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# ANTIULCER EFFECTS OF AQUEOUS EXTRACTS OF STEM-BARK OF *DOLICHANDRONE FALCATA* (AEDF) AGAINST ASPIRIN-INDUCED ULCEROGENESIS IN RATS

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**ABSTRACT**

The study aimed to investigate the mechanism underlying theantiulcer effects of aqueous extracts of stem-bark of *Dolichandrone falcate* (AEDF) against aspirin-induced ulcerogenesis in rats. Acute gastric ulcer was induced by orally administering 200 mg/kg aspirin suspended in 1%v/v tween 80solution in rats.The volumes of the gastric content, pH, total & free acidity of gastric juice weremeasured and ulcer index &percentage of ulcer protection were calculated.The present results suggested that *Dolichandronefalcata*decreased ulcer index and increased percentage of ulcer protection by significant reduction of volume of the gastric content, total & free acidity of gastric juice inversely increases the pH. This effect may protect the gastric mucosa against ulceration by antisecretory and antiulcerogenic property of *Dolichandrone falcate*.

## INTRODUCTION

Ancient day's peptic ulcer disease was very often managed surgically, with resulting high morbidity and mortality rates. After 1970's, histamine $H_2$-receptor antagonists introduced and it's effectively suppressed the gastric acid secretion leads greatly improved clinical outcomes [1]. Symptoms of peptic ulcer disease commonly include epigastric pain, postprandial pain and nocturnal pain, pain that can wake the patient from sleep, and pain relieved by food or antacids. Earlier studies pathophysiology of peptic ulcer disease focused on abnormalities in the secretion of gastric acid and pepsin, and on the suppression of acid as a treatment strategy. But today, gastric hypersecretion associated with gastrinoma in Zollinger–Ellison syndrome, antral G-cell hyperplasia, an increase in parietal-cell mass, and a physiological imbalance betweenthe antagonistic gastric hormones gastrin and somatostatin—is still an important issue in peptic ulcer disease [2]. Moreover, Psychologic stress, cigarette smoking, alcohol consumption, use of nonsteroidal anti-inflammatory drugs (NSAIDs) including aspirin, potassium chloride, immune suppressive medications, and an age-related decline in prostaglandin levels have all been shown to contribute to peptic ulcer disease.In developing countries, about 70% population were relies on traditional system of medicine for their primary health care needs [3]. Many plants based medicines have been screened and reported to be useful in treating and managing ulcer with growing interest in natural medicine.

*Dolichandronefalcata* Seem.,Bignoniaceae, is a is a small deciduous tree with bluish grey bark, peeling in irregular woody scales and also commonly known as Medshingi. It growing on hedges of cultivated fields and frequently in hill forest, occasionally seen in dry scrub

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forests.*Dolichandronefalcata* bark is traditionally used in the treatment of fractured bones and used as a fish poison. In this plant Chrysin (flavone) was identified and reported for different biological activities such as anti-oxidant, anti-allergic, anti-inflammatory, anti-cancer, antiestrogenic and anxiolytic activities by previous authors [4-10]. In Ayurveda, the stem bark of *Dolichandronefalcata* is used for cure the ulcer, pain and epilepsy. But still no depth scientific study has been performed on*Dolichandrone falcate* stem-bark pharmacological properties. The aim of present study was to investigate the antiulcer effect of aqueous extract of stem bark of *Dolichandronefalcata* in different animal models. This is being carried out with the intention of giving a scientific validity and justification of such herb indicated for the treatment of ulcer and related disorders.

## MATERIALS AND METHODS

### Plant collection and Preparation of plant extract

The stem-bark of *Dolichandronefalcata* was collected from the forest of agasthyamalai hills, Tirunelvelidistrict, Tamilnadu, India. It was identified and authenticated by Dr.V.Chelladurai, Research Officer Botany. C.C.R.A.S., Govt. of India. The collected stem-bark of *Dolichandronefalcata* was shadow/air dried in room temperature without sunlight. The dried material was extracted in 1 litre of boiling water for 2-3 h and concentrated to half of the volume by boiling in a water bath. The yielded brownish extract was cooled and filtered using Whatman filter paper. The filterate extract was concentrated up to 100 ml on rotavapour under reduced pressure. The yield value was found to be 12.5%. The concentrated plant extract was lyophilized into powder used for the further pharmacological study which is suspended to 1% tween 80.

### Animals

Albino Wistar strain of rats, weighing about 180-220 g were obtained from Department of Pharmacology, Southern Institute of Medical Sciences, Guntur. Andhra Pradesh, India and used for the screening models. According to guidelines, animals were kept in animal house at an ambient temperature of 25°C and 45–55% relative humidity, with 12 h each of dark and light cycles. Animals were complete fed pellet diet and water *adlibitum*. For screening anti-ulcer efficiency purpose the animals were kept fasting overnight but were allowed free access to water.The experimental protocol was approved by the Institutional animal ethical committee.

### Acute toxicity study

The acute oral toxicity study was done for aqueous extract of stem-bark of *Dolichandronefalcata* (AEDF) according to OECD 420 guideline using fixed dose method Animals were divided into two groups, three animals each, fasted overnight. The started dose AEDF 2000 mg/kg b.wt.was administered to the Group 1 & 2 respectively. After oral administration of AEDF, the behavioral changes and signs of toxicity such as body temperature, CNS activity, urination, defecation etc were observed for 24 hrs. If AEDF does not showed any toxicity symptoms, lower dose 200 mg/kg b.wt. and higher dose 400 mg/kg b.wt. were selected for further studies [11].

### Aspin induced gastric ulcer model

Healthy animals were selected and divided into four groups, six rats each.

Group 1 served as vehicle control group, received 1% v/v tween 80 orally. (1ml/kg b.wt)

Group 2 served as Negativecontrol group, received only aspirin (200 mg/kg, b.wt. p.o.) suspended in 1% v/v tween 80

Group 3 served as standard group, received Omeprazole (20mg/kg, b.wt. p.o) suspended in 1%v/v tween 80

Group 4&5 served as test groups, received AEDF (200 & 400 mg/kg, b.wt. p.o.) suspended in 1% v/v tween 80respectively.

Single dose of aspirin (200 mg/kg, b.wt. p.o.) was given to all groups of animals 45mins after oral administration (Omeprazole & AEDF) of vehicle and test drugs.All group animals were sacrificed by cervical dislocation 4 hrs later & the stomach was then isolated & cut along the grater curvature and washed carefully with normal saline. The ulcers score was observed by a person unaware of the experimental protocol in the glandular portion of the stomach [12].

Ulcer score was estimated as follows: 0: No ulcer, mild ulcer: 1, moderate ulcer: 2, severe ulcer: 3, severe ulcer with perforation: 4.

Mean ulcer score was calculated and the percentage of ulcer protection was determined as follows

$$\text{Ulcer Protection (\%)} = \frac{C - T}{T} \times 100$$

Where, C indicates Control mean ulcer index

T indicates test mean ulcer index

$$\text{Acidity} = \frac{\text{Vol of NaOH} \times \text{Normality of NaOH}}{0.1\ \text{N}} \times 100\ \text{mEq/L/100g}$$

### Determination of gastric volume

The dissected stomach was separated and the gastric contents were transferred in to the centrifuge tube, and centrifuged at 1000 rpm for 10 minutes. The supernatant liquid was then transferred to a measuring cylinder, and the gastric volume was measured [12,13].

### Determination of pH of gastric content

1 ml of the gastric juice was collected, and pH was directly estimated by using pH strip [14].

**Determination of free acidity and total acidity**

The gastric contents were collected and centrifuged for the estimation of total acid present in the gastric juice [15].

Acidity was calculated by using formula;

$$\text{Acidity} = \frac{\text{Vol. of NaOH X Normality of NaOH}}{\text{Vol. of Gastric juice used}} \text{ m. Eq. /dl.}$$

**Statistical analysis**

The data were expressed as mean ± standard error mean (S.E.M).The Significance of differences among the group was assessed using one way and multiple comparison test and ANOVA(one-way analysis of variance). The test followed by Dunnett's test p values less than 0.05 were considered as significance.

**RESULTS AND DISCUSSION**

In acute oral toxicity study, in which the animals treated with the AEDF at a higher dose of 2000 mg/kg did not showed any significant abnormal signs, behavioral changes, body weight changes, or macroscopic findings at any time of observation and end of the 14 days of observation. This study indicated the safety of the extract. In aspirin induced gastric ulcer, AEDF showed a significant reduction in ulcer index when compared tonegative control ($p<0.001$).Both doses of AEDF 200mg/kgand 400mg/kg treated group showed significant reduction ($P<0.01$) in gastric volume and total & free acidity andinversely increased the pH ($p<0.001$) when compared tonegative control.The AEDF showed significant anti-ulcer effect against ulcers induced by aspirinin a dose dependent manner. AEDF at a dose of 200 and 400 mg/kg body weight showed protective effect of 57.58 and 71.77%, respectively, whereas Omeprazole showed protection index of 82.44 % at a dose of 20 mg/kg body weight. The results were shown in Table 1.

Aspirin suppresses gastroduodenal bicarbonate secretion, reduces endogeneous prostaglandin biosynthesis and disrupts the mucosal barrier as well as mucosal blood flow in animals**.** It leads tomucosal damage by interfering withprostaglandin synthesis, increasing acid secretion andback diffusion of H ions [16,17]. In stomach, prostaglandins play a vital protectiverole by prostaglandins synthetized in large quantities by the gastrointestinal mucosa can prevent NSAIDs induced acute gastric ulcersand gastro duodenalulceration [18-20].From these results where the ulcer index, gastric volume and total & free acidity were significantly decreased andinversely increased the pHin AEDF (200mg/kgand 400mg/kg) treated groups and Omeprazole treated group (Table 1). These parameters results suggested that AEDF treated groups showed severity of ulcer was decreased by maintaining mucosal membrane and antisecretoryeffect [21-23].

**Table 1. Efficiency of AEDF on acid secretary parameters in aspirininduced gastric ulcer**

| Groups | Gastric Volume (ml/100g) | pH | Ulcer index | % of ulcer protection | Free acidity (mEq/dl) | Total acidity (mEq/dl) |
|---|---|---|---|---|---|---|
| 1- Control (1%v/v tween 80) | 2.52 ± 0.21 | 2.85±0.12 | 0.17 ±0.02 | 98.64 | 4.26± 0.19 | 5.62 ± 0.03 |
| 2-Aspirin induced | 7.25± 0.33** | 2.16 ±0.14** | 12.47± 0.52** | - | 7.52± 0.32** | 8.56 ± 0.42** |
| 3-Omeprazole 20mg/kg, b.wt. p.o | 3.21 ± 0.52** | 3.42 ± 0.17** | 2.19± 0.41** | 82.44 | 3.16±0.33** | 4.14 ± 0.13** |
| 4- AEDF 200mg/kg, p.o | 6.14± 0.17b** | 2.82 ± 0.24* | 5.29±0.27** | 57.58 | 6.54±0.24** | 7.85 ±0.27* |
| 5- AEDF 400mg/kg, p.o | 4.62 ± 0.11b** | 3.14 ± 0.22** | 3.52± 0.19** | 71.77 | 4.42± 0.25** | 5.33 ± 0.23** |

*Comparisons were between: Group IIvs Group I&Group III- V. Values are expressed as mean ± SEM of 6 animals. Statistical Significance test for comparison was done by one way ANOVA followed by Dunnett's test. Symbols represent statistical significance: ** P < 0.01, * P < 0.05, ns- non a significant.*

**CONCLUSION**

Antiulcer efficiency of AEDF at 200& 400mg/kg of b.wt. is likely mediated which might be similar to that of Omeprazole which equally reduced theseverity of gastric ulcer developed by aspirin. Omeprazole is a well-known proton pump inhibitors act by irreversibly blocking the H/K adenosine triphosphataseenzyme system of the gastric parietal cells. AEDF showed significant anti-ulcer activity in aspirin induced gastric ulcer in rat model by decreasing the gastric secretions and by enhancing prostaglandins ($PGE_2$) levels. Overall, AEDF at 200& 400mg/kg of b.wt.has shown a substantial and significant protection against aspirin induced gastric ulcer model.

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