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Effect of zinc oxide nanoparticles and zinc oxide on clinical, hemato-biochemical, body weight, trace elements and wool zinc changes in lambs

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ABSTRACT

This study aimed to compare between the effect of zinc oxide nanoparticles (NPs) and zinc oxide on clinical, body weight, hematological and biochemical changes in lambs. we used thirty-five Rahmani weaned lambs at Animal Production Research Institute (APRI), in Serwa station, Damietta for six weeks. The lambs were randomized into seven groups (each of five). Group A received no treatment (control). Group B (mixed small dose) received 15 ppm ZNO NPs and 15 ppm ZNO. Group C received 30 ppm ZNO NPs. Group D received 30 ppm ZNO. Group E (mixed large dose) received 30 ppm ZNO NPs and 30 ppm ZNO. Group F received 60 ppm ZNO NPs. Group G received 60 ppm ZNO. All parameters were determined at zero day before starting to feed on the experimental ration and after the 6th week. Wool samples were collected for monitoring zinc, copper, and calcium. It was concluded that small doses of zinc oxide nanoparticles can be used for treatment of zinc deficiency in lambs, improving plasma and wool trace element profile and the hematobiochemical picture. It also improved the body weight gain and increased growth rate in growing lambs with minor adverse effect on liver and kidney functions.

1. INTRODUCTION

In ruminants the zinc is very vital trace element (Mandal et al., 2007). Zn affects growth, immune state, and reproduction by enhancing enzyme acting of all animals (Chesters, 1997). Also, required to activation of many enzymes and is necessary for RNA, DNA formation and absorbing of amino acids in lambs (McDowell, 1995). Likewise, Zn mends the hoof and wool quality (Kessler et al. 2003). It's main for activation of some hormones containing insulin, hormone of growth and many sex hormones. Zn is not stocked in the animal body and should be added daily in animal diet (Zalewski et al. 2005).

Signs of an absence in Lambs may reduce of feed intake. (McDowell et al., 1993), reduction of growth rate, decrease immune state in growing lambs (Droke and Spears 1993), loss the hair around the eye and mouth, and inflammation of skin around the nose, eye and mouth and Para keratosis. these signs determined by Ott et al. (1964).

This work aims to monitor the Effect of Zinc Oxide Nanoparticles and Zinc Oxide on Clinical, Hemato-biochemical, Body weight, Trace elements and Wool zinc changes in lambs.

2. MATERIAL AND METHODS

2.1. Animals and experimental design:

The experiment was conducted from June to August 2021 on thirty-five dewormed and de-ticked Rahmani weaned lambs with average weight (15-16 kg) and average age (2-3 months) at Animal production research institute (APRI) from Agricultural research center (ARC) in Elserw Station - Damietta. The lambs were randomized into seven groups (each of five). Group A received no treatment and kept as control. The other 6 groups received either small (30 ppm) or large (60 ppm) doses of ZNO or ZNO NP alone or mixture of them. Live body weight of lambs was recorded Biweekly. The ration content and structure are shown in Table (1). The experiment was approved under the ethical number (BUFVTM 03-03-22).

Table 1 Chemical Composition of feed stuffs to lambs.

Item	Moisture content	Dry Matter %						Chemical composition		
		OM	CP	CF	EE	NFE	Ash	Zn mg/kg	Cu mg/kg	Ca %
Concentrate feed mixture (CFM)	9.3	92.7	14.6	15.1	4.9	58.1	7.3	4.5	2.3	0.80
Rice straw	9.1	84.1	4.0	33.4	1.6	45.1	15.9	2.6	2.0	0.28
Total	18.4	176.8	18.6	48.5	6.5	103.2	23.2	7.1	4.3	1.08

OM: Organic Mater, CP: Crude Protein, CF: Crude Fiber, EE: Either Extract, NFE: Nitrogen Free extract Daily requirement of Zn:20-33 (mg/kg DM of diet). Daily Requirement of Cu: 7-11 (mg/kg DM of diet). Daily Requirement of Ca: 0.20 – 0.82 (mg/kg DM of diet).

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2.2. Preparation and administration of ZNO NPs and ZNO:
Lambs received Nano zinc oxide (ZNO NPs) and zinc oxide (ZNO) from Nawah scientific company which carried by corn starch as a carrier and given orally for 2 months (daily) as a tablet. During the first 2 weeks, lambs received 1.17 g of starch as a tablet orally (daily in early morning). During the second week to sixth week, lambs received 1.20 g of starch as a tablet orally (daily in early morning). In the control group lambs received 1.17 of starch only as a tablet orally (daily in early morning). During the second week to sixth week, lambs received 1.20 g of starch only as a tablet orally (daily in early morning).

2.3. Samples
Blood samples were collected from all animals for CBC analysis. The plasma was separated to measure plasma zinc, copper, and calcium. Serum samples were collected in clean dry labeled Eppendorf tubes and freeze until biochemical analysis to determine the liver and kidney function (AST, ALT, urea, creatinine, total protein, albumin, and globulin). Wool samples (weighing 5 g) were collected by cutting from the left side of lambs, the samples were subjected to cleaning process for removal of foreign substance and washed in warm water with detergent then washed twice in distilled water then left for drying.

2.4. Hematological analysis:
Hemoglobin concentration (Hb), total erythrocytic count (RBCs) total leukocytic count (WBCs) and differential leukocytic counts were determined by Abacus 380 hematology analyzer (Diatron MI PLC. Hungary) (Feldman et al., 2000).

2.5. Biochemical analysis
Urea, creatinine, AST, ALT, total protein, albumin and globulin were determined by spectrophotometer using VITROS 350 AT chemistry system and specific diagnostic kits (Ortho-clinical diagnostic, Inc.). The plasma zinc, copper, calcium, the wool zinc, copper, calcium were determined by ICP MS-MS 8800 (AOAC, (2019).

2.6. Statistical analysis:
Statistical analysis was performed by Costat (version 6:311, CoHort software 798 lighthouses Ave.PMB 320, Monterey, C A, 93940, USA) by using the least significant difference test (LSD). The results were represented as means ± standard deviation (SD) Significant difference was considered when the probability value (P) was less than 0.05.

3. RESULTS

Clinical examination
There was a significant increase ($P < 0.05$) in heart rate of the control group on the 6th week compared to day zero values. There was a significant decrease in heart rate in the groups received small and large single and mixed doses of the ZnO NPs and ZnO compared to zero values. There were no significant changes in body temperature and respiratory rate among the groups (Table 2).

Changes in body weight gain
A significant increase in body weight gain on the 2nd, 4th, and 6th week of lambs in all groups received single and mixed small and large doses of ZnO NPs and ZnO compared with the control group (Table 3).

Table 2 Changes in clinical signs parameters of lambs received different doses of Zinc oxide and Zinc oxide Nano Particles before and after six weeks.

Treatments Parameters	Control		Mixed small dose		30 ZNO NPs		30 ZNO		Mixed large dose		60 ZNO		60 ZNO NPs	
Time periods	Day zero	6 W	Day zero	6 w	Day zero	6 W	Day zero	6 W	Day zero	6 W	Day zero	6 W	Day zero	6 W
Temp (°C)	9.0±0.1a	8.5±0.1a	8.8±0.3a	38.5±0.3a	9.0a±0.3	8.7±0.3a	8.9±0.2a	8.6±0.3a	9.0±0.2a	8.4±0.3a	9.0±0.3a	8.6±0.1a	39.0±0.3a	38.8±0.3a
Heart Rate (beats/minute)	78b±1	81±1a	80±2a	76±3b	84a±4	80±5b	80±3a	75±3b	81±3a	75±4b	82±2a	79±2b	79±3a	75±2b
Resp. Rate (breaths/minute)	20a±1	18±1a	20±1a	19±1a	20a±2	19±1a	21±2a	19±2a	20±2a	18±1a	21±2a	20±1a	19±2a	18±2a

The results are presented as means± SD. Different letters of the same row indicated significant changes at P< 0.05.

Table 3 Changes in body weight gain in lambs received different doses of Zinc oxide and Zinc oxide Nano Particles after 2nd, 4th, and 6th weeks.

Treatments Weight gain	Control	Mixed small dose	30 ZNO NPs	30 ZNO	Mixed large dose	60 ZNO NPs	60 ZNO
2 weeks	0.8±0.3b	1.5±0.5a	1.3±0.3a	1.6±0.4a	1.5±0.3a	1.6±0.4a	1.6±0.2a
4 weeks	1.5±0.3b	2.5±0.9a	2.8±0.5a	2.7±0.4a	2.5±0.3a	3±0.6a	3.2±0.5a
6 weeks	2.2±0.4b	4±0.94a	4.5±0.52a	2.4±0.56a	3.9±0.25a	4.4±0.63a	4.6±0.61a

The results are presented as mean ± SD. Different letters of the same row indicated significant changes at P< 0.05

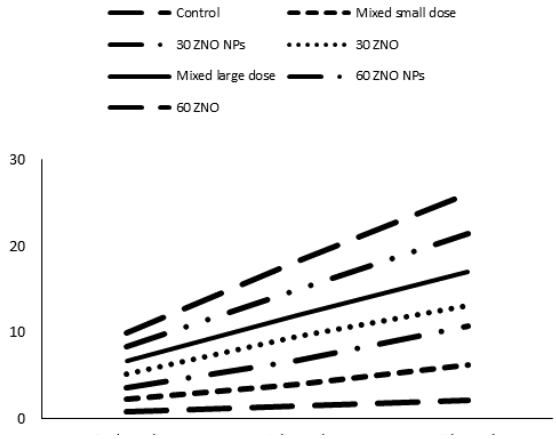

Figure 1: Changes in body weight gain in lambs received different levels of ZnO and ZnO NPs

Hematological findings

The Hb concentration in lambs of the control group showed a significant decrease on the 6th week compared to day zero-day. The Hb in lambs received (small mixed dose), (30 ZnO NPS), (30 ZNO), (large mixed dose), (60 ZNO NPS) and (60 ZNO) showed a significant increase on the 6th week compared to zero values. The RBCs count in lambs of the control group showed a significant decrease in the 6th week compared to zero values. The RBCs count in lambs received (small mixed dose), (30 ZnO NPS), (30 ZNO), (large mixed dose), (60 ZnO NPS) and (60 ZNO) showed a significant dose), (60 ZNO NPs) and (60 ZNO) showed a significant increase ($p<0.05$) on the 6th week compared to day zero. The Neutrophil % in lambs of the control group, lambs received (small mixed dose), (30 ZNO) and (60 ZNO) showed a significant decrease ($P< 0.05$) on the 6th week compared to day zero. No significant changes in monocyte % and eosinophil % was detected among the groups after zinc supplementation. The PLTs count in lambs of the control group showed a significant decrease ($p<0.05$) on the 6th week compared to day zero. The PLTs count in lambs received (small mixed dose), (30 ZNO NPs), (large mixed dose), (60 ZNO NPs) and (60 ZNO) showed a significant increase ($p<0.05$) on the 6th week compared to day zero. (Table 4).

Biochemical changes

The serum urea level in the control group showed a significant decrease in the 6th week. The serum urea level in all groups which received small and large doses of ZnO and ZnO NPs showed a significant increase on the 6th week compared with day zero. The serum creatinine level in all groups which received small and large doses of ZnO and ZnO NPs showed a significant increase on the 6th week compared with the zero-day. Whereas serum creatinine was not changed in the control group after 6 weeks compared to day zero.

The serum AST level of lambs in the control group showed a significant decrease on the 6th week compared to day zero. The serum AST level in all groups which received single and mixed small and large doses of ZnO and ZnO NPs showed a significant increase on the 6th week compared with day zero. The serum ALT level of lambs in the control group and lambs received (60ZNO NPS) and (60 ZNO) showed a significant decrease on the 6th week compared with the day zero. The serum ALT level of lambs received (30 ZNO) showed a significant increase on the 6th week compared with the day zero values.

The serum total protein level of lambs in the control group and lambs received (30 ZNO), (large mixed dose), (60ZNO NPS), and (60 ZNO) showed a significant increase in the 6th week compared with the zero-day. The serum albumin level of lambs received (60 ZnO NPS) and (60 ZNO) showed a significant increase on the 6th week compared with day zero. The serum globulin level of lambs in all groups which received single and mixed small and large doses of ZnO and ZnO NPs showed a significant increase on the 6th week compared with day zero. (Table 5)

The plasma Zinc level in the lambs in the control group showed a significant decrease on the 6th week compared with the zero-day. The plasma Zinc level of the lambs received (small mixed dose), (30 ZNO NPS), (30 ZNO), (large mixed dose), (60 ZNO NPS), and (60 ZNO) showed a significant increase on the 6th week compared with the zero-day. Lambs received larger doses of Zn (either mixed or single) have significantly higher plasma Zn compared to low doses of zinc intake. The plasma Cu level of the lambs in the control group showed a significant decrease on the 6th week compared with day zero. The plasma copper level of the lambs received (small mixed dose), (30 ZNO NPS), (30 ZnO), and (large mixed dose) showed a significant increase on the 6th week compared with the day zero. The plasma calcium level of lambs received (small mixed dose), (30 ZNO NPS), (30 ZNO), (large mixed dose) and (60 ZnO) showed a significant increase in the 6th week compared with the zero-day. -The calcium in the group which took (60 ZNO) had a higher increase compared to either zero-day or other groups.

The wool Zinc level of the lambs in the (control group) showed a significant decrease on the 6th week compared with the zero-day. The wool Zinc level of the lambs received (small mixed dose), (30 ZnO NPS), (30 ZNO), (large mixed dose), (60 ZNO NPS), and (60 ZNO) showed a significant increase on the 6th week compared with the zero-day. The wool copper level of the lambs in the (control group) showed a significant decrease on the 6th week compared with the zero-day. The wool copper level of the lambs received (small mixed dose) and (30 ZNO NPS) showed a significant increase on the 6th week compared with the zero-day. (Tables 6,7).

Table 6 Changes in Plasma Zn, Cu and Ca levels in lambs received different doses of Zinc oxide and Zinc oxide Nano Particles

Treatments / Parameters	Control		Mixed small dose		30 ZNO NPs		30 ZNO		Mixed large dose		60 ZNO NPs		60 ZNO	
	Day 0	6 W	Day 0	6 W	Day 0	6 W	Day 0	6 W	Day 0	6 W	Day 0	6 W	Day 0	6 W
ZN PPM	0.72±0.01a	0.57±0.01d	0.67±0.03b	0.87±0.01a4	0.70±0.01b	0.87±0.01a4	0.66±0.02b	0.87±0.01a4	0.63±0.1b	0.91±0.01a3	0.70±0.01b	1.01±0.01a1	0.70±0.01b	1±0a2
CU PPM	0.46±0.01a	0.36±0.02d	0.36±0.03b	0.45±0.02a	0.39±0.01b	0.42±0.01a	0.38±0.01b	0.42±0.01a	0.40±0.01b	0.50±0.01a	0.40±0.01a	0.41±0.01a	0.41±0.01a	0.42±0a
Ca mg/dl	9.4±0.7a	9.6±0.8a	9.2±2.6b	10.1±1.4a	9.8±1.6b	10.7±4.3a	9.5±2.1b	11.1±1.8a	9.6±0.8b	11.5±4.4a	11.0±6.1a	11.3±6.3a	10.3±4.1b	12.2±9.6a

The results are presented as means± SD different letters of the same column denote significant changes at $p <0.05$
Normal value of zinc: 80-120 ug/dl. Normal value of copper: 60-100 ug/dl. Normal value of calcium: 9.5 - 12.8 mg/dl.

Table 7 Changes in Wool Zn, Cu and Ca levels in lambs received different doses of Zinc oxide and Zinc oxide nano particles.

Treatments / Parameters	Control		Mixed small dose		30 ZNO NPs		30 ZNO		Mixed large dose		60 ZNO NPs		60 ZNO	
Time periods	Day 0	6 W	Day 0	6 W	Day 0	6 W	Day 0	6 W	Day 0	6 W	Day 0	6 W	Day 0	6 W
ZN PPM	0.52±0.01a	0.4 ±0.01b	0.52±0.01b	0.70±0.04a	0.50±0.01b	0.86±0.04a	0.50±0.01b	0.79±0.04a	0.45±0.1b	0.84±0.04a	0.51±0.01b	1±0.07a	0.50±0.01b	0.85±0.03a
CU PPM	0.37±0.01a	0.34±0.01b	0.34±0.01b	0.37±0.01a	0.34±0.01b	0.378±0.01a	0.36±0.01ab	0.38±0.01a	0.37±0.01a	0.38±0.01a	0.36±0.01ab	0.38±0.01a	0.38±0.01a	0.39±0a
Ca mg/g	9.8±1.6a	9.7±1.1ab	9.6±1.6ab	9.8±1a	9.7±0.57ab	9.8±1.7a	9.6±2.6ab	9.7±0.7ab	9.6±1.9ab	9.6±0.8ab	9.9±1.2a	9.6±1ab	9.8±2ab	9.7±1.1ab

The results are presented as means± SD. Different letters of the same row denote significant changes at p <0.05
Normal value of zinc: 54.2 -74.7 ug/g. Normal value of copper: 2.7- 3.9 ug/g. Normal value of calcium: 9-11.8 mg/g

Table 4 Changes in hematology parameters in lambs received different doses of Zinc oxide and Zinc lambs received different values of Zinc oxide and Zinc oxide Nano Particles before and after six weeks.

Treatments / Parameters	Control		Mixed small dose		30 ZNO NPs		30 ZNO		Mixed large dose		60 ZNO NPs		60 ZNO		Reference values
Time periods	Day zero	6 W	Day zero	6 W	Day zero	6 W	Day zero	6 W	Day zero	6 W	Day zero	6 W	Day zero	6 W	
Hb (g/dl)	10.14±0.4a	9.02±0.2b	8.92± 1.1b	10.52±0.65a	9.14±0.7b	10.8± 0.54a	9.4± 0.9ab	11.34±0.41a	8.52± 0.4b	10.46±0.66a	9.32± 0.4b	10.96±0.7a3	9.12± 1.2b	11.06±1.12a	9-14
RBCs (106/l)	9.82± 1.6a	7.51± 0.4b	7.47 ± 1.9b	9.74±0.54a	7.01±0.7b	9.60± 0.9za	8.29 ± 1.5b	9.91± 1.52a	7.47± 1.0b	9.04± 0.46a	8.96± 1.3b	10.80±1.7a1	7.86± 0.4b	9.78±0.63a	8.2-12.3
PCV %	29.36±1.1a	31.42±2.1a	28.12±3.6a	29.82±2.2a	25.4± 2.3 a	30.38± 35 a	26.0 ± 1.3a	31.4± 3.5a	26.26±3.1a	29.28±3.1a	28.75± 4.7a	31.8±2.1a	27.96±2.6a	29.9±2.9a	25-38
Plats (109/l)	7657± 626 a	6806±936 b	7727±1024 b	8458±4964a	8230± 762b	9053 ±8231a	8315±620a	8351± 6745a	6612± 1408b	8492± 9493a	6627±1413b	8529± 303a2	7920±422b	8315±10216a	2600-10000
WBCs (103)	13±2a	9±2 b	13 ±3b	18 ±31a	12±2b	16 ± 25a	12± 2b	17± 12a	12± 2b	17± 23a	11± 2b	16.6± 1.14a4	12±2b	15±66a	5-17
Neutrophils %	54±7a	43±3 b	56±10a	43±5b	48±5a	48±8a	52±9a	48± 5b	45± 3ab	47± 7a	43± 12a	43±6a	48±5 a	40±3b	15-86
Lymphocytes %	39±10b	52±43a	39±8b	51±5a	40±7 a	47 ± 7 a	42±9a	49± 5a	48± 4a	49± 8a	46± 9b	53±6a	44±6b	55±4a	20-57
Monocytes %	4±2a	3±1a	3±2a	4±2 a	3±1a	4 ±2 a	3±1a	3± 1a	3± 1a	3± 1a	4± 1a	3±1a	4±1a	4±2a	5-6
Eosinophil %	1±0.5a	1±0.4a	2±0.5a	1±0.5a	1±0.4a	1±0.5a	1±0.4a	1± 0.5a	2± 0.4a	1± 0.4a	2± 0.7a	1±0.4a	2±0.4a	1±0.5a	0-1.2

The results are presented as means± SD. Different letters of the same row indicated significant changes at p <0.05.

Table 5 Changes in kidney and liver function in lambs received different doses of Zinc oxide and Zinc oxide Nano Particles before and after six weeks.

Treatments / Parameters	Control		Mixed small dose		30 ZNO NPs		30 ZNO		Mixed large dose		60 ZNO NPs		60 ZNO		Reference values
	Day zero	6 W	Day zero	6 W	Day zero	6 W	Day zero	6 W	Day zero	6 W	Day zero	6 W	Day zero	6 W	
Urea (Mg/dl)	34.5±1.5a	32.5±1.5b	37.1±8.3b	41.6±6a	25.5±7.6b	28.3±7a	26.9±7.6b	33.7±8.1a	36.6±7.4b	40.4±6.3a	28.6±6.7b	33.8±8.3a	31.8±9.7b	35.6±8.0a	10-35
Creatinine(Mg/dl)	0.6±0.1a	0.6±0a	0.6±0.1b	0.8±0.2a	0.5±0.1b	0.7±0.1 a	0.5±0.1b	0.8±0.1a	0.6±0.1b	0.8±0.1a	0.6±0.1b	0.8±0.1a	0.6±0.1b	0.9±0.1a	1.2-1.9
AST (u/l)	116±20.3a	71±5b	97±12b	121±15a	106±18b	126±14a	87±10b	133±27a	86±11b	117±8a	98±21b	129±17a	100.2±20b	125±21a	60-280
ALT (u/l)	24.8±2.5a	21.2±2.0b	29±9.6a	29.8±5a	27.2±3.6a	26.2±7.4a	24.6±0.8b	29.8±6.4a	22.6±3.8a	24.8±8.2a	26.4±3.6a	22.6±5.2 b	27.2±16.7a	18.8±7.4b	22-38
Total protein (g/dl)	4.98±0.1b	5.6±0.4a	5.2±0.3a	5.9±0.3a	5.0±0.3a	5.7±0.4a	4.98±0.2b	6.1±0.1a	5.3±0.2b	6.2±0.5 a	4.96±0.2b	5.9±0.3a	5.0±0.4b	5.9±0.1a	2-6
Albumin (g/dl)	2.1±0.1a	2.3±0.1a	2.5±0.3a	2.6±0.3a	2.5±0.3a	2.4±0.3a	2.4±0.1a	2.5±0.1a	2.3±0.1a	2.5±0.1a	2.0±0b	2.5±0.1a	2.0±0.2b	2.4±0.2a	2.4-3
Globulin (g/dl)	2.8±0.1a	3.3±0.3a	2.7±0.2b	3.2±0.2a	2.5±0.1b	3.3±0.1a	2.5±0.1b	3.6±0.1a	3.0±0.1b	3.6±0.4a	2.8±0.1b	3.4±0.2a	2.9±0.2b	3.4±0.3a	2.4-3

The results are presented as means± SD. Different letters of the same row denote significant changes at p <0.05.

4. DISCUSSION

The body temperature was normal in all groups agreed with Alsaad et al. (2010). The temperature was similar in all groups. The heart rate was significantly higher in the control group after the 6th week compared to zero. However, there was a significant decrease in the heart rate of the groups that received a small and large dose of the ZnO NPs and ZnO. This result agreed with Ibrahim et al. (2016). There was a significant ($p < 0.05$) increase in pulse rate from the 8th week in zinc-deficient sheep.

A significant increase in the 6th week in the body weight gain of lambs in all groups received small and large doses of ZnO NPs and ZnO compared with the zero-day and the control group. These results are relevant to those obtained by Ibrahim, et al. (2016) who found a significant decrease in body weight from the 6th Week in zinc-deficient sheep. On the other hand, singh, et al. (2019) did not find any effect on body weight gain in Iranian Angora goat kids.

About hematological changes, there was a significant decrease in Hb in the 6th week in the control group than that of all treatments supplemented by either ZnO or ZN NPs. There was a significant decrease in RBCs in the 6th week in the control group than those other treatments. The same result showed by Alsaad et al. (2011) and Ibrahim, et al. (2016). Anemia observed in zinc-deficient sheep may be attributed to decrease range of cell replications and protein synthesis and these results were agreed with the results get by Eze et al. (2015) who observed that Zn supplementation can be useful in the management of anemia in rats.

There was a significant decrease in WBCs in the 6th week in the control group than that of all other treatments. This result suggests that zinc is an important element in maintaining the cellular immunity in sheep (Ibrahim, et al. 2016). Our study agreed with Sobhanirad et al., (2014) who showed a significant change in all the lambs' hematological parameters between the groups according to Zn supplementation. Ismail and El-Araby (2017) found that highly significant increase in WBCS in all rabbit groups supplemented by ZnO NPs. There was a significant increase in lymphocytes in the 6th week in the control group and in all other treatments supplemented with ZnO and ZnO NPs. The recent study is nonaligned with the result of Ibrahim et al (2016) who told There were a significant decrease in lymphocytes from the 2nd week in the control group than that in all treatments.

On the contrary, Elamin et al., (2013) reported no effect on Hb concentration, WBCs and RBCs count in kids of goats which supplemented by zinc. Likewise,Milani et al., (2017) in pigs and Ramulu et al., (2015) in calves of buffalo showed no significant changes in all the hematological parameters between groups which supplemented by conventional zinc and ZnO Nps, Likewise, Ismail and El-Araby (2017) reported non noticeable change in the Hb concentration and RBCs count in rabbits. The difference between studies could be attributed to the level of Zn supplementation.

Salama et al., (2003) explained that the increase in the concentration of Zn can inhibit absorption of iron and copper which are needed for RBCs and WBCs formation and maturation.

In our study the urea level in the control group showed a significant decrease on the 6th week compared with zero-day and an increase in the urea levels in all groups received small and large doses of ZnO NPs and ZnO compared with the day zero and 6th week. The result disagreed with Dresler et al., (2016) referenced a highly decreasing in the urea level in the end of the experimentation.

Increase in the serum creatinine level in all groups received small and large doses of ZnO NPs and ZnO compared with Day zero and 6th week. The result agreed with Najafzadeh et al., (2013) determined that after orally supplementation of ZNO NPs there was a significant increase in creatinine level, Also, Ismail and El-Araby (2017) declared the rabbits after supplemented with ZNO NPs in diets there was a significant increase in creatinine level.

the significantly increased activity of the AST enzyme in all groups that received small and large doses of ZnO NPs and ZNO decrease the activity of the ALT enzyme in groups that received 60 ppm ZNO NPs and 60 ppm ZNO. The result of current study disagreed with Fazilati, (2013) who determined that ZNO NPs lead to a significant increase of ALT in males of rats. Also, Jung et al (2010) demonstrated that the mice ALT and AST were significantly increased in the ZNO compared to control. The serum AST, ALT, and urea, in our study are within the normal range, which agreed with Saleh and Saleh, (2003). Mohamed et al., (2017) found no difference between the non-treated groups and groups taken Nano zinc of ewes pregnant and lactating. Wang et al. (2006) compared between micro-particles of Zn and Nano particles of Zn in the diet rats' diet and measured liver enzymes and told that the micro-particles lead to liver cells damage and more severe than Nano particles. The only explanation to these differences may be due to the doses and time exposure to the ZNO NPS. Sharma et al., (2009) reported that if ZNO NPs increased more than 50 mg/kg it can cause oxidative stress and increase ALT and AST level.

Total protein, albumin, and globulin are raised; the results of the present study agreed with Mohamed et al. (2015) who pointed that a significantly increased in total protein and albumin in NP-Zn groups compared with the control group. Dresler et al., (2016) showed that a significant increase in the total protein levels by adding Zn in diets. These results disagreed with Ismail and El-Araby (2017) who found that rabbits supplemented with ZnO NPs lead to a extremely significant decrease in total protein. The significant increase in albumin in lambs received large doses of ZNO NPs and ZNO, agreed with Dresler et al., (2016) who showed that calves supplemented by different sources of Zinc had significant increase in albumin concentration. The significant increase in the globulin level in all groups of small and large doses of ZNO NPs and ZNO agreed with Gaafar et al., (2011) in lactating Friesian cows and Ramulu et al., (2015) reported that in calves groups which supplemented with Zn there was a significant increase in globulin level.

The present study showed a significant increase in plasma zinc level in all groups that received small and large doses of ZNO NPs and ZNO and there was a significant decrease in the plasma Zinc level in the control group compared with other groups. Similar results by Khalil et al (2013) showed an increasing in plasma Zn concentration from the 2nd weeks to 6th weeks and Jia et al. (2008) who adding inorganic source of zinc in goats ration and measured plasma zinc level and found that there was a significant increase in plasma zinc level compared with the control group. Likewise, Phiri et al. (2009) found a significant increase in plasma Zn concentration in goats supplemented with zinc oxide. In this current study, the increase in plasma copper and calcium level in all groups with small and large doses of ZNO NPs and ZNO agreed with Bedi, (1976) has reported that an increase in the plasma calcium level after adding of Zn in calves' diets.

Zn supplementation had no effect on level of blood calcium in Cashmere goats Jia et al., (2009) and Goat kids Khalil Zabolil el at (2013).

5. CONCLUSION

It was concluded that small doses of zinc oxide nanoparticles can be beneficial for treatment of zinc deficiency in lambs, improving plasma and wool trace elements and the hematobiochemical picture. It also improved the body weight gain and increased growth rate in growing lambs with minor adverse effect on liver and kidney functions.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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