

**GRAPE SEED EXTRACT- A THERAPEUTIC REVIEW**

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***Corresponding author e-mail:** sravanthi_1521@yahoo.com**ABSTRACT**

Grapes along with their leaves and sap have been traditional treatments in Europe for thousands of years. Grape seed extract is derived from the ground-up seeds of red wine grapes *Vitisvinifera*, Family: Vitaceae. Grape Seed is a great source of polyphenols-flavonoids, Essential Fatty Acid-linoleic acid, vitamin E, and oligomeric-proanthocyanidin(OPC), Gallic Acid, Resveratrol. Grape seed extract is now used to treat a number of diseases. Human case reports and results from basic research provide preliminary evidence that grape seed extract may affect diseases, hypertension, high levels of blood cholesterol, platelet aggregation, inflammation, reduce the risk for cancer, to treat diabetic retinopathy and neuropathy and various other conditions. As a nutritional supplement the extract is available in liquid, capsule or tablet form. It can be used as a nutritional supplement in various health conditions under the supervision of a doctor.

KEYWORDS: Oligomericproanthocyanidin, hypertension, anti oxidant.**INTRODUCTION**

Grapes have been heralded for their medicinal and nutritional value for thousands of years. Egyptians ate grapes at least 6,000 years ago, and several ancient Greek philosophers praised the healing power of grapes. European folk healers made an ointment from the sap of grapevines to treat skin and eye diseases. Grape leaves were used to stop bleeding, inflammation, and pain, such as the kind brought on by haemorrhoids. Unripe grapes were used to treat sore throats, and dried grapes were used for constipation and thirst. Round, ripe, sweet grapes were used to treat a range of health problems including cancer, cholera, smallpox, nausea, eye infections, and skin, kidney, and liver diseases. Due to their nutritional and medicinal properties grapes, their seeds, and leaves have been used in many home remedies for centuries.¹

Botanical source: Scientific name: *Vitisvinifera*, Family: Vitaceae, Common name: grape vine. *Vitisvinifera* is a high climbing vine, with stems up to 35m long in the wild. Tendrils growing

opposite leaves². Leaves palmately lobed, hairy/bristly on underside. Flowers form in dense panicles that develop into bunches of berries-‘grapes’. Stem bark tends to peel.

Grape Seed Extract(GSE) is derived from the seeds of *Vitisvinifera*. Red grape seeds are generally obtained as a by-product of wine production. The typical commercial opportunity of extracting grape seed constituents has been for chemicals known as polyphenols having antioxidant activity in vitro.³ It is sold commercially in the form of nutritional supplements.⁴ As a nutritional supplement the extract is available in liquid, capsule or tablet form.⁵

Grape Seed is a great source of polyphenols - flavonoids, Essential Fatty Acid - linoleic acid, vitamin E, and oligomericproanthocyanidin(OPC), Gallic Acid⁵. The highest concentration of proanthocyanidins is found in the skin or membrane of the grape seed^{6,7}. Total proanthocyanidin content consumed in 100 g of dry grape seed is approximately 3,500 mg Proanthocyanidins are one type of naturally occurring plant compounds called

bioflavonoids.⁶ The most active proanthocyanidins are those bound to other proanthocyanidins: mixtures of proanthocyanidin dimers, trimers, tetramers, and larger molecules such as PCO^{9,10,11}. These great components make grape seed extract an asset in the treatment of many minor to severe health conditions. It has also been used in the production of massage oils and balms, hair and hygienic products, face and body moisturizers, shampoos as well as in sunblocks and sunburn ointments. A polyphenol contained in grape seeds is resveratrol, which is under study for its possible effect on cancer cell growth, proliferation or apoptosis, among other potential chemopreventive mechanisms.



Grape seeds are known for their proanthocyanidins, which prove to be 20 times stronger than vitamin E and 50 times stronger than vitamin C – which make it one of the best free radical fighters on the planet. It also acts as a blood thinner.⁴ Due to the possible action of proanthocyanidins on limiting platelet adhesion,¹² grape seed extract may act as a blood-thinner, increasing clotting time.

Oligomeric proanthocyanidin the most important flavonoid antioxidant compound found in grape seed known to be extremely powerful antioxidant and they may help to lower high blood pressure, slow skin aging and even help to prevent cancer. Gallic acid is a phytochemical found in grape seeds. It seems to have anti-fungal, anti-viral and antioxidant properties.⁴

Grape seed extract has been shown to dramatically reduce the risk of prostate cancer, fight infection, improve sugar levels, increase cognitive ability by slowing down the aging of the brain, boost “good” cholesterol (HDL) and strengthen blood vessels.³ Current research suggests that grape seeds are a way of preventing and treating the following condition

High Blood Pressure

In a study of subjects with metabolic syndrome, researchers found that four weeks of treatment with grape seed extract lowered both systolic and diastolic blood pressure.³ There are benefits of grape seed for those that suffer from high blood pressure and complications associated with diabetes, including retinopathy.¹³

Alzheimer’s Disease³

Grape seed extract may help delay the development of Alzheimer’s disease, according to an animal study published in 2009. In tests on mice, scientists discovered that grape seed extract eased inflammation and prevented the accumulation of substances known to form the brain plaques associated with Alzheimer’s disease.

Cancer Prevention

There are studies that show regular consumption of grape seed extract may be responsible for both preventing cancer and triggering cancer cells to commit apoptosis. A further study concluded it may help prevent liver damage and other side effects caused by chemotherapy.³

A Science Daily research report by Professor Agarwal showed that grape seed extract inhibited the growth of colorectal tumors both in-vitro and in mice.³ Dr. Rajesh Agarwal and his team determined that supplementing mice with grape seed extract (GSE) reduced the growth of certain cancers by up to 67%, lowered the rate of progression of deadly tumors and DNA damage while inducing apoptosis of the cancer cells.¹³ GSE killed the cancer cells by knocking out one of several vulnerable paths necessary for growth, and left the healthy tissue untouched. The team determined that GSE damages both the cancer cells’ DNA (via increased reactive oxygen species) and stops the pathways that allow repair. They found that GSE created an environment that is unfavorable for cancer cell growth. Cancer cells require a specific environment, blood supply and metabolic nutrients to be able to propagate. If any of these pathways are disrupted, cancer cell death occurs. The scientists commented Mice have been used to study specific cancer cell lines because they parallel tumor progression and metastasis in a manner similar to humans.

Nutrition experts recommend supplementation with an organically harvested grape seed extract (150 mg per day) to support brain health and fight cancerous tumor development.¹³

Prostate Cancer

The Vitamin and Lifestyle study which followed over 30,000 men for 10 years found that a high (average) dosage of grape seed extract supplementation lowered the risk of prostate cancer by 62 %. Even average users of grape seed extract – experience a 41 % lower incidence of prostate cancer¹⁴.

In 2009 research, from the City of Hope, in California had concluded that grape seed extract reduced a protein that produces new blood vessels essential to growing cancers.

Use of any grapeseed supplements was associated with a 41% (HR 0.59, 95% CI: 0.40-0.86) reduced risk of total prostate cancer.¹⁵ Grapeseed may be a potential chemopreventive agent. However few articles say as current evidence is limited, it should not yet be promoted for prevention of prostate cancer.

Squamous Cell Carcinoma

A study carried out by the department of Dermatology, University of California in June of 2011 involving 830 people comparing various vitamins found that the group taking grape seed extract experience a 74 % reduction in squamous cell carcinoma.³

According to a study conducted by the University of Colorado Department of Pharmaceutical Sciences involving mice, gallic acid can help to inhibit the growth of prostate cancer cells. Gallic acid is considered to be one of the more active compounds in grape seed extract.⁴

Breast cancer

According to research done by the Department of Pharmaceutical Sciences, University of Colorado Health Sciences Center. Taking grape seed extract in conjunction with chemotherapy agents may be a powerful tool for treating breast cancer. Studies in test tubes have found that grape seed extract can potentially prevent the growth of cancer cells from breast, stomach, colon, prostate and lung cancer.⁴

Edema

The most positive scientific evidence according to the University of Maryland Medical Center shows that it may help with edema and chronic venous insufficiency. One study of breast cancer patients showed that taking 600 mg a day helped to reduce edema, that resulted from breast cancer surgery.¹⁶ It has also reduced swelling due to sports injuries in human studies

Circulatory & Vascular Disorders

The primary grape seed extract benefit, the one that has been studied the most, is to treat and prevent circulatory and vascular disorders. It may be

beneficial for those that suffer from varicose veins and atherosclerosis.¹⁴ Several studies have shown that the compounds in grape seed are effective for reducing chronic venous insufficiency symptoms pools of blood in the legs which cause pain, swelling, fatigue and visible veins.⁴

Because of the grape seed extract benefit to the circulatory system, it may reduce the risk of blood clots in the brain and heart.¹⁴

Allergies, Hay Fever

Grape seed extract is one of the botanicals that can reduce allergies. It inhibits the production of inflammatory compounds that cause allergic reactions, particularly things like hay fever¹⁴. It does this without causing the unwanted side effects that accompany antihistamines.

Fatty Liver

The significance of grape seed extract treatment in adult patients with non alcoholic fatty liver disease (NAFLD) was investigated in comparison to treatment with vitamin C. Grape seed extract (GSE) has been found to reduce the severity of ischemic/reperfusion-induced organ injury through its ability to balance the oxidant-antioxidant status, to inhibit neutrophil infiltration and to regulate the release of inflammatory mediators.¹⁷

Wrinkles, Sagging Skin

Grape seed benefits for the skin's health. Because of its antioxidant activity, it protects collagen fibers from the damage that free radicals can do. Because of its anti-inflammatory activity, it helps prevent chronic inflammation from damaging collagen fibers and slows down the wrinkle formation.¹⁴

Grape seed extract is considered to improve night vision, but scientific evidence is less.¹⁴ That is also a benefit of vitamin A. The combination of the two could help more.

Studies indicated that Grape seed extract known to be extremely effective at reducing oxidative stress during exercise. Trial was conducted by Dr. Glenn Vile in conjunction with Hort Research, a New Zealand research Institution. Results indicate that the rowers given GSE experienced a significant reduction of lactate dehydrogenase (LDH), a chemical marker for exercise-induced oxidative stress.¹⁸ The reduction level was 34% +/- 6%. There are 13 clinical trials (January, 2012) assessing potential effects of grape seed extracts on human diseases, such as breast cancer, blood estrogen levels in postmenopausal women, and coronary artery disease.¹⁹ Grape seed extract is also an aromatase inhibitor *in vitro*,²⁰ i.e. it may suppress the conversion of testosterone to estradiol. tooth decay – seed

phenolics may inhibit oral sugar metabolism and retard growth of certain bacteria that cause dental caries.²¹ wound healing – OPCs induced vascular endothelial growth factor and accelerated healing of injured skin in mice²². Osteoporosis – grape seed extracts enhanced bone density and strength in experimental animals²³

Grape seed extract has also been shown to protect against bacterial infections, such as *Staphylococcus aureus*. It also exhibited anti-viral activity^{24,25}, hepatoprotective activity²⁶. Some studies mostly in animals support these uses.

Grape seed extract is sometimes suggested for the following, although evidence is slight:

- Alzheimer's disease
- Diabetes (improving blood sugar control) A study in rats suggests that oral administration of 50 to 100 mg/kg grape seed proanthocyanidins for 72 hours may protect pancreatic tissue in experimental diabetes mellitus.²⁷
- Treating haemorrhoids
- Protecting against oxidative rancidity and bacterial pathogens

Other preliminary research on disease models

- liver function²⁸
- blood flow and fluid balance²⁹
- bones³⁰ – grape seed extracts enhanced bone density and strength in experimental animals

Side effects:

Herbs, however, contain components that can trigger side effects and interact with other herbs, supplements, or medications. For these reasons, one should take herbs with care, under the supervision of a health care provider qualified in the field of botanical medicine. Common side effects include nausea, itching, dizziness, stomach upset, diarrhoea, headache, sore throat, cough, and rash.

Adverse Reactions

Grape seed is contraindicated in patients with known hypersensitivity. One trial of 35 patients with chronic venous insufficiency receiving grape seed extract 300 mg every 8 hours for 28 days reported 2 patients with gastralgia, 1 with a headache, and 1 experiencing an allergic reaction.³¹

Possible Interactions:

Grape seed extract can potentially affect medications metabolised by the liver. It could interact with drugs like blood thinners, NSAID painkillers (like aspirin, Advil, and Aleve), certain heart medicines, cancer treatments and others.

Numerous medications are metabolised by the liver. Also, OPCs in grape seed extract may interact with the following:

Anticoagulants (blood thinners): Grape seed extract may act as a blood thinner, and could increase the risk of bleeding if taken with other blood thinners such as (Coumadin), clopidogrel (Plavix), or aspirin. It should be used with caution or avoided in persons with bleeding disorders.

Phenacetin: OPCs in grape seed may fasten the metabolism of Phenacetin. This may decrease the effectiveness of the Phenacetin.

Precautions:

Grape seed extract is considered to be safe when taken for up to three months at a time. Given the lack of evidence about its safety, it is not recommended for pregnant, breastfeeding women and also for children.⁴ People allergic to grapes should not use grape seed extract

Indications:

The standardized extracts of grape seed may be used to treat a range of health problems related to free radical damage, including heart disease, diabetes, and cancer. It may help with common cardiovascular conditions such as high blood pressure and atherosclerosis. Supplementing with grape seed may be recommended for patients suffering from vision problems, diabetes, edema, nerve damage and chronic venous insufficiency. It may also be useful for simply improving immune strength, slowing the aging process and improving overall well-being because of the high content of protective antioxidants⁴

Rich in potent antioxidants, almost anyone can benefit from grape seed extract when taken as a nutritional supplement to help prevent disease, boost immune health and slow the aging process. For those who are at a higher risk for heart disease, cancer and age-related diseases such as macular degeneration, supplementing may be even more important.⁴

Safe Use and Proper Dosage:

Adults can take from 25 to 150 mg, one to three times daily to boost antioxidant activity. A maximum of 900 mg/day has been used. A high-quality extract that is standardized to 40 to 80 percent proanthocyanidins or not less than a 95 percent OPC content. For treating certain conditions such as chronic venous insufficiency higher doses are recommended⁴.

REFERENCES

1. <http://www.umm.edu/altmed/articles/grape-seed-000254.htm#ixzz2K8An6CS0>
2. <http://www.edenproject.com/visit-us/whats-here/plant-a-z/grape-vine>
3. http://en.wikipedia.org/wiki/Grape_seed_extract
4. http://www.naturalhealth365.com/food_news/grape-seeds.html
5. <http://www.healthguideinfo.com/nutrition-information/p120833/>
6. Somerville R. The Complete Guide to Alternative and Conventional Medications. Alexandria. 1ed VA. Time-Life Custom Publishing:1997.
7. Augustin M, Vivas N. J Wine Res 1997;8:159-169.
8. GuL, Kelm MA, Hammerstone JF. J Nutr, 2004;134:613-617.
9. Joshi SS, Kuszynski CA, Bagchi D. Curr Pharm Biotechnol, 2001;2:187-200.
10. Teissedre PL, Fankel EN, Waterhouse AL, Peleg H, German JB. J Sci Food Agric, 1996;70:55-61.
11. El-Mallah MH, Murui T. Journ Royal Stas, 1993;119:45.
12. Shanmuganayagam, Dhanansayan, Beahm, Mark R, Osman, Hashim E, Krueger, Christian G, Reed, Jess D, Folts, John D. The J Nut, 2002;132 (12): 3592-8.
13. http://www.naturalnews.com/034893_grape_seed_extract_cancer_cells_DNA.html#ixzz2K8814pAT
14. http://www.HealthyBodySupplements.com/Herbal_Extracts.html
15. Brasky TM, Kristal AR, Navarro SL, Lampe JW, Peters U, Patterson RE, White E. Nutr Cancer, 2011; 63(4):573-82.
16. <http://www.umm.edu/altmed/articles/grape-seed-000254.htm>
17. ManouchehrKhoshbaten, Akbar Aliasgarzadeh, KooroshMasnadi, Sara Farhang, Mohammad K. Tarzamani, HosainBabaei, JavadKiani, Maryam Zaare, FarzadNajafipoor. Saudi J Gastroenterol, 2010 July; 16(3): 194-197.
18. http://www.naturalnews.com/025249_grapes_grapeseed_extract_cancer.html#ixzz2K8AKg8vB
19. <http://clinicaltrials.gov/ct2/results?term=grape+seed+extract>
20. Kijima I, Phung S, Hur G, Kwok SL, Chen S. Cancer Research, 2006;66 (11): 5960-7.
21. Smullen J, Koutsou G.A, Foster H.A, Zumbé A, Storey DM. Caries Res, 2007; 41 (5): 342-9.
22. Khanna Savita, Venojarvi Mika, Roy Sashwati, Sharma Nidhi, Trikha, Prashant Bagchi, Debasis Bagchi, Manashi Sen, Chandan K. Free Rad Biol and Med, 2002;33 (8): 1089-96.
23. Yahara N, Tofani I, Maki K, Kojima K, Kojima Y, Kimura M. J of musculoskeletal & neuronal interactions, 2005;5 (2): 162-9.
24. Su, X; d'Souza, DH. Appl and env microbiol, 2011;77 (12): 3982-7.
25. Nair, Madhavan P, Kandaswami, Chithan, Mahajan, Supriya, Nair, Harikrishna N, Chawda, RAM, Shanahan, Thomas, Schwartz, Stanley A. Biol Res 2002;35 (3-4): 421-31.
26. Pan Xijuan, Dai Yujie, Li Xing, Niu Nannan, Li Wenjie, Liu Fangli, Zhao Yang, Yu Zengli. Toxicol and Appl Pharmacol, 2011;254 (3): 323-31.
27. El-Alfy AT, Ahmed AA, Fatani AJ. Pharmacol Res, 2005;52:264-270.
28. <http://www.fasebj.org/search?author1=Josep+Maria+Del+Bas&sortspec=date&submit=Submit>
29. <http://www.umm.edu/altmed/articles/grape-seed-000254.htm>
30. <http://dx.doi.org/10.1016/j.phytochem.2007.09.014>,
31. <http://www.drugs.com/npp/grapeseed.html>