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DETERMINATION OF ACUTE AND SUBACUTE TOXICITY OF SIX PLANT EXTRACTS

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ABSTRACT

Determining the toxicity of a plant extract is an important preliminary step, depending on which the therapeutic dose is adjusted. In the current study we proposed to test acute and subacute toxicity for six vegetal extracts using swiss albino healthy mice: Tragopogon pratensis, Dorycnium pentaphyllum subsp herbaceum, Acanthus balcanicus, Tamarix ramosissima, Carduus acanthoides compative with Vaccinium myrtillus (bilberry). The acute toxicity study revealed the lack of toxicity for the tinctures Acanthi balcanici herba, Dorycnii pentaphylli herba, Tragoponis pratensis folium, Tamaricis ramosissimae folium et flos, Myrtilli fructus, even at the gavage dose of 5 g / kg and the toxicity of tincture Cardui acanthoiditis folium, at a dose of 4g / kg. The subacute toxicity study demonstrates the lack of toxicity for all tinctures studied at the 400 mg / kg dose by gavage, a dose representing 1/10 of the dose that is supported by all animals in determining acute toxicity.

ORIGINAL RESEARCH ARTICLE

INTRODUCTION

Using plant extracts to treat various diseases is a common approach, being recommended by the patient's physician. Natural supplements have been traditionally promoted and used for centuries in Asian and Indian medicine, and later in American folk medicine. The active principles of leaves, flowers, bark, stem or seeds can treat or prevent diseases, patients being encouraged to trust the beneficial effects of the ingredients contained[1]. The Society has questioned the limits, abilities, efficacy, and safety of allopathic therapy over time, creating an opportunity to demonstrate the therapeutic potential of alternative medicine.

In the modern era of pharmaceutical development, was established the identification and isolation of plants active constituents and the chemical-activity structure relations. Another stage in the pharmaceutical evolution was the awareness that plants and their derivatives can present in addition to the therapeutic effect a toxic effect. The systematic scientific studies of the active principles contained open the horizons of modern pharmacology and toxicology

Plant products contain contraindications, precautions, drug interactions and consequences of overdose (serious intoxication, hypersensitivity reactions, anaphylactic shock)[2]. The evaluation of adverse and potentially toxic effects of a plant extract intended to be used in human therapy is an essential part of the evaluation of the drug profile[3].

Toxicity assessment is crucial and usually includes the determination of acute, sub-acute, chronic toxicity, mutagenic and toxic to reproduction[4]. Low-potentially toxic

drugs or plant extracts are tested on laboratory animals, determining LD_{50} (g / kg body weight). Depending on the LD_{50} value, the toxicity is established, knowing the limits for the delimitation of toxicity: highly toxic (LD_{50} of 5 mg / kg), very toxic (LD_{50} between 5 - 50 mg / kg), toxic (LD_{50} 50 - 300 mg / kg body weight), moderately toxic (LD_{50} 300 - 2000 mg / Kg body), poorly toxic (LD_{50} 2000 - 5000 mg / kg body weight), practically non-toxic (LD_{50} above 5000 mg / kg body weight) [5].

MATERIAL AND METHOD

Using healthy mice, we investigated the acute and subacute toxicity of the tinctures of some very rarely studied plant species: *Tragopogon pratensis*, *Dorycnium pentaphyllum subsp herbaceum*, *Acanthus balcanicus*, *Tamarix ramosissima*, *Carduus acanthoides* compared to the toxicity of a plant already use in therapy, *Vaccinium myrtillus* (bilberry).

The plant products to be tested were harvested from species from the Botanical Garden of the University of Craiova from April to June 2012. The plants were dried in well-ventilated areas, the vegetable products being then brought to a suitable degree of crushing with the help of a electric grinders.

Vegetable products were used in the form of tinctures, obtained by simple percolation, in a plant / solvent ratio (ethanol 70o) of 1: 5 (F.R.X.). The test sample of each tested tincture is found in the Pharmacognosy Laboratory Collection of the Faculty of Pharmacy in Craiova.

For acute and subacute toxicity testing we used Swiss albino mice, healthy males, weighing between 29-35 grams and aged 6-8 weeks, which were purchased from biobase Faculty of Medicine and Pharmacy, Craiova.

Animals were kept throughout the experiment in polypropylene cages containing sawdust as a litter in a well-ventilated room. In each box we assigned a group of experiment, which was maintained under standard laboratory conditions: 24-28 ° C, 60-70% relative humidity, 12 hours light / dark alternation. Animals were fed with standard food and water *ad libitum*.

In the acute toxicity test, we performed experimental lots of 4 mice, males and females, to which we administered a single dose of the tinctures studied (1,2,3,4,5 g / kg) by gavage. We had a control group, which received gavage with physiological serum.

After administration of the extracts, animals were constantly analyzed at two-hour intervals for 72 hours, following toxicity and lethality. The monitored parameters address the phenomenon of death (seizures, apnea, coma) and behavioral change (walking, eyelid position, sedation or agitation, excessive salivation, transit disturbance, sleep duration, fur and mucous membranes, tremors, photophobia).

In the subacute toxicity test, we performed experimental batches of 4 mice, males and females, which we administered 400 mg / kg gavage of the tinctures daily for 14 days. We also had a contro group, which received gavage with physiological serum.

Animals were weighed initially before testing, then daily for two weeks each morning. Animals were monitored daily at 4 hour intervals.

During the two weeks were followed: food consumption, water, spontaneous motility, breathing amplitude, behavioral change, urine and faeces[6].

RESULTS AND DISCUSSIONS

Following the test of acute toxicity of plant extracts using healthy mice at doses of 1, 2, 3, 4, 5 g / kg, we noticed a lack of toxicity for *Acanthi herbal tinctures*, *Dorycnii pentaphylli herba*, *Tragoponis pratensis folium*, *Tamaricis ramosissimae folium et flos* , *Myrtilli fructus*, no animal in the test batches died and had no behavioral changes. The *Cardui acanthoiditis folium* tincture exhibited toxicity starting at a dose of 4g / kg, its dosing of 5g / kg produced the death of all animals by seizures at ranging from 30 minutes to one hour. (Table 1).

Table 1 Testing of acute toxicity of tinctures

Tincture tested	1g/kg	2g/kg	3g/kg	4g/kg	5g/kg	LD 50
Cardui acanthoiditis folium	no toxic effects	no toxic effects	no toxic effects	sedation, piloerection, large respiratory movements, tremor, photophobia, loss of recovery reflexes	Convulsions, death	4g/kg
Acanthi balcanici herba	no toxic effects	no toxic effects	no toxic effects	no toxic effects	no toxic effects	> 5g/kg
Dorycnii pentaphylli herba	no toxic effects	no toxic effects	no toxic effects	no toxic effects	no toxic effects	> 5g/kg
Tragoponis pratensis folium	no toxic effects	no toxic effects	no toxic effects	no toxic effects	no toxic effects	> 5g/kg
Tamaricis ramosissimae folium et flos	no toxic effects	no toxic effects	no toxic effects	no toxic effects	no toxic effects	> 5g/kg
Myrtilli fructus	no toxic effects	no toxic effects	no toxic effects	no toxic effects	no toxic effects	> 5g/kg

Acanthi balcanici herba, Dorycnii pentaphylli herba, Tragoponis pratensis folium, Tamaricis ramosissimae folium et flos, Myrtilli fructus tinctures fall into the category of practically non-toxic substances because the animals tested did not show signs of toxicity. The maximum tolerated dose value for these extracts is greater than 5g / kg body weight. Tincture *Cardui acanthoiditis folium* is poorly toxic at the dose of 4 g / kg, resulting in toxicity and lethality.

In the subacute toxicity test, we administered oral plant extracts for two weeks at a dose of 400 mg / kg body weight, not observing behavioral changes in the animals. Vegetal extracts did not have a fatal effect, no mortality, no toxic effects.

CONCLUSIONS

1. Toxicity testing of plant extracts is a preliminary study of great importance because it establishes the therapeutic limits.
2. To determine the toxicity of tinctures *Acanthi balcanici herba, Dorycnii pentaphylli herba, Tragoponis pratensis folium, Tamaricis ramosissimae folium et flos, Myrtilli, Cardui acanthoiditis folium* we administered gavage to mice with increasing doses of the samples to be analyzed. (1,2,3,4,5 g / kg).
3. Laboratory animals were monitored during the experiment, the parameters being mortality and behavioral change (walking, eyelid position, sedation or agitation, excessive salivation, transit disturbance, sleep duration, fur and mucous membrane appearance, tremor of the extremities, photophobia, respiratory movements).
4. The acute toxicity study revealed the lack of toxicity for the tinctures *Acanthi balcanici herba, Dorycnii pentaphylli herba, Tragoponis pratensis folium, Tamaricis ramosissimae folium et flos, Myrtilli fructus*, even at the gavage dose of 5 g / kg and the toxicity of tincture *Cardui acanthoiditis folium*, at a dose of 4g / kg.
5. The subacute toxicity study demonstrates the lack of toxicity for all tinctures studied at the 400 mg / kg dose by gavage, a dose representing 1/10 of the dose that is supported by all animals in determining acute toxicity.

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