ACADEMICIA: An International Multidisciplinary Research Journal
ISSN: 2249-7137 Vol. 14 Issue 12, December, 2024 SJIF 2022= 8.252
A peer reviewed journal

A REVIEW ON PHYTOCHEMICAL CONSTITUENTS, ANTI-OXIDANTS AND ANTI-DIABETIC ACTIVITY OF GRAPE (VITIS VINIFERA) SEED

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DOI: 10.5958/2249-7137.2024.00024.0

ABSTRACT:

Grape seed, a byproduct of the grape industry, is recognized for its high content of bioacztive polyphenols, particularly proanthocyanidins, which exhibit potent antioxidant and antidiabetic effects. These compounds have demonstrated significant potential in combating oxidative stress and managing blood glucose levels, two key factors implicated in the development and progression of diabetes mellitus. This review highlights current research on the antioxidant and antidiabetic properties of grape seed extract (GSE). Antioxidant activity in GSE is primarily attributed to its ability to scavenge free radicals, reduce oxidative stress, and prevent cellular damage. In the context of diabetes, GSE compounds are noted to improve insulin sensitivity, lower blood glucose, and inhibit carbohydrate-digesting enzymes, which together aid in controlling blood sugar levels. Both in vitro and in vivo studies indicate that GSE may help protect pancreatic beta-cells from oxidative damage, potentially preserving their function. These findings suggest that grape seed extract could serve as a promising natural supplement for the prevention and management of diabetes and related oxidative stress. However, further clinical studies are warranted to establish optimal dosages and long-term safety in human populations.

KEYWORDS: *Antioxidants, Proanthocyanidins, Oxidative Stress,Antidiabetic Activity, Insulin Sensitivity, Blood Glucose Control, Free Radicals, Polyphenols.*

INTRODUCTION:

Grapes (*Vitis vinifera*), one of the most widely cultivated fruit crops globally, are valued not only for their delicious flavor but also for their therapeutic potential. Among the various parts of the grape, grape seeds have gained significant attention in recent years due to their high content of polyphenolic compounds, particularly proanthocyanidins.Antioxidant and antidiabetic qualities

are just two of the many health advantages that these natural antioxidants provide. A tiny but powerful source of minerals and antioxidants, grape seed is made from the seeds of grapes, often the common grape *Vitis vinifera.*(Dan-Dan Zhou,et ,al.,2022) It has drawn notice due to its high concentration of potent substances that provide a number of health advantages, including as flavonoids, polyphenols, and proanthocyanidins. Grape seeds are frequently leftovers from the production of wine and are turned into supplements, extracts, and oil that are utilized in the food, cosmetic, and medical sectors.The seeds are also a source of healthy fatty acids and can be cold-pressed into grape seed oil, known for its light flavor and high smoke point, ideal for cooking and salad dressings. This oil is rich in vitamin E, which benefits skin health, and linoleic acid, an essential omega-6 fatty acid. (Muhamad Insanu ,et,*al*.,2022).The ability of grape seed extract (GSE) to neutralize free radicals, lower oxidative stress, and prevent cellular damage is primarily responsible for its antioxidant activity. This is important for managing a number of chronic diseases.

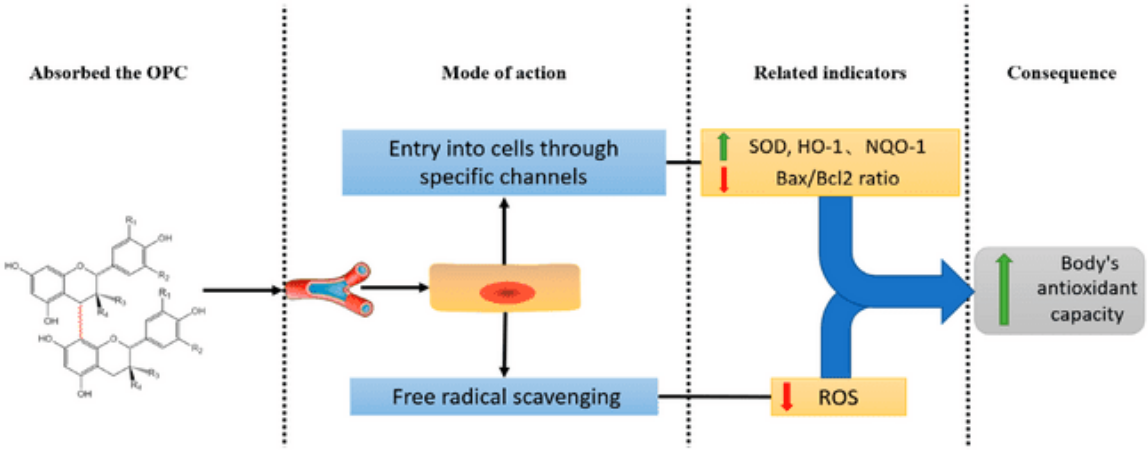
2. Biochemical Composition of Grape Seed

The biochemical structures of grape seed components, especially proanthocyanidins, flavonoids, and phenolic acids, are crucial for understanding their antioxidant and health-promoting properties. Below are the key components of grape seeds, their chemical structures, and some references for further reading.

2.1. Proanthocyanidins (Oligomeric Proanthocyanidins - OPCs)

Proanthocyanidins are flavonoid compounds composed of catechins or epicatechins. They are often found as dimers, trimers, or larger oligomers in grape seeds.The most prevalent polyphenols in grape seeds, oligomeric proanthocyanidin complexes (OPCs), are responsible for their powerful antioxidant properties.Basile, M., et al. (2001) Because of their potent ability to neutralize free radicals, proanthocyanidins can stop oxidative damage to tissues and cells. They lower blood pressure, increase blood circulation, and prevent cholesterol oxidation, which is associated with a lower risk of atherosclerosis. Because OPCs can strengthen collagen and elastin and protect against UV-induced skin damage, they are used in skin care products.

Structure of Proanthocyanidin (Dimer): Chemical formula of catechin: C15H14O6

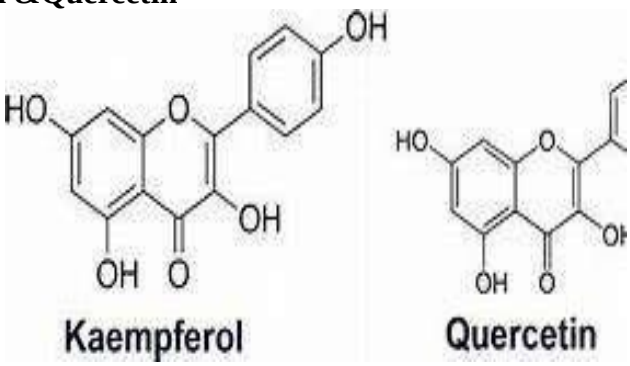


2.2 Flavonoids

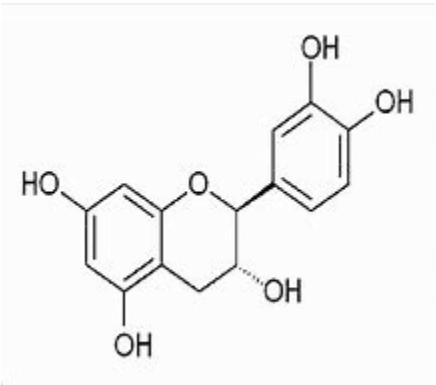
Polyphenolic substances called flavonoids play a major role in grape seeds' antioxidant potential. Kaempferol and quercetin are important flavonoids found in grape seeds. These flavonoids have

antioxidant qualities and are comparable to those in chocolate and green tea. Conditions like arthritis and cardiovascular illnesses can benefit from flavonoids' ability to control inflammatory pathways. (D'Archivio, M., et al. (2010))According to recent studies, epicatechins and catechins may shield brain tissue, which could help treat neurodegenerative diseases. Certain flavonoids included in grape seeds have the ability to stop bacteria from growing, which may boost immunity and encourage a balanced microbiome. Including the well-known health benefits of myricetin and quercetin-3-β-D-glucoside.(Roychowdhury, et *al*., (2001))

Structure: Kaempferol &Quercetin



2.3. Tannins are polyphenolic chemicals that give many plant-based foods and drinks their astringent flavor. Gallo tannins and ellagitannins are examples of hydrolysable tannins that give grape seeds their astringent flavor. Tannins, like other polyphenols, aid in scavenging free radicals and shielding cells from harm.(Li, S., et *al.*, (2009)) According to studies, tannins may have anti-cancer properties by causing apoptosis, or programmed cell death, and preventing the proliferation of cancer cells. By influencing gut flora, tannins may promote gut health by enhancing digestion and lowering gastrointestinal tract inflammation.

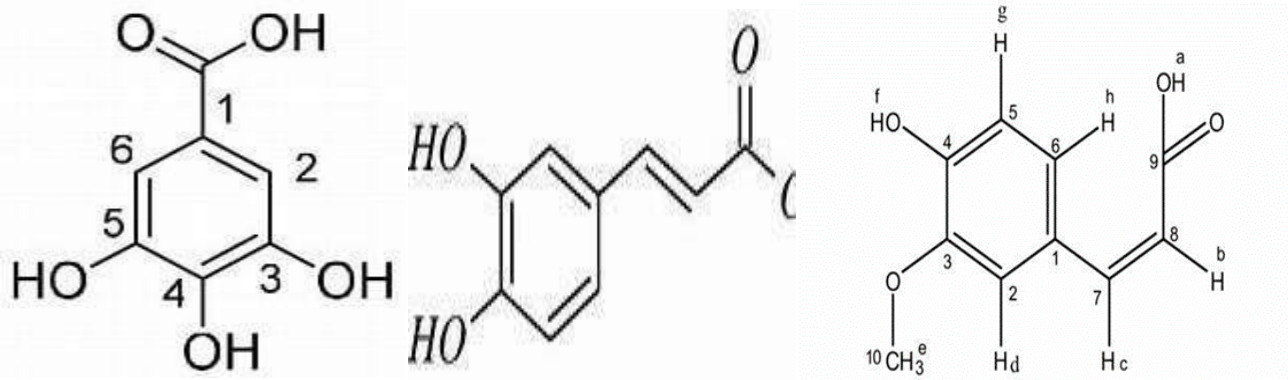


4.4. Phenolic Acids (Gallic Acid, Caffeic Acid, Ferulic Acid)

Phenolic acids are another class of antioxidant compound in grape seeds, contributing to their broad-spectrum health benefits.These compounds help prevent oxidative stress and reduce inflammation in the body, which are linked to chronic diseases.Studies have shown that phenolic acids can protect the liver from toxin-induced damage.Gallic acid, in particular, has shown promising anti-cancer effects in lab studies, with the potential to inhibit tumor growth.Gallic acid

is a phenolic compound commonly found in grape seeds. It contributes to the seeds' antioxidant and anti-inflammatory properties. (MontagutG,et.*al* 2010)

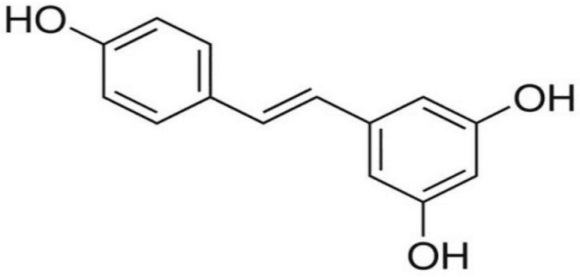
Structure of Gallic Acid **Caffeic Acid** **Ferulic Acid**



2.5. Resveratrol

Resveratrol, which has significant health advantages, is found in modest amounts in grape seeds but is more prevalent in grape skins.Resveratrol is well known for supporting the longevity and health of cells. It causes certain aging-related cellular proteins (sirtuins) to become active.By decreasing inflammation and shielding blood vessels from harm, this substance enhances heart health.In animal models, resveratrol has been investigated for its capacity to suppress tumor formation and stop the growth of cancer cells.

Resveratrol chemical structure

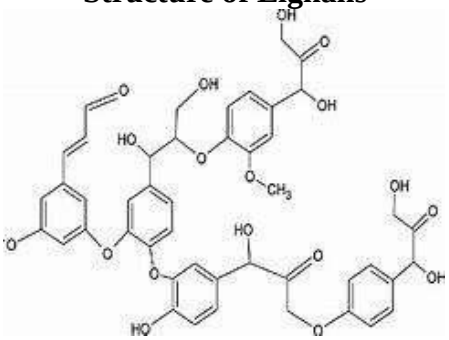


2.6. Lignans

Lignans are a class of phytoestrogens, plant compounds with estrogen-like effects, contributing to hormone balance.Lignans can help modulate estrogen activity in the body, potentially benefiting conditions related to hormone imbalance, such as menopausal symptoms.They help reduce oxidative stress and inflammation, supporting cardiovascular and overall health.Lignans

have shown anti-cancer effects, particularly in hormone-sensitive cancers like breast cancer, by modulating hormone metabolism and activity.

Structure of Lignans



3.1. Antioxidant Activity of Grape Seed Extract

The seeds of *Vitis vinifera* grapes are used to make grape seed extract (GSE), which is high in bioactive substances, mostly polyphenols including proanthocyanidins, flavonoids, and other antioxidants. These substances have garnered interest due to their potential in the treatment of diabetes and oxidative stress. Here's a closer look at how GSE demonstrates these advantageous qualities:

The antioxidant and antibacterial qualities of grape (Vitis vinifera L.) stem phenolics during long-term storage are the main topics of the study by MatthausS . (2008) in Industrial Crops and Products. According to the study, grape stems are an excellent source of flavonoids, ortho-diphenols, and total phenols, among other phenolic components. These substances effectively inhibited the development of both Gram-positive and Gram-negative bacteria and shown consistent antioxidant action.The antioxidant capacity of grape seed extract is one of its most notable benefits. GSE has been shown to have a higher antioxidant potential compared to vitamins C and E due to its high proanthocyanidin content. These compounds scavenge free radicals and inhibit lipid peroxidation, which protects cells and tissues from oxidative damage. Studies have shown that regular consumption of grape seed polyphenols can help lower oxidative stress markers, which in turn reduces the risk of developing oxidative-stress-related diseases.

Polyphenol Content: GSE is highly valued for its concentrated polyphenols, especially proanthocyanidins, which are powerful antioxidants. These compounds scavenge free radicals, reduce oxidative damage, and protect cells from reactive oxygen species (ROS) which contribute to aging and chronic diseases.The effect of N ε-carboxymethyllysine (CML), its precursor glyoxal, and AGE-modified BSA on serotonin release from human parietal cells in culture is

examined in the work by Holik et al. (2018). According to the results, AGE-modified BSA has a lowering effect on serotonin release, whereas CML can considerably boost it. This study sheds light on the intricate relationships between serotonin release and advanced glycation end products (AGEs), which may help us comprehend how dietary AGEs affect health.

Oxidative Stress Reduction: By reducing ROS, GSE helps lower oxidative stress in the body. Since oxidative stress is linked to cellular damage and inflammation, this protective effect can aid in maintaining cellular integrity.

Lipid and DNA Protection: Studies indicate that GSE's antioxidants not only protect cells but also stabilize cellular membranes, reduce lipid peroxidation, and prevent DNA damage, contributing to the prevention of oxidative stress-related conditions.

3.2. Antidiabetic Activity of Grape Seed Extract

Research in Phytotherapy Research (2014) indicated that grape seed extract, particularly its proanthocyanidin content, exhibited anti-inflammatory and anti-oxidant effects, which contributed to improving insulin sensitivity and reducing diabetes-induced complications.The positive effects of grape seed extract in the treatment of diabetes have been the subject of numerous investigations. By increasing insulin sensitivity, boosting glucose absorption, and lowering postprandial glucose spikes, grape seed polyphenols may aid in blood sugar regulation. There are several different ways that GSE works to prevent diabetes. First off, oxidative damage is a major factor in the development of diabetes, and its antioxidant qualities aid in shielding pancreatic beta cells from this harm. GSE has also demonstrated promise in blocking enzymes such as alpha-glucosidase, which slows the breakdown and absorption of carbohydrates and aids in blood glucose regulation.

Blood Glucose Control: Research shows that GSE may lower blood glucose levels by inhibiting carbohydrate-digesting enzymes, particularly alpha-amylase and alpha-glucosidase. By slowing carbohydrate absorption, GSE helps reduce postprandial (post-meal) blood sugar spikes.**Anti-Diabetic** activity. The insulin resistance index and the homeostasis model evaluation improved in Wister female rats given a daily dose of 25 mg grape seed procyanidin extract/kg body weight for 30 days, according to Montagut et al. Furthermore, the primers Glut4, Irs1, and Pparg2 were downregulated in the mesenteric white adipose tissue (WAT), suggesting that grape seed procyanidin has a long-term positive effect on glucose homeostasis. The oligomeric structures of the grape seed procyanidin extracts accelerated the absorption of glucose by binding to the insulin receptor and triggering its autophosphorylation, according to another study by Montagut et al.

Insulin Sensitivity: Grape seed polyphenols are suggested to enhance insulin sensitivity by improving insulin receptor function and signaling pathways, helping the body utilize glucose more effectively and potentially reducing insulin resistance. Given its potential benefits, GSE is being studied as a natural supplement to assist in the management of type 2 diabetes. By inhibiting digestive enzymes related to carbohydrate breakdown, GSE reduces the rapid release of glucose into the bloodstream.The suppression of the digestive enzymes α-amylase and α-glucosidase is one of the best-established processes. In the digestive system, these enzymes are in charge of converting complex carbs into glucose.According to Samir Felhi. et.al(2016)grape seed extracts can reduce the rate at which glucose is absorbed by blocking these enzymes, hence averting sharp increases in blood sugar levels after meals. Research has demonstrated that grape

seed extracts, especially those high in proanthocyanidins, have strong inhibitory effects on both enzymes, which suggests that they could be used to treat postprandial hyperglycemia.

Protection of Beta Cells: Pancreatic beta cells, responsible for insulin production, are vulnerable to oxidative stress, which is heightened in diabetic conditions. GSE has shown protective effects on beta cells by neutralizing ROS and reducing inflammation, which could help preserve insulin production over time.A study published in the Journal of Food Science (2012) found that grape seed extract significantly inhibited the activity of α-amylase and α-glucosidase, which helped reduce blood glucose levels in vitro.Another study in Molecules (2018) highlighted that grape seed extract prevented β-cell apoptosis in diabetic rats, showing its potential to protect the pancreas from the damage caused by prolonged high blood sugar.

Anti-Inflammatory Effects: Chronic inflammation is closely associated with diabetes, and the anti-inflammatory properties of grape seed polyphenols help reduce inflammatory markers, providing a complementary benefit in managing diabetes.Several animal studies and limited human trials have supported the antidiabetic potential of grape seed extract.Sano, A, et.*al*,. (2016). For instance, animal studies have shown that GSE supplementation can improve glucose tolerance, reduce fasting blood glucose levels, and enhance antioxidant enzyme activities. In clinical studies, while more research is needed, some evidence suggests that GSE can lower blood glucose and improve lipid profiles in diabetic patients.

CONCLUSION

Overall, grape seed extract holds promise as a natural antioxidant and antidiabetic agent. Its high polyphenolic content offers protection against oxidative stress and supports blood glucose regulation, potentially reducing the risk of diabetes complications. However, further human clinical trials are necessary to solidify its efficacy, establish proper dosages, and fully understand the long-term effects of GSE in diabetic patients. Animal studies highlight that GSE can improve glucose tolerance, reduce insulin resistance, and protect against diabetes-induced oxidative damage.Although limited, some clinical trials indicate GSE's potential in managing blood glucose levels and improving oxidative stress markers in individuals with diabetes, suggesting promising outcomes for future research. Due to its antioxidant properties, GSE may help prevent or delay complications related to chronic diseases by combating oxidative stress.Overall, GSE presents an interesting natural approach to diabetes management, but further clinical studies are needed to determine optimal dosages and confirm its long-term effects.

Acknowledgement

I would like to thank so many persons who have unwaveringly stood beside me while I was completing my research work, guiding and supporting me. I wouldkeep the list short and sweet, to start with **Dr. M.Velvizhi,** my supervisor Assistant Professor, P.G. and Research Department of Nutrition and Dietetics, Muslim Arts College, Thiruvithancode, Kanyakumari District, *Affiliated to ManonmaniumSundaranar University, Tirunelveli, Tamil Nadu,* India. And Thank you Madam, for giving me an opportunity to do this doctoral research, guidance & support, throughout my doctoral research and support to publish articles from this research work and also in thesis writing. Without you my doctoral research would not have seen the light ofthe day.

I extend my sincere thanks to **Dr. A. Ponni Principalincharge , Sourashtra College for Women, Madurai** for his suggestions and exuberant guidance all through the process of this work.

I am Indebted forever to my Parents, Husband, brothers and Sisters for the perennial support and for being pillar of strength in my Life. To conclude, what we are is God's gift to us; what we become is our gift to God. Thanks Almighty!!

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