Nanoparticle based drug delivery system: Advantages and applications

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Abstract

There has been a considerable research interest in the area of drug delivery systems using nanoparticles. Nanostructured biomaterials have unique physicochemical properties such as ultra small and controllable size, large surface area to mass ratio, high reactivity and functionalizable structure. It alter and improve the pharmacokinetic and pharmacodynamic properties of various types of drug molecules that are capable of targeted delivery of both imaging agents and anticancer drugs and early detection of cancer lesions, determination of molecular signatures of the tumor by noninvasive imaging and, most importantly, molecular targeted cancer therapy. These properties can be applied on drug to overcoming some of the limitations in traditional therapeutics. They have been used in vivo to protect the drug entity in the systemic circulation, restrict access of the drug to the chosen sites and to deliver the drug at a controlled and sustained rate to the site of action, minimizes undesirable side effects of the drugs and allow for more efficient use of the drug. It should be present at appropriate concentrations at the target site, and it should not lose its activity or therapeutic efficacy while in circulation. Here, we review various aspects of nanoparticle formulation, characterization, effect of their characteristics and their applications in delivery of drug molecules, improving the targated delivery of therapeutic agents, the potential of nanomedicine, development of novel and more effective diagnostic and screening techniques to extend the limits of molecular diagnostics and challenges in synthesizing nanoparticle platforms for delivering various drugs.

Keywords: Drug delivery, microbes, liposomes, polymeric nanoparticles, ceramic nanoparticles, dendrimers.

Introduction

The predominant methods to deliver drugs are oral and injection. The drug is expected to circulate whole body affecting the cell and organ that are dysfunctioning as well as those which are healthy. It may cause serious side effects. The efficacy of drug is limited by their potential to reach the site of therapeutic action, only a small amount of dose reaches the target site and majority of drug is distributed to the rest of the body with it's physiochemical and biochemical properties, therefore developing a drug delivery system that optimizes the action of drug while reducing the side effects in vivo is a challenging task. Nanoparticles are solid colloidal particles (1-1000A^0). Nanoparticles are specially designed to absorb or encapsulated a drug, thereby protecting it against chemical and enzymatic degradation. It can be used as adjuvant in vaccine or drug carrier in which the active ingredient is dissolved, entrapped, encapsulated, adsorbed or chemically attached. Depending upon the method of preparation, nanoparticles, nanospheres or nanocapsules in which drug is confined to a cavity surrounded by a unique polymeric membrane, while nanosphere are matrix system in which the drug is physically and uniformly dispersed (Peer *et al.,* 2007). The major goal in designing nanoparticles as delivery system is to release pharmacologically active agents for site-specific action of drug at optimal rate and dose (Jain *et al.,* 2010). In the recent years, biodegradable polymeric nanoparticles have attracted the attention of numerous researchers in the controlled release of drugs due to its inherent capacity in targeting particular organ/tissue.

Drug delivery alternatives:

In addition to the oral and injection routes, drugs can also be administered through other means, like transdermal, transmucosal, pulmonary and implantation. The materials used are biological, polymers, silicon based materials, carbon based materials are structured in nanoscale forms. Table 1 summarized the materials and structures currently being investigated at nanoscale for drug delivery application (Hughes *et al.,* 2005).

Advantages over traditional drug delivery:

Conventionally drugs are taken via orally or through injection which circulate through out the body which may causes harmful effect on the cells or tissues or organs. Protein and peptide drugs are poorly absorbed after oral administration because of their susceptibility across the intestinal epithelium. Conventional drug delivery needs high doses to make up the bio-availability (Zhang *et al.,* 2008; Jain *et al.,* 2010). The advantages of using nanoparticles as a drug delivery system include the following.

1. Controlled and sustained release of the drug during the transportation and at the site of localization, altering organ distribution of drug and subsequence clearance of the drug so as to achieve increase in drug therapeutic efficiency and reduction in side effects.
2. Drug can be incorporated in to the system without any chemical reaction; this is an important factor for preserving the drug.
3. Controlled release and drug degradation charecteristics can be readily modulated.

4. There is no wastage of drug and thus enhanced bio-availability of drug at specific site in right proportion for prolonged period of time.
5. It improve the solubility of poorly water soluble drugs, prolong half life of drug systemic circulation by reducing immunogenicity, release drug at sustained rate and lower the frequency of administration .
6. It provides comfort and compliance to the patient and yet improves the therapeutic performance of the drug over conventional systems.

Importance of nanoparticles in drug delivery:

When drugs is loaded into nanoparticles through physical encapsulation, adsorption or chemical conjugation, the pharmacokinetics and therapeutic index of the drugs can be significantly improved in contrast to the free drug counterparts. Many advantages of nanoparticle-based drug delivery have been recognized, including improving serum solubility of the drugs, prolonging the systemic circulation lifetime, releasing drugs at a sustained and controlled manner, preferentially delivering drugs to the tissues and cells of interest, and concurrently delivering multiple therapeutic agents to the same cells for combination therapy (Zhang *et al.,* 2008; Davis *et al.,* 2008). Nanostructures biomaterials and nanoparticles have unique physicochemical properties such as ultra small and controllable size, large surface area to mass ratio, high reactivity, and functionalizable structure. Biological membranes and access cells, tissues and organs are eligible for entrance of nanoparticles. These cells are not crossed by the larger-sized particles easily (Rao *et al.,* 2010) i.e. by conventional medicine.

Table 1. Materials and structures currently being investigated at nanoscale for drug delivery application.

Drug delivery technology	Material	Nanostructure forms
Biologic	Lipid Peptide Nucleic acid Polysaccharide	Vesicles Nanotubes Nanoparticles
Polymeric	Poly(lactid acid) Poly(glycolic acid) Poly(carpolactone) Poly(ethylene glycol)	Vesicles Spheres Nanoparticles
Silicon based	Silicon Silicon dioxide	Porous nanoparticles Nanoneedles
Carbon based	Carbon	Nanotubes
Metallic	Gold Silver Platium	Nanoparticles Nanoshells

Nanoparticle mediated drug delivery system:

Nanoparticles can offer significant advantages over the traditional delivery mechanisms in terms of high stability, high specificity, high drug carrying capacity, ability for controlled release possibility to use in different types of drug administration and the capability to transport both hydrophilic and hydrophobic molecules. The drugs may be enclosed inside the sphere of the nanoparticle or linked to the surface. Once they are at the target site, the drug payload may be released from the nanoparticle by diffusion, swelling, erosion or degradation. Active systems are also possible, e.g. drug release in response to the input of external energy such as targeted ultrasound, light or magnetic field. A few types of nanoparticles including liposomes (Omri *et al.,* 2010), polymeric nanoparticles (Ahmad *et al.,* 2006), solid lipid nanoparticles and dendrimers (Bhadra *et al.,* 2005) have been widely investigated as antimicrobial drug delivery platforms, of which several products have been introduced into pharmaceutical market.

Liposomes for drug delivery:

Liposomes are spherical lipid vesicles with a bilayered membrane structure consisting of amphiphilic lipid molecules. It is used as drug delivery nanoparticle. It can be made of either natural or synthetic lipids. Currently, liposomes are the most widely used antimicrobial drug delivery system (Schumacher *et al.,* 1997; Omri *et al.,* 2002). One of the distinguishing features of liposomes is its lipid bilayer structure, which mimics cell membranes and can readily fuse with infectious microbes. By directly fusing with bacterial membranes, the drug payloads of liposomes can be released to the cell membranes or the interior of the bacteria (Zhang *et al.,* 2010). It carries both hydrophobic and hydrophilic compounds without chemical modification.

Polymeric nanoparticle for drug delivery:

Biocompatible and biodegradable polymers are used extensively for controlled drug release. Polymeric nanoparticles are structurally stable and properties such as size, zeta potentials and drug release profiles can be tuned by selecting different polymer lengths, surfactants and organic solvents during the synthesis. The surface of polymeric nanoparticles typically contains functional groups that can be chemically modified with targeting ligands (Ahmad *et al.,* 2006; Pandey *et al.,* 2006). The drugs can be either absorbed to the nanocapsules during
the polymerization process or covalently conjugated to the surface of the nanoparticles after they are formed.

Dendrimers for drug delivery:

Dendrimers are highly ordered and regularly branched globular macromolecules. It consists of three regions: a core, layers of branched repeat units emerging from the core, and functional end groups on the outer layer of repeat units. The highly-branched nature of dendrimers provides large surface area to size ratio and allows great reactivity with microorganisms in vivo (Balogh *et al.,* 2001; Devarakonda *et al.,* 2005). Both hydrophobic and hydrophilic agents can be loaded

Table 2. Nanoparticles for antimicrobial drug delivery.

Formulation	Drug	Targeted microorganism	Activity	References
1,2-dipalmitoyl-sn-glycero-3-phosphocholine (DPPC) and cholesterol	polymyxin B	*Pseudomonas aeruginosa*	1)Decreased bacteria count in lung 2)Increased bioavailability 3)Decreased lung injury caused by bacteria	Omri *et al.,* 2010
Soybean phosphatidylcholine (PC) and cholesterol	ampillicin	*Micrococcus luteus* & *Salmonella typhimurium*	1)Increased stability 2)Full biological activity of ampicilin was observed.	Schumacher *et al.,*1997
Alginate nanoparticle	Rifampicin, isoniazid, pyrazinamide, & ethambutol.	*Mycobacterium turberculosis*	1) High drug payload 2) Improved pharmacokinetic 3) High therapeutic efficacy	Ahmad *et al.,* 2006
Poly-lactide-co-glycolide (PLG)nanoparticle	Rifampicin, isoniazid, pyrazinamide & ethambutol.	*Mycobacterium turberculosis*	1) Enhanced bioavailability 2)Improvied pharmacodynamic	Pandey *et al.,* 2006
Polyamidoamine (PAMAM) dendrimers	Niclosmide	Tapeworm	1)Improved water solubility 2) Controllable drug release	Devarakonda *et al.,* 2005
Pegylated lysine based copolymeric dendrimer	Artemether	*Plasmodium falciparum*	1) Increased drug stability 2) enhanced solubility 3) Prolonged drug circulation half-life	Balogh *et al.,*2001

into dendrimers. Hydrophobic drugs can be loaded inside the cavity in the hydrophobic core, and hydrophilic drugs can be attached to the multivalent surfaces of dendrimers through covalent conjugation or electrostatic interaction.

Ceramic nanoparticles:

Ceramic nanoparticles are inorganic systems with porous characteristics. Because these particles can be easily engineered with the desired size and porosity, growing interest has recently emerged to utilize ceramic nanoparticles as drug vehicles. Most of the research has been exploring typical biocompatible ceramic nanoparticles such as silica, titania, alumina etc. In cancer therapy because of their physiological stability, hybridizing ceramic nanoparticles with DNA offers a potential therapy to target liver cancer cells (Yih *et al.,* 2006)

Future opportunities and challenges

Nanoparticles provide massive advantages regarding drug targeting, delivery and release and with their additional potential to combine diagnosis and therapy, emerge as one of the major tools in nanomedicine. The main goals are to improve their stability in the biological environment, to mediate the bio-distribution of active compounds, improve drug loading, targeting, transport, release, and interaction with biological barriers. The cytotoxicity of nanoparticles or their degradation products remains a major problem, and improvements in biocompatibility obviously are a main concern of future research (Bawa *et al.,* 2005, Pragati *et al.,* 2009; Wadher *et al.,* 2009).

Conclusion

Nanoparticle mediated drug delivery is going to have a great potential impact on the society. It will drastically improve patient's quality of life associated with healthcare, early detection of pathologic conditions, reduce the severity of disease and result in improved clinical outcome for the patient.

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