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Evaluation of methanolic extract of Slippery elm bark for its Anti-ulcer activity on Albino Wistar Rat

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ABSTRACT:
The objective of present study was to evaluate the anti-ulcer activity of hydro-alcoholic extract of Slippery Elm Bark.Mainly secretion of gastric acid and pepsin causes ulcer in patients. Plant extracts and polyherbal formulations are two of the most appealing sources of new drug. This type of extract formulations are showing good results in the treatment of gastric ulcers. In this study anti-ulcer activity was investigated by aspirin induced gastric ulcer in albino wistar rats. The extract was given at the dose of 150mg/kg (SELD- Slippery elm low dose) and 250mg/kg (SEHD- Slippery elmhigh dose) in the experimental models. Ranitidine (20mg/kg) was used as standard drug. SELD and SEHD showed 42 % and 77 % ulcer inhibition respectively, whereas ranitidine 60 % against aspirin induced ulcer model. In the models methanolic extract of Slippery elm bark has shown significant anti-ulcer activity in dose dependent manner.

INTRODUCTION:

Problem currently, ulceration is being intentional about staff requirements at the of increased of world and and is a major cost of morbidity and health care. Ulcer is: GI disease (10% worldwide) population [1].

WHO reports according to which Strategies Used to estimate years of life lost due to the leading causes of death in people ≤19 years of age: 2018, from a total death in India of 55,560 India of 0.63% because of ulcer at world No. 60 the age-adjusted death rate is 5.58 per 100,000[2];

Ulcer: a defect of the mucosal integrity duodenal barrier) and lead to a local active inflammation, defect or excavation[3]. A gastric ulcer develops in the stomach and it is the part of small intestine first one duodenum ulcer. A common cause of food poisoning and a major GI (Gastrointestinal)DataReader imbalances of the same, taking place therein. Risk factors like gastric acid, pepsin, bile, H. factors (5-7), and the American Gastroenterological bicarbonate secretion, the integrity of the(pg: 8) constitutive resistance of the mucosal cells [4]. Common causesof ulcer are Helicobacter pylori, chronic use of reductive drugs, etc. Various factors such as the use of NSAIDs, smoking, alcohol consumption, and higher stress levels, etc. Belching, vomiting, which have the feature of upper stomach pain, further common side effects include bleeding, perforation, and Ulcer– This condition is known to lead to blockage of stomach so, ulcer treatment is symptoms based decrease, ulcers healing and stop preventing The Suppresses acid (ulcer medications). Secretione.g., proton-pump inhibitor, H_2 antagonist, and Prostaglandin analogs

or inhibit stomach-produced acid i.e. antacids.

Other than that, most of these drugs have been found to have adverse effects. Due to numerous side these include side effects of synthetic drugs, medicinal plants etc. are considered primary to producing new drugs because they cause less or no side effects and it is also not too cost-effective and effective, less poisonous[5].

The plant Slippery elm commonly known as belongs to the family Ulmaceae. Geographic distribution ranging along the eastern and central United States. Its name is derived from the viscous, slimy liquid created when the inner bark is chewed, which was common among Native Americans and early pioneers as a relief to dehydration and hunger. The inner bark is the only part of the tree known to be used for medicinal purposes, and the remainder of the tree has no significant commercial value. The inner bark is thin, tough, and flexible with a fibrous texture. The hue of the natural bark is a reddish-yellow or reddish-brown color, although when dried and in powder form (as is commonly used in medicinal applications) the color is grayish [6-12]. The bark containsmucilage – Uronic acid, Pentose, Hexose, Methyl Pentose (rhamnose,galactose). Tannins , oxalate acid, flavonoids, phytosterols, salicylic acid, capric acid,caprylic acid, decanoic acid[12-14].

According to the Natural Medicines Comprehensive Database, slippery elm is used for the treatment of coughs, sore throat, colic, diarrhea, constipation, hemorrhoids, irritable bowel syndrome (IBS), cystitis, urinary inflammation, urinary tract infections, syphilis, herpes, expelling tapeworms, protecting against stomach and duodenal ulcers, for colitis, diverticulitis, GI inflammation, and acidity [15].In traditional Oriental medicine, elm bark has been used for edema, inflammation,and cancer [16].Present study was designed to scientifically evaluate the antiulcer activity of slippery elm bark extract at different doses.

MATERIALS AND METHODS:

Experimental Animals:

Female albino wistar rats of 150-200g were usedthroughout the experiment. They were placed inpolypropylene cages (32×24×16cm). The animals werepurchased from authorized animal breeder. The animals were kept in CPCSE approved DayanandCollege Of Pharmacy animal house (approval no:2193/PO/Re/S/22/CPCSEA), well maintained under standard hygienic conditions, at a temperature of 22±2°C, 65% relative humidity, and 12-hours light and dark cycle. Commercial food pallets and tap water ad libitum were provided. All the experiments were performed in between 10am to 6pm.

Drugs and chemicals used:

Sodium hydroxide (LobaChemie Pvt. Ltd.), hydrochloric acid (LobaChemie Pvt. Ltd.), diethyl ether (Merck Specialties Pvt. Ltd., Mumbai.), ranitidine (Acilocmanufactured by Cadila Pharmaceuticals Ltd.), aspirin, distilled water.

Preparation of extract formulation:

The Bark of Slippery elm were purchased fromlocal market. They were washed by clean and fresh water to remove the unwanted particles. The Bark were dried, powdered and then extracted with 70% methanol insoxhlet apparatus for about 48 hours. Then the extract was dried by using a water bath and kept at 4^0C in refrigerator until the experimental testing.

Preliminary phytochemical investigations of the extract:

Methanolic extract of Slippery elm bark was evaluated for phytochemical investigation[17]and presence of phytoconstituents like mucilage – Uronic acid, Pentose, Hexose, Methyl Pentose (rhamnose, galactose). Tannins, oxalate acid, flavonoids,phytosterols, salicylic acid,capricacid,caprylicacid,decanoic acid etc. were observed.

Experimental design:

For this study the animals were divided into four groups of five animals in each group.

- **Group I**

The animals of this group was untreated and known as control.

- **Group II**

This group received the treatment of ranitidine 20 mg/kg ip.

• Group III

This group received aspirin (200mg/kg) orally

• Group IV

This group was treated with 150 mg/kg dose of Slippery elm bark extract orally and known as SELD.

• Group V

This group was treated with 250 mg/kg dose of Slippery elm bark extract orally and known as SEHD.

Aspirin induced ulcer[18-20]:

In this model ulcer was induced by aspirin administration. Prior to the start of the experiment, all the rats were kept for 24 hours fasting and given free access to drinking water. The animals were given treatment as per their groups, after 45 minutes of treatment, all rats were received aspirin (20mg/kg, ip) to induce gastric ulcer. After 4 hours the animals were sacrificed by inhalation of anesthetic ether. The stomachs were isolated, dissected and cleaned to remove gastric contents and blood by using distilled water. The number of ulcers and the severity scores were recorded. The acidity, ulcer index and percentage of ulcer inhibition was calculated by the formulas described below.

$$\text{Acidity} = \frac{\text{Volume of NaOH} \times \text{Normality}}{\text{MEq/L/100 g}} \times 100$$

Formation of any lesion in the stomach wall was observed and examined, the number of ulcers were recorded and scored as:

0 = No ulcer; 1 = Superficial ulcers; 2 = Deep ulcers; 3 = Perforation.

Mean ulcer score for each animal was expressed as ulcer index (UI):

UI = UN + US+ UP × 10–1

UN = Mean value of ulcers/animal

US = Average of severity score

UP = Percentage of animals with ulcers

The acidity and ulcer index of the treated animals were compared with controls. The ulcer inhibition (%) was calculated as:

$$\text{Inhibition (\%)} = \frac{\text{Mean ulcer index of control - Mean ulcer index of test}}{\text{Mean ulcer index of control}} \times 100$$

Statistical analysis:

The experimental result were shown as mean±SEM for each treatment group. The significance of activity was assessed using one-way ANOVA, Dunnett's post- parametric test between the data of control and treated groups. *$p<0.001$ was considered statistically significant.

RESULTS AND DISCUSSION:

Gastric ulcer occurs because of imbalance in the aggressive and defensive factors. The basolateral membrane of parietal cell has four important receptor namely muscarinic (M1), histaminic (H2), gastrin (G) and prostaglandin (P), among them M1, H2 and G are responsible for positive action on proton pump, may enhance acid secretion in stomach [21]. Prostaglandin produces inhibitory signal on proton pump, reduces the acid secretion. On the other hand it enhances the mucus production which produces a protective layer in stomach.

Ulcer is a burning issue mostly in the Eastern India, may be due to incorporation of more spices in the dishes of this region. Lots of drugs from different medicinal system like allopathic, homeopathic, Ayurveda and unani are available to combat this situation. As per, depending upon the seriousness of the situation may many combination drug therapy are also used in India, but the most popular antiulcer drugs from allopathic system has major draw-backs like side effects and high cost. Some of the herbal drugs has a certain level of anti-ulcer activity but there are always scopes for exploration of new molecules which can be easily available and cost-effective.

In this study Slippery elm bark have been investigated for its antiulcer activity by using aspirin induced ulcer. In all the model ranitidine (H2 antihistaminic) has been taken as taken as standard drug. The selection of the drug as a standard has come to the idea due to its no anti- androgenic and CNS effect.

Aspirin is an acetyl salicylic acid derivative, nonselective COX-2 inhibitor, used as an analgesic. Due to non-selectivity on COX pathway it also induces ulcer in the patient and has side effect. Because of blockage of COX-1 pathway prostaglandin synthesis get inhibited and causes damage in the mucosal layer of stomach. By using this phenomena aspirin has been used as an ulcer inducer in preclinical antiulcer screening since long time.

In aspirin induced ulcer model the control has shown ulcer index 0, in the other hand aspirin induced, ranitidine, SELD and SEHD have shown ulcer index 13.98±0.5122, 5.540±0.2250, 7.358±0.1706 and 2.950±0.2102respectively. Ranitidine is a standard drug has shown total acidity of 3171±67.36, at the same time SELD and SEHD have shown 4527±37.85 and 3600±93.54 respectively and all of these three has shown significant level of decrease in total acidity while compared with untreated control i.e. 2448±2051 and aspirin induced 5472±33.65(Table 1).

Figure 1: Sample of dissected stomach and formation of ulcer in aspirin induced ulcer model. (a) Aspirin treated, (b) Ranitidine, (c) SELD, (d)SEHD, (e) Control n-saline.

All values are shown as mean ± SEM, n = 6. ***p < 0.001 was considered statistically significant compared with control group.

Table 1: Effect of control, ranitidine and different extracts of Slippery elm in aspirin induced ulcer model

Group	Free acidity	Total acidity	Ulcer index	%Protection	%Ulceration
Control (n-saline)	**916.3±49.32**	**2448±2051**	**0**	**0**	**0**
Induced (Aspirin 200mg/kg)	**1768±30.34**	**5472±33.65**	**13.98±0.5122**	**0**	**100**
Standard (ranitidine 20mg/kg)	**1004±20.32**	**3171±67.36**	**5.540±0.2250**	**60±2**	**40**
MESEB (150mg/kg)	**1227±25.51**	**4527±37.85**	**7.358±0.1706**	**42±2**	**58**
MESEB (250mg/kg)	**1067±20.69**	**3600±93.54**	**2.950±0.2102**	**77±2**	**23**

CONCLUSION:

This study was designed to assess whether the chemical constituents of Slippery elm could promote ulcer healing in experimentally produce ulcer in rat. The observation substantiated the use of Slippery elm bark in future for treatment of ulcer.

In this study the Slippery elm bark were extracted in soxhlet apparatus by using 70% methanol. The extract was formulated and given orally, decreased the ulcer induce as well as the total acidity. Acidity is a parameter directly influence the chance of formation of ulcer.

Lipid peroxidation is an important process of several types of wound and ulcer[22]. Any drug that inhibits lipid peroxidation[23] is believed to increase the circulation thereby preventing the cell damage, promoting DNA synthesis followed by reconstitution of broken wound or ulcer. The antioxidant property of Slippery elm may be most responsible for its anti-ulcer activity.

Though several types of medications are also available for the treatment of ulcer still Slippery elm can bring a new era in the treatment of ulcer which is easily available and affordable.

CONFLICTOFINTEREST:

The authors have no conflict of interest regarding this investigation.

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