

Uses of Nanotechnological Feed Additives and Nanofeeds in Poultry Feeding

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Abstract

In poultry, which has an important place in meeting the need for healthy animal protein, the production of ration substance compositions with alternative sources is one of the popular topics of the last period. Nanoparticles produced by nanotechnology of various minerals added to poultry diets are increasingly being used as feed additives that can reduce feed costs, reduce the risk of environmental waste, replace antibiotics and do not pose residue risk in animal products, both in terms of supporting growth and development and strengthening the immune system. The aim of this study was to bring together the studies on the effects of using nanoparticles as feed additives on growth, development performance and immune system in poultry.

Introduction

In order to meet the need for sufficient and healthy animal protein for the rapidly growing human population, it is estimated that 200 million tons of meat production is required annually (Ghasemzadeh, 2012). In view of the rapid production and cost of meat production, poultry meat production comes to the forefront, which leads to an increase in the number of studies on alternative poultry meat production, especially chicken meat. In order to ensure the continuity of production, issues such as reducing production costs, sustainability of animal health and product health are being discussed. In recent years, the development of alternative feeds has made it possible to increase the feed utilization rate, protect animal health and obtain clean products. Intensive efforts are also being made to develop raw materials that do not compete with humans and to produce relatively

inexpensive, high-quality products with a lower environmental impact in animal nutrition.

Infection with microbial agents adversely affects growth, development, and yield characteristics and is one of the major threats to the poultry industry, causing economic losses. Infectious diseases, generally controlled by vaccination and the use of antibiotics, are associated with the emergence of drug resistance in susceptible microbial populations (Doyle et al., 2006). Some countries have restricted the use of antibiotics as growth promoters as well as chemoprophylactics against poultry diseases because the residual concentrations of these drugs in poultry products may pose a risk to consumer health (Ohimain & Ofongo, 2012). Researchers are therefore looking for consumer-friendly and residue-free alternatives to develop a profitable poultry business.

Feed additives can only be placed on the market if they have been scientifically evaluated and approved as having no adverse effects on human or animal health or the environment, and if they can increase growth and/or egg production efficiency, prevent diseases, and improve feed utilization. Five categories of feed additives are defined: zootechnical (enzymes, probiotics, prebiotics, some phytogenics), nutritional (vitamins and amino acids), technological (organic acids, antioxidants, pellet binders, etc.), sensory (flavourings) and coccidiostats. However, the use and development of enzymes, phytogenics and probiotics in poultry nutrition has gained momentum (Pirgozliev et al., 2019).

In light of these increases, modern technologies such as nanotechnology will be used in agriculture and food to improve health, performance, productivity, efficiency and unit production. Nanomaterials may play an important role in facilitating the productivity gains needed to transform agriculture and, in the context of this review, the poultry industry.

Over the past decade, there has been a significant increase in interest in investigating the potential use and efficacy of nanomaterials in animal production. The main applications of these nanomaterials in animal nutrition as supplements, drugs and probiotics are being rigorously investigated. The major application of nanotechnology in poultry nutrition is mainly in the form of nanominerals due to their increased bioavailability and reduced antagonistic behavior in the intestine (Gopi et al., 2017). Nano-Zn supplementation improved growth performance in broilers (Mohammadi et al., 2015a). Similarly, the addition of silver (nano-Ag) and selenium (nano-Se) nanoparticles to broiler diets has been shown to reduce oxidative stress due to their strong antioxidant activity (Ahmadi & Kurdestani, 2010a; Aparna & Karunakaran, 2016). Furthermore, copper nanoparticles (nano-Cu) not only improved growth performance but also enhanced immune responses in poultry (Wang et al., 2011). It has also been reported that the supplementation of nano-Fe improved the growth performance and hatchability of poultry (Saki & Abbasinezhad, 2014; Sizova et al., 2015).

In this study, studies on growth and development and immunological effects of nanoparticles as feed additives in poultry diets were evaluated.

THE EFFECTS OF NANOPARTICLES ON GROWTH AND DEVELOPMENT CHARACTERISTICS

The high surface area to volume ratio makes gold nanoparticles an attractive option for use in poultry. Their surface can be coated with hundreds of molecules. Supplementation of chicken embryos in-ovo with golden nanoparticles, taurine or taurine conjugates has been shown to improve pectoral muscle organization through the activation of molecular mechanisms such as the expression of nuclear antigens of proliferative cells to enhance growth performance (Zielinska et al., 2009).

Copper is an essential trace mineral involved in many physiological and biochemical processes, such as angiogenesis, vasculogenesis, hemoglobin synthesis, and redox processes (Mroczek-Sosnowska et al., 2015). Nanocopper stimulated vascular development at the molecular and systemic level, prolonging the predominance of hyperplasia over hypertrophy until the end of embryogenesis and improving performance in broilers and layers (Leeson, 2009; Karimi et al., 2011). Muscle growth during embryogenesis depends on vascular development stimulated by copper, and the number of muscle fibers is mainly determined during the prenatal period. This stimulation of cell proliferation by copper can have a significant effect on the subsequent growth of chickens (Mroczek-Sosnowska et al., 2016). Sawosz et al. (2018) reported that it was possible to reduce the level of copper supplementation in chicken feed and its excretion into the environment using nanocopper. Another study reported that in-ovo injection of nanocopper on different days during incubation significantly altered oxygen consumption and heat production, indicating changes in metabolic rate. This may be related to reduced fat oxidation and suppression of organ development (Anwar et al., 2019).

Zinc is an essential trace element for growth, wound healing, immune function, fertility, metabolism and ROS scavengers in animals (Feng et al., 2010; Liu et al., 2011). The bioavailability of organic zinc is higher than that of inorganic zinc, but its use in animal nutrition is limited due to its higher cost (Anwar et al., 2019). However, high levels of zinc in the diet can lead to excessive excretion, which can be a source of contamination (Broom et al., 2003). High levels of zinc supplementation can also have an effect on the balance of other elements in the body and on the stability of vitamins and other nutrients. In addition, long-term exposure may increase the risk of residues (Sundaresan et al., 2008). The effects of interactions between different fatty acids, zinc sources and levels on carcass and meat quality characteristics of broiler chicks showed that using palm oil containing nano-zinc oxide at 80 mg/kg in the diet improved carcass characteristics and meat quality of broilers reared under summer heat conditions (Selim et al., 2014). An adequate dietary concentration of nanocopper was shown to improve growth performance and antioxidant capacity in broilers at a dose of 20 mg/kg (Zhao et al., 2014). The addition of nanocopper to the dry diet improved the carcass yield and increased the relative weight of the digestive and lymphoid organs of broilers in the initial period as compared to the wet diet (Mohammadi et al., 2015b; Esfahani et al., 2015). Essential minerals for optimal poultry growth and performance are calcium and phosphorus. Reducing calcium and phosphorus in poultry diets can result in bloody meat and broken bones during carcass processing (Chen & Moran Jr., 1995). Supplementing minerals in nano form increases their bioavailability and utilization efficiency. By reducing the amount of mineral supplementation, nano-sized calcium-phosphorus supplementation can improve broiler

growth performance and reduce feed costs. Since phosphorus is an expensive mineral source, its requirement as dicalcium phosphate can be replaced with the nano form of Ca-P at levels as low as 50%. Compared to the control, birds fed 50% and 60% Ca-P-NP had significantly higher BW gains. Birds fed 50% Ca-P NPs substitution had the best FCR, which was significantly different from the control group (Vijayakumar & Balakrishnan, 2014).

Adding Se-NPs to chicken feed has significant effects on broiler growth (Cai, 2012). The addition of Se-NPs at a dose of 0.3 mg/kg to the feed increased the growth rate of broiler chickens, as reported by Senthil Kumaran et al. (2015). Furthermore, nano vitamin D3 affects the quality of femur and production performance of chickens (Yang et al., 2014). Supplementation of poultry with nano minerals and vitamins reduces stress and improves productivity and meat quality. Therefore, Se-NPs can be used as potential anti-stress factors in poultry to increase production.

EFFECTS OF NANOPARTICLES ON THE IMMUNE SYSTEM

Ag NPs showed antimicrobial activity against *Escherichia coli* and *S. aureus* with cell wall disruption at minimum inhibitory concentrations of 100 and 50 ppm (Cho et al., 2005). NPs attach to pathogens and remove them from chicken's body. Elkloub et al. (2015) found that broilers fed with Ag-NPs at a dose of 4 ppm per kilogram of feed demonstrated a reduction in the number of harmful bacteria (*E. coli*), while the population of beneficial lactobacilli remained unaltered. Due to these antimicrobial activities, these Ag-NP were reported to improve growth performance, body weight (BW), feed intake (FI) and feed conversion ratio (FCR) at 900 ppm (Ahmadi, 2009).

From an immunological perspective, it is accepted that phagocytosis of Ag-NPs stimulates inflammatory signalling by accumulating reactive oxygen species (ROS) in macrophage cells, followed by secretion of activated macrophage cell-derived tumor necrotic factor alpha (TNF- α). As TNF- α levels increase, it causes cell membrane damage and apoptosis. Incorrect recognition of Ag-NPs as foreign particles by immune cells can lead to a multi-level immune response and ultimately to toxicity in the host (Park et al., 2010). Conversely, when Ag-NPs are spontaneously recognized or in the absence of immune recognition, their ability to stimulate an immune response may be the determinant of Ag-NPs' fate in the host. In vivo studies have shown that NPs can promote inflammation (Nygaard et al., 2009). The immune defense and T helper 1 (Th1)/T helper 2 (Th2) cell balance may be affected by the inflammatory response induced by NPs. Grodzik and Sawosz (2006) evaluated the effect of Ag-NPs at 10 ppm on fetal bursa Fabricius and growth, showing decreased size and number of follicles and no significant effect on growth of chickens. Ahmadi and Kurdestany (2010b) investigated the changes in the relative weight of the

bursa after application of 20, 40 and 60 ppm concentrations of Ag-NPs. The results reported decreased follicle size and number. This may be due to the antimicrobial properties of Ag-NPs affecting the microbial populations in the gut. Ag-NPs transport available oxygen and certainly reduce the growth of anaerobic microorganisms. This in turn has negative effects on the growth of the bursa Fabricius.

Matsumura et al. (2003) suggest that the same effect of Ag-zeolite may be due to Ag⁺ uptake in bacterial cells when they come in contact with Ag-zeolite, which inhibits cellular functions and damages the cell. On the other hand, it could be explained by the formation of reactive oxygen molecules that inhibit the cellular respiration. It is logical that for the growth and development of the bursa in healthy broilers, the presence of microorganisms in the gastrointestinal tract is necessary. Ag NPs do not appear to affect immunoglobulin M (IgM) and immunoglobulin G (IgG) levels (Pineda et al., 2012). Furthermore, Ag-NPs together with amino acids (cysteine and threonine) were shown to enhance innate and adaptive immunity in chickens during embryonic development (Bhanja et al., 2015; Saki et al., 2017). Another study reported antiviral activity of Ag NP solution against infectious bursal disease virus in embryonic chicken eggs (Pangestika & Ernawati, 2017).

Au-NPs are attractive for use in poultry because their surface can be coated with hundreds of molecules due to their high surface area-to-volume ratio. In-ovo supplementation of chicken embryos with Au-NPs, taurine, or taurine-conjugated Au-NPs improved pectoral muscle organization by activating molecular mechanisms such as nuclear antigen expression of proliferating cells to enhance growth performance (Zielinska et al., 2010). Improvements in growth performance can be maximized by controlling infectious diseases. However, early detection of disease is essential. Therefore, an effective on-farm disease control program for early detection of diseases is essential for profitable poultry production. Nanotechnology provides a platform for rapid and early detection of various poultry diseases. Au-NPs were used in diagnostics to detect avian influenza H5 hemagglutinin-derived peptides with a detection limit of 2.2 pg/mL (Jarocka et al., 2014). Au NPs have been used to coat an immobilized polyvinylidene difluoride membrane with some of the immunodominant sequences of the non-structural 1 protein of the avian influenza virus for the detection of this virus in the serum of infected birds (Emami et al., 2012).

Chitosans are thought to possess a variety of biological effects, including immunomodulatory and antimicrobial activity (Jan et al., 2012; Alishahi 2014). It is used as effective adjuvant for the delivery of biological substances such as drugs and vaccines. Compared to chitosan-free vaccines, chitosan-adjuvanted vaccines increased antibody titres against influenza. Wang et al (2011) reported that the addition of Cu-loaded chitosan NPs at a dose of 100 mg/kg can improve growth performance, immunity, protein synthesis and caecal microbiota in broilers. In another

study, avian influenza (H9N2) vaccine-loaded chitosan-NPs induced protective antibody titres after single vaccination and required low antigen dose (Khalili et al., 2015). Chitosan NPs loaded with Newcastle disease virus (La Sota) showed stronger cellular, humoral and mucosal immune responses when administered by the intranasal route (Dai et al., 2015).

METABOLISM and POSSIBLE SIDE EFFECTS of NANOFEEDES

Nanoparticles can enter the gut by several routes, including direct ingestion from feed or water and therapeutic nanodrug delivery. Inhalation of nanoparticles can also enter the GI after clearance from the respiratory tracts (Surai et al., 2017). Due to gastrointestinal barriers, bioavailability is generally reduced with oral administration. Intestinal mucosa and liver are associated with incomplete absorption. Nanoparticles, however, have shown 100% bioavailability when administered by intravenous injection due to direct entry into the systemic blood circulation (Geraet et al., 2014). Nanoparticles diffuse through intestinal mucus to reach intestinal cells and blood more rapidly (Surai et al., 2017). Little is known regarding gastrointestinal uptake of nanoparticles. Studies have shown that, depending on size, nanoparticles either pass through the gastrointestinal tract without absorption and are rapidly eliminated from the body (Geraet et al., 2014), or that nanoparticles cross the intestinal mucosa and enter the bloodstream, from where they are transferred to other organs. The physicochemical properties of these particles (e.g., charge, size, and solubility) have a significant impact on their fragmentation, absorption, distribution, and excretion (Choi & Choy, 2014). Recent studies have proposed a possible mechanism for the conversion of nano-Se to selenite in monogastric animals, suggesting that the gut microbiota can convert nano-Se to selenite, Se-phosphate and/or H₂Se, ultimately leading to the synthesis of selenoprotein (Thulasi et al., 2013; Surai et al., 2017).

Nano minerals tend to be rapidly distributed from the circulation into tissues. Primarily, the highly perfused reticuloendothelial system (RES), including organs such as the spleen and liver, are target tissues for nano minerals. Nanoparticles have even been observed in protective membranes, although at lower levels (Geraet et al., 2014). The tissue distribution patterns of ZnO nanoparticles are highly dependent on the animal, the exposure route and the physicochemical properties of ZnO nanoparticles. Studies have shown that kidney and liver are common target tissues for nano-ZnO, regardless of exposure routes, physicochemical properties, and animals tested. There is also evidence that the clearance of ZnO nanomaterials may be largely dependent on faecal excretion (Choi & Choy, 2014).

Toxic effects have been reported in addition to the benefits of nanoparticles. Toxicity of conventional

sources of Zn in food and feed has been reported. Zn toxicities are mediated by oxidative stress, lipid peroxidation, cell membrane damage and oxidative DNA damage (Lin et al., 2009). The toxic effects of nanoparticles are generally size dependent, and nano-sized Zn has been shown to be more toxic than micro-sized Zn at the same dose (Chen et al., 2007). In a similar way, copper nanoparticles cause systemic toxic effects with morphological and functional changes in the liver, the spleen and the kidneys. In summary, the in vivo toxicity of Cu nanoparticles as compared to their ionic form is most likely related to their higher solubility and biodistribution in physiological media (Wang et al., 2014). Nano-Cu toxicity caused decreased growth parameters and increased malonaldehyde concentration (indicator of cellular oxidation), total SOD activity, total GSH-Px concentration and Na(+)/K(+)-ATPase activity. However, adverse effects were observed in the brain (Suttle, 2010). The literature recommends further studies on the toxic effects of nanoparticles.

CONCLUSION

In conclusion, it is seen that nanoparticles used as feed additives in poultry provide advantages such as increasing growth and development performance, strengthening the immune system and reducing feed costs. The use of these minerals produced by nanotechnology is an important development in terms of reducing the risk of environmental waste and providing natural alternatives to antibiotics. Considering the economic perspective that this method brings to poultry farming, the economic advantages of using nanoparticles as feed additives can play an important role. The reduction in feed costs, coupled with improved growth and development performance, could positively impact farmers' profit margins. Furthermore, factors such as reduced use of antibiotics, reduced risk of residues in animal products and reduced risk of environmental waste can increase sustainability and consumer confidence in the sector. However, factors such as the cost, production processes and commercial viability of this technology need to be evaluated in more detail. In conclusion, the economic advantages of using nanoparticles to farmers require a comprehensive economic analysis in terms of long-term profitability and sustainability in the sector. These studies can be considered as an important step to increase productivity and sustainability in poultry farming. However, research in this area needs to be further deepened and long-term impacts need to be evaluated more comprehensively.

Author Contributions

First Author: Conceptualization, Data Curation, Formal Analysis, Investigation, Methodology, Visualization and Writing -original draft, Funding Acquisition, Project Administration, Resources, Writing -review and editing.

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