

NANOPARTICLES: A REVIEW BASED ON NANOTECHNOLOGY-BASED DOSAGE FORM

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ABSTRACT:

This review provides a brief study of nanoparticles, which are produced through nanotechnology, and their evolution in the pharmaceutical industry. It has developed as one of the most promising fields in modern pharmaceutical sciences. Although the research on nanopharmaceuticals is still in its early stages, the safety and the effects of the dosage form should be carefully considered. The pharmaceutical industry has traditionally relied on tablets, capsules and injections, which are conventional dosage forms. These conventional dosage forms have several limitations, due to which the need for a nanotechnology-based dosage form was created. Nanoparticles are novel dosage forms which has better bioavailability, disintegration rate, dissolution rate, stability, controlled and sustained drug release. They also work on targeted sites, providing efficient drug delivery. Nanoparticles offer the ability to overcome biological barriers and enhance patient compliance. There are various types of nanoparticles, like polymeric nanoparticles, solid lipid nanoparticles, nanostructured lipid carriers, metallic nanoparticles, nanocrystals, and dendrimers. These submicron-sized particles have been developed for the treatment of various diseases like cancer, infectious diseases, and neurological disorders, and used for personal diagnostics. Nanoparticles can cross blood blood-brain barrier, so they are also used for the treatment of Alzheimer's and brain tumors. Despite their advantages, there are also many challenges. This review provides a detailed review of nanoparticles, their type, applications, composition, methods of preparation, evaluation techniques, marketed products, and recent research /advances in the field of nanotechnology-based drug delivery.

INTRODUCTION:

The evolution of pharmaceutical dosage forms has shifted from conventional formulation to more advanced and targeted nanotechnology-based dosage forms. Nanotechnology breakthroughs have occurred in almost every field of science, and they make life easier in this era. The field of nanotechnology is one of the fastest-growing areas of scientific research and development. Nanoparticles are increasingly being explored for their potential applications in medicine. The prefix 'nano' refers to a Greek prefix meaning 'dwarf' or something very small. [1]. Nanoparticles are colloidal carriers with a size range typically between 1-100 nm used for delivering therapeutic agents in a controlled and site-specific manner. Drug delivery systems (DDS) have been used in past eras to treat numerous ailments. In a conventional drug delivery system (CDDS), the effectiveness depends on the route of administration; drugs are usually delivered via oral, nasal, inhaled, mucosal, and through parental routes. The conventionally delivered drugs are absorbed less, distributed randomly, have less bioavailability, damage unaffected areas, are excreted early, and take a prolonged time to cure the disease. They are less effective in many ways. Due to these, the novel drug delivery systems were introduced (NDDS). It enhances drug effectiveness in many ways. The drug delivery systems (DDS) have been developed in recent years to control drug release. In 1959, Feynman was the first physicist to introduce the notion of nanotechnology in the lecture entitled "There's plenty of room at the bottom" at the California Institute of Technology (Caltech). In this lecture, Feynman made the hypothesis "Why can't we write the entire 24 volumes of the Encyclopedia Britannica on the head of a pin?", and described a vision of using machines to construct smaller machines and down to the molecular level. This new idea demonstrated that Feynman's hypotheses have been proven correct, and for this reason, he is considered the father of modern nanotechnology

Definition:

Nanotechnology is the study of extremely tiny things and is basically the hub of all science disciplines, including physics, chemistry, biology, engineering, information technology, electronics, and material science. The structures measured with nanotechnology range from 1-100 nm at the nanoscale level, and due to their submicroscopic size, they exhibit unique material characteristics that make them useful in a wide range of fields such as engineering, drug delivery, catalysis, and nanomedicine. They also play a significant role in targeting diseases like melanoma, cancer, cardiovascular disease (CVD), skin diseases, liver disorders, and many others. Therefore, drugs linked with nanotechnology can enhance the efficiency of medicines and their bioavailability. The relation between nanoparticles and medicine was demonstrated in the late 1970s.

One of the most promising areas of nanoparticle research among the many biomedical applications is drug delivery. As drug carriers' nanoparticles can be designed to help deliver therapeutic agents to particular cells or tissues, this can increase pharmacological efficacy and reduce systemic toxicity. Drug efficacy can be increased and side effects can be lessened by engineering nanoparticles to have particular surface characteristics that enable them to target diseased cells while avoiding healthy ones. To ensure the optimal therapeutic concentration for extended periods of time, they can also be set up to release encapsulated drugs gradually and regulatedly. Nanoparticles can be used to identify specific biomolecule samples or as contrast agents in medical imaging, in addition to their application in drug delivery. Even though nanotechnology is still in its early stages, the incorporation of nanoparticles into therapeutic and diagnostic platforms has enormous potential to transform the identification, management and treatment of a broad range of medical conditions.

History:

The historical development of nanoparticle-based drug delivery has evolved through key milestones over the past seven decades. Petros and his colleague reported that polymers and drugs were conjugated in 1955, followed by the introduction of the first controlled-release polymer device in 1964. In 1965, Bangham discovered the liposome, marking a major advancement in nanotechnology. Albumin-based nanoparticles were developed in 1972, and liposome-based drug formulations appeared in 1973. The first micelle formulation was created and approved in 1983, while the FDA approved the first controlled formulation in 1989. Subsequently, in 1990, the first polyethylene glycol (PEG) conjugated protein product entered the market.^[2]

Advantages:

Both passive and active drug targeting following parental administration are made possible by altering the nanoparticles' surface characteristics and particle size. These nanoparticle systems can be delivered via a variety of methods, such as oral, nasal, and parental administration.^[3]

Characterizing and analyzing the behavior of nanoparticles is further supported by Raman scattering with surface enhancement. Nanoparticles allow precise drug distribution to small or localized regions within the body. To achieve site-specific targeting, targeting ligands may be conjugated to the nanoparticle surface, or magnetic guidance can be applied.

Effective control of the rate of particle disintegration and release behavior of encapsulated drugs can be achieved by modifying matrix composition. As a result, release kinetics can be better controlled. Furthermore, drug transportation across the cellular barrier is facilitated by nanoparticles.

Preparing nanoparticles usually requires the same raw material as emulsions. These systems ultimately improve drug absorption, lower toxicity and lessen the possibility of negative drug action

They can cross biological barriers such as blood brain barrier to release the drug at the targeted site.

Disadvantages:

Nevertheless, there are also drawbacks to nanoparticles. This includes the possibility of cytotoxicity, high manufacturing costs, difficult characterization and regulatory obstacles.

Nanoparticles are extremely reactive in the cellular environment due to their large surface area relative to their size, which could result in undesirable biological interactions.

The synthesis and production of nanoparticle formulations are often associated with high costs, leading to an increase in the overall expenses of these materials.

Furthermore, there are serious biological risks due to their capacity to penetrate the dermal cellular layers, which raises questions regarding toxicity, carcinogenicity and irritation. The potential for toxicity from the solvents used

in the preparation of nanoparticles further complicates their safety profile.

Variable gelatin behavior during formulation procedures may also affect the stability and functionality of the finished product.^[4]

Classification:

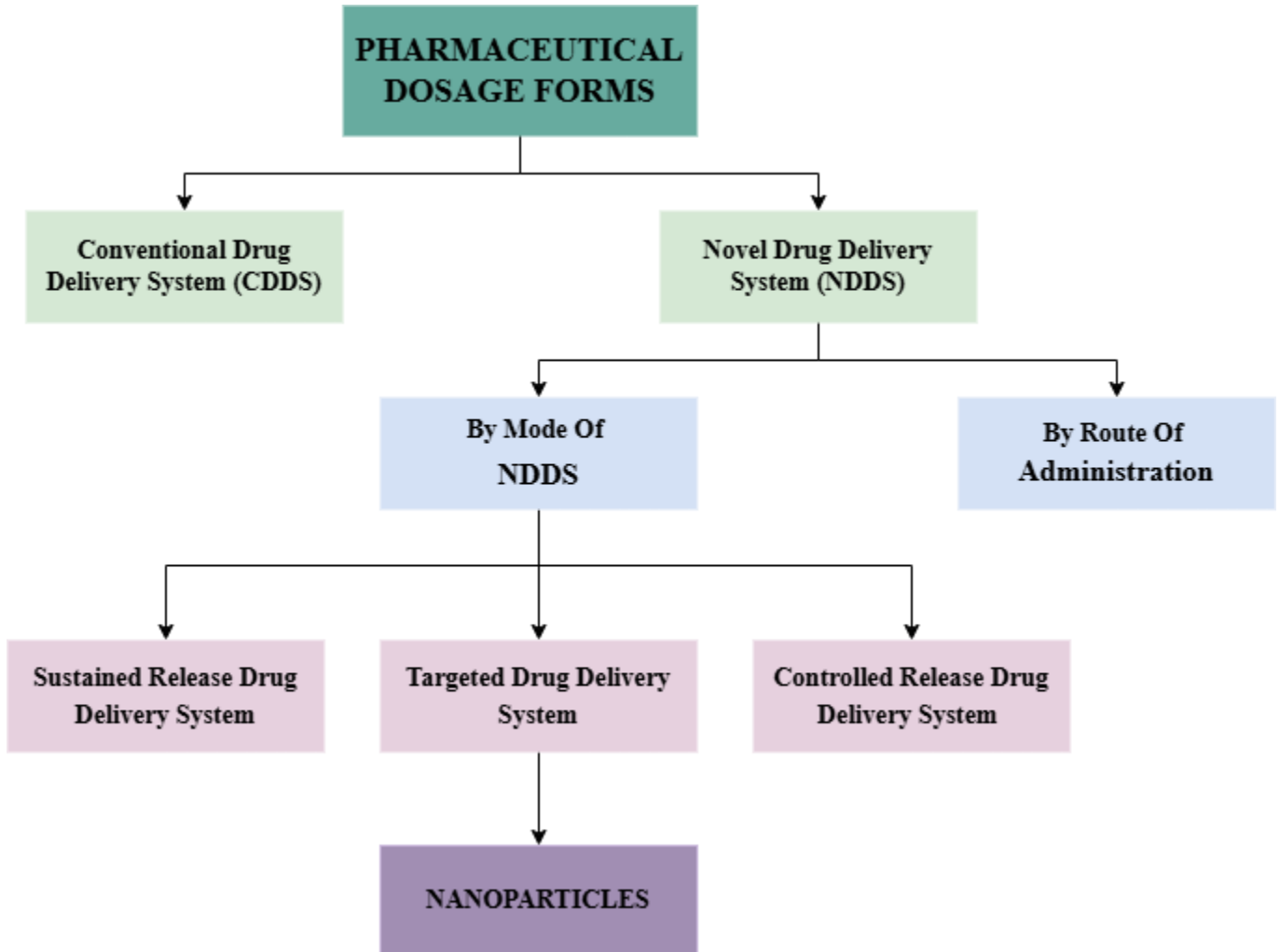
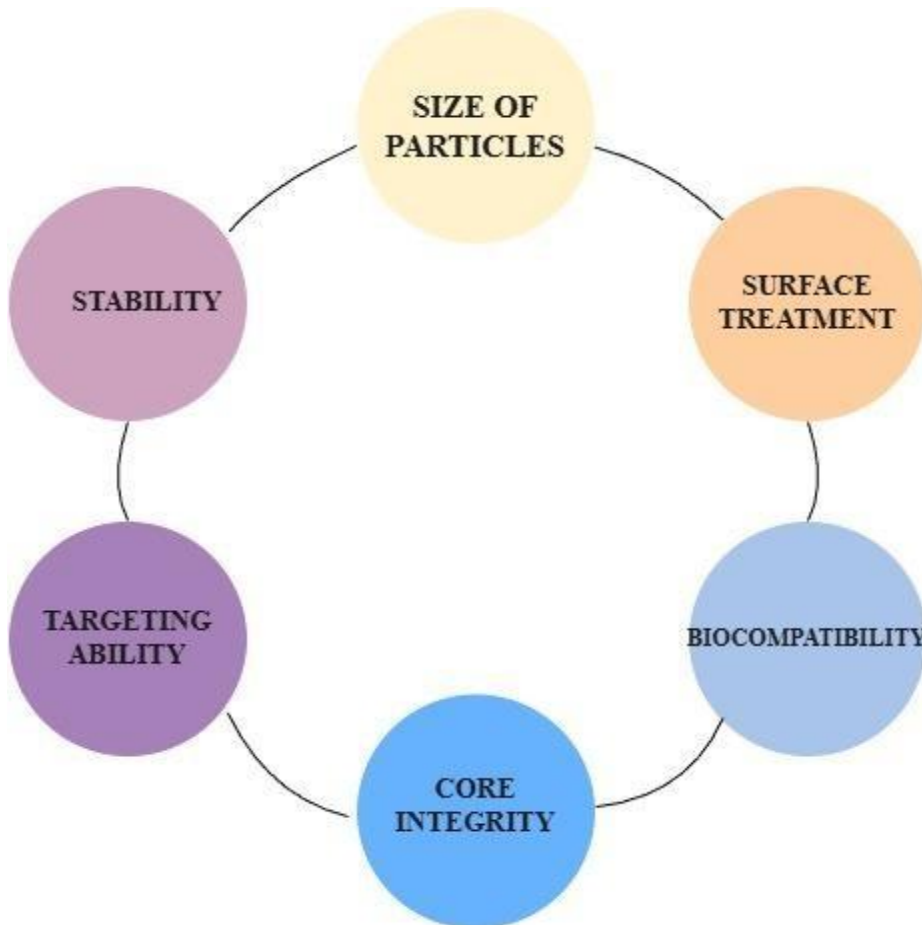


Figure 1 classification of pharmaceutical dosage forms

As shown in Figure 1, the pharmaceutical dosage forms are broadly classified into conventional drug delivery systems (CDDS) and novel drug delivery systems (NDDS) based on their design, function, and method of delivering the active pharmaceutical ingredient to the body. To achieve therapeutic effects, conventional dosage forms comprise solid, liquid, semi-solid, and gaseous preparations that release the drug immediately or over a short period. Examples include tablets, capsules, syrups, ointments, injections, and aerosols, which are designed primarily for ease of administration and patient compliance. They are mainly divided into two types: By mode of NDDS and by route of administration. these systems enable site-specific drug release, side effects, and enhance therapeutic efficiency. As a result, the classification shows how modern systems, which emphasizes precision and sustained drug action, have evolved from traditional forms that focused on dosage convenience.

Ideal characteristics:**Figure 2 ideal characteristics of nanoparticles**

The biophysical and chemical characteristics of nanoparticles, including their size, shape, surface charge, surface chemistry, hydrophobic properties, roughness, hardness, and combinability, can greatly influence the effectiveness of targeted drug delivery using these nanoparticles. Understanding how the body handles foreign particles is crucial before going into the details of the ideal medicine delivery system driven by nanoparticles. Three main routes exist for nanoparticles to enter the body: oral consumption, direct injection, and inhalation. The first thing that happens when particles enter systemic circulation is that they interact with proteins before being distributed to various organs. Once absorbed from blood capillaries, the particles can be further dispersed and eliminated via the lymphatic system. The system has three main goals; two of them are drug delivery. In the first stage of fluid recovery, fluids are filtered out by the blood capillaries through the lymphatic system. The second one is immunity; the system recovers excess fluids while absorbing chemicals and foreign cells from the tissues. As the fluids are filtered back into the blood, the lymph nodes identify any foreign objects that make their way through anything that macrophages perceive as alien will be taken up and removed from the body. This process can be affected by the shape and size of the particle. as shown in Figure 2 there are various ideal characteristics of nanoparticles.

1. Size of particle:

As the size of particles decreases, their surface area relative to volume increases. This suggests that a greater quantity of the drug is positioned nearer to the particle's surface compared to larger molecules. Being located at or near the surface would allow for a faster release of the drug. It's beneficial to create nanoparticle systems with a high surface area to volume ratio. However, it is important to check for toxicity regularly. As mentioned earlier, the size of the nanoparticle affects its biological behavior. Remember that the vascular and lymphatic systems help filter and remove foreign substances and chemicals. This is yet another consideration that needs to be factored into the design of the ideal nanoparticle system. Research has demonstrated that particles measuring 200 nm or more generally trigger the activation of the lymphatic system and are removed from circulation more rapidly. Therefore, based on the evaluation and discussion of the literature thus far, it appears that an optimal size for a nanoparticle is around 100 nm. At this size, the particle can traverse the blood-brain barrier, provide an adequate amount of drug delivery due to its high surface area to volume ratio, and evade prompt clearance by the lymphatic system.

2. Surface treatment:

The surface chemistry of nanoparticles, including their charge and the chemical groups they carry, plays a crucial role in their reactivity and can ultimately influence their functionality. Numerous nanoparticles have been altered to modify their surface chemistry for particular applications. You can change the surfaces of nanoparticles with different groups, like polymers, antibodies, or small molecules. This helps to target specific cells or tissues. It is crucial to assess the stability, specificity, and effectiveness of these modifications when designing the nanoplatform. The higher the hydrophobicity of a nanoparticle, the greater its chances of being eliminated because of the stronger interaction with blood components. Since hydrophobic nanoparticles are readily cleared, it seems reasonable to think that modifying their surface to become hydrophilic would prolong their circulation time. The surface of NPs can be modified to control their interactions with biological systems, such as by attaching targeting ligands or protective coatings.

3. Biocompatibility:

The material must exhibit biocompatibility, meaning it should not provoke any negative reactions in biological systems, such as inflammation, toxicity, or an immune response. Nanoparticles (NPs) can be designed to interact safely with biological systems, minimizing the chances of toxicity or immune responses. Biocompatible NPs can be utilized in many applications such as drug delivery, imaging, and tissue engineering.

4. Core integrity:

Certain nanoparticles, like iron oxide, are recognized for their high reactivity, so it is essential to ensure that the iron oxide core remains stable and does not degrade or form aggregates in biological environments.

5. Targeting ability:

NPs can be designed to specifically target tissues, cells, or intracellular compartments, which may lead to improved efficacy and safety in drug delivery or imaging.

6. Stability:

NPs such as metallic-organic frameworks are stable to different biological conditions and can provide stability during storage, allowing for longer-term storage and transportation.

TYPES:

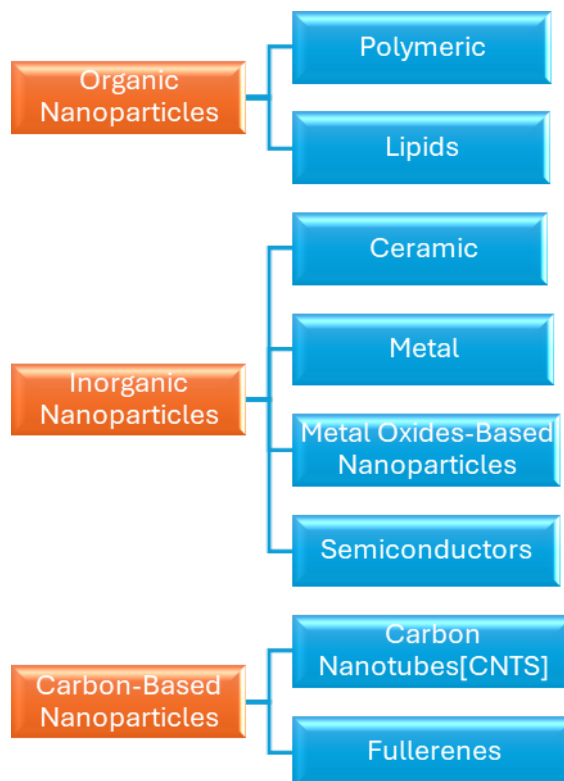


Figure 3 types of nanoparticles

As shown Figure 3 in Nanoparticles can be classified into different types. Here, we have covered various types according to their chemical composition. Based on this, they are classified into organic nanoparticles, inorganic nanoparticles, and carbon-based nanoparticles.

Organic nanoparticles:

This class of nanoparticles, which is more unstable due to its high sensitivity to heat and light, is comprised of proteins, carbohydrates, lipids, polymers, dendrimers, and other organic materials. Organic nanoparticles are often formed through non-covalent intermolecular interactions. These nanoparticles are usually biocompatible, genuine biodegradable materials, while others such as micelles, liposomes (as shown in Figure 4) have a hollow core structure.[5]

Most lipid nanoparticles are spherical and measure from 10 to 100 nm in diameter. Lipid nanoparticles are composed of a solid core with lipids and soluble lipophilic molecules in the matrix, while surfactants/emulsifiers stabilize the outer core. The use of this type of nanoparticle has been documented in the biomedical field, demonstrating a role in drug delivery and in RNA release in cancer care. In particular, lipid nanoparticles have shown Organic success as drug delivery vehicles, especially with poorly soluble oligonucleotides in gene therapy. Depending on the preparation method for the organic nanomaterials, polymeric nanoparticles can have different structures, such as nanocapsules or nanospheres, nanogels, or nanomicelles. Nanospheres can be thought of as matrix-like structures wherein the active compounds and polymer are uniformly distributed throughout the material. On the other hand, although the nanocapsule and nanosphere structures look similar, nanocapsules consist of a core-shell structure with polymer layers surrounding the active molecular located in the center of the nanoparticle. Some benefits of polymeric nanoparticles are controlled release, the ability to protect drug molecules during transport in the internal and external environmental, the ability to amalgamate therapy and imaging, and selectivity. Polymeric nanoparticles have been found to be most often in drug delivery and diagnostics than any others. The drug delivery systems with polymeric nanoparticles have the advantages of significant biodegradability and biocompatibility.

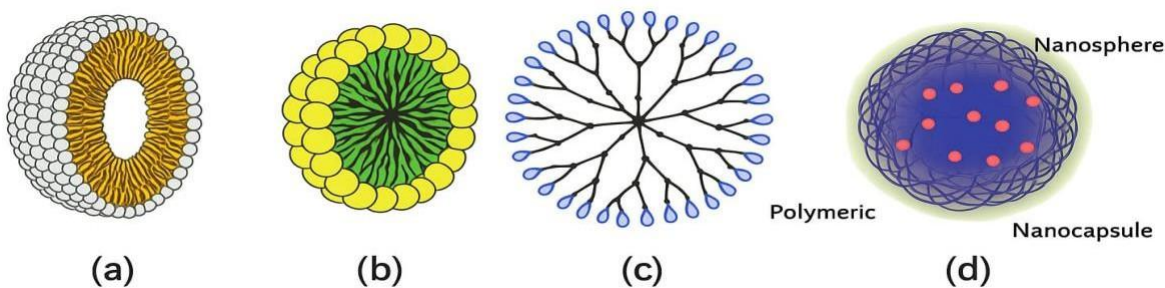


Figure 4 organic nanoparticles: (a) liposomes (b) micelles (c) dendrimers (d) polymers

Inorganic nanoparticles:

Inorganic nanoparticles are also called as non-carbon-based nanoparticles. This group of nanoparticles are not carbon-based or organic-based. They can be further classified into three groups: ceramic, metal, metal oxides-based nanoparticles, and semiconductor.

Ceramic nanoparticles (shown in Figure 5) are generally identified as having oxides, carbides, carbonates and phosphates. They exhibit high thermal and chemical resistance and are used in photocatalysis, photodegradation of dyes, and biological imaging. Ceramic nanoparticles are especially beneficial in drug delivery applications. When you can control several properties like size, surface area, surface area to volume ratio and porosity, these nanomaterials can be effective drug delivery methods. The various biomedical fields have reported ceramic nanoparticles as drug delivery systems for various disease treatment including bacterial infections, glaucoma, and sometimes cancer. More recently, researchers have developed these nanoparticles for use in bone repair.

Metal nanoparticles (shown in Figure 5) are a category of nanoparticles formed from metal precursors, which can be synthesized using chemical, electrochemical, or photochemical methods.

In the chemical methods, the metal nanoparticles are formed from the chemical reduction of metal-ion precursors in solution with chemical reducing agents. The resulting nanomaterials have high energy at the surface and are capable of selectively adsorbing small molecules.

The most common types of metal nanoparticles are silver, gold, palladium, titanium, zinc, and copper nanoparticles.

Metal nanoparticles are applied in different areas of research including biomolecule detection and imaging, environmental and bioanalytical applications, and many more. Gold nanoparticles are used to coat samples before scanning electron microscopy (SEM) analysis to increase SEM and quality electron microscope images.

Metal nanoparticles play an important role in drug delivery by providing a platform for delivery of a variety of therapeutic agencies, including antibodies, nucleic acids, peptides, and more.

Due to their plasma resonance characteristics, metal nanoparticles possess unique optoelectrical properties. The characteristics of metal's nanoparticles, shape, facet, and size define their synthesis. All of the metal's nanoparticles are synthesized. The examples include well-known metal nanoparticles of aluminium, gold, iron, lead, silver, cobalt, zinc, and copper. Besides their small size (10–100 nm), surface properties (surface area to volume ratio, surface charge, pore size, and surface charge density), shapes (spherical, rod, hexagonal, tetragonal, cylindrical, and irregular), color, and environmental factors (microbes, sunlight, moisture, air, and heat) all contributed to their unique properties of the nanoparticles.

NPs made from metals that can be converted into their Oxides are called Metal oxides-based NPs (shown in Figure 5). Compared to their metal counterparts, NPs from metal oxides have special features. Further examples of some Metal oxide-based NPs include; magnetite and iron oxide (Fe_2O_3) (Fe_3O_4), silicon dioxide (SiO_2), titanium, aluminium oxide (Al_2O_3), cerium oxide (CeO_2) Titanium dioxide (TiO_2), zinc oxide (ZnO), These NPs depend on discovered metal oxides that are found to have more responsiveness and efficacy.

Semiconductor nanoparticles (shown in Figure 5) consist of nanoparticles with characteristics of metals and non-metals and can be found in groups II-VI, III-V or IV-VI of the periodic table. These types of nanoparticles exhibit wide bandgaps that when tuned exhibit varied properties. Some examples of semiconductor nanoparticles are GaN, GaP, InP, InAs from group III-V; ZnO, ZnS, CdS, CdSe, CdTe are II-VI semiconductors while silicon and germanium are group IV.

Applications of semiconductor nanoparticles include photocatalysis, electronics devices that are found in computers, cell phones, television remote controls and satellite/cable dishes, nanophotonics, or applications based on water splitting.[6]

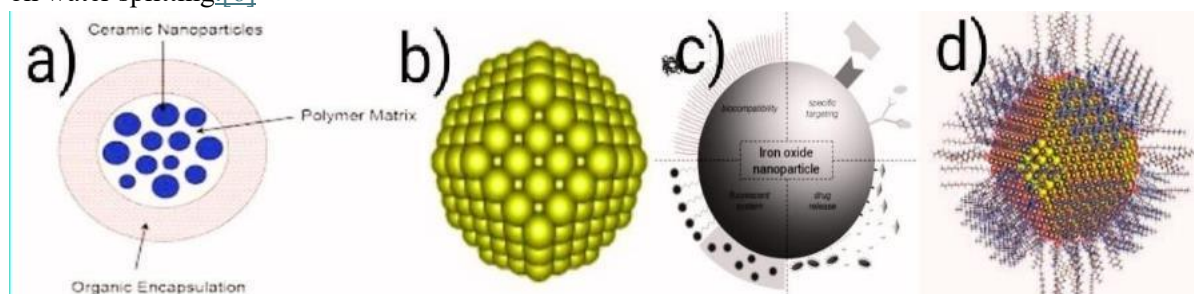


Figure 5 inorganic nanoparticles (a) ceramic NPs (b) Metal NPs (c) Metal oxide-based NPs (d) semiconductor NPs

NPs can be used in a long list of applications due to their unique physical and chemical properties that do not exist in their larger-dimension counterparts of the same materials

Carbon-based nanoparticles:

As per the name, they are made from carbon atoms that is why they are called carbon-based nanoparticles. The two most recognized types of nanoparticles in this group are carbon nanotubes (CNTs) and fullerenes (as shown in Figure 6). These nanoparticles are primarily used for reinforcement applications because they are extremely strong- in fact, sometimes 100 times stronger than steel.

CNTs can be described in terms of single-walled carbon nanotubes (SWCNTs) or multi-walled carbon nanotubes (MWCNTs). CNTs are also very important in nanotechnology because of their length to diameter ratio-is greater than 1,000,000! They can be very interesting in terms of their conductivity- they are thermally conductive in the length direction and not conductive across the tube.

Fullerenes are carbon allotropes that are arranged in a hollow cage-like structure (of sixty or more carbon atoms). Buckminster fullerenes are made of 60 carbon atoms in a hollow, football-like shape. The carbon atoms in these

materials are arranged in a combination of both pentagonal and hexagonal arrangements, and have their own wide variety of applications.[7] Because of their electrical conductivity, structure, high strength, and the ability to accept electrical charges, fullerenes have been used in many commercial applications. So far, CNTs have already been used to build transistors, aircraft, sensors and biosensors, as well as delivery vehicles for drugs, batteries, and energy storage devices. CNTs are also used to reinforce concrete, and to remediate water.

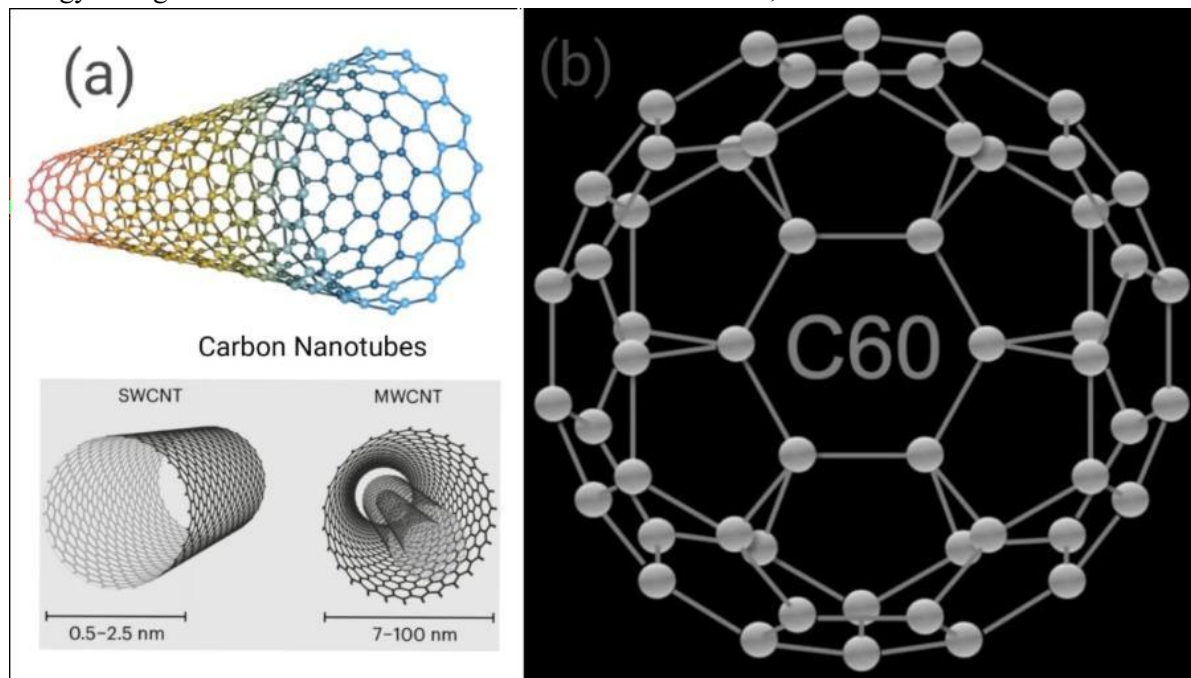


Figure 6 carbon-based nanoparticles (a) carbon nanotubes (CNTs) (b) fullerenes

APPLICATIONS:

Every specialty of medicine has begun to take an interest in Nanoparticles because they can deliver drugs in the eventually optimum dosage range, often leading to greater therapeutic efficacy of the medication, reduced side effects, and improved patient adherence. Nanoparticles (NPs) have distinct and improved physical and chemical properties, which are useful in various applications across different fields. NPs are appealing to various applications in the environment because of their small size and unique physical and chemical properties. Material properties can be positively affected by nanotechnology that can strengthen and lighted the material, make it more durable, make it more reactive, make it more sieve-like, or create better electrical conductors.

Applications in drug and medications:

Nano-sized inorganic particles, which can be either simple or complex, display unique physical and chemical properties and represent an increasingly important class of materials in the growth of new nanodevices that can be used in many physical, biological, biomedical and drug delivery applications. Metallic and semiconductor nanoparticles (NPs) have enormous potential for cancer diagnosis and therapy through their enhanced light scattering and light absorption properties as a result of the LSPR effect. For example, Au NPs can efficiently absorb light and convert that energy into localized heating of the NP, which can be utilized for selective photothermal therapy of cancer (i.e., cancer cell death via heating of tumor tissue). Gd based NPs also showed great promise as a therapeutic agent for tumor growth inhibition, metastasis inhibition, and tumor-specific enhancement for magnetic resonance imaging. Moreover, Au NPs exhibit special optical properties that makes them a promising candidate for photodynamic therapy of cancer (the use of a light activated drug to kill cancer cells). Targeted drug delivery is another potential important application of NPs. For example, ZnO and Fe₃O₄ NPs were effectively used for targeted drug delivery and selective killing of tumor cells. [8]. The advancement of hydrophilic NPs as drug delivery systems has posed a major challenge over the past few years. Among the various approaches, polyethylene oxide (PEO) and polylactic acid (PLA) NPs have been demonstrated to be very promising systems for delivering drugs via the intravenous route. Furthermore, NPs have been utilized in various medical applications including cellular imaging, biosensors for detecting DNA, carbohydrates, proteins, and heavy metal ions, blood glucose levels, and medical diagnosis to identify bacteria and viruses. For example, Au NPs were conjugated with SARS-CoV-2 antigens for the rapid, 10–15 min detection of SARS-CoV-2 IgM/IgA antibodies in blood samples. In addition, due to their antimicrobial and antibacterial properties, NPs such as TiO₂,

ZnO, CuO, and BiVO₄ are increasingly being utilized in many medical products including catheters.

Because they can protect against degradation, target specific sites of action, and minimize toxicity or other side effects, liposomes have emerged as a possibility as an alternate method of drug delivery rather than conventional dosage forms. But sadly, the activity of development liposome drugs has been limited due to associated health concerns like very low encapsulation efficiency, quickly leaking into blood components, very poor storage, and stability over time. In addition, polymeric NPs have certain advantages over the liposomes mentioned above. For example, NPs would increase the traversability of drug or material and offer desirable benefice-controlled drug release behavior as well.

In the last two or three decades, there has been some interest in developing biodegradable NPs as impactful drug delivery vehicles. Many polymers have been studied in drug delivery research because they effectively deliver drugs to the targeting site thus increasing therapeutic benefit and reducing side effects. The controlled release of a pharmacologically active drug at the precise site of action, at the therapeutically optimum degree, and dosing regimen, has been a major goal of designing such devices.

It is also used in tissue engineering. Nanoparticles (NPs) can facilitate the growth and repair of tissues and organs. Specifically, titanium dioxide nanoparticles (TiO₂ NPs) have been studied for tissue engineering applications due to an observed growth promoting effect on bone cells.

Certain NPs, including silver nanoparticles (AgNPs) and copper nanoparticles (CuNPs), display potent antimicrobial characteristics and are being investigated for incorporation into the wider array of medical products including wound dressings and medical devices.

In conclusion, NPs display an exciting possibility to be utilized in medicine and are currently under investigation for numerous applications. Nevertheless, the potential risks and benefits of applications of NPs in medicine should always be appropriately highlighted and managed to support safe and responsible usage.

Application of nanoparticles in treatment of kidney diseases:

Nanoparticles have been integrated into treatments for urology and nephrology concerning kidney diseases. Ferumoxytol has been combined with nanoparticles for individuals suffering from chronic kidney disease or end-stage renal disease when their bodies no longer produce enough erythropoietin. Since many such diseases originate in this area, PEGylated gold nanoparticles can be directed to the mesangium, which comprises specific contractile cells that form the main body of the glomerulus in the kidney. Rhein, an anthraquinone derivative utilized for treating diabetic nephropathy and other kidney-related conditions, has been repurposed to enhance its therapeutic effects through nanoparticle technology. Nanoparticles incorporating Rhein were developed using triblock amphiphilic polymers, particularly polyethylene glycol-co-polycaprolactone-co-polyethylenimine. The nanoparticles measured about 75 nm in size, which is considered optimal for delivering drugs specifically to the kidneys. The results demonstrated that both the distribution of the drug to the kidney and its therapeutic effects were improved.

Application in cancer therapy:

The therapies currently employed to treat cancer patients have successfully saved numerous lives; however, the adverse effects of these treatments can be severe, impacting the entire body due to the lack of specificity of chemotherapeutic agents. Cancer is an intricate biological condition and can be regarded as a collection of various diseases. One key characteristic of cancerous cells is their propensity to divide and multiply uncontrollably. Presently, chemotherapy primarily targets all rapidly dividing cells for destruction. The drawback of this approach is that it also eliminates other swiftly proliferating cells in the body, such as those found in hair follicles and the intestinal lining, causing patients to endure significant life-altering side effects. The introduction of nanoparticles has opened up a new path for chemotherapy. With carefully engineered nanoparticles, the targeted delivery of drugs to the tumor site or specific groups of cells can largely circumvent the toxic impact on other healthy tissues and organs. Various systems have been explored and tested to provide this type of therapy.

Dendrimers are complex macromolecules characterized by extensive branching and numerous functional groups that can attach to drug, targeting, and imaging agents. The absorption, distribution, metabolism, and elimination (ADME) profile of these molecules relies on several structural characteristics. Nanoparticle therapies utilizing dendrimers have the potential to enhance the therapeutic effectiveness of cytotoxic medications by incorporating biocompatible elements, as well as through surface modifications like PEGylation, acetylation, glycosylation, and various amino acids.

Bioavailability is one of the concerns in cancer therapy. Micelles and liposomes provide an alternative strategy to

deliver chemotherapy. Micelles also are effective in solubilizing insoluble drugs because of the hydrophobic core and hydrophilic surface. When micelles are additionally PEGylated on their surface, the micelles can passively transport through the fenestrated vasculature in tumors and inflamed tissues, increasing the concentration in tumors. Currently, there are several polymeric micelles with anti-cancer therapies, such as NK012, NK105, NK911, NC-6004, and SP1049C, listed in clinical trials, and Genexol-PM (paclitaxel) has been approved for breast cancer patients. [9]

Application of nanoparticles in treatment of skin diseases:

Polymeric nanoparticles (PNPs) are extensively adopted nanoparticles for delivering therapeutics transdermally. PNPs derived from chitosan and alginate could treat acne, and they demonstrated enhanced antibacterial efficacy against *Propionibacterium acnes* compared to benzoyl peroxide alone. Aside from polymeric nanoparticles, electrospun fibers have high surface area-to-volume ratio, to allow for dispersion of both hydrophobic and hydrophilic drugs and therefore function well for topical administration.

Liposomes, solid lipid nanoparticles (SLN), and nanostructured lipid carriers (NLC) bind to skin surface and facilitate lipid transfer between the outer most layers of stratum corneum and the carrier thereby improving drug absorption. Glucocorticoids and T-cell suppressors, cyclosporin and tacrolimus have been used to treat inflammatory skin conditions, psoriasis and atopic eczema, in lipid-based carrier systems. Modifying surface of SLN with retinyl palmitate improved cutaneous dispersion compared to neutral SLN. Newer studies suggest adding retinol into Compritol based SLN increased release rates or drug compared to conventional carriers.

Application of nanoparticles in HIV and AIDS treatment:

Untreated human immunodeficiency virus (HIV) infection can develop into an incredibly serious condition called acquired immune deficiency syndrome (AIDS), in which a person's immune system is severely compromised. When the first antiretroviral treatment for the disease was released, individuals were required to take as many as thirty to forty pills daily. As mentioned, much has changed in the area of HIV/AIDS research over the past ten years, and at present, individuals take only a few pills each day. The research noted above describes a method for providing ARV drugs both intracellularly and to the brain via polymeric nanoparticles. In addition to this potential of polymeric nanoparticles in enhancing and developing treatments, there is also potential to harness the power of polymeric nanoparticles in conjunction with HIV vaccines to prevent HIV infection.

Drugs aimed at treating HIV can be divided into different classes based on what stage of the HIV lifecycle they work in efficiently. The incorporation of nanotechnology has played an important role in improving the delivery of antiretroviral drugs and enhancing patient compliance. Studies have indicated that nanoparticles carrying an antiretroviral drug can specifically target monocytes and macrophages in vitro. The central nervous system (CNS) also represents another area where HIV can infect and replicate, leading to serious HIV-associated neurocognitive disorders (HAND). It is known that nanoparticles can cross the blood-brain barrier (BBB) and enter the CNS through endocytosis or phagocytosis, and many publications have demonstrated their successful use in delivering anti-HIV medication. [9]

Medical and Healthcare applications:

Nanotechnology is already expanding the range of medical tools, knowledge, and therapies available to clinicians. Nanomedicine refers to the use of nanotechnology in medicine, and it leverages the natural scale of biological phenomena to develop effective measures to prevent, diagnose, and treat disease.

Nanotechnology is causing a significant advancement in imaging and diagnostic modalities, allowing for more timely diagnosis, more individualized treatment options, and higher rates of therapeutic success. The use of nanotechnology is currently being investigated for the diagnosis and treatment of atherosclerosis (the build-up of plaque in arteries). In one instance, the researcher created a nanoparticle that mimicked the body's "good" cholesterol known as HDL (high-density lipoprotein), which assists in reducing plaque.

Commercial applications have employed gold nanoparticles as probes for detecting targeted nucleic acid sequences. Additionally, gold nanoparticles are being studied clinically as a potential treatment for cancer and other diseases. Researchers in the field of nanotechnology are working on several therapeutics, in which a nanoparticle can encapsulate or assist in delivering medication straight to cancer cells while minimizing the possibility of harm to healthy tissue. This could fundamentally change how doctors treat cancer and reduce the toxic effects of chemotherapy significantly.

Research on the use of nanotechnology in regenerative medicine has emerged in several application areas, such as bone engineering and neural tissue engineering. For example, new materials can be designed to produce a

crystal mineral structure like that of human bone, or as a restorative resin for dental applications. There is also ongoing research to figure out ways to grow complex tissue, which may one day be able to develop human organs for transplant. Researchers are even evaluating the potential use of graphene nanoribbons for spinal cord repair. Early research shows that neurons grow in good conditions when placed on a conductive graphene surface. Nanomedicine research is investigating whether nanotechnology can help improve vaccinations, such as enabling needleless delivery of vaccines, as well as design a universal scaffold for the annual flu vaccination that includes more strains of the flu virus and requires less development for each ensuing year. [10]

Applications in electronics:

NPs have numerous potential uses in imaging applications or electronics because of their new electronic and optical properties. For example, NPs based on Gd aid in the quality of imaging and agent dose for administration of the contrast agent in MRI. For instance, Gd₂O₃ NPs as a contrast agent was even found to be more efficient than Gd-DOTA, the standard agent use, when used in the same concentration. At the same time, GdPO₄ NPs were also effective at detecting tumors with MRI with 1/10 of the dosage required for Gd-DTPA agent. Once again, NPs even allow for the imaging and tracking of a single molecule where significant insight regarding cellular processes such as organization of membrane proteins or interaction with other proteins, for instance, was derived from tracking a single toxin receptor with an Eu³⁺-doped oxide NP with a localization precision of 30 nm.

Application of nanoparticles in vaccination against COVID-19

Since early on in 2020, and continuing to the present, scientists and researchers have been invested in a special focus on developing therapeutics to address the global outbreak of COVID-19 virus infections. During 2021, the importance of using nanoparticles in designing therapeutics to recognize, to treat, and to promote lasting human immunity to COVID-19 was noted. The critical piece of information that hastened the research and development of COVID-19 nanoparticle-based vaccines (CNPBV) was the described genomic structure of coronaviruses and the previously recognized sequence of the proteins that form the surface of the virus.

The spike proteins of COVID-19 virus attached to the outer surface of the virus are known to have a high binding affinity towards nano-formulations, as well as an affinity to bind to the human host cell receptors. The spike protein played an important role in the development of CNPBV. A novel vaccine developed with the use of nanotechnology received Food and Drug Administration (FDA) approval and has had tremendous efficacy in preventing COVID-19 in a vaccinated population, and resulted in 90% efficacy amongst many vaccine variants that were moderately efficacious in helping to control and decrease the global spread of the COVID-19 pandemic. The two examples of vaccines are the Pfizer-BioNTech (BNT162b2 vaccine) and Moderna (mRNA-1273 vaccine). The Pfizer-BioNTech (BNT162b2) and Moderna vaccine (mRNA-1273) utilize mRNA to encode the spike glycoprotein (S) of the COVID-19 virus by encapsulating the modified mRNA (coding for the virus's glycoprotein) into lipid nanoparticles. The encapsulation of the modified mRNA prepares and delivers the protein antigen (spike protein) to immune cells, activating T cell activity and inducing antibody immune responses to form in the human body. [11].

DRUG SELECTION CRITERIA:

When it comes to the development of a successful nano-drug delivery system, the selection of an appropriate drug for the nanoparticle formulation is one of the most important steps. Some drugs are not as suitable for formulation into a nanoparticle as others, since the physicochemical properties of the drug, along with its biopharmaceutical properties, impact the formulation's performance, stability, and overall efficacy. Appropriate drug selection helps ensure high encapsulation efficiency, controlled release, and increased bioavailability, which is key for the successful development of nanomedicine.

Physicochemical properties:

When formulating with nanoparticles, the physicochemical properties of the drug will be the first and most thought about parameters. When using nanoparticles, we prefer drugs that have low to moderate molecular weight and usually have molecular weight of lower than 1000 Da because of easy encapsulation and effective diffusion across biological membranes. One of the main advantages to using nanoparticles is the increased solubility of drugs that have low water-solubility or lipophilicity. Therefore, these drugs are considered ideal candidates for nanoparticle-based drug delivery approaches, as nanoparticles can dramatically improve their dissolution rates and bioavailability. It is also worth noting that stability of the drug in both chemical and physical formulations and storage must be considered to ensure no degradation during processing occur. In terms of encapsulation, the partition coefficient (Log P) ideally is between 1 and 3 to ensure the drug has a

balance of hydrophilic and lipophilic properties necessary to interact with both the aqueous and lipid phases of the nanoparticle carrier. The melting point of the drug must also be considered; compounds with melting points that are too high might have low entrapment efficiency, which would lend to poor drug loading into a nanoparticle formulation.

Pharmacokinetic and biopharmaceutical factor:

Both pharmacokinetic and biopharmaceutical means the same in drug selection. However, drugs with poor bioavailability, significant first-pass metabolism, or short biological half-life will benefit from nanoparticle systems the most. Nanoparticles will either enhance absorption, escape hepatic metabolism, and provide sustained or controlled release dosing. Likewise, drugs requiring site-specific delivery (anticancer, antiviral, brain-targeting) will also benefit from nanoparticle formulations, enhancing drug concentration delivery while limiting systemic side effects.

Therapeutic and clinical aspect:

From a therapeutic perspective, potent medications are preferred in the context of nanoparticles, as low dosing tends to produce clinically relevant therapeutic impact when administered to the site of action. Drugs with a narrow therapeutic index or dose-dependent toxicity can also benefit since nanoparticles can mediate release and maintain more stable drug concentrations in plasma, thereby decreasing toxicity.

Compatibility with carrier material:

Another critical aspect is the compatibility of the drug with carriers, which are polymers, lipids, or surfactants. The drug should not chemically react with the excipients, as these interactions may compromise stability and/or efficacy. Also, drugs with potential for controlled or stimuli-responsive release are ideal for inclusion into drug delivery systems using nanoparticles.

In conclusion, all of these are important to ensure the nanoparticles improve therapeutic efficacy and reduced toxicity, which will ultimately lead to better patient compliance.

COMPOSITION/EXCIPIENTS:

Liposomes:

Liposomes are also categorized to four types due to their structure based on number and amount of bilayers present: small unilamellar vesicles (SUV), large unilamellar vesicles (LUV), multilamellar vesicle (MLV), and multivesicular vesicles (MVV). With respect to only hydrophilic molecules, the encapsulation of liposomes is negatively correlated to liposome bilayers and positively correlated to size. The amount of medicine encapsulated by liposomes is based on both the size and number of bilayers. The optimum range for drug delivery using liposome is typically 50 to 150 nm in size. Many variables influence liposome-cell interactions, such as composition, liposome diameter, surface charge, the presence of a targeting ligand on the liposome surface and the biological but biological environment.

Liposomes can be produced from both synthetic and natural phospholipids. Liposome composition has a significant influence on particle size, rigidity, fluidity, stability, and electric charge. In structure, liposomes are spherical or multi-layered spherical vesicles that form when diacyl-chain phospholipids, or lipid bilayer phospholipids self-assemble in aqueous media. The bilayer phospholipid membrane is composed of a hydrophobic tail and a hydrophilic head, yielding an amphiphilic structure

1. Natural lipids:

Glycerophospholipids are the most prevalent component of membrane bilayers in normal cells. Phospholipids consist of two fatty acids and the glycerol unit is attached to a phosphate group (PO_4^{2-}). Furthermore, the phosphate can form an additional bond to the small, important chemical which is choline. Natural sources of phospholipids include egg yolks and soy beans. The hydrocarbon chain of natural phospholipids, being unsaturated, means that they are not as stable as synthetic phospholipids during liposome formation. Along with unsaturated fatty acids, palmitic acid (hexadecanoic acid, $\text{H}_3\text{C}-(\text{CH}_2)_{14}-\text{COOH}$) and margaric acid (heptadecanoic acid, $\text{H}_3\text{C}-(\text{CH}_2)_{15}-\text{COOH}$) are examples of saturated fatty acids in natural phospholipids for example, egg yolk lecithin contains the unsaturated fatty acid oleic acid (9Z-octadecenoic acid). Egg phospholipids and PCs contain the fatty acid patterns of palmitic (C16:0), stearic (C18:0), oleic (C18:1), linoleic (C18:2) and arachidonic (C20:4) acids; and about 95% of the soybean derived fatty acid pattern consists of palmitic (C16:0), stearic (C18:0), oleic (C18:1), linoleic (C18:2) and linolenic (C18:3) acids.

2. Synthetic lipids:

Synthetic phospholipids are formed after the chemical modification of the polar and non-polar sections of natural phospholipids. The modification will give rise to an endless array of unique and classified phospholipids. Saturated synthetic phospholipids primarily come from stearic and/or palmitic fatty acids.

3. Surfactants:

Surfactants altered a liposome's encapsulation and release properties by decreasing the surface tension between disparate immiscible phases. Surfactants are single acyl-chain amphiphiles that improve the deformability of nanovessels by disrupting the lipid bilayer of liposomal nanoparticles. The surfactants commonly used in liposome formulations include sodium cholate, span 60, Span 80, Tween 60, and Tween 80. The provision of surfactants to liposomes has been employed to enhance skin penetration of encapsulated pharmaceuticals. Transfersomes, or ultra deformable liposomes, are surfactant-based nanovesicles that have been investigated for potential use in transdermal delivery of drugs. Edge activators (surfactants) are the major component responsible for the deformation of liposomes. Edge activators can change the lipids in the vesicle's bilayers to be less rigid. Unlike traditional liposomes, these nanovesicles can respond to osmotic pressure and perform rapid shape change with less energy. Ultra deformable liposomes demonstrated increased drug transepidermal flow, making it a better nanovehicle for supplying topical antihypertensive medications. [12]

Solid-lipid nanoparticles:

SLNs consist of a solid lipid, an emulsifier, and water/solvent. Any solid lipid can be used: Triglycerides (tristearin), partial glycerides, fatty acids (stearic acid, palmitic acid), steroids (cholesterol), and waxes (cetyl palmitate) are all candidates as lipids. The lipid dispersion has been stabilized with various emulsifiers and their combinations (Pluronic F 68, F 127). The combination of emulsifiers can be more effective in preventing particle agglomeration. The lipids employed in the SLN lipid matrix are physiological lipids that allow a lower risk of acute and chronic damage. Several emulsifiers are suited for parenteral delivery based on the delivery method.

Nanostructured lipid carriers (NLCs):

The nanostructured lipid carriers (NLCs) are generally composed of lipids which can be solid as well as liquid, surfactants, organic solvents and other agents like counter-ions and surface modifiers.

1. Lipids:

Lipid is the primary element of nanostructured lipid carriers and provides the formulations' stability, sustained release, and drug-loading potential. NLC has been developed from solid lipids including fatty acids, triglycerides, diglycerides, monoglycerides, steroids, and waxes. The selection of a lipid is important before it is used to create nanocarriers. The specifics of the lipid type and structure will influence various characteristics of nanocarriers. The most practical criterion for selecting a lipid is the solubility or apparent partition coefficient of the bioactive in the lipid. The solubility of drug molecules in lipid is important because it will influence drug loading and the encapsulation efficiency. Other lipid factors which may impact the quality of NLC include the appearance of lipid crystals, the hydrophilicity of lipids, and changes in composition variability.

2. Surfactants:

Both the types and levels of surfactant influence the activity and quality of NLC. The decision of surfactant is a major factor influencing the toxicity, physical stability, and crystallinity of NLC. Surfactant systems also affect the drug permeation rate and the extent of drug dissolution. Surfactants are selected based on their effect on particle size, lipid modification, hydrophilic-lipophilic balance (HLB) value, and route of administration. Surface active agents (emulsifiers) are amphipathic molecules that adsorb at the interface by reducing the tension between the lipid and aqueous phases. While forming NLC, the crystallization of colloid particles takes place simultaneously with solidification, however the surface area of the phases increases markedly as crystallization occurs and this phenomenon globally destabilizes the system.

3. Other ingredients:

To overcome the challenge of encapsulating water-soluble active pharmaceutical ingredients, organic salts and ionic polymers can function as counter-ions during the nano structural carrier formation. Surface-modifiers represent a different excipient class used in the formation of nano-lipid carriers (NLC) to limit the phagocytosis of NLC by macrophages of the reticuloendothelial system (RES). Lipid particles can be coated with hydrophilic polymers, such as PEG, poloxamines, or poloxamers to prolong the amount of time active pharmaceutical ingredients remain in the body's systemic circulation. Another advantage of surface modification may include improved biocompatibility and physical stabilization, targeted medication delivery, and improved transportability

across epithelium. [13]

Dendrimers:

Dendrimers are relatively new types of three-dimensional, hyperbranched, monodispersed polymers with a central core, branches, and terminal functional groups attached to the branches. Their large interior cavities, functionalized surfaces incorporating various chemical groups for extensive modification, and good biocompatibility make them excellent drug delivery vehicles. Dendrimers are also more precise in molecular weight, are more water-soluble, and possess biocompatibility with polyvalency compared to conventional polymers. The dendrimers that have been made and used as drug delivery vehicles for natural products include polyamidoamine (PAMAM), polylysine (PLL), polypropylene (PPI), and polyglycerol (PG). These dendrimers can be used to target drug delivery through a variety of routes, including oral, ophthalmic, intravenous, subcutaneous, and intraperitoneal.

Dendrimers administer drugs in two distinct ways. The first is through non-covalent interactions, in which drugs are covalently bound to dendritic polymers, and the covalent bond is usually a cleavable functional group such as esters, amines, or carbamates that can be used to rapidly and effectively control drug release. The second is through covalent interactions, in which drugs are covalently linked to dendritic polymers, which keeps the drug available and protected upon reaching its target location and helps increase bioavailability. [14]

Polymeric nanoparticles:

The solubility and oral bioavailability of active pharmaceutical ingredients (APIs) can be limited when presented as classic solid positioned dosage forms (e.g., oral tablets). However, the encapsulation of an API in a functionalized polymeric nano-structure has shown to be a unique delivery option which could improve therapeutic effect by prolonging the half-life of the drug while also lowering toxicity. Polymeric core-shell nanoparticles (NPs) are a new and exciting class of nano-carriers that could facilitate API encapsulation by way of accumulation of the API in a hydrophobic polymeric decadence established as part of the core.

Poly(lactic acid)-poly(ethylene glycol) (PLA-PEG) polymer nanoparticles have been extensively investigated as vehicles for anticancer drug delivery. PLA is commonly used as a drug carrier. To improve dispersion stability and blood circulation time of the NP form, hydrophilic PEG is required to modify the PLA surface, which is hydrophobic and not easily dispersible in water. Emulsion solvent separation or emulsion solvent diffusion methods are often employed to prepare PLA-PEG NPs. There are several examples in the literature of PLA-PEG-based NPs efficiently encapsulating and conjugating multiple active pharmaceutical ingredients (APIs), including peptides, nucleic acids, and chemotherapeutic agents. [15]

All the excipients used in composition should be non-toxic and approved for pharmaceutical use. Excipients must support sterilization especially for parental formulations. They must be listed in pharmacopeia or have GRAS (generally recognized as safe) status.

MANUFACTURING:

Nanoparticles are manufactured using two techniques.

Top-down method:

Using the top-down method, a bulk material, or larger particles, undergoing many methods in producing nanoparticles. Examples of the methods are:

Mechanical attrition Nanolithography

Laser ablation sputtering

The methods described above are typically implemented to convert a bulk material into powder and then take that powder and use it to produce nanoparticles. [16]

1. Mechanical attrition:

Mechanical attrition (MA) is a technique that was introduced in the industrial realm for the preparation of powders for new alloys and phase mixtures that has evolved since the 1970's. It allows to solve the limitations on quantity for the preparation of nanocrystals and obtain nanocrystalline powders in large volumes. MA offers many possibilities to develop different kinds of structures in nanostructured powders, such as crystalline/crystalline and crystalline/amorphous, or different atomic bonds such as metal/metal, metal/semiconducting or metal/ceramic. One major advantage of the mechanical attrition process is that it can be performed at low temperatures and the resultant grains newly formed will grow at very low rates. The ability to produce engineered advanced materials with specific grain structures or designs at an interface boundary can all be realized through this method. Two methods for making nanopowders via mechanical milling have been developed. The first method can be achieved

by milling a single-phase powder in an interstitial balance point between fracturing and cold welding to avoid excessive cold welding of particles larger than 100 nm. The grain size is reduced from 50–100 μm to 2–20 nm. Mechanical attrition is especially sensitive to contamination, although controlling the atmosphere allows chemical reactions to take place between the powders being milled and the atmosphere. This has led to an innovative, and cost-effective practice to create various types of nanopowders which is referred to as Mechanochemical Processing (MCP), considered to be the second of the mechanical attrition process. A standard ball mill is an example of MCP where it can function as a chemical reactor at low temperatures.

2. Nanolithography:

Nanolithographic methods are appropriate for the fabrication of one-dimensional nanostructures, nanocatalysts, semiconductors, and more. Methods include electron-beam or focused-ion-beam writing, proximal probe patterning, X-ray lithography, etc. In addition, nanolithography employs dry and wet etching for fabrication purposes. Furthermore, 'lithography' within the context of nanostructure fabrication should be interpreted as not just a top-down process but also as bottom-up assembly. Via nanolithography, nanostructures, or arrangements of nanostructures, can be produced in a directed growth technique or can be constrained growth between one to a few nanometers. These methods are advantageous in that they can yield significant quantities of one-dimensional nanostructures from a large variety of available materials.

Template fabrication is one of the most widely recognized and possibly the least costly methods for nanolithography, employing templates on the order of nanometers. This technique is well suited to the growth of nanowires, via electrodeposition to take advantage of the nanopore, sol-gel, or in a vapor phase. Since the templates can be removed from the wire, it allows for independent controls of the structures. First, templates of ordered nanopores must be fabricated, then the pores can be filled with the desired material either via electrodeposition, sol-gel, or in a vapor phase.

SPM-based nanolithography is a recognized technique for fabricating nanometer-scale patterns. The method has been used to pattern metallic and semiconducting surfaces. The patterns can then be transferred to a substrate, in a fashion analogous to optical or electron beam lithography. This technique is suitable for nanoelectronic device fabrication. One major advantage of SPM-based lithography is that the same SPM can be used to generate the traces and then subsequently image them.

3. Laser ablation sputtering:

The laser ablation process has two critical components: a high-powered laser that utilizes an optical focusing system and an apparatus to employ the metal target. The laser beam is focused upon the target surface and the laser causes a supersonic jet of vaporized material to be expelled orthogonally from the surface of the target in the form of a vapor plume. The vapor plume then expands into the surrounding gas environment, and the resultant particles are carried by the carrier gas to the collector for products. The major advantage of the process is the ability to use metals and metal oxides as precursors, and to produce materials with high crystalline quality. The density of the particles and their size-distribution depend on the condition used in the ablation chamber (e.g., ambient air, argon, and water), the target material and the operating conditions of the laser (e.g., wavelength, pulse duration, energy, repetition rate, scanning speed of the beam, etc.). (manufacturing nanomaterials).

Bottom-up method:

The bottom-up approach to synthesizing nanoparticles consists of atoms coming together to form larger particles (a cluster) of small parts, which in turn come together to give rise to nanoparticles. There are many means of bringing together the small particles to form larger particles.

Sol-gel method Hydrothermal method Electrochemical deposition Spinning

Pyrolysis

Chemical vapor deposition

These are the means of converting atoms into nanoparticles. The following figures illustrate the bottom-up approach of nanoparticle synthesis.[\[17\]](#)

1. Sol-gel method:

The method is to chemically turn a sol into a gel. This method is often used to make metal oxide nanoparticles. The following are the steps involved in this procedure.

The method is to chemically turn a sol into a gel. This method is often used to make metal oxide nanoparticles. The following are the steps involved in this procedure.

Preparation of SOL:

Metal salts, or organic materials, are dissolved in a suitable solvent. The resulting solution contains the compounds acting as precursors to give you the nanoparticles.

Hydrolysis:

A hydrolyzing agent, or water, is added to the sol. This hydrolyzing agent is responsible for breaking the precursor molecules down to form a gel network.

Condensation:

The hydrolyzed products then condense, combining smaller nanoparticles into larger nanoparticles. Also, during this time, water and/or other byproducts would be removed.

Aging:

The network that is created is allowed to age. Ageing improves the structure of the network, such as crystallinity and uniformity.

Drying:

The gel is dried using various methods, such as freeze-drying. **Calcination:**

The final product undergoes high temperatures to remove any organics in the material, and this grows the particles. This method is cost-effective and easy to control the shape and sizes of the particles. These characteristics make them applicable for both research and industrial applications.

2. Hydrothermal method:

This is the bottom-up approach for making nanoparticles. This is a procedure that produces the nanoparticle under high temperature and pressure conditions in aqueous media. The steps in the process are:

Preparation of solutions:

Metal salts or other chemical precursors that are easily soluble in the solvent (often water) are prepared as a solution, or precursor solution.

Heating and packing:

The pressure vessel is sealed with the reaction mixture. The hydrothermal reactor is used to heat the vessel. The aqueous environment allows the reaction to happen at elevated temperatures and pressures. The reaction continues until nucleation occurs, which leads to the formation of nanoparticles.

Cooling:

Once the reaction period has elapsed, the reactor is allowed to cool at room temperature to yield stable nanoparticles.

Gathering and purification:

The particles are isolated from the reactant mixture via centrifugation, filtration, or precipitation methods. They are subsequently cleaned of contaminants or subjected to other various purification procedures.

As water is employed as a solvent, this is a green process. Furthermore, this process provides an accurate means for size and particle structure control.

3. Electrochemical decomposition:

Electrochemical deposition is used to create metallic nanoparticles. Electrochemical deposition involves delivering the metal ions onto the cathode surface by passing an electric current through the electrolyte. The stages of this process include:

Electrolyte preparation:

The electrolyte is formed by dissolving metallic salts in a suitable solvent.

An electrolyte is inserted into the cathode and anode of an electrochemical cell, which is linked to a power source.

Deposition:

When an electric current is conducted through the electrodes, metallic ions start to accumulate on the surface of the cathode. Nanoparticles are accumulated on the cathode surface.

The process is quick and does not require any oxidizing or reducing chemicals. The product is controlled for size and shape through the process. In addition, the absence of unwanted byproducts makes this process feasible for factories and laboratories.

4. Spinning:

The spinning method utilizes centrifugal force to rapidly solidify a liquid precursor to form nanoparticles. Often, metal and metal oxide-based materials are produced through this method.

In this method, a precursor solution or suspension is placed on top of a rapidly rotating disk. As the disk spins, centrifugal force thins the liquid precursor. Nanoparticles are formed when the solvent quickly evaporates from

the liquid precursor.

The size, shape, or content of nanoparticles can be affected by the following factors: Choice of Precursor Solution, Duration of Spinning, and Speed of Spinning.

The reasons that the spinning method is preferred are its simple nature, its easily scalable, and it is able to produce nanoparticles that have a high surface area and a uniform size distribution. It can produce colloidal nanoparticles of metals, metal oxides, and hybrid materials. For example, magnesium hydroxide nanoparticles are frequently produced using a spinning disk reactor, which serves as a precursor to both magnesium oxide and other magnesium-based materials.

Despite its advantages, spinning has disadvantages, just like all other techniques. Such disadvantages include a lack of control over the size/shape of nanoparticles and significant undesirable agglomeration issues. Careful consideration of the advantages and disadvantages of this technique is necessary prior to using it in the synthesis of nanoparticles.

5. Pyrolysis:

It involves breaking down precursor gases at high temperatures without oxygen. This allows nanoparticles to be produced with exact sizes and shapes.

The process consists of dispersing a precursor in a suitable solvent or carrier gas and heating it until the precursor begins its breakdown, forming reactive species. The reactive species then continue to nucleate and grow into nanoparticles.

Researchers can control the parameters to create nanoparticles with the right composition and shape. These parameters are:

Choice of Precursor Material, Reaction Temperature, Rate of Heating, Reaction Time, and Presence of Catalyst.

While pyrolysis has several advantages over traditional nanoparticle synthesis methods, such as scalability, increased flexibility in the choice of precursors, and the ability to generate nanoparticles in multiple morphologies (e.g., powders or colloidal suspensions), it also has several challenges in the reproducibility of size or size distribution of nanoparticles. Thus, it is important for researchers to carefully evaluate the trade-offs when using pyrolysis for nanoparticle synthesis.

6. Chemical vapor deposition:

In Chemical Vapor Deposition (CVD), precursor gases needed to produce nanoparticles are chosen. The reaction chamber of a reactor, heating element, and substrate or receptor offers a controlled environment. Heating the chamber causes the precursor gas to decompose or react. Gases then diffuse on the heated substrate and adsorb on the substrate. Surface reactions produce nucleation centers. The nucleation centers diffuse and coalesce, resulting in nanoparticles being formed. Precursor gases are removed when the appropriate size and shape have been achieved, leaving the nanoparticles available to be collected on the substrate. For example, the CVD of methane on Cu foils has been used to successfully synthesize nanoparticles, such as large-area graphene.

The process comprises the next actions:

Selection of Precursor Gases:

This stage involves selecting the correct gases that contain the specific elements or compounds necessary to form nanoparticles. The type of precursor gas used determines the properties of the newly formed nanoparticles. Consequently, different precursor gases will create nanoparticles with different properties.

The Design of the Reactor:

At this stage, the operator is creating an environment around the substrate, heating element and reaction chamber that is controlled. This provides a means with which one can monitor and change reaction conditions.

Heating and Activation of the Reaction Chamber:

For this stage to occur, the temperature in the reactor needs to be increased to assist in the breakdown of the precursor gases. This allows for the right reaction kinetics to occur and avoids side reactions from taking place, with controlled temperature and decomposition. Carbon nanotubes, or CNTs, are also produced through CVD. Heating and activating the reaction chamber are a crucial process. The temperature and flow rate of the hydrocarbon gas need to be closely monitored for the precursors to break down and form hydrocarbon reactive for the production of CNTs.

Adsorption of Precursor Gases on the Substrate:

At this stage, the precursor gases are allowed to fill the reaction chamber and contact the heated substrate. This allows the gases to spread and utilize the adsorption mechanism to adhere to the substrate surface. This step is

significantly dependent on the substrate properties, temperature, and pressure.

Initiation of Nucleation:

Once the precursor gases are adsorbed on the substrate surface, chemical reactions occur that produce nucleation sites. The nucleation sites are the fundamental units of synthesis and particle growth, and involve the breaking down of precursors and the generation of reactive species.

Encouraging Nanoparticle Growth:

The number of available nucleation centers continues to increase as more precursors are deposited on their surfaces. The growth could be guided by surface diffusion, coalescence, and aggregation. Some factors that could rate-limit the growth process include temperature, gas composition, and reaction time.

Removing Precursor Gases:

Once the nanoparticles of the desired size and shape are produced, the precursor gases are removed from the reactor. This is accomplished simply by turning off the gas flow and cooling the reactor.

Collecting Nanoparticles from the Substrate:

Once the precursor gases have been removed, the nanoparticles that have formed generally stick to the surface of the substrate and remain there. They can be removed from the substrate and then characterized for various applications.

The steps described represent the entire the Chemical Vapor Deposition (CVD) process for producing nanoparticles. At each step, researchers are able to manipulate certain parameters in order to optimize characteristics of the final nanoparticles.

Steps for manufacturing:

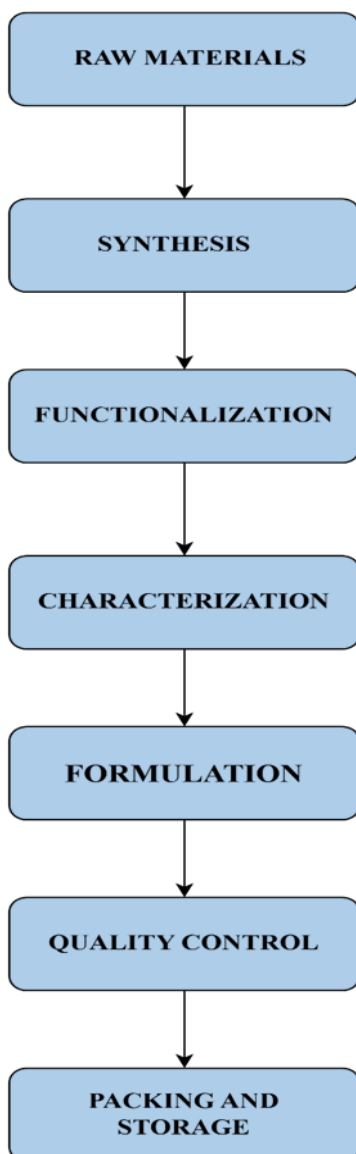


Figure 7 manufacturing steps

As shown in Figure 7 the manufacturing of nanoparticles involves series of steps. Firstly, raw material is selected by ensuring the purity and quality of raw materials which are further synthesized by top-down or bottom-up methods to prepare nanoparticles. These nanoparticles are further functionalized by modifying the surface to enhance stability, targeting ability, and interaction with biological systems. characterization is an important step which involves physiochemical properties including size, shape, and surface area. After characterization, the nanomaterials are incorporated into drug delivery systems or diagnostic platforms during formulation. Next step is quality control after which packing and storage protocols are implanted ensuring to maintain the stability and integrity of nanoparticles.

Evaluation:

the tests to evaluate the quality of nanoparticle formulations are as follows [18]:

Examine particle size:

The nanoparticle diameters (350 - 600 nm evaluated by the scanning electron microscopy) varied according to the polymer load.

Examine Scanning Electron Microscopy (SEM):

Particle shape and surface morphology of the nanoparticles were conducted using the electron scanning microscopy technique. After lyophilisation and full dryness, the samples were attached to aluminium stubs using sticky tape and a surface coating of gold produced using a sputter coater. The samples were then observed for morphology at an acceleration voltage of 20 kV.

Atomic Force Microscopy (AFM) studies:

AFM studies were performed to characterize the surface morphology of fabricated drug-loaded nanoparticles. The nanoparticle suspension was prepared using milli-Q water and then deposited on a clean glass surface and allowed to air dry overnight prior to being viewed with an AFM with silicon pyramidal cantilever probes with a force constant of 0.2 N/m. All measurements were taken in intermittent contact mode to minimize sample surface damage, with the amplitude feedback function in the attractive force's regime used to regulate the tip-to-sample distance. The amplitude and cantilever signal in the tracing direction were reported, and images were obtained at a scan speed of 2 Hz with a resonant frequency of 312 kHz.

Research utilizing differential scanning calorimetry (DSC):

The DSC assessment determined the physical state of the native drug in the nanoparticles. Approximately 2 mg of native drug, polymer, and nanoparticles were each weighed and placed into separate sealed standard aluminium pans. Scans were performed at a rate of 10°C per minute between 25°C - 300°C in a nitrogen atmosphere, with an empty aluminium pan served as the reference.

X-ray diffraction study:

An XRD-6000 diffractometer was utilized to conduct X-ray diffraction analysis. The crystallinity of the formulation and the pure drug were evaluated using X-ray diffraction analysis. The powder was placed in an aluminium sample holder. Cu radiation was generated at 30 mA and 40 kV. Samples were scanned within a range of 10° utilizes a 10° min⁻¹ scan speed. As previously stated, the samples were scanned to 90°.

Zeta potential measurement:

A zetasizer (Malvern Instruments) was used to calculate the zeta potential of the drug loaded chitosan nanoparticles in a micro electrophoresis flow cell from the measured electrophoretic mobility. Each sample was measured in triplicate in water at a temperature of 25 °C.

In order to determine the percentage of drug entrapment efficiency:

nanoparticle suspensions were prepared and subjected to centrifugation at 2000 rpm for 30 minutes. After collecting the supernatant, the supernatant was removed and particles rinsed with water and centrifuged. The UV-Visible Spectrophotometer was then used to analyse the amount of free drug in the supernatant.

Drug Entrapment (%) = $\frac{\text{Amount of drug added} - \text{Amount of free drug}}{\text{Amount of drug added}} \times 100$.

Reverse Phase High Performance Liquid Chromatography (RP-HPLC) method for the evaluation of Entrapment Efficiency (EE) and Loading Capacity (LC):

The RP-HPLC technique was utilized to determine the Entrapment Efficiency (EE) and Loading Capacity (LC). In brief, 20 µ L of sample was manually injected into the HPLC after the methanolic solution of the drug-loaded nanoparticulate was prepared to be 1 mg/ml. The system was equipped with a Sard M20 A PDA detector and a Shimadzu LC-20 AD PLC pump. Shimadzu CLASS-VP Version 6.12 SP1 equipment was used to monitor and integrate the output signal. The chromatographic separation was accomplished using a Phenomenex C18 (150

mm × 4.6 mm, 5 μm) analytical column. After being filtered through a 0.45 μm membrane, the mobile phase consisting of methanol and water (75:25; v/v) was degassed by ultrasonication. All measurements were taken at 282 nm, keeping the flow rate constant at 1.0 mL/min and using a thermostat to maintain ambient conditions in the column. The concentration of the drug in the sample was calculated using the peak area corresponding to the standard curve under the same conditions as used to make the standard curve.

In vitro drug diffusion study using EGG membrane:

The egg shell was immersed in concentrated hydrochloric acid (HCl) for two hours. The diffusion cell was connected to the separated membrane. Next, 10 ml of phosphate buffer (pH 7.4) and 20 mg of drug was placed into the diffusion cell. The receptor compartment of a 100 ml beaker was filled with 50 ml of phosphate buffer (pH 7.4). The assembly was attached to a magnetic stirrer. Samples were withdrawn at intervals over six hours, and samples were analyzed at a specific wavelength using UV-visible spectrophotometer.

An initial in vitro release of nanoparticles was performed using standard diffusion cell equipment:

It consists of two open ends with one end attached to a sigma dialysis membrane that served as the donor compartment. The dissolving medium was a freshly prepared phosphate buffer saline pH 7.4. The sigma membrane was immersed in the dissolving medium overnight. The medium was agitated with a magnetic stirrer, and the temperature was maintained at 37 °C ± 0.5 °C. Five millilitres of the sample was periodically taken out and analyzed with a spectrophotometer.

Study of In Vitro Release Kinetics:

The drug release data was fit to a zero order, first order, Higuchi, and Korsmeyer-Peppas model to characterize the mechanism of drug release.

1. Zero Order Kinetics:

These types of systems are described using a zero-order rate equation, in which the rate of drug release is independent of drug concentration.

For a zero-order release, the relationship between different parameters is:

$$Q_1 = Q_0 + K_0 t$$

2. First Order Kinetics:

The release from a system in which the release rate is dependent on concentration is described by a first order equation.

The kinetic equation for first order release is:

$$\log Q_t = \log Q_0 + K_1 t / 2.303$$

3. The Higuchi model:

Higuchi defines drug release as a diffusion process, following Fick's law and proportional to the square root of time.

$$Q_t = KH t^{1/2}$$

4. The Korsmeyer-Peppas model:

It is often used to describe drug release behavior from polymeric systems when the mechanism of drug release is unknown or when there are multiple types of release phenomena involved. The release mechanism can be determined from this model by fitting the first 60% of the drug release data.

$$\log (M_t/M_\infty) = \log KKP + n \log t$$

In vivo biodistribution of drug-loaded nanoparticles:

For the in vivo biodistribution studies, three sets of three Wistar rats weighing between 100-150 grams were used. Group 1 had free drug treatment, group 2 had drug-loaded nanoparticle treatment, and group 3 had a solvent control treatment. Each mouse in each group had free IV injected drug and drug-loaded nanoparticles with a pH 7.4 solvent control with a dosage of 3.6mg/kg body weight. After the eighteen-hour drug injection, the animals were euthanized, blood was collected and plasma separated, and several organs were collected and homogenized in phosphate buffer, such as the liver, lungs, kidney, and spleen.

Accelerated stability study:

Following the encapsulation of the nanoparticles in borosilicate glass vials, the samples were placed into environmental simulation chambers to achieve consistent climate conditions. The storage conditions of the stability study and the time points the samples were analyzed were based on recommendations by the International Conference on Harmonization (ICH). The drug-loaded Eudragit®RS100 nanoparticles were characterized over a six-month period at regular intervals by dispersing 1 mg of the drug-loaded Eudragit®RS100 nanoparticles in 10

ml of distilled water to observe for any degradation. Sometimes, studies were done in triplicate. Then, zeta sizer which is based on quasi-elastic light scattering was used to evaluate particle size and the zeta potential at a wavelength at 25 degrees Celsius. RP-HPLC was done to evaluate the chemical stability (drug content) of the formulation at 282 nm.

Marketed Examples:

Table 1: marketed example

Brand name	company	Nanoparticle type	strength	application	Approximate cost
Doxil® / Caelyx®	Janssen (Johnson & Johnson)	Liposomal doxorubicin	20 mg/10 mL vial	Ovarian cancer, multiple myeloma, Kaposi's sarcoma	~₹25,000–30,000 per vial
Daunorubicin	DaunoXome (Galen)	Liposomal daunorubicin	20mg/vial	Karposi sarcoma	~₹145-1000
Cytarabine	DepoCyt© (Pacira Pharms Inc)	Liposomal cytarabine	100mg/vial 500mg/vial 1000mg/vial	Lymphoma	~₹98-145 ~₹341-600 ~₹920-1750
Vincristine	Marqibo (Acrotech)	Liposomal vincristine	1mg/1mL vial	Acute lymphocytic blood clot	~₹40-250
Certolizumab pegol	Cimzia (UCB)	PEGylated antibody fragment (Certolizumab)	200mg/vial	Chron's disease, rheumatoid arthritis, psoriasis, ankylosing spondylitis	~₹3000-50000
Glatiramer acetate	Copaxone (Teva)	Random copolymer of l- glutamate, l- alanine, l-lysine and l-tyrosine	20mg/mL vial	Multiple sclerosis	~₹360-900
Pegfilgrastim	Neulasta (Amgen)	PEGylated GCSF protein	6mg/vial	Leukopenia by chemotherapy	~₹1,500-5,000
Paclitaxel	Abraxane (Abraxis Bioscience)	Protein NP	30mg/vial, 100mg/vial, 300mg/vial	Breast cancer	~₹450-1500 ~₹4000-6000 ~₹1200-12,000
Verapamil HCl	Verelan PM (Schwarz Pharma)	PLGA nanoparticles	5mg/10mL vial	Hypertension, angina, and rhythm disorders	~₹40
Aprepitant	Emend (Merck)	Nanocrystal	150mg/vial	Vomiting agent	~₹1,725-2,800
Tizanidine HCl	Zanaflex (Covis)	Nanocrystal	2mg	Muscle relaxant	~₹210-250
Olanzapine	Zyprexa (Lilly Pharma)	Nanocrystal	10mg/vial	Schizophrenia	₹200–300+ (varies by market)
Naproxen sodium	Naprelan (Almatica)	Nanocrystal	500mg	Anti-inflammation	~₹299
Fenofibrate	Stanlip (sun pharma)	Nanocrystal	145 mg, 160 mg, 200 mg	Hyperlipidemia	~ ₹82–₹208
Sirolimus	Rapamune (PF Prism CV)	Nanocrystal	100mg/vial	Immunosuppressant	~ ₹2,35,000 per vial

Megestrol acetate	MegaceES (Endo Pharms Inc)	Nanocrystal	40 mg tablets; 160 mg tablets; 40 mg/5 mL suspension	Anorexia	₹400–₹500 per strip of 30 tablets (40 mg); ~₹1,200–₹1,500 per bottle of suspension
Methylphenidate HCl	Ritalin LA (Novartis)	Nanocrystal	10 mg, 18 mg, 36 mg, 54 mg	Mental stimulant	~ ₹150–₹250
Theophylline	Elixophyllin Nostrum Labs Inc	Nanocrystal	200 mg/5 mL vial	Bronchial dilation	~₹1,500–1,600
Brinzolamide	Azopt (Novartis)	Nanocrystal	1% w/v, 5 mL bottle	Glaucoma	~ ₹200–₹300 per bottle
Iron sucrose	Venoferr (Am Reagent)	Inorganic/metallic NPs	100 mg/5 mL vial	Chronic renal failure with iron deficiency	~₹200–300
Sodium ferric gluconate	Ferrlecit (sanofi avertis)	Inorganic/metallic NPs	62.5 mg/5 mL vial	Chronic renal failure with iron deficiency	~ ₹150–250
Ferric carboxymaltose	Injectafer/ (am reagent)	Inorganic/metallic NPs	500 mg/10 mL vial	Iron deficiency anemia in chronic kidney disease	~ ₹1,700–4,500
Abraxane®	Celgene (Bristol Myers Squibb)	Albumin-bound paclitaxel nanoparticles (nab-technology)	100 mg/vial	Breast cancer, NSCLC, pancreatic cancer	~₹18,000–22,000 per vial
Genexol-PM®	Samyang Biopharm (South Korea)	Polymeric micelles (PEG– PLA)	30 mg/vial	Breast and ovarian cancers	~₹12,000–15,000 per vial
Marqibo®	Spectrum Pharmaceuticals	Liposomal vincristine sulfate	5 mg/31 mL vial	Acute lymphoblastic leukemia (ALL)	~₹60,000–70,000 per vial
Comirnaty® (Pfizer-BioNTech COVID-19 vaccine)	Pfizer & BioNTech	Lipid nanoparticles (LNPs) encapsulating mRNA	30 µg/dose	COVID-19 prevention	~₹1,200–1,500 per dose (govt. procurement lower)
Spikevax® (Moderna COVID-19 vaccine)	Moderna	Lipid nanoparticles (LNPs) encapsulating mRNA	100 µg/dose	COVID-19 prevention	~₹2,000–2,500 per dose (varies by country)
Covovax®	Novavax / Serum Institute of India	Recombinant protein subunit	5 µg recombinant	Prevention of COVID-19 infection	Around ₹900– 1,200 per dose in
		vaccine formulated with Matrix-M™ adjuvant nanoparticles	spike protein + 50 µg Matrix-M adjuvant per dose		private markets (lower under government procurement)

Recent research/advances

Within the last couple of years, nanomedicine has rapidly evolved, with several significant developments enhancing the safety and efficacy of pharmaceutical interventions. In the year 2025, the emphasis lies in the development of more responsive, focused, and intelligent nanoplatforms. Further are some recent advances in nanoparticles in pharmaceutical industry.

Nanovaccines on cancer theranotics:

The immune system's accumulation, development, and activation is largely defined by the multiple properties of nanomaterials. Nanomaterials can be employed to create cancer vaccines called nanovaccines that allow for targeted delivery and implementation via nanocarriers and nanoplatforms. Nanovaccines provide increased efficacy, extended antitumor immunity, and minimized side effects. Nanomedicine has instigated innovative strategies for cancer treatment, which includes prevention and diagnostics. Cancer vaccination has the potential to be a new adjunctive to standard treatment for cancer. These vaccines will teach the immune system of a patient to detect and kill cancer cells. In doing so, these vaccines may create immunological memory, which could lead to a long-term protection for tumour recurrence, and create a directed antitumor immune response to directly kill the tumour with minimal side effects. The significant benefits of nanovaccines include their ability to co-deliver adjuvants and antigens, to assist phagocytosis and processing by antigen-presenting cells (APCs), and to amplify the adaptive immune response. The NPs maintained antigen release, protected antigens from degradation by intracellular proteases, and greatly increased nanovaccine stability.^[19]

The application of artificial intelligence (AI) to nanomedicine:

Artificial intelligence (AI) in nanomedicine provides the advantages of better-structured therapies and improved efficiency, allowing us to achieve significant breakthroughs. AI would help facilitate the progress and use of nanomaterials in the medical domain by applying its predictive and pattern-identifier capacity to analyze large sets of information more efficiently.

The ability of Artificial Intelligence (AI) to analyze large and complicated datasets, including genomic data and patient medical records, is transforming the field of nanomedicine. AI can create reliable diagnostic tools and individualize treatment regimens, working with the patterns and trends that are found in datasets. For example, AI algorithms can analyze medical images and identify early signs of disease, and predict whether patients will respond to specific nanomedicine treatments.

By anticipating the physicochemical characteristics and biological interactions of nanoparticles that result in increased efficacy and safety, AI algorithms enhance the development of nanomedicine. The synthesis process is guided towards nanomaterials with certain desirable qualities when the size, shape, and surface characteristics of nanomaterials are predicted for specific applications like medication delivery or imaging. Researchers can identify safer and more biocompatible nanoparticles for medical uses by forecasting their toxicity and immunogenicity. Predicting surface alterations that will enhance drug-release properties and targeting capabilities is necessary for nanomaterial optimization.

Through precise prediction of how nanomaterials will engage with biological systems, artificial intelligence (AI) in nanomedicine removes barriers for development and discovery. There are many applications to optimize formulations and to identify new disease-specific targets. Through the analysis of large and complex databases of nanomaterial properties, scientists are able to predict how nanomaterials will interact with biological systems to match specific nanomaterials for imaging and drug delivery applications. Using AI-based computer simulations, scientists are able to predict how nanomedicines will be distributed and processed in the whole body. This ability to predict allows scientists to optimize formulations and delivery methods for improved safety and therapeutic window outcomes. Scientists can develop nanomedicines that are more effective and safer, for instance, by personalizing them for specific health conditions and genotypes of patients; developing nanomedicines with increased effectiveness and decreased adverse effects.

Illness management approaches could be transformed by diagnostic systems applying artificial intelligence. These systems study medical records to help identify patients more likely to develop certain diseases. This identification method enables an early intervention in nanomedicine that can either stop the progression of a disease or reduce its severity.

AI contributes to the design and execution of clinical trials by selecting optimal patient groups, predicting treatment outcomes, and continuously monitoring patient responses in real-time. The use of AI technology is expected to improve clinical trial management by improving efficacy and efficiency within the scope of nanomedicine. Clinical trial efficiency can be improved through the implementation of AI algorithms that can analyze demographic data and determine the population most likely to benefit from certain nanomedicines. AI technology enables on-demand forecasting of probabilities of treatment success or failure, which allows for optimized patient stratification and treatment. Real-time monitoring also enables treatment to be modified quickly when there are early reports of side effects associated with the administration of nanomedicine. [20]

Targeted drug delivery:

Nanomedicine is still all about targeted drugs. By engineering nanoparticles to recognize and bind to specific cellular markers, therapeutic agents may directly be administered to diseases without harming healthy cells or minimally causing side adverse effects. Due to the development in ligand engineering, including fragments of antibodies, peptides, and aptamers, the selectivity of nanocarriers for tumors, inflammatory tissues, and infected tissues improved. The nanocarriers responsive to inputs derived from the tumor microenvironment have been of interest because of their ability to release medication payloads due to internal stimuli, such as pH, redox gradients, or enzymatic activity, as well as external stimuli, such as heat, light, or magnetic fields. For example, acid-sensitive liposomes containing doxorubicin are currently used to target the delivery by taking advantage of the acidic tumor microenvironment. [21]

Smart nanosensors and wearables:

Nanosensors are changing the landscape of diagnostics through their ability to provide ultrasensitive, point-of-care monitoring of biomarkers associated with cancer, cardiovascular disease, and neurodegeneration. When integrated into wearable platforms, these nanosensors are able to continuously monitor physiologic states, including blood glucose levels, inflammatory markers, and circulating tumour DNA. New implantable nanosensor devices hold the potential to create responsive and autonomous therapeutic systems through their ability to monitor therapeutic response and disease recurrence in real-time. [22]

Conclusion:

In this review, we presented a detailed overview of NPs, their types, applications, drug selection criteria, composition, manufacturing, evaluation, marketed examples, and recent advances. Pharmaceutical sciences have been transformed by nanoparticles that enhance drug delivery by addressing challenges associated with conventional dosage forms. Due to their unique properties (e.g., size, tunable surface characteristics, and ability to penetrate biological walls), nanoparticles can serve as efficient carriers for targeted and controlled drug delivery. A range of different nanoparticles has been considered for pharmaceutical applications including polymeric nanoparticles, solid lipid nanoparticles, nanostructured lipid carriers, metallic nanoparticles, nanocrystals, and dendrimers. All of these nanoparticle types possess varying advantages in drug loading and release characteristics, and they allow delivery of drugs while considering biocompatibility when developing formulations for specific targets to treat diseases such as cancer, neurological disorders, and infectious diseases.

The choice of drug in nanoparticle-based drug delivery is based on various criteria that include solubility, lack of Thermal stability, therapeutic index, and site-specific properties. Many poorly soluble or unstable drugs are considerably benefited by encapsulation in nanoparticles, which provide significant enhancement in drug bioavailability, yet minimize systemic toxicity. The construction of nanoparticles usually involves a core component, such as lipid, polymer, or metal particle, and excipients such as surfactants, stabilizers, and targeting ligands, which will act as either separate functional components or work collaboratively. The core and all excipients act in concert to determine the particle's stability, release behavior, and interaction with biological systems.

Manufacturing methods substantially influence the quality and performance of nanoparticles. High-pressure homogenization, ultrasonication, solvent evaporation, or microemulsion processes are typically implemented to achieve the desired particle size, morphology, and reproducibility. Each of these methods has its unique benefits and limitations that influence its scalability and cost. In addition, evaluation parameters associated with particle size distribution, zeta potential, entrapment efficiency, in vitro drug release, and stability studies will largely

determine if a nanoparticle formulation is safe, effective, and consistent.

Several nanoparticle-based products have successfully been marketed, indicating the clinical effectiveness of nanotechnology in drug delivery. Examples of such products would be Doxil® (liposomal doxorubicin), Abraxane® (albumin-bound paclitaxel), and Covovax (recombinant serum), where each nanoparticle-based delivery system had enhanced pharmacokinetics or improved efficacy than their conventional drug counterparts. Recent studies still broaden the horizons of nanopharmaceuticals by developing multifunctional and stimuli-responsive systems and hybrid nanoparticles or personalized nanomedicine. Advances in surface engineering, the conjugation of ligands, and smart release systems are driving next-generation therapeutics for the drug delivery field. Although challenges exist regarding toxicity, regulatory approval, and manufacturing cost, nanotechnology incorporated in new drug delivery systems provides great future promise. As such, assessing the mechanisms of the varieties of nanoparticles, their composition, ways to prepare them, and how to evaluate them will be critical in harnessing their full potential and flourishing in pharmaceutical experience.

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