

# PHARMACOLOGY

## THE EFFECT OF A SUBSTANCE WITH THYROID ACTION (IODIZED CASEIN) ON THE COURSE AND OUTCOME OF CORASOLE INTOXICATION IN MICE

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O. D. Kozlov [1] demonstrated that one of the agents disturbing the processes of conjugated phosphorylation (separating respiration from phosphorylation), — 2,4 — dinitrophenol (DNP) — decreases the number of convulsive attacks and lowers the death incidence in animals with corasole intoxication. One of the explanations for these findings linked the effect of DNP with its effect on the processes of conjugated phosphorylation. In order to verify this assumption it was decided to investigate the effect of other inhibitors of respiratory phosphorylation on the course and outcome of corasole intoxication. Thyroxin is such a substance, a substance natural to the organism and whose separating action was demonstrated by a number of authors in experiments on isolated tissues [4, 5, 6, 7, 8, 9 and others].

### EXPERIMENTAL METHOD

Our experiments were carried out on adult male mice weighing from 16 to 22 g. At first, O. D. Kozlov's experiments were performed and his findings of favorable effects of DNP on the course of corasole intoxication confirmed: in 5 mice given DNP (20  $\gamma$ /g) 15 minutes prior to subcutaneous injection of corasole (80  $\gamma$ /g) the number of convulsive attacks was 14 instead of 38 as in control mice.

As we did not have thyroxin available, preparations with thyroid action were employed in our experiments. Thyroidin, which according to findings on mice tested for resistance to lowering of atmospheric pressure in the pressure chamber (a generally accepted biological test for thyroidin), was available but found to be ineffective. Therefore a series of experiments was undertaken employing iodized casein (IC) — a preparation producing an action analogous to that of thyroxin.

Two series of experiments were carried out with IC. In the first series of 20 mice a suspension of IC (1 ml containing 4 mg IC) was administered subcutaneously three times (1 ml every other day). The control series of 20 mice received the same number of injections of a casein (C) suspension only. Twenty-four hours following the last injection, 20 mice (10 experimental and 10 controls) were tested for resistance to lowering of atmospheric pressure in the pressure chamber. The remaining 20 mice were given corasole. It was administered subcutaneously in a 1% solution of 80  $\gamma$ /g. In the second series of experiments IC was given six times.

### EXPERIMENTAL RESULTS

As we did not observe any significant difference in the results in both series of experiments, the findings are summarized and presented in the table.

As seen in the table, IC does not influence mortality of mice with corasole intoxication when administered in doses which distinctly decrease resistance of mice to lowering of atmospheric pressure; the number of

fatalities remains the same as in experiments with preliminary administration of unlodized casein (IC does not influence the number of convulsive attacks either).

Thus, of the two separating agents, DNP improves the course and outcome in corasole intoxication whereas the preparation with thyroid action is without any effect.

As is already known, animals with thyrotoxicosis have symptoms resembling those in dinitrophenol and dinitrocresol intoxications; weight loss, rise in body temperature and increased metabolism. On the other hand, as opposed to thyroidin, dinitrocresol cannot eliminate the development of myxedema and DNP does not hasten (as opposed to substances with a thyroid action) metamorphosis of the tadpole.

#### The Effect of Iodized Casein (IC) on Resistance of Mice to Lowering of Atmospheric Pressure and to Corasole Intoxication

In the pressure chamber				Outside the pressure chamber			
preparation	total number of animals	animals which perished at 270 mm of Hg		preparation	total number of animals	animals perished	
		total number	%			total number	%
C	20	0	0	C + corasole	20	10	50
IC	20	17	85	IC + corasole	20	8	40

There are a number of reports in the literature testifying to the differences in the effect of thyroidin and DNP on the processes of conjugated phosphorylation. The effects on these processes are more distinct when the aid of magnesium salts is enlisted; the magnesium cation inhibits the separating effect of thyroidin but does not influence the effect of DNP [2, 3, 10 and others].

The lack of effect of substances with thyroid action on the course and outcome of corasole intoxication can serve as a new index for differentiating the effects of these substances from DNP. The mechanism of the favorable effect of DNP on the course of corasole intoxication deserves further study.

#### SUMMARY

It was demonstrated that the symptoms of corasole intoxication become less intense as a result of preliminary administration of 2,4-dinitrophenol, disturbing the processes connected with phosphorylation. Iodized casein, like substances with thyroid action, disturbs the processes of conjugated phosphorylation, but has no effect on the course and the outcome of corasole intoxication (as distinguished from 2,4-dinitrophenol).

#### LITERATURE CITED

- [1] O. D. Kozlov, *Biull. Eksperim. Biol. i Med.* 39, 4, 44-46 (1955).
- [2] T. M. Brody and J. A. Bain, *J. Pharmacol. a. Exper. Therap.* 1954, 119, 2-3.
- [3] T. M. Brody, *Pharmacol. Rev.* 1955, v. 7, pp. 335-363.
- [4] F. L. Hock and F. Lipmann, *Proc. Nat. Acad. Sc.* 1954, v. 10, pp. 909-921.
- [5] H. A. Lardy and G. Feldott, *Ann. New York Acad. Sc.* 1951, v. 54, pp. 636-647.
- [6] G. F. Maley and A. Lardy, *J. Biol. Chem.* 1953, v. 204, pp. 435-444.
- [7] G. F. Maley and A. Lardy, *J. Biol. Chem.* 1955, v. 215, pp. 377-388.
- [8] C. Martius and B. Hess, *Arch Biochem.* 1951, v. 33, pp. 486-487.
- [9] C. Martius, H. Bieling and D. Nith-Litzow, *Bioch. Ztschr.* 1955, Bd. 327, S. 163-169.
- [10] D. F. Tapley, C. Cooper and A. L. Lehninger, *Bioch. biophys. Acta*, 1955, v. 18, pp. 597-598.