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TOXICOLOGIC CHARACTERISTIC OF THE PREVENTIVE IODINE-CONTAINING PREPARATION "VANGTSEYOD"

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SUMMARY

The Amur Oblast belongs to biogeochemical province with low contents of iodine in the soil, water and air, which leads to the thyroid gland disorders in animals, weakened immunity system and, consequently, to the increased sensitivity to diseases. A new iodine-containing preparation "Vangtseyod" has been developed basing on natural zeolites from Vanga deposits to prevent iodine deficit in young cattle. The distinctive feature of the Vanga deposit zeolite in comparison with other deposits of the Amur Oblast and the Far East is that it contains more effective clinoptilolite and heulandite minerals, characterized by the low contents of harmful compounds. Studies of the preparation safety performed on white mice showed that "Vangtseyod" does not have acute toxicity. It's inclusion into mice diet at 1.0 and 2.0 g/kg dose during two months did not induce any signs of chronic intoxication as 100% mice of experimental group survived in comparison with the control group (57%). Feeding mice with the preparation at 1.0 g/kg dose facilitated improved protein and carbohydrate metabolism.

Key words: iodine insufficiency, weakening of the immune system, preventive iodine-containing preparation.

INTRODUCTION

Thyroid gland diseases in animals stand out among non-contagious diseases due to their wide spread and the economic damage they cause. Sustained iodine deficiency is the major factor in the etiology of endemic goiter; its outbreaks result in significant mortality of young animals (up to 68%) out of the total number of births [5].

The Amur Oblast belongs to a biogeochemical region with the low content of iodine in soil, water and air, which leads to thyroid gland disorders in livestock. Hypo- and dysproteinemia, hypoglycaemia, mineral metabolism disorders were found in young cattle in the iodine deficiency zone. Metabolic process disorders and immune deficiency were most pronounced in 10-day-old calves and grew more profound subsequently [2].

At present, there are quite a lot of preparations for iodine replenishment in animal bodies. But the low effectiveness of potassium iodide is accounted for the weak iodine/potassium bond limiting the shelf life of the preparations.

Natural zeolites are effectively used in veterinary medicine for non-contagious disease prevention and treatment [1]. Zeolites possess buffering, ion-exchange and sorption properties, they are the source of many macro- and microelements, are able to immobilize the enzymes of the gastrointestinal tract thus increasing their activity and stability [3]. Zeolites can prolong the effect of drugs and are good stabilizers. They are found to have a favourable impact on natural resistance and immunity of animals [4].

More than 10 zeolite deposits have been detected and developed in the Amur Oblast with the Vanginskoye and Kulikovskoye deposits being the most promising of them with respect to their use in agriculture.

Based on their petrographic characteristics, the zeolites of the Vanginskoye deposit are classified as heulandite-clinoptilolites, which have a more effective composition and the lower content of compounds hazardous for the body as compared with the zeolitic tuff of other deposits of the Amur Oblast and the Far East.

In order to improve the natural resistance and the metabolic processes in young cattle, a preventive iodine-containing preparation was developed on the basis of the natural zeolites of the Vanginskoye deposit.

The aim of the work is to study the toxicological properties of the developed "Vangtseyod" preparation.

MATERIALS AND METHODS

The work was conducted at the biochemistry laboratory and the animal facilities of the Far East Zone Research Veterinary Institute.

Table 1
Morphological and biochemical blood parameters in the mice fed the diet containing the "Vangtseyod" preparation

Parameters	Group of animals	
	control group (n=7)	test group (n=10)
Erythrocytes, 10^{12}/l	4.94 ± 0.36	5.75 ± 0.33
Leukocytes, 10^{9}/l	4.68 ± 0.52	6.33 ± 1.35
Haemoglobin, g/l	125.97 ± 3.58	142.37 ± 4.02
Total protein, g/l	56.80 ± 1.13	61.9 ± 1.43
Urea, mmole/l	4.81 ± 0.34	4.98 ± 0.29
Glucose, mmole/l	5.93 ± 0.34	5.16 ± 0.45
Total calcium, mmole/l	2.24 ± 0.10	2.32 ± 0.04
Inorganic phosphorus, mmole/l	2.03 ± 0.09	2.19 ± 0.17

The preventive iodine-containing preparation "Vangtseyod" was tested for its acute and chronic toxicity in white mice. To determine the acute toxicity the mice were given the preparation mixed with feed. The initial dose of the preparation was 1.0 g/kg of body weight, in 2 days the dose was increased up to 2.0 g/kg, then up to 4.0 g/kg; from then on, the dose of the preparation was doubled every 2 days in order to determine the median lethal dose (LD_{50}). The preparation was tested for its chronic toxicity in mice weighing 20–22 g after its single administration with feed at doses of 1.0 and 2.0 g/kg of body weight. The testing period was 60 days.

The systemic effect of the preparation on the bodies of the laboratory animals was assessed based on the physical condition of the animals, their morphological and biochemical blood parameters.

The amount of leucocytes, erythrocytes, haemoglobin was determined in blood. Total protein was determined using the biuret test, glucose, urea, calcium, phosphorus – by means of spectrophotometry using commercial test kits for the determination of the mentioned substrata.

RESULTS AND DISCUSSION

The preparation delivered to the mice at an initial dose of 1.0 g/kg of body weight did not have any effect on the systemic condition of the animals. The mice consumed all the feed, were mobile, showed an active response to the environment. When the preparation was given to the mice at a maximum dose of 16.0 g/kg, they ate 47.6% of the preparation. No signs of intoxication were detected – the animals were mobile, showed an active response to external irritants. Prior to the beginning of the experiment and upon its completion, test and control group animals were weighed, and at the end of the experiment blood samples were collected for morphological and biochemical tests.

Morphological and biochemical blood parameters of both test and control group mice indicated the absence of acute intoxication signs (Table 1). The comparative haematological analysis of test and control group animals showed a significant increase in haemoglobin by 13% ($p < 0.01$) in test group mice. The levels of erythrocytes and leukocytes were 1.2 and 1.3 times higher, respectively, in test group mice as compared to those in control group mice, but remained within the normal range. Biochemical testing of animal sera showed that the total protein content had significantly increased by 9% ($p < 0.05$) in mice fed with the preparation and was within the normal range. It was not possible to determine the median lethal dose (LD_{50}) because all the mice had survived the administration of the maximum dose of the preparation.

The analysis of white mouse body weight dynamics showed weight gains in both control group and test

Table 2
Morphological and biochemical blood parameters in mice after 60 days of preparation administration

Parameter	Group of animals		
	control group (n=4)	test group 1 1.0 g/kg (n=5)	test group 2 2.0 g/kg (n=5)
Erythrocytes, 10^{12}/l	7.93 ± 0.53	6.78 ± 0.79	7.08 ± 0.26
Leukocytes, 10^{9}/l	4.44 ± 1.63	4.20 ± 0.46	3.95 ± 0.77
Haemoglobin, g/l	129.60 ± 1.76	127.94 ± 2.23	130.04 ± 4.92
Total protein, g/l	61.88 ± 7.34	68.76 ± 4.25	64.13 ± 2.69
Albumins, g/l	28.43 ± 1.56	34.06 ± 1.02*	35.53 ± 2.60*
Urea, mmole/l	2.46 ± 0.54	2.34 ± 0.15	2.59 ± 0.60
Glucose, mmole/l	3.83 ± 0.15	6.01 ± 0.74*	3.73 ± 0.46
Total calcium, mmole/l	1.17 ± 0.08	1.49 ± 0.06*	1.35 ± 0.15
Inorganic phosphorus, mmole/l	2.07 ± 0.29	1.78 ± 0.19	2.03 ± 0.11

*$p < 0,05$

group. In particular, the weight gain in the group fed with the iodine-containing preparation was 9.2%, and in the control group – 4.8%. Consequently, animals fed with the preparation showed a more intensive growth as compared to the control ones (the difference was 4.4%).

Thus, supplementing the diet of the white mice with the preventive iodine-containing preparation based on natural zeolites did not have any negative effect on the biochemical and morphological blood parameters in the animals, promoted average daily weight gain that evidences the safety of the preparation.

When the preventive preparation was added to the diet of the white mice at doses of 1.0 and 2.0 g/kg of body weight no signs of chronic toxicity were detected in 60 days. Throughout the experiment the mice were mobile, showed an active response to the environment, consumed all the feed, their oral mucosae were pink, the hair coat was sleek and shiny (Figure 1).

Control group mice demonstrated hair loss, were aggressive, ate their offspring, and attacked the weaker ones (Figure 2). The survival rate in control and test group was 57.1% and 100%, respectively.

Morphological and biochemical blood parameters in test and control mice indicated the absence of chronic intoxication (Table 2).

Erythrocyte, leukocyte, haemoglobin levels in the blood of test and control group animals did not differ significantly.

Increase in total protein by 6.8 and 2.3 g/l and in albumin by 5.6 and 7.1 g/l were detected in the sera of test group mice as compared to the controls. Glucose concentration in the sera of test group 1 mice was 56.9% higher as compared to that in control group animals. Feeding mice with the preventive preparation at a dose of 1.0 g/kg of body weight promoted the normalization of protein and carbohydrate metabolism.

Calcium and phosphorus content was not significantly different in the sera of test and control group mice.

Consequently, the preventive preparation is not chronically toxic for white mice. The administration dose of 1.0 g/kg can be considered optimal, since the biochemical blood parameters in the mice fed with the preparation at the said dose and at a dose of 2.0 g/kg were not significantly different.

Figure 1. Test group mice (on day 40 of the experiment)

Figure 2. Control group mice (on day 40 of the experiment)

CONCLUSION

The developed preventive iodine-containing preparation "Vangtseyod" is neither clinically nor chronically toxic. No signs of chronic intoxication were detected when the diet of white mice was supplemented with the preparation at doses of 1.0 and 2.0 g/kg of body weight for two months as evidenced by 100% survivability of mice in the test groups as compared to the control group (57%). Feeding mice with the preventive preparation at a dose of 1.0 g/kg of body weight promoted the normalization of protein and carbohydrate metabolism.

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