A GENERAL MECHANISM FOR OXIDATIVE PHOSPHORYLATION[1]

by

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Received January 3, 1961

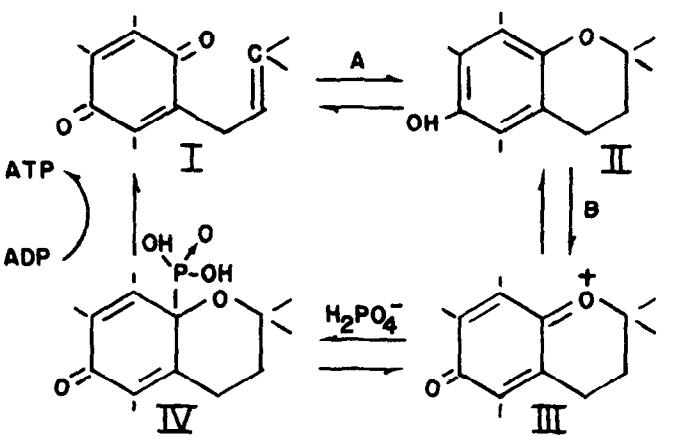
We have recently presented evidence requiring the cyclization of the isoprenoid side chain of vitamin K_1 in order for it to restore oxidative phosphorylation in ultraviolet irradiated liver mitochondria (Dallam & Taylor, 1959). At that time we pointed out the chemical similarity of the quinones of the vitamin K, ubiquinone and vitamin E groups, i.e., all are fully substituted and all possess an isoprenoid side chain with unsaturation at the β,γ position. We also presented alternative chemical mechanisms for the introduction of inorganic phosphate into these quinones or corresponding tocopherols, possessing the above requisites. These mechanisms required cyclization of the side chain to form a chroman either prior to or accompanying oxidation reduction. In these and other (Wessels, 1954, Clark et. al., 1958, Harrison, 1958 and Chmielewska, 1960) proposed chemical mechanisms of quinol phosphates participating in phosphorylation associated with oxidation, the reaction preceeding ATP formation involved oxidation of a quinol phosphate in the presence of a suitable acceptor such as ADP.

A newly proposed mechanism for oxidative phosphorylation is presented below. The necessity for revision of our original proposal, and those of

1 Supported by grants from the American Heart Association, The National Science Foundation (G-1157), and the United States Public Health Service (H-2102C)

2 A portion of this work was done during the tenure of an Established Investigatorship of the American Heart Association

others, is due to an apparent discrepancy between the various proposals and the existing data. The fact that P_i-ATP exchange occurs rapidly and equally well either in the presence or absence of substrate (Boyer, et. al., 1954) would almost demand that the intermediate compound, X~P, does not require oxidation for exchange. Thus, it would appear that the previously proposed mechanisms are incorrect. The mechanism presented, therefore, may more accurately depict the chemical mechanisms of mitochondrial oxidative phosphorylation when and if quinones are involved.



Compound I can be any fully substituted paraquinone possessing an isoprenoid side chain adjacent to one of the quinoid groups, i.e., vitamin K, ubiquinone and the group of oxidized E vitamins. Compound II results from reduction by one of the members of the respiratory chain and is oxidized by another member to yield III. Compound III is held in its electrophilic configuration presumably by the enzyme and in the presence of nucleophilic inorganic phosphate yields IV which can then donate the energized phosphate to ADP under proper conditions yielding ATP and the starting quinone.

We are investigating the validity of the above proposal through the aid of synthetic compounds and are, for the present, accepting this scheme as a working hypothesis.

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