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Mini Review

# Nano Drug Delivery Systems and their Applications in Veterinary Medicine

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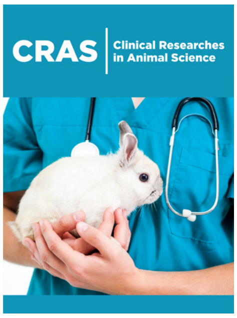


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### Abstract

Nanomaterials and nano-drug delivery systems are emerging technologies in human and veterinary medicine. Nano-drug delivery systems have very important advantages, such as increased stability, high bioavailability and low toxicity. Although nano-drug delivery systems have been mainly used in human medicine, veterinary clinical applications are increasing. In this mini review, common nano-drug delivery systems and their applications in veterinary medicine were evaluated.

**Keywords:** Nanomaterials; Drug delivery; Veterinary medicine

## Introduction

Nanotechnology is one of the most important scientific developments of last decades. Nanoparticles are defined as particles that have three dimensions of the order of 100nm or less. Nano-based materials have major advantages against macroscale entities: small size with high surface to volume area, enhanced reactivity, solubility, diffusivity, thermal and electrical characteristics, low toxicity etc. Thanks to these novel properties, nanomaterials are used in different areas such as electronic, industry, textile, renewable energy, agriculture, food sector and medicine [1,2]. In the medical field, nanomaterials give many new opportunities to diagnosis, treatment and prevention of diseases. Low bioavailability and higher accumulation of drugs than toxic levels are common problems in pharmacology. Therefore, nanoparticle drug delivery systems which target to deliver therapeutic compounds to the effect site in the body are one of main applications of nanotechnology. Although many studies regarding nano-drug delivery systems have been performed in human medicine, there are important applications of nanomaterials in veterinary medicine, too [3]. Common nano-drug delivery systems used in veterinary medicine can be indicated as liposomes, micelles, solid lipid nanoparticles, polymeric nanoparticles, dendrimers, carbon nano tubes, fullerens and metallic nanoparticles [1,3,4].

## Discussion

Liposomes are considered as the first developed nano-drug delivery systems which are 50-200nm. Liposomes consist of double layers of phospholipids with polar ends inside and outside and a polar end in between. This structure is basically similar to the cell membrane; thus, liposomes are very biocompatible systems. In addition, their drug binding capacity is very high for both hydrophilic and lipophilic drugs [1,5]. Liposomes are most investigated and used nano-drug delivery systems in veterinary medicine. Liposomes containing some antibacterial agents, such as gentamycin, tobramycin and other aminoglycosides were determined more effective than single antibiotics in mastitis and pulmonary infections of cattle. Also, liposomes have been used with antifungal and antiviral drugs, and efficacy of these systems was higher than their conventional counterparts [3]. Another important usage area of liposomes is cancer therapy. Liposomal doxorubicin and cisplatin were determined very effective in several cancer types, such as oral melanoma, oral sarcoma, and anal gland adenocarcinoma in cats and dogs [6]. Some other liposomes were used as the carrying system for chicken and sheep vaccines. In addition, liposomal hydromorphone and diclofenac were used for postoperative and osteoarthritis pains in dogs and horses, respectively [7].

Other important lipid-based nano-drug delivery systems are micelles and solid lipid nanoparticles. Micelles are very similar to liposomes, but they are single layered, with dimensions of around 10 nm. The most important advantages of micelles are that they can be easily obtained, radioactively labelled and they increase the absorption of vitamins, enzymes and steroids [1,5]. Micelles were used with insulin in dogs, diminazene in sheep, paclitaxel in mast cell tumors in dogs, vitamin E in racehorses and piglets, propofol and ivermectin in horses, and tilmicosin in broiler chickens. Generally, more effective and safer results were obtained with micellar nano-drug delivery systems [3,8]. Also, there are reports regarding usage of micelles as a carrying system with Fasciola hepatica antigen in sheep and Newcastle disease vaccine in birds [8]. Solid lipid nanoparticles are manufactured with lipids that are solid at room and body temperature and stabilized with surfactants. Solid lipid nanoparticles have excellent physical stability for parenteral applications; thus, they are protecting the added unstable drugs against degradation while maintaining controlled drug release [1]. Solid lipid nanoparticles have been used with various drugs in veterinary medicine, including tilmicosin in broiler chickens [3] and enrofloxacin in pigs [9]. In a recent study, solid lipid nanoparticles were reported as a potential adjuvant for inactivated foot and mouth disease virus vaccine [10].

Polymeric nanoparticles are produced from polymers and generally used for targeted drug delivery. Because, polymeric nanoparticles provide decreased toxicity and good biocompatibility, increased solubility in biological fluids, decreased drug resistance and good immuno-stimulatory effects. Especially polyethylene glycol and other biologically inert natural polymers are widely used in drug delivery systems by covalently bonding to the surface of nanoparticles [1,3]. Polymeric nanoparticles were generally investigated for antibiotics and other chemotherapeutics to target Mycobacterium tuberculosis, Pseudomonas aeruginosa, Staphylococcus aureus, Escherichia coli, Brucella abortus, toxoplasmosis, HIV, anthrax, Plasmodium vivax and Influenza Virus [3,8,11]. Dendrimers are one of polymeric drug carrier systems consisting of nucleus, branching units around the nucleus and surface groups called functional groups. The first developed dendrimer family is polyamidoamines and they have been widely used in veterinary medicine as antimicrobial agents, a tool for MRI imaging and gene transfer. Amphotericin B was used with anionic linear globular dendrimer for leishmaniasis, and increased efficacy and reduced toxicity were observed. Dendrimers are also very beneficial for cancer therapy. In addition, a dendrimeric epitopes were used in treatment of classical swine fever virus in domestic pigs. Dendrimers were used as the adjuvant in foot-and-mouth disease and animal rabies vaccines [1,3,8,12].

Carbon nanotubes are hexagonal nets of carbon atoms with a length of 1-100 nm and a diameter of 1 nm. There are two types of carbon nano tubes in use today: single-walled and multi-walled nanotubes. Carbon nanotubes can easily pass-through membranes due to their needle-like shape and have a potential to be used as a drug delivery system. Other carbon-based nanoparticles are fullerenes. They are similar to carbon nano tubes, but carbon numbers are different (28->100). Chemically modified fullerenes are used alone or as drug release systems by binding to carbon nano tubes for neuroprotective, antiviral, antibacterial, antitumoral, antiapoptic and antioxidant substances. However, there are conflicting toxicity reports about carbon nanoparticles, and it was reported that especially single walled carbon nano tubes caused cytotoxic effects and oxidative stress formation in cell lines. Therefore, veterinary clinical usage of carbon-based nanoparticles is limited and generally studies on experimental animals are available [1,8].

Metallic nanoparticles consist of metal elements in the nano-range. Because of their small size and surface modifications, metallic nanoparticles can remain in circulation for a long time and be effective by targeting primarily tumour sites. Silver and gold nanoparticles are widely used in drug delivery systems. There are reports regarding silver nanoparticle loaded vaccines. However, the main research subject is the antibacterial effect of silver nanoparticles. Silver nanoparticles have synergistic effects with antibiotics, such as gentamicin and penicillin G. In addition, there are many studies about antibacterial effect of silver nanoparticles alone against various animal bacteria, including antibiotic resistant strains, in goats, piglets and dogs. Also, beneficial effects of silver nanoparticles against aflatoxicosis in chickens and some tumours in cats were reported [1,3]. Gold nanoparticles are accepted more biocompatible. Gold nanoparticles were investigated in various cancer types in cats and dogs, and against Corynebacterium pseudotuberculosis in goats and sheep. Also, gold nanoparticles and gold-based test strips were used for the rapid detection of several infection agents, such as foot-and-mouth disease virus, bluetongue virus, Salmonella typhimurium and S. enteritidis. Similarly the metallic nanoparticles, metal oxides, such as iron oxide and zinc oxide, were used as antibacterial, wound healing, antineoplastic, and angiogenic agents in veterinary medicine [3].

## Conclusion

Nanotechnology and nanomaterials are involving our lives more and more every day, and the number of products containing nanoparticles is increasing rapidly. Nanomedicine is one of main fields of nanotechnology and nano-drug delivery systems are an important part of medical applications. Thanks to nanoparticles, stability, bioavailability and biocompatibility of drugs can be increased. Nano-drug delivery systems have been mainly used in human medicine and applications in veterinary medicine are limited, still. Many reports have been performed in frame of research and mainly in experimental animals. However, clinical administration of various nano-drug delivery systems to animals is getting more. In this mini review, importance of nano-drug delivery systems in veterinary medicine was tried to be emphasized and some important veterinary clinical applications were summarized. It is obvious that the impact of nano-drug delivery systems in veterinary medicine will increase in the future, however it should be considered that further studies regarding efficacy and safety of nano-drug delivery systems are needed in different animal species.

## Conflict of Interest

The authors declare that there is no conflict of interest.

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