

# EFFECT OF OCTADINE AND BRETYLIUM ON THE CONTENT OF ADENINE NUCLEOTIDES IN THE VASCULAR WALL

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Experiments on rabbits showed that a single injection of octadine (guanethidine) (10 mg/kg) 3 h, or of bretylium (10 mg/kg) 1 h, before the investigation caused no change in the content of adenine nucleotides or inorganic phosphorus in the wall of the aorta. A decrease in the catecholamine level was observed after administration of octadine. Bretylium, whether injected once or repeatedly, caused no change in the tissue catecholamine concentration. Repeated injection of these preparations in the same doses daily for 10 days caused an increase in the AMP level but no significant change in the concentrations of the other adenine nucleotides or of inorganic phosphorus. The increase in the AMP level could be one possible mechanism of the pharmaco-mechanical relaxation of the smooth muscle of the vessel wall.

Key words: adenine nucleotides; blood vessel wall; catecholamines; sympatholytics.

ATP is known to play an important role in the storage of catecholamines in the adrenergic neuron [10, 11]. Pharmacological agents liberating biogenic amines from tissue depots have been shown to induce corresponding changes in the content of the components of the adenosine phosphate system [2, 5, 6, 12, 15]. It was accordingly decided to study the effect of the sympatholytics octadine (guanethidine) and bretylium, which interfere with the storage and liberation of biogenic amines, on the content of adenine nucleotides, inorganic phosphorus, and catecholamines in the wall of the rabbit aorta.

## EXPERIMENTAL METHOD

Experiments were carried out on 65 rabbits weighing 1.7-2.3 kg. The catecholamine content in the wall of the aorta was determined by Osinskaya's fluorescence-analytical method [3] with certain modifications [4] and expressed as micrograms noradrenalin base per gram wet weight of tissue. Separation of ATP, ADP, and AMP was carried out by high-voltage electrophoresis on paper [14].

The adenine nucleotides were estimated quantitatively on the SF-4A spectrophotometer by measuring the extinctions at a wavelength of 260 nm. Inorganic phosphorus was determined by Delory's colorimetric method in Grigor'eva's modification [1]. To rule out possible fluctuations in the parameters studied, each series of experiments was accompanied by its own control.

Octadine (10 mg/kg) was injected intramuscularly 3 h, and benactyzene (10 mg/kg) intravenously 1 h, before the investigation. These substances were reinjected intramuscularly in the same doses for a period of 10 days.

## EXPERIMENTAL RESULTS AND DISCUSSION

The data given in Table 1 show that a single injection of octadine and bretylium caused no change in the concentrations of the adenosine phosphates and inorganic phosphorus in the rabbit aortic wall. Under the influence of octadine the catecholamine level fell by 41% below the control. Bretylium, whether injected

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TABLE 1. Effect of Octadine and Bretylium on Content of Adenine Nucleotides, Inorganic Phosphorus, and Catecholamines in Wall of Rabbit Aorta ( $M \pm m$ )

Experimental conditions	ATP	ADP	AMP	Total adenine nucleotides	Inorganic phosphorus (in mg %)	Total content of catecholamines (in $\mu$ g noreadrenalin/g wet weight of tissue)
	$\mu$ moles/g tissue					
Control	$0,38 \pm 0,03$	$0,34 \pm 0,03$	$0,33 \pm 0,03$	$1,06 \pm 0,06$	$17,32 \pm 0,8$	$0,85 \pm 0,14$
Octadine (10 mg/kg, 3 h later)	$0,33 \pm 0,04$	$0,30 \pm 0,04$	$0,33 \pm 0,04$	$0,95 \pm 0,04$	$16,45 \pm 1,3$	$0,35 \pm 0,08$
P	$>0,25$	$>0,25$	$>0,5$	$>0,25$	$>0,5$	$<0,01$
Bretylium (10 mg/kg, 1 h later)	$0,41 \pm 0,06$	$0,32 \pm 0,04$	$0,37 \pm 0,05$	$1,09 \pm 0,09$	$15,48 \pm 0,8$	$0,59 \pm 0,11$
P	$>0,1$	$>0,5$	$>0,5$	$>0,5$	$>0,1$	$>0,25$
Control	$0,24 \pm 0,02$	$0,28 \pm 0,02$	$0,25 \pm 0,007$	$0,77 \pm 0,03$	$22,18 \pm 1,28$	—
Octadine (10 mg/kg, for 10 days)	$0,20 \pm 0,01$	$0,33 \pm 0,03$	$0,34 \pm 0,03$	$0,87 \pm 0,06$	$23,96 \pm 1,45$	—
P	$>0,5$	$>0,25$	$<0,05$	$>0,1$	$>0,25$	—
Control	$0,29 \pm 0,01$	$0,28 \pm 0,05$	$0,28 \pm 0,04$	$0,86 \pm 0,08$	$17,85 \pm 0,6$	—
Bretylium (10 mg/kg, for 10 days)	$0,26 \pm 0,02$	$0,32 \pm 0,03$	$0,37 \pm 0,05$	$0,95 \pm 0,06$	$19,37 \pm 1,24$	$0,95 \pm 0,18$
P	$>0,5$	$>0,5$	$<0,02$	$>0,25$	$>0,25$	$>0,5$

Legend. P calculated relative to the control.

once or repeatedly, did not change the catecholamine content. Repeated injections of these preparations were accompanied by elevation of the AMP level without any significant changes in the concentrations of the other adenine nucleotides or of inorganic phosphorus.

The results of the investigation were interpreted from the standpoint of the concept of a functionally active "nucleotide-independent" and a stable "nucleotide-dependent" fraction of the catecholamines in the adrenergic neuron [13].

The fact that the ATP level showed no significant change in these experiments under the influence of the sympatholytics is further confirmation of the currently held opinion that catecholamines are liberated from the functionally active fraction under the influence of octadine [7-9]. Correspondingly bretylium, which does not affect the catecholamine level in the aortic wall, does not change the ATP concentration in it.

Regardless of its effect on the catecholamine level, the repeated injection of octadine and bretylium, resulting in chronic pharmacological desympathization, leads to an increase in the AMP content. This effect, in turn, could be one mechanism of the pharmacomechanical relaxation of the smooth muscle of the blood vessel wall [16].

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