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Study of antidiarrhoeal activity of piperine

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ABSTRACT

Antidiarrhoeal effect of piperine was evaluated in castor oil and magnesium sulphate induced diarrhoea in mice. Effect of piperine was also studied on intestinal propulsive movement and intestinal fluid accumulation in mice. Piperine, at a dose of 5 to 20 mg/kg showed antidiarrhoeal activity in castor oil and magnesium sulphate induced diarrhoea. It has also produced antimotility and antisecretory activity in castor oil induced intestinal transit and intraluminal fluid accumulation in mice. These results suggest that piperine possesses antidiarrhoeal effect may be due to its antimotility and antisecretory effect.

Key words: Piperine, diarrhoea, intestinal transit, intestinal secretion.

INTRODUCTION

Diarrhoea is a condition of passage of loose, watery stools with increased frequency [1, 2]. It involves both an increase in the motility of the gastrointestinal tract, along with increased secretion, and a decrease in the absorption of fluid and thus a loss of electrolytes and water [3]. It is one of the major health threats to populations in tropical and subtropical poor countries, responsible for about 5 millions deaths annually [4]. Several antidiarrhoeals are available in both the modern and traditional medicines. Despite the availability of several remedies to treat diarrhoea including botanicals and chemical agents, yet there is a great need for the evaluation of newer, economical and cost effective agents to meet the challenges of upcoming era regarding disease burden [5].

Piperine is an alkaloidal constituent of black pepper [6]. It has the ability to increase the bioavailability of certain nutrients and drugs, such as: beta carotene, curcumin, selenium, pyroxidine (B6), glucose, and amino acids. [7] It is used all over the world for various illnesses. In Mexico for instance, it is used to treat stomach aches, malaria, and as an anti-inflammatory agent. Morocco uses it to treat weight loss and leukemia. Indonesia uses it to reduce or prevent headache and fever, as a treatment for snake poisoning, and to treat epilepsy. [8, 9] Present study was conducted to investigate the antidiarrhoeal effect of piperine and mechanism of antidiarrhoeal activity of piperine.

MATERIALS AND METHODS

Drugs

i) Piperine – Sigma chemicals Ltd., ii) Castor oil (refined pure) – Paras Chemical Industries, iii) Loperamide hydrochloride – Cipla Pharmaceuticals Ltd., iv) Chlorpromazine hydrochloride – Rhone Poulenc (India) Ltd., v) Activated Charcoal – E. Merck, vi) Magnesium sulphate – Merck, vii) Atropine sulphate – Sigma chemicals Ltd.

Animals

“Swiss albino mice” of either sex, weighing; 20 – 25 gm obtained from VIPER, Pune, were used for the experiments. They were kept in standard environmental condition, fed standard food and water ad libitum. All experiments were performed after an overnight fast. The study was approved by Institutional Animal Ethical Committee of Government College of Pharmacy, Aurangabad, Maharashtra, India (GCPA/IAEC/2011/235, 11/03/2011).

Experimental procedure for antidiarrhoeal activity

Acute toxicity

Initially the piperine was studied for acute oral toxicity as per revised OECD guidelines number 423. Piperine was used for the study at the dose of 5, 10 and 20 mg/kg because it has not shown any toxicity up to 50 mg/kg.

Castor oil induced diarrhea

The animals were divided in to control, positive and test groups containing six in each group. Each mouse was kept for observation under a glass funnel, the floor of which was lined with blotting paper and observed for 4 h. Diarrhea was induced by administering 0.2 ml. of castor oil orally to mice. The control group received only distilled water (10 ml/kg, p.o.); the positive control group received loperamide (2 mg/kg, p.o.); test group received piperine at doses of 5, 10, 20 mg/kg, p.o., body weight 30 min before the administration of castor oil. During an observation period of 4 h, the parameters observed were: onset of diarrhoea, total weight of stool output, total weight of wet stools, total number of stool output, and number of wet stools. [10]

Magnesium sulphate induced diarrhea

A similar protocol as for castor oil induced diarrhoea was followed. Magnesium sulphate was given in the dose of 2 g/kg, p.o., to the animals 30 min after pre-treatment with distilled water (10 ml/kg, p.o.) to the control group, loperamide (2 mg/kg, p.o.) to the positive control group, piperine at doses of 5, 10, 20 mg/kg, p.o., to test group. [11]

Gastrointestinal motility by charcoal meal

The animals were divided in to control, positive and test groups of six mice each. Each animal was given orally 0.2 ml of charcoal meal (3% charcoal in 5 % gum acacia). The test groups received the piperine at doses of 5, 10, 20 mg/kg, p.o., body weight immediately after charcoal meal administration. The positive control group received atropine sulfate (5 mg/kg, i.p.), while the control group received distilled water (10 ml/kg, p.o.). After 30 min., the animals were sacrificed and the movement of charcoal from pylorus to caecum was measured. The peristaltic index, which is the distance travelled by charcoal meal to the total length of small intestine expressed in terms of percentage. [12]

Small intestinal secretions

Effect of piperine on intestinal secretion was indirectly studied by entero-pooling assay. The mice were divided into different groups and treated with piperine (5, 10, 20 mg/kg, p.o.),

distilled water (10 ml/kg, p.o.) and standard chlorpromazine (30 mg/kg, i.p.) before the oral administration of castor oil 0.2 ml per mouse. These mice were sacrificed 30 min later and entire small intestine from each animal was weighed and their group average was calculated. The difference in the weight of intestine in control and castor oil treated group was considered as the castor oil induced accumulation of intestinal fluid. [13]

Statistics

The results of all experiments were reported as mean \pm S.E.M. Statistical analysis was carried out using Student's 't'-test. A level of significance of $P < 0.05$ was regarded as statistically significant.

RESULTS

Effect of piperine on castor oil induced diarrhoea

In the course of observation for 4 h. after castor oil administration, all the mice in control group produced copious diarrhoea. Pretreatment of mice with the different doses of piperine caused a significant dose dependent decrease in the frequency of purging (reduction of number of wet stools and total no of stools) and, weight of wet stools. Piperine showed dose dependent inhibition of castor oil induced diarrhoea in albino mice. This effect was significant at 20 mg/kg in comparison to control group, however, this activity was less as compared to loperamide as shown in Table 1.

Table 1: Effect of piperine on castor oil induced diarrhoea in mice

Group	Dose (mg/kg)	Onset of diarrhoea (min)	Total weight of stools (g)	Weight of wet stools (g)	Total number of stools	Number of wet stools	% Inhibition
Control		53 \pm 2.11	0.372 \pm 0.010	0.35 \pm 0.010	13.33 \pm 0.33	11.00 \pm 0.36	
Piperine	5	69 \pm 2.47	0.305 \pm 0.009	0.285 \pm 0.006	10.66 \pm 0.42	8.83 \pm 0.40	19.69
Piperine	10	75 \pm 3.17	0.275 \pm 0.007	0.252 \pm 0.005	9.5 \pm 0.42	7.83 \pm 0.30	28.81
Piperine	20	79 \pm 2.94	0.240 \pm 0.006	0.215 \pm 0.005	9.16 \pm 0.47	7.33 \pm 0.33	33.36
Loperamide	2	223 \pm 5.16	0.036 \pm 0.002	0.030 \pm 0.003	1.00 \pm 0.25	0.83 \pm 0.16	92.45

Values are mean \pm standard error of mean. Each value represents average of six determinations. $P < 0.05$ vs. control, student's 't' test.

Effect of piperine on magnesium sulphate induced diarrhoea

All the mice in control group produced diarrhoea after magnesium sulphate administration during the observation period of 4 h. Pretreatment of mice with the different doses of piperine caused a significant dose dependent decrease in the frequency of purging (reduction of number of wet stools and total no of stools) and, weight of wet stools. Piperine showed dose dependent inhibition of magnesium sulphate induced diarrhoea in albino mice. This effect was significant at 20 mg/kg in comparison to control group, however, this activity was less potent as compared to loperamide (Table 2).

Table 2: Effect of piperine on magnesium sulphate induced diarrhoea in mice

Group	Dose (/kg)	Onset of diarrhoea (min)	Total weight of stools (g)	Weight of wet stools (g)	Total number of stools	Number of wet stools	% Inhibition
Control		41 \pm 2.06	0.32 \pm 0.01	0.291 \pm 0.009	11.50 \pm 0.42	8.16 \pm 0.30	
Piperine	5	57 \pm 2.31	0.251 \pm 0.008	0.215 \pm 0.007	8.66 \pm 0.33	6.00 \pm 0.36	26.47
Piperine	10	61 \pm 2.37	0.232 \pm 0.006	0.207 \pm 0.005	8.16 \pm 0.47	5.66 \pm 0.33	30.63
Piperine	20	68 \pm 2.50	0.204 \pm 0.006	0.184 \pm 0.006	8.00 \pm 0.36	5.16 \pm 0.47	36.76
Loperamide	2	207 \pm 6.58	0.030 \pm 0.004	0.027 \pm 0.006	0.83 \pm 0.16	0.66 \pm 0.21	91.11

Values are mean \pm standard error of mean. Each value represents average of six determinations. $P < 0.05$ vs. control, student's 't' test.

Effect of piperine on small intestinal transit

The results revealed that piperine inhibited the castor oil induced gastrointestinal transit of charcoal in mice by dose dependent manner. Maximum effect was produced at 20 mg/kg in comparison to control group, however, this activity was less as compared to atropine sulphate as shown in Table 3.

Table 3: Effect of piperine on castor oil induced intestinal transit in mice

Group	Dose (/kg)	Percent intestinal transit	% Inhibition
Normal		73.30 ± 1.60	
Control		81.33 ± 2.13	
Piperine	5	65.34 ± 2.17	10.85
Piperine	10	62.13 ± 1.71	15.23
Piperine	20	59.33 ± 1.65	19.05
Atropine sulphate	5 mg	32.29 ± 1.02	55.94

Values are mean ± standard error of mean. Each value represents average of six determinations. $P < 0.05$ vs. control, student's 't' test.

Effect of piperine on small intestinal secretion

Piperine, dose dependently reduced the castor oil induced intraluminal accumulation of fluid. Maximum effect was produced at 20 mg/kg in comparison to control group, however, this activity was less as compared to chlorpromazine as shown in Table 4.

Table 4: Effect of piperine on castor oil induced intraluminal fluid accumulation in mice

Experimental Group	Dose (/kg)	weight of small intestine mg	Castor oil induced intraluminal fluid (mg)	% Inhibition
Normal		1123 ± 25		
Control		1628 ± 23	505 ± 40	
Piperine	5	1489 ± 26	366 ± 33	27.52
Piperine	10	1444 ± 22	321 ± 31	36.43
Piperine	20	1380 ± 24	257 ± 28	49.10
Chlorpromazine	30 mg	1176 ± 24	53 ± 8	89.50

Values are mean ± standard error of mean. Each value represents average of six determinations. $P < 0.05$ vs. control, student's 't' test.

DISCUSSION

Castor oil induces diarrhoea by causing increased secretion of fluid and electrolytes into the lumen of the bowel by intestinal mucosa, resulting in fluid accumulation and a watery luminal content that flows rapidly through the small and large intestines. [14] This is brought about by the irritant effect of ricinoleic acid liberated by pancreatic lipases, which hydrolyse the oil derived from the seeds of *Ricinus communis*. [15] As piperine effectively inhibited the castor oil induced diarrhoea, it can be assumed that the antidiarrhoeal action was exerted by antisecretory mechanism.

Magnesium sulphate increases the volume of the intestinal content by preventing the reabsorption of water and sodium chloride. It also promotes the liberation of cholecystokinin from duodenal mucosa, which increases the secretion and motility of small intestine. [16] Piperine found to reduce the diarrhoeic condition in this model. Piperine may have increased the absorption of water and electrolyte from the gastrointestinal tract.

GI motility describes the contraction of the muscles that mix and propel contents in the gastrointestinal tract. Charcoal meal test in mice is a method used to study the effect of drugs on the motility of intestine. [17] In present study Piperine was found to be the inhibitor of intestinal motility.

Castor oil produces permeability changes in the intestinal mucosa membranes to water and electrolytes resulting in fluid and watery luminal content that flows rapidly through small and large intestines [18]. Piperine inhibited the castor oil induced intestinal fluid accumulation.

CONCLUSION

Piperine possesses antidiarrhoeal effect may be due to its antimotility and antiseretory effect.

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