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Review

Plant sterols from foods in inflammation and risk of cardiovascular disease: A real threat?

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ABSTRACT

High dietary intakes of cholesterol together with sedentary habits have been identified as major contributors to atherosclerosis. The latter has long been considered a cholesterol storage disease; however, today atherosclerosis is considered a more complex disease in which both innate and adaptive immune-inflammatory mechanisms as well as bacteria play a major role, in addition to interactions between the arterial wall and blood components. This scenario has promoted nutritional recommendations to enrich different type of foods with plant sterols (PS) because of their cholesterol-lowering effects. In addition to cholesterol, PS can also be oxidized during food processing or storage, and the oxidized derivatives, known as phytosterol oxidation products (POPs), can make an important contribution to the negative effects of both cholesterol and cholesterol oxidation oxides (COPs) in relation to inflammatory disease onset and the development of atherosclerosis. Most current research efforts have focused on COPs, and evaluations of the particular role and physiopathological implications of specific POPs have been only inferential. Appreciation of the inflammatory role described for both COPs and POPs derived from foods also provides additional reasons for safety studies after long-term consumption of PS. The balance and relevance for health of all these effects deserves further studies in humans. This review summarizes current knowledge about the presence of sterol oxidation products (SOPs) in foods and their potential role in inflammatory process and cardiovascular disease.

Contents

Abbreviations: ACAT2, acyl-CoA: cholesterol acyltransferase; ASVD, atherosclerotic vascular disease; COPs, cholesterol oxidation products; HDL, high density lipoprotein; HUVECs, umbilical venous endothelial cells; ICAM, intercellular adhesion molecule; IL, interleukin; LCAT, lecithin–cholesterol acyltransferase; LDL, low-density lipoprotein; LXR, liver X receptor; SREBP, sterol regulatory binding protein; MAPK, mitogen-activated protein kinases; MCP, monocyte chemotactic protein; MIP, monocyte inflammatory protein; MMPs, metalloproteinases; MTP, microsomal triglyceride protein; NFkB, nuclear factor kappa B; POPs, phytosterol oxidation products; PPAR, peroxisome proliferator activator receptor; PS, plant sterols; SOPs, sterol oxidation products; TGF-β1, growth factor β1; TLRs, toll-like receptors; TNFα, tumor necrosis factor α; TRIF, TIR domain-containing adapter-inducing interferon-β; VCAM, vascular cell adhesion molecule; ZDF, zucker diabetic fatty.

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1. Introduction

Western lifestyle together with a high content of animal fats and particularly cholesterol in the diet, are the main contributors to chronic diseases such as atherosclerosis (also known as arteriosclerotic vascular disease or ASVD) (Bonow, 2002; Xu et al., 2013). Although atherosclerosis usually manifests in later life, its early phases are present in teenagers and young adults (Toth, 2008). Atherosclerotic plaque formation has long been considered a cholesterol storage disease (Baigent et al., 2011); however, today atherosclerosis is considered a more complex disorder in which both innate and adaptive immune-inflammatory mechanisms play a major role (Tedgui and Mallat, 2006; Libby, 2007, 2012), in addition to interactions between the arterial wall and blood components. Moreover, atherosclerosis is associated to metabolic and neuroendocrine diseases such as diabetes, obesity and non-alcoholic fatty liver disease (Beckman et al., 2002; Wee et al., 2008; Yu et al., in press).

ASVD affects arterial blood vessels, which develop a chronic inflammatory wall response, and is promoted by low-density lipoproteins (LDL; plasma proteins that carry cholesterol and triglycerides) in the absence of adequate removal of fats and cholesterol from the accumulated macrophages by functional high-density lipoproteins (HDL). Several inflammatory mediators (including cytokines, chemokines and matrix metalloproteases), growth factors and hormones orchestrate recruitment and activities of inflammatory cells in the plaque, with the subsequent induction of a systemic proinflammatory state, involving the adipose tissue and liver (Cybulsky and Gimbrone, 1991; Hansson, 2005). Beyond genetic risk factors, hyperlipidemia with high levels of cholesterol in the systemic circulation is considered the main contributor to endothelial injury.

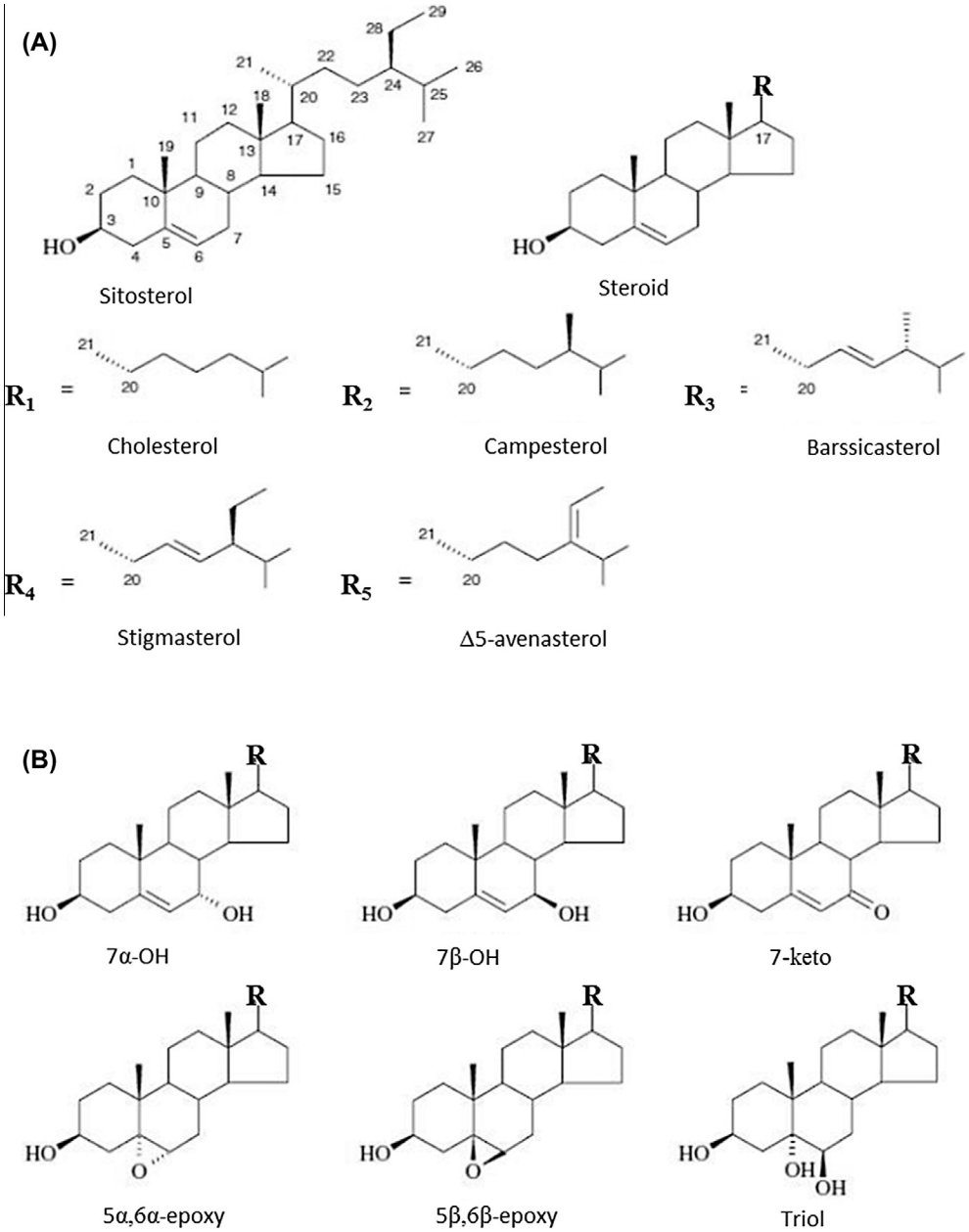

Fig. 1. Structures of the main sterols (A) and their oxidation products (B).