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Action of a Sulfonated Succinic Acid on the Respiratory Metabolism of Frog Tissues.*

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In the succinic acid cycle outlined by Szent-Gyorgyi[1] succinic acid serves in a catalytic capacity as a carrier between metabolites and the cytochrome - cytochromeoxidase - oxygen complex. In this scheme succinic acid is oxidized to fumaric acid. This reaction is catalyzed by succinic dehydrogenase and is reversible. Thus, the action of succinate serves the dual role of substrate and reversible catalyst-carrier in the respiratory enzyme system.

From a series of sulfonated succinic acid derivatives, it was considered of theoretic interest to investigate the action of potassium-sulfon-succinic acid. This compound contains a ($SO_2 \cdot OK$) group replacing one of the hydrogen atoms of the ethane residue.

A series of experiments on frog skin and muscle were carried out using the Warburg manometric technic. The tissues were suspended in Ringer-Phosphate, pH 7.5. Succinic acid and potassium-sulfon-succinic acid were neutralized with sodium hydroxide before use.

The oxygen consumption of frog skin was not noticeably influenced by the presence of 0.1 mg glucose or 0.04 mg succinate, the respiratory rate diminished with time (10 to 20% in 2 hours). The addition of 0.04 mg potassium-sulfon-succinate inhibited oxygen consumption 20 to 40%.

The respiratory rate of sliced and minced muscle falls off rapidly with time, decreasing as much as 80% in 2 hours. The addition of 0.1 mg glucose did not arrest this fall. However, 0.04 mg succinate had a marked effect, increasing oxygen consumption 100% or more and maintaining this increased rate for several hours.

In contrast, the addition of 0.04 mg of potassium-sulfon-succinate to muscle resulted in a 25 to 30% depression of oxygen consumption compared to untreated controls to which no succinate had been added.

The addition of succinate in catalytic amounts (40 γ) increased the oxygen consumption of muscle by 30 to 40% and also maintained this rate for more than an hour. Upon the addition of 0.04 mg potassium-sulfon-succinate to the tissue, the oxygen uptake of which was accelerated by succinate, there resulted a 75% diminution of the oxygen uptake.

Conclusion. From these observations, it would appear that potassium-sulfon-succinate is not utilized as a substrate nor acts as a reversible carrier. It is capable, however, of inhibiting the catalytic activity of succinate when the latter is present in minute quantities.

This latter inhibition presents an analogy to the activity of para-aminobenzoic acid and the sulfa drugs. Owing to the widespread distribution of succinate in tissues and bacteria, the possible bacteriostatic action is being investigated.

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[1] Szent-Gyorgyi, A., *Z. f. Physiol. Chem.*, 1935, **236**, 1.