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Anti-ulcer Activity of *Excoecaria agallocha bark* on NSAID-induced Gastric Ulcer in Albino Rats

P. Thirunavukkarasu, L. Ramkumar and T. Ramanathan

Centre of Advanced Study in Marine Biology, Annamalai University,
Parangipettai-608 502, Tamil Nadu, India

Abstract: The plant extract of *Excoecaria agallocha* bark herbal preparation that has been suggested as useful in the treatment of varies diseases (anti tumor, anti microbial, anti wound killing agents and anti oxidant). In this, study to determine the gastro protective effect of *E. agallocha* in a model of NSAID induced ulcer rat. The lyophilized extract was given by oral gavages (125 and 62.5mg/kg) three times at 12 h intervals before administering dicolofenac 100mg/kg. Pretreatment with the extract resulted in a significant decreased of the ulcerated area. The volume and acidity of the gastric juice decreased in the pretreated rats. The plant extract was elevated in the gastric juice of untreated rats, showed hear normal levels in the pretreated rats. The *E. agallocha* was able to decrease the acidity and increase the mucosal defense in the gastric areas, there by justifying its use as an antiulcerogenic agent.

Key words: *Excoecaria agallocha* · NSAID · Gastric ulcer · Albino rats · Mangrove

INTRODUCTION

Peptic ulcer is a conglomerate of heterogeneous disorders, which manifests itself as a break in the lining of the gastrointestinal mucosa bathed by acid and/or pepsin. Non Steroidal anti-inflammatory drugs (NSAID) ingestion is associated with erosions, petechiae, type C gastritis, ulceration, interference with ulcer healing, ulcer complications and injury to the small and large intestine [1]. Although a number of antiulcer drugs such as H_2 receptor antagonists, proton pump inhibitors and cytoprotectants are available for ulceration all these drugs have side effects and limitations Herbal medicine deals with plants and plant extracts in treating diseases. These medicines are considered safer because of the natural ingredients with no side effects [2]. *E. agallocha* L. (Euphorbiaceae) is a small mangrove tree that grows widely in the tidal forests and swamps of the Sundarbans and other coastal areas of Bangladesh [3].This plant is also found in the countries of temperate and tropical Asia, Australasia and South-western Pacific (This plant has traditionally been used to treat sores and stings from marine creatures and ulcers, as a purgative and an emetic and the smoke from the bark to treat leprosy [3]. The bark oil has been reported to be effective against rheumatism, leprosy and paralysis. However, the milky sap of this tree can cause temporary blindness if it enters the eyes. The sap can also cause skin blisters and irritation. Clinical trials carried out on this plant showed its potential as anti-HIV, anticancer, antibacterial and antiviral agent [4] *E. agallocha* is a commonly available mangrove plant in almost all the coastal states of India. It is traditionally used by the local people as folk medicine in various diseases like epilepsy, toothache, ulcer etc [5,6].

MATERIALS METHODS

The plant sample was collected from Parangipettai. The Bark were cut into small pieces and shade dried for the experimental studies. Dried leaves were powdered and then the extract was prepared. The cold water extract was prepared by keeping leaf powder in cold water (1:50 W /v) for 48hours and Then it was filtered with the help of Whatman paper No. 1 filter paper and filtrate was lyophilized. The hot water extract was prepared by boiling leaf powder in distilled water (1:10 w/v) at 90° c for one hour. Then it was filtered by whatman No.1 filter paper and the filtrate was lyophilized. Both the lyophilized samples were stored at dry place [7].

Corresponding Author: Mr. L. Ramkumar, CAS in Marine Biology Annamalai University,
Parangipettai-608 502, Tamil Nadu, India

Animal Model: Healthy Female albino Wister rats of 150-165 gms were used throughout the study. They were maintained in a controlled environmental condition of temperature and humidity on alternatively. All animals were fed with standard pellet diet and water *ad libitum.*Animal experimental studies were conducted according to the guidelines of institutional animal ethical committee. All the animals were grouped into seven groups and each group had 5 animals. Group-1 Was Negative control (without any treatment fed with normal water), Group-2 Positive control treated with NSAID, Group-3 Pretreated animals with low dose (cold water Extract) and then treated with NSAID, Group-4 pretreated animals with high dose (cold water extract) and then treated with NSAID, Group-5 Pretreated animals with low dose (hot water extract) and then treated with NSAID, Group-6: Pretreated animals with high dose (hot water extract) and then treated with NSAID and Group-7: Standard control pretreated with omeprazole+ and then treated with NSAID [7].

Dose Selection and Mode of Administration: All the animals fed by oral gavages with the help of feeding tube. The doses determined as low dose at rate of 62.5 mg/ kg of the body weight and high dose at the rate of 125 mg/kg of the body weight for both the sample. Then Non steroidal Anti-Inflammatory Drug Diclofenac sodium used as the ulcerogenic agent at the dose of 100 mg/kg of body weight [7]. Standard anti ulcer drug Omeprazole used at the rate of 20 mg/ kg of body weight.

***In vivo* Protocol:** All the groups of animal were kept for overnight fasting fed only with the tap Water. The animals of group 3, 4, 5 and 6 were treated with the sample extract different doses.This treatment was given thrice at the 12 hours interval. Animals of group 7 were treated with Ranitidine simultaneously. After one hour of last administration of sample extract the NSAID was given by Oral gavages to group 2 to group 7 animals. After 6 hours of NSAID administration, the animals were sacrificed by cervical dislocation [8].

The animals were dissected and the stomach was taken out. Finally the ulcers were observed macroscopically. The observation was made for any bulging or inflammation in the stomach. The Stomachs were opened along the greater curvature and the mucosa was exposing for evaluation. The ulcer scores (US) were calculated as the arithmetic mean for each treatment.

RESULTS AND DISCUSSION

The defense mechanism of the gastrointestinal mucosa against aggressive factors such as HCl, bile acid and NSAIDs, mainly consists of functional, humoral and neuronal factors. Mucus-alkaline secretion, mucosal microcirculation and motility act as functional factors, while prostaglandins and nitric oxide act as humoral factors and capsaicin sensitive sensory neurons act as neuronal factors. In recent experiments, it has been found that heat shock proteins (HSPs), specifically HSP70 and HSP47 are involved in the gastric protection. The HSC70 (a constitutive form of HSP70) is co precipitated with COX-1 and the neuronal form of nitric oxide synthase after treatment with a mild irritant (20% ethanol). A positive relationship between enhanced interaction of HSC70 with either Cyclooxigenase-1 or nitric oxide synthase and mucosal defence mechanisms and ulcer healing, most probably through protecting key enzymes related to cytoprotection [9].

Pretreatment with the mangrove reflected a clear tendency to increase PGE_2 production in spite of NSAID-induced depletion, at the considerably high dose of Diclofenac used (100 mg/kg) [7]. These results may be attributed to the polyphenolic compounds found in the mangrove plants. Phenols stimulate PGE_2 formation based on their action as co substrates for the peroxidase reaction [10]. Since the leaf extract of E. *agallocha* also has the protective effect on the stomach against NSAID-induced gastric ulcer and this may attributed to polyphenolic compounds.

[11] Have evaluated the anti-ulcer effect of *Rhizophora mangle* bark on the gastric ulcer induced by using ethanol-hydrochloric acid in rats which causes the mucosal damage in it. They have used the drug cimetidine as standard. The effect of these agents on the quality and quantity of the gastric mucus were also determined by giving oral dosage of the aqueous extract of the sample at different dose. Oral doses at 500 mg/kg body weight gave the highest level of gastric protection. Mucus content increased, accompanied by a proportional increase in proteins. In this present study, positive control (Diclofenac Sodium) was caused damage on the glandular mucosa (2.40±0.37)

On the other hand, tannins may prevent ulcer development due to their protein precipitating and vasoconstricting effects [12]. Their astringent action can help precipitating microproteins on the ulcer site, thereby

Table 1: Ulcer Score at different concentration of Plant extract

Group Name	Concentrations (mg/kg of body weight)	Ulcer score
Negative control	-	-
Positive control	100	2.40±0.37
Low Dose (cold extract)	62.5	1.542±0.478
High Dose (cold extract)	125	1.275±0.25
Low Dose (hot extract)	62.5	1.3±0.408
High Dose (hot extract)	125	1.115±0.25
Standard control	20	0.625±0.25

forming an impervious layer over the lining that hinders gut secretions and protects the underlyinjg mucosafrom toxins and other irritants [13-15]. This propensity to bind with proteins also explains the fact that polyphenols inhibit enzymes tested *in vitro*. The major active principles of the red mangrove are polyphenols, represented in their majority by polymeric tannins (80%) and hydrolysable tannins (20%) and catechin, chlorogenic, Gallic and elagic acids as well as gallotannins, elagitannins and condensed tannins. These substances characterized by their polyphenolic nature, have shown cytoprotective properties [16] and have been associated to antiulcerogenic activity in other plants [17,18]. Since *E. agallocha* also had shown same but less anti ulcer activity in comparisons to *Rhizophora mangle.* So, it may be considered that *E. agallocha* also have tannins or polyphenolic compounds which are responsible for its anti ulcer property. In phytochemical analysis of the *E. agallocha* three new highly oxygenated dipterpenoids Excolabdone A, Excolabdone B and Excolabdone C are found. In this study, contrast to it the pretreatment with hot water and cold water extract, at doses of 62.5 mg/ kg and the body weight 125 kg decreased the ulcerated area to high dose-cold extract (1.115± 0.25) and high dose-hot extract (1.275±0.25), followed by low dose-cold extract and low dose-hot. This was compared to the effect exerted by standard control (Omeprazole) (0.625±0.25) (Table 1).

Based on the comparison with the *R. mangle* it is expected that the wound healing capacity of *E. agallocha* during ulcer is due to several mechanisms, such as coating the wound, forming complexes with proteins of cell wall, chelating free radicals and reactive oxygen species, stimulating the contraction of the wound and increasing the formation of new capillaries and fibroblasts [19].

CONCLUSION

The present study showed that pretreatment with the leaf extract (both hot water and cold water) of *E. agallocha* caused a beneficial effect on NSAID-induced gastric ulcer in rats as evidenced by the reduction in the ulcer score.

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