

Nanoparticles

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Abstract: *Nanoparticles typically range in size from 1 to 100 nm in one (or more) dimensions. In general, nanoparticles are characterized as inorganic, organic, or carbon particles on a nanometric scale, and their properties are superior to those of bigger materials. They exhibit improved qualities such as strength, sensitivity, high reactivity, stability, surface area, and so on as a result of their small size. They were synthesized using a variety of technologies for research and commercial applications, which are categorized into three types: chemical, physical, and mechanical procedures that experienced significant progress. This work presents an overview of nanoparticles, their types, characterisation, production processes, and applications in the field of environment.*

Keywords: Nanoparticles, Types, Synthesis, characteristics and applications.

I. INTRODUCTION

Nanoparticles are important components of nanotechnology. Nanoparticles range in size from 1 to 100 nm and are composed of metal, metal oxides, organic materials, and carbon^[1] Aside from their substance, nanoparticles vary in dimension, shape, and size^[2] Surfaces can be uneven, with surface variances, or homogeneous. Some nanoparticles are crystalline or amorphous, having single or many crystal solids that are either agglomerated or loosely packed^[3] Most drug candidates are insoluble or weakly soluble in water throughout the synthesis process, posing a significant challenge to the pharmaceutical industry. Drug insolubility is primarily due to its complex and massive molecular structure. More than 65% of new active pharmaceutical ingredients (APIs) are water-insoluble or poorly soluble. These drugs are classified as class II of the Biopharmaceutics Classification System (BCS) due to their low aqueous solubility and high permeability. The rate of absorption is limited by the dissolving stage. The pharmaceutical industry is working to increase the dissolving of weakly watersoluble medications, which is crucial for increasing bioavailability. For example, they improve drug/protein stability and provide controlled release features. This review primarily examined the creation of various nanoparticles by chemical, physical, and biological approaches. Biological approaches are more cost-effective and less damaging than chemical or physical methods. The article discusses nanoparticle properties and their potential applications.

Classification of Nanoparticle

Nanoparticles are classed as organic, inorganic, and carbon-based.

Organic nanoparticles: include micelles, dendrimers, ferritin, and liposomes. Nanoparticles are non-toxic and biodegradable. Some particles, such as liposomes and micelles, have hollow cores called nano capsules. They are sensitive to thermal and electromagnetic radiation^[4].

Organic nanoparticles are commonly employed in biomedical applications, such as drug delivery, due to their efficiency and ability to target particular areas of the body.

Examples of organic nanoparticles include liposomes, dendrimers, and micelles.

Inorganic nanoparticles: These are particles that do not contain carbon. Metal and metal oxide-based nanoparticles are typically classified as inorganic nanoparticles.

Metal nanoparticles NPs: can be synthesized from almost any metal^[5]. Metals often utilized in nanoparticle synthesis include aluminum (Al), cadmium (Cd), cobalt (Co), copper (Cu), gold (Au), iron (Fe), lead (Pb), silver (Ag), and zinc. Nanoparticles can be manufactured via chemical, electrochemical, or photochemical processes. Chemical techniques include the metal Nanoparticles are created by reducing metal-ion precursors in solution with chemical reducing agents. These can adsorb tiny compounds. Have a high surface energy. Nanoparticles have various applications, including research, biomolecule detection and imaging, and environmental and bioanalytical applications. Gold nanoparticles are used to coat samples for SEM analysis. This enhances the electronic stream, resulting in high-quality SEM images. Metal nanoparticles are widely used in research due to their superior optical characteristics.

Ceramic nanoparticles:- These inorganic solids consist of carbides, carbonates, oxides, and phosphates created through heat and cooling. They come in several forms, including polycrystalline, dense, amorphous, porous, and hollow. Researchers are focusing on these nanoparticles for their potential applications in catalysis, photocatalysis, and dye degradation. Nanoparticles with controlled physical properties can be used in medication delivery systems to target cancers, glaucoma, and certain bacterial infections.

Semiconductor nanoparticles:- exhibit characteristics similar to metals and nonmetals.

They are classified in the periodic table as groups II-VI, III-V, or IV-VI. Particles with large bandgaps exhibit varying characteristics depending on tuning. They are utilized for photocatalysis. Application areas include electronics, photo-optics, and water splitting. Semiconductor materials have qualities similar to metals and nonmetals, making them widely used in literature. Semiconductor nanoparticles include GaN, GaP, InP, and InAs from group III-V; ZnO, ZnS, CdS, CdSe, and CdTe from group II-VI; and silicon and germanium from group IV.^[6]

Polymeric NPs: are organic-based and commonly referred to as polymer nanoparticles (PNPs) in the literature. Depending upon the Nanospheres or nano-capsules are used in their preparation. The matrix particles have a solid overall mass, whereas the other molecules are adsorbed on the spherical surface's outer edge.

In the latter situation, the particle entirely encapsulates the solid mass. PNPs have numerous applications in the literature due to their ease of functionality.

Polymeric nanoparticles offer benefits such as controlled release, drug protection, therapy-imaging integration, and selective targeting. Their uses include medicine delivery and diagnostics. The medication delivery using polymeric Nanoparticles are very biodegradable and biocompatible.

Lipid-based nanoparticles: Lipid nanoparticles are typically spherical, with diameters ranging from 10 to 100 nm. The structure consists of a lipid core and a matrix of soluble lipophilic molecules. Surfactants and emulsifiers help stabilize the nanoparticles' exterior core. Nanoparticles have medicinal applications such as medication delivery and RNA release in cancer therapy.

Carbon-based nanoparticles: consist of two primary materials: carbon nanotubes (CNTs) and fullerenes. CNTs are graphene sheets wrapped into tubes. These materials are 100 times stronger than steel, making them ideal for structural reinforcement. Carbon nanotubes are classed as either single-walled (SWCNTs) or multi-walled (MWCNTs). CNTs are remarkable in that they are thermally conductive along their length but non-conductive across the tube. Fullerenes are carbon allotropes with a hollow cage structure made up of 60 or more atoms. C-60's structure, known as Buckminsterfullerene, resembles a hollow football. Carbon units in these structures are arranged in pentagons and hexagons^[7]. These have commercial applications. Properties include electrical conductivity, structure, high strength, and electron affinity. Single-walled (SWNTs), double-walled (DWNTs), and multi-walled carbon nanotubes (MWNTs) refer to rolled sheets with one, two, or more walls. Carbon precursors, particularly atomic carbons, are deposited on metal particles using laser or electric arc vaporization of graphite. Recently, they have been produced using chemical vapor deposition (CVD) techniques. These materials have unique physical, chemical, and mechanical properties, making them useful as fillers, gas adsorbents for environmental remediation, and support medium for inorganic and organic catalysts. They are also used in nano-composites^[8].

Synthesis of Nanoparticles:

Several approaches have been used to create nanoparticles (NPs) with precise form, size, and dimensions. structure. There are two ways for synthesizing NPs: top-down and bottom-up (Arole et al., 2014; Hasan, 2015; Khan, 2020; Khan et al., 2019; Rane et al., 2018). The methods are classified depending on their operations and reaction circumstances (Scheme 1 & 2).

A. Top-down Approach

The top-down strategy entails breaking down the bulk material into nanosized particles. This is a damaging method. Topdown techniques are easier and involve removing or dividing bulk material or miniaturizing production procedures to achieve desired structures with appropriate attributes^[9]. Common methods for producing nanoparticles include mechanical milling, nanolithography, laser ablation, sputtering, and thermal breakdown^[10].

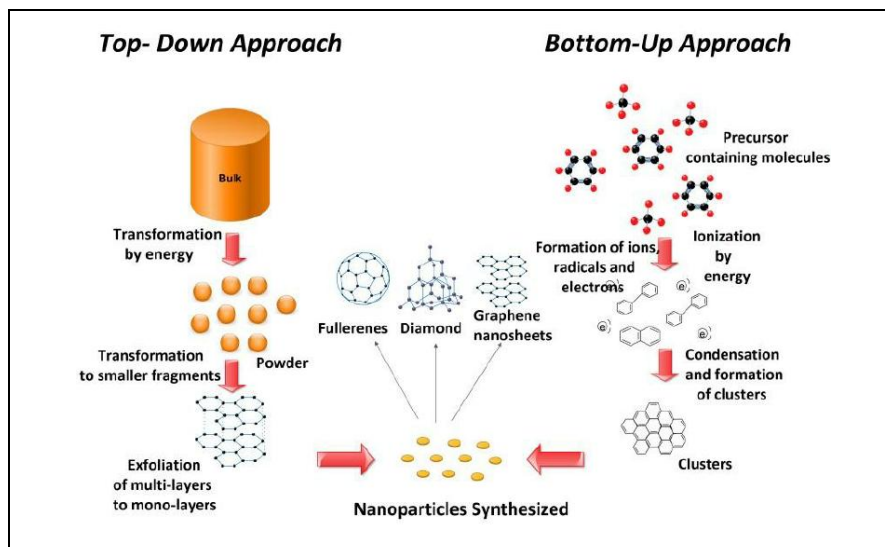


Fig: Schematic representation of Top-down approach & Bottomup approach

B. Bottom-Up Approach:

The bottom-up approach, also known as the constructive method, involves building nanoparticles from clusters formed by atoms. This procedure often incorporates sedimentation and reduction techniques. This strategy can reduce waste, making it more cost-effective. Examples of this approach include sol-gel, spinning, green synthesis, CVD, pyrolysis, and biosynthesis^[11].

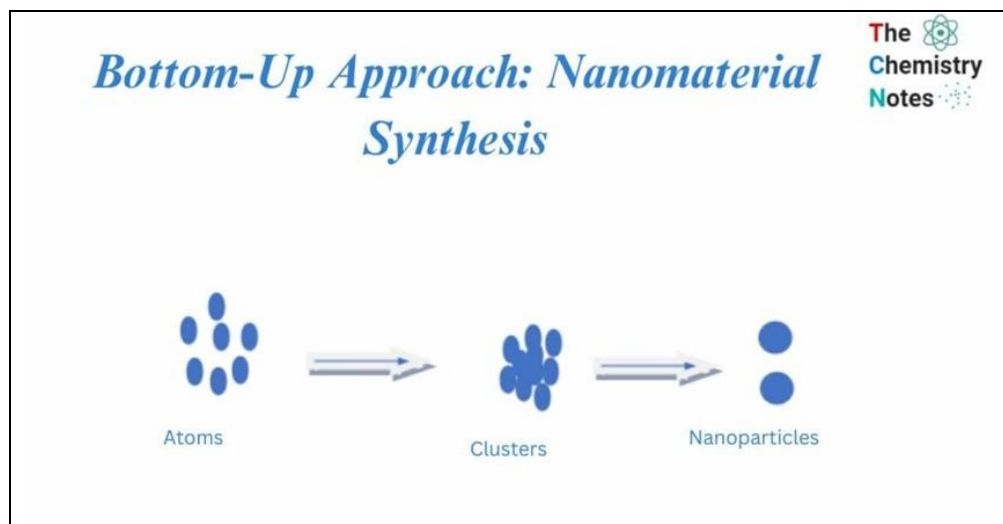


Fig: Bottom- up approach

Characterization of Nanoparticles

Zeta potential: The zeta potential of a nanoparticle is widely used to determine its surface charge. It reflects particles' electrical potential and is influenced by their composition as well as the medium in which they are scattered. Nanoparticles having a zeta potential between -10 and +10 mV are roughly neutral, while those with zeta potentials above +30 mV or below -30 mV are strongly cationic or anionic^[12]. The zeta potential can also be utilized to assess whether a charged active substance is encapsulated inside the nanocapsule or adsorbed on the surface. The magnitude

of the Zeta Potential offers information regarding particle stability; higher magnitude potentials exhibit increased electrostatic repulsion and thus increased stability.

0-5 mV: Particles tend to agglomerate or aggregate

5-20 mV: Particles are minimally stable

20-40 mV: Particles are moderately stable

40+ mV: Particles are highly stable

It is vital to note that the amount of the charge on the nanoparticle surface is affected by the pH of the solution. The Henry equation is then used to compute the zeta potential (ζ):

$$\mu = \frac{2\zeta\epsilon}{3\eta_0} f(\kappa a) \quad (1)$$

Where:

μ = electrophoretic mobility

ζ = zeta potential

ϵ = dielectric permittivity

η_0 = viscosity

$f(\kappa a)$ = function describing the relationship between particle radius a and the Debye length $1/\kappa$,

UV-visible absorption spectroscopy: Absorption spectroscopy is used to determine a solution's optical characteristics. Light is passed through the sample solution, and the amount of light absorbed is measured. When the wavelength is changed and the absorbance is determined at each wavelength. The absorbance of a solution can be used to calculate its concentration using Beer-Lambert's Law^[13]. The optical measurement of a UV-visible spectrophotometer has a different absorbance peak, such as 410nm.

X-ray diffraction (XRD) analysis: X-ray diffraction is a well-established technique for determining crystallographic structure and shape. The intensity **Microscopic techniques** increases or decreases depending on the amount of ingredient. This approach is used to determine the metallic nature of particles, provides information on translational symmetry, size, and shape of the unit cell from peak positions, and information on electron density within the unit cell, specifically where the atoms are placed from peak intensities^[14]. The XRD patterns were calculated using a Rotaflex diffraction meter with Cu K radiation and a resolution of 1.5406 Å. Crystallite size is estimated using the Scherrer equation:

$$CS = K/\cos$$

Where CS is the crystallite size. The constant $[K] = 0.94$ represents the full width at half maximum [FWHM] in a radius $[\beta] = \text{FWHM} \times \pi / 180\lambda$. $\text{Cos} = \text{Bragg angle}$. Several researchers have investigated X-ray diffraction analysis using various nanoparticles to determine the high crystallinity of the generated sample.

Fourier Transform Infrared [FTIR] spectroscopy: It compares infrared intensity to light wavelength and is used to evaluate the nature of related functional groups and structural properties of biological samples including nanoparticles. The computed spectra clearly show the well-known relationship on nanoparticle optical characteristics. The green silver nanoparticle generated using diverse leaf extracts was analyzed using Fourier Transform Infrared [FTIR] Spectroscopy, which revealed distinctive peaks.

Microscopic techniques: These techniques, SEM and TEM, are primarily employed for morphological research of nanoparticles^[15]. Many studies used these methods to demonstrate that the produced nanoparticles were more or less homogeneous in size and shape.

Transmission electron microscopy (TEM): Transmission electron microscopy is a microscopy technique in which an electron beam passes through an ultra-thin object, interacting with it as it does so. An image is composed of The interaction of electrons passed through the specimen produces an image that is magnified and focussed onto an imaging device, such as a fluorescent screen, a layer of photographic film, or a sensor, such as a CCD camera^[15]. TEM is a prominent analytical approach in a variety of scientific domains, including both physical and biological sciences. TEMs have applications in cancer research, virology, materials science, pollution, nanotechnology, and semiconductors.

Scanning electron microscope: The characteristics of Scanning electron microscopic examination is used to determine the size, shape, and morphology of produced nanoparticles. SEM provides high-resolution photographs of a sample's surface when requested. The scanning electron microscope operates on the same concept as an optical microscope, but it detects electrons scattered from the material rather than photons. An electric potential can accelerate electrons, causing their wavelength to be shorter than that of photons^[15]. This means the SEM can magnify images up to 200,000 times. Measures and characterizes particle size, using a conductive or sputter coated sample with a sensitivity of 1 nm.

Applications of Nanoparticles:

General applications of organic nanoparticles

Micelles:

- In treatment of malignant tumours
- Reduces enzymatic degradation and inactivation of drugs
- Improves stability of the drugs
- Reduces critical micellar concentration

Liposomes: Liposomes have also been utilized to supplement dairy products with vitamins, increasing their nutritional value while also aiding in the digestion of dairy product ingredients. Typically, phospholipids are utilized to build the bilayer, and the most common phospholipids are phosphatidyl choline (neutral charge), negatively charged phosphatidic acid, phosphatidyl glycerol, phosphatidyl serine, and phosphatidyl ethanolamine. Archaeosomes are liposomes composed of one or more of the polar ether lipids isolated from Archaeobacteria. In comparison to liposomes (which are made of ester phospholipid), archaeosomes are more thermostable and resistant to oxidation, chemicals, and enzymatic hydrolysis.

Dendrimers: Dendrimers can be employed in a variety of applications, including gene transport, conjugate systems, boron neutron capture therapy, molecular recognition, and medication delivery^[16] It can be used as a contrast agent in magnetic resonance imaging (MRI), but more importantly, as a carrier for drug administration in cancer treatment. Enzymatic degradation and inactivation are inhibited, increasing medication stability. Polymeric micelles are most commonly employed in the treatment of malignant tumors.

General Applications of Inorganic Nanoparticles

Therapeutic applications of metallic nanoparticles

As anti-Infective Agents: Metallic nanoparticles have been described as an HIV prevention therapy. Several investigations have revealed that silver acts directly on the virus as a virucidal agent by binding to the glycoprotein gp120. This binding prevents CD4-dependent virion binding, reducing HIV-1 infectivity^[17] Additionally, metallic nanoparticles have been shown to be efficient antiviral agents against herpes simplex virus, influenza, and respiratory syncytial viruses.

As anti-Angiogenic: Angiogenesis is the formation of new blood vessels that occurs throughout normal development and in some diseases. It is essential in a variety of disorders, including cancer and rheumatoid arthritis. Angiogenesis is carefully regulated in normal settings by pro-angiogenic growth factors (VEGF, PDGF, and TGF-B) and anti-angiogenic factors (platelet factor 4, TSP-1). In sick situations, angiogenic is activated. Some studies have found that these agents cause major side effects such as deadly hemorrhage, thrombosis, and hypertension. It could be overcome if these nanoparticles alone are effective as an anti-angiogenic agent^[17]

In Tumour Therapy: In vitro, bare gold nanoparticles were shown to suppress the action of heparin-binding proteins such as VEGF165 and bFGF, while in vivo, VEGF promoted angiogenesis. Further research has shown that heparin binding proteins are absorbed and denatured on the surface of AuNPs^[18] The researchers also discovered that surface size has a significant influence in the therapeutic efficacy of AuNPs. Mukherjee and colleagues also investigated the effect of gold nanoparticles on VEGF-mediated angiogenesis in a mouse ear model that had been injected with an adenoviral vector expressing VEGF.

In Multiple Myeloma: Researchers developed a nanoparticle-based treatment that effectively treats mice with multiple myeloma. Multiple myeloma is a malignancy of plasma cells.

In Leukaemia: B-chronic Lymphocytic Leukaemia (CLL) is an incurable illness characterized by apoptosis resistance. Co-culture with an anti-VEGF antibody was reported to induce more Gold nanoparticles were selected because to their biocompatibility, large surface area, surface functionalization, and ease of characterization. VEGF antibodies were linked to gold nanoparticles and tested for their ability to kill CLL B cells^[19]

In Rheumatoid Arthritis: Scientists at the University of Wollongong (Australia) have developed a new class of anti-arthritis medication that might be used by gold nanoparticles and has less adverse effects. New research has demonstrated that gold particles can enter macrophages and prevent them from causing inflammation without killing them. According to a study published in the Journal of Inorganic Biochemistry, reducing the size of gold into tiny nanoparticles (50 nm) allowed for more gold to reach immune cells while causing less harm^[19]

In Photo Thermal Therapy: Gold nanoparticles absorb light intensely because they convert photon energy into heat fast and efficiently. Photothermal therapy (PTT) is an invasive treatment that converts photon energy into heat to kill cancer. Gold nanoparticles have proven more useful for treating cancer^[20]

Therapeutic applications of ceramic nanoparticles: Ceramic nanoparticles, such as titania, have also been introduced to polymer matrices to modify the composite surface chemistry, topography, and wettability (surface energetics), with the goal of promoting osteogenic responses on the material surfaces^[21]

Adding functionalized magnesium oxide, zirconia, sulfate, and calcium carbonate to polymethylmethacrylate (PMMA) bone cement improves its cytocompatibility, X-ray radiopacity, and antibacterial potential.

BaSO₄ nanoparticles have been shown to have antibacterial properties against *Staphylococcus aureus* and *Pseudomonas aeruginosa*, making them viable anti-infective additions for bone cement, implant coating, and medical tubing.

As a result, researchers all around the world use these nanoparticles for a variety of applications, including catalysis, photocatalysis, dye photo degradation, and imaging. Nanoceramics are used in medical technology to heal bones^[22]

Ceramic nanoparticles are also utilized in energy supply and storage, communication, transportation systems, construction, and medical technology.

One of the most common applications of nanoceramics has been in biomedicine and medical technology, notably bone healing. Bioactive ceramics have characteristics similar to bone and can work as a nanoscaffold to promote bone regrowth.

Nanoceramics have also been suggested as a potential application in energy supply and storage, communications, transportation systems, aircraft, and construction. They have also found applications in electronics as insulators, semiconductors, conductors, and magnets^[21,22]

Nanoceramics may also be used as armor to replace stiff, robust layers of woven fiber that absorb impact. A strong body armor with ceramic inserts and steel or titanium panels is being developed to provide better protection against blunt damage and high-velocity bullets. The inserts could absorb the projectile's kinetic energy and dissipate it by localized breaking of the ceramic insert.

Therapeutic applications of Polymeric nanoparticles:

They develop novel medication delivery systems for the treatment of neurodegenerative and brain-related illnesses.

Polymeric nanoparticles protect pharmaceuticals by encapsulating, entrapping, conjugating, or adsorbing them on their surfaces.

Polymeric nanoparticles transport cargo molecules across the BBB via endocytosis and transcytosis routes.

The polymeric covering is considered to minimize immunogenicity and limit nanoparticle phagocytosis by the reticulo-endothelial system, leading in higher drug levels in organs like the brain, intestines, and kidneys.

Gene therapy for breast cancer cells has shown anti-proliferative effects.

Therapeutic applications of lipid-based nanoparticles:

These are commonly utilized for cancers such as GIT, lung, breast, pancreatic, and prostate cancer^[23]

It improves phytomedicines' transdermal entry into the skin.

SLNs enhance the therapeutic efficacy of eugenol and effectively prevent *Candida* infection in oral candidiasis.

Improves antibacterial activity.

Therapeutic applications of semiconductor nanoparticles:

Semiconductor nanoparticles have received a lot of attention for their therapeutic applications in emerging technologies like nanoelectronics, nanophotonics, energy conversion, non-linear optics, miniaturized sensors and imaging devices, solar cells, catalysis, detectors, photography, biomedicine, and so on^[24]

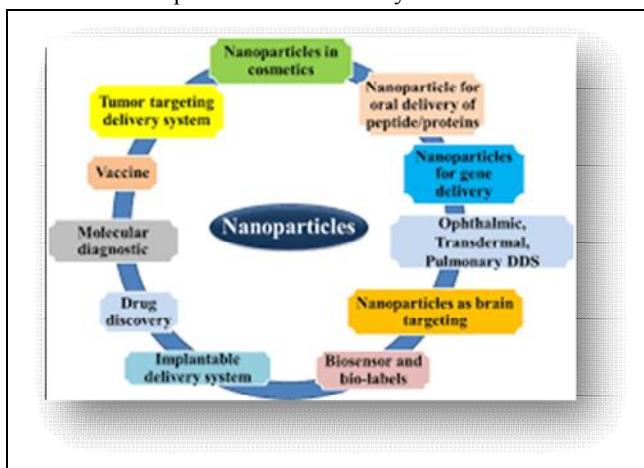
Therapeutic applications of carbon-based nanoparticles:-

Drug and Gene Delivery: Carbon-based nanoparticles, particularly those based on graphene, are frequently used for medication delivery. The π -conjugated structure of six-atom rings of carbon can be thought of as a planar aromatic macromolecule. This novel structure has a high loading capacity for a wide range of fluorescence probes and medicines. The chemical modification of graphene allows for conjugation with targeting ligands, resulting in targeted drug delivery. Both in vitro and in vivo investigations have shown that graphene can deliver anti-cancer medications to the desired site of tumor cells rather than normal or healthy cells.

Bioimaging: Carbon-based materials have long been studied in a variety of imaging applications. Examples include fluorescence imaging (FL), two-photon FL, Raman imaging, magnetic resonance imaging (MRI), tomography (CT), photoacoustic imaging (PAI), computed positron emission tomography/single photon emission computed tomography (PET/SPECT), and multimodal imaging. Recently, a new type of carbon-based nanomaterial, carbon quantum dots, has sparked intense interest in bioimaging applications.

Energy sources: Carbon-based nanomaterials have been extensively studied as catalysts and important components of hydrogen storage systems. Carbon-based materials are ideal as electrodes in capacitors and batteries due to their inherent properties. CNTs have demonstrated a high reversible capacity for usage in lithium-ion batteries and a range of fuel cell components. Because of their great electrical conductivity, CNTs can also be utilized as current collectors and gas diffusion layers. CNT and graphene are ideal electrode catalyst supports in fuel cells due to their high surface area and thermal conductivity.

Nanoparticles for drug administration into the brain: The blood-brain barrier (BBB) is the most significant barrier to the creation of novel treatments for the central nervous system. The BBB is distinguished by relatively impermeable endothelial cells with tight connections, enzymatic activity, and active efflux transport mechanisms. It efficiently blocks the transfer of water-soluble molecules from the bloodstream into the CNS, and it can also lower the concentration of lipid-soluble molecules in the brain through the action of enzymes or efflux pumps^[25] As a result, the BBB only allows selective movement of chemicals that are required for brain activity



II. CONCLUSION

The preceding review demonstrates that nanoparticulate systems have significant potential for converting poorly soluble, poorly absorbed, and labile biologically active substances into promising deliverable medications. The core of this system can contain a wide range of medicines, enzymes, and genes and has a lengthy circulation duration due to the hydrophilic shell, which hinders recognition by the reticular-endothelial system. To optimize this drug delivery system, a better understanding of the many mechanisms of biological interactions, as well as particle engineering, is required.

Further advancements are required to make nanoparticle technology a viable practical use as the next generation of medication delivery systems.

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