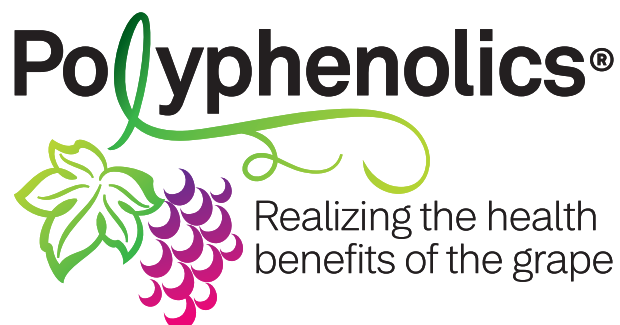
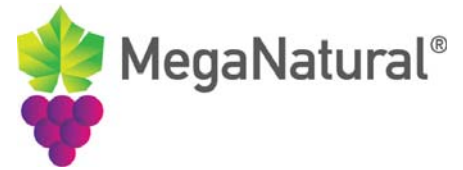


# MegaNatural® Grape Seed Extracts and their role in Sports Nutrition



Authored by: James A. Kennedy, Ph.D.

# MegaNatural® Grape Seed Extracts And Their Role In Sports Nutrition



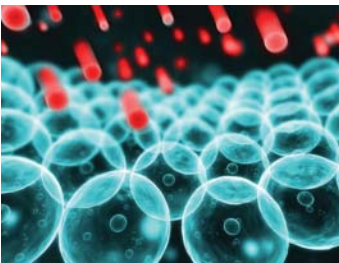
## MegaNatural® grape seed extracts may help support your Sports Nutrition needs

Proper nutrition is critically important whether you are a competitive athlete at the top of your game or you're just staying active as part of your strategy to remain healthy. At Polyphenolics we understand that healthfulness is critical to happiness and believe that our MegaNatural® grape seed extracts should play an important role in helping you to stay active, here is why.



## Oxidative Stress

From the sunlight that we love so much to the air that we respire, the human body is under constant exposure to oxidative stress. With that said, when we exercise, our bodies often operate beyond our ability to manage oxidative stress. Specifically, we breathe harder and our hearts beat faster to ensure that we receive the extra oxygen that we need. It is in times of this additional level of stress that supplementing our antioxidant system with antioxidants may be beneficial. MegaNatural® grape seed extracts are one possible way to help us cope with the oxidative stress that our bodies experience during exercise.\*



## Free Radicals

When we breathe harder, we experience an increase in oxidative stress caused by the production of damaging free radicals. The production of these free radicals is a normal part of living and our bodies have an elegant antioxidant system for coping with these potentially damaging substances. Exercise increases the production of these radicals, and radical production can exceed the antioxidant system. Left unchecked, these radicals can lead to cellular damage. MegaNatural® grape seed extracts are rich in antioxidants and may reduce free radicals.\*

## What differentiates MegaNatural® grape seed extracts from others?



Polyphenolics' MegaNatural® grape seed extracts are traceable to the exact California vineyard they were grown in. Not all grape seed extract suppliers are able to make the same claim. Through relentless testing and painstaking record keeping, Polyphenolics is able to guarantee that MegaNatural® grape seed extracts remain adulterant free. Because ensuring the safety of consumers is of utmost importance, Polyphenolics is a proud supporter of the American Botanical Council's Botanical Adulterants Program.

MegaNatural® advantages above competitors:

- Patented Process
- Unique Composition
- Highly Consistent
- Clinically Shown
- Relentlessly Tested
- FDA No-Objection GRAS
- 100% Water Soluble
- 100% California-grown Grapes
- 100% Pure Grape Seed Extract
- Successful use in Sport Nutrition products for years



\*This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

# MegaNatural®-Gold grape seed extract: Powerful Antioxidant Activity



One of the richest sources of natural antioxidants is grape seed extract.

Not all antioxidants are the same or as effective. MegaNatural®-Gold a unique form of grape seed extract is an antioxidant, and because it can be absorbed into our bodies, MegaNatural®-Gold increases the antioxidant activity of blood plasma in human subjects.\*

## MegaNatural® -Gold

*A unique form of grape seed extract that has been clinically shown to be an effective antioxidant.\**

- A daily serving of grape seed extract has been found to improve the antioxidant status after thirty days, in elite athletes
- Moreover, clinical studies have found that grape seed extract supplementation improves the performance in elite athletes.
- Clinical studies show that MegaNatural®-Gold remains active in the bloodstream for over four hours.
- When MegaNatural®-Gold is taken in combination with either Vitamin C or Vitamin E, the vitamin's antioxidant capacity is doubled.
- MegaNatural®-Gold is a natural option to include when considering supplemental antioxidants as part of your sports nutrition program.\*

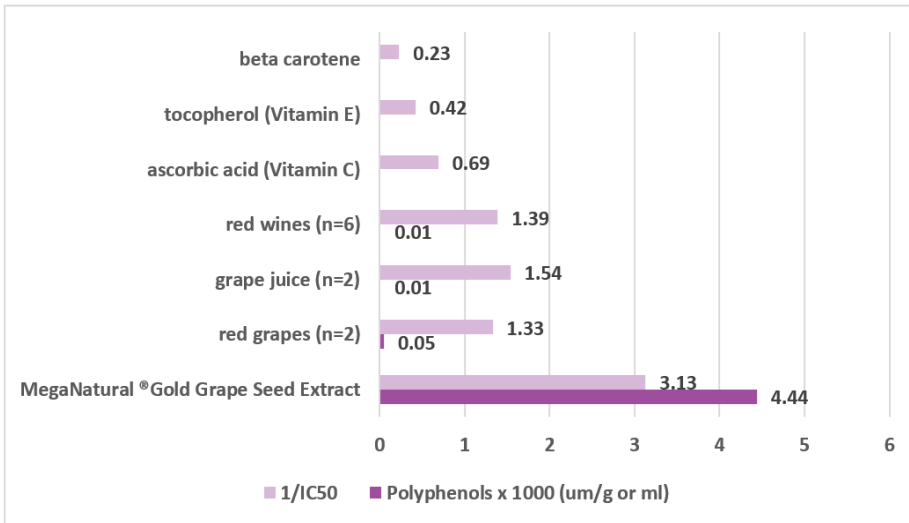


Fig. 1. Quantity and quality of pure antioxidants and antioxidants in foods, beverages, and extracts. Adapted from Vinson et al., 2001.

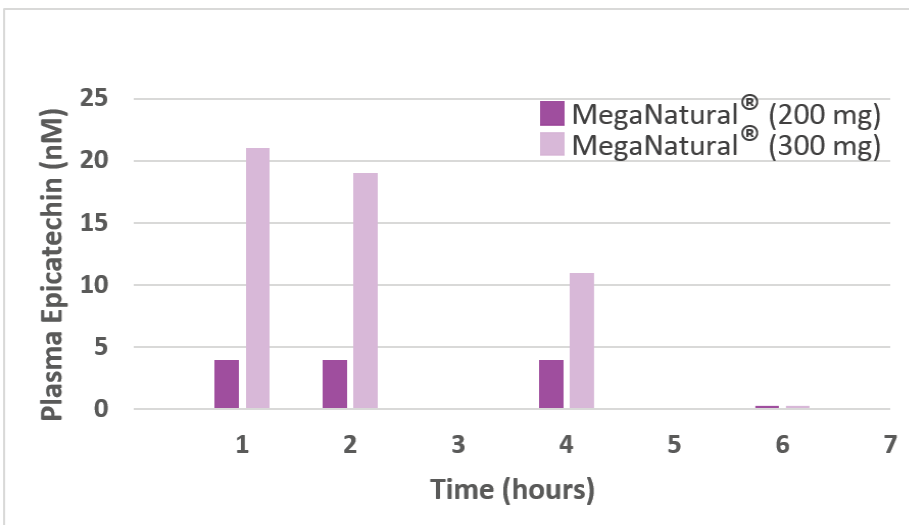


Fig. 2. Average change in plasma epicatechin in nine subjects given 200 and 300 mg of MegaNatural®-Gold. \*P < .01 versus 200-mg dose. Adapted from Vinson et al., 2001.

## Safety

In addition to the natural benefits of our MegaNatural® grape seed extracts, it is also important to note that our clinically studied grape seed extracts are produced using a patented hot water extraction process for maximum effectiveness. Our grape seed extracts have been granted a no-objection generally recognized as safe (GRAS) status by the Food and Drug Administration (FDA).

- Non-toxic, Non-clastogenic
- FDA No-Objection GRAS
- Free of Side Effects
- Relentlessly Tested
- Highly Consistent
- Hot Water Extracted
- Safe History



\* This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

# MegaNatural®-BP grape seed extract: Multiple benefits in one supplement



## + Another MegaNatural® Antioxidant

Like MegaNatural®-Gold, MegaNatural®-BP is also a powerful and effective antioxidant.\*

## + Helps maintain healthy Nitric Oxide levels

Many athletes seek out sports nutrition supplements that promote Nitric Oxide benefits. Nitric Oxide is important in maintaining the function of the interior lining of your arteries (endothelium). MegaNatural®-BP has been clinically shown to help support endothelial function by maintaining healthy nitric oxide levels within the normal range. This helps support healthy vasodilation and blood flow.\*

## + Helps maintain healthy Blood Pressure levels

As for that beating heart, we know that the health of our cardiovascular system is key to optimal health and well-being. Studies have shown that an increase in dietary flavonoids are associated with a reduction in cardiovascular disease. In line with this, our MegaNatural®-BP has been shown to positively impact biochemical markers associated with cardiovascular health. Moreover, MegaNatural®-BP has been clinically studied in humans and has been found to support heart health.\*

One of the key indicators of a healthy heart is healthy blood pressure. Blood pressure is measured in two numbers: the higher number represents systolic blood pressure (the force when the heart contracts); the lower number represents diastolic blood pressure (the force when the heart rests). Below 120/80 mmHg is considered healthy. Systolic blood pressure is known to rise during exercise. This isn't a problem if the increased demands are occasional, such as during intense exercise. However, if your blood pressure has been slowly increasing over the years into the prehypertension range, this puts tremendous stress on such an important organ. MegaNatural®-BP has been shown in three human clinical studies to help maintain healthy blood pressure within the normal range.\*

## *MegaNatural®-BP*

*A unique form of grape seed extract is an antioxidant that helps support endothelial function by maintaining healthy nitric oxide levels that are within the normal range. This helps support healthy vasodilation and blood flow.\**

## *MegaNatural®-BP*

*A unique form of grape seed extract that has been clinically shown to maintain healthy blood pressure levels within the normal range.\**

### • Nationally Recognized

MegaNatural®-BP is the recipient of the prestigious Frost & Sullivan 2010 North American Product Differentiation Excellence of the Year Award, "in recognition of Polyphenolics' sharp focus on research and development, technological process innovation, and associations with major research organizations and universities resulting in a strikingly differentiated grape seed extract."

### • Intellectually Protected

MegaNatural®-BP is protected by a portfolio of intellectual property, including four patents — a production flow process patent (U.S. patent No. 6,544,581 B1), a method of use patent (U.S. patent No. 7,651,707 B2), a composition patent (U.S. patent No. 7,767,235 B2), an exclusive production process patent (U.S. patent No. 8,075,929 B2), — and a trademarked brand name. Several patents have also been issued worldwide. This portfolio clearly differentiates MegaNatural®-BP from commodity grape seed extracts.



Formulating with MegaNatural® grape seed extracts  
MegaNatural® Grape Seed Extracts are 100% water soluble, so they can easily be added to functional beverages without precipitating out of solution. They can also be included in capsules, shots, shakes, gummies, gels, bars, powder mixes, etc.

\* This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

# MegaNatural®-BP: The patented grape seed extract with clinically shown health benefits



As a science-driven organization, Polyphenolics has invested heavily in original research on MegaNatural®-BP at both the laboratory and clinical levels. Why is original research important?

Because multiple factors — from the grape varieties chosen, to the time of harvest, to the extraction technique — can influence the constituent profile of the finished product. The only way to know if a particular extract has biological efficacy is to test the specific composition of the extract.

## Mechanism of Action

Edirisinghe I, Burton-Freeman B, Kappagoda CT Mechanism of the endothelium-dependent relaxation evoked by a grape seed extract. *Clin. Sci.* 2008; 114: 331-337.

How does MegaNatural® BP work? Research using animal models indicates that it activates the enzyme nitric oxide synthase (eNOS) to produce nitric oxide (NO).

NO is a gaseous compound that acts as a cellular messenger. When NO is present in the inner lining of the blood vessels (endothelium), it causes the surrounding smooth muscle to relax. This endothelium-dependent relaxation of the blood vessels then supports healthy blood flow.\*

## Human Clinical Trial #1

Sivaprakasapillai B, Edirisinghe I, Randolph J, Steinberg F, Kappagoda T. Effect of grape seed extract on blood pressure in subjects with the metabolic syndrome. *Metabolism.* 2009; 58:1743-1746.

Study Type: randomized, double-blind, placebo-controlled

Methodology: Twenty-five subjects were randomized into three groups: a.) placebo, b.) 150 mg MegaNatural®-BP per day and c.) 300 mg MegaNatural®-BP per day. Each group took their respective treatment for four weeks.

Results: Blood samples showed MegaNatural®-BP to be well-absorbed after a single dose, with a steep rise in polyphenols 90 minutes after ingestion. After four weeks, both dosages of MegaNatural®-BP were found to help maintain blood pressure levels (both systolic and diastolic) within the normal range.\* In addition, both dosages decreased levels of oxidized LDL cholesterol, with the 300 mg dosage reaching statistical significance compared to baseline. Low levels of oxidized LDL are correlated to arterial health.\*

## Human Clinical Trial #2

Robinson M, Lu B, Edirisinghe I, Kappagoda CT. Effect of grape seed extract on blood pressure subjects with pre-hypertension. *J. Pharm. Nutri. Sci.* 2012;

Study Type: randomized, double-blind, placebo-controlled

Methodology: All 30 subjects began the trial by taking a placebo for two weeks. Then, they were randomized into two groups: a.) placebo and b.) 300 mg MegaNatural®-BP per day. Each group took their respective treatment for eight weeks.

Results: After eight weeks, MegaNatural®-BP was found to help maintain blood pressure levels (systolic and diastolic) within the normal range.\*

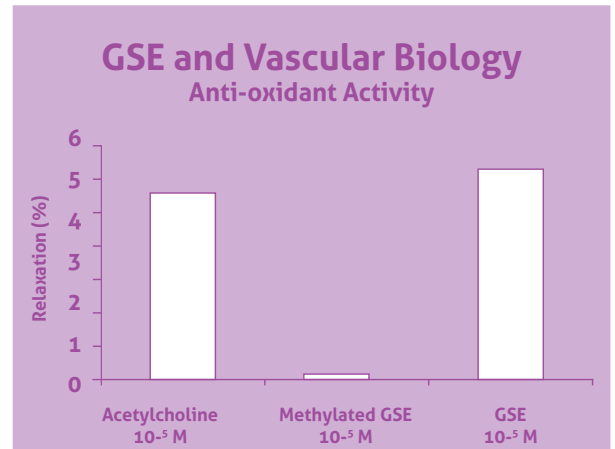
## Human Clinical Trial #3

Park E, Edirisinghe I, Choy YY, Waterhouse A, Burton-Freeman B. Effects of grape seed extract beverage on blood pressure and metabolic indices in individuals with pre-hypertension: a randomised, double-blinded, two-arm, parallel, placebo-controlled trial. *Brit. J. Nutr.* 2016; 115: 226-38.

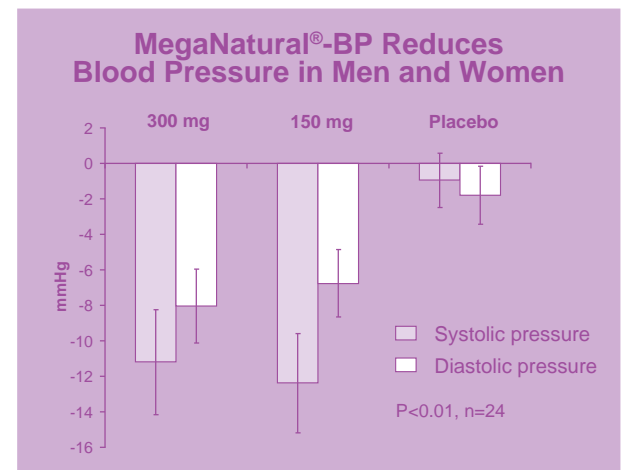
Study Type: A single-center, randomized, double-blinded, placebo-controlled, 12-week, parallel study

Methodology: 29 middle age adults with pre-hypertension consumed a fruit-flavored beverage placebo or 150 mg MegaNatural®-BP twice per day (300 mg per day) in a fruit-flavored beverage for six weeks, preceded by two week placebo run-in and four week no-beverage follow-up.

Results: After six weeks, MegaNatural®-BP was found to help maintain blood pressure levels within the normal range.\* After four weeks discontinuation of GSE beverage, blood pressure increased to original levels.



A study in rabbit aortic rings shows MegaNatural® BP causes a relaxation of the blood vessels which is similar to that elicited by acetylcholine – a known vasodilator\*.



MegaNatural®-BP was found to help maintain blood pressure levels within normal range.\*

\* This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

## About Polyphenolics

Founded in 1996, Polyphenolics is a science-driven organization dedicated to researching and developing innovative products using grape-seed-derived polyphenols to deliver specific and documented health benefits.



## Vertical Integration

As a division of Constellation Brands, the largest premium wine company in the world, Polyphenolics has access to an abundant supply of fresh wine grapes, grown in California's Central Valley, and retains complete control over the entire manufacturing process — from the initial selection of wine grapes to the final extraction of finished material. The company goes beyond federally mandated traceability requirements, documenting all aspects of growing, treating, and processing the grapes. Through painstaking supply chain documentation and laboratory testing, Polyphenolics can substantiate freshness, identity, domestic origin, and absence of chemical contaminants and genetic modification.

## References

- Camic CL, Housh TJ, Zuniga JM, et al. Effects of arginine-based supplements on the physical working capacity at the fatigue threshold. *J. Strength Cond. Res.* 2010; 24: 1306-12.
- Caselli S, Segui AV, Quattrini F, et al. Upper normal values of blood pressure response to exercise in Olympic athletes. *Am. Heart J.* 2016; 177: 120-8.
- Choy YY, Quifer-Rada P, Holstege DM, et al. Phenolics metabolites and substantial microbiome changes in pig feces by ingesting grape seed proanthocyanidins. *Food Funct.* 2014; 5: 2298-2308.
- Close GL, Hamilton DL, Philp A, et al. New Strategies in sport nutrition to increase exercise performance. *J. Free Radic. Biol. Med.*; 2016; 98: 144-158.
- Corder R, Wood EG, Khan NQ. Evaluation of the Antioxidant, vasodilator, anti-proliferative, and anti-adhesion properties of MegaNatural Whole Grape Extract, MegaNatural Grape Seed Extract, and MegaNatural Grape Skin Extract. William Harvey Institute. 2002. Unpublished Manuscript.
- Corder R, Brown RE, Wood EG, et al. Evaluation of MegaNatural Whole Grape Extract, MegaNatural Grape Seed Extract, and MegaNatural Grape Skin Extract. William Harvey Institute. 2002. Unpublished Manuscript.
- Corder R, Warburton RC, Khan NQ, et al. The procyanidin-induced pseudo laminar shear stress response: a new concept for the reversal of endothelial dysfunction. *Clin. Sci.* 2004; 107: 513-517.
- Di Lorenzo C, Sousa LP, Pastor RF, et al. Beneficial effects of non-alcoholic grape-derived products on human health: A literature review. Bio Web of Conferences , 38th World Congress of Vine and Wine, 2015.
- Edirisinghe I, Burton-Freeman B, Kappagoda CT Mechanism of the endothelium-dependent relaxation evoked by a grape seed extract. *Clin. Sci.* 2008; 114: 331-337.
- Kar P, Laight D, Rooptait HK. Effects of grape seed extract in Type 2 diabetic subjects at high cardiovascular risk: a double blind randomized placebo controlled trial examining metabolic markers, vascular tone, inflammation, oxidative stress and insulin sensitivity. *Diabet. Med.* 2009; 26: 526-531.
- Kim JK, Nho HS, Park SK. Effect of Grape Seed Extract on Exercise Performance in Elite Basketball Players. Manuscript to be submitted for publication.
- Quifer-Rada P, Choy YY, Calvert CC, et al. Use of metabolomics and lipidomics to evaluate the hypocholesterolemic effect of Proanthocyanidins from grape seed in a pig model. *Mol. Nutr. Food Res.* 2016; 00: 1-9
- Park E, Edirisinghe I, Choy YY, Waterhouse A, Burton-Freeman B. Effects of grape seed extract beverage on blood pressure and metabolic indices in individuals with pre-hypertension: a randomised, double-blinded, two-arm, parallel, placebo-controlled trial. *Brit. J. Nutr.* 2016; 115: 226-38.
- Robinson M, Lu B, Edirisinghe I, Kappagoda CT. Effect of grape seed extract on blood pressure subjects with pre-hypertension. *J. Pharm. Nutri. Sci.* 2012; 155-159.
- Rodriguez-Mateos A, Vauzour D, Krueger CG, Shanmuganayagam D, Reed J, Calani L, Mena P, Del Rio D, Crozier A. Bioavailability, bioactivity and impact on health of dietary flavonoids and related compounds: an update. *Arch. Toxicol.* 2014; 88: 1803-1853.
- Sivaprakasapillai B, Edirisinghe I, Randolph J, Steinberg F, Kappagoda T. Effect of grape seed extract on blood pressure in subjects with the metabolic syndrome. *Metab. Clin. Exp.* 2009; 58: 1743-1746.
- Vinson JA, Proch J, Bose P. MegaNatural Gold grapes seed extract: In Vitro antioxidant and in vivo human supplementation studies. *J. Med. Food.* 2001; 4: 17-26.
- Wang X, Ouyang YY, Liu J, Zhao G. Flavonoid intake and risk of CVD: A systematic review and meta-analysis of prospective cohort studies. *Br. J. Nutr.* 2014; 111: 1-11.
- Wright JR Jr, Williamson JD, Whelton PK, et al. A Randomized Trial of Intensive versus Standard Blood-Pressure Control. *New Engl. J. Med.* 2015; 373: 2103-16.



## For more information, contact:

Gregory A. Arabatzis  
Director of Global Sales  
908-941-6535  
gregory.arabatzis@cbrands.com

Customer Service: 866.308.7678

Polyphenolics, a division of Constellation Brands