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Red wine benefits and side effects: a Review

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Abstract Various studies indicate that a moderate and regular red wine consumption is associated with human health benefits. Clinical and experimental data have highlighted that red wine may protect against cardiovascular diseases, atherosclerosis, certain types of cancer, type 2 diabetes, neurological disorders, age-related macular degeneration and have positive effects on lung function or aging. One of the components of red wine, resveratrol is known and proven by numerous studies that have antioxidant properties. Red wine contains, however, antioxidants more powerful than resveratrol, like quercetin, cathechins and epicatechins. Research has proved that quercetin has antihypertensive effect with protection against LDL cholesterol oxidation and promotes balanced blood pressure and the ability to inhibit platelet aggregation. The nature of wine protective constituents is unclear and their action is incompletely understood. It seems that bioactive compounds are benefic due to their antioxidant, lipid regulating, and anti-inflammatory effects. Despite many beneficial effects of red wine, questions about moderate alcohol consumption remain.

Key words

red wine, antioxidants, polyphenols, resveratrol, quercetin, cancer, catechin, epicatechin

Scholars of the ancient world, Plinius, Paracelsus or Galenus, mentioned the potential beneficial effect of red wine. Father of the medicine - Hippocrates, suggest the use of red wine as a tranquilizer, diuretic and analgesic but also for treating wounds or disinfection of gastrointestinal mucosa, advice given also by Cesar to the Roman soldiers [2]. Red wine is made from dark-coloured (black) grape varieties. The colour of the wine can range from intense violet, in young wines, through to brick red for mature wines or brown for older red wines. Juice from fresh red or black grapes is greenish-white. Longer the skins of the grapes are kept in contact with the juice while making the wine, the darker and more intense the color of the wine becomes. The red colour comes from anthocyan pigments (also called anthocyanins) present in the skin of the grape [13]. The opacity of a wine tells what kind of grape was used to make the wine and it can also tell the age of a wine. Blue marks at the edge of the glass indicate a higher pH. Among beverages (water, tea, beer, wine, coffee, juices, milk), red wine is the only one whose organoleptic properties improve with time and this is called ageing [5]. Normally, anthocyanins are mainly located in the grape skins, with exceptions of "teinturier" grapes, which have anthocyanins in both of the skin and the pulp [2]. Tannins of the wine contain some flavonoid polyphenols. Unlike other drinks, a moderate consumption of red wine can: prevent the breast cancer because polyphenols reduce the estrogen level and increase the testosterone in premenopausal women; prevent dementia because resveratrol can scavenge the platelets and therefore maintain the blood vessels open and flexible for a good circulation to the brain. Neafsey and Collins (2011) [24] from the Department of Molecular Pharmacology and Therapeutics Loyola University Chicago, specified that "moderate red wine drinkers had a 23% lower risk of developing dementia compared to people who rarely or never consumed the alcoholic beverage"); prevent blinding diseases through resveratrol that can stop the blood vessel growth in the eye; red wine may protect the brain from stroke damage, due to the resveratrol action which increases the level of the enzyme heme oxygenase, responsible for protection of nerve cells in the brain and increase the brain resistance to ischemic stroke [14]; improving lung function and preventing lung cancer specially in smokers [9]; protect from prostate cancer due to the action of flavonoids and resveratrol which act as an estrogen, counterbalance androgens, reducing levels of testosterone that stimulate the prostate [18]; resveratrol, quercetin, cathechines and anthocyanins improve sensitivity to insulin, inhibit hyperglycemia, improve beta-cell function preventing type 2 diabetes [35].

Resveratrol in red wines

Resveratrol (trans-3, 5, 4'-trihydroxystilbene) is a phytoalexin produced naturally by several plants - including skin of red grapes. Phytoalexins are

antibiotics produced by plants when under attack by pathogens such as bacteria or fungi (Botrytis cinerea). Vine grapes grown in cooler climates have higher resveratrol levels than those from warmer climes. Level of resveratrol in wine and wine-products, varies from a region to another and from one year to year. The richest red wines in polyphenols and resveratrol respectively are obtained from grape varieties Pinot Noir, Syrah, Cabernet Sauvignon, Cabernet Franc, and Merlot [22]. Resveratrol might be a key ingredient in red wine that helps prevent damage to blood vessels, reduces low-density lipoprotein (LDL) cholesterol (the "bad" cholesterol) and prevents blood clots. Several studies reported that resveratrol can have a protective role in myocardial ischemia reperfusion injury [25].

Resveratrol cardiovascular effects

Drinking red wine, as reported by many studies, is considered healthy and may reduce the occurrence of coronary heart diseases, diabetes mellitus and neurodegenerative disorders [28]. Emphasis the beneficial cardiovascular effects are often associated with “French paradox”, which refers to foods high in fat and at the same time, reduced incidence of cardiovascular disease, knowing the French people preference for red wine [30]. One of the components of red wine, resveratrol is known and proven by numerous studies that have antioxidant properties. Having high hydrophilic and lipolytic properties is considered a best protective antioxidant than C and E vitamins [12]. Red wine contains, however, antioxidants more powerful than resveratrol, like quercetin and epicatechin [6]. Resveratrol can be regarded as preventive agent in fight against atherosclerosis in individuals considered lower risk for this condition [1]. As evidenced by medical studies, beneficial cardiovascular effects of red wine are due to release of NO in vessel walls of the circulatory system, with a vasodilator potential, of the anti-inflammatory action, and antioxidant effect. On the other hand though there must be a balance of consumption in order not to skid towards excessive alcohol consumption associated with liver disease as cirrhosis, or cancer [2]. Red wine consumption is associated with HDL, fibrinolysis (breakdown of a clot) and antioxidant activity increasing, and in the same time with the reduction of myocardial ischemic reperfusion injury the molecule involved in blood pressure regulation - endothelin-1 and to the decreasing of platelet aggregation (clumping) [21].

Resveratrol cancer - related effects

Many studies qualified resveratrol found in grape skins and red wine, with the potential of cancer cells restriction and initiation of apoptosis (cancer cell death), making it potentially useful in prevention and treatment [10]. Research concerning health benefits of red wine are only at the beginning, and its content in resveratrol is relatively small compared to the experimentally amount proven to be necessary for health benefits, but recent studies have revealed that even small amounts of resveratrol helps to health improvement [31]. In vitro studies have shown that resveratrol has multiple anti-cancer effects, and can act as an antioxidant to prevent DNA damage that can lead to tumor formation. This natural compound has the ability to decrease DNA binding activity of a transcription factor (nuclear factor κB (NF-κB)), which is upregulated in cancers and influence the transcriptions of genes implicated in tumors growth [26]. Results of the studies made by Carter and al (2014) [7], shows that resveratrol and other components from grapes could possible be used to decrease the risk of developing colon cancer, but is less efficient against already established colon cancer. There are limited clinical trials data concerning resveratrol use as an option for cancer prevention and therapy, therefore, much more human research are needed [7].

Resveratrol anti-aging effect

Some researchers believe that resveratrol can activate SIRT 1 gene that is responsible for organism protection against obesity and diseases of aging. The opinion of the most scientists is that a glass of red wine per day is associated with health benefits and a lower risk to develop coronary heart disease. Polyphenols molecules from red wine, like resveratrol or quercetin, behave like antioxidants and radical scavengers helping to prevent heart diseases by lowering LDL and increasing HDL levels of cholesterol [6]. Resveratrol and quercetin are single molecular entities, not essential nutrients. The most intriguing question is what doses of resveratrol or quercetin may help humans to achieve the beneficial health that already have been observed in studies performed on animals. Extrapolating animal dosage to human, the recommended daily dose should be of 500 mg. To achieve this amount, a person should consume about 50 bottles of red wine a day, which is obviously impossible. Studies carried out in last decades prove that procyanidins, compounds found in red wine, keep the blood vessels healthy [11].

Quercetin in red wines

One of the most important flavonoids present in red wine is quercetin, with a more powerful antioxidant effect than the resveratrol. Research has proved that quercetin has antihypertensive effect, due to the vasodilatory exertion action on vascular smooth muscles and also has the ability to inhibit platelet aggregation [17]. Lab tests have shown that quercetin has also an antioxidant action with protection against LDL cholesterol oxidation and promotes balanced

blood pressure. In the same time, quercetin inhibit histamine release and influences intracellular enzymes and protection against stress by suppressing the enzyme necessary for cortisol release (hormone produced when body is stressed) and contributes to the relaxation of the airway smooth muscle [15]. Studies also demonstrated that quercetin improves the contractile function of the left ventricle in experimental myocardial infarction with subsequent 24-h reperfusion" [29]. Besides beneficial effects, quercetin can have possible interactions with anticoagulants, fluoroguinolones, and corticosteroids, cyclosporine or in chemotherapy [3]. Quercetin can have also side effects, like the inhibition of the enzyme (CYP3A4) involved in many common drugs metabolism [4].

Catechins and epicatechins in red wines

Catechins and epicatechins are classified as flavanols and high concentrations can be found in red wine. The catechin group of flavanols are major components in wine and are reported to have antioxidant, antimicrobial, antimutagenic and anticarcinogenic activities. Catechins are the most powerful antioxidants associated with several beneficial effects like increasing the ability of plasma to scavenge free radicals, blood vessel dilation, fat oxidation and reducing of LDL [34]. Catechins have the properties to destroy free radicals. In addition catechins have anti-bacterial action (sterilizing effect), reduce the risk of heart disease (stopping the platelets from forming clots, lowering blood pressure, cholesterol levels, and reducing stress) [23]. The highest concentration of catechins and epicatechins is found in Pinot Noir red wine [19].

Red wine side effects

There are many positive health benefits assigned to the moderate consumption of red wine but more than the recommended amount increase the risk of heart disease, hypertension, stroke, depressive disorders, neuro-degeneration, osteoporosis or obesity [27]. There are contraindications for consumption of red wine for patients with liver disease, pregnant women or children. Having vasodilating properties red wine could interact with antihypertensive medications [33]. Too much red wine consumption can lead to liver cirrhosis, cardiovascular disorders such as alcoholic cardiomyopathy, high blood pressure, the onset of acute or chronic pancreatitis, sleeping and neurological disorders, physical and mental health impairment and not ultimately to alcoholism developing [32]. Because during the vegetation period in vine are applied many treatments, some contaminants including pesticides and fungicide residues can reach into wine [8]. After long term consumption, toxic levels of lead, nickel, chromium and vanadium is likely to accumulate in the body [20].

Conclusions

There is a lot of evidence about moderate and regular consumption of red wine on health benefits, especially of polyphenols. Red wine compounds increase HDL level and reduce the bad cholesterol (LDL). Polyphenols provide cardioptotection, neuroprotection and act as antioxidants and chemopreventive agents. The healthiest wines are those rich in tannic and procyanidin like Pinot Noir, Shirah, Cabernet Sauvignon, Cabernet Franc and Merlot. Antioxidants more powerful than resveratrol found in red wine are catechins and epicatechins. Red wine has health benefits if the consumption is regular and moderate. However, the mechanism action in the body of the polyphenols from red wine and the necessary amount for health benefit are largely unknown and future research in this area will be needed.

Bibliography

1.Agarwal B., Campen M.J., Channell M.M., Wherry S.J., Varamini B., Davis J.G., Baur J.A., Smoliga J.M., 2013, Resveratrol for primary prevention of atherosclerosis: clinical trial evidence for improved gene expression in vascular endothelium, Int J Cardiol. Jun 5; 166(1):246-8. doi: 10.1016/j.ijcard.2012.09.027.
2.Böhm M., Rosenkranz St., Laufs U., 2004, Alcohol and red wine: impact on cardiovascular risk, Nephrol. Dial. Transplant. 19 (1): 11-16, doi: 10.1093/ndt/gfg340.
3.Boots A.W., Haenen G.R., Bast A., 2008, Health effects of quercetin: from antioxidant to nutraceutical. Eur J Pharmacol, 582(2-3):325-37.
4.Boots A.W., Li H., Schins R.P., Duffin R., Heemskerk J.W., Bast A., Haenen G.R., 2007, The quercetin paradox. Toxicol Appl Pharmacol, 222(1):89-96.
5.Brouillard R., Chassaing S., Fougerousse A., 2003, Why are grape/fresh wine anthocyanins so simple and why is it that red wine color lasts so long? Phytochemistry. Dec;64(7):1179-86.
6.Brouillard R., George F., Fougerousse A., 1997, Polyphenols produced during red wine ageing. Biofactors 6(4):403-10.
7.Carter L.G., D'Orazio J.A, Pearson K.J., 2014, Resveratrol and cancer: focus on in vivo evidence, Endocrine Related Cancer, 21(3): R209–R225.
8.Cesnik H.B., Gregorcic A., Cus F., 2008, Pesticide residues in grapes from vineyards included in integrated pest management in Slovenia. Food Addit. Contam. Part A Chem. Anal. Control Expo. Risk Assess. 25:438-443.
9.Chao C., 2011, 2007, Associations between Beer, Wine, and Liquor Consumption and Lung Cancer Risk: A Meta-analysis, Cancer Epidemiol Biomarkers and Prevention, November 16; 2436, pp. 471-486, doi: 10.1158/1055-9965.EPI-07-0386.

10.Clement MV, Hirpara JL, Chawdhury SH, Pervaiz S., 1998, Chemopreventive agent resveratrol, a natural product derived from grapes, triggers CD95 signaling-dependent apoptosis in human tumor cells. Blood. 92:996–1002.
11.Das D.K., Mukherjee S., Ray D., 2010, Resveratrol and red wine, healthy heart and longevity. Heart Fail Rev. 2010 Sep;15(5):467-77. doi: 10.1007/s10741-010-9163-9.
12.Dell'Agli M., Busciala Alessandra, Bosisio Enrica, 2004, Vascular effects of wine polyphenols, Cardiovascular Research 63 593– 602.
13.Dobrei A., Poiană Mariana, Sala F., Alina Ghiţă, Gergen I., 2011, Changes in the chromatic properties of red wines from Vitis vinifera L.cv. Merlot and Pinot Noir during the course of aging in bottle, Food Journal of Agriculture & Environment, Helsinki, Finlanda.
14.Doré S., Sampei K., Goto S., Alkayed N.J., Guastella D., Blackshaw S., Gallagher M., Traystman R.J., Hurn P.D., Koehler R.C., Snyder S.H., 1999, Heme oxygenase-2 is neuroprotective in cerebral ischemia, Mol. Med.,5 pp.656–663.
15.Egert S., Bosy-Westphal A., Seiberl J., 2009, Quercetin reduces systolic blood pressure and plasma oxidised low-density lipoprotein concentrations in overweight subjects with a high-cardiovascular disease risk phenotype: a dboule-blinded, placebo-controlled cross-over study. Br J Nutr. 102(7):1065-74.
16.Fei He, Na-Na Liang, Lin Mu, Qiu-Hong Pan, Jun Wang, Malcolm J.Reeves, Chang-Qing Duan, 2012, Anthocyanins and Their Variation in Red Wines I. Monomeric Anthocyanins and Their Color Expression, Molecules *17*, 1571-1601; doi:10.3390/molecules17021571.
17.Formica J.V., Regelson W., 1995, Review of the biology of Quercetin and related bioflavonoids. Food Chem Toxicol. 33:1061–80.
18.Gill C., Walsh S.E., Morrissey C., Fitzpatrick J. M., Watson W. R. G., 2007, Resveratrol sensitizes androgen independent prostate cancer cells to death-receptor mediated apoptosis through multiple mechanisms Volume 67, Issue 15, 1 November 2007, Pages: 1641–1653, DOI: 10.1002/pros.20653.
19.Goldberg D.M., Karumanchiri A., Tsang E., Soleas G.J., 1998, Catechin and Epicatechin Concentrations of Red Wines: Regional and Cultivar-Related Differences, Am. J. Enol. Vitic, vol. 49 no. 1, pp. 23-34.
20.Hague, T., Petroczi A., Andrews P.L., Barker J., Naughton D.P.. 2008. Determination of metal ion content of beverages and estimation of target hazard quotients: A comparative study. Chem. Central J. 2:13. doi: 10.1186/1752-153X-1-13.
21.Heneman K., Zidenberg-Cherr S., 2008, Some facts about catechin, University of California, Agriculture and Natural Resources, http://nutrition.ucdavis.edu/content/infosheets/fact-pro-catechin.pdf.
22.Kalra N, Roy P, Prasad S, Shukla Y., 2008, Resveratrol induces apoptosis involving mitochondrial pathways in mouse skin tumorigenesis. Life Sciences, 82:348–358. doi:10.1016/j.lfs.2007.11.006.
23.Lee H.S., Widmer B.W., 1996, Phenolic compounds. In: L.M.L. Nollet, ed. Handbook of food analysis. New York, Marcel Dekker, 821-894.
24.Neafsey E.J., Collins M.A., 2011, Moderate alcohol consumption and cognitive risk, Neuropsychiatric Disease and Treatment,Volume 7, Issue 1, Pages 465—484.
25.Ray P.S., Gautam M., Gerald A., Cordisalberto A., Bertelli E., Das D.K., 1999, The red wine antioxidant resveratrol protects isolated rat hearts from ischemia reperfusion injury. Free Radical Biol Med., 27:160–9.
26.Roy P, Madan E, Kalra N, Nigam N, George J, Ray RS, Hans RK, Prasad S, Shukla Y., 2009, Resveratrol enhances ultraviolet B-induced cell death through nuclear factor-κB pathway in human epidermoid carcinoma A431 cells. Biochemical and Biophysical Research Communications. 384:215–220.
27.Saremi, A., Arora R., 2008. The cardiovascular implications of alcohol and red wine. Am. J. Ther. 15:265-277.
28.Smoliga J.M., Baur J.A., Hausenblas H.A., 2011, Resveratrol and health-a comprehensive review of human clinical trials. Mol Nutr Food Res. 2011; 55:1129–1141.
29.St. John Sutton M.G., Sharpe N., 2000, Left ventricular remodeling after myocardial infarction pathophysiology and therapy, Circulation, 101: 2981-2988, doi: 10.1161/01.CIR.101.25.2981
30.Szmitko P. E., Verma S., 2005, Red Wine and Your Heart, Circulation, 111: e10-e11, doi: 10.1161/01.CIR.
31.Tome-Carneiro J, Larrosa M, Gonzalez-Sarrias A, Tomas-Barberan FA, Garcia-Conesa MT, Espin JC., 2013, Resveratrol and clinical trials: the crossroad from in vitro studies to human evidence. Current Pharmaceutical Design. 19:6064–6093.
32.Walzem R.L. 2008. Wine and health: State of proofs and research needs. Inflammopharmacology 16:265-271.
33.Ward N.C., Hodgson J.M., Croft K.D., Burke V., Beilin L.J., Puddey I.B., 2005, The combination of vitamin C and grape-seed polyphenols increases blood pressure: A randomized, double-blind, placebo-controlled trial. J. Hypertens. 23:427-434.
34.Williamson G, Manach C., 2005, Bioavailability and bioefficacy of polyphenols in humans. II. Review of 93 intervention studies. American Journal of Clinic Nutrition. 81:243S-255S.
35.Zunino S., 2009, Type 2 diabetes and glycemic response to grapes or grape products. J. of Nutrition 139:1794S-1800S.