

EFFICACY OF TOLTRAZURIL AGAINST EXPERIMENTALLY INDUCED COCCIDIOSIS IN CHICKEN

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ABSTRACT

The efficacy of toltrazuril (25 m/kg B.Wt.) against experimental mixed Eimeria species infection in chicken (120 Cobb broiler chicks) was investigated. The infection was initiated with sporulated oocyst (50.000) on the 21st day of age .Performance parameters, daily oocyst count, mortality rate, lesions score and some biochemical parameters were evaluated. Our results revealed that, administration of toltrazuril in drinking water at 1st and second schizogony stage was more valuable in treatment of chicken coccidiosis due to improvement in body weight, weight gain and feed conversion ratio. Moreover, a significant reduction in daily oocyst count also, there was no significant change of ALT, AST, ALP, uric acid and creatinine.

Key words: toltrazuril, broiler chicken , coccidiosis

INTRODUCTION

In developing countries animal production is being subjected to great pressure to satisfy the demand for animal protein required by the continued increase in human population (FAO, 1998). Among the animal production activities, poultry sector has been adversely affected by a variety of constraints. One of these constraints, poultry diseases continue to play the major central role in hampering its development (Rushton et al., 1999).

Coccidiosis is a common enteric parasitism that significantly influences poultry production, causing economic losses of about 1.5 billion \$ every year worldwide (Stevens, 1998). It is caused by intestinal protozoan parasites of the genus Eimeria. It results in reduced

productivity, depressed immune system, and causes major losses of livestock (Suo & Li, 1998; Lillehoj & Lillehoj, 2000) as well as poor feed conversion, high mortality and high morbidity rates (Allen & Fetterer, 2002).

Despite prophylactic administration of anticoccidials in feed, there are many reports of clinical and sub-clinical coccidiosis occurring as a result of insufficient effective medications with conventional anticoccidials (Chapman, 1987). Many medications are required to fulfill some main criteria including a high level of efficacy against all developmental stages of pathogenic Eimeria species infecting poultry and they did not interfere with the immune response of the host during and after treatment of coccidial infection.

One of these drugs is toltrazuril, a symmetrical triazinon, which has been introduced recently and brought substantial progress in treatment of various *Eimeria* infections (Greuel et al., 1989). This compound is efficient against schizonts and gametes of coccidia strains (*E. tenella*, *E. acervulina* and *E. maxima*) in poultry (Mehlhorn et al., 1984). Coccidia become inaccessible to toltrazuril only after the oocyst wall has been formed.

The aim of our study was to measure the efficacy of toltrazuril against experimental infection with mixed *Eimeria* species in chicken, and to study their expected; if any; effects on performance, mortality rate and some biochemical parameters of chicken.

MATERIALS AND METHODS

Drug:

Toltrazuril (Tolycox 2.5%) ®: Toltrazuril is mixed in the drinking water at a dose of 7 mg / kg body weight per day for two consecutive days. Therefore, the recommended therapeutic dose of toltrazuril 2.5% is 25 mg / liter drinking water Vertommen and Peek, (1990).

Experimental chicken:

One hundred and twenty 1-day old Cobb broiler chicks were purchased from local hatchery. Chicks were reared under standard management practices. All the chicks were kept on broiler starter ration up to 2 weeks of age and later on fed on broiler finisher ration. Commercial ration was free from any medications especially, anticoccidials. The birds were reared on the sawdust litter. The feed and water were provided ad-libitum to all the birds. Lighting was provided for 24 hr through out

the experimental period. All birds were vaccinated against Newcastle disease by Hitchner B1 live attenuated virus vaccine at 7 day old and at 18 day old by Lasota via drinking water.

Experimental Mixed *Eimeria* sporulated oocyst:-

For this purpose, a field strain of *Eimeria* species was isolated from naturally infected chicken. The preparation of the *Eimeria* oocyst for experimental infection.

A. Propagation and isolation of oocysts for the experimental infection.

1. Collection and concentration of oocyst:-
According the method described by Soulsby (1968).
2. Sporulation of collected oocysts:-
According the method described by Long (1971),
3. Technique of experimental infection:-
The chicks were infected at three weeks age (21 day) by inoculation of the suspension of 50,000 oocysts of mixed *Eimeria* species (Donal, 1989). The inoculation was carried out with the help of a rubber tube introduced into the esophagus.

B. Grouping & Experimental design:-

One hundred and twenty (120) (1 day old) Cobb chicks were used in this study and were divided into 4 main groups each of 45 chicks (except group 1 and group 2 were 15 chicks) as the following:

Group 1 ; 15 broiler chicks were kept as control negative (non infected non treated).

Group 2 ; 15 broiler chicks were kept as non infected treated with toltrazuril (25mg/L in drinking water / day).

Group 3 : 45 broiler chicks were experimentally infected with 50,000 sporulated oocysts of mixed *Eimeria* species at 3 weeks age and non-treated.

Group 4 : 45 broiler chicks were experimentally infected with 50,000 sporulated oocysts of mixed *Eimeria* species at 3 weeks age and treated with toltrazuril (25 mg/L in drinking water / day). Further subdivided into three subgroups (each contains 15 chicks).

- **Subgroup 1 :** treated with toltrazuril on the 1st, 2nd & 3rd day post infection (to detect the effect of the drug on the 1st generation schizont).
- **Subgroup 2 :** treated with toltrazuril on the 4th & 5th day post infection (to detect the effect of the drug on the 2nd generation schizont).
- **Subgroup 3 :** treated with toltrazuril on the 6th day post infection (to detect the effect of the drug on the gametocytes).

C. Efficacy of the toltrazuril:-

The efficacy of toltrazuril was evaluated by the daily count of *Eimeria* oocysts in the dropping of the experimentally infected chicks, severity of the clinical symptoms induced by the disease, body weight gain, lesions score and feed conversion, in the experimentally infected chicken.

1. Oocysts counting:-

The daily output of *Eimeria* oocysts in the droppings of the infected chicks was counted from the 7th to the 12th day by using McMaster counting slide (Tracy and Webster, 1996).

2. Lesions score:

The severity of lesion was evaluated to determine the efficacy of the drug according to

Johnson and Reid, (1970). The score was adopted between 0 and + 4.

3. Clinical symptoms :

The bloody droppings were the main clinical symptoms of coccidiosis. The intense of bloody droppings in infected non treated group in comparison with the treated group was considered one of the most important mean of evaluation the drug efficacy. Therefore, chicken were continuously examined for recording the clinical symptoms.

4. Evaluation of growth performance parameters:

a- Body weight and body weight gain:

Ten chicks of each group were wing tagged and weighed at the day 20 before experimental infection of chicken to obtain the average body weight then weighed weekly. Weights of the chicks were used for the average body weight and calculating the average body gain per chick in each group by difference between the value of body weight at a particular week from the corresponding value of the next week.

b- Feed intake & feed utilization

According the method described by Ensminger (1980).

D. Biochemical parameters analysis:

Blood samples were collected from wing vein of five chicks from each group in clean dry tubes after the end of each treatment as the following:

- On the 4th day post infection in the (subgroup 1) of the group 4.
- On the 6th day post infection in the (subgroup 2) of the group 4

- On the 7th day post infection in the (subgroup 3) of the group 4.

Beside non infected non treated, non infected treated with (toltrazuril (25mg/L in drinking water / day) and infected non treated group.

- Serum samples were carefully separated by centrifuged at 3000 r.p.m for 10 minutes and kept in a clean epindorff tubes at -20°C until assayed.

D. a. Determination of serum transaminases:

The serum levels of alanine aminotransferase (ALT) and serum serum aspartate Aminotransferase (AST) were measured colorimetrically according to the methods described by **Reitman and Frankel, (1957)**.

D. b. Determination of serum alkaline phosphates:

Alkaline phosphatase is determined by a colorimetric method according to **Roy, (1970)**.

D.c. Quantitative determination of serum uric acid :

Serum uric acid is determined by a colorimetric method according to **Schultz & Kaplan et al., (1984)**.

D.d Determination of serum creatinine:

Creatinine is measured by a colorimetric method with deproteinisation according to the method described by **Bartels et al., (1971)**.

Statistical analysis:

The obtained data in the present study were statistically analyzed for analysis of variance (ANOVA) and least significant difference (LSD) as described by **Snedecor and Cochran, (1981)**.

RESULTS AND DISCUSSION

1. Effects of toltrazuril on daily oocyst count/gm faeces:-

Regarding the effect of the tested drug on the daily (7th, 8th, 9th, 10th, 11th, and 12th post infection) oocyst count, the obtained data revealed a flatulent significant decrease in total oocyst count in all treated groups in comparison to the infected non treated group Table (1). The obtained results agree with that recorded by **Edgar (1955)** who stated that, the numbers of oocysts discharged are scanty at first appearance and increased rapidly during the subsequent day or two until they reach a peak, then declined rapidly. Moreover, many publications have shown that, oocyst production correlates poorly with weight development, intestinal lesions, and even with mortality in highly pathogenic species *E.Tenella* and *E.Necatrx* (**Weber and Frigg, 1986**).

Our data revealed that, the lowest significant decrease in oocyst count was 51.9 ± 0.40 on the 7th day post infection (PI) in toltrazuril treated group (at 4th and 5th day PI) in comparison with infected non treated group (764.0 ± 30.72). Whereas, the most obvious significant decrease in oocyst count on the 12th day post infection was 4.5 ± 0.057 at 1st, 2nd and 3rd PI in comparison with the infected non treated group (89.0 ± 0.58). The obtained results demonstrated that, toltrazuril treatment was highly efficacious on the basis of the prevention of mortality, and reductions in oocyst output this agreed with **Ramadan et al., (1993a, b)**. On a similar ground, **Vertomen and Peak (1990)** recorded that; toltrazuril was active against sexual stages of coccidia. In addition, **Ramadan et al., (1997)** stated

that, the oocyst counts of chicken treated with toltrazuril at different dose levels were significantly lower than those of the undedicated infected control.

2. Effect of toltrazuril on growth performance parameters:

a- Effect on Body weight (gm):

The effect of toltrazuril on average body weight of experimentally infected chicken with mixed *Eimeria* species was summarized in Table (2).

The mean average body weights of broiler chicks at 20 days old before infection were nearly similar, indicating that all groups were homogenous. On the other hand, the average body weight in infected non treated group was significantly decreased (1497.0 ± 112.23) at 41 days of age in comparison with the non infected non treated group (1669.5 ± 52.85). This result confirmed by **Mc Dougald and Reid (1979)** who stated that, the protozoan parasites of the genus *Eimeria* multiply in the intestinal tract and cause tissue damage with resulting interruption of feeding and digestive processes of nutrient absorption, dehydration and blood loss. On a similar ground, **Fernando and McCrew, (1973)** reported that, *Eimeria* infection causes changes in the intestinal morphology, reduction in the absorption capacity, increase the rate of replacement and turnover of the intestinal cells, increase tissue edema, and increase in feed passage time thus, alteration of feed intake and overall decrease in body weight and weight gain.

The average body weight at 34 days (13 days post experimental infection) of age, revealed a significant increase at 1st, 2nd and

3rd post infection in toltrazuril treated group (1260 ± 60.60). This finding is agreed with that recorded by **Mathis et al., (2004)** and **Mundt et al., (2005)** who stated that, toltrazuril provided in drinking water improved weight gain and feed conversion of broiler chicken and has a highly beneficial effect for the animal in regards to health status.

Similarly, at 41 days of age, generally all infected treated groups elicited a significant increase in average body weight in comparison with the infected non treated group. The most prominent significant increase was noticed in toltrazuril treated group at 4th and 5th day post infection (1811.5 ± 56.39). This result may be due to the effect of drug on all intracellular developmental stages including those of schizogony and gametogony (**Kitandu and Juanova, 2008**). Moreover, toltrazuril produced healthier gut epithelium thus, enhancement the absorption of nutrients.

b- Effect on total body weight gain (gm):

The obtained data reflected the effect of the administered drug on body weight gain was illustrated in Table (3). The infected non treated group elicited a significant decrease in body weight gain at 27, 34 and 41 days (211.5 ± 17.48 , 374.5 ± 8.44 & 378.0 ± 83.86 , respectively) compared with non infected non treated group. In comparison with the infected non treated group, a significant increase (1286.0 ± 39.25) in total body weight gain was recorded in toltrazuril infected treated group at 4th & 5th days post infection. This finding supported by **Epe et al., (2005)** who showed that, toltrazuril it resulted in significantly higher body weight. Also, **Clacksons et**

al, (2007) said that, toltrazuril significantly increase daily weight gain.

c. Effect on feed conversion ratio (FCR):

The effect of toltrazuril on feed conversion ratio of experimentally infected chicken was tabulated in Table (4). The infected non treated group showed highly increased feed conversion ratio (2.59 ± 0.32) at 27 days. At 34 days, the obtained data showed, a significant increase in feed conversion ratio of toltrazuril treated group at 4th and 5th day PI (3.38 ± 0.26). These results are in accordance with that obtained by and Cleaskens et al., (2007) who declared that, toltrazuril caused a significant increase in feed conversion ratio.

The obtained total feed conversion ratio at 41 days clearly demonstrated that, there was no significant difference between all toltrazuril treated subgroups and the non infected non treated group, this indicating an improvement in feed conversion ratio. Our finding is in consistence with that previously reported with Mathis et al., (2004) who noticed that toltrazuril provided in drinking water for broiler chicken improved both weight gain and feed conversion

3. Clinical examination of the chicken:

a- Clinical signs:-

The non infected non treated group was apparently healthy showed good appetite, good feathering and normal dropping. No mortalities were recorded. While, the infected non treated group was severely affected and symptoms of depression, anorexia, loss of appetite, ruffled feather and bloody diarrhea were clearly observed. The mortality rate was 13.3% (Table, 5). The appearance of the symp-

toms was prominent at the 7th day (beginning of oocyst excretion in droppings) till 12th day post infection. The obtained results were supported by those obtained by Hofstad et al., (1984) and Orbay et al., (1989) in infected non treated chickens.

Toltrazuril treated group evoked mild clinical symptoms, and slightly bloody diarrhea. General health conditions of birds were slightly affected especially, the groups treated at 1st, 2nd and 3rd post infection and at 4th and 5th day PI. The mortality rate was 2.2. These results are agree with results recorded by Epe et al., (2005) in calves, Ocal et al., (2007) in goats and Allam et al., (2008) in chicken. They found that, toltrazuril reduced the clinical signs and improved the healthy status of infected groups as evidenced by the decreased mortality rates, lesion scores and oocyst output.

B. Lesion score:

Lesions score was demonstrated in Table (5). Non infected non treated group showed no clinical symptoms and the post mortem examination revealed Score 0: where no macroscopic lesion. The wall of the intestine was thin and showed a characteristic longitudinal grooves and mucosal folds. The contents of the intestine were homogeneous and creamy. While, the infected non treated group showed Score 4 lesions: where the caecal wall was distended with blood or large caseous plugs. Fecal debris was no longer visible; it is enclosed in the caseous plugs and the extent of hemorrhages gives the intestine a dark color: the intestinal contents consist of red or brown mucous. Distension may spread along the entire length of the intestine. This result is

supported by that obtained by **Johnson and Reid, (1970)**.

The results of toltrazuril treated group (at 1st, 2nd, 3rd and at 4th, 5th day PI) revealed a Score 1 lesion: small petechiae and white spots can easily be observed on the serous membrane. The damage was difficult to notice on the mucosal side and some petechiae were scattered on the caecal wall. The caecal contents were normal. The obtained result is in accordance with that confirmed by **Laczay et al., (1995)** who reported that, toltrazuril is more effective in reducing intestinal lesions when treatment was initiated 24 hours post infection. Similar result was recorded by **Sameh et al., (2005)**. The author found that, toltrazuril evoked a significant decrease in oocyst count/gm droppings and lesion scores.

4. Effect of medications on some biochemical parameters:

The results obtained, regarding the effect of toltrazuril on the liver and kidney functions of both experimentally infected or non infected chicken were summarized in Tables (6), (7) and (8).

4.1- Liver function:-

The obtained results in Table (6) revealed a non significant changes in both alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels in infected non treated and toltrazuril treated group at 1st, 2nd, 3rd days post infection (at 1st schizogony stage) this confirmed with **Majkic-Singh, (1993)** who stated that, intestinal coccidiosis of rabbit did not alter significantly the activity of these enzymes because it originates mainly from liver. On the other hand the level of alk-

aline phosphatase (ALP) showed a significant decrease in non infected treated group and was 158.2 ± 26.54 , compared with the infected treated groups which showed a significant increase (402.2 ± 47.16) in comparison with the infected non treated group (322.4 ± 49.60).

Nearly similar findings were obtained at 4th, 5th days post infection (at 2nd schizogony stage) regarding the levels of ALT, AST in non infected toltrazuril that, elicited a significant increase of both enzymes, this may attributed to the metabolic pathway of toltrazuril in liver. Moreover, **Eraalan, (2004)** stated that, toltrazuril itself led to oxidative damage at the specific period and dosage. In addition, alkaline phosphatase was highly increased in infected non treated group (883.20 ± 64.61) this findings agreed with **Kulstic et al., (1999)** who stated that, alkaline phosphatase elevated during intestinal coccidiosis in rabbit as, this enzyme is synthesized in the small intestine wall and liver. However, the pathological process was confined to intestine, the liver showed signs of enhanced activity so, the enzyme level elevated and due to the disrupted intestinal barrier and the activity was increased in the circulation. While, the level of ALP was significantly decreased in both non infected treated (158.30 ± 26.54) and infected treated (719 ± 19.84), compared with the infected non treated group (Table, 7).

Treatment at 6th day post infection (at gamctogony stage) revealed a significant increase (79.9 ± 7.25) in ALT level of non infected toltrazuril treated groups. Similarly, there was a significant increase in the level of AST (299.5 ± 17.5) in the same treated groups. The alkaline phosphatase level showed a signifi-

cant increase in infected non treated group (499.40 ± 64.59). On the other hand the levels of alkaline phosphatase (ALP) elicited a significant decrease in non infected treated group (158.2 ± 26.54) and infected treated group (355.4 ± 65.23) compared with infected non treated group (Table, 8).the findings was supported by **Kulisc et al., (1999)**. The non significant changes in both alanine aminotransferase (ALT) and aspartate aminotransferase (AST) of all infected toltrazuril treated sub-groups were reinforced by **Ocal et al., (2007)** who stated that, toltrazuril treatment in goat kids evoked a non significant changes in ALT and AST.

4.2- kidney function:-

The obtained data at 1st schizogony stage showed no significant change in uric acid level except in infected non treated group

the results showed a significant decrease (5.14 ± 1.13). At 2nd schizogony stage uric acid value showed no significant changes in comparison with non infected non treated groups. (Table, 7). At gametogony stage the highest uric acid value was recorded in infected non treated (13.22 ± 2.60). While creatinine showed a significant increase (1.4 ± 0.29) in non infected treated with toltrazuril (Table, 8). A similar result obtained by **Allam et al., (2008)** who, attributed the high value of creatinine and uric acid to the high protein level of the consumed diet. Moreover, **Allen, (2002)** reported that, oxidative stress occurs during the acute phase (days 5-7 post infection) of primary avian coccidia infections. This is a period of much host tissue destruction that is associated with maturation and shedding of oocysts and uric acid increased 138% at 32 hr PI .

Table (1): Effect of toltrazuril daily oocyst count/gm faeces of experimentally infected with mixed *Eimeria* species. (Mean±S.E) X10³ n=3

Groups	Time of drug administration during life cycle	Days post infection					
		7 th	8 th	9 th	10 th	11 th	12 th
G1 (Non Infected non treated)	—	0.0	0.0	0.0	0.0	0.0	0.0
G3 (Infected non treated)	—	764±30.72 ^a	862.7±11.27 ^a	600±2.31 ^a	423.5±12.50 ^a	711.5±1.15 ^a	89±0.58 ^a
G4 (Infected treated with toltrazuril) (25 mg/liter)	G4.A (at 1 st &2 nd &3 rd days)	85.6±2.66 ^c	111.4±1.15 ^d	226±5.19 ^b	88.7±1.21 ^c	16.8±0.58 ^d	4.5±0.057 ^d
	G4.B (at 4 th & 5 th days)	51.9±0.40 ^d	650.6±17.23 ^b	100.4±1.15 ^c	164.2±16.86 ^b	35.6±1.15 ^c	12.6±0.577 ^c
	G4.C (at 6 th days)	383.5±10.97 ^b	366.4±27.17 ^c	93.4±1.19 ^d	43.9±11.59 ^d	47.6±1.15 ^b	18.9±1.15 ^b

Table (2): Effect of toltrazuril on average body weight (gm) of experimentally infected chicken with mixed *Eimeria* species. (Mean ± S.E) n=10

Groups	Time of drug administration during life cycle	Average body weight before infection (at 20 days)	Average body weight (gm)		
			at 27 days	at 34 days	at 41 days
G1 Non infected non treated	--	540.5±15.02 ^a	815±16.67 ^b	1218.5±30.78 ^{ab}	1669.5±52.85 ^{ab}
G3 Infected non treated	--	533±17.78 ^a	744.5±33.43 ^c	1119±28.96 ^b	1497±112.23 ^c
G4 (Infected treated with toltrazuril) (25 mg/liter)	G4.A (at 1 st &2 nd &3 rd days)	529.5±14.19 ^a	870±36.90 ^a	1260±60.60 ^a	1771.5±66.21 ^{ab}
	G4.B (at 4 th & 5 th days)	525±19.07 ^a	884±15.98 ^a	1223.5±43.37 ^{ab}	1811.5±56.39 ^a
	G4.C (at 6 th days)	536±18.16 ^a	825.5±21.27 ^b	1161±36.47 ^{ab}	1671±102.56 ^{ab}

Means within the same column bearing different superscripts are significant at (p<0.05)

Table (3) : Effect of toltrazuril on body weight gain (gm) in experimentally infected chicken with mixed *Eimeria* species. (Mean \pm S.E) n=10

Groups	Time of drug administration during life cycle	Body weight gain (gm)			
		At 27 days	at 34 days	at 41 days	Total
G1 (Non infected non treated)		274.5 \pm 4.79 ^a	403.5 \pm 15.31 ^a	451 \pm 27.24 ^{bc}	1129 \pm 38.31 ^b
G3 (Infected non treated)		211.5 \pm 17.48 ^c	374.5 \pm 8.44 ^b	378 \pm 83.86 ^c	964 \pm 95.26 ^c
G4 (Infected treated with toltrazuril) (25 mg/liter)	G4.A (at 1 st & 2 nd & 3 rd days)	340.5 \pm 23.44 ^a	390 \pm 26.87 ^a	511 \pm 16.58 ^{ab}	1242 \pm 53.53 ^{ab}
	G4.B (at 4 th & 5 th days)	359 \pm 6.35 ^a	339.5 \pm 27.71 ^b	588 \pm 19.46 ^a	1286 \pm 39.25 ^a
	G4.C (at 6 th days)	289.5 \pm 7.20 ^b	335.5 \pm 16.13 ^b	510 \pm 67.56 ^{ab}	1135 \pm 85.95 ^{ab}

Means within the same column bearing different superscripts are significant at (p<0.05)

Table (4) : Effect of toltrazuril on feed conversion ratio in experimentally infected (with mixed *Eimeria* species) chicken. (Mean \pm S.E) n=10

Groups	Time of drug administration during life cycle	feed conversion ratio (%)			
		At 27 days	at 34 days	at 41 days	Total
G1 (Non infected non treated)	-----	1.9888 \pm 0.03 ^{bc}	1.7889 \pm 0.057 ^d	1.8794 \pm 0.12 ^b	1.8570 \pm 0.06 ^d
G3 (Infected non treated)	-----	2.5909 \pm 0.32 ^a	2.4661 \pm 0.052 ^{bc}	4.2260 \pm 2.41 ^a	3.1499 \pm 0.32 ^a
G4 (Infected treated with toltrazuril) (25 mg/liter)	G4.A (at 1 st & 2 nd & 3 rd days)	2.1679 \pm 0.16 ^b	2.6074 \pm 0.21 ^{bc}	2.0425 \pm 0.06 ^b	2.2222 \pm 0.11 ^{cd}
	G4.B (at 4 th & 5 th days)	2.1527 \pm 0.03 ^{bc}	3.3175 \pm 0.26 ^a	1.8733 \pm 0.06 ^b	2.2892 \pm 0.06 ^c
	G4.C (at 6 th days)	2.4446 \pm 0.06 ^{ab}	2.8747 \pm 0.16 ^{ab}	3.1721 \pm 0.58 ^b	2.7356 \pm 0.23 ^b

Table (5) : Effects of toltrazuril on mortality rate and lesion score in experimentally infected (with mixed *Eimeria* species) chicken .

group	Time of drug administration during life cycle	Mortality rate		Lesion score
		No.	%	
G1 (Non infected non treated)	-----	0/15	0	0
G2 Non infected treated with toltrazuril (25 mg/liter)	----	0/15	0	0
G3 (Infected non treated)	----	6/45	13.3%	4
G3 (Infected treated with toltrazuril) (25 mg/liter)	G3.1 (at 1 st & 2 nd & 3 rd days)	0/15	1/45	1
	G3.2 (at 4 th & 5 th days)	0/15		1
	G3.3 (at 6 th days)	1/15		3

Table (6) : Effect of toltrazuril on some biochemica l parameters in serum of experimentally infected chicken with mixed *Eimeria* species at 1st Schizogony stage (1st, 2nd and 3rd days post challenge). (Mean±S.E) n=5

Groups	Biochemical parameters				
	Liver functions			Kidney functions	
	ALT (U/L)	AST (U/L)	ALP (IU/L)	Uric acid (mg/dl)	Creatinine (mg/dl)
G1 Non infected non-treated	50.9±1.27 ^b	235.2±5.29 ^b	301.2±11.93 ^c	7.74±0.18 ^a	0.54±0.04 ^b
G2 Non infected treated with tolt. (25 mg/liter)	79.9±7.25 ^a	299.5±17.5 ^a	158.2±26.54 ^d	8.28±0.52 ^a	1.4±0.29 ^a
G3 Infected non treated	45.9±0.97 ^b	226.8±4.95 ^b	322.4±49.60 ^b	5.14±1.13 ^b	0.4±0.04 ^b
G4.A Infected & treated with tolt. (25 mg/liter)	49.7±0.85 ^b	214.6±4.23 ^b	402.2±47.16 ^a	8.26±0.17 ^a	0.56±0.04 ^b

Table (7): Effect of toltrazuril on some biochemical parameters in serum of experimentally infected chicken with mixed *Eimeria* species at 2nd Schizogony stage (3rd & 4th days post challenge). (Mean±S.E) n =5

Groups	Biochemical parameters				
	Liver functions			Kidney functions	
	ALT (U/L)	AST (U/L)	ALP (IU/L)	Uric acid (mg/dl)	Creatinine (mg/dl)
G1 Non infected non-treated	50.97±1.28 ^b	235.27±5.29 ^b	301.20±11.93 ^c	7.74±0.19 ^{a,b}	0.54±0.04 ^b
G2 Non infected treated with tolt. (25 mg/liter)	79.97±7.25 ^a	299.56±17.57 ^a	158.20±26.54 ^d	8.28±0.53 ^a	1.40±0.29 ^a
G3 Infected non treated	49.07±0.56 ^b	214.74±6.66 ^b	883.20±64.62 ^a	8.20±0.15 ^a	0.54±0.04 ^b
G4.B Infected & treated with tolt. (25 mg/liter)	47.57±0.43 ^b	226.05±4.38 ^b	719.00±19.84 ^b	6.12±0.55 ^{a,b}	0.50±0.03 ^b

Means within the same column bearing different superscripts are significant at (p<0.05)

Table (8): Effect of toltrazuril on some biochemical parameters in serum of experimentally infected chicken with mixed *Eimeria* species at gametogony stage (6th day post challenge). (Mean±S.E) n =5

Groups	Biochemical parameters				
	Liver functions			Kidney functions	
	ALT (U/L)	AST (U/L)	ALP (IU/L)	Uric acid (mg/dl)	Creatinine (mg/dl)
G1 Non infected non-treated	50.97±1.28 ^b	235.27±5.29 ^b	301.20±11.93 ^c	7.74±0.19 ^b	0.54±0.04 ^b
G2 Non infected treated with tolt. (25 mg/liter)	79.97±7.25 ^a	299.56±17.57 ^a	158.20±26.54 ^d	8.28±0.53 ^b	1.40±0.29 ^a
G3 Infected non treated	50.56±1.93 ^b	221.76±9.08 ^{bc}	499.40±64.59 ^a	13.22±2.60 ^a	0.62±0.07 ^b
G4.C Infected & treated with tolt. (25 mg/liter)	49.52±0.86 ^b	211.92±5.36 ^c	355.40±65.23 ^b	6.19±0.26 ^c	0.52±0.04 ^b

Means within the same column bearing different superscripts are significant at (p<0.05)

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المعروف في وظائف الكلى والكبد والكلى والكلى.
 تظهر لم تظهر تغيرات في وظائف الكلى والكبد والكلى والكلى في الأشهر الثلاثة الأولى من الحمل بعد الولادة. وقد أظهرت نتائج الفحوصات المخبرية في الأشهر الثلاثة الأولى من الحمل بعد الولادة. وقد أظهرت نتائج الفحوصات المخبرية في الأشهر الثلاثة الأولى من الحمل بعد الولادة. وقد أظهرت نتائج الفحوصات المخبرية في الأشهر الثلاثة الأولى من الحمل بعد الولادة.

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