

Substituted Methyl Benzimidazole Carbamate (CDRI Compound 81–470) in the Mass Treatment of Poultry Round Worms

Suman GUPTA¹, N. L. PAL¹, S. CHANDRA¹, G. K. JAIN² and J. C. KATIYAR¹

¹Division of Parasitology and ²Division of Pharmaceutics
Central Drug Research Institute, Lucknow-226001, India

Abstract: Methyl 5 [4- (2-pyridinyl) -1- piperazinylcarbonyl] -1-H- benzimidazol -2- yl carbamate: (CDRI Comp. 81/470) has consistently exhibited broadspectrum anthelmintic efficacy both against adult and larval stages of various helminth parasites of experimental and domestic animals by oral or parenteral route. The compound incorporated in transdermal tape has also yielded anthelmintic action.

In order to increase solubility and to make mass administration easier, two formulations e.g. soluble and dispersible, were prepared and found effective in control testing against various helminth parasites of rodents.

Both the preparations were put to trial at 3 dose schedules to ascertain their utility for mass treatment of poultry carrying *Ascaridia galli* infection. Though the three dose schedule (20 mg/kgx1, 10 mg/kgx2, 5 mg/kgx3 days) were found to have parallel efficacy, 5 mg/kgx3 days dose requiring lesser compound than single administration was suggested useful in mass therapy.

Thus, either of the preparations could be safely used for the control of poultry roundworms. However, the dispersible formulation having longer shelf-life and convenience of packaging and transportation may be preferred over the soluble preparation.

Key words: Anthelmintic, CDRI Comp. 81/470, Poultry round worms, Efficacy, Soluble formulation, Dispersible formulation, *Ascaridia galli*

INTRODUCTION

Methyl [5-{(4-(2-pyridinyl)-1-piperazinyl)-carbonyl}-1-H-benzimidazole-2-yl]-carbamate (CDRI compound 81/470) possesses significant efficacy against adult and metamorphic forms of a variety of enteric and tissue dwelling helminths by oral and parenteral routes (Katiyar *et al.*, 1984; 1987; 1988). The compound has been found safe in acute (Katiyar *et al.*, 1984), subacute and chronic toxicity studies (unpublished). The compound incorporated in transdermal tape has also shown excellent action (Jain *et al.*, 1991; Gupta *et al.*, 1992). Trials with the compound carried out in domestic animals have endorsed high order of efficacy against enteric helminths (Katiyar *et al.*, 1984).

In order to enhance bioavailability (Nagaraja *et al.*, 1995) and consequently the efficacy, two formulations, soluble and dispersible preparations were made and evaluated in control testing against various helminth parasites of rodents. Both the preparations were found

equally effective (Gupta *et al.*, 1996).

Since a large population of domestic animals/poultry suffer from one or the other helminth parasites, they often require frequent treatment. *Ascaridia galli* is often debilitating parasite of small intestine of chicken and other domestic and wild birds. It is commonly encountered in crowded unsanitary outer doorpens. Severe infections in young birds during development of the parasite in tissue causes debility, ruff feathers, drooping wings, haemorrhagic diarrhoea, anorexia and reduces growth rate (Levine, 1968; Soulsby, 1978). Heavy infections may cause intestinal obstruction or perforation and severe egg drop in layers and may ultimately lead to great morbidity and mortality resulting into heavy economic losses to the entrepreneurs. Drawing the advantage of solubility/dispersibility of the compound, the two preparations through drinking water were put to trial to ascertain their utility for mass treatment of poultry carrying *Ascaridia galli* infection.

MATERIALS AND METHODS

Infected birds:

Fowls (1.5 ± 0.2 kg) carrying natural infection of *A. galli* (confirmed by stool examination) at different farms were selected for the study. The birds were killed under deep ether anaesthesia.

Preparation of soluble/dispersible formulations:

Soluble formulation:

Soluble formulation was prepared as per method of Jain *et al.* (1991). Briefly, 100 mg/ml solution of comp. 81/470 was prepared by dissolving 1 g of compound in 5 ml lactic acid at room temperature. To the resultant solution 5 ml of distilled water was added, pH of the solution was adjusted to 3.0 by adding, in portion, solid sodium bicarbonate. The solution was filtered through a sintered funnel to remove any undissolved or suspended impurities.

Dispersible preparation:

Drug suspension powder containing drug was prepared by homogeneously blending 50 % compound 81/470, 48 % lactose, 1 % carbopol-940, 0.5 % sodium bicarbonate and 0.5 % of permicol orange red powder, a permissible food colour additive (unpublished data).

Drug Testing:

Soluble and dispersible formulations were simultaneously evaluated. Both the preparations were initially tried by force feeding at different dose schedules (20 mg/kgx1; 10 mg/kgx2 days; 5 mg/kgx3 days), against confirmed (positive by stool examination) *A. galli* infection in fowls to ascertain their efficacy potential. Six birds were used at each dose level and two replicates were carried out. All birds were sacrificed by deep ether anaesthesia and their intestine were searched for presence of worms (Katiyar *et al.*, 1984).

For mass therapy both the preparations were given in drinking water. Each bird consumes about 125 ml of water in 24 hours. Three dose regimens [20 mg/kgx1 (0.06 % concentration); 10 mg/kgx1 (0.03 % conc.) days and 5 mg/kgx3 (0.015 % conc.) days] were employed. For each dose level, a flock of 200 birds was selected. Prior to medication drinking water was withheld for 6 hours. Desired amount of drug formulation was suspended in 10 liters of drinking water and divided into four containers each having 2.5 liters of medicated water and provided to the flock (assuming that each thirsty bird (1.5 ± 0.2 kg) consumes about 50 ml of water in 3–4 hours).

The efficacy assessment was made on the basis of stool examination (3–4 fecal samples of each bird) conducted at random (40–50 birds in each flock) on day -1 and day +4 of treatment by the following formula.

$$\% \text{ efficacy} = \frac{\text{No. of positives pre-treatment} - \text{No. of positives post-treatment}}{\text{No. of positives pre-treatment}}$$

Postmortem of certain randomly selected birds from infected treated and control flocks was also conducted for critical examination (Katiyar *et al.*, 1984). Two replicates of each dose schedule were done.

Statistical Analysis

Standard normal deviate test for proportion was used to compare responses between the groups.

RESULTS

Efficacy by force feeding:

The efficacy of soluble and dispersible preparations of compound 81/470 is presented in Table 1.

In single dose schedule of 20 mg/kg, both dispersible and soluble preparations were equally effective. In lower multiple doses, soluble formulation was found to exhibit better activity than dispersible preparation. Soluble formulation at 10 mg/kgx2 days dose cleared 100 % of the treated birds whereas dispersible preparation could remove ascarids from only 66 % of the treated birds ($p < 0.05$).

Efficacy by mass feeding:

On the basis of activity witnessed in force feeding with both the formulations, it was decided to try all the doses in mass feeding to select appropriate regimen for large scale treatment.

Table 1: Efficacy of soluble and dispersible preparations of compound 81/470 against *Ascaridia galli* in fowls by oral route

Formulation	Dose mg/kg (route)	No. cleared*		Percent efficacy	Significance
		No. treated			
Soluble	20×1	12/12		100.0 ^a	b vs b ¹ (p<0.05)
	10×2	12/12		100.0 ^{b+}	
	5×3	9/12		75.0 ^c	
Dispersible	20×1	12/12		100.0 ^{a1}	c vs c ¹ NS (p>0.05)
	10×2	8/12		66.6 ^{b1}	
	5×3	8/12		66.6 ^{c1}	

*Results of two replicates

In the experimental birds, the overall positivity rate for ascarids was approximately 50 %. The soluble preparation in single dose of 20 mg/kg resulted in complete elimination of parasites from 93.3 % birds whereas dispersible preparation cleared 83.3 % of the treated birds (Table 2).

Table 2: Efficacy of soluble and dispersible preparations of compound 81/470 in mass treatment

Dose mg/kg	Soluble preparation		Dispersible preparation		Significance
	No. examined*		No. examined*		
	No. cleared	Percent efficacy	No. cleared	Percent efficacy	
20×1	90/84	93.33 ^a	90/75	83.33 ^{a1}	a vs a ¹ (p<0.05)
10×2 days	90/80	88.88 ^b	90/85	94.44 ^{b1}	b vs b ¹ (NS p>0.05)
5×3 days	90/84	93.33 ^c	90/77	85.55 ^{c1}	c vs c ¹ (NS p>0.05)

*Results of two replicates

In multiple doses of 10 mg/kg×2 and 5 mg/kg×3 days both the preparations were more or less equally efficient (NS, p>0.05) whereas single dose of 20 mg/kg of soluble preparation exhibited better response than dispersible formulation. Five birds from each of the treated groups (negative for ascarid ova) were sacrificed and their intestines were searched for worms. No parasite could be traced in any of these birds.

DISCUSSION

Benzimidazoles constitute an important class of anthelmintics. These are notoriously insoluble in water (Toeco *et al.*, 1965; Sharma and Srivastava, 1988). For routine deworming of livestock harbouring helminth parasites, an anthelmintic which could be solubilized/dispersed in water would be more suitable for mass treatment. Through drinking water uniform distribution and quick intake of drug can be assured when given to fasted livestock in comparison to solid feed. With this view two pharmaceutical preparations, soluble form and dispersible form were made (Jain *et al.*, 1991) and their potential was examined in mass treatment in various dose schedules.

Certain anthelmintics, like albendazole have been claimed to be effective in single dose. However, patients often require repeat drugging. Compound 81/470 in three dose schedules (20 mg/kgx1, 10 mg/kgx2 days, 5 mg/kgx3 days) was found to have parallel efficacy in mass treatment of birds. In large scale trials, it may be possible that multiple dose schedule may prove better than the single ones. Moreover, in multiple doses, fowls who do not succeed in taking drugs at the time of first administration for various reasons (crowding, illness etc.), will get access to drug on subsequent days and such schedule should yield better efficacy. In the present study 5 mg/kgx3 days dose needed lesser compound than single administration (20 mg/kgx1). Thus, emphasis may be laid to use in practice 5 mg/kg dose for 3 consecutive days.

Although both the formulations elicited comparable efficacy against poultry roundworms in mass feeding, the dispersible formulation having longer shelf-life (unpublished data) and convenience of packaging and transportation may be preferred over the soluble preparation.

Thus, compound 81/470 possessing many desirable characteristics and showing high anthelmintic efficacy could be safely used for the control of poultry round worms.

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