

Controversial acute toxicity of Saussurea dry extract E.Yu. Avdeeva, Ya. E. Reshetov, E.I. Gulina, A.G. Miroshnichenko, M.V. Belousov Federal State Budgetary Educational Institution of Higher Education "Siberian State Medical University" of the Ministry of Health of the Russian Federation (Tomsk)

Acute toxicity of the dry Saussurea controversa extract  
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#### SUMMARY

Determined the acute toxicity of dry extract of controversial saussurea (*Saussurea controversa* DC.), Which has osteogenic, immunomodulatory and anti-inflammatory activity. According to the results of toxicometry, observations of experimental animals for 14 days after acute administration and necropsy data, the studied extract according to the classification of Hodge and Sterner belongs to low-toxic substances, and according to GOST 12.1.007-76 - to low-hazard substances (IV hazard class), which along with its high biological activity, it provides a prospect for its further study and implementation in medical practice.

Keywords: *Saussurea controversa* DC, acute toxicity.

#### RESUME

Acute toxicity of dry *Saussurea controversa* extract possessing osteogenic, immune modulating and anti-inflammatory activity was determined. According to the results of toxicometry and observations of experimental animals for 14 days after acute administration, as well as necropsy data, the dry *Saussurea controversa* extract according to the classification of Hodge and Sterner refers to low-toxic substances, which, along with high biological activity gives the prospect for its further study and implementation in medical practice.

Keywords: *Saussurea controversa* DC, acute toxicity.

Scientific interest in the search for new medicinal products from medicinal plant materials and the introduction into official practice of plants used in traditional medicine remains quite high. Preparations based on medicinal herbal raw materials are in great demand among the population due to their environmental friendliness, availability and effectiveness, and are also distinguished by their mild action and the possibility of long-term administration.

*Saussurea* extract controversial (*S. controversa*), obtained using optimal parameters of extraction of target components, is a promising source of funds that stimulate the hematopoietic function of the bone marrow, with osteogenic and immunotropic activity [1]. To create a new drug, in addition to proving its effectiveness, it is necessary to assess its safety [2]. The aim of this work was to determine the acute toxicity of the controversial *Saussurea* dry extract.

#### MATERIALS AND METHODS

Dry extract *S. controversa* was obtained as described in [1], using 40% aqueous ethanol (n = 3, 1:15, t = 60, 80 ° C). The acute toxicity of the dry extract was determined in accordance with the guidelines for conducting preclinical studies of drugs [3].

The experiments were carried out on white Wistar rats of both sexes weighing 280–300 g (laboratory of biological models, Siberian State Medical University, Tomsk). The animals were kept in standard vivarium conditions with free access to food and water. During the experiments, we were guided by the principles set out in the directives of the European Community (86/609 / EEC) and the Declaration of Helsinki. Local Ethical Approval

Committee of the Federal State Budgetary Educational Institution of Higher Education of the Siberian State Medical University (conclusion No. 5539 dated 02.10.2017).

The animals were divided into three groups: intact (group 1) and receiving doses, respectively, 2000 (group 2) and 5000 mg / kg (group 3). The extract was introduced through a tube into the stomach in the form of an aqueous suspension. Acute toxicity was assessed by neuro-somatic parameters, blood test data, weight coefficients and macroscopic examination of internal organs. The observation period was 14 days. Blood analysis was performed on an automatic hematology analyzer for veterinary medicine PCE 90 Vet (USA, High Technology).

## RESULTS AND DISCUSSION

For the primary assessment of the safety of the dry extract, its acute toxicity was investigated. In the group of rats receiving a dose of 2000 mg / kg (group 2), after the introduction of the extract, a slight decrease in mobility was observed in comparison with intact animals during the day, but in general, the animals differed little from the intact ones. In animals of group 3, during the first five hours after administration of the extract, a clinical picture of intoxication was observed, lethargy, lethargy, ptosis, and bradypnea were noted (Table 1). After 24 hours, the animals of group 3 developed lacrimation, symptoms of conjunctivitis, which persisted for 4 days. There were no significant differences in the dynamics of body weight, heart rate, water and food consumption in the groups of intact animals and those receiving the extract.

Table 1

Neuro-somatic indices and weight coefficients (VK) of rat organs  
after the introduction of dry extract of controversial Saussurea ( $X \pm x$ ,  $n = 10$ )

Defined parameters	intact	2000 mg / kg	5000 mg / kg
Body weight, g (before introduction / after 2 weeks)	336 ± 32/346 ± 34	327 ± 15/305 ± 23	300 ± 24/290 ± 34
Respiratory rate / min (after 1 h)	132 ± 10	128 ± 12	112 ± 12
Heart rate cuts / min (after 1 h)	252 ± 10	244 ± 16	228 ± 10
Number of movements in the open field / min (after 3 h / 24 h)	37 ± 3/32 ± 5	27 ± 8/22 ± 5	32 ± 20/18 ± 13
Water consumption ml / rat (1/2/3 and 4 days)	25/33/52	32/48/73	27/15/50
Feed consumption g / rat (1 and 2 days / 3 and 4 days)	34/32	33/36	30/28
Reaction to stimuli (within 3 h / 24 h)	- / -	- / -	- / -
Ptosis (within 3 hours)	-	-	-
VK hearts	0.0038 ± 0.0005	0.0035 ± 0.0005	0.0033 ± 0.0002
Liver VC	0.0389 ± 0.0013	0.0376 ± 0.0034	0.0338 ± 0.0028
VC of the spleen	0.0044 ± 0.0006	0.0047 ± 0.0014	0.0060 ± 0.0028-
Kidney VC	0.0078 ± 0.0004	0.0080 ± 0.0010	0.0075 ± 0.0007
Note: "-" - the phenomenon was not observed.			
-- the differences are significant in comparison with the group 1.			

There were no significant differences in the hemogram of intact animals and group 2. In group 3, there was a tendency to an increase in the number of leukocytes, monocytes and lymphocytes (Table 2), the hemoglobin content decreased, the number of

platelets, which may indicate some toxic effect of the extract *S. controversa* indose of 5000 mg / kg for the hematopoietic system.

The weight coefficient of the spleen in rats of group 3 was increased in comparison with intact animals. The weight coefficients of the remaining organs of the experimental animals receiving the extract, as well as their macroscopic features, did not differ from the intact ones. Complications and death of animals were not observed.

Thus, the results of toxicometry and observation data of experimental animals for 14 days after acute administration, as well as data of necropsy, allow the dry extract of the controversial saussurea to be classified as low-toxic medicinal substances according to the classification of Hodge and Sterner. Guided by the accepted GOST (12.1.007-76), the investigated extract belongs to the IV hazard class - low-hazard substances.

table 2

Data of blood tests after administration of dry extract of controversial Saussurea ( $X \pm x$ ,  $n = 10$ )

Defined parameters	intact	2000 mg / kg	5000 mg / kg
erythrocytes	7.69 ± 0.53	7.10 ± 1.30	7.87 ± 0.56
average erythrocyte volume	53.05 ± 0.70	56.44 ± 2.52	53.05 ± 1.25
red blood cell distribution	12.37 ± 1.16	13.88 ± 2.97	12.23 ± 1.38
leukocytes	10.51 ± 1.93	9.46 ± 3.54	13.12 ± 2.40
lymphocytes	6.90 ± 1.69	6.12 ± 2.89	8.67 ± 1.80
granulocytes	3.23 ± 0.39	3.08 ± 0.75	3.92 ± 0.67
monocytes	0.38 ± 0.07	0.26 ± 0.09	0.52 ± 0.09
hemoglobin	135.00 ± 8.90	133.8 ± 23.69	135.75 ± 8.84
average hemoglobin content in erythrocyte	17.50 ± 0.37	18.78 ± 0.89	17.18 ± 0.38
average concentration hemoglobin in erythrocytes	330.67 ± 4.13	334.00 ± 3.53	325.00 ± 7.74
hematocrit	40.77 ± 2.70	39.98 ± 6.72	41.67 ± 1.95
platelets	912.33 ± 188.27	825.40 ± 238.83	387.67 ± 214.08-
thrombocyte	0.550 ± 0.12	0.510 ± 0.12	0.25 ± 0.13
average platelet volume	6.31 ± 0.22	6.26 ± 0.40	6.35 ± 0.41
platelet distribution	16.02 ± 0.44	16.18 ± 0.34	16.77 ± 0.61

Note: - - differences are significant in comparison with group 1.

#### CONCLUSIONS

1. The controversial Saussurea extract belongs to low-toxic substances according to the classification Hodge and Sterner.

2. The controversial Saussurea extract belongs to the IV hazard class - low-hazard substances (according to GOST 12.1.007-76).

3. The conducted experimental toxicological study allowed to establish that the absence of toxicity of the Saussurea extract is controversial, gives a prospect for its further study and implementation in medical practice (taking into account the previously established high biological activity).

#### LITERATURE

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