

Active International Research into Cardiometabolic and Liver Effects of a Proprietary Calabrian Bergamot Citrus Extract

By James Ehrlich, MD and Jay Williams, PhD

A team of Italian physicians and food scientists are leading an aggressive international research agenda into the salutary cardiovascular, metabolic, and hepatic properties of a juice extract of the bergamot citrus fruit (*Citrus bergamia*, Rutaceae), endemic to Calabria, Italy. After developing one of Europe's top medical research facilities at the Interregional Research Center for Food Safety and Health at the University of Catanzaro, the group has recruited academic physicians from Rome, Australia, and the United States to study the properties of a highly concentrated juice extract called BergaMet™ (Bergamot Polyphenol Fraction/BPF 38%). Over the past few years, the group has organized international symposia, published book chapters, and has authored numerous publications concentrating its efforts on three key areas affecting at least 30% of western civilization -- high cholesterol, metabolic syndrome, and fatty liver disease.

Safe and effective management of dyslipidemia (elevated cholesterol) with a “natural statin”

It is well known that statin cholesterol medications have a long list of adverse side effects, including muscle aches, memory loss, and an elevated risk for diabetes. Finding a natural and safe lipid-lowering alternative is a topic of increased interest among clinicians and proactive citizens. Bergamot polyphenolic fraction (BPF) has been shown to lower LDL-cholesterol, raise HDL-cholesterol and favorably improve the dangerous lipoprotein particle characteristics seen in most Americans who consume excessive carbohydrates. Dietary polyphenols (especially bioflavonoids) may prevent atherosclerosis due to their anti-oxidative and anti-inflammatory properties. Among the citrus family (Rutaceae), bergamot fruits contain a very high content of flavonoids, including “statin-like” bruteridin and melitidin, two polyphenols which contain the same HMG-CoA reductase enzymatic activity found in all pharmacologic statins.

Unlike pharmacologic statins that deplete coenzyme Q10 and can cause muscle aches, BergaMet has no known adverse side effects and does not deplete this critical enzyme involved in muscle strength and activity. Furthermore, it appears that the citrus extract also inhibits the reabsorption of cholesterol in the intestines, a mechanism similar to ezetimibe, a drug that has recently shown additional benefits in heart attack risk. A recent *Wall Street Journal* article on the clinical effectiveness of extracts from Calabrian bergamot acknowledged that only the highly concentrated proprietary extract BergaMet (38% BPF) has been proven in published research as highly effective in lowering blood cholesterol while improving various metabolic risk markers such as blood sugar, insulin resistance, and inflammation.

Patients with established coronary disease or vascular atherosclerosis still need to be on pharmacologic statins because of their proven ability to stabilize plaque and lower risks for heart attacks and strokes. Since statin side effects are related to dose, research efforts have focused on whether the addition of BergaMet to a drug statin could allow physicians to prescribe lower doses of a drug while achieving adequate lipid reduction and additional benefits ascribed to the natural supplement.

New published research reveals that BergaMet™ (Bergamot Polyphenol Fraction/BPF 38%) enhances and complements the lipid lowering effect of rosuvastatin (Crestor™) when given to patients with elevated cholesterol. Led by cardiologists Franco Romeo and Vincenzo Mollace, the findings were published in the December 2013 issue of the *International Journal of Cardiology*. {Romeo & Mollace 2013}

In the study, 77 patients with elevated low-density lipoprotein (LDL) and triglycerides were divided into four groups to investigate the lipid-lowering and vascular-protective effects of placebo, BPF 38% alone, rosuvastatin alone, and their combination. The combination of 1000 mg of BPF 38% with 10 mg or 20mg rosuvastatin demonstrated an enhanced effect on all lipid parameters and significant positive effect on biomarkers of vascular protection and reductions in oxidative stress. As stated by Professor Mollace, “the paper shows, for the first time, that BPF 38% leads physicians to a better management of statin-based treatment of hyperlipemia. Moreover the added value for using BPF 38% in combination with statins is represented by significant improvement of serum triglyceride and glycemia leading to better vasoprotection.”

Adding BergaMet significantly lowered blood sugar levels, raised high-density lipoprotein (HDL) and lowered triglycerides to an extent that cannot be achieved by a statin alone. Beyond this “complementary effect”, the combination of BergaMet™ and a statin allows a physician to lower the dose of the statin drug while achieving lower cholesterol levels and improving overall metabolism and vessel health.

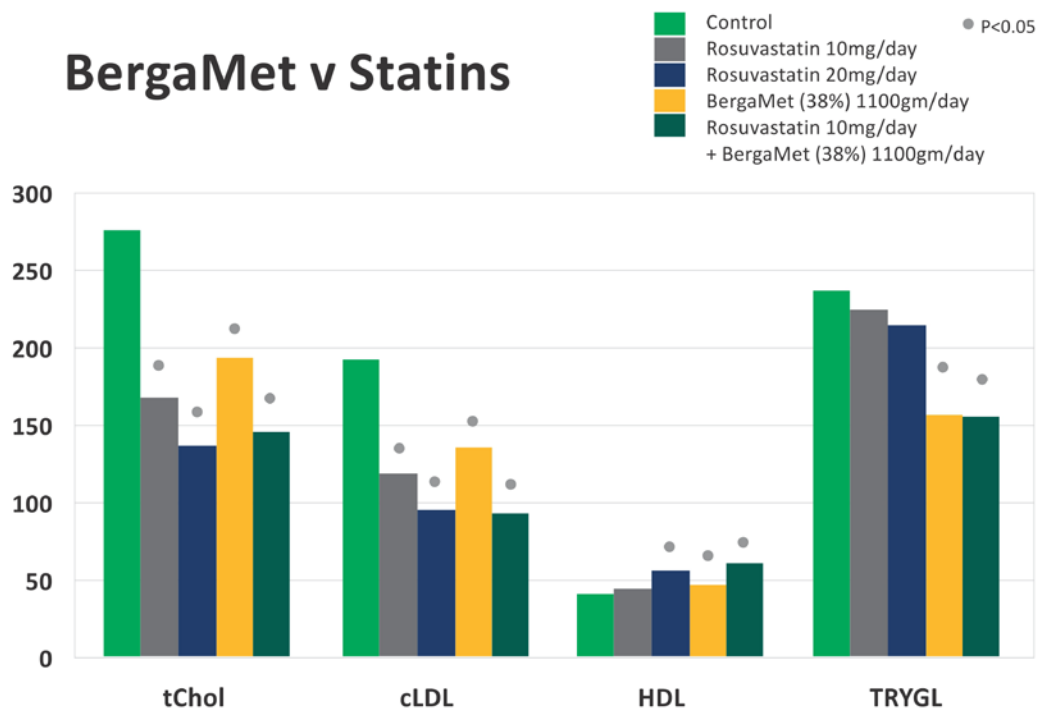


Figure 1

Addressing the “Epidemic of the 21st Century”—the Metabolic Syndrome

About 35% of US citizens have a dangerous constellation of risk factors termed the “metabolic syndrome” that is associated with insulin resistance and a high risk for type 2 diabetes, cardiovascular events and mortality. Fueled by excessive carbohydrate intake and sedentary living, this epidemic manifests itself clinically by expanding abdominal waistlines (visceral adiposity), hypertension, elevated blood sugars, and abnormal cholesterol levels including triglyceride elevation. Recent peer reviewed research published in the *Journal of Metabolic Syndrome* revealed that high dosages of 38% BPF causes striking decreases of all risk factors involved with the metabolic syndrome. Gliozzi M, Walker R, Mollace V (2014) Bergamot Polyphenols: Pleiotropic Players in the Treatment of Metabolic Syndrome. *J Metabolic Syndr* Vol 3 Issue 2

Most patients lose belly fat and achieve favorable improvements in blood sugar (averaging 23% reduction), blood pressure, and lipid profiles. The paper reviewed the various mechanisms of action of the citrus extract related to insulin resistance and the development of atherosclerosis (plaque formation in arteries). Of particular interest has been demonstration of important actions of the product linking its inhibition of oxidative stress to improvements in both vascular health and atherosclerosis (Figure 2).

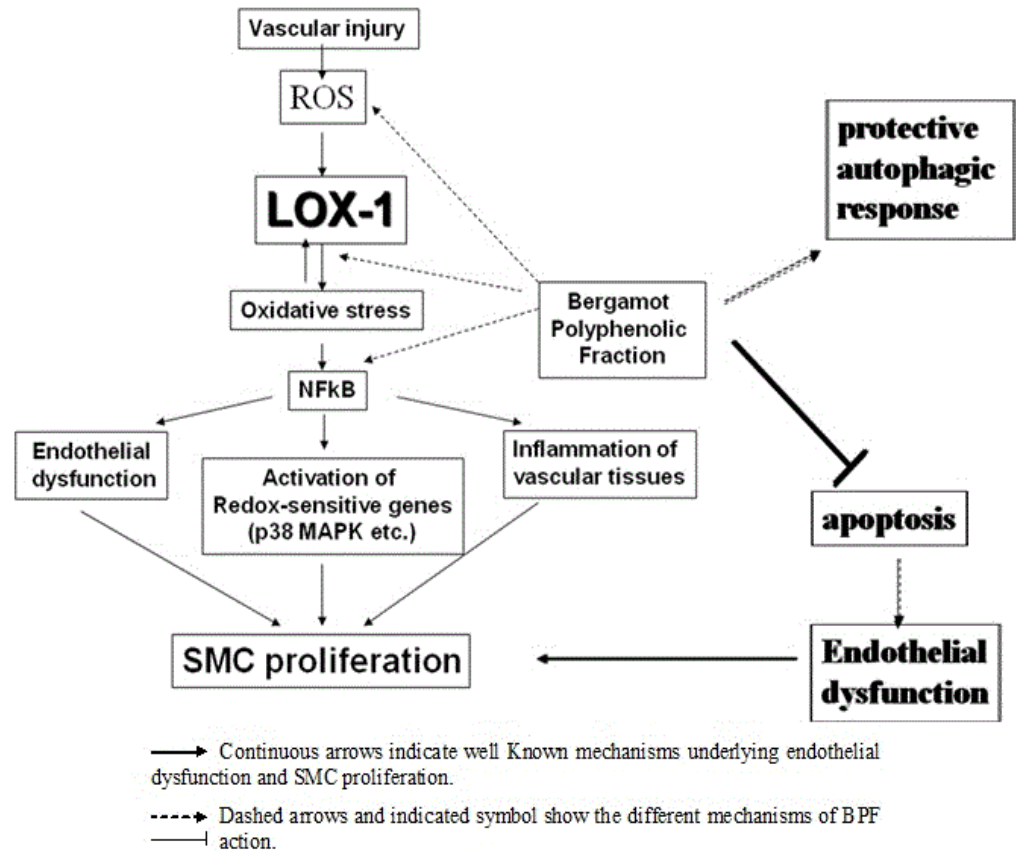


Figure 2

Various mechanisms proposed for Bergamot polyphenol vascular protective effect

Hope for Patients with Non-Alcoholic Fatty Liver Disease

At the 2014 Annual Scientific Meeting of the American College of Gastroenterologists, a coauthor of this paper (JE) presented [data demonstrating](#) that 38% BPF significantly improved liver structure and function in patients with both metabolic syndrome and fatty liver disease. The study involved authors from 3 continents and was published in *Advances in Biological Chemistry*. Since fatty liver disease is the hepatic manifestation of the metabolic syndrome and bergamot was previously shown to be beneficial in subjects with this precise “pre-diabetic” condition, the investigators sought to establish the potential value of 38% BPF in patients with both metabolic syndrome and non alcoholic fatty liver disease (NAFLD).

In a group of 107 patients with confirmed NAFLD and metabolic syndrome, BPF 38% given twice per day before meals significantly improved all measured biochemical and ultrasonographic characteristics of both

NAFLD and metabolic syndrome in 120 days without reported side effects (Figure 3). There was a striking improvement in hepatic function (biochemical) and structure (echogenic visual loss of hepatic fat) accompanied by lower levels of inflammation. [Gliozzi, M, Walker, R, Ehrlich J, Mollace V et al., *Advances in Biological Chemistry*, 2014, 4, 129-137

As there are currently no approved conventional pharmaceutical drugs for NAFLD, this study suggests that BPF 38% may represent a safe and important therapeutic option for these conditions. The research team is currently exploring the feasibility of entering an FDA process leading to botanical drug approval for BPF for this condition.

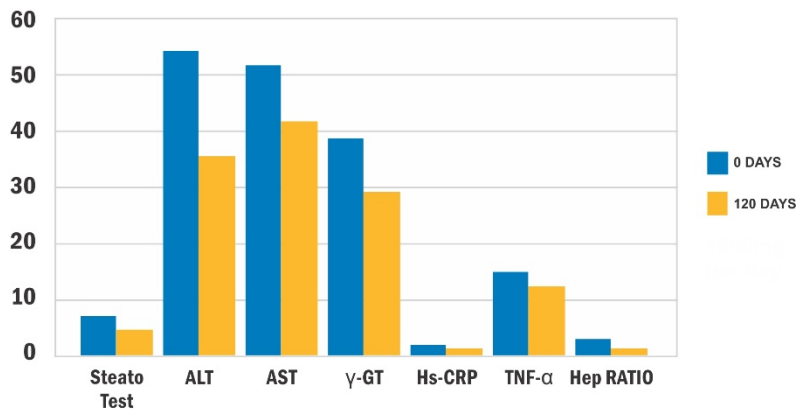


Figure 3

[Significant improvements in liver structure (ultrasound), liver function biochemistry and inflammatory markers after 4 months BPF therapy of patients with both metabolic syndrome and NAFLD

Over the past four years, Australian cardiologist Ross Walker MD the author of *The Cell Factor* (Macmillan Australia 2002) has treated over 4000 patients with 38% BPF. "It has been so gratifying to witness 1000's getting superb results. So many of my patients get side effects from drugs or prefer a more natural approach. I either use BergaMet alone or combine it with low dose statins depending on the clinical situation."

Walker continues "BPF 38% has also been shown to have beneficial effect on maintaining healthy vessels (endothelial function and arterial stiffness). It is therefore my medical opinion that it should be used in:

- *All patients over the age of 50 to maintain normal arterial function and flexibility.
- *All patients with metabolic syndrome.
- *All patients who are statin intolerant as an alternative to maintain healthy LDL and HDL subfractions
- *All patients at low risk for vascular disease who have lipid abnormalities."

Dr. Walker maintains that the high dose 38% BPF may be the most important nutritional product created in the last 30-50 years. "I know of no other supplement or drug that can match its value in addressing so many risk factors contributing to heart disease and diabetes".

Conclusion

A highly concentrated extract (BergaMet/BPF 38%) from the Calabrian bergamot citrus (*Citrus bergamia*, Rutaceae) is being intensely investigated for its potential value in cardiometabolic risk reduction. Recent studies have confirmed that the product significantly addresses all of the major components of the metabolic syndrome including dyslipidemia (cholesterol), blood sugar, abdominal fat and blood pressure while improving vascular function. BergaMet has established itself as a natural supplement to lower cholesterol with and without statins and to treat non-alcoholic fatty liver disease.

References

Romeo F, Mollace V. Bergamot polyphenolic fraction enhances rosuvastatin-induced effect on LDL-cholesterol, LOX-1 expression and protein kinase B phosphorylation in patients with hyperlipidemia. *Int J. Cardiol.* 2013;170:140-145.