

REVIEW

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Berry seed oils as potential cardioprotective food supplements

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Abstract

Background: There is a tendency to search for new, unconventional plant oils with health-promoting properties, preferably unrefined, which besides having an interesting fatty acid profile contain a high level of biologically active compounds. This review is focused on selected berry seed oils as potential cardioprotective food supplements, that is, strawberry, red raspberry, and blackcurrant seed oil, and their chemical composition and nutritional quality.

Main text: Berry seed oils are rich in essential fatty acids both from n-6 and n-3 family. The content of polyunsaturated fatty acids in selected oils was reported as follows (as percentage of total fatty acids): red raspberry seed oil, 85% (linoleic acid, 54%; α -linolenic acid, 32%); blackcurrant seed oil, 81.5% (linoleic acid, 48%; α - and γ -linolenic acid, 30%); and strawberry seed oil, 78% (linoleic acid, 42%; α -linolenic acid, 36%). Worthy of notice is also the presence of γ -linolenic acid in blackcurrant seed oil (approximately 17%). In addition, the seed oils are abundant in other bio-active compounds, such as sterols, tocopherols, and phenolic compounds. Except for blackcurrant seed oil, health-promoting aspects of the proposed seed oils have not been extensively investigated in *in vivo* studies. But, there are available studies on laboratory rats suggesting cardioprotective properties of these oils. Especially, a potent triglyceride-lowering effect of blackcurrant, strawberry, and raspberry seed oil was visible. The tested berry seed oils also ameliorated the inflammatory state in the organism and the liver fat content. Nevertheless, the consumption of the berry seed oils, especially together with an unbalanced diet, induced also some unfavorable changes in the organism.

Conclusion: The proposed berry seed oils can be considered edible and potentially cardioprotective supplements; however, there is a need for extensive *in vivo* researches that could confirm their properties, check the safety of their consumption, and allow to select the most suitable ones.

Keywords: Blackcurrant seed oil, Cardiovascular disease, Metabolic syndrome, Raspberry seed oil, Strawberry seed oil

Background

Cardiovascular disease (CVD) refers to maladies of the arteries supplying muscles of the heart (coronary heart disease), the brain (cerebrovascular disease), and the extremities, especially the legs (peripheral vascular disease). They are the leading cause of mortality worldwide, accounting for around 18 million deaths each year. Approximately 50% of these deaths are from coronary heart disease and further 25% from cerebrovascular disease [1]. There are many risk factors for the development of CVD among these smoking, dyslipidemia, raised blood pressure, physical inactivity, obesity, and diabetes are considered to be the most important [1, 2]. In this context, especially important is

also the metabolic syndrome (MS) defined as a cluster of interrelated risk factors for CVD, increasing the risk of their development from three to four times. According to the newest standardized criteria, clinical diagnosis of the MS is based on the determination of central obesity, raised blood pressure, and a low concentration of high-density lipoprotein (HDL)-cholesterolemia, as well as elevated glycemia and triglyceridemia. Three abnormal findings out of the five qualify a person to suffer from the MS [3].

CVD can be characterized as involving processes of atherosclerosis, thrombosis, and changes to the function of the arterial lining, whereas in the MS, insulin resistance is a distinguishing disturbance that often occurs. Nevertheless, the pathogenesis of both these diseases is strongly connected, and oxidative stress resulting from an imbalance between energy intake and its expenditure is postulated as one of the most important causative factors

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[4]. It is suggested that if the imbalance occurs, a substrate-induced increase in citric acid cycle activity generates an excess of mitochondrial reduced nicotinamide adenine dinucleotide and thus increases the production of reactive oxygen species, particularly superoxide anion. Chronic overproduction of these species may disturb the oxidative/antioxidative balance of the body, which stimulates compensatory mechanisms that protect cells of selected tissues (particularly muscle and adipose ones) against further insulin-stimulated glucose and fatty acid uptake and therefore oxidative damage. As a result, an increased postprandial concentration of glucose (impaired glucose tolerance) and free fatty acids in the blood may occur. Secondly, elevated glycemia intensifies oxidative stress in the body, as well. Such a situation may lead to the injury of selected cells that are especially sensitive to oxidative stress, such as pancreatic beta and endothelial ones [4, 5]. Beta cell damage is the critical step to the development of type 2 diabetes, whereas endothelial dysfunction, as a consequence of endothelial cell damages, is thought to be a key event in the development of atherosclerosis. Furthermore, oxidative stress is also linked with inflammation processes, and the pathways that generate the mediators of inflammation, such as adhesion molecules and interleukins, seem to be all induced by this state [4, 6]. Indeed, inflammation is an intrinsic element of atherogenesis and the MS being present through all stages of their development [1, 6]. Therefore, the acute phase proteins, C-reactive protein, fibrinogen, and serum amyloid A appear to be associated with risk for CVD; however, a number of other surrogate markers for systemic inflammation have also been suggested, including proinflammatory cytokines, such as interleukin 6, tumor necrosis factor- α , and growth factors; however, these markers remain inferior to C-reactive protein in terms of their discriminatory power to predict CVD risk [1].

Main text

Role of unsaturated fatty acids in the management of MS and CVD

The development and progression of MS and CVD are strongly related to lifestyle factors; among the most important ones are nutritional faults, which can be easily corrected compared with others, affording a real chance to prevent disease development, as it was stated in the report of WHO and FAO experts [7]. Apart from many changes in an everyday diet, such as caloric restrictions, a reduced intake of cholesterol or salt, and an increased consumption of unsaturated fatty acids at the expense of saturated ones, with mono- and polyunsaturated fatty acids therein (MUFA and PUFA, respectively), is a basic recommended nutritional strategy. It is well established that replacing saturated fatty acids by either MUFA or n-6 PUFA reduces LDL-cholesterolemia. Unsaturated fatty acids, such as

linoleic acid or MUFA, also enhance HDL-cholesterolemia, which assists in the removal of triglycerides from the bloodstream. Numerous mechanisms whereby dietary unsaturated fatty acids could reduce CVD risks have been identified, yet the exact one is still unclear. However, these include effects on blood lipid concentration, blood pressure, inflammatory response, arrhythmia, and endothelial and platelet function, along with many other effects as yet undefined [8]. Most of the abovementioned effects concern mechanisms underlying cardioprotective effects of n-3 PUFA, namely eicosapentaenoic acid and docosahexaenoic acid found in fish oils, and α -linolenic acid whose large quantities are present in some plant oils, such as linseed oil or rapeseed oil. First of all, n-3 PUFA have the ability to respond to inflammation in atherogenesis through direct and indirect mechanisms. A direct mechanism through which n-3 PUFA decrease inflammation includes their rapid effect on the regulation of transcription factors, and indirect modes of actions include the production of three- and five-series eicosanoids and inflammation-resolving lipid mediators, as well as suppression of acute phase proteins, especially C-reactive protein. In the context of transcription factors regulation, n-3 PUFA inhibit NF- κ B activity (an inflammatory signaling pathway), downregulate gene expression involved in fatty acid synthesis through sterol regulatory element binding protein 1c, and upregulate gene expression involved in fatty acid oxidation by means of peroxisome proliferator-activated receptor α . Interestingly, inflammation is stimulated by triglycerides that are independent risk factors for CVD, while supplementation of n-3 PUFA can decrease blood triglyceride concentration through the inhibition of hepatic very low-density lipoprotein/triglyceride synthesis and secretion. n-3 PUFA have also beneficial effects on vascular endothelial function by decreasing endothelial activation, which contributes to early phases of atherogenesis [9]. Moreover, there are also findings indicating on a very important role of n-3 PUFA in the improvement of platelet function in healthy subjects and in patients with CVD [10]. It has been suggested that these PUFA can be incorporated into platelets, improve their oxidative stability, and reduce their aggregation and activation [10–13].

Generally, cardioprotective effects of n-3 PUFA and mechanisms underlying them are relatively well recognized. Nevertheless, latest studies indicate that n-6 PUFA can be very important in this context as well. For example, high plasma phospholipid concentration of linoleic acid, but not other n-6 PUFA, was inversely associated with total mortality and coronary heart disease mortality in older adults [14]. Moreover, the study by Nagai et al. [15] even suggested that lower circulating n-6 but not n-3 PUFA level on admission was significantly related to worse clinical outcomes in acute decompensated heart failure patients. Contrary to n-3 and n-6 PUFA, epidemiological

and interventional studies suggest that MUFA themselves, found in high quantities in olive oil and rapeseed oil, appear not to provide cardioprotection [16]. Nevertheless, what is especially important from the MS' perspective is that the role of MUFA as cytoprotective agents in pancreatic β -cells is gaining more and more scientific attention. Overall, the elevated concentration of free fatty acids in the blood is thought to be cytotoxic to β cells, similar to glucose. Nonetheless, it is suggested by *in vitro* studies that some unsaturated fatty acids, especially MUFA, can improve β cell viability, mainly through the rapid inhibition of caspase 3 activity [17]. It remains unclear, however, whether this response represents cause or effect.

Selected berry seeds as a source of potential cardioprotective oils

One of the richest sources of PUFA are edible plant oils, among which the most popular are those obtained from seeds of rape, sunflower, and soybean. However, in the food industry, there is a tendency to search for new, unconventional plant oils with potential health-promoting properties, preferably unrefined, which besides having an interesting fatty acid profile contain additional bio-active compounds. For instance, more and more attention is being received by oils from such sources, as amaranth seeds or sea buckthorn fruits, which are especially abundant in biologically active squalene or carotenoids, respectively. Interestingly, sea buckthorn oil may be extracted from the seeds and also from the pulp and the seed oil contains more PUFA, whereas the pulp oil contains more MUFA and is additionally rich in carotenoids [18]. Nevertheless, it is worth emphasizing that other important sources of edible oils could be searched for among seeds of fruits, whose intensive cultivation for industrial processing is common worldwide. For example in Poland, according to the Statistical Yearbook of Agriculture, the overall production of fruits in 2009 amounted to approximately 3.8 million tons, which is of significance in the European Union. Among the fruits, berries take an important part with the most popular strawberries (199 thousand tons), blackcurrants (196 thousand tons), and red raspberries (82 thousand tons) [19]. In the industrial production of juices, jellies, and jams, most processors consider fruit seeds to be removed from the pulp during processing, which improves the end product. As a consequence, waste products including seeds are for potential use. Unfortunately, fruit seeds alone or, which is even more often, together with pomace as by-product of juice production, are often dumped or composted. However, this approach has recently been changed and fruit seeds from waste streams are more and more often utilized worldwide, among others for the production of oils, which assures technical progress in fruit processing and gives reasons for more fulfilled utilization of raw materials [20]. Worthy of notice is that, in general, fruit seeds contain considerable quantities

of oil, for example, for berry seeds the mass fraction of oil is most frequently above 20% [21, 22]. Surprisingly, fruit seed oils are not popular as edible products and so far they are used in cosmetics, more specifically in so-called nutricosmetics. However, there are some exceptions, as for example grape seed oil whose presence is common in the food market or to a lesser extent blackcurrant seed oil, which among others is used as an ingredient in infant formulas, due to the presence of γ -linolenic acid just as in human milk. Blackcurrant seed oil is newly available on the market as a dietary supplement in a tablet form, as well.

Obviously, fruit seed oils produced from waste streams are valuable to the market from the economical point of view. Nevertheless, some of them seem to be especially nutritious and have interesting chemical composition, which is of particular importance in the context of CVD prevention, as well as MS treatment. Berry seed oils are rich in essential fatty acids and have a favorable low n-6/n-3 ratio. For instance, this ratio equals 1.69 and 1.16 for red raspberry and strawberry, respectively [22]. It ought to be emphasized that the recommended n-6 to n-3 ratio in an everyday diet equals 4–6 to 1, and it seems to be important when the CVD prevention is considered [8]. Nevertheless, newer recommendations suggest that focusing on the ratio can distract away from absolute intakes of n-3 fatty acids, the increase of which should be considered as more important [23]. More in detail, the content of PUFA in selected oils was reported as follows (as percentage of total fatty acids): red raspberry seed oil, 85% (linoleic acid, 54%; α -linolenic acid, 32%) [22], blackcurrant seed oil, 81.5% (linoleic acid, 48%; α - and γ -linolenic acid, 30%) [24], and strawberry seed oil, 78% (linoleic acid, 42%; α -linolenic acid, 36%) [22]. Worthy of notice is also the presence of γ -linolenic acid in blackcurrant seed oil (approximately 17%). Chemical structure of PUFA that are present in the berry seed oils is shown on Fig. 1.

Berry fruits including their seeds are very rich in other nutrients and bio-active compounds that can play an important role in cardioprotection. For example, cranberries are rich in folic acid and the consumption of cranberry juice was able to improve some cardiovascular risk factors, including a decrease in blood homocysteine level [25]. However, an important question is the extent to which bio-active compounds can be extracted together with fatty acids during cold pressing of berry seeds and it seems that the extracted amounts can be of significance. For instance, blackcurrant seed oils obtained from Canadian crops was reported to be especially abundant in sterols (6.5 g/100 g of oil on average) [26]. Tocopherols were present in large quantities in red raspberry seed oil (2.11 g/kg oil), whereas in strawberry seed oil, significant amounts of phenolic compounds were determined (approximately 9 mg/g oil with 6.6 mg/g of p-coumaric acid, therein) [21]. Both tocopherols and phenolics are antioxidants with potent

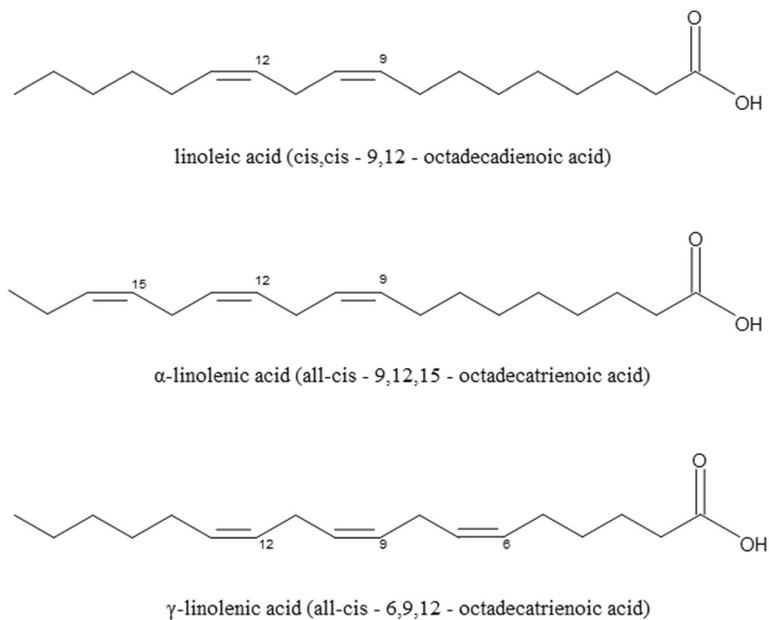


Fig. 1 Chemical structure of polyunsaturated fatty acids (PUFA) present in selected berry seed oils; n-6 PUFA—linoleic acid and γ -linolenic acid, n-3 PUFA— α -linolenic acid

preventive effects on CVD, whereas phytosterols, such as β -sitosterol, inhibit cholesterol absorption in the intestine, thus exhibiting the cholesterolemia-lowering properties.

In vivo researches

The chemical composition of the oils presented here points that a cardioprotective activity is possible; however, its recognition including the extent of positive effects should be confirmed in biological studies and then potentially also in clinical trials. Except for blackcurrant seed oil, nutritional and health-promoting aspects of the proposed seed oils have not been extensively investigated in biological studies. But, there are experimental studies performed in rats and conducted by the first author of this mini-review, in which it was concluded that blackcurrant, strawberry, and raspberry seed oil can be a valuable source of essential fatty acids in the daily diet and can be potentially used in the management of some disorders related to obesity and CVD [27–29]. A potent triglyceride-lowering effect of blackcurrant, strawberry, and raspberry seed oil was especially visible, and the effect was as efficient as that of some lipid-lowering drugs available on the market. The tested berry seed oils also ameliorated the inflammatory state in the organism and the liver fat content, which is a common disorder present in obese subjects. Nevertheless, the consumption of the berry seeds oils, especially together with an unbalanced diet, induced also some unfavorable changes in the organism. The consumption of black currant seed oil led to the increased risk of liver injury, whereas in the case of strawberry and

raspberry seed oils some disorders in the metabolism of the large intestinal bacteria were noted.

Some interesting studies regarding the biological activity of blackcurrant seed oil are already available in the literature. In a randomized, double-blind, crossover study including two 4-week periods with the supplementation of oils, serum concentrations of LDL-cholesterol were significantly lower after blackcurrant seed oil compared to fish oil [30]. In another study, 8-week supplementation with blackcurrant seed oil led to the 40% reduction of blood pressure reactivity in men [31]. In a study in rats, 48-week feeding showed effectiveness of a relatively small amount of blackcurrant seed oil in reducing the susceptibility to ischemic arrhythmia in rats [32]. Moreover, the use of blackcurrant seed oil has also been considered for the treatment of inflammatory disease [33].

Conclusions

The proposed berry seed oils can be considered as edible and potentially cardioprotective; however, there is a need for extensive in vivo researches that will confirm their activity and allow to select the most suitable ones. Moreover, it has to be stressed that safety aspects of fruit seed oils should also be touched in future researches. Overall, safety of novel foods is an essential research area, especially when they are produced using unconventional methods, or from unconventional sources, as in the case of fruit seed oils. Complex toxicological reports are already available in the literature for some fruit seed oils (for example, acute toxicity, subchronic toxicity), as for example for

pomegranate seed oil that was not toxic to rats [34] or, on the contrary, custard apple (*Annona reticulata* L.) seed oil whose toxicity was notable in mice [35]. It is especially important regarding berry seed oils, because it is known that they can accumulate pesticides to some degree [36]. Furthermore, it is a completely open issue how such oils could be exactly applied in the food/pharmaceutical industry. If they were to be used as a standard food additive (for example, for salad preparation), ingredients of functional foods or dietary supplements, these would be established in further research, such as organoleptic analyses or pharmaceutical formulation. In this context, an important question is if rather low oxidative stability of berry seed oils signalized in the literature will not be an important obstacle in their use [22].

Abbreviations

CVD: Cardiovascular disease; HFL: High-density lipoprotein; LDL: Low-density lipoprotein; MS: Metabolic syndrome; MUFA: Monounsaturated fatty acids; PUFA: Polyunsaturated fatty acids

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