The sharp decrease in the glucose consumption of the ischemized myocardium under the influence of intravenous injection of sodium succinate and α-ketoglutarate, established by these experiments, calls for further analysis, as also does the demonstration of the wide range of doses of α-ketoglutarate causing maximal stimulation of CCC and the study of the mechanism of this effect.

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GLUCOSE TOLERANCE AND INSULIN SENSITIVITY OF RATS POISONED WITH *Amanita phalloides*

N. I. Chuchukalo

UDC 615.918:582.28/.015.4:612.122.1

The effect of *Amanita phalloides* toxins on glucose tolerance and insulin sensitivity was studied. *Amanita* toxins were injected intraperitoneally in a dose of LD_{50} into male albino rats. Amanita toxins were found to disturb glucose tolerance, to increase the utilization of glucose by the tissues, and to make the animals more sensitive to insulin. These effects may be the result of depression of the insulin-activating capacity of the liver and potentiation of the function of the islet-cell apparatus of the pancreas.

KEY WORDS: *Amanita phalloides* toxins; glucose tolerance; insulin sensitivity.

The toxins of *Amanita phalloides*, namely amanitines and phalloidines, if administered to animals, cause degenerative changes in many organs and disturbances of all types of metabolism [2, 3]. Profound disturbances of the protein-synthesizing and carbohydrate functions of the liver, manifested by hypoglycemia, depletion of the glycogen reserves in the liver, and hyperinsulinemia, have been found [5-7].

The object of the present investigation to study glucose tolerance and insulin sensitivity in rats poisoned with *Amanita* toxins.

EXPERIMENTAL METHOD

Experiments were carried out on 110 noninbred male albino rats weighing 160-180 g. The toxins were injected intraperitoneally into the animals in a dose of LD_{50}. Physiological saline was injected into the control rats. In the glucose tolerance test, glucose was injected intraperitoneally in a dose of 1 mg/g body weight of the 40% solution [1] and the blood sugar was determined in the fasting state and 15, 30, 60, and 120 min after loading. Insulin sensitivity was judged from changes in the blood sugar level 10, 30, and 60 min after subcutaneous injection of insulin in a dose of 0.07 unit per animal. Blood sugar was determined by the orthotoluidine method. Analysis of the blood sugar curves involved determination of: the hyperglycemic coefficient

Department of General Biology, Ternopol' Medical Institute.

(Presented by Academician of the Academy of Medical Sciences of the USSR S. N. Golikov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 86, No. 9, pp. 319-321, September, 1978. Original article submitted December 28, 1977.

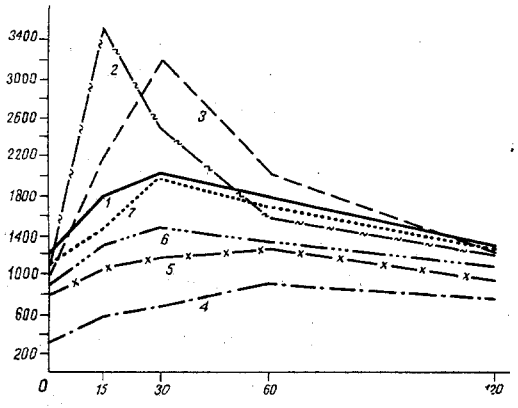

Fig. 1

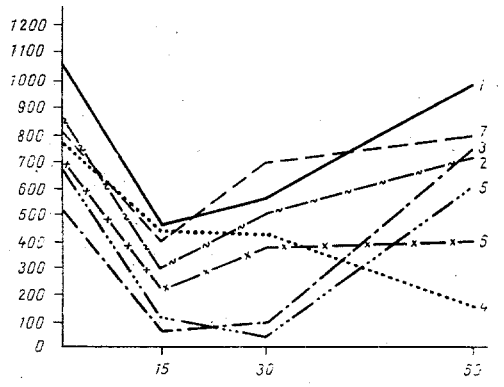

Fig. 2

Fig. 1. Glucose tolerance in rats poisoned with Amanita toxins. Abscissa, time (in min); ordinate, blood sugar (in mg/liter). Curves: 1) after glucose loading in control group of rats; 2) 6 h, 3) 12 h, 4) 24 h, 5) 3 days, 6) 7 days, 7) 20 days after poisoning.

Fig. 2. Insulin sensitivity in rats poisoned with Amanita toxins. Curves: 1) control; 2) 1 h, 3) 12 h, 4) 24 h, 5) 3 days, 6) 7 days, 7) 20 days after poisoning. Remainder of legend as in Fig. 1.

TABLE 1. Changes in HC, PHC, and UC of Glucose in Rats Poisoned with Amanita phalloides Toxins (M ± m)

Time of investigation	HC	PHC	UC
Контроль	1,81±0,24	1,0±0,34	2,04±0,12
After poisoning with toxins:			
1 h	2,70±0,12*	0,87±0,07	2,76±0,11*
3 h	4,49±0,50*	1,35±0,18*	5,37±0,29*
6 h	4,96±1,20*	1,37±0,12	5,15±1,50*
12 h	5,47±0,90*	1,38±0,19	6,21±0,79*
24 h	2,25±0,33	1,30±0,08	2,05±0,54
on 3rd day	1,87±0,34	1,80±0,24*	1,15±0,17*
» 5-th »	1,65±0,13*	0,98±0,14	1,44±0,21*
» 7-th »	1,97±0,21	1,19±0,30*	2,25±0,70*
» 10-th »	2,26±0,20*	1,11±0,30	5,38±1,61*
« 20-th »	2,00±0,19	0,79±0,09*	2,80±0,31*

Legend. Asterisk indicates $P < 0.05$ compared with control.

(HC), the posthyperglycemic coefficient (PHC), and the glucose utilization coefficient (UC) [4]. The investigations were carried out 1, 3, 6, 12, and 24 h and 3, 5, 7, 10, and 20 days after poisoning. Five rats were used each time.

The numerical results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

The fasting blood sugar of the control rats were 983.0 ± 37.0 mg/liter. After glucose loading the blood sugar began to rise 15 min after the injection and reached a maximum after 30 min (1800.0 ± 100.0 mg/liter), after which it fell, to reach its initial level by the 120th minute. The values of the coefficients were: HC 1.81 ± 0.25, PHC 1.0 ± 0.34, UC 2.04 ± 0.12. In the same group of animals the blood sugar concentration after injection of insulin fell to its lowest level after 15 min (to 450.0 ± 50.0 mg/liter); it began to rise after 30 min and regained its initial values after 60 min.

The fasting blood sugar concentration in the rats poisoned with Amanita phalloides toxins was significantly lowered at all times of the experiments. The blood sugar curves of the animals 1, 3, 6, and 12 h after

poisoning were uniform in character: during the first 15 min after glucose loading, the blood sugar rose to 2-4 times its initial level ($P < 0.05$), it fell after 30 min, and by 120 min it had regained its initial values (Fig. 1). The values of HC, PHC, and UC were significantly higher than in the control (Table 1).

The curves after glucose loading 1, 3, and 5 days after poisoning with the Amanita toxins showed only a very small rise in the blood sugar level, followed by a rapid fall, to reach initial values after 120 min.

Sensitivity to insulin 1 and 6 h after the beginning of the experiment was reduced, but between 12 h and 10 days after the beginning of the experiment it was high (Fig. 2).

The lowered glucose tolerance during the first 12 h after injection of the toxins could reflect a low liver glycogen concentration and an active response of the islet-cell apparatus of the pancreas to hyperglycemic stimulation [8]. The increase in all coefficients indicates the more intensive utilization of glucose at the periphery. The marked insulin sensitivity was due to a decrease in the activity of the antiinsulin regulators, such as the insulinase system. The writer has shown that insulinase activity of liver homogenates of poisoned rats during the first 10 days after the beginning of the experiment was relatively low (down to 26% compared with 95% in the control). The blood insulin activity of the rats at the same periods of the experiment was high, 1.5-2.8 times higher than in the control animals.

Amanita toxins thus disturb glucose tolerance, increase the utilization of glucose by the tissues, and increase the sensitivity of the animal to insulin. These effects may be the result of depression of the insulin-activating system of the liver and stimulation of the function of the islet-cell apparatus of the pancreas.

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