
Maestro For Cardiometabolic Harmony
BERGAMONTE®
Musica Universalis ~ "Music of The Spheres"
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Clinically Proven • Highly Effective • Metabolic Syndrome Agent

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Bergamonte® BPE Complex: Maestro for Cardiometabolic Harmony

Imagine metabolic balance is like ***Musica universalis*** – when our solar system is in balance, creating a harmonic order.

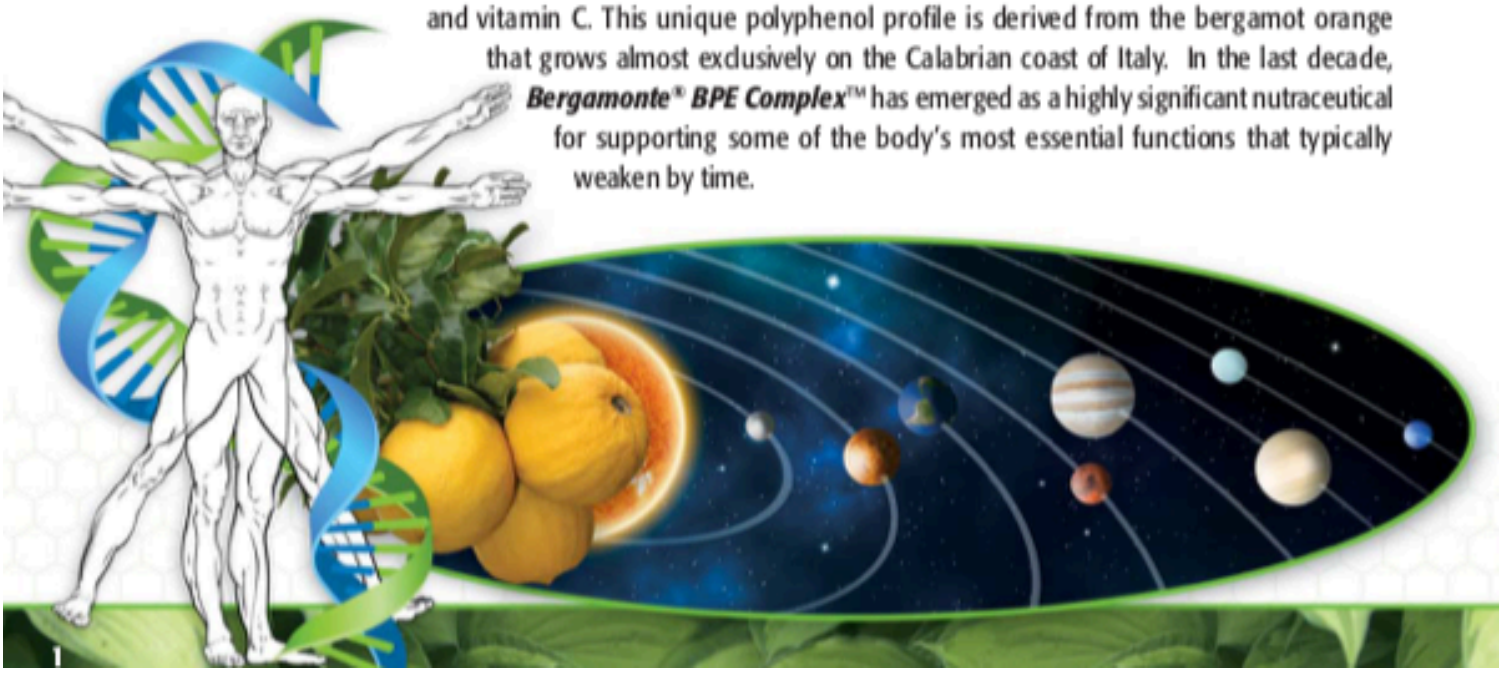
Metabolic imbalance, known as metabolic syndrome (or ***MetS***) can have profound ill effects on health and truncate longevity. Aging, the cumulative effects of time, brings with it many physical changes. Modern Western lifestyles have been found to impact aging by way of development of metabolic syndrome, itself the "perfect disharmony" leading to chronic degenerative and potentially deadly diseases. A supplement from citrus can help reduce risk and delay onset of ***MetS***, in conjunction with a mindfully healthy lifestyle.

Over time, without noticing, our bodies begin to have difficulty in managing healthy cholesterol levels, blood sugar metabolism, and weight control – leading to potential development of metabolic syndrome. ***MetS*** can cause numerous health conditions such as increased blood pressure, insulin resistance, excess body fat around the waist, and abnormal cholesterol or triglyceride levels – that occur together, increasing your risk of heart disease, stroke and diabetes, and diminish quality of life.

However, it is known that most individuals can significantly slow down the development of any of these conditions – and therefore, metabolic syndrome itself – through healthy lifestyle management including being physically active, losing weight (and fat), and eating nutritiously. Taking dietary supplements such as ***Bergamonte® BPE Complex™***, which research has demonstrated has powerful applications for metabolic syndrome and a related condition called non-alcoholic fatty liver disease, can additionally help combat these age-related health conditions.

Bergamonte® BPE Complex™ is the very first supplement that supports individuals who have both metabolic syndrome and non-alcoholic fatty liver disease.

Bergamonte® BPE Complex™, a standardized extract of Citrus bergamia risso, is rich in polyphenols such as neoeriocitrine, naringine, neohesperidine, melitidine, brutieridine. it also contains a high amount of both pectin and vitamin C. This unique polyphenol profile is derived from the bergamot orange that grows almost exclusively on the Calabrian coast of Italy. In the last decade, ***Bergamonte® BPE Complex™*** has emerged as a highly significant nutraceutical for supporting some of the body's most essential functions that typically weaken by time.



The Concept of Body Balance

In the time of Galileo, music and astronomy were functionally intertwined, and the planets' harmonious movements created Musica universalis – the music of the spheres. Much like Musica universalis – when our body's elements are moving in harmony, we have good health and well-being.

In relation to human physiology, the planets can be classified into four different functional groupings, as follows:

The Luminaries: the Sun & Moon
These "planets" provide most of the light in the heavens. Similarly, they represent the main power sources of the bodymind that drive all its functions.

The Personal Planets: Mercury, Venus & Mars
These rapidly moving planets represent important factors that define basic characteristics of your personality: how you think (Mercury), how you love (Venus), and how you fight (Mars). In Medical Astrology, they flesh out and expand on the core functions of the Sun, Moon and Ascendant.

The Social /Developmental Planets: Jupiter & Saturn
These slower moving planets aren't so personal, and define how we relate to larger groups of people, and to society in general. Medically, they're important regulators of the overall metabolism and govern the slower growth and developmental processes of the organism.

The Outer Planets: Uranus, Neptune & Pluto
Whereas the seven classical planets are sufficient to represent all the basic, ordinary functions of the bodymind, the outer planets represent certain extraordinary functions or capabilities that could even be called paranormal.

The Four Humors

Ancient medicine practitioners diagnosed conditions based on four physical qualities, which were believed to determine behavior of the human body...

Melancholic...
- Humor: Black Bile
- Element: Earth
- Season: Winter
- Age: Old Age
- Qualities: Cold & Dry
- Organ: Spleen
- Planet: Saturn

Phlegmatic...
- Humor: Phlegm
- Element: Water
- Season: Autumn
- Age: Maturity
- Qualities: Cold & Moist
- Organ: Brain
- Planet: Moon

Choleric...
- Humor: Yellow Bile
- Element: Fire
- Season: Summer
- Age: Childhood
- Qualities: Hot & Dry
- Organ: Gall Bladder
- Planet: Mars

Sanguine...
- Humor: Blood
- Element: Air
- Season: Spring
- Age: Adolescence
- Qualities: Hot & Moist
- Organ: Heart
- Planet: Jupiter

According to the American Heart Association, approximately 47 million Americans are living with metabolic syndrome (***MetS***), which results in slowing them down.

Metabolism is the process by which your body converts what you eat and drink into energy. It may be tempting to blame your metabolism for weight gain; however, metabolism is much more than weight control. During this complex biochemical process, calories in food and beverages are combined with oxygen to release the energy your body needs to function.

MetS as defined by the National Institutes of Health, is a group of risk factors linked to development of heart disease, diabetes and stroke, among other conditions. Risk for metabolic syndrome increases with age. People with abdominal obesity, who lead an inactive lifestyle, and are genetically predisposed to insulin resistance, are at the greatest risk for metabolic syndrome. Some people are at risk for metabolic syndrome because they take medicines that cause weight gain or changes in blood pressure, blood cholesterol, and blood sugar levels. These medicines most often are used to treat inflammation, allergies, HIV, depression, and other types of mental illness.

There are five metabolic risk factors that can be easily identified by the individual and his/her physician. You may have one of any of these risk factors by itself. However, according to NIH, you must have at least three of the metabolic risk factors to be considered to have metabolic syndrome.

PHATS is a mnemonic to remember Metabolic Syndrome:

P ~ *Pressure*
H ~ *HDL Cholesterol*
A ~ *Abdominal Obesity*
T ~ *Triglycerides*
S ~ *Sugar*

Pressure: Elevated blood pressure, which damages the heart and can lead to plaque buildup. Blood pressure readings of 130 mm Hg systolic and 85 mm Hg diastolic and greater are considered too high.

Low levels of high-density lipoprotein (HDL): HDL (the good cholesterol) sweeps low-density lipoprotein (LDL) and very low density lipoprotein (VLDL) out of the body and helps remove cholesterol from arteries by carrying the cholesterol from tissues or cells to the liver for catabolism. LDL and VLDL tend to accumulate when HDL is low, which is a significant risk factor for developing heart disease. Ideally, an individual would have high HDL and corresponding low to normal LDL. An HDL cholesterol level of <50 mg/dL for women and <40 mg/ dL for men (or being on medicine to treat low HDL cholesterol) is a metabolic risk factor.

Belly fat and large waistline (abdominal obesity): This used to be called "middle-age spread," and is often mistaken as being "something that just happens when you get older." Believing in this myth is dangerous, because excess fat in the abdominal area is a much greater risk factor for heart disease than excess fat in the hips, thighs or arms. The general rule is that abdominal fat is a key risk factor for women with waist circumference more than 35 inches, and men with more than 40 inches. Through diet, exercise and supplements such as ***Bergamonte® BPE Complex™***, middle-age people can have slimmer abdominal areas, thus lowering this risk factor.

According to one researcher, "Accumu- lated visceral adipose tissue produces and secretes a number of adipo-cytokines, such as TNF-α [tumor necrosis factor-alpha] and IL-6 [interleukin-6], which induce development of hypertension."

High triglyceride levels (also known as hypertriglyceridemia): Normal levels are 150 mg/dL, and lower; borderline to high is 150 to 199 mg/ dL, high is 200 to 499 mg/dL. A triglyceride level of 150 mg/dL or higher is a metabolic risk factor.

Sugar High fasting blood glucose levels: Normal fasting blood glucose is 100 mg/dL and lower. A fasting blood sugar level over 100 mg/dL is a metabolic risk factor. About 85 percent of people who have type 2 diabetes – the most common type of diabetes – also have metabolic syndrome. These people have a much higher risk for heart disease than the 15 percent of people who have type 2 diabetes without metabolic syndrome.

Balancing Hunger Hormones

A central issue within the sphere of MetS is increased appetite. Appetite is regulated by hormones leptin and ghrelin, and when these are in balance, we eat the amount of foods in normal range and maintain reasonably healthy weight. Adiponectin is a protein that must also be in harmony with leptin and ghrelin.

Leptin is a hormone that is produced by the body's fat cells. It is often referred to as the "satiety hormone" or the "starvation hormone." Its main role is regulating how many calories we eat and burn, as well as how much fat we carry on our bodies.

Ghrelin is a hormone produced in the gut. It is often termed the hunger hormone, and sometimes called lenomorelin. It travels through your bloodstream and to your brain, where it tells your brain to become hungry and seek out food. Ghrelin's main function is to increase appetite. It makes you consume more food, take in more calories and store fat.

Adiponectin is a protein secreted from adipose tissue. Plasma levels of adiponectin are especially low in individuals with visceral obesity and are associated with raised levels of several different markers of inflammation. Obese people have lower blood levels of adiponectin than normal weight individuals. Furthermore, reduction of obesity increases adiponectin levels.

Inflammation: A Related Condition

Those individuals with metabolic syndrome have another imbalance to try to address: they also tend to present with chronic inflammation – a key player in the development of heart disease and many other serious health conditions.

Metabolic overload evokes stress reactions and activates inflammation. Over nutrition, physical inactivity, and aging result in excess cytokines such as IL-6, TNF-α and C-reactive protein (CRP). These pro-inflammatory cytokines lead to insulin resistance and diabetes in metabolically predisposed individuals.

Statins Don't Create Balance

When cholesterol levels rise (specifically, total cholesterol, low-density lipoproteins and very low-density lipoproteins), physicians turn to a class of pharmaceuticals known as statins – HMG-CoA reductase inhibitors. These are chemicals that block the liver from producing an enzyme that is responsible for creating and releasing LDL. That blue prescription pad can call for any of the following: Atorvastatin, simvastatin, rosuvostatin, pravastatin and eztemibe.

There is currently no one "simple" pharmaceutical intervention that can address the many aspects of metabolic syndrome. Many drugs that address cholesterol, diabetes, or blood pressure exert various side effects that can lead to other health issues. Statin cholesterol lowering drugs are among the most widely prescribed drugs on the market, with more than one in four Ameri- cans over the age of 45 taking them. This already inflated number is set to increase significantly due to the U.S. Preventive Services Task Force recommending statins to healthy adults over the age of 40 as a form of preventive medicine.

However, for some people statins have a dark side. Statin-consuming folks don't actually feel the intended benefits, but they may feel the side effects, which may include muscle pain and weakness, felt often in the thighs, upper arms, lower back and shoulders; liver damage, and increased blood sugar levels. Further, statins also increase risk of side effects when combined with many other drugs. Meanwhile, less common side effects, such as depression, loss of ability to concentrate, and memory issues have been known to occur in statins users too.

3 Reasons To Avoid Statins

1~ They Don't Support against Met S: Statin drugs work to lower cholesterol, but there are far more factors contributing to cardiovascular health than just your cholesterol levels. There is evidence showing that statins may worsen overall heart health.

2~ Statins Deplete Your Body of Coenzyme Q10 (CoQ10): All cells in the body need and use CoQ10 for energy production. The heart is the most energy-de- manding organ in the body. The depletion of CoQ 10 caused by statin drugs is why risk of acute heart failure increases.

3~ Increased Risk of Other Serious Diseases: Research has shown that long-term statins use (10 years or longer) more than doubles risk of breast cancer and prostate cancer. Statins have also been shown to increase insulin resistance and increase diabetes risk by raising blood sugar. Memory loss and other neurodegenerative disease are widely reported in association with statin use. Statins users are more likely to suffer from musculoskeletal conditions, injuries and pain than non-users.

Therefore, the challenge is to provide consumers with a dietary supplement that they can rely on for cholesterol control – without all the side effects of statins – while also lessening the other factors of metabolic syndrome. Bergamonte® BPE Complex™ just may be that solution.

The Maestro: Bergamonte® BPE Complex™

When the body is out of balance because of ***MetS*** and related inflammation, it's like the music of the spheres being in chaos. But there is a solution, like a maestro to bring out the harmony once again – the Italian superfruit known as ***Bergamonte® BPE Complex™***, from the Calabrian bergamot.

Italy is renowned for its olive oil, wine, and so many other gustatory delights, including the juicy, rotund Bergamot citrus fruit (technically known as Citrus bergamia Risso), which grows almost exclusively in Italy's coastal Calabria region (southern Italy).

Bergamot juice was traditionally consumed by the local population as a remedy for supporting healthy cholesterol levels and promoting overall cardiovascular fitness. This traditional usage of bergamot has been rediscovered and validated by research teams in Italy using modern scientific methods.

The juice and albedo (the white inner portion of a citrus-fruit rind) of bergamot is high in Vitamin C and Pectin, and have a unique profile of flavonoid and glycosides, such as neoeriocitrin, neohesperidin, naringin, rutin, neodesmin, rhoifolin, and poncirin.

Naringin is a powerful antioxidant. Studies have shown that naringin has cholesterol lowering effect, reduces LDL oxidation and can help to prevent hypercholesterolemia. In clinical trial with 60 hypercholesterolemic subjects, 400mg of naringin supplementation for 8 weeks was found to lower the plasma total cholesterol by 14% and low-density lipoprotein cholesterol concentrations by 17%. The apolipoprotein B levels (particles that transport cholesterol and triglycerides in the blood stream) in the hypercholesterolemic subjects were significantly lowered after naringin treatment. In addition, the erythrocyte superoxide dismutase and catalase activities in the hypercholesterolemic group were significantly increased.[1] Naringin is an aldose reductase inhibitor which means that it can help fight retinal disease linked to diabetics.

Neoeriocitrin and rutin have been found to exhibit a strong capacity to prevent LDL from oxidation. Treatment of Neohesperidin significantly decreased

fasting glucose, serum glucose, and glycosylated serum protein in diabetic model mice. Neohesperidin significantly increase glucose tolerance and insulin sensitivity, and decreased insulin resistance in the diabetic mice. In addition, Neohesperidin significantly decreased serum triglycerides, total cholesterol, and inhibited lipid accumulation in the liver. Epididymal adipocyte were also decrease via the activation of the AMPK pathway.[2]

People use pectin for cholesterol, triglycerides, balance blood glucose, and support weight loss. In guinea pig fed with high cholesterol diet, researcher had found citrus pectin significantly reduced LDL in a dose-response manner from 29% to 67%, increased apolipoprotein B/E receptors, decreased hepatic cholesterol and acyl-CoA: cholesterol acyltransferase (ACAT) activity.[3]

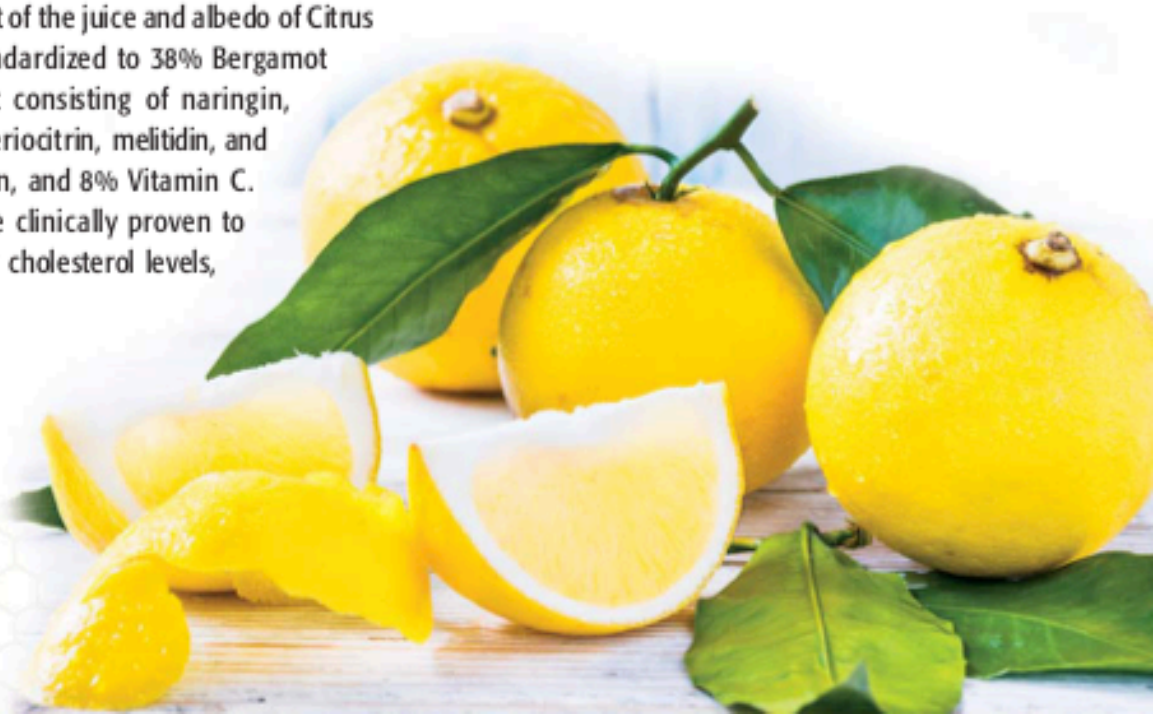
Importantly, bergamot juice is rich in brutieridin and melitidin, novel compounds found only in Bergamot, with molecular structure resembles that of statins, with an ability to inhibit HMG-CoA reductase, which catalyzes the mevalonate biosynthesis, a key intermediate in cholesterol metabolism.

Bergamonte® BPE Complex™ contains bioactive compounds of extract of the juice and albedo of Citrus bergamia Risso, standardized to 38% Bergamot Polyphenolic Extract consisting of naringin, neohesperidin, neoeriocitrin, melitidin, and brutieridin., 8% Pectin, and 8% Vitamin C. These flavonoids are clinically proven to help support healthy cholesterol levels, healthy blood glucose activity, increase HDL cholesterol levels, and promote healthy weight management.

The research on ***Bergamonte® BPE Complex™*** is so compelling that Health Canada has allowed the following claims for supplements containing ***Bergamonte® BPE Complex™***:

- ***Helps maintain/support healthy (total, LDL, HDL,) cholesterol levels***
- ***Helps maintain/support cardiovascular health***
- ***Helps maintain/support healthy glucose levels***
- ***Helps maintain/support healthy weight management***
- ***Provides powerful antioxidants***

Bergamonte® BPE Complex™ is a unique bergamot extract with human clinical studies, showing efficacy in several parameters of metabolic syndrome and NAFLD, making it highly relevant for nearly 50 million Americans. In addition, for those who would rather not take statins for cholesterol management, ***Bergamonte® BPE Complex™*** may be an effective alternative or an adjunct, depending upon the individual.

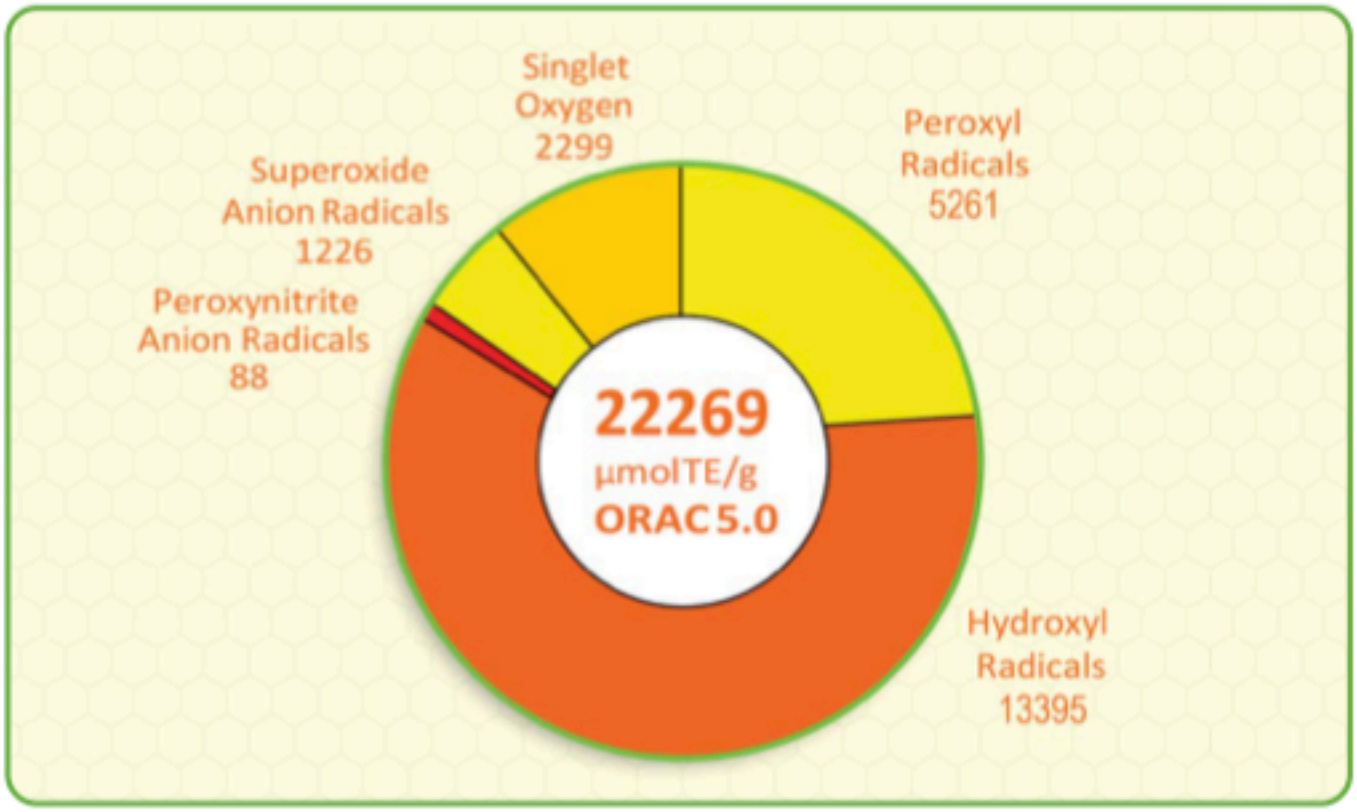


How Does Bergamonte® BPE Complex Work™?

Bergamonte® BPE Complex™ has several mechanisms of action that teams of researchers revealed. And they all work harmoniously to bring the body back into balance to age more robustly and increase overall well-being.

Bergamonte® BPE Complex™ Scavenges Free Radicals

Bergamonte® BPE Complex™ is a powerful antioxidant with total ORAC value over 22,000 umole/g. Bergamot flavonoids inhibit the free radical formation and prevent LDL-C oxidation.



Bergamot Polyphenols Inhibits HMG-CoA Reductase

In a study published in the Journal of Natural Products July 2009, researchers discovered two novel statin-like compounds in the bergamot fruit that has 3-hydroxy-3-methylglutaric acid (HMG) bound to neohesperidin and naringin to become new compounds named brutelidine and melitidin. These novel compounds act as direct HMGCoA reductase inhibitors, to catalyze the HMGCoA to mevalonate (a key intermediate in cholesterol metabolism.) Inhibition of the HMGR enzyme is reported to significantly decrease cholesterol levels and reduce the risks of stroke.

HMG-CoA reductase is an enzyme linked to the liver's cholesterol production. Mel- itidin and brutieridin inhibit the liver's ability to produce LDL, resulting in reduced cholesterol levels in liver cells, which then meet their cholesterol requirements by taking up cholesterol circulating in the blood, via LDL receptors. LDL receptors break down the circulating cholesterol, resulting in healthy LDL levels in the blood- stream.[10,11]

Bergamot Polyphenols Inhibits Phosphodiesterases (PDEs)

Bergamot flavonoids mediate their beneficial effects on lipid and glucose homeo- stasis by PDE4 and PDE3B modulation. PDE4 plays a critical role in cAMP (cyclic adenosine monophosphate), which regulates energy metabolism, AMPK, triglyceride hydrolysis, and glucose metabolism. PDE3B is crucial for triglyceride and cholesterol metabolism, as well as glucose homeostasis. Dysregulation of PDE3B can cause development of fatty liver, common in metabolic syndrome and type-2 diabetes patients.[5]

Bergamot Polyphenols Activates AMPK

AMP (adenosine monophosphate)-activated protein kinase (AMPK) is a master regulator of the metabolic pathways involved in ATP production. Because excess abdominal fat is a factor in metabolic syndrome, stimulating fat burning helps to lessen this symptom. The flavonoids in ***Bergamonte® BPE Complex***™ stimulate AMP-activated protein kinase (AMPK) and stimulate glucose uptake. AMPK plays a central role in regulating healthy glucose, lipid metabolism and energy production. AMPK activation can prevent abdominal fat accumulation, regulate glucose tolerance, normalize liver markers, and reduce oxidative stress and inflammation in the liver and heart. Bergamot flavonoids activate the glucose transporter GLUT1 in all cells and upregulation and translocation GLUT4 to the cell membrane in muscle cells.[5]

In rat model of hepatic steatosis induced by cafeteria diet, higher AMPK phosphorylation levels were observed accompanied by significant decrease in blood triglyceride and glucose levels. Analysis of AMPK expression from patients with metabolic syndrome taking 650mg of BPF twice daily leads to increased AMPK levels.

Bergamot Polyphenols Activates Cholesterol 7R-hydroxylase

Bergamot Polyphenols activate cholesterol 7R-hydroxy lase, an enzyme that converts liver cholesterol to neural sterol and bile acids (this is a key pathway for cholesterol elimination). The increased bile acids fecal excretion leads to a decrease in hepatic cholesterol content, which in turn stimulates LDL receptor expression and lowers blood cholesterol levels.

Bergamot Polyphenols Reduces Inflammation

One team of researchers looked at the role of Bergamot Polyphenols in inflammatory response. In an in vitro assay, they demonstrated that the bergamot polyphenols inhibited both gene expression and secretion of pro-inflammatory cytokines (IL-6, IL-1b, TNF-α) through inhibiting NF-kB activation. They concluded, "These results suggest that these bergamot polyphenols may be useful for the development of alternative pharmacological strategies aimed at reducing the inflammatory process."[13]

Bergamot Polyphenols Balance Hunger/Appetite

Studies have shown that administration of ***Bergamonte® BPE Complex***™ significantly reduced ghrelin by -6.89% (650mg) and -14.90% (1300mg) respectively after 90 days. Additionally, ***Bergamonte® BPE Complex***™ significantly increased adiponectin by +18.65% (650mg) and +21.76% (1300mg). This was accompanied by a reduction of body weight by -10.04% (650mg) and -14.91% (1300mg), as well as reduction of BMI by -10.12% (650mg) and -15.85% (1300mg) respectively after 90 days.[14]

Proof of Efficacy: From Animal Models to Human Studies

Bergamonte® BPE Complex™ is a unique citrus extract from Calabria, Italy, different than Citrus aurantium from China or other countries. There are now over 200 research papers published on Bergamot Polyphenols with several human clinical studies, showing efficacy in several parameters of metabolic syndrome and NAFLD, making ***Bergamonte® BPE Complex™*** highly relevant for nearly 50 million Americans. In addition, for those who would rather not take statins for cholesterol management, ***Bergamonte® BPE Complex™*** may be an effective alternative, or an adjunct, depending upon the individual.

There Are Now Over 200 Research Papers Published On Bergamot With Several Human Clinical Studies

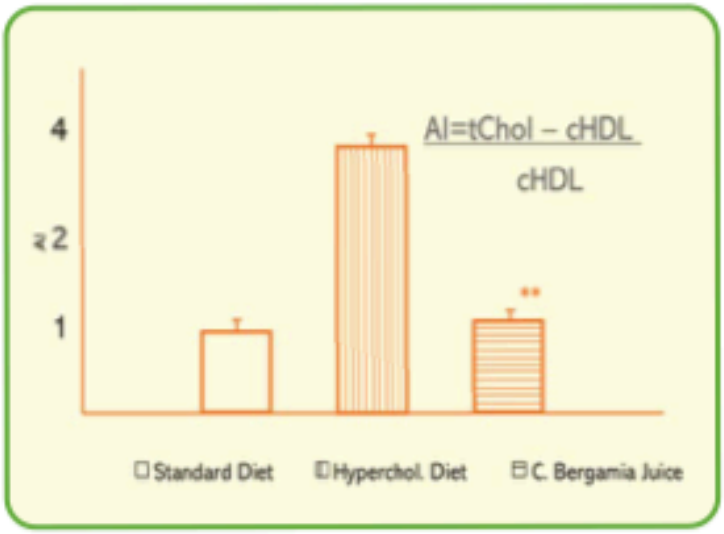
Bergamot Juice Reduces Aterogenic Index

In research published in the *Journal of Agricultural and Food Chemistry*, 2007, the effects bergamot juice on lipid metabolism were evaluated in diet-induced hypercholesterolemia experimental rat model.

	Total Cholesterol	HDL Cholesterol	LDL Cholesterol	Triglycerides
Bergamot Juice (1ml/day)	-29.27%	+27.61%	-51.72%	-46.12%

The administration of bergamot juice for 30 days provoked a significant reduction in serum levels of cholesterol (29.27%), triglycerides (46.12%), and LDL (51.72%) and an increase in HDL (27.61%) levels versus hyperlipidemic controls. The HDL pathway of removing LDL and VLDL for catabolism by the liver plays a very important role in reducing the cholesterol levels in blood and peripheral tissue and inhibiting atherosclerosis plaque formation. Because cholesterol was significantly suppressed, and HDL was significantly increased, as a result Aterogenic Index (AI) were significantly reduced in the bergamot group.

Output of total bile acids and neutral sterols were found to be enhanced significantly by 42.22% and 30.96% in the Bergamot group. The conversion of cholesterol to bile acids is the major pathway of cholesterol elimination, and it accounts for about 50% of daily cholesterol excretion. The increase in the excretion of bile acids seem to activate cholesterol 7R-hydroxylase, enhancing the conversion of liver cholesterol to bile acids for excretion



Bergamot Polyphenolic Fraction Cholesterol Studies

In research published in Fitoterapia 82 (2011) 309–316, researchers examined the hypolipemic and hypoglycemic activity of Bergamot Polyphenolic Fraction (BPF) from animal models to human clinicals.

In one study, 237 individuals were given either placebo or BPF standardized to 30% naringin, neoeriocitricin, neohesperidin, melitidin, and brutelidin daily for 30 days. There were 104 people with isolated hypercholesterolemia (LDL>130), 42 with mixed hyperlipedemia (high cholesterol and high tryglyceride), 59 people with metabolic syndrome (mixed hyperlipemia and hyperglycemia), and 32 who were previously on statins.

All individuals were given either placebo (500mg maltodextrine + 50mg ascorbic acid), or (500 mg BPF + 50mg ascorbic acid) or (1,000 mg BPF + 100mg ascorbic acid) daily for 30 days. There were also 32 patients in the post-statins group, who stopped simvastatin therapy due to muscular pain and a significant elevation of serum creatine-phospho-kinase (CPK); they waited 60 days as a washout period and were given (1500mg of BPF + 150mg ascorbic acid) daily.

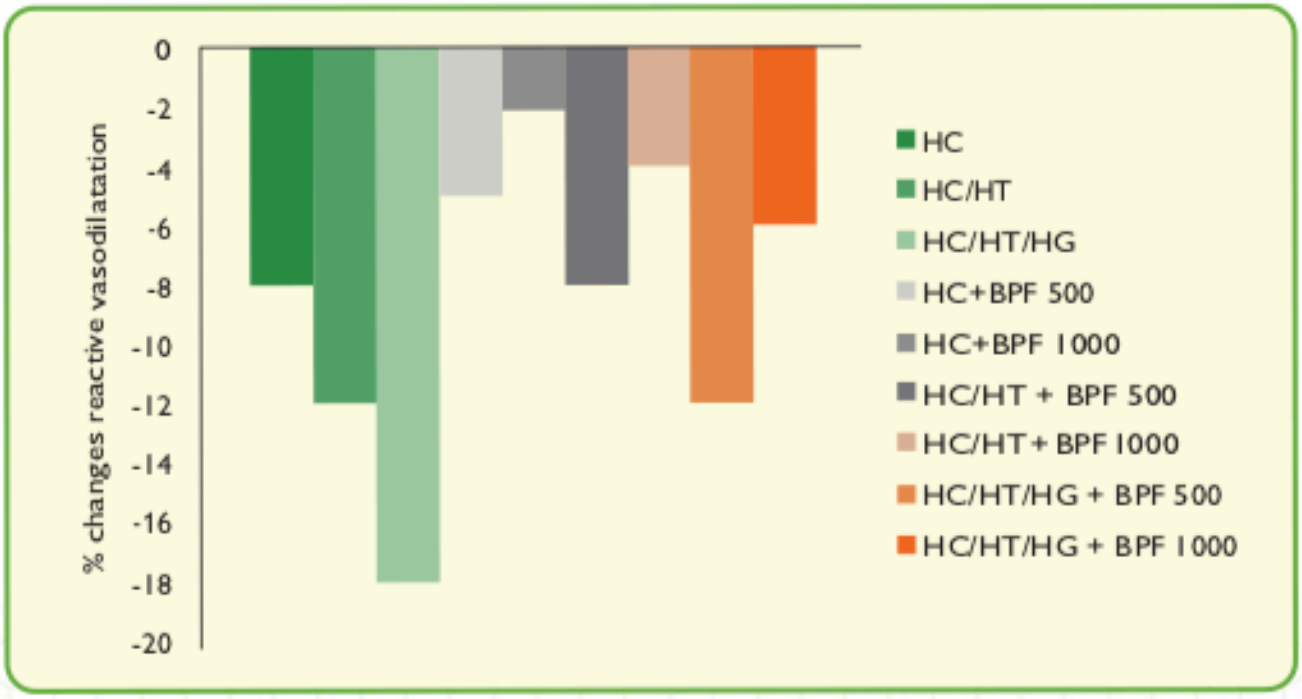
	Total Cholesterol	HDL - C	LDL - C	Triglycerides	Blood Glucose
Placebo (n=66)	-0.1%	+1.2%	-1.1%	+0.1%	+0.5%
30% BPF 500mg/Day (n=69)	-21.8%	+22.3%	-24.1%	-32%	-18.9%
30% BPF 1000mg/Day (n=70)	-29.4%	+40.1%	-36.0%	-41%	-22.4%
Post Statin Group (1500mg 30% BPF/Day) (n=32)	-25%	+23.8%	-27.6%	N/A	N/A

The researchers showed that BPF led to a strong reduction in total cholesterol, LDL, and a significant increase in HDL in the majority of the subjects. No significant changes in the mean cholesterol parameters were recorded after 30 days in the placebo groups. Further, the researchers observed significant reduction in triglyceride levels especially in participants with hypertriglyceridemia and metabolic syndrome. Volunteers with metabolic syndrome experienced a highly significant reduction in blood glucose levels. Patients that are taking 1000mg 30% BPF are getting better result compared to the 500mg 30% BPF group.

The effect on HDL was very striking: 22.3% to 40.1% increase. The conclusion is that BPF therapy leads to a significant reduction of coronary artery disease risk as confirmed in this human study. Experts believe HDL cholesterol may act in a variety of helpful ways that tend to reduce the risk for heart disease:

- ***HDL cholesterol scavenges and removes LDL cholesterol.***
- ***HDL reduces, reuses, and recycles LDL cholesterol by transporting it to the liver where it can be reprocessed.***
- ***HDL cholesterol acts as a maintenance crew for the inner walls (endothelium) of blood vessels. Damage to the inner walls is the first step in the process of athero- sclerosis, which causes heart attacks and strokes. HDL scrubs the wall clean and keeps it healthy.***

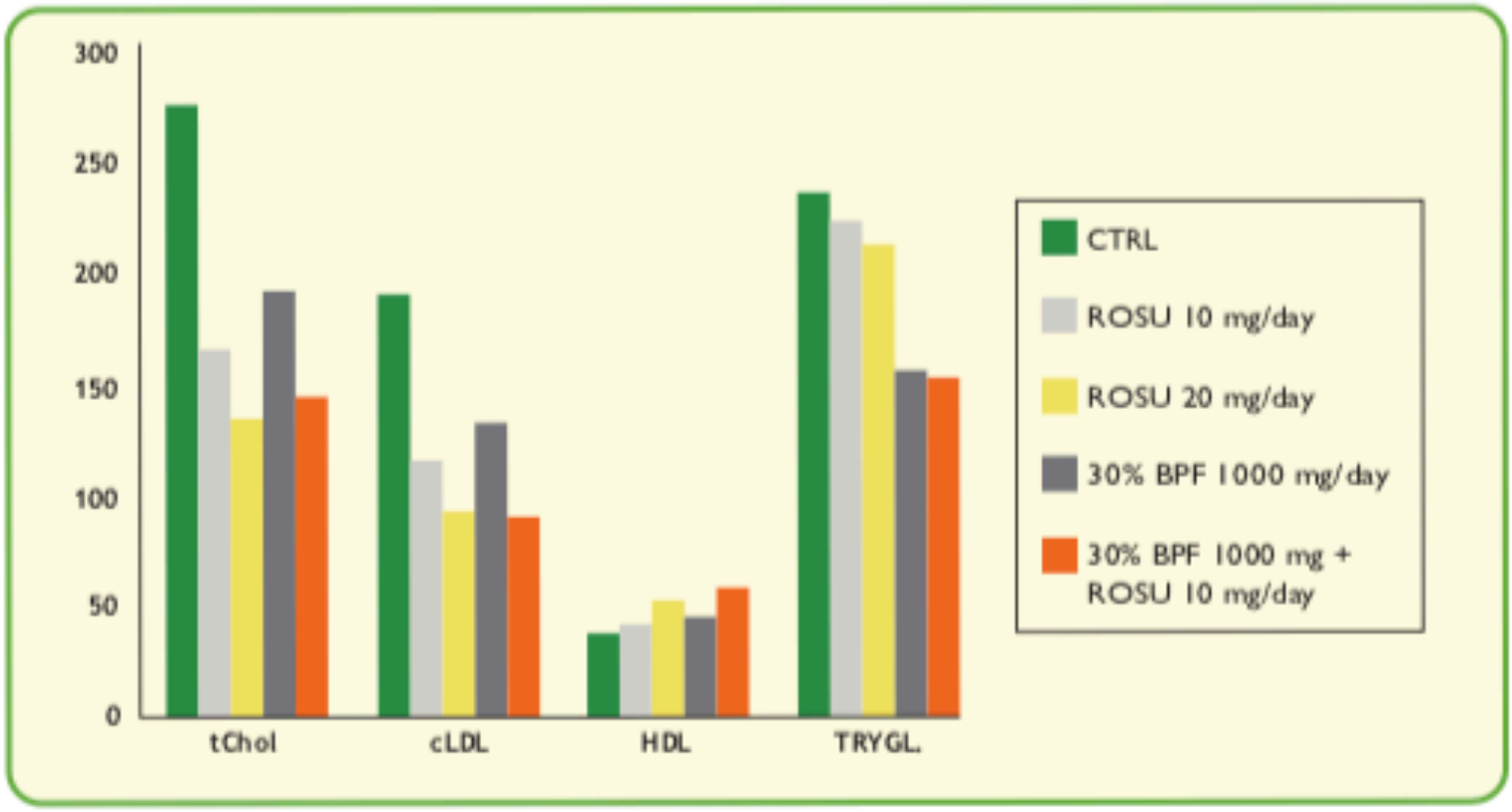
In the post-statins group, BPF offers a safe alternative for individuals exhibiting statin toxicity. A 24-hour urinary MVA excretion test showed decreased from a baseline value of 2.12 to 1.34 µmol/day.



Bergamot Polyphenolic Fraction Complements Statins

Statins are the most commonly prescribed pharmaceuticals used to reduce cardio-metabolic risk – addressing unhealthy cholesterol profiles. Statins inhibit the activity of 3-hydroxy-3-methyl-glutaryl-CoA (HMG-CoA) reductase, a key intermediate in cholesterol metabolism. Despite the significant clinical benefits provided by statins, many people, those with diabetes or metabolic syndrome, do not achieve their recommended LDL-C and HDL-C target goals with statins alone. Moreover, statins have been reported to cause dose-related side effects.

A randomized placebo-controlled study published in the International Journal of Cardiology 2013, recruited 77 individuals all with elevated LDL and triglyceride levels. The individuals were randomly assigned to five groups: placebo, 10mg of rosuvastatin (rosu), 20mg of rosuvastatin, 1000mg BPF + 100mg ascorbic acid, and 1000mg of BPF + 100mg ascorbic acid +10mg of rosuvastatin for 30 days.



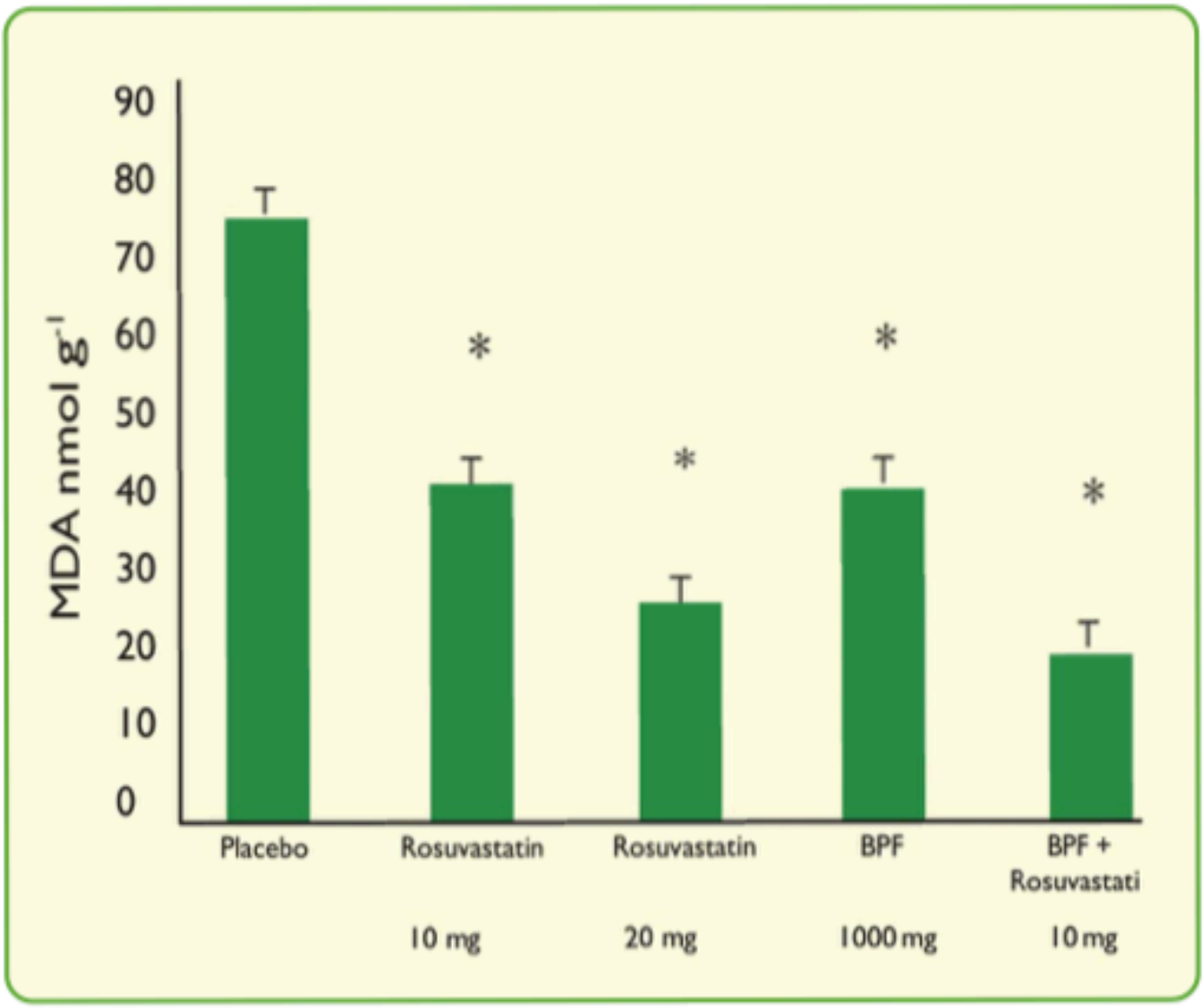
	tChol	cLDL	HDL	TRYGL
Basal	278 + 4	191 + 3	38 + 2	238 + 5
Placebo (n=15)	275 + 4	190 + 2	38 + 3	235 + 5
Rosu 10mg (n=16)	195 + 3*	115 + 4*	42 + 3*	200 + 4*
Rosu 20mg (n=16)	174 + 4*	87 + 3*	48 + 3*	202 + 5*
30% BPF 1000mg (n=15)	191 + 5*	113 + 4*	45 + 4*	165 +3*
30% BPF 1000mg + Rosu 10mg (n=15)	172 + 3*	90 + 4*	52 + 4*	152 + 5*

No change in serum total cholesterol, LDL-C, HDL-C and triglycerides was found in the placebo group. 10mg and 20mg rosuvastatin groups produced a significant reduction of total cholesterol and LDL compared to placebo. Minimal reduction in triglycerides and elevation in HDL-C were observed.

Oral administration of 1000mg BPF daily showed the same reduction in total cholesterol and LDL-C as 10mg of rosuvastatin; the reduction in triglyceride and increase in HDL-C were much more significant in the 1000mg BPF group compared to the 10mg rosuvastatin group.

The combination of 1000mg of BPF combined with 10mg of rosuvastatin produced a significant decrease in total cholesterol and LDL, nearly the same as 20mg of rosuvastatin. In addition, triglycerides were reduced by 42% and HDL was increased by 34%, an effect which was significantly higher compared to the use of 20mg of rosuvastatin alone.

Oxidative stress increased concentration of oxyLDL and is followed by an inflammatory response in vascular tissues which is accompanied by the overexpression of LOX-1 (oxidized low-density lipoprotein receptor). The basal levels of malondialdehyde (MDA, a marker of lipid peroxidation) and LOX-1 expression have been previously found elevated in patients with hyperlipidemia compared to a group of normolipidemic individuals. Those who took 1000 mg BPF daily, rosuvastatin (10 and 20mg), or a combination of both (1000mg BPF plus 10mg Rosu) had significantly decreased malondialdehyde, oxyLDL receptor LOX-1 and phosphoPKB, which are all biomarkers of oxidative vascular damage.



This study yielded data showing that 1000mg of BPF exerted a vasoprotective action via its antioxidant ability, enhanced the reduction in triglycerides, and increased HDL-C. Overall, the researchers concluded that Bergamot Polyphenolic Fraction allows the reduction of daily dose of rosuvastatin while achieving target lipid values in patients with mixed dyslipidemia.

This effect was characterized by a significant reduction in total cholesterol, LDL, accompanied by amplified reduction in triglycerides, increase in HDL, resulted in an enhanced expression of protein kinase B levels in PMNs of hyperlipidemic patients.[10]

	Baseline	38% BPF	% Change
BMI (kg/m2)	29.4 ± 2.01	28.2 ± 1.53	-4.0%
Fasting plasma glucose (mg/mL)	118 ± 1.4	98 ± 0.8*	-16.9%
Total Cholesterol (mg/dL)	245 ± 8.3	182 ± 7.1*	-25.7%
LDL-C (mg/mL)	162 ±4.3	101 ± 1.8*	-37.7%
HDL-C (mg/mL)	38 ± 3.8	49 ± 4*	+28.9%
Triglycerides (mg/mL)	232 ± 5.1	160 ± 4.8*	-31.0%

VLDL is made up of cholesterol, triglycerides, and proteins. They move cholesterol, triglycerides, and other lipids around the body. VLDL contains the highest amount of triglycerides and is an unhealthy cholesterol because it encourages the buildup of cholesterol on the walls of arteries. Patients taking BPF showed significant reduction in large VLDL particles by 57.1% and medium VLDL by 54.8%

Plasma lipoprotein plasma	Baseline	38% BPF	%Change
VLDL	55.3 ± 6.4	44.5 ± 5.2*	-19.5%
LDL	22.6 ± 1.7	18.0 ± 0.8*	-20.35%
HDL	7.5 ± 0.8	9.6 ± 0.9*	+28%
Plasma lipoprotein particles, nmol/L			
Total VLDL	83 ± 14	4 ± 12*	-34.9%
Large VLDL	4.2 ± 2	1.8 ± 1.3*	-57.1%
Medium VLDL	31 ± 9	14 ± 8*	-54.8%
Small VLDL	43 ± 9	38 ± 10	-11.6%

LDL (LDL-P) particle number measures the actual number of LDL particles. Studies show that people whose LDL particles are predominantly small and dense, have a threefold greater risk of coronary heart disease. Furthermore, the large and fluffy type of LDL may be protective. What is significant about this study is that it unveils that BPF decreased the mean concentration of intermediate density lipoprotein (IDL) particles by 50.6%, decrease small LDL by 37.9%, while increase the protective large LDL by 54%. Moreover, 120-day supplementation with BPF led to 20% increase of total HDL particles, mainly due to the increase of 200% of the large HDL.

Plasma lipoprotein particles, nmol/L	Baseline	38% BPF	%Change
Total LDL	1477 ± 75	1293 ± 101*	-12.5%
IDL	77 ± 16	38 ± 10*	-50.6%
Large LDL	424 ± 87	653 ± 95*	+54.0%
Small LDL	986 ± 105	612 ± 98*	-37.9%
Total HDL	30 ± 2	36 ± 3*	+20.0%
Large HDL	5 ± 3	15 ± 4*	+200%
Medium HDL	7 ± 4	7 ± 3	unchanged
Small HDL	18 ± 5	14 ± 4*	-22.2%

	Baseline	38% BPF	%Change
Steato test	0.74 ± 0.12	0.44 ± 0.09*	-99.4%
ALT (U/L)	54 ± 5.4	36 ± 5.3*	-33.3%
AST (U/L)	52. ± 6.4	41 ± 5.2*	-21.2%
γ-GT (IU/L)	38 ± 5.2	29.33 ± 1.1*	-22.8%
Hs-CRP (mcg/dl)	1.2 + 0.8	0.94 + 0.6*	-21.6%
TNF-α (pg/mL)	14.4 ± 1.9	10.7 ± 1.7*	-25.7%
Hepatorenal index	2.8 ± 0.4	1.5 ± 0.5*	-46.4%

The improvement of steato test and hepatorenal index in patients with MS and NAFLD following BPF supplementation are confirmed by the significant reduction in serum liver enzyme - ALT and AST.

This led to the conclusion that Bergamot Polyphenolic Fraction may help improves both liver function and signs of chronic liver inflammation, as confirmed by reduction of TNF-α and CRP.

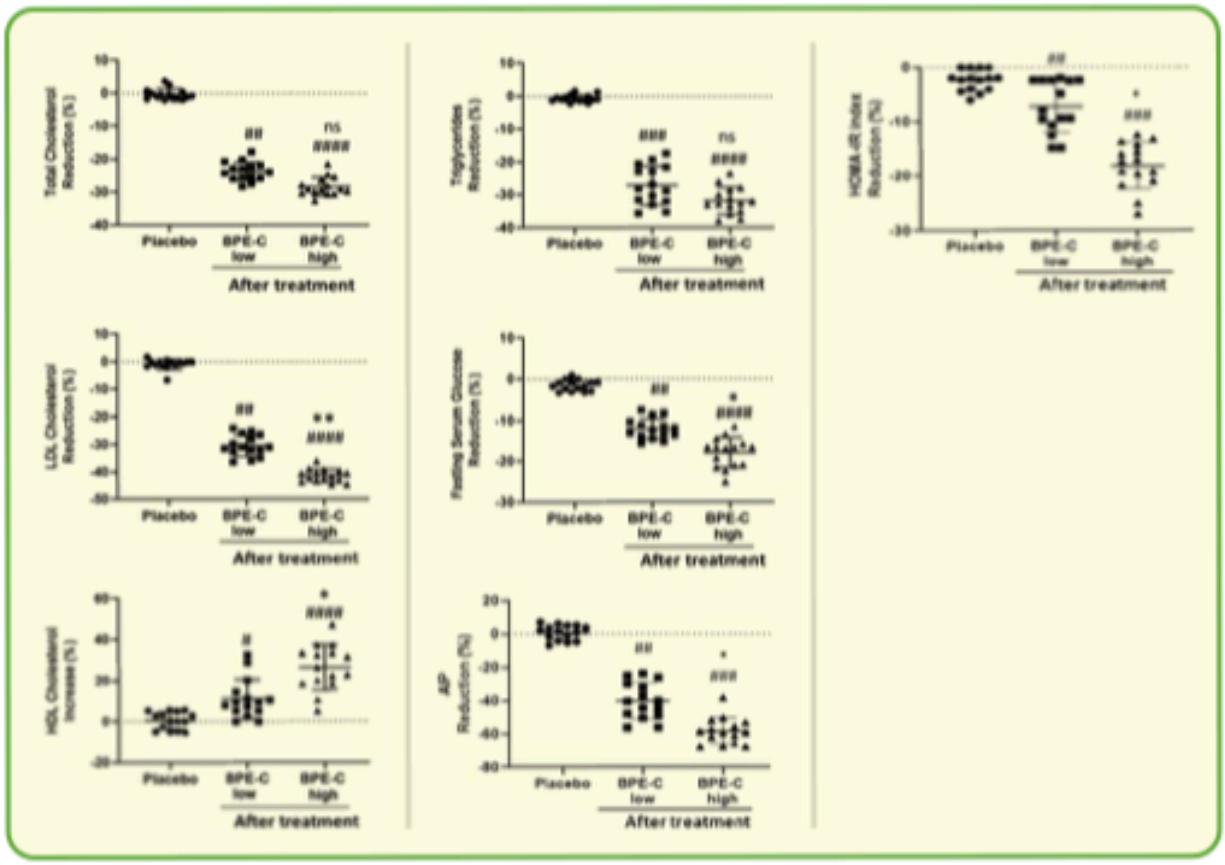
A new double-blind randomized study published study of 52 obese patients with atherogenic index of plasma (AIP) over 0.34 and mild hyperglycemia compared two doses of BPE-C (650 and 1300 mg daily) with placebo for 90 days. BPE-C reduced significantly fasting glucose by 18.1%, triglycerides by 32% and cholesterol parameters by up to 41.4%, leading to a powerful reduction of AIP (below 0.2) in the high dose group. The homeostasis model assessment of insulin resistance (HOMA-IR) and insulin levels were also reduced. Moreover, BPE-C decreased body weight by 14.8% and body mass index by 15.9% in BPE-C high group. This correlated with a significant reduction of circulating hormones balancing caloric intake, including leptin, ghrelin and upregulation of adiponectin. All effects showed a dose-dependent tendency. This study suggests that food supplements, containing full spectrum of bergamot juice components, such as BPE-C efficiently induce a combination of weight loss and insulin sensitivity effects together with a robust reduction of atherosclerosis risk. 14

This study correlates to and validates a recent study on rats to determine anti-obesity effects. The rodents were fed a basal diet (lean and CTR group) or basal diet supplementation with Bergamonte BPE-Complex extract at 10 and 30 mg per kg, for 28 days.

Body and adipose tissue weights in 5% of the supplement group were found to be significantly lower than the control group. Fasting blood glucose and HOMA-IR levels were also improved, as were serum triglyceride and free fatty acid levels, which were reduced in both Bergamonte BPE-Complex dosage groups. The researchers also noted that the rats in the BPE-C group showed heightened glucose tolerance. The researchers concluded, "These results suggest that dietary BPE-C is beneficial for improving diabetes by decreasing lipid levels." 15

	T Chol % Change	LDL % Change	HDL % Change	TRYG % Change	F GLU % Change	HOMA -IR
Placebo (n=15)	-0.31%	-0.94%	0.50%	-0.62%	-1.56%	2.00%
650mg BPE-C (n=15)	-23.70%	-30.42%	10.94%	-27.09%	-12.08%	-8.33%
1300mg BPE-C (n=15)	-28.35%	-41.38%	26.37%	-31.89%	-18.00%	-16.66%

	BW % Change	BMI % Change	Leptin (ng/ml)	Ghrelin (pg/ml)	Adiponectin (mg/ml)
Placebo (n=15)	-2.77%	-3.60%	1.36%	-0.61%	-3.63%
650mg BPE-C (n=15)	-10.04%	-10.12%	-12.30%	-6.89%	18.65%
1300mg BPE-C (n=15)	-14.91%	-15.85%	-21.36%	-14.90%	21.76%



FAQs About Bergamonte® BPE Complex™

What claims can be made for Bergamonte® BPE Complex™?

Follow your regulatory counsel's guidance on label and marketing claims, but some claims to consider for products containing Bergamonte® can include: Multiple human clinicals allow for the following claims*:

- ***Helps support healthy Cardiovascular Function***
- ***Helps support Healthy Cholesterol Levels***
- ***Encourages Healthy Weight Management***
- ***Helps support Healthy Blood Glucose Levels***
- ***Helps support Healthy Liver function***
- ***Enhance Nitric Oxide***
- ***Provides Antioxidants***

What forms of Bergamonte® BPE Complex™ are available?

Bergamonte® BPE Complex is available in conventional and organic. All are kosher and halal certified.

What are the dosage amounts for Bergamonte® BPE Complex™?

1,000 mg to 1500 mg daily for 1 to 6 months, or until optimal healthy cholesterol levels are achieved. Maintenance dose thereafter for healthy cholesterol should be 500 mg to 1000 mg daily.

Where does the bergamot fruit come from in Bergamonte® BPE Complex™?

We only use citrus bergamot fruits that are harvested and grown in the rich soils of Calabria on the southern coast of Italy. These bergamot fruits are harvested using traditional sustainable farming techniques handed down by generations of local farmers in Calabria.

Is Bergamonte® BPE Complex™ GRAS? (Generally Recognized As Safe)

Yes, bergamot is on the FDA GRAS list. It is the same Bergamot found in Earl Grey Tea.

Glossary of Terms

AMPK: A biochemical that informs cells when to store and use energy; when it becomes sluggish, it can lead to fat generation.

FFAs: Free fatty acids, which are high in overweight and obese individuals; FFA release into the bloodstream can cause peripheral insulin resistance.

GLUT1 and GLUT4: Insulin-independent glucose transport regulates insulin sensitivity. GLUT1 is insulin- independent and is widely distributed in different tissues.GLUT4 is insulin-dependent and is responsible for the majority of glucose transport into muscle and adipose cells in anabolic conditions.

HDL: High-density lipoprotein, the "good" cholesterol. The higher this number, the lower the "bad" cholesterols – low-density lipoprotein and very low-density lipoprotein.

IL-2 and IL-6: Interleukins. IL-2 is a type of cytokine signaling molecule in the immune system. It is a protein that regulates the activities of white blood cells that are responsible for immunity. IL-6 is secreted by T cells to stimulate an immune response.

HMG-CoA reductase: A rate-limiting enzyme for cholesterol synthesis. Statins have been developed to inhibit this enzyme, but statins have dangerous and unpleasant side effects.

LDL: Low-density lipoproteins, the bad cholesterol, high levels of which can lead to heart disease.

LOX-1: lectin-type oxidized LDL receptor, which acts like a scavenger, binding and regulating oxidized LDL.

Metabolic Syndrome: A condition that develops when five health conditions exist, high triglycerides, low HDL, high LDL, high abdominal fat, and high blood pressure.

NAFLD: Non-alcoholic fatty liver disease, a condition where the liver has more fat than it should, which acts like a dogged vacuum cleaner.

NASH: Nonalcoholic steatohepatitis is liver inflammation and damage caused by a buildup of fat in the liver, a precursor to NAFLD.

NFκβ: Nuclear factor-kappa B is a protein complex that controls transcription of DNA, cytokine production and cell survival.

PDE: Phosphodiesterase, an enzyme that breaks down certain nucleotide strands such as DNA and RNA.

PKB: Protein kinase B plays a key role in multiple cellular processes such as glucose metabolism, apoptosis, cell proliferation, transcription and cell migration.

PMN: Polymorphonuclear leukocytes, a special family of white blood cells.

TC: Total cholesterol, a measure of LDL, VLDL and HDL.

TNF-α: Tumor necrosis factor alpha is a cell-signaling protein (cytokine) involved in systemic inflammation and is one of the cytokines that make up the acute phase reaction.

VLDL: Very low-density lipoprotein, which carries triglycerides.