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NANOPARTICLE DRUG DELIVERY SYSTEM: AN OVERVIEW

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ABSTRACT

Drug delivery is a comprehensive and distinct area of research that is gaining the interest of pharmaceutical researchers, physicians, and industry. In addition to having an impact on the development and efficacy of new therapeutic strategies like gene therapy, peptide and protein delivery, and anticancer drug delivery, a safe and targeted drug delivery has the potential to enhance the performance of some conventional medicines that are currently on the market. Recently, pharmacokinetic and pharmacodynamic characteristics of numerous types of pharmacological compounds have been altered and improved physically using particulate systems like nanoparticles. NPs are extremely small materials, ranging from 1 to 100 nm. Based on their characteristics, shapes, or sizes, they can be divided into many classes. Due to their large surface area and nanoscale size, NPs possess distinct physical and chemical characteristics. Because of their tiny size, nanoparticles exhibit improved properties such as high reactivity, strength, surface area, sensitivity, stability, etc. which have been developed in recent years for a wide variety of therapeutic applications. Nanoparticles are the most effective drug delivery system due to their high stability and controlled drug release. Consequently, drugs that are both hydrophilic and hydrophobic can be delivered via nanoparticles. Nanoparticles have been reducing the adverse effects and enhances the therapeutic efficacy of medications.

KEYWORDS: Nanoparticles, Nanotechnology, Particulate System, Drug Delivery, Targeting, Bioavailability.

INTRODUCTION

The complexity of certain diseases and the toxicity associated with some treatments increasingly demand novel routes for drug delivery. This includes not only therapeutic drug administration methods, but also the use of vectors to facilitate their application and diffusion into the human body.[1]

Drug delivery systems (DDSs) have been used in past eras to treat numerous ailments. All medicines rely on pharmacologic active metabolites (drugs) to treat diseases. In conventional drug delivery systems (CDDSs), drugs were delivered usually via oral, nasal, inhaled, mucosal, and shot methods. The conventionally delivered drugs were absorbed less, distributed randomly, damaged unaffected areas, were excreted early, and took a prolonged time to cure the disease. Due to all such reasons, the controlled-release drug delivery system was developed. Such evolution in the DDS enhances drug effectiveness in many ways.[2]

Nanotechnology is a known field of research since last century. Nanotechnology produced materials are of various types at nanoscale level. The fundamental component of nanotechnology is the nanoparticles. Nanoparticles (NPs) are wide class of materials that include particulate substances. The nanoparticles exhibit a unique physical, chemical and biological properties at nanoscale compared to their respective particles at higher scales. Nanoparticles can be defined as particulate dispersions or solid particles with a size range of 10-1000nm. The drug is dissolved, entrapped, encapsulated or attached to a nanoparticle matrix.

The nanoparticles are of different shape, size and structure. It may be spherical, cylindrical, tubular, conical, hollow core, spiral, flat, etc. or irregular. The surface can be a uniform or irregular with surface variations. Some nanoparticles are crystalline or amorphous with single or multi crystal solids either loose or agglomerated. Depending on the overall shape these materials can be 0D (zero dimension), 1D (one dimension), 2D (two dimension) or 3D (three dimension). The importance of these materials realized when researchers found that size can influence the physiochemical properties of a substance e.g. the optical properties.

NPs are not simple molecules itself and therefore composed of three layers i.e. (a) The surface layer, which

may be functionalized with a variety of small molecules, metal ions, surfactants and polymers. (b) The shell layer, which is chemically different material from the core in all aspects, and (c) The core, which is essentially the central portion of the NP and usually refers the NP itself.[3,4,5]

Nanotechnology basically deals with design, production and characterization of nano sized particles. Nano sized particles are basically small objects that act as a whole unit in accordance with their transport and properties. They can also be designed to improve the pharmacological and therapeutic effects of the drugs. They also have a very high surface area and they permit many functional groups to be adhered to them which in turn can bind to tumor cells. They have proven to be an excellent replacement for radiation and chemotherapy as they can easily assemble in the micro environment of the tumor. Recent studies have developed a number of nano-sized particles such as metals, semiconductors and polymeric particles utilized in molecular imaging and particulate delivery vehicles. Basically, nanotechnology deals with construction of artificial cells, enzymes and genes or repair in the synthesis of protein. Depending upon the method of preparation, nanoparticles, nanospheres or nanocapsules can be obtained. Nanocapsules are systems in which the drug is confined to a cavity surrounded by a unique polymer membrane, while nanospheres are matrix systems in which the drug is physically and uniformly dispersed.[6]

In pharmaceutical research and clinical settings, nano-particulate pharmaceutical drug delivery systems (NDDSs) are commonly used to increase the efficacy of medicines. Liposomes, polymers, micelles, metal nanoparticles, carbon nanotubes, solid lipid nanoparticles, noisomes and dendrimers are various types of nanoparticles that can be used to deliver drugs and target diseases. Drug-related problems such as low water solubility, poor bioavailability, and off-target delivery can be solved using NDDSs. NDDSs have been used to improve drug stability, to improve distribution time, and to target specific sites in the body.[7]

Recent developments in nanotechnology have shown that nanoparticles have a great potential as drug carriers. The major goals in designing nanoparticles as a delivery system are to control particle size, surface properties and release of pharmacologically active agents in order to achieve the site-specific action of the drug at the therapeutically optimal rate and dosage regimen.

Nanoparticles (NPs) have wide-spread applications in various sectors ranging from agriculture to medicine. In medicine, nanoparticles are continuously being improved for drug delivery, screening of various diseases and tissue engineering. The market of nanotechnology and drug delivery systems based on this technology will be widely felt by the pharmaceutical industry. In recent years, the number of patents and products in this field is increasing significantly.[8]

ADVANTAGES OF NANOPARTICLES[9]

- ✓ Enhancement of solubility and bioavailability
- ✓ Enhancement of pharmacological activity
- ✓ Sustained drug delivery
- ✓ Protection from degradation
- ✓ Enhancement of permeability
- ✓ Decreased side effects compared to conventional drug delivery
- ✓ Improved therapeutic effect
- ✓ Easy to alter the size and surface charge of nanoparticles, hence, could be used for both passive and active drug targeting after parenteral administration.
- ✓ Nanocarriers are generally made of biodegradable substances, therefore, do not remain in the body.

CLASSIFICATION OF NANOPARTICLES

- **Organic nanoparticles:** Micelles, dendrimers, ferritin and liposomes, etc. are commonly known polymers or organic nanoparticles. These nanoparticles are non-toxic, biodegradable, and some particles such as liposomes and micelles have a hollow core also known as nano capsules and are sensitive to thermal and electromagnetic radiation such as heat and light. The organic nanoparticles are most widely used in the biomedical field for example drug delivery system as they are efficient and also can be injected on specific parts of the body which is also known as targeted drug delivery.[10]

Advantages: Biocompatible, biodegradable, nontoxic.
Disadvantages: Low stability, reproducibility, drug entrapment issues.[11]

- **Liposomes:** Liposomes are particles formed by hydrating dried phospholipids. Liposomes are spherical vesicles composed of phospholipid bilayers with a particle size distribution between 10 and 1000 nm. They are made with lipid particles and surface adjustment to produce particles of various shapes, compositions, scales, and versatility.[12]

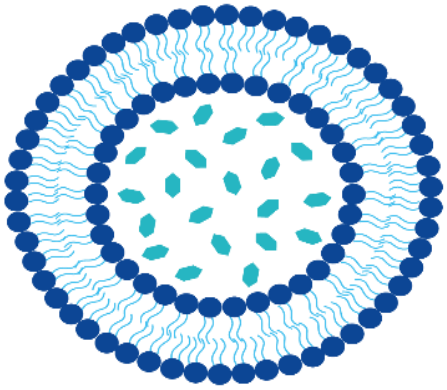

Fig no.1: Schematic representation of liposome.

Advantages: Biodegradable and biocompatible, protects entrapped drug and provides sustained release.
Disadvantages: Low stability, tends to agglomerate.[13]

- **Dendrimers:** Dendrimers are synthetic, well-defined and highly mono-dispersed symmetric molecules which have a repetitive branched pattern. Dendrimers arise from two Greek words: 'Dendron' meaning tree and 'Meros' meaning part. Molecular chemistry and polymer chemistry both exhibit well-defined characteristics features of Dendrites. Usually, dendrimers have hyper-branched structures with a core in which therapeutics and imaging agents have been trapped.

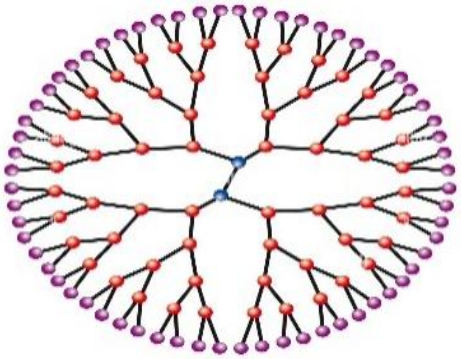

Fig no.2: Schematic representation of dendrimer.

Advantages: Water soluble and biocompatible, flexibility in conjugation chemistry, good pharmacokinetic behaviour.

Disadvantages: Poor drug release profile, rapid clearance, toxic effects.

- **Nanotube:** A nanotube is a nanometer scale tube like structure. Nanotubes are members of the fullerene structural family. Their name is derived from their long, hollow structure with the walls formed by one-atom-thick sheets of carbon called graphene. Nanotubes are categorized as single-walled nanotubes (SWNTs) and multi-walled nanotubes.

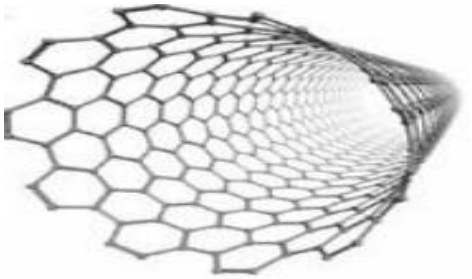

Fig no.4: Schematic representation of nanotube.

Advantages: Protects entrapped drug and provides sustained release, large surface area.

Disadvantages: Poorly soluble in water, non-biodegradable, poor pharmacokinetics.[14,15]

- **Polymeric nanoparticles:** Polymeric nanoparticles (PNPs) can be synthesized from natural or synthetic materials, as well as monomers or preformed polymers — allowing for a wide variety of possible structures and characteristics. Polymeric NPs are ideal candidates for drug delivery because they are biodegradable, water soluble, biocompatible, biomimetic and stable during storage. It can be prepared as nanospheres or nanocapsules by different methods such as nanoprecipitation, double emulsification, polymer coating and emulsification diffusion.

Fig no.3: Schematic representation of polymeric nanoparticle.

Advantages: Controlled synthesis and great deal of flexibility in conjugation of multiple bioactive agents, excellent stability.

Disadvantages: Agglomeration, nanotoxicity with non-biodegradable polymers.[16]

- **Inorganic nanoparticles:** In the field of modern material science, Inorganic nanoparticle has been developed the role based upon their unique physical properties and particularly in biotechnology. Nanoparticles that lack carbon atoms are known as inorganic nanoparticles. Inorganic nanoparticles are typically defined as those composed of metals or metal oxides. Based upon these two factors of inorganic nanoparticles they have certain physical properties that mainly include size-dependent optical, magnetic, electronic, and catalytic properties.

Advantages: Smaller particle size, improved stability, enhanced magnetic properties.

Disadvantages: Low biocompatibility, lack of biodegradability, high cellular toxicity.[17]

- **Fullerenes:** Fullerenes (C_{60}) is a carbon molecule that is spherical in shape and made up of carbon atoms held together by sp^2 hybridization. About 28 to 1500 carbon atoms forms the spherical structure with diameters up to 8.2 nm for a single layer and 4 to 36 nm for multi-layered fullerenes.

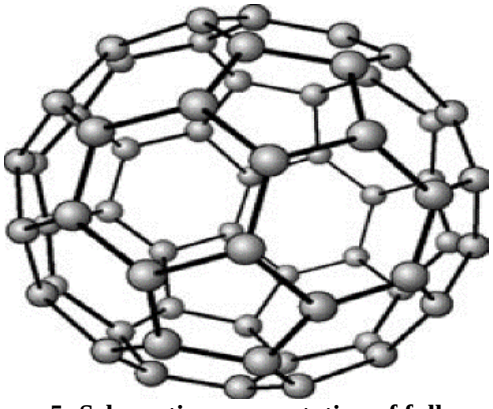

Fig no.5: Schematic representation of fullerenes.

Advantages: Low cost, large surface area, long-term storage, highly stable.
Disadvantages: Lower catalytic activity, unclear catalytic mechanism.[18]

- **Nanocrystal:** A nanocrystal is a type based upon material particle having at least one dimension smaller than 100 nanometres and mainly composed of atoms in either a single or poly-crystalline arrangement. Nanocrystals are aggregates of around hundreds or thousands of molecules that combine in a crystalline form, composed of pure drug with only a thin coating comprised of surfactant or combination of surfactants.

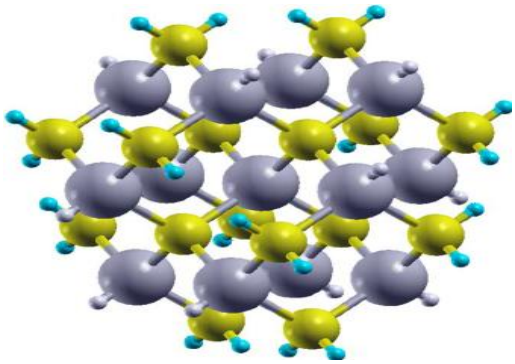

Fig no.6: Schematic representation of nanocrystal.

Advantages: Improve bioavailability of water-insoluble compounds, enhances particle stability.

Disadvantages: Time consuming, costly, specialized equipment is needed.[19]

- **Solid lipid nanoparticles:** Solid lipid nanoparticles (SLNs) are made of solid lipids and stabilized with emulsifying agents in an aqueous dispersion. They resemble with nanoemulsion only replacing liquid lipid with a solid lipid. Their high degree of biocompatibility, physiochemical properties and ability to enhance absorption of hydrophobic drugs through lymphatic uptake has made them popular compounds to utilize in drug carrier systems.

Fig no.7: Schematic representation of solid lipid nanoparticle.

Advantages: Long physical stability, limited side effects, controlled and sustained drug release, improved drug bioavailability.

Disadvantages: Low drug payload for hydrophilic drugs, drug expulsion, drug burst release by erosion mechanism.[20]

- **Nanoemulsion:** Nanoemulsions and self-emulsified drug delivery systems (SEDDS) have gained a lot of interest in recent years as a way to increase the bioavailability of medicines of low aqueous solubility. Nanoemulsions are non-homogenous systems made up of immiscible liquids where one is disseminated as droplets in the other. When integrated into aqueous phases under mild mixing, SNEDDS are isotropic mixes of oil, surfactant, co-surfactant, and drug that produce oil-in-water (o/w) nanoemulsions.

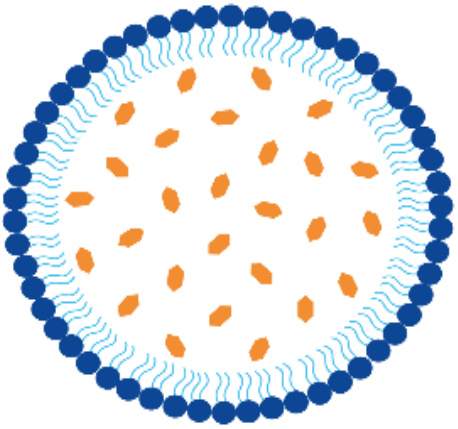

Fig no.9: Schematic representation of nanoemulsion.

Advantages: Biocompatible/ biodegradable, improves solubility, highly stable to gravitational separation and aggregation.

Disadvantages: High amounts of surfactant needed to achieve oil droplets of nanometric sizes.[21]

- **Niosome:** Niosomes are a type of molecular cluster formed in an aqueous phase by the self-assembly of non-ionic surfactants. Niosomes have a unique

architecture that allows them to function as a new delivery method that can accommodate both lipophobic and lipophilic agents. Niosomes consist of non-ionic surfactants, they are characterized by their non-toxicity, high stability and they are considered to be a replacement to liposomes.

Fig no.8: Schematic representation of noisome.

Advantages: Controlled and targeted drug delivery, stable and osmotically active, nontoxic, nonimmunogenic, biocompatible and biodegradable.

Disadvantages: Physically instable, expensive, insufficient drug loading capacity, leakage of entrapped drug.[22]

METHODS OF PREPARATION OF NANOPARTICLES: Nanoparticles are aimed to be prepared from a variety of materials such as proteins, polysaccharides and synthetic polymers.

- **Solvent evaporation method:** In this method, the polymer is dissolved in an organic solvent such as dichloromethane, chloroform or ethyl acetate, which is also used as the solvent for dissolving the hydrophobic drug. The mixture of polymer and drug solution is then emulsified in an aqueous solution containing a surfactant or emulsifying agent to form an oil in water (o/w) emulsion. After the formation of stable emulsion, the organic solvent is evaporated either by reducing the pressure or by continuous stirring. Particle size was found to be influenced by the type and concentrations of stabilizer, homogenizer speed and polymer concentration. In order to produce small particle size, often a high-speed homogenization or ultrasonication may be employed.
- **Spontaneous emulsification or solvent diffusion method:** This is a modified version of solvent evaporation method. In this method, the water-miscible solvent along with a small amount of the water immiscible organic solvent is used as an oil phase. Due to the spontaneous diffusion of solvents an interfacial turbulence is created between the two phases leading to the formation of small particles. As the concentration of water miscible solvent increases, a decrease in the size of particle can be achieved.
- **Polymerization method:** In this method, monomers are polymerized to form nanoparticles in an aqueous solution in which drug may be dissolved. Drug may also be incorporated by absorption onto the nanoparticles after polymerization completed. The nanoparticle suspension is then purified to remove various stabilizers and surfactants employed for polymerization by ultracentrifugation and resuspending the particles in an isotonic surfactant-free medium. This technique has been reported for making polybutylcyanoacrylate or poly(alkylcyanoacrylate) nanoparticles.
- **Coacervation or ionic gelation method:** The nanoparticles preparation is carried by using biodegradable hydrophilic polymers such as chitosan, gelatin and sodium alginate. Developing a method for preparing hydrophilic chitosan nanoparticles by ionic gelation. In this method, positively charged amino-group of chitosan interacts with negative charged tripolyphosphate to form coacervates with a size in the range of nanometer.[5]
- **High-pressure homogenization (HPR):** HPR is a technique commonly used in the preparations of SLNs and liposomes. HPR can be performed as either a hot homogenization or a cold homogenization. For hot HPR techniques, a drug is usually dissolved in lipid being melted at 5 - 10°C above its melting point. The melt is then dispersed under a hot aqueous surfactant solution that is being heated at the same temperature. The resulting solution is then homogenized to form a hot oil in water nanoemulsion and cooled to room temperature to enable recrystallization and the formation of SLNs. In cold HPR techniques, the drug containing melt is cooled to form a solid lipid.[12]
- **Supercritical fluid technology:** Supercritical fluid technology has been utilized as an alternative to manufacture biodegradable micro and nanoparticles since supercritical fluids are ecologically friendly. Even though environment friendly and suitable for mass production, supercritical fluid technology needs specific expensive equipment. Supercritical fluids are fluids, when are at a temperature higher than its critical temperature, still remain homogenous, regardless of pressure. Supercritical CO_2 (SC-CO_2) is the most broadly applied supercritical fluid due to its moderate critical conditions, non-flammability, considerable price and safety.[21]
- **Salting Out Method:** Salting out is based on the separation of a water-miscible solvent from aqueous solution via a salting-out effect. Salting-out is based on the separation of a water miscible solvent from aqueous solution via a salting-out effect. Polymer and drug are initially dissolved in a solvent which is subsequently emulsified into an aqueous gel containing the salting-out agent (electrolytes, such as magnesium chloride and calcium chloride, or

non- electrolytes such as sucrose) and a colloidal stabilizer such as polyvinylpyrrolidone or hydroxyethylcellulose. This oil/water emulsion is diluted with a sufficient volume of water or aqueous solution to enhance the diffusion of solvent into the aqueous phase, thus inducing the formation of nanospheres.[23]

- **Solvent Displacement / Precipitation method:** Solvent displacement involves the precipitation of a preformed polymer from an organic solution and the diffusion of the organic solvent in the aqueous medium in the presence or absence of surfactant. Polymers, drug, and or lipophilic surfactant are dissolved in a semi-polar water miscible solvent such as acetone or ethanol. The solution is then poured or injected into an aqueous solution containing stabilizer under magnetic stirring. Nano particles are formed instantaneously by the rapid solvent diffusion. The solvent is then removed from the suspensions under reduced pressure. Nano precipitation method is well suited for most of the poorly soluble drugs.[24]

CHARACTERIZATION OF NANOPARTICLES

- **Drug Entrapment Efficiency:** The nanoparticles were separated from the aqueous medium by ultracentrifugation at 10,000 rpm for 30 min at 50C. Then the resulting supernatant solution was decanted and dispersed into phosphate buffer saline pH 7.4. Thus the procedure was repeated twice to remove the unentrapped drug molecules completely. The amount of drug entrapped in the nanoparticles was determined as the difference between the total amount of drug used to prepare the nanoparticles and the amount of drug present in the aqueous medium.

Drug Entrapment efficiency (%) = Amount released from the lysed nanoparticle /Amount of drug Initially taken to prepare the Nanoparticles X 100

- **Particle size:** Particle size and size distribution are the most important characteristics of nanoparticle systems. They determine the *in-vivo* distribution, biological fate, and toxicity and targeting ability of nanoparticle system. Different techniques used to estimate the size of the NPs include scanning electron microscopy (SEM), transmission electron microscopy (TEM), X-ray diffraction (XRD), atomic force microscopy (AFM), and dynamic light scattering (DLS). It has been found that particle size affects the drug release. Smaller particles offer larger surface area. As a result, most of the drug loaded onto them will be exposed to the particle surface leading to fast drug release.[5]

- **Zeta potential:** The Zeta potential of a nanoparticle is commonly used to characterized the surface charge property of nanoparticles. It reflects the electrical potential of particles and is influenced by the composition of the particle and the medium in which it is dispersed. Nanoparticles with a zeta potential between −10 and +10 mV are considered approximately neutral, while nanoparticles with zeta potentials of greater than +30 mV or less than −30 mV are considered strongly cationic and anionic, respectively.[10]

- **Surface morphology:** Nanoparticles can take on a wide variety of shapes, and their surfaces can be patterned in a variety of ways, both of which are important for utilizing their properties. There are many different shapes, some of which are spherical, flat, cylindrical, tubular, conical, and irregular. The surfaces of these shapes can be crystalline or amorphous, and they can be uniform or have irregularities. Imaging methods using electron microscopy, such as scanning electron microscopy (SEM) and transmission electron microscopy (TEM), are typically used to determine the surface. When it comes to imaging using electron microscopy, the particles in the liquid phase are captured either electrostatically or through filtering while the particles in the gaseous phase are deposited on a surface for subsequent analysis.[17]

- **Polydispersity Index:** Polydispersity index is a parameter to define the particle size distribution of nanoparticles obtained from photon correlation spectroscopic analysis. It is a dimensionless number extrapolated from the autocorrelation function and ranges from a value of 0.01 for mono dispersed particles and up to values of 0.5-0.7. Samples with very broad size distribution have polydispersity index values > 0.7.[25]

- ***In-vitro* drug Release:** The drug loading of the nanoparticles is generally defined as the amount of drug bound per mass of polymer (usually moles of drug per mg polymer or mg drug per mg polymer); it could also be given as percentage relative to the polymer. The technique used for this analysis is classical analytical methods like UV spectroscopy or high performance liquid chromatography (HPLC) after ultracentrifugation, ultra-filtration, gel filtration, or centrifugal ultrafiltration. Quantification is performed with the UV spectroscopy or HPLC. Drug release assays are also similar to drug loading assay which is assessed for a period of time to analyze the mechanism of drug release.

- **Drug release kinetics:** In order to understand the kinetics and mechanism of drug release, results of in vitro drug release study of the prepared NPs were fitted into various kinetic equations like zero order (cumulative % remaining vs. time), first order (log % drug remaining vs. time), Higuchi's model (cumulative % drug release vs. square root of time), Peppas (log % drug release vs. log time).[26]

MARKETED NANOFORMULATIONS[7,12]

Brand name	NP type	Drug loaded on NPs	Therapeutic class	Company
Doxil	Liposome	Doxorubicin	Chemotherapeutic	Baxter Hlthcare Corp
DepoCyt	Liposome	Cytarabine	Chemotherapeutic	Sigma-Tau
Cimzia	Polymeric NP	Certolizumab pegol	TNF inhibitor	UCB
Oncaspar	Polymeric NP	Pegaspargase	Chemotherapeutic	Sigma-Tau
Somavert	Polymeric NP	Pegvisomant	Acromegaly	Pfizer
TriCor	Nanocrystal	Fenofibrate	Hyperlipidemia	Abbvie
Emend	Nanocrystal	Aprepitant	Anti-emetic	Merck
Megace ES	Nanocrystal	Megestrol acetate	Appetite stimulant	Par Pharmaceutical
Femara	Solid lipid NP	Letrozol (LTZ)	Antineoplastic	Novartis
Somatuline depot	Nanotube	Lanreotide acetate	Chemotherapeutic	IPSEN Pharma

APPLICATIONS OF NANOPARTICLES

The main application involved in use of nanoparticles for biomedical applications, such as drug and gene delivery, cancer treatment and diagnostic tools, food etc. has been extensively studied throughout the past decade and also nanoparticle created a huge interest due to their very small size and large surface-to-volume ratio, and they display absolutely novel uniqueness contrast to the large particles of bulk material. Very recently, nanoparticles have gained significance in the field of Biomedicine. Nanoparticles have potential application in medical field including diagnostics and therapeutics.

1. **Nanoparticles for oral delivery of peptides and proteins:** Significant advances in biotechnology and biochemistry have led to the discovery of a large number of bioactive molecules and vaccines based on peptides and proteins. Development of suitable carriers remains a challenge due to the fact that bioavailability of these molecules is limited by the epithelial barriers of the gastrointestinal tract and their susceptibility to gastrointestinal degradation by digestive enzymes. Polymeric nanoparticles allow encapsulation of bioactive molecules and protect them against enzymatic and hydrolytic degradation. The gastrointestinal tract provides a variety of physiological and morphological barriers against protein or peptide delivery, e.g., (a) proteolytic enzymes in the gut lumen like pepsin, trypsin and chymotrypsin; (b) proteolytic enzymes at the brush border membrane (endopeptidases); (c) bacterial gut flora; and (d) mucus layer and epithelial cell lining itself. One important strategy to overcome the gastrointestinal barrier is to deliver the drug in a colloidal carrier system, such as nanoparticles, which is capable of enhancing the interaction mechanisms of the drug delivery system and the epithelia cells in the GI tract.[5]
2. **Nanoparticles in drug delivery:** The most significant advantages of nanoparticles used on drug carrier are high stability, high carrier capacity, expediency of accommodation of both hydrophilic, hydrophobic substances and various routes of administration including oral application and inhalation. Certain drugs cannot pass the first pass metabolism. The nanoparticles can be modified to overcome this and they also allow controlled sustained drug release from the matrix. These attributes can enhance the bioavailability of the drug and also in the reduction of the dosing frequency.[6]
3. **Nanoparticles for drug delivery into the brain:** The blood-brain barrier (BBB) is the most important factor limiting the development of new drugs for the central nervous system. 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 can also reduce the brain concentration of lipid-soluble molecules by the function of enzymes or efflux pumps. Consequently, the BBB only permits selective transport of molecules that are essential for brain function.[10]
4. **Nanoparticle in cancer treatment:** There are a variety of nanoparticle systems currently under investigation to be applied in biomedical with the emphasis on cancer therapeutics and explored for biomedical applications with some particular emphasis for cancer therapeutics; hence some precious metals (mainly gold and silver systems, Au, and Ag) and some magnetic oxides (in particular magnetite Fe_3O_4) received much interest including quantum dots and some of what is called natural nanoparticles.[14]
5. **Nanoparticles in Cosmetics and Sunscreens:** Traditional sunscreen that offers protection from ultraviolet (UV) rays is not stable over the long term when it is used. Numerous benefits can be gained from the use of sunscreen that contains nanoparticles, such as titanium dioxide. Some sunscreens make use of titanium oxide and zinc oxide nanoparticles due to the UV protection that these nanoparticles provide. Titanium oxide and zinc oxide nanoparticles are both transparent to visible light, and they also absorb and reflect UV rays. Some lipsticks employ iron oxide nanoparticles as a pigment.[17]
6. **Nanoparticles in vaccination against COVID-19:** During the year 2020 and now, all scientists and researchers are concentrating their efforts on creating remedies to combat the worldwide epidemic of the COVID-19 virus. In the year 2021, the importance of nanoparticle technology in the

development of therapeutic formulations for the diagnosis, treatment, and promotion of long-term human immunity against COVID-19 was highlighted. The backbone in succession and acceleration of the time required for creation of COVID-19 nanoparticle-based vaccines (CNPBV) was the recorded genome structure from Corona viruses and the pre-knowledge of the sequence of the protein laying the virus surface.[21]

7. **Nanoparticles for Gene delivery:** Polynucleotide vaccines work by delivering genes encoding relevant antigens to host cells where they are expressed, producing the antigenic protein within the vicinity of professional antigen presenting cells to initiate immune response. Such vaccines produce both humoral and cell-mediated immunity because intracellular production of protein, as opposed to extracellular deposition, stimulates both arms of the immune system.[27]
8. **Nanoparticles for diagnosis and bioimaging:** A number of molecular imaging techniques are available such as optical imaging (OI), magnetic resonance imaging (MRI), ultrasound imaging (USI), positron emission tomography (PET) and others have been reported for imaging of *in vitro* and *in vivo* biological specimens. The current development of luminescent and magnetic nanoparticles advances bio-imaging technologies. Two different types of nanoparticles have been widely used for imaging; luminescent nanoprobes for OI and magnetic nanoparticles for MRI. Gold nanoparticles are being used for detection of cancer.[28]

CONCLUSION

In this review, we provided a comprehensive overview on NPs, their types, characterizations, and applications. Biologically active substances that are poorly soluble, poorly absorbed, and labile can be transformed into potentially deliverable pharmaceuticals via nanoparticulate systems. The hydrophilic shell of this systems core, which hinders identification by the reticular-endothelial system, results in a long circulation time and the ability to enclose a variety of drugs, enzymes, and genes. Because of their small size and large surface area, NPs are a good candidate for a wide range of applications. Due to their small size and relative mobility, NP have a relatively higher intracellular uptake than microparticles and are accessible to a wide range of biological targets. NPs can minimize drug toxicity and enhance drug safety parameters also by enhancing the pharmacokinetic and pharmacodynamic characteristics of a variety of drugs. NP formulations present a highly feasible alternative in the field of developing novel drugs. Because of its effectiveness and environmental friendly property, nanotechnology is improving our everyday lives by enhancing the performance and efficiency of everyday objects. The concept of nanoparticle has to be developed further in order to become a realistic, practical application as the next generation of drug delivery system. Finally, this study will help the researchers by providing the necessary information to recognize and study the nanoparticles.

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