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# Peroxide dependence of polyunsaturated fatty acid oxygenation in platelets and endothelium

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## Introduction

The oxygenated metabolism of arachidonic acid (AA) in platelets and endothelium has been well described [1] but that of polyunsaturated fatty acids (PUFAs) of nutritional value is much less documented. It is generally assumed that these PUFAs are less efficiently converted by cell oxygenases and early investigations with seminal gland microsomes led to the concept that this conversion requires a certain "peroxide tone" [2]. Some evidence will be provided for such a peroxide requirement in blood platelets and endothelial cells.

## Results and discussion

Amongst icosapolyenoic acids – namely AA, dihomogammalinolenic acid (DHLA), 5,8,11-icosatrienoic acid (20:3n-9) and icosapentaenoic acid (EPA) – EPA appears as the poorest substrate of platelet cyclo- and lipo-oxygenase. In the presence of either AA or its lipoxygenase product 12-hydroperoxy-eicosatetraenoic acid (12-HPETE), the oxygenation of icosapolyenoic acids by intact human platelets is very markedly increased, the increase being the most efficient for EPA [3]. Since the reduced product of 12-HPETE, namely 12-HETE, is devoid of any potentiating effect, it is concluded that platelets may produce substantial amounts of oxygenated derivatives from minor PUFAs when peroxides are provided. This is of physiological relevance since 12-HPETE is expected to be formed from endogenous AA during platelet activation. Investigations with cultured endothelial cells from human umbilical veins also revealed that AA potentiates the oxygenation of EPA into both PGI3 and primary prostaglandins PGE3 and F3$\alpha$. This suggests that AA, or most probably 15-HPETE formed in the endothelium [4], stimulates the oxygenation of EPA at the cyclooxygenase rather than at the prostacyclin synthase level [5].

In relation to the peroxide dependence of PUFA oxygenation, it has been found that platelets from elderly people produced more oxygenated metabolites (thromboxane B2, 12-hydroxy-heptadecatrienoic acid and 12-HETE) from exogenous AA than platelets from middle-aged volunteers [6]. We could then argue that this might be linked to the decreased platelet vitamin E observed in the aged population [7]. However, the enrichment of normal platelets with $\alpha$-tocopherol, by both *in vitro* and *in vivo* approaches, failed to affect the cyclooxygenation and the lipoxygenation of exogenous AA as well as the potentiating effect of AA upon the lipoxygenation of EPA. This leads us to speculate that vitamin E might not be able to counteract the peroxide dependence of PUFA specific oxygenation in normal platelets. A relative vitamin E deficiency, as found in platelets from elderly people or diabetics, would however accentuates this specific oxygenation [8].

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