# **Grape Seed SAP**

Science-based grape seed extract for antioxidant properties and inflammation

Grape seed extract (GSE) contains proanthocyanidins, which have been demonstrated to exhibit a wide spectrum of pharmacological, therapeutic and chemoprotective properties. Studies have demonstrated that GSE can reduce inflammation by inhibiting the formation of inflammatory cytokines and reducing inflammatory mediators. GSE can ameliorate atherosclerosis by reducing inflammation, decreasing MDA-LDL, and by decreasing foam cell formation. GSE has been found to be cytotoxic toward human breast, lung and gastric adenocarcinoma cells.

Many pharmaceuticals can damage various organ systems. GSE has been studied and has the ability to protect multiple organs from toxicity caused by drugs or chemicals. GSE is a powerful antioxidant that has a wide range of health benefits and has been shown to have better free-radical scavenging ability than vitamins C or E or  $\beta$ -carotene.

## **ACTIVE INGREDIENTS**

#### Each non-GMO vegetable capsule contains:

Grape (Vitis vinifera) seed extract, 80% oligomeric proanthocyanidins 500 mg

#### This product is non-GMO.

**Contains no:** Gluten, soy, wheat, corn, eggs, dairy, yeast, citrus, preservatives, artificial flavor or color, starch, or sugar.

Grape Seed SAP contains 60 capsules per bottle.

### **DIRECTIONS FOR USE**

**Adults: Take 1 capsule daily** or as directed by your healthcare practitioner. Consult a healthcare practitioner for use beyond 3 months. Use for a minimum of 1 month to see beneficial effects.

## **INDICATIONS**

#### **Grape Seed SAP** can be used:

- · As a systemic anti-inflammatory to reduce formation of inflammatory cytokines and inflammatory mediators.
- · To help treat and prevent atherosclerotic plaque.
- · As a tool to protect multiple organs from a variety of toxic drugs.
- · To help prevent breast cancer caused by low-dose carcinogen exposure. and is:
- · An effective treatment to reduce oxidized LDL.
- · An adjunctive treatment for breast, lung, or gastric adenocarcinomas.
- · A powerful antioxidant with better free-radical scavenging ability than vitamins C or E, or β-carotene.

## **SAFETY**

Grape seed extract has been studied for both acute and long-term use and has been found to be safe and not cause any detrimental side effects for doses up to 500 mg/kg<sub>hw</sub>/d in vivo.<sup>[7]</sup>

## **PURITY, CLEANLINESS, AND STABILITY**

All ingredients listed for all **Grape Seed SAP** lot numbers have been tested by a third-party laboratory for identity, potency, and purity.



Scientific Advisory Panel (SAP): adding nutraceutical research to achieve optimum health

**60 CAPSULES** 



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## **Grape Seed SAP**

## Research Monograph

Grape seed extract (GSE) is sourced from the seeds of red grapes, which are known for their high proanthocyanidin content. Proanthocyanidins have remarkable antioxidant properties and have the ability to reduce oxidative stress and free-radical damage. This affords them the ability to protect the cardiovascular system, to reduce inflammation, to be chemoprotective, and to potentially protect us from the progression of several chronic diseases.

### **GSE AND INFLAMMATION**

A study performed on rice mice and rats with experimentally induced inflammation demonstrated that proanthocyanidins (PAs) from GSE exerted an anti-inflammatory effect.<sup>[2]</sup> Animals were dosed at 10 mg/kg proanthocyanidins, which had the effect of inhibiting β-NAG and NOS activity as well as lowering the values of NO, IL1β, TNF-α, and PGE<sub>2</sub>. The inhibitory effects of the PAs were compared to dexamethasone at 2 mg/kg and found to be superior.<sup>[2]</sup> Another study performed on human umbilicalvein endothelial cells using 50–100 mcg/ml GSE demonstrated that this dose was effective at reducing inflammation induced by TNF-α in the HUVEC.<sup>[3]</sup> This finding suggests that consumption of GSE may be beneficial for inflammatory atherosclerosis.<sup>[3]</sup>

### **GSE AND CARDIOVASCULAR HEALTH**

Atherosclerosis is a condition that affects the arteries, in which fatty plaques develop on the inner arterial wall; this in turn leads to obstructed blood flow.[4] Malondialdehyde-modified LDL (MDA-LDL) is a chemical modification thought to reflect the naturally occurring oxidation of LDL.[5] It is the oxidized LDL that adheres to the arterial wall. In a human clinical trial on patients with elevated LDL cholesterol, subjects were given either placebo, 200 mg, or 400 mg GSE, and lipid values were assessed at 6 and 12 weeks. [6] The placebo group had no change in MDA-LDL levels, whereas the group who received 200 mg showed a non-statistically significant decrease in MDA-LDL and the group who received 400 mg GSE showed a statistically significant decrease in MDA-LDL levels.[6] In a study performed on hamsters (hamsters possess lipid profiles similar to those of humans), animals were fed a hypercholesterolemic diet, which resulted in foam-cell formation in the arteries. Foam-cell development is an early marker of atherosclerotic changes. The animals were then supplemented with 50 mg/kg or 100 mg/kg GSE, and the atherosclerosis was reduced by approximately 50% and 63%, respectively.[4]

## GSE ORGAN PROTECTION FROM PHARMACEUTICALS

In this study, GSE was given to animals for 7–10 d prior to drug/chemical exposure, while the control group received no GSE. [1] Experimenters then administered various drugs, including acetaminophen, amiodarone, doxorubicin, cadmium chloride, and dimethylnitrosamine. The treatment group was provided complete protection as per serum chemistry changes including ALT, blood urea, nitrogen, and creatine kinase. GSE was able to inhibit both forms of cell death (necrosis and apoptosis) and reduce DNA damage that is typically triggered by these drugs. Upon organ examination, similar patterns to those of the serum

analysis were also seen, with there being limited hepatoxicity from acetaminophen, pulmonary toxicity from amiodarone, cardiotoxicity from doxorubicin, nephrotoxicity from cadmium chloride, and spleenotoxicity from dimethylnitrosamine. <sup>[1]</sup> The only organ that had only partial protection was brain tissue from damage due to *O*-ethyl-*S*,*S*-dipropyl phosphorodithioate. These results suggest that GSE is a bioavailable agent that provides significant organ protection against a multitude of drug and toxin exposure. <sup>[1]</sup>

#### **GSE AND CANCER**

Breast cancer is currently the most common cancer that occurs in women. A study was performed using GSE as a preventative measure to protect women from ongoing low-dose carcinogen exposure.[8] The study used a model system and measured both biological and molecular targets and found that GSE was indeed valuable for preventing human breast-cell carcinogenesis induced by repeated exposures to low doses of various environmental carcinogens.[8] GSE was found in another study to be a possible adjunctive treatment for breast cancer, as it demonstrated the ability to arrest the cell cycle of the breastcancer cell MCF-7 in the S phase. [9] GSE also has the ability to inhibit the proliferation of some colorectal carcinoma cell lines, and was associated with a mechanism that causes apoptosis of the mitochondrial membrane in these cells.[10] Tumour-cell migration is the main mechanism by which metastasis occurs. A study examined the ability of GSE to prevent metastasis of nonsmall cell human lung cancer cells. Using an in vitro migration assay, it was found that treatment of A549 and H1299 cells with GSPs resulted in a concentration-dependent inhibition of migration of these cells.[11] More human clinical trials need to be performed, but based on current research, GSE could be useful for both prevention and treatment of various breast-cancer cell

#### **REFERENCES**

- Bagchi, D., et al. "Protection against drug- and chemical-induced multiorgan toxicity by a novel IH636 grape seed proanthocyanidin extract." Drugs Under Experimental and Clinical Research Vol. 27, No. 1 (2001): 3–15.
- Li, W.G., et al. "Anti-inflammatory effect and mechanism of proanthocyanidins from grape seeds." Acta Pharmacol Sinica Vol. 22, No. 12 (2001): 1117–1120.
- Chao, C.L., et al. "Grape seed extract ameliorates tumor necrosis factor-α-induced inflammatory status of human umbilical vein endothelial cells." European Journal of Nutrition Vol. 50. No. 6 (2011): 401–409.
- Vinson, J.A., et al. "Beneficial effects of a novel IH636 grape seed proanthocyanidin extract and a niacin-bound chromium in a hamster atherosclerosis model." Molecular and Cellular Biochemistry Vol. 240, No. 1–2 (2002): 99–103.
- Amaki, T., et al. "Circulating malondialdehyde modified LDL is a biochemical risk marker for coronary artery disease." Heart Vol. 90, No. 10 (2004): 1211–1213.
- Sano, A., et al. "Beneficial effects of grape seed extract on malondialdehyde-modified LDL." Journal of Nutritional Science and Vitaminology Vol. 53, No. 2 (2007): 174–182.
- Ray, S., et al. "Acute and long-term safety evaluation of a novel IH636 grape seed proanthocyanidin extract." Research Communication in Molecular Pathology and Pharmacology Vol. 109, No. 3–4 (2001): 165–197.
- Song, X., et al. "Grape seed proanthocyanidin suppression of breast cell carcinogenesis induced by chronic exposure to combined 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone and benzo[a]pyrene." Molecular Carcinogenesis Vol. 49, No. 5 (2010): 450–463.
- Chen, C., et al. "Grape seed extract inhibit proliferation of breast cancer cell MCF-7 and decrease the gene expression of survivin." Zhongguo Zhong Yao Za Zhi Vol. 34, No. 4 (2009): 433–437.
- Hsu, C.P., et al. "Mechanisms of grape seed procyanidin-induced apoptosis in colorectal carcinoma cells." Anticancer Research Vol. 29, No. 1 (2009): 283–289.
- Punathil, T. and S.K. Katiyar. "Inhibition of non-small cell lung cancer cell migration by grape seed proanthocyanidins is mediated through the inhibition of nitric oxide, guanylate cyclase, and ERK1/2." Molecular Carcinogenesis Vol. 48, No. 3 (2009): 232– 242.