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

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Abstract

Terminalia is a genus which has extensive utilization by people worldwide in tradicional 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 standart drug, carbenoxolone 200 mg/kg. Therefore, EETB showed gastroprotective effect which should be subject to further studies.

Keywords: Terminalia brasiliensis, gastric ulcer, gastroprotective effect.

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 tradicional medicine in Brazil, Africa and India, as well as a considerable number of those also have phamacological activities discribed, such as antidiabetic, antimicrobial, antifungical, antioxidant, antiespasmolitic, 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 with 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, culminanting 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 it 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 mm^2 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).

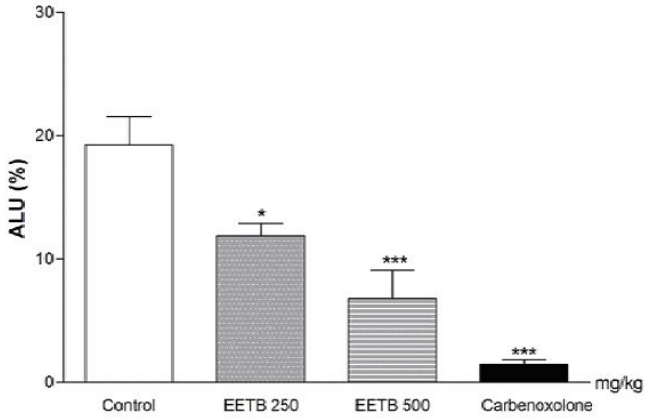

Figure 1: Percentage of area of ulcerative lesions in stomachs of female Wistar rats treated with water (control group), EETB in different doses (250 or 500 mg/kg) and carbenoxolone (200 mg/kg). * $p<0.05$ and ***$p< 0.001$ versus control group.

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 sulfhydril 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.

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References

1. Katerere, DR, Gray AI, Nash RJ, Waigh RD. Phytochemistry 2003, 63, 81; Saleem A, Husheem M, Härkönen P, Pihlaja K. J. Ethnopharmacol. 2002, 81, 327.
2. Carpano SM, Spegazzini ED, Rossi JS, Castro MT, Debenedetti SL. Fitoterapia 2003, 74, 294.
3. Khan MR, Kihara M, Omoloso AD. Fitoterapia 2002, 73, 737; Mau JL, Ko PT, Chyau CC. Food Res. Int. 2003, 36, 97; Rao BK, Sudarshan PR, Rajasekhar MD, Nagaraju N, Rao CA. J. Ethnopharmacol. 2003, 85, 169.
4. Singh V et al. Cultivation, processing and quality evaluation of medicinal & aromatic plants. Training course material. Institute of Himalayan Bio resource Technology (CSIR) 2003; 17.
5. Valsaraj R, Pushpangadan P, Smitt UW, Adsersen A, Christensen SB, Sittie A, Nyman U, Nielsen C, Olsen CE. J. Nat. Prod.1997, 60, 739.
6. Araujo, DS, Chaves, MH. Triterpenóides pentacíclicos das folhas de Terminalia brasiliensis. Quím. Nova, São Paulo, v. 28, n. 6, Dec. 2005.
7. Corrêa, MP.; Dicionário das Plantas Úteis do Brasil, Impressa Nacional: Rio de Janeiro, 1974, vol. 5, p. 195.
8. Klein-Júnior LC, Gandolfi, RB, Santin JR, Lemos M, Cechinel-Filho V, Andrade SF. 2010. Antiulcerogenic activity of extract, fractions, and some compounds obtained from Polygala cyparissias St Hillaire & Moquin (Poligalaceae). Naunym-Schmiedberg's Archives of Pharmacology 381, 121–126.
9. Yuan Y, Padol IT, Hunt RH. 2006. Peptic ulcer disease today. Nat. Clin. Pract. Gastroenterol. Hepatol. 3, 80–89.
10. Laine L, Takeuchi K, Tarnawski A. 2008. Gastric mucosal defense and cytoprotection: bench to bedside. Gastroenterology 135, 41–60.
11. Daniela M, Sewerynek E, Reiter RJ, Ortiz GG, Poeggeler B, Nistico G. 1997. Suppressive effect of melatonin administration on ethanol-induced gastroduodenal injury in rats in vivo. Br. J. Pharmacol. 121, 264–270.
12. Guslandi M, 1987. Effects of ethanol on the gastric mucosa. Dig. Dis. Sci. 5, 21–32.
13. O'Malley P, 2003. Gastric ulcers and GERD: the new "plagues" of 21st century update for the clinical nurse specialist. Clin. Nurse Spec. 17, 286–289.
14. Malfertheiner P, Chan FKL, McColl KEL. 2009. Peptic ulcer disease. The Lancet, 374, 1449–1461.
15. Sheen E, Triadafilopoulos G. 2011. Adverse effects of long-term proton pump inhibitor therapy. Digestive Diseases and Sciences 56, 931–950.
16. Morimoto Y, Shimohara K, Oshima S, Sukamoto K. 1991. Effects of the new antiulcer agent kb-5492 on experimental gastric mucosal lesions and gastric mucosal defensive factors, as compared to those of terpenone and cimetidine. Jpn J Pharmacol, 57: 495-505.
17. De-Faria, FM, Almeida, ACA, Luiz-Ferreira, A, et al. Mechanisms of action underlying the gastric antiulcer activity of the Rhizophora mangle L. Journal of Ethnopharmacology 2012; 139(1): 234–243.
18. Freitas, FFBP, Fernandes, HB, Piauilino, CA, et al. Gastroprotective activity of Zanthoxylum rhoifolium Lam. in animal models. Journal of Ethnopharmacology 2011; 137(1): 700–708.
19. Brzozowski, T, Konturek, PC, Sliwowski, Z, et al. Interaction of nonsteroidal anti-inflammatory drugs (NSAID) with Helicobacter pylori in the stomach of humans and experimental animals. Journal of Physiology and Pharmacology 2006; 57, 67–79.
20. Takayama, C, De-Faria, FM, Almeida, ACA, et al. Gastroprotective and ulcer healing effects of essential oil from Hyptis spicigera Lam. (Lamiaceae). Journal of Ethnopharmacology 2011; 135(1), 147-155.
21. Lemos, M, Santin, JR, Júnior, LCK, et al. Gastroprotective activity of hydroalcoholic extract obtained from the leaves of Brassica oleracea var. acephala DC in different animal models. Journal of Ethnopharmacology 2011; 138(2), 503-507.
22. Araújo, DS, Chaves, MH. Pentacyclic triterpenoids from the leaves of Terminalia brasiliensis. Química Nova 2005; 28(6), 996-999