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Role of Nanotechnology in Animal Nutrition, Health and Reproduction

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Abstract

Nanotechnology is considered the most exponential technology in the veterinary sciences, especially animal breeding. It has also worked wonders in providing good habitual conditions and a properly livable environment for animals supported by good hygiene and proper maintenance of animal feed. The achievements of nanotechnology in every field are surprisingly amazing but its lead in the field of livestock is pre-eminent. Nanotechnology is facilitating veterinary science by aiding in the diagnosis and therapeutic purposes. The scope of nanotechnology is not just limited to better and increased animal reproduction and breeding, but it also has made its way to animal nutrition, therapeutics, diagnosis, and animal hygiene. Different nanoparticles with magnetic properties are useful in diagnostics along with other techniques like magnetic resonance imaging (MRI). In medicine, nanoparticles act as carriers for different drugs and growth promoters. The antimicrobial properties of various nanoparticles make them more significant for both animal and public health. Nanotechnology as an alternative to antibiotics has cast a good reflection on the sector of public health. In this review, we discussed the advantageous nature and significance of nanomaterials in contrast to nanoparticles. The paper also entitles the application and exquisite performance of nanotechnology in veterinary sciences.

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Introduction

Nanotechnology is an emerging field in today's era. Simply it is defined as working with small things. But in detail it is a highly advanced area of trace backing and investigation of things governed by a systematic way of manipulation, study, analyzing, tracking and using physical means for the study of a subject [1]. It deals with the technology, research, and development at the atomic, subatomic, and molecular levels that are mainly in the range of 1-100 nanometers. The concept of nanotechnology was first given by a scientist named Richard Fehmarn and the specific term nanotechnology was termed by Tokyo professor Norio Taniguchi. Nanotechnology has a widespread canvas of applications in different sectors that include the medicine and drug delivery, energy sector, development of quantum computers, reactivity, and strength of material [1]. Nanotechnology has many branches under its umbrella that are nanoengineering green nanotechnology, wet nanotechnology, and many more yet to be discovered. It has its use in many places like carbon nanotubes, thin nanofilms, nanoscale transistors, drug delivery techniques by using dendrimers, water filtration techniques, etc. [2].

A very important advantage of nanotechnology is related to biological systems and in it the ability to manipulate the size of resulting particles and devices. The small size of the nanoscale particles allows them to interact easily with the biomolecules on the surface of the cell and within the cell. Although we are having a general sense of this, the technological base in nanotechnology is created sufficiently to enable biologists to make the ready and easy use of their instruments, tools, and materials. The agricultural producers and manufacturers of food can get a very long-term benefit from nanotechnology. It is best explained and understood as a conceptual and logical approach to the design of intricate macroscopic structures by using nanometer-scale building blocks [3]. Nanotechnology plays a significant role in animal sciences in different ways. Biocides are very crucial to minimize the risk of antimicrobial resistance by replacing the overuse of antibiotics. This can eliminate the threat of drug residues in animal by-products that are prepared for human consumption. Nanotechnology has also changed nutrient bioavailability by making it more profitable for animals. Nanostructure particles have made veterinary medicine more advanced by playing a key role in diagnostics and therapeutic techniques.

Nanoparticles have a wide range of applications in animal production, and this analysis aims to highlight some of these whiles also identifying possible future applications. Nanoparticles are currently on the market, and as technology progresses, their characteristics will be carefully tuned for a larger range of uses. Nanotechnology in animal production is still in its early stages, but promising results from feeding, biocidal, remedial, and reproductive studies are prompting more research [4]. Despite their minute volume, nanoparticles hold extraordinary features and hence prove themselves to be the future of numerous fields. In the division of veterinary sciences, the use of nanotechnology is increasing day by day. As veterinarians, we must raise awareness and enlighten the way towards the advancement of technologies and increase their efficacy while keeping the cost-benefit ratio and feasibility in mind. The use of nanotechnology can further be utilized and explored by our fellow scientists and students. The following research article might help the aspirants to navigate the north of their studies.

Nanotechnology and its types

Nanotechnology is the upcoming and blooming field of the 21st century. In nanotechnology, we aim to take the maximum benefit from the four kinds of effects, first is the usage of new biological, chemical, and physical properties that are caused by size scaling. In these techniques, the effects of quantum become more organized for the structures under 50 nm. Second is the usage of new phenomena to do the size reduction up to the point where the interaction and communication between the physical, chemical and biological phenomena become comparable to the small and nano size of the particle, crystal, and respective microstructure grain. The third is the making of new atomic, macromolecular, and molecular structures by using various routes like chemistry, nanofabrication, and manipulation. Fourth is the important increase in the degree of complexity and speed of processes in a specialized system. Nanotechnology is also applied to biological systems [2, 3]. Nanoparticles are synthesized by different methods but there are mainly 2 ways for it, the bottom-up approach and the top-down approach. The top-down synthesis is a method that

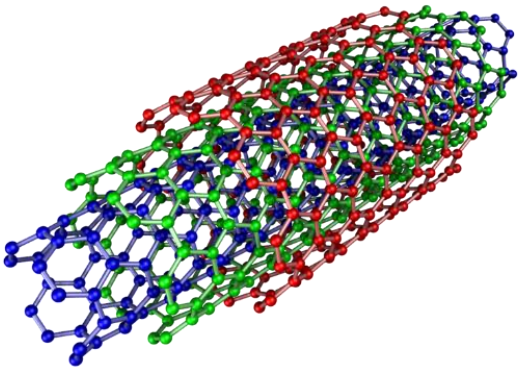

Fig. 1 Multi-walled carbon nanotube multi-walled carbon nanotubes. Wikimedia Commons. Available at: https://commons.wikimedia.org/wiki/Category:Multi-walled_carbon_nanotubes

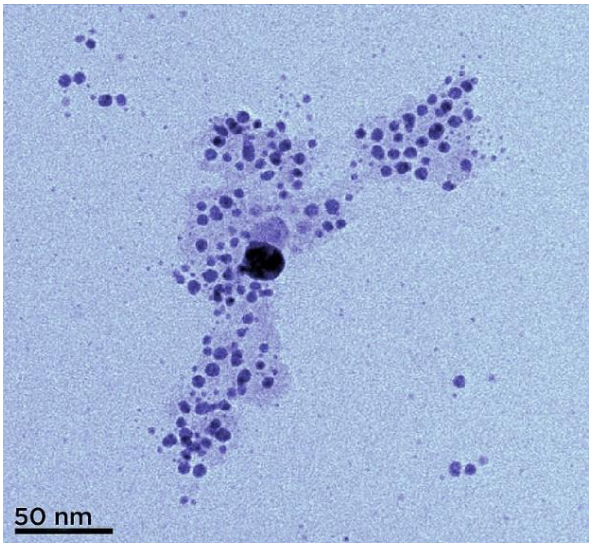

Fig. 2 Electron micrograph of silver nanoparticles. Wikimedia Commons. Available at: https://commons.wikimedia.org/wiki/File:TEM;_Silver_Nanoparticles_(5978792602).jpg

uses a destructive approach. In it, we start from a larger molecule, which is decomposed into smaller units, and these smaller units are further converted into nanoparticles. The next way for the synthesis of nanoparticles is bottom-up synthesis. It is a reverse process of a top-down approach. In this, the nanoparticles are formed from the simpler substances, and this approach is also called as a building up approach [3]. This field is the latest and newly emerging field of the current era. It was initiated by a Noble laureate Richard P. Feyn. Nanoparticles are not simple particles themselves. They consist of 3 layers, first is the surface layer, which is communicated with a lot of various small molecules, ions of metal, surfactants, and polymers. The second layer is the shell layer, the layer that is different from the core in its all properties of a chemical nature. The 3rd layer is the core layer, which is the very essential part of the nanoparticles, and mainly refers to the nanoparticles [5]. Carbon nanotubes are distinctive because of their size, shape and physical properties and play a significant role in drug delivery and diagnostics. Metallic nanoparticles also play the same role by carrying drugs to targeted cancerous sites and performing the functions of biosensors as well. These include silver, gold, and other metallic nanoparticles. Carbon nanotubes and nanowires are significant for detecting mutations in DNA and vary in diameter (0.5-3 nm) and length (20-1000 nm). The nanotubes can be useful to find disease proteins. Dendrimers are used in diagnostic imaging and controlled drug release due to their small sizes. The size of nanocrystals varies from 2.0 to 9.5 nm, and they enhance the quality of less soluble active ingredients. A quantum dot is also a type of nanocrystal. Nano-shells are applicable in imaging tumor growth [6].

Role of nanotechnology in animal nutrition

Organic nanoparticles include plant-derived feed additives, fat, protein, and sugar molecules. These are also known as nanocapsules when they act as vehicles and increase nutrient bioavailability. This is achieved by changing feed functionality. They don't alter the taste and appearance of the feed. The location of a nutrient in the body can also be found by the use of this technology. Nutrient bioavailability can be measured in this way [7]. Casein phosphoproteins allow transportation of various nutrients from mother to young by assembling them around them. Nanoparticles boost the growth rates of livestock by enhancing nutrient cargo bioavailability and providing extra support for weanlings [4]. Encapsulating materials with nanoparticles increase their surface area concerning volume and decreases pore size that results in improved solubility and diffusion. They can easily enter the cell because of their small size [8]. Improvement in intestinal health, blood lipid profiles, and increased efficiency of diet are the benefits of dietary fibers. Cellulose nanofibers can be used as their replacement. They are reactive and resistant to gastric juices they regulate microbes

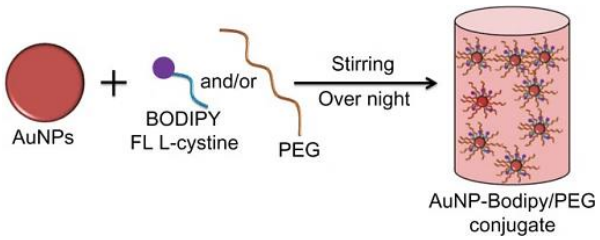

Fig. 3 Gold nanoparticles conjugation for targeted drug delivery. Wikimedia Commons. Available at: https://commons.wikimedia.org/wiki/Category

of the digestive tract. They help in the absorption of aflatoxins and mycotoxins. They inhibit the growth of bacteria and fungi. Excess fat accumulation in the blood can also be prevented by using Nano cellulose [9]. Nano-emulsified oil forms decreased transformation rate of polyunsaturated fatty acids to saturated fatty acids in a bio hydration environment. It helps in animal nutrition because polyunsaturated fatty acids have toxic effects on animal rumen [10, 11]. Nanoparticles stay inside the GIT for a longer period, which increases nutrient absorption from the GIT [12]. Minerals in the form of nanoparticles decrease intestinal mineral antagonism as a result, environmental pollution and excretion are reduced [13]. Copper is a trace mineral. Copper nanoparticles enhance immunity in birds, act as growth promoters and increase nutrient digestibility [14]. Decreasing the level of methane production is necessary for reducing greenhouse gases and improving feed conversion efficiency [15]. Zinc oxide nanoparticles decrease the level of methanogenic archaea, which produce CH_4 from CO_2. The length, width, and surface area of villi increase by the intake of zinc oxide nanoparticles [16]. The inclusion of zinc nanoparticles in the animal diet decreases the mortality rate and increases the live weight of broilers. This will have a positive effect on the broiler's health [17]. Zinc oxide nanoparticles increase chymotrypsin activity in the pancreas. Protease and chymotrypsin activity is increased in the small intestine. This increases nutrient bioavailability in animals [18]. Selenium deficiency affects the functioning of the immune system, liver necrosis, muscular dystrophy, thyroid dysfunction, etc. Biogenic selenium nanoparticles are manufactured to increase selenium bioavailability. This plays a positive role in animal nourishment [19]. Ferrous oxide and copper nanoparticles improve microbial growth and manage equine gut health. Calcium, zinc, and silver nanoparticles are used to prevent periodontal disease in horses [20]. Silver nanoparticles and hydroxyproline help to form stronger collagen fibers. It increases the blood vessel size, cartilage collagen fiber lattice size, and bundle thickness [21]. Taurine enhances cellular function and muscle overuse affects taurine levels due to the production of reactive oxygen species [22]. Taurine depletion can be overcome by the intake of taurine nanoparticles, which increase muscle organization [23].

Role of nanotechnology in diagnosis, detection and treatment

Nanotechnology has several advantages in medical diagnostics. It made diagnosis easy and accurate where small samples and less time are required [4]. Metallic nanoparticles with magnetic properties are used for diagnostic purposes. The specific particles spread in the body can be seen by magnetic resonance imaging (MRI). Iron oxide nanoparticles (NPs) are commonly used as magnetic resonance (MR) contrast agents when high intracellular levels are necessary to represent signal variations [24]. Many concerns about drug delivery systems for cancer therapy exclusively nonspecific drug distribution have been resolved by carbon nanoparticle CNPs. The anti-cancer medication methotrexate was then conjugated to the functioned particles, which are then employed as fluorescent nano-carriers [25]. Gold nanoparticles (GNPs) in conjugation with amoxicillin (β-lactam antibiotic) show many positive aspects of nanotechnology. This GNP and amoxicillin conjugate acts more effectively against G-positive and G-negative type bacteria. It also overcomes the threat of antibiotic resistance by keeping control over *β*-lactamase secreted by *Staphylococcus aureus*, which is resistant to methicillin [26]. Gold nanoparticles (AuNPs) carry the drugs without causing toxicity where the gold core is responsible for stability and the monolayer tunes the surface properties [27]. Gold nanoparticles (AuNPs) can also carry proteins and successful conjugation with Albumin protein enhances the accuracy to target specific tissues or organs in the body, thus highlighting the importance of nanomedicine and nano pharmacology. AuNPs can be stabilized by different macromolecules such as chitosan, a non-toxic biopolymer. Au NPs had been taken into consideration because of the most exciting nanomaterial due to their precise optical,

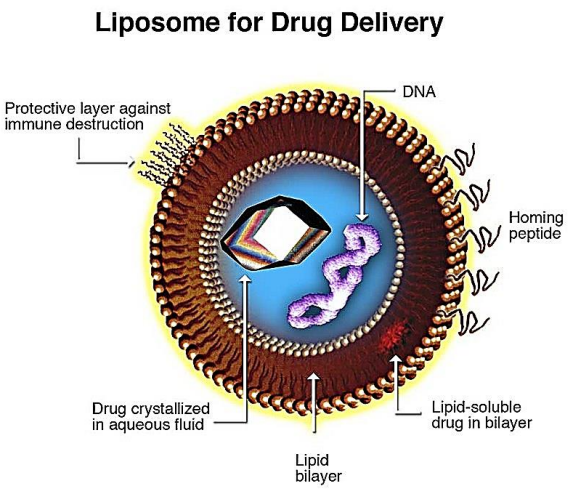

Fig. 4 liposome for drug delivery nanocarriers. Wikipedia Commons. Available at: https://en.wikipedia.org/wiki/Nanocarriers

electronic, sensing, and biochemical properties. AuNPs had been carried out for scientific imaging, drug delivery, and tumor remedy in the early detection, diagnosis, and remedy for diseases [28]. In veterinary medicine, different antibiotics with magnetic markers are significant to human health and food safety as they facilitate in the removal of *Salmonella typhi* from the skin of the chicken. In addition to this, some Nano detectors improve farm security by detecting foot and mouth virus (FMV). In pigs, growth hormones are carried by using nanoparticles to enhance the production and in sheep and other livestock animals, NPs are used as a vaccine carrier [29]. The antifungal actions of a few metallic nanoparticles (silver oxide, titanium dioxide) have been reported. Zinc nanoparticles (ZnNPs) showed efficient results in the case of buffalo dermatological conditions caused by certain agents and antimicrobial activity against pathogens that can also cause mastitis. In addition to antimicrobial activities, silver nanoparticles also possess anti-inflammatory and anti-cancerous features. Different nanosensors show their efficiency in detecting and diagnosing techniques in veterinary medicine such as iron oxide nanosensors coated with silica are helpful to detect *Mycobacterium avium* paratuberculosis and *Escherichia coli* O157:H7. Recently glucose and sucrose-derived nanostructures acted as nanocarriers by taking anti-cancerous agents to the lungs to treat carcinoma. In the same manner, iron oxide NPs carry the drugs to target cancerous tissue. Nanoparticles having platinum may also act as a good anti-cancerous agent [30]. For transdermal issues, mostly micellar nanoparticles (MNPs) are used. In racing, horses micellized vit E supplementation control the oxidative status and this strategy improves the oxidative situation in sows as well. MNPs improve the bioavailability of tilmicosin in broiler chickens. Synthetic polymeric nanoparticles can be used as a carrier to target diseases such as toxoplasmosis, HIV, TB, *Brucella abortus* and anthrax. In veterinary medicine, dendrimers are effective to carry drugs for cancer treatment. Metallic NPs are suitable for bio-imaging and tumor therapy. In veterinary dermatological issues, some ointments are formulated by using nanotechnology. Gold NPs are useful to detect infectious bursal disease (IBD), FMD virus and Bluetongue virus. ZnNPs are used to treat udder infections caused by *E. coli*. The use of graphite NPs in veterinary sciences is limited [31]. Liposomes are 100 to 2.5 mm synthetic vesicles that carry the drug in an aqueous phase encapsulated by a lipid bilayer. They mainly carry different cosmetic and pharmaceutical ingredients to different targeted sites. This mode of drug delivery has certain flaws such as burst release of carrying agent and instability [31]. Liposome-supported drug-carrying was successfully done in dogs and various anti-parasitic vaccines were trialed in livestock which was based on liposomes. Mastitis in cattle was cured by gentamycin enclosed in liposomes and

Table 1 Nano-size drug delivery system [33].

Types	Sizes	Characteristics	Sub-types	Examples
Nano-emulsions	20-200 nm	Emulsions including two immiscible liquids		
Nanoparticles	10 nm-2.5 µm	Made of lipid, polymers, metal	Nanocapsules Nanospheres	Lipidics, solid lipidics, polymerics Polymeric or Metallic
Liposomes	80 nm-100 µm	Vesicles of concentric lipid bilayers separated by aqueous compartments		

showed efficient results against diseases caused by multidrug-resisting pathogens [31]. By facilitating drug delivery of diminazene, nanotechnology proved to help treat trypanosomiasis [32].

Role of nanotechnology in animal reproduction

Nanoparticles are small but have phenomenal features. Nano applications in the field of animal sciences and reproduction have been proven diverse and effective. Modulating drugs' behavior and consequently, their biological effect is the principle of nanotechnology in animal reproduction. The reproductive capacity of an animal determines the future outcome and productivity of the animal. Nanotechnology is used in creating the male effect. It is the effect of male pheromones on the sexual activity of the female as it activates the female sex hormones. The nano delivery system of the pheromones can be made through nasal sprays as it is perceived by the olfactory receptors. It also aids in hormonal-based treatment as it can be used to mimic high molecular weight hormones, but being low molecular weight, it enhances the absorption of hormones, which it wouldn't otherwise [34]. Breeding management is a critical part of rearing farm animals. Nanotechnology has given a solution to this time-consuming problem in the form of nanotubes. Nanotubes can be placed intra-dermal, which shows a level of sex hormones. This helps in detecting estrus in animals as it measures the estradiol antibody [35]. Some metal nanoparticles have shown negative effects upon usage. Improper use of such nanoparticles leads to toxicity. Toxicity is a negative impact of the nanoparticle itself, but it can be used as a contraceptive as it produces sterility in animals, *e.g.*, the use of cadmium [36]. The use of nanoparticles seems to be a hope for improving pharmaceutical attributes. It increases the efficacy of the drug by crossing the blood-tissue barrier, increasing shelf life, increasing intestinal absorption and rapid onset with reduced side effects. Such improvement is based on the chemical structure of the compound. Some nanoparticles have antioxidant properties, which protect the sperm from reactive oxygen species, *e.g.*, cerium oxides can save oxygen and act as ROS and saves sperm functionality during cooling. It also seems to increase sperm motility in the ram. It is also used to increase the conception rate and improve progeny by detecting and removing defective spermatozoa. For example, ferrous oxide due to its magnetic properties can attach to the defective spermatozoa with the help of lectins or antibodies [37]. There are also some controversial impacts of nanoparticles. The use of zinc oxide showed a cytotoxic effect on testicular cells and their primary effect is on the process of maturation in spermatogenesis. Gold is also a widely used nanoparticle, but it also reduces sperm motility and morphology. ln order to increase the efficacy

Table 2 Use of nanoparticles in semen preservation and purification.

Nano products	Function	Positives	Species	References
Nano lecithin	Semen dilution Promotes cryosurvival	Minimize apoptosis Increase motility Enhance sperm membrane functionality	Buck	[40]
Zinc nano-complex	Used as a supplement in semen extender	Promotes activity of mitochondria Lowers lipid peroxidation. Improves function of the sperm plasma membrane.	Bull	[41]
Cerium oxide nanoparticles	Supplements semen extender	Promotes the plasma membrane integrity Protects DNA of spermatozoa Improve motility of sperm	Rams	[42]
Nanoparticles of selenium	Act as antioxidants	Improve sperm quality after thawing Minimize apoptosis Lowers sperm damage Reduce lipid peroxidation	Bull	[43]
Nano water (NW)	Replaced deionized water (DW) as an extender medium	High diffusivity Low viscosity Low density Have antimicrobial properties.	Rams	[44]
Fe_3O_4 Nanoparticles	Purification of fresh or extended semen	An inexpensive way to purify semen	Bull Pig	[45] [46]

of technologies like artificial insemination, nanoparticles are proved to be effective, *e.g.*, quantum dots are photostable and biocompatible nanoparticles that help to study and visualize the cellular events during fertilization at the deeper tissue level [38]. Cycle management of females greatly depends upon exogenous hormones. But administering such hormones creates concerns like residual hormones in the meat leading to public health concerns. The efficacy of the exogenous hormones can be increased by introducing the nano hormones delivery system, where there will be fewer chances of side effects and improved fertility rate with reduced doses. The problems like intrauterine growth restriction can be avoided using nanoparticles, as they can be used as a targeted delivery system to the placenta. This approach seems to be effective in dealing with pregnancy complications as it can directly affect the targeted receptors. The future of nanotechnology in the field of animal reproduction is bright as it has proven itself to be cost-effective, efficient and safe for environmental and public health also. The success of nanotechnology in this field can be achieved by further research and investigation before its application [39].

Conclusions

The review paper has lime lighted the use of nanoparticles in various ways for animal production and what prospective opportunities can be availed. Nanomaterials are getting so much fame and have become the first choice because of their cost-effectiveness and low rate of risk to the users. Moreover, there are many future incentives attached to them as they can surely upgrade veterinary science. They are not just cost-effective but time savers. The nanomaterials showed that antibiotics could not do for a long time, but they can do in a few minutes like the elimination of bacterial infection. There are many uses of nanoparticles in animal production and this review serves to highlight these uses and to identify potential opportunities for future applications. Nanotechnology presents a great deal of versatility nanomaterials assisting veterinary and medical sciences in the field of diagnosis, treatment, medication, enhanced reproduction, and nutrition as discussed above. Nanomaterials offer a vast number of breakthroughs like cost-effectiveness, lower risk to consumers, and a faster approach that will further advance the clinical aspect of veterinary sciences in the future.

Conflict of interest

The authors declare no conflict of interest.

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