

## THE INFLUENCE OF DIMEDROL ON CARBOHYDRATE METABOLISM

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It has been established experimentally that histamine can lead to a depletion of the reserves of glycogen in the liver of animals. We have shown that by using an antihistaminic agent, dimedrol, the opposite effect can be produced.

The principal task of the research set forth below was to make clear to what extent the observed effect of dimedrol depends on its dose.

It was also important to determine the influence of dimedrol on epinephrine hyperglycemia. Komrad, Harvey, et al. [1, 2] have shown that many antihistaminic agents reduce the hyperglycemia produced by epinephrine. In this respect dimedrol has not been studied.

### EXPERIMENTAL METHODS

Experiments were performed on rabbits (predominantly males) weighing about 2 kg, which were kept on an ordinary food ration. Dimedrol was injected intravenously: 1, 2, 3 and 5 mg per kg of body weight. On the day following injection the rabbits were killed by decapitation. The organs which were the object of the examination were frozen with liquid nitrogen, and their glycogen content determined (according to Pfluger's method).

The influence of dimedrol on the blood sugar content was examined in rabbits which were previously without food for 18-20 hours. In the first series (9 rabbits) dimedrol was injected intravenously: 2-3 mg/kg. After 30-60 minutes 0.1 mg of epinephrine was injected subcutaneously.

In the second series of experiments (15 rabbits) dimedrol was injected in a dose of 1-2 mg/kg; 0.1 mg of epinephrine was injected on the following day.

The control rabbits in each series of experiments (10 and 11 animals) were only injected with epinephrine in the same dose as were the experimental animals. Blood sugar content was determined by Hagedorn and Jensen's method. Blood samples were taken on an empty stomach and 30, 60, 90 and 120 minutes after the injection of epinephrine.

### EXPERIMENTAL RESULTS

It was discovered that dimedrol in doses of 1-2 mg/kg produced in the rabbits somewhat of a state of retardation. With larger doses of 3-5 mg/kg, excitation, tremor and ataxia were noted in the animals. The indicated phenomena lasted 15-20 minutes.

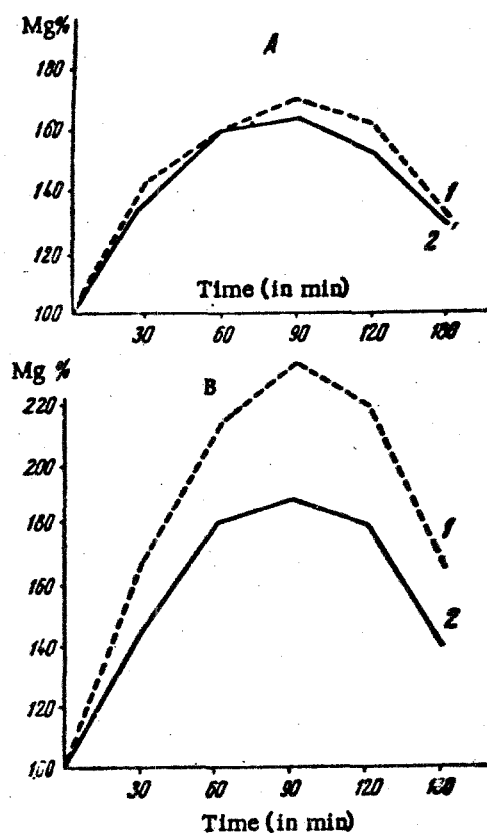
From the data cited in the table it is evident that, as a result of the use of dimedrol in doses of 1-2 mg/kg, the glycogen content of the heart and liver of the animals increased, while that of skeletal muscle remained

unchanged. With larger doses of dimedrol (3-5 mg/kg), a decrease in the glycogen content of the liver and skeletal muscle was observed. The glycogen content of the heart did not change.

#### The Influence of Dimedrol on the Glycogen Content of the Heart, Skeletal Muscle and Liver of Rabbits

Amount of dimedrol injected (in mg/kg)	Number of Animals	Glycogen content (in % of the gross weight of tissue)		
		Heart	Skeletal muscle	Liver
Control . . . . .	20	$0.378 \pm 0.019$	$0.380 \pm 0.044$	$4.540 \pm 0.313$
1 . . . . .	7	$0.574 \pm 0.087$	$0.362 \pm 0.044$	$5.860 \pm 0.370$
2 . . . . .	7	$0.708 \pm 0.170$	$0.430 \pm 0.032$	$5.510 \pm 0.560$
3-5 . . . . .	12	$0.377 \pm 0.047$	$0.264 \pm 0.030$	$3.930 \pm 0.565$

The changes in glycogen content corresponded, evidently, to that functional state in which the rabbits were found following their injection with dimedrol. The excited state and the tremor, which were observed in the animals with injection of dimedrol in a dose of 3-5 mg/kg, may promote the depletion of carbohydrate reserves in the liver and skeletal muscle, while the slow-down of the animals noted with small doses may promote the accumulation of glycogen in the heart and liver.



Change in blood sugar content of rabbits of the first (A) and second (B) series of experiments. 1) Epinephrine (control); 2) epinephrine+dimedrol (experiment).

Curves of the change in blood sugar content are drawn in the diagram, each point of which represents the average value calculated from the data on the blood sugar content of the individual experimental and control animals for the duration of the examination.

It can be noted that the glycemic curve for the first group of rabbits (A), which were injected with dimedrol 30-60 minutes prior to the epinephrine, does not differ from the corresponding curve for the control group of animals.

The curve for the rabbits of the second series of experiments (B), which were injected with dimedrol a day before the epinephrine, differs from the glycemic curve for the control animals and shows a considerable decrease in the hyperglycemia produced by the epinephrine.

Thus, from the data obtained it is apparent that the influence of dimedrol on carbohydrate metabolism under definite conditions results in an increase in the glycogen content of the liver and heart and in a reduction of epinephrine hyperglycemia.

This influence depends on the doses of dimedrol employed and on the time it is used.

#### LITERATURE CITED

- [1] S. C. Harvey, C. Y. Wang and M. J. Nickerson, *Pharmacol. Exptl. Therap.* Vol. 104, No. 3, pp. 363-378 (1952).
- [2] E. L. Komrad and E. R. Loew, *Pharmacol. Exptl. Therap.* Vol. 103, No. 2, pp. 115-122 (1951).