologies (ART)” include methods including “in vitro fertilization (IVF)” and “Intracytoplasmic sperm injection (ICSI)”, in which an egg is fertilized outside of the body. In vitro fertilization (IVF) is used to treat female menopause and inexplicable infertility, whereas in vitro sperm injection is used to treat male infertility.Recent breakthroughs in biotechnological reproduction techniques include the generation of transgenic animals and cloning. RT has long-term impacts on animal breeding because it boosts the reproduction rate and decreases generation time. Emerging biotechnologies like "Multiple Ovulation and Embryo Transfer (MOET)", "In Vitro Fertilization (IVF)", and others were necessary for the most successful reproductive technologies like AI and ET and cloning, as a primary instrument for rapidly changing the genetic makeup of populations of animals.

### *3.1.3. Use of Transgenic Technology in Animal Breeding:*

Transmission of certain genetic variants across members of different species or even other kingdoms affects the recipients' phenotypic expression In contrast to 'conventional' improvement approaches that relyon these gene-by-gene methods rely exclusively on phenotypic data, which might lead to more extensive alteration of animal genomes for animal breeding.Transgenesis refers to a technique wherein a gene or a segment of a gene is transferred into the genomes of a different organism. Potential applications for transgenic animals include the research of gene function processes, altering animal characteristics to increase the production of high-value proteins, and raising animal production and disease resistance while establishing animal models for human diseases. Many laboratories announced their successful transfer of genes and the creation of mouse models in the early 1980s.Several laboratories announced their successful introduction of foreign genes .and the creation of transgenic mice in the early 1980s. Transgenic animals include those produced via any molecular change of endogenous genomic DNA, including but not limited to embryonic stem (ES) cell transplantation, DNA microinjection, and the production of "knockout" mice [13].

Currently, transgenic animal technologies are in the process of completely altering how cattle are raised in the home. Transgenesis refers to the process by which an alien inserts a gene of interest into a host organism's DNA from a different species and then perpetuated it via offspring. It can speed up and simplify the process of genetic improvement in animals. Transgenic animal breeding was first developed to boost agricultural output by creating stronger, faster-growing, more meat-bearing breeds [23].

Transgenic organisms are created by first cloning the transgene encoding the desired characteristic into a vector which may be either synthetic, viral, or plasmid DNA, and then inserting this hybrid vector into the host genome. More methods for creating transgenic animals have proven to be effective, while others are still in the research phase and might need some refinement. Microinjecting a transgene into the pronucleus of an embryo just after fertilization is the most common technique for creating transgenic animals, but other techniques, such as transgenic a version of somatic cell nuclear transfer, furthermore somatic cell nuclear transfer (SCNT) has been developed [24].

*3.2.Animal Genetic Engineering Applications:*

*3.2.1. Increase animal disease resistance:*

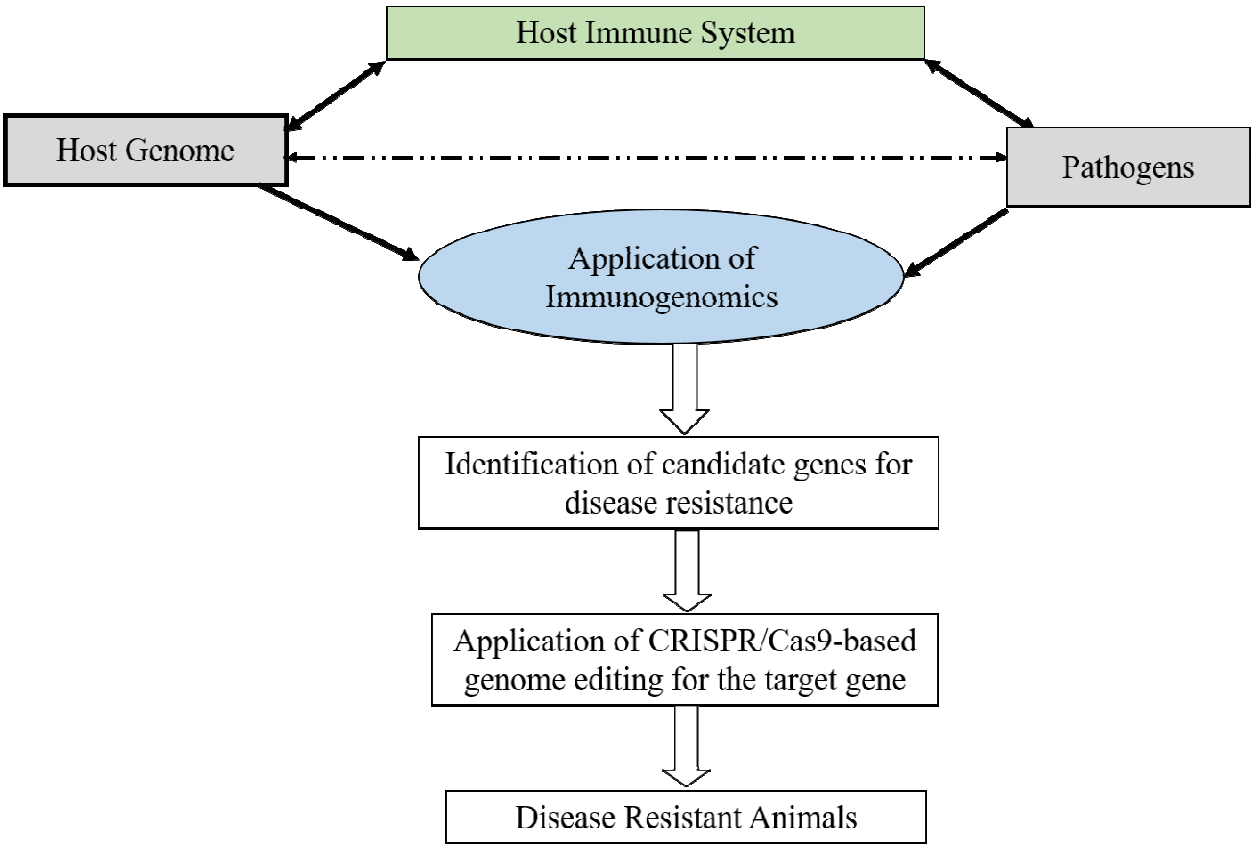


**Figure 1:Diagram illustrating the use of Immunogenomics and genome editing to create disease-resistant animals.**

By inserting certain genes into animals, genetic engineering of animal production offers the potential to increase disease resistance.The discovery of individual genes in the major histocompatibility complex (MHC) that control the immune response was a pivotal moment in the evolution of our knowledge of genetics underlying disease resistance and susceptibility. Many new tools for treating animal diseases have been developed thanks to advances in animal biotechnology. First, genetic selection may be used by the cattle industry to screen for traits associated with disease resistance, allowing for the establishment of populations of animals that are more resilient to sickness. The second way in which genetic engineering improves animal health is by allowing breeders to make use of previously unavailable disease-resistant genes [25].

Disease resistance occurs when a host can slow down or stop the spread of an illness caused by a virus, bacteria, fungus, parasite, or another pathogen. Infection and disease pathogenesis are controlled by interactions between the host immune system, invading pathogens, and the host genome shown in Figure 1. A host's innate immune system is its first line of defense against pathogen attack, and genes involved in inducing adaptive immune systems are among the most promising prospects for disease resistance [26].The heterogeneity in genetic resistance to illness is mostly attributable to the host's immunological response to an infection. As a result, knowledge of immunology and genetics together would help describe the illness phenotype. Immunogenomics refers to the use of genetic technology to better understanding immunology. Immunogenomics is the integrative examination of immunological and genomic data on host immune responses to infectious diseases, and it contributes to the identification of possible disease-resistance genetic variants in cattle.

### *3.2.2. "Increase meat and milk production":*

There is hope for "value-added" production in the animal agricultural sector because of therise in meat and milk production via the use of genetic engineering. This is because genetic engineering may either raise the concentrations of proteins that already exist or produce whole new proteins.With the world's population constantly rising, they must find ways to boost the milk and meat supply of animals via genetic engineering. Milk from transgenic mice with an enhanced human lysozyme content has greater anti-microbial characteristics, which in cows might decrease mammary gland infections and perhaps eradicate undesired microorganisms in the guts of people who ingest the milk. In addition to their high value as a source of protein, cattle are often recognized as the most productive livestock animals.

Milk from a transgenic cow has been shown to have changed casein levels ranging from 10 to 20%, which may hasten cheese's maturation by increasing proteolysis. Transgenic mouse studies showed the benefits of introducing genes to the milk protein system, like the casein gene or the human lysozyme gene.Both growth hormone-releasing factor (GRF) and insulin-like growth factor I (IGF-I) are proteins whose production is controlled by genes that were discovered to have effects on growth in mouse and lamb studies. Transgene effects in pigs have been shown to enhance IGF-I levels and growth hormone, which in turn decreases body fat and increases muscle fiber diameter, without causing any severe pathological consequences [4].

### *3.2.3. Improving the production of Wool:*

Wool is a natural fiber that is widely used to make outerwear and is a crucial economic factor for many nations. The study of sheep biology has yielded fundamental insights into the wool-growing process, and plans include capitalizing on the development and use of recombinant DNA technology to boost the performance and efficiency of wool production.One area of

attention for genetic engineering in animals has beenenhancing the hair, wool, and fiber harvesting process to provide better quality, more abundant, and simpler fabric and yarns. Transgenic techniques have been investigated for their potential to improve the thickness, smoothness, and crimping of wool and hair fibers from sheep and goats [27].

The goals are to optimize sheep wool production and to alter the fiber's characteristics. To improve wool production, researchers initially attempted to introduce bacterial genes for cysteine biosynthesis into the sheep genome. This was carried out because research suggests that cysteine is a crucial building block in the production of wool. Unfortunately, the transgenic sheep's rumen did not produce enough of these enzymes using this method. One area of interest for genetically engineered livestock has been the regulation of hair, wool, and fiber for use in the manufacturing of cloth and yarn [28]. Fiber flexibility and stiffness may be enhanced by transgenic approaches as well. Transgenic modification of wool in the future will concentrate on the fibers' exteriors. Garments constructed from certain fibers may shrink less if their surface contacts were reduced.

### *3.2.4. Vaccine Production:*

To vaccinate an animal, it is often injected with weakened live, dead, or inactivated versions of the virus or its toxin. The vast majority of vaccinations on the market today are either inactivated bacterial toxins, live attenuated organisms, or dead microorganisms. The majority of the molecular components found in killed vaccines are likely unnecessary and even hazardous since the immune system only responds to a few protective immunogens. Modern technological advancements provide alternatives to traditional immunizations that have fewer of these side effects. Generally speaking, recombinant vaccines may be broken down into three distinct types: those containing live GMOs, those containing inactivated recombinant components, and those containing genetic material [29].

#### *i. Live Genetically Modified Vaccine:*

Live genetically modified vaccines fall into two broad categories: those that employ bacteria or viruses with one or more genes eliminated or inhibited, and those that use viruses or bacteria as vectors to deliver a foreign gene from another disease agent. Vaccines with the disease-causing agent's genes deleted or inactivated are created. Vaccines often include the immunization is effective, the deletion or blocking of two (double-knockout) or more genes is required, and also it is stable and unable to mutate into a harmful agent. Animals have been inoculated against diseases by eating plants whose DNA was taken from other organisms. These plants include potatoes, soybeans, and maize.

#### ii. *Recombinant Inactivated Vaccine:*

Subunit vaccines, such as recombinant inactivated vaccines, comprise only a small portion of the entire organism. Synthetic peptides called subunit vaccines are the smallest immunogenic components of proteins. Subunit vaccines are made up of purified proteins that were either taken directly from the infectious pathogen or produced in vitro using cloned genes. Recombinant proteins may be expressed in either a cell-free system or a whole-cell system, but there are many more expression methods available.

Both prokaryotic (from bacteria) systems like E. coli and eukaryotic (from mammals, birds, insects, or yeast) platforms are examples of whole-cell expression systems. Virus-like particles (VLPs) are a kind of recombinant subunit vaccine made by simultaneously expressing one or

more clone genes encoding the structural proteins of a virus. All of these VLPs have immunogenic properties. However, subunit vaccinations need an adjuvant to be fully effective.

*3.3.Genetic Engineering's Limitations:*

*iii. Genetic engineering ethical concerns:*

At any point in a genetically altered animal's life cycle, ethical questions about the animal's well-being may emerge.There have been various difficulties discovered throughout the impact analysis consultations and peer-driven recommendations development phase of the Canadian Council on Animal Care (CCAC). The CCAC follows the Three Rs, a set of standards for the welfare of the animals used during a scientific investigation (Reducing the number of animals employed, Refining procedures and husbandry to reduce pain and suffering, and replacing animals with non-animal substitutes whenever feasible).

iv. *Antibiotic Resistance:*

In people and animals alike, the potential loss of antibiotic efficiency due to the usage of antibiotic resistance flag genes is a significant cause for worry. Antibiotic resistance is potentially contagious because of the widespread availability of antibiotic resistance is becoming more common due to the spread of antibiotic-resistant bacteria in soil, the environment, and animal and human diets. This might happen if microorganisms in the environment or the stomachs of animals or people acquire antibiotic-resistance molecular markers via the horizontal transfer of genes.Many bacteria are capable of acquiring and passing on genes from their environment, including antibiotic resistance marker genes. These genes might be acquired by pathogenic bacteria, leading to treatment difficulties due to antibiotic resistance.

v. *Economic Constraints:*

Infrastructural development is a fundamental necessity for establishing businesses based on biotechnology. Although research and development spending on biotechnology is on the increase in developing countries, there is still a severe lack of seed money for biotech startups. Financing early phases of company growth might be accomplished through seed investment, increased access to loans, and venture capital.

## 4. CONCLUSION

The fields of medicine and agriculture both rely heavily on the innovations made possible by genetic engineering.As a result, several industries have reaped enormous financial benefits. The use of genetic engineering has the potential to save endangered species. According to existing state and federal animal rights regulations, any reasonable animal genetic engineering must be legalized. As with other basic advancements in biological science, genetic engineering may give practical advantages to humanity if used wisely.Genetically engineered animals have the potential to increase both human and environmental health, and also the better manufacturing characteristics of genetically modified foods could help meet the world's demand for more effective, better quality, and lower-cost sources of food.A wide range of hitherto impossible biological uses would become possible with this method.Gene exchange between organisms has the potential to disrupt the natural genetic balance and produce undesirable effects, raising concerns about health and ethics in addition to financial constraints.

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# CHAPTER 21

# AN ANALYSIS OF THE USE OF MITOCHONDRIAL DNA IN FORENSIC SCIENCE

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**ABSTRACT:**

Mitochondrial DNA (mtDNA) has a variety of features that make it a helpful tool in forensics, including its characteristics of high copy number, no recombination, and maternal inheritance. Screening of ancient bones, teeth, and hair, in addition to other biological materials with low DNA content, may be done using sequencing of the regulatory region or the whole mitochondrial genome for mtDNA type. When compared to nuclear DNA, mitochondrial DNA mutates at a rate 10 times faster. Because of this characteristic, species development can be extremely advantageous in the hereditary, line for many generations and can be employed in a range of different research techniques. This study discusses the importance of mtDNA and modern forensic methods. In this study, the author also covers the mitochondrial DNA profiling techniques that are used for human identification and their application in the most important instances involving human identification and focuses on the most important forensic concerns.

**KEYWORDS:**

Forensic Science, Mitochondrial DNA (mtDNA), Human Identification.

## 1. INTRODUCTION\

The mitochondria in a cell are responsible for releasing usable energy from the nutrients they take in.Every cell has hundreds to thousands of mitochondria floating about in the cytoplasm, the fluid surrounding the nucleus. Mitochondria have a little quantity of their DNA in addition to the chromosomes found in the nucleus.Human nucleated cells include mitochondria, membrane-bound organelles that produce Adenosine triphosphate (ATP). Mitochondrial DNA is located inside mitochondria (ATP). Because mitochondria have a lot in common with bacteria, scientists believe they evolved from prokaryotes to become endosymbionts of eukaryotic cells [1].

From its conception, forensic science has been at the forefront of solving identification mysteries in instances involving murder, kidnapping, terrorism, disappearances, and natural disasters. Despite their accuracy, STR markers may not amplify in situations when insufficient template DNA is available (perhaps because of significant degradation, alterations, or low copy numbers) [2].The sequencing of Mitochondrial DNA (mtDNA) is a method that can and should be employed in such situations, and the FBI laboratory recently did so in a criminal case. Almost all eukaryotic cells include organelles called mitochondria, which are responsible for converting chemical energy into a form (adenosine triphosphate) that may be quickly used [3].

Forensic uses of human genetic identification depend on the delineation of genetic profiles. An individual's genetic profile, often known as a genetic fingerprint, is a phenotypic characterization of a subset of genomic regions that seems to be unique to that person. Current international

guidelines proposegenetic fingerprinting based only on profiles derived from autosomal short tandem repeats (STR), following suggestions made by the "European DNA Profiling Group (EDNAP)". Furthermore, autosomal DNA is often severely damaged or unavailable in instances requiring human identity. Because of its use in such situations, mtDNA research for human detection has become standard practice.However, in contrast to nuclear markers, mtDNA findings of sequence identities are not about one person but about a group of people who have the same maternal ancestry[4].

Mitochondria have a significant role in determining the cause of nuclear DNA loss, restriction, or damage; a human liver cell contains about 2,000 mitochondria, whereas a mature red cell has none, and oocytes have hundreds of thousands [5].Forensic human identification using autosomal genetic markers is facilitated by a practically unique mix of short tandem repeats (STRs). These are short sequences of typically four nucleotides. The allelic type is determined by the total number of repetitions. In contrast, as shown in Figure 1, the mtDNA sequence does not identify a single person but rather a family tree of women who share a common maternal ancestor.

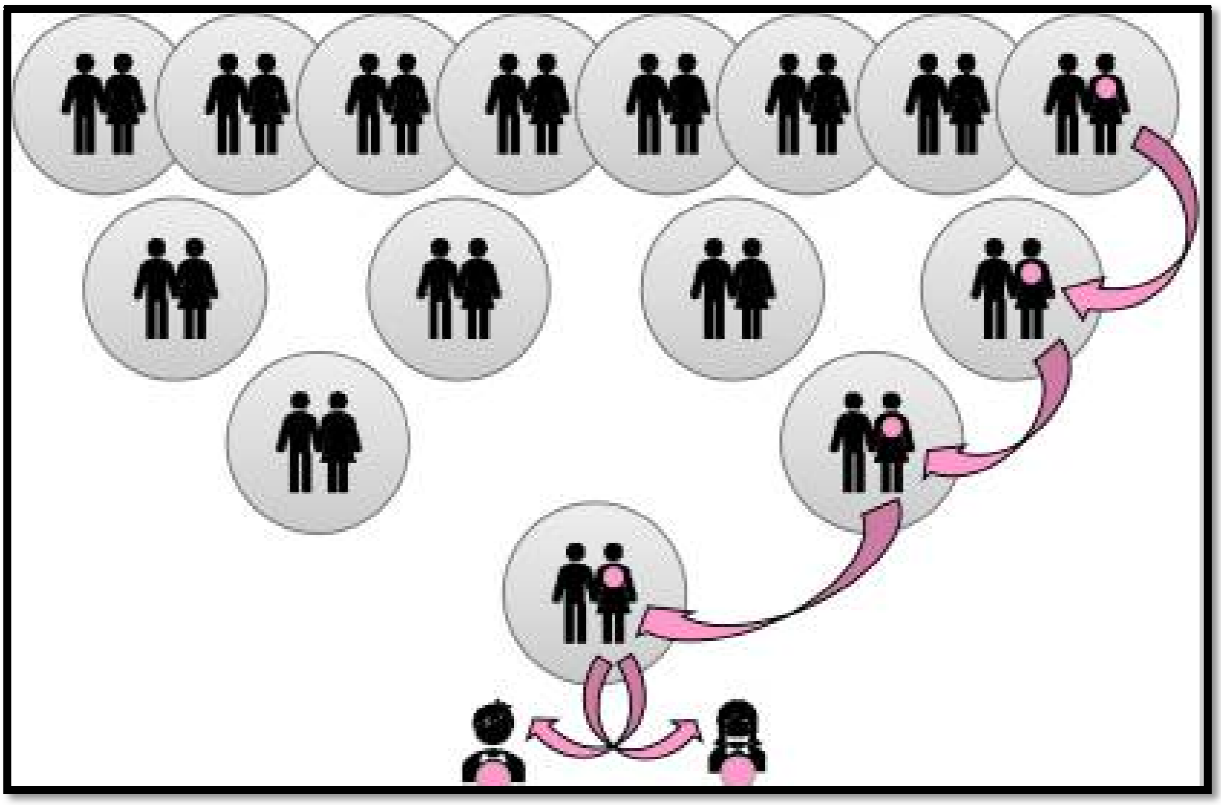

**Figure 1: Displays the Female ancestors with the same haplotype in their mtDNA have been traced back four generations** [6]**.**

Characteristic only of mammalian, plant, and fungal cells, mitochondria are subcellular organelles with a specific function. They are the major power source for the many cellulars and organismal processes that need them. The quantity of mitochondria in cells that need a lot of energy to function varies greatly.They are situated near the site of the highest energy expenditure inside the cell. Their population expands autonomously by the division that occurs independently of the cell cycle during the interphase [7].Comparing all human mtDNA to the

reference sequence based on data from the University of Cambridge[8] is the gold standard. Polymorphism refers to any variation seen in the Cambridge sequence of the mitochondrial DNA.

## 2. LITERATURE REVIEW

Vikas Kumar et al. analyzed their study that DNA sequencing to identify probable animal items from east India. The author took adequate safety measures when handling samples and performed the project at ZSI, Kolkata. Most of the 21 seized wildlife items are recognized by Cytb, one by COI, and another by both. All amorphous specimens are reliably recognizedby examination of sequence similarity (99.9%-100%), genetic distance, and NJ phylogenetics.The author concluded that five of the most endangered animal species in east India were found to be involved in the ongoing illicit trade. Evidence from this research supports the use of techniques for identifying animals that are based on their DNA in the course of forensic investigations involving animal crimes [9].

Juan M. Bueno et al. conducted their study that Normal aging affects the various tooth structures, especially the dentine. Age may be estimated with the use of these variations, which are helpful in forensic science. In this work, we examine whether MP signals may be used to predict the onset of dentine aging. These shifts have been quantified using “two-photon excitation fluorescence (TPEF)” and “second-harmonic generation (SHG)” images to create an aging index (INAG). According to the findings, INAG declines dramatically with age. Collagen's inner qualities also change with age, as does the size of the dentine that surrounds the tubules. This evidence demonstrates the technique's use in forensic age assessment after catastrophes (both natural and man-made) when a complete fingerprint database may be unavailable.

Mona Sivaneri et al. discussed in their study thatstandards established by the American Dentistry Association (ADA) must be included in dental and dental hygiene programs. Ten maxillary molar radiographs were taken.Radiographs were taken of a single tooth that had been heated to 600 degrees Fahrenheit (315.6 degrees Celsius) for 15 minutes. It was tested on 152 dental students by having them compare the heat-altered radiograph to a regular one. Students also completed a 10-question dental forensics survey.Pupils matched in both the original and the heat-altered radiographs in 92.1% of cases. Five poll items received 70% accurate answers. Neither dental class nor sex was statistically significant. While dental students are good at matching radiographs, they require additional dental forensics understanding [10].

## 3. DISCUSSION

Each mitochondrion has two to five complete genome copies and has its genome, which is organized in a histone-free, double-stranded, circular fashion and is comparable to the bacterial genome. Mitochondrial genomes are similar to bacterial genomes in that they consist of two to five full copies of DNA structured in a histone-free, double-stranded, circular format. The frequency of the heavy (H) and light (L) segments in mitochondrial DNA is set by the local distribution of nucleotides. Most of the mtDNA molecule is made up of these sections,they contain 37 rRNA and tRNA-producing genes and almost all 13 polypeptides have been linked to oxidative phosphorylation.Evidence that mitochondria originate in bacteria is provided by the existence of intron-less genes in mtDNA genomes; nuclear DNA from a human cell is unable to recreate mitochondrial [11].

The procedures used by the majority of labs that provide mtDNA service are standard. Reference samples of blood, which are rich in DNA, and all other samples are treated with the utmost care from collection to sequencing. The fundamental motivation for this method is to prevent samples from being mixed.The investigation relies heavily on a PCR-based amplification technique that zeroes in on the controlhypervariable areas HVR Types I and II. Mitochondrial DNA (mtDNA) analysis consists of several steps, including visual examination, Automated DNA sequencing, data processing, information analysis after sample preparation, DNA extraction, PCR amplification, post-amplification quantification, and purification [12].

*3.1.Human mtDNA has the following characteristics that make it suitable for forensic testing:*

Due to its circular shape and subcellular sequestration, the mtDNA genome is less prone to degradation than nuclear DNA, making it useful for assessing poor quality and low quantity DNA samples and providing an alternative approach to discovering possible family ties. Importantly, the three fundamental drawbacks of mtDNA analysis low discriminatory power, costly method, and heteroplasmy do not make the technology ineffective. In any case, there are a few specialized qualities that stand up to forensic analysis.

*i. High copy number:*

Mitochondrial DNA (mtDNA) is far more abundant than nuclear DNA (between 200 and 1,700 copies per cell) and has a lower base content, making it more economical. Most often, the ratio of mtDNA copies to nuclear DNA (cDNA) copies is used to describe mtDNA content. Forensic studies that need a tiny or degraded quantity of extracted DNA might benefit greatly from mtDNA typing owing due to a cell's large number of mitochondrial DNA molecules and their extra nuclear cytoplasmic location.When the polymorphism markers in nuclear DNA cannot be typed successfully, mtDNA typing is a viable option due to its higher survival rate [13].

*ii. Maternal mode of Inheritance:*

If there are no mutations, all maternal relatives' mtDNA sequences are identical, even those of siblings. This might be useful for identifying the remains of the missing when identified maternal relatives can give reference samples for a quick comparison to the mtDNA type in the issue. Both inter- and intraspecific hybridization of birds, mice, and mussels have shown paternal inheritance of mtDNA. Human mtDNA has traditionally been thought of as a genetic trait passed down only via mothers[14].One of mtDNA's greatest advantages is that it is inherited uniparentally, allowing researchers to follow related lineages across time and reveal a population's maternal ancestry without the sometimes perplexing effects of nuclear DNA's biparental inheritance and recombination, which can be useful in situations of presumed exemption diagnostics in human identification.

Additional people with mitochondrial myopathies were not found to have a paternal inheritance pattern. It is important to note, however, that mtDNA haplotypes that are passed down just one parent at a time represent information from a common, non-recombining maternal ancestry. Nuclear DNA marker recombination findings can be utilized for identification and authentication, but mtDNA information cannot [15].

*iii. Lack of recombination:*

Since recombination does not occur in the maternal line, close female relatives who are many generations removed from the original evidence (or biological material) may be used as a

comparative sample. In the conclusion, studies invalidated the authors' claims that phylogenetic trees constructed from mtDNA sequences and numerical evaluations of mtDNA sequences presented recombination evidence due to an excessive amount of homoplasmic sites and a correlation between genetic linkage and distance throughout the mtDNA genome [16].Even though the resulting research indicates an overabundance of homoplasmic sites, no recombination evidence was identified when researchers correlated linkage unbalance and proximitycollection of whole mtDNA sequences. This discrepancy is likely attributable to the varying mutation rates observed in human mtDNA. Recombination isn't taken seriously as a big problem since paternal mtDNA leaking is so uncommon. In the lack of recombination evidence, mtDNA sequences are assumed to have originated from a single locus, or haplotype between mtDNA molecules and the haploid mtDNA genotype in an individual [17].

*3.2.Forensic Human Identification Using Mitochondrial DNA:*

Forensic analysis routinely involves comparing the mtDNA sequences of the control and at least one other sample. Researchers could rule out the possibility that two sequences came from the same origin if there is an obvious discrepancy between them. More nucleotide changes between the two sequences are often accepted as an exclusions situation by forensic routine labs, despite this not being explicitly mentioned in any study publication or guidance manual.If the mtDNA sequences are the same then it is impossible to rule out the possibility that the samples come from the same mother. Heteroplasmy at identical nucleotide positions in both samples also cannot be disregarded [18].

A further helpful technique for characterizing biological evidence is provided by mtDNA sequencing. Although its value in determining an individual's identity is restricted due to the absence of recombination, its large copy number makes it particularly useful for confirming maternal ancestry or in situationsIf nuclear DNA is in little supply, such as when looking at hair, teeth, and bones. For obvious reasons, it is often utilized in ancient DNA analysis and victim identification during disasters (DVI).

In forensic DNA typing, short tandem repeats (STRs) or microsatellites are often genotyped to identify people, establish a relationship between a suspect and a crime, or both, or clear an individual of wrongdoing. When first discovered in the 1980s [19],During a forensic investigation, STRs have become the "gold standard" for identifying humans. Their building blocks include single, double, triple, quadruple, Penta, and Hexa-deoxyribonucleotides.An individual could be homozygous (having two copies of the gene) or heterozygous (having one copy of the gene) (with a different number of repeats). Genotyping in forensic DNA testing makes use of tetra nucleotide repetitions.The ability of STRs markers to perform multiplexed tests on more than 10 STR loci quickly and easily is one of their key benefits. This quality provides a higher level of identification for certain biological samples.

*iv. Analysis of the Y□chromosome:*

Since it is exclusively found in men, the Y chromosome may be used as a helpful tool in forensic medicine. Thus, Y chromosomes are often sought by police at crime scenes. Analyzing the YSTR component may also provide light on the male component when discussing the male-female ratio in bodily fluid combinations like rapes. It is well knowledge that rapists who have had a vasectomy or are azoospermic will not leave any sperm behind and that spermatozoa cannot be detected with a microscope. YSTR profiling is very helpful in these situations since it may provide details about the rapist's identity.

*v. An examination of DNA from mitochondria (mtDNA):*

As a result of the transmission of mitochondrial DNA (mtDNA) from mother to child, all members of a matriarchal family have the same haplotype. Its benefit comes from the fact that, in comparison to nuclear DNA, its 200-1700 copies per cell have a better chance of survival. Thus, forensic uses of mtDNA include the analysis of ancient or badly deteriorated biological materials, as well as an examination of samples with a low quantity of DNA example: hair follicles and shafts. Mitochondrial DNA successfully identified both Nicholas II and his brother Georgij Romanov (mtDNA).

*3.3.Techniques for the Positive Identification of Forensic Biological Evidence:*

It's crucial to pay close attention to details at the crime scene and any biological specimens that may be there. Following the appropriate crime scene collecting procedures is the first and most important step in determining whether or not to do mtDNA analysis on the collected samples. If the samples contain bodily fluids, they must be compared to a human reference specimen tofind out whether or not they originated from human beings. Additionally, forensic anthropologists must study samples of deteriorated skeletons, teeth, bones, and skull remnants, comparing them to human reference samples to validate their identity.

*vi. Collection and Preservation of Samples:*

Standard operating protocol (SOP) for the scene of the criminal process is accompanied by sample collection from the crime site, however, Because of the inherent rigidity, the Standards of Procedure for Handling Crime Scenes are very important in the case of a mass tragedy or bioterrorism might be Impractical and Unmanageable. As a result, discussion among the many institutions engaged in response should provide best practice possibilities.If new information is discovered at the crime scene or other points of the investigation, the plan may need to be adjusted.Therefore, the presence of a biological agent is not the only piece of circumstantial evidence to evaluate. Traditional evidence in this case like fingerprints, electronic documents, and evidence collection, together with related chemical and physical indicators like byproducts, may help determine who committed a crime.

Obtaining the proper kind, amount, and quality of data to back attribution requires careful consideration of the location of the sample, the technique of sampling, and the number of samples to gather. In addition, it is critical to preserve the evidence's integrity as much as possible during the time of collection and its subsequent preservation, since any compromise to this might result in the loss of important and trustworthy forensic information.Accordance with established principles (for forensic investigations) in combination with professional expertise (such as different biochemical expertise, investigative expertise, and good judgment) is probably the best and most largely acknowledged methodology for the advancement of a sample selection in a particular case. The collection, transport, and storage of samples have a major impact on the reliability of the findings. Once the samples have been identified as coming from a person, they are separated into various containers or plastic bags and given a unique number that represents the number of the crime scene [20].

vii. *Preparation of the Samples:*

Once forensic scientists have obtained exogenous human DNA samples, the first step is cleaning. Human tissue and blood samples are frozen at -20 degrees Celsius until analysis. To get rid of dirt and debris that can be stuck to the bone and tooth samples, sanding is performed.

To get rid of dirt, bacteria, and other tiny particles, a hair sample should be rinsed and subcultured for 30 minutes.Cut off 3 to 5 centimeters with the use of forceps and a scalpel, of the hair or hair shaft. Now is the moment to get a photo of the actual cutting. To test the nuclear DNA as well, you should clip the hair away from the root while taking the mitochondrial DNA sample. Return the unused hair to its original packing by sticking it to the back of a post-it note.

viii. *Extraction of mtDNA:*

DNA is isolated from other biological elements including proteins, cofactors, ions, and so on by extracting the sample using phenol/chloroform or alkaline chemicals. A pure DNA sample is obtained through centrifugation, sedimentation, and filtering. Fast extraction may be obtained using commercialized extraction, which has been verified almost in all forensic labs. The use of HVR-I and HVR-II primers in a polymerase chain reaction (PCR) is then used to amplify, quantify, and sequence the material.

*ix. Sequencing of mtDNA:*

mtDNA sequencing may be done in a variety of ways, each adapted to fit the specific resources available in a given facility. A Next Generation Sequencer is often used for direct sequencing (NGS). European DNA profiling group (EDNAP) commissioned three laboratories to analyze the mitochondrial DNA (mtDNA) HVR-1 region from blood samples using their standard protocols and methods.When looking for a match with a maternal line or the FBI information, the sequences are compared. The study is evaluated to see whether any parts of the process need to be replicated, and if so, how. Furthermore, the FBI's mtDNA database is examined for the detected mitochondrial sequenceswhether it comes to inclusion or matching.The “DNA Analysis Scientific Working Group” (SWGDAM) manages these records. According to the nucleotide locations that have been recorded, the analysts then listed the total number of occurrences of this sort of observation.

Through NGS genetic analysis, researchers were able to glean as much information as possible from severely degraded samples in the aftermath of mass fatalities. When there are several perpetrators and victims, whole genome sequencing may provide important leads by revealing mutations and SNPs. When evidence and reference samples are unclear, it is recommended that a population database be consulted to transmit information regarding the rarity of the mtDNA profile. The databases often include information from the most common types of people who could provide evidence. Forensic uses of these databases must take into account their accuracy and breadth of coverage.

*3.4.Biomarkers that are emerging in forensic identification:*

Because of technological advancements, forensic genetics would continue to improve and refine its procedures.One of the most crucial processes in forensics is determining where any samples of biological evidence came from. Over the last five years, studies have shown that mRNA, or messenger RNA, might be useful in forensics. Blood and saliva, among others, contain mRNA that is quite stable, due to the work of Zubakov et al.[21].Recent research on RNA or DNA co-extraction by the European DNA Profiling Group (EDNAP) demonstrated the superiority of mRNA over DNA as a method for determining the characterization of semen and saliva in forensic situations. In the field of forensics, mRNA is used with Real-Time Reverse Transcription - Polymerase Chain Reaction (RTPCR) techniques for the identification of skin.

In 2009, Hanson et al.[22], began investigating miRNA for forensic applications in the detection of bodily fluids. New markers are more persistent than mRNA markers because of their smaller size (about 18-22 bp), making them less susceptible to degradation. Improvements have been made in "postmortem pharmacogenetics" and "forensic molecular pathology" during the last decades.Forensic molecular pathology and postmortem pharmacogenetics have both seen major developments since the beginning of the decade. Postmortem evaluation of the gene CYP2D6, which embeds a drug-metabolizing enzyme and whose variability could induce pharmacological properties and, eventually, death, is a useful technology in the field of forensic medicine. Molecular treatment of the genetic cardiac arrhythmia or long QT disease, both of which result in unexpected death. These types of studies are examples of how forensics is constantly adapting to accommodate new information.

## 4. CONCLUSION

Around the globe, mtDNA type has been used to identify victims of crimes big and little, terrorist attacks, natural catastrophes, and instances of missing individuals. Overwhelming strides have been made in mtDNA typing, with analyses of tiny fragments now taking days and several whole genomes being sequenced in a matter of hours.The mitochondrial DNA (mtDNA) genome is a potential ancestry-revealing lineage genetic basis, particularly their susceptibility to certain diseases.Growing biotechnologies provide the police with an almost ideal resource. There is no reason to doubt the superiority of molecular genetic typing over other methods, which has been true for some time now. Some aspects of mtDNA analysis are unique, while the same quality assurance, quality control, and many explanatory principles in use for PCR-based DNA assays are applicable.Due to its great efficiency in recovering copious but degraded mtDNA from difficult samples, the short amplicons technique ought to be a standard in the testing arsenal of organizations dealing with missing individuals and catastrophic disasters. Sample collection for mtDNA analysis in a forensic laboratory may be done with the use of all available current technology.

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# CHAPTER 22

# NOVEL TREATMENT STRATEGIES FOR SKIN CANCER, FOCUSING ON NANOTECHNOLOGY

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**ABSTRACT:**

The fatality rate from melanoma is the highest of all skin cancers. Melanoma may be effectively treated if identified early. Skin cancer is quite frequent among people nowadays. According to reports, the most prevalent cause of skin cancer is overexposure to sunlight, which carries hazardous radiations known as ultraviolet rays. Chemotherapy and radiation treatment are two therapeutic techniques used for distinct forms of skin cancer. Clinical trials using nanotechnology are progressing quickly, and novel theranostic substances that combine diagnostic and therapeutic approaches are opening up new avenues of research and development. The study begins with a rapid of the most up-to-date data on skin cancer's epidemiology, pathogenesis, diagnostics, and treatment options, and then moves on to discuss contemporary methods of treating the disease, with an emphasis on the recent advancements in nanotechnology-based therapies and this study also discusses the latest breakthroughs in the research and development of nanoparticles for use in melanoma therapy and diagnostics.

**KEYWORDS:**

Cancer, Melanoma, Nanotechnology, Skin.

## 1. INTRODUCTION

Over the past 50 years, the number of new instances of melanoma has gradually increased, and now exceeds 160,000 globally [1]. About 5% of melanomas develop in extracutaneous locations like the mucous membranes of the respiratory, digestive, and genitourinary systems; uvea; leptomeninges [2]. Although this accounts for a very small percentage (approximately 1%) of cutaneous malignant neoplasms,with the highest fatality rate and most metastatic potential, melanoma is the most dangerous kind of skin cancer.Skin cancer begins in melanocytes, For the most part, melanoma is to blame for skin cancer deaths. Death rates and other measures of morbidity are very diverse among countries, being almost unheard of in certain mostly Caucasian nations yet common in others in Africa and Asia [3].

In the majority of instances, surgical removal ofcurative treatment is available for early-stage melanoma that has not progressed to other organs. There are reports of a 97 to 99.8 percent cure rate after chemosurgery for individuals with relapsed or refractory melanoma. Furthermore, additional traditional medicines like chemotherapy, radiation, surgical intervention, and immunotherapy are required to treat metastatic, irremovable melanoma. Neither the treatment results nor the patient reactions to these treatments have been adequate [4].

Skin melanocytes are the site of genesis for the malignant tumor known as melanoma. The condition manifests when melanocytes become malignant cells. Melanocytes, the cells responsible for producing melanin,may be discovered in the dermal basement membrane of the

epidermis. Melanin provides the skin with its normal hue. Skin darkens with exposure to light, whether natural or artificial because melanocytes produce more pigment.Any part of the skin is fair game for melanoma development, but the legs are a common site for both sexes because of the abundance of fatty tissue there. Melanoma may also develop in other common locations, including the neck and face. Melanoma is a kind of cancer that affects the skin that spreads deeply into human tissue. Because of this, melanoma develops in numerous phases, starting in the outermost layer of skin and progressing down into the deeper layers of the dermis. Melanoma therapy varies depending on the stage of the disease [5].

Melanoma is more likely in those who have fair skin than those with darker pigmentation. Routine melanoma screening has not been studied to determine its efficacy for persons without a personal or family history of the disease. Dermatologists often advise against checking for skin cancer, but early identification and treatment of melanoma, a potentially fatal form of the illness, is crucial. Three-dimensional photography is a technique dermatologists may use to examine the patient from every angle [6].Being out in the sun for long periods is linked to an increased risk of acquiring skin cancer, particularly melanoma. To prevent melanoma, people should limit their sun exposure. Normal moles and atypical moles are the two main types of moles that may be seen in the human body. Having atypical moles puts us at a greater possibility of getting melanoma.

The medical applications of nanotechnology, which include the creation, study, and use of nanoscale materials,are the focus of a lot of research and discussion these days. Nanotechnology's potential in cancer detection and therapy has been explored at length, and the field of melanoma research has benefited from the findings in some ways. Nanoparticles are a very efficient drug delivery technology, boosting the efficiency of cancer treatments by delivering anticancer medications directly to the tumor site [7]. With the use of nanotechnology, imaging agents may be encapsulated in nanoparticles and delivered directly to the site of the tumor, aiding in the diagnostic process. Recent advancements in melanoma detection and therapy using nanotechnology are summarized in this study.

## 2. LITERATURE REVIEW

Fabrizio Ayala et al. stated in their study that Optical radiation refers to all forms of electromagnetic radiation (UV, visible, and infrared) having wavelengths between 100 nm and 1 mm. The purpose of this study was to synthesize the findings from the previous 15 years of research on the link between optical radiation exposure and the development of melanoma and other malignancies. Sunlight is directly linked to skin cancer. The author concluded that Public education campaigns on the dangers of sun exposure are still crucial [8].

Victor Emmanuel Gadelha Pinheiro et al. evaluated in their study rarely sternectomy performed for skin cancer. Data for the study were culled from the medical records of patients seen at Ceara Cancer Institute between 2008 and 2018. All of the patients were above the age of 60 when diagnosed, and they had all spent considerable time in the sun. Most patients responded well to therapy, and many made a full recovery. Based on the research, the author decided for patients with locally advanced skin cancer, sternectomy is still a potential cure option [9].

Jessica N. Kimmel et al. discussed in their study Patients suffering from being affected by “inflammatory bowel disease (IBD)” are more probable to get skin cancer. Individuals with inflammatory bowel disease (IBD) less than 18 years old were enlisted to fill out an online questionnaire.The average age of the patients was 43.50 years; 63.0% were female; 67% had

Crohn's disease; 31% had ulcerative colitis, and 2% had indeterminate colitis. The majority of persons suffering from inflammatory bowel disease know there's a correlation between sun damage and their condition, yet they still don't take enough precautions to avoid skin cancer. This highlights the need for healthcare providers to educate the IBD community on additional skin cancer preventive measures [10].

Lilian de Oliveira Nunes et al. conducted a study that Lesion identification on the skin has been accomplished using Raman spectroscopy. In this study, the author used FT-Raman spectroscopy to examine and compare eight sets of tissue samples, each of which had been histopathologically confirmed to be either BCC or benign tissue. It turns out that the 1220-1300 cm-1 and 1640-1680 cm-1 shift regions are where these samples vary most spectrally. Here, the author may find the vibrational bands associated with amide III and amide I. Utilizing main components analysis on each of the 13 samples allowed for a 100% sensitivity and specificity in determining tissue type [11].

## 3. DISCUSSION

There are presently a variety of therapy choices to choose from, each of which is tailored to the specifics of a patient's illness stage, tumor location, and health status. Traditional methods have been around for quite some time, and they include things like removing tumors surgically and using chemotherapeutic medications and radiation. However, the effectiveness of these therapies has traditionally been low, providing only temporary protection against the illness. In the case of chemotherapy, this was often attributable to the development of resistance to medications like Placlitaxel, platinum, and dacarbazine, which had previously been used with more effectiveness as a first-line treatment for other types of cancers [12].

Recent years have seen a surge of study into potential alternative treatment techniques as scientists attempt tofind strategies to decrease the negative effects of chemotherapy by just affecting cancer cells and not healthy ones.One relatively new approach to enhancing the efficacy of traditional and cutting-edge pharmacological anticancer therapies is the use of nanotechnologies [13]. For example, the most recent innovation in medication delivery, nanoparticles (NPs), have allowed for significant advancements to be made. Due to their composition and diminutive sizes, NPs have been shown to target tumor cells with exceptional selectivity and accuracy.

### *3.1.Recommended MelanomaPossible Adverse Effects of Treating Skin Cancer:*

Alternative treatments for melanoma skin cancer include excision and immunotherapy, surgical intervention, chemotherapeutic, and radiation treatment. Stage-appropriate melanoma skin cancer therapy will be administered. Patients may have unintended consequences if the treatment is not optimal for them [14].Effective treatments for mucosal melanoma include surgery, adjuvant therapy, radiotherapy, photodynamic therapy, medical therapy, and a switch to mucosal melanoma treatment indicated in Figure 1 are the most common forms of contemporary melanoma care.Biopsy, extended resection, metastasis, lymph node dissection, and sentinel lymph node biopsy (for those at stage III of the disease) are all popular surgical treatments. The diagnostic phase and risk level of patients are the primary considerations in adjuvant treatment decisions for melanoma.

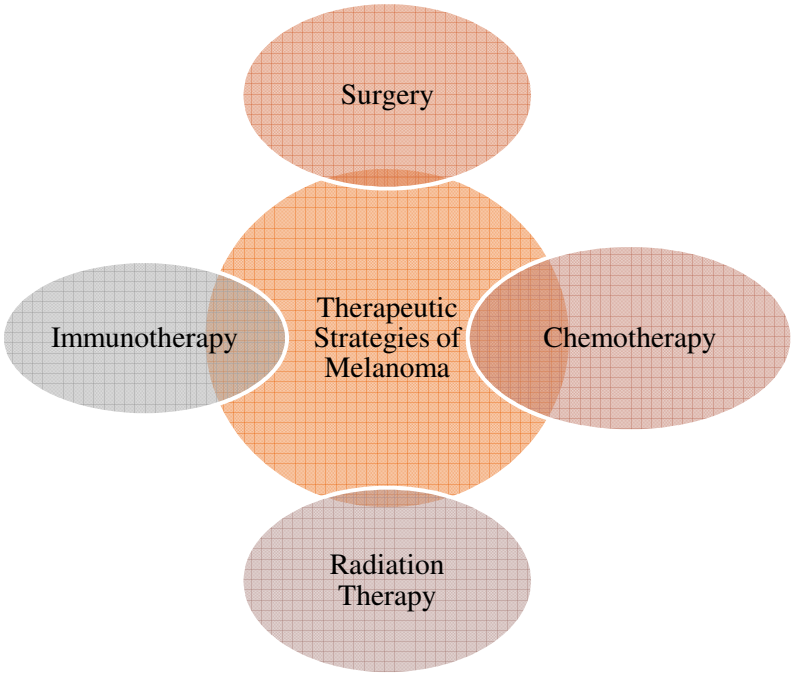


**Figure 1: Therapeutic approaches for patients with melanoma.**

### *3.1.1. Surgery:*

Surgery is the main therapeutic option for most types of melanoma skin cancer, and it is often successful in treating melanoma in its earlier stages. Even though this option helps guarantee that cancer has been eradicated or that malignant cells have not been left behind, a significant number of patients choose not to go this route since it may result in scarring. In certain instances, particularly when a broad excision is being performed, this may be rather painful. On the other hand, some medical professionals believe that it has the potential toprolong the patient's life or, at the very least, lessen the pain induced by illness progression.With early detection, the prognosis for people with melanoma is excellent; the five-year survival rate is believed to be over 99 percent. When cancer spreads to the lymph nodes, survival rates drop to 68%, and when it spreads to other organs, survival rates drop to 30% [15].

The main therapy for localized melanoma is surgical excision of the tumor and associated healthy cells; in addition, individuals whose tumors are more than 0.8 millimeters thick or thinner than this but ulcerated (stage pT1b or above) undergo sentinel lymph node biopsy.Melanoma is diagnosed when cells are in the sentinel lymph nodes, it is occasionally necessary to removeevery lymph node in the afflicted area. Although surgical removal of metastatic tumors is a possibility in certain cases, this is not intended to be a curative therapy for patients with the advanced metastatic illness.

### *3.1.2. Immunotherapy:*

The immune system's capacity to recognize and avoid attacking healthy tissue is important to its function. Specifically, it employs proteins called "checkpoints" that are located before eliciting an immunological response, immune cells must first be activated or destroyed. These checkpoints are also used by melanoma cells to evade immune system assault. Fortunately, numerous medicines target these checkpoint proteins, reviving the immune system's attack on melanoma cells. Response rates, long-term disease control, and overall patient survival were all

significantly improved by these so-called checkpoint inhibitors [16].Drugs used in immunotherapy are sometimes delivered in the form of nanoparticles to lessen the likelihood of undesirable side effects.Ya o et al. created and evaluated a new nanoparticle encasing Interleukin IL-2 in a xenografted carcinoma murine model. Synthesis of the nanoparticle required the combination of IL-2 plasmid, folate-conjugated cyclodextrin, or low-molecular-weight polyethyleneimine (600 Da) [17].

### *3.1.3. Targeted Therapy:*

Because melanoma cells are distinct from healthy cells, they were the specific focus of the medicine in targeted treatment. This alternative has a different mode of action than chemotherapy and has fewer negative effects, such as weakness and hair loss. While it does have some generally accepted side effects, sometimes it may have major consequences including irregular heartbeat, severe liver damage, or an allergic response. Due to the high risk of adverse effects, targeted medicines are seldom the first choice for treating melanoma. To combat cancer, several regulators of intracellular signaling pathwayshave come to be recognized as playing a pivotal role in the development and progression of many forms of cancer, particularly melanoma [18].

Through the stimulation of many signaling pathways, it may raise cancer rates and worsen patient outcomes.Inhibitors of the mitogen-activated protein kinase (MAPK) pathwayhave been delivered by nanotechnology. Chitosan nanoparticles improved therapeutic effectiveness by transporting VEGF siRNA to the downstream target protein. In a recent study, Yin et al. employed functional graphene oxide to transport plasmid-derived small interfering RNAs (siRNAs) and the transcription factor Signal transducer and activator of transcription 3 (STAT3) [19].

### *3.1.4. Chemotherapy:*

As with other types of cancer, skin cancer may be treated with chemotherapy. The medicine it employs is effective against cancer cells. Drugs may either be injected directly into a vein or given orally as a tablet. They target cancer cells that have spread to other organs after entering the bloodstream. It's useless, yet it helps some people feel better or live a little longer anyhow. Hair loss, diarrhea, and exhaustion are all adverse effects of chemotherapy, just as they are of immunotherapy and targeted treatment. This seems to provide patients with a second chance to choose this therapy option.

For melanoma, chemotherapy is the go-to standard treatment. Cancer cells and healthy cells alike are vulnerable to the cytotoxic effects of chemotherapy. As a result of their extreme toxicity, only extremely low doses may be safely administered. DTIC, vinblastine, and temozolomide are often used chemotherapeutic drugs for melanoma.Some studies have shown that administering chemotherapeutic drugs in the form of nanoparticles improves therapy effectiveness while decreasing adverse effects. Gold nanoparticle delivery of the chemotherapeutic drug Dox was shown to be very effective against a melanoma cell line in a study by Zhang et al.[20].

### *3.1.5. Radiation Therapy:*

Treatment with radiation involves exposing the cancerous tissue to high-energy radiation, usually in the form of x-rays or particles. Melanomas of the skin are seldom treated with radiation treatment, although in cases when surgery is not an option, such as in individuals with diabetes mellitus, radiation may be utilized. The dangers of radiation exposure are generally localized to

the region where it is present. Mutations in skin color, hair loss, nausea, and exhaustion are all possible adverse effects.Skin cancer treatment with radiation has been around for about a century. There has been constant progress made in the methods used to give superficial irradiation during this long period. More recently, electron beamshave been produced as a therapy for many forms of skin cancer, allowing for more effective and less harmful therapy for skin cancer. All secondary skin lesions are included in this category, as well as primary skin malignancies.

*3.2.Skin Cancer(Melanoma) Treatment Using Nanotechnology:*

Early evaluations are performed to ascertain the presence of melanoma and at what stage the cancer is. High survival rates among melanoma patients are contingent on the disease being detected at an early stage. Multispectral digital image analysis, RNA microarray, dermatoscopy, and reflectance confocal microscopy are just a few examples of modern technologies that have been utilized to enhance diagnosis alongside traditional methods like the naked eye and histological inspection [21].During melanoma therapy, it is important to utilize your best judgment to determine whether the method being used is effective and if there are ways toincrease the effectiveness of therapy for the patient. To get to this conclusion, imaging the tumor's size, as well as its vascular structure, is required. Nanotechnology is currently being used.

Due to the photophysical properties that nanoparticle quantum dots (QDs) possess, these dots have shown to be effective in the early detection of melanoma. These qualities include high brightness, emission wavelength tuning with size, a wide activation strong photostability, thin emission profile, and broad spectral range, shown to be an effective method for enhancing melanoma diagnosis [22].Folic acid conjugation or the use of antibodies against elevated antigens in cancer cellsare two examples of cancer-targeting chemicals that might be attached to quantum dots (QDs).

Dendrimers were used to track melanoma that has spread throughout the body. Fluorescent dendrimers decorated with amino acids including arginine, glycine, and aspartic acid have been the focus of recent studies. This research aimed to visualize tumor size and vascular structure through fluorescence or nuclear magnetic resonance (NMR) spectroscopy after the nanoparticles had aggregated in the tumor. Furthermore, the reticuloendothelial system and the kidney were shown to be the primary sites of particle accumulation. Dendrimers have the potential to aid in the detection of melanoma metastases, but further research is required before this can be accomplished [23].

Several forms of cancer have benefited from the use of nanomaterials as Drug Delivery systems (DDSs), andmelanoma detection and treatment with nanotechnology is an area of active research. Nanomaterials' size and surface features make it possible for targeted medications enveloped or loaded with them to readily breachbiological barriers and also be administered specifically to melanoma cells, where their cytotoxic effects may be seen.Graphene is coiled into one or more sheets to create carbon nanotubes (CNTs), which are molecular tubes (a single layer of carbon atoms). Single-walled (SWNT) and multi-walled (MWNT) nanotubes. Assembling new chemical groups on the tip or side wall allows for surface modifications that are crucial to their uses. Indeed, CNTs' biocompatibility and also the possibility of delivering vast cargoes of pharmaceuticals and biomolecules have made them increasingly significant in recent years [24].

*3.3.Melanoma diagnosis and prognosis:*

Non-melanoma skin cancer (NMSC) may show itself with or without pigmentation, and they always have distinct boundaries and consistent color. Although they have a lower risk of leading to death as compared to malignant melanoma, they are more challenging to diagnose. Any mole that exhibits symptoms of inflammation, such as bleeding or leaking, should be reported to a dermatologist for further examination. In addition, a suspicious mental image should be formed for any lesion that exhibits a change in feeling (for example, one that begins to itch), size, or shape. There is not much diagnostic significance attached to the existence of hair in the lesion.

The development of theranostic nanomedicine, which employs nanoparticles in both diagnostic and therapy, is a recent scientific achievement.The potential of nanoparticles to transport many medications at once is exploited by embedding imaging agents into the particles, allowing for real-time monitoring of therapeutic drug effectiveness. This might be useful for monitoring medication responses and assessing treatment effectiveness. Researchers may also benefit from the data since it might help them create nanoparticles with the properties they need. Nanoparticles utilized for theranostic purposes, such as liposomes and polymersomes, are now the most popular options.Signs were detected using the immunohistochemical technique. Melanoma has several cytomorphological variations, which may make histological identification challenging.Melanoma may be mistaken for othercarcinomas, neuroendocrine tumors, sarcomas, lymphomas, and even germ cell carcinomas are all subsets of cancer. Because of this, melanoma is often diagnosed by the use of immunohistochemistry testing for melanocytic markers of differentiation [25].

### *3.4.The Possible Role of Nanotechnology in the Future Treatment of Skin Cancer:*

No of the ailment, new treatment methods should be more effective, less expensive, and maintain or improve patient safety. To get there, we need a therapy that has high yields of reaching the intended spot per unit mass of the drug, extremely little probable toxicity, and excellent patient compliance. All of these benefits may be obtained using nanotechnology-based formulations. Since they may be adorned with targeting moieties (like antibodies), they can be more effective in delivering and releasing their payloads in a regulated fashion [26].

Knowing the potential benefits of such formulations, there is a great deal of interest in studying them and a strong desire to implement them into clinical practice as soon as their safety has been shown. At least two nanotechnology-based formulations are now in use for the treatment of cancer, and they have been authorized for usage. Taking into account everything said, there are several optimistic (at least study) developments regarding skin cancer therapy that might potentially indicate considerablechanges in the expected outcome of skin cancer therapy. Novel nanosized formulations in a variety of forms have been produced and are undergoing testing at this time.Rapid and precise monitoring of cancer-related chemicals is now possible thanks to nanotechnology, allowing researchers to see molecular alterations in even a tiny fraction of cells.Revolutionary new highly effective pharmaceuticals might be developed using nanotechnology. Nanotechnology-based such as nanoliposomes could play a crucial part in the management of melanoma that has spread to other organs because of their potential to target drug delivery at the cellular scale by bypassing biological membranes in the body.

## 4. CONCLUSION

Melanoma is a seriously deadly kind of skin cancer. Because of the disease's heterogeneity and complexity, diagnosis and treatment may be challenging. New methods for diagnosing and treating melanoma will be possible if we learn more about the molecular pathways that drive its

development and help melanomas hide from the immune system. However, new technologies are being developed that may give more objective techniques for detecting and prognosticating melanoma, which would enhance health outcomes.Due to environmental changes that have increased the exposure of skin to UV radiation, skin cancer has become one of the most frequent forms of cancer worldwide.

Rising rates of skin cancer may be traced to a variety of factors, including environmental exposure and family history.Even with advances in medicine, metastatic melanoma remains a challenging illness to treat.The genesis of the illness is better understood; early diagnosis is possible; distinct molecular types of the disease have been identified, and unique and efficient drug delivery methods are crucial for increasing therapy success. There is hope that advances in nanotechnology may lead to more effective methods of detecting and treating melanoma. Before certain nanoparticles may be employed in therapeutic settings, further research is necessary to determine how to mitigate any negative effects.

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