Natural Products Chemistry & Research

Yeung, Nat Prod Chem Res 2015, 3:2
http://dx.doi.org/10.4172/2329-6836.1000e111

Editorial Open Access

# Omega -3 Fatty Acid for Cardiovascular Prevention

***Pollen K Yeung****

*College of Pharmacy and Department of Medicine, Dalhousie University, Halifax, NS, Canada B3H 4R2*

Cardiovascular disease including stroke is one the leading cause of death and disability and an enormous economic burden to our societies. Based on the latest statistics released for heart and stroke disease, an estimated 83,600,000 adults in the United State (US) (>30%) have one or more types of cardiovascular disease (CVD) of whom more than 90% have hypertension, 18% have coronary heart disease (CHD), close to 10% have myocardial infarction (MI) and 8% have stroke. The total direct and indirect cost in the US alone for treatment of cardiovascular diseases (hospitalization, drugs, home healthcare, etc.) and loss of productivity and morbidity is estimated at close to $315 billion US per year [1]. Thus prevention by better diagnosis and improved treatment strategies could provide a huge saving for the health care cost worldwide. Despite advancement in modern cardiovascular medicine, the prevalence of hypertension, ischemic heart disease (IHD) and stroke is still on the rise particularly in industrialized societies and in the obese and elderly population, and that finding an optimum drug therapy to slow disease progression remains a therapeutic challenge.

In addition to diet and exercise, natural products and nutraceuticals are increasingly used in our societies to enhance health, slow down aging, and prevention of chronic diseases [2-5]. One of the most widely recognized natural health products which have potential cardiovascular protective effect is omega-3 fatty acid (Omega-3) [6-10]. Omega-3 is a polyunsaturated fatty acid (n-3 PUFAs) made up mainly of eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) in the form of fish oil, and alpha linolenic acid (ALA) if it is from plant source such as flaxseed oil [11,12]. Although there are evidences suggesting that EPA and DHA may have differing effects on cellular and cardiovascular functions, these differences are mostly quantitative and most studies do not differentiate their effects separately [13,14]. In general, Omega-3 influences the physical nature of cell membranes and membrane protein-mediated responses, eicosanoid generation, cell signaling and gene expression in many different cell types, and have an effect on glucose and lipid metabolism. It also has pleiotropic effects which include lowering of blood pressure, anti-platelet and anti-oxidant properties, improved endothelial function and increased high-density cholesterol levels [15-18]. These effects are often evidenced by improvements in disease biomarker profiles or in health-related outcomes. As a result, they may play an important role to protect against cardiovascular morbidity and mortality, and might be beneficial in rheumatoid arthritis, diabetes, inflammatory diseases, childhood learning and behaviour, cancer prevention, and adult psychiatric and neurodegenerative illnesses [7,19-24]. It has been shown recently that Omega-3 can protect myocardial infarction (MI) from ischemia/reperfusion injury in an isolated rat heart model [25] and promote early metabolic recovery after coronary artery bypass grafting (CABG) surgery [26]. However, despite the abundance of evidences to support the potential of Omega-3 for cardiovascular protection in experimental models, the protective effects have not been confirmed unequivocally by controlled clinical trials which could be related to factors such as inadequate power in the studies, inadequate exposure to Omga-3, and patient heterogeneity [27]. There are also evidence to suggest that Omega-3 may enhance the therapeutic effects of conventional medicines for hyperlipidemias [28], although solid data supporting or against use of the combinations are very limited. While the mechanism for protective effects of these natural health products are not fully understood, they could be related to their anti-oxidant, anti-inflammatory and anti-ischemia properties [18,23,24,29] which are important contributing factors for ischemia preconditioning and cardiovascular protection. Furthermore, there are evidence to suggest that DHA may inhibit first pass metabolism by cytochrome P-450 isozymes (CYP450), which could enhance oral drug absorption and improve safety and efficacy profiles of many cardiovascular drugs [30,31] and that they may be incorporated in traditional cardiovascular drug therapies. Thus in view of the increasing use of Omega-3 and other natural health products in North America and around the world to enhance cardiovascular health, and the sparsity of information available for possible interaction with prescription medications, there is an urgent need for more mechanistic research to study the cardiovascular effect of Omega-3 and its combinations with traditional medicines to justify their role for cardiovascular protection and prevention in complementary medicine.

In summary it is conceivable Omega-3 has significant potential for cardiovascular prevention as a stand-alone nutritional supplement and as an adjunct to complement the therapeutic effect of traditional cardiovascular medicines. However, there are a number of challenges which need to be overcome in order to exploit the full potential of Omega-3 in cardiovascular prevention and in complementary medicine. First clinical trials to study the cardiovascular effects of Omega-3 should be designed to understand the mechanism behind the health benefits and has adequate power to answer the underlying question. Secondly, there is a need for identifying systemic biomarkers which can be implemented in both experimental animal studies and clinical trials to assess the cardiovascular health benefits of Omega-3 [32]. Thirdly, despite its promising potential for health management, there is a need for better understanding of the importance of Omega-3 and other anti-oxidants in mitochondrial energetic and whole body energy metabolism in disease management, and their contribution to the safety and effectiveness of traditional cardiovascular medicines. Finally, more data on the long-term safety and the true cost-effectiveness and risk-benefit ratio of Omega-3 will further advance our knowledge of using the natural product as a potential therapeutic agent for widespread use in a general population and for management of CVD.

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***Corresponding author:** Pollen K. Yeung, Department of Pharmacy and Medicine, Dalhousie University, Halifax, NS, Canada, B3H 4R2, Tel: 902-4943845; Fax: 902-4941396; E-mail: Pollen.Yeung@Dal.Ca

**Received** January 27, 2015; **Accepted** January 29, 2015; **Published** February 07, 2015

**Citation:** Yeung PK (2015) Omega -3 Fatty Acid for Cardiovascular Prevention. Nat Prod Chem Res 3: e111. doi:10.4172/2329-6836.1000e111

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