



**MegaNatural<sup>®</sup>BP**

grape seed extract —  
blood pressure maintenance

The patented grape seed extract  
with clinically shown health benefits

## MegaNatural®-BP:

The patented grape seed extract with clinically shown health benefits

One of the key indicators of a healthy heart is healthy blood pressure. But what is blood pressure exactly, and why is it so important?

Blood pressure measures the amount of force exerted against the walls of the arteries in response to the pumping action of the heart. The intensity of that force depends on the volume of blood being pumped and the flexibility of the arteries.

Like a balloon being filled with water, pressure rises when the arteries contain a large amount of blood. Similarly, when the arteries lose some of their natural balloon-like flexibility, they can no longer expand easily to accommodate increased blood flow — again causing an increase in 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 mmHg/80 mmHg is considered healthy.

### Why Maintaining Healthy Blood Pressure Is So Important

When blood pressure is healthy, the heart can pump blood at a relaxed pace. Once pressure in the arteries rises, the heart has to work harder to keep blood flowing. This isn't a problem if the increased demands on the heart are occasional, such as during intense exercise. However, forcing the heart to pump hard all the time puts tremendous stress on such an important organ.

As mentioned previously, arterial inflexibility leads to increased blood pressure. Unfortunately, the opposite is also true: elevated blood pressure causes the arteries to become even stiffer. Thus a vicious self-perpetuating cycle is initiated.

### The Promise of MegaNatural®-BP

Fortunately, there is a natural way to help maintain blood pressure levels within a healthy range: polyphenols.\* Naturally occurring in fruits, vegetables and red wine, polyphenols are a class of phyto-nutrients that have been scientifically demonstrated to support cardiovascular health.\* One of the largest natural depositories of polyphenols is grape seed extract.

Manufactured exclusively by Polyphenolics, a division of Constellation Brands — the world's leading premium wine company — MegaNatural®-BP is a patented grape seed extract with clinically shown benefits. In fact, three placebo-controlled human clinical trials conducted by researchers at the Department of Preventative Cardiology, University of California Davis School of Medicine, have found that MegaNatural®-BP supports blood pressure within the normal range.\* No other grape seed extract can say the same, since MegaNatural®-BP has a unique structure and composition.

# The MegaNatural®-BP Advantage: MegaNatural®-BP versus Commodity Grape Seed Extracts

Grape seed extracts abound. Only MegaNatural®-BP delivers all of the following advantages:

## EFFICACY

### • Clinically Researched

MegaNatural®-BP is backed by three placebo-controlled human clinical trials showing it supports blood pressure within the normal range.\* Importantly, additional research shows that commonplace grape seed extract does not have the same effect.

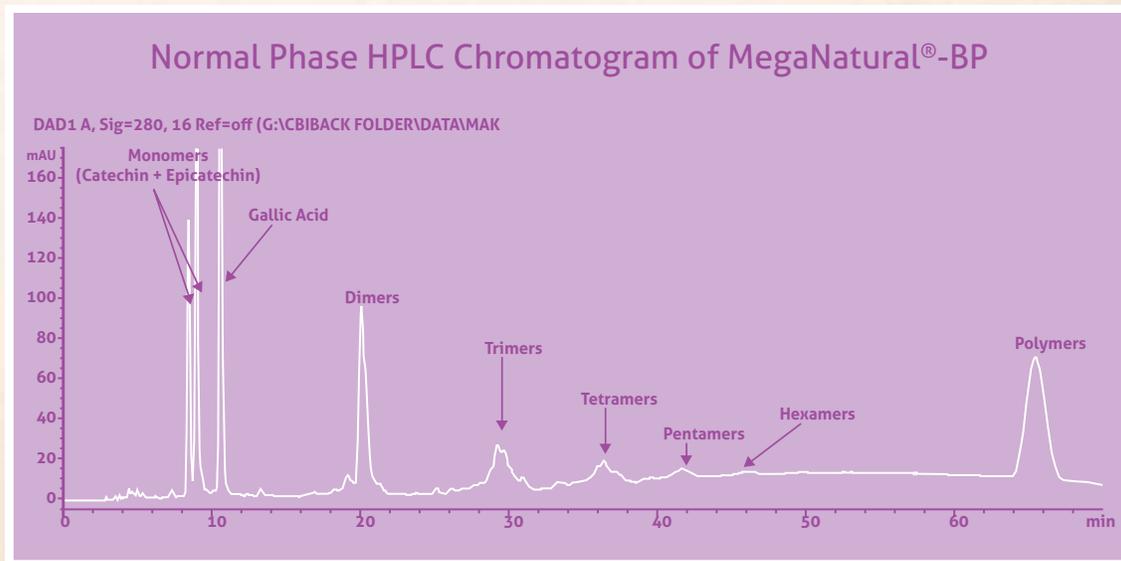
### • U.C. Davis-associated

MegaNatural®-BP has the exclusive privilege of being associated with the Department of Preventive Cardiology at U.C. Davis, where researchers have conducted several clinical and in vitro studies on the ingredient.

## ACTIVITY

### • Structurally Unique

By investing heavily in research that identifies and “captures” the molecular structures within grape seed shown to provide specific health benefits, Polyphenolics has developed a grape seed extract that is structurally unique, providing 90-95% total polyphenols — the biologically active constituents.



MegaNatural®-BP is structurally unique, providing 90-95% total polyphenols (as monomers, oligomers, and polymers).

### • Improved Bioavailability

Because MegaNatural®-BP is selectively extracted to include a higher percentage of lower molecular weight polyphenols, it has improved bioavailability and greater absorption compared to other grape seed extracts.

## QUALITY

- **Vertically Integrated**

As a division of Constellation Brands, Polyphenolics has access to an abundant supply of quality U.S.-grown grapes and maintains total control over the entire manufacturing process, from raw material procurement to final extraction.

- **Environmentally Friendly**

The relationship between Polyphenolics and its parent company results in a uniquely sustainable model of agriculture wherein all parts of the grape are utilized. The grape juice is used to make wine, the unfermented grape seeds are used to manufacture MegaNatural<sup>®</sup>-BP and the grape skin and pulp provide the raw materials for producing MegaNatural<sup>®</sup>-GSKE Grape Pomace Extract.

## SAFETY

- **Non-toxic, Non-clastogenic**

MegaNatural<sup>®</sup>-BP has been the subject of two published safety studies: a three-month oral toxicity study in rats and a high-dose clastogenic study in mice (clastogens are substances that cause damage to chromosomes). MegaNatural<sup>®</sup>-BP was shown to be non-toxic and non-clastogenic.

- **GRAS (Generally Recognized As Safe)**

After submitting the above safety studies to FDA, MegaNatural<sup>®</sup>-BP received No-Objection GRAS status, making it safe for use in foods, medical foods and beverages, in addition to dietary supplements.

- **Free of Side Effects**

Clinical studies confirm MegaNatural<sup>®</sup>-BP is free of side effects, making it a safe and reliable option for people looking to maintain blood pressure within a healthy range.\*

- **Relentlessly Tested**

Every lot of MegaNatural<sup>®</sup>-BP is rigorously tested for heavy metals, pesticides and microbiological contaminants to ensure purity and safety.

- **Chemical-free**

MegaNatural<sup>®</sup>-BP is manufactured through a patented hot-water-based extraction process, without any traces of toxic chemicals or solvents in the final ingredient.

- **Safe History**

Millions of MegaNatural<sup>®</sup>-BP capsules have been sold in the market for the past five years, providing further evidence of its safety.

## RELIABILITY

- **100% Water-soluble**

MegaNatural<sup>®</sup>-BP is 100% water-soluble, so it can be easily added to functional beverages without dissipating out of solution.

- **Highly Consistent**

The consistency of every batch of MegaNatural<sup>®</sup>-BP is verified through specialized HPLC testing, the accepted protocol for measuring polyphenol profiles. Consistent activity guarantees consistent results.

## DIFFERENTIATION

- **Nationally Recognized**

MegaNatural<sup>®</sup>-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<sup>®</sup>-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<sup>®</sup>-BP from commodity grape seed extracts.

## Original Research on MegaNatural®-BP

While it may come as a surprise, the vast majority of raw materials in the marketplace today rely on “borrowed” science — studies performed on materials other than their own — to support their claims. MegaNatural®-BP is the rare exception.

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, Tissa Kappagoda C. *Clin Sci (Lond)*. 2008; 114:331-7.

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, known as the 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; 155-159.

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.\*

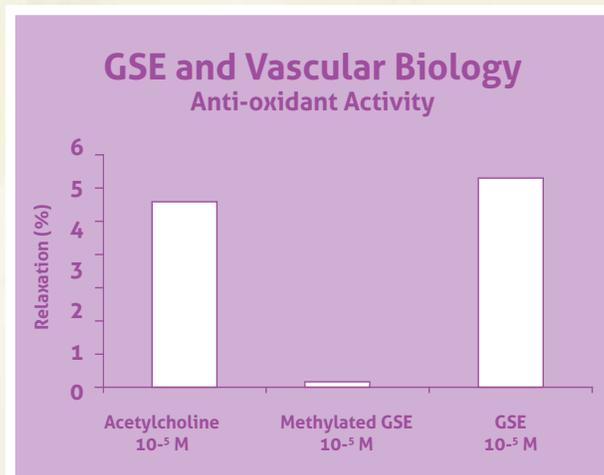
### Human Clinical Trial #3

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: randomized, double-blind, placebo-controlled.

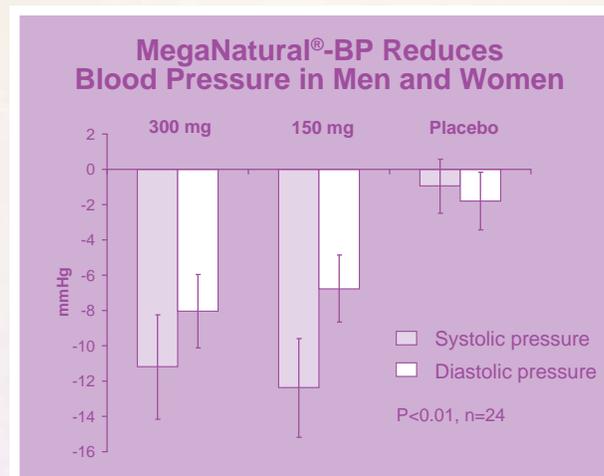
Study Type: A single-center, randomized, double-blinded, placebo-controlled, 12-week, parallel study

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 returned to baseline.



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.\*

## 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, 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 handling the varietal grapes. Through painstaking supply chain documentation and laboratory testing, Polyphenolics can substantiate freshness, identity, domestic origin, and absence of chemical contaminants and genetic modification.

## Dedication to Science

Polyphenolics has invested considerable resources into identifying the particular molecular structures within grape seed that provide the greatest health benefits. In addition, Polyphenolics relentlessly tests its products for:

- Efficacy, through human clinical trials
- Mechanism of action, through laboratory research
- Consistency, through HPLC testing
- Safety, through microbiological, pesticide and heavy metal testing

## Social and Environmental Responsibility

The relationship between Polyphenolics and its parent company Constellation Brands results in a uniquely sustainable model of agriculture, wherein seed, juice and pomace products from wine production — which would normally be thrown away — are used to develop healthful extracts for nutritional purposes. Additionally, the company is dedicated to reducing its carbon footprint by utilizing solar power to generate much of the electricity needed to operate its facilities.

## The Family of MegaNatural® Ingredients

In addition to its flagship ingredient MegaNatural®-BP, Polyphenolics offers an entire family of ingredients under the MegaNatural® brand name.



### MegaNatural® Gold Grape Seed Extract

A high-quality grape seed extract with a guaranteed minimum of 90% standardized polyphenols and an Oxygen Radical Absorption Capacity (ORAC) value greater than 13,000/gram



### MegaNatural® Whole Red Grape Juice Extract

An extract of whole red grape juice, providing a constituent profile similar to bilberry extract, with greater than 15% anthocyanins and 45% total polyphenols



### MegaNatural®-GSKE Grape Pomace Extract

An extract made from grape skins and grape seeds that boasts a high total polyphenol content (80%) and an ORAC value greater than 11,000/gram



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A division of Constellation Brands