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Original Article

Anti-ulcer activity on Siddha herbo-mineral formulation of Arputha Mathirai in aspirin induced gastric ulcer in rats

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ABSTRACT

The present study was to analyse the siddha drug arputha mathirai for anti-ulcer activity in aspirin induced in rats. Arputha mathirai was used to treat eri gunmam (peptic ulcer). Arputha mathirai at the dose level 200mg/kg and 400mg/kg were administered orally. Anti-ulcer effects were compared with standard drug omeprazole 20mg/kg b.w.,p.o.). The effect was assessed by parameters like pH, free acidity, total acidity and ulcer index. These observations helped us to conclude that Arputha mathirai 200mg/kg and 400mg/kg is endowed with antiulcer property.

Key words: Arputha mathirai, Aspirin, Peptic ulcer, Omeprazole.

INTRODUCTION

Ancient siddha literatures notified the diseases as 4448. Among them, the diseases pertaining to gunmam are 8. Eri gunmam is one of the 8 types of gunmam mentioned in yugi vaithiya cinthamani 800.[2] Gunmam is a clinical entity which depresses both body and mind since it is called as gunmam. The signs and symptoms of Eri Gunmam in siddha literature may be correlated with peptic ulcer disease in modern disease of classification. So it is considered to evaluate a classical siddha herbo mineral formulation "Arputha mathirai" mentioned in kosayee anuboga vaithiya brahma ragasiyam, part-II,[1] for the treatment of Eri Gunmam (Peptic ulcer). Peptic ulceration is one of the common disease affecting millions of people. It is now considered to be one of the modern age epidemics affecting nearly 10% of world population.[3] There is a rich abundance of plants reputed in traditional medicine to possess anti-ulcer properties. [4] Peptic ulcer, also known as 'ulcus pepticum' are ulcers which occur in that part of the gastrointestine which is exposed to gastric acid and pepsin, i.e., the stomach and duodenum. However, the etiology of peptic ulcer is not clearly known. It results probably due to an imbalance between the aggressive (acid, pepsin and H-pylori) and the defensive (gastric mucus and bicarbonate secretion, prostaglandin, nitric oxide and innate resistance of mucosal cell factors. [5] Complications such as obstruction, haemorrhage and perforations may occur. [6] In a gastric ulcer, generally, the acid secretion is normal or low. In a duodenal ulcer, acid secretion is high in half of the patients but normal in the rest. Gastric and duodenal ulcers are common pathologies that may be induced by a variety of factors such as stress, smoking, nutritional deficiencies and noxious agents including non-steroidal anti-inflammatory drugs (NSAID).[7]

MATERIALS AND METHODS

Trial drug: Arputha Mathirai:
Cuminum cyminum – 70 grams
Piper nigrum -70 grams
Zingiber officinale – 70 grams
Piper longum – 70 grams
Allium sativum – 70 grams
Ferula asafoetida – 70 grams
Purified rock salt – 70 grams
Purified sulphur – 70 grams
Citrus limon – sufficient quantity.

Preparation: All the drugs are powdered and grounded with lemon juice for 12 hours and rolled into pills of 500mg and dried. It is stored in an air tight container.

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Experimental animals: Albino rats (wistar rats) of either sex, weighing (160-250 g) were procured from animal housing facility, K.k College of pharmacy, Gerugambakkam, Chennai. All animals were placed in a polypropylene cages in a controlled room temperature 24℃±1℃ and relative humidity of 60-70 % in animal house. The animals were maintained in standard pellet diet and water ad libitum. They were acclimatized to laboratory condition for seven days before commencement of the experiment. All the protocols and the experiments conducted in strict compliance according to ethical principles and guidelines provided by committee for the purpose of control and Supervision of Experiments on Animals **(KKCP/2013/008/CPCSEA)**.

Animal experimentation protocols are approved by Institutional Animal Ethical Committee.

Acute toxicity studies: The Acute toxicity studies were performed in accordance with the OECD 423 guidelines. Female Wistar rats weighing 100-150gm were selected and divided into groups containing three animals in a group. The single dose of the Arpudha mathirai starting from 50mg/kg up to 2000mg/kg (5, 50,300,2000mg/kg) was administered orally. The drug treated animals were carefully observed individually for the toxicity signs and mortality. The parameters such as changes in skin and fur, eyes and mucous membranes, respiratory, circulatory, autonomic and central nervous system, behavioural pattern, convulsions, tremors, salivation, lethargy, diarrhoea, sleep and coma were observed. From the maximum dose 1\5th or 1\10th of the dose was considered as therapeutic dose for further study. Based on these findings, no toxic effect was observed up to 400 mg/kg of Arputha mathirai treated via oral route over a period of 28 days. So, it can be concluded that the Arputha mathirai can be prescribed for therapeutic use in human with the dosage recommendations of up to 400mg/kg. Body weight p.o.

Table 1: ACUTE TOXICITY STUDY PARAMETERS

S.no	Parameters	Observation
1.	Motor activity	No effect
2.	Tremors	No effect
3.	Convulsion	No effect
4.	Piloerection	No effect
5.	Straub reaction	No effect
6.	Loss of lighting effects	No effect
7.	Sedation	No effect
8	Muscle relaxation	No effect
9	Hypnosis	No effect
10	Analgesia	No effect
11	Ptosis	No effect
12	Lacrimination	No effect
13	Change in skin colour	No effect

ANTI-ULCER ACTIVITY

Aspirin Induced Gastric Ulcers:

Principle: Aspirin is a NSAID which inhibit the synthesis of prostaglandins. Prostaglandins protect the gastric mucosa by producing leukotrienes and bicarbonate ions. Aspirin also inhibit the gastric peroxidase and may increase mucosal hydrogen peroxide and hydroxyl ions level to cause oxidative mucosal damage.

Procedure: Albino rats of either sex weighing between 150-250 gms were divided into five groups and each consisting of six rats.Group I receives vehicle control (2ml/kg ,p.o.) Group II receives Standard drug omeprazole, .Group III: Received Arpudha Mathirai 200mg/kg and Group IV: Received Arpudha Mathirai 400mg/kg The animals are fasted for 24 hours.The test drug in varying concentrations based on the design of the experiment is administered orally 30 minute prior to aspirin at dose of 500 mg/kg.4hours later the rats are sacrified by using anaesthetic ether and their stomaches dissected and they were opened along greater curvature for the determination of gastric lesions. Ulcer index calculated by nothing the number of ulcers per animal and severity scored by observing the ulcers microscopically with the help of 10 X lens.

Ulcer assessment [16]: The stomachs were harvested, opened along the greater curvature and the mucosa was exposed for macroscopic evaluation. The ulcerated area was assessed and the ulcer index (UI, mm2) was calculated as the arithmetic mean for each treatment. Following the

analysis, the mucosal layer was blotted dry and scraped off the underlying muscularis externa and serosa.

Ulcer Scoring [16]: After sacrificing the rat, stomach was removed and opened along the greater curvature, and washed it slowly under running tap water. Put it on the glass slide and observe under 10X magnification for ulcer. Score the ulcers as below.

0= Normal coloured stomach; 0.5= Red colouration
1= Spot ulcers; 1.5= Haemorrhagic streaks
2 = Ulcers ≥ 3mm but ≤ 5mm
3 = Ulcers >5 perforation

Mean ulcer score for each animal is expressed as Ulcer Index.

Ulcer index [17]

Ulcer index was calculated as
Ulcer index = 10/x
Where x = Total mucosal area/Total ulcerated area.

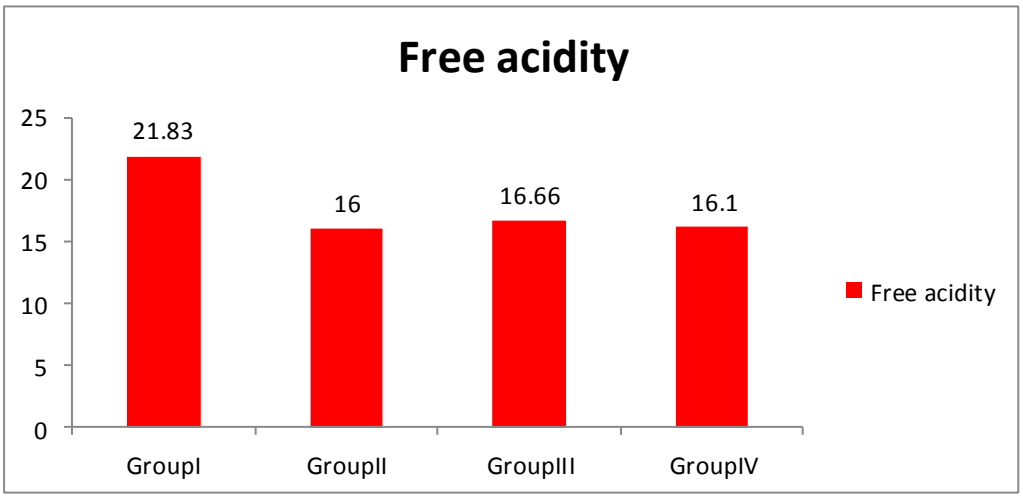
RESULTS

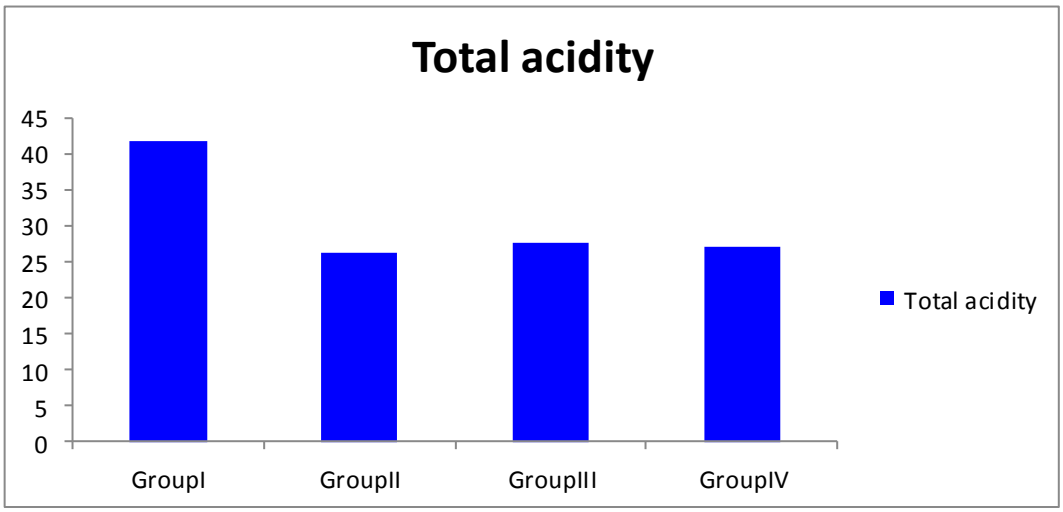
Effect of Free Acidity and Total Acidity: The free acidity and total acidity was determined based on the titre values. The free acidity and total acidity of Test drug on albino rats decreased significantly in comparison with the standard group treated with omeprazole.

Table: 2. Effect of Arpudha Mathirai on Free Acidity and Total Acid

Group No.	Body wt. gms	Treatment	Free acidity	Total acidity
I	155.67±0.56	Control (distilled water 2ml/kg)	21.83 ± 0.833	41.66 ± 0.760
II	164.23±1.23	Standard drug Omeprazole (20 mg/kg)	16.0 ± 0.61**	26.33± 1.05**
III	172.09±2.67	Arputha Mathirai(200mg/kg)	16.66±1.89*	27.50±1.62
IV	164.23±1.46	Arputha Mathirai(400mg/kg	16.1±1.90**	27.16±1.08*

Values are expressed in terms of mean ± SEM of 6 rats (ANOVA); Effects are statistically significant; *P<0.05;**p<0.01 (in comparison with Standard)





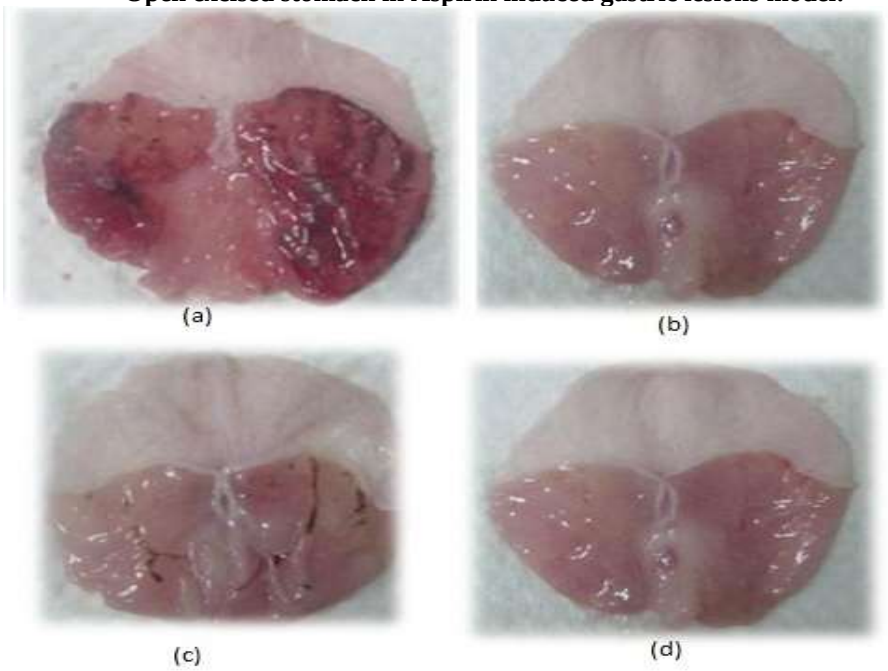
Ulcer index: The ulcer index was calculated by taking the mean ulcer score of each group. Then the mean ulcer score graph was plotted with groups on x-axis and ulcer index on y-axis. The histograms of different groups were then interpolated by comparing the ulcer index of group I with group II, III and IV. It was noticed that the ulcer index of Dose group (Dose-I & II) was significantly less when compared to the standard group (Group-II) treated with Omeprazole significantly.

Table: 3. Effect of Arputha Mathirai on Ulcer index and Percentage of ulcer protection

Group No.	Body wt. gms	Treatment	Ulcer Index	Percentage of ulcer protection
I	182.12±0.67	Control (distilled water 2ml/kg)	5.666 ±0.19	-
II	188.34±1.46	Standard drug Omeprazole (20 mg/kg)	1.083 ±0.24	77.5**
III	178.18±2.87	Arputha Mathirai(200mg/kg)	2.41 ±0.35	57.42
IV	169.67±1.23	Arputha Mathirai(400mg/kg	1.5±0.22	73.49*

Values are expressed in terms of mean ± SEM of 6 rats (ANOVA); Percentage protection = (Control mean ulcer index – Test mean ulcer index)/Control mean ulcer index ×100; Effects are statistically significant; *P<0.05;**p<0.01 (in comparison with Standard)

Open excised stomach in Aspirin induced gastric lesions model:



a: Inhibition in gastric lesions at control(distilled water 2ml/kg)
b: Absence of gastric lesions in Omeprazole (20mg/kg)
c: Fraction inhibition in gastric lesions at Arputha Mathirai (200mg/kg)
d. Fraction inhibition in gastric lesions at Arputha Mathirai (400mg/kg)

Bio Statistical Analysis: Since the p value is significant in all symptoms except diarrhoea. So there is significant reducing of symptoms among the patients for the treatment of Eri Gunmam(Peptic Ulcer). Hence it is concluded that the treatment was effective and significant. McNemat test, C.I: 95%, *P<0.05; **P<0.01

DISCUSSION

The gastro protective effects of Arputha mathirai were investigated against aspirin-induced ulcer model in rats. It has shown significant gastro protective effects against these models. Arputha mathirai has shown significant reduction in ulcer index as compared to control group in aspirin induced gastric ulcer model in both doses. Arputha mathirai 200mg/kg.,400mg/kg., has also significantly decreased ulcer index as compared to control group. Further the acid secretory parameters like total acidity, volume of gastric acid secretion and total acid output were also studied in aspirin-induced gastric ulcer model. Significant reduction was observed in total acid output and volume of gastric acid secretion although total

acidity was observed to be reduced insignificantly against aspirin-induced gastric ulcer model as compared to control group.

CONCLUSION

Administration of the Arputha mathirai significantly decreased the gastric volume in comparison with rats treated with Omeprazole. Comparing the gastric volume and acidity, the gastric volume gets decreased, simultaneously the gastric acidity also decreased significantly. This study demonstrates that the Arputha mathirai has a potent ulcer healing effect.

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