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Review

Application of Nanotechnology in Veterinary Medicine - An Overview

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Abstract

Nanoparticles are small, nanoscale particles that range in size from 1 to 100 nm and can contain either inorganic or organic substances. Nanoparticles possess unique qualities due to their unique morphology, size, structure, and surface characteristics. Applications of nanotechnology are becoming more widely acknowledged as viable instruments in modern disinfectants, veterinary care, drug delivery, illness diagnostics, and vaccine production. Numerous medical applications, such as gene delivery, vaccination, medication, diagnosis, and treatments, have made use of nanotechnology. By developing new small-scale tools and materials that are beneficial to living things, nanotechnology has transformed almost every field of veterinary and animal research and opened up new avenues for the use of molecular biology and biotechnology. Among the many types of nanomaterials used in therapy, drug delivery, immunization, and disease detection are metallic nanoparticles, quantum dots, carbon nanotubes, magnetic nanoparticles, fullerenes, liposomes, and dendrimers.

Keywords: Antimicrobials, Diagnostic Tools, Nanotechnology, Nano Medicine, Nano Vaccines.

Introduction

A material, substance, or element's structure can be altered at the nano scale, a process known as nanotechnology. At the Nobel Prize lecture in 1959, Richard Feynman introduced the idea of nanotechnology by speculating that it would never be able to build a material atom by atom (Feynman, 2018), after Fullerenes were discovered (Iijima, 1991), and carbon nano tube production (Prow *et al*., 2005). Once thought to be science fiction, nanoscience and nanotechnology are now recognized as practical technologies (Underwood & Eps, 2013). Nanotechnology later received contributions from other fields of endeavor. A new discipline known as nanomedicine has emerged as a result of the growing interest in using nanotechnology in medicine (Haley & Frenkel, 2008). Veterinary medicine items that are commercially available now include nanoparticle medicines that have been verified by science (Blanco *et al*., 2008). This demonstrates how nanotechnology research is becoming more and more relevant to veterinary practice.

Advantages of Nanoparticles

In the biomedical industry, nanoparticles are also organized so that drugs and biomolecules can be inserted and not broken at unwanted places, which can help the medication reach the target site more successfully. By increasing the penetration and retention impact, nanoparticles can frequently prolong the circulation time of therapeutic compounds loaded on nanomaterials and boost their residence at the target site through leaky vasculature (Wang *et al.,* 2007; Gelperina *et al.,* 2005).

Advantage includes –

i. The capacity to adjust particle characteristics including size and shape to attain the best possible passive or active medication targeting.
ii. Distinct administrative routes.
iii. Higher carrier capacity.
iv. Enhanced absorption capacity.
v. Nanoparticles have more cellular uptake and mobility than microparticles.
vi. Steady, controlled medication delivery at the intended location.
vii. less hazardous as compared to other substances.
viii. The capacity to modify a specific particle to endure harsh pH, processing, and enzymatic conditions.
ix. Longer retention duration of NPs at the mucosal surface with the use of formulation ingredients that are mucoadhesive.
x. Longer circulation times led to better pharmacokinetic and pharmacodynamic outcomes (Reverberi *et al* 2016; Yao *et al*., 2015; Zhang *et al* 2011; Nair *et al*., 2010).

Classification of Nanoparticles

Nanoparticles are classified numerously based on their origin, form, structure and purpose of administration.

Organic Nanoparticles

Many people are aware of ferritin, dendimers, micelles, liposomes, and other organic NPs or polymers. These nanoparticles (NPs) are biodegradable and harmless. Some particles, such as micelles and liposomes, have hollow cores that are known as nanocapsules. These particles are also susceptible to light, heat, and electromagnetic radiation. Their unique characteristics make them a great substitute for drug delivery. Their field of use and performance are determined by their stability and delivery methods, which include either an absorbed or trapped drug system, in addition to their typical properties such as size, structure, and surface morphology. Because they work well and may be injected at a specified location, organic nanoparticles are employed in biomedicine applications such as medication delivery systems (Tai *et al*,. 2007).

Inorganic Nanoparticles

These comprise nanoparticles based on metal, oxide, and carbon.

Metal: Based nanoparticles, or metal-based NPs, are created by both constructive and destructive means from metals to nanometric sizes. Metals such as silver, cadmium, cobalt, copper, iron, lead, gold, and zinc are frequently utilized in the creation of nanoparticles.

When oxygen is present at ambient temperature, iron nanoparticles rapidly oxidize to iron oxide, increasing their reactivity in comparison to other iron nanoparticles. This is how metal **Oxide:** Based nanoparticles (NPs) are created. The primary reason for synthesizing metal oxide nanoparticles (NPs) is their enhanced reactivity and efficiency (Mohantya *et al.*, 2014).
Carbon: based nanoparticles are defined as those that are composed solely of carbon. These fall into the following categories: nanosized activated carbon, graphene, carbon nanotubes, carbon nanofiber, black carbon, and fullerenes (Torres et al., 2016).

Structure of Nanoparticle and Their Use

Polymeric Nanoparticles: There are two types of polymers: synthetic polymers, such as polyethylene glycol (PEG), and proprietary polymers, which are based structurally on polysaccharides, such as chitosan and inulin. Dendimers share a structure with one another, but the branches that emerge from the center have different spreading foci. This kind of nanoparticle is typically used in antibody readiness as New Castle (Riley & Vermerris, 2017).

Liposomes: These spherical, non-destructive, biodegradable PEGylated particles were described. Their fluid spotlight features adjustments that dissolve in water. Similarly, the non-water dissolvable treatments are encased in a double layer of phospholipid shell, which disperses the particles. Additionally, they could be utilized to mask other antigens (Thulasi *et a*l., 2013). The particles are shielded from the body's immune system because of the external polyethylene glycol layer that coats their exterior. Furthermore, chelated antibodies can be fixed on the outside of liposomes. In general, this kind of nanoparticle is represented by its ability to transfer both water-soluble and water-insoluble solutions (Elgqvist, 2017). Their biodegradable structure portrays them as highly prosperous. Another type of liposome is called an immunooliposome; these can be attached to external antigens for vaccination purposes, or they can be linked to antibodies that are summoned to attack harmful bodily cells (Meena *et al.,* 2018; Jurj *et al.,* 2017). Lastly, because liposomes are thought to be extremely biodegradable and biocompatible materials with a high ability to stack both water soluble and water insoluble compounds concurrently, they have a great use in the delivery of pharmaceuticals. One method of releasing the laden medicines is through simple diffusion. In any event, their inadequate quantity, quick accumulation, and quick arrival of the loaded medications are a true barrier (Manuja *et al*.,2012)

Fullerenes and Bucky Tubes: Fullerenes are carbon nanoparticles with a ball like structure that are stable and capable of interacting with cells or pathogens. Bucky tubes are hollow, spherical structure that can be used as biosensors for various substances. Nanotubes can infiltrate cells to treat disease because of their needle like structure, much like immunoglobins (Patil *et al.,* 2009).

Respirocytes and Microbivores: Respirocytes follow the components of red and white blood cells on their own. Microbivores catch infections while they economically and efficiently supply the tissues with oxygen and avoid the accumulated carbon dioxide exceptional management sensors. The eliminated microorganisms underwent an enzymatic transformation into their initial building blocks, which included unsaturated lipids, nucleotides, and amino acids (Rodriguez *et al*., 2017).

Nanoshells: These are spherical structures with an exterior gold coating attached, which are irradiated with an infrared laser to analyze malignant tumors. They can be used as an adjuvant for radiotherapy since they lessen the force of the X-beam. In addition, gold nanoparticles are non-toxic and biocompatible with the body (Rodriguez *et al*., 2017).

Quantum Dots: These incredibly tiny jewels, which range in size from 2 to 10 nm, have the ability to semiconduct when exposed to light, which makes them useful for optoelectronic applications (Awate *et al.,* 2013). The components of semiconductors are made up of cadmium, zinc, and selenium (Thulasi *et al*., 2013). They consist of an inorganic material center and a shell that can tolerate a fluid covering that can be coupled to various biomolecules.

There is a crystal in the middle. The color of the lights that have been released depends on the size of the stone before. They are able to construct modest and straightforward long-term experiments that typically last for a few days or longer (Patil *et al.*, 2009).

In general, immunodiagnostics and diagnostics can be performed using quantum dots (Riley & Vermerris, 2017).

Solid Lipid Nanoparticles: Lipids that are evenly distributed and suspended in a fluid mixture. They can be utilized to treat cancer because they include a lipophilic center. It is possible to conjugate many hydrophilic medications or antibiotics to their outer hydrophilic shell. Additionally, the outer shell increases the bioprofitability of the medicine. Furthermore, cationic solid lipid nanoparticles can lawfully bind nucleic acid segments through electrostatic linkage, enabling their application for high-quality treatment (Jurj *et al.*, 2017). These nanoparticles can be administered by a variety of routes, including topical, oral, and subcutaneous injection. They can efficiently deliver the drugs inside the central nervous system since they can pass across the blood-brain barrier. The evaluation of using fluid lipid nanoparticles, in addition to storage lipid NPs, is presently being conducted (Riley & Vermerris, 2017; Jurj *et al.*, 2017).

Magnesium Oxide Nanoparticles: The primary characteristic of this category is their ability to be guided to target cells through the circulation due to an external magnetic field. They work better for drug delivery, thermal treatment, and imaging (Patil *et al.*, 2009). Their structure consists of an iron core encircled by a fluorescent silica outer layer, which is where the drug attachment happens. An outer layer that is polymer-based helps to regulate the particles. They are used in a few appealing resonance medicinal applications for disease conclusion and treatment as multi-useful theranostic buildings due to their beautiful suited ties. To prevent particle aggregation and shield the particles from the immune response, polyethylene glycol is utilized to coat the particles. By enhancing light retention, silica coatings make malignancy imaging easier (Jurj *et al.*, 2017).

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Dendimer: Made of incredibly small polymers, these hyperbranched nanomaterials are remarkably dissolved in aqueous solution and smaller than human cells (Kudel *et al.*, 2015; Chakravarthi & Balaji,2010). When introduced into the flow, their small size and conduction arrangement keep any unwanted resistance reactions at a safe distance (Kudel *et al.*, 2015). They have the appearance of a 3D extended atom tree. Medication is coupled to or may be conjugated inside the circle on the dendimer surface. Dendimers can be stacked with a variety of water-soluble and water-insoluble restorative medicines through physical and chemical connection. These medications can also be put within the vacant centers through nonbonding stacking. The expansion of solidity and increased restorative productivity can result from the covalent conjugation of dendimers and stacking pharmaceuticals. They are essential to the treatment of cancer. Dendimers are distinguished by their enormous, intricately branching structure. Imaging-related medications may include dendimers in them. Numerous investigations have demonstrated the high efficacy of dendimer-loaded nanocomposites as antibacterial agents against Staphylococcus aureus, E. coli, and pseudomonas aeruginosa. The loading of their radioactive or pharmacological storage components causes the tumor to migrate. Ultimately, signals are delivered with the execution of dangerous cells in the event that treatment is successful. In a work led by Landers, scientists coupled sialic acid with dendritic polymers to prevent flu infections. The preparation was found to be effective in eradicating and inactivating infections (Manuja *et al*., 2012).

Nano-emulsion: As bactericidal and virucidal drugs, nanoemulsions show promise for restorative benefits. When oil droplets adhere to the envelope or layer of a bacterial or viral coat in an animal's body due to surface tension, they mix and cause the treatment to enter the microbial cells. Furthermore, nanoemulsions can be used as delivery systems for antigens. Multiple antigens can be integrated into a single nanoparticle (Thulasi *et al*.,2013). They are greasy, nanoscale droplets in water that have a tiny layer of surfactant on them to help with physical adjustment. The two types of nanoemulsions are water in oil and oil in water. For nanoemulsions delivered by low essentiality methods, room temperature and 4 degrees Celsius are the optimal stockpiling temperatures, and the capacity time is more than two months (Chakravarthi & Balaji, 2010). The water/oil nanoparticle emulsions' ability to continuously release the antigens makes them adjuvants that enhance the arrival of antibodies at high titres. A few analysts notice the signs of fat drops on red blood cells and sperm cells when they are administered systemically (Kudela *et al*., 2015). Several audits concluded that using nanoemulsion on eukaryotic cells was safe and did not cause any problems.

Nano-bubbles: These are stable at ambient temperature, but when exposed to ultrasonic sounds and slightly heated, they group together to produce microbubbles. Their primary function is the delivery of medications, particularly those that are intended to enter cancerous areas. Gene therapy also makes use of liposomal nano bubbles (Anton & Vadamme, 2011).

Aluminosilicate Nanoparticles: These are short-chain polyphosphate and silica nanoparticles combined to speed up the body's natural clotting process. Consequently, reduces bleeding (Kang *et al*., 2004).

Polymeric Micelles: These contain a hydrophobic core that makes it easier for medications that are hydrophobic to be transported. They have a soluble layer covering the hydrophobic core, which makes them extremely water soluble. It is also mentioned that amphiphilic polymers like PLGA and ecaprolactone were used in their creation. paclitaxel and amphotericin B are two examples of less water-soluble medicines that are typically supplied for targeted drug transport [Sayed & Kamel, 2018; Prabhu *et al*, 2015).

Polymer Coated Nanocrystals: These help to organize a robust nanosuspension that is dependent on macrophages for delivery to HIV infection sites and sequestration, while also preventing aggregation (Elsabahy *et al.*, 2012).

Polymeric Nanospheres: Consistent circular structures with a pore size of less than a micron are made from either biodegradable or non-biodegradable polymers. Novel approach to transdermal drug delivery, it might be applied to the study of type 2 human epidermal growth factor receptor and in vitro integrin cancer cell proliferation (Mieszawska *et al*., 2013).

Metallic Nanoparticles: Among the several metals employed in the nano system is gold, which is mostly used in cancer treatment. Another kind of metallic nanoparticles include those made of silver, manganese, and platinum. These particles all have a metallic core covered in a coating of protection. Metallic nanoparticles are additionally loaded with a variety of antibodies and chelated radionuclide. In order to keep a strategic distance from non-specific binding, particles are linked to polyethylene glycol, which shields them from immune attack [33]. Certain metallic nanoparticles, particularly bimetallic ones, such as silver/gold (Alshatwi *et al.*, 2015), silver/selenium (Muktar *et al*., 2015), or gold/platinum, have been used to treat various diseases.

Possible Applications of Nanotechnology in Veterinary Science

Therapeutic Purposes

Nanoparticles are relatively new to the veterinary and animal processing fields, despite their lengthy history of use as therapeutic and diagnostic instruments in the human medical industry. Because of growing concerns about microbiological antibiotic resistance, the cattle industry's development demands have recently centered on the use of antibiotics as growth boosters, which leads to the development of antibiotic resistance (Muktar *et al*., 2015). Therefore, we need alternatives to antibiotics in order to use nanoparticles as antimicrobials. Global veterinary practice is thought to be significantly impacted by nanotechnology. Recently, the use of devastating clones of antibiotics against a variety of bacteria that cause chronic animal illness, such as Brucella, Mycobacterium bovis, streptococcus, and Rhodococus equi, has helped establish nontoxic antimicrobials agents to address antibiotic resistance. Their most common use is in drug delivery systems with nanoparticles (Woundenberg *et al*., 2005). Utilizing technology to help deliver unstable and insoluble pharmaceuticals has the following benefits: it maintains the concentration of the active ingredient at the anticipated site of action, has little systemic toxicity, and requires less clearance than the original drug (Parveen *et al*., 2017). Compared to traditional medications, the nanoparticle compositions require lower therapeutic dosages. This characteristic is crucial to veterinary medicine because it permits the use of smaller dosages of medications and encourages the elimination of pharmaceutical residues, especially antimicrobials found in carcasses and other animal products, as well as a decrease in treatment expenses (Jurj *et al.*, 2017). Tissue engineering, or the regulation and healing of damaged tissue, is possible with the use of nanotechnology. Traditional medical procedures like organ transplants and artificial implants may be replaced by tissue engineering. The development of a carbon nanotube scaffold in bones is one such instance. Because of their small size, they can evade the reticuloendothelial system's detection and destruction by passing through various physiological barriers or even through cell or nuclear membranes to reach their target sites (Talukdar *et al*., 2014). Because they are biocompatible, nanoparticles can readily integrate with an organism's biological system without causing an adverse immune reaction or inflamation (Troncarelli *et al*., 2013). When it comes to the delivery of antibiotics, nanominerals, hormones, antioxidants, vitamins, nucleic acids, and imaging agents, nanoparticles offer a sustained release/long acting smart drug delivery tool (Krishnan & George, 2014). Enable robust pathogens that are resistant to several antibiotics (such as MRSA and XDR/TDR/MDR TB). Intracellular pathogens, such as leishmaniasis and brucella, as well as both chronic and non-chronic infectious illnesses (Meena *et al*., 2018).

Diagnostic Applications

Disease Diagnosis: Thanks to advancements in nanotechnology, diagnostic instruments and treatments are now more effective in terms of sensitivity, specificity, speed, and cost. Numerous nanomaterials, such as metal nanoparticles, polymeric nanoparticles, nanoemulsion, liposomes, and nanocrystals, have been employed in the detection of veterinary diseases. In a review provided the most recent updates on the diagnostic tests using nanomaterials for six new and reemerging diseases in poultry and livestock: post-weaning multisystemic wasting syndrome (antibody mediated gold, platinum, and silica dioxide nanospheres), Anthrax (biosensor with single stranded modified gold nanoparticles probes), Brucellosis (biosensor with oligonucleotide modified gold nanoparticles based colometric assay), and aflatoxicoxicosis (aptasensor with gold nanowires/graphene oxide). creation of a lateral flow immunoassay based on blue silica nanoparticles (Si NPs) for the quick and accurate diagnosis of human brucellosis. Lipopolysaccharide of brucella and Staphylococcal protein A were utilized in the development of a Si NPs based lateral flow immunoassay that could identify the target antibody on serum samples[GE and others]. In the work, an alternative molecular method based on an E. coli expression system was used to generate the capsid protein of porcine circovirus type 4 (PCV4) [WANG and others].

Imaging Techniques: The body is scanned for metastatic lesions and early cancer diagnosis is made possible by the pairing of nanoparticles with antibodies specific to tumors (Manuja *et al.*, 2012). They are more radiant, remain in the body for a longer period of time, and permit repeated administration of the imaging agent without hepatic or renal restrictions. Therapeutic and research microsurgeries can employ nanorobotics. Additionally, they are able to carry nanocameras to aid in surgeries in real time. By using high density nano-array chips, thousands of proteins, genes, antigens, or disease biomarkers can be found at once, making it a quick screening and diagnostic tool (Daneesh *et al.*, 2011).

Prophylactic Use

Nano-carriers and nano-adjuvents are highly advantageous because they increase the stability and encapsulate therapeutic agents at the site, mask the taste and odor of the medicine, control the drug's release, and protect it from external sources.

Nano-Vaccines: NPs, are used to boost immune responses. They are crucial for inducing humoral and cell-mediated immune responses, which fight pathogens and stop illness from spreading. They are also crucial in the antigen-presenting cells' activation. When NPs are employed as nano-adjuvants, the release of antigens is slowed, increasing the vaccine's efficacy. To increase the effectiveness of the vaccine, NPs loaded with antigens are directed towards lymph nodes. In vaccinations, polylactic co-glycolic acid is employed. A glucosamine polymer called chitosan is employed in the respiratory tract-administered tuberculosis vaccination. Liposomes coated with neoglycolipids, which contain oligomannose residues (OMLs) and aid in inducing Th 1 cells and T lymphocytes, are part of the vaccine against Neospora caninum (Riley & Vermerries, 2017). Additional instances comprise recombinant B. anthracis spore-based vaccines in nanoemulsion form as well as influenza vaccines. PLGA nanoparticles are included in the oral forms of the Bordetella pertussis vaccine, Tetanus toxoid, Helicobacter pylori vaccine, and Bovine para influenza type 3 vaccine. Artificial Leishmania One vaccination that is administered subcutaneously and placed onto chitosan nanoparticles is the SOD vaccine. A vaccine based on gold nanoparticles is administered to prevent foot and mouth disease. (Nishikawa, 2017; Jurj *et al.*, 2017; Marees et al., 2016).

Conclusion

The development of novel, unusual, and accurate techniques for the diagnosis and treatment of animal illness is greatly aided by NPs. NPs have a critical role in animal security, growth, vaccination, and cleanliness. NPs have a great deal of potential for use in biomedical applications because of their distinct biological and chemical properties. They can be sent and used for the transportation of medications, veterinary care, and illness treatment. The idea of nanoparticles, their classification, their benefits, and their possible application as therapeutic agents in veterinary medicine for prevention and disease detection have all been covered in this research. Therapeutic nanoparticles of the new generation are very particular to their targets; distinct NPs were created to treat diverse cancer cell morphologies and genotypes, including malignant tumors that are resistant to cancer stem cells and chemotherapy. They can work in a variety of ways. For instance, nanoparticles can kill cancer cells by delivering chemotherapeutic agents, heating the cells, attacking the cells selectively with the immune system, or turning off the genes that cause apoptosis and initiating programmed cell death. They can even use multiple of these methods at once (Sridharan & Gogtay, 2016). The removal of metastatic cancer cells away from the initial lesion is made possible by the combination of nanoparticles and antibodies specific to tumors (Mohantya *et al*., 2014). expand the possibilities for bone grafting and tissue engineering, and offer fresh perspectives on gene therapy delivery of proteins, RNA, DNA, or tiny peptides inside of cells. RBCs (oxygen and carbon dioxide gas exchangers) and WBCs (circulating pathogens) can be replaced by the produced microparticles.

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Contribution by Authors

Each co-author contributes equally.

Conflict of Interests

There is no conflict of interest.

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