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Review article

NANO-DRUG DELIVERY SYSTEM: APPLICATIONS IN VETERINARY MEDICINE AND ANIMAL HEALTH

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Abstract: Nano-drug delivery systems have several advantages compared to the traditional forms of drugs. A nanocarrier sytem transport the drug to the site of action, hence, its influence on vital tissues and undesirable side effects can be minimized. Accumulation of therapeutic compounds in the target site increases and, consequently, the required doses of drugs are lower. Cell-specific targeting can be accomplished by attaching drugs to specially designed nanocarriers. Various nanostructures, including liposomes, polymers, dendrimers, carbon materials, and magnetic nanoparticles, have been tested as carriers in drug delivery systems.
Keywords: Nano-drug delivery, Nanotechnology, Veterinary application.

Introduction

Nanoparticles are defined as the science and engineering involved in the design, synthesis, characterization and application of materials and devices whose smallest functional organization ranging between 1-100 nm in at least one dimension (Muller *et al.,* 2000). Nanotechnology has the potential to revolutionize veterinary medicine, animal health and other areas of animal production. In the twenty first century, nanotechnology may offer a vast number of breakthroughs that will advance the practice of clinical veterinary medicine. Nanoparticle-based drug delivery improves the solubility of poorly water-soluble drugs, prolongs the half-life of drug, releases drugs at a sustained rate or in an environmentally responsive manner and thus lowers the frequency of administration, delivers drugs in a target manner to minimize systemic side effects, and delivers two or more drugs simultaneously for combination therapy to generate a synergistic effect and suppress drug resistance (Agnieszka *et al*., 2012). A few types of nanoparticles including polymeric nanoparticles, lipid nanoparticles liposomes, dendrimers, carbon materials, and magnetic nanoparticles have been widely investigated as drug delivery platforms, of which several products have been introduced into pharmaceutical market.

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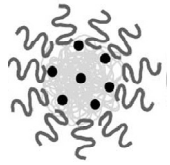
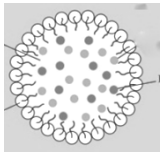
Polymeric nanoparticles (PNPs)

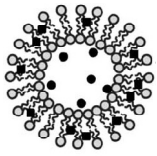
PNPs are made from variety of natural and synthetic polymers which are considered as the most promising drug carrier. PNPs are structurally stable and can be synthesized with a sharper size distribution. The surface of PNPs contains functional groups that can be chemically modified with either drug moieties or targeting ligands delivery (Agnieszka *et al*., 2012). PNPs are usually coated with nonionic surfactants in order to reduce immunological interactions as well as intermolecular interactions between the surface chemical groups of PNPs (Torchilin, 2008).



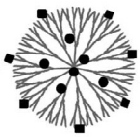
Polymeric nanoparticle



Lipid nanoparticle



Liposomes



Dendrimer

Carbon nanotube

Lipid Nanoparticles

Solid lipid nanoparticles (SLNs), Nanostructured lipid carriers (NLCs) and Lipid drug conjugates (LDC) are types of carrier systems based on solid lipid matrix.

Solid lipid nanoparticles (SLNs): SLNs are particles made of solid lipids, e.g., triglycerides, complex glyceride mixtures or waxes stabilized by various surfactants (Muller *et al*., 2000). The main characteristics of SLNs include a good physical stability, protection of incorporated drugs from degradation, controlled drug release, and good tolerability (Mehnert and Mader, 2001).

Nanostructured lipid carriers (NLCs): The modifications of SLN are NLCs and it is called as second generation of lipid nanoparticles. NLCs are produced by mixing solid lipids with liquid lipids, which leads to special nanostructure with increased payload and prevented drug expulsion (Wissing *et al*., 2004).

Lipid drug conjugates (LDC): LDCs are developed in order to expand applicability of lipid based carriers to lipophobic drug molecules (Wissing *et al*., 2004).

Liposomes

Liposomes are nano/micro-particular or colloidal carriers, usually with 80-300 nm size range. 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 (Silva *et al*., 2011).

Dendrimer nanocarriers

Dendrimers are defined as highly ordered and regularly branched globular macromolecules produced by stepwise iterative approaches (Svenson and Tomalia, 2006). The structure of dendrimers consists of three distinct architectural regions: a focal moiety or a core, layers of branched repeat units emerging from the core, and functional end groups on the outer layer of repeat units. The presence of several surface functional groups enables a sumultanoeus interaction with a number of receptors, thus, it enhances biological activity. The drug may be encapsulated in the internal structure of dendrimers or it can be chemically attached or physically adsorbed on dendrimers surface (Menjoge *et al.,* 2010)

Carbon nanomaterials

Carbon nanocarriers used in delivery systems are differentiated into nanotubes (CNTs) and nanohorns (CNH).

Nanotubes (CNTs): CNTs are characterized by unique architecture formed by rolling of single (SWNCTs – single walled CNTs) or multi (MWCNTs – multi walled CNTs) layers of graphite with an enormous surface area and an excellent electronic and thermal conductivity (Beg *et al*., 2011). Biocompatibility of nanotubes may be improved by chemical modification of their surface (Shin et al., 2011). Drug release from CNTs can be electrically or chemically controlled. To prevent the unwanted release of the drug, the open ends of CNTs were sealed with (Luo *et al*., 2011).

Nanohorns: It is single-wall nanotubes which does not require a metal catalyst for the formulation, thus, they can be easily prepared with very low cost and are of high purity (Shiba *et al*., 2006).

Magnetic nanoparticles

Magnetic nanoparticles are easy handling with the aid of an external magnetic field, the possibility of using passive and active drug delivery strategies, the ability of visualization, and enhanced uptake by the target tissue resulting in effective treatment at the therapeutically optimal doses (Arruebo *et al.,* 2007).

Problems in nano-drug delivery

Nanocarriers used for medical applications have to be biocompatible and nontoxic. Undesirable effects of nanoparticles strongly depend on their size, shape, amount, surface chemistry, the route of administration, reaction of the immune system and residence time in

the bloodstream. It is accepted that nanoparticles with a diameter of 10–100 nm have optimal pharmacokinetic properties for *in vivo* applications. Due to a number of factors which may affect the toxicity of nanoparticles, toxicological studies of each new nano-drug delivery formulation are needed (Ai *et al*., 2011).

Conclusion

With continued research and development efforts, nanotechnology is expected to have a tremendous impact on veterinary medicine and animal health for decades to come. Nanotechnology is beginning to change the scale and methods of drug delivery.

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