

SUCCINIC ACID: ABSTRACTS

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suc·ci·nate (sks-nt) n.

A salt or an ester of succinic acid.

The American Heritage® Dictionary of the English Language

Inhibition of lipid peroxidation* by idebenone in brain mitochondria in the presence of succinate.

Suno M, Nagaoka A., Central Research Division, Takeda Chemical Industries, Ltd., Osaka, Japan. PMID: 2764644

*The process whereby free radicals “steal” electrons from the lipids in our cell membranes, resulting in cell damage and increased production of free radicals

Lipid peroxidation in brain mitochondria was induced by NADH in the presence of ADP and FeCl₃. A novel quinone compound, idebenone, inhibited this peroxidation and the inhibition was markedly enhanced by succinate, a substrate of mitochondrial respiration. The concentration of succinate required to exert the maximal effect was 1.5 mM. The concentration of idebenone giving 50% inhibition (IC₅₀) was 0.5 and 84 microM in the presence and absence of succinate, respectively, indicating that **succinate enhances the inhibition by 170-fold**. These results indicate that idebenone is changed through complex II to its reduced form, which protects mitochondria against lipid peroxidation.

The life-extending gene Indy encodes an exchanger for Krebs-cycle intermediates.

Knauf F, Mohebbi N, Teichert C, Herold D, Rogina B, Helfand S, Gollasch M, Luft FC, Aronson PS. Biochem J. 2006 Apr 12. PMID: 16608441

A longevity gene called Indy (for "I'm not dead yet"), with homology to mammalian genes encoding Na-dicarboxylate cotransporters, was identified in *Drosophila melanogaster*. **Efflux of [14C]-citrate from INDY-expressing oocytes was greatly accelerated by the addition of succinate to the external medium**, indicating citrate-succinate exchange. We conclude that INDY functions as an exchanger of dicarboxylic and tricarboxylic Krebs cycle intermediates. The effect of decreasing INDY activity, as in the long-lived Indy mutants, may be to alter energy metabolism in a manner that favors life span extension.

Cardioprotective effect of succinate against ischemia/reperfusion injury.

Sakamoto M, Takeshige K, Yasui H, Tokunaga K. Division of Cardiovascular Surgery, Research Institute of Angiocardiology, Faculty of Medicine, Kyushu University, Fukuoka, Japan. Surg Today. 1998;28(5):522-8. PMID: 9607905

We investigated the protective effects of succinate, which is a respiratory substrate and a potential antioxidant, on myocardial ischemia/reperfusion injury with the whole heart. Isolated rat hearts were loaded with 25-min normothermic global ischemia followed by 30-min reperfusion in a working heart model. **Succinate administered either before reperfusion or added to the cardioplegic solution improved the postischemic cardiac function significantly**. The hearts arrested with succinate-supplemented cardioplegic solution replenished high-energy phosphates and

maintained the total adenine nucleotides during the reperfusion period, whereas those arrested with succinate-nonsupplemented cardioplegic solution replenished the high-energy phosphates less, and also lost total adenine nucleotides during that period. We thus conclude that **succinate administered before reperfusion may decrease the degree of mitochondrial damage** during reperfusion and thereby reduce the amount of myocardial ischemia/reperfusion injury.

Postischemic administration of succinate reverses the impairment of oxidative phosphorylation after cardiac ischemia and reperfusion injury.

Cairns CB, Ferroggiaro AA, Walther JM, Harken AH, Banerjee A. Colorado Emergency Medicine Research Center, Department of Surgery, University of Colorado Health Sciences Center, Denver 80262, USA. *Circulation*. 1997 Nov 4;96(9 Suppl):II-260-5. PMID: 9386108

CONCLUSIONS: Cardiac ischemia and reperfusion results in a defect at mitochondrial complex I but not complex II. Cytochrome a,a₃ undergoes anomalous oxidation during ischemia. Postischemic administration of **succinate infusion restores the cytochrome a,a₃ redox state balance and myocardial function after IR.**

Effect of succinate on mitochondrial lipid peroxidation. 2. The protective effect of succinate against functional and structural changes induced by lipid peroxidation.

Tretter L, Szabados G, Ando A, Horvath I. *J Bioenerg Biomembr*. 1987 Feb;19(1):31-44. PMID: 3032929

The damaging effects of ADP/Fe/NADPH-induced lipid peroxidation were studied on the enzymes and membranes of rat liver mitochondria. Succinate, an inhibitor of mitochondrial lipid peroxidation, prevented or delayed most of the damage caused by the peroxidation on different mitochondrial structures and functions. There were marked abnormalities on the electrophoretic pattern of mitochondrial proteins during the course of lipid peroxidation. The disappearance of particular polypeptide bands and the accumulation of high-molecular-weight aggregates could be observed. Succinate was found to delay these effects. As a consequence of lipid peroxidation the succinate oxidase activity of mitochondria was decreased. The succinate dehydrogenase enzyme and the component(s) of the respiratory chain were inactivated. From the matrix enzymes the glutamate dehydrogenase retained its full activity but the NADP-linked isocitrate dehydrogenase was inactivated. The mitochondrial membranes became permeable to large protein molecules. Succinate prevented the inactivation of isocitrate dehydrogenase and delayed the release of protein molecules from mitochondria.