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Application of Nanoparticles in Biomedical Field: An Overview

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Abstract: *The use of nanotechnology has resulted in significant advancements across a wide range of industries in recent years. Nanomaterials are the cornerstone upon which nanotechnology is built. It is clear that nanoparticles possess unique properties when contrasted with bulk materials. Noble metal nanoparticles (NMNs) have become a famous nanomaterial due to the compelling visual and chemical properties that they possess due to their composition. Today, NMNs have a wide variety of applications, including but not limited to the following: catalysis, biosensors, bioimaging, theragnostic, antimicrobial, cosmetics, medical devices, and a seemingly endless number of other applications. Following is some of the topics that have been discussed in this chapter of the book: the current state of nanotechnology; techniques for characterising nanoparticles; optical properties; various applications of nanoparticles in medical biotechnology; "and synthetic strategies for nanoparticles, including top-down, bottom-up, and biological approaches.*

Introduction

It is widely believed that nanotechnology will be the most transformative breakthrough of the new century. A wide range of fields, including biology, electronics, energy, the environment, and catalysis, have all been significantly influenced by the revolutionary advancements that it has brought forth. According to the year 2000, the term "nanotechnology" is often used to refer to any technology that was produced in the nanoscale realm and has genuine, meaningful applications. Nanomaterials are the cornerstone upon which nanotechnology is built. "During the annual meeting of the American Physical Society in 1959, Richard Feynman delivered a lecture with the title "There's plenty of room at the bottom," which ignited a significant amount of interest in nanomaterials around the world. In his discussion of tuning things at the microscopic scale to its extreme limits, he laid out a number of solid assumptions, including information on the microscopic scale, comparisons of the sizes of biological systems, the development of miniaturisation through evaporation, the construction of microscopic machines, and the manipulation of individual atoms to our specifications. These are just some of the many solid assumptions he laid out. Taniguchi was the first person to use the term "nanotechnology" in a scientific publication in 1974. He did so in order to describe the exact engineering that is required in the manufacturing of small semiconductors. The scanning tunnelling microscope, which was developed by Binning and Rohrer in 1986, has, on the other hand, aroused a serious interest in nanotechnology and nanoscience. Through the passage of time, it contributed to the development of the atomic force microscope, which was created by Christoph Gerber and Calvin Quate." This microscope was able to exceed the diffraction limit of the optical microscope by almost three orders of magnitude in terms of atomic resolution. During the year 1985, Kroto and his colleagues made the discovery of fullerene, which is a carbon material that has a spherical form and a diameter of just one nanometre. Through his book "Engine of Creation," which was published in 1986, Eric Drexler discussed molecular nanotechnology and contributed to the dissemination of several facets of nanotechnology to a more general audience than only scientists. Since then, a great number of key improvements have been achieved, including the discovery of carbon nanotubes, the development of technology for nano-imprinting, and research into the photocatalytic activity of TiO_2 nanosheets, amongst a great number of other developments. With the goal of gaining a deeper understanding of nanotechnology, the National Nanotechnology Initiative (NNI) was established by the government of the United States of America in the year 2001. Due to the fact that nanotechnology has developed into a large and separate area, a number of academic books have been produced to record the development of nanomaterials and the diverse uses that they have encountered. "Nature Nanotechnology, Nano Letters, Journal of Nanoscience and Nanotechnology, Academy of Computer Science Applied Nanomaterials, Journal of Nanoparticle Research, and a great deal of other publications are among them." There is no way to stretch the truth if one were to assert that nanotechnology is indispensable to each and every technological innovation that has occurred in the 21st century. A wide number of sectors, notably those dealing with medical biotechnology, have reaped significant benefits from it.

Objective

- To use nanoparticles in the area of biomedicine.
- To better diagnostics and imaging.

Properties of Nanoparticles

The quantum phenomena that are responsible for the distinctive optical, magnetic, electrical, mechanical, and other properties of nanomaterials are the outcome of these phenomena.

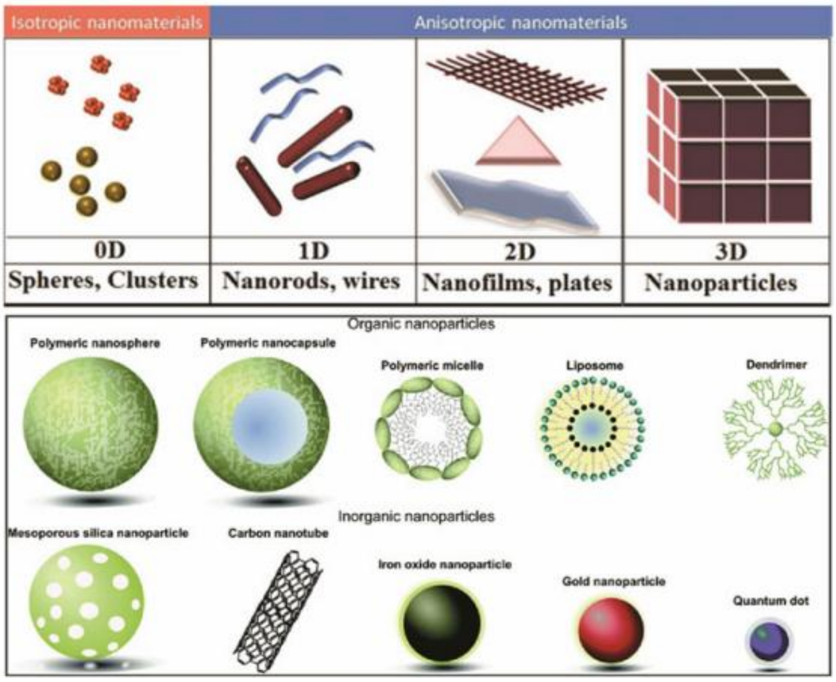

Fig. 1: Nanomaterials are categorised according to their size (top panel), kind of material (bottom panel), and figure obtained with consent. With permission, this figure was used from 2017

Physiological, chemical, and physical aspects of the substance. The capability of accurately regulating the size, shape, and composition of nanomaterials in order to vary their optical and chemical properties is a fascinating component of this technology.

Optical Properties

Because of their remarkable optical and catalytic features, noble metal nanoparticles (NMPs) have attracted the attention of many different kinds of nanomaterials. All of the noble metals, such as gold, silver, platinum, and tin, are included in the category of nanoparticles. Light engages in a variety of interactions with NMPs. The light that strikes NMPs induces a phenomenon known as localised surface plasmon resonance (LSPR) at a particular frequency of light radiation. This phenomenon, in turn, amplifies a variety of interactions between light and matter. These interactions include boosts of the electric field (EF) as well as a significant increase in selective light absorption and scattering that occurs. Extremely minute particle

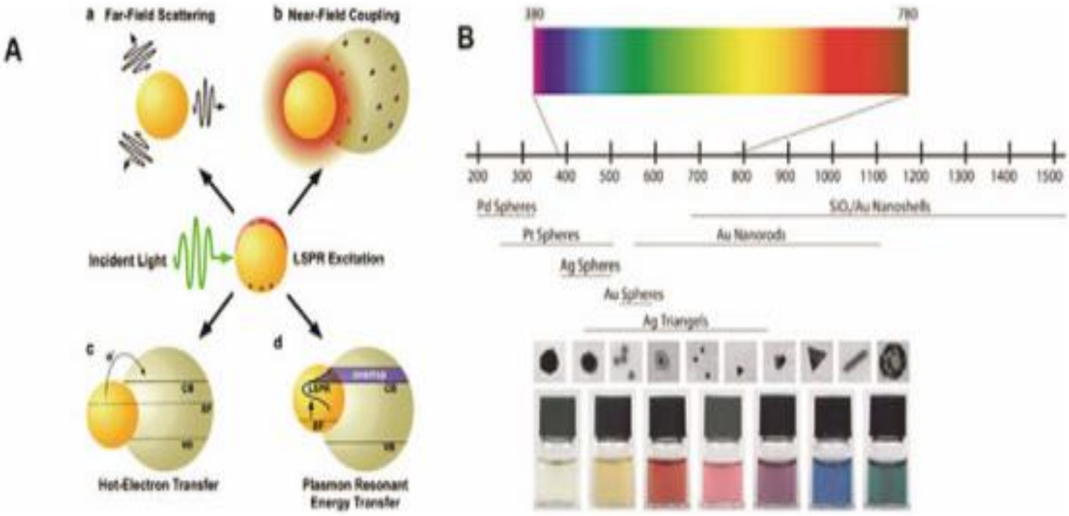

Fig. 2: (A) Diagrammatic representation of how light interacts with plasmonic nanoparticles. With permission, this figure is derived from Erwin et al. (2016) (B). The size, shape, and composition of NPs have a significant impact on their optical characteristics. The figure was obtained with permission

Nanoparticles that exhibit LSPR phenomena when light interacts with them are referred to be plasmonic nanoparticles of this kind.

"As shown in Figure 2A, the LSPR technique has the potential to create a number of different processes on the surface of nanoparticles. These processes include far-field scattering, near-field coupling, hot-electron transfer, and plasmon resonant energy transfer. You may easily modify LSPR by modifying the size, shape, and composition of various NMPs. This is a very straightforward process. The evidence shown in Figure 2B demonstrates that non-metallic compounds (NMPs) with different morphologies and compositions (Au, Ag, Pt, and Pd) absorb and emit electromagnetic radiations at different frequencies. In the broad new field of nanoplasmonics, the features of various nanomaterials in terms of how they interact with light have being investigated. Plasmonic nanomaterials have molar coefficients that are several orders of magnitude higher than those of ordinary organic fluorophores. This enables them to possess the ability to absorb and scatter certain electromagnetic wavelengths."

According to Wong et al. 2020, plasmonic nanoparticles have a wide range of applications in the field of biomedicine. Some of these applications include biosensors, photothermal therapy (PTT), optoacoustic imaging (OI), bioplasmonics, and theragnostic applications. In addition to their remarkable surface-to-volume ratio (S/V), quantum size effects, interfacial chemistry, and surface chemistry, nanometer-sized particles (NMPs) exhibit particular catalytic properties.

Toxicity of Nanoparticles

Nanotoxicity is the term used to describe the negative consequences that nanoparticles have. The field of study known as nanotoxicology investigates the potentially catastrophic impacts of nanomaterials and nanoparticles. The study of nanotoxicology, which is a subfield of nanoscience, is concerned with the possible adverse consequences that nanoparticles may encounter. Nanotoxicological research is now being conducted in order to ascertain whether or not these qualities provide a risk to people, animals, and the environments in which they are found. “As an example, we can see in Figure 1 that nanoparticles are known to cause damage to the central nervous system, the cardiovascular system, the respiratory system, and the vascular system.”

Classification of Nanoparticles

According to the basic criteria for identifying nanoparticles, the number of dimensions that fall inside the nanometre range is the most important factor. Nanoparticles may be broken down into two major categories: an organic nanoparticle and an inorganic nanoparticle. “In the organic realm, lipid nanoparticles (micelles, liposomes, and nanocapsules) in the inorganic realm, dendrimers, hybrids, nanospheres, compact polymeric, and nanocapsules in the inorganic realm, fullerene, quantum dots, and certain metallic nanoparticles (Silica, Palladium, Silver, Lead, Gold, Platinum, Ruthenium, copper, and so on) are the components that make up the inorganic nanoparticles.” Micelles are a kind of lipid bilayer that come together to form a spherical shape when they are submerged in water. Micelles exhibit a trait known as amphipathicity, which is characterised by their ability to respond to the hydrophobic and hydrophilic properties of fatty acids (lipid polymers) as they form. When the molecules come into contact with water, they experience hydrophobic interactions, which are principally responsible for the formation of their spherical shape. When they are not separated from water, hydrophobic tails are surrounded by water, which creates a systematic cage around them. Dendrimers are molecules that have structures that are well-defined, identical, and monodisperse. They are nanosized and radially symmetrical across their whole structure. Dendrimers are molecules that are circular in shape, include many atoms, and have an abnormally high number of branches. “They possess synthetic elasticity and have the potential to be used in a broad range of applications, including drug delivery, electronics, and catalysis. It is simple to regulate the size of this nanoparticle by adjusting the number of production processes.”

Liposomes are spherical vesicles that are comprised of phospholipid bilayers that surround them. They are created by the combination of cholesterol and phospholipids that exist naturally in the body. The fact that they are both hydrophobic and hydrophilic, in addition to their size, makes them intriguing drug delivery systems. The phospholipid concentration, surface charge, size, and production procedure are all factors that have a significant influence on the features of these substances. Unilamellar designs, sometimes known as single-layer designs, are the most common. The most important advantages of liposomes are their total recyclability, compatibility, absence of toxicity, and absence of immunogenicity that they possess. These particles are referred to as nanospheres, and their diameters may range anywhere from ten to two hundred nanometres. To be amorphous implies to lack form. It has been shown in recent research that the hydrophobic portions of these particles are very vulnerable to phagocyte invasion that is mediated by opsonin. There are times when it adsorbs to the surfaces of the nanoparticles, transforms into a liquefiable condition, gets trapped inside the nanoparticle (a "nanosphere"), or is enclosed in a polymeric shell (a "nanocapsule"). Specifically, a nanocapsule is composed of two components: the shell and the inside space, which may be filled with any substance that the user desires. The chemicals that make up nanocapsules are called phospholipids, and they have two different ends: one hydrophobic and one hydrophilic. These molecules spontaneously fold into capsules when they are exposed to water, with the hydrophobic end on the inside and the hydrophilic end on the exterior of the capsule.

The fullerene molecule is made up of carbon molecules, and it has a huge number of bonds that are very symmetrical and stable. Fullerenes that contain sixty carbon atoms are the most frequent kind, and the stiff icosahedron, which is a polyhedron with twenty faces, is the one that is most often used. Benzene's three-dimensional counterparts are considered to be one of these substances. Fullerenes are compounds that possess remarkable strength and resilience to pressure than other molecules.

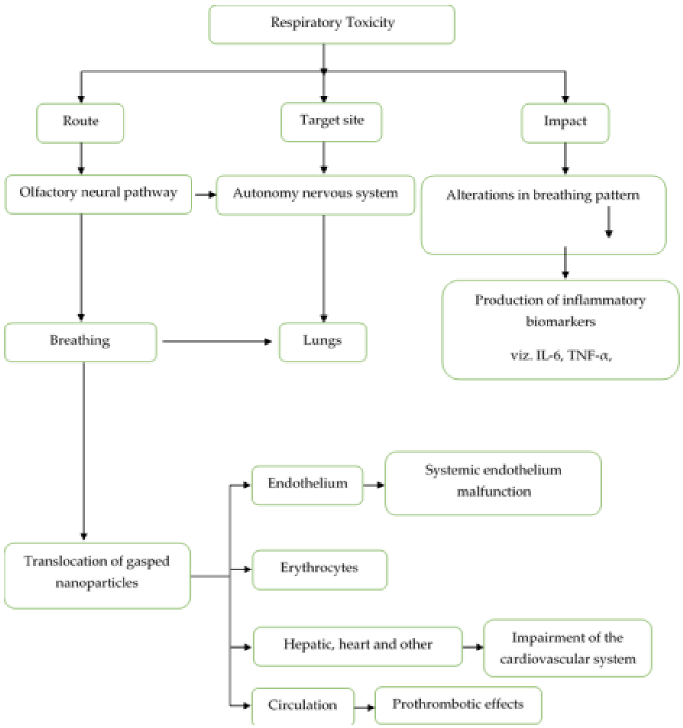

Figure 3: Schematic diagram of the main system impacts relevant to nanoparticles treatment and probable mechanism linked to those effects

One kind of semiconductor is a quantum dot. In these little devices, there are a few droplets of electrons enclosed inside them. A few nanometres in size is another name for these crystals, which are also known as nanometre crystals. There are several applications for inorganic quantum dots, and they are nanometric. Inorganic compounds such as silica, gold (Au), silver (Ag), or platinum (Pt) may be used in the production of nanoparticles. Inorganic nanoparticles may be synthesised utilising a range of different procedures, which results in the formation of a three-dimensional structure that is highly structured and hard.

"Strategies for Synthetic Nanomaterials

When describing the process of synthesising nanomaterials, the terms "top-down approach" and "bottom-approach" are often used. Both of these approaches are fundamental strategies. The bottom-up approach, on the other hand, includes first breaking a bulk material into tiny pieces, which are then ground, crushed, and shaped into nanomaterials of varied sizes. The top-down method involves breaking a bulk material into smaller bits.

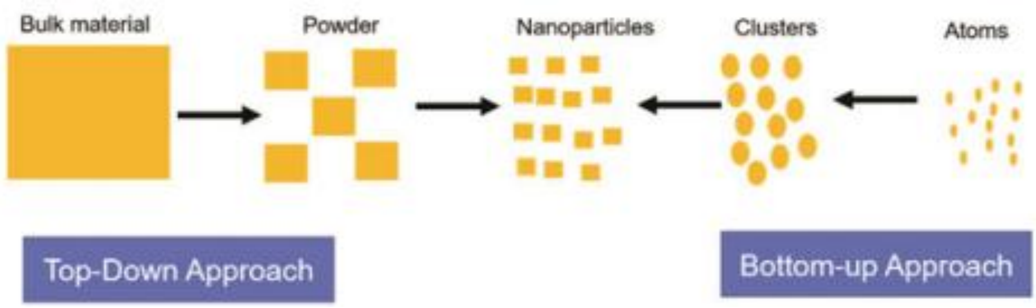

Fig. 4: Diagrammatic Representation of Nanomaterials' Synthesis Techniques

"The creation of nanomaterials involves the methodical assembly of atoms and molecules, which is accomplished via the utilisation of a wide range of capping ligands and surfactants (Fig. 4). In contrast to bottom-up approaches, which only permit the synthesis of homogeneous nanomaterials with consistent size, shape, and composition, top-down methods allow for the fast synthesis of nanomaterials in huge numbers. This is the primary advantage of top-down methods. The synthetic techniques may be classified as either physical, chemical, or biological, depending on the method that is used for the synthesis of NMPs. Synthesis of a broad variety of nanoparticles for a variety of applications is accomplished via the use of a variety of synthetic processes." There are a variety of shapes that these nanoparticles may take, such as spheres, cubicles, rods, stars, prisms, plates, nano-hollow spheres, flowers, tubes, octahedral, and tetrahedral nanoparticles. In Figure 3.6, a model system is used to illustrate the different synthetic strategies that may be used to fabricate silver nanoparticles. These methodologies include both top-down and bottom-up approaches. By using these synthetic procedures, it is also possible to complete the synthesis of additional NMPs at the same time.

Top-Down Synthetic Strategies

When using top-down synthetic techniques, one of the most important principles is to reduce the size of bulk materials to the nanometre scale or smaller, depending on the requirements. These synthetic technologies, which make use of either conventional workshop skills or microfabrication procedures, include milling, cutting, moulding, and carving large materials to exact sizes and forms. "These processes are all included in the synthetic technologies. A description of the top-down strategies that are the most often used in nanoparticle synthesis is included in the following paragraphs."

Pyrolysis

Pyrolysis is the primary method that is used in the synthesis of nanoparticles composed of noble metals. Utilising this method to produce powdered nanoparticles is the most common and straightforward approach to achieving economic viability for these particles. First, a gas or liquid is heated to a vapour pressure that is high enough to pass through the aperture, and then it is burnt to form ash. This process is completed in this location. An enduring

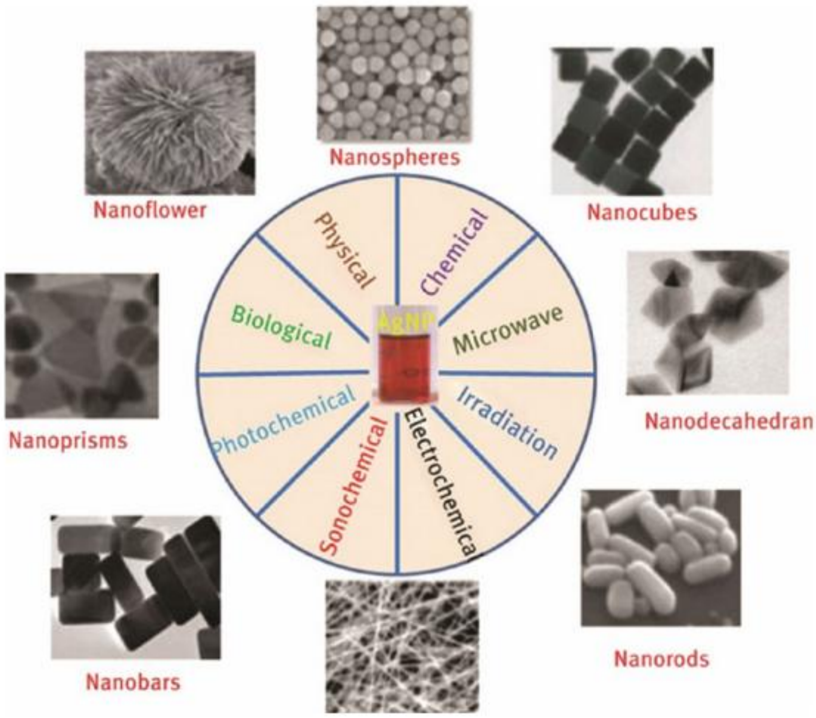

Fig. 5: Diagrammatic Representation of the Production of Ag NPs as a Model System using Several Synthetic Techniques

The nanoparticles were extracted from the ash by further processing. This technique has a number of drawbacks, the most significant of which are that (i) it results in the formation of large clumps or agglomerates of nanoparticles that are of varying sizes, and (ii) it requires a significant amount of energy to maintain a high temperature and pressure.

Attrition (Milling)

The reduction of macro and micro-scale materials to nano-size particles may be accomplished by the use of a ball mill, attrition, or milling. The ceramic processing industry and industries based on powder metallurgy have depended on this method for a considerable amount of time. The attrition process is based on a basic concept that is determined by the amount of energy that is transmitted from the milling medium to the sample. The transfer of kinetic energy from balls to samples is the means by which this approach accomplishes the decrease of grain size in macro-scale materials. There are a number of parameters that influence the milling process, and therefore, the size and composition of the nanoparticles. These factors are directly related to one another. Among these are the kind of milling, the temperature of the milling, the length of the milling, the intensity of the milling, the surrounding environment of the milling, and the quantity of powder. A number of milling devices, including shaker mills, tumbler mills, vibratory mills, attrition mills, planetary mills, and others, have been developed to circumvent these limitations and perform exceptionally well in certain applications. You may be able to alter the operating parameters, milling capacity, and accessories of the equipment in order to control the amount of heat and separate nanoparticles of varied sizes. When opposed to the mechanochemical approach known as "dry milling," liquid-aided grinding provides a number of advantages, including improved nanoparticle quality, reduced energy and material waste, and increased time efficiency. "Dry milling"

Because of this technology, the production of nanoparticles on a huge scale has never been simpler than it is now. This procedure makes it simpler to build a broad range of alloys and nanocomposites, in contrast to more conventional methods of synthesising nanoparticles, such as chemical reduction, sonochemistry, electrochemistry, and all of these other methods. One of the disadvantages of the milling process is that it might result in the generation of disordered crystals, which is one of its potential outcomes. There are also trace quantities of N2 and O2 in the sample, as well as trace amounts of Fe. These pollutants are often caused by milling equipment, environmental variables, surface flaws, and the generation of internal tension. Surface defects have a substantial influence on the physicochemical properties of nanoparticles due to the high aspect ratio that nanoparticles possess.

Micropatterning

“This technique, which is used extensively in the field of nanoelectronics, is referred to as the "art of miniaturisation of patterns." It is often used in the domains of bioengineering, cell biology, and biomaterials engineering, among other areas of study. Numerous techniques for micropatterning, including photolithographic procedures, have been developed over the course of the last several years. There are many different types of lithography, some of which include soft lithography, colloidal lithography, E-beam lithography, scanning probe lithography, and nano-imprint lithography. A well-controlled focused beam of electromagnetic radiation (EMR), which may include light (UV-Visible), X-rays, electrons, and ions, is used to remove and shape specific nano-size structures on a precursor material known as "resist." The fundamental concept that underpins this method is to create systematic nano-design patterns on the "resist" material.”

Bottom-Up Synthetic Strategies

This technique includes the slow assembly of atoms and molecules into nanoparticles in the presence of capping ligands or surfactants, with the intention of enhancing the chemical properties of the nanoparticles. It is possible that molecular recognition and/or molecule self-assembly are the sources of inspiration for this method. When it comes to the synthesis of nanoparticles, there are a number of different capping ligands that may be used. The function of these ligands is to control the structure and growth of the particles. On the other hand, in contrast to the top-down strategy, this technology makes it possible to create nanoparticles that are uniform in distribution. The bottom-up method allows for the modification of NMPs in terms of their size, shape, and composition with relative simplicity. Additionally, the synthesis of their optimum crystalline structures may be accomplished for a wide range of applications. Listed below are explanations of the most common bottom-up synthetic methodologies, followed by a review of the advantages and disadvantages associated with each of these strategies.

Chemical Reduction Method

This is the method that is used the majority of the time while synthesising NMPs. This technique includes decreasing ionic salts, which are metal ions, by using a variety of reducing agents, while simultaneously including capping ligands and stabilising agents. “When it comes to the production of NMPs, it is common practice to make use of a wide range of reducing agents, such as sodium hydroxide, sodium bihydride, hydrogen, alcohols, carbon monoxide, and hydrazine. In the field of NMP synthesis, the Lee-Meisel and Creighton techniques are the two most often used solution-based methods. For the most part, the Lee-Meisel method is used in the process of synthesising silver nanoparticles. The method comprises the use of metal precursor salts, such as silver nitrate and silver sulphate, and the reduction of these salts by the utilisation of a mixture of hydrogen, sodium citrate, and sodium hydroxide at a range of temperature settings. Changing the pH of the reaction conditions is a straightforward method for easily controlling the size and shape of silver nanoparticles. Ag nanoparticles with a wide range of morphologies were manufactured by the use of this technique. In the presence of high pH values, the slow reduction kinetics of Ag nitrate led to the formation of spherical and rod-shaped Ag nanoparticles.” On the other hand, the slow kinetics of Ag nanoparticles under conditions of lower pH (5.5-11.1) led to the observation of their triangular and polygonal shapes. Simply keeping an eye on the pH of the reaction conditions is all that is required to easily regulate the morphologies of silver nanoparticles using this method.

The reduction of Au+3 ions with a variety of reducing chemicals may allow for the creation of nanoparticles of gold in a manner that is analogous. It was shown in 1951 that it is possible to produce 20 nm Au nanoparticles by reducing an aqueous solution of HAuCl4 with citrate that was present. Turkevich technique is the name of this method of approaching the problem. In Fig. 6, transmission electron micrographs of gold nanoparticles with diameters of 10, 20, 50, and 100 nm are shown. These nanoparticles were produced using the Turkevich process. Over the course of the 1970s, the Frens adopted a number of modifications to this method. At the beginning of the 1990s, Brust was the one who came up with the method for producing gold nanoparticles. On the other hand, the Turkevich technique depends on an aqueous solution to produce gold nanoparticles, in contrast to the Brust method, which employs an organic solvent for the material synthesis. In spite of the fact that a number of different methods were developed for the manufacturing of gold nanoparticles, they were all, in essence, replicas of the first strategies that had been recorded in the past for the production of platinum nanocubes via the utilisation of the fundamental chemical reduction process. The manufacture of lead nanoparticles may also be accomplished via the use of the chemical reduction method.

In spite of the fact that it is widely regarded as a straightforward and time-honored method for the production of nanoparticles, including NMPs, the chemical reduction approach is not devoid of undesirable characteristics.

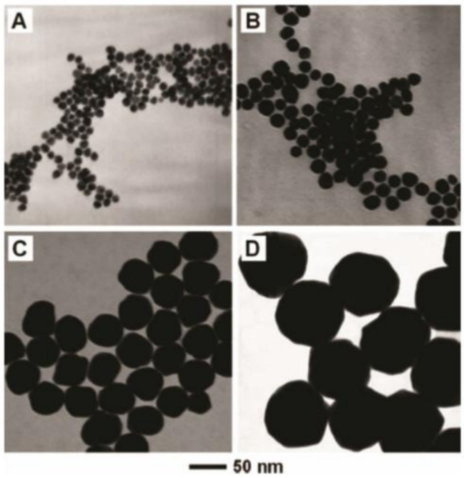

Fig. 6: TEM Pictures of Au Nanoparticles Synthesised using the Turkevich Technique at Various Sizes: (A) 10, (B) 20, (C) 50, and (D) 100 nm. With Permission, this Figure was Borrowed from Njoki et al. 2007

In order to successfully synthesise nanoparticles using this method, it is often necessary to subject the material to very high temperatures and pressures, in addition to a significant amount of time. In addition to this, the reaction makes use of a significant quantity of very hazardous substances, which may have an effect on the surrounding environment. "Due to the presence of capping ligands on the surface of nanoparticles, their usage in biological applications is restricted to a limited extent."

Electrochemical Method

In order to establish metal nanoparticles, they were the pioneers in the use of an electrochemical method. The dissolution of a metal sheet at the anode and the subsequent reduction of the intermediate metal salt at the cathode were the two steps that were used in the production of metal nanoparticles employing their method. Through the use of a number of electrochemical techniques that have surfaced over the course of the last ten years, it is possible to produce nanoparticles that exhibit a broad range of shapes, aspect ratios, and configurations. This was made feasible by the emergence of a wide variety of electrochemical technologies, which allowed for the synthesis of various NMPs.

Microemulsion Method

This approach was first put to use in the early 1980s for the purpose of synthesising nanoparticles of platinum, palladium, and rhodium. The process of synthesising nanoparticles includes dispersing and mixing salts and reducing agents with surfactants in either water-in-oil or water-in-water emulsions. Another approach involves combining surfactants with salts. Following the synthesis of the micelles, the manufacturing of nanoparticles started with the mixing of reactants and nucleation that was brought about by inter-micellar collisions brought about by the Brownian motion of the micelles. As a method for the synthesis of a wide variety of nanoparticles in microemulsions that include either water or oil, or both, this technique has garnered an enormous amount of appeal. Using this method, it is possible to easily synthesise nanoparticles that are monodisperse and thermodynamically stable, which is a significant advantage.

Microwave Method

In this method, the synthesis of NMPs is accomplished by the utilisation of microwave irradiation, with the precursors consisting of a solution of polymer surfactants and metal salts. Since the invention of our one-pot approach, the process of synthesising metal nanoparticles has never been simpler. Simply adjusting and standardising the parameters of the reaction makes it possible to easily tune the size, shape, and composition of the NMP. Excellent review articles are accessible for anybody who is interested in learning more about the microwave method for synthesising MNPs. These publications can be found in a variety of different places.

Laser Ablation

The process of laser ablation, which is a flexible method for the production of nanomaterials, involves piercing a solid surface with a beam of laser light. After being exposed to laser light with a low flux power, the material is heated to the point where it goes through a process of vaporisation or sublimation. The wavelength of the laser and the optical properties of the material both have a significant role in determining the amount of material that can be removed from a solid surface. This technology has lately acquired momentum as a potential new approach to the manufacture of nanoparticles. It is an alternative for the chemical reduction method, which has been gaining popularity. Taking this strategy has a number of advantages, the most important of which is that it does not exclude any excess chemicals from the synthesis process. This makes it possible to easily adjust the size and form of NMPs. The production of silver nanoparticles on a metal plate in conjunction with the use of sodium dodecyl sulphate as a surfactant. This technique resulted in the production of a large number of ligand-free NMPs. This method has the potential to be used in the production of NMPs in large quantities, with the ability to modify their dimensions, characteristics, and composition.

Conclusion

There have been revolutionary advancements brought about in the twenty-first century as a result of nanotechnology, which has developed into an independent and advanced technology. Nanoparticles, which are the basic units of nanotechnology and have a size range of one to one hundred nanometres, possess unique chemical and optical properties that are used in a wide variety of technological applications. The size, shape, and composition of nanoparticles have a significant impact on the chemical and optical properties that they possess. Large-scale nanoparticles with a wide range of properties have been manufactured by the use of synthetic procedures, which also serve as powerful instruments for directing the growth of these nanoparticles. With the assistance of cutting-edge technology, it is now possible to investigate the many features of nanoparticles of every kind. A wide variety of applications, including theranostics, biosensors, antibacterial agents, and bioimaging agents, are among the numerous possible applications of plasmonic nanoparticles in the area of biomedicine. It is possible that in the future, nanotechnology may give novel solutions to a significant number of the most important issues facing the globe, so enabling us to lead better lives in general.

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