ACTION OF THE HEMOCYTOCARDIOTOXIN FROM THE VENOM OF THE CENTRAL ASIAN COBRA ON ARTIFICIAL PHOSPHOLIPID MEMBRANES OF DIFFERENT COMPOSITIONS

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The selective hemolytic and cytotoxic action of the venoms of snakes of the family Elipidae and of the hemocytocardiotoxins (HTs), membrane-active polypeptides, isolated from them have been reported on many occasions [1-8]. Although attempts to connect the resistance of individual types of cells to HTs with the features of the phospholipid composition of their cytoplasmatic membrane have been unsuccessful [1], nevertheless it has been suggested that the resistance depends on the ratio of lecithin and sphingomyelin in the membrane [9]. We have shown previously [10] that in artificial phospholipid membranes (APMs) and liposomes from total brain (or erythrocyte) phospholipids the HT isolated from the venom of the central Asian cobra [11] induces permeability for univalent cations and causes the issuance of K^+ from liposomes charged with it. In view of the established selective action of this HT [8], it appeared of interest to investigate its influence on the permeability of APMs formed from the combined phospholipids of different compositions from pure phospholipids.

The results obtained (Table 1) show that the HT of the central Asian cobra in a concentration of $2 \cdot 10^{-7}$ M changes almost identically (by a factor of approximately 20) the conductivity of the ATMs formed from the phospholipids isolated from the erythrocytes of the rat, the rabbit, man, the guinea-pig, and cattle brain in which the ratio of lecithin to sphingomyelin varies from 3 : 2 to 4 : 1. The only exception is formed by membranes from oxidized cholesterol, where the effect was considerably less. The HT-induced issuance of K^+ from liposomes prepared from sphingomyelin alone was the same as from liposomes formulated from the total phospholipid (Fig. 1).

Thus, the stability of erythrocytes or other types of cells to a hemocytocardiotoxin does not depend on the ratio of lecithin and spingomyelin in their membranes, which agrees well with the fact that camel erythro-

TABLE 1. Influence of the Hemocytocardiotoxin from the Venom of the Central Asian Cobra on the Conductivity of Various APMs

Lipids forming the APM	Lecithin: sphingomyelin ratio	Permeability, mho/cm²	
		control	$2 \cdot 10^{-7}$ M HT
Human erythrocytes	1,2 : 1,0–3 : 2	$0,5 \cdot 10^{-8}$	$0,13 \cdot 10^{-6}$
Rabbit erythrocytes	2,2 : 1,0–3 : 2	$0,67 \cdot 10^{-8}$	$0,12 \cdot 10^{-6}$
Rat erythrocytes	4 : 1	$0,66 \cdot 10^{-8}$	$0,20 \cdot 10^{-6}$
Guinea-pig erythrocytes	4 : 1	$0,77 \cdot 10^{-8}$	$0,23 \cdot 10^{-6}$
Cattle brain erythrocytes	1,7 : 1,0	$0,48 \cdot 10^{-8}$	$0,15 \cdot 10^{-6}$
Lecithin (Olaine factory)	—	$0,77 \cdot 10^{-8}$	$0,14 \cdot 10^{-6}$
Oxidized cholesterol	—	$0,13 \cdot 10^{-7}$	$0,62 \cdot 10^{-7}$

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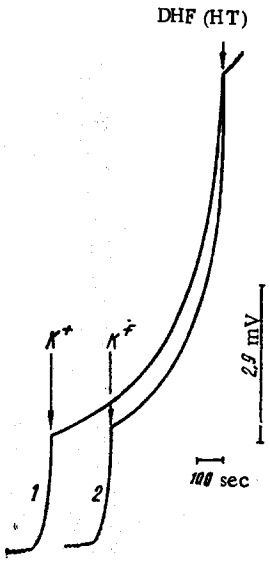

Fig. 1. Hemocytocardiotoxin-induced issuance of K^+ from liposomes: 1) liposomes prepared from cattle brain sphingomyelin; 2) from the total phospholipids of human erythrocytes. The suspensions of liposomes were standardized spectrophotometrically. Final concentrations: toxin $2.7 \cdot 10^{-7}$ M; K^+ added $2.2 \cdot 10^{-6}$ M. (Medium: 150 mM NaCl, 5 mM tris, pH 7.5.)

cytes, in the membrane of which there is a large amount of lecithin, are resistant [12]. The resistance of sheep erythrocytes also probably cannot be connected with the absence of lecithin from their membrane [13].

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