Editorial

A key role for dietary bioactives in the prevention of atherosclerosis

Prevention of chronic noncommunicable diseases—which include cardiovascular conditions, some cancers, chronic respiratory conditions, and type-2 diabetes, is a major focus of modern nutrition research. These chronic conditions affect people of all ages, nationalities, and classes, and are reaching epidemic proportions worldwide [1]. They account for ~60% of all deaths worldwide, and have a significant economic impact owing to a reduced economic productivity [2]. Coronary heart disease (CHD) is one of the most important noncommunicable diseases, and is rapidly becoming a primary cause of premature death worldwide. The observed decline in CHD since the 1980s has slowed due to an increasing incidence of major diet and lifestyle-related risk factors such as obesity, hyperlipidemia, and diabetes mellitus [3]. Essential strategies for CHD disease risk reduction in the population therefore include an increased understanding of nutrient benefit in foods, as well as the development of new biomarkers for risk and early disease detection.

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Until recently, most epidemiologic and clinical investigations of diet and CHD have been dominated by the diet-heart hypothesis, which proposes a principal role of dietary saturated fat and cholesterol in the cause of atherosclerosis and CHD in humans [4]. This hypothesis was based on the fact that most epidemiological studies found that increased serum cholesterol predicted the risk of CHD in human populations. An abnormal lipoprotein profile (i.e., increased levels of total and LDL cholesterol and lowered levels of HDL cholesterol), as well as an increased systolic blood pressure, are currently the main modifiable classic risk factors for CHD, and these factors are included in the Framingham risk score. It is now easy to understand how scientific results relating to dietary fatty acids, which are known to affect lipoprotein metabolism, continue to affect nutritional guidelines. For example, the replacement of partially hydrogenated oils (rich in trans fatty acids) by unprocessed oils in food products is likely to prevent many myocardial infarctions [5]. However, beneficially altering lipoprotein metabolism is not the only way to decrease CHD risk. In the past two decades, the understanding of how dietary compounds influence risk of CHD has grown substantially, mainly through studies investigating the molecular mechanisms of atherosclerosis as well as the execution of carefully controlled dietary intervention studies. A number of studies in this issue show novel ways by which fatty acids, bioactive plant compounds, and micronutrients not only affect lipoprotein metabolism, but also have the ability to modulate important antiinflammatory and antioxidant pathways. Indeed, we now know that the effects of diet on CHD can be mediated through multiple biological pathways, heightening the need to find more intermediate end points as markers of CHD risk [6].

The underlying causes of all CHDs involve atherosclerosis and thrombosis [7]. Atherosclerosis is a multifactorial chronic inflammatory disease of the arterial wall involving an extension of the arterial intima with lipids, cells, and components of the extracellular matrix. During the first stage of atherosclerotic plaque development, the arterial lumen is virtually preserved and major symptoms remain rare events. Only a few of these atherosclerotic lesions develop a considerable necrotic core and eventually rupture, leading to acute, occlusive thrombosis and subsequent cardiovascular events such as myocardial infarction, stroke, sudden cardiac death, or unstable angina [8]. Nutrition is likely to affect the early stages of atherosclerosis development, but mechanisms, involving metabolic, oxidative, and inflammatory stress factors, are complex and remain poorly understood. Our diets are made up of many different food compounds and nutrients and most of these may uniquely affect risk of developing vascular disease. Indeed, fatty acid isomers or plant polyphenols that are structurally very similar could have, depending on, for example, receptor affinity, completely divergent actions on gene regulation and modulation of

biochemical pathways. In addition, our genes can also affect the way diet influences the development of atherosclerosis. The use of genetically modified mouse models has significantly increased our understanding of the genetic and molecular mechanisms of atherosclerosis [9] and continue to do so as evident from this special issue. In addition, advances in nutrigenomic technologies, such as nutrigenetics, transcriptomics, proteomics, and metabolomics, linked to network and pathway analysis, will undoubtedly improve our understanding of the complex molecular interplay between genotype, phenotype, and diet, and simultaneously expand the discovery of novel mechanistic biomarkers [10].

Baukje de Roos
Rowett Institute of Nutrition & Health University of Aberdeen, Aberdeen, UK

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