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Cardioprotective effect of alcohol consumption: contemporary concepts

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Abstract

Coronary atherosclerosis is the major cause of death in Western civilization. Epidemiological, experimental and clinical investigations have shown that diets supplemented with moderate quantities of alcoholic beverages lead to biochemical changes, that are widely regarded to prevent atherosclerosis. Oxidized LDL-C particles are able to penetrate arterial walls and cause atherosclerotic occlusions of the arteries. The cardioprotective effect of alcoholic beverages is related to their biologically active antioxidant compounds, ethanol and phenolics, which are able to prevent oxidation of LDL-C. Among alcoholic beverages red wine appears to be the best choice. © 2002 Elsevier Science Inc. All rights reserved.

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1. Introduction

Coronary atherosclerosis is still the major cause of death in Western industrial countries; one of every three cases of death in men as well as in women [1,2]. Atherosclerosis is a multifactorial process based on various risk factors. According to Ross [2], the form and content of the advanced lesions of atherosclerosis demonstrate the results of three funda-

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mental biological processes: (a) accumulation of intimal smooth muscle cells, together with variable numbers of accumulated macrophages and T-lymphocytes; (b) formation by the proliferated smooth muscle cells of large amounts of connective tissue matrix, including collagen, elastic fibers, and proteoglycans; (c) accumulation of lipids, principally in the form of cholesteryl esters and free cholesterol within the cells as well as in the surrounding connective tissues. The main target of atherosclerosis are arteries. The pathological damage, can be found practically in every artery. The most important clinical damage is in the coronary arteries, coronary artery disease (CAD) is a consequence. Occlusion of coronary arteries leads to myocardial infarction, which in some cases can be fatal. Elevated levels of total cholesterol, low-density cholesterol (LDL-C), triglycerides, apolipoproteins B and C-III and reduced level of high-density cholesterol (HDL-C) and apolipoprotein A-I are major risk factors for atherosclerosis [3,4]. One of the important mechanisms in development of atherosclerosis is the oxidation of cholesterol-rich LDL-C particles [5,6]. Oxidation of lipids enhances their atherogenicity and facilitates penetration into arterial wall. The support of the theory that oxidized LDL-C is responsible for the pathological features of atherosclerotic lesions derives from the findings in cultured cell systems that oxidized LDL-C causes the aforementioned cellular changes. This theory is similar in many aspects to updated versions of the “response to injury” theory of atherogenesis, with oxidized LDL-C playing a central role as an agent that caused injury to, or dysfunction of, the endothelium [7]. A hypothetical sequence of one version of the oxidative theory was described by Chisolm and Penn, [7]. VLDL and LDL enter into and accumulate in the arterial intima, processes that are governed by endothelial vesicular transport rates, local endothelial cell turnover, plasma concentration of lipoproteins, and the size of intima. Increases in the intimal pool size of these lipoproteins and binding to connective tissue elements increase the residence time of the lipoproteins in the intima, which, in turn, increases the probability of opportunistic oxidation. The oxidation may be by reactive oxygen from isolated macrophages or intimal smooth muscle cells or from the endothelium. Once oxidized, the modified lipoproteins may injure or activate endothelium, increasing the turnover of these cells and allowing the entry of more plasma macromolecules. Oxidized LDL can also facilitate monocyte invasion of the intima by eliciting secretion of monocyte chemoattractants and surface expression of monocyte binding proteins. Oxidized LDL and lysophosphatidylcholine emanating from it may act as chemoattractants for monocytes. Further potential atherogenic actions of oxidized LDL include serving as a ligand for foam cell formation by promoting migration and proliferation of smooth muscle cells, and by killing cells and thereby contributing to the accumulation of dead-cell debris.

Thus, according to this theory, prevention of atherosclerosis should be based against LDL-C oxidation [8]. In 1993, Frankel et al., [9] showed that resveratrol inhibits human LDL-C oxidation. Later these authors [10] demonstrated inhibition of the oxidation of human low-density lipoprotein by phenolic substances of red wine. It was shown, that intensive multiple risk factor reduction has a beneficial effect on coronary atherosclerosis in men and women: the disease regression is twice as frequent in the risk reduction group as in control [11]. An integral part of the preventive measures are antiatherosclerosis diets with limited quantities of fats and an increased amounts of vegetables and fruits [12,13].

2. Alcoholic beverages

It was shown that moderate consumption of alcohol beverages has a cardioprotective effect [12,13,18]. In Western countries alcohol beverages are an integral part of diet and provide about 4 to 6% of the average energy intake [14–19].

It was reported that consumption of alcohol beverages negatively influences protein metabolism [20–22]. Some authors have found that acute ethanol ingestion reduced synthesis rates of intestinal contractile proteins [23]. The effect of ethanol on skeletal muscle was studied and an impaired synthesis of protein was found [24]. Proteins are oxidatively modified in plasma of acute alcoholics [25]. Even short-term moderate beer consumption leads to certain changes in plasma proteins [26,27]. In spite of these facts, consumption of alcoholic beverages is relatively high. One of the reasons of high alcohol consumption are the data, which have shown that diets, supplemented with various kinds of alcoholic beverages have a positive influence on CAD [28–32]. Alcohol intake was studied among 51,529 male health professionals [33]. It was found that inverse relation between alcohol consumption and risk of CAD is causal. The published results of the most comprehensive study have summarizing data of alcohol consumption and mortality among middle-aged and elderly U. S. adults [32]. Among 490,000 men and women, in the U.S.A. those who used alcohol beverages, 46,000 died during nine years of follow-up. Thun et al., [32] have compared cause-specific death rates and death from all causes across categories of base-line alcohol consumption. The rates of death from all cardiovascular diseases between the ages of 35 and 69 were 30 to 40 percent lower among men and women reporting one drink daily than among nondrinkers.

Intake of food products, containing high quantities of cholesterol is positively correlated with morbidity and mortality from CAD [2]. Total consumption of saturated fats in France is equal to that of other developed countries, while French mortality from CAD is only one-third of the average [34]. The distinguishing feature of French diet is a regular consumption of red wine with meals. Therefore, the frequent consumption of wine often red wine could explain in part the low French mortality from CAD [31]. Epidemiological, experimental and clinical investigations have demonstrated that diets supplemented with moderate quantities of alcoholic beverages lead to some positive biochemical changes, which are widely regarded as indicators of improved prevention of atherosclerosis [12,13,31,35,36]. It was found an improved lipid metabolism, an increased antioxidant and anticoagulant activities in the blood of consumers [12,13,29–31].

There are two major differences of opinions about the biologically active compounds of these beverages (we do not mention the role of vasorelaxing components of grapeskin as less scientifically grounded). Some authors have demonstrated that ethanol itself is responsible for the cardioprotective effect [35–42]. Other studies have shown that consumption of wine leads to the most beneficial effects [28,30,31]. Opponents claim that methodological problems of the above mentioned studies limit their validity [37–41]. They insist that the biologically active part of all alcoholic beverages is only ethanol itself. However, other scientists have demonstrated that the phenolic substances in wine are playing a major role in its cardioprotective effect [43–50].

As far as back as in 1979, Leger et al. [28] reported a strong and specific negative

association between CAD deaths and alcohol consumption in both sexes. They analyzed consumption of three main beverages, wines, beers, and spirits. and came to the conclusion that “of the three alcohol components, wine had the strongest negative association with CAD”. These findings were supported by Friedman and Kinbal [30]. In the well-known Framingham Heart Study they found that in nonsmokers beer and wine show greater reductions in CAD mortality than spirits. Also Renaud and Lorgeil [31] attributed the French paradox to moderate wine consumption. They postulated that an increased anticoagulant activity (inhibition of platelet reactivity) by wine might be one explanation of this well-known paradox. Some additional studies were performed in the following years [43–52]. These studies do not have methodological problems as in questionnaires of epidemiological retrospectives. It was shown *in vitro* that phenolic substances in red wine inhibit oxidation of human low-density lipoproteins [9,10,50]. It was demonstrated that phenolics of beer and wine protect serum low-density lipoprotein against atherogenic modification [46]. Experiments on laboratory animals support this point of view [35,36,47,51]. It was found that red wine affects peroxidation of plasma and erythrocytes of rats [47] and low-density lipoprotein oxidation and atherosclerosis in aorta and coronary artery in Watanabe heritable hyperlipidemic rabbits [51]. Other investigators have shown that the biologically active compounds of alcoholic beverages are phenolics [35,36,48,49]. Two experiments on rats: with dry matter and with alcohol-containing and alcohol-free different alcoholic beverages were performed [36]. These studies showed that both original and lyophilized wine and beer increase antioxidant activity and improve lipid metabolism by reducing plasma total cho-

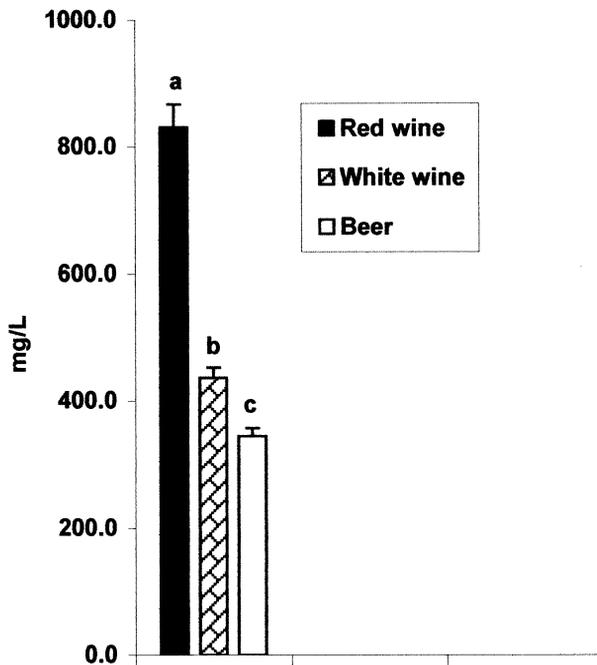


Fig. 1. Content of total polyphenols in three alcoholic beverages. Means ± SD (vertical lines). Bars with different letters are significantly different ($p < 0.05$). From Gorinstein et al (2000).

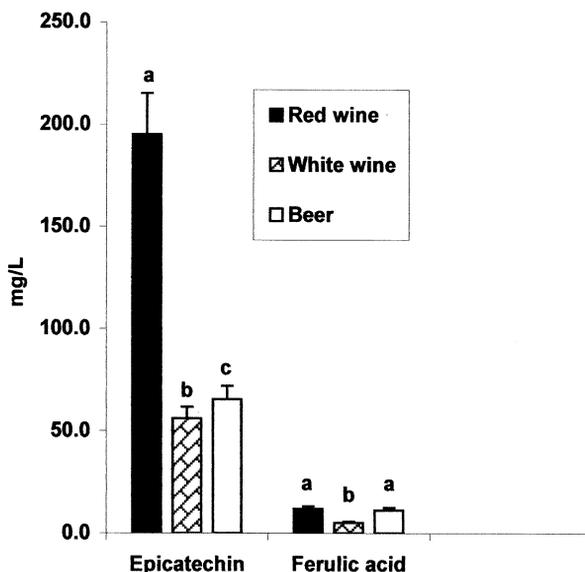


Fig. 2. Content of epicatechin and ferulic acid in three alcoholic beverages. Means \pm SD (vertical lines). Bars with different letters are significantly different ($p < 0.05$). From Gorinstein et al (2000).

lesterol (TC), LDL-C, triglycerides, lipid peroxides and elevating HDL-C/TC ratio. There were no significant differences in the results of the experiments performed on groups of rats fed basal diet supplemented with original or lyophilized wine and beer [35,36]. Similar results were obtained in investigations on humans. Serafini et al. [48] demonstrated that alcohol free red wine enhances plasma antioxidant capacity. Also Carbonneau et al. [49] observed an improvement in antioxidant status of plasma and in LDL-C after consumption of phenolic mixture of red wine. These experiments on laboratory animals and humans underline the probable role of phenolics in alcoholic beverages.

Phenolic compounds of alcoholic beverages protect serum LDL-C against atherogenic modification [46]. Therefore, it could be concluded that the choice of alcoholic beverage must be based on their phenolic content [53]. This postulate may be wrong [35]. Among three alcoholic beverages (red wine, white wine and beer) the highest content of total polyphenols is in red wine and the lowest—in beer (Figure 1) and this difference is significant ($p < 0.0025$) [54]. However, the influence of diet, supplemented with beer on lipid metabolism and antioxidant activity is higher than of diets supplemented with white wine [35]. The contents of epicatechin and ferulic acid (Figure 2) are significantly higher in beer than in white wine ($p < 0.05$ and $p < 0.0025$, respectively) [54]. Therefore, not only the level of total polyphenols is important, but also the contents of some essential phenolics. The high content of the above-mentioned phenolics is the most plausible explanation of the higher biological activity of beer versus white wine. This suggestion was later supported by the findings of Paganga et al. [55]. It was found that the antioxidant activities of 1 glass of red wine (150ml) are equivalent to 12 glasses of white wine and only to 3.5 glasses of beer (500ml).

According to the majority of the reviewed studies, it can be concluded that the main

biologically active components of alcoholic beverage are phenolic compounds. Both the total polyphenol content and the phenolic composition are important. Therefore, the choice of alcoholic beverage must be based on both indices.

To the rhetorical question of Klatsky and Armstrong [18] “do red wine drinkers fare best?” there is a clear-cut answer. Among alcoholic beverages red wine has the highest content of total polyphenols and the highest content of some essential phenolics. Therefore, according to above mentioned [31,43,44,46–49,55] and our own studies [35,36,54], among the alcoholic beverages red wine is the best choice for prevention of atherosclerosis.

3. Conclusion

Atherosclerosis is still one of the major cause of death in Western industrial countries. The prevailing oxidative theory of the development of atherosclerosis states that only rich in cholesterol oxidized LDL particles are able to penetrate arterial walls. There is an inverse relation between moderate consumption of alcoholic beverages and risk of atherosclerosis. The cardioprotective effect of alcoholic beverages is related to antioxidant activity of their components, first of all phenolics, which prevent oxidation of LDL-C. Among alcoholic beverages red wine is the best choice for prevention of atherosclerosis. Consumption of alcohol beverages negatively influences protein metabolism and there is a need for further investigations.

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