LETTER TO THE EDITOR

Reactions of Biological Antioxidants: III. Composition of Biological Membranes

Sir. It has been proposed that vitamin E and some part of the coenzymes Q (CoQ) may function together as biological antioxidants (Mellors and Tappel, J. Biol. Chem. 241:4353-4356, 1966). The quantitative levels of the reactive compounds in such function still remain a question in order to judge the validity of the proposal. The question of whether or not the quantities of vitamin E and CoQ in biological membranes relative to peroxidizable unsaturated lipids are of reasonable magnitude to suggest that they may act as effective antioxidants can be answered by considering the lipid composition of the largely membranous mitochondrion. In highly active biological cells, a significant part of the vitamin E and most of the CoQ are found in mitochondria.

We wish to report the results of the calculation of ratios of the unsaturated fatty acids in mitochondria to the total α-tocopherol (α-T) and CoQ, which have been reported for mitochondria. Only data reported for the analyses of rat liver mitochondria and beef heart electron transport particle could be found that included fatty acid composition, CoQ, and α-T determinations based on a common denominator, i.e., weight per cent dry protein. Rat liver mitochondria can contain 384 μmoles fatty acid esters per gram of dry tissue fraction, which contains 63 wt % protein (Getz and Bartley, Biochem. J. 78:307-312, 1961; Getz et al., Biochem. J. 83:181-191, 1962). Of the total mitochondrial fatty acid esters, 49.6 mole % are polyunsaturated fatty acids (PUFA) (Getz, et al., Biochem. J. 83:181-191, 1962). There were 0.66 μmole CoQ per gram protein in a rat liver mitochondrial fraction (Lester and Crane, J. Biol. Chem. 234:2169-2175, 1959). The electron transport particle of beef heart contained 4.2 mg CoQ per gram protein and 0.45 mg α-T per gram protein (Crane, et al., Biochim. Biophys. Acta 31:476-489, 1959).

To calculate mole % CoQ from weight per cent, we chose to consider CoQ_{10} (mol wt 863), which represents the least effect on the results by giving a lower mole ratio of PUFA to biological antioxidant, rather than CoQ_6 or others. In the absence of definitive in vivo studies, we also chose to consider that one tenth of the CoQ might function as an antioxidant. This, in effect, assigns 90% of the function of CoQ to the tasks in electron transport and oxidative phosphorylation, etc., while also minimizing the involvement of CoQ in antioxidant function. It is important too to point out that there are molar excesses of endogenous CoQ over individual cytochromes (Redfearn, Vit. Hormones 24:465-488, 1966), indicating that there could be functions other than those now commonly associated with CoQ.

Calculations from the above values show that the mitochondria may contain both 4.87 μmoles CoQ_{10} per gram protein and 1.04 μmoles α-T per gram protein. Thus, there can be a molar ratio of CoQ_{10} to α-T of 4.7 to 1.0 in the mitochondria. Based, then, on the 0.66 μmole CoQ per gram, there may be 0.14 μmole α-T per gram protein. From the latter value and a calculated 302 μmole PUFA per gram protein, the mitochondrial membrane lipids may have ca. 2100 molecules of PUFA moieties for each molecule of α-T. Similarly, ca. 4600 molecules of PUFA for each CoQ molecule is calculated from 0.066 μmole CoQ per gram for antioxidant function. The combined antioxidant capacity of α-T and CoQ in this model may represent levels of about 0.07 mole % or about 0.1 wt % of the peroxidizable PUFA in mitochondrial membrane lipids.

These calculated levels of biological antioxidants in the membrane are consistent with levels for antioxidant activity in many other systems (Scott, G., "Atmospheric Oxidation and Antioxidants," Elsevier Publishing Co., New York, 1965, p. 282). For example, 0.01 wt % α-T inhibits in vitro oxidation of menhaden oil (Olcott and Einsett, JAOCS 35:159-160, 1958). We conclude from the calculations that biological antioxidants are normally present at adequate levels relative to unsaturated lipids to protect them in membranes from becoming peroxidized significantly in vivo.

It is extremely interesting that Bieri and Poukka (J. Nutr. 100:557-564, 1970) found in rat erythrocytes 1100 molecules of polyunsaturated fatty acids for each molecule of α-T, which was involved in preventing 10% hemolysis in vitro, in cases where the lipids were controlled by diets. The ratios calculated here agree well with these experimental findings.

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