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# A COMPLETE ANALYSIS OF THE HEALTH BENEFITS, PHYTOCHEMICAL COMPOSITIONS, AND INDUSTRIAL USE OF POLYHYDROXYFLAVAN OLIGOMERS IN GRAPE SEEDS (VITIS VINIFERA)

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## ABSTRACT

Polyhydroxylflavan oligomers are polymers that can be found in abundance in grape seeds. Due to its conjugated and colonic metabolites, grape seeds have been shown to have significant health benefits. A reciprocal interaction between grape seed polyhydroxyflavan oligomers and the gut flora is possible. Particularly, it has been shown by a number of in vitro and in vivo investigations that grape seed polyhydroxyflavan oligomers seem to have pharmacological effects. They may have anti-oxidative damage defense as well as anti-diabetic, anti-cholesterol, and anti- platelet properties. With an emphasis on investigations of the phytochemical components, pharmacological characteristics, and industrial uses of grape seeds, this review aims to provide an overview of the existing literature on grape seed proanthocyanidins, which are composed of polyhydroxyflavan oligomers.

**Keywords:** Grape Seeds, Colonic Metabolites, Oligomers, Investigations, Phytochemical Components.

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## 1. INTRODUCTION

Among the most widely produced fruit crops worldwide are grapes (*Vitis spp*.). Every year, over 75 million tons are produced, with 41% growing in Europe, 29% in Asia, and 21% in the US. Their harvesting takes place in temperate regions with typical climatic patterns of warm summers and mild winters [1]. Grapes are used to make wine from about 50% of them, fresh fruit from about 1/3 of them, and refined grape seed oil, dried grapes (raisins), juice, jam, and vinegar from the remaining grapes [2]. A fruit with a high calorie content (65 kcal/100 g), a low glycemic index, and one of the highest carbohydrate contents (17 g/100 g) is the grape. Grapes are one of the best sources of polyphenols and a great source of manganese and potassium. They are also a good source of vitamins B6, C, and thiamine.

Ancient Greek and Roman civilizations used grapes to make wine [3]. For every kilogram of crushed grapes used in the winemaking process, more than 0.3 kg of solid byproducts are created [4]. Approximately two thirds of the solids are composed of grape marc, the primary byproduct [4]. 50% of grape marc is made up of grape skins, 25% are seeds, and 25% are stems [4].

As such, grape seeds are an industrial byproduct of the wine-making process itself. Antioxidant chemicals found in grape seeds range from 38 to 52% on a dry matter basis [6, despite being a rather affordable supply [5]. If no extracts are obtained from the grape seeds, they are considered waste [7]. The industry produces around 10–12 kg of grape seeds for every 100 kg of wet residue. There are extremely little amounts of low molecular weight proanthocyanidins. The greater molecular weight proanthocyanidins are linked to astringency and tanning characteristics. Concise tannins, which are polymers or oligomers of flavan-3-ol molecules, are also known as catechin tannins or proanthocyanidins and are insoluble in water. [8].

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Up till Dec, 2023, a PubMed, Medline (OvidSP), and Google Scholar electronic literature search was done. From references found in the retrieved papers, more articles were found. The following search terms were combined: phytochemical, antioxidant, anthocyanins, proanthocyanidins, grape, grape seed, and pharmacological. Only English-language publications on the pharmacological characteristics and phytochemical composition of grape seeds were included in the search. Studies that involve human beings will be prioritized for this examination.

## 2. HISTORICAL PERSPECTIVE

TIn Southwest Asia, the area around the Caspian Sea is thought to be the grape's native habitat. It was in the early 1900s when research into the bioactive elements of grape seed extracts began. When researching on the segregation of vitamin C, 1937 Nobel Prize winner Albert Szent-Gyorgyi [12] found flavonoids, which he dubbed “vitamin P”. Following this, Professor Jacques Masquelier hypothesized that since pine bark displayed effects similar to those of ascorbate, it had to include flavonoids and vitamin C. He called these flavonoids "pycnogenols," a term that is no longer used in science but is instead used to identify proanthocyanidins that were extracted from the bark of French maritime pines.

In 1947, Masquelier developed and received a patent for a method of separating proanthocyanidins from oligomeric grape seeds [13]. He also noted that bioflavonoids obtained from grape seeds seemed to have a higher concentration and antioxidant action than those derived from pine bark [14]. Tannins were defined by [15] in the decade that followed the 1952 publication of the name "flavonoids" by Geissmann and Hinreiner.

## Pharmacological Properties

Grape seeds contain significant levels of proanthocyanidins, which have drawn consumer attention due to possible health benefits [16]. Strong antioxidant action, scavenging of reactive oxygen and nitrogen species, immunological function modulation, platelet activation, and generating nitric oxide (NO) release from endothelium have all been demonstrated in vitro by proanthocyanidins [16]. Proanthocyanidins also stop low-density lipoprotein (LDL) cholesterol from rising in concentration and slow the development of atherosclerosis [17].

## Anti-Diabetic

According to Montagut *et. al.,* [18], Wister female rats given a daily dose of 25 mg grape seed procyanidin extract/kg body weight for 30 days showed improvements in the insulin resistance index and the homeostasis model assessment. Additionally, the mesenteric white adipose tissue (WAT) showed downregulation of the primers Glut4, Irs1, and Pparg2,

indicating that grape seed procyanidin has a long-term beneficial impact on glucose homeostasis. Another work by Montagut *et.al.,* [19] showed that the grape seed procyanidin extracts' oligomeric structures stimulated the absorption of glucose by engaging with the insulin receptor and causing its autophosphorylation.

## Anti-Platelet

It was observed that grape seed extracts (5–50 µg/mL) reduced platelet adhesion, aggregation, and superoxide anion generation [20]. Grape seed extracts were also shown to display anti-platelet effect. The authors additionally discovered that grape seed extract reduced platelet processes more effectively than the pure resveratrol solution.

## Anti-Cholesterol

Grape seed extracts reduce postprandial oxidative stress by increasing the plasma antioxidant concentration and preventing the increase of lipid hydroperoxides, according to a study by Natella *et. al.,* [21] that looked at the effects of supplementing a single high-fat meal with 300 mg of proanthocyanidin-rich grape seed extracts in eight male adults. This enhances the ability of LDL activate serum paraoxonase (PON), preventing the rise in lipid peroxides that occurs after a meal. One enzyme linked to high-density lipoprotein (HDL) is serum paraoxonase, which reduces LDL oxidation by hydrolyzing lipoprotein peroxides [22].

## Anti-Inflammation

Rats administered grape-seed procyanidin extracts showed decreased body weight and plasmatic systemic indicators of TNF- and CRP, according to Terra *et.al.,* [23]. Furthermore, procyanidin extracts from grape seeds lowered IL-6 and enhanced the expression of adiponectin. Reduced expression of mucin-like receptor 1 (EMR1), a particular marker of macrophage F4/80, is also associated with grape seed procyanidin extracts, indicating a decrease in macrophage infiltration of WAT. Thus, frequent ingestion of foods high in procyanidins may help prevent obesity-related low- grade inflammatory disorders marked by aberrant cytokine production and macrophage buildup in WAT.

According to Pinent *et.al.,*'s study [24], which examined the impact of grape seed procyanidins on glucose metabolism in streptozotocin-induced diabetic rats, grape seed procyanidins promoted the absorption of glucose in L6e9 myotubes and 3T3-L1 adipocytes in a way that was dose-dependent. Furthermore, procyanidins found in grape seeds induced the translocation of glucose transported-4 to the plasma membrane. Procyanidins may have actions similar to those of insulin in cells that are susceptible to the hormone. Thus, all of these results pointed to the inhibition of mRNA levels by procyanidins in grape seeds and the reduction in the risk of diseases linked to obesity and high-fat diets.

## Anti-Aging

Balu *et.al.,* [25] conducted a study on male albino rats of the Wister strain to examine the impact of grape seed extracts on the accumulation of oxidative DNA damage associated with aging. The results showed that the extracts prevented the build-up of age-related oxidative DNA damage products, such as 8-hydroxy-20-deoxyguanosine (8-OHdG) and DNA protein cross-links, in the spinal cord and in different brain regions, such as the striatum, cerebral cortex, and hippocampus.

A different study by Balu *et.al.,* [26] found that in male albino rats given grape seed extract supplements, lipid peroxidation and antioxidant defenses returned to normal. This suggests that grape seed extracts could be used to enhance antioxidant status and reduce the incidence of lipid peroxidation caused by free radicals in the aged rats' central nervous systems.

## Anti-Tumour

Anti-tumor activities have also been demonstrated by grape seed extracts. Numerous experiments on human colorectal carcinoma, head and neck squamous cell carcinoma, and prostate cancer cells have produced encouraging results [27]. Consequently, it is proposed that adding grape seed extract supplements could function as a potent anti-tumor agent in clinical situations.

## Other Pharmacological Properties

Grape seed extracts decreased brain weight loss from 20% in vehicle pups to 3% in treated pups ($p < 0.01$), according to a study by Feng *et.al.,* [28]. When measuring the amount of brain damage in pups with neonatal hypoxia ischemic brain injury, the loss of brain weight was utilized. Furthermore, the cortical, hippocampal, and thalamus histopathologic brain scores were all improved by grape seed extract. The authors proposed that lipid peroxidation might be inhibited and hypoxic ischemic brain injury could be decreased by using grape seed extract treatment.

## Toxicity

Additionally, after consuming pills containing 200 mg and 400 mg of grape seed extract, participants' physiological and clinical laboratory tests showed no aberrant alterations, according to Sano *et.al.,* [29]. Furthermore, these subjects' urine sedimentation tests yielded no troubling results, indicating that the 200 and 400 mg grape seed extract pills are safe to take.

## Industrial Applications

According to Mielnik *et.al.,* [30], adding grape seed extracts prior to cooking greatly enhanced the lipid stability of turkey breast meat during the cooking process and while being chilled. The study examined the effects of four different concentrations of grape seed extracts (i.e., 0.0, 0.4, 0.8, and 1.6 g/kg) on cooked turkey breast meat. As the concentration of antioxidant was raised from 0.4 g/kg to 1.6 g/kg, the authors found that grape seed extract was more effective at preventing oxidation.

Consequently, it is hypothesized that grape seed extracts may be a very powerful antioxidant that prevents cooked turkey meat from oxidizing lipids while it is being chilled. Similarly, when grape seed extracts were added during chilled storage, Brannan [31] similarly showed a decrease in the indicators of lipid oxidation and sensory ratings for important qualities in ground chicken. According to research by Brannan and Mah [32], 0.1% grape seed extract can successfully prevent the development of primary oxidation products (like hexanal and lipid hydroperoxides) and secondary oxidation products (like TBARS) in meat systems that are either raw or cooked and are stored in the refrigerator or freezer. According to certain theories, the in vivo mechanism of grape seed extract antioxidant activity involves oxygen radical scavenging [34], intransitive stress inhibition [33], and nitric oxide enzymatic synthesis promotion [34].

## CONCLUSIONS AND FUTURE RESEARCH

The antioxidant potential of grape seeds is high. In addition to their anti-diabetic, anti-cholesterol, and anti-platelet qualities, they may offer protection against oxidative harm to health. It is believed that the polyphenols found in grape seeds are primarily responsible for their health advantages. Numerous meta-analyses have demonstrated the possible health advantages of dietary polyphenols on major chronic non-communicable diseases. Thus, more research is needed to screen for specific polyphenol elements in grape seeds that have been shown to have health benefits.

This is because it is only until the composition of grape seeds is accurately identified and standardized that a cause-and-effect relationship between the consumption of grape seeds and its health consequences can be established. The impacts of incorporating these advantageous polyphenol components from grape seeds into food systems utilizing cutting-edge technology also require a great deal of research. More investigation is required to determine grape seed extract's function as an antibacterial agent in food safety as well as its efficacy in the food ecosystem.

## CONFLICTS OF INTEREST

None.

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## REFERENCES

Brannan, R.G. Effect of grape seed extract on descriptive sensory analysis of ground chicken during refrigerated storage. Meat Sci. 2009, 81, 589–595.

Brannan, R.G.; Mah, E. Grape seed extract inhibits lipid oxidation in muscle from different species during refrigerated and frozen storage and oxidation catalyzed by peroxynitrite and iron/ascorbate in a pyrogallol red model system. Meat Sci. 2007, 77, 540–546.

Roychowdhury, S.; Wolf, G.; Keilhoff, G.; Bagchi, D.; Horn, T. Protection of primary glial cells by grape seed proanthocyanidin extract against nitrosative/oxidative stress. Nitric Oxide 2001, 5, 137–149.

Bagchi, D.; Bagchi, M.; Stohs, S.J.; Das, D.K.; Ray, S.D.; Kuszynski, C.A.; Joshi, S.S.; Pruess, H.G. Free radicals and grape seed proanthocyanidin extract: Importance in human health and disease prevention. Toxicology 2000, 148, 187–197.

Fine, A. M. (2000). Oligomeric proanthocyanidin complexes: History, structure, and phytopharmaceutical applications. Alternative Medicine Review, 5(2), 144–151.

Frank, D. N., Amand, A. L. S., Feldman, R. A., Boedeker, E. C., Harpaz, N., & Pace, N. R.

(2007). Molecular-phylogenetic characterization of microbial community imbalances in human inflammatory bowel diseases. Proceedings of the National Academy of Sciences, 104(34), 13780–13785.

Estreicher, S.K. Wine. In The Encyclopedia of Ancient History; Bagnall, R.S., Brodersen, K., Champion, C.B.,Erskine, A., Huebner, S.R., Eds.; JohnWiley & Sons, Inc.: Oxford, UK, 2013; pp. 1–5.ISBN 9781444338386.

Duba, K.S.; Fiori, L. Supercritical CO2 extraction of grape seed oil: Effect of process parameters on the extraction kinetics. J. Supercrit. Fluids 2015, 98, 33–43.

Cádiz-Gurrea, M.; Borrás-Linares, I.; Lozano-Sánchez, J.; Joven, J.; Fernández-Arroyo, S.; Segura- Carretero, A. Cocoa and grape seed byproducts as a source of antioxidant and anti- inflammatory proanthocyanidins. Int. J. Mol. Sci. 2017, 18, 376.

Maier, T.; Schieber, A.; Kammerer, D.R.; Carle, R. Residues of grape (Vitis vinifera L.) seed oil production as a valuable source of phenolic antioxidants. Food Chem. 2009, 112, 551–559.

Matthäus, B. Virgin grape seed oil: Is it really a nutritional highlight? Eur. J. Lipid Sci. Technol. 2008, 110, 645–650.

Serrano, J., Puupponen-Pimiä, R., Dauer, A., Aura, A. M., & Saura-Calixto, F. (2009). Tannins: Current knowledge of food sources, intake, bioavailability and biological effects. Molecular Nutrition & Food Research, 53(S2), S310–S329.

Sun, B.; Spranger, M.I. Review: Quantitative extraction and analysis of grape and wine proanthocyanidins and stilbenes. Ciência e Técnica Vitivinícola 2005, 20, 59–89.

He, F.; Liang, N.;Mu, L.; Pan, Q.;Wang, J.; Reeves,M.J.; Duan, C. Anthocyanins and their

variation in red wines I. Monomeric anthocyanins and their color expression. Molecules 2012, 17, 1571–1601.

Yilmaz, Y.; Toledo, R.T. Health aspects of functional grape seed constituents. Trends Food Sci. Technol. 2004, 15, 422–433.

Szent-Györgyi, A. (1936). Vitamin P: Flavonols as vitamins. Nature, 138(3479), 27. Tan, R.-R., Zhang, S.-J., Li, Y.-F., Tsoi, B., Huang, W.-S., Yao, N., ... Tang, L.-P. (2015).

Fine, A. M. (2000). Oligomeric proanthocyanidin complexes: History,structure, and phytopharmaceutical applications. Alternative Medicine Review, 5(2), 144–151.

Masquelier, J. (1991). Historic Note on OPC, Procyanidines de France. In. Martillac,France.

Bate-Smith, E., & Swain, T. (1962). Comparative biochemistry. Eds. Mason, HS, Florkin, M, 3, 764.

Varzakas, T.; Zakynthinos, G.; Verpoort, F. Plant food residues as a source of nutraceuticals and functional foods. Foods 2016, 5, 88.

Quesada, H.; del Bas, J.M.; Pajuelo, D.; Diaz, S.; Fernandez-Larrea, J.; Pinent, M.; Arola, L.; Salvado, M.J.; Blade, C. Grape seed proanthocyanidins correct dyslipidemia associated with a high-fat diet in rats and repress genes controlling lipogenesis and VLDL assembling in liver. Int.journal of Obes. 2009, 33, 1007–1012.

Montagut, G.; Bladé, C.; Blay, M.; Fernández-Larrea, J.; Pujadas, G.; Salvadó, M.J.; Arola, L.; Pinent, M.; Ardévol, A. Effects of a grapeseed procyanidin extract (GSPE) on insulin resistance. J. Nutr. Biochem. 2010, 21, 961–967.

Montagut, G.; Onnockx, S.; Vaqué, M.; Bladé, C.; Blay, M.; Fernández-Larrea, J.; Pujadas, G.;Salvadó, M.J.; Arola, L.; Pirson, I.; et al. Oligomers of grape-seed procyanidin extract activate the insulin receptor and key targets of the insulin signaling pathway differently from insulin. J. Nutr. Biochem. 2010, 21, 476–481.

Olas, B.; Wachowicz, B.; Tomczak, A.; Erler, J.; Stochmal, A.; Oleszek, W. Comparative anti- platelet and antioxidant properties of polyphenol-rich extracts from: Berries of Aronia melanocarpa, seeds of grape and bark of Yucca schidigera in vitro. Platelets 2008, 19, 70–77.

Natella, F.; Belelli, F.; Gentili, V.; Ursini, F.; Scaccini, C. Grape seed proanthocyanidins prevent plasma postprandial

oxidative stress in humans. J. Agric. Food Chem. 2002, 50, 7720–7725.

Aviram, M.; Rosenblat, M.; Bisgaier, C.L.; Newton, R.S.; Primo-Parmo, S.L.; La Du, B.N. Paraoxonase inhibits high-density lipoprotein oxidation and preserves its functions. A possible peroxidative role for paraoxonase. J. Clin. Investig. 1998, 101, 1581–1590.

Terra, X.; Pallarés, V.; Ardèvol, A.; Bladé, C.; Fernández-Larrea, J.; Pujadas, G.; Salvadó, J.; Arola, L.; Blay, M. Modulatory effect of grape-seed procyanidins on local and systemic inflammation in diet- induced obesity rats. J. Nutr. Biochem. 2011, 22, 380–387.

Pinent, M.; Blay, M.; Bladé, M.C.; Salvadó, M.J.; Arola, L.; Ardévol, A. Grape seed-derived procyanidins have an antihyperglycemic effect in streptozotocin-induced diabetic rats and insulinomimetic activity in insulin-sensitive cell lines. Endocrinology 2004, 145, 4985–4990.

Balu, M.; Sangeetha, P.; Murali, G.; Panneerselvam, C. Modulatory role of grape seed extract on

age-related oxidative DNA damage in central nervous system of rats. Brain Res. Bull. 2006, 68, 469–473.

Balu, M.; Sangeetha, P.; Haripriya, D.; Panneerselvam, C. Rejuvenation of antioxidant system in central nervous system of aged rats by grape seed extract. Neurosci. Lett. 2005, 383, 295–300.

Park, S.Y.; Lee, Y.H.; Choi, K.C.; Seong, A.R.; Choi, H.K.; Lee, O.H.; Hwang, H.J.; Yoon, H.G.

Grape seed extract regulates androgen receptor-mediated transcription in prostate cancer cells through potent anti-histone acetyltransferase activity. J. Med. Food 2011, 14, 9–16.

Feng, Y.; Liu, Y.M.; Fratkins, J.D.; LeBlanc, M.H. Grape seed extract suppresses lipid peroxidation and reduces hypoxic ischemic brain injury in neonatal rats. Brain Res. Bull. 2005,66,120–127.

Sano, A.; Uchida, R.; Saito, M.; Shioya, N.; Komori, Y.; Tho, Y.; Hashizume, N. Beneficial effects of grape seed extract on malondialdehyde-modified LDL. J. Nutr. Sci. Vitaminol. 2007, 53, 174–182.

Mielnik, M.B.; Olsen, E.; Vogt, G.; Adeline, D.; Skrede, G. Grape seed extract as antioxidant in cooked, cold stored turkey meat. Food Sci. Technol. 2006, 39, 191–198.