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A REVIEW ON NANOPARTICLES: INTRODUCTION, CLASSIFICATION, SYNTHESIS AND APPLICATIONS

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ABSTRACT

The pharmacokinetic and pharmacodynamic characteristics of several kinds of pharmacological molecules have recently been changed and improved by the physical usage of particulate systems, such as nanoparticles. In vivo, they have been utilized to protect the drug entity in the systemic circulation, limit the drug's access to certain areas, and transport the drug to the site of action at a steady and regulated rate. It is evident that drug delivery research is shifting from the micro to the nanoscale. Thus, nanotechnology is becoming a medical discipline that is anticipated to yield substantial therapeutic advantages. One of the hardest jobs for pharmaceutical formulation researchers is creating efficient nanodelivery systems that can deliver a medication precisely and securely to the intended site of action. To sustain promising scientific results and therapeutic advancements, they are working to restructure and add additional indications to the current blockbuster medications. The primary nanodelivery technologies include

liposomes, lipid or polymeric nanoparticles, and nanoemulsions. Particulate vesicle systems have been used as drug carriers for both small and large molecules in a significant amount of research conducted in recent years on the basis of novel drug delivery methods. Drugs' medicinal efficacy and adverse effects have been enhanced using nanoparticles. In general, a variety of processes have been used to create nanoparticles, including ionic gelation or co-acervation of hydrophilic polymers, polymerization of monomers, and dispersion of preformed polymers.

KEYWORDS: Nanoparticles, Nanotechnology, Nano drug delivery, Targeted drug delivery.

1. INTRODUCTION^[1-5]

The minuscule components that comprise the universe's entirety are known as particles. In particle physics, a particle is considered elementary if it cannot be divided into smaller components. A variety of different particle types with different sizes and properties can be found. All scientific and engineering disciplines where phenomena at the nanoscale level are utilized in the creation, characterization, development, and application of materials, structures, and equipment are collectively referred to as nanotechnology. Important molecules found in the human body and food components are among the many examples of nanometersized structures (Referred to as nanoscale) that appear in the natural world. Although many advancements have included nonmaterial for a number of years, it was only in the last 25 years that it became feasible to intentionally and consciously change molecules and structures within this range of sizes. The regulation at the nanometer scale is the sole thing that distinguishes nanotechnology from other technological domains. Specifically, the various facets of nanotechnology do possess the capacity to significantly impact civilization. It goes without saying that both individuals and companies would find great benefits from the application of nanotechnology. Some of these applications call for contemporary materials with radically different properties depending on nanoscale activity, where novel processes are associated with quantum fluctuations not observed at larger scales and extremely high surface-area-to-volume proportions observed in these measurements. These include components of the kind of much thinner membranes used in electronics and catalysis, twodimensional nanotubes and nanowires for optical and magnetic structures, and nanoparticles used in coatings, medications, and cosmetics.

A large class of raw materials known as nanoparticles is made up of particles having at least one diameter smaller than 10 nm. Depending on the finished design, these materials or objects can be zero, one, two, or three dimensions. Since researchers have found that scale can alter the physio-chemical properties of the material's surface, such as its optical qualities, the importance of such materials has been acknowledged. Nanomaterials made of gold (Au), silver (Ag), platinum (Pt), and palladium (Pd) come in a variety of colors, including wine red, yellowish-gray, black, and dark black. These nanoparticles represented various sizes and shapes, colors, and other features that may be applied to bioimaging devices. In their structure, nanoparticles are complexes made up of three outer lines: the shield sheet, which is

made up of surface layers that can be coated with various minute substances, trace metals, polymers, and surfactants; the inner part, which has an inner component of the nano-particle and usually corresponds to the nanosphere itself; and the outer lines, which are made up of surface layers that have different chemistry from the nano-particle's center (core).

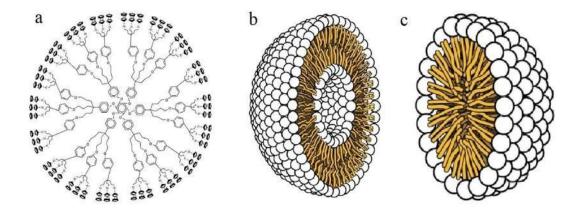
Nanotechnology and nanoscience, which research and apply incredibly small materials, are new and unique methods for diagnosing and treating cancer. Using nanoparticles for local medication delivery has garnered a lot of interest in chemoprevention and/or chemotherapy in recent years. The use of nanotechnology in cancer treatment has advanced thanks to new techniques that address and lessen the drawbacks of current treatments and/or cancer diagnosis. It can identify a single diseased cell, and it can also administer medications directly to the cancerous cells identified during the in-vivo investigation. Nanotechnology advancements have also improved the speed and sensitivity of identifying biochemical indicators of cancer. Following a final diagnosis of oral cancer, an integrative approach which includes chemotherapy, radiation, and surgery is frequently employed to treat OSCC. On the other hand, conservative chemotherapy medications might have a number of harmful side effects and be ineffective. Numerous nanoparticles have been employed as technological catalysts for advancement in in situ drug delivery in order to overcome these challenges. Particles of sizes ranging from 1 to 500 nm are known as nanoparticulate drug delivery systems, and they can increase treatment effectiveness while lowering adverse effects by delivering therapeutic chemicals to specific target areas in the body. In addition to their composition, nanoparticles differ in size, shape, and dimensions. There are several types of nanoparticles: one-dimensional, like graphene, two-dimensional, like carbon nanotubes, three-dimensional, like gold nanoparticles, and zero-dimensional, like nanodots, with length, width, and height fixed at a single point. In the current review, we give a summary of the various facets of nanoparticle formulation, classification, the influence of its characteristics, its usage in the dispersion of API molecules, and its therapeutic benefits, with a particular emphasis on pharmaceutical applications.

2. Classification of nanoparticles^[6-10]

1. Organic nanoparticles

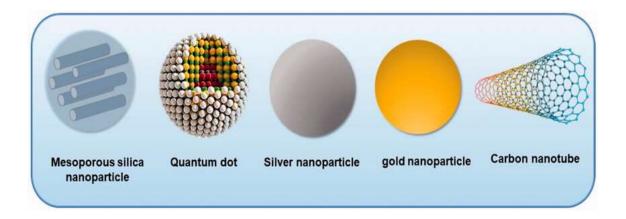
These nanoparticles, known as organic nanoparticles (ONPs), are made from organic molecules that are 100 nm or less in size. Liposomal, ferritin, dendrimers, micelles, and other well-known organic nanoparticles or polymers are examples of this class.

In addition to being biodegradable and non-toxic, micelles and liposomes are nanoparticles with a hollow interior called a nanocapsule that are sensitive to heat and electromagnetic radiation (heat and light). They are better choices for the delivery of medications due to their unique characteristics. Although size, content, surface shape, and other factors are important, the drug's area of application and efficiency are affected by its carrying capacity, stability, and delivery systems, whether it is an adsorbed drug system or an entrapped drug. In the biomedical field, organic nanoparticles are widely used, for instance in drug delivery systems, due to their effectiveness and the ability to be injected into particular bodily parts (a technique known as targeted drug delivery).



2. Inorganic nanoparticles

Carbon-atom-free nanoparticles are referred to as inorganic nanoparticles. Metal or metal oxide-based nanoparticles are commonly referred to as inorganic nanoparticles.



3. Metal-Based Nanoparticles

Metal-based nanoparticles can be created constructively or destructively to reach nanometric sizes. Just about all metals can be synthesized as nanoparticles. The production of

nanoparticles commonly uses metals including aluminum (Al), cadmium (Cd), cobalt (Co), copper (Cu), gold (Au), iron (Fe), lead (Pb), silver (Ag), and zinc (Zn). Excellent UV-visible sensitivity, electrical, catalytic, thermal, and antibacterial qualities are all attributed to metal nanoparticles' quantum effects and massive surface-to-volume ratio. There are a lot more atoms on the surface because of the smaller particle size. Nanoparticle size and shape influence the surface area to volume ratio, which in turn influences characteristics like conductivity and UV-visible sensitivity. Among the numerous attributes that are impacted by variations in surface area are the electronic energy levels, electron affinities, electronic transitions, magnetic properties, phase transition temperature, melting point, and affinities to polymeric, biological, and organic substances. A combination of the quantum size mechanisms and the Coulomb charging effects gives nanoparticles their charge. Combining the quantum size with the Coulomb charge effect yields a variety of fascinating features that are not present in the same bulk material. Sharp-edged and spherically shaped particles are especially vulnerable to quantum events. Catalysis, sensing, and imaging all make use of nanoparticles because of their size-dependent properties.



• Silver nanoparticles

Silver nanoparticles, or AgNPs, range in size from 1 to 100 nanometers. Because of their small size, high surface area-to-volume ratio, and capacity to absorb and scatter visible and near-infrared light, they possess special physical and chemical properties. Compared to their bulk counterparts, silver nanoparticles may have extra antibacterial qualities not exhibited by

ionic silver due to their comparatively tiny size and high surface-to-volume ratios, which result in chemical and physical changes in their properties.

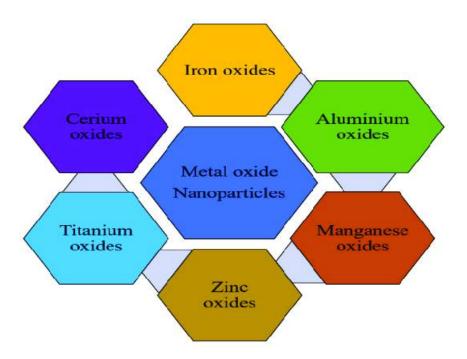
Gold nanoparticles

Gold nanoparticles (AuNPs) are gold particles that are nanometers in size. They can absorb and scatter light in the visible and near-infrared spectrums and have special physical and chemical characteristics.

Anisotropic AuNPs were discovered by scientists at the turn of the 20th century. In his work published in 1909, Zsigmond stated that gold particles "are not always spherical when their size is 40 nm or lower." He also discovered different-colored anisotropic gold particles. In 1925, Zsigmondy was awarded the Nobel Prize for "his demonstration of the heterogeneous character of colloidal solutions and the methods he utilized" as well as for creating the ultramicroscope, which enabled him to observe the shapes of Au particles. He saw that gold often crystallized like a leaf with six sides. Due to their optical, electrical, and molecular recognition properties, AuNPs are the subject of much research. They have many potential or promised applications in a variety of sectors, such as materials science, electronics, electron microscopy, and nanotechnology.

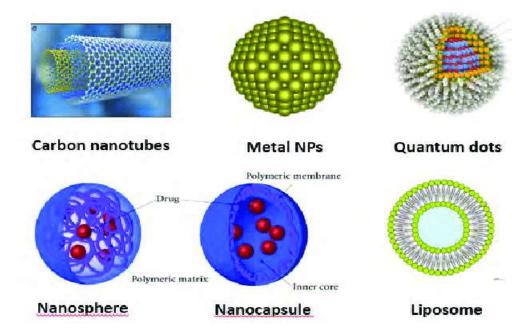
4. Metal Oxide-Based Nanoparticles

Metal oxides have garnered increasing attention from researchers in recent decades. Ionic compounds called metal oxides are created when positive metallic ions and negative oxygen ions interact. Because of the electrostatic contacts between the positive metal ions and the negative oxygen ions, ionic connections are robust and long-lasting. For example, when iron (Fe) nanoparticles are exposed to oxygen at ambient temperature, they easily transform into iron oxide (Fe2O3) nanoparticles, which significantly increases their reactivity compared to iron nanoparticles. These oxide-based nanoparticles are created to alter the characteristics of their metal-based equivalents. To benefit from their increased efficiency and reactivity, metal oxide nanoparticles are frequently created. Aluminum oxide (Al2O3), zinc oxide (ZnO), titanium oxide (TiO2), and silicon dioxide (SiO2) are some of the most often synthesized oxides. In contrast to their metal counterparts, these nanoparticles exhibit exceptional properties.



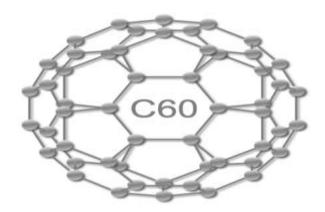
5. Carbon-Based nanoparticles

The evolution of human civilization on Earth has been significantly influenced by carbon. It produces bonds with unparalleled strength when mixed with other materials. Over the past few decades, a diverse range of carbon-based nanomaterials have been developed through various synthesis techniques. They have been used in a wide range of industries due to their unique shape and diverse characteristics. Carbon-based nanomaterials offer a number of possible applications, such as energy production and storage, wastewater and water treatment, Carbon may take on a variety of allotropic and biological usage. Buckminsterfullerene, diamond, and graphite are instances of allotropes. The most thermodynamically stable of them all is graphite. Batteries, electrodes, solar panels, and other electronic devices may all make use of it due to its high conductivity. Stacks of graphene sheets make up graphite. A new kind of carbon called graphene is made up of a single layer of atoms organized in a honeycomb pattern on a two-dimensional sheet. Because of its great strength, it is a very helpful building component for the production of various types of carbon nanoparticles. Carbon nanotubes (CNTs) are yet another new type of carbon. Despite being synthesized in various ways, graphene, fullerene, and carbon nanotubes all have similar chemical and physical characteristics. Due to their age, fullerenes are the most unlikely to form the basis for derivatives and composites. However, graphene and carbon nanotubes (CNTs) hold great promise as viable alternatives in a variety of disciplines and have a great deal of room for further research. Adsorption, separation, catalysis, and many other processes have demonstrated the exceptional adsorbent properties of activated carbon.



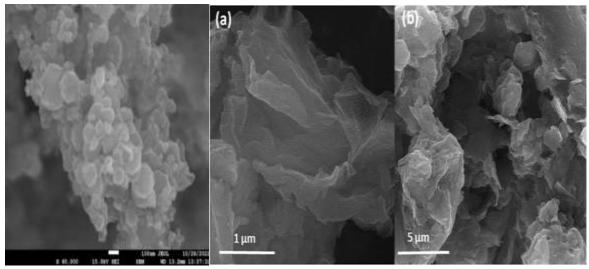
6. Fullerenes

One of the most prominent and often used fullerenes is buckminster fullerene, or C60. It resembles a soccer ball due to the cage-like configuration of its 60 carbon atoms, each of which has three bonds. There are twenty hexagons and twelve pentagons in the C60 structure. For this structure, two well-established characteristics are resonance stabilization and icosahedral symmetry. The field of material science uses it because of its unique collection of physicochemical properties. Recently, C60-based nanostructures—such as nanorods, nanotubes, and nanosheets—have become widely used in a variety of nanotechnology and nanoscience domains. Because of its versatility, C60 can be employed in a variety of ways to accelerate the reactions of a broad spectrum of chemicals. It can be included into systems to enhance particular behaviors due to its special characteristics. Through covalent, endohedral, and supramolecular transformations, C60 can be molecularly altered and polymeric material synthesized for use in environmental applications.



7. Graphene and Graphene Oxide(GO)

A very versatile type of the carbon allotrope are carbon nanotubes (CNTs). The structure is long, cylindrical, and tubular, and it is made from rolled-up graphene sheets. Many concentrically interlocked nanotubes combine to form multi-walled carbon nanotubes (MWCNTs), whereas a single layer of carbon atoms makes up single-walled carbon nanotubes (SWCNTs). While MWCNTs can have a diameter of over 100 nm, SWCNTs can only have a maximum of 3 nm. MWCNTs have a higher mechanical strength than SWCNTs due to the many carbon atom layers they include. It has been discovered that CNTs have a substantially higher Young's modulus and tensile strength than typical metals like steel and iron. SWCNTs' exceptional twisting capabilities make them ideal for use as sensors. Research on composites uses MWCNTs because of their exceptional endurance. There have been reports of CNTs being used in mechanical, electrical, chemical, and biological applications. CNTs are essential for vacuum microelectronics, electron field emission systems, and electrochemical and energy storage applications. In the electrical industry, they are advantageous due to their consistent shape and precise accuracy. CNTs can store hydrogen as well. Their remarkable capacity for absorption makes them perfect for this purpose. To reduce the overall weight of mechanical composites, carbon nanotubes (CNTs) are commonly used as reinforcing and filler materials.



Graphene Graphene Oxide (GO)

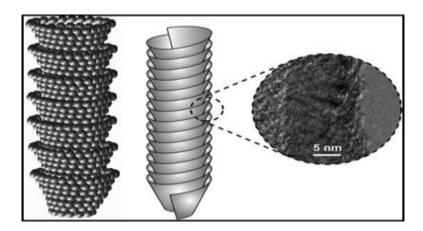
8. Carbon Nanofiber (CNFs)

Carbon nanofibers (CNFs) are hollow-cored nanofibers composed of one or two graphite layers arranged parallel to or at an angle to the fiber axis in degrees. The neighboring layers are layered in a number of ways, including bamboo-like, parallel, and cup-stacked. In the

instance of CNFs, spherical nanostructures are created by stacking graphene layers in the shape of cones, cups, or plates. Cylindrical carbon nanotubes, or CNTs, are produced when graphene-containing CNFs are rolled up. CNFs have gotten less attention because of their smaller diameters, lower densities, and superior mechanical properties (because of fewer microstructural flaws). CNFs, on the other hand, are perfect substitutes for CNTs because to their low price and broad availability. Since carbon fibers are used in many different industries, understanding how they originate and the factors that control their shape is crucial. However, due to their low cost of synthesis, CNFs can be studied and tested in order to apply the knowledge gained to more expensive CNTs.

Compared to CNFs, MWNTs are two to three times more expensive to produce, whereas SWNTs are significantly more expensive. Research into novel fabrication techniques ought to result in further drops in the already low cost of fabrication. CNFs' special qualities have led to their increased utilization. Researchers currently frequently use CNFs to create composite materials that perform significantly better than the most advanced materials available.

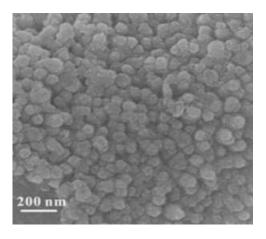
A lot of interest has been shown in CNFs because of their special electrical, thermal, and mechanical properties. The reason these CNFs are utilized in electrical applications is because they need less loading to achieve the necessary electrical conductivities. The post-treatment techniques and the synthesis method (catalysts, feedstock, etc.) both affect the structure of CNFs and their properties.



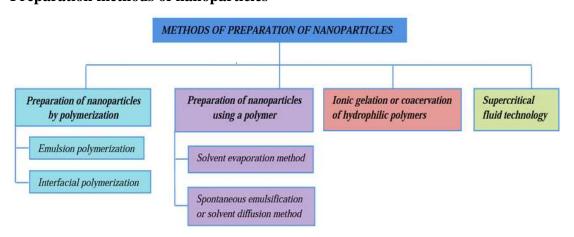
9. Activated carbon or charcoal

Charcoal, also referred to as activated carbon, is a kind of carbon that has undergone processing to produce incredibly tiny pores and a very small volume. Its synthesis aims to offer a large surface area for chemical reactions or adsorption. As a result, activated carbon is

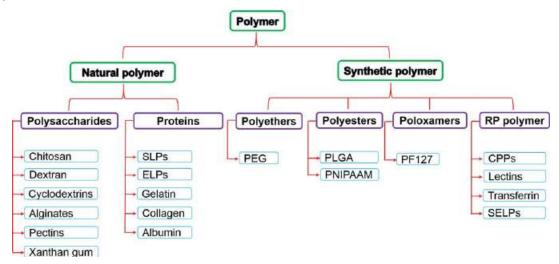
frequently used as an adsorbent to eliminate pollutants from water purification processes. It is frequently employed in the purification of colors and gasses as well as the extraction of minerals from water. The problem is that the efficiency of the removal is low. Nanoporous activated carbon is a functional kind of activated carbon that is used to obtain the required efficiency. The majority of nanoporous formations are composed of carbon. Hydrogen and oxygen are also present, albeit in smaller amounts. Depending on the precursor, manufacturing technique, and post-synthesis processing, there may also be inorganic materials, nitrogen, sulfur, and phosphorus. Oxygen groups are the most noticeable when looking at the nanoporous surface. Because of its excellent pore form (Micropores or micro + mesopores) and heteroatoms (Such as oxygen, nitrogen, and sulfur), nanoporous activated carbon finds widespread use.



3. Preparation methods of nanoparticles $^{[11-15]}$

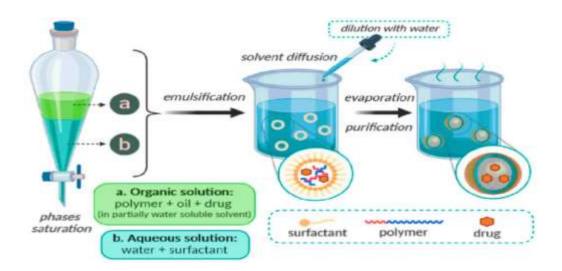


Polymers



1. Solvent evaporation method

The first technique created to create polymeric NPs from a premade polymer was solvent evaporation. In order to produce nanospheres, this method first requires the fabrication of an oil-in-water (o/w) emulsion. Figure 2 depicts the entire procedure. First, the active ingredient is added by dissolving or dispersion, and an organic phase is made up of a polar organic solvent in which the polymer is dissolved. Chloroform and dichloromethane have been employed extensively, but more frequently in the past. Because of their toxicity, ethyl acetate has taken their place. It has a better toxicological profile and is therefore more appropriate for use in biomedical applications. It has also been common practice to prepare an aqueous phase that contains a surfactant, such as polyvinyl acetate (PVA).

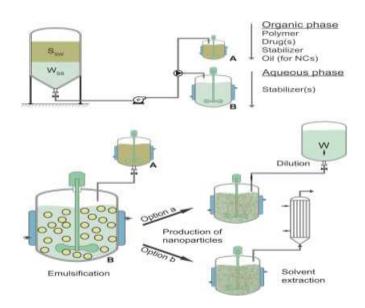


A surfactant is used to emulsify the organic solution in the aqueous phase. It is then usually treated using ultrasonication or high-speed homogenization to produce a dispersion of

nanodroplets. Once the polymer solvent has evaporated and been allowed to permeate into the continuous phase of the emulsion, NPs are suspended. Evaporation of the solvent occurs either by slow, lowered pressure (as occurs with dichloromethane and chloroform, for example) or by continuous magnetic stirring at ambient temperature (for more polar solvents). For long-term storage, the solidified nanoparticles can be collected and cleaned by centrifugation after the solvent has evaporated. They can then be freeze-dried. With this technique, nanospheres can be produced.

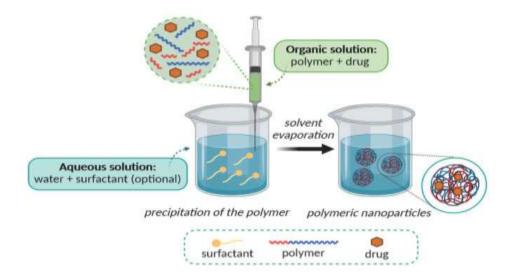
2. Emulsification/Solvent diffusion method

This technique involves combining an aqueous solution with a surfactant and a partially water-miscible solvent that contains a polymer and drug to generate an o/w emulsion. To guarantee an initial thermodynamic equilibrium of both phases at room temperature, the internal phase of this emulsion is made up of a somewhat hydro-miscible organic solvent, such as benzyl alcohol or ethyl acetate, which has been saturated with water beforehand. Colloidal particles are formed as a result of solvent diffusion from the dispersed droplets into the external phase caused by the subsequent dilution with a significant volume of water. Nanospheres are typically made in this way, but nanocapsules can also be made by adding a tiny bit of oil (such as triglycerides C6, C8, C10, and C12) to the organic phase. Evaporation or filtration are the last methods for removing this stage, which depends on the organic solvent's boiling point. NPs with dimensions ranging from 80 to 900 nm can ultimately be obtained. Despite the need to remove a large amount of the aqueous phase from the colloidal dispersion and the possibility of the hydrophilic drug diffusing into the aqueous phase, this technique is widely used to produce polymeric nanoparticles.



3. Nanoprespitation

This technique, also known as the solvent displacement method, calls for two solvents that are miscible. An organic solvent that is miscible, like acetone or acetonitrile, dissolves a polymer to form the internal phase. Evaporation can readily remove them due to their immiscibility in water. As the organic solvent is displaced from a lipophilic solution to the aqueous phase, the technique's basic idea is the interfacial deposition of a polymer. A watermiscible solvent with an intermediate polarity is used to dissolve the polymer. This solution is then gradually added to an aqueous solution while being stirred (dropwise) or at a regulated rate. The nanoparticles develop instantly in an effort to evade the water molecules because of the polymer solution's rapid spontaneous migration into the aqueous phase. The polymer precipitates as nanocapsules or nanospheres as the solvent diffuses out of the nanodroplets. Although the process can be switched without affecting the creation of nanoparticles, the organic phase is typically added to the aqueous phase. Although their presence is not necessary to ensure the creation of nanoparticles, surfactants can typically be added to the process to maintain the stability of the colloidal suspension. The resulting nanoparticles are often better than those made by the emulsification solvent evaporation process because they have a restricted size dispersion and a well-defined size. One technique that is commonly used to create polymeric nanoparticles (NPs) with dimensions of approximately 170 nm is nanoprecipitation, which also makes it possible to obtain nanospheres or nanocapsules. When the active ingredient is dissolved or distributed throughout the polymeric solution, nanospheres are produced. The drug is first dissolved in an oil, which is subsequently emulsified in an organic polymeric solution before the internal phase of the emulsion is distributed in the external phase, resulting in nanocapsules.



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4. Evaluation of nanoparticles^[16-19]

✓ Analysis of particle size

The nanoparticles' size was measured using a scanning electron microscope. Particle sizes vary from 350 nm to 600 nm, depending on the polymer content.

✓ Scanning Electron Microscopy (SEM)

Nanoparticles' particle shape and surface morphology were examined using scanning electron microscopy. Adhesive tapes were used to place lyophilized samples that were completely dry on aluminum stubs. A sputter coater was used to apply a gold coating, and morphology was assessed at a 20 kV acceleration voltage.

✓ Differential Scanning Calorimetry (DSC)

A DSC analysis (DSC-60, Shimadzu, Japan) was used to determine the physical state of the natural medication and identify the nanoparticles. In separate sealed standard aluminum pans, approximately 2 mg of native drug, polymer, and nanoparticles were added. The pans were then heated to varying temperatures between 25 and 300 °C at a rate of 10°C/min in a nitrogen environment. An aluminum pan, empty, was the standard.

✓ X-ray diffraction analysis

The X-ray diffraction analysis was conducted using an XRD-6000 diffractometer. Analysis was done to determine the crystallinity of the pure medication and the diffraction of X-ray formulation. The powder was put in an aluminum sample holder. Cu radiation was produced at 30 mA and 40 kV. As previously stated, samples were scanned at a speed of 10° min-1 between 10° and 90°.

✓ Analysis of Fourier Transform Infrared (FTIR) Spectroscopy

FTIR examination of the chemical stability and potential chemistry (Perkin Elmer, FTIR Spectrometer, SPECTRUM RX I, USA) can be performed to evaluate the interaction between the drug and polymer. Samples were individually mixed with 200–400 mg of potassium bromide and crushed for two minutes at a pressure of 200 kg/cm2 to produce the pellets. Analysis was made possible by positioning the pellets of the natural medication, polymer, and drug-loaded nanoparticles on the light path. To scan all samples, an average of 32 interferograms with a resolution of 2 cm1 over a range of 4000-400 cm1 was employed.

✓ Study of accelerated stability

The nanoparticles were housed in climatically controlled environmental simulation chambers along with the samples in borosilicate glass vials. International Conference on Harmonization (ICH) rules are followed regarding the number of samples used in safety assessments and storage conditions. During the course of six months, the drug-loaded Eudragit®RS100 nanoparticles were physically and chemically characterized at regular intervals to check for any deterioration. This was done by dispersing 1 mg of the nanoparticles in 10 ml of distilled water. Three duplicates of the study were occasionally conducted. The size of particles and the zeta potential at a specific wavelength and 25°C were measured using a Zeta sizer, which is based on quasi-elastic light scattering. To test the formulation's chemical stability (drug content), RP-HPLC was employed at 282 nm.

Zeta potential analysis

Nanoparticle surface charge in colloidal fluids is measured using zeta potential. The Stern layer is a thin layer that forms on the surface of NPs as a result of counter-ions being drawn to their surface charge. The NPs diffuse through the solution, carrying this layer with them. NP zeta potential is the name given to the electric potential at this layer's edge. The devices known as zeta potential analysers are used to measure this potential. Higher absolute levels of zeta potential suggest more stable NPs, and zeta potential values are predictive of NP stability.

Examples: NPs with zeta potentials more than +30 mV or less than -30 mV are regarded as stable, and the zeta potential is a useful indication of NP stability. Numerous biogenic NPs have had their zeta potentials evaluated. Ziziphus jujuba leaf extract yielded Ag NPs with a zeta potential of -26.4 mV. Other organisms' Ag NPs have varying zeta potential values. For instance, Ag NPs made from the peel extract of Punica granatum have a zeta potential of – 40.6 mV, which indicates their higher stability, whereas Ag NPs made from Aspergillus tubingensis have a zeta potential of +8.48, which indicates their relative instability. Zeta potential values are also influenced by the sample's pH; the higher the pH, the lower the zeta potential value. It is not specific to silver that various zeta potential values for the same type of NPs depend on the organism used to synthesise them; Se NPs also exhibit varying potential values based on the organism utilised to synthesise them.

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5. Applications of nanoparticles



6. CONCLUSION

In this review article we have given a brief overview of nanoparticles. Their structure, classification, method of synthesis, and applications in various fields.

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