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Essential fatty acids and their metabolites could function as endogenous HMG-CoA reductase and ACE enzyme inhibitors, anti-arrhythmic, anti-hypertensive, anti-atherosclerotic, anti-inflammatory, cytoprotective, and cardioprotective molecules.

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Abstract

Lowering plasma low density lipoprotein-cholesterol (LDL-C), blood pressure, homocysteine, and preventing platelet aggregation using a combination of a statin, three blood pressure lowering drugs such as a thiazide, a beta blocker, and an angiotensin converting enzyme (ACE) inhibitor each at half standard dose; folic acid; and aspirin-called as polypill- was estimated to reduce cardiovascular events by approximately 80%. Essential fatty acids (EFAs) and their long-chain metabolites: gamma-linolenic acid (GLA), dihomo-GLA (DGLA), arachidonic acid, eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) and other products such as prostaglandins E1 (PGE1), prostacyclin (PGI2), PGI3, lipoxins (LXs), resolvins, protectins including neuroprotectin D1 (NPD1) prevent platelet aggregation, lower blood pressure, have anti-arrhythmic action, reduce LDL-C, ameliorate the adverse actions of homocysteine, show anti-inflammatory actions, activate telomerase, and have cytoprotective properties. Thus, EFAs and their metabolites show all the classic actions expected of the "polypill". Unlike the proposed "polypill", EFAs are endogenous molecules present in almost all tissues, have no significant or few side effects, can be taken orally for long periods of time even by pregnant women, lactating mothers, and infants, children, and adults; and have been known to reduce the incidence cardiovascular diseases including stroke. In addition, various EFAs and their long-chain metabolites not only enhance nitric oxide generation but also react with nitric oxide to yield their respective nitroalkene derivatives that produce vascular relaxation, inhibit neutrophil degranulation and superoxide formation, inhibit platelet activation, and possess PPAR-gamma ligand activity and release NO, thus prevent platelet aggregation, thrombus formation, atherosclerosis, and cardiovascular diseases. Based on these evidences, I propose that a rational combination of omega-3 and omega-6 fatty acids and the co-factors that are necessary for their appropriate action/metabolism is as beneficial as that of the combined use of a statin, thiazide, a beta blocker, and an angiotensin converting enzyme (ACE) inhibitor, folic acid, and aspirin. Furthermore, appropriate combination of omega-3 and omega-6 fatty acids may even show additional benefits in the form of protection from depression, schizophrenia, Alzheimer's disease, and enhances cognitive function; and serve as endogenous anti-inflammatory molecules; and could be administered from childhood for life long.

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