



## Antiulcerogenic activity of ethanol extract of the bark from *Terminalia catappa* in gastric ulcer model induced by ethanol in *Rattus norvegicus*

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### Abstract

*Terminalia* is a genus which has extensive utilization by people worldwide in traditional medicine and has also several pharmacological activities described. Accordingly, this study evaluated the antiulcerogenic activity of ethanol extract of the bark from *T. catappa* (EETC) by using the model of acute gastric ulceration induced by ethanol. EETB 250 mg/kg showed good results in reducing the gastric lesion area, while EETB 500 mg/kg protection was higher than one of the standard drug, carbenoxolone 100 mg/kg. Thus, EETC exhibits notable gastroprotective effect, showing that additional studies are necessary.

Keywords: Antiulcerogenic, *Terminalia catappa*, Combretaceae

## Introduction

Peptic ulcer disease is among the most serious diseases in the world and can be defined as mucosal lesions that penetrate the muscularis mucosae layer and form a cavity surrounded by acute and chronic inflammation (1). Despite the pathophysiology of the gastric ulcer has not been completely elucidated, it is thought to be caused by an imbalance between aggressive factors (leukotrienes, acid-pepsin secretion and reactive oxygen species), and protective factors in the stomach, such as mucus and bicarbonate secretion, cell regeneration, enzymatic and non-enzymatic antioxidants, blood flow and prostaglandins (2,3).

It is currently known that the two main causes of gastric ulcer are infection by *Helicobacter pylori* and chronic use of nonsteroidal anti-inflammatory drug (NSAID) (4). Other factors are involved in gastric ulcer aetiology as well, like excessive alcohol consumption, smoking, diet, genetic factors, emotional stress and use of other drugs such as corticosteroids, bisphosphonates, anticoagulants and chemotherapeutic (5, 6).

The treatment currently available of peptic ulcer includes antacids, histamine (H<sub>2</sub>) receptor blockers, proton pump inhibitors, sucralfate, bismuth salts, prostaglandins analogs, anticholinergic, among others (7). Nevertheless, most of these drugs present undesirable side effects and important drug interactions and represent a high cost for the patient, often leading to non-adhesion to the treatment (8).

Therefore, it is important that studies be carried out to search for new potential antiulcer drugs. In this context, it is largely known the folk use of medicinal plants in the treatment of gastric ulcers. Hence several experimental studies have demonstrated that medicinal plants extracts are important sources for chemical compounds with gastroprotective activity (9).

*Terminalia arjuna*, *Terminalia pallida* and *Terminalia fagifolia* exhibited antiulcerogenic activity, indicating that this genus probably has

others species with the same potential (8, 10, 11). *Terminalia catappa* L., which belongs to the family Combretaceae, is commonly known as “castanhola” (12). It has antioxidant, hepatoprotective, anti-inflammatory and antidiabetic effects, but there is no reference regarding its possible gastroprotective effect (13-15). Thus, the aim of this study was to evaluate the antiulcerogenic activity of ethanol extract (EETC) of *T. catappa* L. in *Rattus norvegicus*.

## Methods

### Plant material and preparation of ethanol extract

The aerial parts of *T. catappa* were collected in the campus of the Federal University of Piauí. The dried and powdered aerial parts (2 kg) were extracted three times over 72 h with 95% ethanol at room temperature. The extractive solution was concentrated under vacuum conditions and yielded approximately 205 g (10 % yield) of crude ethanol extract (EETC).

### Animals

Male and female Wistar albino rats, weighting 250–320 g, coming from the biotherium of the Department of Biophysics and Physiology (CCS/UFPI), maintained under controlled temperature (24 ± 1 °C) and 12–12 h light:dark cycle and allowed free access to food and water. After a fasting period of 24 h, they were acclimatized to the test environment for 2 h before the experimentation. The project was approved by the Ethics Committee for Animal Experiments – CEEA/UFPI, with the report number 42/09.

### Chemical and Drugs

The following drugs and chemicals were used: absolute ethanol (Quimex, Brazil), carbenoxolone (SIGMA, USA). All the drugs were dissolved in distilled water. The concentration of ethanol was adjusted for treatment to result in a volume of 250

mL/kg and 500 mL/kg, while carbenoxolone had its concentration set at 100 mg/kg.

### **Absolute ethanol-induced gastric ulcer**

The animals were orally treated with 5 ml/kg of water (control group, n=10), carbenoxolone (100 mg/kg, n=6) and EETB (250 mg/kg, n=8, and 500 mg/kg, n=8). After one hour, gastric lesions were induced by absolute ethanol (1 mL/animal, orally). Thirty minutes after administration of the ulcerogenic agent the animals were euthanized through an intraperitoneum overdose of sodium thiopental (100 mg/kg) and the stomachs were removed and opened along the lesser curvature. The contours of the body of the stomach and areas of ulcerative lesion (ALU) were drawn on transparent sheets, and the ALU's were measured by planimetry in mm<sup>2</sup>, and then calculating as percentage of body area of the stomach, by means of software ImageJ (16).

### **Statistical analysis**

The data were expressed as mean  $\pm$  standard error of the mean (SEM). The values were compared by one-way ANOVA followed by Tukey's post-test. The significance level was set at 5% ( $p < 0.05$ ).

### **Results**

The reduction of the absolute ethanol-induced gastric lesions was statistically significant compared the control ( $17.1 \pm 2.06$ ), in animals treated with carbenoxolone ( $4.0 \pm 0.98$ ,  $p < 0.001$ ) and EETC at doses of 250 mg/kg ( $2.5 \pm 0.82$ ,  $p < 0.001$ ) and 500 mg/kg ( $0.07 \pm 0.03$ ,  $p < 0.001$ ). Moreover, the gastroprotection induced by EETC at dose of 500 mg/kg (99.9%) was statistically higher than that one observed in carbenoxolone (Fig. 1).

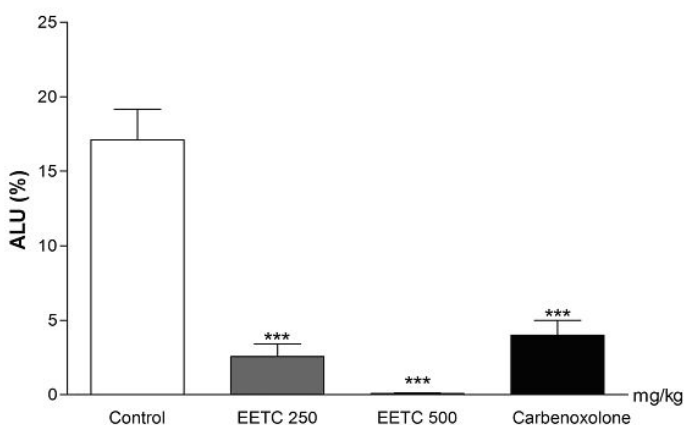


Figure 1: Percentage of area of ulcerative lesions (ALUs) in stomachs of animals treated with water (control group), EETC in different doses (250 and 500 mg/kg) and carbenoxolone. \*\*\* $p < 0.001$  versus control group.

### **Discussion**

The current study investigated the gastroprotective effect of ethanol extract of the bark from *Terminalia catappa* (EETC) in models of gastric ulcers induced by ethanol.

Absolute ethanol gastric ulcer is a classic ulcer model frequently used for the evaluation antiulcerogenic activity of medicinal plants. It is responsible for a large portion of gastric ulcers by altering the balance between the protective agents and perpetrators of the gastric mucosa. This effect is explained by reduced blood flow to the gastric mucosa, as well as reducing the production of mucus in the gastric lumen, is also reducing prostaglandins. It also has the ability to cause ischemia, increased gastric vascular permeability, increased amounts of histamine, sodium and potassium efflux and calcium influx, generation of free radicals, reduced glutathione and production of leukotrienes (17).

On the other hand, carbenoxolone is used as a standard gastroprotective drug. It is able to protect the gastric mucosa by means of increasing of prostaglandins production and inhibition of prostaglandins degrading enzymes. Furthermore, this drug increases production of mucus by surface mucous cells and production of nitric oxide, and hence promotes vasodilation, increasing blood flow

to tissue (18).

In this model, EETB showed a gastroprotective effect, reducing the gastric lesions in a dose-dependent manner when compared to control group, besides the higher dose of the extract was more effective than standard drug. This effect indicates that EETB contains biologically active molecule (s) with gastroprotective activity, likely related to factors linked to the preservation of the mucus layer and the control of blood flow in the stomach, both of them known to be altered by ethanol (19).

The genus *Terminalia* includes plants which are a rich source of secondary metabolites, such as pentacyclic triterpenoids and their glycosides derivatives, flavonoids, tannins and other aromatic compounds. Several ethnopharmacologic studies revealed the wide pharmacological potential of *Terminalia* plants, revealed by biological activities, such as antifungal, antimicrobial, antioxidant, antidiabetic, anti-HIV-1 and antimalarial ones (20). Therefore, further studies are needed to evaluate possible substances and possible mechanisms underlying this gastroprotective effect verified with *T. catappa*.

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