**THE OMEGA 3 EPA:DHA 6:1 CAUSES REDOX-SENSITIVE PI3-KINASE/AKT-DEPENDENT ACTIVATION OF ENDOTHELIAL NO SYNTHASE**

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Intake of fish oil-derived omega 3 products eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) is associated with a reduced risk of cardiovascular diseases. This study examined whether the EPA:DHA ratio and purity affects the ability of omega 3 products to cause endothelium-dependent relaxations and to clarify the pathway leading to endothelial NO synthase (eNOS) activation. Vascular reactivity was assessed in organ chambers using porcine coronary artery rings, and the phosphorylation level of Akt and eNOS in cultured coronary artery endothelial cells by Western blot.EPA:DHA 1:1 caused potent relaxations in intact but not in endothelium denuded coronary artery rings. EPA:DHA 6:1 induced greater endothelium-dependent relaxations than the EPA:DHA 1:1, EPA and DHA alone, and an EPA:DHA 6:1 with a reduced EPA + DHA content. Relaxations to EPA:DHA 6:1 were reduced by NG-nitro L-arginine (NLA, an eNOS inhibitor), not affected by TRAM34 plus apamin (APA, two inhibitors of endothelium-derived hyperpolarizing factor) and abolished by the combination NLA, and TRAM34 plus APA. They were insensitive to indomethacin (inhibitor of cyclooxygenases) and significantly reduced by inhibitors of oxidative stress, PP2 (Src kinase inhibitor) and wortmannin (PI3-kinase inhibitor). EPA:DHA 6:1 caused phosphorylation of Akt and eNOS, which were reduced by inhibitors of oxidative stress. Thus, the ability of omega 3 products to cause endothelium-dependent relaxations involving predominantly NO in coronary arteries is dependent on the EPA plus DHA content and the EPA:DHA ratio. The EPA:DHA 6:1-induced activation of eNOS is mediated by the redox-sensitive PI3-kinase/Akt pathway leading to eNOS phosphorylation at Ser 1177.