EFFECT OF CARBAMATE PESTICIDES ON NUCLEIC ACID METABOLISM IN THE RAT LIVER AND SPLEEN

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UDC 615.285.7:632.95:547.495.1].014.42:[612.35+612.411].015.348

A single injection of maximal tolerated doses of carbamate pesticides into albino rats stimulates activity of ribonuclease and desoxyribonuclease in the liver and spleen. The RNA and DNA content in the liver rises or is unchanged. The content of nucleic acids in the spleen in most cases shows a tendency to fall.

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Among the many substances used in plant protection at the present time derivatives of carbamic acid are becoming increasingly important. These compounds possess a broad spectrum of action and compare favorably with other pesticides because of their relatively lower toxicity for warm-blooded animals.

Investigation of the toxic properties of preparations and the establishment of normal standards are not always enough, if it is borne in mind that the action of toxic chemicals may not be confined to visible disturbances of the organism's responses but may also give rise to deep-seated changes in vitally important systems of the living cell, often persuing a latent course. The study of carbamate from these standpoints is particularly important because some of these preparations (Zineb, Ziram) are known to have harmful effects on the generative function and on the progeny [2, 3].

In the present investigation the action of some carbamic acid derivatives on nucleic acid metabolism was studied in the liver and spleen of rats.

EXPERIMENTAL METHOD

The effect of carbamates on nucleic acid metabolism was studied by determination of the content of the nucleic acids themselves and also by investigation of the activity of enzymes involved in the first stages of nucleic acid breakdown: ribonuclease (RNase) and desoxyribonuclease (DNase). The action of members of three groups of carbamates was studied: carbamaic acid esters (Sevin, Carbin), thiocarbamates (Diptal), and dithiocarbamates (tetramethylthiuram disulfide, or TMTD).

The investigations were carried out on young male albino rats weighing 120-150 g. The preparations were introduced into the animal's stomach once only, in the form of aqueous suspensions or oily emulsions, in maximal tolerated doses. The rats were sacrificed by decapitation 18 h after administration. Activity of the enzymes and the content of nucleic acids in the liver and spleen were studied.

RNase activity was determined by the method of Fiers and Stocks [5], and DNase activity by De Duve's method [4]. RNA was estimated quantitatively by the method of Fleck and Munro [6], and DNA by the method of A. S. Orlov and E. I. Orlova [1], followed by spectrophotometric examination of the samples.

Activity of the enzymes was expressed in micrograms phosphorus of nucleic acids per milligram enzyme nitrogen, and the nucleic acid content in milligrams of nucleic acids per gram tissue. All the results were analyzed by statistical methods.

EXPERIMENTAL RESULTS

The study of the effect of carbamates on activity of enzymes depolymerizing nucleic acids showed that after administration of maximal tolerated doses of preparations activity of RNase and DNase was increased by comparison with their activity in the control group (Table 1).

Kiev Research Institute of Work Hygiene and Occupational Diseases (Presented by Active Member of the Academy of Medical Sciences of the USSR L. M. Shabad). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 66, No. 10, pp. 46-48, October, 1968. Original article submitted June 19, 1967.

TABLE 1. Activity of RNase and DNase of Liver and Spleen of Rats Receiving Maximal Tolerated Doses of Carbamates by a Single Intragastric Injection (μg phosphorus of nucleic acids/mg nitrogen)

Statistical index	Tissue	Control group	RNA				Control group	DNA			
			Sevin	Carbin	Diptal	TMTD		Sevin	Carbin	Diptal	TMTD
$\bar{X}$	Liver	16.7	40.7	37.7	22.5	29.5	14.4	25.9	18.02	14.08	48.2
$S\bar{X}$ ±		1.22	4.3	2.87	1.7	4.29	1.58	2.9	1.11	3.3	8.98
t		–	4.9	7.8	2.55	3.88	–	3.62	3.9	0.18	5.8
P		–	< 0.001	< 0.001	< 0.02	< 0.001	–	< 0.001	< 0.001	> 0.5	< 0.001
$\bar{X}$	Spleen	36.1	57.9	66.7	47.3	64.9	17.9	39.5	38.1	38.03	55.2
$S\bar{X}$ ±		2.69	4.2	4.18	3.2	6.5	1.7	3.7	3.5	6.97	7.88
t		–	4.5	6.3	2.2	4.6	–	5.9	3.5	4.15	6.6
P		–	< 0.001	< 0.001	< 0.05	< 0.001	–	< 0.001	< 0.001	< 0.001	< 0.001

TABLE 2. Content of RNA and DNA in Liver and Spleen of Rats Receiving Maximal Tolerated Doses of Carbamates by a Single Intragastric Injection (in mg RNA and DNA/g tissue)

Statistical index	Tissue	Control group	RNA				Control group	DNA			
			Sevin	Carbin	Diptal	TMTD		Sevin	Carbin	Diptal	TMTD
$\bar{X}$	Liver	4.08	4.66	5.31	6.17	4.92	2.24	2.52	2.29	1.9	2.77
$S\bar{X}$ ±		0.24	0.17	0.21	0.41	0.48	0.85	0.61	0.16	0.09	0.28
t		–	1.75	6.3	4.7	1.38	–	2.9	0.22	0.8	2.04
P		–	> 0.1	< 0.001	< 0.001	> 0.1	–	< 0.01	> 0.5	> 0.5	< 0.05
$\bar{X}$	Spleen	5.3	4.99	6.11	3.04	4.19	12.34	11.61	10.59	9.26	10.71
$S\bar{X}$ ±		0.42	0.75	0.56	0.48	0.52	0.42	0.52	0.46	0.35	0.49
t		–	1.07	1.2	2.8	1.65	–	1.23	2.8	5.3	2.7
P		–	> 0.1	> 0.1	< 0.05	> 0.1	–	> 0.1	< 0.02	< 0.001	< 0.01

EXPERIMENTAL RESULTS

The study of the effect of carbamates on activity of enzymes depolymerizing nucleic acids showed that after administration of maximal tolerated doses of the preparations activity of RNase and DNase was increased by comparison with their activity in the control group (Table 1).

In most cases a tendency was observed for the content of nucleic acids in the spleen to fall, in agreement with the observed increase in enzyme activity.

In the liver, on the other hand, an increase in the content of nucleic acids under the influence of carbamates was most frequently observed. The RNA content, for example, increased during exposure to all the substances tested (increase statistically significant in the case of Carbin and Diptal. The DNA content in the liver changed in different directions. The largest increase was produced by Sevin and TMTD, while under the influence of Diptal the DNA content in the liver was actually reduced slightly (Table 2).

Whatever the nature of the increase in enzyme activity of the nuclease, it is evidence of increased activity of nucleic acid breakdown under the influence of carbamates.

When the results concerned with the effect of carbamates on activity of enzymes depolymerizing nucleic acids and the content of these acids in the investigated tissues are compared, it should be noted that an increase in nuclease activity in the liver was accompanied by an increase in the RNA content. The DNA content also showed a tendency to increase. This fact may indicate that, besides an increase in activity of depolymerizing enzymes, activation of synthetic processes also takes place as a response reaction of the body. This activation of synthesis can be interpreted as the result of the action of protective forces or compensatory mechanisms. In most cases a slight decrease in the RNA and DNA level was observed in the

spleen, although this decrease was not considerable and did not correspond to the observed increase in nuclease activity. This suggests activation of nucleic acid synthesis in the spleen also, more especially because in some cases (Carbin poisoning), an increase in the RNA content was observed in the spleen.

Carbamates possibly disturb nucleic acid metabolism and stimulate their breakdown, thereby creating physiological conditions in the cell for synthetic activity of the nucleases.

It should be noted that different members of the carbamates used in the investigation gave effects of similar type on nucleic acid metabolism, i.e., they possess a common action despite differences in their chemical structures and properties. This is in full agreement with published data relating to the action of various carbamates on the chromosomal apparatus of plants.

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