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A brief review on Nanoparticals and their importance in Pharmaceutical science.

Pallavi V.Jagtap[1] Samiksha P.Ambadkar[2],Tanuja N.Mundane[3],Prof. Narendra D. Umale[4], Prof. Dnyanesha N. Somnathe[5],Dr. H S.Sawarkar[6]

[1,2,3] Student of B.Pharm II Year
[,3,4,5] Assistant Professor, Department of Pharmaceutical Chemistry
[6]Principal,& HOD Department of Pharmaceutical Chemistry
Dr .Rajendra Gode College Of Pharmacy,Amravati

ABSTRACT:

Generally, nanoparticles can be categorised by their origin, size, shape and properties such as Organic, inorganic or carbon based. Nanoparticles size ranges from 1 nm to 100 nm with one or more dimensions. Nanoparticles can be synthesized using various methods for research and commercial uses which are categorised into physical, chemical and mechanical processes. They have some properties such as strength, sensitivity, high reactivity, stability, surface area, etc. Nanoparticles can have both the desirable and undesirable effects on living cells. Nanoparticles used in variety of fields including medicine, environmental sciences, analytical chemistry, agriculture, etc. This paper has been prepared to provide a review of nanoparticles including their types characteristics, synthesis and applications.

INTRODUCTION:

Nanoparticles are the essential building blocks of nanotechnology. Nanoparticles are the spherical, polymeric particles composed of natural or artificial polymers. Nanoparticles vary in different dimensions, shapes, and size in addition to their material composition. Nano particle are the tiny particles and their size ranges from 1nm to 100 nm which is smaller than the width of human hair and are made up of a variety of materials including metals, metal oxides, organic matter, carbon nanotubes, polymers and dendrimers. The application of nanoparticles in various fields such as molecular biology, physics, organic and inorganic chemistry, medicines and material science has significantly increased in recent times. Nanoparticles have a large surface area to volume ratio because of their small size which results in a number of unique properties such as reactivity, drug carriers, antimicrobial activity, melting point and vapour pressure, quantum effects, solar radiation absorption. The surface can be irregular with variations or uniform. Among nanoparticles, some are crystalline and others are amorphous, existing as single or multi crystal solids which can be either agglomerated or loose. It has been noted that transitioning from bulk materials to nanoscale can alter their physicochemical properties, making them useful in various biomedical applications. Nanoparticles are particularly appealing for many biomedical uses primarily because of their high surface-to-volume ratio, which allows them to interact with molecular or cellular processes and potentially affect their functions. Drug delivery systems are among the most promising applications for human healthcare and represent a rapidly advancing area in medical sciences.
Nanoparticles can be classified in various ways depending on their composition. Based on the type of material they are made of, the classification can be as follows:

1. **Organic Nanoparticles:**

These are nanoparticles composed of organic materials such as polymers, lipids, proteins, or other carbon-based organic compounds. They are typically used in drug delivery, biotechnology, and imaging.

Micelles, dendrimers, ferritin, and liposomes are well-known types of polymers or organic nanoparticles. These nanoparticles are non-toxic and biodegradable, and certain particles, like liposomes and micelles, feature a hollow core, often referred to as nano capsules. They are responsive to thermal and electromagnetic radiation, including heat and light. Organic nanoparticles are extensively utilized in the biomedical sector, particularly for drug delivery systems, due to their effectiveness and ability to be administered precisely to targeted areas of the body, a process known as targeted drug delivery.

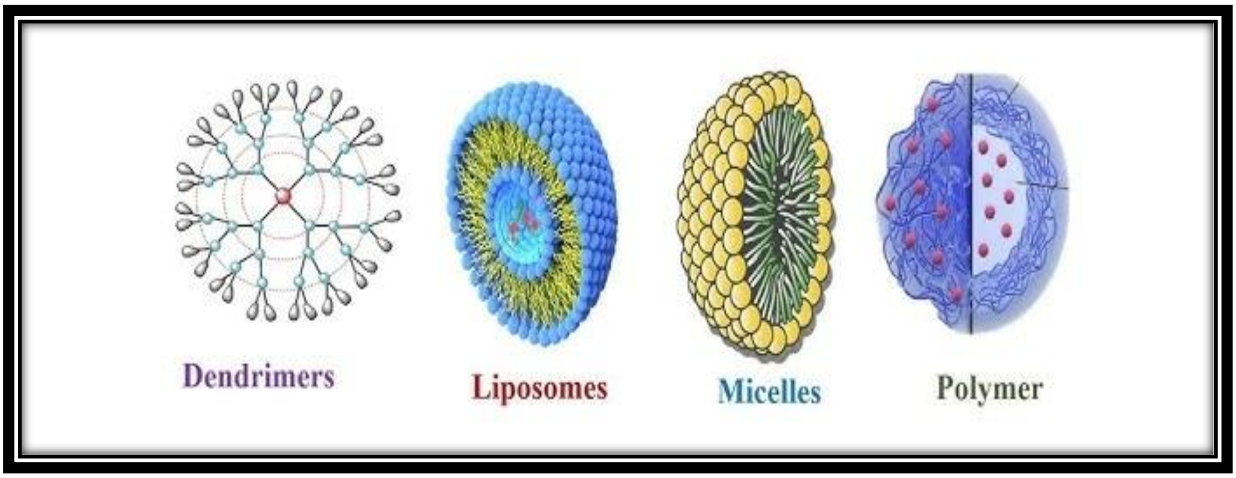

Fig. Organic nanoparticle

2. **Inorganic Nanoparticles:**

These nanoparticles are composed of inorganic materials, often metals or metal oxides. They are widely used in catalysis, electronics, and medical applications.

- **Metal nanoparticles:** Nearly all metals can be converted into their nanoparticle forms. Composed of metals like aluminium (Al), cadmium (Cd), cobalt (Co), iron (Fe), lead (Pb), zinc (Zn), gold (Au), silver (Ag), copper (Cu), and platinum (Pt). They have unique optical and electronic properties. These nanoparticles can be produced by chemical, electrochemical, or photochemical techniques. In chemical method, the metal nanoparticles are acquired by decreasing the metal ion precursors in solution by chemical reducing agents.

- **Metal oxide nanoparticles:** Made from metal oxides like titanium dioxide (TiO_2), zinc oxide (ZnO), or iron oxide (Fe_3O_4), often used in photocatalysis, sensors, and biomedical applications. Metal oxide-based nanoparticles are created to enhance the characteristics of their corresponding metal nanoparticles. For instance, iron (Fe) nanoparticles quickly oxidize to form iron oxide (Fe2O3) when exposed to oxygen at room temperature, which significantly boosts their reactivity in comparison to iron nanoparticles.

- **Quantum dots:** Semiconductor nanoparticles that exhibit unique optical properties, useful in imaging and sensing.

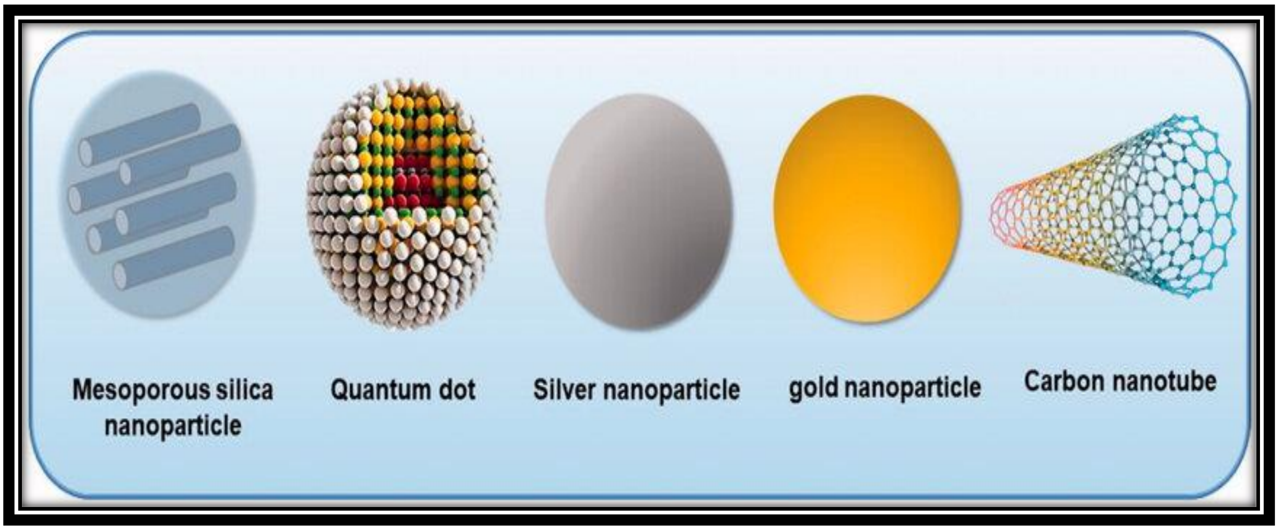

Fig. Organic nanoparticle

3. **Carbon-Based Nanoparticles:**

These are nanoparticles that consist mainly of carbon atoms, and they exhibit unique properties due to the bonding structures of carbon.

- **Carbon nanotubes (CNTs):** Cylindrical nanostructures made of carbon atoms. They are used in electronics, materials science, and energy storage.
- **Fullerenes (buckyballs):** Molecules composed of carbon atoms arranged in a spherical shape.

- **Graphene:** A single layer of carbon atoms arranged in a hexagonal lattice. It has exceptional electrical, mechanical, and thermal properties.
- **Graphene oxide:** A derivative of graphene with oxygen-containing groups, useful in various applications like sensors and energy storage. These are used in various fields including electronic, energy and nanocomposites.
- **Composite Nanoparticles:** These are made by combining two or more different materials, typically to enhance properties such as strength, conductivity, or biocompatibility.
  Example: Core-shell nanoparticles, hybrid nanoparticles.

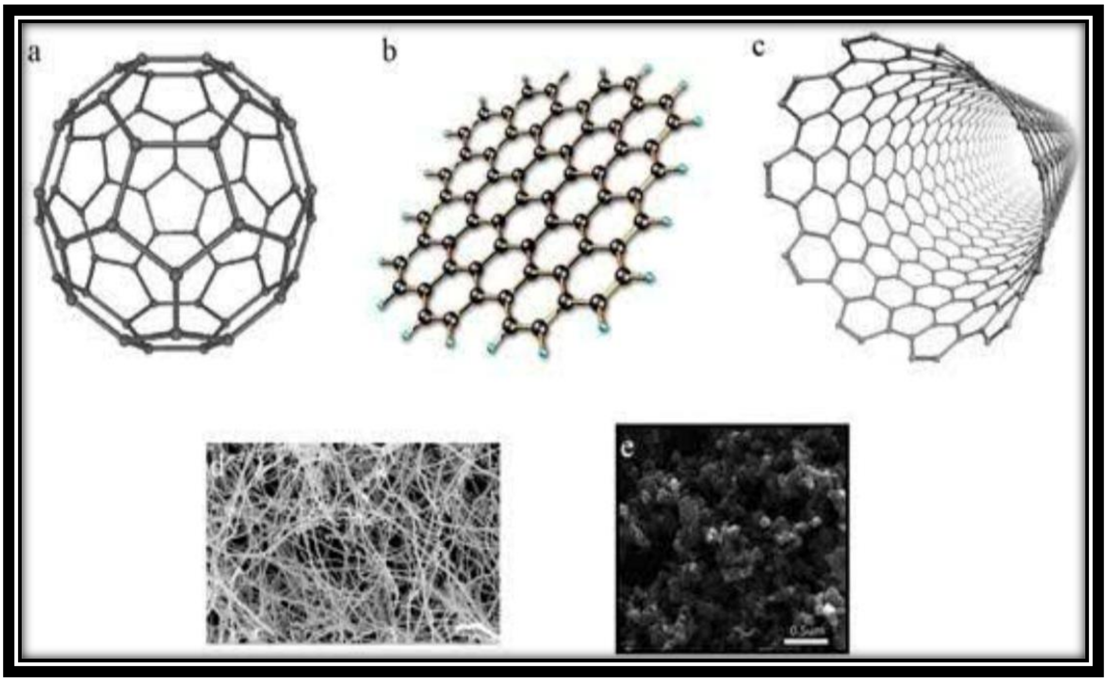

Fig. Carbon-based nanoparticles

Nanoparticles are materials with sizes typically in the range of 1 to 100 nanometers. They exhibit unique properties, such as increased surface area, quantum effects, and reactivity, which can differ significantly from those of bulk materials. Below are some references and important concepts related to nanoparticles:

Key Concepts: Synthesis of nanoparticles : There are various methods that are classified into bottom up and top-down method.

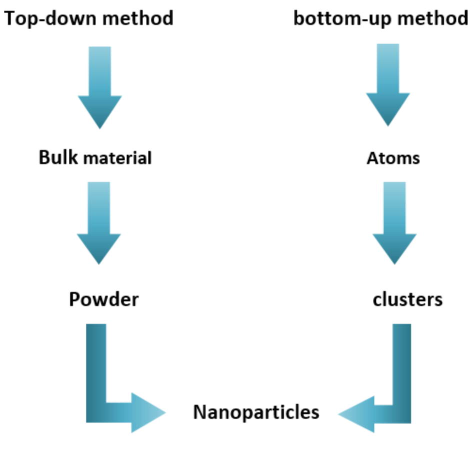

Fig. Synthesis of nanoparticles

Top-down : Methods like grinding or lithography, where larger pieces of material are broken down into nanoparticles.

Certainly! The top-down method for nanoparticle synthesis is a process where larger particles or bulk material are broken down into smaller nanoscale structures. This approach is typically used to create nanoparticles from larger pieces of material, as opposed to the bottom-up method, which builds nanoparticles from smaller units like atoms or molecules.

Mechanical milling, nanolithography, laser ablation, sputtering and thermal decomposition are commonly employed methods for synthesizing nanoparticles.

1. **Mechanical milling :** Among the different top-down techniques, mechanical milling is the most commonly utilized method for producing a variety of nanoparticles. This process involves milling and post-annealing of nanoparticles during their synthesis, where various elements are ground in an inert atmosphere. Key factors affecting mechanical milling include plastic deformation, which influences particle shape, fractures that reduce particle size, and cold welding that results in an increase in particle size.
2. **Nanolithography :** Nanolithography involves the fabrication of structures at the nanometric scale, with at least one dimension measuring between 1 to 100 nm. There are several nanolithographic techniques, including optical, electron-beam, multiphoton, nanoimprint, and scanning probe lithography. Typically, lithography refers to the process of printing a specific shape or structure onto a light-sensitive material, which selectively removes parts of the material to achieve the desired design. One of the primary benefits of nanolithography is its ability to create anything from a single nanoparticle to a cluster with specific shapes and sizes. However, the drawbacks include the need for sophisticated equipment and the associated costs.
3. **Laser ablation :** Laser ablation synthesis in solution is a widely used technique for producing nanoparticles from different solvents. Laser beam irradiation of a metal submerged in a liquid solution creates a plasma plume that generates nanoparticles. This method is a dependable top-down approach that offers an alternative to the traditional chemical reduction of metals for synthesizing metal-based nanoparticles. The advantage of this method, it allows precise control over nanoparticle size. It produces nanoparticles with minimal contamination, leading to high purity. The disadvantage is the laser equipment and maintenance can be expensive. And it can produce fewer nanoparticles compared to other methods, making it less efficient for large- scale production.

Bottom-up method: The bottom-up or constructive approach involves building material from atoms to clusters to nanoparticles. The most commonly used bottom-up methods for nanoparticle production include sol-gel, spinning, chemical vapor deposition (CVD), pyrolysis, and biosynthesis.

1. **Sol-gel :** The sol is a colloidal solution of solids suspended in a liquid phase, while the gel is a solid macromolecule immersed in a solvent. Sol-gel is the preferred bottom-up method due to its simplicity, as it allows for the synthesis of a wide range of nanoparticles. This wet-chemical process involves a chemical solution that acts as a precursor for an integrated system of discrete particles. Metal oxides and chlorides are typically used as precursors in the sol-gel process.
2. **Spinning :** The synthesis of nanoparticles through spinning is conducted using a spinning disc reactor (SDR). This reactor features a rotating disc within a chamber where physical parameters, such as temperature, can be controlled. Typically, the reactor is filled with nitrogen or other inert gases to eliminate oxygen and prevent unwanted chemical reactions. The disc rotates at various speeds while the liquid, which includes the precursor and water, is pumped in. The spinning action causes the atoms or molecules to fuse together, resulting in precipitation, which is then collected and dried. Various operating parameters, such as liquid flow rate, disc rotation speed, liquid-to-precursor ratio, feed location, and disc surface characteristics, influence the properties of the nanoparticles synthesized from the spinning disc reactor (SDR).

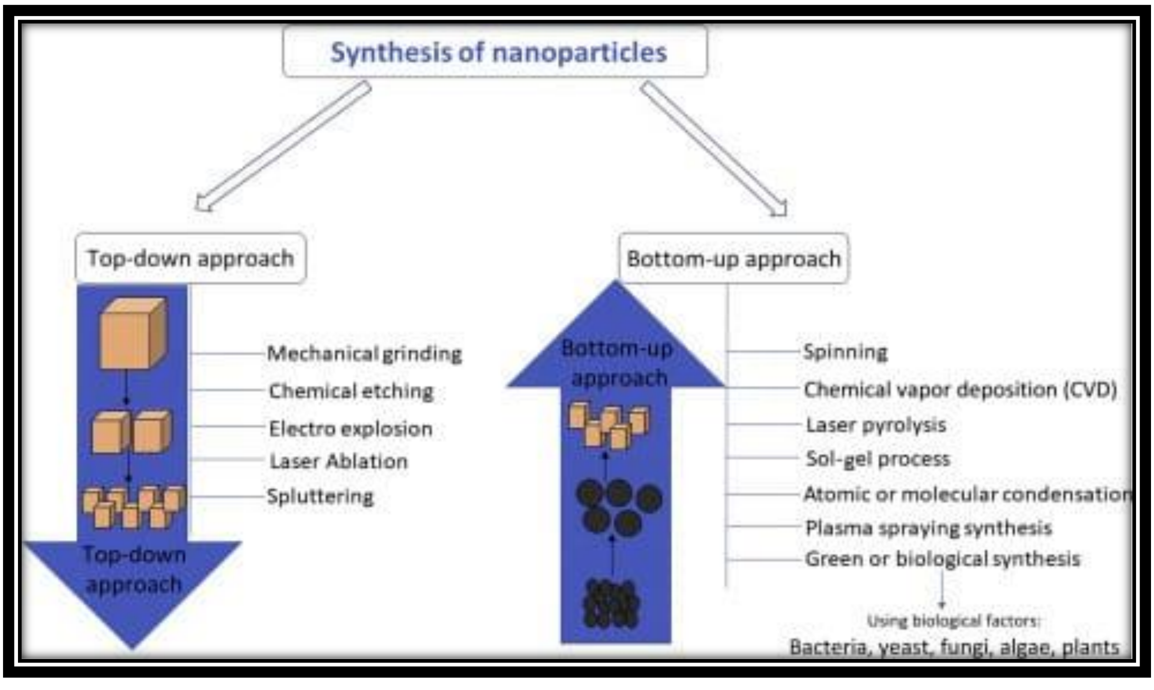

Fig. Synthesis of nanoparticles

Characterization of Nanoparticles:

- **Zeta potential:**

  The zeta potential of a nanoparticle is commonly utilized to characterize its surface charge properties. It indicates the electrical potential of the particles and is affected by both the composition of the particles and the medium in which they are dispersed. Nanoparticles with a zeta potential between -10 and +10 mV are regarded as approximately neutral, while those with a zeta potential greater than +30 mV or less than -30 mV are considered strongly cationic and anionic, respectively.

  It is essential to note that the magnitude of the charge on the nanoparticle's surface is influenced by the pH of the solution. The Henry equation is then employed to calculate the zeta potential, z:

$$U_E = \frac{2\varepsilon\zeta}{3\eta} f(\kappa a)$$

Where U_E: electrophoretic mobility
ε: dielectric constant
ζ: zeta potential
η: viscosity
$f(\kappa a)$: Henry's function

- **UV-visible absorption spectroscopy:**

Absorbance spectroscopy is employed to assess the optical properties of a solution. Light is passed through the sample solution, and the amount of light absorbed is measured. As the wavelength is varied, the absorbance is recorded at each wavelength. This absorbance can be utilized to determine the concentration of a solution using Beer-Lambert law. The optical measurements taken with a UV-visible spectrophotometer reveal different absorbance peaks, such as at 210 nm.

- **X-ray diffraction(XRD) analysis:**

X-ray diffraction (XRD) analysis is a powerful technique used for characterizing the crystallographic structure of nanoparticles. When X-rays are directed at a sample, they are diffracted by the crystal lattice, producing a diffraction pattern. By analyzing this pattern, information about the particle size, crystal structure, phase composition, and lattice parameters of nanoparticles can be determined. XRD is particularly useful for confirming the crystallinity of nanoparticles, identifying different phases (e.g., amorphous vs crystalline), and estimating particle sizes using the Scherrer equation.

Microscopic techniques: SEM AND TEM techniques are mainly used for morphological studies of nanoparticles.

- **Transmission electron microscopy:**

Transmission electron microscopy is a technique that involves transmitting a beam of electrons through an ultra-thin specimen, where the electrons interact with the specimen during their passage. An image is generated from the interactions of the transmitted electrons; this image is then magnified and focused onto an imaging device, which could be a fluorescent screen, a layer of photographic film, or a sensor like a CCD camera. TEMs are utilized in various fields, including cancer research, virology, materials science, pollution studies, nanotechnology, and semiconductors.

- **Scanning electron microscopy:**

The characterization of scanning electron microscopy analysis is used to determine the size, shape, and morphology of the formed nanoparticles. Scanning electron microscopy operates on the same principle as an optical microscope, but it measures the electrons scattered from the sample instead of photons. Since electrons can be accelerated by an electric potential, their wavelength can be made shorter than that of photons. SEM provides high-resolution images of the sample's surface as required.

Properties of nanoparticles:

1. Size and Shape: Nanoparticles typically range from 1 to 100 nm in size. Their shape (spherical, cylindrical, rod-shaped, etc.) can influence their physical, chemical, and biological properties.

2. Surface Area: Nanoparticles have a high surface-to-volume ratio, which increases their reactivity and interaction with surrounding environments compared to bulk materials.

3. Surface Charge: The surface charge of nanoparticles affects their stability, dispersion in solutions, and interactions with biological systems. It can be manipulated for targeted drug delivery or other applications.

4. Optical Properties: At the nanoscale, materials often exhibit unique optical properties, such as quantum dots showing size-dependent fluorescence or plasmonic nanoparticles exhibiting enhanced light absorption and scattering.

5. Magnetic Properties: Magnetic nanoparticles, like those made of iron oxide, can exhibit superparamagnetism, which is useful in applications such as targeted drug delivery or MRI imaging.

6. Mechanical Properties: Nanoparticles can have enhanced mechanical strength, flexibility, or toughness due to their small size and high surface energy.

7. Thermal and Electrical Conductivity: Nanoparticles may show improved thermal conductivity and electrical properties, which are important for electronics and energy storage applications.

8. Chemical Reactivity: Due to their large surface area and unique electronic properties, nanoparticles can exhibit increased chemical reactivity compared to bulk materials.

9. Biocompatibility and Toxicity: Biocompatibility is a crucial property for nanoparticles used in biomedical applications. The toxicity largely depends on the material, size, shape, and surface chemistry of the nanoparticles.

These properties are essential in determining the applications of nanoparticles in fields such as medicine, electronics, energy, and environmental protection.

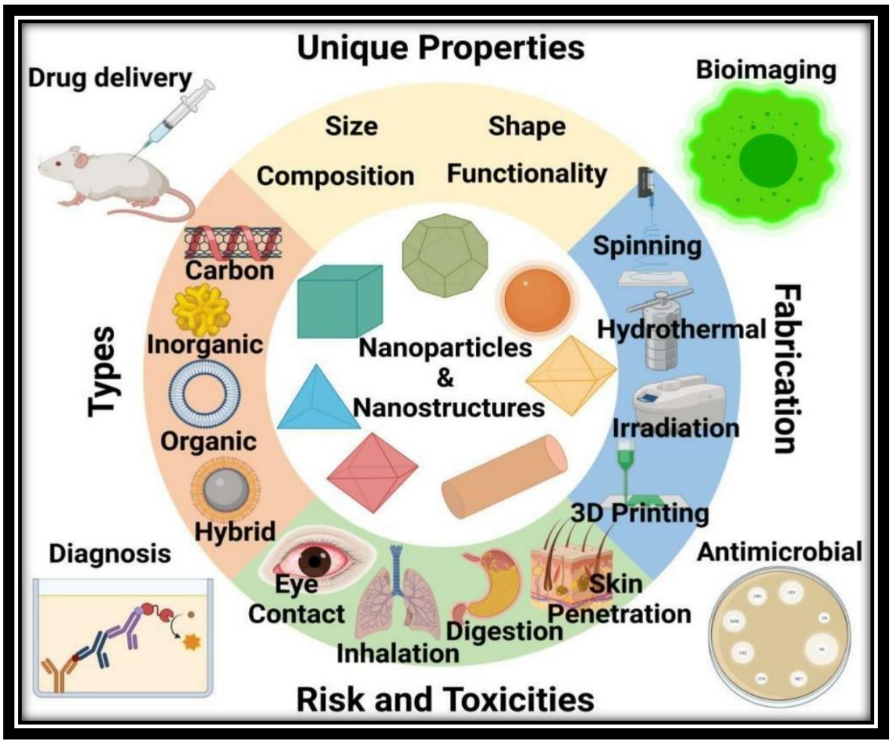

Fig. Properties of nanoparticles

Applications:

General application of organic nanoparticles:

1. Micelles

Organic nanoparticles, specifically micelles, are widely used in various applications due to their unique structure and properties. Micelles are colloidal structures formed by the self-assembly of amphiphilic molecules (molecules that have both hydrophilic and hydrophobic regions) in an aqueous environment. Here are some key general applications of organic nanoparticles in the form of micelles:

- **Drug Delivery**

Targeted Drug Delivery: Micelles are often used as drug carriers in pharmaceutical formulations due to their ability to encapsulate both hydrophobic and hydrophilic drugs. This allows for the targeted and controlled release of drugs, enhancing therapeutic effectiveness and minimizing side effects.
Cancer Treatment: Micelles can be engineered to deliver chemotherapeutic agents specifically to cancer cells by exploiting their unique ability to accumulate in tumors (due to the enhanced permeability and retention effect).

Gene Delivery: Micelles can also be used to deliver nucleic acids (DNA, RNA) in gene therapy, protecting the nucleic acids from degradation while aiding in their cellular uptake.

- **Cosmetics and Personal Care**

Solubilizing Active Ingredients: In the cosmetics industry, micelles help in solubilizing hydrophobic ingredients, allowing them to be incorporated into water-based products. This is particularly useful in products like shampoos, body washes, and facial cleansers.
Skin Penetration Enhancement: Micelles can enhance the penetration of active ingredients into the skin, improving the effectiveness of skincare products.

- **Environmental Applications**

Pollutant Removal: Micelles are used in environmental remediation, particularly in the removal of hydrophobic pollutants such as oils and heavy metals from water. Micelles can encapsulate pollutants and facilitate their removal.
Water Purification: By utilizing micelles' ability to trap organic contaminants, they can be used in water filtration systems to clean polluted water.

- **Food Industry**

Encapsulation of Nutrients: Micelles can encapsulate nutrients, such as vitamins and antioxidants, improving their stability, bioavailability, and controlled release in the body.
Flavor and Aroma Enhancement: Micelles are sometimes used to encapsulate in flavors and aromas, allowing for better preservation and slow release during food processing.

- **Diagnostics and Imaging**

Imaging Agents: Micelles can serve as carriers for imaging agents (e.g., MRI contrast agents, fluorescent dyes) in medical diagnostics, helping to enhance the imaging of tissues and organs.
Biosensing: Micelles can be used in biosensors for detecting various biological markers or pathogens due to their tunable properties.

- **Nanomedicine Research**

Study of Drug Mechanisms: In nanomedicine research, micelles are utilized to study drug interactions, mechanisms of action, and to optimize drug formulations for better therapeutic outcomes.

Overall, micelles as organic nanoparticles have diverse applications across the pharmaceutical, environmental, cosmetic, and food industries, leveraging their unique self-assembling capabilities and versatility.

2. **Liposomes:**

Liposomes have also been utilized to enhance dairy products by adding vitamins, thereby increasing their nutritional value and assisting in the digestion of components naturally present in dairy products. Archaeosomes are a type of liposome composed of one or more polar ether lipids derived from archaebacteria. Additionally, they exhibit greater resistance to low pH and bile salts that are typically found in the gastrointestinal (GI) tract.

3. **Dendrimers:**

Dendrimers can also be applied in various fields such as gene delivery, conjugation systems, boron neutron capture therapy, molecular recognition, and drug delivery. Dendrimers can capture and remove contaminants from water due to their high surface area. Dendrimers can be functionalized with imaging agents for enhanced detection in medical imaging (e.g., MRI, PET).

General applications of inorganic nanoparticles:

Therapeutic application of metallic nanoparticle

1. **In anti -Infective agents:**

Metallic nanoparticles have been characterized as a therapeutic option for preventing HIV. Additionally, it has been reported that these metallic nanoparticles are effective antiviral agents against herpes simplex virus, influenza, and respiratory syncytial viruses.

2. **In anti-angiogenic:**

Angiogenesis is the process of forming new blood vessels and occurs during normal development as well as in certain disease states. It plays a significant role in a number of diseases, such as cancer and rheumatoid arthritis. Under diseased conditions, angiogenesis is activated. This can potentially be countered if these nanoparticles can prove to be effective as anti-angiogenic agents on their own.

3. **Therapeutic application of ceramic nanoparticles:**

Ceramic nanoparticles, like silica or hydroxyapatite, are used in therapeutic applications due to their biocompatibility and stability. They are employed in drug delivery systems for controlled and targeted release, improving the effectiveness of treatments while minimizing side effects. In cancer therapy, they enhance drug delivery and can act as radiosensitizers or facilitate hyperthermia. Additionally, in bone tissue engineering, ceramic nanoparticles such as hydroxyapatite promote bone growth and repair. Their versatility makes them promising tools in diverse medical therapies.

4. **Therapeutic application of polymeric nanoparticles:**

- They develop innovative drug delivery systems for the treatment of brain-related diseases.
- Polymeric nanoparticles offer protection to the drug. These nanoparticles deliver cargo-loaded molecules across the blood-brain barrier by utilizing endocytosis and transcytosis pathways.
- They have also been applied in gene therapy for breast cancer cells, leading to anti-proliferative effects.

General application of carbon-based nanoparticles:

Carbon-based nanoparticles, such as carbon nanotubes (CNTs) and graphene, are used in various therapeutic applications due to their biocompatibility and functionalization potential. They are employed in drug delivery for controlled, targeted release, and in cancer therapy for efficient drug delivery and photothermal treatment. Additionally, they possess antibacterial and antiviral properties, aiding in infection control. In tissue engineering, they promote stem cell growth and tissue regeneration. These versatile nanoparticles hold great promise in diverse medical fields.

Materials like graphene oxide can absorb light and convert it into heat, which, when directed at cancer cells, can induce cell death through localized heating. Carbon nanoparticles can deliver chemotherapeutic drugs directly to tumor sites, increasing treatment effectiveness while reducing systemic toxicity.

Conclusion:

The previous discussion indicates that nanoparticulate systems hold significant potential, as they can transform poorly soluble, poorly absorbed, and unstable biologically active substances into effective deliverable drugs. The core of these systems can encapsulate a range of drugs, enzymes, and genes, and they are characterized by an extended circulation time thanks to the hydrophilic shell, which helps evade recognition by the reticuler endothelial system.

To enhance the effectiveness of this drug delivery system, a deeper understanding of the various mechanisms of biological interactions and advancements in particle engineering are essential. Moreover, further developments are necessary to convert the concept of nanoparticle technology into a feasible and practical application, paving the way for the next generation of drug delivery systems. This could lead to improved patient outcomes and more targeted therapies in the future.

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