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Wine health properties

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Abstract
Introduction: Wine is worldwide known drink with a long history. It is popular in many cultures and diets. It is a component of Mediterranean diet, which is an example of healthy eating. Red wine seems to be an essential component of the diet, since moderate consumption of wine is associated with lower risk and mortality from cardiovascular disease.
The aim of the study: The purpose of this systemic review was to collect and analyse available data about health properties of wine.
Material and method: Standard criteria were used to review the literature data. The search of articles in the PubMed database was carried out using the following keywords: wine, alcohol, cardiovascular, polyphenols.
Description of the state of knowledge: Pro-health properties of alcohol depends mainly on the content of polyphenols. The most biologically active polyphenol is resveratrol. Light drinking of wine has multiple beneficial effects. It decreases level of total plasma cholesterol, low-density lipoprotein and increases high-density lipoprotein, lowers blood fibrinogen, thromboxane A, platelet stickiness, reducing insulin resistance, inhibits inflammation, improves endothelial function, fibrinolysis and increases plasma concentration of atrial natriuretic peptide. In addition it may have neuroprotective effect and beneficial effect on gut microbiota.
Summary: Moderate wine consumption can be beneficial for our health, may protect against cardiovascular disease, atherosclerosis, hypertension, certain types of cancer, type 2 diabetes, neurological disorders and metabolic syndrome. Nevertheless, any amount of alcohol consumed can lead to alcohol addiction and there is a very thin line between drinking small amounts and abuse. Furthermore, there are studies indicating that small amounts of alcohol can also have a negative impact on health. This subject still needs more studies and clinical trials.

Keywords: wine, polyphenols, alcohol

1. Introduction

Red wine is a worldwide known drink with a long history since it was popular even in ancient times [1]. Wine can be found in many cultures, but especially in Mediterranean diet [2]. Low to moderate red wine consumption can be beneficial for our health since it is associated with lower mortality from cardiovascular and cerebrovascular disease [3]. However, it is very important to emphasize that it only applies to light drinking. It is well known that alcohol can have many negative and serious health effects. Harmful use of alcohol is responsible for 5.9% of all deaths, and 5.1% of the global burden of disease [4]. Nevertheless, the French paradox exists and is associated with a daily glass of wine [5]. Red wine seems to have some positive effects, so the aim of this article is to discuss how it can influence our health.

2. Polyphenols

Red wine is known as a source of phenolics since it contains 10-fold more phenolic compounds than white wine [6]. For white wines the concentration of polyphenol content is around 50-400 mg/L, while for red wines it is 900-1400 mg/L. The differences in concentration appear due to differences in enological practices and regarding grape like variety, soil and climate. Red wine phenolics can be divided into two major groups: flavonoids (flavan-3-ols, the flavonols, and the anthocyanins) and non-flavonoids (hydroxycinnamates, hydroxybenzoates and the stilbenes) [7,8]. The benefits of red wine are studied since the discovery of the French paradox [9], which is low rates of coronary heart disease and low risk of cardiac mortality in the French populace despite of high intakes of dietary cholesterol and saturated fat [10]. These phenolics reduce low-density lipoprotein

(LDL) cholesterol oxidation and reduce platelet aggregation which contribute to lower risk of coronary diseases [11]. Both long-term abuse of alcohol and binge drinking are associated with atrial fibrillation. However, this relationship is not that certain with light and moderate drinking [9]. Studies show that light-to-moderate alcohol consumers have an increased survival compared to abstainers [11]. All the benefits are associated with flavonoids that are polyphenolic compounds. It is commonly known that high intake of fruits and vegetables is beneficial for our health [12,13].One of the reasons is high content of flavonoids in these foods [13].

Flavonols are a diverse family of monomeric (catechin, epicatechin), oligomeric and polymeric (proanthocyanidins, also called condensed tannins) chemical compounds. The astringency, bitterness, and structure of wines depend on catechin and epicatechin which can be found in skin and seeds of grape [6]. Anthocyanins are pigments found in plants, flowers and fruits [7]. Tannins may be divided into two groups: hydrolysable tannins and condensed tannins (also named catechin tannins or proanthocyanidins) [14]. Many studies show the beneficial effects on health of tannins mostly due to its antioxidant properties and, thus, could help in the prevention of inflammation disorders, cardiovascular diseases, or have protective effects to lower the risk of various cancers [14,15]. Another compound is resveratrol that is responsible for multiple biological effects. However, the way of action of resveratrol is not fully known yet [16]. The variety of molecular targets of resveratrol seems to be the key of its mechanism of action [16,17]. Studies showed that resveratrol has beneficial effect on cardiovascular system [18,19,20], cancer treatment [21,22], has antioxidant and immunomodulatory effects for some autoimmune diseases [23], anti-diabetic effects [24] and neuroprotective activity [25].

3. Wine and cardiovascular health

Drinking wine definitely has an impact on functioning of the cardiovascular system. Moderate wine intake reduces cardiovascular risk [26]. It decreases level of total plasma cholesterol, low-density lipoprotein (LDL) and increases high-density lipoprotein [11]. It also causes less LDL oxidation, which in vessel wall promotes atherosclerosis [27]. In addition to the positive effects on cholesterol, the wine has many other positive effects. It lowers blood fibrinogen, thromboxane A, platelet stickiness. This effects decrease clot formation in atherosclerotic blood vessels [27]. It lowers the risk of type 2 diabetes mellitus, probably by reducing insulin resistance, inhibits inflammation, improves endothelial function, fibrinolysis and increases plasma concentration of atrial natriuretic peptide [28,29,30]. Wine contains resveratrol(3,5,4'-trihydroxy-trans-stilbene) – one of the most biologically active polyphenols [26].It lowers production of reactive oxygen species (ROS) , because it inhibits NADPH-oxidase by down-regulating its expression and activity [31]. ROS cause oxidative stress and contribute do development of cardiovascular disease, such as ischemic heart disease, hypertension, cardiac hypertrophy, atherosclerosisand congestive heart failure [26]. Literature reports that resveratrol may have anti-arrhythmic effects and may act as inhibitor of both intracellular calcium release and pathological signaling cascades in atrial fibrillation [9]. There are several preclinical studies on animal models that show protective effect of resveratrol on cardiovascular disease, such as hypertension, hypercholesterolemia, ischaemic heart disease, diabetes and atherosclerosis [32,33,34,35,36]. Moderate wine drinking may decrease psychological stress, which is a possible coronary artery disease risk factor. All of these effects are related to “light” drinking, which is defining as less than 3 standard drinks per day, heavy drinking(≥ 3 standard drinks per day)can be catastrophic in terms of cardiovascular health [27]. On the other hand alcohol abuse has undoubtedly negative effects including alcohol dependence syndrome, liver cirrhosis, alcoholic cardiomyopathy, systemic hypertension, hemorrhagic stroke, heart rhythm disturbances, encephalopathies, polyneuropathy, dementia [27,37].

The epidemiological data indicate that light drinking has a beneficial effect on health [4]. One meta-analysis shows that drinking wine has a protective effect against cardiovascular risk and reduces total mortality, which is probably associated with the presence of high concentrations of polyphenols in wine. We do not observe this effects in drinking spirits, due to the lowest polyphenolic concentration [26,38]. Two studies show that low and moderate wine drinking, decrease mortality of coronary artery disease [39,40]. Nevertheless, one study of 32 826 women enrolled in the Nurses Health Study followed up from 1990 to 1998 and 18 225 men enrolled in the Health Professionals Follow-Up Study followed up from 1994 to 2000 and second prospective study among 85,709 women, 34 to 59 years of age show no differences in health benefits between moderate drinking of any types of drink [41,42].

4. Wine and cancer prevention

Ethanol is classified by International Agency for Research on Cancer (IARC) as carcinogenic to humans. Its carcinogenic effect depends on the amount of alcohol consumed and increases with increasing consumption of ethanol. Epidemiological data are hard to analyze due to the presence of other risk factors for cancer such as smoking, diet, family history or hormone-replacement therapy [11].Available data is still inconclusive in terms of low alcohol intake and reduced risk of cancer. There is evidence that wince consumption decreases the risk of cancer of upper digestive tract, lung, colon, basal cell carcinoma, non-Hodgkin lymphoma and prostate [43,44]. The protective effect of moderate wine consumption on cancer may be mainly attributed to polyphenols [43]. As with cardiovascular disease, resveratrol seems to have the greatest importance. Studies show that “light” drinking of wine may reduce the risk of developing lung cancer [45]. A study on female with non-Hodgkin's lymphoma showed that moderate wine intake increased 5-year survival to 75% from 69% in abstainers [46]. However, excessive alcohol consumption increases the risk of death of people with non-Hodgkin lymphoma compared to abstainers [47]. Drinking about 1 glass of wine per day decreases the risk of developing Barrett’s esophagus, compared to heavy-drinkers and abstainers [48].There are several mechanisms in which resveratrol inhibits promotion and progression of the cancer process. This mechanisms are inhibition of cytochrome P450 enzymes, antioxidant, anti-inflammatory activities, and effects on cell cycle, cellproliferation and apoptosis [43]. Anti-tumor initiation activity of resveratrol is based on its antioxidant properties. Oxidative stress plays a dominant part in the causation of carcinogenesis [21]. Studies conducted in vitro have discovered that resveratrol exerts an anti-proliferative activity by inducing apoptosis [49]. It also modulates signal transduction, immune response, transcription factors, growth factors, cytokines, caspases, interleukins, prostaglandin synthesis and cell cycle-regulating proteins [11].Experimental studies show its anticarcinogenic properties [50]. It should be remembered that moderate drinking of alcohol has many disadvantages. There are reports that even light or moderate alcohol consumption can contribute to development of breast cancer, which is caused by increased levels of estrogen and the production of reactive oxygen species during alcohol metabolism [51,52]. Another study also shows that alcohol consumption increases the risk of breast cancer in post-menopausal women [53].

5. Wine and diabetes mellitus type 2

Type 2-diabetes mellitus is affected mainly by lifestyle. The aim of therapy for diabetes is to keep the blood glucose level at optimum level. One of the therapeutic goals is inhibition of α-glucosidase [7]. Several studies show that red wine contains compounds that show strong inhibitory effect on α-glucosidase and α-amylase. α-glucosidase catalyzes the disaccharides distribution and α-amylase breaks down long-chain carbohydrates [54]. These effects may contribute to better control of postprandial glycemia. Wine flavonoids also inhibit glucose absorption in the intestine by sodium-dependent glucose transporter 1 (SGLT1). It stimulates insulin secretion and reduces hepatic glucose output [7].Flavonoids can also activate AMP-

activated protein kinase (AMPK). AMPK activation modulates glucose and fatty acid metabolism, mitochondrial function, endoplasmic reticulum stress, autophagy, and apoptosis. In study on type 2 diabetic mice the AMPK activation was often accompanied by the up-regulation of glucose transporter 4 (GLUT4) in skeletal muscle and the down-regulation of gluconeogenesis in the liver. This mechanism improves insulin sensitivity in the skeletal muscle and liver [55,56].

6. Neuroprotection

Neurodegenerative diseases, like Alzheimer's disease or Parkinson's disease, are mostly age-dependent disorders [57]. It is believed that onset of those diseases and subsequently neuronal death appears before first symptoms can be noticed. That means we do not know when was the beginning of the disease nor how late the treatment started. Moreover, there is not enough information about how to prevent neurodegenerative diseases [58]. A study of Parkinson's disease showed that intake of dietary antioxidants was associated with a lower risk of Parkinson's disease [59]. A concept of wine-related compounds having neuroprotective and neurorescue effects starts to be accepted. Not only because of antioxidant activities of those compounds, but also via suppressing neuroinflammation, modulating signalling pathways, decreasing mitochondrial dysfunction and anti-aggregating properties [60]. Resveratrol shows antioxidant and anti-inflammatory effects, but the problematic issue is poor absorption of resveratrol [61]. Another study also indicates resveratrol as a potetnial substance in Alzheimer's disease treatment due to its multiple mechanisms in neuroprotection [62]. Wine polyphenols seems to be potentially neuroprotective agents, however, more clinical trials on this subject are needed [63].

7. Microbiota

Microbiota is as name for microorganisms that can be found on a given habitat. Large intestine is a place where bacterial density reach 10^{11}–10^{12} bacteria per gram [64]. The composition of gut microbiota is changing throughout life especially during development and diet is one of the influencing factors [65]. The bioavailability of polyphenols is very low, so the vast majority of them persist into the colon [66,67]. Polyphenols may be considered as a potential substance in preventing or treating inflammatory gut disorders due to their antioxidant properties [68]. Polyphenols after intestinal transformations, firstly because of digestive enzymes and then due to the action of microbiota, may show strong antiviral, antibacterial, and antiparasitic activities [69]. However, these effects are not the only benefits of polyphenols, since there is a new concept of polyphenols as potential prebiotic candidates [66]. The meaning of the word ‘probiotic’ is ‘for live’ in greek, but another, more specific definition is that it is “a nondigestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon” [70]. Studies showed that two of the wine phenolic compounds are able to promote the growth of beneficial bacteria and the inhibition of pathogenic bacteria [71]. One of the studies which was a randomized, crossover, and controlled trial compared changes in micobiota of the participants who were asked to drink red wine, de-alcoholised red wine and gin for a specific period of time. Study showed significant changes in the fecal microbiota of all the participants depending on the kind of beverage consumed [72]. An increase of Bacteroides and Clostridium frequencies and a disappearance of Prevotellaceae were noticed after the period of ethanol (gin) consumption. The other thing is that the diversity of the fecal microbiota was higher after the red wine period. Phenolic compounds of red wine caused increase in the concentration of Firmicutes and Bacteroidetes, Enterococcus, Prevotella,Bifidobacterium, Bacteroidesuniformis, Eggerthellalenta, and Blautiacoccoides–Eubacterium rectal. At the same time, there were no significant changes in Lactobacillus species concentration. These results showed that small ethanol doses plus polyphenol intake for a short time can modulate the composition of gut microbiota [72]. Another study

indicating that flavanols are able to influence the growth of specific large-intestinal bacteria showed this ability of monomers catechin and epicatechin. Both of them, but in particular catechin is responsible of the growth of C. coccoides–Eubacterium recital, which is a group of bacteria linked to the positive effects at the cellular and systemic level. Moreover, an increase of bifidobacteria was also noticed after catechin exposure, and this bacterial group present an ability to inhibit the growth of pathogenic micro-organisms [73]. It has been suggested the consumption of red wine increased the diversity of microbiota [74].

8. Summary

All the protective effects on cardiovascular system, cancer prevention, type 2-diabetes mellitus, neuroprotection and microbiota composition that seem to come from red wine consumption are associated with the phenols contained in it. That means that moderate wine consumption that is a part of Mediterranean diet can be beneficial for our health. Nevertheless, any amount of alcohol consumed can lead to alcohol addiction and there is a very thin line between drinking small amounts and abuse. Furthermore, there are studies indicating that small amounts of alcohol can also have a negative impact on health. This subject still needs more studies and clinical trials.

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