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REVIEW ARTICLE

Nanoparticles: Advances in Drug Delivery Systems

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ABSTRACT

Breakthroughs in nanotechnology promise in revolutionize drug manufacturing, drug delivery medical diagnostics. Nanoparticles have unique properties as compared to micro and macro particles. Nanotechnology is expected to bring revolutionary changes in the field of life sciences including drug delivery, diagnostics, nutraceuticals and production of bio–materials. Different types of nanoparticulate materials used in electronics, magnetic pharmaceuticals, cosmetics, energy, catalytic and materials industries. The US FDA specifies that nanotechnology involves: research and technology development at atomic, molecular or macromolecular levels, in the length scale of approximately 1-100 nm ;creating and using structures, devices and systems that have novel properties and functions because of their small and/or intermediate size; and the ability to control or manipulate on atomic scale. Nanoparticles have range of potential application in short term in new cosmetics, textiles and paints. These technologies can increase the potency of traditional small molecules of drugs in addition to potentially providing a mechanism for treating previously incurable diseases. This paper focus on the types of nanoparticles, their advantages, disadvantages and applications.

Keywords: Nanotechnology, Nanosuspension, Nanoparticles, solid lipid Nanoparticles (SLN)

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INTRODUCTION

The word "Nano" is derived from Greek word Dwarf , means "a billionth " .A Nanometer is billionth of a meter , which is 250 millionth of an inch , about 1/80,000 of the diameter of a human hair or 10 times of the diameter of hydrogen atom[1]. The term 'Nanotechnology' was coined by Prof. Norio Taniguchi, Tokyo Science University in 1974 to describe the precision manufacture of materials with nanometers tolerances and was unknowingly appropriated by Drexler in his 1986 book 'Engines of creation: The Coming Era of Nanotechnology [2].

Nanoparticles are sub-nano sized colloidal structure of synthetic or semi synthetic polymer .The first reported nanoparticles were based on non biodegradable polymeric system [3] (polyacrylamide, polymethyl-methaacrylate, polystyrene).The polymeric nanoparticles can carry drug(s) or proteineous substances, i.e. antigen(s). These bioactives are entrapped in polymer matrix as particulates or solid solution or may bound to particle surface by physical adsorption or chemically. The drug(s) may be added during preparation of nanoparticle or to the previously prepared nanoparticles. The term particulates is suggestively general and doesn't account for morphological and structural organization of
system. Nanomedicine is an emerging field of medicine with novel applications.

Nanomedicine is a subset of nanotechnology, which uses tiny particles that are more than 10 million times smaller than the human body. In nanomedicine, these particles are much smaller than the living cell. Because of this, nanomedicine presents many revolutionary opportunities in the fight against all types of cancer, neurodegenerative disorders and other diseases.

TYPES OF NANOPARTICLES APPLIED IN DRUG DELIVERY

The types of nanoparticles applied in the drug delivery system include:

Sl.no	Type of Nanoparticles	Material used	Applications	Ref.
1	Nanosuspensions and Nanocrystals	Drug powder is disperse-d in surfactant solution	Stable system for controlled delivery of poorly soluble drug	[4]
2	Solid lipid Nanoparticles	Melted lipid dispersed in Aqueous surfactant	Least toxic and more stable Colloidal carrier systems as alternative materials To polymers	[5]
3	Polymeric nanoparticles	Biodegradable polymers	Controlled and targeted drug delivery	[6]
4	Polymeric micelles	Amphiphilic block co polymers	Controlled and systemic Delivery of water insoluble Drugs	[7]
5	Magnetic Nanoparticles	Magnetite Fe2O3,Meghe Mite coated with dextran	Drug targeting diagnostics to in medicine	[8]
6	Carbon Nanotubes	Metals ,semiconductors	Gene and DNA delivery	[9]

		or carbon	Controlled release of drug	
7	Liposomes	Phoshpolipid vesicles	Controlled targeted drug delivery	[10]
8	Nanoshells	Dielectric core and metal shell	Tumor targeting	[11]
9	Ceramic Nanoparticles	Silica,alumina,titania	Drug and biomolecule delivery	[12]
10	Nanopores	Aerogel,which is produced-ed by cell gel chemistry	Controlled release drug carriers	[13]
11	Nano wires	Silicon, cobalt, gold or Copper based nanowires	Transport electron in nano Electronics	[14]
12	Quantum dots	cdSe-cdS core shell	Targeting ,imaging agent	[15]
13	Nano films	polypeptides	Systemic or local drug Delivery.	[16]
14	Ferrofluids	Iron oxide magnetic Nanoparticles surrounde-d by polymeric layer.	For capturing cells and other biological targets.	[17]

All the Nanoparticles listed above are explained in brief:

1. Nanosuspension

A suspension of drug nanoparticles in a liquid is called as nanosuspension. A size of nanoparticle lies in between 200 to 500 nm and outstanding feature of nanosuspension is the increased saturation, solubility, increased dissolution rate of compound. The saturation and solubility increases [18] below a particle size of 1 mcm. An additional feature of nanosuspension is that they may induce changes in the crystalline structure increase the amorphous fraction in particle or even creating completely amorphous particles. Nanoparticles and Nanosuspensions show an increased adhesiveness to tissue [19]. The oral administration of drug in the form of nanosuspension has been reported [20] to enhance absorption rate and bioavailability.

Examples of Nanosuspension: Nanosuspension of ibuprofen is prepared by emulsion-solvent diffusion technique for the purpose of improving ocular availability[21] whereas nanosuspension of Danazole is formulated by nanocrystal technology to improve bioavailability.

2. Solid lipid Nanoparticles (SLN)

The solid lipid nanoparticles are sub micron colloidal carriers (50-1,000nm) which are composed of physiological lipid, dispersed in water or in aqueous surfactant solution. In order to overcome the disadvantages associated with liquid state of oil droplets, liquid lipid replaced by a solid lipid ,which eventually transformed into solid lipid nanoparticles [20].

3. Polymeric nanoparticles [22]

The drug is dissolved, entrapped, absorbed, attached or encapsulated into nanoparticle matrix. Depending on the method of preparation, nanoparticles, nanospheres or nanocapsules

can be obtained with different properties and release characteristics for encapsulated therapeutic agent .Nanoparticles are vesicular systems in which the drug is confined to a cavity surrounded by unique polymer membranes, where as nanospheres are matrix systems in which the drug is physically and uniformly dispersed. The advantages of using nanoparticles for drug delivery result from their two main basic properties. First nanoparticles, because of their small size, can penetrate through smaller capillaries and are taken up by cells, which allow efficient drug accumulation at the target sites. Second, the use of biodegradable materials for nanoparticle preparation allows sustained drug release within the target site over a period of days or even weeks .

4. Polymeric micelles

Polymeric micelles have been extensively studied as drug carrier [23]. Polymeric micelles have better thermodynamic stability in physiological solution, as indicated by their low critical micellar concentration, which makes polymeric micelles stable and prevent their rapid dissociation *in vivo*.

Micelles have a fairly narrow size distribution in the nanometer range and are characterized by their unique core-shell architecture, in which hydrophobic segments are segregated from the aqueous exterior.

Micellar systems are useful for the systemic delivery of water-insoluble drugs [24]. Drugs can be partitioned in the hydrophobic cores of micelles and the outer hydrophilic layer from stable dispersion in aqueous media which can then be administered intravenously. The distribution of drug-loaded polymeric micelles (less than 100 nm in diameter), following intravenous administration, polymeric micelles have been shown to have prolonged systemic circulation time because of their smaller size and hydrophilic shell, which minimizes their uptakes by the reticuloendothelial system. Polymeric micelle-incorporated drugs may accumulate to a greater extent than free drugs into tumors and demonstrate reduced distribution in nontargeted areas.

5. Magnetic Nanoparticles

Magnetic nanoparticles are powerful and versatile diagnostic tool in field of medicine. Magnetic immunoassay techniques have been developed in which the main field generated by the magnetically labeled target detected directly with sensitive magnetometer. Superparamagnetic nanoparticles are used as contrast agents in magnetic resonance imaging .The magnetic nanoparticle are coated with inorganic core of iron oxide with polymer such as dextran. Magnetic nanoparticles of indomethacin demonstrated selective targeting under magnetic field of 8000 Oe-strength, following normal administration, the drug concentration was higher in the liver and spleen where endocytosis and phagocytosis could occur [25].

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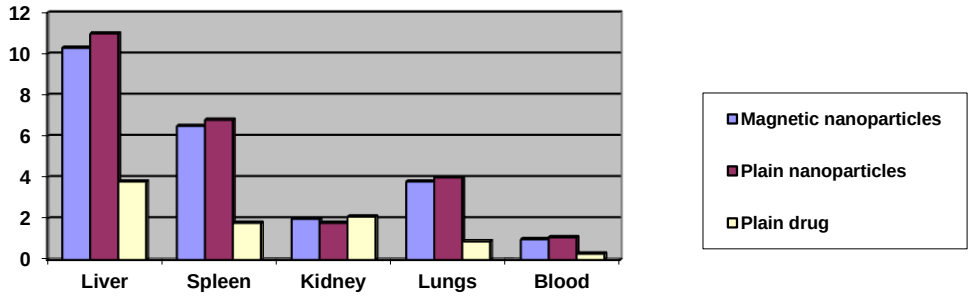

Figure. In vivo organ distribution of indomethacin loaded PMMA Plain & Magnetic nanoparticles after IV administration.

6. Carbon Nanotubes

Carbon nanotubes are a new form of carbon molecule around in a hexagonal network of carbon atoms, these hollow cylinders can have diameter as a small as 0.7nm and reach several millimeters in length [26]. Each end can be opened or closed by a fullerene half molecule. The small dimensions of nanotubes, combined with their remarkable physical, mechanical and electrical properties, make them unique materials .The mechanical strength of carbon nanotubes is more than sixty times greater than that of the best steels, even though they weigh six times less. They also represent a very large specific surface area, are excellent heat conductors and display unique electronic properties, offering three dimensional configurations. They have higher capacity for molecular absorption [27].

7. Liposomes

Liposomes have been used as a versatile tool in biology, biochemistry and medicine. Liposomes are small artificial vesicles of spherical shape that can be produced from natural non toxic phospholipids and cholesterol.Because of their size ,hydrophilic and hydrophobic character, as well as biocompatibility,liposomes are promising system for drug delivery. Properties of Liposomes vary substantially with lipid composition,size,surface charge and the method of preparation .They are therefore classified into three classes based on their size and number of bilayers. Small unilamellar vesicles (SUV) are surrounded by a single lipid layer and are 25-50nm in diameter. Large unilamellar vesicles (LUV) are heterogeneous group of vesicles similar to SUVs and are surrounded by a single lipid layer. Multilamellar vesicles (MLV) consist of several lipids separated from one another by a layer of aqueous solution .Drugs associated with liposomes have markedly altered pharmacokinetic properties compared to drugs in solution.They are also effective in reducing systemic toxicity and preventing early degradation of the encapsulated drug after introduction to the target organism [28].

8. Nanoshells coated with gold

Gold nanoshells are new composite nanoparticles that combine infrared optical activity with the uniquely biocompatible properties of gold colloid. Metal nanoshells are concentric

sphere nanoparticles consisting of a dielectric (typically gold sulfide or silica) core and a metal (gold) shell. By varying the relative thickness of core and shell layers, the plasmon-derived optical resonance of gold can be dramatically shifted in wavelength from visible region of highest physiological transmissivity. By varying absolute size of the gold nanoshell [25], it can be made to either selectively absorb(for particle diameter < 75nm) or scatter incident light. Because the gold shell layer is deposited using the same chemical method used to grow gold colloid, the surface properties of gold nanoshells are virtually identical to those of gold colloid. Gold nanoshells can be used to ablate breast cancer cells.

9. Ceramic nanoparticles

The newly emerging area of using inorganic (ceramic) particles with entrapped biomolecule has potential applications in many frontiers of modern materials science including drug delivery system. The advantages of ceramic nanoparticles include easy preparation with desired size, shape and porosity, and no effect on swelling or porosity with no change in pH.

10. Nanopores

Materials with defined pore-sizes in the nanometer range are of special interest for a broad range of industrial application because of their outstanding properties with regard to thermal insulation, controllable material separation and release and their applicability as templates or fillers for chemistry and catalysis [29]. One example of nanoporous material is aerogel, which is produced by sol-gel chemistry.

11. Nanowires

Nanowires are conductive or semi conductive particles with a crystalline structure of a few dozen nm and a high length /diameter ratio. Silicon, Cobalt, Gold or Copper-based nanowires have already been produced [26]. They are used to transport electrons in nanoelectronics they could be composed of different metals, Oxides, sulphides and nitrites.

Advantages of Nanoparticles

1. Fairly easy preparation.
2. Targeted and drug delivery.
3. Due to their small size Nanoparticles penetrate small capillary and are taken up by the cell which allows for efficient drug accumulation at the target sites in the body.
4. Good control over size and size distribution.
5. Good protection of the encapsulated drug.
6. Retention of drug at the active site.
7. Longer clearance time.
8. Increased therapeutic efficacy.
9. Increased bioavailability.
10. Dose proportionality.

11. Stable dosage forms of drug which are either unstable or have unacceptably low bioavailability in non-nanoparticulate dosages forms.
12. Increased surface area results in a faster dissolution of active agents in an aqueous environment.
13. Faster dissolution generally equates with greater bioavailability.
14. Smaller drug doses.
15. Reduction in fed/fasted variability.
16. Less toxicity.

Disadvantages of Nanoparticles:

1. Extensive use of polyvinyl alcohol as a detergent –issues with toxicity.
2. Limited targeting abilities.
3. Discontinuation of therapy is not possible.
4. Cytotoxicity.
5. Pulmonary inflammation and pulmonary carcinogenicity.
6. Alveolar inflammation.
7. The disturbance of autonomic imbalance by nanoparticles having direct effect on heart and vascular function.

Therapeutic Applications of Nanoparticles

Nanoparticles with different compositions and characteristics and investigated for various therapeutic applications as follows:-

- Carriers of drugs and biological agents
- Carriers of gene and DNA
- Carriers of antigens & vaccines
- Controlled & targeted drug delivery
- Carriers of diagnostic agent
- Carriers of MRI contrast

CONCLUSION

Nanoparticles represents promising drug carrier for various drug delivery systems Nanotechnology is breakthrough technology pervading all fields newer applications of this field are being explored worldwide. Nanoparticles represents a technology to overcome solubilities and bioavailability problems of drugs which can be generally applied to all poorly soluble drugs. Any drug can be transformed to drug nanoparticles leading to increasing saturation solubility, dissolution rate and providing in general feature of an increased adhesiveness to surfaces. Nanoparticulate drug delivery system is increasingly viewed as an advantageous solution for biological drugs. In addition, nanoparticles provide efficient treatment by enabling targeted and

controlled release thus in feature nanoparticulate drug-delivery system seem to be a viable and promising stratergy for the biopharmaceutical industry.

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