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EVALUATION OF ANTI-ULCER POTENTIAL OF SIDDHA FORMULATION AGASTHIYAR ELATHY CHOORANAM IN ASPIRIN-INDUCED ULCERATED RATS

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ABSTRACT

Peptic ulcer is one of the world's major gastrointestinal disorders and affecting 10% of the world population. Peptic ulcer disease is a disease located in the gastric or duodenal part of the gastrointestinal tract that mainly involves the mucosa layer. An estimated 15000 deaths occur each year as a consequence of peptic ulcer. Proton pump inhibitors are among the most commonly used and overprescribed medications in the world. The side effects of the PPIs, such as a headache, diarrhea, constipation, and abdominal discomfort becomes serious concern upon long-term usage. The potential of herbal supplements as source of new drugs still offers a large field for scientific research. But only a fraction of them has already been assessed for its efficacy still huge number of formulation belongs to Indian system of traditional medicine is yet to be explored. The main aim of the present study is to evaluate the anti-ulcer potential of the siddha drug Agasthiyar elathy chooranam (AEC) in aspirin ulcerated rats. Results of the study clearly indicates that ulcerative score of the rats belongs to aspirin group has shown the increased intensity and severity of the ulcer induction. There was significant decrease in the ulcerative score observed in trial drug AEC treated rats at both the dose level of 500 and 1000 mg/kg which reveals the anti-ulcer potential of the formulation. It was concluded from the outcome of the present study that formulations like AEC may be utilized for primary health care because of better acceptability, better compatibility with the human body and no side effects on clinical usage.

KEY WORDS: ***Gastrointestinal disorders, Siddha drug, Agasthiyar elathy chooranam, Anti-ulcer potential, Aspirin, Ulcerative score***

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1. Introduction

Peptic ulcer disease was traditionally thought to be the result of increased acid production, dietary factors, and even stress. However, Helicobacter Pylori infections and the use of nonsteroidal anti-inflammatory drugs (NSAIDs) including low-dose aspirin are now the more popular etiologies leading to the development of peptic ulcer disease [1-3]. Other factors such as smoking and alcohol may also contribute.

The recent approach to peptic ulcer is managed by inhibition of gastric acid secretion, promotion of gastro-protection, blocking apoptosis and stimulation of epithelial cell proliferation for effective healing. The conventional drugs used in the treatment of ulcer include histamine receptor antagonists, prostaglandins analogues, proton pump inhibitors, cytoprotective agents, antacids and anticholinergics, but most of these drugs produce undesirable side effects or drug interactions and may even alter biochemical mechanisms of the body upon chronic usage [4].

Even among traditional medicinal plants there is still a large percentage that has not been studied to confirm their efficacy and safety in humans [5]. Herbal preparations have been used to treat human gastric ulcer for millennia. Several controlled clinical studies have demonstrated that herbal medicines are effective in treating human gastric ulcer. Patients with gastric ulcer showed improvement after administration of the herbal supplements [6,7].

Agasthiyar Elathy Chooranam is a siddha polyherbal formulation that majorly comprises of the following ingredients such as Eletteria cardamomum, Syzygium aromaticum, Rock salt, Myristica fragrans, Costus speciosus, Rhus succedanea, Piper nigrum, Piper longum, Dried Rizhome of Zingibero fficinalis, skin of Terminalia chebula, skin of Terminalia bellirica, Dried fruit of Emblica officinalis, Nardostachys grandiflora, Cleodendrum serratum, Flower of Michelia champaca .But still now there is no proper documentary evidence available on the anti-ulcer property of this novel drug. Hence present study aimed at investigating anti-ulcer potential of the siddha drug Agasthiyar elathy chooranam (AEC) against aspirin ulcerated rats.

2.Materials and Methods

2.1. Experimental Animals

Healthy adult Wistar albino rats of either sex weighing between 200-220 g were used for the study. The animals were housed in poly propylene cages and were kept in well ventilated with 100% fresh air by air handling unit. A 12 light / dark cycle were maintained. Room temperature was maintained between 22 ¬+ 2o C and relative humidity 50–65%. They were provided with food and water ad libitum. All the animals were acclimatized to the laboratory for 7 days prior to the start of the study. The experimental protocol was approved by The Institutional Animal Ethics Committee of Sathyabama Institute of science and technology, Chennai, Tamil Nadu, India. The IAEC approval number: SU/CLATR/IAEC/X/089/2018.

2.1. Animal grouping and Methodology [8]

The animals were grouped into four groups of 6 animals each. Group I (Control group) -received normal saline, Group II – Ulcer control rats received 200mg/kg of Aspirin , p.o for the period of 7 days (Day 1 to 7). Group III (Low dose treated group): Aspirin ulcerated rats was treated with 500mg/kg of AEC,p.o for the period of 07 days 1 hr prior to the administration of aspirin. Group IV (High dose treated group): Aspirin ulcerated rats was treated with 1000mg/kg of AEC,p.o for the period of 07 days 1 hr prior to the administration of aspirin.

2.2. Sample Collection

At the end of the study, before sacrifice, the animals were fasted for overnight with free access to water. Animals were sacrificed with excess anesthesia. The stomach was removed and opened along the greater curvature. The stomach was gently rinsed with water to remove the gastric contents and blood clots. The inner surface of free stomach was examined for gastric lesions. The number of ulcers was counted. Ulcer scoring was carried out according to the method by as given below.

The scores were:

0 = no ulcer, 1 = superficial ulcer, 2 = deep ulcer and 3 = perforation

2.2.1. Ulcer score [9]

Ulcer index was measured by using the following formula

$$UI = UN + US + UP \times 10^{-1}.$$

Where UI is the ulcer index; UN is the average number of ulcers per animal; US is the average number of severity score and UP is the percentage of animals with ulcers.

2.2.2. Percentage inhibition of ulceration [10]

Percentage inhibition of ulceration was calculated as follows:

$$\%\ \text{inhibition of ulceration} = \frac{\text{UI of Control} - \text{UI of Test}}{\text{UI of Control}} \times 100$$

There was a low percentage of ulcer in the study drug treated animals.

2.3. Histopathological Analysis [11]

Sample obtained were immersed in 10% formalin for 24 h-48h for histopathological examination. After standard processing, the cut tissue was embedded in paraffin (Leica TP1020 tissue processor) and cut into 5 µm thick sections in a rotary microtome (Leica RM2255 - Fully Automated Rotary Microtome). The sections were stained with haematoxylin-eosin (Merck). Histological measurement and photographs were taken with Olympus CX31, Trinocular Biological Microscope (magnification 10x & 40 x).

2.4. Statistical Method

The statistical analysis was carried by one-way analysis of variance ANOVA (GRAPH PAD PRISM 5 computer program). Results are expressed as ±SEM. The data were statistically analyzed by ONE WAY ANOVA followed by Dunnett's multiple comparison test. Probability P values < 0.05 were considered as significant.

3.Results

3.1. Effect of AEC on ulcer severity score on aspirin ulcerated rats

It was observed from the results of the present analysis that ulcerative score of the rats belongs to group II rats has shown the intensity and severity of the ulcer induction by aspirin in the experimental animals. There was significant decrease in the ulcerative score observed in trial drug treated rats which reveals the anti-ulcer potential of the formulation. It was further observed that there was a significant increase in the percentage protection offered by the trial drug AEC at both the dose of 500 and 1000 mg/kg. As shown in table 1 and figure 1.

Table 1: Effect of AEC on Ulcer Index of Aspirin ulcerated rats

Group	Treatment and Dose	Aspirin Induced Ulceration		Percentage of Ulcer Protection
		Ulcer Severity Score	Ulcer Index	
I	Normal Saline	0.0 ± 0.0	-	100
II	Aspirin 200mg/kg	2.83 ± 0.16	11.47 ± 0.04	-
III	Aspirin + 500 mg/kg of AEC	1.16 ± 0.54*	7.39 ± 0.24*	35.49*
IV	Aspirin + 1000 mg/kg of AEC	0.5 ± 0.22*	5.18 ± 0.08*	54.81*

Values represent mean ± SEM of 6 experimental animals. * P< 0.05; ** P< 0.01; *** P < 0.001.

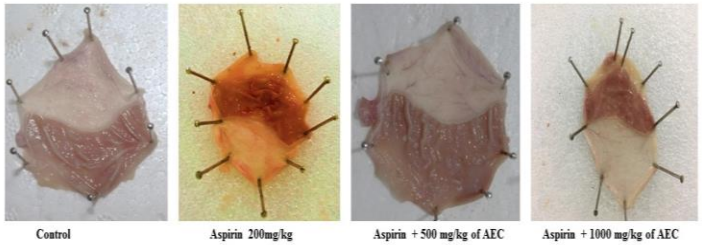

Figure 1: Effect of AEC on gross anatomy of rat stomach aspirin ulcerated rats

3.2. Effect of AEC on Histopatholgy of aspirin ulcerated rats under low and high power magnification

Histopathological analysis report has revealed regular histology of Inner circular muscle, gastric pit and muscularis mucosae were observed in sample belongs to group I rats. Derangement of Mucosal barrier with deeper perforations up to sub-mucosal layer were observed in aspirin alone treated rats. Marginal degeneration of gastric gland and pits were observed in sample belongs to group II rats. The continuity of mucosa was marginally improved normal with mild evidence of ulceration in sample belong to group III animals. Prominent mucosal wall with regular arrangement of connective tissue were observed in group IV samples. As shown in figure 2.

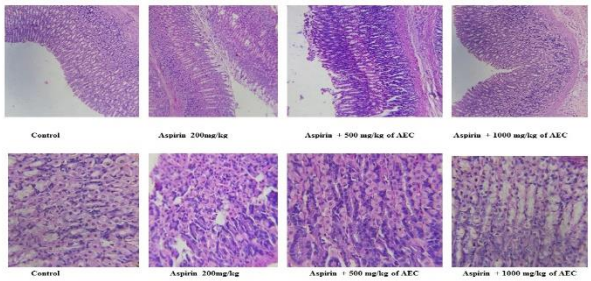

Figure 2: Histopathology of rat stomach belongs to control , aspirin ulcerated and treatment group rats under low and high power magnification

4.Discussion

Peptic ulcer disease (PUD) is a disease located in the gastric or duodenal part of the gastrointestinal tract that mainly involves the mucosa layer. The two main risk factors for PUD are Helicobactor pylori (H. pylori) infection and medication consumption, especially of nonsteroid anti-inflammatory drugs (NSAIDs) [12]. The prevalence of PUD ranges from 0.12 to 1.5% and increases with age [13]. The major symptom of uncomplicated PUD is upper abdominal dyspepsia such as bloating, early satiety, and nausea [14].

Annual incidence estimates of peptic ulcer hemorrhage and perforation were 19.4–57 and 3.8–14 per 100,000 individuals, respectively. The average 7-day recurrence of hemorrhage was 13.9% and the average long-term recurrence of perforation was 12.2% [15]. In the Indian pharmaceutical industry, antacids and antiulcer drugs share 6.2 billion rupees and occupy 4.3% of the market share [16].

The main mechanism of NSAID-associated damage of the gastroduodenal mucosa is the systemic inhibition of constitutively expressed cyclooxygenase-1 (COX-1), which is responsible for prostaglandin synthesis, and is associated with decreased mucosal blood flow, low mucus and bicarbonate secretion, and the inhibition of cell proliferation. NSAIDs inhibit the enzyme reversibly in a concentration-dependent manner. The co-administration of exogenous prostaglandins and cyclooxygenase-2 (COX-2)-selective NSAIDs use reduces mucosal damage and the risk of ulcers [17]. However, the different physicochemical properties of NSAIDs cause differences in their toxicity [18]. NSAIDs disrupt mucus phospholipids and lead to the uncoupling of mitochondrial oxidative phosphorylation, thus initiating mucosal damage. In the present investigation ulcerative score of the rats belongs to group II rats has shown the intensity and severity of the ulcer induction by aspirin in the experimental animals. There was significant decrease in the ulcerative score observed in trial drug treated rats which reveals the anti-ulcer potential of the formulation. It was further observed that there was a significant increase in the percentage protection offered by the trial drug AEC at both the dose of 500 and 1000 mg/kg.

Ulcers are an open sore of the skin or mucus membrane characterized by sloughing of inflamed dead tissue [19]. Ulcers are lesions on the surface of the skin or a mucous membrane characterized by a superficial loss of tissue. Ulcers are most common on the skin of the lower extremities and in the gastrointestinal tract, although they may be encountered at almost any site. There are many types of ulcer such as mouth ulcer, esophagus ulcer, peptic ulcer, and genital ulcer. Of these peptic ulcer is seen among many people. The peptic ulcers are erosion of lining of stomach or the duodenum [20]. The two most common types of peptic ulcer are called “gastric ulcer” and “duodenal ulcer.” The name refers to the site of ulceration.

In the present study regular histology of Inner circular muscle, gastric pit and muscularis mucosae were observed in sample belongs to group I rats. Derangement of Mucosal barrier with deeper perforations up to sub-mucosal layer were observed in aspirin alone treated rats. Marginal degeneration of gastric gland and pits were observed in sample belongs to group II rats. The continuity of mucosa was marginally improved normal with mild evidence of ulceration in sample belong to group III animals Prominent mucosal wall with regular arrangement of connective tissue were observed in group IV rats.

5.Conclusion

Gastric ulcer becomes a global issue due to its annual mortality and morbidity reported throughout the world especially in the developing countries like India. Need of alternate medicine is of paramount importance due to limitation and restrictions in using conventional anti-ulcer agents which offered threatening side effects. Only few of the herbal medicine have been scientifically validated for the claimed medicinal effects, hence slowing down the pace of drug discovery from such herbal source. Among the factors

responsible for this is the myth surrounding herbal medicine especially in developing nations as well as dosages administered. It was concluded from the outcome of the present study that formulations like Agasthiyar elathy chooranam may be utilized for primary health care because of better acceptability, better compatibility with the human body and no side effects on clinical usage.

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6. References

1. Lanas A, Chan FKL. Peptic ulcer disease. Lancet. 2017 Aug 05;390(10094):613-624.
2. Gisbert JP, Legido J, García-Sanz I, Pajares JM. Helicobacter pylori and perforated peptic ulcer prevalence of the infection and role of non-steroidal anti-inflammatory drugs. Dig Liver Dis. 2004 Feb;36(2):116-20.
3. Kavitt RT, Lipowska AM, Anyane-Yeboa A, Gralnek IM. Diagnosis and Treatment of Peptic Ulcer Disease. Am. J. Med. 2019 Apr;132(4):447-456.
4. Bandyopadhyay U, Biswas K, Chatterjee R, Bandyopadhyay D, Chattopadhyay I, Ganguly CK, et al. Gastroprotective effect of Neem (Azadiracta indica) bark extract possible involvement of H+K+ATPase inhibition and scavenging of hydroxyl radical. Life Sci. 2002;71:2845–65.
5. Rates SMK. Plants as source of drugs. Toxicon. 2001;39:603–613.
6. Ge Y, Cui JC, Zhou RL. [Clinical and experimental study on separately decocted and mingly decocted jianweishu granule] Zhongguo Zhongxiyi Jiehe Zazhi. 2002;22:420–422.
7. Wei BH. [Clinical and experimental study on the prescription of jianpi yipi] Zhongxiyi Jiehe Zazhi. 1989;9:537–59, 516.
8. Santin JR.Antiulcer effects of Achyrocline satureoides (Lam.) DC (Asteraceae) (Marcela), a folk medicine plant, in different experimental models", Journal of Ethnopharmacology.2010; 130:334-341.
9. Zhongzhi Wang. Protective Effects of Ginger against Aspirin-Induced Gastric Ulcers in Rats. Yonago Acta Med. 2011 Mar; 54(1): 11–19.
10. Shyamal K. Das. The Protective Role of Aegle Marmelos on Aspirin–Induced Gastro-Duodenal Ulceration in Albino Rat Model: A Possible Involvement of Antioxidants. Saudi J Gastroenterol. 2012 May-Jun; 18(3): 188–194
11. Suvarna, S.K., C.Layton and J.D. Bancroft.Bancroft's theory and practice of histological techniques. 7th edn, Churchill Livingstone, London.2013.
12. Malfertheiner P. The intriguing relationship of helicobacter pylori infection and acid secretion in peptic ulcer disease and gastric cancer. Dig. Dis. 2011;29:459–464.
13. Sung J.J., Kuipers E.J., El-Serag H.B. Systematic review: The global incidence and prevalence of peptic ulcer disease. Aliment. Pharmacol. Ther. 2009;29:938–946.
14. Suerbaum S., Michetti P. Helicobacter pylori infection. N. Engl. J. Med. 2002;347:1175–1186.
15. Lau JY, Sung J, Hill C, Henderson C, Howden CW, Metz DC. Systematic review of the epidemiology of complicated peptic ulcer disease: incidence, recurrence, risk factors and mortality. Digestion. 2011;84(2):102–113.
16. Hoogerwerf WA, Pasricha PJ. Agents Used for Control of Gastric Acidity and Treatment of Peptic Ulcers and Gastro Esophageal Reflux Diseaseedition. 10th edition. New York, NY, USA: McGraw-Hill; 2001:1005–19.
17. Bhala N., Emberson J., Merhi A., Abramson S., Arber N., Baron J.A., Bombardier C., Cannon C., Farkouh M.E., FitzGerald G.A., et al. Vascular and upper gastrointestinal effects of non-steroidal anti-inflammatory drugs: Meta-analyses of individual participant data from randomised trials. Lancet. 2013;382:769–779.
18. Bjarnason I., Scarpignato C., Takeuchi K., Rainsford K.D. Determinants of the short-term gastric damage caused by NSAIDs in man. Aliment. Pharmacol. Ther. 2007; 26:95–106.
19. Chan FKL, Graham DY. Review article: prevention of non-steroidal anti-inflammatory drug gastrointestinal complications—review and recommendations based on risk assessment.

Alimentary Pharmacology and Therapeutics. 2004;19(10):1051–1061.

20. Debjit B, Chiranjib C, Tripathi KK, Pankaj, Sampath Kumar KP. Recent trends of treatment and medication peptic ulcerative disorder. International Journal of PharmTech Research. 2010;2(1):970–980.

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