



## BIOCHEMICAL EFFECTS OF ANTI PROTOZOA ON GASTROINTESTINAL TRACT ENZYMES AND RELATED HORMONES IN RABBITS

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### ABSTRACT

This study aimed to evaluate the biochemical effects of some anti protozoa agents as propolis and toltrazuril in the treatment of coccidiosis disease and their effects on certain gastrointestinal enzymes and related hormones in rabbits. The rabbits were divided into four equal groups each of six rabbits, group 1 control non infected group. However, group 2, 3, 4 were infected with 40,000 sporulated oocysts of *Eimeria* for each rabbit. Group 2 infected non-treated all over the experimental period. Group 3 (propolis treated group) rabbits treated orally with propolis at a dose of 200 mg/kg body weight for 2 weeks after two weeks of infection. Group 4 (toltrazuril treated group) rabbits treated orally with toltrazuril at a dose of 20 mg/kg body weight for 2 weeks after two weeks of infection. Blood samples were collected before, during and after treatment at 2, 4, 6 weeks post infection for biochemical determination. The obtained results revealed that, administration of sporulated oocyst of *Eimeria* species to normal rabbits exhibited marked decrease in amylase, lipase, gastrin, catalase and GST, with an increase in ALT, AST, GGT, ALP and L-MDA compared to control group. In toltrazuril treated group these parameters remains changed after two weeks of treatment. While after two weeks post stoppage of treatment all parameters changed towards the normal values in the control group, and rabbits faeces was free from *Eimeria* oocysts. On the other hand rabbits treated with propolis showed improvement of all parameters and reversed towards normal control value and rabbits faeces were free from *Eimeria* oocysts, in addition increase of appetite and body weight was also obtained. These results concluded that, propolis is a drug of choice for treatment of rabbit coccidiosis.

**KEY WORDS:** propolis, toltrazuril, *Eimeria* spp., amylase, lipase, gastrin and antioxidant.

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### 1. INTRODUCTION

Coccidiosis remains a serious problem on rabbit farms, causing high mortality with significant economic losses worldwide (1). The characteristic symptoms associated with hepatic coccidiosis in rabbits include loss of appetite, anorexia, hair loss, diarrhea, yellowish mucous membranes, fatigue, abdomen swelling and significant loss in body weight, (2), as well as increases in serum AST, ALT and GGT activities

depending on hepatocellular damage and cholestasis which have been reported in the rabbits with hepatic coccidiosis, (3). The authors add that, parasitic infection causes change in lipid peroxidation which consider one of the best indicators of the level of reactive oxygen species (ROS) that induced systemic biological damage (4). However antioxidant system plays a role in the protection of the phagocytic leukocytes against their own products and oxygen

radicals, (3). Most of the current anti coccidial drugs show low efficacy and cause deleterious side effects (5). The extensive use of chemical anti coccidial drugs in controlling this disease has led to the development of drug-resistant parasites as well as the side effects of some anti coccidial drugs will have serious consequences for future disease control, (6). Therefore, to combat the disease there is a pressing need to identify new effective drugs that are safe for the animals and the environment. Toltrazuril, a broad-spectrum anticoccidial drug against different *Eimeria* species, is used for the treatment of coccidiosis in rabbits, (7). The drug is effective on both schizont and gamont stages of *Eimeria*, (8). Propolis (bee glue) is a natural dark-coloured, resinous sticky substance produced by honey bees by mixing their own waxes with resins collected from plants, and is used as a sealant and sterilant in their nests (9). Its properties are mostly attributed to the phenolic components such as flavonoids, (10), that are thought to be responsible for many of its biological and pharmacological activities, (11). The anticoccidial efficacy of Propolis against coccidia of rabbits has been reported, (5). A pronounced decrease in the activities of serum ALT, AST, ALP and GGT after oral treatment with aqueous propolis extract in toxicity induced by 4-tert-OP in rats indicate hepato-protected effects of propolis, (12). There for, this study aimed to evaluate the biochemical effects of some anti protozoa agents as propolis and toltrazuril in the treatment of coccidiosis and their effects on certain gastrointestinal enzymes and related hormones in rabbits via determination of Serum Amylase, Lipase, Gastrin, Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Gama glutamyltransferase (GGT), Alkaline phosphatase (ALP), L-malondialdehyde (L-MDA), Plasma Catalase and Glutathione-s-transferase (GST).

## 2. MATERIAL AND METHODS

### 2.1. *Experimental Animals:*

24 male rabbits, weighting 750 – 900 gm were used in the experimental investigation of this study. Animals were housed in clean separate metal cages. Rabbits were kept at a constant environmental and nutritional condition throughout the period of experiment. The animals were left 10 days for acclimatization before the beginning of the experiment.

### 2.2. *Drugs:*

Propolis: Liquid dark-colored natural Propolis (dissolve 20gm of pure liquid propolis in 100 ml distilled water). Toltrazuril: Toltrazuril Solution 2.5% (Zhejiang Mingzhu Animal Health Products Co., Ltd. China). It is a triazinon derived compound and its chemical structure is as follows: 1-methyl-3-(3-methyl-4-(4-(trifluoromethyl) thio) phenoxy) phenyl-1,3,5-triazine 2,4,6 (1H,3H,5H)-trione, (13).

### 2.3. *Rabbit infection:*

Each rabbit was infected by oral administration of 40,000 sporulated *Eimeria* oocysts. Preparation of sporulated *Eimeria* oocysts was carried out by concentration-flotation technique for positive faecal samples obtained from infected rabbits according to, (14). *Eimeria* species were identified after sporulation of faeces in a thin layer of 2.5 % (w/v) potassium dichromate for one or two weeks at 25 °C, according to, (15). Oocysts per gram of feces (OPG) were estimated by McMaster technique according to, (16)

### 2.4. *Experimental design:*

After faecal examination occurred and all rabbits faeces free from any oocyst. Rabbits were divided into four equal groups, each group contain six male rabbits as follow:- Group 1: Control normal group: Contained 6 non-infected male rabbits and saved as healthy control group. Groups 2, 3, 4 infected orally with 40,000 sporulated oocysts *Eimeria* speices and left without

treatment for two weeks before the onset of anti protozoa drugs administration.

Group 2: Infected non-treated group: Included 6 infected male rabbits left without treatment all over the experimental period. Group 3: Propolis treated group: Comprised 6 infected male rabbits and treated orally with propolis at a dose of 200 mg/kg body weight (Daily) for 2 weeks, (17). Group 4: Toltrazuril treated group: Contain 6 infected male rabbits and treated orally with toltrazuril at a dose of 20 mg/kg body weight (Daily) for 2 weeks, (18).

#### 2.5. Sampling:

Faecal samples: Faecal samples were collected from all animals groups four times along the duration of experiment. 1- At the onset of the experiment (before experimental infection). 2- Two weeks post infection (before anti protozoa drugs treatment). 3- Four weeks post infection (two weeks after drugs administration). 4- Six weeks post infection (two weeks after stoppage drugs administration). Blood samples: Blood samples were collected after over night fasting from all animals groups three times along the duration of experiment. 1- Two weeks post infection (before anti protozoa drugs treatment). 2- Four weeks post infection (two weeks after drugs administration). 3- Six weeks post infection (two weeks after stoppage drugs administration).

#### 2.6. Biochemical analysis:

Serum and Plasma (EDTA plasma) were separated by centrifugation at 3000 r.p.m for 10 minutes. The clean, clear serum and plasma were received in dry sterile tubes using sterilized pipettes for determination of Serum amylase (19), lipase (20), gastrin (21), alanine amino transferase (ALT) (22), aspartate amino transferase (AST) (22), Gamma-glutamyltransferase (GGT) (23), Alkaline phosphatase (ALP) (24) and L-malondialdehyde (L-MDA) (25) in addition to Plasma catalase (26) and GST (27).

### 3. RESULTS

The obtained data in table (2) revealed that administration of sporulated oocyst of *Eimeria* spp. to normal rabbits exhibited a non significant decrease in serum amylase after 2 weeks of infection this decrease become significant decrease after 4 and 6 weeks as well as a significant decrease in lipase and gastrin was recorded after 2, 4 and 6 weeks of infection compared to control group. In addition, infected rabbits showed loss of appetite and body weight. Regarding propolis treated group a significant increase in serum amylase, lipase and gastrin were recorded after 2 weeks from beginning of treatment, which became non-significant increase in serum lipase only after 2 weeks from of stoppage treatment compared to control group. In addition treated rabbits showed marked increase in appetite and body weight. Concerning toltrazuril treated group a significant decrease in serum amylase, lipase and gastrin after 2 weeks from beginning of treatment, which became a non-significant increase in serum amylase and gastrin after 2 weeks from stoppage treatment compared to control group. However a decrease in appetite through drug administration period and loss of body weight. The recorded data in table (2,3) revealed that, administration of sporulated oocyst of *Eimeria* spp. to normal rabbits exhibited a significant increase in serum ALT, AST, ALP activities after 2,4 and 6 weeks of infection and a non significant increase in serum GGT activity after 2,4 and 6 weeks of infection when compared with control group. Propolis treated group showed a non-significant decrease in serum ALT and AST activities, while slight increase in serum GGT and ALP activities was recorded after 2 weeks from beginning of treatment and after 2 weeks from stoppage of treatment compared to control group. In toltrazuril treated group a significant increase in serum ALT, AST and ALP activities, while a non significant increase in serum GGT activity were

recorded after 2 weeks from beginning of treatment compared to control group. After 2 weeks from stoppage of treatment, these parameters decrease towards the control group.

Administration of sporulated oocyst of *Eimeria* spp. to normal rabbits (table3) exhibited a significant increase in serum L.MDA concentration after 2, 4 and 6 weeks of infection however plasma catalase and GST activities showed non significant decrease after 2 weeks of infection this decrease became significant after 4 and 6 weeks of infection compared to control group. Treatment of infected group with propolis showed a non-significant decrease in serum L.MDA concentration however non-significant increase in plasma catalase and GST activities was recorded after 2 weeks from beginning of treatment and after 2 weeks from stoppage of treatment when compared with infected nontreated group. Regarding toltrazuril treated group a significant increase in serum L.MDA concentration was recorded however plasma catalase and GST activities revealed a significant decrease after 2 weeks from beginning of treatment compared to control group. These results changes towards the control group after 2 weeks from stoppage treatment.

#### 4. DISCUSSION

The obtained data in table (2) revealed that administration of sporulated oocyst of *Eimeria* spp. to normal rabbits exhibited anon significant decrease in serum amylase after 2 weeks of infection this decrease become significant decrease after 4 and 6 weeks as well as a significant decrease in lipase and gastrin was recorded after 2, 4 and 6 weeks of infection compared to control group. In addition infected rabbits showed loss of appetite and body weight. These observations were similar to the reported studies of (2) who recorded that the characteristic symptoms associated with coccidiosis in rabbits include loss of appetite, anorexia, hair loss, diarrhea,

yellowish mucous membranes, fatigue, abdomen swelling and significant loss in body weight. The recorded results might be attributed to the damage of the intestinal epithelium caused by the multiplication of *Eimeria* stages that impaired absorption, utilization and assimilation of some elements such as iron and copper (28), this might be lead to loss of appetite and reduce level of digestive enzymes and hormones. Regarding propolis treated group a significant increase in serum amylase, lipase and gastrin were recorded after 2 weeks from beginning of treatment which became non significant increase in serum lipase only after 2 weeks from of stoppage treatment compared to control group. In addition treated rabbits showed marked increase in appetite and body weight. Similar results was obtained by (29) who repoted that, 0.02 and 0.03 g/L propolis caused an increase in the level of amylase and decrease in the levels of aspartate aminotransferase and alkaline phosphatase, attributed these results to the anti coccidial efficacy of Propolis against coccidia of rabbits that prevent the damage of the intestinal epithelium caused by the multiplication of *Eimeria* stages which impaired absorption, utilization and assimilation of some elements such as iron and copper (28), accompanied with increase of appetite and digestive enzymes and hormones in propolis treated group. Authers suggestion stated that propolis might contain digestive enzymes. As, general medicinal uses of propolis have also been described that propolis was included in treatment of digestive tract disorders and immune system support (30). Concerning toltrazuril treated group a significant decrease in serum amylase, lipase and gastrin after 2 weeks from beginning of treatment which became anon significant increase in serum amylase and gastrin after 2 weeks from stoppage treatment compared to control group. However a decrease in appetite through drug administration period and loss of body weight this might be due to long term of administration,

Table (1): Effect of treatment with propolis and toltrazuril on presence or absence Eimeria oocyst in faeces of experimentally infected rabbits with Eimeria spp.

Durations weeks	Animal groups			
	Control	Infected	Propolis treated	Toltrazuril treated
Before infection	(-ve)	(-ve)	(-ve)	(-ve)
Before treatment	(-ve)	(+ +)	(+ +)	(+ +)
Two weeks after treatment	(-ve)	(+ + +)	(-ve)	(-ve)
Two Weeks Post stoppage Treat.	(-ve)	(+ +)	(-ve)	(-ve)

(+) less than 1000 oocyst/gm. (+ +) from 1000 – 2000 oocyst/gm. (+ + +) more than 2000 oocyst/gm.

but after the end of drug administration period the appetite return to normal range. These results might be due to the anticoccidial efficacy of toltrazuril against coccidia that prevent the damage of the intestinal epithelium caused by the multiplication of Eimeria stages and impaired absorption, utilization and assimilation of some elements such as iron and copper (28), that leads to increase in appetite, digestive enzymes and hormones in toltrazuril treated group to return nearly normal control group. The recorded data in table (2,3) revealed that, administration of sporulated oocyst of Eimeria spp. to normal rabbits exhibited a significant increase in serum ALT, AST, ALP activities after 2,4 and 6 weeks of infection and a non significant increase in serum GGT activity after 2,4 and 6 weeks of infection when compared with control group. These observations were came in accordance with the reported studies of (3) who recorded that, the increases in serum AST and ALT activities depending on hepatocellular damage and in serum GGT activity due to cholestasis which have been reported in the rabbits with hepatic coccidiosis. Similarly, a significant increase in serum ALT, AST, ALP, GGT and total bilirubin was recorded in lamb with coccidiosis compared to normal control group, (31). These results attributed to the epithelial tissues damage of the intestinal walls caused by the parasites

and its toxins, (32). Propolis treated group showed a non significant decrease in serum ALT and AST activities, while slight increase in serum GGT and ALP activities was recorded after 2 weeks from beginning of treatment and after 2 weeks from stoppage of treatment compared to control group. These observations were similar to the reported studies of (33), who recorded that the rise in AST, ALT, ALP and GGT activities induced by Thioacetamide administration was significantly reduced by administration of Aqueous extract of propolis or Oil extract of propolis when combined with Thioacetamide, suggesting that propolis protective activity might be due its effect against cellular leakage and loss of functional integrity of the cell membrane in hepatocytes. Moreover, it was reported that propolis reduce the damage caused by coccidiosis mean it has hepatoprotective action that may be due to the antioxidant effect of propolis which was previously confirmed by (34). In toltrazuril treated group a significant increase in serum ALT, AST and ALP activities, while a non significant increase in serum GGT activity were recorded after 2 weeks from beginning of treatment compared to control group. After 2 weeks from stoppage of treatment these parameters decrease towards the control group. The elevation that occurred after 2 weeks from beginning of treatment

Table ( 2 ) : Effect of treatment with propolis and toltrazuril on serum amylase, lipase, gastrin, ALT and AST in experimentally infected rabbits with Eimeria spp.

Duration period	Groups	Parameters				
		Amylase activity (U/L)	lipase activity (U/L)	Gastrin conc. (Pg/ml)	ALT activity (IU/L)	AST activity (IU/L)
Before treatment	Control	323.33 <sup>A</sup> ±29.81	3.42 <sup>B</sup> ±0.18	87.93 <sup>B</sup> ±0.94	40.97 <sup>A</sup> ±2.33	41.87 <sup>A</sup> ±2.68
	Infected	290.00 <sup>A</sup> ±21.93	2.98 <sup>A</sup> ±0.06	83.46 <sup>A</sup> ±1.37	68.13 <sup>B</sup> ±4.24	62.60 <sup>B</sup> ±7.93
	Propolis treated	285.33 <sup>A</sup> ±36.99	2.99 <sup>A</sup> ±0.14	83.17 <sup>A</sup> ±1.11	69.13 <sup>B</sup> ±4.46	61.40 <sup>B</sup> ±5.69
	Toltrazuril treated	281.33 <sup>A</sup> ±35.04	2.94 <sup>A</sup> ±0.17	82.80 <sup>A</sup> ±1.56	67.13 <sup>B</sup> ±6.35	59.27 <sup>B</sup> ±2.15
Two weeks after treatment	Control	336.00 <sup>C</sup> ±32.52	3.45 <sup>B</sup> ±0.25	89.69 <sup>B</sup> ±2.42	40.33 <sup>A</sup> ±2.08	39.40 <sup>A</sup> ±0.95
	Infected	228.67 <sup>B</sup> ±27.71	2.80 <sup>A</sup> ±0.11	80.01 <sup>A</sup> ±1.78	69.63 <sup>B</sup> ±3.5	55.23 <sup>B</sup> ±2.57
	Propolis treated	426.67 <sup>D</sup> ±25.69	4.12 <sup>C</sup> ±0.14	113.00 <sup>C</sup> ±2.3	35.70 <sup>A</sup> ±3.09	37.83 <sup>A</sup> ±4.71
	Toltrazuril treated	169.00 <sup>A</sup> ±21.7	2.73 <sup>A</sup> ±0.15	79.64 <sup>A</sup> ±4.51	99.23 <sup>C</sup> ±5.4	65.17 <sup>C</sup> ±7.22
Two weeks post stoppage treatment	Control	322.67 <sup>B</sup> ±18.89	3.75 <sup>C</sup> ±0.15	89.49 <sup>B</sup> ±1.26	39.83 <sup>A</sup> ±0.91	40.50 <sup>A</sup> ±1.48
	Infected	183.33 <sup>A</sup> ±36.99	2.67 <sup>A</sup> ±0.22	76.49 <sup>A</sup> ±2.65	60.37 <sup>B</sup> ±0.56	52.37 <sup>B</sup> ±2.37
	Propolis treated	414.67 <sup>C</sup> ±28.42	4.00 <sup>C</sup> ±0.24	99.75 <sup>C</sup> ±2.80	37.73 <sup>A</sup> ±3.15	39.03 <sup>A</sup> ±3.46
	Toltrazuril treated	352.00 <sup>B</sup> ±28.04	3.41 <sup>B</sup> ±0.26	90.97 <sup>B</sup> ±1.32	54.27 <sup>B</sup> ±3.28	44.43 <sup>A</sup> ±5.89

Table ( 3 ) : Effect of treatment with propolis and toltrazuril on serum GGT, ALP, L-MDA, Plasma catalase and GST in experimentally infected rabbits with Eimeria spp.

Duration period	Groups	Parameters				
		GGT activity (U/L)	ALP activity (IU/L)	L.MDA conc. (nmol/ml)	catalase activity (U/L)	GST activity (U/L)
Before treatment	Control	15.20 <sup>A</sup> ±2.07	67.90 <sup>A</sup> ±5.28	3.94 <sup>A</sup> ±0.2	405.00 <sup>A</sup> ±23.71	80.93 <sup>A</sup> ±6.04
	Infected	16.23 <sup>A</sup> ±2.39	80.47 <sup>B</sup> ±4.07	5.04 <sup>B</sup> ±0.39	387.00 <sup>A</sup> ±28.22	78.50 <sup>A</sup> ±9.12
	Propolis treated	16.67 <sup>A</sup> ±0.84	79.03 <sup>B</sup> ±1.44	5.01 <sup>B</sup> ±0.33	385.67 <sup>A</sup> ±31.18	77.87 <sup>A</sup> ±1.30
	Toltrazuril treated	16.03 <sup>A</sup> ±2.69	77.57 <sup>B</sup> ±6.11	5.01 <sup>B</sup> ±0.44	383.33 <sup>A</sup> ±37.56	77.37 <sup>A</sup> ±7.00
Two weeks after treatment	Control	15.30 <sup>A</sup> ±1.65	68.87 <sup>A</sup> ±2.71	3.93 <sup>A</sup> ±0.16	407.33 <sup>B</sup> ±21.88	82.03 <sup>C</sup> ±5.32
	Infected	16.67 <sup>A</sup> ±1.60	79.30 <sup>B</sup> ±3.4	5.92 <sup>C</sup> ±0.39	364.00 <sup>A</sup> ±26.65	69.43 <sup>B</sup> ±3.45
	Propolis treated	15.83 <sup>A</sup> ±1.31	68.90 <sup>A</sup> ±6.35	3.45 <sup>A</sup> ±0.23	412.00 <sup>B</sup> ±25.97	89.57 <sup>C</sup> ±5.36
	Toltrazuril treated	17.97 <sup>A</sup> ±1.08	79.47 <sup>B</sup> ±5.09	4.42 <sup>B</sup> ±0.24	355.00 <sup>A</sup> ±18.58	58.33 <sup>A</sup> ±3.78
Two weeks post stoppage treatment	Control	14.73 <sup>A</sup> ±2.46	75.17 <sup>A</sup> ±7.06	3.98 <sup>A</sup> ±0.13	402.00 <sup>B</sup> ±29.26	80.67 <sup>C</sup> ±2.78
	Infected	16.27 <sup>A</sup> ±0.92	87.33 <sup>C</sup> ±9.13	5.95 <sup>B</sup> ±0.54	356.33 <sup>A</sup> ±22.26	61.00 <sup>A</sup> ±9.28
	Propolis treated	15.00 <sup>A</sup> ±1.48	77.47 <sup>AB</sup> ±7.99	3.62 <sup>A</sup> ±0.36	406.00 <sup>B</sup> ±10.6	84.00 <sup>C</sup> ±5.76
	Toltrazuril treated	15.67 <sup>A</sup> ±3.03	85.07 <sup>BC</sup> ±6.33	3.84 <sup>A</sup> ±0.2	383.67 <sup>AB</sup> ±19.78	74.93 <sup>B</sup> ±3.32

may be attributed to long term of administration of toltrazuril and these effects removed after 2 weeks from stoppage of treatment. These results that obtained after 2 weeks from stoppage treatment are similarly (35) recorded that coccidiosis in kids induced a significant increase in serum AST-ALT, alkaline phosphatase, urea and creatinine. The authors added that all above biochemical parameters returned to the normal level after treatment by toltrazuril.

Moreover, (3) attributed the increases in serum AST, ALT and GGT activities to hepatocellular damage and cholestasis which have been reported in the rabbits with hepatic coccidiosis. However the infected group treated with toltrazuril showed no abnormal clinical findings and had a significant decrease in epg values, suggesting that this treatment was effective. The increase in liver enzymes after 2 weeks from beginning treatment might be due to long term administration of drug that might cause stress on liver enzymes, but after two weeks post treatment these enzymes showed marked decrease compared to infected group that became near to control group which confirm the anticoccidial efficacy and hepatoprotective effects of toltrazuril. Administration of sporulated oocyst of *Eimeria* spp. to normal rabbits (table3) exhibited a significant increase in serum L.MDA concentration after 2, 4 and 6 weeks of infection however plasma catalase and GST activities showed non significant decrease after 2 weeks of infection this decrease became significant after 4 and 6 weeks of infection compared to control group. These observations were hand by hand to that of (3) who reported that, the increase in plasma MDA levels in the infected rabbits suggested that *E. stiedae* caused lipid peroxidation resulting from the destruction of the liver parenchyma and bile duct. In addition the decrease in erythrocyte GSH-Px, CAT and SOD activities might be associated with excessive free radicals relasing during the infection or a decrease

in production of these enzyme as a result of liver damage.

Malondialdehyde (MDA), the stable end product of lipid peroxidation. It often represent the first parameter analyzed for proving the involvement of free radical damage. Lipid peroxidation produces a progressive loss of cell membrane integrity, impairment in membrane transport function and disruption of cellular ion homeostasis (36). However, the antioxidant system plays a role in the protection of the phagocytic leukocytes against their own products and oxygen radicals, some investigation have revealed that parasitic infection causes change in lipid peroxidation parameters (3). Treatment of infected group with propolis showed a non significant decrease in serum L.MDA concentration however non significant increase in plasma catalase and GST activities was recorded after 2 weeks from beginning of treatment and after 2 weeks from stoppage of treatment when compared with infected nontreated group, this might be due to antioxidant effects of propolis. Similarly, of (37) declared that propolis cause reduction in MDA levels and increase in SOD, GSH-Px, and CAT activities. Moreover, (12) reported that, Simultaneous treatment with aqueous propolis extract significantly abolished the enhancing effect of the toxic 4-tert-OP on hepatic lipid peroxidation that was expressed by a lower level of MDA in hepatocytes. The author added that administration of aqueous propolis extract alone induced a significant increase in total antioxidant capacity, GST, SOD and CAT compared to control group. The antioxidant activity of propolis and its polyphenolic/flavonoid components are related to their ability to chelate metal ions and scavenge singlet oxygen, superoxide anions, proxy radicals, hydroxyl radicals and peroxynitrite, (38).

Regarding toltrazuril treated group our results showed a significant increase in serum L.MDA concentration however plasma catalase and GST activities revealed a significant decrease after 2 weeks from



beginning of treatment compared to control group. These results changes towards the control group after 2 weeks from stoppage treatment, the results might be due to long administration of drug while after two weeks from stoppage treatment due to antioxidant and anticoccidial effects of toltrazuril (18) the auther recorded a significant reductions in erythrocyte GSHpx, GR-ase, SOD, and catalase activities in Eimeria-infected kids compared to control. However, increasing in these parameters was observed after treatment, particularly with Toltrazuril accompanied with a significant decrease in erythrocyte GSH concentration of infected group compared to control, which was significantly increased after treatment with Propolis and Toltrazuril. On the other hand, significant elevations in serum MDA and nitric oxide were recorded in infected animals, which had been significantly reduced after treatment with Propolis and Toltrazuril.

### CONCLUSION

There for, it was cocluded that, uses of propolis (natural drug) and toltrazuril (synthetic drug) as anti protozoal compounds were effective in treatment of coccidiosis however propolis was more safe and without any harmful effect as it showed efficient role as hepatoprotective and antioxidant with effective antiprotozoa agent.

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## التأثير الكيميائي الحيوي لمضادات الطفيليات وحيدة الخلية على انزيمات الجهاز الهضمي والهرمونات التابعة لها في الأرنب

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### الملخص العربي

زاد في الآونة الأخيرة استخدام العديد من الأدوية المضادة للطفيليات وحيدة الخلية نظرا لانتشار هذه الطفيليات وتأثيرها الضار على الثروة الحيوانية. ومن أكثر هذه الطفيليات انتشارا هو طفيل الأيميريا الذي يتسبب في إصابة الحيوانات بمرض الكوكسيديا. ونظرا لوجود آثار جانبية للعديد من هذه الأدوية لهذا تهدف الدراسة دراسة التأثيرات الكيميائية الحيوية لمضادات الطفيليات وحيدة الخلية على الخمائر والهرمونات التابعة للجهاز الهضمي في الأرنب تم استخدام نوعين من الأدوية التولترازوريل كعلاج كيميائي والبروبوليس (صمغ النحل) كمادة طبيعية. تم إجراء التجربة على عدد 24 أرنب تم تقسيمهم الى 4 مجموعات. المجموعة الأولى: -تعتبر المجموعة الضابطة. تم عمل عدوى لكل الأرنب الموجوده بالمجموعات الثانية والثالثة والرابعة وذلك بتجريب الأرنب لطفيل الأيميريا (40000 طفيل لكل أرنب). المجموعة الثانية: -تحتوي على 6 أرنب تم تجريعهم بالطفيل ولم يتم علاجهم حتى نهاية التجربة. المجموعة الثالثة: -تحتوي على 6 أرنب تم تجريعهم بالطفيل ثم بعد أسبوعين من العدوى تم علاجهم بمادة البروبوليس عن طريق التجريع والجرعة هي 200 مجم / كجم من وزن الجسم يوميا ولمدة أسبوعين. المجموعة الرابعة: -تحتوي على 6 أرنب تم تجريعهم بالطفيل ثم بعد أسبوعين من العدوى تم علاجهم بمادة التولترازوريل عن طريق التجريع والجرعة هي 20 مجم / كجم من وزن الجسم يوميا ولمدة أسبوعين. تم تجميع عينات البراز من كل المجموعات أربع مرات: -قبل العدوى وبعد أسبوعين من العدوى (قبل بداية العلاج) وبعد 4 أسابيع من العدوى (بعد نهاية فترة العلاج مباشرة) وبعد 6 أسابيع من العدوى (بعد أسبوعين من نهاية العلاج) لفحصهم تحت الميكروسكوب. تم تجميع عينات الدم من كل المجموعات ثلاث مرات :- بعد أسبوعين من العدوى (قبل بداية العلاج) وبعد 4 أسابيع من العدوى (بعد نهاية فترة العلاج مباشرة) و بعد 6 أسابيع من العدوى (بعد أسبوعين من نهاية العلاج) لقياس بعض التحاليل البيوكيميائية وهي :- الأميلاز و الليبيز و الجاسترين و الألانين أمينو ترانس فيراز و الأسبرتات أمينو ترانس فيراز و الفوسفاتيز القاعدي و الجاما جليوتاميل ترانس فيراز و الألبومين و البروتين الكلي و البيليروبين الكلي و ال مالون داي ألدهيد و الهيموجلوبين و انزيم الكتاليز و الجلوتاثيون اس ترانس فيراز. أوضحت الدراسة أن العدوى بطفيل الأيميريا أدى الى حدوث تغيرات في القياسات البيوكيميائية كزيادة في وظائف الكبد وانزيم ال مالون داي ألدهيد ونقص انزيمات وهرمونات الهضم والهيموجلوبين وانزيم الكتاليز و الجلوتاثيون اس ترانس فيراز. وأن استخدام كلاً من البروبوليس (كعلاج طبيعي) والتولترازوريل (كعلاج كيميائي) كان له دور فعال حيث أنهما قضيا نهائياً على طفيل الأيميريا. ولكن استخدام البروبوليس لفترات طويلة اتضح أنه أكثر أماناً وليس له آثار جانبية بالمقارنة بالتولترازوريل. حيث أن تناول البروبوليس أدى الى زيادة في انزيمات وهرمونات الهضم وتحسين وظائف الكبد وزيادة نسبة الهيموجلوبين والمحافظة على مضادات الأكسدة. يتضح مما ذكر أنه يمكن استخدام البروبوليس كمضاد للطفيليات وحيدة الخلية وفي تحسين عملية الهضم وكفاتح للشهية وفي المحافظة على وظائف الكبد وكمضاد للأكسدة.

(مجلة بنها للعلوم الطبية البيطرية: عدد 25 (2): 113-124, ديسمبر 2013)