

Nanomedicine: A Novel idea in Veterinary Therapeutics

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DOI: 10.5281/zenodo.6059800

Introduction

Human medicine has been transformed by nanotechnology, especially in the fields of imaging and drug delivery. In 1974, Professor Noro Taniguchi coined the word "nanotechnology" (Kreuter, 2007). The European Science Foundation's Medical Standing Committee described nanomedicine as "the science and technology of diagnosing, treating, and preventing disease and traumatic injury, relieving pain, and maintaining and improving human health, using molecular tools and molecular knowledge of the human body, using molecular tools and molecular knowledge of the human body." At the same time, the National Institutes of Health in the United States considers nanomedicine to be "a branch of nanotechnology that refers to extremely specific medical therapies at the molecular scale for curing disease or repairing damaged tissues, such as bone, muscle, or nerve" (Webster, 2006). Nanoparticle research in medicine has mainly focused on the targeted delivery of therapeutic agents, vaccine production, and novel diagnostic methods. Nanoparticles have provided successful and scientifically validated solutions in some of these fields, resulting in their incorporation into marketable goods that are now spreading to veterinary animals. Over speculation on the potential of futuristic nano-inventions in the early stages of growth, on the other hand, can obscure the practical progress that is being made. This article focuses on the basic principles behind the use of nanoparticles for drug delivery, diagnostics and vaccine formulation.

Nanoparticles: What are they?

Professor Peter Speiser devised a technique for controlled drug release in the form of Nano-particles, which are miniaturized delivery systems (Bírrenbach and Speiser, 1976). Over 200 nanoparticle drug delivery systems are in the works, with at least 30 nanoparticle-based

therapeutic products licensed for human usage and a comparable number in clinical trials (Bawa, 2008). Many of these formulations are too costly for veterinary usage, but many nanoparticle formulations are already on the market and as nanoparticle production facilities scale up for commercialization, these formulations will become more accessible for veterinary use. Via four main pathways, nanoparticles increase the therapeutic index of the pharmaceutical agents they hold. To begin with, they make it possible to use substances that would otherwise be insoluble or dysfunctional. Second, they raise the concentration of the pharmaceutical at its target site of action, increasing efficacy. Third, they reduce systemic toxicity and drug concentration in healthy tissues due to preferential accumulation at target sites. Fourth, nanoparticles have lower clearance than the parent compound, allowing for a method of long-term controlled release over days or even weeks (Fahmy *et al.*, 2005). The nanoparticle must be filled with an appropriate amount of pharmaceutical, carried to the target tissue, and then released at the target site to form a viable drug delivery system. Drugs may be loaded into nanoparticles either through encapsulation inside the particle or by surface attachment (Lu *et al.*, 2007). The reticuloendothelial system opsonizes nanoparticles and then absorbs them, reducing the number of nanoparticles in circulation and being able to extravasate (Laverman *et al.*, 2000). To solve this, nanoparticles can be coated with hydrophilic compounds, the most common of which is polyethylene glycol (PEG), which decreases opsonization and extends the time in circulation (arulsudar *et al.*, 2004). Targeting nanoparticles to particular tissues by changing their charge or covering them in a material that is naturally taken up by that tissue is a more cost-effective method of developing targeted nanoparticles for veterinary use, and this method has been successfully used to improve nanoparticle adherence to and absorption through the blood-brain barrier for the treatment of neurological diseases (Lu *et al.*, 2006). Nanoparticles are widely used in drug delivery for cancer, inflammation, and analgesia, among other indications. Several studies have tested nanoparticle formulations explicitly for veterinary use, despite the fact that there are still wide areas of nanotechnology that have yet to be explored for veterinary use (Wang *et al.*, 2009; Wunsch *et al.*, 2009; Riffault *et al.*, 2010; Wiese *et al.*, 2010; Underwood *et al.*, 2012) and more work will be undertaken as development costs fall.

Use in diagnostics:

Imaging agents may be loaded onto nanoparticle platforms to detect abnormal tissues and particular cell types. Nanoparticles are used to visualize, characterize, and quantify cellular

processes in living organisms at a macroscopic or molecular level. Some nanoparticles have inherent imaging properties, whereas others can be loaded with an imaging contrast agent to enable pathological tissues to be detected (Bentolila *et al.*, 2009). To target a specific cell type or pathway, these nanoparticles use passive delivery mechanisms or are conjugated to different ligands. The initial research centered on the macroscopic use of nanoparticles in conjunction with traditional imaging modalities such as radiography, magnetic resonance imaging (MRI), nuclear scintigraphy, positron emission tomography (PET), and computerized tomography (CT) to diagnose tumors and inflammatory foci. Nanoparticle imaging may be particularly useful in veterinary animals, where lesion localization may be more difficult and there are fewer alternative agents/imaging modalities. Radiolabelled liposomes, for example, have the ability to detect tumors or septic foci in large animals where traditional imaging is not possible. Nanoparticle-based imaging techniques have been widely used in animal disease models to assess the bio-distribution of potential nanoparticle-drug delivery systems on a larger scale. Functionalized nanoparticles have been successfully linked to biological molecules such as antibodies, peptides, proteins, and nucleic acids to create novel diagnostic assays (Luchini *et al.*, 2010). These techniques, when combined with spectroscopy, flow cytometry, and histological methods, form a powerful new medium for mapping the molecular profiles associated with disease and infection, as well as a highly sensitive, amplification-free method of pathogen detection (Halfpenny and Wright, 2010). Although further research is needed until this complex device can be used in the clinic, there are a number of nanoparticle-based detection systems that have been successfully validated in the veterinary sector for the detection of viral, parasitic, and bacterial pathogens (Yuan *et al.*, 2009).

Use in vaccine delivery:

The novel nanoparticle-based adjuvants are highly configurable and can be designed for lower dosage frequency through a convenient administration route in order to elicit a particular immune response, such as intranasal administration to better target mucosal immunity (Scheerlinck *et al.*, 2006). This makes them ideal for veterinary species where large numbers of animals need to be handled at once in a commercial unit, or where traditional vaccination is impractical due to complex management structures or limited accessibility (e.g. wildlife). Emulsions, liposomes, polystyrene nanobeads, immune-stimulating complexes, and inorganic particles are examples of nanoparticle adjuvants approved for veterinary use (or in clinical trials)

(Scheerlínck *et al.*, 2006). Nanoparticle adjuvants for veterinary use must be cheap, safe, simple to administer, and biodegradable in species used for human consumption (aucouturier *et al.*, 2001). To date, more than 40 diseases of animal species including equine influenza and *Streptococcus equi* infection in horses (Moreín *et al.*, 2004), foot-and-mouth disease, bovine virus diarrhoea virus, and *Toxoplasma gondii* in ruminants (Cubillos *et al.*, 2008); Newcastle disease and H5N1 influenza in poultry (Zhang *et al.*, 2010), enterotoxigenic *E. coli* and atrophic rhinitis in swine (Kang *et al.*, 2008), and parvovirus and atopic dermatitis in dogs (Moreín *et al.*, 2004) have nanoparticle vaccine delivery systems that are successfully developed.

Conclusions:

The advent of nanotechnology into the pharmaceutical industry has revolutionized drug delivery options, allowing for the development of new drugs with greater precision and fewer side effects. Nanomedicines have made it possible to provide novel formulation options for molecules and compounds derived from biotechnology. Veterinarians are now using nanoparticle drug carriers to revisit difficult disease entities with a new perspective and expand their pharmaceutical arsenal. Nanotechnology in veterinary medicine allows for improved medication, vitamin, mineral, and vaccine delivery through methods that are suitable for bulk application to wildlife and large-scale production systems, as well as simple, sensitive on-site diagnostic tests for a variety of veterinary diseases. This has the potential to improve herd management and productivity of animals that provide food. Collaboration between different disciplines, such as human and veterinary medicine, engineering, and materials science, will extend existing expertise and make it more applicable to veterinary applications.

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