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Effect of catechin on gastric ulcers induced by ethanol in rats

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Abstract

Catechins is a class of flavonoid compounds present in many plants, including *Terminalia fagifolia*, *Brysonima crassa, Camellia sinensis* and *Vitis sp.* In this study, we evaluated the possible antiulcerogenic activity of (+)-catechin administered orally in the model of gastric ulcer induced by ethanol. Females *Rattus norvegicus* (168 ± 2.5 g) distributed in groups of 6-7 animals, fasted for 24 hours were treated orally with water (5 mL/kg, control group), vehicle (1% Tween-80 in water, 5 mL/kg), catechin (1, 10, 50 and 125 mg/kg) and carbenoxolone (200 mg/kg). After 1 hour of treatment, gastric ulcers were induced by administration of 99.5% ethanol orally (5 mL/kg). Thirty minutes later, all animals were euthanized by an overdose of sodium thiopental (100 mg/kg). After laparotomy, the stomachs were removed and opened by the lesser curve to determine the area of ulcerative lesion (AUL), calculated as a percentage of body area of the stomach (mean ± SD) using the *ImageJ* software. The data were analyzed by ANOVA followed by Dunnett's post-test. There was no significant difference ($p>0.05$) in the AUL of the animals treated with catechin at doses 1, 10, 50 and 125 mg/kg compared to groups administered water or vehicle. Carbenoxolone showed significant reduction ($p< 0.001$) of the AUL compared to control group. Therefore, catechin, administered orally, does not present antiulcer activity in ethanol-induced gastric ulcers in rats.

Keywords: catechin, antiulcerogenic activity, flavonoids

Introduction

Flavonoids are a class of polyphenolic compounds and are widely distributed in vegetables, fruits, seeds, flowers, bark and other products derived from these, such as wine and tea [1,2,3,4,5]. An important effect of flavonoids is their ability to act as antioxidants [1,3]. *In vitro* experiments also demonstrated that these compounds have anti-inflammatory, antiallergic, antiviral and anticarcinogenic properties [3].

Catechins is a class of flavonoid compound present in many plants, including *Brysonima crassa, Camellia sinensis* and *Vitis sp.* [6,7,8,9]. The presence of (+)-catechin has been detected in the ethanol extract from leaves of *Terminalia fagifolia* [10]. Studies indicate that flavonoids have antioxidant properties and this property can be related to the presence of the gastric antiulcer activity in some plants [8]. Catechins have been widely reported in the literature due to their antioxidant and antitumor activities [11].

The ethanol extracts of the leaves and bark of *Terminalia fagifolia* present antiulcerogenic activity in the model of ethanol-induced gastric ulcer, as well as cytotoxic and antioxidant activities [10,12]. Literature report that catechin (25 mg/kg) administered intraperitoneally presents gastroprotective activity in histamine-induced ulcers in rats [13]. The aim of this study was to evaluate the possible antiulcerogenic activity of (+)-catechin administered orally in the model of gastric ulcer induced by ethanol in rats.

Methods

Animals

Rattus norvegicus females were used, with body mass 168 ± 2.5 g, from the Animal Facility of the Center for Research on Medicinal Plants - UFPI. The rats were adapted at the Experimental Research Laboratory, Department of Biophysics and Physiology, UFPI, staying in polyethylene cages, lined with wood shavings, and kept under controlled conditions. Water and feed were offered *ad libitum.* All animals were handled in accordance with the approval of the Ethics Committee on Animal Experimentation of UFPI under number 042/09.

Induction of ulcers and treatment

Twenty-four hours before the experiment, the animals were subjected to a fasting with free access to water. After the fasting period, animals were randomized (6-7 animals) in seven groups and treated orally with distilled water (5 mL/kg, control group), vehicle (1% Tween-80 in water, 5 mL/kg), catechin (1, 10, 50 or 125 mg/kg) and carbenoxolone (200 mg/kg, standard group). One hour after treatment, gastric ulcers were induced by administration of 99.5% ethanol at a dose 5 mL/kg orally. Thirty minutes later, all animals were euthanized by an overdose of sodium thiopental (100 mg/kg). The animals were placed in a supine position on operating table and underwent laparotomy. The stomachs of each group were removed and then opened by the lesser curvature, washed and placed between two glass plates, with a slight compression of a plate over another for better observation of ulcers.

Determination of the area of ulcerative lesion (AUL)

From the observation of the stomach, the magnitude of the ulcerative effect of ethanol on the gastric mucosa will be evaluated by determining the area of ulcerative lesions (AUL) of each stomach.

The AUL is calculated by dividing the sum of the areas with ulcerative lesions by the total area of the body of the stomach, using the *ImageJ* software, and expressed as a percentage of body area of the stomach.

Statistical Analysis

Results are presented as mean and standard error of the mean (Mean ± SEM) for each group.

The statistical analysis was performed by ANOVA followed by Dunnett's post-test for comparison between groups. The significance level is set at $p<0.05$.

Results

There was no significant difference ($p>0.05$) in the AUL of the animals treated with catechin at doses 1, 10, 50 and 125 mg/kg compared to control group and vehicle. Carbenoxolone elicited a significant reduction ($p< 0.001$) of 92% in AUL compared to control group (Table 1).

see Table 1.

Discussion

Oral administration of ethanol clearly produced considerable necrotizing areas in gastric mucosa in all experimental and control group. Induction of stomach ulcers after treatment with ethanol results from the solubilization of the constituents of gastric mucus associated with an increased flow of Na^+ and K^+ within the lumen, pepsin secretion and the loss of H^+ ions and histamine present in the lumen. Ethanol is also responsible for the reduction of tissue levels of DNA, RNA and proteins causing damage to the gastric blood flow and ulcerated areas [8].

The lesions induced by ethanol in the stomach are also associated with excessive production of free radicals, which attack essential cell constituents such as nucleic acids, proteins and lipids as well as damage to the membranes, cell death, exfoliation and epithelial erosion [14,15]. In recent years, a great interest in the study of antioxidants has been due mainly to the findings on the effects of free radicals in the body. Antioxidants are known for their excellent ability to inhibit lipid peroxidation and scavenge free radicals [8].

Flavonoids have a considerable performance in antioxidant activity mainly due to the presence of a catechol nucleus [16]. Catechins (catechin, epicatechin and epigallocatechin-3-gallate) are among the main flavonoids responsible for protecting the body against reactive oxygen species [2]. Many studies indicate the antiulcerogenic property of flavonoids and that this may be related to antioxidant activity [17]. Studies have shown that catechin and epicatechin are better free radical scavengers than the antioxidant compounds that are already recognized in the literature as α-tocopherol, L-ascorbate (vitamin C) and β-carotene [4,10].

In Brazil, many studies of medicinal plants has been performed in order to treat digestive diseases, among them gastric ulcers [18]. Experimental studies performed in the Center for Research on Medicinal Plants-UFPI detected the presence of antiulcer activity in ethanol extract of leaves and stem bark *Terminalia fagifolia* [12]. The antioxidant activity present in the ethanolic extract of leaves of this plant has been justified by the main substance isolated, (+)-catechin [10]. Gastroprotective activity was also noted in *Byrsonima crassa* and the presence of catechin and epicatechin in methanol extract of leaves of *B. crassa* [8]. Studies have reported the beneficial effects of flavonoid epigallocatechin-3-gallate in the healing of gastric ulcers due to their antioxidant activity, prostaglandin synthesis and ability to form mucin [19].

In this study, catechin orally at doses 1,10,50 and 125 mg / kg does not show antiulcer activity in ethanol-induced gastric ulcers in rats, thus indicating that this substance alone is not related to the antiulcerogeic activity demonstrated for the ethanolic extract of the leaves and bark of *Terminalia fagifolia* using this experimental model of gastric ulcers in rats.

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Treatment	Dose (oral)	Area of ulcerative lesion (%) Mean ± SEM	Protection (%)
Water (control)	5 mL/kg	20,94 ± 2,28	0,0
Tween-80 1%	5 mL/kg	17,42 ± 1,71	NS
Catechin	1 mg/kg	19,83 ± 3,42	NS
	10 mg/kg	18,70 ± 3,72	NS
	50 mg/kg	19,30 ± 6,16	NS
	125 mg/kg	26,28 ± 1,20	NS
Carbenoxolone	200mg/kg	1,67 ± 0,85*	92,2

Table 1: Area of ulcerative lesion (%) in stomachs of female Rattus norvegicus treated with water (5ml/kg), 1% Tween-80 (5ml/kg), catechin (1, 10, 50 and 125mg/kg) and carbenoxolone (200 mg / kg).

* p <0.001 compared to control and 1% Tween-80 (ANOVA and Dunnett's post-test). NS: no significant difference.