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Review Article

Biological and medicinal properties of grapes and their bioactive constituents: an update

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Running Head: Biological applications of grapes

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ABSTRACT

Grape is one of the most valued conventional fruits, worldwide. Though most of the parts of grapevine are useful, primarily, grape is considered as a source of unique natural products not only for the development of valuable medicines against a number of diseases but also for manufacturing variety of industrial products. Over the last few decades, apart from the chemistry of grape compounds a considerable progress has been made towards exploring the biological activities of various grape derived constituents.. Today, it is well established that in addition to food, grape is a major source of several phytochemicals. The main biologically active and well characterized constituent from grape is resveratrol which is known for various medicinal properties for in human diseases. This review is an attempt towards discussing the roles of various grape derived phytochemicals in relation to various diseases.

Key words: Grapes, Resveratrol, Phytochemicals, Biological functions

INTRODUCTION

Since the times of human civilization, medicinal plants have always remained a part and parcel of human society to combat and treat different diseases. Particularly, in Indian system of medicine such descriptions have been documented Rigveda, Charak Samhita and Sushruta Samhita. According to the estimates of World Health Organization nearly 75% of world population currently uses herbs and other traditional medicines to treat diseases of different natures.[1] Nevertheless, current scenario indicates that, the medical as well as pharmaceutical research is being carried out towards characterization and development of pant derived natural components to treat various human ailments.[2]

Grape is well recognized worldwide for over 2000 years as one among the edible sweet fruits, and recognized for wide spectrum of biological properties.[3] Its taxonomic position is- Group: Thalamifloreae, Order: Rhamnales, Family: *Vitaceae*, Genus: *Vitis,* Species: *vinifera.* Various chemical studies on the products of fruit and other parts of grape plant have been attempted, mainly, during the fifties of the 20th century. A brief sketch of chemical structures of some of the important biological active gape derived compounds has been depicted in figure 1.

GRAPE: A GOOD SOURCE OF NUTRIENTS

The grape belongs to the berry family as it is found attached to the stem. Many berries make up the cluster or bunch of grapes. Grape fruit is one of the most palatably edible food having many established nutritional and medicinal properties for consumers. Grapes are good source of carbohydrates, proteins, fats and other nutrients like boron, an important element for the bone formation and osteoporosis. Additionally, grape contains significant amount of potassium, vitamin C and A, and also has a little amount of calcium.

The essential parts of the berry include: skin, pulp, and seeds. The composition, in terms of nutrients, of grape has been summed-up in Table-1.

BIOLOGICAL ACTIVITIES OF GRAPE

Though a large number of compounds have been isolated from grape, only some of them have been found to be having biological activities described in Table-2. Particularly, resveratrol, a major compound extracted from the skin and seeds of grape, has been reported having several biological activities.

Antioxidant property

Oxidative stress is a hallmark of various health problems. Resveratrol (3,5,4'-trans-trihydroxystilbene) is a natural phytoalexin abundantly found in grapes and red wine, which has potent antioxidant property. Over the years several analogues i.e. 3,4-dihydroxy-trans-stilbene (3,4-DHS), 4,4'-dihydroxy-trans-stilbene (4,4'-DHS), 4-hydroxy-trans-stilbene (4-HS) and 3,5-dihydroxy-trans-stilbene (3,5-DHS), of resveratrol have been synthesized and have been found to have attenuating effect on free radical-induced peroxidation of rat liver microsomes.[4] Thus, all these trans-stilbene derivatives are potent antioxidants against both 2,2'-azobis(2-amidinopropane hydrochloride) (AAPH) and iron-induced peroxidation. The most potent antioxidant activity was noticed with 3,4-DHS followed by 4,4'-DHS, resveratrol, 4-HS, 3,5-DHS respectively.[4] Further, resveratrol was also reported to show strong inhibitory effect on the 2,3,7, 8-tetrachlorodibenzo-p-dioxin (TCDD)-induced aryl hydrocarbon receptor DNA binding activity as well as on the expression of CYP1A1 and CYP1B1 which are known to oxidise 17-beta-estradiol to produce catechol and estrogens. Thus, resveratrol protects the tissues from oxidative as well as catechol estrogens induced damages.[4] It is thought that antioxidative effect of

resveratrol is mediated through inhibition of NF-kappa B, or the oxidative damage mediated through the angiotensin II type 1 receptor.[5] In another attempt, the proanthocyanidin, a variant of resveratrol, isolated from grapes seed extract also exhibited antioxidant protection in smokeless tobacco (STE)-induced cellular injury, and this activity has been ascribed to be due to alteration in Bcl-2 and p53 expression in in-vitro and in-vivo system.[6]

Moreover, skin and seeds of grape are good sources of phytochemicals like gallic acid, catechin and epicatechin that are appropriate raw substrates for the production of anti-oxidative dietary supplements.[7] Anti-oxidant thio-conjugates could also be obtained from the white grape pomace.[8] Analysis of concord grape juice (CGJ) has shown that it is a rich source of flavonoids, having greater antioxidant efficacy, as seen *in vitro,* than α-tocopherol (Vit E)[9]. Further, CGJ has also been found to increase serum antioxidant capacity and thereby protective, better than α-tocopherol, against LDL oxidation in healthy adults. Thus, Byrne et al[9] concluded that, CGJ flavonoids are potent antioxidants that protects the host against oxidative stress, reduce the risk of free radical damage and onset of chronic diseases. Surprisingly, dried grape seeds, obtained after the color extraction and alcohol distillation of wine pomace, still kept considerable flavanol content with high antioxidant activity, even after exposure to high temperatures.[10] Regarding, polyphenol, diprim, is a natural polyphenol from Amur grapes crest and it has been documented to promote inhibition of lipid peroxidation and glutathione-saving effect which might be due to polyphenols in it that capture free radicals.[11] On the basis of these observations the consumption of grape fruit and/ or its constituents may be compelling therapeutic regimens to suppress oxidative stress related threats.

Anticarcinogenic activity

Cancer is the rapidly growing health problem which is a biggest challenge to researchers and medical professionals to be opted for various prevention and therapeutic strategies. Dietary intake of many vegetables and fruits including grapes has been found to reduce the risk of occurrence of cancer.[12] Resveratrol is well characterized to have anticarcinegnic effects as well as antineoplastic properties. The molecular mechanisms for these effects are supposed to be associated with mitochondrial release of cytochrome c, formation of the apoptosome complex, and caspase activation.[13]

The antiproliferative and proapoptotic effect of resveratrol in breast cancer cells are thought to be through accumulation of ceramide and phenolic moiety of stilbenoids, which is necessary to induce ceramide-associated growth inhibition.[14] The inhibitory effects of red wine polyphenolics on human breast cancer cells has been demonstrated to be due to inhibition of cell proliferation by flavonoid which in turn could be related to the inhibition of calcium and calmodulin associated phosphodiesterase activity indicating that flavonoids interfere with the function of second messenger calcium. Thus, certain grape wine ingredients that have anticancer properties may be helpful for developing functional neutraceuticals with anti-cancer properties.[15] Resveratrol treatment of MCF-7 cells at low concentrations is known to result in inhibition of the cell growth at the S-phase transition of the cell cycle. On the other hand, high concentration of resveratrol does not induce S-phase accumulation. The growth suppression by resveratrol might be due to apoptosis, which involves activation of caspase-9, decrease of Bcl-2 as well as Bcl-XL, and increase Bax levels.[16] Resveratrol has also been reported to suppress the proliferation of human prostate cancer cells with a typical apoptotic feature, interfering with the expression of HSPs70.[17] Kubota et al[18] , in their experiments with A549, EBC-1 and Lu65 lung cancer cells, found that resveratrol could inhibit (50%) the growth of cells and could enhance the

activity of paclitaxel, a chemotherapeutic agent lung cancer treatment. Based on these findings, Kubota et al[18] recommended that resveratrol could be involved in an adjuvant to anti-carcingenic therapy for lung cancer.

Aromatase is considerably expressed in breast cancer tissue as compared to that of normal tissue. Red wine extract fraction procyanidin B dimers also have good inhibitory action on aromatase activity and could play role in treating the breast cancers.[19] Epigallocatechin-3-gallate another component from grapes that has been demonstrated to possess have high anti-neoplastic potential due to its programmed cell death induction.[20] In conclusion, grapes may be considered as alternative/ complementary therapeutic regimen to prevent and/ suppress tumor progression in various cancer types.

Effect on apoptotic cell death

Apoptosis is an important cellular process, which participates in the homeostasis of various pathophysiological conditions. Various natural components are characterized to play an important role to regulate the apoptotic rate *in-vitro* and *in-vivo* and here we have discussed the role of grape constituents in relation to apoptosis. Resveratrol has been reported to induce activation of apoptosis signal-regulating kinase 1 that activates the downstream kinases c-Jun N-terminal kinase and p38 mitogen-activated protein kinase and lead to regulation of apoptotic cell death.[21] Also, Su et al,[21] have reported that resveratrol activates small GTP-binding protein Cdc42 and apoptotic signal-regulating kinase 1/ c-Jun N-terminal kinase/ FasL signaling cascade in HL-60 cells which led to subsequent apoptosis. Regarding the effect of resveratrol on cell growth, it has been found to inhibit the growth of human prostate carcinoma cells[22] and human breast cancer cell line MCF-7.[14] This type of anti-proliferative effect of resveratrol has been associated with the inhibition of D-type cyclins and cyclin-dependent kinase 4 expressions, and the

induction of tumor suppressor p53 and cyclin-dependent kinase inhibitor p21WAF1/CIP. Moreover, the kinase activities of cyclin E and cyclin-dependent kinase 2 are known to be inhibited by resveratrol without alteration of their protein levels. Further, resveratrol treatment has also been demonstrate to up-regulate the Bax protein and mRNA expression in a dose-dependent manner without significantly affecting the Bcl-2 and Bcl-xL levels. It is considered that these effects are caused through involvement of activation of caspase-3 and caspase-9.[22] Kim et al [23] and Hayashibara et al [24] have reported that resveratrol inhibited the growth of human T cell lymphotrophic virus-1-infected cell lines, at least in part, by inducing apoptosis mediated by downregulation in survivin expression. In a study with breast cancer cells resveratrol has been found to induce apoptosis via p53-dependent pathways.[25] Additionally, Heyneanol A, a tetramer of resveratrol, isolated from the roots of *V. amurensis*, has been found to induce cytochrome c released from mitochondria into the cytosol and subsequent caspase activation.[26]

Anti-inflammatory and Immunomodulatory properties

The role of inflammation is very wide in various immuno-pathophysiological conditions. The main target of current research is to identify anti-inflammatory natural components to treat various inflammatory diseases. Thus far several evidences have established that resveratrol has potent anti-inflammatory and immunomodulatory activities. Martin et al,[27] reported that resveratrol considerably reduced the colonic injury, index of neutrophil infiltration and the levels of the cytokine *in-vivo*. However, resveratrol could not revert the increased prostaglandin E_2 levels but produced a significant fall in the prostaglandin D_2. It targeted prostaglandin H_2 synthases, COX-1 and COX-2, that catalyzed the synthesis of prostaglandins via sequential cyclooxygenase while peroxidase reactions were inhibited.[27,28] Resveratrol inactivated COX-1 and offered a design of selective COX-1

inactivator that worked at the peroxidase active site.[29,30] Resveratrol inhibited phorbol ester (PMA)-mediated induction of COX-2 in human mammary glands and oral epithelial cells. Treatment of cells with PMA induced COX-2, causing a marked increase in prostaglandin E_2. Resveratrol also inhibits PMA-mediated activation of protein kinase C.[31] The resveratrol and quercetin have been identified as novel non-steroidal compounds with anti-inflammatory activity that has applications for the treatment of inflammatory diseases. These molecules inhibit both interleukin-8 and granulocyte-macrophage colony stimulating factor released from A549 cells. Resveratrol, but not estradiol inhibited cytokine-stimulated inducible nitric oxide synthase expression and nitrite production in human primary airway epithelial cells.[28] Grape melanin also interferes with the prostaglandin, the leukotriene and complement system mediated inflammation.[32] Melanin also reduces the cytokines IL-1, IL-6 and TNF-α in adjuvant induced disease rats.[32]

The inhibition of cyclooxygenase, induction of CD95 signaling-dependent apoptosis, effects on cell division cycle and modulation of NF-kB activation, suggest a possible effect of resveratrol on the immune system. Resveratrol induces the development of cytokine-producing $CD4^+$ and $CD8^+$ T cells by stimulating peripheral blood mononuclear cells with anti-CD3/anti-CD28 *in-vitro*.[33] The phagocytosis rate has been found to increase human promonocytic cell line, when treated with resveratrol and quercetin, while both polyphenols demonstrated the cytostatic activity and prointraphagocytic effect on U937 cell growth.[34]

Antidiabetic Property

Currently a big part of adult population is suffering from diabetes and its prevalence is increasing day-by-day. Till now no therapy is available to treat diabetes and various therapeutic strategies have also been applied to suppress increasing prevalence of diabetes. Among these strategies the use of various natural components is in common use,

worldwide, in which grapes and its constituents are one. Bolton et al,[35] demonstrated that the insulin response of the whole grape fruit was significantly higher than that of juice alone. This led to a speculation that the glucose in grapes is more insulinogenic than those in oranges and apples. The plasma insulin and glucose responses to fruit depended on the fiber and glucose content.[35] Oleanolic acid and aleanolic aldehydes present in grape skin have insulin secretor activities.[36] Resveratrol inhibits the glucose uptakes by human trasformed myelocytic cells.[37] Grape seed extract, chromium polynicotinate and zink monothionine combination enhances the insulin sensitivity and lowers the glycosylated proteins.[38] In addition, these combinations can markedly lower systolic blood pressure in normotensive rats, lessen oxidative damage and decreased glycosylated haemoglobin without any toxicity.[39] Flavonoids and epicatechin isolated from grapes stimulate β-cell regeneration and ameliorate chemically-induced diabetes in animals.[40] Recently, it has been shown that resveratrol activated SIRT-1 deacylase and protected high fructose induced diabetes.[41] Milne et al[42] reported that analogues of resveratrol improved energy homeostasis and insulin sensitivity.

Cardioprotective effects

Among biggest health problems, cardiovascular diseases are one, which are affecting around 12% adult population in the world. The pathophysiology of cardiovascular diseases is very complex thereby it termed as metabolic syndrome. Cardioprotective effects of various natural components have been investigated; here we are discussing the role of grapes. Purple grapes have partial antithrombotic effects due to the availability of phytochemicals.[43] Epidemiologic studies suggest that red wine from grapes is associated with a reduced incidence of mortality and morbidity from coronary heart diseases, which might be due to changes in lipid metabolism, antioxidative effect and changes in

hemostasis. It has been reported that, moderate taking of red wine increased HDL cholesterol, decreases LDL cholesterol, decreased the fibrinogen level and inhibited platelet aggregation. This could positively influence stress, fear, anxiety and depression.[44] In a study from the University of Wisconsin reported that, grape juice improved blood flow by 6.4% and protected LDL from oxidation.[45] Research revealed that the flavonoids in grape juice decreased the tendency of blood to clot and regular use of grape juice could reduce the risk of cardiovascular disease, a safer way to achieve protection against heart disease than wine.[45] Grape juice also inhibits platelet activity and protects against epinephrine activation of platelets as well as enhances endothelial production of nitric oxide.[46,47]

Grape seed extract reduces malonaldehyde content of heart, indicating reduction of oxidative stress during ischemia and reperfusion.[48] The hearts of the grape seed extract fed persons are resistant to myocardial ischemia reperfusion injury, suggesting a cardioprotective role of grapes.[48] The cardioprotective effect has been attributed to antioxidants present in the polyphenol fraction of red wine. The wine extract as well as resveratrol and proanthocyanidins are equally effective in reducing myocardial ischemic reperfusion injury that suggests that polyphenolic antioxidants in wine play a vital role in cardioprotection.[49] In concert, grape seed proanthocynidins extract significantly reduced the appearance of apoptotic cardiomyocytes and appearance of the reactive oxygen species in the ischemic/reperfused hearts, while functioning as an *in vivo* antioxidant.[50] The proanthocyanidin-fed animals were resistant to myocardial ischemia reperfusion injury as evidenced by improved recovery of post-ischemic contractile functions.[51,52] The flavonoids in grapes are good inhibitors of plasminogen activator *in vitro* appeared proanthocyanin**.** Hence grape juice may be a useful alternative dietary supplement to red wine without concomitant intake of alcohol.[53]

Resveratrol is a potent antiarrhythmic agent with cardioprotective properties and the same could be correlated with upregulation of nitric oxide (NO) production.[54] Resveratrol suppresses both the serum triglyceride and very-low-density lipoprotein and low-density lipoprotein (VLDL and LDL)-cholesterol levels. This hypocholesterolemic action of resveratrol is partly attributed, to an increased excretion of neutral sterols and bile acids into feces.[55] The increase in tyrosine phosphorylation of Iκ-Bα, p50-NF-κB, and p65-NF-κB suggests the involvement of such alterations in the modulation of NF-kappaB transcription activity which shows the cardiovascular protective effects and suggests antiatherogenic activities of the compound on endothelial cells.[56] Resveratrol has been found to pharmacologically precondition heart through the upregulation of nitric oxide (NO).[57] NO being a free radical with vasodilator properties exerts dual effects on tissues and cells in biological systems. The high level of flavonoids, catechins, tannins and other polyphenolics in red wine induce NO formation in endothelial cells to improve circulation and suppress induction of inducible NO synthase.[58] Its beneficial effects in focal cerebral ischemia may be due to its anti-platelet aggregation activity, vasodilating effect, antioxidant property or by collective effects of all these.[59] In ovactamized, resveratrol acts like mammalian estrogens, thus lowering blood pressure and increasing dilatory responses to acetylcholine.[60]

Neuroprotective property

Increasing prevalence of neurodegenerative diseases, attracting researchers to testify various components which can be used to treat/ prevent neurodegeneration. Investigations whether polyphenolic antioxidants offer protective effects beyond the cardiovascular system, and whether polyphenols from other plant sources offer beneficial effects to human health of interest**.** Animal models have provided information clearly indicating the

ability of grape polyphenols to ameliorate neuronal damages due to chronic ethanol consumption. Resveratrol has shown protective effects on neuron cell death induced by ethanol and other oxidative agents.[61] The resveratrol is a potent neuroprotective agent in focal cerebral ischemia.[60] Recently, it has been reported that, resveratrol protected ethanol induced neurotoxicity.[62] The neuroprotective effect of resveratrol might be due to its anti-oxidant and ion-channel regulatory (Ca^{++} channels) properties.

Effect on obesity and ageing

Obesity is the main growing health problem leads to immature morbidity and mortality in the major part of population. The main cause of obesity is intake of high energy (fat) intake through food. One of the strategies to inhibit prevalence of obesity may be suppression of fat absorption from gastrointestinal tract. The grape seed extract enriched with compounds which inhibit gastrointestinal digestion of lipids through inhibition of lipase enzymes (pancreatic lipase, lipoprotein lipase, and hormone-sensitive lipase *in vitro*) may provide a safe, natural, and cost-effective weight control treatment. Thus, grape seed extract may have its potential application as a treatment for obesity.[63] Recently it has been reported that, various analogues of resveratrol have capacity to reduce insulin resistance by enhancing energy homeostasis.[42]

Accelerated aging is another health threat, affecting hundred percent populations and sometimes leads to premature mortality in major population. Aging is a progressive accumulation of changes as the time progresses and is responsible for ever-increasing likelihood of disease and death. The precise cascade of pathological events responsible for aging mainly is the enhanced production of free radicals. The deleterious effects of free radicals on proteins, nucleic acids and fats as well as enhanced glycosylation of proteins and DNA are prevalent during aging. Partial insulin resistance may be a common etiology,

behind the pathobiological alterations of advancing age. As grape seed proanthocyanidin extract has demonstrated to improve insulin sensitivity and ameliorate free radical formation by reducing the signs/symptoms of chronic age-related disorders.[39] Resveratrol and various anthocyanins of grapes have been well established for anti-aging effects through various mechanisms, in which anti-oxidant property is the chief mechanism.[64]

Hormonal agent and antipyretic property

Resveratrol has been shown to be a non-flavonoid phytoestrogen, and to act as an estrogen receptor super-agonist in MCF-7 cells, transiently transfected with estrogen-responsive reporter constructs. Several additional hydroxystilbenes, including diethylstilbestrol and piceatannol, were tested, and all showed estrogen receptor but superagonism was specific to resveratrol.[65] Grape seeds and anthocyanins inhibited the apyrase (an enzyme which hydrolyses ATP and ADP) and ecto-ATPase that is related to the integrity of the endothelium and the synthesis and release of nitric oxide. In addition grape seeds and anthocyanins activate P2y1 and/or P2Y2 purinoceptors of endothelial cells, trigger the synthesis and release of nitric oxide that leads to relaxation and reducing the body temperature.[66]

Antiviral and anti-encephalitozoon activities

Resveratrol has been studied to show anti-herpes simplex virus activity as 12.5 and 25% of resveratrol cream, which effectively suppressed lesion formation.[67] Hepatitis is a widespread form of viral infection of the liver that is among the several causes of the population disablement. The grapes have been shown to improve the systemic condition of hepatitis-affected liver in experimental animals.[68] The resveratrol synergistically enhances the anti-HIV-1 activity of the nucleoside analogues zidovudine, zalcitabine, and

didanosine. Moreover, resveratrol at 10 μM was not toxic to cells, and by itself reduced viral replication by 20 to 30 percent.[69] Stilebenes are phenolic molecules that have antifungal effects in plants.[70]

Microsporidians of the genus Encephalitozoon are an important cause of disease in immunocompromised patients. Resveratrol at 50 μM showed significant sporicidal activity, while at 10 μM resveratrol also inhibited intracellular development of the parasite, without affecting host cell viability.[71]

Other health beneficial effects of grapes

The resveratrol is suggested to be a potent anti-glomerulonephritic food factor capable of suppressing proteinuria, hypoalbuminemia and hyperlipidemia.[72] The glycosylation of resveratrol by resveratrol glucosyltransferase is distinct from the glucosyl transferase(s) active on the other phenolics.[70] Resveratrol diffuses rapidly across the intestinal epithelium.[73]

CONCLUSION AND PERSPECTIVES

Grape fruits liked by consumers worldwide for high taste is blessed with a bundle of nutritional properties. The health favorable properties in active ingredients are prevalent in different parts (e.g. fruit, stems, and seeds) of grapes. This further adds to the benefits of this fruit thereby tempting one for its addition in the diet of humans to stay away from disease, infections and relaxants**.** Keeping all the facts described here, it is worthwhile mentioning that grape taking grape in regular diet could help a lot in maintaining good health. Similarly, the purified products obtained from the fruit could prove to be potential agents in prevention and treatment of several diseases.

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Table :1 Grapes nutrients

Proximates		Lipids:	
Water :	74.796 gm	Fatty acids, total satutrated:	0.105 gm
Energy :	61.740 kcal	14:0 :	0.003 gm
Energy:	257.600 kj	16:0:	0.090 gm
Protein:	0.580 gm	18:0:	0.012 gm
Total lipid (fat):	0.322 gm	Fatty acids, total monounsaturated:	0.013 gm
Ash:	0.524 gm	18:1, undifferentiated:	0.01 gm
Carbohydrates, by difference:	15.778 gm	Fatty acids, total poly unsaturated:	0.094 gm
Fibre, Total dietary:	0.920 gm	18:2, Undifferentiated :	0.073 gm
Minerals		18:3, undifferentitated:	0.022 gm
Calcium :	12.880 mg	Amino acids	
Iron:	0.267 mg	Tryptophan:	0.003 gm
Magnesium:	4.600 mg	Threonnine :	0.016 gm
Phosphorus-	9.2 mg	Isoleucine:	0.005 gm
Potassium:	175.72 mg	Leucine:	0.012 gm
Sodium:	1.840 mg	Lysine: 0.013 gm	
Zinc:	0.037 mg	cystiene:	0.009 gm
Copper	0.037 mg	Phenylalanine :	0.012 gm
Magnese:	0.661 mg	Tyrosine :	0.010 gm
Selenium:	0.184 mcg	Valine:	0.016 gm
Vitamins		Arginine:	0.042 gm
Vitamin C, Total ascorbic acid:	3.680 mg	Alanine :	0.024 gm
Thiamine:	0.085 mg	Aspartic acid:	0.071 gm
Riboflavin	0.052 mg	Glutamic acid:	0.121 gm
Niacin:	0.276 mg	Glycine:	0.017 gm
Pantothenic acid:	0.022 mg	Proline :	0.019 gm
Vitamin B6:	0.101 mg	Serine :	0.028 gm
Folate, total-	3.680 mcg		
Vitamin A, IU:	92.00 IU		
Vitamin A, RAE-	4.600 mcg_RAE		
Vitamin E:	0.313 mg_ATE		

Source : USDA National Nutrient Database for Standard Reference, Release 15 (August 2002)

Table 2: Some bioactive compounds from Grapes

Grape compound	Source	Biological Activity	Reference
Resveratrol	Fruit Skin and Seeds	Antioxidant	Cai et al 2003
		Anticarcinogenic	Kim et al 2003
		Anti-inflammatory	Martin et al 2004
		Antiarthritic	Donnelly et al 2004
		Cardioprtective	Miura et al 2003
		Hypoglycaemic	Park et al 2001
		Antiviral	Docherty et al 2004
		Phytoestrogen	Gehm et al 2004
Heyneanol A	Roots of *Vitis amarensis*	Apoptotic inducing	Lee et al 2004
Gallic acid	Fruit skin and Seeds	Antioxidant	Yilmaz et al 2004
Catechin	Fruit skin and Seeds	Antioxidant	Yimaz et al 2004
		Antidiabetic	Chakravarthy et al 1981
Epicatechin	Fruit skin and Seeds	Antioxidant	Yilmaz et al 2004
		Antidiabetic	Chakravarthy et al 1981
Epigallocatechin-3-gallate		Antineoplastic	Borska et al 2003
Thiconjugates	White grape	Antioxidant	Selga et al 2004
Flavonoids	Concord grape juice	Antioxidant	Byrne et al 2002
		Antidiabetic	Chakravarthy et al 1981
		Anticarcinogenic	Hakimmudin et al 2004
Proanthocyanidins	Dried seeds	Antioxidant	Gonzalez et al 2004
		Antipyretic	Mender et al 2003
Diprim	Amur grape crest	Antioxidant	Kushnerova et al 2002
Quercetin		Anti-inflammatory	Donnelly et al 2004
		Immunomodulatory	Donnelly et al 2004
Melanin		Anti-inflammatory	Avramidis et al 1998
		Immunosuppressive	Avramidis et al 1998
Oleanolic acid & Aleanilic acid	Grape skin	Insulin secretor	Zhang et al 2004
Tannins		Blood pressure regulator	Achike et al 2003

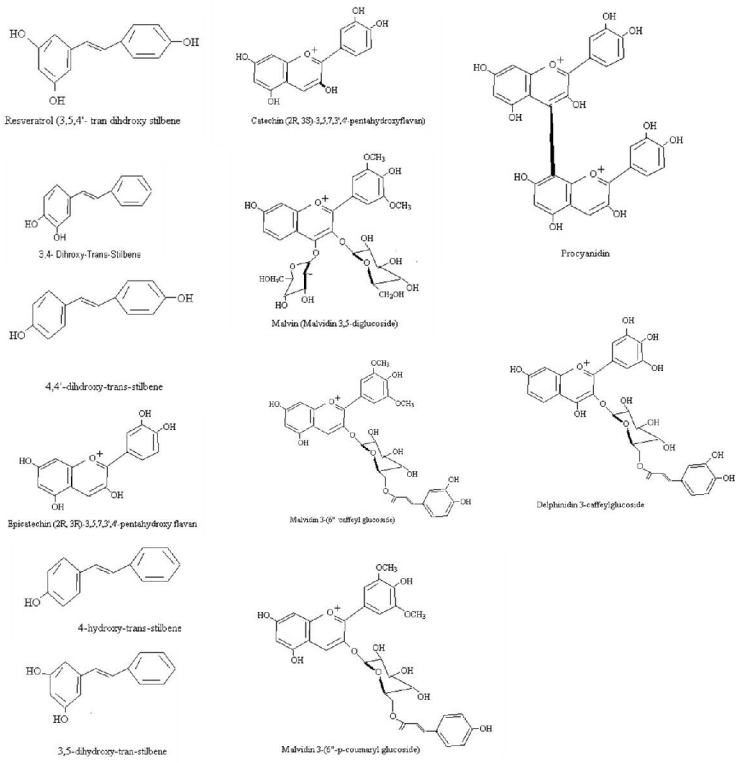

Fig.1. Chemical structures of well identified biological active compounds from grapes.

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