

INACTIVATION OF COBALT IN THE ORGANISM BY ETHYLENEDIAMINOTETRAACETATE

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In the last few years there has appeared in foreign literature a large number of experimental investigations establishing the possibility of coupling in the organism by means of sodium ethylenediaminetetraacetate the ions of various metals with the formation of water-solvent complex compounds.

A particularly stable complex compound of sodium ethylenediaminetetraacetate is formed with calcium ions, on which basis it was recommended as an anticoagulant [8] and for coupling the calcium in various clinical indications [5, 6]. In addition, it has been used for experimental therapy in poisoning by heavy metals: lead [2], vanadium [7] and also for acceleration of extraction from the organism of radioactive elements, for example, yttrium [3].

Child [3] showed that sodium ethylenediaminetetraacetate prevents polycythemia in rats caused by cobalt salts. The quantitative relationship between it and cobalt in this work remained unexplained, since the solutions of the substances in question were added to the food of the animals.

The possibility of detoxication of cobalt ions with the help of sodium ethylenediaminetetraacetate is of special interest in connection with the fact that radioactive cobalt in the last few years has been widely employed in radio therapy. The purpose of the present work was to find to what extent and in what quantitative ratios sodium ethylenediaminetetraacetate may serve as an antitoxic for the cobalt ions. For this purpose, the most convenient is that variant of the experiment in which the biologically determined amounts of cobalt would be the smallest possible, which simplifies the task of establishing the quantitative ratios between sodium ethylenediaminetetraacetate and cobalt. We chose detoxication of hydrocyanic acid by a cobalt salt. The doses of cobalt nitrate and cyanide were obtained by us from the work of V. M. Rozhkov, N. S. Stepanenko and K. M. Usova [1].

EXPERIMENTAL METHODS

The work was conducted on 160 white female mice weighing 18-22 g. The aqueous solutions of sodium ethylenediaminetetraacetate, cobalt nitrate and potassium cyanide were introduced subcutaneously in various parts of the body of the animal.

It was clear in the preliminary experiments that the mice tolerated without symptoms of intoxication sodium ethylenediaminetetraacetate at a dose of 300 γ /g.

Three series of experiments were conducted. In the first control series (40 mice) the toxic effect of potassium cyanide (dose 10 or 12 γ /g) was evaluated; in the second control series (45 mice) the detoxicating effect of cobalt (introduced in a dose of 20 or 30 γ /g body weight, 20-40 minutes before cyanide). In the third series, (75 mice) we determined the suppression of the detoxicating effect of cobalt by means of sodium ethylenediaminetetraacetate (introduced in doses of 35, 100, 200 and 300 γ /g body weight, 15-30 minutes before cobalt; the cyanide as in the second series was introduced 20-40 minutes after cobalt). The gram-molecular ratios between the doses of sodium ethylenediaminetetraacetate and cobalt in the various groups of the third series of experi-

ments were 1:1, 2:1, 4:1, 6:1, 9:1. The table shows only three groups with the coefficients 2, 6 and 9.

EXPERIMENTAL RESULTS

Cobalt reduced sixfold the percentage of animals in which convulsions occurred and fully prevented a fatal outcome upon introduction of cyanide.

There was a perceptible inhibition of the detoxicating effect of cobalt under the influence of sodium ethylenediaminetetraacetate even with a coefficient of 2; in more than half the animals convulsions occurred, and 20% of the mice died. According to the degree of increase in the coefficient, the suppression of the cobalt effect was intensified. With a coefficient of 9, the toxic effect of cyanide was particularly evident. The percentage of animals with convulsions and which died in the third and first series of experiments proved to be similar (see Table).

Inactivation of Cobalt by Sodium ethylenediaminetetraacetate (EDTA).

Series of Experiments	M- EDTA	Number of animals		
	M Co (NO ₃) ₂	Total	With con- vulsions	Died
First (KCN)		40	40 (100)	39 (97)
Second [Co(NO ₃) ₂ and KCN]		45	8 (17)	0 (0)
Third EDTA, [Co(NO ₃) ₂ and KCN]	2	20	11 (55)	4 (20)
	6	20	15 (80)	11 (55)
	9	10	9 (90)	8 (80)

As can be seen from the data presented, with the aid of sodium ethylenediaminetetraacetate, it is possible to couple the ions of cobalt; sodium ethylenediaminetetraacetate suppresses detoxication of cyanide by cobalt nitrate as a result of which the toxic effect of cyanide is sharply apparent.

The optimal dose of sodium ethylenediaminetetraacetate is that which, in the gram-molecular relationship is 9 times greater than the dose of cobalt nitrate.

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