gradual increase in amplitude of the type A contractions during consecutive periods of work is evidently attributable to recovery of communication between Auerbach's plexus and the smooth muscles. On the other hand, average doses of m and n cholinoblockers in mixtures of the ganglion blocker with oxyphenonium and atropine enable a conduction block to be obtained from the vagus nerves to the intramural plexuses while retaining normal conduction between the latter and the effector cells.

In the light of these findings it is possible to choose vagolytic mixtures which would protect the digestive tract and, in particular, the stomach against the action of increased tone of the vagus nerves while preserving normal functional activity of Auerbach's plexus [1].

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EFFECT OF FUROSEMIDE AND ETHACRYNIC ACID ON SODIUM TRANSPORT AND POTASSIUM SECRETION

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Like strophanthin K, ethacrynic acid increases the sodium concentration and reduces the potassium concentration in frog urinary bladder tissue, with the result that potassium secretion is reduced; furosemide does not change these concentrations. The results point to differences in the intracellular action of furosemide and ethacrynic acid.

KEY WORDS: *furosemide; ethacrynic acid; sodium transport, potassium secretion; frog urinary bladder.*

Inhibition of the reabsorption of chlorine ions is now ascribed an important role in the mechanism of action of the most effective modern diuretics (furosemide and ethacrynic acid) [6]. Meanwhile, previous investigations showed that these substances inhibit sodium transport [3, 8]. Both these diuretics increase the potassium excretion by the kidney [2]; this could depend both on their direct effect on one component of the system secreting this

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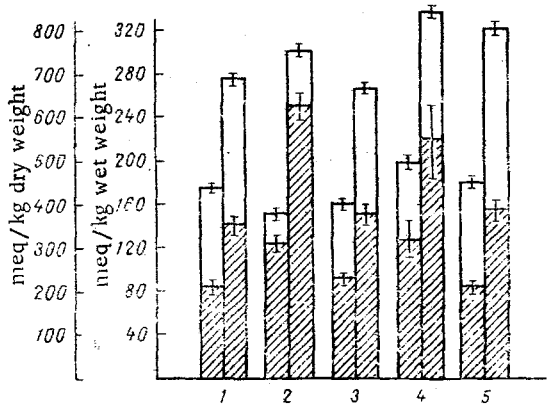

Fig. 1. Sodium and potassium concentrations in frog urinary bladder tissue. Column on left of each pair represents meq/kg wet weight, column on right meq/kg dry weight. 1) Control; 2) incubation for 4 h with $1.8 \cdot 10^{-5}$ M strophanthin K; 3) 0.1 mg/ml furosemide; 4) 0.5 mg/ml ethacrynic acid; 5) $1 \cdot 10^{-4}$ M nystatin. Unshaded part of columns represents sodium, shaded part potassium.

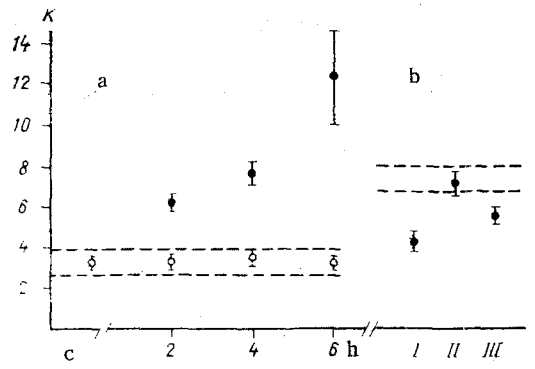

Fig. 2. Secretion of potassium by frog urinary bladder cells. Abscissa: a) time of experiment (in h); b) effect on potassium secretion produced by nystatin, $1.8 \cdot 10^{-5}$ M, $1.8 \cdot 10^{-5}$ M strophanthin K (I), 0.1 mg/ml furosemide (II), and 0.5 mg/ml ethacrynic acid (III); C) control; ordinate, potassium concentration (in meq/liter) in solution near mucous membrane of urinary bladder. Broken line indicates potassium concentration in experiments without addition of nystatin (a) and after incubation for 4 h with 10^{-4} M nystatin (b).

cation and on a change in the transport of sodium and chlorides. In the later case, during their action the change in the character of potassium secretion would be accompanied by an increase in the tissue sodium concentration.

The investigation described below was carried out to study these problems.

EXPERIMENTAL METHOD

The isolated urinary bladders of frogs (*Rana temporaria*) were filled with Ringer's solution and incubated in aerated Ringer's solution [4]. At the end of the experiment pieces of tissue were weighed on VLAO-100 microanalytical scales, dried to constant weight, incinerated in a quartz dish with concentrated HNO_3, after which the sodium and potassium concentrations were determined with the Flapho-4 flame photometer. The tissue sodium and potassium concentrations under these experimental conditions are a reliable criterion of the level of work of the ion pumps of the cells, for the potassium concentration in this tissue depends mainly on its accumulation by the epithelial cells [3]. The intracellular ionic composition was not determined by the inulin method, for the flow of water through this tissue from the mucous to the serous membrane elutes the inulin from the tissue, so that incorrect experimental values are obtained [3].

EXPERIMENTAL RESULTS AND DISCUSSION

In the tissue of the amphibian urinary bladder, which resembles the renal tubules in its ability to transport ions, sodium absorption and potassium secretion are determined by the functional capacity of the epithelial cells of the mucous membrane [3]. Ion transport is largely dependent on Na,K-ATPase, inhibition of which by strophanthin K increases the sodium concentration in the tissue and reduces its potassium concentration (Fig. 1). Furosemide had no effect on the distribution of the tissue electrolytes, whereas ethacrynic acid caused a marked increase in the tissue sodium concentration. Both diuretics were added to the solution in contact with the mucous membrane, for in the nephron they act on the reabsorption of ions from the lumen of the tubules. The results are unequivocal evidence of differences in the cellular effects of furosemide and ethacrynic acid. In vivo, the binding of ethacrynic acid with cysteine in the blood possibly reduces its effect on the cellular mechanisms of sodium transport, whereas its action on active chloride transport remains unaffected [5].

Potassium secretion in the renal tubule, skin, and urinary bladder [3], according to recent findings, is a passive process. Potassium enters in exchange for sodium through the basal plasma membrane, it accumulates in the cell, and its secretion depends on the potassium permeability of the apical plasma membrane and on the magnitude of the potential gradient on this membrane favoring potassium secretion. In the frog skin nystatin increases the potassium permeability of the apical cell membrane, thus creating the conditions for its secretion [1]. On the addition of nystatin to the Ringer's solution in contact with the mucous membrane of the bladder, in a concentration of $1 \cdot 10^{-4}$ M it was found to increase the potassium permeability of the apical membrane. Time-dependent potassium secretion was observed under these circumstances (Fig. 2). The secretion of potassium into the solution next to the mucous membrane caused no change in the intracellular sodium and potassium concentrations. Nystatin applied on the side of the serous membrane had no effect on potassium permeability. The next experiments were carried out during incubation of the urinary bladders with $1 \cdot 10^{-4}$ M nystatin for 4 h. Furosemide did not affect potassium secretion but ethacrynic acid reduced it. The action of ethacrynic acid was evidently connected with inhibition of the sodium pump and a decrease in the amount of intracellular potassium available for secretion (Fig. 1).

There are thus significant differences between the cellular action of furosemide and of ethacrynic acid. Whereas the mechanism of action of furosemide is based mainly on its effect on chloride permeability [3, 7], ethacrynic acid also acts on sodium transport and increases the tissue sodium concentration. Neither substance has any direct effect on the potassium secretory system. The increase in the excretion of potassium by the kidney under the influence of both substances probably depends on a decrease in the reabsorption of chloride and the increase in electronegativity of the lumen of the tubule.

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