Review Article

Importance of Metal Nanoparticles in Veterinary Medicine

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Received: 06/12/2022
Accepted: 25/12/2022

ABSTRACT To increase the effectiveness of animal production, many businesses that specialize in the creation of novel nanomaterials have launched poultry and cattle production systems. Metal nanoparticles are sometimes added to animal diets as supplements, but the effects are not always clear-cut. The literature is replete with reports on the varied impacts of this kind of animal supplementation. The purpose of the paper is to describe what is currently known about the potential use of nano-metal forms in animal feeding as well as any potential advantages and disadvantages. The benefits of using nanoparticles as feed additives have most frequently been seen in improvements of the feed conversion rate, more significant average daily gains, or increases in body weight. However, the impact of adding nanoparticles to meals was sometimes imperceptible. Positive effects are thought to result from the powerful antibacterial activity of nanoparticles, particularly against Gram-negative and Gram-positive bacteria. The investigation of avian and animal progeny systems for increasing production efficiency and meeting consumer demand for premium meat and poultry product. Due to the small size of nanoparticles, they pass through the gastrointestinal tract walls very quickly and have a variety of significant effects on different body systems. This gives researchers the chance to work with nanomaterials by researching a variety of veterinary fields, such as production, reproduction, disease control, and working with biological materials.

Keywords: metal, nanoparticles, poultry, Feed additives, Production, reproduction.

INTRODUCTION

Nano is a phrase that derives from the Latin word "nanus," which signifies dwarf, lesser, or very little minute particle (1 nm equals 10^-9 m) **(Youssef et al. 2019).** Essential minerals with sizes ranging from 1 to 100 nm called nano-minerals could replace traditional forms of elements in an animal's diet **(Mohamed et al. 2016).** They are utilized because of qualities including their tiny size, high surface area, superior uniformity, and physical reactivity **(Scott et al. 2018).** The most well-known Nano-particles include aluminium **(Li et al. 2011**), copper (**Refaie et al. 2015**), zinc (**Joshua et al. 2016**), silver (**Grodzik and Sawosz 2006**), calcium (**Matuszewski et al. 2020**), gold (**Sanati et al. 2019**), magnesium **(Mazaheri et al. 2019; Abdelnour et al. 2021),** selenium **(Zhang et al. 2008**), iron (**Pilaquinga et al. 2021),** nickel (**Gong et al. 2016**), titanium (**Li et al. 2011**).Some nanoparticles are crystalline or amorphous, and they may contain one or more loose or clumped crystals. (**Abd Elghany et al. 2017**). The total dosage needed to be reached favorable serum concentrations at Nano levels is lower than it is for their Normal counterparts (Normal bulk materials). Like a standard bulk zinc supplement, feeding with Nano-zinc oxide (ZnO) supplementation improved intestinal morphology, daily gain average, and plasma zinc level (at high dose) (**Wang et al. 2018)**.

Classification of Nanoparticles:

They are typically divided into three categories based on their composition: organic, inorganic, and carbon as following:

1. **Organic Nano-minerals**: that include polymers as dendrimers, micelles, liposomes and ferritin which are nontoxic, biodegradable and may have hollow core (micelles & liposomes) sensitive for heat and light (**Tiwari et al. 2008).**

2. **Inorganic Nano-minerals:** which include metal based, and metal oxides-based nanoparticles.

- **Metal Based Nanoparticles** as aluminium (Al), cadmium (Cd), cobalt (Co), copper (Cu), gold (Au), iron (Fe), lead (Pb), silver (Ag) and zinc (Zn) **(Salavati-niasari et al. 2008).**

- **Metal Oxides Nanoparticles**: which include oxides of nanoparticles as iron oxide (Fe2o3) and zinc oxide, which are synthesized mainly to increase efficiency and reactivity **(Tai et al. 2007).**

3. **Carbon Based Nanoparticles:** made completely form carbon which include fullerenes (C60), graphene (allotrope of carbon), carbon nanotubes (CNT), carbon nanofiber and carbon black **(Bhaviripudi et al. 2007).**

Synthesis of Nanoparticles:

they are synthesis by various methods which divided mainly into 2 methods bottom-up or top- down method as the following:

1- **Bottom-up method:** which include building up of material from atom to cluster to form finally nanoparticle, including many ways as sol-gel, spinning, chemical vapour deposition, pyrolysis and bio-synthesis.

- **Sol-gel:** colloidal solution of solids suspended in liquid phase, it is wet chemical process contains chemical precursor solution (metal oxides and chlorides) **(Ramesh et al. 2013).**
- **Spinning:** rotate disc inside champer /reactor where temperature and other physical parameters can be controlled, reactor filled with nitrogen which remove oxygen and avoid reactions **(Tai et al. 2007).**
- **Chemical Vapour Deposition:** is dopsition of a thin film of gaseous reactants onto a substrate **(Bhaviripudi et al. 2007).**
- **Pyrolysis:** it involves burning a precursor (liquid or vapour) with flame at high pressure through a small hole **(Kammler et al. 2001).**
- **Biosynthesis:** is a green and environmental approach by using bacteria, plant extracts, fungi, etc. **(Kuppusamy et al. 2014).**

2- **Top-down method:** reduction of bulk material to nano-metric scale particles, it includes mechanical milling, nanolithography, laser ablation, sputtering and thermal decomposition.

- **Mechanical milling**: it used for milling of nanoparticles during synthesis in an inert atmosphere **(Yadav et al. 2012).**
- **Nanolithography**: is printing process of required shape or structure on light sensitive material that removes part of material to create desired shape and structure **(Hulteen et al. 1999).**
- **Laser ablation**: irradiation of a metal submerged in liquid solution by a laser beam condenses a plasma plume that produces nanoparticles **(Amendola et al. 2009).**
- **Sputtering**: it is deposition of nanoparticles on surface by ejecting particles by colliding with ions **(Shah and Gavrin 2006).**
- **Thermal decomposition**: is an endothermic chemical decomposition produced by heat that breaks the chemical bonds in the compound **(Salavati-niasari et al. 2008).**

Effect of Nano particles on growth performance:

It was reported that minerals NPs were rapidly absorbed and systemically distributed to many organs such as liver, kidney, spleen, duodenum, and other organs in rats after oral administration **(Krause et al. 2020).**

As a result of the extensive usage of feed additives containing essential minerals in nano form, such as Nano zinc, Nano selenium, and Nano copper **(Gopi et al. 2017),** to increase feed conversion, performance, and efficiency **(Abd ElGhany et al. 2019).** Another finding showed that it greatly enhances feed efficiency by promoting intestinal health, protein, lipid, and carbohydrate metabolism **(Kechrid and Bouzerna 2004; Surai et al. 2017).** It is an essential component of more than 300 enzymes that work together to produce and degrade proteins, lipids, carbohydrates, and nucleic acids as well as to process other micronutrients **(O'Dell et al. 2000; Salgueiro et al. 2000).** In contrast, animals with zinc deficiencies grow more slowly, consume less food, have lower levels of growth hormone and insulin-like growth factor I, and produce less insulin-like growth factor I. **(McDonald 2000).**

Hassan et al. 2017 demonstrated that feeding growing rabbits raised in hot environments ZnO-NPs source supplementation boosted their productivity. Compared to alternative sources. Others came to the conclusion that the Cu-small NP's size, which can enhance GIT uptake, can make them more efficient than bulk Cu at lower doses **(Civardi et al. 2015).** Utilizing another nanominarals, such as Cu_NPs, allows them to enter the small intestine and then spread throughout the body, including the blood, brain, heart, kidney, spleen, liver, and intestine **(Hillyer et al. 2001)** Cu-NP has been demonstrated to improve growth performance and feed utilization when used as a feed supplement for piglets, poultry, and fish **(Mroczek et al. 2015; El Basuini et al. 2016).** According to research by **Miroslavikov et al. 2015,** there is a connection between the amount of arginine in the liver and chicken growth, which was boosted by a single intramuscular injection of Cu-NP. Since Lactobacillus fermentum is one of the main targets of antibiotic growth promoters, a study showed that the antimicrobial properties of chitosan implanted with Cu-NP reduce gut bacteria like *E. coli*, *Enterococcus faecalis, S. aureus*, and, in particular, *Lactobacillus fermentum*. This suggests that the Cu-NP could be used to reduce unwanted levels of microbial populations without causing cytotoxicity **(Rajasekaran and Santra 2015).** Others have claimed that supplementing the feed of chickens with more copper lowers the number of *clostridia* in the hens' GIT. Generally speaking, Cu salts have a higher concentration (up to 200 mg/kg) than Cu-NP (below 50 mg/kg) that has an impact on coliform bacteria populations. Although 150 mg/kg of copper enhanced the population of *lactobacilli* in the GIT contents, the higher concentration had no noticeable impact **(EFSA 2016).** It has been established that adding Cu-NP to chicken diets as a supplement may have positive effects on growth, feed efficiency, and chicken health by harming pathogens, reducing the production of bacterial toxins, increasing the synthesis of vitamins and other growth factors, and enhancing nutrient absorption by reducing intestinal epithelium thickness and intestinal mucosal epithelial cell turnover and motility (**Prescott and Baggot 1993**).

Studies contrasting the inorganic forms of copper with copper nanoparticles (Cu-NP) revealed that the latter improved piglet growth. Additionally, compared to CuSO4, Cu availability was dramatically increased and the stool Cu level was decreased **(Gonzaliez Eguia et al. 2009).** The advantages of include Cu-NP in fish diets have been shown in a number of research. In a study by **El Basuini et al. 2016,** different concentrations of Cu-NP were investigated. The results showed that 2 and 4 mg/kg of Cu-NP caused the highest final body weight, better feed efficiency, protein retention, immune response, and antioxidant defense system compared to CuSO4 and the control groups.

In a similar manner, rabbits fed meals supplemented with different concentrations of Cu-NP outperformed the control group in terms of performance and body weight **(Refaie et al. 2015).** Application of silver nanoparticle mouthwash after making an incision on the tongues of rabbit models considerably decreased the number of microorganisms in the oral cavity, according to **Amir Hossein et al. 2022** additionally, the healing of surgical wounds was significantly improved by mouthwash containing silver nanoparticles. The mouthwash formulation with a silver nanoparticle weight percentage of 9.80% and a particle size of 5 nm may be a suitable alternative for use following oral surgical operations. Contrarily, nano-silver had no impact on performance. Bursa weight considerably decreased when compared to control treatment ($p>0.05$), with the treatment added with 25 ppm nanosilver showing the lowest weight among the treatments **(Farhad and Ardashir 2010).**

Effect of Nano particles on Immunity:

Researches stated that, minerals NPs have a significant impact on both cellular and humoral immunity and play a critical role in the immune system. It is crucial for the process of genetic expression **(Sunder et al., 2008).** It might affect the thymus gland's release of thymulin, which encourages the growth of T cells. Consequently, its absence has an impact on the thymus gland and immune system **(Mocchegiani et al. 1998).** Other researchers came to the conclusion that dietary Zn supplementation could modify superoxide dismutase (SOD) activity **(Alissa et al. 2004),** improve the immune response of male guinea pigs in comparison to inorganic Zn sources **(Shinde et al. 2006),** and raise broiler total IgM and IgG antibody titres **(Bartlett and Smith 2003).** In order to fight off infections and repair damaged tissues, Cu plays a function in immune system stimulation **(Failla et al. 2003).** Furthermore, it promotes the elimination of free radicals that cause severe cell damage **(Tapiero et al. 2003).** Copper is necessary for the growth of antibodies and white blood cells in addition to the production of antioxidant enzymes **(Sharma et al. 2005).** Additionally, copper is essential to the body's enzyme systems for the creation of red blood cells, the immunological system, and the metabolism of iron. Additionally, Cu speeds the growth of the nervous system by increasing dopamine synthesis and encourages the formation of connective tissues like collagen and elastin **(Mroczek et al. 2013).**

As a result, any exposure to silver nano-materials may trigger a series of inflammatory reactions involving the activation of neutrophils, macrophages, and helper T cells, finally leading to the release of a wide variety of cytokines, including tumor necrosis factor (TNF-), Interleukins (IL-1, IL-6, IL-12, IL-18). On the other hand, immune cells clarify silver nano-materials for foreign particles. Systemic inflammation may result from unintended cytokine level rise brought on by nanomaterials. Including the Mitogen-activated protein kinase (MKK), c-Jun N-terminal kinase (JKK), and Nuclear Factor-k (NF-k) pathways **(Elsabahy 2013).** Therefore, the material chemistry of silver-coated implants can dramatically affect the immune response and the regulation of the release of cytokines from monocytes and macrophages. Additionally, it may cause an immune reaction. **(Rochford et al. 2012).**

Antioxidant Effect of Nano- particles:

By modulating inflammatory cytokines, zinc, an essential trace mineral, helps to manage oxidative stress, promote development, and strengthen the immune system. The formation of monosodium urate crystals results in gouty arthritis, which is an inflammation of the joints and other tissues **(Mubin et al. 2019).** By preventing the generation of OH^-1 (hydroxide ion) in an antagonist transition metal-catalyzed process (the reaction fenton), zinc's antioxidant function has been demonstrated **(Jomova and Valko 2011).** Any OH^-1 generation results in severe, localized, chronic damage to cellular constituents **(Powell 2000).**

Several studies have demonstrated that adding Cu-NP to animal diets increased SOD activity **(Refaie et al. 2015).** In addition, silver NPs can be used to lower ROS levels, which can be utilized to regulate the immune system since when R.O.S levels are high, immune cells become dysfunctional, which frequently results in immunosuppression **(Schieber et al. 2014).**

Antimicrobial effects of Nanoparticle:

Zinc oxide NPs which consider as promising antiviral agent against viruses as H1n1 influenza virus infection **(Ghaffari et al. 2019),** also silver NPs has potant antiviral activity against H1N1 influenza virus **(Xiang et al. 2011).** Zn is used as an antimicrobial material and can improve kidney and liver functions **(Chrastinová et al. 2018; Fawaz et al. 2019).**

Gram-positive and Gram-negative bacteria are immune to Cu-NP **(Alzahrani et al. 2016).** Furthermore, according to **Shobha et al. 2014,** Cu-NP prevents the growth of the bacteria S. aureus, B. subtilis, and E. coli, as well as Micrococcus luteus, Klebsiella pneumoniae, and Pseudomonas aeruginosa **(Ramyadevi et al. 2012).** By raising Cu- NP concentrations, E. coli and B. subtilis bacterial subsistence rates are reduced **(Yoon et al. 2007).** Additionally, other evidence showed that Cu-NP has been utilized as a disinfectant for a long time due to its antibacterial qualities **(Sanchez et al. 2016).** With regard to a variety of Gram-positive, Gram-negative, aerobic, anaerobic, and even vancomycin-resistant species, silver nanoparticles have antimicrobial properties **(Allaker et al. 2010).**

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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Cite this Paper

Mahboba Abd Elwanees Zaky, Said Ibrahim Fathalla, Sherif Mohamed Shawky, Ahmed M.A. El-Seidy, Ibrahim Said Abu-alya, and Shimaa Ramadan Masoud (2023). Importance of Metal Nanoparticles in Veterinary Medicine. MJVM., Vol. (3), Issue (1) Special Issue of 2nd Sci Conference of Fac Vet Med Matrouh University, pages (50-57).
DOI:10.21608/MJVM.2023.182170.1016.

About the Journal

Matrouh Journal of Veterinary Medicine (MJVM)
The official journal of the faculty of veterinary medicine, Matrouh University, Egypt.
Publisher: *Matrouh University, Egypt.*
ISSN (Online):2735-458X
ISSN (Print): 2735-4903
Indexed in EKB Database