HOSTED BY
ELSEVIER

Contents lists available at ScienceDirect

Asian Pacific Journal of Tropical Biomedicine

journal homepage: www.elsevier.com/locate/apjtb

Original article http://dx.doi.org/10.1016/j.apjtb.2016.04.001

Preliminary studies of acute and sub-chronic toxicity of the aqueous extract of *Guibourtia tessmannii* (Harms) J. Leonard stem barks (Caesalpiniaceae) in mice and rats

Noreen Orianna Koumba Madingou[1,2*], Aristide Traore[3], Alain Souza[4], Marlaine Michelle Boukandou Mounanga[1], Raissa Reine Aworet Samseny[1], Sylvin Ouedraogo[3], Alfred Sababenedyo Traore[2]

[1]*Laboratory of Pharmacology and Toxicology, Pharmacopoeia and Traditional Medicines Institute, BP 1935 Libreville, Gabon*

[2]*Research Center in Biological, Food and Nutritional Sciences, University of Ouagadougou, 03 BP 7129 Ouagadougou, Burkina Faso*

[3]*Department of Medicine and Traditional Pharmacopoeia/Pharmacy, Health Science Research Institute, 03 BP 7192 Ouagadougou 03, Burkina Faso*

[4]*Department of Biology, Faculty of Sciences, University of Sciences and Technique of Masuku (USTM), BP 941 Franceville, Gabon*

ARTICLE INFO

Article history:
Received 10 Sep 2015
Received in revised form 19 Sep, 2nd revised form 19 Oct, 3rd revised form 2 Nov, 4th revised form 9 Nov, 5th revised form 30 Nov 2015
Accepted 20 Dec 2015
Available online 22 Apr 2016

Keywords:
Guibourtia tessmannii
Stem barks
Plant extract
Herbal medicine
Toxicity

ABSTRACT

Objective: To investigate the toxicity of aqueous extract of *Guibourtia tessmannii* (Harms) J. Leonard (*G. tessmannii*) and evaluate its safety.
Methods: NMRI mice were used to determine the acute toxicity of *G. tessmannii*. Increasing concentrations of the plant extracts were administered intraperitoneally or by force-feeding. General behavior and death were monitored and recorded daily for 7 days. In order to determine the sub-acute toxicity of the extract, several doses were administered by oral gavage daily for 28 days in adult Wistar rats. Different parameters were assessed including body weight, food and water intake, biochemical parameters and several vital organ weights.
Results: LD_{50} of 328.78 mg/kg was obtained by *i.p.* route and more than 5000 mg/kg was obtained in acute toxicity by oral route. In sub-acute toxicity, no significant alteration was observed in body weight or vital organs, food and water intake, and biochemical parameters.
Conclusions: The results showed that the aqueous extract of *G. tessmannii* has low toxicity intraperitoneally and no sub-acute toxicity via oral intake.

1. Introduction

It is well known that plants are an important source of drugs worldwide [1–3]. Indeed, over 50% of chemical drugs used for the treatment of various diseases are derived from vegetables [4]. In the case of cardiovascular diseases, drugs such as digitoxin, digoxin, lanatosides A, B, C, are derived from *Digitalis purpurea* and *Digitalis lanata* which are traditionally used by indigenous people as poison [5]. However, the traditional usage of plants is not always a guarantee of the plant safety. In accordance with Ashafa *et al.* [3], it is plausible to assume that a history of a plant usage does not proof its safety.

In Gabon, the use of medicinal plants is claimed to have an important role in health care system. However, several deaths are regularly reported by practitioners using traditional medications due to overdosing. Moreover, in this country, few scientific

*Corresponding author: Noreen Orianna Koumba Madingou, Laboratory of Pharmacology and Toxicology, Pharmacopoeia and Traditional Medicines Institute, BP 1935 Libreville, Gabon.
Tel: +226 241 06 39 16 83
E-mail: madnoreen01@gmail.com

Foundation Project: Supported by the doctoral training funds no. 84722652 USTM/4802 AC-USTM, of the University of Sciences and Technique of Masuku.
Peer review under responsibility of Hainan Medical University. The journal implements double-blind peer review practiced by specially invited international editorial board members.

studies have been conducted to investigate the potential toxicity or eventual side effects of traditional recipes in experiments. *Guibourtia tessmannii* (Harms) J. Leonard (*G. tessmannii*) is one of the most abundantly used medicinal plant in Central Africa for many purposes such as the treatment of cardiovascular diseases [6–8], and its aphrodisiac effects in Cameroon [9].

Phytochemical studies performed on *G. tessmannii* revealed the presence of bioactive compounds such as tannins, phenolic, triterpenoids and alkaloids [6,7]. In order to study the biosafety of this extract in the present study, we determined the acute and sub-acute toxicity effect of the extract of this plant.

2. Materials and methods

2.1. Plant material

Stem barks of *G. tessmannii* were collected in the south of Gabon in August 2010. The plant was authenticated in the Gabon National Herbarium, the Institute of Pharmacopeia and Traditional Medicine, Libreville (Gabon) where a voucher specimen (SRFG 879 LBV) was deposited.

2.2. Aqueous extract

The stem barks of the plant were sun-dried and crushed into powder using mortar and Culatti micro-crusher. The powder obtained (1 kg) was macerated in 2000 mL of water during 48 h at room temperature and filtered using a Whatman millipore filter. The filtrate was lyophilized at −40 °C. The powder obtained (67.7 g) was stored at 5 °C until further use.

2.3. Animals

NMRI mice weighing 19–30 g were used in the acute toxicity test. Animals were provided by the Health Science Research Institute (IRSS), Ouagadougou (Burkina Faso). For the sub-acute toxicity, albino Wistar rats weighing 180–300 g were used. These animals were provided by the Institute of Pharmacopoeia and Traditional Medicine, Libreville, Gabon. All animals were housed under standard laboratory conditions [(25 ± 1) °C] with free access to food and water. Experimental protocols were carried out and followed the Guide for the Care and Use of Laboratory Animals of Gabon.

2.4. Acute toxicity tests

The oral acute toxicity test and the intraperitoneal acute toxicity test were performed. Male and female NMRI mice were randomly distributed into two control groups and 8 treated groups with 10 animals in each group. Among the 8 treated groups, 5 groups of animals were subjected to the intraperitoneal acute toxicity test (5 males and 5 females), and 3 groups of animals were subjected to the oral acute toxicity test, in the same proportions. The two control groups received the water orally or by *i.p.* (0.5 mL vehicle). For the oral acute toxicity test, the treated groups received increasing doses of plant extract (2000, 3000 and 5000 mg/kg weight). Regarding the intraperitoneal acute toxicity test, increasing doses of the plant extract (150, 250, 300, 500 and 600 mg/kg weight) were administered.

Animals were deprived of food and water overnight prior to the drug administration. The mice were observed at 0, 30, 60 and 120 min after treatment. The animals were observed for morbidity and mortality once a day, for up to 14 days, with food and water provided. The number of survivors after 7 days period was recorded [10–12]. The toxicological effect was assessed on the basis of mortality, which was expressed as LD_{50} [13].

2.5. Sub-chronic toxicity

Wistar rats (180–250 g) of both gender were divided into four groups of 6 animals each (3 males and 3 females) and were housed under standard conditions and room temperature [(25 ± 1) °C].

The control group received the vehicle (0.5 mL) and the others received increasing oral doses of the plant extract (150, 1500 and 3000 mg/kg weight) by gavage.

Sub-chronic toxicity was evaluated after a single daily administration of extract *per os* for a period of 28 days. Animals were observed daily. Clinical signs, behavioral pattern, food and water intake, and body weight were monitored. At the end of the 28 days period, animals were deprived of food and water for 15 h and then sacrificed for serum biochemical analyses and organs weighing.

For serum biochemical analyses, blood samples collected from the heart were dispensed into plain tubes and were centrifuged at 3500 r/min for 10 min. The serum samples obtained were then used for biochemical parameters analysis such as: aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphate (ALP), total protein, creatinine, urea, total cholesterol, using an automated biochemistry analyzer (Selectra XL Vital Scientific, Elitech Group Company).

Vital organs such as heart, lungs, liver, kidneys, spleen, testes, ovary and uterus were carefully dissected, washed with normal buffer, weighed and examined macroscopically.

2.6. Statistical analysis

Data were expressed as mean ± SEM. They were analyzed by GraphPad Prism version 5.0 for Windows. Data were assessed by One-way ANOVA followed by Dunnett's multiple comparison test. *P* values less than 0.05 were considered as statistically significant.

3. Results

3.1. Acute toxicity study in mice

Oral administration of increasing doses of the aqueous extract of *G. tessmannii* (2000, 3000 and 5000 mg/kg) did not produce any abnormal behavioral responses in male and female mice during the 14 days of observation. No mortality was recorded at all dose levels. Orally, the LD_{50} appeared to be > 5000 mg/kg.

When administered intraperitoneally, the aqueous extract of *G. tessmannii* (150 mg/kg body weight to 600 mg/kg body weight) showed a LD_{50} at 328.78 mg/kg body weight. Table 1 summarizes treatment-related responses observed in acute intraperitoneal toxicity study.

3.2. Sub-chronic toxicity study in rats

3.2.1. Mortality and general behavior

Oral ingestion of the aqueous extract of *G. tessmannii* (150 mg/kg body weight to 3000 mg/kg body weight) for 28