

Preliminary tests on acute oral toxicity and intestinal motility with extract of pulverized bark of *Endopleura uchi* (Huber) Cuatrec. (Humiriaceae) in mice

Testes preliminares de motilidade intestinal e toxicidade oral aguda com extrato de cascas pulverizadas de *Endopleura uchi* (Huber) Cuatrec. (Humiriaceae) em camundongos

Pruebas preliminares de motilidad intestinal y de toxicidad oral aguda con extracto de corteza en polvo de *Endopleura uchi* (Huber) Cuatrec. (Humiriaceae) en ratones

Flávio Augusto Sanches Politi

Departamento de Fármacos e Medicamentos, Faculdade de Ciências Farmacêuticas de Araraquara, Universidade Estadual Paulista "Júlio de Mesquita Filho", Araraquara, São Paulo, Brasil

Hérica Regina Nunes Salgado

Departamento de Fármacos e Medicamentos, Faculdade de Ciências Farmacêuticas de Araraquara, Universidade Estadual Paulista "Júlio de Mesquita Filho", Araraquara, São Paulo, Brasil

Raquel Regina Duarte Moreira

Departamento de Princípios Ativos Naturais e Toxicologia, Faculdade de Ciências Farmacêuticas de Araraquara, Universidade Estadual Paulista "Júlio de Mesquita Filho", Araraquara, São Paulo, Brasil

Rosemeire Cristina Linhari Rodrigues Pietro

Departamento de Fármacos e Medicamentos, Faculdade de Ciências Farmacêuticas de Araraquara, Universidade Estadual Paulista "Júlio de Mesquita Filho", Araraquara, São Paulo, Brasil

ABSTRACT

The aim of this work was to analyze the acute oral toxicity and the effects on intestinal motility of the extract obtained through decoction 20% (m/v) of *Endopleura uchi*, popularly known as "uxi-amarelo", a native plant from the Brazilian Amazon. The plant is used indiscriminately against several diseases: arthritis, cholesterol, diabetes, ulcers, myomas, and intestinal illnesses in general, among others. The present results show that there were no significant alterations in intestinal motility and that the extract does not present signs of toxicity, showing its safety for consumption purposes.

Keywords: *Endopleura uchi*; Gastrointestinal Motility; Acute Toxicity; Phytotherapy; Plant Extracts.

INTRODUCTION

Endopleura uchi (Huber) Cuatrec. [synonym of *Sacoglottis uchi* Huber] (Humiriaceae) is a Brazilian species native to the *terra firme* (non-flooded) forests and is scattered throughout the Amazon Basin. The plant is locally known as *uchi*, *uxi-amarelo*, *cumatê*, *pururu*, *uxi-liso*, *uxi-ordinário* or *uchi-pucu*^{3,7}. Although no studies have been conducted to confirm its efficacy or safety, the bark from this plant is widely sold at fairs, markets and even magistral pharmacies

throughout the country for the treatment of arthritis, cholesterol, diabetes, inflammation and intestinal diseases². Based on this information and considering that the use of this drug occurs mainly in the form of maceration or tea, the aims of this study were to conduct a preliminary evaluation of the effects of the drug decoction (20% w/v) on mice intestinal motility and to verify its acute oral toxicity.

This research and both of its assays were approved by the Research Ethics Committee of Faculdade de Ciências Farmacêuticas, Universidade Estadual Paulista "Júlio de Mesquita Filho" (UNESP), Araraquara, São Paulo State, Brazil, protocol CEP/FCF/CAr. N. 40/2008.

MATERIALS AND METHODS

PLANT MATERIAL AND EXTRACT PREPARATION

Finely pulverized *Endopleura uchi* (Huber) (Humiriaceae) bark was purchased from the company Sítio da Mata (batch: Uxi03/01; Prod. Inscr.: 024.308.176; harvest: 01/Sep/2005; expiry date: 30/Sep/2008), located on Rodovia Cajuru, Cássia dos Coqueiros, São Paulo State, Brazil.

Correspondence / Correspondência / Correspondencia:

Rosemeire Cristina Linhari Rodrigues Pietro
Faculdade de Ciências Farmacêuticas de Araraquara
Rodovia Araraquara-Jaú, km 1
CEP: 14801-902 Araraquara-São Paulo-Brasil
Tel: +55 (16) 3301-6965
E-mail: pietrorc@fcar.unesp.br

Translated by / Traduzido por / Traducido por:

American Journal Experts

The aqueous extract was prepared by decoction at 20% (w/v), using 200 g of the drug in 1,000 mL of distilled water. The solutions were placed in beakers and then on a plate heated to 100° C. Following 15 min of boiling, these solutions were filtered and then lyophilized. The extracts obtained were weighed and stored in desiccators to prevent moisture absorption.

ACUTE ORAL TOXICITY TEST IN MICE

According to Guideline 423 of the Organisation for Economic Co-operation and Development (OECD), 20 adult male Swiss mice (*Mus musculus*) weighing 29-35 g were used in the study. They were divided into four groups (n = 5), according to the doses received by oral gavage⁶. Single doses were used throughout the study. The administered concentrations were 500 mg/kg, 1,000 mg/kg and 2,000 mg/kg, and distilled water was used for the control group. The animals were kept in cages inside a room with a 12 h light/dark cycle at 20° C. They were fasted for 12 h before and received food and water again 4 h after the administration of the extracts¹. Following treatment, the mice were observed at 30, 60, 120, 240 and 360 min and every 24 h during a 14-day period. During examination, the following parameters were assessed: heart rate, respiratory rate, number of deaths and side effects (e.g., piloerection, diarrhea, sialorrhea, hypnosis and seizures).

INTESTINAL MOTILITY TEST IN MICE

Two experimental groups were assessed during this study (n = 10). The treatment group was exposed to aqueous extract of *E. uchi* (200 mg/kg), and the negative control group was treated with saline solution (10 mL/kg). Both groups received the oral solution via gavage. The animals received a suspension of 10% activated charcoal in a 5% gum arabic solution (0.5 mL/animal) also by gavage 90 min after the initial treatment. The mice were sacrificed in a CO₂ chamber 45 min after charcoal treatment and immediate removal of the intestine, from the pylorus to the beginning of the cecum, was performed. For analyses, we measured the total length of the small intestine and the distance traveled by the activated charcoal suspension. The activity of intestinal transit was determined according to the methods used in Janssen and Jageneau⁴ and Wong and Wai⁸. Statistical analysis was performed using a Student's t-test (P < 0.05).

RESULTS

The results revealed no signs of systemic toxicity in mice treated with *E. uchi* aqueous extract obtained by decoction at 20% (w/v). Death or changes in animal behavior were not observed, nor were there any changes in animal body weight.

Compared to the negative control (saline), the assay measuring intestinal transit in mice demonstrated that there was a reduction in the distance activated charcoal traveled

following administration of the extract obtained by decoction at 20% (w/v) of powdered *E. uchi* bark (Table 1). Concerning P < 0.05, however, the calculated "t" value (t = 0.9057) was lower than the standard "T" value (T = 2.101), suggesting that the extract treatment did not differ significantly from the control.

Table 1 – Distance traveled by activated charcoal in the intestine of mice following administration of either the decoction at 20% (w/v) of powdered *E. uchi* bark or the control saline solution*

Treatment	Dose (mg/kg)	Mean distance (cm)
Decoction 20%	200 mg/kg	43.81 ± 11.84
Negative control	10 mL/kg	48.00 ± 8.58

* The results represent the average of three determinations ± the standard deviations.

DISCUSSION

The assay measuring the intestinal transit distance in mice demonstrated that there was a small reduction in distance traveled by the activated charcoal in animals treated with the extract obtained by decoction at 20% (w/v) when compared to the negative control (saline). According to the results of the Student's t-test, however, the distance traveled by the activated charcoal in the extract-treated sample was not statistically different from the distance observed in the control group. Based on this analysis, we cannot conclude that the extract treatment altered the intestinal motility of the animals. In order to produce more comprehensive and conclusive results, single compounds or fractions of the extract could be tested in the same model.

According to the results from the acute oral toxicity tests in mice, systemic toxicity was not observed following administration of the extract obtained by decoction at 20% (w/v). Exposure to the extract was not lethal nor did it result in any observed physiological or behavioral changes in the animals. According to the toxicity classification of Larini⁵, which classifies oral toxic agents as extremely toxic (LD₅₀ lower or equal to 25 mg/kg), highly toxic (LD₅₀ between 100 and 500 mg/kg), moderately toxic (LD₅₀ between 500 and 2,000 mg/kg) and little toxicity (LD₅₀ above 2,000 mg/kg), our results indicate that *E. uchi* bark extract exhibits low toxicity.

E. uchi is heavily marketed and is used in the form of powdered samples to treat various diseases. As there are few studies on this plant, our study represents an initial contribution to the preclinical data regarding its toxicity and effect on intestinal motility. Additional studies using extracts obtained by other procedures and different solvents with a broader range of treatment groups are necessary to increase the available preclinical information on this plant.

CONCLUSIONS

The assay measuring intestinal transit distance in mice receiving the aqueous extract obtained by decoction (20% w/v) revealed no significant changes in the motility of activated charcoal. In the acute oral

toxicity test in mice, the animals did not show any signs of behavioral or physiological changes, nor was the compound lethal. Based on these results, we were unable to detect any signs of toxicity at the tested concentration, suggesting safety following extract consumption.



Testes preliminares de motilidade intestinal e toxicidade oral aguda com extrato de cascas pulverizadas de *Endopleura uchi* (Huber) Cuatrec. (Humiriaceae) em camundongos

RESUMO

O objetivo deste trabalho foi avaliar os efeitos sobre a motilidade intestinal e a toxicidade oral aguda de extrato obtido por decoção 20% (m/v) de *Endopleura uchi*, popularmente conhecido como uxi-amarelo, planta nativa da Região Amazônica brasileira, utilizada indiscriminadamente para o combate de diversas doenças: artrite, colesterol, diabetes, úlceras, miomas, afecções intestinais de uma forma geral, entre outras. Os resultados mostraram que não houve alteração significativa na motilidade intestinal e que o extrato não apresenta traços de toxicidade, conferindo segurança para seu consumo.

Palavras-chave: *Endopleura uchi*; Motilidade Gastrointestinal; Toxicidade Aguda; Fitoterapia; Extratos Vegetais.

Pruebas preliminares de motilidad intestinal y de toxicidad oral aguda con extracto de corteza en polvo de *Endopleura uchi* (Huber) Cuatrec. (Humiriaceae) en ratones

RESUMEN

El objetivo de este estudio fue evaluar los efectos sobre la motilidad intestinal y la toxicidad oral del extracto obtenido por decocción al 20% (m/v) de *Endopleura uchi*, cuyo nombre común brasileño es "uxi-amarelo". Se trata de una planta nativa de la Región Amazónica brasileña, utilizada de forma indiscriminada en la lucha contra diversas enfermedades: artritis, colesterol, diabetes, úlceras, fibromas, trastornos intestinales en general, entre otras. Los resultados mostraron que no hubo alteraciones significativas en la motilidad intestinal y que el extracto no muestra indicios de toxicidad, proporcionando seguridad para su consumo.

Palabras clave: *Endopleura uchi*; Motilidad Gastrointestinal; Toxicidad Aguda; Fitoterapia; Extractos Vegetales.



REFERENCES

- 1 Brito ARMS. Toxicidade aguda (dose simples). In: Manual de ensaios toxicológicos *in vivo*. Campinas: UNICAMP; Rio de Janeiro: Editora Três; 1994. p. 15-22.
- 2 Corrêa MP. Dicionário das plantas úteis do Brasil e das exóticas cultivadas. Rio de Janeiro: Imprensa Nacional; 1984. Vol. 6, 764 p.
- 3 Cuatrecasas JA. A taxonomic revision of Humiriaceae, contributions from the United States National Herbarium. Bull US Nat Mus. 1961; 35(Pt 2):25-214.
- 4 Janssen PA, Jageneau AH. A new series of potent analgesics: dextro 2:2-diphenyl-3-methyl-4-morpholino-butyrylpyrrolidine and related amides. I. Chemical structure and pharmacological activity. J Pharm Pharmacol. 1957 Jun; 9(6):381-400.
- 5 Larini L. Toxicologia. São Paulo: Manole; 1987. p. 301.
- 6 Organization for Economic Cooperation and Development. OECD Guidelines for testing of chemicals, No 423: Acute oral toxicity - Acute toxic class method, adopted. Paris: OECD; 1996.
- 7 Schultes RE. De plantis Toxicariis e mundo novo tropicale commentationes. XXI. Interesting native uses of the Humiriaceae in the northwest Amazon. J Ethnopharmacol. 1979 Jan;1(1):89-94.
- 8 Wong CL, Wai MK. Effects of aspirin and paracetamol on naloxone reversal of morphine-induced inhibition of gastrointestinal propulsion in mice. Eur J Pharmacol. 1981 Jul;73(1):11-9.