Nanomaterials and its biomedical applications: Current status and future aspects

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***Abstract*- The investigation of systems at the molecular and cellular levels of the cells is known as nanotechnology. In order to create exact applications in the biological domains, the scheming of nanomaterials has lately emerged as a major study objective.**

Recent developments in nanotechnology have made it necessary to create novel materials with a variety of purposes. The exceptional physiochemical functions of nanoparticles are attributed to their decreased size. These include enhanced surface area, molar extinction coefficients, heightened absorption and reactivity, adjustable plasmonic features, quantum phenomena as well as magnetic and optical characteristics.

Understanding the fundamentals of analytical chemistry, physical sciences, and, primarily, molecular biology for the study of incredibly small objects is made easier by nanotechnology. It describes how nanoparticles are used in processes like wound healing and drug delivery. Nanotechnology has a wide range of uses in biomedical engineering and medicine, including tissue and implant engineering, diagnosis, and treatment. The most recent research on creating carbon-based nanomaterials for a range of biological uses, such as cancer treatment, drug transport, and biosensing, is also summarized in this review

***Key words:* Biosensing, cancer treatment, drug delivery, nanotechnology, nanomaterials, and nanomedicine.**

I. INTRODUCTION

A prefix called Nano{N} can be used to describe 109 of any parameter. The renowned material scientist Richard P. Feynman introduced the concept of nanotechnology within his landmark talk, ""Enough Space at the Bottom," presented at the December 1959 meeting of the American Physical Society [1]. In the near future, entire equipment for clinical use and a useful set of research tools will be made available thanks to nanomedicine, a subfield of nanotechnology[2]. In order to further apply molecularly linked nanotechnology to the creation of biological instruments and pharmaceuticals, nanomedicine primarily focuses on nanomaterials, biological devices, and nano electronic biosensors[3]. Recent scientific advancements in the fields of disease detection, therapeutic planning , and drug of delivery are largely due to nanotechnology.

Nanomedicine is the term used to describe the use of nanotechnology in the diagnosis, treatment, monitoring, and control of biological systems[4]. Furthermore, a variety of nanostructures have been investigated in order to assess their characteristics and potential uses in biosensors. Nanotubes, nanofibres, nanorods, nanoparticles, and thin films are all included in these structures[5].

Nanotechnologies with a variety of specializations, such as data management, medicine delivery, water purification, and the development of nanoscale materials for use in industry and health care[6]. Smart nanomaterials are materials that respond to a variety of stimuli by changing their own properties, including shape, surface area, size, permeability, solubility, and mechanical qualities. [7]. Overall, the most recent advancements in cellular and subcellular nanodevices could be persuasive in rational and therapeutic applications, giving researchers and medical professionals one of the most powerful instruments at their disposal to tackle urgent concerns, treat human sickness, and troubleshoot age-related health problems. [8].

Because of their many benefits, including their high flexibility, vast surface area, and exceptional characteristics, nanomaterials hold a great deal of promise to address these issues [9].Applications for bioassay that use nanomaterials, such as biosensors, biomedical devices, and biofuel cells, have received special attention[10].

CLASSIFICATION OF NANOMATERIALS:

- Nanospheres
- Nanorods
- Nanocore shells
- nanotubes

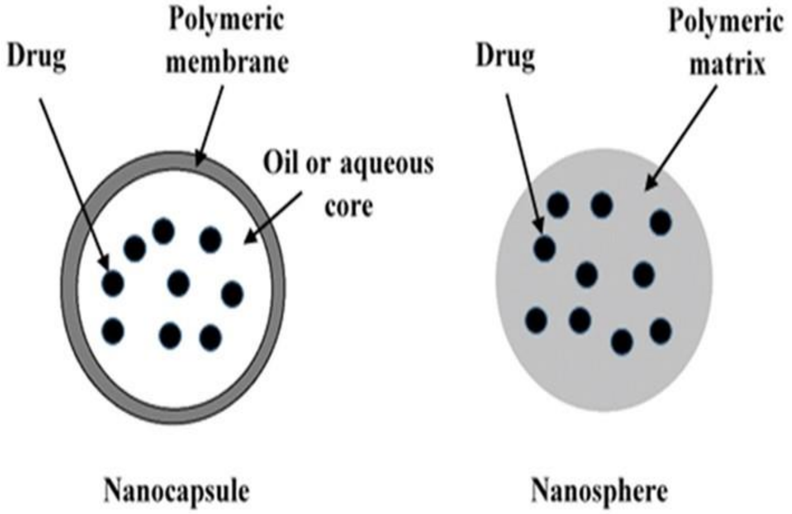
- Quantum dots
- nano bubbles
- Nanocrystals and nanocubes structures

1. NANOSPHERES:

The core of nanosphere innovation is the production of spherical particles with average diameters measured in nanometers through the combination of polymeric, inorganic, or both types of materials.

They are ideal for these uses because of their size at nanoscale and ability to contain and discharge medicinal or active substances [11]. To ensure maximum fusing into the nanospheres, either the aqueous phase or the oil phase molecules can be loaded with the medicines and active compounds.

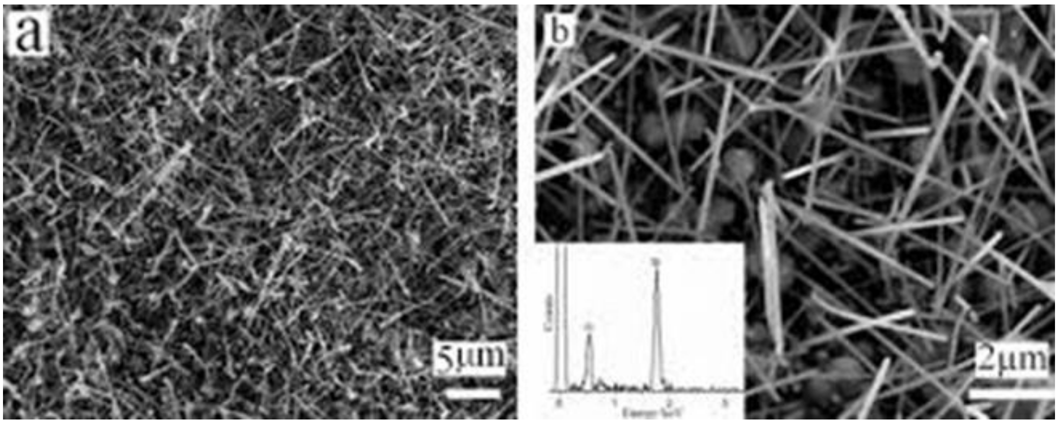
Several forms of electron microscopy can be used to characterize the nanospheres' size, shape, and drug encapsulation. The diameter, size, and form of the nanospheres can be managed by changing the homogenizer speed, precursor surfactant or stabilizer ratio, and pioneer concentration[12].



2. NANORODS:

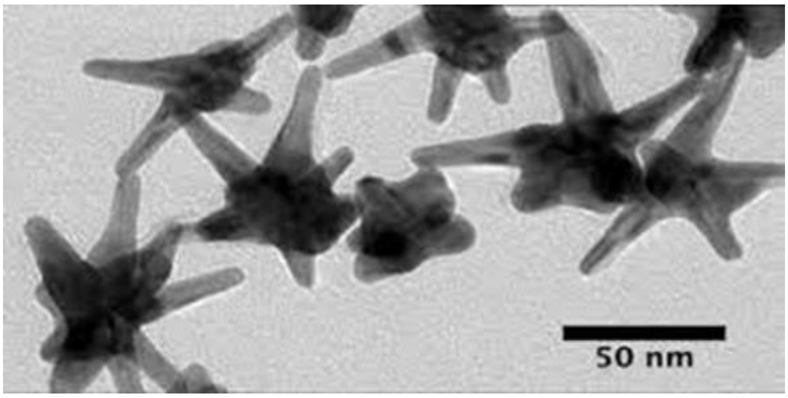
Aspect ratios of three to five are found in the regions of two of the faces of nanorods, which are nanoparticles smaller than 100 nm.Due to modifications made to the plasma medication profiles, these drug nanocarriers will improve therapeutic efficacy and lessen side effects. [13].

The methods of internalization, drug release, and immune response can be affected by the size of the NPs, even though they either passively or actively infiltrate the cells[14].



3. NANOSTARS:

Numerous metallic nanostructures in the form of stars have been created for various biological purposes. This method improves the biocompatibility of the GNS by creating a star-shaped gold nanoparticle without the need for the deadly surfactants that are typically used for GNS production. GNSs were employed to investigate the penetration of nanoparticles into cerebrum tumors across the blood-membrane barrier[15]. The multifunctional GNS test was used in this evaluation for both imaging and treatment, according to in vivo research.This was done to use radio-labelling, CT, and two-photon luminescence (TPL) imaging to investigate how the size and infusion portion of NPs affect their biodistribution and intra-tumoral conveyance. [16].



4. NANOCORE SHELLS :

The potential applications of core-shell 730onmaterial and nanostructures in various domains, especially in the transport of bioactive chemicals, have made them an important research topic in the last few decades[17].

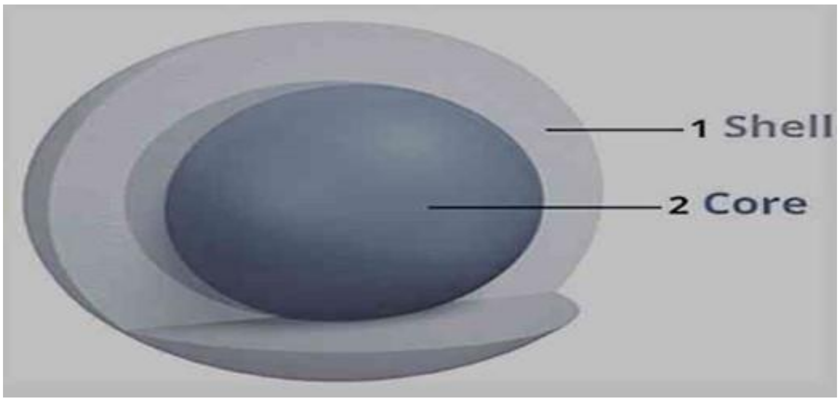
Different core shell structures exist, such as

a) metal core and different metal shell
b) metal core and non metallic shell
c) metal core and polymer shell
d) non-metallic core and non-metallic shell
e) polymer core and non-metallic shell
f) polymer core and polymer shell

In this sense, core-shell NPs could be very important in biomedical applications.

They are regarded as controller-released drug carriers [18].

Since core-shell designs may transfer the active components slowly following localization into the cancer tissue, they enhance the practical applications of NPs in the market for targeted anti-tumor drugs. [19].



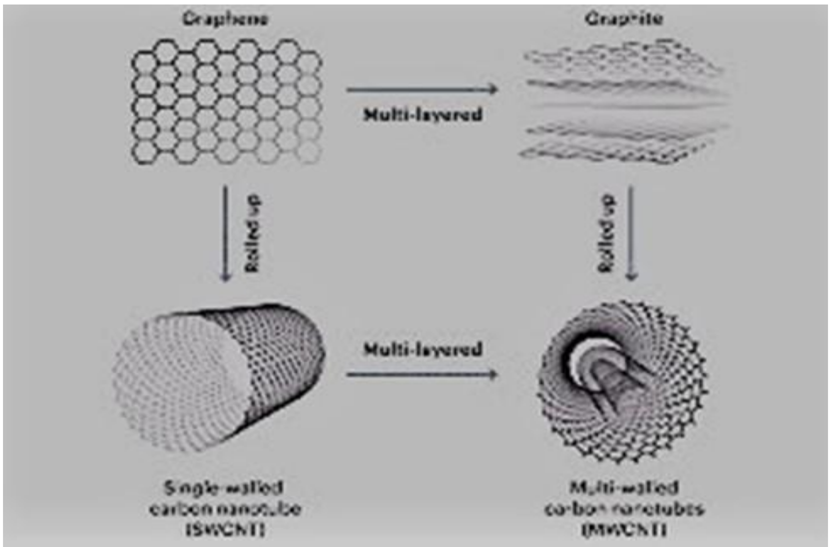
5. NANOTUBES:

The most well-known type of nanotube is the carbon nanotube, which was created in 1991.

Two types of nanotubes that can be differentiated from one another by their architectures are single-walled carbon nanotubes (SWCNTs) and multiwalled carbon nanotubes (MWCNTs). [20].

Once bioactive compounds like drugs or genes have been functionalized with ammonium or carboxylic groups to make them soluble, nanotubes can be utilized as a transport mechanism for those molecules.

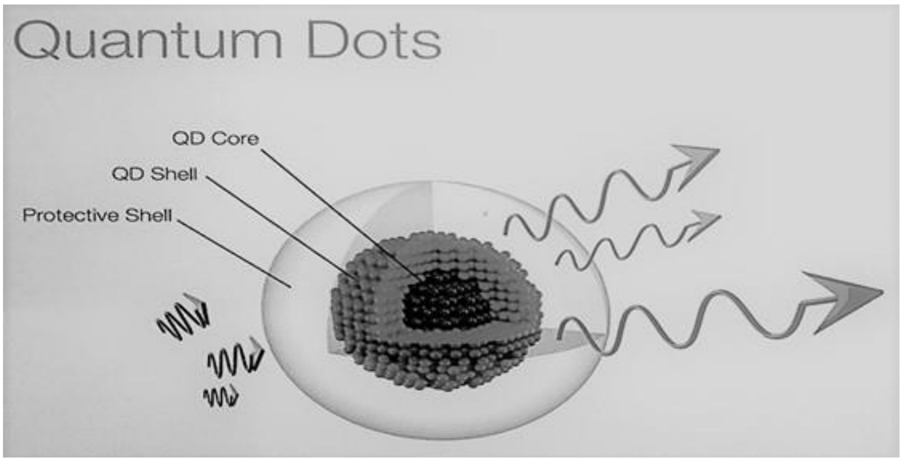
Amphotericin B has shown enhanced drug delivery via nanotubes into cells when compared to drug delivery without nanotubes. [21].



6. QUANTUAM DOTS :

Higher electrical and optical qualities in materials at the nanoscale (2–10 nm) than at the broader scale are referred to as quantum dots, and this defines them as highly recommended for semiconductor applications[22].

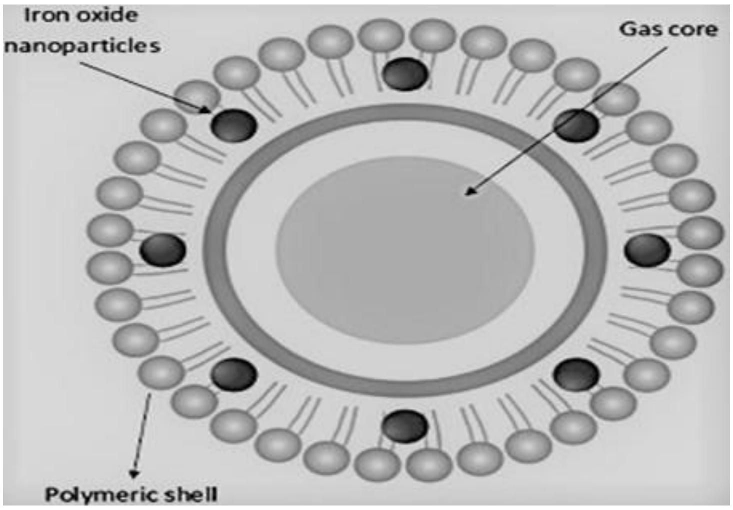
Moreover, QDs can be utilized to map tumors and oversee appropriate treatment for individuals with malignancies by imaging their tumors. Because of their remarkable distinctiveness, they make good candidates for using in model animals and cell diagnostics. They might also take the place of the organic pigments that were initially used for the same porous materials due to their established limitations and downsides. 23].



7. NANO BUBBLES :

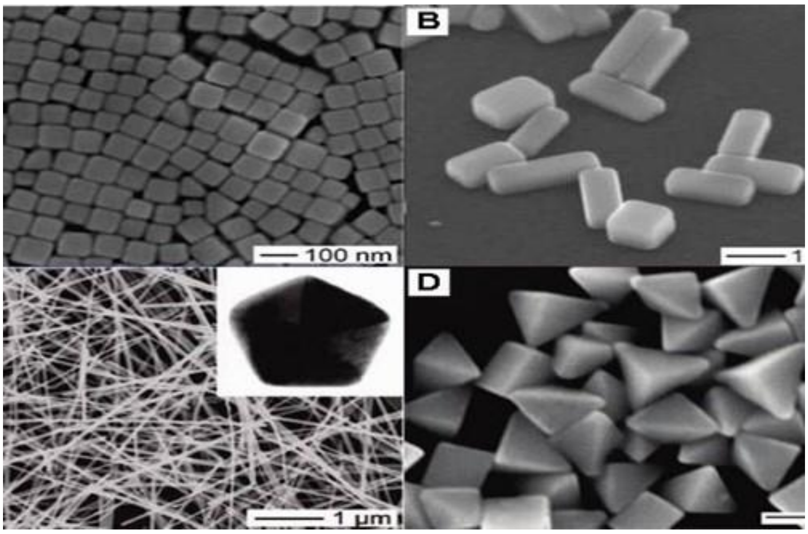
Disease-treating medications can be manufactured into formations resembling nanoscale bubbles, or nanobubbles. The body temperature causes them to become unstable, which is how pharmaceuticals are delivered by nanobubbles. They then aggregate to create microbubbles with the help of external ultrasonic stimulation, which releases the active chemicals that are enclosed in the nanobubbles[24].

Further research is necessary to determine the efficacy of this method in treating various cancers. In addition to being used to treat cancer, nanobubbles can also be used as a carrier for non-viral vectors that can be used to treat or diagnose certain diseases using ultrasound imaging. In addition, they are being investigated in conjunction with ultrasound as a corrective measure for clot removal in vascular frameworks. [25].



8. NANOCRYSTAL AND NANOCUBE STRUCTURES :

The ability of metallic or bimetallic nanoparticles (NPs) to transition from one desired shape to another is important for both nanotechnology and nanoscience. In the realm of nanosensors, nanocube shapes have garnered significant interest among nanocrystals.To prepare larger particles, this process involves first synthesizing small metal nanoparticles (NPs) as seeds, or nucleation sites, which are then mixed with a growth solution[26].



Techniques used in the production of nanomaterials

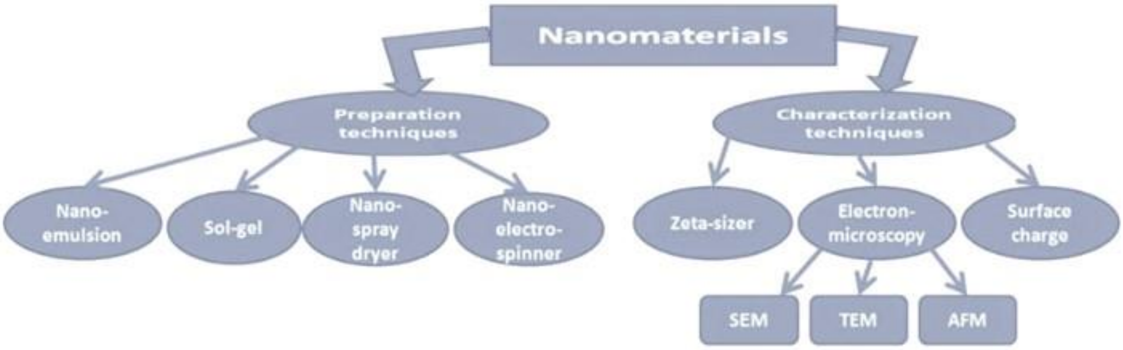
Methods used in the creation of nanomaterials: There are two distinct processes for the synthesis of nanomaterials and the formation of nanostructures.

1. **Top down approaches** is used to describe the process of gradually reducing a bulk material into nanopartBottom icles through milling and attrition.
2. **Bottom up approach** refers to processes when materials self-assemble to make themselves [27].

- **Inorganic nanoparticles** (NPs): NPs are widely used in the pharmaceutical business because they offer substitutes for conventional antibiotics and anti-cancer medications, which generates new opportunities for their application in this domain.
- **Chemical precipitation:** Because of its cost and convenience of usage, the chemical precipitation method is frequently employed to produce different nanomaterials for use in biomedical applications
- **Sol gel technology:** The synthesis of NPs for biomedical applications has made great use of the sol-gel processing approach.
- **Nanopolymers:** The choice of an appropriate process for NP creation is based on the physicochemical properties of the medicine to be employed as well as the polymer. A range of materials, such as proteins, polysaccharides, and synthetic polymers, can be used to create NPs[28].

Nanocomposites:
Multiphase materials with one or more constituent particles smaller than 100 nm are called nano composites. The pharmaceutical sector has made considerable use of nano composite-based polymers; in fact, the majority of pharmaceutical formulations available today are hydrogels consisting of biopolymers loaded with active chemicals or nano-metal oxides[29].

Characteristion of nanoparticles:
Particle size distribution, diameter, and shape—all of which may be found using a variety of characterization techniques—are crucial criteria to consider when assessing the proposed NPs.



1.Dynamic Light Scattering:
Dynamic light scattering (DLS) is still one of the fastest technologies available for NP characterisation and is usually preferred by scientists that are interested in NP design.

2. Scanning Electron Microscopy:
The form, surface properties, and diameter of NPs can be ascertained using a variety of microscopic techniques, the most notable of which being scanning electron microscopy (SEM). When utilizing a DLS zetasizer on the same sample, the findings should match the particle size found by SEM[30].

3. Transmission Electron Microscopy:
Because of their small sizes, there is very little opportunity to use conventional techniques for detecting the size and shape of NPs. Remarkably, transmission electron microscopy (TEM) techniques provide optional information on the intended nanomaterials, such as diffraction, image recording, and spectroscopic data[31].

4. Atomic force microscopy:
This technique is also known as scanning force microscopy. Compared to ordinary light microscopy, atomic force microscopy (AFM) offers 100 times higher demand resolution tens of nanometers.AFM has two different modes for recording images: modalities of contact and non-contact. The appropriate mode is determined solely by the characteristics of the specimen[32]. The most accurate representation of size, size distribution, and actual image is provided by AFM, which helps to clarify the effects of various biological situations.

Nanotechnology in antimicrobial techniques:
With the use of nanoparticles and infrared light rays, scientists are creating an anti-microbial method that will destroy bacteria. This technique is mostly used to clean devices, particularly those used in hospitals to treat biomedical wastes[33].

Cream containing nanoparticles has shown promise in treating infections caused by microbes. Nitric oxide gas, which is used to destroy bacteria and lessen diseases linked to germs, is present in nanoparticles. A recent development in antibiotic-containing nanotechnology is the burn dressing, which is covered with nanocapsules[34].

Nanotechnology in drug delivery:

In the near future, nanomedicine will be significant primarily in the scientific and technological domains. Nanomedicine mostly uses nanoparticles to inject or administer medications, as well as other chemicals like heat, light, or other substances to identify certain tumor-related cells that produce carcinomas or cancers[35].

For example, cancer cells are the only cells that nanoparticles target; healthy cells are not. A therapeutically relevant nanoparticle that can be swallowed and that enters the bloodstream after passing through the intestines and stomach walls is being developed by researchers worldwide[36].

Advances in nanomaterials in biomedicine:

Since many nanoparticles have detrimental impacts on living things, there is reason for concern regarding the growing use of these materials.

The increasing use of nanoparticles raises concerns because many of them have negative effects on biological organisms. The necessity for published data analysis according to certain medical specialties has arisen from the development of ever-new nanomaterials and research into the potential use of these materials in biomedicine[37].

One of the most significant issues is the effective transport of therapeutic nucleic acids into cells, which is being addressed by the development of a wide range of nanostructures.

Nanomaterial’s for biomedical applications:

Depending on where they come from, natural or synthetic nanomaterials fall into one of two groups when it comes to bioactive nanomaterials.

The following are some common uses of nanomaterials in the medical field:

- Diagnosis
  - ☐ Bioimaging
  - ☐ Biosensors

- Therapy
  - ☐ Regenerative medicine
  - ☐ Cancer treatment
  - ☐ Antibacterial agent
- Drug delivery
- Gene delivery
- Medication delivery

Their mechanical, biocompatibility, degradation, and bioactivity qualities determine how they are used in the human body. Biomaterials have been approved for use in biomedical applications thus far, including medication delivery devices, plastic surgery, joint replacements, heart valve replacements, and other restorative procedures [38].

Regenerative medicine and the therapeutic use of antibacterial and anticancer drugs are generally included in the category of biomedical applications.

Regenerative medicine:

When used properly, nanomedicine can replace a damaged body part with new tissue or an organ by utilising nanomaterials as a vehicle for biological molecules and medication delivery as well as a substrate for cell development and proliferation. [39].

One of the most important problems in regenerative medicine is nerve creation. Restoring nerve tissue at damaged sites remains a major problem to date. Many kinds of nanomaterials have been developed and are being investigated for the prevention or treatment of nerve injury.

Certain inorganic compounds, including magnetic NPs, silica NPs, metallic NPs, and quantum dots, have been utilized to help injured nerves regenerate. Conversely, unique organic nanomaterials have been researched for applications involving the regeneration of neural tissue. Among the natural nanomaterials are carbon-based nanomaterials, liposomes, dendrimers, micelles, nanofibre, and polymeric nanoparticles. Applications for nanomaterials in bone, ligament, vascular, and bladder tissue regeneration have also been demonstrated.Humans are susceptible to various wound effects that might arise from many sources. Nonetheless, the development of a wound involves four main phases: hemostasis, inflammation, proliferation, and maturation[40].

The most effective method for treating wounds has been shown to be the use of nanoparticles (NPs) loaded with antibiotics or antibacterial compounds. One kind of polymer nanomaterials is nanofibres that are loaded with medicines, bioactive compounds, and antibacterial agents[41].

Fundamentally, these nanofibres provide a multitude of uses, especially in the healthcare sector, due to their increased surface-area-to-volume ratio, simple surface functionalization, and changeable porosity.

The nanobiosensor is based on an anodic aluminium oxide (AAO) chip and works on the principles of localised surface plasmon resonance (LSPR) and interferometry. 42].

Gene delivery system:

Scientists use NPs as drug carriers because prolonged sustained medication administration is sought in many scenarios to produce improved results and improved patient consistency. One of the most sought-after goals in drug quality is targeted medicine delivery. NPs can be used to focus on a variety of phases, including cells, tissues, and organs, particularly when it comes to the organelles found within the cells[43].

Numerous tumour forms have permeability in their veins. Because of the enhanced permeability and retention (EPR) effect, flowing nanoparticles (NPs) having a diameter of between 100 and 300 nm would pour through the perforations and gather inside the tumour. [44].

For head and neck squamous cell cancer (HNSCC), a supra-portion intra-blood vessel CDDP mixture was particularly employed to solve these issues and enhance the therapeutic efficacy of cisplatin (CDDP). Recently, a variety of restorative stages of nanoparticles have been produced, including liposomes, NPs, and polymeric micelles. These stages were motivated by the possibility of drug delivery systems (DDS) to be precisely given to tumours with little adverse effects and reduced circulation in normal tissues. [45].

In gastric cancer, NC-6004, a CDDP-joining polymeric micellar nanoparticle, improved anti-tumor movement and reduced CDDP's nephrotoxicity and neurotoxicity. It is a long-standing and well-established fact that a material's surface area grows as its volume decreases per unit. This fundamental concept is important for advances in drug delivery molecules that use nanoscale components [46].

Nanoparticles for bioimaging:

Nanoparticle-based optical imaging agents have improved stability both in vitro and in vivo, resistance against photobleaching, high quantum yield, high absorbance, resistance against metabolic disintegration, non-toxicity, and near-infraded emission..For deep tissue cancer imaging, it is appealing to produce nanoparticles having NIR excitation and emission. In this regard, recently announced NIR Qdots exhibit considerable promise[47]. It has been shown that virus-magnet hybrid nanoparticles are capable of both gene expression and MR imaging.

Controlled drug delivery using nanoparticles :

The goal of nanomedical techniques to drug delivery is to create nanoscale molecules or particles that will guarantee a medicine's stability and bioavailability.Drug delivery based on nanotechnology provides improved drug targeting, controlled release, and penetration.

Due to the fact that conventional drug delivery methods employing nanoparticles or nanocapsules are not target cell selective, they may have toxicities and side effects on sensitive normal cells[48].

Many nanoparticulate systems, including biodegradable chitosan, liposomes, PEG, dextran, silica, and gelatin, and non-biodegradable polymers like PMMA, polyacrelamide, polysterene, polycynoacrelate, polyphosphazene derivatives, etc., were studied for the purpose of therapeutic gene administration. [49].

The basic concept of antibody or ligand targeted therapeutics is that selective delivery of drugs to cancerous tissues can be enhanced by combining drugs with molecules that bind to antigens or receptors that are either specifically expressed on target cells or enable the targeted delivery of drugs to cancer cells.

The use of nanostructured materials is becoming more and more effective in the diagnosis of illnesses of the central nervous system.A viable substitute for delivering medications through the blood-brain barrier is the use of nanoparticles.There's proof that treating brain tumors in particular with a combination of drugs and nanoparticles can help treat brain illnesses. Anti-HIV medications, anti-infective medicines, and other delivery systems based on nanoparticles can also be very successful[50].

The various classes of smart nanomaterials are distinguished by the stimuli that are applied.Due to these unique materials' capacity to react to one or more stimuli, their primary uses in the biomedical sector

Table: Examples of nanomaterials and their biomedical applications

stimuli	***nanomaterial***	***application***

Temperature	poly(ethylene oxide) Poly(propylene oxide PEO-PPO-PEO	Oral drug delivery wound healing
Temperature	Gold nanoparticles-pluronic	drug delivery photo thermal platform
Temperature	copolymers/poly(lactic acid-co-Glycolic acid)	Tissue engineering
Temperature	collagen or chitosan based	drug delivery
Electrical	Fe3O4/PolyanilineFe3O4	Anti microbial drug delivery
Light	poly(ethylene glycol)PEG	Switchable fluorescent Probes

Nanotubes used for cancer therapy

Because of their many uses in biological applications, carbon nanotubes are highly adaptable materials. These are the appealing options to carry genes, proteins, and anticancer medications for chemotherapy.

Additionally, CNTs' potent NIR light absorption makes them effective photothermal agents. created MWCNT functionalized with iRGD polyethyleneimine (PEI) and conjugated with candesartan. Using plasmid AT, the functionalized iRGDPEI-MWCNT-CD was put together.IRGD and CD were used to target αvβ3-integrin and AT1R of tumour endothelium and lung cancer cells, respectively. The CD treatment demonstrated synergistic downregulation of VEGF and successfully prevented angiogenesis when used in conjunction with pAT. Combined photothermal and chemotherapeutic treatment using a DOX-loaded TAT-chitosan functionalized MWCNT nanosystem was recently conducted. In order to induce apoptosis in cancer cells, the Dong-woo group used a PEG-coated CNT-ABT737 nanodrug specifically targeted at the mitochondria. In the end, the material showed effective in vivo medicinal qualities..

Conclusion:

Drugs can be effectively delivered to target cells by using nanoparticles, which also lessen damage to healthy cells. A recent development in nanotechnology aids in the treatment of damaged cells while sparing healthy cells.

For use in medication and gene delivery applications, nanomaterials with various compositions and a variety of chemical and biological characteristics have been thoroughly studied. Over the past 20 years, a great deal of research has been conducted on carbon-based nanotubes (CBNs), one of the most widely used forms of nanomaterials.

Nanomaterials based on CBN might be used in the future to provide biomedical uses. Despite their potentially harmful effects on biological systems, a number of chemical modification techniques have been developed and successfully used in bio-applications, including drug delivery, tissue engineering, biomolecule detection, and cancer therapy.

The literature study indicates that nanotechnology has had a noteworthy influence on the biomedical profession, leading to remarkable advancements in the synthesis of usable nanomaterials for a range of medical applications.This overview emphasizes how far nanotechnology has come in the previous 20 years and why it is so important for future research into smart materials for biomedical applications.

By creating multifunctional nanoplatforms, new techniques and approaches for clinical oncology nanomedicine in the future can be produced with improved diagnostic and therapeutic efficacy. A number of intricate biological in vitro barriers are still challenging to achieve, including enhancing biocompatibility, stability, and biodegradability as well as guaranteeing non-toxicity and exact control of response locations of stimuli-responsive nanoplatforms.Despite these obstacles, understanding plasmonic nanoparticles opens up a world of possibilities for improved prognostic monitoring and diagnosis leading up to point of care testing. With its innovative approach that seamlessly transitions from in vitro research to clinical trial applications in the field of oncology, nanomedicine holds great potential.

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