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Grape: A Medicinal Fruit Species in the Holy Qur'an and its Ethnomedicinal Importance

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Abstract: Islam is a religion of the complete code of life. The Ethical teaching of the Holy Qur'an and the tradition of the Prophet Muhammad (PBUH) are intimately linked to the biomedical ethics. The Holy Qur'an is the absolute reference book describing, inter alia, the importance of plants used for diverse ailments in different Surahs. In the current study, ethnomedicinal importance of grape, *Vitis vinifera* L., was studied. The name of the grape appears as Inab and it is narrated eleven times in the Holy Qur'an in different Surash-Verses-Al-Baqara: 266, Al-An'aam: 99, Ar-Ra'd: 4, An-Nahl: 11, 67, Al-Israa: 91, Al-Kahf: 32, Al-Muminoon: 19, Yaseen: 34, An-Naba: 32 and Abasa: 28. In addition, Hadith, Islamic history and books on medicinal plants, scientific publications also looked for the realistic ethnomedicinal importance of this plant. The main aim of this study was to accrue the advanced knowledge on grape in terms of its ethnomedicinal importance in the light of Islamic point of view. It contains important bioactive compounds including flavonoids, polyphenols, anthocyanins and stilbene derivatives resveratrol that have different therapeutic effects like anti-oxidative, anti-carcinogenic, antimicrobial, antiviral, anti-aging, anti-inflammatory, anti-diabetic, cardioprotective, hepatoprotechtive and neuroprotective activities. Furthermore, it has extensive nutritional values and usages.

Key words: Bioactives · Ethnomedicine · Grape Production · Holy Qur'an · Hadith · Medicinal Plant

INTRODUCTION

The last revealed Book, the only one perfect and complete celestial guidance from Allah Subhanu Wa Ta'ala (SWT), is the Holy Qur'an which exists in the world as a guide of mankind [1]. The Holy Qur'an is the endless and perpetual basis of Islam and it was revealed upon the Prophet Mohammad (Peace Be Upon Him [PBUH]) in the mid of 5th century through the Angel Gabriel (Alaihe Salaam) during the twenty-three years of Muhammad's messengership. It comprises many signs and verses that are attracting people towards Islam. Moreover, the Holy Qur'an invites human to study in depth and think over the creations of Allah SWT, over again and again [2]. It has been claimed that the Holy Qur'an covers every aspect of life and full of wisdom from the very beginning. Almighty Allah SWT proved it more than 1400 years ago by saying:

"We have neglected nothing in the Book." [Holy Qur'an, 6:38] [3].

There are many natural resources such as soil, water, air, plants, fruits and animals which have been created by Allah SWT for human beings and all of these have been described in the Holy Qur'an [4]. Among these natural resources, the importance of medicinal plants focuses in different Surahs, for example, Al-Baqara, Ar-Rad, Al-Anaam, Al-Araf, An-Nahl, Al-Isra, Al-Kahf, Maryam,

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Taha, Al-Ambiya, Al-Mumenoon, An-Noor, As-Shuara, Luqman, Saba, Ya Seen, An-Najm, A-Qamar, Al-Rahman, Al-Waqia, Al-Insan, An-Naba, Abasa and At-tin [3]. Allah SWT says:

"And in the earth are neighboring tracts and gardens of vines and green crops (fields) and date-palm, growing into two or three from a single stem root, or otherwise (one stem root for every palm), watered with the same water; yet some of them We make more excellent than others to eat. Verily, in these things there are Ayat (proofs, evidences, lessons, signs) for the people who understand" (Holy Qur'an, 13:4) [3].

Our Holy Prophet (PBUH) used and recommended medicinal plants for the treatment of various ailments. Traditionally many plants are still using today. There are many edible and non-edible plants (such as ginger, pomegranate, grape and banana), which are cited in the Holy Qur'an, are using as remedies for various ailments such as cough, intestinal bleeding and diarrhea. Therefore, plants mentioned in the Holy Qur'an have been attracted by the botanists, biochemists and pharmacognosist (Natural drug specialists) for research purposes [5]. In the Holy Qur'an, about nineteen medicinal plants have been identified. These plants are Camphor, Date palm, Fig, Ginger, Grape, Garlic, Lentil, Olive, Onion, Pomegranate, Sweet basil, Athel tamarix, Tooth-Brush Tree, Mustard, Cucumber, Arak, Summer squash, Acacia and Cedrus [6]. Among these documented plants, grapes and its bioactives have shown profuse pharmaceutical and pharmacological activities against diseases. It also used as foods due to containing high nutritional values. Grape is mentioned as 'Inab' in the Holy Qur'an and in Malaysia, it is known as Anggur. It has been cited 11 times in the Holy Qur'an in different Surahs' and Verses- Al-Baqara: verse 266, Al-An'aam: verse 99, Ar-Ra'd: verse 4, An-Nahl: verse 11and 67, Al-Israa: verse 91, Al-Kahf: verse 32, Al-Muminoon: verse 19, Yaseen: verse 34, An-Naba: verse 32 and Abasa: verse 28 [3].

The Prophet (PBUH) said that there is a cure for every disease and encouraged early Muslim scholars to engage in botanical and other natural products, chemical and biomedical research to seek out a cure for every disease known to them. In Hadith, book 76, chapter 1, number 5678, The Prophet (PBUH) said:

"There is no disease that Allah has created, except that He also has created its treatment" Narrated by Abu Huraira (Rahmatullahi Alahei [RA]) [2].

Moreover, some verses in the Holy Quran also emphasis that every disease has a medicine. For example:

"Say: It is for those who believe, a guide and a healing" (Fussilat 41: verse 44) [3].

"And We send down of the Quran that which is a healing and a mercy to those who believe" (Al-Israa' 17: verse 82) [3].

The importance and uses of the grapes aslo focuses on some Hadiths of Prophet Muhammad (PBUH). One Hadith narrated by Abu Huraira (RA): The Prophet (PBUH) said:

"Don't call the grapes Al-Karm, (because) Al-Karm is the heart of the Mumin" [7].

In another Hadith also narrated by Abu Huraira (RA): Rasulullah (Sallallahu Alayhi Wasallam) said,

"You have resaisins (Munaqqa) which make the colour of the face handsome and remove the phlegm" [7, 8].

In one more Hadith narrated by Abdullah bin Abbass (R.A):

"Raisins were soaked for Rasulullah (Sallallahu Alayhi Wasallam). He used to drink this syrup that day, the next day and sometimes the third day" [7].

The necessity of eating grape also highlighted in the following Hadith. In book 67, chapter 89, number 5197, Narrated Abdullah bin Abbass (RA): He (PBUH) said,

"I saw Paradise (or Paradise was shown to me) and I stretched my hand to pluck a bunch (of grapes) and had I plucked it, you would have eaten of it as long as this world exists" [2].

Grapes are widely used to prepare juice or drink and also for alcoholic drink (wine). The drinks prepared from honey or grapes are permissible to drink as long as it is fresh (not fermented). However, alcoholic drinks were strictly prohibited in Islam. In book 74, chapter 2, number 5580, Narrated Anas (R.A.):

"Alcoholic drinks were prohibited at the time we could rarely find wine made from grapes in Al-Madina, for most of our liquors were made from unripe and ripe dates" [2].

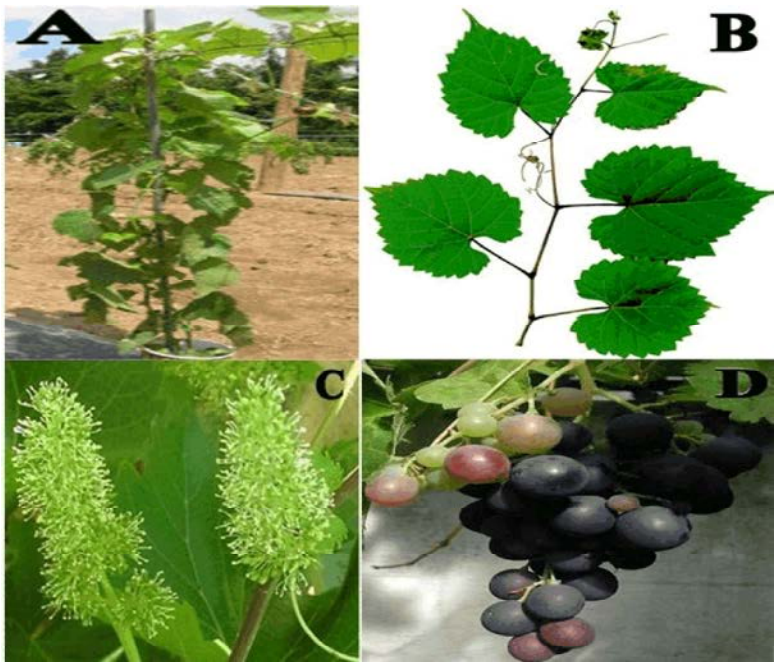

Fig. 1: Grapevine (*V. vinifera*) plant. [A] Adult grapevine plant, [B] Leaves (adult leaves and tendrils), [C] Flower at bloom and [D] Bunch of fruits

In another Hadith, book 74, chapter 2, number 5581, Narrated by Ibn 'Umar: 'Umar stood up on the pulpit and said,

"Now then, prohibitions of alcoholic drinks have been revealed and these drinks are prepared from five things, i.e., grapes, dates, honey, wheat or barley. And an alcoholic drink is that, that disturbs the mind" [2].

The grapes commonly known as grapevine (*Vitis vinifera* L.) and it is a historically important fruit plant. Traditionally, grape has been used as important source of medicine as well as nutritions. The fruit of grapes used as dietary supplement and other parts including seeds, leaves, skins are used in herbal medicine for centuries [9]. The leaves of grapes are rich in tannins, flavonoids and procyanidins [10] and possess astringent and haemostatic properties. In the traditional healing system, it is used for the treatment of diarrhea, hemorrhage, varicose veins, hemorrhoids, inflammatory conditions, hepatitis and free radicals related diseases. It is also used externally in Anatolia for centuries to heal wounds and drain furuncles. Furthermore, the juice of the leaves possesses antiseptic activity which is recommended to use even for eye wash [9, 11]. Grapes also used as its raw form or used by making juice, jam, jelly, vinegar, wine, grape seed oil, raisins and grape syrup [12, 13]. The raisins is one of the important nutrients and it is a source of carbohydrates. The grapes have shown multidimensional uses and there have several existing scientific publications as proved of traditional uses of this plant. Hence, in the current study, the main aim was to accrue the advanced knowledge on grape from the Holy Qur'an, Hadith, Islamic literature and books and scientific publications in terms of its ethnomedicinal importance in the light of Islamic point of view.

Plant Description: The *Vitis vinifera* L., bleongs to the family *Vitaceae*, is a liana with flaky bark. The young grapevine consist very pliable trunk and must need support. It has a weak stem and the branches have long shoots. The secondary shoots developed from the primary long shoots and the tendrils assist it to hold on to other structure [14]. The height of the plant is approximately 35 miter and leaves (Figure 1B) are alternate, pentagonal in shape [15], lobed and broad. The length of leaves ranged from 5 to 20 cm. Flowers form branched clusters of one to three per shoot (Figure 1C). The fruit is a fleshy berry, known as a grape. In cultivated grapevine, the fruit is upto 3 cm long and can be white, green, purple, or red; in the wild species it is very smaller, usually 6 mm diameter and ripens dark purple to blackish with a pale wax bloom [14, 16].

Scientific Classification

Kingdom:	Plantae
Division:	Magnoliophyta
Class:	Magnoliopsida
Order:	Vitales
Family:	*Vitaceae*
Genus:	*Vitis*
Species:	*V. vinifera*

Binomial name: *Vitis vinifera* L.

Evolution and History: The grapevine has about 60 [17, 18] or 70 [19] *Vitis* species and many cultivars cultivated widely for fruit, juice and mainly for wine. It is classified as *V. vinifera* L. subsp. *vinifera* (or sativa), derives from wild progenitor, *V. vinifera* subsp. *sylvestris* and the domestication started 6,000–8,000 years ago in the Near East [18, 20]. *Vitis* genus has major agronomic importance. The *V. vinifera* widely used in global wine industries among all the grape species. It has proposed that *V. vinifera* emerged 65 million years ago to Eurasia and still exist both forms in Eurasia and in North Africa. The historical separation into subspecies occurred due to the morphological differences [17]. The geographic disjunction has shown for wild grapes (*Vitis* spp.) including the 34 American species, the 37 Asian species and the rare European–Middle Asian wild grapevine (*V. vinifera* subsp. *sylvestris*). *V. vinifera* subsp. *sylvestris* is believed to be the living ancestor of modern grapevine cultivars [19]. It is generally grows along river banks and in alluvial and colluvial deciduous and semi-deciduous forest [18]. The wild type grapevine widely distributed but the progressive has declined due to introduced of anthropogenic pressure on their natural habitats and pathogens populations from North America during the second part of the 19th century [21]. The grapevine cultivation and domestication have emerged between the seventh and the fourth millennium BC, in a geographical area between the Black Sea and Iran. After that the cultivated forms was spread by humans in Near East, Middle East and Central Europe. For this reason, these areas might comprise secondary domestication centers. In fifth millennium BC, the viticulture would have started in Greece and Crete. Archaeological studies have exposed a considerable development of viticulture and viniculture between the first and the end of the second century AD [18]. The extensive knowledge of viniculture and viticulture has been documented wisely from the archaeological and historical standpoint to develop the model of development, expansion and diffusion. However, the identity, history and biogeography of ancestral cultivars and mechanisms of grapevine domestication and varietal diversification remain obscure.

Distribution and Production: The *V. vinifera* is a perennial treelike and tendrils-climbing vascular plants which is distributed through Asia Minor to and then introduced in Europe. At present, it is domesticated in all temperature regions of the world. It is also commonly found in Asian and European countries, Turkey, Greek, Arabian countries, India, Pakistan, France, Germany [11, 22, 23]. It is one of the largest fruit crops in the world and total grape production was about 67.09 million metric tons (MMt) in 2011 all over the world [24]. The top 20 countreis of grape production in 2011 is shown in Figure 2. The highest production of grapes in 2011 was found in China mainland (about 9.07 MMt) and the lowest production was found in Republic of Moldova (about 0.59 MMt). The total dedicated area for the grapes cultivation was about 7,586,600 ha around the world and it is increasing about 2% per year. The grapes are used for production of wine (71%), as a fresh fruit (27%) and as a dried fruit (2%) [25, 26].

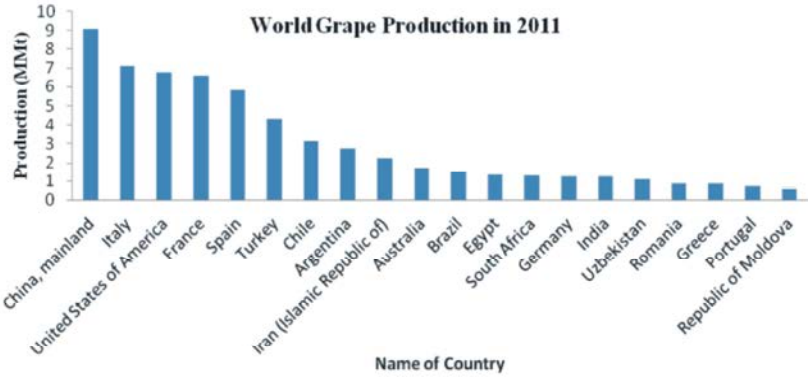

Fig. 2: The world grape production. Top 20 countries- ranking highest to lowest (left to right). MMt: Million Metric tons. Source: Adopted from Food and Agriculture Organization (FAO) [24].

Table 1: Nutrients data of *Vitis vinifera*

Nutrient	%	Prox.	g/100g	Mineral	Conc. (mg/100g)	Vitamin	µg/100g	Anti-nutrient	Conc. (mg/100g)
Moisture	81.50	Energy	57 kcal	Pb	0.01	Thiamine	69	Oxalate	99
Ash	0.100	Water	84.29	Cd	0.01	Riboflavin	70	Phytate	0.28
CL	0.180	Protein	0.81	Ca	44.54	Niacin	188	CG	0.033
CP	0.820	Fat	0.47	Fe	0.43	Vit. B5	50		
CF	0.720	CHO	13.93	Mg	14	Pyridoxine	86		
Sol CHO	16.72	Fibre	3.90	Mn	0.07	Folate	2		
				P	20	Vit. B12	0		
				K	203	Vit. C	10.8 mg		
				Na	1	Vit. K	22		
				Zn	0.11				

CF: Crude fibre, CG: Cyanogenic glycosides, CHO: carbohydrate, CL: Crude lipid, Conc.: Concentration, CP: Crude protein, Prox.: Proximate, Sol: Solution Vit.: Vitamins [Source: 27, 28]

Table 2: Pharmacological activities of bioactive compounds of grapes

Types	Bioactives	Source	Activity	Reference
Flavonoid Phenolics	Flavonoids	Seed, leaves and skins	Antioxidant, antibacterial, antiviral, anti-inflammatory, antimutagenic and antitumor, antidiabetic and antilipoperoxidant	[9, 36-39]
	Anthocyanins	Seed, Skin and grape juice	Antioxidant and antilisteric	[40-42]
	Proanthocyanidin	Seed	Antidiabetic, antibacterial and Antiatherosclerotic,	[37, 43, 44]
	Tannins	Seed and leaves	Antihypercholesterolemic, antilipoperoxidant and antidiabetic	[9, 45, 46]
	Procyanidins	Seed	Antihyperglycemic, antihyperlipidemic and hepatoprotective	[44, 47, 48]
	Catechin	Seed	Antioxidant	[41, 42]
	Epiatechin	Seed	Antioxidant	[41, 42]
	Quercetin	Skin and grape juice	Antioxidant, Preserve β-cell mass, reduce oxidative stress in pancreas, Antidiabetic, Anticancer and inhibit platelet aggregation	[41, 42, 49]
Non-Flavonoid Phenolics	Resveratrol	Skin	Antidiabetic, anticancer, antibacterial, antiviral, anti-inflammatory, antihyperglycemic, antilipidemic, estrogenic, antiatherosclerotic and inhibit platelet aggregation	[42, 50-57]
Extract	Crude extract	Root	Antidiabetic and hepatoprotective	[58]
	Oil	Grapes	Wound healing	[59]

Nutritional Value: *V. vinifera* is a nutritionally rich fruit. It has a lot of glucose, fructose, sucrose, formic acid, citric acid, specially malic acid and tartaric acid [23]. However, its calorie level is low (57 kcal per 100g grapes). It is a great source of iron, most of the vitamins like vitamin A, vitamin B complex, vitamin C and vitamin K and minerals. The amount of nutrients (per 100g) found in grapes listed out in Table 1. In addition, *V. vinifera* contains some anti-nutrient like oxalate, phytate [12, 27, 28].

Chemical Composition: The fresh grapevine juice usually contains almost 70% to 80% water and the rest are dissolved solids (organic and inorganic compounds); such as sugars, organic acids, phenolic compounds, nitrogenous compounds, aroma compounds, minerals, pectic substances. Sugars that include glucose, fructose and sucrose has a large amount of soluble solid. But their sweetness differs significantly. By calculating in a scale of sugariness, fructose is considered to be 100 whereas sucrose is 84 and glucose is 66. Generally most of the dissoleved solids are found in grapes juice as various forms of organic acids, such as, tartaric acid, malic acid and to small amount, citric acid, amino acid [23]. Among these acids, over 90% are tartaric and malic acids. It also has nitrogenous compounds, such as, amino acids, peptides and proteins. Different grape varieties have different form of nitrogenous content in different concentrations which varies with climate, fertilization, soil and other cultural practices. Pectin substances are found in the cell wall, which exist as cementing agents [29].

The seeds and skins of the fruit are abundant of bioactive compounds, for example, flavonoids, polyphenols, anthocyanins, proanthocyanidins, procyanidines and the stilbene derivative resveratrol [11]. Moreover, there are two foremost phenolic compounds that are found in *V. Vinifera*;(i) flavonoids which are consists of colorless flavan-3-ols, flavonols and anthocyanins (red and blue color) [20] and (ii) phenolic acids including cinnamic and benzoic acid derivatives [30]. The pharmacological activities of common bioactive compounds of grapes are summerised in Table 2.

Active Constituents

Flavonoids: The flavonoids (around 4% to 5% of total bioactive compounds) are commonly found in the seeds

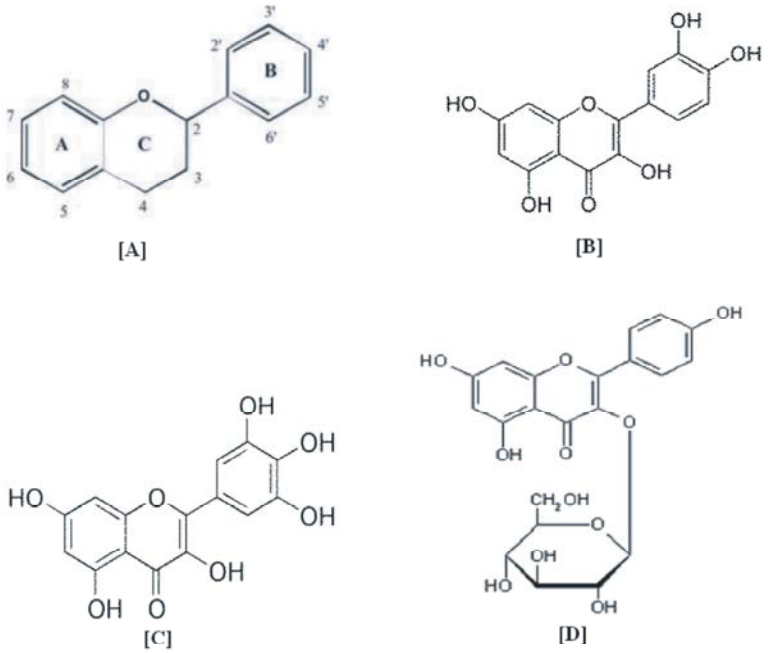

Fig. 3: Chemical structure of flavonoids found in grape. A. Basic structure, B. Quercetin, C. Myricetin, D. Kaempferol-3-O-glucoside.

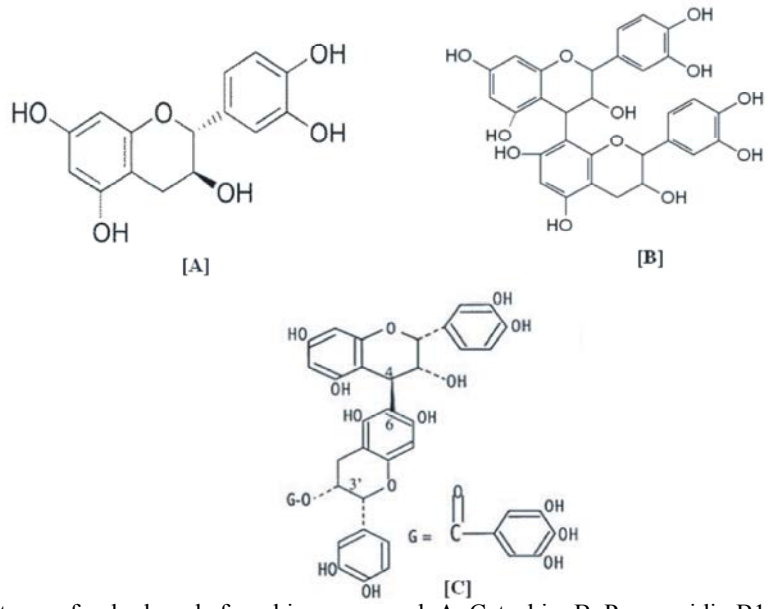

Fig. 4: Chemical structures of polyphenols found in grape seed. A. Catechin, B. Procyanidin B1, C. Procyanidin B5-3'-gallate.

of grapevine. The common flavonoids are kaempferol-3-O-glucosides, quercetin-3-Oglucosides, quercetin and myricetin (Figure 3) [11].

Polyphenols: The grapevine has a largest amount of polyphenols (about 60-70% of total bioactive compounds), which are mostly found in seeds. The commonest polyphenols are flavan-3-ol derivatives such as, (+)-catechins, (-)-epicatechin, (-)-epicatechin-3-O-gallate, procyanidins dimers (B1-B5), procyanidin C1 and procyanidin B5-3'-gallate (Figure 4)[31]. Procyanidins or proanthocyanidins of the grapes are hexamers and acylated procyandins are esters of gallic acid [32].

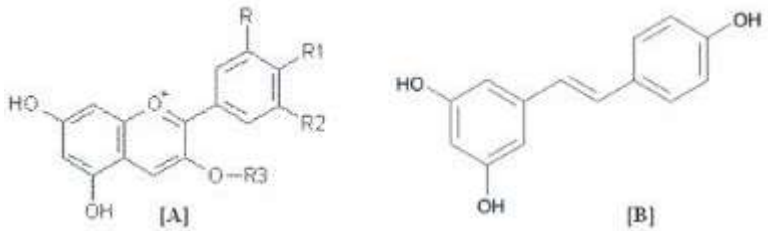

Fig. 5: Chemical structure of [A] anthocyanins and [B] resveratrol in grape.

Anthocyanins: A total of 29 anthocyanins in different concentrations were identified in 110 grape cultivars. Malvidin-derivatives were reported relatively higher in concentration among the anthocyanins (Figure 5[A]) in majority of the cultivars. *V. vinifera* contains only monoglucoside derivatives while the other cultivars had both mono- and di-glucoside derivatives [33]. One the other hand, Wang *et al*. (2003) [34] reported that the *V. Vinifera* also have diglucosides along with monoglucosides. His reported monoglucosieds were 3-glucosides, 3 acetylglucosides, 3-coumaroylglucosidesand 3-caffeoylglucosides and diflucosides were 3,5-diglucosides, 3-acetyl-5-diglucosides, 3-coumaroyl-5-diglucosides and 3-caffeoyl-5-diglucosides of cyanidin, delphinidin, peonidin, petunidin and malvidin.

Stilbene: Plant stilbenes are produced in response to infection and/or injury. It posseses antifungal activity and save the plants from fungal infections. The resveratrol (3,4',5-trihydroxystilbene) is a naturally occurring polyphenol stilbene (Figure 5[B]) that found largely in grapes [31, 35].

Pharmacological Profile

Anti-Hyperlipidemic Aactivity: Effects of the grape seed extracts on the lipid and lipoprotein metabolism could effectively reduce the risk of atherosclerosis and thus helping the patients against the complications caused by the abnormal lipid and lipoprotein metabolisms as well as type 2 diabetes mellitus. The grape seed extracts starts its action from the digestion and absorption by its oligomeric procyanidins and prevent postprandial hyperlipidemia. The actions are inhibition of pancreatic lipase activity, cholesterol esterase activity, cholesterol micellization and bile acid binding [47]. The grape seed's tannins also gave anti-hypercholesteromic action by increasing reverse cholesterol transport and reducing absorption as well as increasing bile acid secretion [45]. In an animal study on Albino Wister rats in cholesterol induced hyperlipidemic model showed that the grape seed extracts significantly decreases serum total cholesterol, low density lipoprotein, very low density lipoprotein and triglyceride levels whereas increase serum high density lipoprotein level [60].

Anti-inflammatory Activity: The methanolic extracts from *V. vinifera* leave demonstrated anti-inflammatory activity in rat and mice. Carrageenan and histamine were used to induce inflammation. There was no toxicity and mortality up to the maximum dose and the extract showed dose dependent significant anti-inflammatory activity compared to the control group [61]. Another study also described similar anti-inflammatory activity of extracts from the grape seeds and skins against 12-O-tetradecanoylphorbol 13-acetate induced inflammation in mice ear. Although application of the extracts separately did not show positive result, but combine use of the extracts showed excellent effectiveness same as to the control drug group [62]. Both the authors stated that the presence of the phenolic compounds, flavonoids, saponins and carbohydrates, are responsible for this anti-inflammatory effect of grape extracts.

Hepatoprotective Effect: There are so many metabolic functions regulated in the liver. The functions may alter in response to hepatic injuries [63]. Ethanolic extract from the grape leaves were successfully demonstrated the hepatoprotective effect against the carbon tetrachloride (CCl_4) induced liver damage. According to the authors, possible mechanisms might be (i) inhibition of cytochrome P450-dependent oxygenase activity, (ii) prevention of lipid peroxidation and (iii) stabilization of the hepatocyte membrane [9]. Another study also demonstrated hepatoprotective activity of grape root extracts against the CCl4 same as to the Silymarin, a well known hepatoprotective agent [58]. Extract from the grape seed also protected the liver from oxidative damage after the ligation of bile duct in rat [64].

Effect on Cardio-Vascular System: The proanthocyanidins rich extract of grape seed showed cardioprotective effects against reperfusion induced injury in isolated rat's heart [65]. It reduced free radicals in myocardium reperfused after an ischemic attack has been suggested as possible mechanism. It also blocks the anti-death signal through inhibition of the pro-apoptotic transcription factor and gene, JNK-1 and c-Jun [66]. Supplementation of procyanidin from grape extraction also found to be effective in decreasing ischemic damage in rat's and rabbit's heart [67]. Suggested mechanisms were (i) increased plasma anti-oxidant level [68] and (ii) enhanced endothelial cells relaxation mediated by Nitric Oxide (NO) synthesis [67]. The procyanidin also noted to be able to prevent the peroxynitric attack to vascular cells by layering on the surface of coronary endothelial cells. Another study revealed that Polyphenolic compounds of grape seed extracts caused an endothelium dependent relaxation of blood vessels which was mediated by activation of the PI3K/Akt signaling pathway through a redox-sensitive mechanism, resulting in phorphorylation of endothelial nitric oxide synthase (eNOS) [69].

Anti-Microbial Activity: Several studies described the anti-microbial activities of extracts from different parts of the grapes due to the presence of the hydroxycinnamic acids [70], flavanols [71, 72], trans resveratrol [50] and tannins [73]. Extracts from the seeds and leaves showed broad spectrum anti-biotic activity against both the gram positive and gram negative microorganisms [38, 73, 74]. These extracts were found to be effective against *Bacillus cereus, Bacillus coagulans, Bacillus subtilis, Staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus subfava, Escherichia coli, Enterobacter aerogenes, Salmonella typhimurium, Pseudomonas aeruginosa, Pseudomonas pseudoalcaligenes, Alcaligenes faecalis, Klebsiella pneumoniae, Proteus vulgaris* and *Candida tropicalis* [73, 74]. Furthermore, the grape seed extracts also able to inhibit effectively the Methicillin resistant Staphylococcus aureus [37]. Anti-listerial and anti-viral effects were also noted for certain extracts from the grape seeds and leaves [40, 75, 76].

Anti-Oxidant Activity: Phenolic components from plants (fruits and vegetables) are well known for their anti-oxidant activities – scavenging of free radicals, inhibition of lipid oxidation, reduction of hydrogen peroxide (H_2O_2) formation and chelating of metal ions. Total phenolic contents and the anti-oxidant activities are directly related to each other. In a research on 12 selected grape varieties available in Portuguese [77], total phenolic contents were reported ranging from 833.73 mg/L to 2005.66 mg/L. Out of them, nine varieties had more than 1000 mg/L of phenolic compounds. In the presence of higher amount of the phenolic compounds, raw grapes and grape products are believed to have positive health effects against the cardio-vaascular diseases, cancerous conditions and neurodegenerative processes. The anti-oxidant activities of the different parts of the grape tree were evaluated using several methods, such as 1,1-diphenyl-2-picryhidrazyl (DPPH) assay, Oxygen radical absorbance capacity (ORAC) assay, Trolox equivalent antioxidant capacity (TEAC) assay, Ferric reducing antioxidant power (FRAP) assay etc. The highest anti-oxidant activity was observed in extracts from the grape seeds followed by the skin and flesh of the grape [78].

Anti-Diabetic Activity: The leaves of *V. vinifera* showed anti-diabetic activity. Grape leaves contains polyphenols, such as stilbene resveratrol, catechin, flavanol, quercetin and anthocyanins exhibited potential to reduce hyperglycemia in type 2 diabetes by improving β-cell function, as well as protecting against loss of β-cell [79]. Extraction from the root of *V. vinifera* was also found to have anti-diabetic effect in streptozotocin induced diabetic rats. The extract was not only reduced fasting blood glucose level but also reduced the liver glycogen levels [9, 38, 46, 47, 80].

Anti-Cancerous Activity: Anti-cancerous activity of the grapes was reported in different articles along with its anti-oxidant activity. Reports suggested that elevated consumption of grape components can reduce the risk of certain cancerous conditions, such as breast cancer, colonic cancer [81] and prostate cancer [82] and melanoma cells [83]. The anti-oxidants are able to arrest cell cycles and enhance apoptosis of cancerous cells. Grapes anti-oxidants showed the ability to modify the estrogen receptors and thus prevent the development of breast cancer. Methanolic extracts of *V. vinifera* also found to be effective in preventing gastric cancer cells [81]. Some varieties of grape extracts which are rich with phenolic compounds showed ability to prevent cancer cell proliferation by suppressing ICAM-1 levels in AGS cells and inducing cell death [51, 84]. The grape juice containing phenolics showed the ability to restrain carcinogen induced DNA adducts formation in rat model [85] and inhibit DNA synthesis in breast cancer cells [86].

Extracts from some certain grape variants were also reported to have anti-proliferative activity in cancer cell proliferation by inhibiting MCF7, NCI-H460, HCT116 and MKN45 [87].

Other Activities: The *V. vinefera* has shown many other activities including above mentioned to cure diseases. The antiviral activity of *V. vinifera* leaves supported the utilization in folk medicine [88]. The high levels of phytochemicals of grapes are able to decrease the risk of chronic diseases. The 10 different cultivars, for instance, 'SV 18315', 'Naples', 'Agawam', 'Aligote', 'V.50151', 'Cabernet Sauvignon', 'Urbana', 'Baco22A', 'Clinton' and 'Campbell Early', have shown the antiproliferative activity which assessed by the inhibition of MCF7, NCI-H460, HCT116 and MKN45 cancer cell proliferation [87]. The neuroprotective activities of *V. vinifera* had also showed the significant result. The seed extracts of grapes are able to protect as well as treatment against lead-induced toxicity in rats. [89]. Another literature had shown the neuroprotective effects where the leaves extracts were found to be able to reduce the protein and lipid damages which induced by hydrogen peroxide in the brain of rats [90].

CONCLUSION

In summary, Islam is the perfect and complete code of life. In the Holy Qur'an, Allah SWT described everythings, negligible. In this study, up-to-date knowledge of *V. vinifera* has been compiled from Holy Qur'an, Hadith, Islamic books and scientific knowledge. It is one of the fruit species cited in the Holy Quran and its bioactives have several pharmaceutical and pharmacological activities such as antioxidative, anti-inflammatory and antimicrobial activities, as well as *in vitro* activity against several cancer cell lines and hepatoprotective and cardioprotective effects. It seems that grape seed extract and its active components such as proanthocyanidins are potent antioxidants. For the proven of pharmacological activity, some *in vitro* and *in vivo* studies already have conducted and they rported prositive results. Hence, systematic studies are required to test a range of concentrations of bioactives *in vitro* and then apply those doses *in vivo* and even in clinical trial to a wide variety of diseaeses. Several i*n vivo* studies clearly demonstrate that bioactives are pharmacologically safe and can be used for the prevention and therapy of various disorders of human. The consumption of grapes and grape juice is likely to have positive effects on human health and especially in postmenopausal women. Grape has both beneficial constituent of sprituality and also for the human physical elements. The findings knowledge may be encouraged the people to use it for various ailments and for human beings as nutrient supplements.

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