Evaluation of the gastroprotective activity of Talinum paniculatum

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Introdução: Gastric ulcers are common digestive disorders which are caused by multifactorial processes including stress, alcohol abuse and non-steroidal anti-inflammatory drugs, smoking, H. pylori and reflux, which induce, through different mechanisms, an imbalance between aggressive or mucosal defense factors. Antibiotics and proton pump inhibitors (e.g. omeprazole) are the main type of drugs used in ulcer treatment, however there is a need to discover new drugs with antiulcer potential, which have fewer side effects and better efficiency. The natural products are a great source of new bioactive compounds that may lead to the discovery of new drugs for the treatment of gastric ulcers. The Brazilian biome has a remarkable potential to be explored in this field. The species Talinum paniculatum, also known as "Erva Gorda" has shown to be a good nutritional source, besides its leaves are used in traditional medicine to treat inflammatory diseases, edemas, scars and skin lesions. Bioactive compounds such as steroidal saponins, tannins and triterpenes were found in the species. In the literature, T. paniculatum leaves also had revealed a high level of phenolic compounds and antioxidant activity in DPPH assay. Due to these discoveries, T. Paniculatum shows to be a species with potential to be explored regarding its gastroprotective activity, that is the main goal of the present study.
Objetivos: General Purpose To evaluate the gastroprotective activity of the ethanol-soluble fraction obtained from the leaves of Talinum paniculatum (ESTP). Specific objectives To evaluate the gastroprotective activity of ESTP against ethanol-induced gastric ulcer; To evaluate the existence of a dose-response relationship in the gastroprotective activity of ESTP; To evaluate ESTP mechanisms of action.
Metodologia: Animals Animal care and experimental procedures followed international standards and ethical guidelines on animal welfare. The experiments were carried out after approval by the institutional ethics committee of the University of Vale do Itajaí (UNIVALI) (Approved number: 021/22p). Male Swiss mice (25-30 g, aged between 3 and 4 months were housed in polypropylene boxes under standard laboratory conditions (12-hour light/dark cycle, and temperature 22 ± 2 ¿C), with free access to feed and water. Eight hours before the experiments, the animals kept fasting. Induction of acute gastric lesions by ethanol. The gastroprotective activity of ESTP was evaluated as previously described by Morimoto et al. (1991) with a few modifications. The mice were divided into groups (n = 6), called: Naive (not received any treatment); Vehicle (VEH: negative control, saline 10 mL/kg, p.o.); Omeprazole (OME: positive control, 20 mg/kg, p.o.), ESTP in three different dosages (30, 100 and 300 mg/kg, p.o. 30 mg/kg, i.p.). The gastric lesions were induced by given to the mice 60% ethanol / 0.3 M HCl (5 mL/kg, p.o.) After one hour of the ethanol administration, the animals were euthanized. The stomachs were dissected and opened along greater curvature and photographed. The

images obtained were used to measure the area of the lesion (mm2) using the ImageG® program. Mechanism of action The gastroprotective mechanisms of ESTP were evaluated as described by Matsuda et al. (1999) with a few modifications. Mice (n = 6) were treated with: an NP-SH chelator (NEM - 10 mg/kg, i.p.), a non-selective NO synthase inhibitor (L-NAME - 70 mg/kg, i.p.), and an inhibitor non-selective cyclooxygenase (indomethacin - 10 mg/kg, i.p, respectively. After 30 minutes, the animals received vehicle (VEH: saline, 10 mL/kg, v.o.) or ESTP (30 mg/kg, i.p.) After 1h, all mice received 60% ethanol / 0.3 M HCl (5 mL/kg, p.o.) to induce gastric lesions. After 1 h of ingestion of acidified ethanol, the animals were euthanized. The stomachs were removed and analyze as described previously.

Resultados: The ethanol induced a mean lesion area in the vehicle group of 11.36 ± 1.65 mm2. Mice that received omeprazole 20 mg/kg has a similar lesion area (11.48 ± 2.52 mm2). ESTP at doses of 30 or 100 mg/kg given orally did not induce a gastroprotective effect. At a dose of 300 mg/kg a reduction of 54% in the lesion area compared to vehicle ($p > 0.06$) was observed. To assess whether this effect could be improved by increasing bioavailability, we further evaluated the effect of intraperitoneal ESTP, which significantly reduced the lesion area by 82% ($p > 0.001$).The pre-treatment with L-NAME (a non-selective nitric oxide synthase inhibitor) or NEM (a non-protein sulfhydryl group chelator) did not interfere with the gastroprotective action of ESTP that reduced the lesion area significantly compared to their respective vehicle groups, even though NEM have exacerbated gastric lesions induced by ethanol. However, when mice were pre-treated with indomethacin (a non-selective inhibitor of cyclooxygenases), the ESTP 30 mg/kg completely lost the ability to decrease the gastric lesions induced by the ethanol, instead, the lesion area was significantly increased in this group.

Considerações finais: The data obtained herein showed a dose-response gastroprotective effect of ESTP. Moreover we have demonstrated that its effect is improved when given by intraperioneal route, indicating low biodisponibility of the product by oral route. In addition the effect of ESTP seems to be dependent of prostaglandins. Finally, our data contribute to validate the traditional use of T. paniculatum for gastric disorders.

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