Gastroprotective effect of ethanol extract of the bark from *Terminalia brasiliensis* in gastric ulcers induced by ethanol

Ponte M.P.T.R.\(^1,2\)\(^*,2\), Nunes A.F.\(^1,2\), Amorim J.F.\(^1\), Paulo D.B.\(^1\), Nunes P.H.M. \(^1,2\), Martins M.C.C.\(^1\)

\(^1\)Department of Biophysics and Physiology, UFPI, Teresina-PI, Brazil
\(^2\)Medicinal Plants Research Center, UFPI, Teresina-PI, Brazil

\(^*\)mpteles@hotmail.com - phone: 558699712352

Abstract

*Terminalia* is a genus which has extensive utilization by people worldwide in traditional medicine with well-reported pharmacological activities. Accordingly, this study evaluated the gastroprotective effect of ethanolic extract of *T. brasiliensis* (EETB) 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 similar to that of the standard drug, carbenoxolone 200 mg/kg. Therefore, EETB showed gastroprotective effect which should be subject to further studies.

Keywords: *Terminalia brasiliensis*, gastric ulcer, gastroprotective effect.
PhOL

Introduction

The genus Terminalia consists of approximately 600 species of plants, widely distributed in tropical and subtropical areas of the world (1). Some species of this genus have widespread utilization on traditional medicine in Brazil, Africa and India, as well as a considerable number of those also have pharmacological activities described, such as antidiabetic, antimicrobial, antifungal, antioxidant, antispasmodic, anti-HIV-1, antimalarial (2-5). The species Terminalia brasiliensis Camb., particularly, has been recently studied due to its phytochemical potential and widespread utilization in folk medicine for gastrointestinal disorders treatment (6,7).

For more than a century, gastric ulcer was the most frequent cause of surgery, with high morbidity and mortality rates and it still affects a great number of people worldwide (8,9). The pathogenesis of gastric ulcer is, therefore, related to an imbalance between the offensive (gastric acid secretion) and defensive (gastric mucosal integrity) factors (10). The infection with Helicobacter pylori and the utilization of non-steroid anti-inflammatory drugs (NSAIDs) in long term treatments are the two main factors which increase the incidence of gastric ulcer development. Furthermore, excessive ethanol consumption induces gastric ulcer once it enhances mucosal permeability and augments the release of vasoactive products, leading to vascular damage and gastric cell necrosis, culminating in ulcer formation (11-13).

Although the modern treatment, performed mainly with antacids, histamine receptor antagonists and proton pump inhibitors, has shown good results, long-term use of some these drugs can induce serious side effects, such as increased susceptibility to pneumonia, enteric infections and hypergastrinemia. Thereby, there is a constant demand for more effective and safer treatments for which plants could be elected (14,15). Regarding the genus Terminalia importance to folk medicine worldwide and extensive pharmacology activities as well as noticing the popular indications of Terminalia brasiliensis, the present work aimed to investigate the gastroprotective activity of the ethanol extract of the bark of Terminalia brasiliensis (EETB) on ethanol-induced gastric ulcers.

Methods

Plant Material

The aerial parts of T. brasiliensis 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 (EETB).

Animal Model

Wistar rats (150-200 g), obtained from the Sectional Vivarium of the Center of Research in Medicinal Plants at the Federal University of Piauí were used. The animals were housed at 24 ± 2 °C under a 12/12 light cycle and were given ad libitum access to water and food. After a fasting period of 24 h, they were acclimatized to the test environment for 2 h before the experimentation. All experiments followed the protocols that were submitted and approved by the Ethics Committee of the Federal University of Piauí (n° 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 carbenoxolone 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

Wistar rats (n=6) were orally treated with water (5 ml/kg), carbenoxolone (100 mg/kg) or EETB (250 and 500 mg/kg). After one hour, gastric lesions were induced by using absolute ethanol (0.5 mL/100g animal p.o.). The animals were euthanized.
by an intraperitoneal overdose of sodium thiopental (100 mg/kg). 30 min after ethanol administration, the stomachs were removed and opened along the greater curvature and the area containing the gastric lesions was measured by planimetry, using a transparent grid. The ulcerous area in each animal was measured in mm² and the ulcerative lesion area (ALU) was determinate utilizing the software ImageJ (16).

**Statistical Analysis**

The data were expressed as mean ± error of the mean (SEM). One-way ANOVA followed by Tukey's test when necessary were used to compare means. The differences between groups were regarded as significant at p<0.05.

**Results**

The reduction of the absolute ethanol-induced gastric lesions area found in animals treated orally with carbenoxolone 200 mg/kg (1.45 ± 0.37, p <0.001) and EETB at doses of 250 mg/kg (11.89 ± 1.14; p <0.05) and 500 mg/kg (6.8 ± 2.31, p <0.001) were statistically significant compared to control group (19.28 ± 2.40). Moreover, the lesion inhibition induced by EETB at a dose of 500 mg/kg (64.8%) was not significantly different from the effect produced by carbenoxolone (92.5%) (Fig. 1).

**Discussion**

The current study investigated the gastroprotective effect of ethanol extract of the bark from *Terminalia brasiliensis* (EETB) 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 and drugs. Ethanol rapidly penetrates the gastric mucosa, and causes membrane damage, erosive hemorrhagic lesions with diffuse coagulative cell necrosis, cell exfoliation, marked vascular congestion and ulcer formation (17). It is known that ethanol increases the oxidative stress, by means of diminishing of catalase levels and non-protein sulphhydryl groups, resulting in an accumulation of free radicals (18). Ethanol also reduces nitric oxide level in the gastric mucosa, which is one of the most important mucosa defensive mechanisms (19). Moreover, this ulcerogenic agent dissolves the constituent gastric mucus and concomitantly decreasing the transmucosal action potential, thus increasing the flow of Na⁺ and H⁺ in the lumen. Ethanol stimulates the secretion of histamine, pepsin and H⁺ ions as well (20).

In this model, EETB showed a gastroprotective effect, reducing the gastric lesions in a dose-dependent manner. 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 (21).

The species of genus *Terminalia* are a rich source of secondary metabolites, such as pentacyclic triterpenoids and their glycosides derivatives, flavonoids, tannins and other aromatic compounds. These plants present several pharmacological activities revealed by extracts or isolated substances, like antifungal, antimicrobial, antioxidant, antidiabetic, anti-HIV-1 and antimalarial (22). Thus, further studies are needed to evaluate possible substances and mechanisms underlying this gastroprotective effect.
Acknowledgments

This work was supported by the Federal University of Piauí

References

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