



Natural Approaches for Reducing Risk Markers of Cardiovascular Diseases Related to Obesity

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Abstract

Raised blood lipid levels are associated with a risk of cardiovascular disease (CVD) and obesity. Despite scientific and technical progress in risk prediction, diagnostics, prognostication and therapy of cardiovascular pathologies it has been shown that nutritional intervention seems to be an effective approach to reduce the risk markers of cardiovascular diseases. Bioactive phytochemicals in food supplements are a trending approach to facilitate dieting and to improve patient's adherence to reducing food and caloric intake. This review focuses on current bioactive compounds that exhibit therapeutic effects through several cellular mechanisms in obesity and related diseases. The information discussed in the present review may provide evidence to spread the use of some effective ingredients from nature for the prevention of cardiovascular disease.

Keywords: Obesity; Cardiovascular disease; Nutrition; Phytochemicals; Cholesterol; Polysaccharides

Introduction

Calorie imbalance is related to a rising prevalence of obesity. Populations of industrialized countries are becoming more overweight as a result of changes in lifestyle, and obesity may well become the most common health problem of the 21st century. Obesity is a major contributor to the prevalence of cardiovascular disease (CVD) in the developed world, and yet has only recently been afforded the same level of attention as other risk factors of coronary artery disease (CAD). Studies indicate that higher levels of body fat are associated with an increased risk for the development of numerous adverse health conditions [1]. Weight loss is increasingly recognized to have major health benefits for overweight people [2] and also increases life expectancy in people having obesity-related complications. While reducing dietary fat content combined with increased physical exercise was shown to be effective in preventing obesity [3], only one third of those trying to lose weight reported eating fewer calories and exercising more [4]. Although weight loss and weight control drugs are becoming extremely common in today's society, the remedies provided by the diet industry have failed in the long-term maintenance of weight loss in obese patients [5]. Moreover, it has been estimated that more than 90% of the people who lose weight by dieting return to their original weight within 2-5 years [6]. Adipose tissue growth involves formation of

neoadipocytes from precursor cells, further leading to an increase in adipocyte size. The transition from preadipocytes into mature adipocytes constitutes the adipocyte life cycle, and treatments that regulate both size and number of adipocytes may provide a better therapeutic approach for treating obesity. Prins and O'Rahilly revealed for the very first time that the decrease of adipose tissue mass that occurs with weight loss may involve the mobilization of lipids through lipolysis or the loss of mature fat cells [7]. While development of obesity is a greater problem during middle age, elderly people can have a relative increase in body fat content accompanied by an accumulation of adipocytes in nonadipose tissues leading to a higher risk of stroke and other cardiovascular diseases

Bioactives from plant extracts represent the most widespread form of medication and a common tool to reduce cholesterol levels and other cardiovascular risk factors. At least 25% of the active compounds in currently prescribed synthetic drugs were first identified in plant sources [8]. Dissatisfaction with the high costs and potentially hazardous side effects of pharmaceuticals have resulted in a larger percentage of people in the United States purchasing and exploring the applications of medicinal plants than before [9]. Several plants like willow, poppy, foxglove, cinchona, aloe and garlic

have been verified as medicinally beneficial through repeated clinical testing and laboratory analyses [10], and a number of plant extracts like green tea [11], garlic compounds [12] and conjugated linoleic acid (CLA) [13] were shown to possess either antidiabetic effects or have direct effects on adipose tissue. Substantial progresses have been made concerning our knowledge of bioactive components in plant foods and their links to obesity. Polyphenols constitute one of the ubiquitous groups of plant metabolites widely found in fruits, vegetables, cereals, legumes and wine [14]. A large number of studies have been carried out to investigate the antiobesity effects of polyphenols like apigenin and luteolin [15], kaempferol [16], myricetin and quercetin [17], genistein and daidzein [18-20], cyanidin [21], grape seed proanthocyanidin extract (GSPE) [22], xanthohumol [23] and epigallocatechin gallate (EGCG) [24]. Likewise, studies involving the effects on lipid metabolism have been carried out with carotenoids like fucoxanthin [25], coumarin derivatives like esculetin [26] and phytoalexins like resveratrol [27]. Other bioactive components of food with antiobesity effects include phytosterols, polyunsaturated fatty acids and organosulfur compounds. The association between lipid and bone metabolism has become an increasing focus of interest in recent years [28], and accumulating evidence has shown that atherosclerosis and osteoporosis, a disorder of bone metabolism, frequently co-exist, therefore the reduction of CVD risk markers could have a positive effect on bone health [29].

Natural compounds used for the reduction of risk biomarkers in CVD

The use of botanicals to diminish the lipid absorption has been widely reported [30]. Plant extracts like *Cissus quadrangularis* [31], *Aralia mandshurica* (aralax) [32], psyllium [33], *Salix matsudana* leaves [34] and *Arachis hypogaea* [35] on lipid metabolism revealed a reduction in serum triglyceride levels. However, there are no major long-term studies demonstrating harm or benefit in using lipid-lowering drugs compared to low-fat diets in children [36].

Phytosterols have been widely studied for their cholesterol-lowering effects and because of the effect on bone health regulating the osteoblasts/osteoclast ratio [37]. Plant sterols like diosgenin, campesterol, sitosterol, stigmasterol and brassicasterol were shown to possess cholesterol lowering effects [38]. Since turnover of cholesterol was shown to bear a relationship to body fat mass [39], phytosterols may also decrease body fat. A number of studies have demonstrated the beneficial effects of polyunsaturated fatty acids (PUFAs) on lipid-related disorders in humans [40].

Adipose tissue mass can be reduced by both inhibiting adipogenesis and inducing apoptosis of adipocytes. Natural products that specifically target both these pathways therefore will have better potential for treatment and prevention of obesity. Polyphenolic compounds are widely found in fruits and vegetables among which flavonoids and several classes of nonflavonoids are usually distinguished. The antiobesity effects and also adipocyte-

specific effects of several polyphenols have been investigated. PUFAs are vital components of the phospholipids of cell membranes and serve as important mediators of the nuclear events regulating the adipocyte-specific gene expression involved in lipid metabolism and adipogenesis [41,42] revealed how the Herbal composition Ob-X reduces abdominal visceral fat in humans and also shown that the visceral fat reduction reduction is linked to the decrease of the triglyceride's levels. Previously [43] suggested that a highly specific *Melissa officinalis* extract can reduce the adipose tissue mass by inhibiting the adipose angiogenesis. The inhibition of the angiogenesis in the adipose tissue seems related to metabolic changes in plasma lipids, liver triglycerides and weight loss.

Although most commonly used dietary supplements like CLA showed an effect on glucose and lipid metabolism, these effects are also likely secondary effects mediated through adipocyte-specific transcription factors and their nuclear receptors [44]. Likewise, although the beneficial effects of organosulfur compounds present in natural food are due to their antioxidant and anticarcinogenic properties [45], the adipocyte specific effects of ajoene, has been reported [46]. Dietary fibre (DF) primarily consists of non-starch polysaccharides, many of which are characterised by their ability to form viscous dispersions and/or gels in water [47]. For example, the consumption of β -glucan, a viscous soluble fibre from barley, can lead to a significant reduction in total cholesterol as well as LDL cholesterol levels [48,49]. Recent reports on the intake of barley and oat β -glucan and konjac glucomannan significantly reducing LDL cholesterol and non-HDL cholesterol levels [50-52]. Several mechanisms have been proposed to explain the beneficial effects of DF on blood lipids, including short chain fatty acid (SCFA) production in the colon, reduced fatty acid synthesis, lowered body weight with fat loss, improved glycaemic control, microbial modulation, reduced inflammation and formation of non-covalent bonds with other dietary components to adsorb or entrap them [53]. Gaining a better understanding of the beneficial influence of increased DF intake on the multiple markers for CVD risk is an important area of preventative health research.

More recently, it has been proven that water soluble polysaccharides from *Agaricus Bisporus* (H2Oslim®) create a cationic polymer when in contact with water, which is able to interact with anionic substances. Polymer-lipid complexes that are formed through bonds can be attributed to the density of positive charges on the polymer. [54] Because of the indigestibility of this amino polysaccharides-lipid complex, the lipid absorption by the intestine is highly reduced. These characteristics make H2Oslim® helpful in the treatment of high blood fat, hyper lipemia and high blood cholesterol, hypercholesteremia or hypertriglyceridemia. It seems that such complexes, are able to reduce the amount of lipid and cholesterol available for absorption and assimilation by the body, decreasing the most noteworthy risk markers in cardiovascular diseases in the occidental adult population.

Conclusion

Obesity is a risk factor for diseases like non-insulin-dependent diabetes mellitus, cardiovascular diseases and certain cancers. Dietary bioactives derived from natural products have shown interesting effects on adipose tissue like inducing apoptosis, decreasing lipid accumulation and inducing lipolysis. Since a number of complex interconnected cell signaling pathways are involved in regulating all the above-mentioned processes, lipid trapping strategies and targeting the adipocytes with bioactives from ingredients could result in enhanced effects. This strategy can be achieved by exerting beneficial effects through additive or synergistic actions of several natural compounds acting at single or multiple target sites associated with physiological processes like apoptosis, adipogenesis lipolysis or inhibiting the lipid absorption. These strategies seem an effective approach in the reduction of cardiovascular risk markers.

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