Material e Métodos

Os óleos essenciais foram obtidos no Departamento de Química Orgânica e Inorgânica da Universidade Federal do Ceará e Cetamina foi obtida na sua forma comercial (Ketalar®, Parke-Davis, Brasil).

Foram utilizados camundongos albinos (*Mus musculus*) variedade Swiss webster, adultos do sexo feminino, pesando entre 25-30 g, provenientes do Biotério Central da Universidade Federal do Ceará, mantidos à temperatura ambiente, com ciclos de 12 em 12 h, recebendo ração padrão (Purina Chow) e livre acesso a água.No modelo do tempo de sono induzido por Cetamina 150 mg/kg os animais foram divididos em 11 grupos. O primeiro grupo (controle) foi tratado oralmente com veículo (VEH) (Tween 80 à 2% em água destilada, 10 ml/kg). Os demais grupos foram tratados oralmente com óleos essenciais de *Psidium guyanensis* (OEAA), *Psidium pohlianum* (OEAD), *Psidium guajava* (OEAG), *Rosmarinus officinalis* (OEA) e *Lippia alba* (OEC), nas doses de 200 e 400 mg/lg. Uma hora depois do tratamento, o tempo de sono foi induzido pela administração intraperitoneal de cetamina (150 mg/kg). Iniciado o período de sono, os animais, em seus respectivos grupos, foram posicionados em decúbito dorsal, em local de adequada observação. Os animais foram observados durante todo o período de sono, sendo este tempo registrado em minutos, tendo como situação de retorno ao estado de alerta o momento no qual o animal alterou sua posição de decúbito.

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Effect of *Plantago australis* leaves on different gastric ulcer models

M.E. Bürger*; P.C. Ghedini; B. Baldisserotto; N.M.S. Palmeiro; C.E. Almeida; C.F. Lenzi; A.C. Silva; C.Q. Oliveira

Departamento de Fisiologia, Universidade Federal de Santa Maria, 97105-900, Santa Maria, RS, Brazil
mariliseeb@smail.ufsm.br

Abstract

The anti-ulcerogenic effect of the crude ethanolic extract (CEE) of *Plantago australis* leaves was tested against ethanol-, indomethacin-, and cold restrain-induced stress ulcers. The CEE (500 and 1000 mg/kg) reduced the lesion index (LI) and the ulcer index in ethanol-induced ulcers, and the dose of 1000 mg/kg increased the amount of mucous. The highest dose of the CEE reduced the LI of cold restraint-induced stress ulcers when compared to the control group. The indomethacin-induced ulcers were not affected by this extract.

The genus *Plantago* (Plantaginaceae) has several species with laxative, diuretic, anti-inflammatory, anti-bacterial, anti-diarrhoeic, cicatrizing, and other medicinal properties[1]. One of these species, *Plantago australis* Lam., is found in almost all Latin America and west of United States. This plant is commonly used to give medical care to throat infections, wounds, boils and varicose veins. In addition, it has been used to treat inflammations and diarrhoea[2]. Therefore, the aim of this study was to investigate the effect of the crude ethanolic extract (CEE) of *P. australis* leaves on different gastric ulcer models on rats.

The doses of 500 and 1000 mg/kg of the *P. australis* CEE reduced the lesion index (LI) of ethanol-induced ulcers in 27.65% (4.16 ± 0.40) and 40.69% (3.41 ± 0.35), respectively, when compared with the control group (5.75 ± 0.21). These doses of the CEE also decreased in 81.3% (12.0 ± 2.97) and 95.8% (2.66 ± 0.49), respectively, the ulcer index (UI) with relation to the control group (64.2 ± 5.76). The dose of 1000 mg/kg increased the mucous secretion (328.76 ± 10.71) with relation to control group (252.46 ± 12.99), but the dose of 500 mg/kg did not change this parameter (282,63 ± 26,39). The CEE did not showed any significant effect on the determination of non-proteic sulphide groups (GSH) or on the indomethacin-induced ulcers. The highest dose of the CEE reduced the LI of cold restraint-induced stress ulcers (4.16 ± 0.60) when compared to the control group (6.5 ± 0.76).

Ethanol is highly corrosive to the rat gastric mucosa. It promotes superficial cellular necrosis and release of histamine and leucotrine C4. These tissue-derived mediators act on gastric microvasculature, starting events that result in mucosal and possibly submucosal tissue destruction[3]. The results of our

study suggested P. australis CEE prevented the necrotic action of these mediators on the gastric microvasculature.

Indomethacin inhibits gastroduodenal bicarbonate secretion due to the reduction of endogenous prostaglandin biosynthesis as well as gastric mucosal blood flow. When an anti-ulcer agent reduces the effect of indomethacin, probably its effect is through the mediation of endogenous prostaglandins[4]. As *P. australis* CEE had no effect on indomethacin-induced lesions, it is suggested that its action is not related to the cytoprotection mediated by prostaglandins.

An increase of the acid secretion is usually associated with the occurrence of stress-induced lesions[5]. Typical antisecretory drugs, which are H2-receptor antagonists (cimetidine, ranitidine, and famotidine), inhibited stress-induced ulcers[6,7]. The *P. australis* CEE (dose of 1000 mg/kg) reduced the LI of cold restraint-induced stress ulcers, but additional studies are needed to determine if the effect of this CEE is also due to a decreased acid secretion.

Material and Methods

The plant (*P. australis*) was collected in Santa Maria, Rio Grande do Sul state, South Brazil, on October and November 1997. A voucher specimen was registered in the herbarium of the Department of Biology of the Universidade Federal de Santa Maria (SMDB nº 6369). The leaves were maintained in a ventilated oven (40 ºC) for drying and stabilization, and the material was then pulverized in a Willye mill. The obtained CEE (70%) was lyophilized and stored at -12 ºC. The yield of the dried residue was 18.74%.

The procedures for ethanol-induce ulcers were an adaptation of the method of Robert et al[8]: after a 24 h fast, male Wistar rats (200-300 g) (groups of 6 animals) received by gavage 500 or 1000 mg/kg CEE. Control animals were similarly treated with distilled water only. Sixty minutes after this procedure, every animal received by gavage 1ml of ethanol 60%. One hour later the rats were killed, the stomachs removed, and opened along the small curvature to assess the lesion index (LI) (lesions preceding ulcers) and the ulcer index (UI). The stomachs were then divided in half for mucous quantification according Corne[9] and determination of non-proteic sulphide groups according to Sedlak and Lindsay[10].

For indomethacin-induced ulcers, groups of 6 male rats (24h fasting) received by gavage distilled water (control), 500 or 1000 mg/kg CEE, and ranitidine (50 mg/kg). After 60 min indomethacin was injected subcutaneously (30 mg/kg), according to Djahanguri[11]. The rats were killed six hours later and the LI and UI determined.

Cold restraint stress ulcers were induced according to Senay and Levine[12]. After a 36 h fast, groups of 6 female Wistar rats (200-300 g) received by gavage distilled water (control), 500 or 1000 mg/kg CEE, and ranitidine (50 mg/kg). After 60 min the animals were immobilized individually at 4 °C for 4 h. Then the rats were killed, the stomachs removed, and the LI and UI determined.

All values are expressed as mean±SEM, an statistical differences among the experimental groups were assessed by one-way analysis of variance and the Dunnet test, with the aid of the Instat 2.06 test. The minimum significant level was $P<0.05$.

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