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(REVIEW ARTICLE)

Application of Nanoparticle in the Veterinary Medicine

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Abstract

Nanotechnology is a modern and developed technology, which have great importance in many fields of medicine (diagnosis and treatment). Also, it used to prevent and solve many problems related to animal production and health. The Nanosystems are including metallic nanoparticles, liposomes, polymeric Nanospheres, polymeric micelles, carbon nanotubes, functionalized fullerenes, polymer-coated Nanocrystals, dendrimers and Nanoshells. Our review showed a details classification of nanoparticles and their uses. Nanoparticles have several features depended on the size, colossal surface. The development of antibiotics nanoparticle is very important and has an excellent impact in treating bacterial infections wherever the antibiotics nanoparticle gives high therapeutic effect without negative side effects. Our review showed some aspects of the nanoparticles' classification and their uses in general form and veterinary medicine, focusing the light on nanoparticle applications in the nutrient, Biocides, meat and egg quality, milk, animal treatment diseases, and reproduction the animals.

Keywords: Nanoparticle; Diagnosis; Treatment; Medicine

1. Introduction

Nanotechnology is quickly developing science which started work in 1974 about work on materials that has (1-100) nm in size [1, 2, 3, 4]. The word (Nano) is taken from the Latin word (nanus), that indicate to implies tiny size, wherever the (1) nm equals to (10^9) meter [5, 6]. Nanotechnology is a science interested in many fields such as agriculture, science, and medicine [7].

In addition to that, the nanomaterial has an effective impact on in-vivo and in-vitro researches [8]. The Nanoparticles have more powerful physicochemical effects than the non-nanoparticles because they have many surfaces to volume proportion, huge surface, higher reactivity, bioactivity, bioavailability, site-specific targeting stability and therapeutics effects [9, 10].

Nanotechnology has great importance in medication application through its extraordinary capacity to get organs, tissues and cells more than macroparticles. Therefore, it has low toxicity [9, 11, 12] . The drugs could react with the nanoparticles or linked it with their surface [13].

The nanoparticle was used in medicine to increase the immune responses of the infection. Traditional therapy has many difficulties during the using [14]. Many countries depended on the economy and investment of the animals.

Although, the rise of many diseases, helpful tools are used and created to recognize and treat animal diseases to increase animal protein production [10].

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Nanotechnology in Veterinary Medicine has an essential role in improving drugs [7]. (Synthesis of the atoms helps us create new medicines to treat viral or bacterial diseases and heal. In addition to that, the production of new drugs can get in the cell [14].

Treatment by nanoparticles is a new strategy used for treatment and diagnosis and can increase the safety and efficacy of drugs. Also, it provides a great chance to develop new agents (15, 16]. Nanopharmaceuticals are beneficial fields of this science with many advantages used in the veterinary world [17].

Objectives of the study

- Showing classification of the nanoparticle
- Showing general and veterinary medicines uses of the nanoparticles

2. Review of literature

2.1. Classification of nanoparticles

The are many kind of classification for move particles:

2.1.1. According to their use in veterinary medicine

A- Polymeric nanoparticles
B- Liposomes
C- Fullerenes and Bucky tubes
D- Microbivores and respirocytes
E- Nanoshells
F- Quantum dots
G- Solid lipid nanoparticles
H- Magnetic iron oxide nanoparticles
I-Dendrimer
J- Nanoemulsion
K- Nanobubbles
L- Aluminosilicate nanoparticles
M- Polymeric micelles
N- Polymer coated Nanocrystals
O- Polymeric Nanospheres
P- Metallic nanoparticles [18, 19, 20, 21]

2.1.2. According to their origin

A- Inorganic nanomaterials
B- Organic nanomaterials
C- Hybrid nanoparticles [22, 23, 24]

2.1.3. According to their shape

A- spheres
B- tubes
C- liquid drops

2.1.4. According to the aim of application:

A- vaccine
B- nutritional
C- therapeutic
D- diagnostic [25]

2.2. General uses of the nanoparticles

2.2.1. Therapeutic uses

- It has physical and chemical properties that make us use it in medicine [26].

- Contains a demonstrative and helpful operator [16].
- Helps us to large amount production of the payloads [27, 28].
- Nanoparticles are work under different temperature and weight [29].
- It can pass over the blood-brain and reach the target and at a high percentage [24].
- It can quickly react with the organism for immunological aims [20].
- Used as capsules or injection [7].
- Used for treatment and diagnosis [30].
- It significantly affects neurotic sores and treatment and improves medication [20].
- Used for releasing hormones, vitamins and antibiotics [31].
- It can cure of intracellular bacteria such as brucella and leishmania and resistant pathogens [32].
- Nanoparticles can be used to treat the malignancy cell by using chemotherapeutic operators [33].
- It used with tumours to prevent metastatic malignant cells to other tissues [34].
- Many substances such as metal, polymers, and lipids are used for nanoparticle production [35], proteins and nucleic acids [22]. Also, antibiotics used for the treatment of bacterial infection such as TB [35].
- The nano-carriers are very important in producing nanomedicine in research medicine and research academic [36].
- It has an essential role in chemotherapeutic production for treating diseases without side effect or cell obstruction such as ovarian carcinomas [33].

2.2.2. Preventive uses

- it provides us with new plans to produce new antibodies with high efficiency [37].
- It is used to develop sensors that give to the patients to measure proteins level [33].

2.2.3. Diagnostic uses

- the nanoparticles with particular tumour antibodies help to treat cancer with better results and a high cure percentage [34].
- the imaging operators have a long time duration of action and efficiently use the imaging substance without side effects on the body organs [38].
- Nanorobotics used scale medical procedures and can carry cameras for discovering the organs during the surgeries [39].
- It is fast screening and diagnostic and can detect the proteins and genes due to high-density nanoarray chips [40].

2.3. Nanoparticles Uses in veterinary medicine

Nanotechnology has a marked effect in veterinary medicine, veterinary diagnostics, tissue reformation, disinfectants and immunization. The Nano-applications are used in many fields that related to veterinary sciences such as animals production, animal health and nutrition, animals breeding and reproduction and treatment of the veterinary diseases [25].

Nanoparticles applications in animal production

The nanotechnology used in animal production by the production of probiotics, vitamins, nutritional supplements and drugs. The nanoparticles used for the detection of diseases. The use of routine antibiotics leave a residue which affects as side effects, while nanoparticles reduces the using of antibiotics due to its small size [41].

Fattal *et al*., [36] studied the effect of the nanoparticles ampicillin on mice that suffer from Salmonella spp. The results showed treated mice with nanoparticles ampicillin showed significant effects. Its lower amount of the required antibiotic is needed to treatment.

Nanoparticles application in animal health and nutrition

Nanoparticles are inexpensive, used in low amounts, and used as growth factors and immune factors, and it form several benefits for animal feeding. It helps to improve fermentation. Nanoparticle zinc oxide is used improvement of growth and increase immune response. Nano zinc decreases the somatic cell count in subclinical mastitis in dairy cows [42].

Microencapsulation is used to protect the food from oxidation, keeps them without analysis for a long time, is used in proteases, and keeps pH stability. Mycotoxicosis is a big problem in human and animals that come from the contamination of food. Nano magnesium oxide and nano-silica have high powerful on mycotoxin such as aflatoxins [43].

Nanoparticles application in inbreeding and reproduction

Treatment and diagnosis of reproductive diseases such as sperm freezing and estrus detection. Reproductive problems such as retained placenta could treat by nanoparticles. The nanoparticles have a significant effect in releasing hormones such as a steroid [44].

The nanotube established in the skin to time measurement of in oestradiol organizes within the blood. Nanotubes can detect oestrus by using fluorescence [45].

Nanoprobes are used to diagnose genital tract diseases, hormonal and metabolic disorders. The sterilization nanoparticles used in the animals depended on the nanoparticles' toxicity that included Cd in low doses. The course of nanoparticles increased reproductive activity efficiency [25].

Nanoparticles application in the treatment of veterinary diseases

Nanotechnology is playing an important role in veterinary diseases [17]. Nanocarrier-mediated therapy has excellent effects in diagnosing and treating the disorders [46]. Quantum dots can use in vivo imaging [47].

Nanotechnology is used to treat the trypanosome. Nanoparticle treatment showed a partial decrease in the allergic [47].

2.3.1. Nanoparticles application in vaccines and adjuvants

Nanoparticles are used in the vaccine production used in the animals due to their high ability to improve immunological reactions. It is also used of adjuvant output to make antigens and vaccines [48]. The nanoparticles are used as carrying on antigens to increase the vaccine's level performance [49].

Nano vaccines in veterinary medicine:

- Nanoemulsion vaccines are included influenza vaccine and anthrax vaccine and.
- oral vaccine loaded on PLGA nanoparticles for production of the Immunoglobulin type G and Immunoglobulin type A such as Bovine para influenza III vaccine, vaccines of the Helicobacter pylori, Bordetella pertussis vaccine, and tetanus toxoid.
- Recombinant Leishmania SOD vaccine
- Empty capsid and center such as vaccines of the virus that used for protection against African horse sickness [50].

2.4. Uses of nanoparticles in veterinary medicine

Nanotechnology has a significant effect on veterinary fields treatment, diagnostics, vaccination and disinfectants. The medicine's vehicle straightforwardly into the target cells empowers utilizing exceptionally low dosages that progressively diminish the medication build-ups and withdrawal period in homestead animals [25].

2.4.1. Nutrient

Casein micelles are nanoparticles present in the milk [50]. Some casein molecules accumulated around Ca and proteins. Vitamin D helped to absorb casein nanoparticles, wherever casein particles release their encapsulated vitamins [51].

Without milk from the mother, weanlings should be considered carbohydrate [52]. Nutritional supplements increase body size as well in weaned animals. Nanoparticles nutrient facilitate and increases growth rates [53].

Orally carrier nanoparticle is very important to the livestock. Each part of the gastrointestinal has a unique environment that contains enzymes and pH level [54]. The nanoparticle made from the canola protein cruciferin showed that hydrophobic compounds and nanoparticles encapsulate hydrophilic protect it from stomach secretion. The nutrients are produced from the nanoparticles and reach to epithelial of the intestinal. The nanoparticle doesn't stay in the intestine because it degradation depending on the cellular uptake and type of nanoparticle [55].

The nanoparticles are bioactive compounds and can add it directly and could be countered by nanotechnological methods. The small size of nanoparticles makes it high bioavailability in the intestinal mucosa [56]. The Ca citrate and Ca carbonate used in the nano to test bioavailability differences by measuring bone density in the lab animals. Administered mice by calcium nano compounds have bone dinner more than administered mice by normal calcium and controls [57].

2.4.2. Biocides

Nanoparticles work as an alternative to antibiotics and prevent pathogens from getting into the animal body. Resistant bacteria emerge from the unregulated use of antibiotics. In agriculture, Prophylactic antibiotic use is a method to prevent the growing problem [58]. Limiting and few used antibiotics is essential to find alternative substances because of the increase in animal production [59]. Elements nanoparticles have positive charges on the bacterial membranes, leading to leakage and bacterial lysis [60]. Kim *et al*., [48] found silver NPS can reduce hemorrhagic growth in intestine inflammation caused by E. coli and yeast isolated from mastitis in cows. Silver is used in dentistry to prevent dental inflammation. positively charged nanoparticles causes reduce bacteria growth [61]. Qi *et al*., [62] examined the chitosan's effect against the bacterial pathogens and found that the bacteria's MIC was smaller than 0.25 μg/mL. Colles, *et, al*. [63] reported that the nanoparticles antimicrobial have significant effects on potential pathogens.

Copper is usually added to the foods to increase the growth and performance [64]. The Copper nanoparticles pass mucosa of the intestine by absorption. Gonzales-Eguia *et al*., [65] found copper NPS improve piglet growth by increasing fat digestion by increasing phospholipase A and lipase in the intestine compared with CuSO4. These piglets become more weight, and the metabolic rates become more. Also, copper nanoparticles positively affect the immune reactions, wherever it showed marked greater total globulin and superoxide dismutase levels. These results concluded that element nanoparticles have significant benefits as antimicrobial and immune stimulator.

Antibiotic-resistance bacteria are spread anywhere; the antibiotics don't affect them. Antibiotics nanoparticle significantly impact resistance bacteria and decrease the dosage of required antibiotics used in the treatment [66] (Kalita *et al*., 2016). Penicillin nanoparticles are effective on the β-lactam ring by binding with β-lactamase in *Staphylococcus aureus* [67]. Penicillin- nanoparticles were tested and showed penicillin- nanoparticle could inhibit MRSA [67]. There was no evidence of the toxicity of antibiotics nanoparticles when it used systemic or topical application in mice [68]. Using tetracycline-chitosan nanoparticles causes a decrease in the bacterial growth of tetracycline-resistant *Escherichia coli* [69].

Antibiotics nanoparticles were targeted gram-negative bacteria in the food, particularly the lipopolysaccharide and endotoxin. Nanotechnology applications are critical in preventing and killing all the pathogens that live in the food; therefore, scientific society uses nanotechnology. Using nanoparticles in the feed not only kills the pathogens; the hydrogels can prevent the growth of the pathogens. The hydrogels used by covering the surfaces to avoid germ adhesion can also bind with viruses [70].

Using the cationic polymers showed toxicity was depending on the polycation type and the polymer molar mass. The unquaternized PDMAEMA can induce hemolysis when administered to the mice. unquaternized PDMAEMA use as a biocide for external purposes only [71].

2.4.3. Meat and egg quality

The nanoparticles are used to enhance meat and egg quality wherever, Wang, and Xu [72] found chromium nanoparticles is very beneficial for pigs production in feed, wherever it causes an increase in muscle mass. Similar effects found in the pigs that fed chitosan nanoparticle [73]. These chromium-chitosan nanoparticles cause an increase in lipase activity in adipose tissue and result in a decrease in the fatty acid and stimuli the immune response [74].

Also, it is noticed that the chromium level was increased in tissues such as the longissimus muscle. Some nanoparticles such as copper and silver were found in the blood-brain barrier [62].

If the nanomaterials were given ti the animals with water or food, they would increase the quality of the products. Chromium nanoparticles have great benefits in poultry feeding and positively affect muscle mass and decrease cholesterol level [75].

Using nanoparticles improve meat quality in the broilers. Conversely but, if the chromium nanoparticles were given to layers, it doesn't cause any marked improvement in body weight [76].

But, Chauke N, Siebrits [77] found that egg quality doesn't improve due to using chromium nanoparticles. In the liver, the nanoparticles are accumulated in the treated experimental. In coccidiosis cases, replacing the antibiotic with silver NPS in water showed improvement of the meat quality [78].

2.4.4. Milk

Mastitis is common in dairy cows caused by several bacterial agents and could use antibiotics to treat. Tilmicosin is a common drug in the treatment of the mastitis but it has side-effects, particularly in the high concentration [79] (Han *et al*., 2009). There are several tries to production tilmicosin NPS with castor oil-solid was, the trials found that time of the half-life of the tilmicosin was five hours in mice, and tilmicosin nanoparticles were 8 days [34].

Treatment by the nanoparticles has the benefit of minimizing the amount of milk wasted. Nanotechnology help to make that quality of milk is safe for human. Han *et al*., [79] used nanoparticle antibody as anti-*S. aureus*, gold nanoparticles, and magnetic nanoparticles to provide a 40 min colourimetric test for the presence of *S. aureus* in milk. Wang *et al*., [80] used similar polyclonal antibodies with gold nanoparticle immunochromatographic to diagnose the toxins in cow milk by using the carcinogenic aflatoxin M1.

Many studies focus on removing harmful components from cow milk; there is some nanoparticle in the milk. Lee et al., [80] used nanoparticle powder oyster with milk and increased the amount of calcium from (100) to (120) mg/mL. Providing the milk with Ca from nanoparticle oyster shell has excellent benefits.

2.5. Treatment of the veterinary diseases

Nanomedicine has many functions, such as diagnostics and therapeutics. Elements nanoparticles are functional as diagnostic tools in biological and medicine research, particularly in drugs and cell research. Magnetic elements nanoparticles such as iron oxide could get inside the cell and can be imaged at a high level using (MRI) [81].

Nanoparticles could be used for fluorescing by light stimulation [82]. Diagnostic nanoparticles have made in molecular technologies to make biological testing. Small volumes of reagents and analytic are produced little waste. Many products are present in the market used for diagnostic aims [82].

Examination of the drug delivery estimated using fluorescent nano-carriers such as light activation, fluorescent nanoglucose- and nanosucrose could be used to determine the bound chemotherapies [82].

The carbohydrate nanoparticles were used in diagnosing lung carcinoma cell in the human [82]. It binding with methotrexate and conjugate nanoparticles, the cytotoxicity treated with methotrexate. The drugs delivery with a nanoparticle used for tracking the drugs by using the light. Carrier nanoparticle could be activated by two-photon- the 3D spatial image of the tissue dimensions [83]). The chemotherapies are also used in a high dose that reduces side effects by increasing accuracy targeting to target sites [84].

The nanotubes could be used in L-lactide's pharmaceutical application [85]. If the enantiomers come together, they interact together, delivering caught materials all the while. There is no necessity for outer upgrades for drug discharge in some light-actuated nanoparticles, just that the two nanotubes interface. Other nanostructured particles can act naturally stacking like egg whites dextran nanoparticles with hydrophobic medications [86].

Albumin of the cow serum mixed with dextran then could use in the medicine by electrostatic and hydrophobic interactions [86].

2.6. Reproduction

Animal production depended on animal's slaughter. The livestock is the produce from individuals who have highly ranked phenotypes and genotypes. The reproductive abilities of breeders provide high value. Most of the nanoparticles have enhancement effects on infertility and spermatozoa. Artificial insemination is methods used for animals that have

pure race used for animal production. These animals choose genetic characters. Artificial insemination is enhanced by integrating nano-methods such as nano purification, gametes, non-invasive bioimaging, and protectants [87].

To enhance the effectiveness of manual semen injection, domesticated animals gamete science and conceptive impediments to treatment should initially be clarified. As of late, quantum specks have been investigated as an examination strategy to improve comprehension of mammalian spermatozoon and oocyte development and their associations in a physiological setting. This self-enlightening, inorganic nanoparticles are important to the field of theriogenology as they are biocompatible, photograph stable, and have a more considerable sign force than natural fluorescent atoms recently used to picture gametes and other cell types in vivo [88].

Long *et al*., [87] have exhibited the constant following capacity of bioluminescent reverberation energy move formed quantum speck nanoparticles in vitro, in situ, and ex vivo are utilizing pig male gametes. Quantum specks can give focused on or non-focused on imaging as a component of their size produced frequencies and formation prospects.

This designed nano molecule gives another intend to imagine the sub-atomic and cell occasions during preparation, along these lines to fluorescent proteins, however at more noteworthy tissue profundities [89]. The signal strength of quantum dabs are portion needy, and a higher focus might be needed for in vivo imaging on more giant creatures. Subsequently, quantum specks' organization ought to be added advanced for biocompatibility as a large number of the current ones incorporate substantial metals, like cadmium and lead, which might be cytotoxic at significant levels (Hasuwa *et al*., 2010). In any case, if quantum spot focuses and surface sciences are painstakingly chosen, cytotoxicity might be diminished or dispensed with Lin *et al*., [90].

Nanopurification of semen can be used to detach hurt sperm from safe, strong sperm. One procedure is to cover alluring nanoparticles with antibodies against ubiquitin, a surface marker of helpless sperm, for a protein-based ejection framework [91]. A lectin-based philosophy features alluring nanoparticles covered with lectins that difficult situation glycan uncovered outside of the sperm through acrosomal hurt [92]. Nanopurified bull spermatozoa (*Bos taurus*) achieved start rates identical to those of unpurified semen at a huge segment of the concentration with no negative impacts declared for inseminated cows or calves [91].

Cryopreservation of sperm can be improved by going to nano-protectant added substances in extenders. Used to weaken sperm, extenders are buffering specialists and furnish sperm with supplements needed for delayed capacity. They serve to secure and contain anti-microbials, to keep bacterial development from influencing sperm quality and tainting inseminated females [93].

Antimicrobial nanoparticles may serve to supplant extender anti-infection agents later on as certain anti-toxins have been appeared to restrain sperm motility and feasibility in a portion subordinate way. Nanoparticles may likewise encourage the expansion of standard items in extenders to build sperm motility. Examination bunches have revealed that the addition of nectar, sugarcane juice, tomato juice, and pineapple juice can expand the survivability of sperm put away at room temperature [94]. While nanoparticles were not associated with those investigations, it is fascinating to know how sperm quality would be affected if every item's helpful gatherings were conveyed through nanoparticle. As sperm can be delivered universally over several days, extenders with a higher limit concerning protecting examples going through freeze-defrost cycles would be gainful [95].

Further headways in regenerative biotechnology might be conceivable with the more important incorporation of nanoparticles in atomic science procedures. Sperm-interceded quality exchange is one such methodology where mesoporous silica nanoparticles can be stacked with nucleic acids and proteins [96].

These nanoparticles can frame a solid relationship with spermatozoa *in vitro* and don't have any modest impacts on sperm capacity or quality. Transfections with polymeric nanoparticles, like PDMAEMA, chitosan, and polyethyleneimine, have been accounted for to be beneficial over conventional viral methodologies gave low convergences of polymers are utilized [97]. The nanopolymer's sub-atomic load has an incredible impact on transfection viability and harmfulness; for example, the ideal atomic load for transfection with PDMAEMA has been resolved to be 60 kDa [97].

With proceeded with investigation and refinement, nanoparticles could assume a considerable part in creature propagation. Nonetheless, it ought to be noticed that some nanoparticles are spermatozoic, which may have genuine outcomes if reproducer proliferation is influenced. Zinc oxide and titanium oxide nanoparticles are two models that decrease in vitro sperm practicality in a portion and time-subordinate way by film debilitating and DNA fracture [98]. Barkhordari *et al*., [99] brooded human sperm with zinc oxide nanoparticles and tracked down that a grouping of 500

μg/mL would altogether build cell demise after 45 min. In comparison, a centralization of 100 μg/mL would fundamentally expand cell passing after 180 min.

Some investigations discovered wild ox sperm brooded in titanium oxide nanoparticles would lessen suitability. Titanium oxide has a job in expanding sperm creation. The nanoparticles likewise have extraordinary advantages in creature creation, veterinary medication [98].

3. Conclusion

Many nanoparticles applications were used commonly in animal production, diagnosis and treatment of the diseases; this review focuses the light on the introduction of the nanoparticle and future opportunities of the nanoparticles. There are several types of nanoparticles present in the market and produced new kinds in the last years. Nanotechnology plays a vital role in veterinary medicine and animal production in reproductive aspects, treatment, mild manufacturer, antibiotics, and reproduction.

In this paper, we reviewed different types of nanoparticles and their classification; besides, we reviewed the role of nanoparticle antimicrobials, nanoparticle vaccine, and nanoparticle adjuvant used in Veterinary Medicine. Our investigation will be proposed to build the adequacy of the chose anti-microbials against pathogenic strains of microscopic organisms, defeat the antimicrobial opposition, decline the harmfulness and improve the chosen bioavailability anti-infection.

Recommendation

Our study recommended as following:

- The importance of using and applying nanoparticle applications in therapeutic drugs such as antibiotics.
- Applying the nanoparticle applications and develop the diagnostic methods for the early diagnosis of the diseases.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declared that there is no conflict of interest

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