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Research Article

Experimental evaluation of prophylactic and curative effect of a herbal drug *Hemidesmus indicus* R.Br. in drug induced ulcers in wistar albino rats

Shishira Bharadwaj[1]*, Shraddha Nayak[2]

[1]Department of Hospital Medicine, Cleveland Clinic, USA.
[2]BMKankanawady Ayurved Mahavidyalaya, Belgaum, India

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***Correspondence:**
Dr. Shraddha Nayak,
E-mail: shradhaayu1@rediffmail.com

ABSTRACT

Peptic Ulcers are the most common condition experienced by most of the people due to urbanized lifestyle. *Hemidesmus indicus* R.Br. is a herbal drug mentioned for its treatment in the ancient Indian traditional medicine**.** To compare the Prophylactic and Curative effects of aqueous and Alcoholic extracts of *Hemidesmus indicus in Drug induced ulcers.* Aqueous and Alcoholic extracts of the drug were studied for their ulcer healing activity in Wistar Albino rats. Ninety Wistar albino rats were divided into nine groups with one control, four prophylactic and four curative groups. Ulcers were induced with Indomethacin in a dose of 20 mg/kg body weight twice in a gap of 15 hours. Aqueous extract was given in a dose of 500 mg/kg body weight and alcohol in a dose of 100 mg/kg body weight. It was found that both have potential ulcer healing activity with alcoholic extract marginally better than aqueous extract. It can thus be concluded that *Hemidesmus indicus* R. Br is a effective drug in peptic ulcers

Keywords: *Hemidesmus indicus* R. Br, Peptic Ulcer, Ulcer healing activity, Wistar albino rats

INTRODUCTION

Modernization, Industrialization and Urbanization, though no doubt is suggestive of advancement of human life as it has gifted to human society many diseases which are innate with urban life styles caused due to stress, injudicial food and habits. Of these Acid Peptic Disease is the most common disorder caused due to such urbanized life styles and in view of its universal distribution and common prevalence, has had more attention directed at it than many other major diseases.[1]

In India, the incidence of Peptic ulcer has been reported highest in the south, in Kerala ad TamilNadu. It has been estimated that 7% of the united States population experience heart burn symptoms daily and almost half of them once in every month. Because of their prevalence, potential for complications and economic consequences, Acid Peptic Disease represent an important group of diseases.[2]

Advancement of Medicine and Pharmacology has thrown open innumerable number of drugs from time to time with newer and potent drugs like antacids, H2 receptor antagonists, proton pump inhibitors and more recently H Pylori eradicators, thus causing a decline in its incidence. Inspite of these advances, management of acid peptic Diseases is still unsatisfactory, because total cure is eluding, recurrence more frequent and most of all, the adverse effects of the drugs like Alkalosis, Hypergastrinemia, Hypochlorhydria, Tumours of enterochromaffin cells, Constipation, Diarrhoea etc.[3]

Long before modern man knew Acid Peptic disease, elaborate description of diseases like Amlapitta (Acid

peptic Disease), Vidagdhajeerna(indigestion), Parinamashoola (Duodenal ulcer) and AmashayagataVrana (Gastric Ulcer) are found in Ayurvedic literature (Indian traditional medicine) centuries ago. Detailed description of its causes like Viruddha (incompatible foods), Dooshita (freezed, canned foods), Amla (alcohol and other beverages), Vidahi (spicy, fried) and other aggravating food substances resulting in symptoms like Avipaka (Indigestion), Tiktamlodgara (Bitter and Sour eructation), Klama (Fatigue), Hritkantadaha (burning sensation in epigastrium and throat) and aruchi (loss of appetite) simulate the salient features of Acid Peptic Diseases.[4] AmashayagataVrana (Gastric Ulcer) has not been directly referred to in Ayurved. Rather causes of Vrana (Ulcer) has been categorized as Nija (endogenous) and Agantuja (exogenous factor) with eight different sites of manifestation among which amashaya (Gastrium) is one.[5] Ulcers caused by drugs (NSAIDs) can thus be safely correlated to Amashayagatavrana (gastric ulcer) and equated to drug induced ulcers.

NSAIDs are non-steroidal anti inflammatory drugs which are the commonly used analgesics and have a wide range of therapeutic applications from simple headache to the management of acute and chronic inflammatory conditions. Their use ranges from one day to few months or even years. With such extensive use, NSAID gastropathy is produced as a common iatrogenic disorder.[1]

Out of these 87 to 90% of patients exhibit gastritis while 10 to 30 % have ulcers. Such NSAID induced ulcers and its healing can be studied scientifically by experimental studies. Wistar albino rat is taken as the ideal model for the study of anti-peptic ulcer healing effect.[6]

Hemidesmus indicus R.Br. (Shveta Sariva in sanskrit) is one of the most easily and abundantly available, and used singly as well as in combinations since ancient period. It is one of the main ingredient in formulations used in Peptic Ulcers.[7] It is said to be used in affections of mucous membrane.[8] Research works have been carried to evaluate its ulcer healing property with different experimental models.[9,10] The current models study only the prophylactic effect of the drug. So in the present study slight modification was made to include curative effect of the drug as well. The present study is focused to assess the anti peptic ulcer effect of the drug in two forms aqueous and alcohol extract both as prophylactic and curative through experimental study in albino rats in drug induced gastric ulcer.

METHODS

Healthy Wistar albino rats of both sexes weighing 100 to 150 gms were obtained from Animal house of Veterinary College, U.A.S, Hebbal, Bangalore. These animals were kept in cage bedding. Each cage contained 10 animals. These animals were allowed to acclimatise to the animal room conditions for one week and were fed with rat pellet feed (Gold Mohur, Hindustan Lever ltd., India) and tap water ad libitum. Identical conditions were maintained for all groups. Animal Ethics committee Clearance was obtained before the commencement of the trial. The experimental study was carried out at Department of Pharmacology, Veterinary College, Hebbal, Bangalore. Phytochemical study was conducted at Government College of Pharmacy, Bangalore.

Source and preparation of the drug

Fresh roots of botanically authenticated *Hemidesmus indicus* R. Br. i.e Shveta sariva was collected from the natural habitat of the plant from various places inand around Bangalore. The roots were washed well, dried, powdered and used for the preparation of aqueous and alcoholic extracts as per standard pharmacopeal procedures.[11,12]

Reagents

Indomethacin (BP74/USNF. I.C.F.I.S. madein Italy), Ranitidine (JB Chemicals and PharaceuticalsLtd. Batch No1075, Mg.2000 lic. No. G/2156A), Ether for Anaesthesia (SD Fine Chemicals Ltd. Batch no.1300a-0100-1301-13)

Schedule of the experiment

Ninety animals were randomly selected with 10 animals in each group and divided into the following groups.

Group I: Normal Group-Ten animals were maintained in the experimental condition with no drug treatment and ulcer induction.

Prophylactic Groups: Forty animals were selected for the trial and divided into four groups of ten animals. The test drugs were administered half an hour earlier to each dosing of Indomethacin. Six hours later the animals were sacrificed, ulcer scoring and other histopathology performed.

Group II-Control Group for prophylactic: Ulcers were induced with indomethacin in a dose of 20 mg/kg body weight in two doses between 15 hours interval[6] but no treatment was given. The animals were instead fed with distilled water half hour before ulcer induction.

Group III-Standard Pretreated Prophylactic: Standard drug: Ranitidine was given half an hour before each dose of Indomethacin in a dose of 27 mg/kg body weight.[6]

Group IV Test drug Pretreated Prophylactic: Aqueous extract of the test drug was administered half an hour before each dose of Indomethacin in a dose of 500 mg/kg body weight.

Group V Alcohol Extract Pretreated Prophylactic: Alcoholic extract of the test drug was administered half an hour before each dose of Indomethacin in a dose of 100 mg/kg body weight.

Curative Groups: Forty animals were randomly selected for the trial with four groups often animals in each group. The Animals were treated with the test drug for the test group, Ranitidine for the standard group and distilled water for the Control Group for two days after induction of the ulcers and the animals were sacrificed at fortyeight hours with over dosage of ether anaesthesia and the stomach observed for Ulcers and investigated for all assessment tests.

Group VI: Control Curative-After induction of ulcers the rats were fed with only distilled water for the next two days after induction of ulcer.

Group VII: Standard Posttreated Curative: Rats in this group were treated with Standard drug: Ranitidine in a dose of 27 mg/kg body weight for the next two days after induction of ulcer orally in a single dose per day.

Group VIII: Aquoeus Extacrt Posttreated Curative: Aqueous extract of the test drug was administered in a dose of 500 mg/kg body weight per day weight for the next two days after induction of ulcer orally in a single dose per day.

Group IX Alcohol Extacrt Posttreated Curative-The test drug was administered in a dose of 100 mg/kg body weight per day weight for the next two days after induction of ulcer orally in a single dose per day.

The dosage of the test drug was extrapolated from human dose and pilot study.

The animals were then sacrificed with overdose of ether anesthesia. The abdomen was opened with a midline incision extending from the xiphoid. The stomach was removed and opened along the greater curvature, inner surface was examined for mucosal integrity and occurance of ulcers under a magnifying lens.

Assessment Parameters

Ulcer scoring: The stomachs were opened as mentioned above, and the inner surface was examined under a magnifying lens and scoring done as follows.[13]

0-Normal
1-scatteredhemorrhagicspots
2-Deeper haemorrhagic spots
3-Haemorrhagicspots +Ulcer
4-Perforation

Histopathology

Animals of all groups were sacrificed after the trial and the stomach with ulcerations collected and preserved in Neutral Buffer Formalin for fixation of tissues. And processed for Histopathology.

RESULTS

The test drug treated groups showed statistically significant reduction in the ulcer scoring when compared to the untreated groups. The mean ulcer scores are given in Table 1, and the comparison between groups by ANOVA of variance in Table 2.

Table 1: Showing the mean values of the Ulcer Score in different groups of prophylactic and curative treatments.

	Control	Standard	Aqueous Test Group	Alcoholic Test group
Prophylactic Treatment	$2.3^{a}\pm$ 0.213	$1^{a}\pm$ 0.298	0.4	0.3
Curative Treatment	$1.3^{b}\pm$ 0.153	$0.3^{b}\pm$ 0.213	-	-

Table 2: Showing the mean and standard error of mean of the Ulcer Scores by ANOVA of variance between the groups ($p \leq 0.01$).

	Control	Standard	Aqueous Test Group	Alcoholic Test Group
Prophylactic Treatment	$2.3^{a}\pm$ 0.2134	$1.0^{b}\pm$ 0.298	$0.4^{bc}\pm$ 0.1632	$0.3^{bcd}\pm$ 0.1527
Curative Treatment	1.3± 0.153	0.3± 0.153	0	0

In the prophylactic group the mean ulcer score values of the test drug groups are significantly lower than the untreated group .The mean values of the ulcer score in the test drug treated groups though statistically not significant are lower than the standard drug treated group. The mean values of the ulcer score between the aqueous and alcohol treated groups though not statistically significant, the alcohol group shows a lower mean value of ulcer score than the aqueous treated group.

In the curative group the mean values of the test drug treated showed total absence of ulcers, when compared to the control group (untreated group) and standard group (Ranitidine treated).

The mean values of the ulcer score of prophylactic and the curative groups of control, standard and test groups (aqueous and alcohol) are given in Table 3.

The mean ulcer score of the test drug groups in the curative treatment when compared to the prophylactic treatment showed that the mean values of the curative

group is statistically significant and lower when compared to the prophylactic group.

Table 3: Showing the mean and standard error of mean of the Ulcer Scores between the prophylactic and curative treatment by student t test (p≤ 0.01).

	Control	Standard	Aqueous Test Group	Alcoholic Test Group
Prophylactic Treatment	2.3	1.0	0.4	0.3
Curative Treatment	1.3	0.3	0	0

Note: the different superscripts column wise indicates significant difference between the means Common superscripts indicate no difference between the means

In histopathological sections the control group showed gross infiltration of lymphocytes and eosinophils with necrosis. The trearment groups showed normal mucosa.

DISCUSSION

Acid Peptic disease is a common disorder encountered by common man and its reference is seen since ancient period.[4] *Hemidesmus indicus* R.Br. is one drug recommended for this condition in traditional Indian Medicine.[8] The test drug showed highly significant ulcer healing effect in both the aqueous and alcoholic extract groups. This ulcer healing effect by the test group was far superior than the ulcer healing effect seen in the standard group healed with Ranitidine. The animals in the group treated with alcohol extract showed marginally better healing effect (which is statistically not significant) when compared to the animals treated with the aqueous extract.

In the prophylactic treatment group there is considerable reduction of ulcers in the test drug treated group when compared to the control and standard groups, thus indicating the superior ulcer healing effect of the drug. But total cure was not seen probably because sufficient time was not given for healing as stomachs were opened within 6 hours of drug administration.

In the curative treatment there was reduction of ulcer score in the control and standard groups probably because of the time factor of 48hours (2 days).But in the test drug treated groups there was total healing of the ulcers showing the superior ulcer healing effect of the drug, which proves that the test drug is highly effective curatively.

The ulcer healing effect observed in the experimental trial can be attributed to the contributive and supportive properties of the drug like Phytochemical constituents which are Tannins, Flavonoids present in the drug.[14]In gastric ulcers, the tannin-protein complex layer is said to protect the stomach by promoting greater resistance to chemical and mechanical injury or irritation, promote tissue repair, and aid in gastrointestinal tract anti-inflammatory processes.[15]Flavonoids on the other hand display several pharmacological properties in the gastroprotective area, acting asanti-secretory, cytoprotective and antioxidant agents. Besides their action as gastroprotective, flavonoids also act in healing of gastric ulcers.[16] Aditionally *Hemidesmus indicus* is found to possess significant wound healing activity.[17,18]

To conclude Aquoeus extract and alcoholic extracts of Hemidesmus indicus R.Br. were analysed pharmacognostically and were found to be within Indian Pharmacopoel standards. Aqueous extract of the drug in the dose of500mg/kg body weight administered orally produced almost complete healing of gastric ulcers at the end of 48 hours after ulcer induction. While alcohol in the dose of 100 mg/kg body weight showed marginally better result though statistically not significant with the curative group better than the prophylactic group. Clinically the drug did not produce any abnormal signs or symptoms, behaviour during the course of the experimental study.

Histopatholigically, the sections of the gastric mucosa in the treated groups showed a normal gastric mucosa while that of the control group showed gross infiltration of lymphocytes and eosinophils with necrosis. Thus Hemidesmus indicus is a promising drug in the treatment of Peptic ulcer.

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