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Efficacy of piperzine citrate, stabilized with Aluminium-Magnesium Silicate, against *Helignosomoides bakeri*

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ABSTRACT

To test effect of a synthetic Aluminium-Magnesium Silicate (AMS) on anthelmintic efficacy of piperazine citrate (PC), 35 mice were infected by dosing each, 0.15 ml *Helignosomoides bakeri* sample which contained 200 infective larvae, per os. Following confirmation of establishment of infection by faecal floatation, they were assigned into seven groups of 5 each, and were treated with piperazine citrate, per os, at rates of 110 mg/kg (PC), 110 mg/kg (PC in AMS), 82.5 mg/kg (PC), 82.5 mg/kg (PC in AMS), 55 mg/kg (PC) and 55 mg/kg (PC in AMS) respectively. The seventh group served as untreated control. Mean Eggs Per Gramm of faeces (EPG) were 375 ± 32.27 , 175 ± 14.43 , 830 ± 1.04 , 70 ± 12.25 , 850 ± 293.06 , 370 ± 58.54 and $2,200 \pm 2.55$ respectively. This showed EPG reduction rates of 83%, 92%, 62%, 97%, 61% and 83% among the respective treated groups.

Keywords: Anthelminthic Resistance; Aluminium-Magnesium Silicate; Stabilization; Piperazine Citrate; *Helignosomoides bakeri*

1. INTRODUCTION

Helminthosis is one of the world's most important parasitoses. It is of both public health and economic importance [1]. Piperazine salts are among the most extensively used anthelmintics in livestock production, because, they are cheap and effective. However, there are increasing reports of development of resistance by helminth parasites against piperazine and other anthelmintics [2-4]. This calls for research for drugs to combine with piperazine salts for treatment of helminthosis, to improve their effi-

cacy, for better performance of livestock and to reduce rate of development of anthelmintic resistance.

Molecules of Aluminium-Magnesium Silicate have positive electrical charges on one of their ends while the other end is negatively charged [5]. So, when in solution, AMS hydrates to form three dimensional colloidal structures. These colloidal structures stabilize active drugs [5]. AMS is therefore used in many pharmaceutical formulations as a stabilizing agent. It has been in use for many decades, with no report of toxicity [6,7]. Schills [8] reported that it is safe for use on food animals. Report of assessment of some minerals for pharmaceutical use, also revealed that when AMS was administered to laboratory animals both by oral route and by topical application, there was no significant adverse side effect [9].

By stabilizing drugs' active ingredients, AMS protects them from destruction. So, it may protect piperazine citrate from being rapidly degraded by metabolic processes. If high concentration of a drug is retained in the blood for longer time after treatment, its therapeutic action increases [10]. However, the natural AMS contains many impurities [5]. If AMS is used at higher doses than presently used, these impurities may lead to adverse reactions. To overcome this problem, Aluminium Silicate and Magnesium Silicate which are also safe for use in pharmaceutical formulations [9] were reacted to get a synthetic AMS [11]. Ability of the synthetic AMS to enhance anthelmintic efficacy of piperazine citrate was tested against *Helignosomoides bakeri*.

2. MATERIALS AND METHODS

Thirty five mice, aged between 8 weeks and 10 weeks were each dosed (per os), 0.15 ml of *H. bakeri* sample which contained 200 infective larvae. Ten days post infection (PI), establishment of infection was confirmed by detection of *H. bakeri* eggs in faeces of the mice, by floatation technique. The mice were then divided into seven

groups of five mice each. Six groups were treated with 110 mg/kg, piperazine, 110 mg/kg, piperazine in a piperazine-AMS drug formulation, 82.5 mg/kg, piperazine, 82.5 mg/kg, piperazine in the piperazine-AMS drug formulation, 55 mg/kg, piperazine and 55 mg/kg, piperazine in the piperazine-AMS drug, respectively. The seventh group served as control. Effect of AMS on anthelmintic efficacy of piperazine was assessed by counting number of *H. bakeri* Eggs Per Gramm (EPG) of faeces of each mouse in the seven groups, by the McMaster method. Mean EPG of the groups were then compared for statistical differences by Analysis of Variance (ANOVA) method.

3. RESULTS

Mean EPG of *H. bakeri* in the control group was 2200 ± 2.25 . Treatment with 110 mg/kg piperazine and with 110 mg/kg piperazine in AMS, reduced the EPG to 375 ± 32.27 and 175 ± 14.43 ($P < 0.05$) respectively. At 82.5 mg/kg, treating with piperazine and with piperazine in AMS reduced the EPG to 830 ± 1.04 and 70 ± 12.25 ($P < 0.01$) respectively. At piperazine dose of 55 mg/kg, mean EPG for the groups of mice treated with piperazine and piperazine in AMS were 850 ± 293.06 and 370 ± 58.54 ($P < 0.05$) respectively. Percentage reduction in mean EPG by 110mg/kg Piperazine, 110 mg/kg piperazine in AMS, 82.5 mg/kg piperazine, 82.5 mg/kg piperazine in AMS, 55 mg/kg piperazine and 55 mg/kg piperazine in AMS were 83%, 92%, 62%, 97%, 61% and 83% respectively.

4. DISCUSSION

Reduction of mean EPG from 2200 ± 2.25 in the control to 375 ± 32.27 , when piperazine was administered at dose of 110 mg/kg, was only 83% whereas to avoid anthelmintic resistance anthelmintics are required to reduce helminth infection by at least 95% [3]. Since 110 mg/kg is the highest dose of piperazine usually employed in treatment of helminthosis in animals, its failure to achieve upto the required 95% reduction in EPG may be one of the reasons for the increase of incidence of anthelmintic resistance by helminths.

It has been suggested that effort be made to find drugs to combine with piperazine salts and other anthelmintics to reduce incidence of resistance observed in treatment of helminthosis in ruminants and in horses [3]. Reduction of EPG by 97% when 82.5 mg/kg piperazine in AMS was used, suggests that AMS may potentiate piperazine to achieve enough anthelmintic clearance to avoid development of anthelmintic resistance.

Reason for failure of 110 mg/kg piperazine in the AMS to achieve upto 95% reduction of EPG is not well understood. However, the observation that when AMS is used

to potentiate active drugs, normal therapeutic doses produce less effect than subnormal doses has been consistent. This has been observed in effect of AMS on Sulphadiazine against Avian Coccidia [12], in effect of AMS on Chloroquine phosphate against plasmodium [13] and in effect of AMS on Ampicillin trihydrate against *Salmonella gallinarum* [14]. It is possible, that by stabilizing these active drugs, AMS enhances their activities such that the normal doses become overdose and thus toxic to treated animals. Toxicity from drugs could lead to immunosuppression which could affect oocysts count per gramme of faeces, parasitaemia, titre of bacteria in bile of treated chickens and number of helminth eggs per gramme of faeces of mice.

Use of 55 mg/kg piperazine in AMS achieved only 83% reduction in EPG which is short of the required 95% reduction in EPG. It is therefore recommended that when AMS is to be used on piperazine for treatment of helminths, piperazine dose should be 82.5 mg/kg. Use of this lower dose of piperazine potentiated with AMS, for treatment of helminthosis has advantages of, better anthelmintic effect, reduction in cost of treatment and reduction in amount of drug residues in meat of treated animals.

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