THE INFLUENCE OF pH ON THE ANESTHETIC ACTION OF POTASSIUM SALTS ON SINGLE CELLS

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A great deal of evidence has accumulated in regard to the important role of potassium in modifying many fundamental physiological processes. The present investigation deals with the effects of K ions on excitatory phenomena in single cells. *Chaos diffluens* (*Amoeba proteus*) specimens taken from standardized cultures were immersed in approximately isosmotic solutions (0.025 M) of KCl. Exposure to such solutions invariably produced anesthesia. The amebae withdrew their pseudopodia, rounded up, and exhibited complete lack of locomotion. This inhibition was reversible. Concomitant with this inhibition of locomotion there was always a very marked decrease in protoplasmic viscosity as measured by the centrifuge method. This effect too was reversible.

These effects of K could be antagonized by Na and Ca ions. This is in agreement with the results obtained by a great many workers on various types of cells, including those of the neuromuscular system of vertebrates. The important fact brought out by the present investigation is the antagonism to K exhibited by H ions. In KCl solutions acidified with HCl, even at a pH of 5.5, the amebae showed some locomotion, while the viscosity values increased, though neither the locomotion nor the viscosity values reached the normal limits. Between a pH of 3.7 and 4.1 the cells were indistinguishable from normal either in appearance, locomotion, or viscosity.

These anesthetic effects of K are in agreement with observations that high concentrations of K cause inexcitability in nerve and produce a decrease in the resting (or injury) potential of nerve fibers. It is well known that resting potentials are essential prerequisites for excitability. Excitation, in fact, involves a momentary reversible depolarization of a normally polarized membrane. It is generally assumed that the normal membrane polarization is due to the orientation of K ions on the external side of a cation-permeable membrane. The cellular anions, being unable to traverse the membrane, remain oriented along the interior side of the cell membrane. In this manner the external side of the membrane becomes positively charged in respect to the cell interior, thus giving rise to the resting potential.

It follows, therefore, that if we place living cells into solutions containing high concentrations of K ions, the tendency of intracellular K to diffuse outward is decreased; it may even be completely abolished or reversed. This, in turn, will decrease or abolish the membrane polarization

and, therefore, the cell excitability. Thus we arrive at a reasonable explanation for the anesthetic properties of K ions.

Now, this tendency for K ions to diffuse outward is dependent not merely on the K concentration gradient but also on the concentration gradient of H ions across the cell membrane. In general, penetrating cations will distribute themselves across an anion-impermeable membrane in accordance with the well known Gibbs-Donnan equation. Thus:

$$\frac{(K)o}{(K)i} = \frac{(H)o}{(H)i}$$

where "o" refers to the concentration of the ion in question outside the cell, while "i" refers to the concentration inside the cell. From the above equation it follows that at equilibrium:

$$(K)o(H)i = (K)i(H)o$$

Therefore, when the cells are placed in a neutral solution of KCl, the equilibrium is disturbed. The product (K)o(H)i may be greater than (K)i(H)o, and the K ions may have a tendency to move inwards instead of outwards. Thus the basis for the usual membrance polarization is abolished and the cell is rendered inexcitable. However, when the same KCl solution is acidified, the product (K)o(H)i becomes relatively lower. The intracellular K once more tends to move outwards, the membrane polarization is restored, and the cell again becomes excitable.

These experiments, together with other unpublished data, furnish a simple physico-chemical explanation for the anesthetic effects of K ions and the antagonistic effects of H ions.