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Original Article

Acute toxicity and antimicrobial activity of leaf tincture *Baccharis trimera* (Less)

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ABSTRACT

Background: The present study aimed to evaluate the possible acute oral toxicity of *Baccharis trimera* leaf dye as well as its antimicrobial activity.
Method: Organization for Economic co-operation and development (OECD) 423 was used to assess acute oral toxicity and as per protocol a dose of 2000 mg/kg of tincture was administered to Wistar rats, male and female, and observed for 14 days. Biochemical and hematological analyzes were performed with sample collected of rat. The dye was evaluated for antimicrobial activity by agar diffusion and microdilution methods, which allow to determine the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) and antibiofilm potential.
Results: The results showed that there was no loss of animals and no significant changes in hematological and biochemical parameters after oral administration of 2000 mg/kg of tincture and was considered safe by the OECD, classified as category 5. The dyeing also showed an important antimicrobial activity against gram positive and gram negative bacteria also significantly decreased the microbial biofilm.
Conclusion: The tincture of *B. trimera* leaf when given orally once can be considered safe and has a relevant antimicrobial potential that should be elucidated in subsequent research.

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At a glance commentary

Scientific background on the subject:

Despite advances in studies for the use of medicinal plants, many people associate the natural origin of products with low toxicity and lack of drug interactions. This belief is considered erroneous, since the plants are xenobiotic and they undergo biotransformation in the human metabolism, being able to form toxic products.

What this study adds to the field:

Considering the wide variety of therapeutic indications and the popular use of the *B. trimera* species, the toxicological study and antimicrobial properties of this plant are relevant for a better knowledge of the effects caused, as well as the safety in the use of the same as a therapeutic resource.

Medicinal plants are misused because they are believed to be a natural product that do not cause toxic or adverse effects, and the popular use of plants by many communities and ethnic groups serves as validation of the effectiveness of these medicines. However, toxicological studies show that plants, in some cases and when used exacerbated, can be harmful or even, in high doses, lethal. The same plant can contain medicinal and therapeutic parts, and also parts with toxic substances harmful to human and animal organisms [1,2].

The frequent appearance of resistant and multi-resistant strains to the usual antimicrobials and the investigation for low-side effect drugs have been contributed to the search for alternative treatments against diseases caused by microorganisms [3,4]. An important public health problem are the nosocomial infections caused by strains resistant to available antibiotics by the pharmaceutical industry, which makes the search for new antimicrobial agents extremely important [5].

A plant belonging to the family Asteraceae, whose species has been identified in pharmacology articles as *Baccharis trimera* (Less.) DC or even *Baccharis genistelloides* var. *Trimera* (Less.) Baker (which are data of *Baccharis crispa* [6]. *B. trimera* (Less) DC) it is a small tree, found in rocky soils and sandy fields of southern Brazil, Paraguay, Uruguay and Argentina. In Brazil, it is popularly known a carqueja, carqueja-amarga, carqueja-do-mato, vassoura [7,8]. Studies published about *B. trimera* describe analgesic [9,10], muscle relaxant effects [11], antidiabetic [12], antioxidant [13], anti-inflammatory [14,15] anthelmintic activity [16] and hepatotoxicity [17]. Silva et al. [8] studied the acute toxicity of *B. trimera* tincture, but only evaluated the mortality and classified the plant as category 5, relatively safe. In subacute toxicity, levels of the enzymes aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were reduced after 28 days of treatment at 200 and 400 mg/kg doses of *B. trimera* dye.

Studies demonstrate the antimicrobial activity of crude extract [18] and essential oil [19,20] against Gram negative, Gram positive and fungi.

Considering its variety of therapeutic indications and its popular use, it is relevant to evaluate the detailed acute toxicity and antimicrobial activity of *B. trimera* tincture for a better knowledge of the effects caused by this plant, as well as the safety of its use as a therapeutic resource.

Materials and methods

Vegetable sample

The *B. trimera* tincture used in the experiments was purchased by Flores e Ervas Com. Fazenda Ltda. (Piracicaba, São Paulo, Brazil), in 2015, registered under the number NPT.0215/082 (Responsible Pharmaceutical: Karina da Silva). The *B. trimera* leafs were macerated and crushed with ethanol (68%) solution.

Animals

For the acute toxicity, Wistar adult rats, male and female, of 6 and 8 weeks of age, weighing 160–200 g, from Biotério Central da Universidade Federal de Santa Maria (UFSM) were used. The animals were separated according to sex and were acclimatized to the new environment for 5 days before the start of the experiment. All of the animals were housed on polypropylene cages, the environment temperature was kept at 24 °C ± 2 °C, and the relative humidity at 45–55%, with a light/dark cycle of 12:12 h. The rats were treated with commercial food and *ad libitum* water. The animals were manipulated and the experiments were performed with approval of the UFSM Ethics Committee (CEUA UFSM; protocol 050/2014).

Evaluation of acute toxicity

The acute oral toxicity of *B. trimera* tincture was evaluated in rats of both sexes, as preconized by the guidance of OCED (Organization for Economic Cooperation and Development-423, approved in 17 of December of 2001) with modifications [21].

According to the guidance of OCED 423, these experiments were performed twice with the use of 3 animals of each sexual category by stage. The animals of the test group received a unique dose of 2000 mg/kg of *B. trimera* tincture, with the help of esophageal probe. The control group was treated by the same route with ethanol (68%) at a 10 mL/kg concentration. The dose used in the experiment of acute toxicity was chosen from dose 2000 mg/kg, as described in the OCED guide. According to the OCED 423 protocol, this assay was performed in two independent experiments to estimate the LD_{50}. In total, 12 male and 12 female rats were used.

After the administration, the animals were individually observed during the first 30 min and daily. After that, the observation was extended for 14 days. The analysis included changes in skin, bristle, eyes and mucosa of respiratory tract, somatomotor activity and behavior. The attention was directed to the analysis of tremors, convulsion, salivation and diarrhea. The weight of each animal was determined just before

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