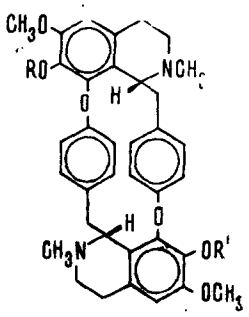

R=R′=CH_3, cycleanine
R=H, R′=CH_3, norcycleanine
R=R′=H, isochondodendrine

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ACTION OF A HEMOCYTOCARDIOTOXIN FROM THE VENOM OF THE CENTRAL ASIAN COBRA ON THE PASSIVE ISSUANCE OF K^+ FROM HUMAN ERYTHROCYTES

O. V. Krasil'nikov, L. Ya. Yukel'son, and B. A. Tashmukhamedov

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It has been shown previously that the hemocytocardiotoxin isolated in the pure form from the venom of the central Asian cobra [1] increases the permeability of artificial phospholipid membranes (APMs) for univalent cations [2]. In view of this, it appeared of interest of investigate this effect on biological membranes.

We studied the issuance of K^+ from erythrocytes treated with the cobra venom hemocytocardiotoxin. The yield of K^+ was recorded in a suspension of erythrocytes in a sucrose medium (300 mM sucrose, 5 mM tris, pH 7.4) with the aid of an LPU-01 laboratory pH-meter with a cation-selective glass electrode previously wetted in a 10 mM solution of KCl. The percentage hemolysis was determined from the amount of hemoglobin liberated, which was measured from the absorption at 540 nm with a correction for the aggregation of the cells, the number of aggregates being counted by means of an optical microscope.

The results obtained show that in a concentration of $1.5 \cdot 10^{-5}$ M the hemocytocardiotoxin stimulates the issuance of K^+ ions from erythrocytes (Fig. 1, curve 4). The efficiency of the process depends almost linearly on the time of incubation of the erythrocytes with the toxin. The hemolytic effect also rises linearly with the time of incubation. However, according to calculations, the amount of K^+ liberated by the erythrocytes as a

Institute of Biochemistry, Academy of Sciences of the Uzbek SSR, Tashkent.

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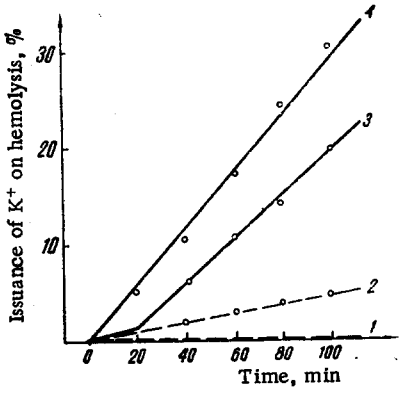

Fig. 1

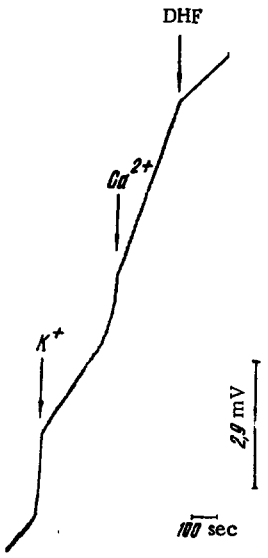

Fig. 2

Fig. 1. Issuance of K^+ from human erythrocytes induced by the hemocytocardiotoxin: 1) hemolysis in the control, 2) issuance of K^+ in the control (with correction for the surface); 3) hemolysis in the presence of $1.5 \cdot 10^{-5}$ M hemocytocardiotoxin; 4) issuance of K^+ in the presence of hemocytocardiotoxin. (Medium: sucrose 295 mM, tris 5 mM, pH 7.4.)

Fig. 2. Influence of hemocytocardiotoxin on the passive issuance of K^+ from human erythrocytes. ε_{750} of the suspension of erythrocytes 0.6; final concentrations: toxin $2 \cdot 10^{-6}$ M; Ca^{2+} $2.5 \cdot 10^{-3}$ M; K^+ added $6.7 \cdot 10^{-6}$ M. Rate of issuance of K^+ ions: in the control $1.5 \cdot 10^{-9}$ g.eq/min; in the presence of the hemocytocardiotoxin $6.0 \cdot 10^{-9}$. after the addition of Ca^{2+} $4.65 \cdot 10^{-9}$ g·eq/min. (Medium: NaCl 150 mM, tris 5 mM, pH 7.4.)

result of hemolysis, i.e., of the destruction of the cell membrane (Fig. 1, curve 3), is less than that found in the experiment. This permits the assumption that the hemocytocardiotoxin induces the issuance of K^+ from erythrocytes which have not yet undergone lysis.

This effect appears more clearly in a suspension of erythrocytes in isotonic NaCl solution (150 mM NaCl 5 mM tris, pH 7.4), where the aggregation of the cells is reduced to a minimum. In this case, the yield of K^+ was recorded by means of a home-made potassium-selective valinomycin electrode with a liquid membrane which, in the medium that we used, responds to a tenfold increase in the concentration of K^+ (beginning from 10^{-4} M) by a linear potential change of 55 mV.

It was established that in a concentration of $2 \cdot 10^{-6}$ M the hemocytocardiotoxin increases the rate of issuance of K^+ from erythrocytes fourfold; the addition of Ca^{2+} ions to the medium in a final concentration of $2.5 \cdot 10^{-3}$ M considerably inhibits this effect of the toxin (Fig. 2). It must be mentioned that Ca^{2+} ions inhibit the well-known biological effects of hemocytocardiotoxins [3].

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