ANTI CESTODAL ACTIVITY OF SOME DERIVATIVES OF THE OPEN LACTAM FORM OF PRAZIQUANTEL (N – ACYL / COO – ALKYL) IN CHICKENS

By

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KEY WORDS

PZQ structure - activity relationship, anticestodal efficacy, *R. tetragona*, chicks.

ABSTRACT

One hundred and eighty, 21 days old male Bovans type chicks allotted to nine groups were infected with *Railietina tetragona* cysticercoids. Six groups were treated with the N-acyl /COO - alkyl derivatives of the open lactam form of praziquantel (OLF - PZQ) in oral doses of 20 mg/kg body weight on days 21 and 24 post - infection. The efficacy of the compounds was evaluated as 62, 70, 44, 44, 20 and 30 % following the first dose and 84, 88, 66, 74, 44 and 48 % after the administration of the second dose in groups 4,5,6,7,8 and 9 respectively. Histopathological, haematological, and biochemical alterations were evaluated and compared with those in infected chicks. Neither clinical signs of toxicity nor severe pathologic -al changes were observed in the birds treated with the different compounds.

INTRODUCTION

Available reports have indicated that knowledge about the efficacy of praziquantel PZQ, as the anthelmintic drug of choice is inadequate (Stelma *et al.*, 1997; Cioli *et al.*, 1995; Fallon *et al.*, 1997) .All the reports dealt with the structure - activity relationship of PZQ emphasized the importance of the pyrazinoxy isoquinoline ring system (Andrews *et al.*, 1983).

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We here report the efficacy and toxicity of N - acyl / COO - aikyl derivatives of OLF – PZQ against mature *Railietina tetragona* infection in Bovans type chicks.

MATERIALS AND METHODS

Birds: One hundred and eighty 1-day- old male Bovans type chicks were bought from Coral Company, Khartoum, and reared at the premises of the Faculty of Veterinary Medicine and Animal Production, Kuku, Khartoum North. The chicks were provided with *ad libitum* feed and drinking water with illumination at night. At the age of 21 days, the chicks were assigned randomly into 9 groups of 20 chicks each. Each group was kept separately under strict conditions to prevent accidental infection with tapeworms.

Infection: *R. tetragona* cysticercoids were recovered by dissection of adult ants, *Tetramorium caespitum* which were found in poultry farms. 10 cysticercoids per chick were fed in gelatin capsules to chicks in nine groups that were previously starved for 5 hours at the age of 21days.One group was kept as control (group 1) uninfected untreated and two other groups were either infected – untreated or vehicle treated.

Compounds and synthesis: OLF-PZQ was obtained by selective hydrolysis of PZQ. The different derivatives were prepared by standard synthetic procedures utilizing conditions, which prevented the chemical cyclization to the parent PZQ (Saeed, 2000). The identities of the prepared compounds were elucidated by spectroscopic means (I.R., H^1 – and C^{13} – NMR., M.S.) as described by (Saeed,2000). The six compounds were:

I) N – (1,2,3,4- tetrahydro – 2 – acetyl – 1 - isoquinolinyl methyl) – N-cyclohexyl carbonyl glycine.

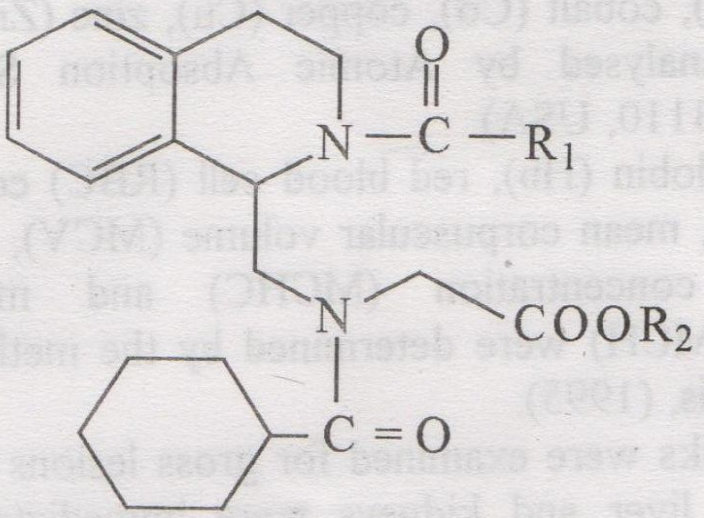
II) Methyl - N – (1,2,3,4- tetrahydro – 2- acetyl –1- isoquinolinyl methyl) – N-cyclohexyl carbonyl glycinate.

III) N – (1,2,3,4- tetrahydro – 2- propionyl –1- isoquinolinyl methyl) – N-cyclohexyl carbonyl glycine

IV) Methyl- N – (1,2,3,4- tetrahydro – 2- propionyl –1- isoquinolinyl methyl) – N-cyclohexyl carbonyl glycinate

(V) N – (1,2,3,4- tetrahydro -2- (ethyl formate) –1- isoquinolinyl methyl) – N-cyclohexyl carbonyl glycine.

(VI) Methyl -N– (1,2,3,4- tetrahydro –2- (ethyl formate) –1-isoquinolinyl methyl) – N- cyclohexyl carbonyl glycinate.



(I) $R_1 = CH_3$, $R_2 = H$, (II) $R_1 = CH_3$, $R_2 = CH_3$.
(III) $R_1 = CH_2CH_3$, $R_2 = H$, (IV) $R_1 = CH_2CH_3$, $R_2 = CH_3$.
(V) $R_1 = OCH_2CH_3$, $R_2 = H$, (VI) $R_1 = OCH_2CH_3$, $R_2 = CH$.

Figure 1: Chemical structures of the compounds tested

Treatment of infected chicks: The compounds (I – VI) were given orally to each chick in groups (4 – 9) respectively at a dose rate of 20 mg / kg / BW at day 21 and day 24 post - infection. Each dose given to chick was dissolved in 15% propylene glycol. Each chick in group (3) was treated with 0.5 ml of 15% propylene glycol, group (2) chicks were kept as infected untreated control and group (1) chicks were uninfected untreated control.

Recovery of worms: Ten birds / group were slaughtered three days after each treatment on days 24 and 27 post - infection. At necropsy, the intestine of each bird was slit open longitudinally after it had been placed in Petri dishes containing warm solution of normal saline. Any visible worms were collected and counted for each chick. Percent efficacy / group was recorded.

Laboratory assays: Blood samples were collected from each chick at slaughter (Days 24 and 27 post- infection) into two dry clean bottles, one of them contained ethylene diamine tetra acetic acid (EDTA) as anticoagulant for haematology and the other without anticoagulant for serobiochemical analysis.

The activity of aspartate amino transferase (AST), and the concentrations of total protein, and uric acid were measured by

commercial kits (Plasmatec Laboratory Products ltd., England). Serum concentrations of sodium (Na), calcium (Ca), magnesium (Mg), iron (Fe), cobalt (Co), copper (Cu), zinc (Zn), and manganese (Mn) were analysed by Atomic Absoption Spectrophotometer (Perkin Elmer 3110, USA).

Haemoglobin (Hb), red blood cell (RBC) counts, packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular haemoglobin concentration (MCHC) and mean corpuscular haemoglobin (MCH) were determined by the methods described by Dacei and Lewis, (1995).

All chicks were examined for gross lesions and specimens of the intestines, liver and kidneys were immediately fixed in 10% formal saline, embedded in paraffin wax, sectioned and stained with haematoxylin and eosin (H & E) for microscopic examination.

Statistical analysis of data: Data were statistically analyzed using SPSS programme, statistical package for windows, version 11.5 (2002). The statistical analysis was carried out at $p < 0.05$.

RESULTS

Efficacy of compounds: No clinical abnormaliteis were seen in the chicks infected with *R . tetragona* at 10 cysticercoids per chick or in the chicks infected and treated at three - day intervals (days 21 and 24) with the different compounds in doses of 20 mg / kg BW. The compounds were well tolerated by the chicks and no death took place during the experiment.

Parasitological findings: The number of worms, *R.tetragona* in the intestines of the chicks were recovered and counted during post – mortem examination of each chick (Tables 1 and 2). It was found that all N – acyl / COO alkyl derivatives of the open lactam form of praziquantel (OLF – PZQ) possessd anticestodal activity which was highest after the second dose especially with regards to compounds I and II.

Pathological findings: Necropsy findings: No significant post- mortem changes were recorded in any of the chicks, which had been slaughtered following completion of the dosing of the different compounds.

Table 1: Efficacy of single dose of N-acyl / COOH and N- acyl / COO alkyl derivatives of the open lactam form of praziquantel against *R. tetragona* infection in chicks

Group / compound	No. of birds/group	No. of cysticercoids/chick	No. of cysticercoids/group	Age of infection	Total No. of worms / group	Efficacy %
1 uninfected – untreated control	10	--	--	--	--	--
2 infected untreated control	10	10	100	21	100	--
3 PRG 0.5 ml	10	10	100	21	100	00
4 (R_1=CH_3,R_2=H)	10	10	100	21	38	62
5 (R_1=CH_3,R_2=CH_3)	10	10	100	21	30	70
6 (R_1=C_2H_5,R_2=H)	10	10	100	21	56	44
7 (R_1=C_2H_5,R_2=CH_3)	10	10	100	21	56	44
8 (R_1=OC_2H_5,R_2=H)	10	10	100	21	80	20
9 (R_1=OC_2H_5,R_2=CH_3)	10	10	100	21	70	30

Table (2) Efficacy of 2 doses, 3 days apart of N-acyl / COOH and N- acyl / COO alkyl derivatives of the open lactam form of praziquantel against *R. tetragona* infection in chicks

Group / compound	No. of chicks/group	No. of cysticercoids/chick	No. of cysticercoids /group	Age of infection	Total No. of worms / group	Efficacy %
1 uninfected – untreated control	10	--	--	--	--	--
2 infected untreated control	10	10	100	21	100	--
3 PRG 0.5 ml	10	10	100	21	100	00
4 (R_1=CH_3,R_2=H)	10	10	100	21	16	84
5 (R_1=CH_3,R_2=CH_3)	10	10	100	21	12	88
6 (R_1=C_2H_5,R_2=H)	10	10	100	21	34	66
7 (R_1=C_2H_5,R_2=CH_3)	10	10	100	21	26	74
8 (R_1=OC_2H_5,R_2=H)	10	10	100	21	56	44
9 (R_1=OC_2H_5,R_2=CH_3)	10	10	100	21	52	48

PRG = propylene glycol (15% solution).

Histopathological findings: The microscopic lesions were mainly observed in the liver, kidneys and intestines.

Liver: Hepatic lesions in chicks infected with *R .tetragona* and given the test compounds were mild and consisted of centrilobular patocelluar necrosis or degeneration with foamy appearance of the cytoplasm of hepatocytes particularly in chicks receiving compounds III (group 6) and IV (group 7). Slight congestion of the hepatic blood vessels and sinusoids and lymphocytic infiltration in the portal area were noticed. No significant lesions were seen in the uninfected - untreated (group 1) chicks.

Kidneys: There was congestion of the renal blood vessels. The epithelial cells of some of the proximal convoluted tubules were degenerated and / or necrotic with acidophilic homogeneous material in the affected renal tubules especially in chicks treated with compounds III and IV (groups 6 and 7). No other renal lesions were seen in treated chicks.

Small intestine: Slight lymphocytic infiltration was observed in mucosa and submucosa of all the chicks infected - untreated and infected - treated groups. Scolicial parts of the worms sometimes were seen in the submucosa of the experimental chicks.

Changes in serum constituents: Significant decreases ($p < 0.05$) were observed in the values of AST and total protein in the test and infected untreated groups in slaughter I and II (Tables 3 a, b). Compared to the uninfected untreated chicks (group 1), a significant increase ($p < 0.05$) was observed in AST activity in the groups treated with compounds V and VI at slaughter I and the groups treated with compounds I, II, III and IV at slaughter I. there was no difference ($p < 0.05$) in total protein concentration between the uninfected – untreated control and the test groups at slaughter I and II, but a significant decrease ($p < 0.05$) in total protein value was observed in the group treated with compound V at slaughter I and the groups treated with compounds V and VI at slaughter II .

No significant differences ($p > 0.05$) in uric acid, sodium or potassium concentration were observed between the test and the uninfected – untreated or the infected - untreated control groups during slaughter I and II. Significant increase ($p < 0.05$) in uric acid

Table 3a: Serobiochemical changes in chicks infected with *R. tetragona* and treated with N-acyl/COOH and N-acyl/COOMe derivatives of the open lactam form of praziquantel.

Group / compound	No. of chicks	Single dose (slaughter I)			2doses, 3 days apart (slaughter II)		
		AST (U/l)	Total protein (g/dl)	Uric acid (mg/dl)	AST (U/l)	Total protein (g/dl)	Uric acid (mg/dl)
1 uninfected – untreated control	10	^{NS} 22.97 ± 1.3 *	^{NS} 5.01 ± 0.9 *	^{NS} 5.3 ± 0.9 ^{NS}	^{NS} 25.42 ± 2.4 *	^{NS} 6.77 ± 0.71 *	^{NS} 5.60 ± 1.2 ^{NS}
2 infected untreated control	10	^{NS} 33.12 ± 0.7 ^{NS}	^{NS} 3.12 ± 0.21 ^{NS}	^{NS} 6.01 ± 0.5 ^{NS}	^{NS} 34.6 ± 6.1 ^{NS}	^{NS} 3.5 ± 0.31 ^{NS}	^{NS} 6.39 ± 1.1 ^{NS}
3 PRG 0.5 ml	10	^{NS} 33.95 ± 0.8 ^{NS}	^{NS} 3.23 ± 0.40 ^{NS}	^{NS} 6.05 ± 0.82 ^{NS}	^{NS} 35.0 ± 1.12 ^{NS}	^{NS} 3.76 ± 0.50 ^{NS}	^{NS} 6.61 ± 1.3 ^{NS}
4 (R_1=CH_3,R_2=H)	10	^{NS} 25.23 ± 2.3 *	^{NS} 6.34 ± 1.1 *	^{NS} 6.1 ± 1.1 ^{NS}	-23.38 ± 1.3 *	^{NS} 7.27 ± 0.6 *	^{NS} 6.69 ± 0.9 ^{NS}
5 (R_1=CH_3,R_2=CH_3)	10	^{NS} 24.98 ± 2.7 *	^{NS} 6.2 ± 0.95 *	-7.16 ± 1.0 ^{NS}	-27.71 ± 1.49 *	^{NS} 7.10 ± 0.51 *	^{NS} 6.81 ± 1.2 ^{NS}
6 (R_1=C_2H_5,R_2=H)	10	^{NS} 26.1 ± 4.2 *	^{NS} 6.14 ± 0.9 *	^{NS} 4.2 ± 0.95 ^{NS}	-31.81 ± 0.8 *	^{NS} 5.92 ± 0.71 *	^{NS} 5.45 ± 2.1 ^{NS}
7 (R_1=C_2H_5,R_2=CH_3)	10	^{NS} 23.41 ± 3.2 *	^{NS} 4.55 ± 0.27 *	-7.07 ± 0.9 ^{NS}	-21.49 ± 4.0 *	^{NS} 6.44 ± 0.64 *	^{NS} 6.56 ± 1.0 ^{NS}
8 (R_1=OC_2H_5,R_2=H)	10	-35.31 ± 3.2 *	-3.85 ± 0.15 *	^{NS} 6.26 ± 1.3 ^{NS}	^{NS} 30.17 ± 6.0 *	-5.42 ± 1.06 *	^{NS} 7.8 ± 2.3 ^{NS}
9 (R_1=OC_2H_5,R_2=CH_3)	10	-33.14± 6.2 *	-4.3 ± 0.9 *	^{NS} 5.75 ± 1.7 ^{NS}	^{NS} 29.71 ± 1.3 *	-5.86 ± 0.27 *	^{NS} 7.77 ± 2.4 ^{NS}

PRG - propylene glycol 15% solution, Mean ± SD. Upper right : compared to infected untreated control, Lower left : compared to uninfected untreated control, NS : not significant,

* significant at $p < 0.05$

Table 3b: Serobiochemical changes in chicks infected with *R. tetragona* and treated with N-acyl/COOH and N-acyl/COOMe derivatives of the open lactam form of praziquantel.

Group / compound	No. of chicks	Single dose (slaughter I)			2 doses, 3 days apart (slaughter II)		
		Ca (mg/dl)	Fe (µg/dl)	Cu (µg/dl)	Ca (mg/dl)	Fe (µg/dl)	Cu (µg/dl)
1 uninfected – untreated control	10	NS 13.05 ± 0.25 *	NS 85 ± 13 NS	NS 19 ± 05 NS	NS 13.00 ± 0.32 *	NS 85 ± 14 NS	NS NS 18.1 ± 03
2 infected untreated control	10	NS 11.60 ± 0.28 NS	NS 82 ± 09 NS	NS 18 ± 03 NS	NS NS 11.70 ± 0.19	NS 89 ± 10 NS	NS NS 18.5 ± 01
3 PRG 0.5 ml	10	NS 11.78 ± 0.12 NS	NS 85 ± 19 NS	NS 20 ± 0.01 NS	NS NS 11.55 ± 0.32	NS 81 ± 12 NS	NS NS 19 ± 0.04
4 (R_1=CH_3,R_2=H)	10	NS 13.81 ± 0.35 *	NS 87 ± 16 NS	NS 16.3 ± 0.8 NS	NS 13.67 ± 0.44 *	NS NS 101 ± 23	NS 18 ± 2 NS
5 (R_1=CH_3,R_2=CH_3)	10	NS 13.4 ± 0.14 *	NS 106 ± 28 NS	NS 16.8 ± 1.3 NS	NS 13.50 ± 0.39 *	NS NS 105 ± 21	·22 ± 01 NS
6 (R_1=C_2H_5,R_2=H)	10	NS 12.80 ± 0.23 *	·116 ± 16 NS	NS 18.6 ± 2 NS	NS 13.50 ± 0.42 *	NS 92 ± 14 NS	NS 21.7 ± 5 NS
7 (R_1=C_2H_5,R_2=CH_3)	10	NS 13.97 ± 0.21 *	·122 ± 20 NS	NS 17 ± 3 NS	NS 13.26 ± 0.29 *	NS 91 ± 10 NS	NS 20 ± 01 NS
8 (R_1=OC_2H_5,R_2=H)	10	NS 13.80 ± 0.24 *	·125 ± 24 NS	NS 20 ± 5 NS	NS 13.10 ± 0.54 *	NS 87 ± 16 NS	·22.7± 01 NS
9 (R_1=OC_2H_5,R_2=CH_3)	10	NS 11.57 ± 0.14 *	NS 80 ± 12 NS	NS 18 ± 6 NS	NS 12.00 ± 0.32 *	NS 84 ± 4 NS	NS 19 ± 5 NS

PRG - propylene glycol 15% solution .Mean ± SD, Upper right : compared to infected untreated control, Lower left : compared to uninfected untreated control, NS : not gnificant, * : significant at $p < 0.05$

Table 4: Haematological changes (Mean ± SD) in experimental chicks infected with *R. tetragona* and treated with N-acyl/COOH and N-acyl/COOMe derivatives of the open lactam form of praziquantel.

Group / compound	No, of chicks	Single dose (slaughter I)			2 doses, 3 days apart (slaughter II)		
		Hb (g/dl)	PCV (%)	RBC ($x10^6$ mm^3)	Hb(g/dl)	PCV (%)	RBC ($x10^6$ mm^3)
1 uninfected – untreated control	10	$_{NS}$ 7.09 ± 0.30 *	$_{NS}$ 25 ± 0.51 *	$_{NS}$ 2.40 ± 0.1 ^{NS}	$_{NS}$ 7.12 ± 0.09 *	$_{NS}$ 24 ± 0.25 *	$_{NS}$ 2.61 ± 0.15 ^{NS}
2 infected untreated control	10	$_{NS}$ 5.48 ± 0.06 ^{NS}	$_{NS}$ 21.31 ± 0.61 ^{NS}	$_{NS}$ 2.15 ± 0.5 ^{NS}	$_{NS}$ 5.88 ± 0.10 ^{NS}	$_{NS}$ 22.5 ± 0.51 ^{NS}	$_{NS}$ 2.22 ± 0.5 ^{NS}
3 PRG 0.5 ml	10	$_{NS}$ 5.50 ± 0.13 ^{NS}	$_{NS}$ 20.5 ± 1.2 ^{NS}	$_{NS}$ 2.20 ± 0.1 ^{NS}	$_{NS}$ 5.95 ± 0.15 ^{NS}	$_{NS}$ 22.8 ± 0.38 ^{NS}	$_{NS}$ 2.31 ± 0.51 ^{NS}
4 (R_1=CH_3,R_2=H)	10	$_{NS}$ 7.14 ± 0.16 *	$_{NS}$ 24.5 ± 1.0 *	$_{NS}$ 2.81 ± 0.5 ^{NS}	$_{NS}$ 6.78 ± 0.21 *	$_{NS}$ 23.5 ± 0.51 *	$_{NS}$ 2.52 ± 0.52 ^{NS}
5 (R_1=CH_3,R_2=CH_3)	10	$_{NS}$ 7.28 ± 0.7 *	$_{NS}$ 24 ± 1.5 *	$_{NS}$ 2.62 ± 0.51 ^{NS}	$_{NS}$ 6.93 ± 0.27 *	$_{NS}$ 23.25 ± 0.53 *	$_{NS}$ 2.24 ± 0.49 ^{NS}
6 (R_1=C_2H_5,R_2=H)	10	$_{NS}$ 7.67 ± 0.21 *	$_{NS}$ 26 ± 0.8 *	$_{NS}$2.80 ± 0.54 ^{NS}	$_{NS}$ 7.11 ± 0.13 *	$_{NS}$ 25.30 ± 0.82 *	$_{NS}$ 2.91 ± 0.81 ^{NS}
7 (R_1=C_2H_5,R_2=CH_3)	10	$_{NS}$ 7.18 ± 0.3 *	$_{NS}$ 26.1 ± 0.8 *	$_{NS}$ 2.29 ± 0.32 ^{NS}	$_{NS}$ 7.67 ± 0.22 *	$_{NS}$ 26 ± 1.71 *	$_{NS}$ 2.54 ± 0.52 ^{NS}
8 (R_1=OC_2H_5,R_2=H)	10	$_{NS}$ 7.35 ± 0.27 *	$_{NS}$ 23.5 ± 0.61 *	$_{NS}$ 2.50 ± 0.16 ^{NS}	$_{NS}$ 7.85 ± 0.46 *	$_{NS}$ 26.5 ± 1.91 *	$_{NS}$ 3.00 ± 0.48 ^{NS}
9 (R_1=OC_2H_5,R_2=CH_3)	10	$_{NS}$ 7.39 ± 0.13 *	$_{NS}$ 26 ± 1.33 *	$_{NS}$ 2.79 ± 0.48 ^{NS}	$_{NS}$ 7.67 ± 0.13 ^{NS}	$_{NS}$ 24.75 ± 1.71	$_{NS}$ 2.97 ± 0.66 ^{NS}

PRG - propylene glycol 15% solution .M ± SD , Upper right : compared to infected untreated control, Lower left : compared to uninfected untreated control, NS : not significant, * : significant at $p < 0.05$

value was observed in the groups treated with compounds II and IV compared to the uninfected – untreated control at slaughter I.

No significant differences ($p > 0.05$) in Mg, Mn and Zn concentrations during slaughter I and II, Cu value during slaughter I and Fe concentration at slaughter II were noticed between the test and control chicks. Significant increase ($p < 0.05$) was observed in Fe value at slaughter I between the groups treated with compounds III, IV and V and the uninfected – untreated control. Significant increase ($p < 0.05$) was observed in Cu value at slaughter II in the groups treated with compounds II and V compared with the uninfected – untreated control. The concentration of Co fluctuated within the normal range. Ca concentration did not significantly change during slaughter I and II, although significant increase ($p < 0.05$) was observed between the test and the infected untreated control during the same periods.

Haematological changes: These data are given in Table 4. Significant increase ($p < 0.05$) was observed in the values of Hb and PCV in the test and infected untreated groups. No significant differences ($p > 0.05$) were observed in the Hb and PCV values between the test and uninfected - untreated groups. No significant differences in RBCs, MCH, MCV or MCHC values between the test and control groups were observed.

DISCUSSION

The findings of this study confirm the susceptibility of Bovans type chicks to infection with *R . tetragona*. Ten cysticercoids per chick were sufficient to induce mature worm infection at day 21 without signs of morbidity or mortality. Worms were easily recovered from the intestinal lumen indicating either free or loose scolicial attachment. Severe lesions may point to embedding of worm scolices in the intestinal lamina propria leading to inflammation and lymphocytic infiltration. It has been reported that adult *R.tetragona* apparently produce little serious effect upon the host except in very heavy infections, in which, they interfere with digestion or cause partial obstruction (Islim *et al*, 1995). Extra

intestinal lesions were attributed to toxins produced by the worm (Abdel Hafiz *et al*, 2000).

The compounds (N-acyl /COOR) represented derivatives of the open lactam form of praziquantel and designed to test the essentially of the pyrazinoxyisoquinoline ring system,for the anthelmintic activity, of praziquantel. These derivatives were designed to block cyclization of the open lactam form structure of the parent praziquantel.

In this class of derivatives, the anticestodal activity decreases with increasing acyl group size, and increases, on the second dose, with esterification of the COOH group .The latter effect is possibly due to increase in lipophilicity. Generally, the carbamate with free or esterified COOH exhibits the lowest anticestodal activity of all other tested derivatives.

In considering the biocyclization of these derivatives to the parent PZQ it was clearly observed the absence of PZQ or any of its metabolites in the sera of these chicks when tested by thin layer chromatography (Saeed, 2000).

It is well known that, the liver is the detoxifying organs while the kidney, is the major organ of excretion in the body. Thus, these organs could be considered as the most sensitive organs to the toxic actions of drugs. The pathological lesions observed in the chicks were mild and could be attributed to physical and/or toxins secreted by the worms. In addition, changes in serum AST activity, total protein and uric acid concentrations were within the normal range. Furthermore, there were no significant changes in other serum constituents and haematological series. These results indicated that slight effect was observed in chicks dosed with the different compounds.

The clinical, serobiochemical and haematological evaluations indicated high efficacy of a new promising cestodicidal remedy against *R. tetragona* infection, a problem in poultry industry - without development of undesirale effects. It is concluded that the pyrazinoxy isoquinoline ring system in PZQ is not essential for anticestodal activity. Further studies should be done to elucidate efficacy on the different cestodes species and other helminthes.

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