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Review Article

A review on emerging paradigm of nanomedicines in current scenario

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Abstract

Due to the severe limitations of conventional pharmaceutical agents, as well as antiquated formulations and delivery systems, nanotechnology plays a significant role in medicine and drug administration. Since several nanotechnology applications have been developed and certain drugs based on nanotechnology are now available on the market, the influence of nanotechnology on healthcare is already apparent. Around the world, more money is being invested in nanotechnology by the public and private sectors. It is anticipated that the application of nanotechnology in medicine, namely in drug delivery, would increase dramatically. For many years, pharmaceutical sciences have employed nanoparticles to reduce the toxicity and side effects of medications. To develop and implement safe nanomaterials for drug delivery in the future, a conceptual understanding of biological responses to nanoparticles is necessary. Strong cooperation between individuals involved in particle toxicity and drug delivery is also necessary to improve this topic by exchanging ideas, methods, and expertise.

Keywords: Drug delivery, Nanotechnology, Pharmacy, Nanomedicine, Healthcare.

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1. Introduction

The molecular fabrication of various functioning systems is known as nanotechnology. These systems are fascinating in a variety of applications, ranging from materials science to biology, due to their distinct physical, electrical, and optical characteristics.1 One of the most well-known fields of research in nanotechnology is nanomedicine. It uses nanotechnology to deliver precisely customized medicinal therapies for prophylactic, therapy, and sickness diagnostics.² Research on nanomedicine has increased over the past few decades, and this has led to global commercialization initiatives that have resulted in the sale of a range of products. Inherent in human nature, curiosity, wonder, and innovation have existed since the dawn of humanity. Throughout the history of our civilization, there has been an increase in interest in scientific efforts to understand the mechanisms behind natural phenomena. Medical and pharmaceutical research has expanded at a never-before-seen pace in recent years. The idea that medical applications of nanotechnology are significantly improving illness detection, treatment, and

prevention is a transition from fantasy to reality. A new field for nanomaterials and biomedicine has emerged as a result of growing interest in the potential medicinal applications of nanotechnology. With therapeutic applications ranging from contrast agents in imaging to carriers for medication and gene transfer into cancerous growths, nanomaterials have lately become important players in modern medicine.

The term "nanomedicine" refers to the application of nanotechnologies in healthcare and medicine. The use of nanoscale technology and nano-enabled practices for disease prevention, diagnosis, monitoring, and treatment is known as nanomedicine.³ In medicine, nanotechnologies hold great promise for everything from drug delivery systems to tissueengineered constructs, implants, and pharmaceutical therapeutics4 to advanced treatments for a wide range of illnesses, including diabetes, cancer, heart disease, musculoskeletal disorders, psychiatric and neurodegenerative diseases, bacterial and viral infections, and cardiovascular disease⁵ [Figure 1]. Disease treatment and diagnosis, disease prevention, pain management, human

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health improvement, nanoscale technology against traumatic injury, and disease treatment options are just a few of the medical applications that are brought together by the broad field of nanomedicine.^{6,7} Therefore, under the general heading of nanomedicine, an interdisciplinary approach is being employed to apply the results of biotechnology, nanomaterials, biomedical robots, and genetic engineering.⁸ The bulk of biological and chemical processes used in the production of medical materials are made more efficient, responsive, and functionally effective by nano-scaling medical technologies. Research therefore shows continued promise for nanomedicine's future applications.^{6,9}

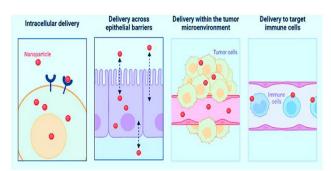


Figure 1: Utility of nanoparticles across various biological barriers.

(Source: Nanomaterials (Basel). 2023 Jan 31;13(3):574. doi: 10.3390/nano13030574).⁷⁴

1.1. Types of nanoparticles

Numerous nanoparticles and nanomaterials have been investigated and approved for use in medicine thus far [Figure 2].

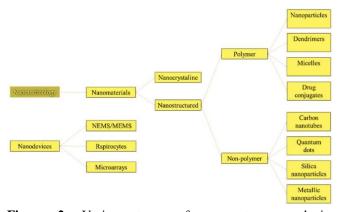


Figure 2: Various types of nanosystems used in pharmaceutical applications

(Source: Nanomaterials (Basel). 2023 Jan 31;13(3):574. doi: 10.3390/nano13030574) [74]

- 1.1.1. Several common types of nanoparticles are covered in the sections that follow.
- 1. Metallic Nanoparticles Iron oxide and gold nanoparticles are examples of metallic nanoparticles. A magnetic core (4-5 nm) and hydrophilic polymers, such as PEG or dextran, make up iron oxide nanoparticles (17–20). A monolayer of surface moieties acting as ligands for active targeting can functionalize gold nanoparticles, which are composed of a core of gold atoms around by negative reactive groups on the surface. ¹⁰ Metallic nanoparticles have been used as drug delivery vehicles, ¹² optical biosensors, ¹² laser-based therapies, ¹² and imaging contrast agents. ¹¹
- 2. Paramagnetic Nanoparticles Magnetic nanoparticles are tiny particles that can be manipulated by magnetic fields. They have a diameter of less than 100 nm. These particle materials are made using magnetic components. The magnetic sensitivity of these nanoparticles determines their classification. Compared to regular contrast forms, paramagnetic nanoparticles have a higher magnetic susceptibility. Both medicinal and diagnostic applications exist for these nanoparticles. Targeting specific organs with paramagnetic nanoparticles is advantageous.¹⁴
- 3. Carbon Nanotubes Carbon nanotubes are cylinder-shaped molecules made of rolled-up sheets of graphene, a single layer of carbon atoms. They might consist of many concentrically interconnected nanotubes or have one or more walls. ¹⁵ As drug carriers, carbon nanotubes can attain significantly high loading capacities because of their large exterior surface area. Carbon tubes have also gained popularity as biological sensors ¹⁸ and imaging contrast agents ^{16,17} due to their distinct optical, mechanical, and electrical characteristics.
- Nanoemulsions Recently, there has been a lot of interest in using self-emulsified drug delivery systems (SEDDS) and nanoemulsions to improve the bioavailability of medications with limited water solubility. Nonhomogenous systems consisting of immiscible liquids that are dispersed as droplets in one another are called nanoemulsions. 19 Oil-in-water (o/w) nanoemulsions are created when SNEDDS, which are isotropic mixtures of oil, surfactant, co-surfactant, and drug, are incorporated into aqueous phases under gentle mixing.²⁰ These systems enhance the oral bioavailability of medications that are poorly soluble in water through a number of mechanisms. Additionally, the oil droplets' tiny size lowers the surface tension between them and the gastrointestinal tract's aqueous medium, facilitating more even and extensive medication distribution throughout the gut.²¹
- 5. Micelles Lipids and amphiphilic molecules combine to form micelles, which are amphiphilic surfactant molecules. Micelles can be utilized to integrate hydrophobic therapeutic medicines because they spontaneously aggregate and self-assemble into

- spherical vesicles with a hydrophilic outer monolayer and a hydrophobic core in aqueous circumstances. Because of the special qualities of micelles, hydrophobic medications can become more soluble, increasing their bioavailability. Micelles have a diameter between 10 and 100 nm. Micelles can be used as therapeutic agents, contrast agents, imaging agents, and drug delivery agents, among other uses.²²
- Nanoshells Nanoshells are changed models for drug targeting, having a silica core and outer layer of metal.²³ These nanoshells are receiving a lot of attention these days. By altering the ratio of the core to the shell, these properties may be modified. nanostructures may now be designed to have certain physical characteristics, such as size and shape. Nanoshells are utilized to construct novel systems with a diversity of morphologies because not all of the materials can be produced in the appropriate morphologies. To attain the proper morphology, particles of shapes might be encased with a thin shell. Because cheap cores may be enhanced with valuable materials, these shells offer the benefit of being reasonably priced. Consequently, the amount of valuable material required to synthesize nanoshells is reduced.24
- Solid Lipid Nanoparticles As a regulated colloidal drug delivery method, solid lipid nanoparticles were created to replace emulsions, liposomes, and polymeric nanoparticles.²⁵ Solid lipids are used to prepare them, and one or more surfactants are used to stabilize them. Compared to other particle carriers, solid lipid nanoparticles have several advantages for drug administration. such as increased tolerability, biodegradability, high bioavailability through the ocular route, and a targeted effect on the brain. 26,27 With the advent of the high-pressure homogenization process. solid lipid nanoparticle research has flourished in recent years. They have been created and researched for several uses. Solid lipid nanoparticles' tiny size made it possible for them to be administered intravenously and utilized for medication site-targeting.
- Dendrimers Dendrimers are macromolecules made up of external functional groups and branching repeating units that extend from a central core. The whole structure, as well as the chemical and physical characteristics, may be altered by these functional groups, which can have cationic, neutral, or anionic terminals. Dendrimers are extremely bioavailable and biodegradable because therapeutic substances can be linked to their surface groups or contained inside their inner space. It has been demonstrated that dendrimer conjugates with peptides or saccharides have better antiviral, antibacterial, and antiprion qualities as well as increased solubility and stability when therapeutic medications are absorbed.²⁸ Dendriplexes, which are polyamidoamine dendrimer-DNA complexes, have been studied as vectors for gene delivery and have the

- potential to enhance medication effectiveness, target drug delivery, and enable successive gene expression. Because of their transformable characteristics, dendrimers are potential particulate systems for biological applications, including drug administration and imaging. 1
- Niosomes A particular kind of molecular cluster called a niosome is created when non-ionic surfactants selfassemble in an aqueous phase. Because of their special structure, niosomes can be used as a novel delivery system for both lipophilic and lipophobic substances.³² Non-ionic surfactants make up niosomes, which are thought to be a viable alternative to liposomes due to their great stability and lack of toxicity. Niosomes function similarly to liposomes in vivo, altering organ distribution, metabolic stability, and the circulation of the contained medication. Apart from the method of manufacture, the bilayer determines the characteristics of niosomes. It has been demonstrated that the intercalation of cholesterol in the bilayers causes the entrapment volume to decrease during formulation, which lowers the entrapment efficiency.³³
- 10. Liposomes Liposomes are spherical vesicles made of lipid bilayers that range in size from 30 nm to several microns. Hydrophilic therapeutic compounds can be incorporated into the aqueous phase of liposomes, whereas hydrophobic agents can be included into the liposomal membrane layer. Because liposomes are so adaptable, macromolecular medications such as solid metals and nucleic acids can be incorporated into them by altering their surface properties using polymers, proteins, and/or antibodies. The first FDA-approved nanomedicine used to treat breast cancer is poly (ethylene glycol) (PEG)ylated liposomal doxorubicin (Doxil®), which increases the effective concentration in malignant effusions without requiring an increase in the total dosage.
- Nanobubbles -Bubble-shaped particles called nanobubbles are created at the nanoscale at the interface of liquids' lipophilic surfaces. They combine to create microbubbles, which are stable at room temperature, until heated to body temperature. They develop in supersaturated fluids because of air gas entrapment caused by gas nucleation at the hydrophobic surface. Plasmonic, bulk, oscillating, and interfacial nanobubbles are the four varieties of these nanoparticles. With the use of ultrasonic exposure, cancer therapy drugs were effectively loaded into these particles, enabling them to target tumour tissues and enhance the absorption of tumour cells.34,35
- 12. Nanocapsules Nanospheres and nanocapsules differ in that the latter are structures in which the drug is distributed across the polymeric matrix, whilst the former are carriers in which the drug is contained in a core surrounded by a polymeric membrane.³⁶ Polymeric nanoparticles can be compared to a matrix where the

- drug is evenly dispersed. The drug may be dissolved, trapped, or encapsulated inside or across the polymeric matrix. Because polymeric nanoparticles allow for customized drug administration, they are a great choice for cancer therapy and other uses.
- 13. Quantum Dots The fluorescent semiconductor nanocrystals known as quantum dots, which range in size from 1 to 100 nm, have demonstrated promise for several biological uses, including cellular imaging and medication administration.³⁷ The shell-core structure of quantum dots is usually made up of elements from the II-VI or III-V groups of the periodic table. Quantum dots have been used in medical imaging because of their unique optical characteristics, size, great brightness, and stability.³⁷
- 14. Polymeric Nanoparticles Researchers are interested in biodegradable polymeric nanoparticles as a drugdelivery method since polymeric nanoparticles are mostly biodegradable and biocompatible. 38,39 They are separated into matrix systems (nanospheres) and vesicular systems (nanocapsules). Researchers have lately investigated advanced modification of natural polymers, including synthetic polyesters. Chitosan is among the most well-known natural polymers. Numerous polymers lessen the harmful effects of synthetic polymers. 40 Because of their greater efficacy and efficiency, natural polymeric nanoparticles outperformed conventional administration methods.

1.1.2. Applications of nanoparticles

- 1. Using Nanoparticles to Treat Renal Disorders Nanoparticles are used to treat renal diseases in urology and nephrology. To treat individuals with end-stage renal illness or chronic kidney disease who do not generate enough erythropoietin, ferumoxytol has been added to nanoparticles. All PEGylated gold nanoparticles can also target the mesangium, which are contractile cells that comprise the central stalk of the kidney's glomerulus, because many illnesses originate in this region. Nanoparticle technology has improved the dispersion and therapeutic effect of Rhein, an anthraquinone derivative used to treat diabetic nephropathy.
- 2. For Chemotherapy-Assisted TB Treatment The altered release behaviour of the anti-TB medication-loaded nanoparticles after oral administration was the cause of their increased effectiveness. Three important medications—pyrazinamide, isoniazid, and rifampin—were co-incorporated into PLG nanoparticles. While free medicines only lasted one day in the plasma after injection, the therapeutic concentrations of these compounds in tissues were maintained for ten days. 42,43
- Topical Medication Delivery Using Nanoparticles for Skin Conditions - The most widely employed nanoparticles for topical medicine delivery are PNPs.⁴⁴ When compared to benzoyl peroxide alone, PNPs derived from chitosan and alginate shown enhanced

- antibacterial effectiveness against Propionibacterium acnes.45,46 Electro-spun fiber mats, in addition to polymeric nanoparticles, have a high surface area-tovolume ratio, which makes them perfect for topical drug delivery and aids in the efficient dispersion of both hydrophilic and hydrophobic drugs. 44,47 The skin's surface is adhered to by liposomes, solid lipid nanoparticles, and nanostructured lipid carriers. To improve drug penetration, liposomes, solid lipid nanoparticles, and nanostructured lipid carriers adhere to the skin's surface and facilitate lipid exchange between the carrier and the outermost layers of the stratum corneum. Lipid-based carrier systems comprising glucocorticoids and T-cell suppressing medications such as tacrolimus and cyclosporin were used to treat inflammatory skin conditions like psoriasis and atopic eczema.
- 4. Using Nanoparticles to Target Infectious Disorders Numerous infectious diseases are being treated with nanoparticles' physical and chemical characteristics. The effectiveness of a therapeutic medication against infectious diseases has increased when it is put onto a nano-vector. Due to its improved pharmacokinetic and toxic properties, polyethylene glycol-modified carbon nanotubes are the most widely used kind of non-viral delivery technology. When it comes to delivering certain medications for the treatment of infectious diseases, they are effective transporters of bioactive compounds. 48,49
- 5. In Management of Alzheimer's One of the most recent methods for improving CNS penetration for the detection and treatment of neurodegenerative illnesses like Alzheimer's disease is medicine administration using nanoparticles. Among the different types of nanocarriers, PNPs are promising because, in addition to opening the blood-brain barrier's tight junctions, they also successfully hide the membrane barrier, limiting the drug molecule's characterizations, extending its release, and shielding it from enzymatic hydrolysis. ^{50,51}
- For Administration of Several Anticancer Drugs A recent medical field called "nano-oncology" uses nanoparticles to treat cancer. Multidrug resistance in cancer tissue is overcome and cancer cell targeting is improved when nanoparticles are used as an effective medicine.52 Α popular polymer for creating nanoparticles, poly(lactic-co-glycolic acid) has been used to create drug-loaded nanoparticles for cancer treatment because of its long-term drug release and biocompatibility. Anticancer medications, including 5-fluorouracil, doxorubicin, paclitaxel, and dexamethasone have all been effectively produced using poly(lactic-co-glycolic acid).
- 7. COVID-19 Immunization Using Nanoparticles Since 2020, every scientist and researcher has focused their efforts on developing solutions to stop the global COVID-19 virus outbreak. The significance of nanoparticle technology in the creation of therapeutic

formulations for the enhancement of long-term human immunity against COVID-19, diagnostics, and therapy was emphasized in 2021.⁵³ The documented genomic structure from Corona viruses and the prior knowledge of the sequence of the protein laying the viral surface served as the foundation for the development of COVID-19 nanoparticle-based vaccines (CNPBV) and sped up the time needed to create them.⁵⁴ There are spikes.

A crucial feature in the creation of CNPBV was the presence of spike proteins on the outer surface of the COVID-19 virus, which had a high connection propensity toward nano-formulations and a strong binding tendency toward host cell receptors.55 Among the many vaccines created with moderate efficacy to combat and slow the spread of the COVID-19 pandemic worldwide, a promising vaccine based on nanotechnology was approved by the Food and Drug Administration (FDA) and demonstrated its significant value in prophylactic against the COVID-19 virus with a high percentage of 90% on the vaccinated population. Among these vaccines are the BNT162b2 vaccine from Pfizer-BioNTech and the mRNA-1273 vaccine from Moderna.⁵⁶ Two vaccines that use mRNA to encode the spike glycoprotein (S) of the COVID-19 virus are Pfizer-BioNTech's BNT162b2 vaccine and Moderna's mRNA-1273 vaccine. The modified mRNA, which encodes the viral glycolprotein, is then incorporated into lipid-based nanoparticles.⁵⁷ The protein antigen (spike protein) is subsequently transported to immune cells by the encapsulated modified mRNA, which promotes T cell activity and triggers antibody immunological responses in the human body.⁵⁸

2. Discussion

Since nanotechnologies provide better-built, safer, cleaner, and longer-lasting approach, and smarter goods for everyday life, agriculture, health, and communications, they have had a substantial influence on practically every industry and aspect of society.⁵⁹ There are two main categories into which nanomaterials are used in common items. First, by contributing some of its special qualities, nanomaterials may be combined or added to an existing product to enhance the composite object's overall performance. Otherwise, because of their unique qualities, nanomaterials like nanoparticles and nanocrystals can be employed directly to make sophisticated and potent devices. The future of almost every economic area may be impacted by the advantages of nanomaterials.⁶⁰

Nanodevices are currently being used in diagnostic sciences to identify diseases quickly and early to prescribe additional medical procedures. In order to gain understanding of potential treatments, it also makes use of nanotechnology to study disease propensity at the cellular and molecular level. By increasing the precision, sensitivity, and speed of medical examinations, nanotechnology holds the potential to completely transform the diagnostics industry. 62

Nanoparticle-based diagnostic imaging is one of the profound applications, whereby nanoparticles can be linked to biomarkers to improve the sensitivity, accuracy, and specificity of imaging modalities like positron emission tomography, computerized tomography, and magnetic resonance imaging.⁶³

Another area of application where nanotechnology has made it possible to create extremely sensitive biosensors that can identify even minute amounts of biomolecules in body fluids like blood and urine, hence aiding in early illness diagnosis and treatment. Similar uses may be seen in nanomaterial-based microfluidic devices, which isolate and analyse certain cells, proteins, and genetic material to provide quick and precise illness detection. Another use might be nanopore sequencing, a cutting-edge technique that employs nanopores to identify the sequence of DNA or RNA molecules, enabling quick and precise detection of hereditary illnesses like cancer.

Recent developments demonstrate that the effectiveness and dependability of illness detection may be improved by using nanomedicine in in vitro diagnostic sciences. 68 Subcellular nanodevices are used to do this, using samples made from human tissue, cell cultures, bodily fluids, etc. 63,69,70 The nanomedicine technique is being employed in in vivo diagnostics to create devices that can function, react, and change inside the human body for the express goal of early detection of any abnormalities that can cause toxicity or tumor formation events.⁷¹ Currently, paramagnetic nanoparticles, nanocrystals, quantum dots, nanoshells, and nanosomes are among the nanoparticle forms being used for applications.^{72,73} diagnostic All things considered, nanotechnology has great promise for healthcare diagnostics and is anticipated to be crucial to the advancement of personalised treatment [Figure 3].

Nanotechnologies transformed medical have advancements, particularly in medication delivery, imaging, and diagnostic techniques. Nanotechnology in healthcare and medicine has enormous promise to transform how we identify, cure, and prevent illnesses in the future. To precisely regulate a material's physical, chemical, and biological characteristics, nanotechnology manipulates materials at a scale so tiny that their properties differ greatly from those of their bulk counterparts. This creates new possibilities for the development of sensitive diagnostic instruments, tailored medication delivery systems, and innovative therapeutics. By increasing the solubility, stability, and bioavailability of current medications, nanoparticles can be utilized to increase their efficacy in addition to drug delivery, targeted administration, better medications, restricted doses, and decreased systematic adverse effects. Furthermore, real-time patient health monitoring is made possible by sensors and gadgets based on nanotechnology, which allows for early identification and individualized treatment regimens. Future advancements in nanotechnology could even make it possible to create nanorobots that can move through the bloodstream to target and eliminate cancer cells or transport medication payloads to tissues.

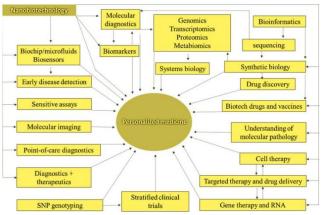


Figure 3: Implementation of Nanotechnology in Development of Personalised Medicine

(Source: Nanomaterials (Basel). 2023 Jan 31;13(3):574. doi: 10.3390/nano13030574) [74]

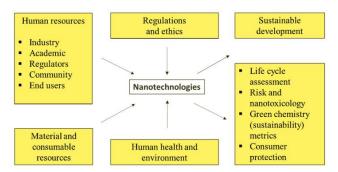


Figure 4: Key Issues to access the effects of nanotechnology on human health

(Source: Nanomaterials (Basel). 2023 Jan 31;13(3):574. doi: 10.3390/nano13030574) [74]

3. Conclusion

In many regions of the world, both the public and commercial sectors are investing more in nanotechnology. The worldwide nanomedicine market was valued at 138.8 billion US\$ in 2016, and it is expected to grow to 350.8 billion US\$ by the end of 2025. This demonstrates how crucial nanotechnology is to the delivery of drugs. The primary benefits of employing nanotechnology to distribute therapeutic medicines include lowering undesired toxicity from nonspecific distribution and enhancing patient adherence, which indirectly lessens the strain on the healthcare system. Scientists are attempting to use nanotechnology for illness diagnosis, treatment, and prevention since they are aware of its advantages. For the upcoming generation of medical scientists, there may also be applications in the development of medical instruments and procedures.

This study review's primary goals are to highlight accepted medical research procedures and compile the many facets of nanomedicine under a single topic. Extensive studies have been carried out to integrate the most recent information on nanotechnology in medicine and treatments from reputable scientific sources. To perform delicate medical operations, nanotechnology is utilized. In the domains of diagnostics, disease treatment, regenerative medicine, gene therapy, dentistry, cancer, the cosmetics medication transport, and industry, therapeutics, nanotechnology is demonstrating effective and advantageous applications. A more planned, structured, and technically programmed sector of nanomedicine will emerge in the future because of close collaboration and association between doctors, clinicians, researchers, and technology. Because illnesses have a pathophysiological base, efforts are being undertaken to overcome obstacles related to the use of nanotechnology in the medical area.

Without a question, by offering a platform for advancements in the biotechnological, medical, industries, nanotechnologies pharmaceutical have contributed to improving patients' quality Additionally, they have made healthcare processes easier, including diagnosis, treatment, and follow-up care. With the goal of making medical procedures more individualized, affordable, and secure, there is a continuous drive to develop and produce new nanomaterials that will enhance illness diagnostics and treatments in a targeted, accurate, powerful, and long-lasting manner. Utilizing the appropriate nanomaterials and minimizing any potential negative consequences are key to the promise of nanotechnology.

Like any other product, there are several issues linked with this technique [Figure 4]. The new nano-based products must undergo risk assessments before being authorized for clinical and commercial use to minimize any possible risks to the environment and public health. To more precisely determine the long-term sustainability and safety of their usage, a thorough life cycle assessment is necessary. Like the in-silico experiments and computational bioinformatics area that were attacked a few years ago, the idea of nanotechnology may appear heretical and Nonetheless, nanobiotechnology is quickly emerging as a cutting-edge 21st-century technology with a wide range of scientific and technological ramifications. Theoretical knowledge exists, and efforts are being made to advance it through practical research. It is anticipated nanotechnology will eventually be required in the medical field rather than being a choice. It is anticipated that technology will have a more significant impact on human life, healthcare, and dentistry than it has in the past once its cost is affordable. Reducing the toxicological hazards and concerns associated with high dosages and overuse of nanomaterials in medication and treatment regimens is crucial. If scientists wish to make nanotechnology in medicine work well, this is crucial. All things considered,

nanotechnology in healthcare and medicine has enormous potential to improve patient outcomes and completely change how we prevent and treat illness.

4. Source of Funding

None.

5. Conflict of Interest

None.

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