REVIEW

ISSN (O): 2349-5332
CODEN: IRJPHY

NANOTECH'S PHARMA FRONTIER: EMERGING TRENDS AND ADVANCES

Bishal Sarkar, Sourav Roy, Shreema Baksi*

IQ City Institute of Pharmaceutical Sciences, Durgapur, India

Submitted on: 18.09.2024; **Revised on:** 24.09.2024; **Accepted on:** 30.09.2024

ABSTRACT:

*Background:*The pharmaceutical industry faces numerous challenges in drug development, delivery, and diagnostics, including: poor drug solubility and bioavailability, leading to reduced efficacy and increased side effects, inadequate targeting, resulting in off-target effects and diminished therapeutic outcomes, limited diagnostic capabilities, making it difficult to detect diseases at an early stage, rising healthcare costs, driven by inefficiencies in drug development and delivery, the need for personalized medicine, tailored to individual patient needs, complexity of biological systems, making it challenging to develop effective treatments. In response to these challenges, the pharmaceutical industry has turned to nanotechnology, a field that harnesses the unique properties of materials at the nanoscale (1-100 nm) to create innovative solutions. Nanotechnology has the potential to revolutionize drug delivery, targeting, and diagnostics.
*Method:*This review article explores the emerging trends and advances in nanotechnology's applications in pharmaceutical research and development, focusing on cutting-edge innovations in drug delivery systems, targeting strategies, and diagnostic tools.
*Results:*Our analysis reveals significant potential for nanotechnology to overcome traditional limitations, enabling improved drug delivery, enhanced targeting, and innovative diagnostics. We identify key advances in nanotechnology-based systems including nnanomaterial's and nanodevices, highlighting their impact on pharmaceutical science.
*Conclusion:*Nanotechnology holds transformative promise for the pharmaceutical industry, offering new possibilities for personalized medicine, tissue engineering, gene therapy, cancer treatment, and improved patient outcomes. This review highlights the exciting frontiers of nanotech's pharma applications, underscoring the need for continued research and development to harness its full potential.

Keywords:

Pharmaceutical nanotechnology, Drug delivery systems, Targeting strategies, Diagnostic tools, Tissue engineering, Gene therapy, Cancer treatment.

Corresponding author: Shreema Baksi
E-mail address: shrima999@gmaill.com

Indian Research Journal of Pharmacy and Science; 40(2024)3110—3126
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1. INTRODUCTION

A growing field of science, nanotechnology has tremendous potential to positively influence the in an unlimited range of applications. First defined in 1958 and evolving through several stages since then, nanotechnology is the combination and development of knowledge gained from various scientific fields such as engineering, chemistry, and engineering, biology, physics, medicine and computer science. Through its constant developments, the field of nanotechnology can create nanomaterials with different functions, properties and additional characteristics that make them unique and improve a wide range of problems facing humanity today, including health, environment, construction and electronics.[1]

Nanotechnology can be defined as the control of the shape and structure of materials at the nano scale for the design, characterization and production of useful structures, devices and systems.Nanoscale refers to objects that are between 1 and 100 nm in size, where 1 nm is equal to 1 × 10^-9 m. Many challenges exist when working at such a small scale, with advanced imaging techniques a prerequisite for studying and improving the behaviour of materials and designing and manufacturing them with particles with high quality. Nanoscale (such as very fine powders, liquids or solids). This is the called a nanoparticle.[2,3] Utilization of technology at the nanoscale is referred to as nanotechnology. The importance of nanotechnology in drug delivery has been demonstrated throughout the last few decades. The word "nano" means "dwarf" in Latin (small). The term "nanotechnology" was first introduced in 1974 by Professor Norio Taniguchi of the Tokyo Science University.[4] Nanotechnology refers to any technology that operates at the nanoscale. The word "nano" refers to a size of 10^{-9} metres. In addition to engineering, electronics, physics, molecular biology, biophysics, medicine, and pharmaceuticals, nanotechnology is a multidisciplinary field. Materials have distinct characteristics at the nanoscale than at the macroscale.These altered drug molecules at the nanoscale can result in improved performance in various dose forms. We can locate the application of colloidal gold in antiquity if we go back in time to the development of nanotechnology in medicine. The development of nanoscience can be traced back to the fifth-century B.C. Greeks and Democritus.[5-6]

Through nanotechnology, a mesoscopic system—a crossover between classical and quantum mechanics—can be connected. The production of natural nano assemblies, including agricultural goods, nanomedicine, and medical treatment and diagnostic tools, is accomplished through the usage of this mesoscopic system. Diagnostic tests and drugs based on nanotechnology are currently being used to limit diseases that were previously incurable.The production and bulk industrial manufacture have also been significantly impacted by this technology. Implementing the reverse engineering approach found in nature, nanotechnology creates materials without using vast amounts of raw materials.[7,8]It makes it possible to produce products at the nanoscale, like atoms, and then creates products that function at a deeper scale.[9,10]

The use of nanotechnology in the formulation of dosage forms has various benefits, including improved solubility, accelerated dissolution, improved stability, decreased dosage, greater bioavailability, and quick onset of action. Nanotechnology is playing a significant part in the fight against a number of fatal diseases, such as cancer. It aids in the early diagnosis of a number of neurological conditions, including diabetes mellitus, viruses, and microorganisms. The development of nanomedicines, diagnosis, tissue engineering, and the creation of biomarkers, biosensors, and targeted drug delivery are all possible uses for nanotechnology in pharmaceutical sciences. Numerous nano-based technologies, including Quantum dots, Dendrimers, Carbon nanotubes, Liposomes, Polymeric nanoparticles, Metallic nanoparticles, Polymeric micelles, Nanocomposites, and many others, are used in the pharmaceutical sciences.[11,12]

2. PHARMACEUTICAL NANOTECHNOLOGY-BASED SYSTEM

It is difficult to create a drug delivery system that maximises a drug's therapeutic effects while minimising its hazardous side effects in vivo.[13]Pharmaceutical nano-systems can be used to manage these difficult tasks. Nanomaterials and nanodevices, which are the two major forms of pharmaceutical nanotechnology and are important in this sector and others, are divided into two categories. Nanomaterials can be sourced from diverse origins, including natural sources (e.g., plant-derived nanoparticles, microbial nanovesicles), chemical synthesis (e.g., sol-gel processing, hydrothermal synthesis), physical methods (e.g., mechanical milling, laser ablation), and biological sources (e.g., biomolecule-based nanomaterials, bio-inspired materials), and are subsequently utilized in various applications, such as biomaterials for orthopaedic or dental implants, scaffolds for tissue-engineered products, and other innovative uses. It is possible to modify or coat them to improve their biocompatibility with living cells. According to Jain, N.K. et al. (2007), these are further divided into nanocrystalline and nanostructured materials. The medications

produced by grinding down nanocrystals in specialised mills can be administered intravenously as nanosuspensions or bronchially via an inhaler. The surface/volume ratio and bioavailability of nearly insoluble medicines are improved by their tiny size. Nanostructured materials are nanomaterials that have undergone processing to create unique shapes and properties. Quantum dots, dendrimers, fullerenes, and carbon nanotubes are a few of these. Nanomaterials are frequently employed in the delivery of pharmaceuticals where they can improve drug solubility and, in addition, provide controlled release and/or drug targeting. They are employed in oral and vaccine administration systems, anti-cancer treatments, gene delivery, inhalers, hormone distribution through the skin, and medicine delivery through the eye. Numerous businesses use nanoparticles to treat cancer. Micro- and nano-electromechanical systems (NEMS/MEMS), microfluidics (the control and manipulation of micro- or nano-litres of fluids), and microarrays (various kinds of biological assays such as DNA, protein, cell, and antibody) are a few examples of the tiny devices known as nanodevices that operate at the nanoscale. Examples include biosensors and detectors for detecting minute amounts of bacteria, airborne pathogens, biological dangers, and disease signatures, as well as some intelligent machines like respirocytes.[14]Nanomaterials used in biosensing of the analytes for promptly diagnosis of relevant diseases enlisted in table 1. Table 2 represents the nanomaterials used in clinical management of several diseases.

Table 1: Nanomaterials implemented in biosensing of the analytes for promptly diagnosis of relevant diseases.

Nanomaterials	Applications	Ref.
Single walled Carbon nanotubes	Monitor blood nitric oxide level in inflammatory diseases	(15)
Graphene oxide	Detect very low level of cancer cells (3-5 cancer cells/ml blood)	(16)
Gold nanoparticle based molecular diagnostic platform	Genetic test for warfarin sensitivity	(17)
Silicon quantum dots and fluorescent nanodiamonds	It can be an ideal diagnostic tool for long-term bioimaging and also a non-toxic vector for drug delivery.	(18)
NanoVelcro chip – anti-EpCAM antibody coated silicon nanowwires overlaid with polydimethylsiloxane	To detect and isolate the circulating tumor cells.	(19)
Silver based nanoparticle and Raman dye-labeled DNA hairpin probes	Targets specific markers in infections	(20)
Gold nanoparticles modified with monoclonal anti-hemagglutinin antibody (mAb)	For detection of influenza A virus in blood. It utilizes the principle of colorimetric immunosensing	(21)
Nanoflares	Enable live cell detection of intracellular mRNA	(22)

Table 2: Nanomaterials implemented in clinical management of several diseases.

Nanomaterials	Applications	Ref.
Nanocrystalline silver	Antimicrobial agent for treatment of wounds	(23)
Biomimetic nanosponge	For detoxification treatment	(24)
Fullerene nanoparticles	Reduce allergic reactions	(25)
Carbon nanotube-based nanofiber scaffold	Cardiac tissue engineering	(26)
Poly(ethylene oxylated) single-walled carbon nanotubes	Maintains brains blood circulation	(27)
Gelatin nanoparticles as acarrier for osteopontin (OPN)	Given intranasally for treatment of ischemic stroke	(28)
Gold/Bismuth based nanoparticles	To concentrate radiation used in radiation therapy to treat cancer tumors	(29)
Fidgetin-like 2 (FL2) small interfering RNA (siRNA) nanoparticles	FL2, the regulator of cell migration is targeted by the nanoparticle encapsulated siRNA, to promote wound closure and regeneration	(30)

3. TYPES OF PHARMACEUTICAL NANOSYSTEMS WITH THEIR APPLICATIONS

3. 1. Liposomes

The first type of nanomaterials used for drug delivery were lipid vesicles known as liposomes, first reported in 1976.[31] Liposomes are spherical vesicles composed of amphiphilic phospholipids and cholesterol that self-assemble into bilayers and encapsulate an aqueous interior. Amphiphilic phospholipid molecules are tries to protect the hydrophobic group from the aqueous environment while maintaining contact with the aqueous phase via the hydrophilic head group.[32] Liposomes can encapsulate aqueous solutions with a hydrophobic outer membrane, so hydrophilic solutes cannot pass through the lipids. Thus, liposomes can carry both hydrophobic molecules (outer membrane) and hydrophilic molecules (inner aqueous core). Depending on the size and number of bilayers, liposomes can be divided into three categories: Multilamellar vesicles, large unilamellar vesicles, and small unilamellar vesicles. Liposomes can be classified into five types based on their composition and intracellular delivery mechanism, conventional liposomes, pH-sensitive liposomes, cationic or immunoliposomes, and long-circulating liposomes. Liposomes deliver their contents to the appropriate site by fusing their lipid bilayer with the cell membrane bilayer. Liposomes can be delivered (randomly) across lipid bilayers by creating liposomes with solutions of DNA or drugs (which cannot normally diffuse across membranes) has been studied. The efficacy of drug delivery systems may be attributed to their small size and reduced drug toxicity, controlled mode of drug release by drug modification pharmacokinetics and biodistribution.[33]Figure 1 illustrates the composition of liposome. Table 3 outlines the benefits of drug load in liposomes.

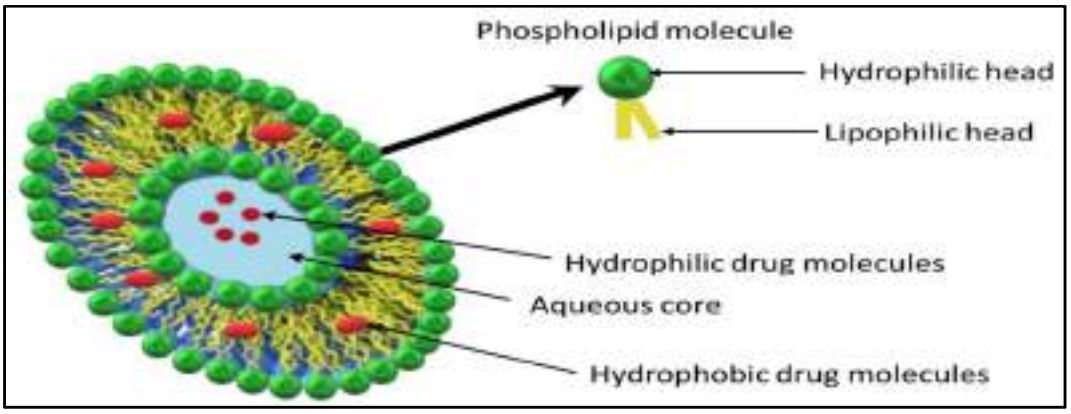

Figure 1: Schematic representation of liposome structure, illustrating the bilayer membrane composed of phospholipids, with encapsulated drug molecules and optional surface modifications for targeted delivery. (34)

Tabe 3: Benefits of drug load in liposomes

Benefits	Drugs
Improved solubility of lipophilic and amphiphilic drugs	Amphotericin B, porphyrins, minoxidil, some peptides, and anthracyclines, respectively; hydrophilic drugs, such as anticancer agent doxorubicin or acyclovir
Site-avoidance mechanism	Doxorubicin and amphotericin B
Improved penetration into tissues	Corticosteroids, anaesthetics, and insulin
Sustained release system of systemically or locally administered liposomes	Doxorubicin, cytosine arabinoside, cortisones, biological proteins or peptides such as vasopressin
Site-specific targeting	Anti-inflammatory drugs, anti-cancer, anti-infection
Passive targeting to the cells of the immune system, especially cells of the mononuclear phagocytic system	Antimonials, amphotericin B, porphyrins, vaccines, immunomodulators

3.2. Dendrimers

Dendrimers are spherical, highly branched synthetic polymers composed of multiple layers with an initiator core and active end groups. These layers are made up of repeating units, and each layer is called a generation. The dendrimer core is

called generation zero. Due to the specific molecular structure of dendrimers, various drugs can be delivered using multivalent surfaces by covalent bonding or electrostatic adsorption.[35] Dendrimers used for drug delivery and imaging are typically 10–100 nm in diameter and have multiple functional groups on their surface, making them ideal carriers for targeted drug delivery. One advantage of dendrimers is that they are similar in size to many proteins and biomolecules such as insulin, cytochrome c, and hemoglobin. The second-generation dendrimers resemble DNA in width (2.4 nm), and his PAMAM dendrimers of the fifth and sixth generation resemble the lipid membranes of cells (~5.5 nm)]. Dendrimers can be loaded with drugs by exploiting the core voids through hydrophobic interactions, hydrogen bonding, or chemical bonding. Recently, a Michigan researcher developed his polyamidoamine-based G5 dendrimers with diameters of ~5 nm and over 100 functional primary amines on the surface. By targeting folic acid and conjugating methotrexate as a therapeutic agent, the G5 dendrimer inhibited tumor growth approximately 10-fold more potently than methotrexate alone.[36]However, dendrimers show great potential for the delivery of anticancer therapeutics when they possess polycationic surfaces capable of multiple interactions with different target receptors. However, polycationic surfaces are also a major drawback in therapeutic delivery applications due to their toxic effects on cell membranes.[37] "Newkome Dendrimer Dentron" is now on sale. PAMAM dendrimers are available directly from Dendritech. Dendrimers structural arrangement is shown in Figure 2. The numerous categories of dendrimers and their respective applications were described in table 4.

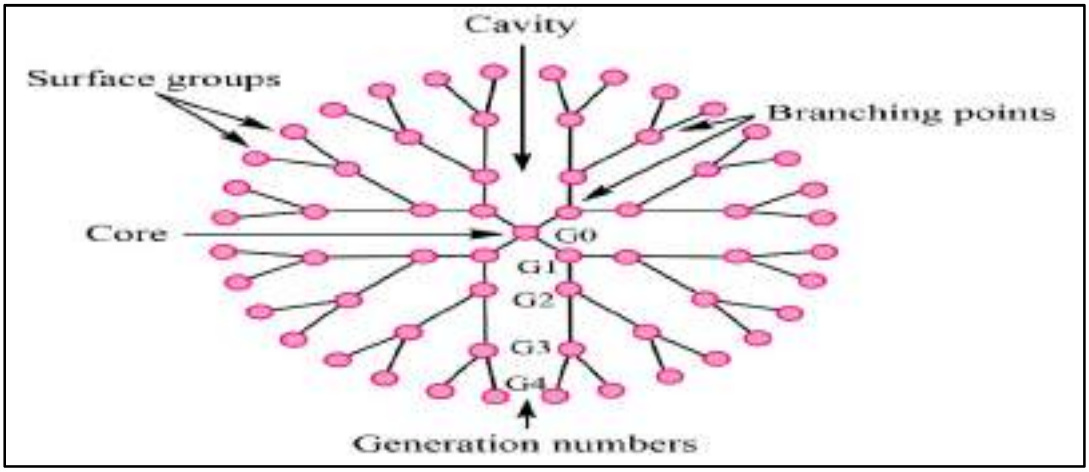

Figure 2. Schematic representation of a dendrimer structure, showcasing its radial architecture with a central core, branching dendrons, and terminal functional groups, highlighting its multivalency and versatility for drug delivery and targeting applications. (38)

Table 4: Various types of dendrimers and their applications

Compound	Types of Dendrimers	Application	References
Camptothecin	PEGylated PAMAM G5 dendrimers–AS1411 antinucleolin aptamers	BALB/c female mice bearing C26 tumors	(39)
Camptothecin	Glucose–PEG–PAMAM–S–CPT–Cy7	Monolayer (2D) and multilayer tumor spheroid (3D) HepG2	(40)
Paclitaxel	dodecyl groups and diethylethanolamine surface-modified cationic PAMAM dendrimers	Murine breast cancer metastasis model	(41)
Paclitaxel	PAMAM G4 dendrimers–succinic acid linker	Human ovarian carcinoma cells A2780	(42)
Berberine	PEGylated PAMAM G4 dendrimers	Human breast cancer cells MCF-7	(43)
Quercetin	PEGylated PAMAM G4 dendrimer–Margetuximab	Human breast cancer cells MDA-MB-231	(44)
Curcumin	PAMAM dendrimers–HCCP linker	Bone marrow macrophage cells BMMs	(45)

3.3. Carbon nanotubes

Carbon nanotubes are used in biology as sensors for detecting DNA and proteins, as diagnostic devices for differentiating different proteins from serum samples, and as carriers for delivering drugs, vaccines, or proteins. It is a carbon cylinder composed of benzene rings.[46] Single-walled carbon nanotubes have been used as a platform to study surface proteins and protein-protein associations and to develop highly specific electronic biomolecular detectors. Carbon nanotubes are hexagonal networks of carbon atoms. The length and diameter of these tubes are 1 nm and lengths between 1 and 100 nm. There are two types of nanotubes: single-walled nanotubes (SWNTS) and multi-walled nanotubes (MWNTS). These are small macromolecules with unique sizes, shapes, and remarkable physical properties. Single-walled graphene oxide, graphene nanosheets, functionalized graphene nanosheets, multi-walled carbon nanotubes prices, multi-walled carbon nanotubes prices containing graphite, OH or COOH graphitized multi-walled carbon nanotubes, OH-functionalized carbon nanotubes, COOH-functionalized carbon nanotubes, NH2 Functionalized carbon nanotubes, in short carbon nanotubes, industrial grade carbon nanotubes, etc. are good example of a commercial product.[47]The structure of carbon nanotubes was depicted in figure 3.

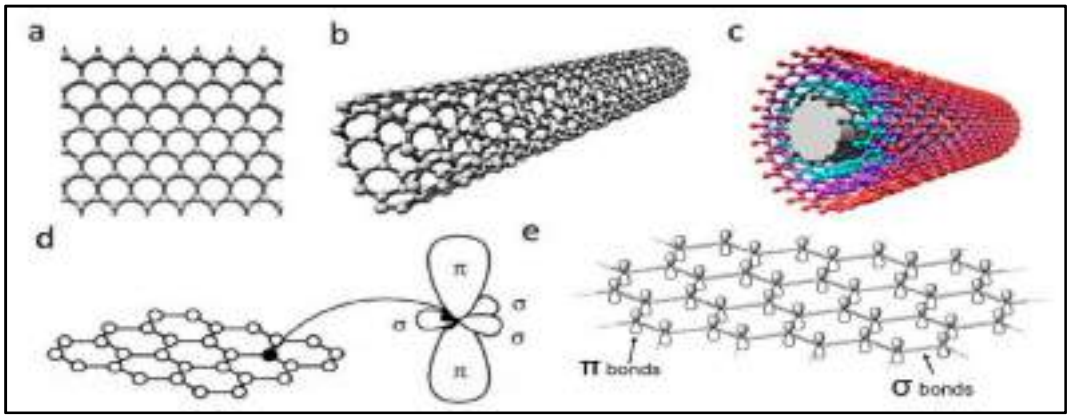

Figure 3: Illustration of a carbon nanotube (CNT) structure, depicting its cylindrical morphology with a hollow interior, composed of rolled graphene sheets with sp2-hybridized carbon atoms. (48)

3.4. Quantum dots

QDs are used to track individual glycine receptors (GlyRs) and analyze their dynamics at neuronal membranes in live cells over time periods ranging from milliseconds to minutes.[49]In recent years, semiconductor quantum dots (QDs) have attracted the attention of many research groups due to their scientific and technological importance in microelectronics, optoelectronics, and cellular imaging.[50] Quantum dots are semiconductor materials consisting of a semiconductor core surrounded by a cladding to improve optical properties. Their properties derive from their physical size with radii between 10 and 100 Å (TheNanotech Revolution in Drug Delivery 2007). Quantum dots are widely used in biological applications that require fluorescence, especially in the immunostaining of proteins, microtubules, actin, and nuclear antigens, such as DNA array technology, cell biology, and immunofluorescence assays.[50]The most commonly used QDs are cadmium selenide (CdSe), cadmium telluride (CdTe), indium phosphide (InP), and indium arsenide (InAs). In biological imaging, these particles act as contrast agents and offer much higher resolution than existing fluorescent dyes. These particles can absorb and re-emit white light within nanoseconds with different volume bandgap energies corresponding to different combinations of particles. Commercial products include lead sulfide (PbS) EviDot® Quantum Dots and PbSEviDots® (850nm to 1500nm) specifications. Quantum Dots structure has been demonstrated in figure 4. The quantum dots employed for drug delivery were reported in table 5.

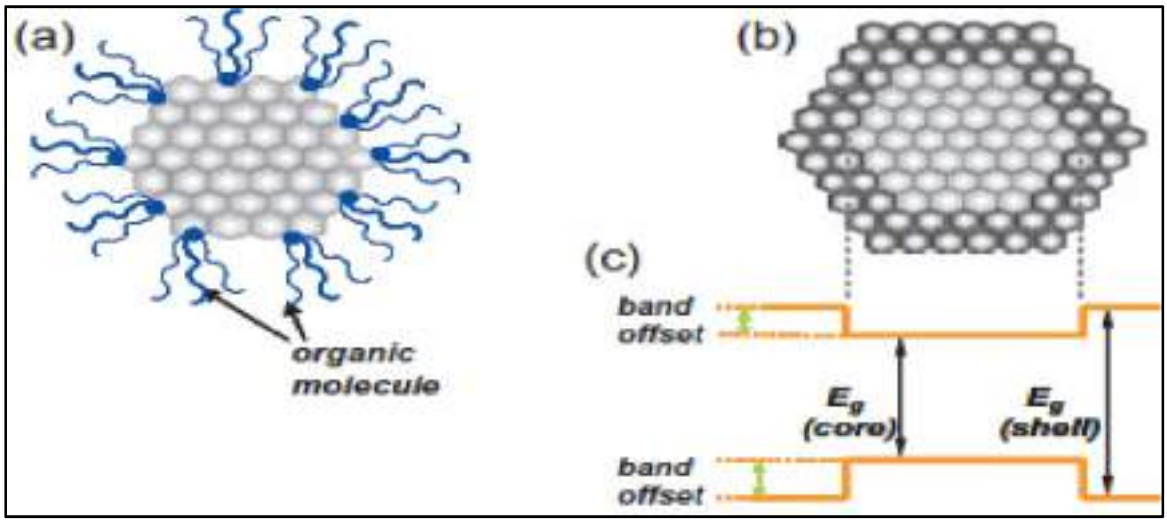

Figure 4. Schematic representation of a quantum dot (QD) structure, showing its nanocrystalline core-shell architecture, comprising a semiconductor material (e.g., CdSe) core surrounded by a passivating shell (e.g., PbS). (51)

Table 5: List of Quantum Dots implemented for Delivering of Drugs.

QD	Drug	Treatment	References
Chitosan encapsulated ZnO	Doxorubicin hydrochloride [DOX]	Leukemia	(52)
Folic acid conjugated Graphene quantum dots	Doxorubicin hydrochloride [DOX]	Cervical cancer	(53)
Manganese-doped zinc sulfide [Mn:ZnS] quantum dots [QDs]	Busulfan	Chronic myelogenous leukemia	(54)
Graphene quantum dots [GQDs]; magnetic mesoporous silica nanoparticles [MMSN]	Doxorubicin	Breast cancer 4T1 cells	(55)
Water soluble graphene quantum dots	Doxorubicin	A549 cell – Lung cancer	(56)

3.5. Polymeric nanoparticles

Polymeric nanoparticles have been developed as effective delivery vehicles due to their passive tumor-targeting properties, resulting in enhanced efficacy and reduced side effects of chemotherapeutic drugs. Furthermore, this unique ability of nanoparticles to preferentially accumulate in and around tumor masses also provides a platform for improving tumor diagnostics and lays the foundation for the development of multifunctional nanoparticle systems in cancer therapy.[57]Build"Polymer nanoparticles" is a generic term for nanospheres and nanocapsules. These are solid colloidal particles with sizes around 10–500 nm.[58]These nanoparticles offer an alternative to the nanosystems mentioned above due to their unique

properties such as biocompatibility, non-immunogenicity, non-toxicity and biodegradability (The Nanotech Revolution in Drug Delivery 2007). Polymers suitable for making nanoparticles include: Poly(alkylcyanocrystallates), poly(mytylidenemalnolate 2.1.2), polyesters, e.g. B. Poly(lactic acid), poly(ecaprolactone) and copolymers thereof. Natural macromolecules such as proteins, polysaccharides, non-polar lipids, metal oxides and silica can also be used to prepare nanospheres.[59]Structure of Polymeric nanoparticles displayed in figure 5.

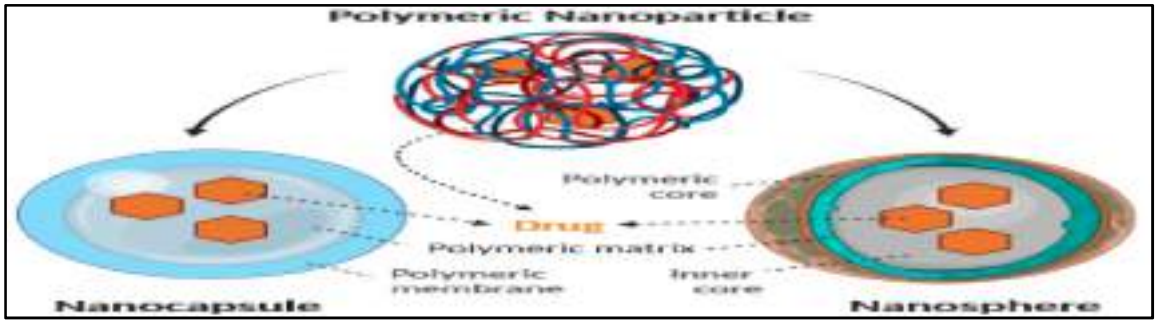

Figure 5. Illustration of a polymeric nanoparticle (PNP) structure, depicting its spherical morphology with a polymeric matrix composed of biocompatible and biodegradable materials, encapsulating a therapeutic agent or drug, and optionally surface-functionalized with targeting ligands or stealth coatings to enhance cellular uptake and biodistribution, highlighting its versatility for controlled drug delivery and targeted therapy. (60)

3.6. Polymeric micelles

Polymeric micelles are nanoparticles composed of a hydrophilic shell and a hydrophobic core. This can be broken down into her two main categories: Hydrophobically configured micelles and polyion complex micelles. The former usually consist of amphiphilic copolymers with hydrophobic and hydrophilic blocks. Equilibrium between these two blocks in aqueous media induces the spontaneous formation of nanosized particles. Most block copolymers use poly (ethylene glycol) (PEG) as the hydrophilic block. Different micellar properties are derived from the properties of hydrophobic core-forming materials, including biodegradable polyesters such as poly (lactic acid) (PLA), poly(caprolactone) (PCL), and poly (glycolic acid) (PGA).[61] They are typically less than 100 nm and their hydrophilic surface protects against non-specific uptake by the reticuloendothelial system. In solution, micelles form as aggregates, in which the molecular components are arranged in globular structures with a hydrophobic core, protected from water by a coating of hydrophilic groups. They are used for systemic delivery of water-insoluble drugs. Commercially available products include CrEL-paclitaxel preparations and phenylboronic acid-introduced polymer micelles. Figure 6 shows the composition of polymeric micelles.

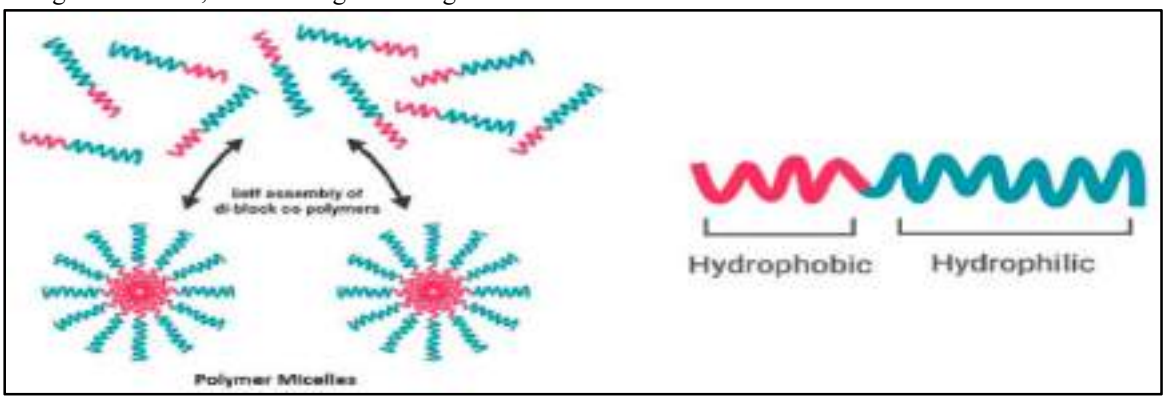

Figure 6. Schematic representation of a polymeric micelle structure, showing its core-shell architecture with a hydrophobic core composed of polymeric chains (e.g., PLGA, PCL) and a hydrophilic shell composed of poly(ethylene glycol) (PEG) or other copolymers, self-assembled to encapsulate hydrophobic drugs or therapeutic agents. (62)

3.7. Metallic nanoparticles

Although nanoparticles of various metals have been manufactured, silver and gold nanoparticles are the most important for biomedical applications and numerous ligands have been attached to nanoparticles such as sugars, peptides, proteins and DNA. Due to their ability to functionalize surfaces, they have been used as an alternative to quantum dots for active bioactive delivery, drug discovery, bioassays, detection, imaging, and many other applications.[63]A commercial product is CdSe, ZnS QDs, palladium and copper metal nanoparticles, silver and gold metal nanoparticles, etc.

4. APPLICATION OF PHARMACEUTICAL NANOTECHNOLOGY

From the concept of nanotechnology, current approaches to drug therapy require drugs to be systemically absorbed to affect a single localized organ, and then attack that organ or its affected areas at the molecular level. Current pharmaceuticals rely on slightly different binding or uptake selectivity's, and even at doses sufficient to be effective against the diseased organ, if binding and uptake is weak throughout the rest of the body, can have serious adverse effects on pharmaceutical nanotechnology is also focused on the following applications.

(i) *Drug delivery*
Nanoparticle-based drug delivery has many advantages, including improve therapeutic efficacy and pharmacological properties of drugs. Nanoparticles improve the solubility of poorly water-soluble drugs, alter their pharmacokinetics, and reduce immunogenicity, thereby increasing drug half-life and increasing specificity for target cells or tissues (thus reducing side effects), to improve bioavailability and decrease drug metabolism, allowing for better control. Simultaneous administration of two or more drugs for therapeutic compound release and combination therapy.[64]

(ii) *Tissue Engineering*
Nanotechnology can help regenerate or repair damaged tissue. "Tissue engineering" uses artificially stimulated cell proliferation using suitable nanomaterial-based scaffolds and growth factors. Tissue engineering has the potential to replace today's conventional treatments such as organ transplantation and artificial implants.[65]Nanotechnology and microtechnology can be combined with biomaterials to create tissue engineering scaffolds that can maintain and control cell behavior.[66]

(iii) *In gene therapy*
Genetic material can be delivered into cells using liposomes that are less than 100 nm. Due to the liver Kupffer cells' quick reception of the polyethylene glycol and galactose-containing liposomes, liver cells are successfully targeted. Therefore, gene therapy for many liver illnesses like Wilson's disease and congenital hemochromatosis may be tried using such liposomal nanoparticles.[67]Additionally, gene therapy for breast cancer cells using polymeric nanoparticles has had an antiproliferative effect.[68]

(iv) *Molecular Diagnostics*
The integration of nanoparticles with other materials based on nanotechnology has the ability to handle this new problem and produce solutions that allow for diagnosis at the level of individual cells and molecules. The most widely utilised QDs in bioimaging are cadmium selenide (CdSe), cadmium telluride (CdTe), indium phosphide (InP), and indium arsenide (InAs), which act as contrast agents and offer far higher resolution than current fluorescent dyes.

(v) *Stem cell therapy*
According to recent studies, nanoparticles may be useful instruments for enhancing stem cell therapy. According to a study reported online on October 5 in Proceedings of the National Academy of Sciences, chemical engineers have effectively employed nanoparticles to improve stem cells' capacity to induce regeneration of injured vascular tissue and lessen muscle atrophy in mice. According to Bulte et al., non-specific membrane adsorption techniques can be utilized to mark human neural stem cells (NSCs) and mesenchymal stem cells (MSCs) using magneto dendrimers made of iron oxide

nanoparticles.According to Noth et al., human mesenchymal stem cells were labelled with super paramagnetic iron oxide particles so that their motility could be followed using MRI after being transplanted for cartilage repair.[69]In stem cell therapy, a blood or bone marrow sample containing the desired adult stem cells is combined with magnetic nanoparticles and antibodies. The target cells are bound by the magnetic particles and are then retrievable by a magnet. This method is employed in cell treatments to separate adult stem cells, which are then transplanted back into the patient, for example, to treat cardiac or blood issues.[70]

(vi) *Cancer treatment*

For application in cancer therapy, colloidal drug delivery systems like liposomes, micelles, and nanoparticles have undergone extensive research. Drug delivery systems' efficiency can be ascribed to factors such as their compact size, decreased drug toxicity, regulated drug release, altered medication pharmacokinetics, and altered biological distribution of the drug.[71]

5. CURRENT NANOTECHNOLOGY ERA

Nanotechnology had progressed since Feynman's initial predictions till 1981, when researchers Gerd Binnig & Heinrich Rohrer, who worked at the IBM Zurich Research Laboratory invent the Scanning Tunneling Microscope (STM).[72,73]The STM's pointed tip approaches a conductive surface with such precision that the atoms' electron wave functions overlap with the surface atoms' wave functions. When a voltage is supplied, electrons "tunnel" (or vice versa) from the atomic structure at the tip into the surface through the vacuum space. The investigators reported the first STM image of the Si (111)-7×7 rebuilt surface in 1983. This surface is currently ordinarily depicted as seen in Figure 7.[74]

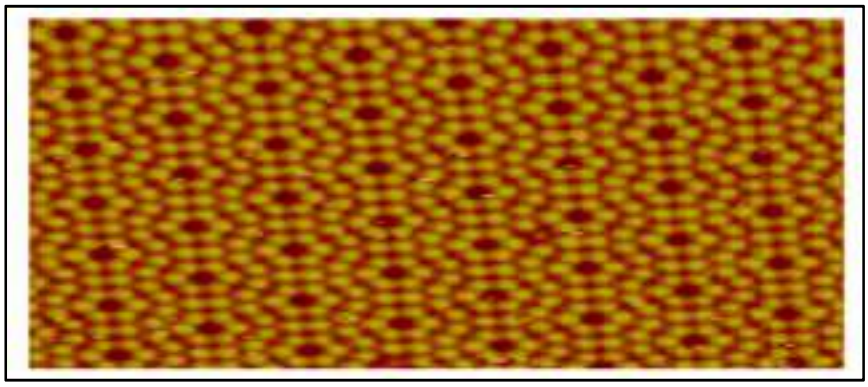

Figure 7: Atomic scale resolution of the uppermost layer of silicon atoms is displayed in this STM image of the Si(111)-7 × 7 rebuilt surface. (75)

A few decades afterwards, in the year 1990, 35 separate xenon atoms were manipulated on a nickel surface by Don Eigler of IBM in Almaden and his fellow researchers to produce the letters of the IBM symbol (Figure 8).[76]

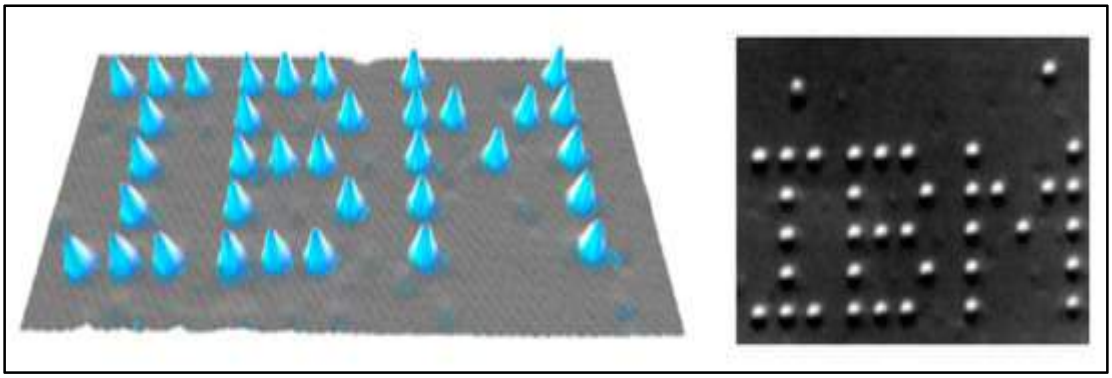

Figure 8. 35 Xenon atoms positioned on a nickel (110) substrate using a STM to form IBM logo. (77)

The STM was created to take pictures of surfaces at the atomic scale, and it has since been used to mold atoms and molecules into structures. The tunneling current can be used to selectively induce or break bonds between molecules. Binnig and Rohrer received the 1986 Nobel Prize in Physics for "their design of the STM." The instruments of choice for nanotechnology researchers nowadays are the atomic force microscope (AFM) & scanning probe microscopes (SPM).[78,79]In 1985, Robert Curl, Harold Kroto, & Richard Smalley additionally discovered that carbon may exist in extremely stable spheres known as fullerenes or buckyballs.[80]In an inert atmosphere, graphite evaporation forms carbon spheres with chemical formulas C60 or C70. It is currently feasible to encapsulate metal atoms to form novel organic molecules, and new carbon chemistries are being created.A few years later, in 1991, Iijima et al. observed them using transmission electron microscopy (TEM) from hollow graphite tubes or carbon nanotubes, forming an additional member of the fullerene family (Fig. 9).[81]

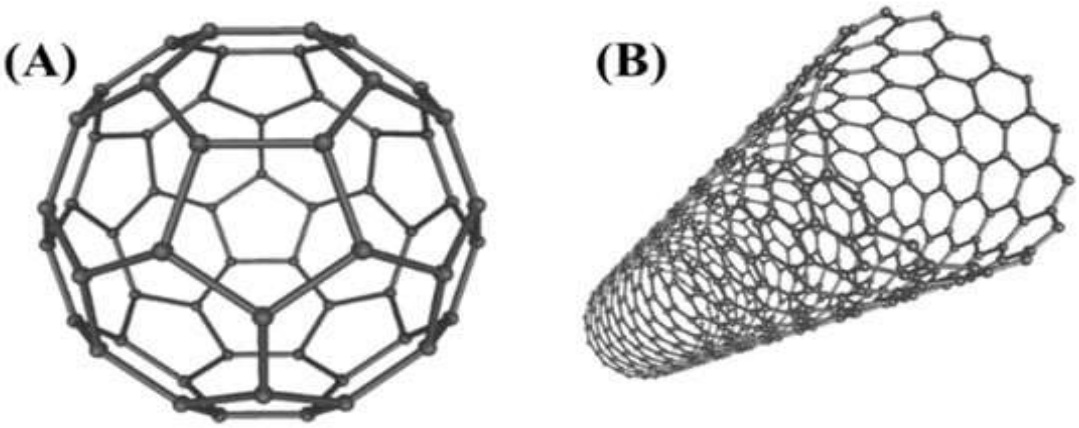

Figure 9. Schematic of a C60 buckyball (Fullerene) (A) and carbon nanotube (B).(82)

Carbon nanotubes have the potential to be helpful in a wide range of nanotechnological applications due to their strength and flexibility. Carbon nanotubes are currently employed in polymers and beton as composite fibers to enhance the bulk product's mechanical, thermal, and electrical characteristics. In addition, they may find use as molecular electrical components, energy storage materials, field emitters, and catalysts. Environmentally friendly and economically viable energy has been produced through nanotechnology in a number of ways, including reduced pollution during the production of materials, competitively priced solar cells, removal of organic pollutants from groundwater, and removal of volatile organic compounds (VOCs) from the air. However, there is a pressing need for study in the underdeveloped field of computational methodologies to nanomedicine.[83,84]The topic of nano informatics was born out of the necessity for computational applications at the nanoscale. Robust algorithms for machine learning and statistical analysis have the potential to significantly aid in the development of more effective nanocarrier designs. These algorithms, which forecast future data with predictive information, are primarily used to forecast the cytotoxicity, absorption, and activity of nanoparticles within cells. Other significant characterizations carried out as part of the assessment of nano informatics include data mining, network assessment, quantitative structure-property relationships (QSPR), quantitative structure-activity relationships (QSAR), and ADMET predictors (absorption, distribution, metabolism, excretion, and toxicity).[85]

To get beyond such in vitro obstacles, nanoinformatics has offered a crucial supplementary platform for nanoparticle creation and analysis. Only the collection, exchange, modeling, visualization, and analysis of crucial data and information at the nanoscale are covered by nanoinformatics.[86] Chemotherapy is also made easier by nanoinformatics, which enhances tumor cell nanomodeling and makes drug-resistant cancers easier to identify. In order to cure cancer with minimal side effects, the most recent nanoinformatics technologies include targeted medication delivery and gene therapy techniques based on hyperthermia.[87]

6. FUTURE ASPECTS OF PHARMACEUTICAL NANOTECHNOLOGY

Pharmaceutical firms are having difficulties. Large pharmaceutical companies are looking for fresh competitive business strategies as the number of

"blockbuster" medicine patents expires rises. By 2011, several medications in America could lose their patent protection, potentially costing the country prescription earnings worth $70-$80 billion. Due to their poor ADMET profiles, the majority of new drugs are unable to enter the market. Drugs with low water solubility have recently been effectively treated using a variety of nanotechnologies. Many pharmaceutical companies are employing nanotechnology to reevaluate medications that were put on hold because of their solubility profiles because they were "difficult" to formulate.[88]Medical diagnosis, effective drug delivery, and the creation of artificial cells are the areas where nanosize materials have found widespread application. According to Freitas, the use of nanotechnology in medicine, or nanomedicine, encompasses three gradually increasingly potent molecular technologies.[89]The notion behind what is needed is apparent; the drug must be targeted to its target, just like a letter is addressed to an addressee. However, the "magic bullet" or "smart medicine" that targets only the organ of interest has not yet been developed.Designing a nanomachine that can simultaneously identify and combat pathogens, detect the change in molecular event throughout the diseased condition, and also monitor the success of treatment is a very intriguing and new future technique. A supply of some sort of "poison" that could be released in a controlled manner, multiple binding sites to measure the concentration of particular molecules, and a small computer would all be included in such a device. Similar devices armed with particular "weapons" could be employed to remove circulatory blockages or locate and eradicate cancer cells. Additionally, it has been suggested that nanorobots could be modified bacteria and viruses that already possess the majority of motorization and genetic information transport capabilities.[90]

7. DISCUSSION

Nanotechnology is transforming pharmaceutical research and development by revolutionizing drug delivery, targeting, and diagnostics. Significant advancements include:

- Nanoparticle-based systems and nano emulsions, enhancing solubility, stability, and bioavailability.
- Active and passive targeting strategies, optimizing treatment efficacy and minimizing off-target effects.
- Nano sensors and imaging agents, enabling real-time monitoring and personalized medicine.
- Therapeutic applications in cancer treatment, gene therapy, and tissue engineering.

The future directions include:

- Personalized medicine, tailoring treatments to individual patients.
- Combination therapies, leveraging synergistic effects.
- Harmonized regulatory frameworks, facilitating innovation and improving patient outcomes.

This multifaceted approach unlocks nanotechnology's transformative potential in pharmaceutical research and development, driving innovation and enhancing patient care.

A comprehensive analysis of the clinical efficacy, application potential, and limitations of various nanomaterials in oncological treatment reveals distinct benefits and challenges across diverse patient populations.

- Liposomes: Enhance chemotherapy delivery, reduce toxicity, and improve efficacy. Prospects include targeted therapy and combination with immunotherapy. However, potential liposome-mediated drug resistance is a limitation.
- Polymeric Nanoparticles (PNPs): Offer controlled drug release, improved bioavailability, and reduced side effects. Prospects include personalized medicine and cancer stem cell targeting. Complexity in synthesis and potential immune responses are limitations.
- Quantum Dots (QDs): Enhance imaging, diagnostics, and photothermal therapy. Prospects include early cancer detection and image-guided surgery. Potential toxicity and limited biocompatibility are limitations.
- Carbon Nanotubes (CNTs): Improve drug delivery and enhance radiation therapy. Prospects include targeted therapy and combination with immunotherapy. Potential toxicity and difficulty in functionalization are limitations.
- Dendrimers: Enhance drug delivery and improve imaging. Prospects include targeted therapy and cancer diagnosis. Complexity in synthesis and potential immune responses are limitations.

As nanotechnology continues to revolutionize the pharmaceutical landscape, it is essential to consider the implications for vulnerable patient populations. The following groups require special attention due

to their unique physiological and pathological characteristics:

1. Pediatric Patients
   - Pharmacokinetic and pharmacodynamic profiles are poorly understood in this population.
   - Immature organ function and developing physiology may enhance susceptibility to nanotoxicity.
2. Geriatric Patients
   - Age-related decline in organ function and clearance necessitates careful dosing and monitoring.
   - Polypharmacy and comorbidities, including renal and hepatic impairment, can exacerbate nanotoxicity.
3. Immunocompromised Patients
   - Altered immune responses and increased susceptibility to opportunistic infections require careful consideration.
   - Immune status and potential for immunotoxicity must be evaluated.
4. Patients with Comorbidities
   - Underlying conditions, such as renal or hepatic disease, can impact nanocarrier distribution and clearance.
   - Disease interactions and potential for exacerbated toxicity must be carefully assessed.

By addressing these considerations, pharmaceutical nanotechnology can continue to advance, providing innovative solutions for vulnerable patient populations while ensuring safety and efficacy.

The advent of nanotechnologies in drug development raises pertinent ethical considerations and societal implications, necessitating a comprehensive examination of their potential consequences on human health, environmental sustainability, and social equity. The ethical issues of nanotechnology include:

- Unintended consequences: Unknown long-term effects on human health and the environment.
- Inequitable access: Nanomedicines may be expensive, limiting access for marginalized communities.
- Privacy concerns: Nano sensors and tracking devices may raise privacy issues.
- Informed consent: Patients may not fully understand nanotechnology-based treatments.
- Patent and ownership issues: Control and profit from nanotechnology-based drugs.

The social impacts of these technologies are as follows:

- Job displacement: Automation in nanotechnology-based manufacturing.
- Economic disparities: High costs of nanomedicines may exacerbate healthcare inequalities.
- Environmental impact: Nanoparticle toxicity and bioaccumulation.
- Public perception and trust: Fear of unknown effects may lead to public skepticism.
- Regulation and governance: Need for clear guidelines and oversight.

These ethical issues and social impacts highlight the need for responsible development, regulation, and communication around nanotechnologies in drug development.

8. CONCLUSION

The enabling technology of the twenty-first century is now thought to be nanotechnology. Today, better composite materials, materials with improved catalytic activity, materials with increased hardness and scratch resistance, and a variety of consumer goods (like cosmetics and sunscreens) that enhance human life are all produced using nanostructured materials and nanotechnology techniques. Pharmaceutical nanotechnology has become a field with immense potential for delivering bioactives and diagnostics in both space and time, as well as for producing intelligent materials for tissue engineering. Through its nano-engineered tools, it offers new prospects, tools, and a wider range of applications that are anticipated to have a significant impact on many areas of disease, diagnosis, prognosis, and treatment of diseases.When more established, traditional technologies may have reached their limits, pharmaceutical nanotechnology offers opportunity to build new, more advanced materials and medical equipment. In light of the financial loss brought on by off-patent medications, it gives industry new hope by offering innovative patent-protective technology. In the future, it will provide us access to cutting-edge nanotechnology that will significantly advance disease detection, diagnosis, therapy, and prevention. Examples include smart medicine and nanorobots.

Despite the significant advancements in nanotechnology, several challenges persist in its applications, necessitating further research and innovation. The current limitations include:

- Scalability and cost-effectiveness in nanomaterial synthesis, hindered by the need for high-energy inputs and complex fabrication processes.

- Uniformity and reproducibility in nanoparticle fabrication, compromised by the inherent variability in nanoscale systems.
- Biocompatibility and toxicity concerns, arising from the interactions between nanomaterials and biological systems.
- Regulatory frameworks and standards for nanotechnology-based products, requiring harmonization and standardization.

To address these challenges, future research directions could focus on:

- Developing novel nanomaterial synthesis methods, such as bottom-up approaches and bio-inspired fabrication, for scalable and cost-effective production.
- Investigating alternative biomaterials and nanostructures, such as graphene and nanocrystalline materials, for improved biocompatibility and reduced toxicity.
- Exploring innovative applications of nanotechnology in personalized medicine and precision healthcare, leveraging advances in genomics and artificial intelligence
- Establishing standardized regulatory frameworks for nanotechnology-based products, incorporating risk assessment and life cycle analysis.

Furthermore, emerging trends and technologies, such as: Artificial intelligence and machine learning in nanotechnology research, enabling predictive modelling and optimization of nanoscale systems. Nanotechnology-enabled Internet of Nano-Things (IoNT) for healthcare applications, facilitating remote monitoring and personalized interventions. Synthetic biology and nano-biohybrid systems for novel therapeutics, harnessing the potential of biological systems and nanoscale materials offer exciting opportunities for future research and innovation. By addressing current challenges and exploring new frontiers, nanotechnology can continue to transform industries and improve human lives.

Abbreviations

NEMS Nano-Electromechanical systems
MEMS Micro- Electromechanical systems
SWNTS Single-walled nanotubes
MWNTS multi-walled nanotubes
STM Scanning Tunnelling Microscope

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CONFLICT OF INTEREST REPORTED: NIL; SOURCE OF FUNDING: NONE REPORTED