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Review Article

Role of Nanoparticles in Animal and Poultry Nutrition: Modes of Action and Applications in Formulating Feed Additives and Food Processing

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Abstract

Nanotechnology is the promising and emerging technology that has tremendous potential to revolutionize agriculture and livestock sectors globally. The concept of nanotechnology was introduced to alter the particle size to few nano meters. The synthesis of nano particles with reducing agents leads to change in physical and chemical characteristics of the molecules/element under study. These nanoparticles have the ability to transport various components under various environmental conditions. Nanoparticles are now-a-days widely used in various sectors, nutrition, therapy, targeted drug delivery, preparations of vaccines and various purifications processes in textile industries, etc. Earlier, the synthesis of these nanoparticles was by chemical method, which leads to excretion of chemicals into the environment. Recently, the preparation of nanoparticles from plant sources-referred as green synthesis is gaining importance. As this process involves plant extracts which consists of sugars, polyphenols, terpenoids, proteins, etc. These phytochemicals acts as a reducing agent to maintain the minerals in reduced state during the synthesis process, their excretory products are highly biodegradable and hence no adverse effect to the environment. In animal nutrition, the nanotechnology is mainly used in preparation of nano-minerals especially trace minerals, whose bioavailability is low. In addition, minerals as nanoparticles reduce intestinal mineral antagonism, thereby reducing excretion and environmental pollution. Studies have suggested that feeding of nanoparticles improved the digestive efficiency, immunity and performance in livestock and poultry. The present review covers various aspects of nanotechnology including production of nanoparticles, their role in animal nutrition and their future prospective.

Key words: Animal nutrition, chemical synthesis, green synthesis, nanoparticles, nanominerals, poultry, production

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INTRODUCTION

The field of nanotechnology brings wide variety to biological research, therapeutic as well as addresses environmental concerns. Nanotechnology is a promising and emerging technology that has tremendous potential to revolutionize agriculture and livestock sector in India as well as all over the globally. Nano is a Latin word meaning 'Dwarf' and the concept that seeded nanotechnology was first explained in 1959 by renowned physicist Richard Feynman. National Nanotechnology Initiative in 2013, USA, elucidated nanotechnology as the understanding and control of matter at the nano-scale dimensions of approximately between 1 and 100 nanometers, at which point unique phenomena enable novel applications. Nanotechnology, by its name it deals with the conversion of larger molecules to nanometer size[1,2]. The process of converting these larger molecules to tiny one causes changes in the innate physical and chemical nature of the base material. These changes includes, change in solubility, absorption, transport mechanism, excretion and importantly antagonisms. The mineral antagonism in the animal/livestock intestine or cellular level leads to mineral imbalance at absorption, transportation and excretion. As the technology engineers to nano level, their properties differ fundamentally and unpredictably compared to a larger scale. Such changes seem to be desirable in various fields such as nutrition, diagnostics, therapeutics, biotechnology, vaccine production, chemical industries etc. The resultant product of this technology has got special properties such as greater penetrability, reactivity, surface area and quantum properties which can be utilized in various scientific fields[3,4].

With regard to animals, its major applications is in administration of nutrients, supplements, probiotics and drugs, diagnosis and treatment of diseases, identity registry for individual animals and in use of hormonal immune-sensors in the management of reproduction. In animal/poultry feeding, the application of nanotechnology is mainly in the form of nano-minerals. This area is of importance as it increases the absorption of trace minerals by reducing the antagonistic effect among the bi-valent cations. This novel strategy can be exploited in livestock and poultry nutrition for efficient uptake of nutrients for better utilization of feedstuff and other supplements. Though the technology holds greater promises for better livestock and poultry production, studies are much limited. Research on nanoparticles upon health and environmental effects is yet another field of concern. This present review covers the types of nanomaterials, its preparation process and their effects of dietary inclusion on animal production system.

TYPES OF NANOMATERIALS

Based on their chemical properties, nanoparticles can be classified into inorganic, organic, emulsions, dispersions and nano-clays. The inorganic nano-particles include inorganic ingredients at nano level and are already approved for use in the feed, e.g., titanium dioxide, a feed colorant can be used in feed packaging process as a ultraviolet barrier. Their intervention in feed and packaging industry involves nano-clay platelets for feed packaging, minerals like silicon dioxide, calcium, magnesium and silver nanoparticles for water purification, antimicrobial packaging and feed storage[5,6.] Organic nano-particles include proteins, fat and sugar molecules. Organic nano-particles through alters feed functionality but can improve their nutritional value. Organic nanoparticles can encapsulate nutrients and transport via the gastrointestinal tract into the blood stream, these are referred to as nano capsules. Hence, with increased bioavailability these capsules are intended to deliver the nutrients without affecting the taste or the appearance. As such encapsulated nano-materials they are incorporated into feeds as micelles, liposomes and in feed packaging systems as biosensors, identification markers, shelf-life extenders and antimicrobials. The nano-emulsions, on the other hand can stabilize and deliver the active components by encapsulating the functional feed ingredients either in oil/water interface or in a continuous phase[7] (Table 1).

PREPARATION OF NANO-PARTICLES

The preparation of nanoparticles varies and depends on the purpose for which they are intended to be. The stability of the active component, toxicity, liberation profile should also be considered. Some methods for the preparation of nanoparticles are emulsion cross-linking, precipitation, spray-drying, emulsion-droplet coalescence, ionic gelationisation, reverse micellar and sieving method[8].

Green synthesis: The term green synthesis indicates that the preparation of a nano-material by exploiting the nanotechnology and plant biotechnology together. The plant extracts plays an important role in reduction of particle size in metal ions. The extracts containing various compounds are such as sugar, alkaloids, polyphenols, proteins, etc. These compounds in addition give stability to the metal ions[9] (Fig. 1). The nano particles synthesized by this method will be of different colors like gold, gray and yellow based on the source of plant material used.

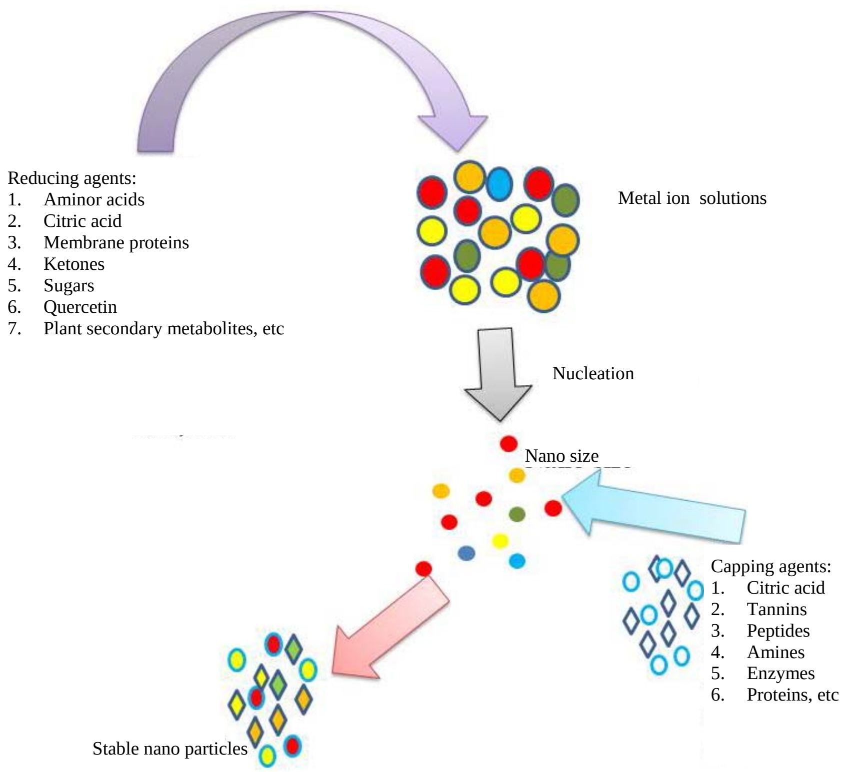

Fig. 1: Synthesis of nano-particles

Table 1: Types of nano-materials used in animal nutrition research

Categories	Examples	Applications
Nanoparticles		
Inorganic	Iron	Food/Feed supplement
	Silver	Food/Feed supplement antimicrobial agent used in feed/food
	Zinc	Food/Feed supplement, colorant
	Platinum	Food/Feed supplement
	Iridium	Food/Feed supplement
Organic	Liposomes	Encapsulation and targeted delivery of feed/food components
	Protein	Re-micelled calcium caseinate from dairy protein. Increased functionality (gelatinization, heat stability and other properties)
	Polymeric	Non-degradable: Polysterene Bio-degradable: Gelatin, Collagen
Nanoemulsions/dispersion		
Emulsions	Oil in water	Stabilisation of biologically active ingredients for delivery of active compounds: extended shelf-life; flavour release; low fat products
Dispersions	Calcium Carbonate	Increased solubility of calcium carbonate can be used at higher additional levels
Nanoclays	Clay composites	Used in packaging materials to extend shelf-life durability and thermal properties

Various researchers have used various plant sources to synthesis these nano-particles, they are as follows: Green nano gold and silver particles have been synthesized from various plant sources, geranium (*Pelargonium graveolens*)[10], leaf extracts of lemongrass (*Cymbopogon flexuosus*)[11], *Cinnamommum camphora*[12], neem (*Azadirachta indica*)[13], *Aloe vera*,[14] tamarind (*Tamarindus indica*)[15], *Abelmoschus esculentus*[16] and extracts of *Emblica officinalis* fruit[17], oat (*Avena sativa*)[18], alfalfa (*Medicago sativa*)[19] and soaked Bengal gram bean (*Cicer arietinum*)[20] and *Piper nigrum* Concoction[21]. The plants such as alfalfa (*Medicago sativa*)[22] and *Brassica juncea* were used for silver[23] and Ag-Au-Cu alloy nanoparticle synthesis. Manganese nanoparticles are synthesized as manganese acetate from lemon extract reducing agent with curcumin as stabilizing agent[24].

The synthesis of nano particles/minerals by this process has two striking advantages over the conventional/chemical synthesis method. Firstly, these nano sized particles possess more permeability through the capillary walls and thereby, they plays an important role in targeted drug delivery. Secondly, this process uses bio-degradable materials which rules out the possibility of environmental accumulation and pollution due to the chemicals[9].

MODES OF ACTION OF NANOPARTICLES

Chen *et al.*[25] specified the different mechanisms of action of nanoparticles as follows:

- Nanoparticles that tends to increase the surface area for better interaction with biological support
- Prolonged the compound residence time in gut
- Reduce the influence of intestinal clearance mechanisms
- Penetrate deep into tissues by fine capillaries
- Cross epithelial lining fenestration
- Enable cells for efficient uptake
- Effective delivery of functional compounds to target sites and thereby better bioavailability

The uptake of nanoparticles from the gastrointestinal tract (GIT) in many ways includes the ingestion and inhalation pathways, oral or smart delivery into GIT (Oral pathway). The absorption, distribution, metabolism and excretion of nanoparticles in the body relies on their physicochemical properties such as solubility, charge and size. The particle size of lesser than about 300 nm can reach the bloodstream, while particles that are smaller than 100 nm can get into various tissues and organs[26]. Through inhalation pathway the inhaled ultrafine particles can get a portal of entry into the central nerve system, bypassing the challenging obstacle of blood-brain barrier. But their reactivity with other substances can have consequences on health and the environment. Recently, bio-functionalized nanoparticles (BN) have got wide acceptance for treatment of enteric infection, as pathogen purging agents prior to transporting and processing[27]. In addition, it has been found that D-mannose can inhibit the bacterial attachment to intestinal cells[28]. Evidence through some preliminary works showed that BN accepted specific for the mannose receptor sites on the Campylobacter cells.

INTERVENTION OF NANOTECHNOLOGY IN ANIMAL AND POULTRY NUTRITION

The application of nanotechnology in animal feeding includes the use of different nanoparticles in the administration of medication, nutrients, probiotics, supplements and other substances (Fig. 2). Recently, feed additives such as trace minerals in the form of nanoparticles can be effectively used to fulfill the requirement of minerals in

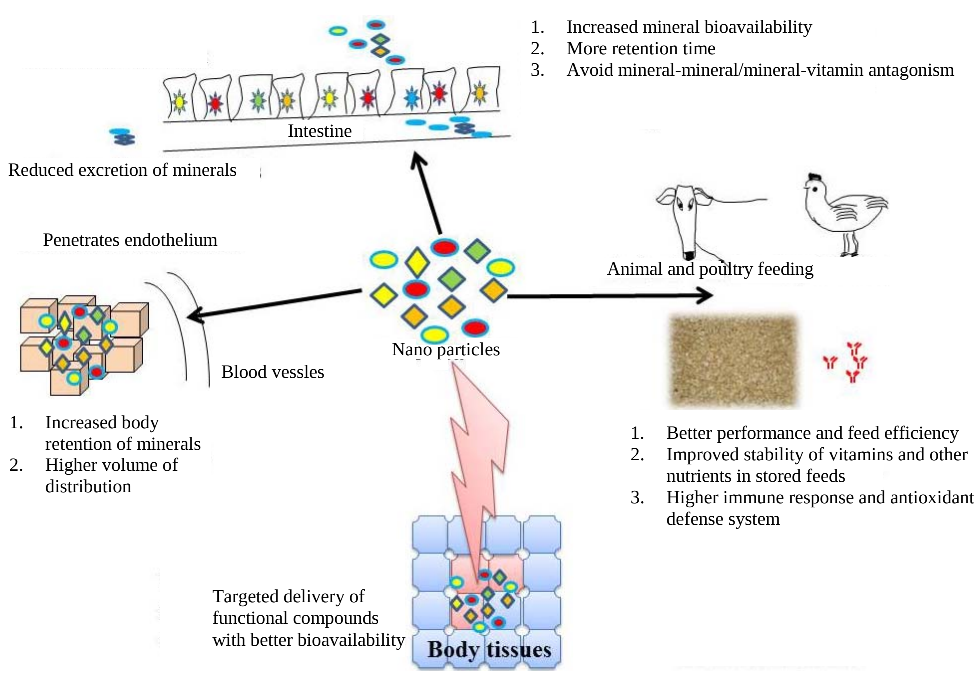

Fig. 2: Applications of nano-particles in animal feeding

the livestock and poultry feed. Such nano additives are expected to have the advantage of better bioavailability, small dose rate and stable interaction with other components. Because of their low dose usage, they can be used as an alternative for antibiotics as growth promoters, eliminate antibiotic residues in the animal products, reduce the environmental contamination and produce pollution-free animal products [26,29]. Nano-additives can also be incorporated in micelles or capsules of protein or another natural feed ingredient.

In sheep, the supplementation of Nano-Selenium at the rate of 3 ppm in basal diet significantly decreased the ruminal pH (range of 6.68-6.80) and ammonia concentration (range of 9.95-12.49 mg/100 mL) and increased total VFA concentration (range of 73.63-77.72 mM) linearly ($p<0.01$) and quadratically ($p<0.01$) with increasing nano-Se supplementation[30]. Similarly, the nutrient utilization and urinary excretion of purine derivatives were also significantly changed ($p<0.01$) by improving the nano-Se supplementation[31].

In another sheep trial, nano-Se had a positive effect against peroxidative damage in blood components when given at 1 mg kg^{-1} of feed[32]. Similarly in male goats, dietery supplementation of nano-Se at the rate of 0.3 ppm showed increase in the final body weight ($p<0.05$) and average daily growth. Whole blood, serum and tissue Se concentration, serum antioxidant enzymes activity were also increased by dietary nano- Selenium supplementation. With respect to the fertility in male goats, supplementation of 0.3 mg kg^{-1} of diet of nano-Se (60-80 nm) lead to favorable effects on testicular microstructure, testicular spermatozoa ultramicroscopic structure, testicular glutathione peroxides activity and semen quality[31].

Dietary supplementation of chromium (Cr) as chromium nanocomposite (CrNano) at the rate of 200 µg in finishing pigs significantly reduced serum levels of glucose, urea nitrogen, triglyceride, cholesterol and non-esterified fatty acid. In contrast, serum levels of total protein, high density lipoprotein and lipase activity were significantly increased. There was also an increase in serum insulin-like growth factor I and reduced serum insulin and cortisol levels significantly. In addition, supplemental CrNano resulted in higher level of immunoglobulins, Ig M and Ig G in plasma[33]. The CrNano also had appreciable effects on carcass characteristics, pork quality, skeletal muscle mass and increased tissue chromium concentration in selected muscle and organs[34]. In piglets, supplementation of nano copper (Cu) at the rate of 50 ppm produced significant improvements in growth performance. The fecal copper level was reduced and the Copper availability was significantly improved as compared to the conventional copper sulphate ($CuSO_4$) group. Also significant differences were observed in the improvement of the digestibility of crude fat and energy in pigs under nano Cu diet. Statistically significant improvements were observed in the IgG, γ-globulin and total globulin protein levels and in the SOD activity of the nanoCu group[35].

Supplementation of metallic silver nanoparticles of 20 and 40 ppm as antimicrobial and growth promoter during the transition phase (5-20 kg weight) of weaned piglets resulted in Coliform reduction in ileal contents. Besides, the concentration of the pathogen *Clostridium perfringens* or *Cl. histolyticum* group in the ileum was reduced with 20 ppm silver[36].

In broiler chicken, supplementation of 1.20 mg kg^{-1} Se (Nano-Se) showed a wider range between the optimal and toxic dietary levels of Nano-Se with efficient retention in the body compared to sodium selenite. Also in the same study, addition of nano-Se (60 nm) to the broiler diet showed an elevation in survival rate, average daily gain and feed to gain ratio with 0.15-1.20 mg kg^{-1} Se concentration[37]. In layer chicks, nano-Se of 0.3 mg kg^{-1} of dry diet was found to have better physiological effects[4].

A study on nano zinc showed that supplementation of 0.06 ppm in the basal diet of broiler birds showed improved immune status and bioavailability compared to inorganic zinc[38]. Moreover, different concentrations of ZnO-nano-particles also found to inhibit the growth of mycotoxic fungi (*A. flavus*, *A. ochraceus* and *A. niger*) and the respective mycotoxins (AFs, OA and Fs). Hence the method can be used for feed treatment to reduce the potential hazards of mycotoxicosis[39].

When broiler birds are fed with nano form of calcium phosphate by replacing upto 50% requirement of dicalcium phosphate, they showed a best feed conversion ratio (1.39 ± 0.02) and differed significantly from the control groups ($p<0.05$)[40].

Nanosilver as a microbicidal preparation reduced the number of Escherichia coli, Streptococcus bacteria, harmful Salmonella and total number of mesophilic bacteria in the litter[41]. Studies have also shown that nanosilver as feed additive had positive selective impact on the count of bacteria in poultry digestive tract. On supplementation of 20, 40 and 60 ppm feed, nano-silver caused dose dependent reduction in the weight of the lymphatic organs[42]. They observed lowest weight at 60 ppm feeding for 42 day of age. This reduction in weight correlated with the antimicrobial property of the Ag-NPs which might result in favorable proportion of non-pathogenic organisms than pathogenic ones in the gut.

Broiler diet enriched with silver nanoparticles had lowered the haemoglobin level, RBC and WBC counts[43]. A study of Andi *et al*.[44] had shown improvement in feed intake, weight gain and feed efficiency of broilers fed nanosilver nanoparticles because of the influence of ionic silver on intestinal harmful bacteria and improved gut health and consequently better nutrients absorption. Loghman *et al*.[1] studied the toxicity of nanosilver and noticed morphological and pathological changes in broiler liver. They concluded that higher levels of nanosilver (8 and 12 ppm) may induce severe lesions in broiler liver.

AS FEED ADDITIVES

Minute micelles (nanocapsules) serve as carriers for essential oils, flavor, antioxidant, coenzyme Q10, vitamins, minerals and phytochemicals with improved bioavailability[45]. Encapsulating the nanoparticles of active ingredients (e.g., polyphenols, minerals and micronutrients) prevent oxidative reactions and off-taste[46]. In food industry, liposomal nanovesicles are employed for the encapsulation and release of nutrients, enzymes, flavors and antimicrobial compounds[47]. Similarly nano-additives can also be capsulated by proteins or other ingredients. Micelles are small spheres of oil coated with a thin layer of bipolar molecules of which one end is soluble in fat and the other in water. They can be suspended in water or contrarily water can be encapsulated in micelles and suspended in oil such as nanocapsules containing omega 3 fish oil with an unpleasant taste[5].

FEED PROCESSING

The nanoscale particles offer a very larger surface area because of their ultrafine size and hence function very efficiently than the macroscale structures. This can lead to the use of micro and nano-sieves with the pore size of micro and nanometer range. Their use in encapsulating the valuable or functional feed ingredients prevents their loss during feed processing. Nanotechnology has started getting momentum in the advancement of functional feed which deliver the nutrients effectively as per the body's need[5]. Research works are in progress for development of "On demand" feeds which can remain latent in the body and deliver nutrients when the need arise. The crucial element in the technology is the inclusion of nanocapsules in the feed to deliver nutrients. Another progress is the addition of nanoparticles to the feed that enables better absorption of nutrients. The 50 nm coiled nanochelates also help deliver nutrients such as vitamins, lycopene and omega fatty acids more efficiently without altering the colour or taste of the feed[7].

RISKS AND HAZARDS

The four essential stages of risk assessment include hazard identification, hazard characterization then exposure assessment and the risk characterization. Substance with high risk but of little exposure may present a lesser risk than substances of limited risk and high exposure for a longer period. Hence, it is of concern to characterize both the nature and exposure time. The application of nanoparticles pose a certain risk of increased bioavailability, induced ROS in the inflammatory digestive diseases, alteration in the nutrient bioavailability by disrupted effects on protein and enzyme stability, possible effects on nanoparticle biocomplexes in the process of heating or storage[7].

REGULATIONS OF NANOTECHNOLOGY

The applications of nanotechnology in animal nutrition require special concern in risk analysis, regulatory policy and oversight[48]. Thus, careful analysis of the potential, technical, societal and policy implications of these emerging applications needs to assessed timely. Regulatory frameworks and various approaches to ensure safety of nano products in agriculture, feed or food is have been accredited in countries around the globe. In India the key piece of regulation for food safety is the Food Safety and Standards Act. The Government had launched in October, 2001 a programme called the Nano Science and Technology Initiative (NSTI), followed by the programme "Nano Mission" in 2007. A series of research activities have been undertaken under this program and only recently some initiatives have started to address risk issues. Standardisation remains an area of concern, as India has only taken initial steps in addressing standardisation issues. The country is still lacking appropriate legislations with regard to nano hazards[49] and in cry for resources and expertise to deal nanotechnology risks[50].

CONCLUSION

Nanotechnology affords novel ways to enhance the growth and production in livestock with the improved feed ingredients, additives, food safety and quality control. Though the technology is attaining constant development with varied applications, studies are limited. The production of nano particles by green synthesis could be exploited as a viable alternative to the chemical synthesis method. Immense research is still needed to support its efficiency and biosafety, avoiding any harm to animals, humans and environment.

SIGNIFICANCE STATEMENT

- Present review gives brief information about the preparation and uses of nano-particles in animal feeding
- Different methods of nano-particles preparation and the advantage of green synthesis where plant extracts containing the secondary metabolites over the chemical synthesis have been detailed
- The nano-particles in animal feeding not only resulted in increased bioavailability of minerals but also reduce their requirements and excretion which will be a huge advantage from environmental friendly point of view

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