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Nanoparticulated Drug Delivery Systems and Its Applications

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ABSTRACT

Recent advancements in nanoparticle-based drug formulations have aided in the treatment of difficult diseases. Nanoparticles vary in size but are typically between 100nm and 500nm. Drug delivery using particulate delivery systems has been the subject of research in recent years. Using nanoparticles as a physical approach, various drug molecules have been modified for both pharmacokinetic and pharmacodynamics properties. To increase therapeutic benefit while minimizing side effects, various polymers have been used in the formulation of nanoparticles for drug delivery research. Nanomedicine and nano delivery systems are a new but rapidly developing science in which nanoscale materials are used as diagnostic tools or to deliver therapeutic agents to specific targeted sites in a controlled manner. Nanotechnology provides numerous advantages in the treatment of chronic human diseases through the site-specific and target-oriented delivery of precise medicines. There have recently been a number of notable applications of nanomedicine (chemotherapeutic agents, biological agents, immunotherapeutic agents, and so on) in the treatment of various diseases. The current review provides an up-to-date summary of recent advances in the field of nanomedicines and nano-based drug delivery systems by conducting a thorough examination of the discovering as well as implementation of nanomaterials in enhancing both the effectiveness of innovative as well as old drugs (e.g., natural products) and selective diagnosis via disease marker molecules. Nanomedicines' opportunities and challenges in drug delivery from synthetic/natural sources to clinical applications are also discussed. In addition, researchers have included information on trends and perspectives in the field of nanomedicine.

INTRODUCTION

Since the last decade, the use of nanoparticles in drug formulation and delivery has grown significantly. Efforts are being made to track the efficacy of nanoparticles in targeted drug delivery applications. The average amount of time and money spent on developing a new chemical or biochemical entity is greater than that required to develop nanoparticle drug delivery systems[1]. On the other hand, incorporating medicine into nanoparticles drug delivery systems improves safety and efficiency factors, as well as patient compliance[2]. The majority of the most recent cancer therapies are based on a nanoparticle approach, because increased permeation increases bioavailability for nanoparticulated drugs, particularly topically administered drugs, the use of nanosuspensions for drug delivery has increased dramatically in recent years[2,3].

One of the most difficult problems in drug discovery and development is creating drugs that have no adverse effects on patients. The vast majority of drug molecules are large organic molecules that are insoluble in water. As a result, considerable effort has been expended in nanosizing drug particles in an amorphous or crystalline nanosuspension for applications in passive targeting via enhanced membrane diffusion[3]. Nanotechnology is a combination of advanced manufacturing science and engineering in which nanometer scaled materials are used. When compared to bulk material, nanosized particles have a higher surface-to-volume ratio. Nanoparticles have also been shown to have numerous applications ranging from agriculture to medicine[4].

Nano-sized inorganic particles, whether simple or complex in nature, exhibit unique physical and chemical properties and are becoming an extremely significant substance in the identification of innovative nanodevices for use in a wide range of physical, biological, biomedical, and pharmaceutical applications[5-7]. The first generation of nanoparticle-based therapy used lipid systems such as liposomes and micelles, both of which are now FDA-approved[8]. Inorganic nanoparticles such as gold or magnetic nanoparticles can be found in these liposomes and micelles[9]. These properties have led to an increase in the use of inorganic nanoparticles for drug delivery, imaging, and therapeutic purposes. Furthermore, nanostructures are said to help prevent drugs from becoming contaminated in the gastrointestinal region and to aid in the delivering of minimally water-soluble drugs to their own target location. Nanodrugs have greater oral absorption because they use absorptive endocytosis uptake mechanisms.

Nanostructures remain in the bloodstream for an extended period of time, allowing amalgamated drugs to be released at the prescribed dose. As a result, they cause fewer plasma fluctuations with fewer side effects. Because these structures are nanosized, they can penetrate the tissue system, allowing for easy drug uptake by cells, efficient drug delivery, and action at the targeted location. Nanostructures are much more readily absorbed by cells than large particles ranging in size from 1 to 10 m[10,11]. As a result, they work together to treat diseased cells more effectively and with fewer or no side effects. Nanoparticles have been found to be useful in acquiring information at all stages of clinical practice due to their use in numerous novel assays to treat and diagnose diseases. The primary advantages of these nanoparticles are related to their surface properties, as various proteins can be attached to the surface. Gold nanoparticles, for example, are used as biomarkers and tumor labels in various biomolecule detection procedural assays.

Metallic, organic, inorganic, mesoporus nanoparticles and polymeric nanostructures, such as dendrimers, micelles, and liposomes, are frequently used in the development of target-specific drug delivery systems. These nanoparticles are specifically tagged with drugs that have poor solubility and absorption ability[10,12]. The effectiveness of these nanostructures as drug delivery vehicles, however, varies depending on their size, shape, and other inherent biophysical/chemical properties. Polymeric nanomaterials with diameters ranging from 10 to 1000 nm, for example, have properties that make them ideal for use as a delivery vehicle[13]. Various synthetic polymers, such as polyvinyl alcohol, poly-l-lactic acid, polyethylene glycol, and poly-(lactic-co-glycolic acid), and natural polymers, such as alginate and chitosan, are widely used in the nanofabrication of nanoparticles due to their high biocompatibility and biodegradability properties[14,16]. Polymeric nanoparticles are classified as nanospheres or nanocapsules, both of which are effective drug delivery systems. Compact lipid nanostructures and phospholipids, such as liposomes and micelles, are also extremely useful in targeted drug delivery.

The use of an ideal nano-drug delivery system is primarily determined by the biophysical and biochemical properties of the targeted drugs chosen for treatment[17]. However, issues such as nanoparticle toxicity must be addressed when considering the use of nanomedicine. Recently, nanoparticles have primarily been used in conjunction with natural products to reduce toxicity concerns. The green chemistry route of designing drug-loaded nanoparticles is widely promoted because it reduces the hazardous constituents in the biosynthetic process. Thus, using green nanoparticles for drug delivery can reduce medication side effects[18].

Furthermore, changes in nanostructure size, shape, hydrophobicity, and surface changes can improve the bioactivity of these nanomaterials.

Given the information above, the goal of this review is to present different nano-based drug delivery systems, significant applications of natural compound-based nanomedicines, and the bioavailability, targeting sites, and controlled release of nano-drugs, as well as other difficulties related to the use of nanomaterials in drugs.

1. Different Types of Nano Carriers

The different types of nanocarriers shown in Figure No 1.

1. Liposomes

Liposomes were the first to be studied as drug carriers. Liposomes range in size from 80 to 300 nm. They are phospholipid and steroid-containing spherical vesicles. Liposomes have been shown to improve pharmacokinetic properties such as therapeutic index of chemotherapeutic agents, rapid metabolism, lower side effects, and increased in vivo and in vitro anticancer activity[4]. The clearance rate by the mononuclear phagocytic system increased with liposome size greater than 100 nm. Liposomes with multiple functions and specific antigens, proteins, and biological substances could be used to create drugs that target specific tissues. It is the most promising type of drug delivery for targeted drug delivery therapy. To incorporate drugs into liposomes, the encapsulation process is used. The pH, liposome composition, osmotic gradient, and environmental conditions all influence drug release from liposomes4. Liposomes interact with cells via lipid transfer, fusion, and adsorption. Liposomal formulations are used in anticancer, antibiotic, anti-inflammatory, and anti-rheumatic drugs. Despite a long history of research, liposomes have yet to make a significant impact. They are commonly found in cosmetic products. Dior created the formulation for the first time in 1986[4-7].

2. Polymeric Nanoparticles

Polymeric nanomaterials are nanoparticle structures with diameters ranging from 10 to 100 nm. Polymeric nanoparticles are made from synthetic polymers such as polye-caprolactone and polyacrylamide, as well as natural polymers such as chitosan and gelatin. There are two types of polymeric nanoparticles: biodegradable and nonbiodegradable. Polymeric nanoparticles are typically coated with nonionic surfactants to reduce immunological and

intramolecular reactions between surface chemical groups. The Food and Drug Administration of the United States has approved biodegradable polymeric nanomaterials such as PLA and PLGA. They are designed in such a way that they can encapsulate a variety of low molecular weight compounds. When chronic dosing is required in formulations, polymeric nanoparticles are more useful in terms of biocompatibility and biodegradation profiles. One disadvantage of polymeric nanoparticles is the difficulty in large-scale manufacturing and production. PLGA nanoparticles are formulated as an emulsifier using a double emulsion solvent evaporation system using oil and water with vinyl alcohol[19-26].

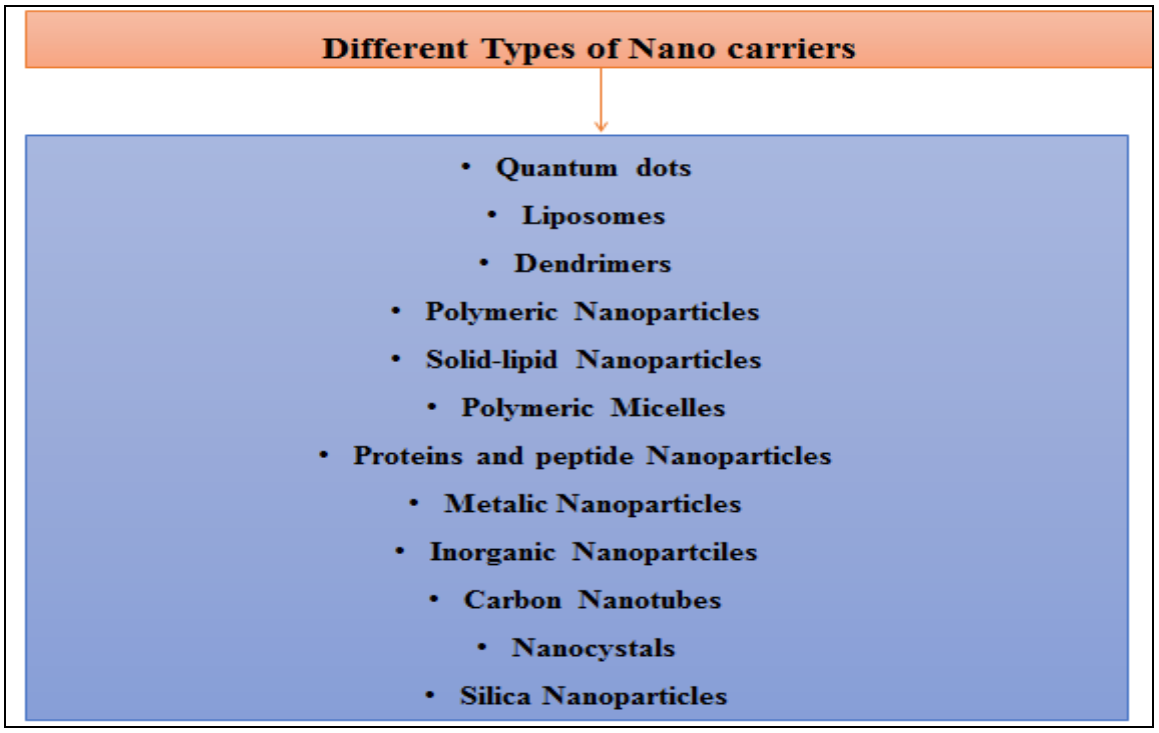

Figure No. 1: Different types of Nano carriers

3. Solid Lipid Nanoparticles [SLN]

Solid lipid nanoparticles were developed in the 1990s as an alternative to emulsions and liposomes. Because of their rigid core of hydrophobic lipids that are solid at room temperature, solid lipid nanoparticles are more stable in biological systems than liposomes. These aggregates are further stabilized by including a high level of surfactants. Because they are biodegradable, solid lipid nanoparticles are less toxic. They can be designed with three different types of hydrophobic designs and have controllable pharmacokinetic parameters. A drug-enriched shell, a drug-enriched core, and a homogeneous matrix are the three designs. SLNPs could be used to deliver drugs orally, topically, or inhalable. SLN particles are

composed of solid lipids such as higher purity triglycerides, complex glyceride mixtures, or waxes stabilized with various surfactants. Nanostructured lipid carriers and lipid drug conjugates are lipid-based nanoparticle modifications that have been developed to overcome the limitations of conventional SLN. By combining liquid and solid lipids, nanostructured lipid carriers are formed, and as a result, special nanostructured lipids are formed, with increased payload and reduced drug expulsion. NLCs are classified into three types: imperfect, multiple, and amorphous[27,78].

4. Dendrimers nanocarriers

Dendrimers nanoparticles are one-of-a-kind polymers with well-defined structure and size. Dendrimers nanocarriers include glycogen, amylopectin, and others. Dendrimers can perform a variety of functions, including solubility enhancement and drug targeting. Dendrimers can be administered via oral, parenteral, nasal, or intraocular routes of administration. Dendrimers can act as vectors in gene therapy. This 3D tree-like branched molecule has some good properties, such as narrow molecular weight distribution, 3D structure tuned by Dendrimers generation and Dendron structure, and flexibility for tailored functional groups with high density on the periphery[28].

5. Carbon nanotubes

Carbon nanotubes were discovered for the first time in 1991. Pyrolysis of metallocenes such as ferrocene, cobaltocene, and nickelocene under reducing conditions produces multiwalled nanotubes. In a similar manner, single-walled carbon nanotubes (SWNT) were created using dilute hydrocarbon-organometallic mixtures. Surprisingly, at 1100ºC, pyrolysis of nickelocene in the presence of benzene yields primarily MWNT. Pyrolysis of nickelocene in the presence of acetylene, on the other hand, produces primarily SWNT, owing to the smaller number of carbon atoms per molecule[29].

6. Silica nanoparticles

Silica nanoparticles are created using sol-gel methods. An efficient co condensation process for mono-disperse silica nanoparticles was demonstrated by researcher18. Aside from this, several other methods for preparing silica nanoparticles have been described and demonstrated, such as Tan group19's organic aqueous biphasic system. MCM-41 is a mesoporous silica nanoparticle that is typically synthesized using sol-gel processes with

surfactants such as C12-trimethylammonium bromide versus C16-trimethylammonium bromide to control pore sizes[30].

7. Polymeric Micelles

Polymeric micelles are nanostructures made of amphiphilic block copolymers that gather in aqueous solution to form a core shell structure. The hydrophobic core can be loaded with hydrophobic drugs (for example, camptothecin, docetaxel, paclitaxel), while the hydrophilic shell makes the entire system water soluble and stabilizes the core. Polymeric micelles are typically less than 100 nm in size and have a narrow distribution to avoid rapid renal excretion, allowing them to accumulate in tumor tissues via the EPR effect. Furthermore, the polymeric shell prevents non-specific interactions with biological components. These nanostructures have a high potential for hydrophobic drug delivery because their interior core structure allows for drug assimilation, resulting in increased stability and bioavailability. Drug targeting using various polymeric micelles as established by various mechanisms of action includes boosted penetrability and holding effect stimuli; complexion of a specific aiming ligand molecule to the micelle surface; or combination of monoclonal antibodies to the micelle corona. Polymeric micelles have been reported to be useful for both cancer drug delivery and ocular drug delivery[30].

8. Inorganic Nanoparticles

Silver, gold, iron oxide, as well as silica nanoparticles are examples of inorganic nanoparticles. Although there aren't as many studies on them as there are on the other nanoparticle types discussed in this section, they do have some potential applications. However, only a few nanoparticles have been approved for clinical use, with the majority still in the clinical trial stage. Metal nanoparticles, such as silver and gold, have unique properties such as SPR (surface plasmon resonance) that liposomes, dendrimers, and micelles do not. They demonstrated several advantages, including good biocompatibility and versatility in surface functionalization[30].

9. Nanocrystals

Nanocrystals are pure solid drug particles with a diameter of 1000 nm. These are pure drugs with no carrier molecules attached and are typically stabilized with polymeric steric stabilizers or surfactants. Nano-suspension is the addition of a surfactant agent to a nanocrystals suspension in a marginal liquid medium. The dispersing medium in this case is

mostly water or any aqueous or non-aqueous medium, including liquid polyethylene glycol and oils[31,32]. Nanocrystals have unique properties that allow them to overcome challenges such as increased saturation solubility, increased dissolution velocity, and increased glueyness to surface/cell membranes.

10. Metallic Nanoparticles

Metallic nanoparticles have gained popularity in a variety of medical applications, including bio-imaging, biosensors, target/sustained drug delivery, hyperthermia, and photo-ablation therapy[33]. Furthermore, the addition of specific functional groups to these nanoparticles allows them to bind to antibodies, drugs, and other ligands, trying to make such processes more showing promise in biomedical applications[34,35]. Although gold, silver, iron, and copper are the most extensively studied metallic nanoparticles, there is a growing interest in other types of metallic nanoparticles, such as zinc oxide, titanium oxide, platinum, selenium, gadolinium, palladium, and cerium dioxide[36,37].

11. Quantum Dots

Quantum dots (QDs) are semiconductor nanocrystals with diameters ranging from 2 to 10 nm and size-dependent optical properties such as absorbance and photoluminescence [38]. The QDs has received a lot of attention in the field of nanomedicine because, unlike conventional organic dyes, the QDs emit in the near-infrared region (650 nm), which is very desirable in the field of biomedical images due to the low absorption by tissues and the reduction in light scattering [37, 38]. Furthermore, QDs of varying sizes and/or compositions can be excited by the same light source, resulting in distinct emission colors across a wide spectral range [38].

12. Protein Nanoparticles

Natural biopolymers are polysaccharides and proteins extracted from biological sources such as plants, animals, microorganisms, and marine sources[39,40]. Protein-based nanoparticles are easily decomposable, metabolizable, and functionalizable for attachment to specific drugs and other targeting ligands. They are normally produced in two ways: (a) from water-soluble proteins such as bovine and human serum albumin, and (b) from insoluble proteins such as zein and gliadin[40]. Coacervation/desolvation, emulsion/solvent extraction, complex coacervation, and electro spraying are the most common methods for synthesizing them. To promote and augment their targeting mechanism, protein-based nanoparticles are chemically altered to combine targeting ligands that identify specific cells and tissues[40].

2. Fundamentals of Nanotechnology Based Techniques in Designing of Drug

Nanomedicine is a branch of medicine that uses nanotechnology to prevent and cure diseases by using nanoscale materials such as biocompatible nanoparticles[41] and nanorobots[42] for a variety of applications such as diagnosis[43], delivery[44], sensory[45], or actuation in a living organism[46]. Drugs with very low solubility have a number of biopharmaceutical delivery issues, including limited bio-access after oral administration, a lower diffusion capacity into the outer membrane, a higher quantity required for intravenous administration, and unwanted side effects preceding the traditional formulated vaccination process. All of these limitations, however, could be overcome by incorporating nanotechnology approaches into the drug delivery mechanism.

Drug design at the nanoscale has received extensive research and is by far the most advanced technology in the field of nanoparticle applications due to potential benefits such as the ability to modify properties such as solubility, drug release profiles, diffusivity, bioavailability, and immunogenicity. This can lead to the development of more convenient administration routes, lower toxicity, fewer side effects, improved bio-distribution, and an extended drug life cycle[17]. The engineered drug delivery systems are either directed at a specific location or are designed for the controlled drug release of therapeutic agents at that location. Their formation involves self-assembly, in which well-defined structures or patterns are formed spontaneously from building blocks[47]. They must also overcome obstacles such as opsonization/sequestration by the mononuclear phagocyte system[48].

Nanostructures can deliver drugs in two ways: passively or autonomously. Drugs are incorporated into the inner cavity of the structure primarily through the hydrophobic effect in the former. Because of the low content of the drugs encapsulated in a hydrophobic environment, when the nanostructure materials are targeted to targeted positions, the intended amount of the drug is released[49]. In the latter case, the drugs to be released are straightforwardly covalently linked to the carrier nanostructure material for simple delivering. The timing of release is critical in this approach because the drug does not reach the target site and quickly dissociates from the carrier, and its bioactivity and efficacy are reduced if it is not released from its nanocarrier system at the appropriate time[49]. Drug targeting is another important aspect that employs nanomaterials or nanoformulations as drug delivery systems and is classified as active or passive. Active targeting involves the use of moieties such as antibodies and peptides in conjunction with a drug delivery system to anchor them to receptor

structures expressed at the target site. The able to prepare drug delivery vehicles complicated propagates through into the blood system and therefore is motivated to the target location by attachment or adhering impacted by properties such as pH, temperature, molecular site, and shape in passive targeting. The prime objectives in the body are cell membrane receptors, lipid components of cell membranes, and antigens or proteins on cell surfaces[50]. Currently, the majority of nanotechnology-mediated drug delivery systems are aimed at cancer treatment and prevention. Some of the most important nanoparticles used in targeting and prevention of cancer mentioned in Table 1.

Table No. 1: Different types of nanoparticles carriers for drug delivery and characteristics

Polymeric nanoparticles	A linker connects drugs to the sides of a linear polymer chain.	These are nontoxic, biodegradable, and water soluble. These nanoparticle drugs can target specific cells that are malfunctioning while leaving normal cells alone. They have the ability to accumulate
Dendrimers	Synthetic polymers with repeating and regular patterning units that emerge radially.	Restricted deterioration, elevated shape and compositional homogeneity, and multifunctionality are all advantages of nanoparticle drugs.
Liposomes	They are lipid bilayer structures that self-assemble.	These nanostructures drugs are simple to implement, capable of targeting specific areas, and are biocompatible and amphiphilic.
Carbon nanotubes	They have a benzene ring as well as carbon cylinders in their structure.	These multifunctional drugs are water soluble and biodegradable due to chemical modification.
Viral nanoparticles	These drugs, which have been chemically modified, are water soluble as well as environmentally benign.	They are multifunctional and can target specific tumors. They are consistent and have well-defined geometry. They are also biochemically interoperable as well as naturally inert.

3. Method of Preparation of Nanoparticles

There are numerous methods for the preparation of nanoparticles. Most useful methods mentioned in Figure No 2.

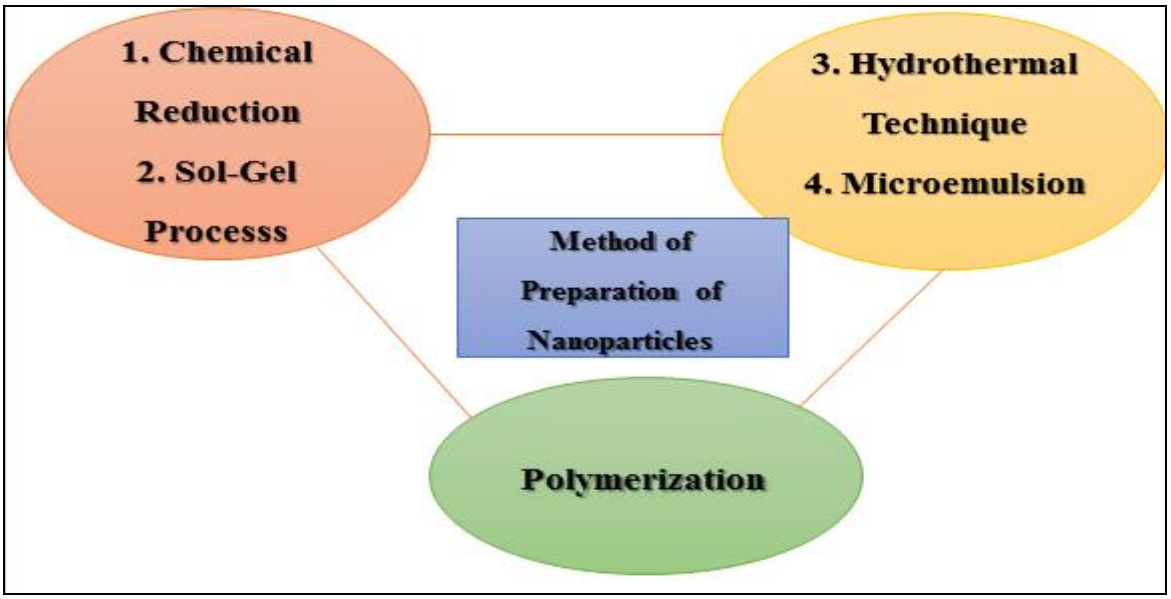

Figure No. 2: Method of Preparation of Nanoparticles

1. Chemical reduction

Chemical reduction of organic and inorganic reducing agents such as sodium citrate, hydrogen, tollens reagent, and sodium borohydride is one of the most commonly used methods to synthesize nanoparticles.

2. Sol-Gel Process

The method employs a wide range of materials for the synthesis of nanoparticles. Sol is formed by dissolving metal oxides such as organic, inorganic, and metal alkoxide. Once the sol has been formed and dried, a polymer network is formed in which the solvent molecules are trapped within the solid. This is known as gel, and it is dried using calcinations to produce the final product.

3. Polymerization

Nanoparticles are formed in this process by polymerizing monomers in an aqueous solution. Drug incorporation is accomplished by either dissolving the drug in the polymerization medium or adsorption of nanoparticles after the polymerizations are completed. Surfactants

and stabilizers have been removed from this nanoparticle suspension. Polybutylcyanoacrylate or poly (alkyl cyanoacrylate) nanoparticles are created using this technique[51,52].

4. Hydrothermal Technique

The synthesis methods of substances in a heated environment are used in the hydrothermal synthesis technique. Synthesis of single nano crystals is accomplished through mineral solubility in hot water under high pressure. Crystal growth is carried out in an autoclave, which contains a steel pressure vessel.

5. Microemulsion

Microemulsion is frequently used in the synthesis of inorganic nanoparticles. Some researchers also proposed methods for creating nanoparticles within the microemulsion. When water droplets in a microemulsion collide, reactant exchange occurs for microemulsion materials that act as reactants. This reaction exchange is quite fats, and precipitation occurs in nano droplets, which is followed by nucleation growth and coagulation of primary particles, resulting in nanoparticle formulation[53,54].

4. Characteristics of Nanoparticles, And Their Effects on Drug Delivery

1. Particle size

Particle size is an important consideration when determining nanoparticle properties. They determine the toxicity, biological fate, and targeting ability of nanoparticle systems. They may also have an impact on drug loading, drug release rate, and nanoparticle stability. Many studies have shown that nanoparticles of sub-micron size have more applications than microparticles. Nanoparticles have higher intracellular uptake than microparticles and can reach a wider range of targets due to their smaller size and mobility. The study discovered that 100nm nanoparticles had a 2.5 times greater uptake than 1µm microparticles. And even the uptake is six times that of 10m micro-particles. Another study demonstrated that nanoparticles penetrated submucosal layers in a rate in situ intestinal loop model, whereas microparticles are restricted to the epithelial lining. Tween 80-coated nanoparticles have crossed the blood-brain barrier. Some cell lines can consume submicron nano particles more efficiently than microparticles[54,56].

The size of the particles will have an impact on drug delivery. Particles of small size will have a large surface area, and the majority of the drug associated with the particle will be at

or near the particle surface, resulting in rapid drug release. Large particles, on the other hand, will have large cores, allowing drug to be encapsulated and resulting in slow drug diffusion. Smaller particles are more likely to aggregate during nanoparticle dispersion, transportation, and storage. It is difficult to create nanoparticles that are small but stable. Photon correlation spectroscopy or dynamic scattering is the most commonly used routine method for determining particle size. The medium's viscosity must be known in order to calculate particle diameter[57].

2. Surface properties of nanoparticles

When nanoparticles are administered, they are easily detected by the body's immune system and cleared by phagocytes for circulation. The amount of proteins adsorbed is determined by the size of the nanoparticles and their surface hydrophobicity, and this influences the in vivo fate of the nanoparticles. Oponization is the process of binding opsonin to the surface of nanoparticles, and it serves as a bridge between phagocytes and nanoparticles. To improve the success rate of nanoparticle-based drug targeting, opsonization must be reduced and nanoparticle circulation in vivo extended. This can be accomplished by:

- Surface coating of nanoparticles with hydrophilic polymers and surfactants.
- Nanoparticle formulation with biodegradable copolymers of PEG, poloxamer, poloxamine, and polysorbate 80.

3. Drug Loading

One of the most important elements of an effective nanostructures drug delivery system is drug loading capacity. The drug loading capacity must be high, which reduces the amount of matrix materials required for administration. There are two methods for drug loading: One method is the incorporation method, in which the drug is incorporated during the nanoparticle production process. The absorption technique is used to absorb drugs after nanoparticles have been formed by incubating the carrier with a concentrated drug solution. The solid state drug solubility in polymer, which is related to drug polymer interactions and molecular weight, determines drug loading and entrapment efficiency.

4. Drug Release

Drug release is critical to the success of a nanoparticulated drug delivery system. Typically, drug release is determined by two factors: drug solubility and desorption of the surface drug,

as well as drug diffusion through a nanoparticle matrix. Whenever it arrives to nano-spheres, the drug will be distributed uniformly and released through matrix erosion under sink conditions. A diffusion process controls the release mechanism if matrix erosion is slower than drug diffusion.

5. Nanoparticulated Drug Delivery Systems and Applications

Several articles, both research and reviews, on nano vehicular intracellular drug delivery systems have recently been published, including one by Prokop and Davidson[58]. This article discusses various aspects of nanodrug delivery systems and their applications in biological systems at the cellular level. Several nano systems and their applications have been examined. Another researcher has gone into great detail about the role of nanotechnology in drug design, citing several drugs and references[59]. Authors describe nanoparticle-based drug delivery systems and their application to chronic pulmonary disease treatment[60]. All of these studies demonstrated that nanoparticulate drug delivery systems are a promising approach to achieving desired drug delivery properties by modifying pharmacokinetic properties. Gupta and Moulik[61] provide a detailed description of nano emulsions. To overcome diseases caused by genes, it is preferable to combat the root cause rather than treat the disease, and gene therapy is a promising strategy[62]. In nano lipoplex gene delivery, researchers have discussed the need for non-toxic and efficient gene delivery vectors[63].

Liposomes are an excellent method to deliver antitumor agents. Furthermore, because of their hydrophobic core, micelles are excellent for making insoluble drugs soluble. Carbon nanotubes are one type of nanoparticle that has shown promising results in the treatment of cancer. It is made of allotropic carbon with a cylindrical framework. They are divided into single-walled and multi-walled carbon nanotubes based on the number of sheets in concentric cylinders. Because carbon nanotubes have hollow interiors, drugs can be easily loaded into them. Through use of nanostructures in diagnostic testing has been widely investigated in recent years[64], as current technology is hampered by inadequacies of fluorescent markers such as fluorescence fading after single use, dyes, and restricted usage. Nanoparticles can help to solve these problems. Theranostic nanoparticles have recently received a lot of attention for diagnostic purposes. Stokes is caused primarily by vascular diseases such as atherosclerosis and hypertension[65]. Nanoparticles have been used to diagnose and detect atherosclerotic plaques. Therapeutic agents are delivered to these plaques using similar

targeting strategies. Detecting the disease early and intervening may prevent the worst outcomes, such as plaque rupture and thrombosis.

Recent Applications

Drug delivery systems can use nanoparticulated systems in a variety of ways. Some recent applications are represented in Figure No. 3.

1. Tumor Targeting

The rationale for using nanoparticles for tumor targeting is based on the following assumptions: (1) Nanoparticles will be able to deliver a concentrated dose of drug in the vicinity of tumor targets due to the enhanced permeability and retention effect of active nanoparticles. (2) Nanoparticles will limit drug distribution to the target organ, reducing drug exposure to healthy tissues. An experiment showed that in mice treated with doxorubicin incorporated into poly (isohexylcynoacrylate) nanospheres, doxorubicin concentrations were higher in the liver, spleen, and lungs than in mice treated with free doxorubicin.

Chinteni et al. wrote a review article on gold nanoparticle applications and methods in cancer therapy. Authors have pointed out that traditional drug delivery has numerous flaws, particularly when it comes to cancer. Gold nanoparticles [GNPs] are one type of nanoparticle capable of treating various cancers with low toxicity and high bioavailability[66]. Gupta Sachin et al. published a review paper on Solid lipid nanoparticles (SLN), a rapidly developing field of nanotechnology with significant possible pharmaceutical applications and research. Because of their unique size-dependent properties, lipid nanoparticles provide the opportunity to develop new therapeutics. The ability to incorporate drugs into nanocarriers provides a replacement method for drug delivery that is used in drug targeting[67].

Dinesh Kumar et al investigated the solvent displacement method for the development of Quercetin-loaded nanoparticles. The nanoparticles were created using a reconfigured solvent displacement method for oral delivery of Quercetin. Quercetin is an anti-oxidant, anti-leishmanial, anti-viral, and anti-inflammatory polyphenol compound found in fruits[68].

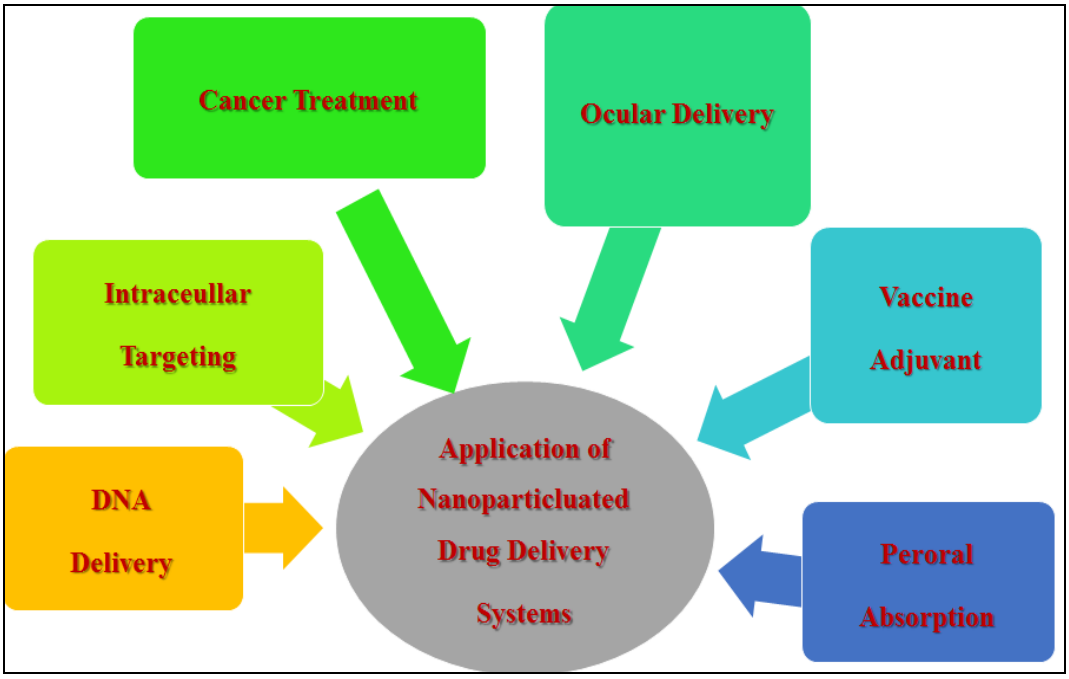

Figure No. 3: Applications of Nanoparticulated system

2. Gene Delivery

Polynucleotide vaccines work besides having to deliver genes that encode applicable antigens to host cells where they are expressed, causing the antigenic protein to be produced in close proximity to professional antigen presenting cells, triggering an immune response. Because intracellular protein production, rather than extracellular protein deposition, stimulates both arms of the immune system, such vaccines produce both humeral and cell-mediated immunity.

3. CNS Delivery

The far more significant element restricting the development of more effective drug for the central nervous system is the blood-brain barrier (BBB). The BBB is characterized by relatively impermeable endothelial cells with tight junctions, enzymatic activity, and active efflux transport systems. It effectively prevents the passage of water-soluble molecules from the blood circulation into the CNS, and it can also lower the concentration of lipid-soluble molecules in the brain via the function of enzymes or efflux pumps. As a result, the BBB only allows for the selective transport of molecules required for brain function. Nanoparticle targeting strategies rely on the presence of and interaction of nanoparticles with specific receptor-mediated transport systems in the BBB. Polysorbate 80/LDL, transferrin receptor binding antibodies (such as OX26), lactoferrin, cell penetrating peptides, and melano-

transferrin, for example, have been shown to be capable of delivering a non-transportable drug into the brain via a chimeric construct capable of receptor-mediated transcytosis. It has been reported that poly(butylcyanoacrylate) nanoparticles can deliver hexapeptidedalargin, doxorubicin, and other agents into the brain, which is significant given the difficulty drugs have in crossing the BBB. Despite some reported success with polysorbate 80 coated NPs, this system has several flaws, including desorption of the polysorbate coating, rapid NP degradation, and toxicity due to the presence of high polysorbate 80 concentrations. The most studied BBB targeting antibody, OX26MAbs (anti-transferrin receptor MAbs), has been used to improve liposome BBB penetration. However, Jiet al. recently demonstrated that in-vivo brain uptake of lactoferrin, an iron-binding glycoprotein of the transferrin (Tf) family, is twice that of OX26 and transferrin[69].

4. Nanoparticles in Inflammation

Aditya et al. prepared silver nanoparticles from cumin oil and assessed the anti-inflammatory action of cumin oil using the albumin denaturation assay technique. The anti-inflammatory activity of prepared nanoparticles was found to be potent, and it was also discovered that increasing the concentration of cumin oil increased the anti-inflammatory activity[70]. Velraj et al investigated the green synthesis of silver nanoparticles from the fruits of Mallotus phillipensis, also known as the "Kamala tree" or "Monkey face tree." The reduction of silver ion into silver particles was used in the manufacturing process. The most recent form of nanotechnology is green synthesis. According to the author's work, green synthesis nanoparticles have potent applications in the biomedical field, but this method is competitively priced and very well adapted for large scale operation for both medical and pharmaceutical applications[71].

5. Diagnostic Testing

Theranostic nanoparticles, or nanoparticles that can be used for both treatment and diagnosis, have recently received a lot of attention[72]. Many classes of nanoparticles have used this strategy, including drug conjugates, dendrimers, surfactant aggregates (micelles and vesicles), core-shell particles, as well as carbon nanotubes. It is able to measure the pathway and localization of these nanoparticles at the target site as well as drug action to assess therapeutic response by combining both drug and imaging agent in one smart formulation[73].

6. Nutraceuticals Delivery

Nutraceuticals are food-derived, standardized components that provide significant health benefits. They are commonly consumed as a supplement to various allopathic treatments, as well as to provide additional health benefits and reduce the risks of a variety of chronic illnesses. Food matrices interactions, aqueous solubility, degradation/metabolism, and epithelial permeability all affect the bioavailability and thus efficacy of orally consumed Nutraceuticals, just like any other drug. The majority of nutraceuticals are lipophilic molecules, such as fat-soluble vitamins (A, D, E, and K), polyunsaturated lipids, and phytochemicals. Again, nanotechnology provides comprehensive assistance, with the majority of studies designed to improve the dissolution processes of nutritional supplements via nanoparticle preparations[74,75].

When compared to Curcumin co-administered with piperine, Curcumin had a 9-fold higher oral bioavailability (absorption enhancer). When compared to Curcumin powder, another study of colloidal nanoparticles of Curcumin dubbed Theracurmin demonstrated 40-fold higher area under the curve (AUC) in rats and 27-fold higher in healthy human volunteers, as well as inhibitory actions against alcohol intoxication[76]. Numerous resveratrol nanoformulations have been reported to enhance the pharmacokinetic profile as well as bioavailability. Polymeric nanoparticles, zein-based nanoparticles, liposomes, cyclodextrins, and dual nanoencapsulation methods are among them. Recently, the neuroprotective effects of resveratrol on the blood-brain barrier were investigated using solid lipid nanoparticles embellished with apolipoprotein E for LDL receptor acknowledgement[77,78].

6. Future Perspectives

Despite widespread recognition of the future potential of nanoparticle as well as nano-drug delivery systems, their actual impact in the healthcare system, including cancer therapy/diagnosis, remains very limited. This is due to the field being a new area of science, with only two decades of actual research on the subject and many key fundamental characteristics still unknown. One major future area of research will be the fundamental markers of diseased tissues, including key biological markers that allow absolute targeting without altering the normal cellular process. Finally, the application of nanomedicine will advance as we gain a better understanding of diseases at the molecular level or that mirrors a nanomaterial-subcellular size comparable marker identification to open up new avenues for new diagnosis/therapy. As a result, understanding disease molecular signatures will lead to

advances in nanomedicine applications in the future. Additional research beyond what we have outlined in this review using known nanoprobes and nanotheragnostics products would be critical for the wider application of nanomedicine.

7. CONCLUSION

The current review examines recent advances in nanomedicines, such as technological advances in the delivery of old and new drugs, along with novel diagnostic methodologies. Novel natural biomaterials have remained in high demand due to their properties of being biodegradable, biocompatible, readily available, renewable, and low toxicity. Beyond identifying such polysaccharides and proteins as natural biopolymers, research on making them more stable in industrial processing environments and biological matrix through techniques such as crosslinking is currently among the most advanced. Polymeric nanoparticles (nanocapsules and nanospheres) synthesized via solvent evaporation, emulsion polymerization, and surfactant-free emulsion polymerization has also received a lot of attention. One of the major areas of research in nanomedicine in recent years has been the incorporation of diagnostics and therapy (theranostic), as exemplified by cancer as a disease model. Since the 1990s, the number of FDA-approved nanotechnology-based products and clinical trials has increase rapidly, and now includes synthetic polymer particles, liposome formulations, micelles nanoparticles, protein nanoparticles, nanocrystals, and a plethora of others, often in combination with drugs or biologics. Although nanomedicine regulatory mechanisms and safety/toxicity assessments will be further developed in the coming years, nanomedicine already has transformed the way we discover and administer drugs in biological systems. Researcher ability to diagnose diseases and even combine diagnosis and therapy has become a reality as a result of advances in nanomedicine.

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