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Impact of supplementation of mineral nano particles on growth performance and health status of animals: A review

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Abstract
Minerals play a vital role in the nutrition of animal production system. Minerals perform digestive and reproductive process and growth of animals. Bioavailability of minerals from its inorganic sources is quite low so these minerals are added 20-30 fold higher than the normal requirement of animals which can lead to excess excretion of these minerals in the faeces resulting in environmental pollution and it may affect the balance of other minerals. Interaction between two minerals or more minerals can reduce bioavailability. Nano minerals improve bioavailability due to the increase in the surface area, higher surface activity, high catalytic efficiency and stronger adsorbing ability. Further, nano encapsulation technique avoids mineral-mineral or mineral-nutrient interaction and enhances their availability. Nano minerals are used for enhancing the bioavailability of minerals in livestock which is helpful in improving growth, production and health status of animals. However, studies explaining the role of nano minerals as a dietary supplement on the performance of the animals are scanty.

Keywords: Bioavailability, growth, nano particle, mineral, surface area

Introduction
Nanotechnology is concerned with materials whose structures exhibit significantly novel and improved physical, chemical, and biological properties due to their nano-scaled particle size [1]. Nano mineral particles refer to the particle having a particle size in the range of 1-100 nm [2, 3]. Nano minerals are widely used in diversified sectors including agriculture, animal, and food systems. These nano minerals also showed their significant effects even at lower doses than the conventional mineral sources. These nano minerals have significant growth promoting, immuno-modulatory, antibacterial effects than the conventional counterparts. They also alter the rumen fermentation pattern on supplementation in the animal feeds. Apart from these, nano minerals are hidden to enhance the reproduction in the livestock and poultry. The nano sized particles are having higher potential than their conventional sources and therefore cut the quantity required [4]. Major source of minerals for animal feed supplementation has been its inorganic salts, such as sulphate, oxide and chloride. However, their bioavailability has been reported to be quite low, hence required in higher amount [5]. Recent studies showed that nano particles of mineral elements have higher bioavailability, because of their novel characteristics, such as, greater specific surface area, higher surface activity, high catalytic efficiency and stronger adsorbing ability [6-8]. The intrinsic properties of nano metals are mainly determined by its size, shape, composition, crystalline structure, and morphology [8-11]. These are stable even under high temperature and pressure and can be easily carried up by the gastrointestinal tract and utilized in the animal system, gaining them more efficient than the larger sized particles. The functional activities such as chemical, catalytic or biological effects of nano minerals are heavily influenced by their particle size. It has been reported that nanoparticle showed new characteristics of transport and uptake [12-14] and reaches deeper into tissues. Also nano particles can translocate via the lymph system to the liver and spleen and deposited in these organs. The objective of the present review was to put light on efficacy of nano minerals on animal growth and health status.

Properties of Nanoparticles
A particle below the size of 100 nanometers (nm) is defined as nanoparticle. The word nano is derived from the Latin word *nanus*, meaning *dwarf*.

The physical, chemical, electrical, optical, mechanical, and magnetic properties of the nanoparticles are quite different from those present at a greater scale [15]. Nanoparticles differ from larger ones, mainly because of the following reasons:

1. Changed stability: The atoms of nanoparticles are less stable than those of larger structures, since the energy required to join adjacent atoms is less and results in change of fusion point of the given element [16].

2. Quantum effects: Quantum Nanostructures behave similar to a single atom. Their spatial arrangement allows them to have properties not proper to the element, such as magnetism in the metals like gold or platinum, when they are in the form of nano particles.

3. Surface area effect: The surface area of the material increases many fold, when it is broken into smaller particles, which increases the rate of the reaction [15].

Nanoparticles can enter the gastrointestinal tract (GIT) in many ways. The smaller is particle diameter, the faster is the diffusion through GIT mucus to reach the cells of the intestinal lining, followed by uptake through the GIT barrier to reach the blood. Uptake occurs variously by passive diffusion across the mucosal cells, via active transport mechanisms and intercellular [17]. Smaller particle size results in better absorption and reaches deeper into the tissues. Nanoparticles can translocate via the lymph system to the liver and spleen, as demonstrated for polystyrene nanoparticles of 100 nm or less [18]. Smaller particles that are capable of being taken up by the villus epithelium [19] may directly enter the bloodstream and are then predominantly scavenged by the liver and the spleen. De Jong *et al.*,[20] demonstrated that tissue distribution of gold nanoparticles after intravenous administration was size dependent with the smallest (10 nm) particles showing wide spread organ distribution. As with absorption, the distribution, breakdown and excretion of mineral particles in the body is dependent on physicochemical characteristics such as solubility, charge and size. It has also been reported that paracellular route of absorption of nanoparticles utilizes less than 1% of mucosal surface area.

Effect of Minerals Nano Particles on the Performance of Animals

As stated earlier, if particle of an element is reduced to nano size (<100 nm), its functional properties changes enormously [10]. Buzea *et al.* [15] reported that surface area of a 0.3 µg C particle of 60 µm dia. is increased to 11.3 mm^2 from 0.01 mm^2, when it is broken to 1 trillion particles of 60 nm dia, providing 1130 times larger surface area for chemical reactions. Thus the bioavailability of the nano sized particles is likely to increase many fold as compared to their normal sized particles. However, reports defining the role of nano sized particles as a dietary supplement on the performance of the animals are scanty. A brief review of such studies available in the literature has been presented below:

Effect on dry matter intake and digestibility of nutrients

Zaboli *et al.* [21] reported that feed intake was not affected in kids supplemented 20-40 ppm nano zinc oxide. However, Ahmadi *et al.* [22] observed that daily feed intake was significantly increased with supplementation of 30-120 ppm of zinc nano particles to broiler as compared to control. Tong *et al.* [23] found that supplementation of 500 ppm nano ZnO improved daily feed intake and decreased faecal score in weanling pigs. Sharma *et al.* [24] observed that the lifetime of the enzymes trypsin and peroxidase increased dramatically, from a few hours to weeks, by attaching them to magnetic Fe nanoparticles. This ability to enhance protein stability by interfacing them with nanomaterials may impact numerous biological processes such as digestion, metabolism and nutrient uptake. Muralisankar *et al.* [25] found that freshwater prawn post larvae supplemented zinc nano particles at 60 ppm level showed significantly improved activities of digestive enzymes (protease, amylase and lipase). Rohner *et al.* [26] also reported that the relative bioavailability and *in vitro* solubility of nanoparticles of Fe was significantly higher than its normal form making it more useful.

Uniyal *et al.* [27] observed that while digestibility of dry matter, organic matter, ether extract, neutral detergent fibre and acid detergent fibre was comparable, crude protein digestibility was significantly higher in group fed organic and commercial nano zinc than other groups. Zhao *et al.* [5] reported that supplementation of nano zinc in broiler at 20, 60 and 100 ppm level significantly increased feed efficiency as compared to control fed 60 ppm zinc oxide. Bunglavan *et al.* [28] reported that digestibility of crude protien and Se absorption were significantly higher in rats supplemented 150 ppb of nano selenium, followed by 37.5 ppb of nano Se group as compared to organic and inorganic selenium supplemented groups. Shi *et al.* [29] reported that nano-Se supplementation at 0.3, 3 and 6 ppm levels in the basal diet decreased ruminal pH and linearly increased total VFA concentration (range of 73.6–77.7mM) with the increasing nano-Se supplementation. The ratio of acetate to propionate was significantly decreased due to increase of propionate concentration. Shi *et al.* [30] observed *in situ* ruminal neutral detergent fiber (NDF) degradation of *Leymuschinensis* (Chinese lime grass) and CP of soybean meal were significantly improved by feeding nano-Se. Gonzales-Eguia *et al.* [31] reported that Cu availability was significantly improved as faeces Cu level was reduced in the 50 ppm nano Cu supplemented piglets as compared to CuSO4 group. Significant improvement was also observed in the digestibility of crude fat and energy by their workers.

Effect on growth performance

Zaboli *et al.* [21] reported that average daily gain was not affected in kids supplemented 20-40 ppm nano zinc oxide. Wang *et al.* [32] found that supplementation of 0-400 ppb Cr loaded Chitosan nanoparticles (Cr-CNP) in the finishing pigs while had no effect on growth performance. However, Uniyal *et al.* [27] reported that growth rate was significantly higher in guinea pigs supplemented 20 ppm commercial nano zinc (30 nm) in the diet compared to control group. Zhao *et al.* [5] also reported that broiler chicks supplemented with nano zinc at 20, 60 and 100 ppm level had significantly higher weight gains as compared to control birds fed 60 ppm Zn as zinc oxide. Tong *et al.* [23] reported that supplementation of 500 ppm nano ZnO improved average daily gain in weanling pigs. Zinc nano particles supplemented freshwater prawn post larvae (60 ppm) showed significantly improved performance in survival and growth [25]. Similarly, Bunglavan *et al.* [28] reported that average daily gain was significantly higher in guinea pigs supplemented with 150 ppb of nano selenium as compared to organic and inorganic selenium for 70 days. Gonzales-Eguia *et al.* [31] reported that supplementation of nano Cu in piglets at 50 ppm level significantly improved their growth rate. Supplemented 150-450 ppb nano Cr to the diet of rats for 8 weeks and found that rats those received Cr nano exhibited no changes in growth rate and food efficiency compared to the control group [33].

Effect on metabolic profile

Gonzales-Eguia *et al.* [31] reported that supplementation of nano Cu in piglets at 50 ppm level had no effect on serum cholesterol concentrations, as well as hematology traits like RBC, WBC, MCV, HGB, HCT, PLT and RDW. Serum glucose, albumine, urea, creatinine and total cholesterol and activity of AST and ALT were comparable in guinea pigs supplemented 150 ppb of nano selenium as compared to organic and inorganic selenium [28]. Muralisankar *et al.* [25] found that freshwater prawn post larvae fed 60 ppm zinc nano particles for 90 days had no effect on activities of metabolic enzymes (GOT and GPT) and the process of lipid peroxidation (LPO) in the hepatopancreas and muscle, however, 80 mg zinc nano particles kg−1 supplemented group showed significant elevations in LPO, GOT and GPT. Similarly, the serum glucose, total protein, albumin, globulin, urea, creatinine and total cholesterol, activities of ALT, AST and ALP were comparable among nano groups and control group [27]. However, Ahmadi *et al.* [22] observed that supplementation of 30-120 ppm of zinc oxide nano particles to broiler significantly decreased serum enzyme activity (ALT, AST, and LDH), LDL, cholesterol and triglyceride level and significantly increased HDL level as compared to control. Lambs were fed 20 mg zinc nano particles per kg body weight daily for 25 days. It was found that activity of creatinine was significantly increased compared with control, the level of the serum ALP was significantly decreased however, other factors did not change significantly [34]. Wang *et al.* [35] observed that supplementation of 200 μg chromium from nano Cr to the finishing pigs resulted in significantly higher serum level of total protein, HDL and lipase activity and reduced serum glucose, urea nitrogen, triglyceride, cholesterol and non-esterified fatty acid levels.

Effect on serum hormone profile

Uniyal *et al.* [27] reported that T3 and T4 hormone levels were not affected by nano Zn fed at 20 ppm level to guinea pigs. However, Bunglavan *et al.* [28] has been found that T3 level was significantly increased and T4 level and ratio of T4:T3 were significantly lowered in nano Se supplemented group as compared to organic and inorganic Se supplemented groups in rats and guinea pigs. Dietary supplementation of 150, 300, and 450 ppb Cr from Cr nano to the diet of rats for 8 weeks, significantly decreased serum concentrations of insulin and cortisol, increased sera level of insulin-like growth factor I [33].

Effect on immunity

Humoral immune response in terms of serum antibody titer against plain *Salmonella pullorum* antigen at 28 days post sensitization was significantly higher in 20 ppm commercial nano zinc fed guinea pigs as compared to control [36]. Gonzales-Eguia *et al.* [31] reported that supplementation of nano Cu in piglets at 50 ppm level significant improved levels of IgG, γ-globulin and total globulin protein. Freshwater prawn post larvae fed 60 ppm Zn nano paricles for 90 days showed significant improvement in immunity status [25]. Serum antibody titer was significantly higher in all the Se supplimented groups compared to control group with best performance in guinea pigs and rats supplemented 150 ppb nano Se [28]. Zha *et al.* [33] has been reported that increased sera level of immunoglobulin G, and enhanced the lymphoproliferative response, anti-SRBC PFC response, and phagocytic activity of peritoneal macrophages on dietary inclusion of 150, 300, and 450 ppb Cr from Cr nano rats.

Effect on antioxidant status

activities of enzymatic antioxidants superoxide dismutase (SOD) and catalase (CAT)] in the hepatopancreas and muscle showed no significant alterations in 10–60 mg kg−1 Zn nano paricles supplemented feed fed PL for 90 days, whereas, 80 mg Zn nano paricles kg−1 supplemented feed fed PL showed significant elevations in SOD and CAT[25]. However, Uniyal *et al.* [27] observed that the SOD activity in erythrocytes was significantly higher in nano zinc supplemented groups compared to control group. Zhao *et al.* [5] reported that supplementation of nano zinc in broiler at 20, 60 and 100 ppm level had significantly higher total antioxidant capability and catalase activity as compared to control fed 60 ppm of zinc oxide. Supplementation of 30-120 ppm of zinc oxide nano particles to broiler significantly increased SOD activity as compared to control [22]. Shi *et al.* [30] reported that serum GSH-Px, SOD and CAT activities were highest in 0.3 ppm nano-Se supplemented goats, followed by selenoyeast and sodium selenite supplemented groups. Significant improvement was observed in SOD activity in pigs fed 50 ppm nano Cu diet [31]. Bunglavan *et al.* [28] have been found that the level of GSH-Px, SOD and catalase activities in erythrocytes were significantly higher in group fed 150 ppb nano Se as compared to organic and inorganic Se fed guinea pigs and rats.

Effect on plasma and tissue minerals status

Zaboli *et al.* [21] reported that serum minerals level were not affected in kids supplemented 20-40 ppm nano zinc oxide. Similarly, no effect was observed in serum copper level in pigs fed nano Cu diet [31]. Serum Ca, P, Fe, Cu and Zn levels were comparable and serum Se concentration was significantly higher in nano Se group than other Se sources [28]. Similarly, Fe, Cu and Zn levels in kidney, liver and testis were comparable but Se was significantly higher in kidney in organic and inorganic 150 ppb Se fed groups as compare to nano Se group in guinea pigs and rats [28]. Uniyal *et al.* [27] reported that serum Ca, P, Cu, Fe, Mn and Co levels were comparable among the zinc nano, organic and inorganic zinc supplemented groups, however, serum zinc levels were significantly higher in groups fed 20 ppm nano zinc and organic zinc compared to inorganic zinc fed group. Najafzadeh *et al.* [34] studied the effect of zinc oxide nano-particles on serum biochemical factors and histological make-up of the liver and kidney in lambs fed 20 mg/kg body weight zinc nano particles daily for 25 days and found increased serum zinc level, however, other factors did not change significantly. Wang *et al.* [35] have been found that retention of Se in the whole blood, serum and some organs was highest in 0.3 ppm nano-Se supplemented goats, followed by selenoyeast and sodium selenite supplemented groups. Wang *et al.* [37] reported that supplementation of nano Cr at the rate of 200 μg in finishing pigs resulted in 184%, 145%, 88% and 52.6% increment of Cr concentration in longissimus muscle, liver, kidney and heart respectively.

Carcass characteristics

Wang *et al.* [37] reported that supplementation of 200 μg nano Cr in finishing pigs resulted in higher carcass lean percentage, larger longissimus muscle area, lower carcass fat percentage and lower back fat thickness. Drip loss in chops from pigs fed nano Cr was decreased by 21.5% and weights of longissimus and semimembranosus muscles were increased by 16 and 15 percent respectively. Similarly Zha *et al.* [38] also reported that supplementation of Cr in the form of Cr-nano and Cr-picolinate might be an effective tool for enhancing carcass traits of broiler chicks in heat-stressed condition. Cr-nano seemed to have greater beneficial effects in comparison with Cr-picolinate.

Conclusions

Minerals as nanoparticles reduce intestinal mineral antagonism, thereby reducing excretion and environmental pollution. Nano minerals are having a great potential as mineral feed supplements in animals even at very lower doses than the conventional sources by increasing their bioavailability in biological system due to the increase in the surface area, surface activity and catalytic efficiency of nano minerals. Present study have recommended that supplementation of nano minerals improved the growth, digestive efficiency, immunity, antioxidant status and other performance of different group of animals.

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