Mechanism Of Suppression Of Microsomal Lipid Peroxidation By Vitamin A

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Previously, we have demonstrated that in vitamin A-deficient rats, their hepatic microsomal drug oxidative activities were greatly affected and such changes could be related to a loss of vitamin A protection against free radical-induced membrane lipid peroxidation (1). To delineate the mechanism of vitamin A protection of membrane lipids from oxidative damage, we examined further the *in vitro* effects of this antioxidant on lipid peroxidation in isolated rat liver microsomes by the thiobarbituric acid (TBA) method as previously described (2). In brief, microsomal lipid peroxidation was initiated by Fe (II)-ADP complex and NADPH (or ascorbate) at 37° and allowed to propagate for 15 min. The reaction was terminated by trichloroacetic acid and boiled at 95° for 15 min in the presence of TBA. The red-coloured complex formed through the condensation of TBA with malondialdehyde generated from the breakdown of polyunsaturated fatty acid hydroperoxides was quantitated colorimetrically at 532 nm. We observed that vitamin A, in a concentration-dependent manner, suppressed both enzymatic (NADPH-dependent) and non-enzymatic (ascorbate-dependent) lipid peroxidation activities in rat liver microsomes. A similar inhibitive effect on Fe (II)-EDTA-initiated peroxidation by vitamin A was also demonstrated in liposomes prepared from liver microsomes. The lack of influence of *in vitro* vitamin A treatment on drug oxidation in liver microsomes further suggests that vitamin A acts mainly as a chemical quencher of reactive intermediate products during the process of lipid peroxidation. Spectroscopic analysis showed the existence of TBA-reactive coloured complexes (λ_{max} 450 and 492 nm) formed during the thermolytic breakdown of peroxidised lipids. This suggests that vitamin A suppresses propagation of reaction products formed during lipid peroxidation, possibly via a free-radical scavenging mechanism.

References

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Abstract 9