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Full Length Research Paper

Anticestodal activity and toxicity of some praziquantel analogues

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Four hundred - 21 days old male Bovans type chicks in 10 groups were infected with *Raillietina tetragona* cystcercoids. 6 groups treated with the N-alkyl/COOR derivatives of the open lactam form of praziquantel (PZQ) in oral dose of 20 mg/kg body weight on day 21 and on day 24 post infection. The open lactam form compounds showed an efficacy of 40, 100, 100, 100, 74 and 56% on the first dose and an efficacy of 50, 100, 100, 100, 100 and 100% respectively on the second dose. Histopathological, haematological and biochemical alterations were evaluated, accordingly no serious signs of toxicity were observed in the birds treated with the different compounds tested.

Key words: PZQ, structure activity relationship, efficacy, toxicity, *Raillietina tetragona.*

INTRODUCTION

Some reports have changed the picture of praziquantel (PZQ) as the anthelmintic of choice, due to the low susceptibility of *Schistosoma mansoni* strain of certain geographic areas (Stelma et al., 1997; Cioli et al., 1995; Fallon et al., 1997). However, Doenhoff and Mattoccia (2006) emphasised that there is currently no evidence to suggest that any schistosomes have developed resistance to PZQ as a result of its wide spread use. All the previous studies concerning the structure activity relationship (SAR) of PZQ emphasis on the pyrazinoxy isoquinoline ring system to be essential for anthelmintic activity (Andrews et al., 1983). Chicken tape worms often cause serious problems in infected flocks (Nurelhuda et al., 1989) and in humans , the mass drug application to eliminate *Taenia solium* have only temporary effects on cysticercosis transmission (Graig and Ito, 2007).

In the present work, a new approach to SAR of PZQ has been adopted, through the functionalization and inter conversion of the open lactam form of praziquantel (OLF-PZQ). This is hoped to produce more effective anthel-mintic compounds. In continuation to our previous reports, which cover the N-acyl /COOR derivatives and N-sulphanilamido/COOR derivatives (Saeed et al., 2003, 2004a, 2005), this paper reports the efficacy and toxicity of the N-alkyl/COOR derivatives of the open lactam form of praziquantel against mature *Raillietina tetragona* infection in bovans type chicks.

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MATERIALS AND METHODS

Birds

Four hundred 1-day old cockerels bovans type chicks were brought from Coral Company, Khartoum and reared on the premises of the Faculty of Veterinary Medicine and Animal Production, Kuku, Khartoum North and provided with ad-libitum feed, drinking water and light at night. At the age of 21 days the chicks were assigned randomly into 10 groups of 40 each. Each group was kept separatedly under conditions preventing accidental infection with tape worms.

Infection

R. tetragona cystcercoids were recovered by dissection of adult ants *Tetramorium caespitum* found in poultry farms. 10 cystocercoids per chick were fed in gelatin capsules to chicks previously starved for 5 h at the age of 21days, for nine groups. A group was kept without infection as a healthy control.

Table 1. Efficacy of N-alkyl/COOH and N-alkyl/COO alkyl derivatives of the open lactam form of praziquantel and praziquantel against *R. tetragona* infection in Bovans-type chicks (n = 20 in each slaughter). a : ($p < 0.001$), b : ($p < 0.01$).

Compound/group No.	days post infection		worms recovered per chick (Mean ± SD)		Total worms recovered		Efficacy %	
Slaughter	1	2	1	2	1	2	1	2
Control healthy	24	27	00±00	00±00	00	00	-	-
Cont..infect. untreated	24	27	10±00	10±00	200	200	00	00
PRG (0.5 ml of 15%/ chick)	24	27	10±00	10±00	200	200	00	00
PZQ I	24	27	00 ± 00 [a]	00 ± 00 [a]	00	00	100	100
OLF-PZQ II	24	27	6.0 ± 00 [a]	5.0 ± 00 [a]	120	100	40	50
III	24	27	00 ± 00 [a]	00 ± 00 [a]	00	00	100	100
IV	24	27	00 ± 00 [a]	00 ± 00 [a]	00	00	100	100
V	24	27	00 ± 00 [a]	00 ± 00 [a]	00	00	100	100
VI	24	27	2.6 ± 0.51 [a]	00 ± 00 [a]	52	00	74	100
VII	24	27	4.4 ± 0.50 [a]	00 ± 00 [a]	88	00	56	100

Test compounds

Synthesis of the test compounds II-VII were described by Saeed et al. (2003).
(I) Praziquantel.
(II) N – (1,2,3,4 - tetrahydro – isoquinolinyl methyl) – N-cyclohexyl carbonyl glycine (open lactam form of praziquantel –OLF –PZQ).
(III) Ethyl - N – (1,2,3,4 - tetrahydro – 2 -ethyl – 1 - isoquinolinyl methyl) – N-cyclohexyl carbonyl glycinate.
(IV) N – (1,2,3,4 - tetrahydro – 2 - ethyl – 1 - isoquinolinyl methyl) – N-cyclohexyl carbonyl glycine.
(V) n – Butyl- N – (1,2,3,4- tetrahydro – 2 - n- butyl – 1 - isoquinolinyl methyl) – N-cyclohexyl carbonyl glycinate.
(VI) N – (1,2,3,4 - tetrahydro-2-n-butyl – 1 - isoquinolinyl methyl) – N-cyclohexyl carbonyl glycine.
(VII) N – (1,2,3,4 - tetrahydro – 2,2 -di methyl – 1 - isoquinolinium bromide methyl) – N-cyclohexyl carbonyl glycine (Figure 2).

Treatment

7 groups were treated with the test compounds which were dissolved in a concentration of 10 mg/ml of 15% propylene glycol. Each chick received a single oral dose of 20 mg kg BW at day 21 and on day 24 post infection . A group was treated with 15% propylene glycol (PRG) which was used as a solvent for the compounds, another group was kept as control infected untreated.

Recovery of worms

Birds were slaughtered 3 days after each treatment. At necropsy, the intestine of each bird was slit open longitudinally in a solution of normal saline and any visible worms were collected and counted for each chick. Efficacy was calculated accordig to the following equation :

% Efficacy = (C – G) X 100 / C
Where : C = Total number of recovered worms in the control infected.
G = Total number of recovered worms in the group.

Biochemical analysis

Blood samples were collected from each chick at slaughter (Day 24 and 27 post infection) into 2 clean dry bottles, 1 of them containing anticoagulant (Ethylene diamine tetraacetic acid, EDTA) for haematological analysis and the other for serum analysis for the activity of GOT and the concentration of total protein, uric acid (Plasmatec Laboratory Products ltd., England), serum concentration of sodium (Na), calcium (Ca), iron (Fe), cobalt (Co), copper (Cu), zinc (Zn), manganese (Mn) and magnesium (Mg) (Atomic Absoption Spectrophotometer, Perkin Elmer 3110, USA).

Haematological analysis

Samples of blood collected at slaughter into clean dry bottles containing anticoagulant (Ethylene diamine tetraacetic acid, EDTA) were used for the determination of haemoglobin (Hb), red blood cell counts (RBCs), packed cell volum (PCV), mean corpuscular volume (MCV) and mean corpuscular haemoglobin concentration (MCHC).

Pathological methods

The post mortem findings were recorded at necropsy and specimens of intestines, liver and kidneys were immediately fixed in 10% formal saline, embeded in paraffin wax, sectioned and stained with haematoxylin and eosin (H & E).

Analysis of data

Data were statistically analyzed using SPSS computer statistical package release 13.5.

RESULTS

Efficacy

No note worthy clinical signs were observed in chicks infected with *R. tetragona* and treated with the different compounds. The compounds were well tolerated by chicks and no death occurred during the experimental period.

The number of worms in the intestines of experimental chicks were recovered and counted during postmortem examination of each chick (Table 1). The total number of

Table 2. GOT activity, total protein, uric acid, sodium (Na) and potassium (K) concentrations (mean ±SD) in sera of chicks infected with *R. tetragona* and treated by N-alkyl/COOH and N-alkyl/COOalkyl derivatives of the open lactam form of praziquantel and praziquantel - Slaughter (1,2) (n = 20) , a : ($p < 0.001$) , b : ($p < 0.01$).

Compound/group No.	GOT U/L (Mean ± SD)		Total protein g/dl (Mean ± SD)		Na mg/dl (Mean ± SD)		K mg/d (Mean ± SD)		uric acid mg/dl (Mean ± SD)	
	1	2	1	2	1	2	1	2	1	2
Cont. healthy	22.97 ± 1.3	25.42 ± 2.4	5.01 ± 0.9	6.77 ± 0.71	307.45 ± 79	305.5 ± 79	28.4 ± 5.3	28.4 ± 5.3	5.3± 0.9	5.6 ± 1.2
Cont. infected untreated	33.12 ± 0.7	34.6 ± 6.1	3.12 ± 0.21	3.5 ± 0.31	325 ± 53	325 ± 53	26.12 ± 4.2	27.5 ± 3.2	6.01 ± 0.5	6.39 ± 1.1
PRG	33.95 ± 0.8	35.0 ± 1.12	3.23 ± 0.4	3.76 ± 0.5	321.55 ± 60	321.3 ± 72	26.35 ± 6.3	27.73 ± 3.1	6.05± 0.82	6.61 ± 1.3
PZQ I	24.87 ± 2.1 [b]	25.0 ± 2.7 [b]	6.00 ± 0.51 [a]	7.39 ± 0.5 [a]	214.53 ± 63	209.5 ± 75	24.2 ± 5.5	24.57 ± 5.4	5.63 ± 1.5	7.2 ± 1.4
OLF-PZQ II	25.96 ± 3.2 [b]	28.63 ± 4.2 [b]	5.95 ± 0.45 [a]	7.28 ± 0.45 [a]	238.3 ± 70	251.1 ± 80	25.2 ± 6.7	24.87 ± 4.7	6.23 ± 1.0	6.79 ± 1.2
III	22.2 ± 0.8 [b]	21.12 ± 1.2 [b]	5.8± 1.02 [a]	7.38 ± 0.17 [a]	258.3 ± 52	280.4 ± 51	23.71 ± 3.2	23.95 ± 7.9	6.51± 0.89	7.34 ± 1.5
IV	23.71 ± 1.4 [b]	21.75 ± 1.7 [b]	5.8 ± 0.5 [a]	7.40 ± 0.62 [a]	210 ± 64	302 ± 60	28.2 ± 3.8	24.7 ± 4.7	6.58 ± 0.9	7.53 ± 2.1
V	23.98 ± 2.1 [b]	21.23 ± 1.3 [b]	5.77 ± 0.19 [a]	6.44 ± 0.5 [a]	241 ± 70	225.8 ± 68	24.6 ± 3.5	24.6 ± 5.2	4.13 ± 1.2	4.22 ± 1.6
VI	24.52 ± 2.2 [b]	22.01 ± 1.4 [b]	5.20 ± 0.7 [b]	7.21 ± 0.6 [a]	225 ± 80	214 ± 57	28.5 ± 3.4	25.1 ± 4.1	4.87± 0.87	4.39 ± 1.7
VII	21.37 ± 1.51 [b]	22.89 ± 1.7 [b]	4.97 ± 0.20 [b]	6.13 ± 0.53 [a]	237 ± 87	358.7 ± 85	27.7 ± 6.0	24.7 ± 5.1	4.95± 0.88	6.45 ± 0.95

worms (efficacy %) in the intestines of the slaughtered chicks at first dose were 200 (00%), 00 (100%), 120 (40%), 00 (100%), 00 (100%), 00 (100%) , 52 (74%) and 88 (56%) and of the second dose were 200 (00%), 00 (100%), 100 (50%), 00 (100%), 00 (100%), 00 (100%), 00 (100%) and 00 (100%) respectively in groups of birds treated with compounds PEG, I(PZQ), II(OLF-PZQ), III, IV, V, VI and VII respectively (Table 1).

Pathology

Lesions in slaughtered chicks consisted of dilatation and congestion of sinusoid hepatic blood vessels were some times congested especially the central veins. Scarcely small haemor- legic foci and individual scattered haepatocytic cell necrosis were also seen. Infiltration and/or small lymphocytic nodules were scattered in the liver paraenchyma adjacent to the portal areas (Figure 1). No significant changes were noticed in the glomeruli, medullary tracts, the cortical intermedia tubles and the ulcer of the experimental chicks. Congestion of the intertobuler and intratobuler veins and individual scattered necrosis of some cortical renal tubules which sometimes might disappear and small foci of lymph could be scattered throughout the renal tissue. Slight to moderate mucosal and submucosal lymphocytic infiltration and slight mucosal errosions were observed in slaughtered treated chicks.

Blood chemistry and haematology

In the first and second slaughters, no significant differences in GOT, total protein, uric acid, sodium, potassium, magnesium, calcium, manganese, iron, cobalt, copper and zinc concentrations were observed between the test and the control healthy groups (Tables 2, 3, 4) . There were significant differences ($p < 0.01$ - 0.001) in the values of GOT, total protein and calcium between the test and control infected untreated groups. At the 2 slaughters, no significant differences in the Hb, PCV, RBCs, MCH, MCV and MCHC values were observed between the test and control healthy groups. A significant differences ($p < 0.01$ - 0.001) in the values of Hb have been observed between the test and the control infected untreated groups (Table 5).

DISCUSSION

The present 6 test compounds (N-alkyl/COOR) represent the first group of 16 derivatives of the open lactam form of praziquantel, designed to test the essentially of the pyrazinoxyisoquinoline ring system for the anthelmintic activity of praziquantel. The 16 derivatives of the 3 types were designed with the idea of blocking the possibility of cyclization of the open lactam form structure of the parent praziquantel. Although among the present series (N- alkyl/COOR), there remain the theoretical possibility of ring closure through N-dealkylation, preliminary investigation of biocyclization in chicks revealed the absence of praziquantel or its metabolites in the chicks given N-Et/COOEt III , N-Et/COOH IV and NH/COOH

Table 3. Mg,Ca,Mn and Fe concentrations (mean±SD) in sera of chicks infected with *R. tetragona* and treated with N-alkyl/COOH and N-alkyl/COO alkyl derivatives of the open lactam form of praziquantel and praziquantel - Slaughter (1,2)(n = 20) , a : ($p < 0.001$) , b : ($p < 0.01$).

Compound/group No.	Mg mg/dl (Mean ± SD)		Ca mg/dl (Mean ± SD)		Mn µg/dl (Mean ± SD)		Fe µg/dl (Mean ± SD)	
	1	2	1	2	1	2	1	2
Cont. healthy	3.50± 0.53	3.55 ± 0.50	13.05 ± 0.25	13.00 ± 0.32	269 ± 50	273 ± 45	85±13	85±14
Cont. infected untreated	3.10± 0.13	3.00 ± 0.31	11.60 ± 0.28	11.70 ± 0.19	280 ± 48	287 ± 49	82±09	89±10
PRG	3.25± 0.3	3.12 ± 0.35	11.78 ± 0.12	11.55 ± 0.32	285 ± 53	290 ± 54	85±19	81±12
PZQ I	3.10± 0.52	2.90 ± 0.45	13.90± 0.13 [a]	13.90 ± 0.41 [b]	250± 50	230 ± 43	93± 23	100 ± 20
OLF-PZQ II	3.50± 0.64	3.80 ± 0.30	12.87 ± 0.40 [a]	13.2 ± 0.80 [b]	270 ± 45	230 ± 37	116 ± 38	87±23
III	3.75± 0.61	2.95 ± 0.53	13.95 ± 0.39 [a]	13.50 ± 0.39 [b]	223 ± 60	225 ± 44	86±15	85.5 ± 10
IV	3.07± 0.64	2.85 ± 0.62	13.00 ± 0.13 [a]	13.47 ± 0.37 [b]	214 ± 60	217 ± 52	90±16	99±18
V	3.50± 0.80	2.97± 0.56	13.77± 0.14 [a]	13.67 ± 0.15 [b]	217± 52	210 ± 56	87± 10	85±05
VI	3.20± 0.49	3.00 ± 0.50	12.67± 0.28 [a]	13.00 ± 0.39 [b]	300± 50	285 ± 50	83± 24	103 ± 14
VII	3.17± 0.40	3.30 ± 0.60	13.77± 0.32 [a]	13.30 ± 0.95 [b]	223± 60	302 ± 48	81± 21	83±11

Table 4. Co,Cu and Zn concentrations (mean ±SD) in sera of chicks infected with *R. tetragona* and treated with N-alkyl/COOH and N-alkyl/COO alkyl derivatives of the open lactam form of praziquantel and praziquantel - Slaughter (1,2) (n = 20) , a : ($p < 0.001$), b : ($p < 0.01$).

Compound/group No.	Co mg/dl (Mean ± SD)		Cu µg/dl (Mean ± SD)		Zn µg/dl (Mean ± SD)	
	1	2	1	2	1	2
Cont. healthy	1.34 ± 0.15	1.30 ± 0.11	19±05	18.1± 03	77.5 ± 9.5	76±10
Cont. infected untreated	2.15 ± 0.31	2.20 ± 0.21	18±03	18.5 ± 01	80±10	79±12
PRG	2.60 ± 0.60	2.51 ± 0.25	20±01	19±04	85±10	84±10
PZQ I	1.30± 0.30 [b]	1.29 ± 0.21	15±01	14.7 ± 2.5	70±20	70±20
OLF-PZQ II	1.72 ± 0.56	1.52 ± 0.23	23±04	20±05	75±10	70±15
III	1.81 ± 0.70	1.60 ± 0.35	24±06	21.5 ± 1.3	95±15	80±28
IV	1.80 ± 0.40	1.70 ± 0.70	20±03	18.7 ± 05	78±02	77±31
V	1.30 ± 0.10 [b]	1.32 ± 0.12	17.7± 01	18±01	73±06	78±02
VI	1.70 ± 0.67	1.87 ± 0.15	22.3 ± 2.1	22.1 ± 8.7	70±02	70±20
VII	1.40 ± 0.30 [b]	1.42 ± 0.23	16.3± 06	17.3 ± 05	77±10	70±20

Table 5. Haematological changes(Hb,PCV and RBCs) in experimental chicks infected by *R. tetragona* and treated with N-alkyl/COOH and N-alkyl/COO alkyl derivatives (mean ±SD) of the open lactam form of praziquantel and praziquantel: Slaughter (1,2) (n = 20) , a : ($p < 0.001$) , b : ($p < 0.01$).

Compound/group No.	Hb g/dl (Mean ± SD)		PCV % (Mean ± SD)		RBCsx10^6 mm3 (Mean ± SD)	
	1	**2**	**1**	**2**	**1**	**2**
Cont. healthy	7.09 ± 0.30	7.12 ± 0.09	25 ± 0.51	24 ± 02.5	2.4± 0.1	2.61 ± 0.15
Cont. inf. Untreated	5.48 ± 0.06	5.88 ± 0.10	21.31 ± 0.61	22.5 ± 0.51	2.15 ± 0.5	2.22 ± 0.5
PRG	5.5 ± 0.13	5.95 ± 0.15	20.5 ± 1.2	22.8 ± 0.38	2.20± 0.10	2.31 ± 0.51
PZQ I	6.90 ± 0.70[a]	7.32 ± 0.18[a]	23 ± 2.6	24 ± 0.82 [b]	2.29± 0.14	2.4 ± 0.47
OLF-PZQ II	7.00 ± 0.11[a]	6.62 ± 0.24[a]	23.75 ± 0.96[a]	23.8 ± 0.28 [b]	2.23± 0.23	2.63 ± 0.65
III	7.60 ± 0.50[a]	6.62 ± 0.23[a]	24.75 ± 0.96[a]	23 ± 0.21	2.45± 0.17	2.72 ± 0.60
IV	7.46 ± 0.39[a]	6.97 ± 0.24[a]	25 ± 0.82 [a]	23.25 ± 0.5	2.52± 0.21	2.74 ± 0.62
V	7.70 ± 0.11[a]	7.84 ± 0.23[a]	24.5 ± 1.3 [a]	25.50 ± 0.31[a]	2.50± 0.32	2.72 ± 0.50
VI	7.14 ± 0.36[a]	7.56 ± 0.23[a]	24 ± 0.61[a]	25.00 ± 0.29[a]	2.26± 0.23	2.41 ± 0.45
VII	7.84 ± 0.30[a]	7.80 ± 0.65[a]	25.25 ± 0.96[a]	27.00 ± 0.6[a]	2.77± 0.42	2.59 ± 0.29

(OLF – PZQ , II) (Saeed et al., 2003, 2004b). For testing the anticestodal activity 2 doses of each derivatives were used. The dose was selected in comparison with praziquantel dose for cestodal infections.

Table 6. Haematological changes (MCH, MCV and MCHC) in experimental chicks infected by *R. tetragona* and treated with N-alKyl/COOH and N-alkyl/COO alkyl derivatives (mean ±SD) of the open lactam form of praziquantel and praziquantel: Slaughter (1,2) (n =20) , a : ($p < 0.001$) , b : ($p < 0.01$)

Compound/group No.	MCH pg (Mean ± SD)		MCV fl (Mean ± SD)		MCHC g/dl (Mean ± SD)	
	1	2	1	2	1	2
Cont. healthy	30.2 ± 3.2	29.83 ± 2.10	100.1± 3.3	96.91 ± 3.8	29.36 ± 1.2	30.51 ± 4.5
Cont. inf. Untreated	26.13 ± 2.1	28.83 ± 6.1	99.06 ± 7.9	92.93 ± 3.7	26.09 ± 3.8	26.65 ± 3.2
PRG	26.01± 3.2	27.95 ± 6.5	98.98 ± 3.4	93.23 ± 4.5	26.39 ± 2.73	26.52 ± 6.4
PZQ I	35.02 ± 4.1[a]	31.65 ± 3.2	104.2 ± 3.2	100.0 ± 5.7	30.03 ± 3.6	30.50 ± 6.8
OLF-PZQ II	32.81± 5.2 [a]	26.97 ± 4.2	102.02 ± 4.2	94.24 ± 2.9	30.81 ± 3.3	31.60 ± 6.5
III	32.91± 4.21[a]	26.87 ± 6.5	95.84 ± 8.3	97.21 ± 2.3	30.75 ± 3.90	29.95 ± 4.5
IV	30.85 ± 6.1[a]	26.92 ± 2.5	99.98 ± 3.5	91.31 ± 5.1	29.82 ± 2.2	30.07 ± 3.5
V	31.1 ± 2.00 [a]	27.33 ± 2.7	96.56 ± 9.2	91.03 ± 5.7	28.05 ± 3.6	30.77 ± 7.6
VI	33 ± 4.20 [a]	32.43 ± 5.1	97.38 ± 8.4	96.83 ± 3.8	30.12 ± 4.2	31.2 ± 5.6
VII	32.11 ± 2.11[a]	32.01 ± 2.3	95.2 ± 4.9	98.01 ± 6.1	31.05 ± 4.2	29.94 ± 5.9

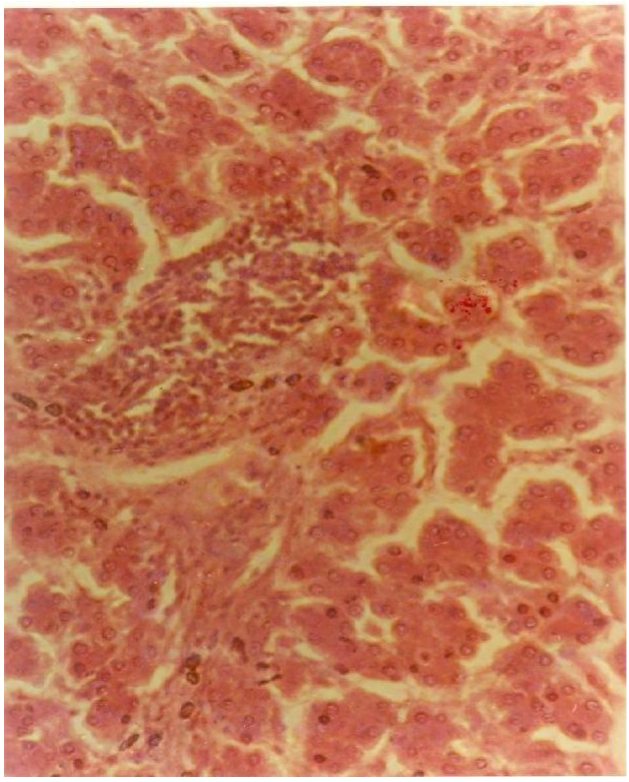
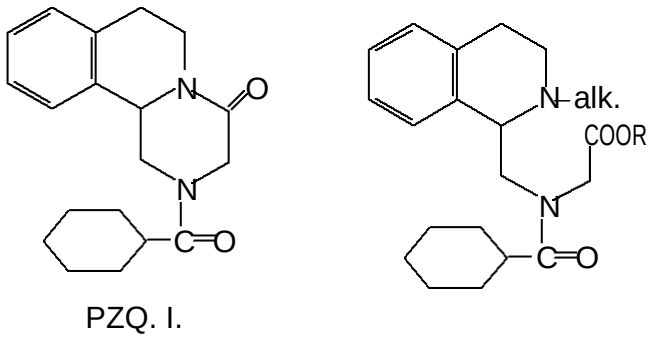


Figure 1. Sinusoidal dilatation and lymphotic infiltration in the portal area in the liver of a chick in the group treated with compound VI (H & E, x 40).



PZQ. I.

Figure 2. Chemical structure of the tested compounds.
II: alk. = H, R = H
III: alk. = CH_2CH_3 , R = CH_2CH_3
IV: alk. = CH_2CH_3, R = H
V: alk. = $CH_2CH_2CH_2CH_3$, R = $CH_2CH_2CH_2CH_3$
VI: alk. = $CH_2CH_2CH_2CH_3$, R = H
VII: alk. = $(CH_3)_2Br$, R = CH_3.

The open lactam form of praziquantel (II) activity could either be intrinsic, or due to partial cyclization to praziquantel or a combination of both effects. Facile cyclization of the esters of the OLF-PZQ (NH/COOR) has been shown to occur at room temperature (Saeed et al., 2003). Should this be the case, then the N-alkyl/COOR derivatives should first undergo N-dealkylation to the NH/COOR form before cyclization could take place. This is not the case since 100% efficacy was obtained for the Et/COOH derivative (IV) compared to 45% for the N-dealkyl (NH/COOH (II)) form. However a possible difference in the N-dealkylation of the ester N-Et/COOEt (III) and the acid N-Et/COOH (IV) should be taken into consideration. Generally, the anticestodal activity seems to reside on N-alkylation regardless of whether the COOH group is free or esterified.

Specuatively, a pseudo base may be obtained from the quaternary ammonium salt (VII) through initial loss of a methyl group. Electronwithrawal by the carbonyl groups may have a facilitating effect. As the process of formation of the pseudobase may take up a week, the considerable increase of anticestodal efficacy of (VII) upon the second dose may be attributed to a time factor upon the first dose for the active species to be generated rather than loading with a second dose.

It is well known that, the liver is the detoxifying organ while the kidney, is the major organ of exrection 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 experimental chicks were mild, in addition, changes in serum GOT activity, total protein and uric acid concentrations were within the normal limits. Furthermore, there were no significant changes in other serum constituents and haematological series. All these results indicated that slight effect was observed in chicks dosed with the different compound. Mild pathological changes observed, could be attributed to the physical and/or toxins secreted by the worms. It was reported that adult worms were most susceptible for treatment (Markoski et al., 2006).

The findings of this study prove the susceptibility of Bovans – type chicks to the infection with *R . tetragona* . 10 cysticercoids per chick were sufficient in this study to promote egg lay after 21 days post – infection accompanied by no signs of morbidity or mortality.Worms were easily recovered from lumen indicating either free or loose scolicial attachment. Severe lesions refer to deep embeding of worm scolices in lamina propria leading to inflammation and lymphocytic infiltraion. It has been reported (Islim et al., 1995) that the adult tapeworms apparently produce little serious effect upon the host except in very heavy infections, in which, they interfere with digestion or cause partial obstruction. Whether extra intestinal lesions exist or not, this may be due to toxins produced by the worm.In the present study , the slaughter / recovery method proved to be reliable in the assessment of anthelmintic drug efficacy in fowl *R.tetragona* infection since 100% adult worms were recovered. All the infected groups have been treated 3 weeks post infection, the time at which the worms of *R.tetragona* reached a mature stage .Praziquantel resulted in complete elimination of worms at the first single dose of 20 mg/kg. This seems to be in good accord with the reported fact (Pawlawski, 1990; Nurelhuda et al., 1989) , that praziquantel is active against taeniasis at lower doses.

The present results highlight a new promising cestocidal remedy to be a highly effective on treatment of *R. tetragona* worm a problem in poultry industry - without any undesirale effects. The results of this study concluded that the pyrazinoxy isoquinoline ring system in PZQ is not essential for anticestodal activity. Further studies should be done on the different cestodes species and other helminthes.

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