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 fullfil 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 1and group2 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 Mc-Master 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:-

egarding 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.Necatrix **(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 McCraw, (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, 2006)**. 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, **Claeskens 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 4^{th} and 5^{th} 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 symptoms was prominent at the 7^{th} 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 1^{st}, 2nd and 3^{rd} post infection and at 4^{th} and 5^{th} 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 alkaline 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, **Eraslan, (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 **Kulisic 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 gametogony 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 **Kulisic et al., (1999)**. The non significant changes in both alanine aminotransferase (ALT) and aspartate aminotransferase (AST) of all infected toltrazuril treated subgroups 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 crteatinine 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 exp erimentally infected with mixed *Eimeria* species. (Mean±S.E) X10 ^{3} n =3

Groups	Time of drug administration during life cycle	Days post infection					
		7th	8th	9th	10th	11th	12th
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 toltrazuri) (25 mg/liter)	G4.A (at 1st&2nd &3rd 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 4TH & 5TH 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 6th 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 a verage 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 weigh before infection (at 20 days)	Average body weigh (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 toltrazuri) (25 mg/liter)	G4.A (at 1st&2nd &3rd days)	529.5±14.19 ^{a}	870±36.90a^{a}	1260±60.60^{a}	1771.5±66.21^{ab}
	G4.B (at 4TH & 5TH days)	525±19.07 ^{a}	884±15.98^{a}	1223.5±43.37^{ab}	1811.5±56.39^{a}
	G4.C (at 6th 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 ± 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±4.79^{b}	403.5±15.31^{a}	451±27.24^{bc}	1129±38.31^{b}
G3 (Infected non treated)		211.5±17.48^{c}	374.5±8.44^{b}	378±83.86^{c}	964±95.26^{c}
G4 (Infected treated with toltrazuri) (25 mg/liter)	G4.A (at 1st&2nd &3rd days)	340.5±23.44^{a}	390±26.87^{a}	511±16.58$^{a\,b}$	1242±53.53^{ab}
	G4.B (at 4th & 5th days)	359±6.35^{a}	339.5±27.71^{b}	588±19.46^{a}	1286±39.25^{a}
	G4.C (at 6th days)	289.5±7.20^{b}	335.5±16.13^{b}	510±67.56$^{a\,b}$	1135±85.95$^{a\,b}$

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 ± 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±0.03^{bc}	1.7889±0.057^{d}	1.8794±0.12^{b}	1.8570±0.06^{d}
G3 (Infected non treated)	-------	2.5909±0.32^{a}	2.4661±0.052$^{b\,c}$	4.2260±2.41^{a}	3.1499±0.32^{a}
G4 (Infected treated with toltrazuri) (25 mg/liter)	G4.A (at 1st&2nd &3rd days)	2.1679±0.16$^{b\,-}$	2.6074±0.21^{bc}	2.0425±0.06^{b}	2.2222±0.11^{cd}
	G4.B (at 4TH & 5TH days)	2.1527±0.03^{bc}	3.3175±0.26^{a}	1.8733±0.06^{b}	2.2892±0.06^{c}
	G4.C (at 6th days)	2.4446±0.06^{ab}	2.8747±0.16$^{a\,b}$	3.1721±0.58^{b}	2.7356±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	Mortakity 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 toltrazuri) (25 mg/liter)	G3.1 (at 1st&2nd &3rd days)	0/15	1/45	2.2%	1
	G3.2 (at 4TH & 5TH days)	0/15			1
	G3.3 (at 6th 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 1 st Schizogony stage (1 st, 2nd and 3 rd 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 ($p<0.05$)

REFERENCES

Allam, H. H.; Bayoumie, H. A. A.; Malhat S. M. H. and Mohamed I. A. A. (2008) : Effect of toltrazuril and amprolium plus in broilers chickens infected with coccidiosis Assuit-Vet.Med. J. Vol :54 no.118 -(253-266).

Allen P., (2002) : Oxidative Stress During Avian Coccidiosis, Poultry Science Association Meeting Abstract.

Allen, P. C. and Fetter, R. H. (2002) : Recent advances in biology and immunobiology of Eimeria species and in diagnosis and control of infection with these coccidian parasites of poultry. Clin Microbiol Rev 15: 58-65.

Bartels H.; et al., (1971) : Mod .method Clin. Chim. Acta 32 , 81.

Chapman, D. H. (1987) : Control of E. tenella, partly resistant to monensin, by including Toltrazuril discontinuously in the drinking water of chickens. J. Comp. Path. 97,21-27.

Claeskens, M.; Verdonck, W.; Heesen, H.; Froyman, R. and Torres, A. (2007) : A field study assessing control of broiler coccidiosis by paracox vaccination or by toltrazuril (baycox) stand -alone treatment. Parasitol Res. (101) :105-112.

Donal P. (1989) : Managing anticoccidial programs. Supplement of the world poultry Mistte P.35.

Edgar, S. A. (1955) : Sporulation of oocysts at species tempretures and notes on the prepatent period of several species of avian coccidian Jour. Parasit. 41:214.

Ensminger, M. E. (1980) : Poultry science 2nd ed. Printed in U.S.A.

EL-Nabtity, S. M.; EL-Sayed, N. A. and Gad, G. N. A. (2005) : Effect of secindazole on Eimeria tenella infection in chickens, 4th Int. Sci. Conf. Mansoura : (1411-1418).

Epe, C.; von Samson-Himmelstjerna, G.; Wirtherlel, N.; von der Heyden, V.; Welzl, C.; Beening, J.; Radeloff, I.; Hellmann K., Schnieder T., and Krieger K., (2005) : Efficacy of toltrazuril as a metaphylactic and therapeutic treatment of coccidiosis infirst-year grazing calves .Parasitol .Res. 97 127-133. Parasitology119: 164-172.

Eraslan, G.; Cam, Y.; Eren, M. and Cemliman, B. (2004) : Chandes in malondialdehyde level and catalase activity and effect of toltrazuril on these parameters in chicks infected with Eimeria tenella Bull Vet Inst Pulawy 48, 251-254.

Fernando, M. A. and McCraw, B. M. (1973) : Mucosalmorphologyandcellularrenewalintheintestineof chickens Following a single infection of Eimeria acervulina. J. Parasitol. 59,493-501.

FAO., (1998) : Village chicken production systems in rural Africa ; household food security and gender issues. FAO animalproduction and health paper 142. FAO, Rome, Italy, pp:1-11.

Greuel, E.; Ruhrmann, U. and Mundt H. C. (1989) : untersuchungen zur wirksamkeit von Baycox bei experimenteller putenkokzidiose prakttierarzt 6: 38-42.

Hofstad, M. S.; barnes, H. J.; Calnek B. W.; Reid, W. M. and Yoder, H. W. (1984) : Diseases of poultry 8th ed. Iowa State Press.

Jeffers, T. K. (1978) : Genetics of coccidia and the host response. In : P.L. Long, K. N. Boorman and B. M. Freeman (Editors), Avian Coccidiosis. Brit. Poult. Sci. Ltd, Edinburgh, pp. 50-125.

Johnson, J. K. and Reid, W. M. (1970) : Anticoccidial drugs: lesion scoring techniques in battery and floor-pen experiments with chickens, Exp. Parasitol. 28, pp. 30-36.

Kitandu, A. and Juranova, R. (2006): Progress in control measures for chicken coccidiosis. ActaVet.Brno.75, 265-276.

Kulisic, Z.; Tambur, Z.; Malicevic, Z. and Mihailovic (1999) : Influence of rabbit infection with intestinal coccidia upon the activity of enzymes primarily not synthesized in the liver, ARS Veterinaria , 15(1):54-57.

Lacazy, P.; Voros, G. and Semjen, G., (1995): comparative studies on the efficacy of sulfachlorpyrazine and toltrazuril for treatment of caecal coccidiosis in chickens. Internalional Journal for Parasitology. Vol. 25. No. 6, pp: 753-756.

Lillehoj, H. S. and E. P. Lillehoj. (2000) : Avian coccidiosis . Areview of acquired intestinal immunity and vaccination strategies . Avian Dis. 44: 408-425.

Long, P. L. (1971) : Maintenance of intestinal protozoa in vivo with particular references of Eimeria and Histomonas Oxoford Black Wells, 65-75.

Majkic-Singh, N. (1993) : Clinical enzymology. Belgrade, Yugoslav Medical Biochemistry Assosiation , p.236-53.

Mathis, G. F.; Froyman, R. and Kennedy, T. (2004) : Coccidiosis control by administering toltrazuril in the drinking water for a 2-day period Veterinary Parasitology121:1-9.

Mc Dougald, L. R. and Reid, W. M. (1979) : Interaction of infectious bursal disease and coccidiosis in layer replacement chickens Avian Dis 23: 999-1005.

Mehlhorn, H.; Ortman-Falkenstein, A.; Haberkorn, A. and Maxima, E. (1984) : The effects of symmetrical triazinetrione on developmental stages of Eimeria tenella, and E. acervulina: alight and electron microscopical study. Z Parasitenkd 70: 173-182.

Mundt, H.; Bougouro, B.; Mengel, H.; Keidel, J. and Daugschies, A. (2005) : Control of clinical coccidiosis of calves due to Eimeria bovis and Eimeria zuernii with toltrazuril under field conditions, Parasitol Res, 97:134-142.

Ocal, N.; Yagci, B. B.; Duru, S. Y. and Kul O. (2007) : Toltrazuril treatment for acute clinical coccidiosis in hair goat kids: clinical, pathological, heamatologic and biochemical findings Medycyna Wet.63(7).

Oraby, F. A.; Kheir El-Din, A. W.; Hilali, M. A.; Edris, G. O.; Aggour, M. G. and Tawfi, A. (1989) : Biological and histopathological studies on Eimeria grenieri in guinea fowl; Alex. J.Vet.Sci 5(2):91-97.

Ramadan, A.; Abo-El-sooud, K. and EL-bahy, M. M. (1997) : Anticoccidial efficacy of toltrazuril and halofuginone against Eimeria tenella infection in broiler chickens in Egypt. Research in Veterinary Science, 62, 175-178 .

Ramadan, A. and Abo-EL-Sooud (1997) : anticoccidial efficacy of toltrazuril and halofuginone against Eimeria tenella infection in broiler chicken in Egypt . J.Research in veterinary science . Vol 62. 172-178.

Ramadan, A.; Afifi, N. A.; Atef, M.; EL-Bahy, M. M. and EL-Mansoury, H. A. (1993a) : Interactive effects of ascogen and anticoccidial compounds in uninfected and Eimeria tenella-infected broiler chicks. World's Poultry Science Association Proceedings, 9th European Symposium on Poultry Nutrition, 5-9 September 1993, Jelenica Gora, Poland. pp 387-392.

Ramadan, A.; Atef, M.; Afifi, N. A.; EL-Bahy, M. M. and EL-Mansoury, H. A. (1993b) : Interaction between nutrigen and some anticoccidial compounds in healthy and Eimeria tenella-infected broiler chicks.

World's Poultry Science Association Proceedings, 9th European Symposium on Poultry Nutrition, 5-9 September 1993, Jelenica Gora, Poland. pp 393-397.

Reitman, S. and Frankel, S. and Amer. J. (1957): Clin. Path., 28-56.

Roy, A. V. Clin. Chem. (1970) : 16 :431.

Rushton, J.; P. K., Thornton and M. J. Otte (1999) : Methods of economic impact assessment. Rev. Sci. Tec. Off. Int. Epiz., 18 : 315-342.

Schultz, A.; Uric acid . Kaplan A., et al., (1984) : ClinChem The C. V. Mosby C. O. St Louis Toronto. Princeton 1261-1266 and 418.

Soulsby E.J . I. (1968): Helminthes, Arthropods and protozoa Domestic Animals. 7th ed. Bailliere-Tindall, London.

Snedecor, G. W. and Cochran, W. G. (1981) : Statistical Methods. 7th Ed. The Iowa State University, Ames, Iowa, USA.

Stevens, D. A. (1998) : Coccidiosis. Pages 591-59 in Encyclopedia of Immunology. 2nd ed. Vol I. P. J. Delves, and I. M. Roitt, ed. Acad. Press, London.

Suo, X. and G. Q. Li. (1998) : Coccidia and Coccidiosis of Domestic Fowl (in Chinese).Chinese Agricultural University Press, Beijing.

Tracy, J. W. and Webster, L. T. (1996) : Drugs used in chemotherapy of protozoal infection p. 987-1008 . In Hardman J.G., and limbird L.E., (ed). The pharmacological basis of theraputics. 9th ed. Mc Graw -lill Bookco., New York, N.Y.

Vertommen, M. H. and Peek, H. W. (1990) : Efficacy of toltrazuril in broilers and development of laboratory model for sensitivity testing of Eimeria field isolates Veterinary Quarterly 12(3): 183-192.

Weber, G. M. and Frigg, M., (1986) : Comparative efficacy of lasalocid and monensin against coccidia of two field isolates, repeatedly propagated in medicated chicks. In: L.R. McDougald, P.L. Joyner and L.P. Long (Editors), Research in Avian Coccidiosis. Univ. Georgia, Atlanta, pp. 363-371.

الملخص العربى

تقييم كفاءة عقار التولترازوريل أثناء العدوى المعملية بالكوكسيديا فى الدجاج

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يعتبر عقار التولترازوريل من أحدث الأدوية المضادة للكوكسيديا والتى أحدثت أثر فعال فى علاج الكوكسيديا ولذا : أجريت هذه الدراسة لتقييم استخدام التولترازوريل أثناء المراحل المختلفة من دوره حياة الكوكسيديا على ١٢٠ كتكوت (نوع كب) وتم تقسيمها إلى (المجموعة الأولى) ضابط سلبى ١٥ كتكوت) والثانية (غير معداه ولكن معالجة ١٥ كتكوت) والثالثة (ضابط إيجابى ٤٥ كتكوت) والرابعة (معداه ومعالجة بالتولترازوريل ٢٥مجم / لتر ماء شرب) وتحتوى على عدد ٤٥ كتكوت والتى قسمت إلى ثلاث مجموعات فرعية كالتالى :

- مجموعة أ : معداة ومعالجة بالتولترازوريل (٢٥ مجم / لتر ماء شرب / اليوم) لمدة ثلاث أيام متتالية بعد العدوى لدراسة التأثير على الطور الأجنسى الأول.
- مجموعة ب : معداة ومعالجة بالتولترازوريل (٢٥ مجم/لتر ماء شرب / اليوم) فى اليوم الرابع والخامس من العدوى لدراسة التأثير على الطور الأجنسى الثانى.
- مجموعة ج : معداة ومعالجة بالتولترازوريل (٢٥ مجم / لتر ماء شرب / اليوم) لمدة يوم واحد فقط (السادس من العدوى).

وقد أعطيت الطور المعداة خليط من الحويصلات المتجرثمة للأيميريا (٥٠٠ر٠٠٠ حويصلة) وتم تقييم القدرة العلاجية من خلال عدة معايير (عدد حويصلات الأيميريا فى الزرق من اليوم السابع للعدوى وحتى اليوم الثانى عشر بالإضافة لتقييم الآداء الإنتاجى ونسبة النفوق وأخذ عينات الدم لفصل المصل وتقييم وظائف الكبد والكلى.

وقد أسفرت النتائج عن مدى فاعلية التولترازوريل فى علاج الكوكسيديا وخاصة عند اليوم الرابع والخامس من العدوى وذلك من خلال قدرته على تقليل عدد حويصلات الأيميريا فى الزرق وزيادة الوزن وتحسين معدلات التحول الغذائى كما أن المجموعات المعالجة لم تظهر تغير ملحوظ فى وظائف الكبد والكلى.