Comparison Of Efficacy Of Ocimum Sanctum Against Gastric And Duodenal Ulcers In Animals

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Citation

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Abstract

This study was conducted with the aim of comparing the efficacy of ocimum sanctum against gastric and duodenal ulcers. The hydralcoholic extract of the plant exhibited significant ulcer protective effect against gastric ulcers in pyloric ligated rats as well as against duodenal ulcers in histamine treated guinea pigs. In both these models of peptic ulcer, significant ulcer protective effects were observed with 100 mg/kg and 200 mg/kg of ocimum sanctum, which were comparable. These effects were also comparable with ranitidine which was used as the standard drug for comparison in both the models. The antiulcer activity of ocimum sanctum could be due to its antisecretory, anticholinergic or antihistaminergic properties. In view of this therapeutic potential, more studies are required to establish ocimum sanctum as a standard drug for peptic ulcer.

INTRODUCTION

An ulcer is a disruption of the mucosal integrity of the stomach and/or duodenum leading to a local defect or excavation due to active inflammation. Ulcers occur within the stomach and/or duodenum and constitute peptic ulcer disease. They are usually chronic in nature. Peptic ulcer probably results due to an imbalance between the aggressive factors like acid, pepsin and Helicobacter pylori (H. pylori) and the defensive factors like gastric mucus and bicarbonate secretion, prostaglandins and innate resistance of the mucosal cells. A variety of psychosomatic, humoral and vascular derangements have also been implicated as contributors to ulcer formation. Non steroidal anti-inflammatory drugs (NSAIDs) are also an important cause of peptic ulcer.[1] The incidence of duodenal ulcers is about 3 times more than that of gastric ulcers. Peptic ulcers occur at all ages but the onset is usually at 20-40 years.[2] They are usually diagnosed in middle aged to older individuals. The male to female ratio for duodenal ulcers is about 3:1 and for gastric ulcers about 1.5 to 2:1.[3] Currently, with the increasing focus on H.pylori, a number of 2-3 drug regimens of 1-2 weeks duration are available but the most effective regimen is difficult to proclaim. Moreover, these may be associated with side effects, poor patient compliance and drug resistance.

Thus, in an effort to overcome the drawbacks observed with the current medications, we chose the plant ocimum sanctum for our study, which has been used for various medicinal purposes like fever, cough, vomiting[4] , mosquito bites and malarial fever[5] fungal infections, earache, skin diseases, gastric and hepatic disorders, snake bite, scorpion sting and genitourinary disorders[6]. It has also been reported to possess antiulcer activity,[7,8,9,10] but the comparative efficacy against gastric and duodenal ulcers has not been reported. Therefore, we decided to compare the efficacy of this drug against gastric and duodenal ulcers in this study.

MATERIALS AND METHODS

ANIMALS

Albino rats: Animals of either sex, weighing between 120-180 gm were used to study the effect on pyloric ligation induced gastric ulceration.

Guinea pigs: Animals of either sex, weighing between 400-600 gm were used for histamine induced duodenal ulcers.

All the animals were caged under standard conditions and were allowed to acclimatise to their surroundings for one week before subjecting them to experimentation. Prior to experimentation permission was taken from institutional ethical committee.

DRUGS AND CHEMICALS

Test drug: Fresh leaves of the plant ocimum sanctum were collected during the month of April from a local area in

Sevagram and were shade dried and powdered. A hydroalcoholic (70% V/V) extract of this powdered form of ocimum sanctum was prepared. This extract was again shade dried and was used to prepare an aqueous solution in desired concentration just before use every time. The same extract was used for all the experiments.

Ranitidine (Ranbaxy, India): It was diluted in distilled water to get the desired concentration. Histamine acid phosphate (BDH, England): It was dissolved in distilled water in desired concentration just before use.

METHOD FOR PYLORIC LIGATION INDUCED GASTRIC ULCERS IN RATS

The animals were kept fasting for 24 hours but were allowed free access to water before experimentation.

They were randomly divided into five groups of six animals each. Group I received distilled water (10ml/kg) orally and served as control whereas group II, III and IV were administered the test drug (ocimum sanctum) in doses of 50 mg/kg, 100 mg/kg and 200 mg/kg respectively. The animals in group V were administered ranitidine (10 mg/kg) orally which served as standard for comparison. After 30 minutes of drug treatment, surgical intervention was done under light ether anaesthesia. The abdomen was opened and pyloric end was ligated with a thread while taking care not to damage its blood supply. Animals were deprived of both food and water during the post operative period and were sacrificed after five hours with an overdosage of ether anaesthesia. The stomach was cut open to examine the ulcers, ulcer index was calculated and the percent animals having ulcers was noted. Histopathological examination of gastric ulcers was also done.

METHOD FOR HISTAMINE INDUCED DUODENAL ULCERS IN GUINEA PIGS

The animals were kept fasting for 24 hours but were allowed free access to water. After 24 hours fast, drug treatment was given and after 30 minutes of drug treatment, the animals were given eight intramuscular injections of histamine acid phosphate in a dose of 0.25 ml/kg of 1 mg/ml solution intramuscularly in the thigh. The injections were spaced at 30 minute intervals. The animals were sacrificed 30 minutes after the eighth injection. The abdomen was opened and duodenum removed. It was cut open to examine the ulcers and their area. The percent incidence of animals showing ulcers was noted. The duodenal specimens were also analysed histopathologically for ulcers.

STATISTICAL ANALYSIS

Data were analysed by student's 't' test and expressed as mean + SEM. P values less than 0.05 were considered significant.

OBSERVATIONS AND RESULTS

Effect on pyloric ligation induced gastric ulcers: (Table-1, Fig-1 A, B, C & D)

In the distilled water (10 mg/kg, orally) treated control group pyloric ligation produced ulcers in 100% animals.

Oral administration of ocimum sanctum extract in the dose of 50mg/kg did not exhibit protection against ulcers and there was no significant decrease in the number of ulcers and the ulcer index. In the dose of 100mg/kg, it showed protection from ulcers in 50% animals and also decreased the number of ulcers and the ulcer index which was statistically significant ($p<0.05$). Ocimum sanctum extract (200 mg/kg, orally) showed protection from ulcers in 66.67% animals and also reduced the number of ulcers and the ulcer index significantly ($P<0.01$). Ranitidine (10 mg/kg, orally), as a standard drug for comparison protected 83.34% animals against ulcers. It also decreased the number of ulcers and the ulcer index significantly ($p<0.001$) in comparison to the control group.

Figure 1

Table 1: Effect of ocimum sanctum extract (OSE) on pyloric ligation induced gastric ulcers in albino rats.

Group (n=6)	Drug	Dose mg.ml'/kg (P.O)	Percent animals showing ulcers	Number of ulcers/stomach (Mean ± SEM)	Ulcer Index (Mean ± SEM)
I	D.W	10*	100	2.33 ± 0.33	1.66 ± 0.42
II	OSE	50	100	2.16 ± 0.30	1.33 ± 0.21
III	OSE	100	50	0.83 ± 0.40*	0.50 ± 0.22*
IV	OSE	200	33.33	0.66 ± 0.49**	0.33 ± 0.21**
V	RAN	10	16.66	0.16 ± 0.16***	0.16 ± 0.16***

n = Number of animals (6 in each group),
P.O = Per orally
SEM = Standard error of mean
D.W. = Distilled water
RAN = Ranitidine

*p < 0.05
** p < 0.01
***p < 0.001

Figure 2

Fig 1 A & B: Effect of ocimum sanctum extract (OSE) on pyloric ligation induced gastric ulcers in albino rats.

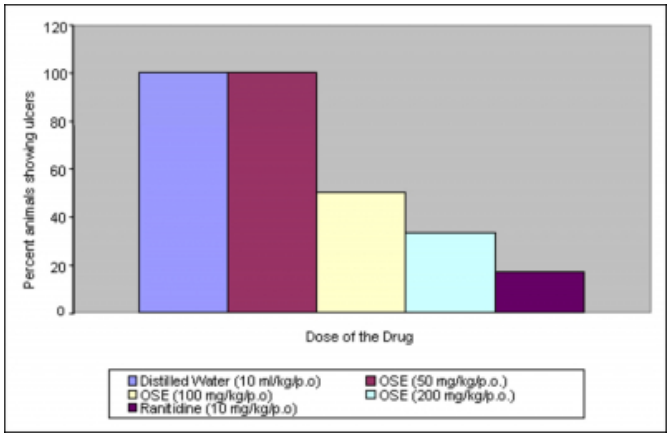


Figure 3

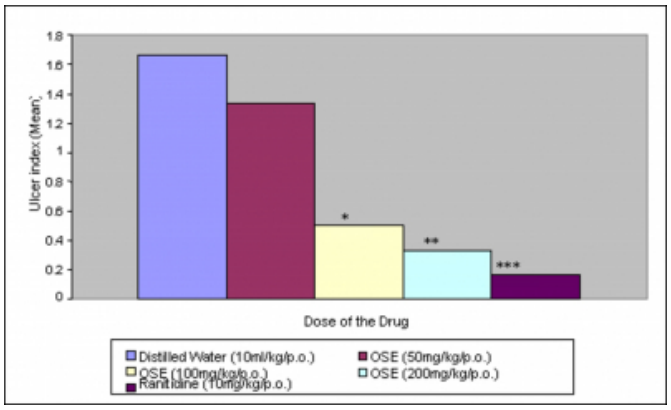


Figure 4

Fig 1 C: Histopathological view of normal rat gastric mucosa

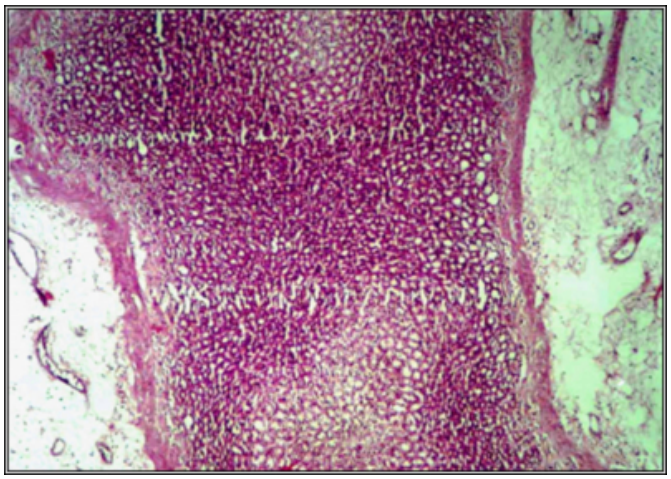
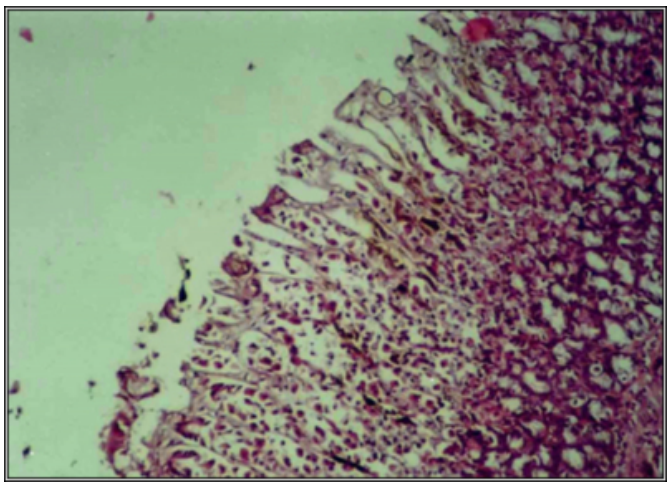


Figure 5

Fig 1 D: Histopathological view showing ulceration of rat gastric mucosa



Effect on histamine induced duodenal ulcers in guinea pigs (Table 2, Fig 2 A, B, C & D)

Histamine acid phosphate produced linear ulcers in 100% animals of the control group. There was no significant protection against ulcers in the dose of 50 mg/kg, orally, of ocimum sanctum extract. Ocimum sanctum extract (100mg/kg, orally) protected 33.34% animals from ulceration and decreased the number and area of ulcers significantly ($p<0.05$). The dose of 200 mg/kg, orally, of ocimum sanctum extract exhibited ulcer protection in 50% animals and also significantly ($p<0.01$) reduced the number and area of histamine induced duodenal ulcers. Ranitidine, protected 83.34% animals against ulcers. It also decreased the number of ulcers and the ulcer index significantly ($p<0.001$).

Figure 6

Table 2: Effect of ocimum sanctum extract (OSE) on histamine induced duodenal ulcers in guinea pigs

Group (n=6)	Drug	Dose mg,ml/kg (P.O)	Percent animals showing ulcers	Number of ulcers/duodenum (Mean ± SEM)	Area of linear lesions (mm^2) (Mean ± SEM)
I	D.W	10ml	100	4.83 ± 0.21	13.50 ± 0.85
II	OSE	50	100	4.16 ± 0.30	12.66 ± 1.53
III	OSE	100	66.66	2.50 ± 0.80*	6.66 ± 2.21*
IV	OSE	200	50	1.83 ± 0.79**	4.50 ± 2.03**
V	RAN	10	16.66	0.83 ± 0.54***	2.33 ± 1.48***

n = Number of animals (6 in each group)
P.O = Per orally
SEM = Standard error of mean
I.U. = International units

*p < 0.05
** p < 0.01
***p < 0.001

Figure 7

Fig 2 A & B: Effect of ocimum sanctum extract (OSE) on histamine induced duodenal ulcers in guinea pigs.

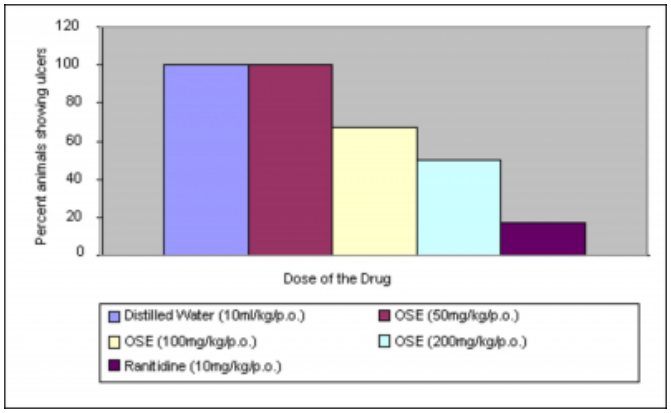


Figure 8

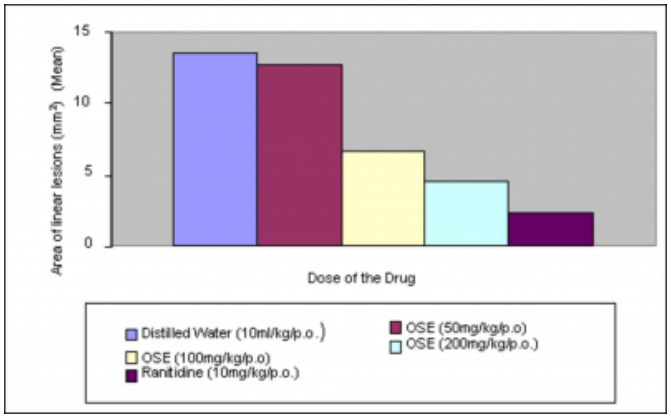


Figure 9

Fig 2 C: Histopathological view of normal guinea pig duodenal mucosa

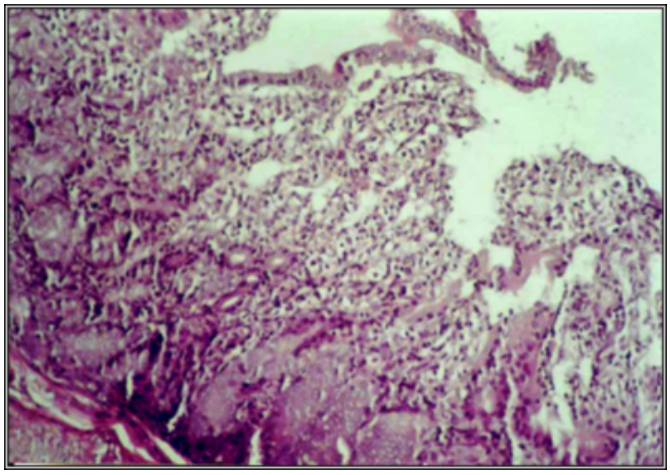
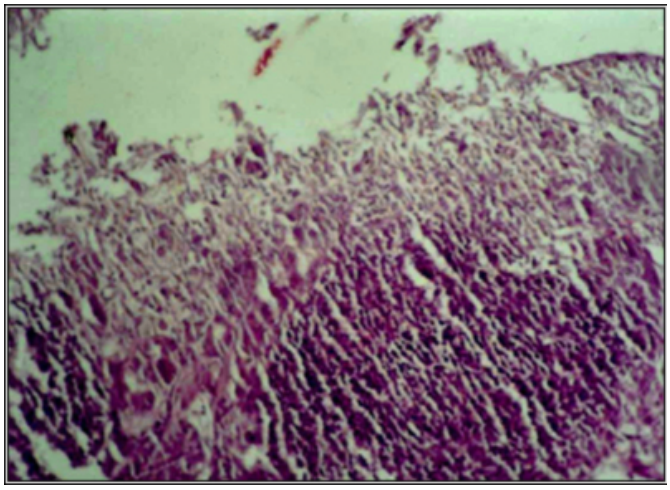


Figure 10

Fig 2 D: Histopathological view showing ulceration of guinea pig duodenal mucosa



DISCUSSION

Peptic ulcers remain a prevalent condition affecting up to 10% of the population and is responsible for considerable morbidity and loss of time from work.[14]

Although a number of effective drugs are available currently for the treatment of peptic ulcer, they are not without disadvantages. Most of the drugs are associated with side effects which leads to noncompliance and therapy failure. This may further lead to recurrence of disease. Antimicrobials in combination with H_2 blockers and proton pump inhibitors are used in many regimens which makes them complex and expensive.[15] This necessitates the constant search for newer drugs which lack the said disadvantages

and provide complete cure. People all over the world are looking to various alternative systems of medicine especially herbal medicines which are non-toxic, claimed to be safe, cost effective and also equally effective in comparison to allopathic drugs.

In the present experimental work, the antiulcer activity of ocimum sanctum has been evaluated against pyloric ligation induced gastric ulcers in rats and compared with its activity against histamine induced duodenal ulcers in guinea pigs. Significant ulcer protective effect was evident from the decrease in the percent incidence, number and severity of the ulcers in the doses of 100 mg/kg and 200 mg/kg of ocimum sanctum leaf extract. The effects were observed in both the models of peptic ulcer and were comparable. Since increased secretion of gastric acid which is an aggressive factor may play a role in the causation of peptic ulcer,[16] our findings suggest an antisecretory activity of ocimum sanctum which may be a mechanism for its antiulcer action in pyloric ligated rats. The extract of ocimum sanctum showed protection against histamine induced duodenal ulcers in guinea pigs which may be due to inhibition of histamine induced acid secretion, since histamine is the chief regulator of gastric acid secretion. Ranitidine also showed protection against ulcers in pyloric ligated rats as well as histamine induced duodenal ulcers in guinea pigs by decreasing the percent incidence, number and severity of ulcers. This may be explained by its H_2 receptor antagonistic activity. Ocimum sanctum is also known to inhibit peristalsis in some animal models[17]. The inhibition of peristalsis by ocimum sanctum in study may be due to anticholinergic action which may be responsible for its antisecretory activity and hence ulcer protection. Since, accelerated gastric emptying of liquids has been noticed in some patients of duodenal ulcer[1], ocimum sanctum by its inhibitory action on peristalsis could probably be useful in these patients. Thus, the inhibition of peristaltic activity by ocimum sanctum may be another mechanism for its antiulcer action where accelerated gastric emptying is the cause of peptic ulcer.

To sum, ocimum sanctum was found to be equally effective against both gastric and duodenal ulcers, and its activity was comparable to ranitidine. This suggests that ocimum sanctum could be a useful drug for the treatment of peptic ulcer. Further studies including clinical trials would be required to completely assess the therapeutic potential of this medicinal plant for future use.

References

1. Valle JD. Peptic ulcer disease and related disorders. In Braunwald E, Fauci AS, Kasper DL, Hauser SL, Longo DL and Jameson JL, editors, Harrison's principles of internal medicine 15th ed (Vol 2). International : Mc Graw Hill; 2001 : p 1649-1664.
2. Chandrasoma P and Taylor CR. Concise Pathology. 2nd ed. International : Appleton –Lange; 1995.
3. Crawford JM and Kumar V. The oral cavity and the gastro- intestinal tract. In: Kumar V, Cotran RS and Robbins SL, editors, Robbins Basic Pathology. 7th ed. New Delhi: Saunders; 2003.p 559.
4. Jain SK and Tarafder CR. Medicinal plant-lore of the Santals (A revival of P.O Bodding's work). Econ Bot 1970 ; 24 : 241.
5. Chopra RN, Roy DN, Ghosh SM. Insecticidal and larvicidal action of the essential oils of ocimum basilicum and ocimum sanctum. J Malaria Inst India 1941 ; 4 : 109.
6. Satyavati GV, Gupta AK and Tandon N. Ocimum sanctum Linn (Tulsi). In: Medicinal Plants of India. Published by ICMR, New Delhi. 1987 ; 27 : 574-575.
7. Jalil A. Clnical trial of Ocimum sanctum (Tulsi) in peptic ulcer and hyperacidity patients. J Res Ind Med 1970 ; 4 (2) : 238-239.
8. Bhargava KP and Singh N. Antistress activity of Ocimum sanctum Linn. Ind J Med Res 1981; 73 : 443-451.
9. Mandal S, Das DN, De K, Ray K, Roy G, Chaudhuri SB, Sahana CC and Choudhuri MK. Ocimum sanctum Linn- a study on gastric ulceration and gastric secretion in rats. Ind J. Physiol Pharmacol 1993 ; 37 (1) : 91-92.
10. Singh S and Majumdar DK. Evaluation of gastric antiulcer activity of fixed oil of ocimum sanctum (Holy basil). J Ethnopharmacol 1999 ; 65 : 13-19
11. Shay M, Komarov SA, Fels D, Meranze D, Gruenstein H and Siplet H. A simple method for the uniform production of gastric ulceration in rats. Gastroenterology 1945 ; 5 : 43-61.
12. Robert A, Nezamis JE and Philips JP. Effect of prostaglandin E1, on gastric secretion and ulcer formation in rats. Gastroenterol 1968 ; 55 : 481
13. Eagleton GB and Watt J. Acute duodenal ulceration in the guinea pig induced by repeated intramuscular doses of aqueous histamine. J Pathol Bacteriol 1967 ; 93 : 694.
14. Howden CW and Hunt RH. Peptic ulcer disease. In: Lewis JH, editor, A pharmacological Approach to Gastrointestinal disorders. Baltimore: Williams and Wilkins; 1994. p 3-1
15. Friedman LS and Peterson WL. In: Fauci AS, Braunwald E, Isselbacher KJ, Wilson JD, Martin JB, Kasper DL, Hauser SL, Longo DL, editors, Harrison's Principles of Internal Medicine. 14th Ed (Vol.2). International: McGraw Hill Co ; 1998. p 1602-1603.
16. Hoogerwerf WA and Pasricha PJ. Agents used for control of gastric acidity and treatment of peptic ulcers and gastroesophageal reflux disease. In: Hardman JG, Limbird LE and Gilman GA, editors, Goodman and Gilman's The Pharmacological Basis of Therapeutics. 10th ed. International : Mc Graw Hill ; 2001. p 1005-1019.
17. Kath RK and Gupta RK. Effects of ocimum sanctum leaf extract (OSE) on peristalsis in guinea pig ileum and frog stomach. J MGIMS Sept 2005, Vol. 10, (ii), 29-33

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