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Review Article

Therapeutic agents for the management of atherosclerosis from herbal sources

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Anu Kajal [a], Lalit Kishore [a], Navpreet Kaur [a], Rakesh Gollen [b], Randhir Singh [a,*]

[a] M. M. College of Pharmacy, M. M. University, Mullana-Ambala, Haryana 133207, India
[b] Department of Pharmacokinetics, KinderPharm LLC, Exton, PA 19341, USA

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ABSTRACT

Purpose: Cardiovascular diseases (CVDs) arising from atherosclerosis are a foremost cause of death and morbidity worldwide. Atherosclerosis and hypertension are the most common factors responsible for CVDs. Due to the increasing prevalence of CVDs caused by atherosclerosis, there is a vital need for precise investigations to rationalize the use of the potential herbal medicines. This review aims to judge current available knowledge of therapeutic agents from herbal sources for management of atherosclerosis.

Method: Bibliographic investigation was done to retrieve available published literature by scrutinizing traditional textbooks and peer reviewed papers, accessing worldwide-accepted scientific databases (Scopus, PubMed, SciELO, NISCAIR, and Google Scholar). The inclusion criterion for the selection of plants was based upon all medicinal herbs and their active compounds with attributed potentials in relieving atherosclerosis.

Result: Wide varieties of plants have been used in the management of atherosclerosis. Overall, 300 articles were reviewed for plant literature, and out of the reviewed literature, 80 articles from year 2000–2016 were selected for the study. The plants were categorized according to the drug targets involved in the pathogenesis of atherosclerosis i.e. modification of lipoprotein levels and adhesion of molecules, LDL oxidation, endothelial dysfunction, plaque formation etc.

Conclusion: Herbs are enacting a reappearance and herbal rebirth is being experienced all over the world. The herbal products signify safety in comparison to the synthetics that are considered as a risk to human beings and to the environment as well. This article may provide the insights of rationale use of medicinal agents from herbal sources based on their mode of action in management of atherosclerosis.

* Corresponding author. M. M. College of Pharmacy, M. M. University, Mullana-Ambala, Haryana 133207, India. Tel.: +91 9896029234; fax: +91 8059930172.
  E-mail address: dahiya_rsd@rediffmail.com; randhirsingh.dahiya@gmail.com (R. Singh).

1.   Introduction

CVDs are considered as the major health care problem that accounts for approximately 30% mortality worldwide (Chapman, 2010). Primarily CVDs include coronary heart disease (CHD), cerebrovascular disease cardiomyopathy, rheumatic heart disease, peripheral arterial diseases, congenital heart disease, deep vein thrombosis, cardiac dysrhythmias, inflammatory heart diseases etc. According to the World Health Organization, CVDs are responsible for about 50% of premature deaths (Amedeo et al., 2000; Mathers and Loncar, 2006). According to the data collected in 2005, the age standardized mortality rate due to CVDs for developing countries like India, China, and Brazil was between 300 and 450 per 100,000 and that for developed countries like the USA and Japan was 100–200 per 100,000.

A statistics indicated that in the USA, more than 900,000 deaths per year are accredited to cardiovascular causes with a cost of around 400 billion US dollars (Thom et al., 2006). Globally, 17.3 million deaths were recorded in 2008 due to CVDs and in 2030 this might reach 23.3 million with expected global cost of 20 trillion US dollars (Mathers and Loncar, 2006).

The etiology of CVDs is very complex but atherosclerosis and hypertension are the most common factors responsible for CVDs (Alain and Karin, 2009). Atherosclerosis or arteriosclerotic vascular disease is a multifaceted disseminated chronic inflammatory disease of the arterial wall that leads to the growth of atherosclerotic plaques in the internal lining (intima) of the arteries (Navab et al., 1996; Stary et al., 1995). Significant genetic components (hypertension, insulin resistance, obesity etc.) and environmental factors (smoking, high fat diet, infectious agents, lack of exercise etc.) are considered as major risk factors responsible for the development of atherosclerosis (Antonio et al., 2003; Goldstein and Brown, 1977). Atherosclerosis and its clinical consequences symbolize a vast and escalating global burden of morbidity and mortality (Murray and Lopez, 1997) in the form of myocardial infarction (MI), peripheral vascular disease, cerebrovascular disease (Ross, 1999) etc.

Over the past few decades, herbal medicines have fascinated a lot of consideration as feasible therapeutic agents in the prevention and treatment of atherosclerosis due to their potential of targeting multiple steps involved in pathogenesis and fewer side effects. Considering this viewpoint, this review is emphasized on plants and parts of plants including the active chemical constituents responsible for attenuation of atherosclerosis via different mechanisms of action.

2.   Materials and methods

In the present review, bibliographic investigation was done to retrieve articles for preclinical studies from worldwide scientific databases like Scopus, PubMed, SciELO, NISCAIR and Google Scholar available during 2005–2015. Botanical names of plants were verified from published literature and database (International Plant Names Index, 2015; The Plant List, 2015). The inclusion criteria for the selection of plants include (i) me-

dicinal plants with reported animal studies targeting steps involved in progression of atherosclerosis, (ii) compounds isolated from medicinal plants with attributed potential in relieving atherosclerosis, and (iii) studies published in the English language and those reporting herbal sources for management of atherosclerosis.

3.   Pathophysiology

Atherosclerosis is considered as a composite syndrome manifesting in arteries especially in major arteries like carotid, coronary, aortic and iliac arteries (Wang et al., 2012). Atherosclerosis resulting from the pathological etiologies and risk factors like hyperlipidemia, hypertension, diabetes mellitus, obesity, and smoking are of main clinical importance (Antonio et al., 2003). Atherosclerosis of this particular etiology is proficiently understood and is illustrated here (Fig. 1).

Being a multistep process, the preliminary steps of atherosclerosis include adhesion of the monocytes to the activated endothelial monolayer leading to migration of the bound monocytes into the tunica intima followed by maturation of monocytes into macrophages. The uptake of lipid globules by macrophages leads to formation of foam cells. The foam cells, under lesion progression, go through an inflammatory process, which leads to migration of SMCs from the tunica media to the tunica intima followed by proliferation of the occupant intimal SMCs and synthesis of extracellular matrix macromolecules such as elastin, collagen, proteoglycans etc. SMCs and plaque macrophages may die during lesion advancing by apoptosis. Extracellular lipid secretion of dead and dying cells can accumulate in central region of plaque and lead to formation of lipid or necrotic core. The most definitive impediment of atherosclerosis i.e. rupturing of plaque or thrombosis, is the last step of the atherosclerotic process which causes interruption of blood flow and other cardiovascular problems (Christopher and Joseph, 2001; Goran, 2005; Sakaruka et al., 2013; Xiao-Hua et al., 2013).

4.   Major targets for anti-atherosclerotic activity

4.1.   Modification of lipoprotein levels

Lipoproteins are composed of lipids (phospholipids and triacylglycerol), proteins and cholesterol. It is well recognized that eminent blood lipid levels amount to the primary risk factor for atherosclerosis. Epidemiological studies have indicated that dyslipidemia and coagulation disturbances are among most considerable risk factors of the development of atherosclerotic conditions (Erqou et al., 2009; Nordestgaard et al., 2010).

In state of hyperlipidemia, excess of LDL infiltrates arteries and is retained in the tunica intima. The retained LDL undergoes oxidative modifications in the sub-endothelial space (Leitinger, 2003; Skalen et al., 2002). The infiltration of LDL can be controlled either by direct lowering of lipoprotein levels of