MECHANISM OF THE DIURETIC ACTION OF STROPHANTHIN

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The possibility that the cardiac glycosides may act directly on the kidneys has been demonstrated by many experimental investigations [2, 5-11] and confirmed clinically [3].

In the author's earlier experiments [1] injection of strophanthin into the renal artery of dogs was accompanied by an increase in the diuresis and sodium excretion. However, this action strophanthin was not exhibited in animals previously receiving desoxycorticosterone acetate (DOCA). Analysis showed that the diuretic and natriuretic effects of strophanthin in dogs are due to a decrease in the reabsorption of water and sodium in the renal tubules.

In the present investigation the effect of strophanthin and DOCA, separately and in combination, was studied on the absorption of water, sodium, and chloride from the small intestine of rats and the action of strophanthin and pituitrin, separately and in combination, on the permeability of the wall of the urinary bladder to water was investigated in frogs.

EXPERIMENTAL METHOD

Rats were anesthetized with urethane and a loop of the small intestine was perfused with a solution containing 0.85% sodium chloride and 0.2% potassium chloride. The volume of fluid introduced into the in-

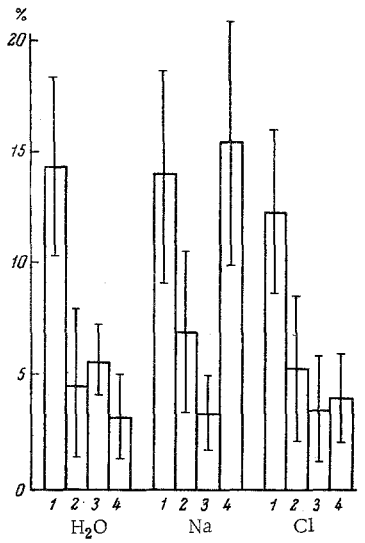

Fig. 1. Effect of strophanthin and DOCA on reabsorption of water, sodium, and chloride from a loop small intestine in rats. 1) Control; 2) strophanthin; 3) DOCA; 4) DOCA + strophanthin.

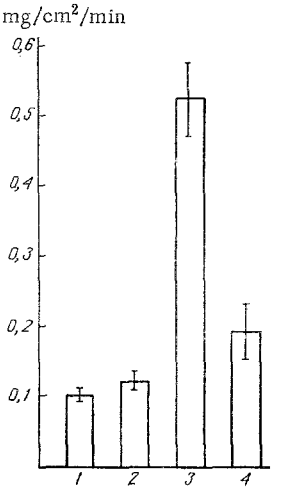

Fig. 2. Effect of strophanthin and pituitrin on permeability of the frog's urinary bladder to water. 1) Control; 2) strophanthin; 3) pituitrin; 4) strophanthin + pituitrin.

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testinal loop and the volume drawn from it were taken into account. The amount of water, sodium, and chloride absorbed was determined from the difference. The intensity of absorption was defined as the amount of the substances absorbed in 2 h from 1 cm^2 of the surface of the intestine and expressed as a percentage of the amount of the substance passing through the intestinal loop during this time.

The experiments on the urinary bladder of the frogs were carried out by the method described by Yu. V. Natochin [4]. The bladder was filled through the cloaca with Ringer's solution diluted 1:10, and was spherical in shape. The filled bladder was removed, weighed accurately to four places, and placed in a vessel containing Ringer's solution which was continuously aerated. Two hours later the bladder was again weighed. The intensity of absorption was calculated from the amount of water (in ml) leaving the bladder per min through 1 cm^2 of its surface.

EXPERIMENTAL RESULTS

The experiments on rats showed that in the experimental conditions described roughly the same proportion (from 12-15%) of water and sodium and chloride ions was absorbed (Fig. 1). Subcutaneous injection of strophanthin in a dose of 1 mg/kg 1 h before the experiment slowed the rate of reabsorption of water three times, of sodium twice, and of chloride 2.5 times. DOCA, injected into the rats in a dose of 5 mg/kg on the day before, and of 2.5 mg/kg 2 h before the experiment gave an effect similar to that of strophanthin, reducing the reabsorption of water, sodium, and chloride 2.5, 4.1, and 3.4 times respectively. Injection of strophanthin into the rats initially receiving DOCA reduced the reabsorption of water and chlorides in the same way as each preparation separately, but the reabsorption of sodium when DOCA and strophanthin were given together (when separately, each depressed sodium absorption) was indistinguishable from its reabsorption in the control (Fig. 1).

Hence, strophanthin and DOCA act in opposite ways on the reabsorption of sodium in the intestine.

The results obtained agree fully with the results of the previous experiments to study the effect of strophanthin, DOCA, and their combinations on the diuresis in rats [1].

The experiments on the frog's bladder showed that the presence of a 10:1 osmotic gradient between the contents of the urinary bladder and the solution bathing the viscus externally led to loss of water from the bladder at the rate of 0.1 mg/cm^2/min (Fig. 2).

When added to the bathing fluid in a concentration of 1×10^{-5}, strophanthin had no marked action on the loss of water from the bladder. Addition of pituitrin in a concentration of 10^{-6} unit/ml to the fluid bathing the bladder, increased the rate of loss of water from the bladder by 5.2 times. The presence of these substances together in the same concentrations made the pituitrin less effective (Fig. 2).

The results of these model experiments show that the effects of strophanthin in stimulating diuresis and the excretion of sodium may be the result of its counter-action to the effect of the mineralocorticoids on the reabsorption of sodium and its simultaneous counteraction to the effect of antidiuretic hormone on the reabsorption of water.

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