

## **Atherosclerotic cardiovascular disease: a review of initiators and protective factors**

### **ABSTRACT**

Atherosclerotic cardiovascular disease (CVD) is a collective term comprising of a group of disorders of the heart and blood vessels. These diseases are the largest cause of morbidity and premature death worldwide. Coronary heart disease and cerebrovascular disease (stroke) are the most frequently occurring diseases. The two major initiators involved in the development of atherosclerotic CVD are vascular production of reactive oxygen species (ROS) and lipid oxidation. In atherosclerosis development, ROS is associated with rapid loss of anti-inflammatory and anti-atherogenic activities of the endothelium-derived nitric oxide (NO $\cdot$ ) resulting in endothelial dysfunction. In part involving activation of the transcription factor NF- $\kappa$ B, ROS have been involved in signaling cascades leading to vascular pro-inflammatory and pro-thrombotic gene expression. ROS is also a potent activator of matrix metalloproteinases (MMPs), which indicate plaque destabilization and rupture. The second initiator involved in atherosclerotic CVD is the oxidation of low-density lipoproteins (LDL). Oxidation of LDL in vessel wall leads to an inflammatory cascade that activates atherogenic pathway leading to foam cell formation. The accumulation of foam cells leads to fatty streak formation, which is the earliest visible atherosclerotic lesion. In contrast, the cardiac sarco/endoplasmic reticulum Ca $^{2+}$ -ATPase (SERCA2a) and hepatic apolipoprotein E (apoE) expression can improve cardiovascular function. SERCA2a regulates the cardiac contractile function by lowering cytoplasmic calcium levels during relaxation, and affecting NO $\cdot$  action in vascular cells, while apoE is a critical ligand in the plasma clearance of triglyceride- and cholesterol-rich lipoproteins.

**Keyword:** Endothelial dysfunction; Hepatic apoE; Inflammation; Lipoprotein oxidation; Matrix metalloproteinases; NAD(P)H oxidase; Reactive oxygen species, ROS; SERCA2a; Thrombosis