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RESEARCH ARTICLE

NANOPARTICLES AS DRUG DELIVERY SYSTEMS

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ABSTRACT

For the past few decades, there has been a considerable research interest in the area of drug delivery using particulate delivery systems as carriers for small and large molecules. Particulate systems like nanoparticles have been used as a physical approach to alter and improve the pharmacokinetic and pharmacodynamic properties of various types of drug molecules. Nanoparticles (NP) are defined as particles with a diameter smaller than 100 nm, are increasingly used in different applications, including drug carrier systems and to pass organ barriers such as the blood-brain barrier. Because of their unique properties Nanocrystals (quantum dots) and other nanoparticles (gold colloids, nanobars, dendrimers and nanoshells) have been receiving a lot of attention for potential use in Therapeutics, and therapeutics drug discovery. The use of nanotechnology in medicine and more specifically drug delivery is set to spread rapidly. Currently many substances are under investigation for drug delivery and more specifically for cancer therapy. Interestingly pharmaceutical sciences are using nanoparticles to reduce toxicity and side effects of drugs and up to recently did not realize that carrier systems themselves may impose risks to the patient. The present paper deals with all these aspects of NP.

INTRODUCTION

Nanotechnology is a modern field of science which plays a dominant role in day to day life aspects. Nanotechnology deals with production, manipulation and use of material ranging in nanometers. Human life gets an impact role in all spheres mainly in the field of nanotechnology .Nanotechnology mainly deals with the Nanoparticle having a size of 1-100 nm in one dimension used significantly concerning medicinal chemistry, atomic physics, and all other known fields .Richard Feynman was the first person who gave a talk in the year of 1959 which many years later inspired the conceptual foundations of nanotechnology. Nanoparticles are defined as particulate dispersions or solid particles with a size in the range of 10-1000 nm. The drug is dissolved, entrapped, encapsulated or attached to a nanoparticle matrix. 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. In recent years, biodegradable polymeric nanoparticles, particularly those coated with hydrophilic polymer such as poly (ethylene glycol) (PEG) known as long-circulating particles, have been used as potential drug delivery devices because of their ability to circulate for a prolonged period time target a particular organ, as carriers of DNA in gene therapy, and their ability to deliver proteins, peptides and genes [1-4]. The reason why nanoparticles (NP) are attractive for such purposes is based on their important and unique features, such as their surface to mass ratio, which is much larger than that of other particles and materials, allowing for catalytic promotion of reactions, as well as their ability to adsorb and carry other compounds. 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 dose regimen. Though liposomes have been used as potential carriers with unique advantages including protecting drugs from degradation, targeting to site of action and reduction toxicity or side effects, their applications are limited efficiency, rapid leakage of water-soluble drug in the presence of blood components and poor storage stability. On the other hand, polymeric nanoparticles offer some specific advantages over liposomes. For instance, they help to increase the stability of drugs/proteins and possess useful controlled release properties [5-8].

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Nanoparticles: The word “nanoparticles” refers to nanostructures particulated, with variable shape, but with at least one dimension in the “nano” scale, that is lower than 100 nanometers (nm). Nanoscale drug delivery technologies offer advantages such as increased bioavailibity, extended drug half-life and reduced off-target toxicities[12]. Furthermore, the new generation of therapeutic nanoparticles is inherently multifunctional: combining active drug compound with selective targeting moieties and, in many cases, imaging agents that permit localization by standard x-ray, magnetic resonance (MR) or positron emission tomography (PET) technologies. Mesoporous silica nanoparticles (MSNs) were used for controlled delivery of various hydrophilic or hydrophobic active agents. Later advances in the MSNs surface properties such as surface functionalization and PEGylation rendered them as a promising drug delivery vehicle for cancer treatment [13]. Polymer systems offer immense flexibility in customization and optimization of nanocarriers to efficiently deliver new therapeutics and provide an integral step in aiding their progression to clinical practice [14]. Nanoparticles are subnanosized colloidal drug delivery systems particle size ranges from 10-1000 nm in diameter. They are composed of synthetic or semi synthetic polymers carrying drugs or proteinaceous substances, i.e. antigen(s). Drugs are entrapped in the polymer matrix particulates or solid solutions or may be bound to particle surface by physical adsorption or in chemical form.Nanoparticles represent very promising carrier system for the targeting of anti-cancer agents to tumors. Nanoparticles exhibit a significant tendency to accumulate in a number of tumors after iv injection. Nanoparticles can also be used in Brain Drug Targeting.Poly (butyl cyanoacrylate) nanoparticles represent the only nanoparticles that were so far successfully used for in vivo delivery of drugs to brain. This polymer has the advantage that it is very rapidly biodegradable.

The advantages of using nanoparticles as a drug delivery system include the following:

- Particle size and surface characteristics of nano particles can be easily manipulated to achieve both passive and active drug targeting after parenteral administration.
- They control and sustain release of the drug during the transportation and at the site of localization, altering organ distribution of the drug and subsequent clearance of the drug so as to achieve increase in drug therapeutic efficacy and reduction in side effects.
- Controlled release and particle degradation characteristics can be readily modulated by
- The choice of matrix constituents. Drug loading is relatively high and drugs can be incorporated
- into the systems without any chemical reaction; this is an important factor for preserving the drug
- Activity.
- Site-specific targeting can be achieved by attaching targeting legends to surface of particles o use of magnetic guidance.
- The system can be used for various routes of administration including oral, nasal, parenteral,intra-ocular etc.

In spite of these advantages, nanoparticles do have limitations. For example, their small size and large surface area can lead to particle-particle aggregation, making physical handling of nanoparticles difficult in liquid and dry forms. In addition, small particles size and large surface area readily result in limited drug loading and burst release. These practical problems have to be overcome before nanoparticles can be used clinically or made commercially available. The present review details the latest development of nanoparticulate drug delivery systems, surface modification issues, drug loading strategies, release control and potential applications of nanoparticles. Liposomes are concentric bilayered vesicles in which an aqueous volume is entirely enclosed by a membranous lipid bilayer mainly composed of natural or synthetic phospholipids. Liposomes are characterized in terms of size, surface charge and number of bilayers. It exhibits number of advantages in terms of amphiphilic character, biocompatibility, and ease of surface modification rendering it a suitable candidate delivery system for biotech drugs. Liposomes have been used successfully in the field of biology, biochemistry and medicine since its origin. These alter the pharmacokinetic profile of loaded drug to a great extent especially in case of proteins and peptides and can be easily modified by surface attachment of polyethylene glycol-units (PEG) making it as stealth liposomes and thus increase its circulation half-life [11-13].

TYPES OF NANOPARTICLES

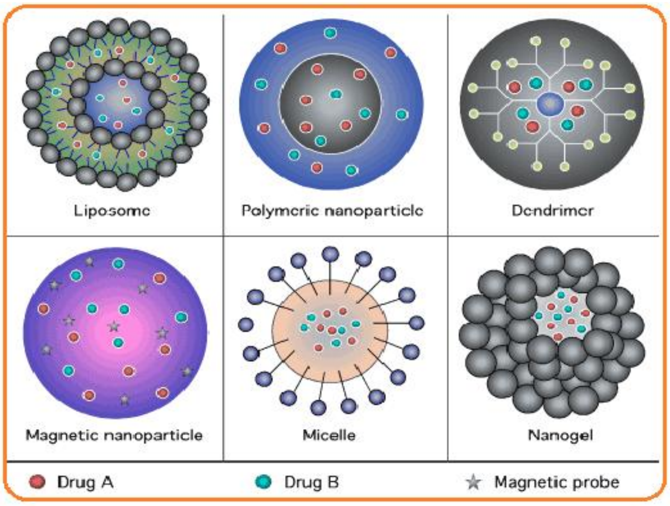

Figure: Schematic diagram representing the various types of nanoparticles Liposomes

Solid lipid nanoparticles: Solid lipid nanoparticles (SLN) were developed at the beginning of the 1990s as an alternative carrier system to emulsions, liposomes and polymeric nanoparticles as a colloidal carrier system for controlled drug delivery. Main reason for their development is the combination of advantages from different carriers systems like liposomes and polymeric nanoparticles. SLN have been developed and investigated for parenteral. pulmonal and dermal application routes. Solid Lipid Nanoparticles consist of a solid lipid matrix, where the drug is normally incorporated, with an average diameter below 1 µm. To avoid aggregation and to stabilize the dispersion, different surfactants are used that have an accepted GRAS (Generally Recognized as Safe) status. SLN have been considered as new transfection agents using cationic lipids for the matrix lipid composition. Cationic solid lipid nanoparticles (SLN) for gene transfer can be formulated using the same cationic lipids as for liposomal transfection agents [14-19].

Polymeric nanoparticles: In comparison to SLN or nanosuspensions polymeric nanoparticles (PNPs) consists of a biodegradable polymer. The advantages of using PNPs in drug delivery are many, being the most important that they generally increase the stability of any volatile pharmaceutical agents and that they are easily and cheaply fabricated in large quantities by a multitude of methods. Also, polymeric nanoparticles may have engineered specificity, allowing them to deliver a higher concentration of pharmaceutical agent to a desired location [14-19]. Polymeric nanoparticles are a broad class comprised of both vesicular systems (nanocapsules) and matrix systems (nanospheres).

Nanocapsules: Nanocapsules are systems in which the drug is confined to a cavity surrounded by unique polymeric membrane whereas nanospheres are systems in which the drug is dispersed throughout the polymer matrix. The various natural polymers like gelatin, albumin and alginate are used to prepare the nanoparticles; however they have some inherent disadvantages like poor batch-to- batch reproducibility, prone to degradation and potential antigenicity. Synthetic polymers used for nanoparticles preparation may be in the form of preformed polymer e.g. polyesters like polycaprolactone (PCL), poly lactic acid (PLA) or monomers that can be polymerized *in situ* e.g. poly alkyl cyanoacrylate. The candidate drug is dissolved, entrapped, attached or encapsulated throughout or within the polymeric shell/matrix. Depending on the method of preparation, the release characteristic of the incorporated drug can be controlled. Polymeric nanoparticulate systems are attractive modules for intracellular and site specific delivery. Nanoparticles can be made to reach a target site by virtue of their size and surface modification with a specific recognition ligand. Their surface can be easily modified and functionalized [14-19].

Nanospheres: From its definition nanospheres are considered as a matrix system in which the matrix in uniformly dispersed. These are spheric vesicular systems.

Dendrimers: Dendrimers, a unique class of polymers, are highly branched macromolecules whose size and shape can be precisely controlled. Dendrimers are fabricated from monomers using either convergent or divergent step growth polymerization. The well-defined structure, mono dispersity of size, surface functionalization capability, and stability are properties of dendrimers that make them attractive drug carrier candidates. Drug molecules can be incorporated into dendrimers via either complexation or encapsulation. Dendrimers are being investigated for both drug and gene delivery, as carriers for penicillin, and for use in anticancer therapy [20-25]

Nanotube: Carbon nanotubes (CNTs; also known as buckytubes) are allotropes of carbon with a cylindrical nanostructure. Nanotubes have been constructed with length-to-diameter ratio of up to 132,000,000:1, which is significantly larger than any other material. These cylindrical carbon molecules have novel properties which make them potentially useful in many applications in nanotechnology, electronics, optics, and other fields of materials science, as well as potential uses in architectural fields. They may also have applications in the construction of body armor. They exhibit extraordinary strength and unique electrical properties, and are efficient thermal conductors. Nanotubes are members of the fullerene structural family, which also includes the spherical bucky balls. The ends of a nanotube may be capped with a hemisphere of the bucky ball structure. Their name is derived from their size, since the diameter of a nanotube is on the order of a few nanometers (approximately 1/50,000th of the width of a human hair), while they can be up to 18 centimeters in length.

Nanowire: A nanowire is a nanostructure, with the diameter of the order of a nanometer (10−9 meters). Alternatively, nanowires can be defined as structures that have a thickness or diameter constrained to tens of nanometers or less and an unconstrained length. At these scales, quantum mechanical effects are important — which coined the term "quantum wires".

Nanocrystals: Nanocrystal is any nanomaterial with at least one dimension ≤ 100nm and that is single crystalline. More properly, any material with a dimension of less than 1 micrometre, i.e., 1000 nanometers, should be referred to as a nanoparticle, not a nanocrystal. For example, any particle which exhibits regions of crystallinity should be termed nanoparticle or nanocluster based on dimensions. These materials are of huge technological interest since many of their electrical and thermodynamic properties show strong size dependence and can therefore be controlled through careful manufacturing processes. Crystalline nanoparticles are also of interest because they often provide single-domain crystalline systems that can be studied to provide information that can help explain the behavior of macroscopic samples of similar materials, without the complicating presence of grain boundaries and other defects. Semiconductor nanocrystals in the sub-10nm size range are often referred to as quantum dots.

Nanobots: Nanorobotics is the technology of creating machines or robots at or close to the microscopic scale of a nanometer (10−9 meters). More specifically, nanorobotics refers to the still largely hypothetical nanotechnology engineering discipline of designing and building nanorobots, devices ranging in size from 0.1-10 micrometers and constructed of nanoscale or molecular components. Potential applications for nanorobotics in medicine include early diagnosis and targeted drug-delivery for cancer, biomedical instrumentation surgery.

Applications of nanotechnology: 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 [26] Very recently, nanoparticles have gained significance in the field of Biomedicine[27] Nanoparticles have potential application in medical field including diagnostics and therapeutics [28].

Application of nanoparticle in drug delivery: Nanoparticle involved in drug delivery – The nanoparticle get entrapment of drugs are either enhanced delivery to, or uptake by target cells and/or a reduction in the toxicity of the free drug to non-target organs.

Applications of nanoparticles in food: Nanofood is a term used to describe foods that use nanotechnology techniques, tools or manufactured nanomaterials that have been added during cultivation, production, processing or packaging. There are several purposes for the development of nanofood.
These include improvement of food safety, enhancement of nutrition and flavor, and cutting production and consumer costs. In addition, nanofood provides various benefits by which

include health promoting additives, longer shelf lives and new flavor varieties The application of nanotechnology in food is rapidly emerging and is involving all areas of the food chain from agricultural applications to food processing and enhancing bioavailability of nutrients.

Application of nanoparticle in gene delivery: Gene delivery it is a technique that plays a vital role that can efficiently introduce gene of interest in order to express its encoded protein in a suitable host or host cell. Now a day, there are different types of primary gene delivery systems that mainly employ viral vectors like retroviruses and adenoviruses, nucleic acid electroporation, and nucleic acid transfection.

Application of 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. There are a variety of nanoparticle systems currently investigated 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 Fe3O4) received much interest including quantum dots and some of what is called natural nanoparticles[29] . The unique up conversion process of UCNPs may be utilized to activate photosensitive therapeutic agents for applications in cancer treatment.

Other applications of nanoparticles: In recent years nanoparticles are involved with new applications in areas like information & communication technology, power engineering, industrial engineering, environmental engineering, chemical industry, medicine, in pharmaceuticals and cosmetics etc. For decades some nanoscale materials have been involved (for e.g. they are used in window glass, sunglasses, car bumpers, paints), whereas others are newly discovered are used as sunscreens and cosmetics, textiles, coatings, sports goods, explosives, propellants and pyrotechnics or their applications are currently under development (e.g. in batteries, solar cells, fuel cells, light sources, electronic storage media, display technologies, bioanalysis and bio detectors, drug delivery systems, medical implants and new organs). All in all, the number of nano products and methods of their use increase continually. This paper has reviewed recent knowledge and built a data base of nanoparticles. This review provides an overview of nanoparticle based upon the characterization methods, types, protocols based upon Strategies used to synthesize nanoparticles and wide range of applications. Our study concludes that nanoparticle has a tremendous growth in recent years. A wide range of opportunities or upcoming projects are available some of the nanoparticles get synthesized are cost effectiveness. For example nanoparticle synthesis using plant sources is largely adopted due to its eco-friendly nature and cost effectiveness etc.

Application of nanoparticle in Healthcare/medical [30-44]

- Targeted drug delivery
- Alternative drug and vaccine delivery mechanisms (e.g. inhalation, oral in place of injection).
- Bone growth promoters
- Cancer treatments
- Biocompatible coatings for implants
- Sunscreens (e.g. using ZnO and TiO2) / cosmetics
- Bio labeling and detection (e.g. using Au)
- Carriers for drugs with low water solubility
- Fungicides (e.g. using ZnO)
- MRI contrast agents (e.g. using superparamagnetic iron oxide)
- New dental composites
- Biological binding agents (e.g. for high phosphate levels)
- Antiviral, antibacterial (e.g. Ag), anti-spore non-chemical creams and
- Powders (using surface tension energy on the nanoscale to destroy biological particles)

Conclusion

Nanotechnology is expected to bring a fundamental change in manufacturing in the next few years and will have an enormous impact on life sciences, including drug delivery, diagnostics, nutraceuticals and production of biomaterials. Engineered nanoparticles (NP) (<100 nm) are an important tool to realize a number of the above applications. The use of Nanotechnology in medicine and more specifically drug delivery is set to spread rapidly. For decades pharmaceutical sciences have been using nanoparticles to reduce toxicity and side effects of drugs. The nanoparticulate systems have great potentials, being able to convert poorly soluble, poorly absorbed and labile biologically active substance into promising deliverable drugs. Further advances are needed in order to turn the concept of nanoparticle technology into a realistic practical application as the next generation of drug delivery system.

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