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Review Article

Vitis vinifera Seeds: Phytochemical Compounds and Pharmacological Properties. A Review

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Abstract

One of the most prominent and valuable fruits is grapes. Grape muscadine seeds possess a broad spectrum of pharmacological potential. The antioxidant potential was shown to be the highest in grape seed compounds. Consumption of proanthocyanidin grapes decreased foam-cell growth in hamsters. Bacteria of both gram-positive and gram-negative varieties were entirely stopped in their tracks by grape seed extracts. Total phenolic content was highest in grape seed extracts, while it was lowest in skin crude extract. Nevertheless, it was found that skin extracts were more beneficial than seed extracts in controlling *Helicobacter pylori*. It is proposed that supplementing grape seed can be an efficient anti- carcinogenic therapy in medical practice. *Vitis vinifera* seed oil contains flavonoids, carotenoid, phenolic, tannin, and stilbene compounds. The total quantity of polyphenolscollected by the cold-pressure method from *Vitis Vinaifera* seed oilis approximately 2.9 mg/kg. Grape seed oils extracted using a cooler pressing method are rich in linoleic acid (LIA). The oil is rich in polyunsaturated fatty acids (PUFA). *Vitis vinaifera* seed oil has potential as a healthy alternative anti-inflammatory treatment. Serious illnesses linked with worldwide-elevated mortality and morbidity rates are commonly associated with inflammatory mechanisms. Grape seed oil also has an impact on certain bacteria, showing an antimicrobial character. Subsequent generations of antimicrobial drugs for use in food and medicine could be transmitted through oil extracted from the *Vitis vinifera* plant.

Keywords: *Vitis vinifera;* Oil; Bioactive Compounds; Antioxidant Effects; Pharmacological Properties

Introduction

About 75 million tons of grapes (*Vitis vinifera*) are produced each year, with Europe (41%), Asia (29%), and the United States (21%) accounting for the vast majority of these regions [1]. The grapes are grown in temperate regions, with typical climatic trends in warm summers and mild winters (Figure 1) [2]. Worldwide, grapes have shown great interest because of the nutritional characteristics of the natural product, and the medication characteristics of its products, including peel and seed extracts. Grapes, all of which belong to the species *Vitis vinifera*, can be subdivided into several subgenera, including those that produce wine, table grapes, and raisins. The key grapes are North American, European, and French varieties [3]. About a third of the grapes are consumed raw, while the remainder are used in primary products like grape seed extract, syrup, and grape seed oil [2].

Catechin and epicatechin are two examples of the polyphenol proanthocyanidins found in abundance in the seeds of the *Vitis vinifera* plant [4]. Furthermore, phenolic substances and proanthocyanidins are concentrated in grape seeds [5]. *Vitis vinifera* is a rich source of monomeric phenolic compounds such as catechins, epicatechin, and epi-3-gallate and is anti-mutagen and antiviral [6]. Flavano-3-ol is also abundant in *Vitis vinifera* seeds, including proanthocyanidins and catechins [7]. In recent years, interest in *Vitis vinifera* seeds has risen rapidly due to the mounting evidence that these seeds may play a role in disease prevention and the enhancement of overall health [8]. They are used for the processing of healthy foods, such as natural antioxidants and dietary supplements [9]. *Vitis vinifera* seeds contain 8%-20% oils (dry core). The amount of oil harvested from a given crop is contingent on many elements, including the method of oil extraction utilized, the solvent, the operating circumstances, the cultivars harvested that year, and the climate [10]. Grape seed oil has traditionally been extracted using either organic solvents or mechanical techniques [11].

Figure 1: Different types of grapes and their seeds [2].

Phytochemical compounds in *Vitis vinifera* Seeds

Seeds from the grape plant have been shown to provide a variety of nutrients, including protein (11%), fiber (35%), minerals (3%), fat (7%-20%), and water (7%). Moreover, grape seed extracts yield a uniform solution consisting of monomers (5%-30%), oligomers (17-63%), and polymers (11%-39%). Grape extracts' color and flavor are mostly determined by a compound called proanthocyanidins. For every 100 grams of dry matter, the levels of overall phenols (gallic acid), entire flavonoids (catechin equivalents), and proanthocyanidins were recorded as 8.58, 8.36, 6.41, and 5.95 milligrams, respectively (Figure 2) [12].

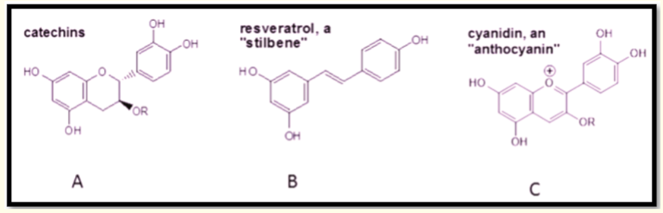

Figure 2: Natural compounds found in *Vitis vinifera* seeds: (A) catechins, (B) resveratrol, and (C) cyaniding [13].

Grape phenolic content can be influenced by factors such as grapevine variety, viticultural methods, and environmental factors. The principal phenolic components found in grape muscadine seeds were epicatechin, catechin, and gallic acid. Muscadine *Vitis vinifera* seeds have been reported to contain 1299 milligrams per 100 grams (mg/100 g), 558 milligrams per 100 grams (mg/100 g), 6.9 milligrams per 100 grams (mg/100 g), 4.3 milligrams per 100 grams (mg/100 g), and 2179 milligrams per 100 grams (mg/100 g) of fresh weight epicatechin, catechin, gallic acid [13].

Pharmacological Properties of *Vitis vinifera* seeds

Listed below and described in Figure 3 are some of the many ways in which the seeds of the vine *Vitis vinifera* have been shown to have pharmacological potential.

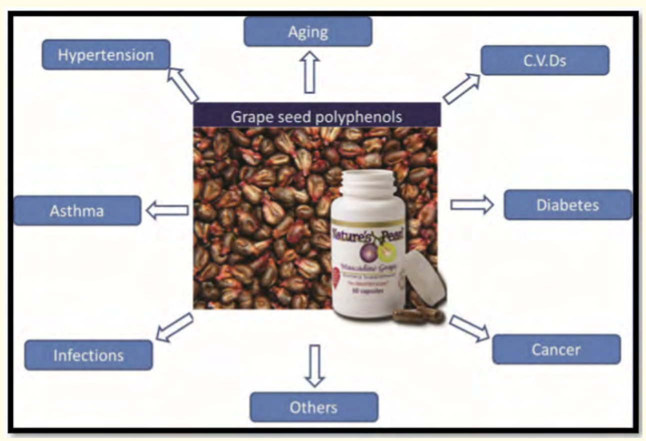

Figure 3: *Vitis vinifera* seeds and their positive health effects [13].

Antioxidant effects

The levels of total cholesterol, oxidised low-density lipoprotein (LDL), and LDL in hypercholesterolemic participants were significantly decreased after two months of supplementation with grape seed proanthocyanidin extracts and chromium polynicotinate, as reported by Preuss., *et al*. [14] in a randomly selected, double-blind, placebo-controlled trial. Furthermore, results showed that the antioxidant potential of grape seed compounds is highest at 281 µM Trolox total antioxidant ability (TEAC)/g fresh weight (FW), followed by the antioxidant potential of grape leaf extract (236 µM TEAC/g FW), grape skin extract, (13 µM TEAC/g FW), and grape wood pulp extract (2.4 µM TEAC/g FW) [13]. Similarly, two experiments have shown that beta-carotene linoleate, linoleic acid, and acid peroxidants are essential for the grape extract to have any antioxidant effect [15]. Procyanidin extracts have been reported to adjust the output of antioxidant systems, and it was suggested that procyanidin extracts of grape seed can increase the cell redox status through the pathways of glutathione metabolism [16]. Grape seed procyanidins have been shown to protect mouse brain cells from ethanol-induced damage [17]. In fact, the consumption of proanthocyanidin grapes in hamsters of 50 mg/kg and 100 mg/kg decreased foam-cell growth by 50% and 63%, respectively [18].

Anti-Inflammatory effects

In a research, rats fed high-fat foods supplemented with grape seed procyanidins (345 mg/kg) of feed for 19 weeks had lower plasma C-reactive protein levels (CRP, a marker of inflammation) than untreated rats, suggesting that this decrease is due to the efficiency of grape seed procyanidins [19]. Moreover, CRP mRNA expression in liver and mesenteric white adipose tissue (WAT) has decreased [20]. Concurrently, Petrescu., *et al*. [20] highlighted that expression of the pro-inflammatory cytokine tumor necrosis factor alpha (TNF-alle) and interleukin (IL-6) component was reduced in the mesenteric white adipose tissue of rats fed a high-fat diet supplemented with grape procyanidins. Moreover, pro-inflammatory mediator concentrations are shown to be extremely resistant to insulin in chronic conditions, including diabetes and obesity [21].

Grape seed procyanidin extracts were shown to lower IL-6 and monocyte chemoattractant protein (MCP-1) production following inflammatory stimulation of pre-treated cell lines of human adipocytes (SGBS) [22]. Procyanidin from grape seed extracts similarly boosts adiponectin activity and reduces IL-6 [23]. Epidermal growth factor 1 module-like mucin-like expression is reduced, which correlates with less macrophage infiltration into WAT in response to grape seed procyanidin extracts [12]. Consumption of procyanidin-rich foods on a daily basis may therefore aid in the prevention of low-grade inflammation situations in obesity, such as those marked by the accumulation of macrophages in WAT and the atypical production of cytokines.

Anti-Diabetic effect

Previous studies have shown that the oligomer structures present in procyanidin grape seed extract stimulate the insulin receptor by associating and inducing autophosphorylation [24]. In addition, oligomeric complexes derived from grape seed fragments have been found to stimulate glucose absorption by interacting with and increasing insulin receptor autophosphorylation [25]. Moreover, procyanidin grape seed had a significant long-term effect on glucose homeostasis, as demonstrated by the enhanced homeostasis model insulin resistance indicator supported by Glut4, Irs1, and Pparg2 down-regulation in mesenteric white adipose tissue in *Wister* female rats after 30 days of treatment with 25 mg procyanidin extraction/Kg body weight per day [26].

Anti-Cholesterol effect

Grape seed extract supplementation significantly altered the methotrexate (MTX) induced alterations in the superoxide dismutase and catalase concentrations of rats [27]. Moreover, combination treatment with grape seed extract may provide protection against the oxidative damage induced by the cytotoxic chemical therapeutic agent MTX [27]. An experiment approved that the malondialdehyde-modified LDL (MDA-LDL) levels were significantly lower in the 400 mg grape seed extract patient group post-experiment compared to pre-experiment levels [28]. As a result, controlling the MDA-LDL level may be included in efforts to prevent or reverse atherosclerosis, leading to more effective regulation of arteriosclerosis pathogenesis [29]. It was found by Al-Otibi., *et al*. [30] that grape seed extracts reduce oxidative stress by increasing antioxidants in the blood and preventing lipid hydroperoxide levels from going up. This study involved eight adult men who participated in a study that looked at what happened after they ate a high-fiber meal supplemented with 300 milligrams of proanthocyanidin-rich grape seed oils. Thus, it strengthens the body's defenses against oxidative modification of LDL cholesterol.

Anti-Microbial effect

Vitis vinifera seeds have shown promise as potentially pathogenic bacteria due to their high polyphenol content [31]. Extracts from grape seeds were shown to be effective against different bacterial species such as *Bacillus cereus* (*B. cereus*), *Bacillus cereus* (*B. cereus*), *Bacillus subtilis* (*B. subtilis*), *Staphylococcus aureus* (*S. aureus*), *Bacillus coagulans* (*B. coagulans*), *Escherichia coli* (*E. coli*), and *Pseudomonas aeruginosa* (*P. aeruginosa*) [15]. Furthermore, research shows that an oil extract from grape seeds effectively inhibits both gram-positive and gram-negative bacteria [31]. In the same consequence's experiments, Ghouila., *et al*. [32] conducted a study demonstrating that grape seed extracts had antibacterial efficacy against *Micrococcus luteus*, *S. aureus*, *E. coli*, *P. aeruginosa*, *Aspergillus niger*, and *Fusarium oxysporum*. Further studies showed that grape seed extracts significantly reduced the growth of *Helicobacter pylori* (*H. pylori*) in test tubes [33]. Although total phenolic content was higher in grape seed extracts, grape skin extracts were shown to be more efficient than seed extracts in inhibiting *H. pylori* growth [34]. For this specific purpose, the component and consistency of phenolics can have an impact on their anti-*H. pylori* effectiveness [35].

Anti-Tumor effect

The extraction of grape seeds also demonstrated anti-cancer benefits [36]. Using grape seed extracts, researchers have shown exceptional outcomes in treating human cancer cells, this includes colorectal cancer, ovarian carcinoma, lung tumors and prostate lumps [37]. Indeed, it is consequently claimed that medical practices can benefit from the use of grape seed extract supplements as an effective anti-carcinogenic treatment [37].

Grape Seed Oil: Constituents and Health Benefits

The interest in grape seed oil as a functional food item has grown primarily because of its significant concentrations of hydrophilic constituents such as phenolic content and lipophilic compounds like vitamin E, unsaturated fatty acids, and phytosterols [38].

Vitis vinifera seed oil constituents

Vitis vinifera seed oil's chemical make-up is linked to the environmental circumstances in which the grape vine variety was grown and the maturity level of its seeds. The pleasant aroma and flavors of grape seed oil have led to a rise in its use as an ingredient in unique ingredients [12].

PHYTOSTEROLS	mg/kg/OIL
Cholesterol	nd–0.10
Cholestanol	nd
Brassicasterol	0.6–0.9
2,4 methylencholesterol	nd–0.18
Campesterol	0.1–9.3
Campestanol	–
Stigmasterol	10.2–10.8
Δ-7 campesterol	0.16–0.27
Δ-5 2,3 stigmastadienol	–
Clerosterol	0.90–0.94
β-sitosterol	66.6–67.4
Sitostanol	3.92–4.70
Δ-5 avenasterol	1.98–2.09
Δ-5 2,4 stigmastadienol	0.41–0.47
Δ-7 estigmastenol	1.99–2.30
Δ-7 avenasterol	0.98–1.10

Figure 4: Main phytosterol content of *Vitis vinifera* seed oil [12].

Grape seed oil is typically extracted using either physical extraction or organic solvents. Nevertheless, the yield through mechanical extraction is lower, but the quality of the commodity is in higher demand. A better return is achieved by removing organic solvents; however, this process necessitates distilling the solvents out first, and the finished product still has some solvent residue. In addition, the supercritical method is being studied as a possible future oil extraction technique because it has the potential to achieve yields comparable to those achieved by mechanical and organic solvent extractions while producing oil of a higher grade. Furthermore, oil is extracted from the seeds of the vine *Vitis vinifera* using a cold pressing method that does not include the use of chemicals or heat. In general, the effectiveness of cold pressing is lower than that of more conventional solvent extractions; nevertheless, more bioactive components are preserved, and the oil is safer because it contains no solvents (figure 4) [10,12].

More recently, researchers highlighted that the many components, such as flavonoids, carotenoids, phenolics, tannins, and stilbenes, found in *Vitis vinifera* grain seed oil are quite impressive [39]. In addition, *Vitis vinifera* seed oil contains 59-360 mg gallic acid equivalents per kilogram of phenols, which are linked to a variety of bioactivities but are best recognized for being powerful antioxidants [40]. Moreover, many different polyphenols may be found in *Vitis vinifera* seed oil, but the most common ones include catechins, epicatechins, trans-resveratrol, and procyanidin B1 [39]. Furthermore, researchers have observed that the total amount of polyphenols extracted by cold-pressing *Vitis vinifera* seed oil is around 2.9 mg/kg, with only trace amounts of catechin (1.3 mg/kg) and trans-resveratrol (0.3 mg/kg) [40].

Whenever it concerns noticeably cooler grape seed oils, linoleic acid (LIA) makes up around 85.0% of total fatty acids (FA). LIA is the foundation of polyunsaturated FA (PUFA) [41]. Beyond that, however, the fatty acid structure of grape oil varies between different grape species [42]. As may be predicted, given the overall amount of phenolic compounds, the polyphenol quality in *Vitis vinifera* seed oil is grossly insufficient. This is likely due to the hydrophilic nature of polyphenols and the poor solubility of clear oil in grape seed manufacturing [40]. When compared, turbid oil collected during the oil process of recovery (squeezed remnants) showed high levels of polyphenols, and its molecules are a particularly rich source of antioxidant polyphenolic chemicals [40].

Vitis vinifera seed oils have a higher concentration of tocotrienols (non-saturated forms of vitamin E) than tocopherols and other components [43]. For In addition, researchers couldn't find any gamma-tocopherol, delta-tocopherol, delta-tocotrienol, or delta-tocotrienol isomers in the grape seed extract, however, total vitamin E, alpha-tocopherol, and alpha-tocopherol equivalents were found in the greatest concentration in grape seed oil [44]. In particular, the vitamin E content of *Vitis vinifera* seed oil is rather high, varying between 1 and 53 milligrams/100 grams of extract oil with a tocopherol content of 148-358, which is greater than other oil extract such as sunflower seed and olive [45]. Whereas grapes may be grown in nearly every region, *Vitis vinifera* oil's vitamin E content is highly temperature-dependent [46]. More recently, many researchers highlighted that vitamin E, which is abundant in *Vitis vinifera* seed oil, is accountable for numerous of the oil's health benefits, including its antioxidant, neuroprotective, and antitumoral properties [47].

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