

Application of zinc oxide nanoparticles on productive performance in rabbit nutrition: A Review

M.A. Hussein, Z.S.H Ismail, A.A.A. Abdel-Wareth*

Department of Animal and Poultry Production, Faculty of Agriculture, South Valley University, Qena 83523, Egypt

Abstract

Nowadays, nanotechnology is more frequently used with the presence of new tools for utilizing nanoparticle-sized essential elements, enhancing the animal's ability to absorb these elements and thereby improving their productive and reproductive performance. Zinc oxide nanoparticles (Nano-ZnO) can promote productive performance, act as antibacterial agents, and influence the immunity and reproduction of the rabbits. Moreover, zinc (Zn) increases semen volume, total live sperm concentration, percentage of sperm motility, and conception rate in heat-stressed rabbits. Several studies have already reported the effects of low and high zinc doses on rabbit performance. The most observed and analyzed reproductive performance variables are semen quality, spermatogonia, and meiosis of spermatocytes. Most of the studies showed slight positive effects; however, significant results were rare. Since there are almost unlimited possibilities regarding the zinc dosage, further research is still required. Nano-sized zinc particles can be used at low doses, resulting in better outcomes than conventional zinc sources. This review provides an overview of and illustrates the positive effects of zinc nanoparticles and their potential application as a mineral supplement to rabbit diets.

Keywords: Nanotechnology; Production; Antimicrobial; Zinc; Rabbits

1. Introduction

Trace minerals are essential for many metabolic processes and physiological functions of animals (McDowell., 2003). Zhao et al. (2014) demonstrated that zinc (Zn) can be incorporated into the diet as inorganic salts, such as ZnO and Zn sulfate (ZnSO₄), and organic chelates, such as Zn propionate and Zn acetate. Although Zn bioavailability in organic sources is greater than that of inorganic

Zn salts, using organic Zn chelates in animal diets is limited because it is not cost-effective. Feng et al. (2009) stated that the high levels of Zn in the supplemented animals have raised concerns about environmental pollution. Therefore, investigating this issue might lead to finding better bioavailable Zn sources and, if possible, reducing the supplemental dose of Zn to the animal feed. Nanotechnology is used to produce nanoparticle-sized Zn a potential alternative both nanoparticle-sized Zn. Utilizing Nano-ZnO exhibited better results and is less toxic than conventional

*Corresponding author: A.A.A. Abdel-Wareth

Email: a.wareth@agr.svu.edu.eg

Received: October 4, 2020;

Accepted: October 13, 2020;

Published: October 13, 2020.

Zn sources and micro-Zn (Wang et al., 2006; Sahoo et al., 2014b).

Recently, in both animal and human models, nanotechnology was employed in the fields of biology, biotechnology, mineral nutrition, physiology, reproduction, and pharmacology. Sindhura et al. (2014) showed that these nanomineral particles have higher potential than conventional sources, thus decreasing the required quantity. Swain et al. (2015) found an added advantage to Nano-ZnO that is they can efficiently be synthesized using any of the physical, chemical, or biological methods which are cost-effective and feasible. Piccinno et al. (2012) demonstrated that, based on the volume of metal nanoparticles produced annually worldwide, Nano-ZnO comes in third place after nano-SiO₂ and nano-TiO₂. Padmavathy and Vijayaraghavan (2008) said that the sudden increased demand of Nano-ZnO is mostly because it possesses better antibacterial properties than conventional Nano-ZnO. Nano-ZnO are used in the food industry as additives and during packaging because of their antimicrobial characteristics (Gerloff et al., 2009; Jin et al., 2009).

Different sources and levels of zinc in rabbit feedstuff had significantly improved immune responses (Luecke et al., 1978; Meshreky et al., 2006; Meshreky et al., 2015). Zn can enhance the carbonic anhydrase activity which catalyzes the conversion of CO₂ + H₂O to HCO₃⁻ that is important for bone development (Fawaz et al., 2019a). Zn is used as an antimicrobial material and can improve kidney and liver functions (Chrastinová et al., 2018; Fawaz et al., 2019b). Moreover, Zn contributes to the secretion and storage of insulin, has a role

in reproduction and growth, and can lead to better intestinal absorption (Chatterjea., 2009). Zn supplementation improves the physical characteristics of semen such as ejaculate volume, sperm motility, count, seminal plasma antioxidants, and fertility rate (Amen and Muhammad., 2016; El-Speiy and El-Hanoun., 2013; Ghasemi et al., 2009; and ElMasry et al., 1994). Most of the studies showed slight positive effects; however, significant results were rare. Since there are almost unlimited possibilities regarding the zinc dosage, further research is still required. Nano-sized zinc particles can be used at low doses, resulting in better outcomes than conventional zinc sources. This review provides an overview of and illustrates the positive effects of zinc nanoparticles and their potential application as a mineral supplement to rabbit diets.

2. *Properties of Nano-ZnO*

Nanominerals with dimensions less than 100 nm are known as nanomaterials which are stable under high pressure and temperature (Stoimenov et al., 2002). “Nano” means one-billionth of something (Ahemad., 2017). With a size range of 1–100 nm, nanomaterials occupy a position in many fields of nanoscience and nanotechnology because of their small size which makes them easily absorbed by the gastrointestinal tract (Feng et al., 2009). Organic and inorganic nanominerals interact more effectively in the animals’ digestive tract due to the larger surface area (Feng et al., 2009; Zaboli et al., 2013). Fawaz et al. (2019a) have concluded that Nano-ZnO could be a potential alternative to other sources of Zn, enhancing the performance and health status of poultry. Hillyer and Albrecht (2001) indicated that nanoparticles of minerals could be absorbed through the

small intestine into the blood and then into internal parts of the animal. Besides, Rosi and Mirkin (2005) discovered that the small particle size of the nanometals greatly affects the functional activities, such as chemical, biological, and catalytic effects of nanoparticles of minerals. Sharma et al. (2012), after 14 days, observed that Nano-ZnO was significantly retained in the liver subacute exposure and when orally administered in the gastrointestinal tract.

3. Recommendation Levels of Zinc in Rabbit Diets

Zn is an important nutrient for rabbits; 50 mg/kg of Zn is required for growing rabbits (NRC, 1977). However, Hassan et al. (2017) reported supplementing rabbit diets with 30 and 60 mg/kg Nano-ZnO and they observed that the optimal concentration is 60 mg Nano-ZnO/kg. Likewise, Ismail and El-Araby (2017) studied the effect of different sources of Zn (ZnO, Nano-ZnO, and the combination of ZnO and Nano-ZnO) at 60 mg/kg and showed that the best results were obtained with 60 mg/kg of the combination of ZnO and Nano-ZnO. Din and Noha (2019) added 30 and 60 mg/kg Nano-ZnO to rabbits' diet and concluded that the recommended level of Nano-ZnO is 60 mg/kg. Moreover, Hassan et al. (2016) added different levels of organic Zn (Zn-enriched spirulina (Zn-Sp)) at 50, 75, and 100 mg/kg to rabbit diets, noting that the best level was at 100 mg/kg. Yan et al. (2017) supplemented the diets with 80 mg/kg from different sources of Zn (ZnSO₄, Zn lactate, Zn methionine (Zn-Me), and Zn glycine) and recommended that Zn lactate is the best source of Zn used to improve the productive performance of rabbits. El-Moghazy et al. (2019) supplemented rabbit diets with 50,

100, and 150 mg/kg of Zn methionine for 8 weeks and recommended Zn-Me at 100 mg/kg. However, Ayyat and Marai (2000) used different concentrations of Zn at 100, 200, 300, and 400 mg/kg in rabbit feed and recommended the supplementation of 100 and 200 mg/kg. Meshreky et al. (2015) reported the supplementation of different concentrations of 100 and 200 mg/kg of ZnSO₄ and Zn-Me and recommended the 200 mg Zn-Me/kg diet. Elsisiet al. (2017) supplemented the male rabbit diets with ZnO at 100 mg/kg and indicated that this level was safe to be used.

4. Antibacterial Activity of Nano-ZnO

Many researchers have identified the antimicrobial action of Nano-ZnO. For example, Arabi et al. (2012) reported that antibacterial activity means a reagent significantly reduces bacteria growth or kills both Gram-positive and Gram-negative bacteria, without being toxic to the surrounding tissues. Bacteria treated with Nano-ZnO had a significant increase in bacteria permeability impacting proper transport throughout the plasma resulting in cell death (Auffan et al., 2009). Arabi et al. (2012) indicated that the antibacterial activity of Nano-ZnO depends on the surface area and concentration, whereas the particle crystalline structure and shape have little effect. However, the size is inversely proportional to the antimicrobial activity of Nano-ZnO, suggesting that the smaller the size of Nano-ZnO, the greater the antimicrobial activity (Shrivastava et al., 2007). Adams et al. (2006) found that nanoparticles have a larger surface area for interaction with the microbial surface to improve microbial effect than the large particles, due to their cytotoxicity to the microorganisms.

Many authors have reported Nano-ZnO mechanisms in acting against pathogenic bacteria. For example, Rajendran et al., (2010) showed that Nano-ZnO inactivate the proteins, in turn reducing the membrane permeability and result in cell death. Padmavathy and Vijayaraghavan (2008) reported that nanominerals slow down bacterial adhesion and biofilm formation. Arabi et al. (2012) found that Nano-ZnO penetrate the bacterial cell, causing cell damage due to the interaction with phosphorus- and sulfur-containing compounds such as DNA. Liu et al. (2009) reported that the inhibitory effect is directly proportional to Nano-ZnO concentrations which distort and destroy the bacterial cell membrane, resulting in intracellular contents leakage and then bacterial cells' death. Therefore, Nano-ZnO is a potential antibacterial agent in agricultural and food safety. Jin et al. (2009) reported that Nano-ZnO exhibited significant antimicrobial effects on three pathogens in growth media (*L. monocytogenes*, *Salmonella enteritidis*, and *E. coli* O157:H7). Nano-ZnO can be used in food systems to effectively inhibit certain pathogens. Arabi et al. (2012) demonstrated that there is another Nano-ZnO antibiotic mechanism indicate: microorganisms are negatively charged whereas metal oxides have a positive charge, creating an "electromagnetic" attraction between the microbe and treated surface; once they interact, the microbe is oxidized and dies instantly. The nonspecific mode of action of nanoparticles against bacteria makes them ideal candidates as antimicrobial agents without risk of developing bacterial resistance (Arabi et al., 2012). Complete bacterial inhibition depends upon the concentrations of Nano-ZnO and on the

number of bacterial cells. Thus, it is evident from the literature that Nano-ZnO have an excellent antibacterial effect and may be incorporated into animal feed as a growth-promoting agent or to prevent the occurrence of diseases. Future studies should investigate using Nano-ZnO as an alternative to conventional Zn sources in animal feed to minimize the use of in-feed antibiotics (Swain et al., 2016).

4. Effects of Nano-ZnO on feed intake and growth performance of rabbits

Several studies have been conducted to explore the effects of using Nano-ZnO on rabbit nutrition and productive performance. Several studies reported that zinc can enhance feed intake. For example, in Hassan et al.'s study (2017), daily feed intake was significantly increased ($p < 0.05$) in rabbit fed diet supplemented with 30 and 60 mg/kg Nano-ZnO compared to the control group. Yan et al. (2017) supplemented the feed with 80 mg/kg from different sources of Zn ($ZnSO_4$, Zn lactate, Zn-Me, and Zn glycine) and observed a significant improvement in average daily feed intake when 80 mg Zn lactate was added to the rabbit fed diet compared to 80 mg $ZnSO_4$ /kg. On the other hand, Hassan et al. (2016) noted that feed consumption was significantly decreased ($p < 0.05$) in rabbit fed diet supplemented with 75 and 100 mg/kg of organic Zn compared to the control group. Elsis, et al. (2017) found that feed intake was not affected in male rabbits fed a diet supplemented with zinc oxide at 100 mg/kg did not. Besides, El-Hamid et al. (2018) found that feed intake was significantly increased ($p < 0.05$) in male rabbits that consumed water with an added 100 mg Zn/liter at compared to the control group. After an 8-week feeding of rabbits diets including high levels of Zn

(100, 200, 300, and 400 mg/kg) no significant differences were observed in feed intake (Ayyat and Marai., 2000). Similarly, no change was observed in the daily feed intake of rabbit fed diet supplemented with different levels of Zn-Me from 50 up to 150 mg/kg (El-Moghazy et al., 2019). Amen and Muhammad (2016) supplemented rabbit diets with pure Zn (100 and 200 mg/kg) and reported that feed intake was not significantly affected. Besides, Meshreky et al. (2015) added different levels and sources of Zn (ZnSO₄ and Zn-Me) at 100 and 200 mg/kg and observed that feed intake was not affected. In another study, Selim et al. (2012) indicated that feed intake of rabbits was not significantly affected when fed diet included 50, 100, 200, and 400 mg/kg. According to previous work, there was no significant change in rabbit feed intake with a dose of 0.083 g/rabbit per day compared to the control group (Attia et al., 2015).

Many studies indicated that dietary treatments including different levels and sources of Zn significantly improved body weight gain as follows. Hassan et al. (2017) observed a significant improvement in daily body weight gain when rabbits consumed different levels of Nano-ZnO at 30 and 60 mg/kg compared to the control group. Besides, after a 60-day feeding, the body weight gain of rabbits fed diets including 20 and 40 mg/kg Zn salt was significantly enhanced compared to the control group (Alikwe et al., 2011). Similarly, Hassan et al. (2016) indicated that daily body weight gain was significantly increased in rabbits fed diet with 75 and 100 mg/kg compared to the control group. Thus, average daily body weight gain was significantly increased in rabbits fed diet

with 80 mg/kg Zn lactate added compared to 80 mg ZnSO₄/kg (Yan et al., 2017). In another study, daily body weight gain was significantly increased in rabbit fed diet supplemented with 100 mg/kg ZnO compared to the control group (Al-Sagheer et al., 2020). Thus, Ayyat and Marai (2000) added high levels of Zn (100, 200, 300, and 400 mg/kg) to rabbit diets and observed a significant increase in body weight gain compared to the control group. Additionally, El-Moghazy et al. (2019) found a significant improvement ($p < 0.0001$) in average daily body weight gain with rabbit fed diet with 50, 100, and 150 mg/kg Zn-Me compared to the control group. Body weight gain was significantly increased with a diet supplemented with 100 and 200 mg pure Zn/kg compared to the control group (Amen and Muhammad., 2016). According to a previous study, after 22 weeks of feeding including 100 and 200 mg/kg of ZnSO₄ and Zn-Me, the body weight gain of rabbits significantly increased (Meshreky et al., 2015). Moreover, diets including 100 mg/kg of ZnO significantly improved body weight gain of rabbits compared to the control group (Al-Sagheer et al., 2020). This result was in line with Elsis., et al. (2017) who observed a significant increase ($p < 0.001$) in body weight gain of male rabbits fed diet with 100 mg/kg compared to the control group. El-Hamid et al. (2018) demonstrated that body weight gain was improved ($p < 0.05$) in male rabbits that consumed water with 75 and 100 mg Zn/liter compared to the control treatment. Uniyal, S. (2015) found that average daily body weight gain was significantly increased with rabbit diets supplemented with 20 ppm commercial

zinc nanoparticles when compared to other groups.

However, Selim et al. (2012) found that body weight gain was not significantly different in rabbit fed diet including 50, 100, 200, and 400 mg/kg. Additionally, in another study, no significant difference was observed in the final body weight with a dose of 0.083 g/rabbit per day for 81 days (Attia et al., 2015).

Hassan et al. (2016) observed a significantly improved feed conversion ratio (FCR) of rabbit fed diet supplemented with 50, 75, and 100 mg/kg compared to the control group. Besides, FCR was significantly improved in rabbit fed diet supplemented with 80 mg/kg Zn lactate compared to 80 mg ZnSO₄/kg (Yan et al., 2017). Diets including pure Zn at 100 and 200 mg/kg significantly improved the FCR of rabbits compared to the control diet (Amen and Muhammad., 2016). Furthermore, Meshreky et al. (2015) noted that FCR was significantly decreased in rabbit fed diet with 100 and 200 mg/kg of ZnSO₄ and Zn-Me compared to the control group. Similarly, Elsis, et al. (2017) found that FCR was significantly lower ($p < 0.001$) in male rabbit fed diet with 100 mg/kg of ZnO compared to the group without supplementation. Additionally, El-Hamid et al. (2018) observed that FCR was improved in male rabbit consumed water with 75 and 100 mg /liter compared to the control treatment.

On the other hand, Hassan et al. (2017) supplemented the feed with 30 and 60 mg/kg Nano-ZnO and noted that the FCR was not affected in rabbits compared to the control group. After an 8-weeks feeding on 50, 100, and 150 mg Zn-Me/kg rabbit diet, FCR was not affected

(El-Moghazy et al., 2019). Selim et al. (2012) observed that FCR was not significantly affected in rabbits fed diet including 50, 100, 200, and 400 mg/kg. In another study, after 81 days, there were no significant differences in FCR of rabbits given a dose of 0.083 g/rabbit per day compared to the control group (Attia et al., 2015). After an 8-week feeding, rabbits' diets including high levels of Zn (100, 200, 300, and 400 mg/kg) had been nonsignificant effects in FCR (Ayyat and Marai., 2000).

5. Effects of Nano-ZnO on Nutrient Digestibility of rabbits

Supplemented the diets with different levels of Zn-Sp of 50, 75, and 100 mg/kg and noted that the digestibility of dry matter, organic matter, crude protein, and ether extract was significantly improved in rabbit fed diet with 100 mg/kg compared to the control group (Hassan et al., 2016). Likewise, Meshreky et al. (2015) found that rabbits fed diets supplemented with Zn-Me or ZnSO₄ of 100 or 200 mg/kg diet improved nutrients digestibility and nutritive, that is, the total digestible nutrients and digestible crude protein. In addition, Elsis et al. (2017) found that the digestibility of dry matter and crude protein was significantly improved ($p < 0.05$) in male rabbit fed 100 mg/kg of ZnO compared to the control. Moreover, Al-Sagheer et al. (2020) reported a significant increase in crude protein and dry matter digestibility in rabbit fed 100 mg/kg ZnO compared to the control group. Similarly, Pinheiro et al. (2004) discovered that the digestibility of crude protein, fat, organic matter, and dry matter was not significantly affected in rabbit fed a 0.1 g Zn bacitracin/kg diet. Shinde et al. (2006) observed that

supplementation of 20 mg/kg of Zn did not significantly affect the nutrient digestibility of pigs compared to the control group. Attia et al. (2015) noticed a significant improvement in crude protein and ether extract digestibility of rabbit given a dose of 0.083 g/rabbit per day; however, ash and dry matter were not affected compared to the control group.

On the other hand, Din and Noha (2019) found that the digestibility of dry matter, crude fiber, crude protein, and ether extract was not significantly affected in rabbit fed diet supplemented with 30 and 60 mg/kg Nano-ZnO. Besides, Uniyal et al. (2017) noted that there were no significant differences observed in nutrient digestibility (dry matter, crude fiber, crude protein, and ether extract) in guinea pigs fed 20 mg/kg of different sources of Zn (ZnSO₄, Nano-ZnO, and Zn-Me).

6. Effects of Nano-ZnO on Carcass Criteria of rabbits

Hot carcass weight and dressing percentage were significantly increased; however, liver weight was significantly decreased in rabbit fed diet with 75 and 100 mg/kg compared to the control group (Hassan et al., 2016). Besides, Al-Sagheer et al. (2020) found a significant increase in carcass weight of rabbit fed diet supplemented with 100 mg/kg; however, liver, kidney, and heart were not different compared with the control group. Diets including 100 mg/kg ZnO did not affect carcass weight, liver, kidney, and heart in male rabbits (Elsisi, et al., 2017). In another study, dressing and liver and kidney percentages were not significantly different in rabbits fed 50, 100, 200, and 400 mg kg⁻¹ ZnO diet compared the control group (Selim et al., 2012).

7. Effects of Nano-ZnO on Blood biochemistry of rabbits

Plasma creatinine concentration did not change in rabbit fed diet supplemented with 30 and 60 mg/kg (Din and Noha., 2019). Additionally, Uniyal et al. (2017) found that serum creatinine concentration was not significantly affected in guinea pigs fed 20 mg/kg Zn, Nano-ZnO, and Zn-Me for 90 days. On the other hand, El-Moghazy et al. (2019) supplemented the diets with different levels of Zn-Me of 50, 100, and 150 mg/kg and observed a significant decrease in creatinine concentration in rabbit fed diet with 50 and 100 mg Zn/kg compared to the control group. Similarly, El-Hamid et al. (2018) found that the serum concentration of creatinine significantly decreased in male rabbits consumed water with 75 and 100 mg Zn/liter compared to the control group. After a 90-day feeding of 30, 40, and 60 mg Nano-ZnO/kg, the serum content of creatinine was linearly decreased ($p < 0.001$) with increased Zn level when compared to the control group (Fawaz et al., 2019b). However, Ismail and El-Araby (2017) observed a significant increase in plasma content of creatinine in rabbit fed diet with 60 mg/kg Nano-ZnO compared to the control group.

Uniyal et al. (2017) found that serum alkaline phosphatase concentration was not affected in guinea pigs fed diet with 20 mg/kg ZnSO₄, Nano-ZnO, and Zn-Me compared to the control group.

Hassan et al. (2016) showed that aspartate aminotransferase (AST) was not affected in rabbit fed different levels of Zn-Sp at 50, 75, and 100 mg/kg. Similarly, Din and Noha (2019) observed that AST concentration was not affected in rabbit fed 30 and 60 mg Nano-ZnO/kg.

Moreover, Al-Sagheer et al. (2020) indicated that rabbit fed diet with 100 mg/kg of ZnO did not affect AST enzyme serum concentration. Besides, Elsisy et al. (2017) suggested that the serum concentration of AST was not different in male rabbit fed diet supplemented with 100 mg/kg ZnO compared to the control group. El-katcha et al. (2018) found that AST enzyme concentrations were reduced in laying hens fed diet supplemented with 30 mg of Nano-ZnO/kg. Furthermore, Fawaz et al. (2019b) observed a linear decrease ($p < 0.001$) in AST concentration in hens compared to the control group.

In other studies, El-Masry et al. (1994) found that serum concentration of glutamic oxaloacetic transaminase was significantly decreased in rabbit fed diet with 35 mg/kg of Zn at compared to the control group. Similarly, El-Hamid et al. (2018) noted that the serum content of AST was lower ($p < 0.05$) in male rabbit consumed water supplemented with 75 and 100 mg Zn/liter than that of the control group.

In contrast, Fazilati (2013) indicated that the serum content of the AST enzyme was significantly increased ($p < 0.05$) in male rats fed 25–200 mg/kg Nano-ZnO. Attia et al. (2015) found a significant increase in plasma content of AST enzyme in rabbit h given a dose of 0.083 g/rabbit per day, compared to the control group. Similarly, Ismail and El-Araby (2017) indicated that the plasma concentration of AST was significantly higher ($p < 0.001$) with ZnO treatment than the control group.

Many studies observed that diets including different levels and sources of Zn significantly influenced the sexual hormones levels. Zn is required to

improve testicular performance, as Zn deficiency leads to decreased testicular growth rate in bull calves (Miller and Miller., 1962; Pitts et al., 1966). El-Masry et al. (1994) noted that serum concentration of testosterone was significantly increased ($p < 0.01$) in rabbit males fed diet supplemented with 35 mg/kg Zn enhancing sperm concentration and sperm motility compared to the control group. Besides, Jalali et al. (2010) observed that plasma concentration of testosterone and serum luteinizing hormone (LH) concentration were significantly increased in male patients treated with 250 mg/day of Zn sulfate; however, follicle-stimulating hormone (FSH) was not affected. Moreover, Dissanayake et al. (2009) found that serum testosterone level was significantly increased ($p < 0.05$) in male rats fed diets supplemented with oral Zn sulfate at 5 mg/day for two weeks compared to rats without treatment. Zn deficiency reduces angiotensin-converting enzyme activity and this leads to inhibition of spermatogenesis and depletion of testosterone (Bedwal and Bahuguna., 1994). Baiomy et al. (2018) reported a significant increase in ejaculate volume, sperm concentration, and fertility rate in rabbit fed diet with 75 and 150 ppm ZnO/kg diet to the group without supplementation. Furthermore, Ogbu and Ezeokoli (2016) and Moce et al. (2000) observed an improvement in the reproductive performance of rabbits fed diet with Zn recording greater ($p \leq 0.05$) ejaculate volume, sperm motility, and fertility rate than those of the control group. This improvement is based on the low sperm count and high percentage and motility of abnormal spermatozoa levels (Raji et al., 2003).

There is also some evidence that Zn is required for the normal functioning of the hypothalamic-pituitary-gonadal axis. Zn supplementation is reported to increase the serum testosterone level in crossbred bulls (Kumar, 2003). In competition studies between Zn and Cu and Fe for membrane binding sites, the potential for the formation of hydroxyl radicals via redox cycling is reduced (Zago and Oteiza, 2001). High levels of seminal reactive oxygen species (ROS) may decrease the effective concentration of seminal Zn (Powell, 2000). Several studies indicated that a decrease in Zn concentration may lead to an increase in oxidation of DNA, proteins, and lipids, causing the loss of spermatozoa membrane integrity and Zn has an important role in inhibiting seminal oxidative stress (Oteiza et al., 1995; Marzec-Wróblewska et al., 2012).

Conclusions

The role of Zn in the animal system is well established and documented. However, Zn from conventional sources is of less benefit to the body and As a consequence, it is mostly excreted to the environment causing environmental pollution. Nano-ZnO is considered a suitable alternative to conventional Zn sources to be used in livestock feeding. Apart from being highly bioavailable, reports have pointed out the growth-promoting, antibacterial, immunomodulatory, and many other beneficial effects of Nano-ZnO, serving all the purposes of the conventional Zn sources and helps in all the physiological functions. Thus, Nano-ZnO may be used at 60 mg/kg in rabbit feed to provide better results than the conventional Zn

sources, indirectly preventing environmental contamination.

References

- Ahemad, M.A.M.N. (2017) 'Effect of dietary nano zinc oxid supplementation on performance of broilers' M.Sc. *Maharashtra Animal and Fishery Sciences University, Nagpur- 440 001. (India).*
- Alikwe, P., Ojiezeh, T. and Olagboye, S. (2011) 'Effects of zinc supplement on rabbits performance and growth rate' *Journal of Agriculture and Social Research, 11:pp. 46-50.*
- Al-Sagheer, A.A., Abdel-Rahman, G., Ayyat, M.S., Gabr, H.A., and Elsisy, G.F. (2020) 'Productive performance response of growing rabbits to dietary protein reduction and supplementation of pyridoxine, protease, and zinc' *Anais da Academia Brasileira de Ciências, 92(3).*
- Amen, M.H.M., and Muhammad, S.S. (2016) 'Effect of zinc supplementation on some physiological and growth traits in local male rabbit' *World Veterinery Journal, 6(3):pp. 151-155.*
- Arabi, F., Imandar, M., Negahdary, M., Imandar, M., Noughabi, M.T., and Akbari-dastjerdi, H., (2012) 'Investigation anti-bacterial effect of zinc oxide nanoparticles upon life of *Listeria monocytogenes*' *Annals of Biological Research 3:pp. 3679-85.*
- Attia, Y., Hamed, R., Abd El-Hamid, A., Shahba, H., and Bovera, F. (2015) "Effect of inulin and mannan-oligosaccharides compared with zinc-bacitracin on growing performance, nutrient digestibility and hematological profiles of growing

- rabbits" *Animal Production Science*, 55(1):pp. 80-86.
- Ayyat, M., and Marai, I. (2000) 'Growth performance and carcass traits as affected by breed and dietary supplementation with different zinc levels, under Egyptian conditions' *Paper presented at the Proceedings of the 8th World Rabbit Congress, Puebla. Colegio de Postgraduados, Montecillo, Spain. Volume C, pp. 83-88*
- Baiomy, A., Hassanien, H. and Emam. K. (2018) 'Effect of zinc oxide levels supplementation on semen characteristics and fertility rate of bucks rabbits under subtropical conditions' *Egyptian Journal of Rabbit Science*, 28:pp. 395-406.
- Bedwal, R., and Bahuguna, A. (1994) 'Zinc, copper and selenium in reproduction.' *Experientia*, 50(7):pp. 626-640.
- Chatterjea, M.N. (2009) 'Textbook of biochemistry' Jaypee Brothers Medical publishers (P) Ltd. 3rd Edition. New Delhi – India.
- Chrastinová, E., Čobanová, K., Chrenková, M., Poláčiková, M., Formelová, Z., Lauková, A., . . . Bučko, O. (2015) 'High dietary levels of zinc for young rabbits' *Slovak Journal of Animal Science*, 48(2):pp 57-63.
- Chrastinová, E., Lauková, A., Chrenková, M., Formelová, Z., Poláčiková, M., Glatzová, E.B., Rajský, M. (2018) 'Efficacy of feed additives on meat quality and numbers of faecal bacteria in growing rabbits' *Journal of Agronomy*, 20. Vol. 1(1): pp. 110-118
- Din, T.-E., and Noha, T. (2019) 'Effects of dietary nano-zinc and nano-selenium addition on productive and physiological performance of growing rabbits at fattening period' *Egyptian Journal of Nutrition and Feeds*, 22(1): pp. 79-89.
- Dissanayake, D., Wijesinghe, P., Ratnasooriya, W., and Wimalasena, S. (2009). 'Effects of zinc supplementation on sexual behavior of male rats' *Journal of human reproductive sciences* 2 (2): pp. 57-61
- El-Katcha, M.I., Soltan, M.A., Arafa, M.M., and Kawarei, E.-S.R. (2018) 'Impact of Dietary Replacement of Inorganic Zinc by Organic or Nano Sources on Productive Performance, Immune Response and Some Blood Biochemical Constituents of Laying Hens' *Alexandria Journal for Veterinary Sciences* 59, 59(1): pp. 48-59
- El-Hamid, A., El-Speiy, M., Hassan, S., and Habbibe, M. (2018) 'Performance, immunity response, blood biochemical and hematological traits of growing male rabbits affected by type water with zinc' *Egyptian Journal of Rabbit Science*, 28(1): pp. 129-155.
- El-Masry, K., Nasr, A., and Kamal, T. (1994) 'Influences of season and dietary supplementation with selenium and vitamin E or zinc on some blood constituents and semen quality of New Zealand white rabbit males' *World Rabbit Science*, 2(3): pp. 79-86.
- El-Moghazy, M., El-Fadaly, H., Khalifa, E., and Mohamed, M. (2019) 'Effect of dietary zinc-methionine on growth, carcass traits, antioxidants and immunity of growing rabbits' *Journal of Animal and Poultry Production*, 10(3): pp. 59-66.

- Elsisi, G.F., M. Ayyat, H. Gabr, and El-Rahman, A. (2017) 'Effect of dietary protein levels and zinc supplementation on growth performance, digestibility, blood constituents and carcass traits of growing rabbits' *Zagazig Journal of Agricultural Research*, 44: pp. 1369-1378.
- Fawaz, M., Abdel-Wareth, A.A.A., Hassan, H., and Südekum, K. (2019b) 'Applications of nanoparticles of zinc oxide on productive performance of laying hens' *SVU-International Journal of Agricultural Sciences*, 1(1): pp. 34-45.
- Fawaz, M., Südekum, K., Hassan, H., and Abdel-Wareth, A.A.A. (2019a) 'Effects of nanoparticles of zinc oxide on productive performance of laying hens.—a review' *SVU-International Journal of Agricultural Sciences*, 1(1): pp. 13-20.
- Hassan, F.A., Amin, F.H., Ali, W.A., El-Aasar, T.A. and Azoz, A.A. (2016) 'Effect of dietary addition of zinc enriched spirulina on growth and physiological performance in growing rabbits' *Egyptian Journal of Rabbit Science*, 26(2): pp. 155-173
- Fazilati, M. (2013) 'Investigation toxicity properties of zinc oxide nanoparticles on liver enzymes in male rat' *European Journal of Experimental Biology*, 3: pp. 97-10.
- Feng, M., Wang, Z., Zhou, A., and Ai, D. (2009) 'The effects of different sizes of nanometer zinc oxide on the proliferation and cell integrity of mice duodenum-epithelial cells in primary culture' *Pakistan Journal of Nutrition*, 8(8):pp. 1164-1166.
- Gerloff, K., Albrecht, C., Boots, A.W., Förster, I., and Schins, R.P. (2009) 'Cytotoxicity and oxidative DNA damage by nanoparticles in human intestinal Caco-2 cells' *Nanotoxicology*, 3(4): pp. 355-364.
- Ghasemi, N., Babaei, H., Azizollahi, S., and Kheradmand, A. (2009) 'Effect of long-term administration of zinc after scrotal heating on mice spermatozoa and subsequent offspring quality' *Andrologia*, 41(4): pp. 222-228.
- Hassan, F.A., Mahmoud, R., and El-Araby, I.E. (2017) 'Growth performance, serum biochemical, economic evaluation and IL6 gene expression in growing rabbits fed diets supplemented with zinc nanoparticles' *Zagazig Veterinary Journal*, 45(3):pp. 238-249.
- Hillyer, J.F., and Albrecht, R.M. (2001) 'Gastrointestinal persorption and tissue distribution of differently sized colloidal gold nanoparticles' *Journal of pharmaceutical sciences*, 90(12):pp. 1927-1936.
- Jalali, G.R., Roozbeh, J., Mohammadzadeh, A., Sharifian, M., Sagheb, M.M., Jahromi, A.H., Afshariani, R. (2010). 'Impact of oral zinc therapy on the level of sex hormones in male patients on hemodialysis' *Renal failure*, 32(4): pp. 417-419.
- Ismail, H.T.H., and El-Araby, I.E. (2017) 'Effect of dietary zinc oxide nanoparticles supplementation on biochemical, hematological and genotoxicity parameters in rabbits' *International Journal of Current Advanced Research*, 6;2: pp. 2108-2115.
- Kumar, R., Singh, G. and R. Misra. (2003) 'Effect of boron, calcium and zinc on gladiolus' *Journal of*

- Ornamental Horticulture*, 6: pp. 104-106.
- Marzec-Wróblewska, U., Kamiński, P. and Łakota, P. (2012) 'Influence of chemical elements on mammalian spermatozoa' *Folia Biol (Praha)*, 58: pp. 7-15.
- McDowell, L.R. 2003 'Minerals in animal and human nutrition (Second Edition)' *Elsevier Science BV, ISBN: 978-0-444-51367-0*.
- Meshreky, S.Z., Allam, S.M., El-Manilawi, M., and Amin, H. (2015) 'Effect of dietary supplemental zinc source and level on growth performance, digestibility coefficients and immune response of new zealand white rabbits' *Egyptian Journal of Nutrition and Feeds*, 18(2 Special): pp. 383-390.
- Miller, J.K., and Miller, W.J. (1962). 'Experimental zinc deficiency and recovery of calves' *The Journal of nutrition*, 76(4):pp. 467-474.
- Moce, E., Arouca, M., Lavara, R. and Pascual, J. (2000) 'Effect of dietary zinc and vitamin supplementation on semen characteristics of high growth rate males during summer season' *Paper presented at the Proceeding Valencia, World Rabbit Congress. Volume A*, pp. 203-209.
- NRC, (1977) 'Nutrient requirement of rabbits' *National Academic of Sciences, National Research Council, Washington, DC, USA*.
- Ogbu, O.A.C. and Ezeokoli, N.C. (2016) 'Supplementary Doses of Zinc: Effects on Male Rabbit Hormonal Levels' *Proc. 21st Ann. Con. Animal Science Association of Nigeria* 18 – 22, Port Harcourt.
- Oteiza, P.I., Olin, K.L., Fraga, C.G. and C.L. Keen. (1995) 'Zinc deficiency causes oxidative damage to proteins, lipids and DNA in rat testes' *The Journal of nutrition* 125: pp. 823-829.
- Padmavathy, N. and Vijayaraghavan, R. (2008) 'Enhanced bioactivity of ZnO nanoparticles- an antimicrobial study' *Sci Technol Adv Mater*, 9: pp. 1-7.
- Piccinno, F., Gottschalk, F., Seeger, S., and Nowack, B. (2012) 'Industrial production quantities and uses of ten engineered nanomaterials in Europe and the world' *Journal of Nanoparticle Research*, 14(9): pp. 1109.
- Powell, S.R. (2000) 'The antioxidant properties of zinc' *The Journal of nutrition* 130: pp. 1447S-1454S.
- Pitts, W., Miller, W., Fosgate, O., Morton, J., and Clifton, C. (1966). 'Effect of zinc deficiency and restricted feeding from two to five months of age on reproduction in Holstein bulls' *Journal of Dairy Science*, 49(8): pp. 995-1000.
- Raji, Y., Udoh, U., Mewoyeka, O., Ononye, F., and Bolarinwa, A. (2003) 'Implication of reproductive endocrine malfunction in male antifertility efficacy of Azadirachta indica extract in rats' *African journal of medicine and medical sciences*, 32(2): pp. 159-165.
- Rosi, N. L., and Mirkin, C. A. (2005) 'Nanostructures in biodiagnostics' *Chemical reviews*, 105(4): pp. 1547-1562.
- Sahoo, A., Swain, R.K. and Mishra, S.K. (2014b) 'Effect of inorganic, organic and nano zinc supplemented diets on bioavailability and immunity status of broilers' *International Journal of Advanced Research* 2: pp. 828-37.
- Selim, N., Abdel-Khalek, A., and Gad, S. M. (2012) 'Effect of supplemental

- zinc, magnesium or iron on performance and some physiological traits of growing rabbits' *Asian Journal of Poultry Science*, 6(1): pp. 23-30.
- Sharma, V., Singh, P., Pandey, A.K., and Dhawan, A. (2012) 'Induction of oxidative stress, DNA damage and apoptosis in mouse liver after sub-acute oral exposure to zinc oxide nanoparticles' *Mutation Research/Genetic Toxicology and Environmental Mutagenesis*, 745(1-2): pp. 84-91.
- Shinde, P., Dass, R.S., Garg, A.K., Chaturvedi, V.K. and Kumar, R. (2006) 'Effect of zinc supplementation from different sources on growth, nutrient digestibility, blood metabolic profile, and immune response of male Guinea pigs' *Biological trace element research*, 112(3): pp. 247-262.
- Sindhura, K.S., Prasad, T., Selvam, P.P. and Hussain, O. (2014) 'Synthesis, characterization and evaluation of effect of phytogenic zinc nanoparticles on soil exo-enzymes' *Applied Nanoscience*, 4(7): pp. 819-827.
- Stoimenov, P.K., Klinger, R.L., Marchin, G.L. and Klabunde, K.J. (2002) 'Metal oxide nanoparticles as bactericidal agents' *Langmuir*, 18(17): pp. 6679-6686.
- Swain, P.S., Rajendran, D., Rao, S., and Dominic, G. (2015) 'Preparation and effects of nano mineral particle feeding in livestock: A review' *Veterinary world*, 8(7): 888.
- Uniyal, S., Garg, A.K., Jadhav, S.E., Chaturvedi, V.K. and Mohanta, R.K. (2017) 'Comparative efficacy of zinc supplementation from different sources on nutrient digestibility, hemato-biochemistry and anti-oxidant activity in guinea pigs' *Livestock Science*, 204:pp. 59-64.
- Wang, B., Feng, W.Y., Wang, T.C., Jia, G., Wang, M., Shi, J.W. (2006) 'Acute toxicity of nano-and micro-scale zinc powder in healthy adult mice' *Toxicol Lett*, 161:pp. 115-23.
- Yan, J., Zhang, G., Zhang, C., Tang, L., and Kuang, S. (2017). 'Effect of dietary organic zinc sources on growth performance, incidence of diarrhoea, serum and tissue zinc concentrations, and intestinal morphology in growing rabbits' *World Rabbit Science*, 25 (1): pp. 43-49.
- Wang, Z.L. (2000) 'Characterization of nanophase materials' *Part Part Sys Char* 18(3):142-165.
- Zaboli, K., Aliarabi, H., Bahari, A.A., and Abbas, A.K.R. (2013) 'Role of dietary nano-zinc oxide on growth performance and blood levels of mineral A study on in Iranian Angora (Markhoz) goat kids' *Journal of Pharmaceutical and Health Sciences*, 2(1): pp. 19-26.
- Zago, M.P. and Oteiza, P.I. (2001) 'The antioxidant properties of zinc: interactions with iron and antioxidants' *Free Radical Biology and Medicine*, 31: pp. 266-274.
- Zhao, C.-Y., Tan, S.-X., Xiao, X.-Y., Qiu, X.-S., Pan, J.-Q., and Tang, Z.-X. (2014) 'Effects of dietary zinc oxide nanoparticles on growth performance and antioxidative status in broilers' *Biological trace element research*, 160(3): pp. 361-367.