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Protective Effect of Terminalia Bellerica Chlorofom Extract for Its Anti-Ulcer Activity

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A B S T R A C T

Peptic ulcer is a most common disease of humans. A number of drugs including proton pump inhibitors and H2 receptor antagonists are available for the treatment of peptic ulcer, but clinical evaluation of these drugs has shown incidence of relapses, side effects like arrhythmias, impotence, gynaecomastia, arthralgia, hypergastrinemia and haemopoeitic changes and drug interactions. The aim of present study was protective effect of terminalia bellerica chloroform extract for it's anti-ulcer activity. Under the research to perform the phytochemical study, acute toxicity studies and aspirin induced ulcer activity. Choloroformic extract of Terminalia belirica, showed the presence flavanoids and their glycosides tannins, triterpenoids, and saponins. These phytoconstituents present in the extract could be the possible agents involved in the prevention of gastric lesions induced by aspirin.

Keywords: Peptic ulcer, Anti-Ulcer, Aspirin, Chloroform, Treminalia Bellerica

A R T I C L E I N F O

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C O N T E N T S

1. Introduction

Peptic ulcer is the most common, chronic gastrointestinal disorder and has become a common global health problem affecting a large number of people worldwide and still a major cause of morbidity and mortality. Geographically, the disease is prevalent throughout the work, in USA annually 3.7 million people are affected by this disease. Approximately 500,000 new cases are reported each year, with 5 million people affected in the United States alone. Interestingly, those at the highest risk of contracting peptic ulcer disease are those generations born around the middle of the 20th century. Ulcer disease has become a

disease predominantly affecting the older population, with the peak incidence occurring between 55and 65 years of age. In men, duodenal ulcers were more common than gastric ulcers; in women, the converse was found to be true. Thirty-five percent of patients diagnosed with gastric ulcers will suffer serious complications. Although mortality rates from peptic ulcer disease are low, the high prevalence and the resulting pain, suffering, and expense are very costly. Ulcers can develop in the esophagus, stomach or duodenum, at the margin of a gastroenterostomy, in the jejunum, in Zollinger-Ellison syndrome, and in association with a Meckel's diverticulum containing ectopicgastricmucosa. Peptic ulcer disease is one of the several disorders.

It is estimated by World Health Organization that, 80% of the world population must rely on traditional medicines for health care; these traditional medicines are mainly plant based. Most of the studies demonstrate the importance of natural products in the drug discovery. The use of phytoconstituents as drug therapy to treat major ailments has proved to be clinically effective and less relatively toxic than the existing drugs. A number of drugs including proton pump inhibitors and H2 receptor antagonists are available for the treatment of peptic ulcer, but clinical evaluation of these drugs has shown incidence of relapses, side effects like arrhythmias, impotence, gynaecomastia, arthralgia, hypergastrinemia and haemopoeitic changes and drug interactions. This has been the rationale for the development of new antiulcer drugs and the search for novel molecules has been extended to herbal drugs that offer better protection and decreased relapse.

Plant Profile:

Botanical name : *Terminalia bellerica*
Family : Combretaceae
Synonyms : Baheda

Fig 1: Macroscopic features of Terminalia bellerica (combertaceae)

Phytochemical Constituents: Glucoside (bellerican), Gallo-tannic acid, colouring matter, resins and a greenish yellow oil. Ellagic acid, gallic acid, lignins (termilignan and thannilignin). 7-hydroxy3'4'(methylenedioxy) flavone and anolignan B. Tannins, ellagic acid, ethyl gallate, galloyl glucose and chebulic acid, phyllemblin, β-sitosterol, mannitol, glucose, fructose and rhamnose.

Traditional Uses:

Fruits are laxative, astringent, anthelmintic, and anti-pyretic, useful in hepatitis, bronchitis, asthma, dyspepsia, piles, diarrhoea, coughs, hoarseness of voice, eye disease and scorpion-string, used as a hair tonic. Decoction of the green fruit is used for cough. Pulp of the fruit is useful in dysenteric-diarrhoea, dropsy, piles and leprosy. Half ripe fruit is used as purgative. Kernel of the fruit is narcotic. Fruits are used in menstrual disorder in khagrachari. Seed oil is used in rheumatism. Gum of the bark is demulcent and purgative. The triterpenoid present in the fruits possess significant antimicrobial activity. Kernel oil has purgative action and its prolonged use was well tolerated in mice.

2. Methodology

Selection of Animals:

Three animals (Albino mice, 25-75 mg) were selected for studies.The chloroform extract of *Terminalia Bellirica* was administered through oral route.Most of the crude extract possess LD5o value more than 2000mg/kg of the body weight of animal used.Dose volume was administered 0.1ml/100mgm body weight to the animal by oral route. After giving the dose the toxic signs were observed with in 3-4 hours.Body weight of animals before and after administration, onset of toxicity and signs of toxicity like changes in skin and fur , eye, and mucous membrane and also respiratory, circulatory, autonomic and central nervous system and somatomotor activity and behavior pattern ,signs of tremors, convulsions ,salivation, diarrhea, lethargy, sleep and coma was also to be noted, if any was observed.

Pharmacological Evaluation

Evaluatioion of Anti-Ulcer Activity

Animals: Male albino rat weighing 150-200g were used in the present study. All the rats were kept at room temperature (22c) in the animal house . All the animals were housed and treated as per the internationally accepted ethical guidelines for the case of laboratory animals. prior top the experiments, rats were fed with standard food and were acclimatized to laboratory conditions. Animal ethics committee and in accordance with the recommendations for the proper care and use of laboratory animals. Animals were divided into five groups of six animals in each group were taken.Male albino rats were divided in to five groups of six animals per group and animals were fasted for 24 hrs prior to the experiment in perforated steel cages to avoid coprophagy, Five groups were made as below.

Experimental Design:

Group 1- Normal control rats served as positive control received normal saline (0.9%Nacl given as 5ml/kg body weight p.o.)

Group 2- (Ulcer control)- ulcer was induced through oral route using aspirin 5mg/kg body weight.

Group 3- Aspirin induced ulcer rats were treated with standard rantidine 200mg/kg body weight.

Group 4- Aspirin induced ulcer rats were treated with CETB 200mg/kg body weight.

Group5-Aspirin induced ulcer rats were treated with CETB 400mg/kg body weight.

One hour after the drug treatment the animals were treated with chloroform extrat of *Terminalia bellerica* (500mg) to induce ulcers. The animals were sacrificed after 1 hr and stomach was opened and percentage inhibition of ulcer was determined.

Pharmacological Studies:

Biochemical Parameters: The stomach was carefully excised keeping oesophagus closed and opened along greater curvature and luminal contents were removed. The gastric contents were collected in attest tube and centrifuged. The gastric contents were analyzed far gastric juice volume, PH. The results are given in table.

Measurement of Gastric Juice Volume and P^H: Gastric juice was collected from aspirin induced ulcer rats. The gastric juice thus collected was centrifuged at3000 rpm for 10 min. The volume of supernatant was measured and expressed as ml/100gm body weight. The ph of the supernatant was measured using digital PH.

Ulcer Index (UI): The mucosa was flushed with saline and stomach was pinned on frog board .The lesion in glandular portion was examined under a 10x magnifying glass and length was measured using a divider and scale and gastric ulcer was scored .Ulcer index of each animal was calculated by adding the values and their mean values were determined.

3. Results and Discussion

Table 1: Phytochemical study of Terminalia Bellerica

Test	Observation
Test For Alkaloids	
Dragendroffs Test	+
Mayers Test	+
Test For Glycosides	
Keller- Killani Test	+
Test For Flavanoids	
Shinoda Test	-
Alkaline Reagent Test	+
Lead Acetate Test	+
Test For Tannins	
$FECL_3$ test	+
Test For Phenol	
$Fecl_3$ test	+
Test For Sterols	
Libbermann- Burchard test	-
Test For Saponins	
Forth test	+
Test For Diterpenes	
Copper acetate test	+
Test For Carbohydrates	
Molisch test	+
Fehlings test	+
Iodine test	+
Test For Protiens and Amino Acids	
Ninhydrin test	+
Xantho protein test	+

Pharmacological Studies

Anti-Ulcer Screening:

Aspirin Induced Ulcer: Aspirin induced gastric damage showed gross mucosal lesion, including long haemorrhage bands and petechial lesion. Animal pretreated with choloroform extract of terminalia belerica and standard drug rantidine showed very mild lesions and sometimes no lesion at all, when compared to ulcer control groups.

Terminalia bellerica showed a dose dependent curative ratio compared to ulcer control groups. The extracts exhibited inhibition percentage of 61,55 at doses of 200 and 400mg/kg doses respectively. The ulcer protective action of extracts at different doses was better as that of standard drug, rantidine which exhibited an inhibition as improved compared to standard drug. Aspirin produces

severe gastric haemorrhagic lesions. The pathogenisis of aspirin induced gastric damage in rats is complicated and involves superficial aggressive cellular necrosis as well as the release of tissue gastric microvasculature, triggering a series of events that lead to mucosal and sub mucosal damage. So the cytoprotective mechanisam of the Terminalia belirica extract may therefore include mechanisms other than simple acid neutralization.

Table 2: Effect of Terminalia Bellerica on Gastric Secretion, Aspirin Induced Ulcer

Group	Ulcer index (ui)	Percentage inhibition (%)	P_H of Gastric Juice
Normal control	00.00	-	
Ulcer control (aspirin 5 mg/kg body weight)	22.8±2.1	85.6%	3.2±0.2
Standard(Ranitidine 20 mg/kg)	8.7±0.9	61%	5.9±1.0
CETB(200mg/kg body weight)	12.2±1.2	46%	4.4±0.6
CETB(400mg/kg body weight)	10±0.4	55%	5.3±0.9

All values are expressed as mean +or- S.E.M: (n+6) animals in each group. **P<0.001, *P<0.01, ulcer control group was compared with normal control group. Ranitidine and extract treated groups were compared with ulcer control group.

Histopathology Studies:

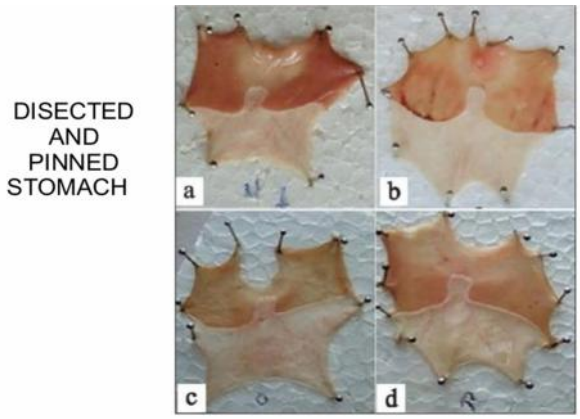

Fig2:Ulcer index in CETB pylorus ligated induced ulcer model (a) Control, (b) Standard Ranitidine treated group, (c) Low dose CETB treated group and (d) High dose CETB treated group

Ulcer Index and CID Parameters:

The effects of chloroform extract of Terminalia bellerica on acid parameters showed significant effect at 100mg/kg dose compared to ulcer control animals. The volume of acid secretion, total and free acidity was decreased and P^H of the gastric juice was increased compared to ulcer control group. But in this gastric environment also able to induce ulcer, so it Can be thought that the antisecretory, activity might not be the main mechanism of action of these extracts.

4. Conclusion

The present study was undertaken to determine the antiulcer activity of the choloroform extract from the fruits of Terminalia bellerica. The preliminary phytochemical investigation showed the presence of alkaloids, saponins, flavanoids, terpenoids, tannins, cardiac glycosides, gums, and phytosteroids. The pharmacological and acute toxicity studies of choloroform extract was performed by following, OCED-423 guidelines .no mortality or acute toxicity was observed (3days) up to 20000mg/kg of body weight. The phyto constituents like flavanoids, tannins, terpenoids, and saponins have been reported in several anti-ulcer literatures as possible gastroprotective agents. Flavanoids, tannins, and triterpenoids are among the cyclo protective active materials for which antiulcerogenic efficacy has been extensively confirmed.It is suggested that these compounds will be able to stimulate mucus, bicarbonate and prostaglandin secretion, and counteract with the deteriorating effect of reactive oxidants in gastrointestinal lumen. Tannins may prevent ulcer development due to their protein precipitation and vasoconstriction effects. Their astringent action can help precipitation micro proteins on the ulcer site, there by forming an impervious layer over the lining that hinders gut secretions and protects the underlying mucosa from toxins and other irritants. Similarly the choloroformic extract of Terminalia belirica, showed the presence flavanoids and their glycosides tannins, triterpenoids, and saponins. These phytoconstituents present in the extract could be the possible agents involved in the prevention of gastric lesions induced by aspirin. Terminalia bellerica showed a dose dependent curative ratio compared to ulcer control groups .The extract exhibited an inhibition

percentage of 55, 66 at doses of 200 and 400 mg/kg doses respectively. The ulcer protective action of extracts at 400mg/kg was good to that of standard drug, ranitidine, which exhibited an inhibition percentage of 66.

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