

Acute Toxicity Evaluation of Aqueous Extract from *Hertia cheirifolia* in Swiss Albino Mice

Mounira Merghem^{1*}, Meriem Hani², Khadidja Dehimi^{1,3}, Yasmine Madi¹, Abderrahim Benslama³

Laboratory of Phytotherapy Applied to Chronic Diseases, Faculty of Nature and Life Sciences, Ferhat Abbas University, Sétif 1, Algeria¹

Laboratory of Natural Resource Valorisation, Faculty of Nature Life Sciences, Ferhat Abbas University Setif-1, 19000, Algeria²

Department of Microbiology and Biochemistry, Faculty of Sciences, University of M'sila, 28000, Algeria³

Corresponding authors: 1*



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ABSTRACT

Hertia cheirifolia L. is a medicinal plant belonging to *Asteraceae* family. It is traditionally used to treat gastrointestinal ailments, infections, and spasms. The aim of this study is to evaluate the oral acute toxicity of aqueous extract from *Hertia cheirifolia* on female Albino wistar mice. Animals were divided into three groups, the first group received distilled water and was used as control; Mice of the second and third groups received the plant extract at doses of 2g/kg and 5g/kg body weight of animals, respectively. The mice were monitored for 14 days for their general behavior, adverse effects and mortality. The results showed that no death or toxic signs were observed, no changes were seen in food consumption, body weight and organ weight in the treated animals compared to the controls. However, an increase in AST and ALT levels was recorded in mice treated with the extract.



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1. INTRODUCTION

The term of medicinal plants include various types of plants used in herbalism which are rich of ingredients used in drug development and synthesis. About eighty percent of the world's population depend on traditional medicine for primary health care. Although the high importance of these natural remedies, there still concerns about their safety on human health whether after instant use or repetitive use [18].

The genus *Hertia*, belonging to the *Asteraceae* family, contains 12 species distributed all over South and North Africa and South-west Asia [2], [15]. It is an aromatic herb that has several functional characteristics including treatment of the pain of stomach, the severe fever and the genital and cutaneous diseases [19]. It is also a source of chemical compounds and extracts containing biologically active constituents that possess spasmolytic and anti-inflammatory activities [3].

Hertia cheirifolia L. (locally known as Kartchoune), an endemic *Asteraceae* species which grows in the border of fields in the eastern part of Algeria and in Tunisia [16], [11]. It is an evergreen sub-shrub growing

in large clumps with ascending and very leafy stems. Leaves are grey-green, alternate, fleshy, and oblong; Flowers are yellow and the flowering period extends from November to December. Fruits are achenes with white pappus that facilitate their dispersion [16]. The leaves of this plant have been used in the traditional medicine to treat rheumatic pains and to reduce hyperglycemia. In addition, some studies suggest that extracts from this plant may possess anti-inflammatory properties [12].

View the use of this plant in many applications in traditional medicine without having adequate information about its safety, this study aim to evaluate the acute toxicity of *Hertia cheirifolia* extract in mice.

2. MATERIALS AND METHODS

2.1 Plant material

Hertia Cheirifolia L. was collected in March, from Beida Bordj in the region of Setif in Northeast Algeria.

2.2 Animal material

Male *Albino Wistar* mice weighing between 35 and 45 g were used for the acute toxicity study. Animals were obtained from Pasteur Institute (Algiers, Algeria) and were kept in the animal house of the faculty of Nature and Life Sciences, University of Setif, at a temperature of 20°C and a photoperiod cycle of 12 hours light/dark. The animals were housed in plastic cages (3 mice per cage) and had free access to standard commercial diet and tap water.

2.3 Preparation of aqueous extract

The aerial parts of the plant were washed in running water, dried and powdered. 50 g of powder was boiled in 500 ml of water for 15 minutes, the resulting was filtered using Wattman filter paper and then evaporated in rotary vacuum evaporator.

2.4 Acute toxicity study

The acute oral toxicity of extract was evaluated using the procedures described by the Organization for Economic Co-operation and Development (OECD) guidelines. Animals were divided into three groups with three animals. The control group was given distilled water. The second and third groups were given a single dose of 2000 mg/kg and 5000 mg/kg of aqueous extract, respectively. Mice were fasted 4 h with free access to water prior to administration of single doses of the extract dissolved in distilled water. The general behavior of mice was continuously monitored after dosing, periodically during the first 24 h (with special attention given during the first 4 hours), and then daily thereafter for a total of 14 days.

At the end of the treatment, animals were fasted overnight, but allowed access to water ad libitum. They were subsequently anesthetized with diethylether and blood samples were obtained by retro-orbital puncture, collected in tube containing heparin and then centrifuged at 4000 r/min at 4°C for 15 minutes to obtain serum (stored at -20°C until analysis). The organs (kidneys, liver, lungs, heart, stomach and spleen) were weighed.

2.5 Body Weight and Food Consumption

The body weight of each mouse was recorded once weekly and the amount of food consumed was measured from the quantity supplied and the amount remaining after 24 hours for 2 weeks of the study period.

2.5 Biochemical analysis

Biochemical analysis was performed using an automatic analyzer (Beckman). Parameters included aspartate aminotransferase (AST) and alanine aminotransferase (ALT).

2.6 Organs weight

After the sacrifice of all animals, the kidneys, liver, heart, lungs and spleen were carefully removed and weighed individually.

2.7 Statistical analysis

Results including mice body weight, organs weight, food consumption and biochemical analysis are expressed as the mean \pm standard deviation of three repetitions.

3. RESULTS

3.1 Mortality and signs of toxicity

The obtained results from the study of the plant aqueous extract acute toxicity for 14 days after oral administration in mice of both doses 2g / kg bw and 5g / kg bw showed no signs of toxicity, and no deaths during the experiment period (Table 1).

Table 1: Mortality and signs of toxicity of *Hertia Cheirifolia* administered orally as one single dose in mice.

Dose (g/kg bw)	Death (D/T)	Adverse effects
0	0/3	Normal
2	0/3	Normal
5	0/3	Normal

3.2 Body weight changes

The body weight of mice treated with the aqueous extract from *Hertia cheirifolia* during 14 days of the experiment is shown in Table 2.

Table 2: Effect of *Hertia cheirifolia* aqueous extract on body weight in mice.

Day	control	2000 mg/kg	5000 mg/kg
1 st Day Body Weight (g)	39.79 \pm 1.62	36.77 \pm 6.55	41.71 \pm 3.48
7 th Day Body Weight (g)	45.62 \pm 1.52	37.8 \pm 6.51	40.30 \pm 2.72

14th Day Body Weight (g)	44.68 ± 2.73	49.54± 4.31	49.25 ± 1.91
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Values are presented as mean ± SD; N= 3.

3.3 Food consumption

The amount of food consumed was measured daily from the quantity of food supplied and the amount remaining after 24 h. According to the results obtained, it seems that there is no change in food intake in mice (Table 3).

Table 3: Effect of *Hertia cheirifolia* aqueous extract on food and water consumption in mice.

Food consumption (g)			
	Control	2000 mg/kg bw	5000 mg/kg
Food	14.002 ± 7.47	13.25 ± 3.79	15.06 ± 7.60

Values are presented as mean ± SD; N= 3.

3.4 Biochemical analysis

The results obtained showed that single doses oral administration of aqueous extract from *Hertia cheirifolia* increased hepatic transaminases (AST and ALT) in mice treated with both doses compared to the control group (Table 4).

Table 4: Effect of *Hertia cheirifolia* aqueous extract on biochemical parameters of mice.

Parameters	Control	2000 mg/kg	5000 mg/kg
ALT(UI/L)	30.85± 29.63	23.30 ± 8.64	64.51 ± 16.05
AST(UI/L)	110.18 ± 30.86	153.75 ± 34.57	204.52 ± 23.46

Values are presented as mean ± SD; N= 3.

3.5 Organs weight

At the end of the experiment, and after the sacrifice and dissection of mice, a macroscopic examination was carried out for the organs removed (liver, kidneys, heart, lungs and spleen). The size and color of these organs have been observed to be normal.

The results demonstrate that aqueous extract of *Hertia cheirifolia* L. has no adverse effect on organs weight (Table 5).

Table 5: Effect of *Hertia cheirifolia* aqueous extract on organs weight in mice.

Organ (g)	Control	2000 mg/kg	5000 mg/kg
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	1.76 ± 0.170	1.54 ± 0,103	1.55 ± 0,128
Liver			
Kidneys	0.18 ± 0	0.16 ± 0,06	0.18 ± 0,022
Lungs	0.07±0.01	0.103 ± 0,020	0.12 ± 0,048
Heart	0.15 ± 0	0.153 ± 0,015	0.15 ± 0,0095
Spleen	0.18 ± 0,075	0.16 ± 0,052	0.15±0,023

Values are presented as mean ± SD; N= 3.

4. DISCUSSION

The symptoms observed (normal, no mortality), suggest that the aqueous extract of the plant is not toxic. These results are similar to those obtained by [5], which showed that no deaths or any change in animal behavior in mice treated by methanolic extract from the leaves of *Hertia Cheirifolia* at 2000mg / kg body weight for two weeks. In the other hand, results obtained by [14], about the administration of another species from the same genus: *Hertia pallens*, caused some symptoms of toxicity (anorexia, jaundice, asphyxia, dyspnea, ...) and the death of animals.

Changes in body weight have been used as an indicator of adverse effects of drugs and chemicals [8]. The change in body weight during the 14 days of acute toxicity study of the aqueous extract from *Hertia cheirifolia* demonstrated that there was not a significant change in the weights of treated mice compared to controls. The change in body weight of mice may correlate with their physiological state, or with a decrease in the amount of food absorbed.

Biochemical examination was performed in order to evaluate any toxic effects on liver. The parameters such as aspartate aminotransferase and alanine aminotransferase, were examined. It is known that the liver plays significant roles in various metabolic processes. The liver plays an important role in xenobiotic function; and therefore, particularly exposed to the toxic effects of exogenous compounds [4].

Serum enzymes like AST and ALT are well-known enzymes used as good indicators of liver function [17], [20] and as biomarkers predicting possible toxicity [13] and any marked necrosis of the liver cells lead to a significant rise of these enzymes in the blood serum [1], [9]. ALT is more specific marker of hepatocellular injury because it occurs exclusively in the liver, whereas AST occurs to some extent also in heart, skeletal muscle, kidney, brain, pancreas and blood cells [10].

In general, alterations of body weight and internal organs weight of mice would reflect the toxicity after exposure to the toxic substances [6]. Organs weight is an important index of physiological and pathological status in animals. The relative organ weight is fundamental to decide whether the organ was exposed to the injury or not [7].

5. CONCLUSION

Acute oral toxicity of aqueous extract from *Hertia cheirifolia* was evaluated according to the OECD guide lines. According to the study results, the nontoxic nature of the plant aqueous extract was confirmed by the normal behavior of animals during the observation period of 14 days, the absence of mortality, the normal food intake and the non-affected body and organs weight, which suggests the safety and harmless effects of the extract even up to 5000 mg/Kg body weight of animals. However, an increase of hepatic transaminases, ALT and AST, was recorded which impose further studies of sub-acute and chronic toxicological evaluations to more investigate the safe use of the *Hertia cheirifolia* extract.

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