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Evaluation of Effect of Halquinol on Intestinal Motility in Rats

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Abstract

Effect of halquinol on intestinal motility was determined by charcoal meal test in Wistar rats. The three treatment groups received halquinol @ 200, 400 and 1000 mg/kg b. wt., P.O. The rats of three treatment groups were also pre-treated with halquinol twice a day at 12 hrs interval for six days at their respective doses. On seventh day, charcoal meal test was carried out. The distance of the small intestine travelled by charcoal meal in rats belonging to 1000 mg/kg b. wt. treatment group was 44.5±8.22 cm which is less compared to control group (61.33±6.39 cm), which reflects decrease in intestinal motility. And peristalsis index in 1000 mg/kg b. wt. treatment group rats was 0.50±0.09 which is comparable to that of the standard group rats whose peristalsis index is 0.37±0.03. Charcoal meal test in the present study indicated that halquinol possess antimotility effect upon pre-treatment with halquinol @ 1g/kg b.wt.

Keywords: Charcoal Meal Test, Halquinol, Intestinal Motility, Wistar Rats

Introduction

Halquinol, a quinoline derivative having antibacterial, antifungal and antiprotozoal activity was introduced across the world to overcome common challenges of modern poultry and swine farming, like pathogenic microbial infections and growth promotion aspects. In Asian countries including India, halquinol is being extensively used as growth promoter in poultry and to control intestinal infections. The present study was undertaken with an aim to determine the effect of halquinol on motility of intestine in Wistar rats as there is paucity of scientific data in this regard.

Halquinol is a mixture obtained by chlorinating quinolin-8-ol. It contains not less than 57 per cent and not more than 74 per cent of 5,7-dichloroquinolin-8-ol, not less than 23 per cent and not more than 40 per cent of 5-chloroquinolin-8-ol and not more than 4 per cent of 7-chloroquinolin-8-ol and the total content of three components is not less than 95 per cent and not more than 105 per cent (Anon., 1980). Halquinol is a broad-spectrum antimicrobial having antibacterial, antifungal, anti-mycoplasmal and anti-protozoal activity (Stewart, 1958; Heseltine and Campbell, 1960; Lamy, 1964; Fiedler and Kaben, 1966; Ellenrieder and Sensch, 1972; Forster and Duggan, 1974; Cosgrove, 1977; Cosgrove and Baines, 1978; Botsoglou and Fletouris, 2001). As halquinol was found to be absorbable to little extent when given to animals by the oral route (Heseltine and Freeman, 1959) and to exhibit activity against a variety of bacteria and fungi, it has potential in the treatment of infections localized within the intestinal tract. Halquinol is one of the popular molecules marketed in South American countries and Asian countries including India, for use in poultry as growth promoter. A tissue distribution study of halquinol in chicken following dietary inclusion by Pavithra *et al.* (2014) has indicated pre-slaughter withdrawal period of 3 days for meat and edible offals. In tests on isolated smooth muscles, Kaul and Lewis (1965) noted that halquinol markedly reduced peristalsis. They also observed that halquinol caused slowing of the movement of the intestinal contents of intact animals. Halquinol reduces the tone and motility of smooth muscle of intestine, thus help in enhancing nutrient absorption (Swick, 1996). These properties provide partial explanation of the improved feed conversion ratio and growth rate due to halquinol supplementation through diet apart from prompt alleviation of the symptoms of diarrhoea. However, the pharmacological effect of halquinol on intestinal motility in animals is poorly understood, and therefore the current study is undertaken in Wistar rats.

Materials and Methods

Effect of halquinol on intestinal motility was determined by carrying out charcoal meal test (Degu *et al.,* 2016). The present study was conducted in Wistar rats. Animals of all the groups were fasted for 18 hours on previous day of conducting charcoal meal test. But all the animals had *ad lib* access to water. Experimental design was as detailed in Table 1.

Table 1: Experimental design for charcoal meal test in rats

Experimental Group	Particulars	No. of animals/group
I	Negative control- vehicle only	6
II	Standard control- Loperamide @ 3 mg/kg b.wt., P.O.	6
III	Halquinol @200 mg/kg b.wt.X7 days, P.O.	6
IV	Halquinol @ 400 mg/kg b.wt.X7 days, P.O.	6
V	Halquinol @ 1000 mg/kg b.wt.X7 days, P.O.	6
	Total No. of Experimental Rats	**30**

Experimental animals belonging to groups III, IV and V were pre-treated with halquinol suspended in tragacanth twice a day at 12 hrs interval for six days @ 200, 400 and 1000 mg/kg b. wt., P.O. On seventh day charcoal meal test was carried out, group I rats received plain vehicle that is tragacanth suspension @ 1mL/100 g b.wt. P.O., group II rats received standard control loperamide @ 3 mg/kg b.wt. P.O. and group III, IV and V rats received halquinol suspended in tragacanth @ 200, 400 and 1000 mg/kg b.wt. P.O. Then one hour later, rats belonging to all the five groups received (*per os*) 5 per cent aqueous charcoal suspension. One hour later after the administration of charcoal, rats in all the groups were sacrificed and small intestine was dissected out from pylorus to caecum. The length of the intestine from pylorus to caecum was measured. The distance of the intestine travelled by the charcoal meal

from the pylorus was measured. The peristalsis index was expressed using appropriate formula. The peristalsis index is the distance of intestine travelled by charcoal meal to the total length of the small intestine expressed in terms of percentage. Halquinol BP 80 (Min. 98% W/W) manufactured and supplied by M/s. Quadragen Vet Health Pvt. Ltd., Bengaluru was used in the present study. Necessary approval from the Institutional Animal Ethics Committee (IAEC) bearing no. VCH/IAEC/2018/72; dated: 18/08/2018, was obtained before the conduct of present animal experiment.

Statistical Analysis

Data were analyzed by one-way ANOVA followed by *post hoc* Tukey's multiple comparison test by using SPSS® statistical software (Version 20.0; 2011, Armonk, NY, USA). Differences between the values were considered significant at $p<0.05$ or lower.

Results and Discussion

The distance travelled by charcoal meal in rats belonging to group V (halquinol @ 1000 mg.kg^{-1}) is significantly ($p<0.05$) less as compared to vehicle or standard positive control group, thus the decrease in intestinal motility by halquinol is evident (Table 2). However, there is no influence of halquinol on intestinal motility when tested at doses below 1.0 g.kg^{-1} b.wt. Peristalsis index of rats belonging to group V is comparable to that of the standard reference drug loperamide. The results of the present study are in agreement with the study by conducted by Kaul and Lewis (1965), where in, halquinol in tests on isolated smooth muscles has reduced the peristalsis of isolated smooth muscles of intestine. Thus, anti-motility effect of halquinol in the charcoal meal test is evident in the current study.

Table 2: Effect of different doses of halquinol on intestinal transit in rats

Parameters	Group I (Control)	Group II (Standard: Loperamide)	Group III Halquinol: 200 mg/kg b.wt	Group IV Halquinol: 400 mg/kg b.wt	Group V Halquinol: 1000 mg/kg b.wt
Mean length of the small intestine(cm)	81.83±2.85	85±5.26	86±5.89	90.33±4.50	89±7.39
Mean distance travelled by charcoal meal (cm)	61.33±6.39^{a}	32±2.38^{b}	61.33±5.59^{a}	62.66±4.61^{a}	44.5±8.22^{b}
Peristalsis index	0.75±0.06	0.37±0.03	0.71±0.08	0.69±0.07	0.50±0.09

Values are expressed as mean±SE ; Data were analyzed by one way ANOVA followed by post hoc Tukey's multiple comparision test; Values bearing dissimilar superscript between column vary significantly (p≤0.05)

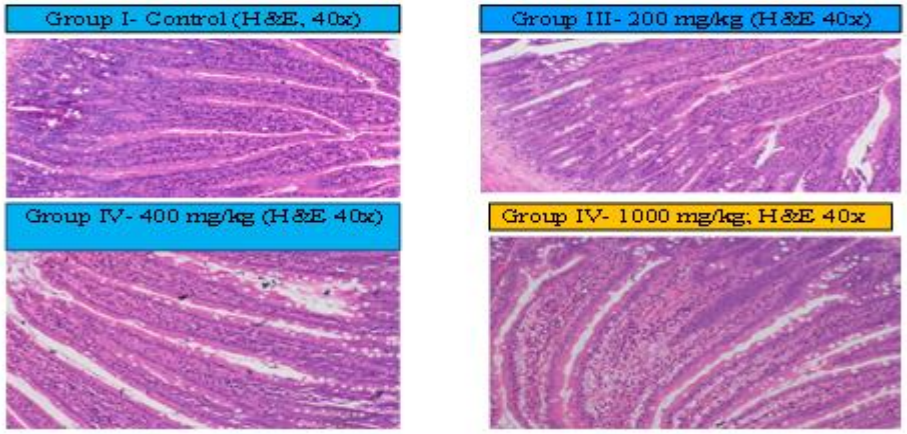

Figure 1: Histopathology of small intestine (ileum) of experimental rats (H&E, 40X)

Histopathology of Intestine

Histopathology of intestinal segment (ileum) under H & E staining was carried out and it was found that halquinol did not induce any toxico pathological changes in the gut in all the tested doses (200, 400 and 1000 mg/kg b.wt. x

7 days, P.O.), except for a slight increase in goblet cell activity in rats receiving halquinol at 1.0 $g.kg^{-1}$. The present finding on histopathology of intestinal segment is in agreement with a repeated dose 28 day oral toxicity study of halquinol in rats conducted by Swetha *et al.* (2007), where in there was an evidence of catarrhal inflammation of intestine characterized microscopically by degeneration of tips of intestinal villi, increased goblet cell activity, infiltration of inflammatory cells in lamina propria in female rats dosed @ 1000 $mg.kg^{-1}$ b.wt. (*per os*) for 28 days.

Conclusion

From the current study it is evident that halquinol possess antimotility effect on intestine by charcoal meal test in Wistar rats upon pre-treatment (@1 g/kg b.wt.). Thus, vast scope exists to exploit halquinol as an antidiarrhoeal agent after appropriate clinical studies.

Conflict of Interests

There is no conflict of interest.

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