precise pharmacological mode of action is unknown. An interaction with K+ ions on transmembrane movement of Ca2+ ions suggests that it may possibly act to lower the internal calcium concentration and so restore the resting condition of the nerve cell more rapidly.


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Adenosine Triphosphate-Dependent Calcium-Transport Systems: Generality of Activation by Potassium Ions

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Despite previous observations (Duggan, 1967), it has only recently been generally accepted (Shigekawa & Pearl, 1976; Duggan, 1977; Jones et al., 1978) that ATP-dependent Ca2+ transport in fragmented sarcoplasmic reticulum is augmented rather than diminished (Gattass & de Meis, 1975) by K+. In skeletal muscle the K+ content of the sarcoplasm is 140–160mmol/litre of fibre water, so the stimulatory effect of K+ has physiological implications. Thus the faster the contraction–relaxation cycle in muscle cells, the higher is the cytoplasmic K+ content (Sreter & Woo, 1963).

As well as its well-recognized role in muscle contraction, Ca2+ mediates the action of a number of hormones in a variety of tissues (Hales et al., 1977), and consequently its concentration must be lowered to revert to resting conditions. Ca2+-transport systems have been reported in brain (Ohtsuki, 1969), kidney (Moore et al., 1974), liver (Bygrave, 1978), adipocytes (Bruns et al., 1976) and platelets (Steiner & Tateishi, 1974). We therefore decided to determine whether ATP-dependent Ca2+ transport, where it could be measured, was generally stimulated by K+. It had already been shown that the system in brain was stimulated by K+ (Duggan & Kelleher, 1975).

Six tissues were studied (liver, spleen, brain, heart, ileum and skeletal muscle) from five animals (rat, rabbit, guinea pig, pigeon and frog). The tissues were homogenized in 0.25 M-sucrose/2.5 mM-Hepes [4-(2-hydroxyethyl)-1-piperazine-ethanesulphonic acid], pH7.4. After centrifugation at 2000g for 10min and 10000g for 20min, the postmitochondrial supernatant was centrifuged at 100000g for 60min. The pellets resulting were resuspended in 0.25 M-sucrose and either used immediately or frozen in liquid N2 and stored at −15°C. All preparations were used within 3 days. Calcium uptake was measured as described by Duggan (1977).

Fig. 1 shows that ATP-dependent Ca2+ transport activity is present to varying extents in the six tissues of the five different animals investigated. In each instance K+ ions have a considerable stimulatory effect. The Ca2+ uptake varied from 12nmol/20min per mg of protein in rat liver microsomal fraction to 500nmol/2min per mg of protein in rabbit skeletal-muscle microsomal fractions, increasing, in the presence of 100mM-K+, to 32 and 1050nmol/min per mg of protein in liver and muscle respectively. With our isolation technique, no Ca2+-transport activity could be demonstrated in rabbit and guinea-pig intestinal preparations, even though there was significant and reproducible activity in the preparations from rat, pigeon and frog. For each tissue an experiment
Fig. 1. Calcium-uptake activities by microsomal fractions from different tissues of various animals
Calcium uptake was measured in a medium containing 5 mM-ATP (imidazole salt), 5 mM-MgCl₂, 5 mM-imidazole oxalate, 100 μM-⁴⁵CaCl₂ and 50 mM-imidazole/HCl, pH 7.0. The incubation temperature was 25°C. (a) Rabbit skeletal muscle; (b) rabbit spleen; (c) rat liver; (d) guinea-pig heart; (e) frog brain; (f) pigeon gut. □, Uptake at 0°C; ○, control medium; ●, control medium plus 100 mM-KCl.

was carried out at 0°C to detect non-specific Ca²⁺ binding and/or exchange with membrane-bound calcium. There was only slight apparent uptake in each instance.

It will be of interest to determine, as one 'descends the evolutionary tree', whether all Ca²⁺-transport activities are sensitive to K⁺.

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