INCREASE IN ^{85}Sr UPTAKE BY ELEVATED CONCENTRATION OF K IN GUINEA PIG TAENIA COLI

Hideaki KARAKI and Norimoto URAKAWA

*Department of Veterinary Pharmacology, Faculty of Agriculture,
University of Tokyo, Bunkyo-ku, Tokyo, Japan*

Received for publication February 12, 1972

In taenia coli, 40 mM K induced a tonic contraction accompanied by an increased oxygen consumption. When Ca in the bathing medium was replaced by Sr, 40 mM K developed little tension but increased oxygen consumption to a similar degree as that in normal medium (1). Although the movement of Ca and its possible relationship to tension development and also to oxygen consumption have been reported in taenia coli in the presence of 40 mM K (2, 3), there are few data concerning a movement of Sr ion in smooth muscle. In the present report ^{85}Sr uptake by taenia coli was studied in comparison with ^{45}Ca movement.

Strips of taenia coli isolated from male Hartley strain guinea pigs were suspended in a bath containing Ca-free Tyrode solution with 0.1 mM ethyleneglycol bis (β -aminoethyl-ether) -N, N'-tetraacetic acid (EGTA). After a preincubation period, 2.5 mM or 8 mM SrCl_2 containing a tracer amount of $^{85}\text{SrCl}_2$ was added to the bath. The amount of ^{85}Sr taken up by taenia coli was counted using well type scintillation detector. In some experiments, the muscle strips incubated with ^{85}Sr for 30 min were washed for 4 min with nonradioactive solution of the same chemical composition as the incubation and the amount of the isotope remaining in the muscle was counted. The tissue Sr fraction which did not exchange within 4 min was named as tightly bound Sr fraction (Sr-TBF) on the analogy of tightly bound Ca fraction (Ca-TBF) reported earlier (2). Tension development, ^{45}Ca movement and extracellular space (ECS) measured with ^{14}C -sorbitol were obtained as described previously (2, 3).

Results are summarized in Fig. 1. The tissue took up approx. 5.3 mM Sr/Kg wet tissue from 8 mM Sr-solution, approx. 1.9 mM Sr/Kg from 2.5 mM Sr-solution and approx. 2.2 mM Ca/Kg from 2.5 mM Ca-solution after a 30 min incubation period. When 2.5 or 8 mM ^{85}Sr was added simultaneously with 40 mM K, replacing 40 mM Na in the external medium with K, the muscle developed tension of only approx. 1 g. The ^{85}Sr uptake increased in the presence of 40 mM K. The increments were approx. 0.7 mM Sr/Kg in 8 mM Sr-solution and approx. 0.5 mM Sr/Kg in 2.5 mM Sr-solution after a 30 min incubation. A similar result was obtained in ^{45}Ca uptake and the increment was approx. 0.6 mM Ca/Kg. The tension development was approx. 10 g in this case. Further, both Sr-TBF and Ca-TBF increased in the presence of 40 mM K, with the increments being approx.

FIG. 1. Uptake of ^{86}Sr and ^{45}Ca by guinea pig taenia coli in the presence or absence of 40 mM K.

$^{86}\text{SrCl}_2$ or $^{45}\text{CaCl}_2$ was added at 0 min. Results were expressed as mM/kg wet tissue. ^{86}Sr and ^{45}Ca uptake by the smooth muscle tissue (Sr : $\circ$, Ca : $\square$) and by the slowly exchanging fraction (Sr-TBF : $\triangle$, Ca-TBF : ∇) in the absence (filled symbols) and presence of 40 mM K (open symbols) are shown. Each point is a mean of 8 experiments. Standard error of mean is shown by vertical bar. For further details see text.

0.4 mM Sr/Kg, 0.3 mM Sr/Kg or 0.5 mM Ca/Kg in 8 mM Sr-, 2.5 mM Sr- or 2.5 mM Ca-solution, respectively. The ECS of the tissue did not significantly change from 40% in the solutions employed in this experiment.

According to a current view, Ca ion acts as a current carrier in the spike generation mechanism and also as a excitation-contraction coupling agent in smooth muscle cells. Further, it is suggested that cytoplasmic Ca ion which increases during muscle contraction acts both on a contractile protein and on a metabolic process in which oxygen is consumed (3, 4), and the Ca ion acting on a contractile protein is continuously accumulated by an active process into a slowly exchanging Ca fraction (5). On the other hand, Sr ion can replace Ca ion for spike generation (6) and for oxygen consumption (1) but only partially replaces the ion in a contractile machinery in smooth muscle (7,8). Further, it is reported that Sr can substitute for Ca in the activation of phosphorylase *b* kinase (9) and miofibrillar ATPase in skeletal muscle (10) and also in the increment in respiration of rat liver mitochondria (11).

The present observation showed that both Ca and Sr entered the smooth muscle cell with amounts of both ions in the tissue and the slowly exchanging fraction increased in the presence of 40 mM K, suggesting that Sr and Ca ions move similarly in smooth muscle cells. These data support the previous suggestion (1) that Sr ion entering the depolarized

smooth muscle cell may stimulate metabolic process(es) resulting in an increase in oxygen consumption. The failure of Sr ion in substitution for Ca ion in contraction may be due to a lower affinity to troponin (8).

Sperelakis (12) reported that both ^{45}Ca and ^{86}Sr uptake by slowly exchanging fraction of cat small intestine increased in a solution in which all NaCl was replaced by KCl. As the difference has been shown between ^{45}Ca movements in taenia coli incubated in 40 mM K solution and high-K, Na-deficient one (13), a comparison to the data of Sperelakis is difficult.

REFERENCES

- 1) URAKAWA, N., IKEDA, M., SAITO, Y. AND SAKAI, Y.: *Jap. J. Pharmac.* **18**, 500 (1968); 2) KARAKI, H., IKEDA, M. AND URAKAWA, N.: *Jap. J. Pharmac.* **19**, 291 (1969); 3) URAKAWA, N., KARAKI, H. AND IKEDA, M.: *Jap. J. Pharmac.* **20**, 360 (1970); 4) SAITO, Y., SAKAI, Y., IKEDA, M. AND URAKAWA, N.: *Jap. J. Pharmac.* **21**, 605 (1971); 5) KARAKI, H. AND URAKAWA, N.: *Jap. J. Pharmac.* (in press); 6) HOTTA, Y. AND TSUKUI, R.: *Nature* **217**, 867 (1968); 7) BANDO, T., AIZU, M., SAKATO, M. AND YANAGISAWA, M.: *Folia pharmac. japon.* **66**, 89 § (1970) (in Japanese); 8) EBASHI, S. AND KODAMA, A.: *Folia pharmac. japon.* **63**, 127 § (1967) (in Japanese); 9) MEYER, W.L., FISCHER, E.H. AND KREBS, E.G.: *Biochemistry* **3**, 1033 (1964); 10) EDWARDS, C., LORKOVIĆ, H. AND WEBER, A.: *J. Physiol.* **186**, 295 (1966); 11) CHAPPELL, J.B. AND GREVILLE, G.D.: *Fed. Proc.* **22**, 526 (1963); 12) SPERELAKIS, N.: *Am. J. Physiol.* **203**, 860 (1962); 13) URAKAWA, N., KARAKI, H. AND IKEDA, M.: *Jap. J. Pharmac.* **18**, 294 (1968)

DIFFERENCE IN ACTIONS OF HARMINE ON THE OXIDATIONS OF SEROTONIN AND TYRAMINE BY BEEF BRAIN MITOCHONDRIAL MAO

Hajime YASUHARA, Sadayuki SHO and Kazuya KAMIJO

*Second Division of the Department of Pharmacology, School of Medicine,
Showa University, Shinagawa-ku, Tokyo, Japan*

Received for publication February 15, 1972

Harmine is known to stimulate the central nervous system and cause hallucinations. It has been used therapeutically since as early as 1920 (1). In 1958, Udenfriend et al. (2) reported that harmala alkaloids are potent inhibitors of monoamine oxidase (MAO) [EC 1. 4. 3. 4. monoamine: oxygen oxidoreductase (deaminating)] and suggested some possible actions of these drugs on amine metabolism in the brain.

In 1928 Hare (3) reported the existence of an amine oxidase and subsequently MAO has been studied intensively with much attention being paid to the "multiplicity" of this enzyme. Harada et al. (4) reported the presence of multiple forms of MAO in brain, but their physiological roles are unknown. To study these enzymes it seemed feasible that if these multiple enzymes in brain mitochondria differ in specificity, it would be possible