

Anthelmintic Efficacy of Tetramisole Against Experimental Infection of Swine Lungworm, *Metastrongylus Apri*

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Introduction

Swine raising in Korea is generally conducted under poor hygienic conditions and on a small scale. Due to this, the animal herds are widely infected with gastrointestinal and pulmonary nematodes. The incidence of *Metastrongylus apri* in Korean pigs was 54.5 percent based on the author's survey conducted in 1967, and the loss due to the parasites is the highest on account of the difficulties of control and the absence of effective anthelmintics.

Tetramisole, developed by Thienpont, has been shown to be highly effective in the control of nematodes found in various animals. This study was conducted to determine the anthelmintic of the chemical, administered via oral and subcutaneous routes, against the immature and mature forms of *Metastrongylus apri*.

Materials and Methods

1. Tetramisole (dl-2, 3, 5, 6-phenyl-imidazo 2, 1-b thiazole hydrochloride): The chemical is a white odourless bitter powder which is soluble in distilled water, methanol and ether. The melting point of tetramisole is 260°C. For oral administration, the chemical may be given as a powder, while a 8 percent aqueous solution may be injected for subcutaneous use.

2. Animals: 72 cross bred pigs which had not been infected with *Metastrongylus apri*, weighing about 30kg were selected and used. Infective larvae were collected from earthworms and

each pig was infected with about 2,000 larvae. Chemical therapy was initiated from 3 to 45 days after infection.

3. Dose and route of administration: Oral administration was performed by mixing tetramisole with a balanced ration. 60 gm of the mixture was administered to each pig. Normal feed was given two hours after the medication. Pigs were dosed at various dosage levels ranging from 5 to 12.5mg/kg.

In these pigs treated parenterally 10mg/kg of the drug was given subcutaneously in single injection at the right side of the neck.

4. Evaluation of anthelmintic activity: All of the animals were subjected to post-mortem examination 7 to 10 days after medication. The worms were collected from bronchia and bronchioles and counted. Fecal egg counts were made using a McNaster EPG counting chamber from 2 days before the medication up to the day of post-mortem examination.

In the evaluation of the anthelmintic efficacy of the chemical emphasis was placed on post mortem worm counts.

Clinical observations on symptoms of possible toxicity were made for two hours post medication.

Experimental Results

1. Anthelmintic effect of various dosage rates:

Infected pigs were divided into four treatment groups based on the dose rate of drug ranging 5 to 12.5 mg per kg of body weight, and one unmedicated control group. The medication was

initiated 40-45 days after infection. The results are presented in Table I and indicate that EPG count tended to slightly increase from the first day but appreciably decrease from the 3rd day after medication. Only one animal of the 5mg/kg

group showed 100 EPG value at 7 days. Four pigs in the 5mg/kg, and another four pigs in the 7.5 mg/kg group had worm burdens at post-mortem examination, but the numbers were much lower than that of control groups.

Table 1. Efficacy of Orally Administered Tetramisole Against Mature Swine Lungworms

Body Weight (kg)	Dose mg/kg	Before Admin.	Average Egg Count (EPG) After Administration (Days)				No. of worms at Necropsy		Total
			1	3	5	7	♀	♂	
35.0		1,200	2,000	300	300	100	56	22	78
39.0		300	400	0	0	0	2	2	4
35.5	5	800	1,000	0	0	0	0	0	0
28.4		1,100	1,300	0	0	0	0	0	0
27.5		500	300	0	0	0	0	0	0
33.05		800	900	100	0	0	0	0	0
33.0		500	200	0	0	0	28	7	35
29.0	7.5	900	1,000	0	0	0	7	2	9
35.5		300	1,200	100	0	0	0	0	0
23.0		1,900	800	100	0	0	0	0	0
45.0		300	200	0	0	0	0	0	0
25.0		200	300	100	0	0	0	0	0
41.0		400	600	100	0	0	0	0	0
20.0	10	600	1,000	300	0	0	0	0	0
20.0		500	300	Accidental Death					
28.0		900	1,300	100	0	0	0	0	0
32.5		1,000	1,200	100	0	0	0	0	0
37.5		1,200	1,100	200	0	0	0	0	0
35.0		700	900	100	0	0	0	0	0
28.5		200	400	0	0	0	0	0	0
31.0	12.5	1,000	900	0	0	0	0	0	0
32.5		200	600	0	0	0	0	0	0
34.0		1,800	400	0	0	0	0	0	0
28.0		700	300	300	400	300	48	22	70
32.5		600	300	700	600	400	72	37	109
37.0	Control	1,100	1,300	1,000	1,000	900	138	71	209
34.5		500	200	200	400	300	105	28	133
34.0		2,600	2,500	1,600	1,600	800	304	78	382

2. Anthelmintic effects at various stages after infection : 25 infected pigs were divided into five groups of five animals each. Four groups of animals received 10mg of tetramisole, per kg of

body weight, added to the feed, at 3, 5, 10 and 15 days after the infection, respectively. Five remaining pigs served as unmedicated controls. The results are presented in Table 2 and indicate

the following : Only one pig showed 100 EPG in the group which were medicated at 15 days after the infection. On the other hand, the control group showed EPG values of 100-300 on the 30th day and 200-700 on the 40th day. At autopsy, one

pig in the group treated on the 3rd day, 3 pig^s in the groups treated on the 5th day and 10th day and 2 pigs in the group treated on the 15th day harboured, 1-23 worms, while control animals harboured 189-409 lungworms.

Table 2. Efficacy of Orally Administered Tetramisole at 10mg/kg Against Swine Lungworms at Immature Stages.

Swine No.	Days after Infection	Average Egg Count (EPG)		No. of Worms at Necropsy		
		30 Days After Infection	40 Days After Infection	♀	♂	Total
31		0	0	0	0	0
32		0	0	0	0	0
33	3	0	0	1	1	2
34		0	0	0	0	0
35		0	0	0	0	0
36		0	0	0	0	0
37		0	0	13	5	18
38	5	0	0	15	2	17
39		0	0	3	1	4
40		0	0	0	0	0
41		0	0	9	2	11
42		0	0	6	0	6
43	10	0	0	0	0	0
44		0	0	0	0	0
45		0	0	1	0	1
46		0	0	0	0	0
47		0	0	3	1	4
48	15	0	0	0	0	0
49		0	0	0	0	0
50		100	100	19	4	23
51		200	700	375	28	403
52		0	200	170	19	189
53	Control	100	400	245	32	277
54		300	500	320	14	334
55		100	300	260	22	282

3. Comparison of oral and subcutaneous routes of administration: 17 infected pigs which were fed for 35 days after the infection, were divided into three groups consisting of 8, 5 and 4 pigs. One group of eight pigs received tetramisole via the subcutaneous route at a dose level of 10mg/kg.

The same dosage was administered orally to five pigs by mixing the chemical with the feed. The remaining four pigs were served as unmedicated controls. The results are presented in Table 3 and indicate the following: Seven out of eight animals in the subcutaneous group and two

out of five in the oral group harboured worms at post-mortem examination. In comparison to the control both treatments were able to control

the worm, and oral administration was more effective.

Table 3. Comparison of the anthelmintic effects of oral and subcutaneous administration of 10mg/kg of Tetramisole against *Metastrongylus apri*.

Route	Swine No.	Body Weight (kg)	Average Egg Count(EPG)		No. of Worms at Necropsy		
			Before Admin.	After Admin. 7th day	♀	♂	Total
S. C.*	56	32	1,100	0	29	11	40
	57	28	1,000	100	26	6	32
	58	28	1,300	100	58	38	96
	59	26	1,800	0	19	5	24
	60	33	500	100	42	25	67
	61	26	2,200	200	52	30	82
	62	27	1,700	0	17	6	23
	63	22	800	0	0	0	0
Oral	64	28	800	0	2	1	3
	65	32	1,600	0	6	1	7
	66	31	900	0	0	0	0
	67	26	2,100	0	0	0	0
	68	24	400	0	0	0	0
Control	69	29	700		172	31	203
	70	31	400		95	13	108
	71	23	1,500		290	32	322
	72	26	1,300		315	27	342

* S. C.Subcutaneous

4. Side reactions of tetramisole observed in the control of swine lungworm : Some side reactions of tetramisole, in the control of swine lungwo-

rm, were observed. These were illustrated in Table 4 and 5.

Table 4. Side-reactions of the administration of Tetramisole orally.

Dose mg/kg	Swine No.	Side-reaction				Increase of Respiration	Duration of Symptom(Min)	Remarks
		Coughing	Vomition	Excitement				
5	1	++	-	-	-	60		
	2	+++	-	-	+	60		
	3	+	-	-	-	70	82worms were found in the vomitus	
	4	++	+++	+	-	90.....		
	5	++	-	++	+	60		
	6	++	-	+	+	70	15worms were found in the vomitus	
	7	+++	++	++	++	50.....		
7.5	8	+++	-	++	++	100		

	9	++	-	+	+	70
	10	+++	±	+	-	50
	11	+	-	+	-	40
	12	++	++	+	+	80
10.0	13	+	-	++	+	40
	14	+	-	-	-	40
	15	++	+	-	+	50
	16	+++	-	++	+	80
	17	++	+	++	+	40
12.5	18	+	-	+	+	50
	19	++	-	+	+	50
	20	+	+	+	-	30
	26	-	-	+	+	30
	27	--	+	+++	++	50
Noninfected Control	28	--	-	+	+	40
	29	-	-	+	-	40
	30	-	-	+	+	30

Table 5. Comparison of the side-reactions of oral and subcutaneous administration of 10mg/kg of Tetramisole.

Route	Swine No.	Body Weight(kg)	Side-reaction			Duration of Symptom(Min)
			Coughing	Vomition	Excitement	
S.C.	56	32	++	-	+	5-30 min.
	57	28	+	-	-	
	58	28	+++	-	++	
	59	26	+++	-	-	
	60	33	++	-	+	
	61	26	++	-	+	
	62	27	+	-	-	
	63	22	+	-	-	
Oral	64	28	++	-	-	15-80 min.
	65	32	+	-	-	
	66	31	+	-	+	
	67	26	+	-	-	
	68	24	+	-	-	

Discussion

A number of methods have been used in the past to control *Metastrongylus apri*, eg. Chemical fumigation, intra-bronchial injection of chlorof-

orm or lugol's solution and subcutaneous administration of 1-2% sodium fluoride solution(11) of 3% phenol solution(2), but the efficacy of these methods is doubtful. Walley reported that Cyanacethydrazide was effective against lungworm of

swine and cattle (14, 15, 16) while Szuki recommended copper sulphate for the purpose (7). In a previous study the author report that Cyancehydrazide and copper sulphate were not effective(3). Di-copper methionate was tested by Osawa (4) and Tamasaki (8, 9, 10) but it was not successful in practical use. Diethylcarbamazine was reported to be effective against immature bovine lung worm(5) and immature *Metastrongylus apri* 14-18 days after infection, (1, 2, 6). Ueno (13) reported that a single subcutaneous dose of tetramisole, developed by Thienpont (12) was effective at 5-20mg/kg. against immature and mature forms of swine lungworms.

In this study, the efficacy of the oral administration of tetramisole was evaluated on the basis of treatment at various intervals after infection, and route of administration. At an oral dose of 5 or 7.5 mgm/kg a few worms were found at post-mortem examination while there were no worms recovered among the groups receiving 10 or 12.5 mg/kg. When tetramisole was given as a single dose of 10 mg/kg. it was revealed that parenteral administration was less effective than oral administration for the removal of adult lungworms. Pigs receiving subcutaneous injections showed more pronounced side effects than those dosed orally.

Side effects such as coughing, vomiting, excitement and increased respiration were observed. The reactions were pronounced from 5 to 30 minutes after medication in parenteral group and 15-100 minutes in oral group. There was no increased severity of side effects with increasing dose levels from 5 to 12.5 mg/kg. Most of the infected animals, when given tetramisole couged intermittently after administration, whereas non-infest pigs showed neither coughing nor vomiting apart from mild and transient reactions. This may suggest that coughing and vomitign were due to *Metastrongylus* infection and tetramisole treatment.

Conclusion

The anthelmintic effects of tetramisole against experimental *Mftastrongylus apri* infection in

pigs was studied. At dose rate of 5, 7, 5, 1⁰ and 12.5 mg per kg of body weight given orally or subcutaneously, the following results were obtained;

1. At a dose rate of 10-12.5 mg/kg of body weight the drug proved to be effective against the worms.

2. Oral administration was believed to be better than subcutaneous injection on the view of the efficacy of the drug and side reactions in the animals.

3. Immature worms of 3-15 days of age were well eradicated as well as mature worms.

4. The main side reactions following the administration of the chemical were coughing, vomiting, excitement and the increased respiration rate. The symptoms were not severe and disappeared in a few hours. At the dose rate of 10-12.5 mg/kg of body weight, the intensity of the dise reactions did not corespond to the increased dose rate.

Summary

Oral and subcutaneous administration of Tetramisole (d1-2, 3, 5, 6-tetrahydro-6-phenyl-imidazo-2, 1-b thiazole hydrochloride) was effective in controlling the adult and immature forms of *Metastrongylus apri* in pigs when administered at the dose of 10-12.5 mg per kg of body weight.

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Tetramisole 에 의한 豚肺虫(Metastrongylus apri) 驅虫 効果에 對하여

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家畜의 線虫類에 驅虫効力이 優秀하다는 Tetramisole을 使用하여 肺虫人工感染豚에 5, 7, 5, 10, 및 12.5mg/kg을 飼料 混與 및 皮下注射로서 驅虫効力을 檢討한 結果 다음과 같은 成績을 얻었다.

1. 投藥別로 보면 10~12.5mg/kg이 가장 優秀하였다.
2. 投藥別로 보면 飼料混與가 皮下注射法보다 優秀하였고 副作用도 적었다.
3. 感染後 4내지 15日째의 幼若虫에도 驅虫效果가 있었다.
4. 主要副作用은 기침, 嘔吐, 興奮, 呼吸數增加等이었으나 一過性으로 곧 消失되었고 投藥을 5~12.5mg/kg 範圍에서는 投藥量이 따른 副作用의 差異는 認定되지 않았다.