MINI REVIEW

Sokoto Journal of Veterinary Sciences
(P-ISSN 1595-093X/ E-ISSN 2315-6201)
Num & Useh /*Sokoto Journal of Veterinary Sciences* (2013) 11(2): 10-14.
http://dx.doi.org/10.4314/sokjvs.v11i2.2

Nanotechnology applications in veterinary diagnostics and therapeutics

SM Num[1] & NM Useh[2]*

1. *Department of Veterinary Pathology and Microbiology, University of Agriculture, Makurdi, Nigeria*
2. *Department of Veterinary Pathology, Ahmadu Bello University, Zaria, Nigeria*

*Correspondence: Tel.: 2348126945597, E-mail: nicodemus.useh@fulbrightmail.org

Abstract

Livestock is an important component of the economy of most countries of the world, as it provides some foreign exchange earnings for social amenities and general development. Disease has been a major setback in livestock production and new diagnostic and therapeutic approaches have evolved over time to strictly identify and treat diseases of animals for the purpose of increased protein supply for human nutrition. In the search for improved diagnostic methodologies, livestock disease diagnostics and therapeutics have moved from the traditional methods to molecular and currently nanotechnology. In this contribution, the authors identified the importance of nanotechnology in veterinary diagnostics and therapeutics and suggest that nanotechnology should be combined with molecular diagnostics and therapeutics to boost the efficiency in the diagnosis and treatment of animal diseases for improved protein supply and food security.

Keywords: Applications, Nanotechnology, Review, Veterinary diagnostics, Veterinary therapeutics.
Received: 28-06-2013 Accepted: 06-09-2013

Introduction

Nanotechnology applies the nanoscale principles and techniques to understand and transform biosystems (living or non living) which uses biological principles and materials to create new devices and systems integrated from the nanoscale. It is engineering at the molecular (groups of atoms) level. Nanotechnology is not confined to one industry or market. Rather, it is an enabling set of technologies that cross all industry sectors and scientific disciplines. Probably uniquely, it is classified by the size of the materials being developed and used, not by the processes being used or products being produced (Chauhan *et al*., 2010).

Diseases of livestock such as helminthosis, trypanosomosis, tick and tick-borne diseases, influenza, clostridial infections, just to mention a few have made news headlines all over the world, because of their devastating effects on livestock population and the potential for some of these to be transmitted to human beings (WHO, 1998, 2012; Engles *et al*., 2002; Thontiravong *et al*., 2012; Useh *et al*., 2012). In some cases, it was difficult for several decades, to distinguish animal and human pathogens that caused similar diseases, because of unavailability of sensitive diagnostic tools and protocols (Nagano *et al*., 2008; Weatherhead & Tweardy, 2012). The National Science and Technology Council of United States of America (2004) defined nanotechnology as "research and development (R&D) aimed at understanding and working with - seeing, measuring and manipulating-matter at the atomic, molecular and supramolecular levels. This correlates to length scales of roughly 1 to 100 nanometers. At this scale, the physical, chemical and biological properties of materials differ fundamentally and often unexpectedly from those of the corresponding bulk materials.'' Veterinary nanotechnology has the potential to improve diagnosis and treatment delivery systems, provide new tools for molecular and cellular breeding, identity preservation of animal history from birth to a consumer's table, the security of animal food products, major impact on animal nutrition scenarios ranging from the diet to nutrient uptake and

utilization, modification of animal waste as expelled from the animal, pathogen detection, and many more (Scott, 2007).

In contemporary veterinary science, if an animal becomes infected with disease, it takes days, weeks, or even months before presence of the disease is detected by whole-organism symptoms. By that time infection may have spread with the need to destroy the entire herd. Nanotechnology operates at the same scale as a virus or a disease-infecting particle, and thus holds the potential for very early detection and eradication. Nanotechnology holds out the possibility that "smart'' treatment delivery systems could be activated long before macro symptoms appear. For example, a smart treatment delivery system could be a miniature device implanted in an animal that samples saliva or other body fluid on a regular basis. Long before a fever or other symptoms develop, the integrated sensing, monitoring and controlling system could detect the presence of disease and notify the farmer and veterinarian to activate a targeted treatment delivery system. Smart treatment delivery systems are envisioned for animal systems such as drugs, nutrients, probiotics, nutraceuticals and implantable cell bioreactors (Scott, 2007).

Nanotechnology applications in veterinary diagnostics and therapeutics

It is believed that in the near future, nanotechnology will play a leading role in global veterinary practice (Feneque, 2003; Scott, 2005). The use of nanotechnology devices for diagnosis of animal diseases or as animal models for the diagnosis of human diseases is great achievement in the one health initiative. Recent reports suggest the use of quantum dots (QD) for *in vivo* imaging in small animal models (Bentolila *et al*., 2009). Functionalized nanoparticles (NPs) conjugated to monoclonal antibodies have been used to rapidly and specifically detect respiratory syncytial virus *in vitro* and *in vivo*. The results suggest that functionalized NPs can provide direct, rapid, and sensitive detection of viruses and thereby bridge the gap between current cumbersome virus detection assays and the need for more rapid and sensitive detection of viral agents (Tripp *et al*., 2007). Several other reports show the usefulness of nanoparticles in disease diagnosis (Na *et al*., 2009; Jackson *et al*., 2011; Schlacter *et al*., 2011; Huang *et al*., 2012).

Nanotechnology is currently employed in the treatment of African animal trypanosomosis (Kroubi *et al*., 2010). It enabled the development of a new drug delivery system against diaminazene (DMZ) a trypanocidal drug registered for veterinary use. The porous cationic nanoparticles used improved the potential targeting of trypanosomes. Similarly, mice pre-treated with protein cage nanoparticles (PCN) independent of any specific viral antigens, were protected against both sub-lethal and lethal doses of two different influenza viruses, a mouse-adapted SARS-coronavirus, or mouse pneumovirus. Treatment with PCN significantly increased survival and was marked by enhanced viral clearance, accelerated induction of viral-specific antibody production, and significant decreases in morbidity and lung damage (Wiley *et al*., 2009). In another report, an aerosol formulation of biodegradable, biocompatible and nontoxic gelatin nanoparticle bound CpG-ODN 2216 was used to treat equine recurrent airway obstruction in a clinical study. Most remarkable was that regulatory anti-inflammatory and anti-allergic cytokine IL-10 expression was significantly triggered by five consecutive inhalations. Thorough assessment of clinical parameters following nanoparticle treatment indicated a partial remission of the allergic condition. The authors concluded that although employed for the first time, the treatment protocol showed the effectiveness of colloidal nanocarrier-mediated immunotherapy in food-producing animals with potential future applicability to other species including human beings (Klier *et al*., 2012).

Nanobiotix technology and its role in cancer therapy is a novel innovation that is already gaining acceptability in diagnoses and therapeutics. It is based on the novel idea of nanotherapeutics, using nanoparticles with control diameter less than 70 nm with a therapeutic core that can be remotely activated by an external energy supply. The nanoparticles are injected into the patient intravenously or intratumoral and target tumor tissues and take 20-48 hours to accumulate selectively in them. Once the particles have been internalized by the cancer cells, an external energy field is applied to activate the nanoparticles and a local physical or chemical effect then destroys the tumor cell (Chauhan *et al*., 2010).

Other authors determined the efficacy of paclitaxel (Tx)-loaded biodegradable nanoparticles (NPs) on tumor inhibition in a murine model of prostate cancer (Sahoo *et al*., 2004). They hypothesized that NPs following conjugation to transferrin (Tf) ligand (NPs-Tf) would enhance the therapeutic efficacy of the encapsulated drug. The antiproliferative activity of NPs was determined in human prostate cancer

cell line (PC3) and their effect on tumor inhibition in a murine model of prostate cancer. NPs (approximately 220 nm in diameter, 5.4% w/w drug loading) under *in vitro* conditions exhibited sustained release of the encapsulated drug (60% release in 60 days). The IC50 (concentration of drug for 50% inhibition of cell growth) of the drug with Tf-conjugated NPs (Tx-NPs-Tf) was about 5-fold lower than that with unconjugated NPs (Tx-NPs) or drug in solution. Animals that received a single-dose intratumoral injection of Tx-NPs-Tf (Tx dose = 24 mg/kg) demonstrated complete tumor regression and greater survival rate than those that received either Tx-NPs or Tx-Cremophor® EL formulation. Overall, sustained release NPs demonstrated greater antitumor activity following their conjugation to Tf ligand.

The immunological properties of a novel nano-bead adjuvant in a sheep (large-animal) model were investigated (Scheerlinck *et al*., 2006). In contrast to alum, antigen covalently coupled to nano-beads induced substantial cell mediated responses along with moderate humoral responses. No adverse reactions were seen at the site of immunization in the sheep. The authors concluded that nano-bead adjuvants in veterinary species may be useful for the induction of immunity to viral pathogens, where a cell mediated response is required. These findings also highlight the potential usefulness of nano-bead vaccines for intracellular pathogens in human beings.

Vaccination against foot-and-mouth disease virus (FMDV) is a major problem, as current vaccines do not allow easy differentiation between infected and vaccinated animals. Furthermore, large scale production of inactivated virus poses significant risks. To address this, Greenwood *et al*. (2008) investigated the feasibility of using inert nano-beads that target antigen to dendritic cells (DCs) to induce immune responses against FMDV-specific synthetic peptides in sheep. It was clear that while single peptides induced responses in most sheep, the combination of multiple peptides either conjugated separately to individual nano-beads or conjugated as a mixture induced significant cell-mediated and humoral immune responses.

There are potential hazards associated with the use of nanotechnology and research is still ongoing to mitigate the hazards. For instance, lipopolysacchride-coated NPs induced lung inflammation which subsequently changed the microenvironment leading to higher translocation rates of NPs to secondary organs (Chen *et al*., 2006). Also under high environmental, occupational or chronic exposure, inhaled engineered NPs can enter olfactory and trigeminal nerve in nasal region and sensory nerve network in tracheobronchial region taking their way to the central nervous system (Simko & Mattsson, 2010). Elder & Oberdorster (2006) found that colloidal gold NPs (50 nm) translocated in the axons of the olfactory nerves to the olfactory bulb after instilled intarnasally in monkeys. Regarding the skin route, there is some evidence that NPs can accumulate around hair follicles and enter the deeper layers when these follicles open during hair growth (Lademann *et al*., 2006). Moreover, it was shown that quantum dots can penetrate the healthy skin (Ryman-Rasmussen *et al*., 2006). Nano-scale structures can directly reach the gastrointestinal tract *via* food, water, drinks, drugs or drug delivery systems. Also, NPs cleared from the respiratory tract *via* the mucociliary escalator can subsequently be ingested into the gastrointestinal tract. The absorption of NPs from the gastrointestinal tract is governed by both the size (Hillyer & Albrecht, 2001) and surface characteristics (Jani *et al*., 1989) of the particles. Jani *et al*. (1990) showed that absorption of 125 iradiolabeled polystyrene NPs was found to be size dependent (50 nm > 100 nm) in rats and was mainly confined to the Peyer's patches of the gut. Most of the studies have demonstrated that NPs undergo limited gastrointestinal absorption and systemic translocation following oral administration (Stern & McNeil, 2008). For example, studies of the oral absorption of ^{14}C-radiolabeled fullerenes and ^{192}Ir NPs in rats observed minimal systemic absorption (Yamago *et al*., 1995).

In developing countries, especially Nigeria where technology is at the lowest level of development, the use of this technology in veterinary diagnostics and therapeutics is almost near impossible in the near future. Moreover, the dearth of trained personnel that will handle and manipulate nanodevices at the level of the farm setting remains a great challenge indeed.

Conclusion

Although there are gaps that need to be filled, veterinary nanotechnology holds a great key in diagnostics and therapeutics of animal diseases and research is being intensified to breach the gaps. It is suggested that in the future molecular diagnostics and therapeutics should be combined with nanotechnology to boost the efficiency in the diagnosis and treatment of animal diseases for

improved protein supply and food security.

Acknowledgement
NM Useh is grateful to United States Department of State for a Senior Fulbright research award at Cornell University, Ithaca, New York where the manuscript was prepared. Authors of the manuscript have no competing interest of any kind.

References

Bentolila L A, Ebenstein Y & Weiss S (2009). Quantum dots for *in vivo* small-animal imaging. *Journal of Nuclear Medicine*, **50**(4): 493-496.

Chauhan R S, Sharma G & Rana J M S (2010). Nanotechnology in health and disease. Bytes and Bytes, Bareilly, UP, India. Pp 1-11.

Chen J, Tan M, Nemmar A, Song W, Dong M, Zhang G & Li, Y (2006). Quantification of extrapulmonary translocation of intratracheal-instilled particles *in vivo* in rats: effect of lipopolysaccharide. *Toxicology*, **222**(3): 195-201.

Elder A & Oberdorster G (2006). Translocation and effects of ultrafine particles outside of the lung. *Clinical, Occupational and Environmental Medicine*, **5**(4): 785-796.

Engels D, Chitsulo L, Montresor A & Savioli L (2002). The global epidemiological situation of schistosomiasis and new approaches to control and research. *Acta Tropica*, **82**(2): 139-146.

Feneque J (2003). Brief introduction to the veterinary applications of nanotechnology. *Nanotechnology Now* www.nanotech-now.com/Jose-Feneque/Veterinary - Applications- Nanotechnology.htm, retrieved 2012-12-15

Greenwood DLV, Dynonc K, Kalkanidis M, Sue Xiangd, Plebanskid M & Scheerlinck JY (2008). Vaccination against foot-and-mouth disease virus using peptides conjugated to nano-beads. *Vaccine*, **26**(22): 2706-2713.

Hillyer J F & Albrecht R M (2001). Gastrointestinal persorption and tissue distribution of differently sized colloidal gold nanoparticles. *Journal of Pharmaceutical Sciences*, **90**(2): 1927-1936.

Huang J, Zhong X, Wang L, Yang L & Mao H (2012). Improving the magnetic resonance imaging contrast and detection methods with engineered magnetic nanoparticles. *Theranostics*, **2**(1): 86-102.

Jackson P, Periasamy S, Bansal V & Geso M (2011). Evaluation of the effects of gold nanoparticle shape and size on contrast enhancement in radiological imaging. *Australas Physics, Engineering, Science and Medicine*, **34**(2): 243-249.

Jani P, Halbert G W, Langridge J & Florence A T (1989). The uptake and translocation of latex nanospheres and microspheres after oral administration to rats. *Journal of Pharmaceutics and Pharmacology*, **41**(12): 809-812.

Jani P, Halbert G W, Langridge J & Florence A T (1990). Nanoparticle uptake by the rat gastrointestinal mucosa: quantitation and particle size dependency. *Journal of Pharmaceutics and Pharmacology*, **42**8(12): 821–826.

Klier J, Fuchs S, May A, Schillinger U, Plank C, Winter G, Gehlen H & Coester C (2012). A nebulized gelatin nanoparticle-based CpG formulation is effective in immunotherapy of allergic horses. *Pharmaceutical Research*, **29(6)**: 1650-1657.

Kroubi M, Daulouede S, Karembe H, Jallouli Y, Howsam M, Mossalayi D, Vincendeau P & Betbeder D (2010). Development of a nanoparticulate formulation of diminazene to treat African trypanosomiasis. *Nanotechnology*, **21**(50): 1-8.

Lademann J, Richter H, Schaefer U F, Blume-Peytavi U, Teichmann A, Otberg N & Sterry W (2006). Hair follicles-a long-term reservoir for drug delivery. *Skin Pharmacology and Physiology*, **19**(19): 232-236.

Na H B, Song I C & Hyeon T (2009). Inorganic nanoparticles for magnetic resonance imaging (MRI) contrast agents. *Advanced Materials*, **21**(21): 2133-2148.

Nagano N, Isomine S, Kato H, Sasaki Y, Takahashi M, Sakaida K, Nagano Y & Arakawa Y (2008). Human Fulminant Gas Gangrene Caused by *Clostridium chauvoei*. *Journal of Clinical Microbiology*, **46**(4): 1545-1547.

National Science and Technology Council (2004). National Nanotechnology Initiative. Committee on Technology. Subcommittee on Nanoscale Science, Engineering and Technology. Supplement to the President's

FY 2004 Budget. www.ostp.gov/NSTC/html/iwgn/iwgn.fy04budsupporl/toc.htm, retrieved 2012-12-15.

Ryman-Rasmussen J P, Riviere J E & Monteiro-Riviere NA (2006). Penetration of intact skin by quantum dots with diverse physicochemical properties. *Toxicological Sciences*, **91**(1): 159-165.

Sahoo S K, Ma W & Labhasetwar V (2004). Efficacy of transferrin-conjugated paclitaxel-loaded nanoparticles in a murine model of prostate cancer. *International Journal of Cancer*, **112(**2): 335-340.

Scheerlinck JPY, Gloster S, Gamvrellis A, Mottram PL & Plebanski M (2006). Systemic immune responses in sheep, induced by a novel nano-bead adjuvant. *Vaccine*, **24**(8): 1124-1131.

Schlachter EK, Widmer HR, Bregy A, Lonnfors-Weitzel T, Vajtai I, Corazza N, Bernau VJ, Weitzel T, Mordasini P, Slotboom J, Herrmann G, Bogni S, Hofmann H, Frenz M & Reinert M (2011). Metabolic pathway and distribution of superparamagnetic iron oxide nanoparticles: *in vivo s*tudy. *International Journal of Nanomedicine*, **6**: 1793-1800.

Scott NR (2007). Nanoscience in veterinary medicine. *Veterinary Research Communications*, **31**(): 139-144.

Scott NR (2005). Nanotechnology and animal health. *OIE Scientific and Technical Review*, **24**(1): 425-432.

Simko M & Mattsson MO (2010). Risks from accidental exposures to engineered nanoparticles and neurological health effects: a critical review. *Part Fibre Toxicology*, **7**: 42.

Stern ST & McNeil SE (2008). Nanotechnology safety concerns revisited. *Toxicological Sciences*, **101**(1): 4-21.

Thontiravong A, Wannaratana S, Tantilertcharoen R, Prakairungnamthip D, Tuanudom R, Sasipreeyajan J, Pakpinyo S, Amonsin A, Kitikoon P & Oraveerakul K. (2012). Comparative study of pandemic (H1N1) 2009, swine H1N1, and avian H3N2 influenza viral infections in quails. *Journal of Veterinary Science*, **13**(4): 395-403.

Tripp RA, Alvarez R, Anderson B, Jones L, Weeks C & Chen W (2007). Bioconjugated nanoparticle detection of respiratory syncytial virus infection. *International Journal of Nanomedicine*, **2**(1): 117-124.

Useh NM, Nok AJ, Ibrahim NDG & Esievo KAN (2012). Anaemia in *Clostridium chauvoei* infection is masked by haemoconcentration. *Veterinarski Arhiv*, **82**(2): 433-447.

Weatherhead, JE & Tweardy, DJ (2012). Lethal human neutropenic entercolitis caused by *Clostridium chauvoei* in the United States: Tip of the iceberg? *Journal of Infection*, **64**(2): 225-227.

Wiley JA, Richert LE, Swain SD, Harmsen A, Barnard DL, Randall TD, Jutila M, Douglas T, Broomell C, Young M & Harmsen A (2009). Inducible bronchus-associated lymphoid tissue elicited by a protein cage nanoparticle enhances protection in mice against diverse respiratory viruses. *PLoS One*, **4**(9): 1-10 e7142.

World Health Organization (WHO) (1998). *Control and surveillance of African trypanosomiasis. Geneva: World Health Organization*, http://whqlibdoc.who.int/trs/WHO_TRS_881.pdf, retrieved 2012-12-18.

World Health Organization (WHO) (2012). *Accelerating work to overcome neglected tropical diseases: a roadmap for implementation. Geneva: World Health Organization*. http://whqlibdoc.who.int/hq/2012/WHO_HTM_NTD_2012.1_eng.pdf, retrieved 2012-12-02.

Yamago S, Tokuyama H, Nakamura E, Kikuchi K, Kananishi S, Sueki K, Nakahara H, Enomoto, S & Ambe F (1995). *In vivo* biological behavior of a water-miscible fullerene: ^{14}C labeling, absorption, distribution, excretion and acute toxicity. *Chemical Biology*, **2**(6): 385-389.