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# Biomedical Effects of Grape Products

*Jamilah M. Hashemi*

Department of Food and Nutrition, King Abdulaziz University, Jeddah, Saudi Arabia

**Abstract:** Studies have shown a reverse relationship between regular consumption of fruits and vegetables and the risk of developing certain diseases. This relationship is due to the phytochemical components found in plant products and their biological effects on human health. Phenolic compounds isolated from grapes include catechins, epicatechin, procyanidin and some dimers and trimers. In this review, we briefly examine the potential of grape phenolic compounds in disease prevention. Evidence was shown to support the positive impact of different grape phenolic compounds such as EGCG and anthocyanin, on human health and disease prevention.

**Key words:** Disease prevention · Antioxidants · Phenolic compounds · EGCG · Grapes

## INTRODUCTION

A grape is a fruiting berry of the deciduous woody vines of the botanical genus *Vitis*. Grapes can be eaten raw or they can be used for making jam, juice, grape seed extract, raisins, vinegar and grape seed oil [1]. They are native to Asia near the Caspian Sea, but they were brought to North America and Europe. This plant's climbing vine has large, jagged leaves and its stem bark tends to peel. The grapes may be green, red, or purple [2]. Grapes are known for their high phytochemicals content. The term “phytochemicals” refers to a wide variety of compounds made by plants, but is mainly used to describe those compounds that may affect human health. Phytochemicals are found in plant-based foods such as fruits, vegetables, beans and grains. Scientists have identified thousands of phytochemicals, although only small fractions have been studied closely [3]. The active compounds from grape extracts, which include the grape seed, grape skin and grape juice, that have been identified thus far include polyphenols such as resveratrol, phenolic acids, anthocyanins and flavonoids. All possess potent antioxidant properties and have been shown to decrease low-density lipoprotein-cholesterol oxidation and platelet aggregation. These compounds also possess a range of additional cardioprotective actions. Antioxidant properties of grape polyphenols are likely to be central to their mechanism(s) of action [4].

**Grape Polyphenols Antioxidant Effects:** Free radicals derived from oxygen, nitrogen and sulfur molecules in the biological system are highly active to react with other molecules due to their unpaired electrons. These radicals are important part of groups of molecules called reactive oxygen/nitrogen species (ROS/RNS), which are produced during cellular metabolism and functional activities and have important roles in cell signaling, apoptosis, gene expression and ion transportation. However, excessive ROS attack bases in nucleic acids, amino acid side chains in proteins and double bonds in unsaturated fatty acids and cause oxidative stress, which can damage DNA, RNA, proteins and lipids resulting in an increased risk for cardiovascular disease, cancer, autism and other diseases. Intracellular antioxidant enzymes and intake of dietary antioxidants may help to maintain an adequate antioxidant status in the body [5]. In a study, examining Oxygen free radical scavenger capacity in aqueous models of procyanidins from grape seeds [6], Epicatechin 3-O-gallate (EGCG) was found to be an effective compound in trapping oxygen free radicals. Later, in 1994, the antioxidative activity of four anthocyanins isolated from the Muscat bailey grape was evaluated according to the amount of malonaldehyde formed by the autoxidation of linoleic acid in Trizma buffer. Hirotoshi and Yamagami [7] found that the monoacylated anthocyanins from the grapes can be used as powerful antioxidants and colorants. Also, in a study by Durak *et al.* [8] the possible

**Corresponding Author:** Jamilah M. Hashemi, Department of Food and Nutrition, King Abdulaziz University, Jeddah, Saudi Arabia.

contribution of black grape ingestion on plasma antioxidant status was investigated. Results suggested that black grape strengthens plasma AOP as does red wine. This result also support the hypothesis that the protective effect of red wine against cellular peroxidation reactions and atherogenesis mainly arises from its flavonoid constituents. Extensive research suggests that grape seed extract is beneficial in many areas of health because of its antioxidant effect to bond with collagen, promoting youthful skin, cell health, elasticity and flexibility [9]. Other studies have shown that proanthocyanidins help to protect the body from sun damage, to improve vision, to improve flexibility in joints, arteries and body tissues such as the heart and to improve blood circulation by strengthening capillaries, arteries and veins [9].

**Grape Seed Effects on Total Lipids:** The effects of monomeric and polymeric grape seed tannins on rat plasma lipoproteins, lipoprotein lipase, hepatic lipase and aortic and hepatic lipid concentration were studied. Tebib *et al.* [10] reported that dietary grape seed tannins was pronounced to have anti-hypercholesterolemic effect by enhancing reverse cholesterol transport and by reducing intestinal cholesterol absorption and increasing bile acid excretion. Also, Rouanet *et al.* [11] investigated the effects of dietary monomeric and polymeric grape seed tannins on the antioxidant activity, total glutathione and level of lipid peroxidation. The lipid peroxidation in plasma and tissues was significantly reduced in the presence of supplemented polymeric tannins as much as in the presence of vitamin E. It is therefore likely that polymeric grape seed tannins function as antioxidants *in vivo*, negating the effects of the oxidative stress induced by both vitamin E deficiency and atherogenic diet. The cholesterol lowering effect of a dietary fiber and polyphenols rich product (DFPP) was evaluated in normo-and hypercholesterolemic rats by Martín-Carrón *et al.* [12]. In hypercholesterolemic rats, serum total cholesterol and LDL-cholesterol concentrations were significantly lower in the DFPP-supplemented group than in the unsupplemented group. These results indicate that the DFPP reduce serum total cholesterol and LDL-cholesterol, as well as the atherogenic index, in hypercholesterolemic rats. Charradi *et al.* [13] studied the gender dependency of fat-induced oxidative stress in the heart and liver, with a special emphasis on the distribution of transition metals, as well as the protective effects of grape seed and skin extract (GSSE). Results showed that, high fat diet treatment altered transition metal homeostasis more drastically in the male heart than in the female liver and grape seed and skin extract efficiently protected these organs against fat-induced disturbances, regardless of gender.

**Grapes and Cancer:** In 1985, the effect of ellagic acid on hepatic and pulmonary xenobiotic metabolism in mice was studied for its anticarcinogenic action, results indicate that both acute and chronic administration of ellagic acid inhibits BP metabolism and/or enhances glutathione S-transferase activity. Thus the modulation of polycyclic aromatic hydrocarbon metabolism by ellagic acid may be related to the anticarcinogenic effects of this compound [14]. In another study, the effect of skin application of grape polyphenolic fraction (GP) to SENCAR mice on 12-O-tetradecanoylphorbol-13-acetate (TPA) and other skin tumor promoter-caused induction of epidermal ornithine decarboxylase (ODC) activity were studied; the results showed GP, specifically its epicatechin derivative (EGCG), could provide anti-tumor-promoting effects against a wide spectrum of skin tumor promoters [15]. The second leading cause of cancer-related deaths in the United States is colorectal cancer. Failure of anti-cancer therapy in colorectal cancer cells involves resistance to death mechanisms. This emphasizes need to develop effective therapies for colorectal cancer patients. Anti-proliferative effect of resveratrol, a natural component of grapes, on human colonic cancer cells were also investigated, resveratrol caused a significant decrease of ornithine decarboxylase (ODC) activity, a key enzyme of polyamine biosynthesis, which is enhanced in cancer growth. ODC inhibition resulted in the reduction of the intracellular putrescine content, indicating that polyamines might represent one of several targets involved in the anti-proliferative effects of resveratrol [16]. Kaurr *et al.* [17] investigated the *in vitro* and *in vivo* anticancer effects and associated mechanisms of grape seed extract (GSE), a rich source of proanthocyanidins, against colorectal cancer. GSE (25-100 ìg/ml) caused a significant dose- and time-dependent inhibition of cell growth with concomitant increase in cell death GSE may be an effective chemopreventive agent against colorectal cancer. Grape seed extract efficacy in inhibiting colorectal cancer metastasis to lung in rats further supports its translational potential in controlling colorectal cancer growth, progression and metastasis in patients [18].

**Grapes and Cardiovascular Diseases:** In 1996, total phenolics content and antioxidant potential of commercial grape Juice were determined; results confirmed that grape juice, especially red grape juice, is a significant source of phenolic antioxidants that protect against CHD [19]. Both *in vitro* incubation and oral supplementation with PGJ decrease platelet aggregation, increase platelet-derived NO release and decrease superoxide production. These findings may be a result of antioxidant-sparing and/or direct effects of select flavonoids found in phenolic grape juice (PGJ). The suppression of platelet-mediated thrombosis represents a potential mechanism for the beneficial effects of purple grape products, independent of alcohol consumption, in cardiovascular disease [20].

**Grapes and Other Diseases:** Flavonoids and related polyphenols, in addition to their cardioprotective, anti-tumor, anti-inflammatory, anti-carcinogenic and anti-allergic activities, also possess promising anti-HIV effects. Investigations of the mechanisms underlying the anti-HIV-1 effects of grape seed extracts may help to identify promising natural products useful in the prevention and/or amelioration of HIV-1 infection [21]. Also, consumption of grape seed extract (GSE) was shown to prevent amyloid-â deposition and attenuates inflammation in brain of an alzheimer's disease Mouse. Polyphenol-rich GSE prevents the A-â deposition and attenuates the inflammation in the brain of a transgenic mouse model and this thus is promising in delaying development of AD [22]. In related study, proteomics technology, namely 2D gel electrophoresis and mass spectrometry, identified quantitative changes in specific proteins induced in adult rat brain following ingestion of a powdered preparation of GSE. In conclusion, is that GSE has neuroprotective activity. The majority of the effects on the proteins detected in this study could be described as protective against age or pathology related cognitive impairment [23].

## CONCLUSION

Although grapes have been consumed for centuries, it has only recently been studied extensively as a health-promoting that may act to prevent a number of chronic diseases and cancers. Numerous studies have indicated that grape consumption may be beneficial in reducing the plasma concentration of cholesterol and preventing atherosclerosis. Although one mechanism for cholesterol reduction may be increased expression of the LDLR. Additional mechanisms and molecular targets should be explored to elucidate the prevention of cardiovascular diseases. The cancer-preventive effects of grapes are widely supported by results from epidemiological, cell culture, animal and clinical studies. Studies showed that polyphenols potently induce apoptotic cell death and cell cycle arrest in tumor cells but not in their normal cell counterparts and that, grape polyphenols affect several biological pathways. Various animal studies have revealed that treatment with grape polyphenols inhibits tumor incidence and multiplicity in different organ sites such as skin, liver and colon. Studies focusing on the purified grapes polyphenol compound (EGCG) should continue to provide researchers an improved understanding of grapes polyphenol absorption, distribution, role in anti-cancer reactions, metabolism and anti-cancer mechanisms. On the other hand, work should continue on synthesizing and evaluating more analogs of grapes polyphenols to find more potent, stable and specific polyphenol proteasome inhibitors as novel anti-cancer agents. A major challenge of cancer prevention is to integrate new molecular findings into clinical practice. Identification of more molecular targets or biomarkers for grapes polyphenols is paramount to cancer prevention and treatment by grapes and will greatly assist in a better understanding of its anti-cancer mechanisms.

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