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COMPARATIVE STUDIES OF ANTIGASTRIC AND ANTIULCER ACTIVITIES AMONG THE THREE HERBAL PLANTS WITH RABEPRAZOLE IN SHAY RATS

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ABSTRACT

A peptic ulcer is an erosion in a segment of the gastro intestinal mucosa, typically in the stomach (Gastric ulcer) or first few centi meters of duodenum (Duodenal ulcer) that penetrates through the muscularis mucosae. Contrary to popular belief, ulcer is not caused by spicy food but instead is most commonly due to either an infection or long-term use of medications. Standard treatment is a combination of drugs including antibiotics and a proton pump inhibitor. Literature suggests that number of synthetic drugs are used in the management of peptic ulcers but elicit several adverse effects. Therefore, Indian herbal plants stand out as being exceptional for its ethnic, ethnobotanical and ethno-pharmaceutical use. In this review attempts have been made to know about some plants which may be used in treatment or prevention of peptic ulcers and a comparative study among each other with the standard drug Rabeprazole, such plants like Abutilon indicum, Elephantopus scaber and Millettia Peguensis proved active in antiulcer therapy. Different extracts of Abutilon indicum, Elephantopus scaber and Millettia peguensis plants were tested for its antigastric and antiulcer activity in shay rat model, out of which the alcoholic extract of the plants afforded more effective antiulcer activity and shows complete inhibition of ulceration which are comparable to the antiulcer activity shown by 2mg/kg of Rabeprazole in shay rat.

KEYWORDS: Antiulcer activity, Herbal plants, Shay.

INTRODUCTION

Peptic ulcers are sores in the lining of the stomach and the duodenum (The first part of the small intestine). Peptic ulcer occurs due to an imbalance between the aggressive (Acid, pepsin and Helicobacter pylori) and the defensive (Gastric mucus and bicarbonate secretion, prostaglandins, innate resistance of the mucosal cells) factors. The cause of most stomach and duodenal ulcers is infection with a type of bacteria called Helicobacter pylori. Other irritants include non-steroidal anti-inflammatory drugs such as aspirin and ibuprofen, alcohol, coffee with or without caffeine, and smoking. A rare cause of peptic ulcer is a condition called Zollinger-Ellison syndrome, in which stomach acid is produced in higher-than-normal amounts. The main risk factors for both gastric and duodenal ulcers are H. pylori infection and NSAID use. However, only a small proportion of people affected with H. pylori or using NSAIDs develop peptic ulcer disease, meaning that individual susceptibility is important at the beginning of mucosal damage. Functional polymorphisms in different cytokine genes are associated with peptic ulcers. For example, polymorphisms of interleukin 1 beta (IL1B) affect mucosal interleukin 1_ production, causing H. pylori-associated gastroduodenal diseases. A peptic ulcer, also known as peptic ulcer disease is an erosion in the wall of the stomach, Duodenum, or oesophagus. As many as 70-90% of such ulcers are associated with Helicobacter Pylori, a spiral-shaped bacterium that lives in the acidic environment of the stomach Ulcers can also be caused or worsened by drugs such as aspirin, ibuprofen, and other NSAIDs. These herbal drugs have been traditionally used for the treatment of various disorders such as liver diseases, fever, asthma, anaemia, chronic dysentery, ulcer and inflammation. Those drugs which are having antioxidant properties can also cure various kinds of ailments. Hence, the attempt was taken the alcoholic extracts of the above plants shows potential antiulcer and antioxidant activities hence the attempt was taken for a comparative study among these three herbal plants with the standard drug Rabeprazole.

MATERIAL AND METHODS

Collection plant materials

The medicinal plants Abutilon indicum, Elephantopus scaber and Millettia Peguensis have been collected from eastern region of India. The plants were identified by Taxonomist and a voucher specimen representing (Herbarium No.2022 A, 3265 A and 5773 C) was submitted at dept. of Botany Utkal University, Odisha.

Preliminary phytochemical screening

Preliminary phytochemical screening of the extract was performed for the presence of alkaloids, flavonoids, glycosides, phenols, saponins, sterols, carbohydrates, and amino acids.

Experimental animals

Swiss albino mice weighing 25-30gm and Wistar rats weighing 180-200 gm of either sex was use in the study. Animals were procured from Laboratory Animal House of U.D.P.S Utkal University, Odisha. All animal experiments strictly complied with the approval of the institutional animal ethical committee. The animals were kept in polyacrylic cages and maintained under standard housing conditions of temperature (24-27°C) and humidity (60-65%) with 12:12 light: dark cycles. They were acclimatized for seven days. Food was provided in the form of dry pellets and water ad libitum.

Acute toxicity test

Acute toxicity studies were performed according to OECD (Organization for Economic Co-operation and Development) guidelines 425. The required dose is administered to animals one at a time by using oral gavage. The animal (Rats) fasted overnight but the water was not withdrawn. The fasted body weight of the rat is determined and Dose is calculated on a body weight basis. After administration of these plant extracts the food is withheld for a further 3-4h. For the limit test, a 4000 mg/kg dose was administered to one animal and then the animal was observed for mortality for a period of 48hrs. The tested rat survived therefore Test was continued by taking 4 more animals. All mice were free of any toxicity as per acceptable range given by the OECD guidelines up to the dose of 4000 mg/kg. From these data and pilot study reports; three different doses were selected for further study.

Antiulcer activity

Pylorus ligation-induced ulcer

Different extracts of the plants Abutilon indicum, Elephantopus scaber and Millettia peguensis were administered for 7 days. On day 7, after the last dose of the plant extract, the rats were kept for 24 hours fasting and care were taken to avoid coprophagy. Under light ether anaesthesia, the abdomen was opened and the pylorus was causing any damage to its blood vessels. The stomach was replaced carefully and the abdominal wall was closed with interrupted sutures. The animals were deprived of water during the postoperative period. Four hours after ligation, stomachs were dissected and contents were collected into clean tubes. The gastric juice was centrifuged at 1000rpm and gastric volume was measured. Free and

total acidities of the supernatant were determined by titration with 0.1 NaOH and expressed as mEq/L /100 Gms. The stomach was cut open along the greater curvature and pinned onto a soft board for evaluating the gastric ulcers and to calculate the ulcer index.

Scoring of the ulcer

Table 1: Scoring observation of Ulcer.

Score	Observation
0	Normal, no ulcer
0.5	Red colouration
1	Spot ulcer
1.5	Haemorrhagic streak
2	Deep ulcer
3	Perforation

The mean ulcer score for each animal will be expressed as the ulcer index. The percentage of ulcer protection was determined as follows

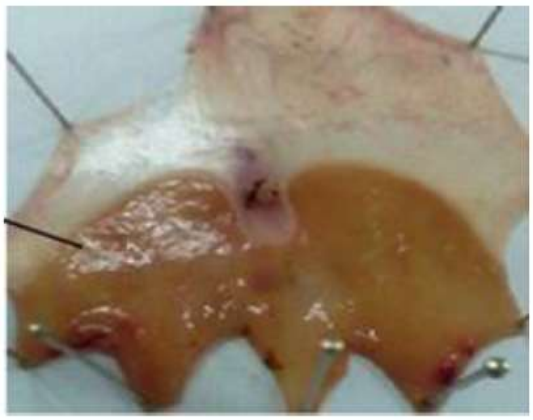
$$\% \text{ protection} = \frac{(\text{control mean ulcer index}) - (\text{test mean ulcer index})}{* \text{ control mean ulcer index}} * 100$$

Statically analysis

The data were expressed as mean +SEM. Results were analysed statically by Way ANOVA followed by Dunnet's TEST using prime of Biostatistics, Version 9. The difference was considered significant if $p< 0.05$. The control group (Group I) is compared with standard and extract doses, * represents significance.

Control

Rabeprazole 2mg/Kg



EEAI 400Mg/kg

EEAI 800Mg/kg

MEES 2OOmg/kg

MEES 4OOmg/kg

MEMP 400mg/kg

MEMP 800mg/kg

Fig. 1: Antiulcer activity of Alcoholic extract of Abutilon indicum, Elephantopus scaber and Millettia peguensis and their comparisons with control and Rabeprazole in shy rats.

Table 2: Effect of Alcoholic extract of Abutilon indicum, Elephantopus scaber and Mellettia peguensis on volume gastric juice, free acidity, Total acidity, Peptic activity, Ulcer index and % reduction in shay rats and its comparison with Rabeprazole.

Group	Treatment	VGJ ml/100gm	FA mg/100gm	TA mg/100gm	PA umol of Tyrosine/ 100gm	Ulcer Index (UI)+
I	Vehicle Control (1% CMC)	5.22±0. 01014(0)	2.7±0. 0601[a](0)	12.4±0. 0557[a](0)	2277.85±7. 72[c](0)	5 (0)
II	EEAI 400mg/kg	4.16±0.056 [c] (15.61)	0.96±0.004[a] (64.17)	1.78±0.036 [b] (85.73)	1409.4±1. 277 [b](36.36)	1+ (80)
III	EEAI 800mg/kg	3.31±0.109 [b] 32.86	1.01±0,054[c] 62.31	1.48±0.043 [a] 88.14	1338.83±0. 760 [a]39.54	0 (100)
IV	MEES 200mg/kg	3.7±0.036[a] (29.11)	1.0±0.025[b] (62.96)	1.71±0.05[b] (86.29)	1393.08±0. 896[c](38.84)	1.25 (75)
V	MEES 400mg/kg	3.65±0.076[a] (30.07)	0.92±0.03[a] (66.66)	1.18±0.4[b] (90.32)	1235.98±0. 620[c](45.73)	0 (100)
VI	MEMP 400mg/kg	4.15±0.042[a] (32.94)	0.88±0.06[b] (67.4)	1.8±0.057[b] (85.48)	1406.65±1. 148[c](38.24)	1.5 (70)
VII	MEMP 800mg/kg	3.37±0.042[a] (35.44)	1.0±0.062[a] (72.96)	1.48±0.047[b] (88.06)	1336.9±1. 473[c](41.3)	0.5 (90)
VIII	Rabeprazole 2mg/kg	1.7±0.036[a] (67.43)	1.0±0.051[a] (62.96)	1.35±0.061[a] (89.11)	1378.55±0. 96[c](39.47)	0 (100)

VGJ-Volume of Gastric Juice

FA-Free Acidity

TA-Total Acidity

PA-Peptic Activity

UI-Ulcer Index

Results are ex pressed means+-SEM of six readings, Significance evaluated by one-way analysis of variances (ANOVA) followed by Dennet's test verses control group.

[a]P<0.005, (n=6),[b]P<0.005,(n=6),[c]P<0.05,(n=6)

Value in () represents percentage in reduction.

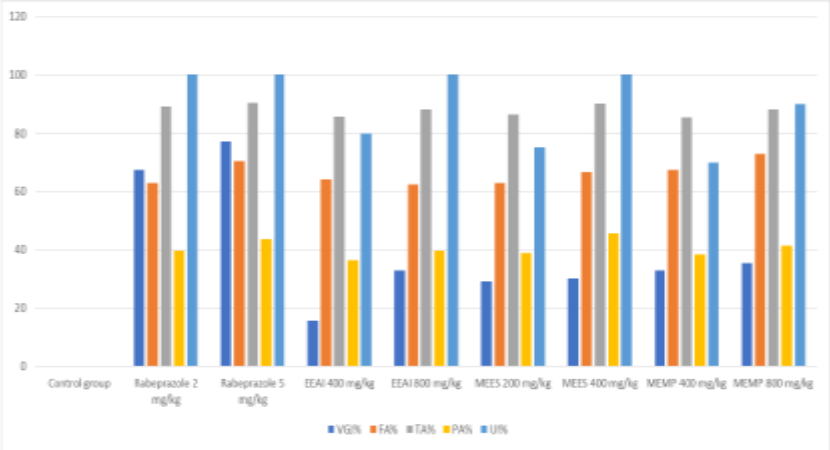


Fig. 2: Graph showing effect of Alcoholic extracts of Abutilon indicum, Elephantopus scaber and Millettia peguensis comparison with Rabeprazole on Pyloric ligation ulcer model in rat % reduction of VGJ, TA, FA, PA & UI.

EEAI-Ethanolic extract of *Abutilon indicum*

MEES-Methanolic extract of *Elephantopus scaber*

MEMP-Methanolic extract of *Abutilon indicum*

RESULTS

It was found that the alcoholic extract of the plants shows more effective antiulcer activity than other extracts so we can compare alcoholic plant extract with the standard drug Rabeprazole. Following results are found during the experimental study.

Rabeprazole 2mg/kg, 5mg/kg inhibited volume of gastric juice (VGJ) 67.43% and 77.01% respectively. Free acidity (FA) 62.96%, and 70.37% respectively Total Acidity (TA) 89.11%, 90.56% respectively. Peptic Activity (PA) 39.47% and 43.79% respectively. And ulcer index (UI) 100% and 100% respectively, Similarly, EEAI 400mg/kg 800mg/kg inhibited volume of gastric juice (VGJ) 15.61% and 32.86% respectively. Free acidity 64.17% and 62.31% respectively. Total Acidity 85.73%, 88.14% respectively. Peptic Acidity 36.36% and 39.54% respectively and ulcer index 80% and 100% respectively.

Similarly, MEES 200mg/kg reduced VGJ, FA, TA, PA and UI by 29.11%, 62.96%, 86.29%, 38.84% and 100% respectively whereas MEES 400mg/kg reduced VGJ, FA, TA, PA and UI by 30.07%, 66.66%, 90.32%, 45.73% and 100% respectively.

Similarly, MEMP 400mg/kg 800mg/kg inhibited volume of gastric juice (VGJ) 32.94% and 35.44% respectively. Free acidity 67.4% and 72.96% respectively. Total Acidity 85.48%, 88.66% respectively. Peptic Acidity 38.24% and 41.3% respectively and ulcer index 70% and 90% respectively.

DISCUSSION

In this study, we evaluated the phytochemistry, the acute toxicity and the anti-ulcer properties of three herbal plants, Abutilon indicum, Elephantopus scaber and Millettia peguensis. The acute toxicity test result showed that all the rats in each of the plants' groups survived, indicating that LD_{50} is greater than 4000 mg/kg (OECD 2001), and that the extracts may be relatively safe. In the phytochemical studies, these plants were shown to possess among others, tannins, flavonoids and saponins which are bioactive metabolites that have been documented to possess antiulcer activities. The evaluation and comparison of the antiulcerogenic properties of extracts of Abutilon indicum, Elephantopus scaber and Millettia peguensis which was done using the Pylorus ligation induced gastric lesion showed that the extracts possess varying degrees of antiulcer properties.

Among all the extract groups the alcoholic extract of Abutilon indicum, Elephantopus scaber and Millettia peguensis were found to be effective at varying degrees in decreasing the mean ulcer indices.

In this study we found Rabeprazole 2mg/kg significantly reduced gastric juice, free acidity, Total acidity, Peptic activity, Ulcer Index as standrd drug consider 100% inhibition of ulcer and all these three herbal plant extracts were compare with the standard drug, Among these three herbal drugs the ethanolic extract of Abutilon indicum 800mg/kg and methanolic extract of Elephantopus scaber 400mg/kg shows significant ulcerogenic activity (100% inhibition of UI) where as methanolic extract of Millettia peguensis 800mg/kg shows moderate ulcerogenic activity (90% inhibition of UI).

CONCLUSION

In conclusion, the oral administration of the plant extracts Abutilon indicum, Elephantopus scaber and Millettia peguensis displayed significant antiulcerogenic activity without much apparent toxicological effects.

Among these three herbal drug Abutilon indicum and Elephantopus scaber shows significant ulcerogenic activity as compare to standard (Rabeprazole) whereas Millettia peguensis shows moderate ulcerogenic activity as compare to standard.

Abutilon indicum and Elephantopus scaber both shows the significant ulcerogenic activity at dose of 800mg/kg and 400mg/kg respectively so in these studies we found that antiulcer properties of alcoholic extract of Elephantopus scaber was better than Abutilon indicum than Millettia peguensis.

The extracts used in combination may appear to be more effective than used singly or not, further studies however are needed to elucidate the exact mechanism(s) of action involved in singly or the additive effect of the combined extracts (polyherb).

These findings, therefore validates their use in herbal medicine in coastal region of India for ulcer therapy.

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