

BERGAMONTE®

• Cholesterol • Glucose Balance • Weight Management



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Bergamot Polyphenolic Extract from H&AD



The History of Bergamot ...

Bergamot (*Citrus bergamia* Risso) is a citrus plant that grows almost exclusively in the narrow coastal Calabria region in Southern Italy, due to sensitivity to the weather and soil conditions. Bergamot juice was traditionally recognized by the local population as a remedy for supporting healthy cholesterol levels and cardiovascular health. The medicinal use of bergamot, forgotten for decades, is now being rediscovered.

The juice and albedo of bergamot have a unique profile of flavonoid and glycosides, such as neoeriocitrin, neohesperidin, naringin, rutin, neodesmin, rhoifolin and poncirin. Naringin has been shown to be beneficial in animal models of atherosclerosis, while neoeriocitrin and rutin have been found to exhibit a strong capacity to prevent LDL from oxidation. Importantly, bergamot juice is rich in brutieridin and melitidin with an ability to inhibit HMG-CoA reductase.

Patented, Standardized, Clinically Tested ...

Bergamonte® contains bioactive compounds of extract of the juice and albedo of *Citrus bergamia* Risso, standardized to polyphenolic flavonoids consisting of naringin, neohesperidin, neoeriocitrin, 1% melitidin, and 2% brutieridin. Bergamonte® is produced using patented extraction technology through collaborative works of various universities and research institutions in Italy.

These flavonoids are clinically proven to help maintain healthy cholesterol levels†, healthy blood glucose level, increase HDL-cholesterol, and promoting healthy weight management.

Benefits of Bergamonte® ...

- **Cardiovascular Health**
- **Supports Healthy Cholesterol†**
- **Supports Healthy Blood Sugar**
- **Healthy Weight Loss**

Citrus Bergamot Differs From *C. Aurantium* ...

Citrus Bergamot differs from *C. Aurantium* because Citrus Bergamot does not contain synepherine, N-methyltyramine, and octopamine, which have been shown in research to constrict arteries, increase blood pressure, increase heart rate, cause heart-rhythm disorders, heart attack, and stroke.

Citrus Bergamot contains melitidin and brutieridin which are absent in *C. Aurantium*. Research has shown that these compounds significantly support healthy total cholesterol†, LDL, triglycerides† and blood glucose levels, while increasing HDL†.

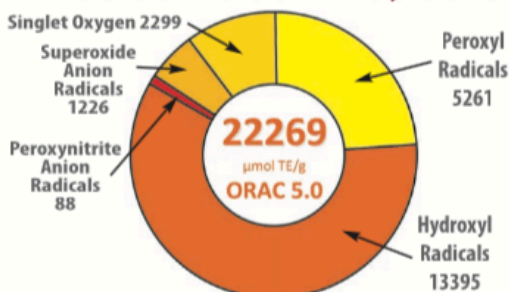
Melitidin and Brutieridin In Bergamot Fruits ...

A research article published in the Journal of Natural Products 2009 showed that bergamot juice contained novel compounds with statin-like properties, having the 3-hydroxy3-methylglutaric acid (HMG) bound to the naringin (melitidin) and neohesperidin (brutieridin).

These novel compounds interfere with the natural synthesis of the cholesterol pathway in the human body: the HMG-CoA substrate interferes with the synthesis of the mevalonate acid, blocking the cholesterol production.

† Already within the normal range

Superior Full-Spectrum Antioxidant ORAC Potency



MODES OF ACTION ...

Inhibiting HMG-CoA Reductase

In a study published in Journal of Natural Products July 2009, it is suggested that brutieridin and melitidin act as direct HMGCoA reductase inhibitors. HMG-CoA reductase is an enzyme linked to the liver's cholesterol production. Melitidin 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 bloodstream.

Inhibiting Phosphodiesterases (PDEs)

Bergamot flavonoids mediate their beneficial effects on lipid and glucose homeostasis 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.

Activating AMPK

Flavonoids in Bergamonte® activate AMPK and stimulate glucose uptake. AMPK plays a central role in regulating healthy glucose, and 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.

CLINICAL TRIAL RESULTS ...

In an unpublished human clinical trial involving 192 patients, the following is the result, after patients consumed 100ml of Citrus Bergamot juice for 30 days.

Bergamot Juice (100 ml/day)				
Total Cholesterol	HDL Cholesterol	LDL Cholesterol	Triglycerides	Blood Glucose
-35.72%	+56.05%	-41.95%	-38.31%	-22%



Hypolipemic and Hypoglycemic Activity of Bergamot Polyphenols

Fitoterapia 82 (Nov 2011) 309–316

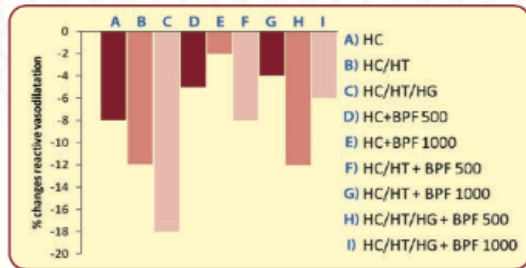
In this study, 237 patients with hyperlipidemia, hypercholesterolemia (HC, cLDL, low cHDL), mixed dyslipidemia (HC and TG), or metabolic syndrome (HC, HT, and HG) were taking either placebo, or Citrus Bergamot juice in either 500mg, 1000mg.

	Total-Chol	HDL-C	LDL-C	Triglycerides	Blood Glucose
Placebo	0.14%	+1.2%	-1.1%	+0.1%	+0.5%
Bergamot Polyphenolic Fraction (500mg/Day)	-20.69%	+22.9%	-24.1%	-29.9%	-18.8%
Bergamot Polyphenolic Fraction (1000mg/Day)	-26.53%	+40.1%	-36.00%	-38.8%	-22.3%



The effect of Bergamot Polyphenolic Fraction (500 and 1000 mg/daily) on reactive vasodilatation in patients suffering from isolated (HC) or mixed hyperlipidemia (HC/HT) and associated hyperglycemia (HC/HT/HG).

Bergamot Polyphenolic Fraction helps support healthy total and LDL cholesterol levels (an effect accompanied by elevation of cHDL), triglyceride levels[†] and support healthy blood glucose. Moreover, Bergamot Polyphenolic Fraction inhibited HMG-CoA reductase activity and enhances reactive vasodilation.



Bergamot Polyphenolic Fraction supports healthy cholesterol levels[†], increased LOX-1 expression and Protein Kinase B phosphorylation

International Journal of Cardiology, 2013

In this open-label, parallel group, placebo-controlled study, 77 patients were randomly assigned either placebo, Rosuvastatin, Bergamot Polyphenolic Fraction or combination of Bergamot Polyphenolic Fraction with Rosuvastatin for 30 days.



	Total-Chol	LDL-Chol	HDL-Chol	Triglycerides
Basal	278 ± 4	191 ± 3	38 ± 2	238 ± 5
Placebo (n=15)	275 ± 4	190 ± 2	38 ± 3	235 ± 5
Rosu 10mg/day (n=16)	195 ± 3*	115 ± 4*	42 ± 3*	200 ± 4*
Rosu 20mg/day (n=16)	174 ± 4*	87 ± 3*	48 ± 3*	202 ± 5*
Bergamot Polyphenolic Fraction 1g/day (n=15)	191 ± 5*	113 ± 4*	45 ± 4*	165 ± 3*
Rosu 10mg + 1g Bergamot Polyphenolic Fraction (n=15)	172 ± 3*	90 ± 4*	52 ± 4*	152 ± 5*

Both doses of rosuvastatin and Bergamot Polyphenolic Fraction were shown to help support healthy cholesterol levels[†] and reduce urinary mevalonate compared to the control group. The benefits are associated with significant reductions of biomarkers used for detecting oxidative vascular damage, including malondialdehyde, oxLDL receptor LOX-1 and phosphoPKB. These suggest several modes of actions of Bergamot Polyphenolic Fraction.

Bergamot Polyphenolic Fraction Effects on LDL Small Dense Particles, Metabolic Biomarkers, and Liver Function

Advances in Biological Chemistry, 2014, 4, 129-137

In this study, 107 patients with metabolic syndrome and non-alcoholic fatty liver disease were given either placebo or 650 mg of Bergamot Polyphenolic Fraction twice a day for 120 days. The Bergamonte[®] group showed significant reduction in fasting plasma glucose, total cholesterol, LDL cholesterol and triglycerides, as well as an increase of HDL cholesterol. Bergamot Polyphenolic Fraction decreased IDL particles by 51%, increased large LDL by 38%, decreased small LDL by 35%, and increased total HDL particles by 20%. Hepatorenal index was significantly reduced by 46%, accompanied by a reduction of hepatic ultrasonographic pattern of steatosis by 99%. This suggests Bergamot Polyphenolic Fraction improves both liver function and inflammation as confirmed by reduction of TNF- α and C-reactive protein.

	Baseline	Bergamot Polyphenolic Fraction	% Change
BMI (kg/m ²)	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%
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%



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Product Comparison ...

	Total-Chol	LDL-Chol	Triglycerides	HDL-Chol	Blood Glucose
BPF	12%-48%	20%-59%	30%-55%	7%-83%	15%-30%
Policosanol	15%-29%	17%-21%	7-12%	8-15%	unknown
Citrus PMF with Tocotrienol	20%-30%	19%-27%	24-34%	0%	0%
Citrus PMF	12%-18%	12%-16%	0%	0%	0%
Phytosterols	15%	9%	0%	0%	0%

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(All research was conducted on BPF, by H&AD)



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