



Bergamot: A promising new cardio-protective nutraceutical

Bergamot is a relative newcomer to the supplement industry. I've heard of its heart benefits, and I've been evaluating it for a couple of years.

I'm an early adopter, but I perform my due diligence before jumping on board with every new craze. It's not enough that a product has a good backstory and scientific evidence to back it up. I've seen many breakthrough candidates with strong research bona fides tank when the rubber meets the road—in clinical practice. ✖

Bergamot is a flavoring ingredient derived from a citrus plant that grows almost exclusively in the coastal region of Calabria, Italy. It is best known as the additive that lends a distinct aroma to Earl Grey tea. Thus, we have confidence that, after years of steady use, it's likely to have a good safety profile.

Bergamot is rich in several phenolic compounds that possess, variously, cholesterol-lowering and antioxidant/anti-inflammatory effects. It may be that exposure to the harsh Mediterranean sun and wind causes plants to elaborate heart-healthy defensive compounds like resveratrol, pterostilbene, pycnogenol, and the polyphenols found in grapeseed and olive oil.

Two constituents of Bergamot are known to inhibit HMG-CoA reductase (HMGCR), a mechanism shared with statin drugs as well as red yeast rice. A special patented extract of Bergamot called called BFP, produced by H&AD srl Italy, has been shown to effectively lower cholesterol.

Animal studies in rats have shown that extracts of Bergamot can lower total cholesterol and LDL while maintaining levels of beneficial HDL. Additionally, markers of inflammation and free radical damage were attenuated, suggesting a protective effect on the endothelium that lines the arteries.

Parenthetically, research on experimental animals suggests a benefit for intestinal inflammation, something I'll keep in mind for my colitis patients.

In a study of human subjects with moderate hypercholesterolemia (e.g. plasma LDL-C concentrations between 160 and 190 mg/dl), BFP produced by H&AD srl was found to improve plasma lipids significantly, demonstrating a 12 and 20 percent decrease in total cholesterol and LDL cholesterol, and a 17% reduction in triglycerides, while HDL increased 8%. The higher the subjects' initial LDL, the more robust the effect. Furthermore, carotid ultrasound revealed that carotid intima-media thickness (IMT), as a marker of subclinical atherosclerosis, decreased after six months of Bergamot supplementation.

Other studies have suggested the BFP is compatible with statin drugs, extending their benefits without compromising their safety.

I decided to field test **Bergamot BPF** by H&AD srl Italy on one of my most challenging patients. She suffers from Type IV Familial Hyperlipidemia, which is not the run-of-the-mill kind of high cholesterol that many people are given statins for.

Many of her family members have early heart disease, and though she's not even 50, an EBT heart scan shows she's developing plaque. She even has cholesterol deposits on her knuckles, a rare phenomenon called **xanthomata**. Before she went on cholesterol-lowering medication, her cholesterol was in the 500s.

Since this a genetic condition of faulty cholesterol metabolism, diet doesn't help much (as it does it most patients with moderately high cholesterol). She's a veritable cholesterol factory.

Even on the highest permissible dose of Lipitor—80 milligrams—her cholesterol only came down to 417!

I decided to try her on **Bergamot BPF** (just one capsule twice daily) for one month while continuing her Lipitor, then had her repeat her cholesterol. I was astounded to see it drop to 327, still not optimal, but a dramatic effect for an over-the-counter supplement. Moreover, her HDL was slightly increased (statins sometimes indiscriminately lower good cholesterol as well as bad). I was also pleased to see that she complained of no side effects, and her blood tests were otherwise normal, without signs of liver function impairment.

Some of you astute *Intelligent Medicine* aficionados may be asking at this point: Why lower cholesterol, when cholesterol doesn't matter according to statin-naysayers?

Well, while it's true that dietary cholesterol may have little to do with cardiac outcomes according to the latest studies, and high cholesterol is now recognized as a survival advantage and a hedge against dementia in the elderly, high blood lipids are associated with heart risk in susceptible individuals.

I selectively use statins in my patients who have demonstrable plaque accumulation on carotid ultrasound, or via EBT heart scans for coronary calcium. For them, lowering cholesterol has a protective effect documented by studies that can't be ignored.

Why not use other natural agents to lower cholesterol? Policosanol and "flush-free" inositol hexanicotinate don't work in my experience, and I've long abandoned them. Pantetheine has mild lipid-lowering effects, but you have to use a lot. Guggulipids were all the rage for a while, but they only work when given in large amounts—several grams. **Kyolic Aged Garlic** extract, olive leaf, berberine, curcumin, **fish oil**, and EGCG all may lower cholesterol a bit, but mostly confer their heart benefits via protection of the endothelium. Bergamot won't supplant them, but teams well with them.

Niacin, on the other hand, very successfully lowers cholesterol and triglycerides, while preserving HDL. But it causes unpleasant flushing at doses needed to impact cholesterol, and it has a tendency to damage the liver, requiring constant monitoring. And besides, studies suggest that, inexplicably, while it improves the lipid profile, that doesn't translate to statistically meaningful reduction in heart attacks or strokes.

Plant phytosterols are promising cholesterol-lowering agents, so much so that they've earned approval from the FDA and the American Heart Association as add-ons to statin therapy. At the Hoffman Center, we use a product called **Cholestepure Plus**

by Pure Encapsulations. It also contains BPF produced by H&AD srl Itlay.

Finally, there's red yeast rice (RYR), which contains meaningful amounts of a proto-statin (Mevacor). But there are problems with standardization. One study of various brands showed they range from almost negligible amounts to clinically meaningful doses of drug-equivalent material. That may sound like a plus, but considering the high-rate of muscle pain and liver abnormalities reported by RYR users, it might be too much of a good thing. Complicating matters, there's evidence that when the manufacturing process goes wrong and quality controls are not in place, there may be toxic impurities in some batches of RYR.

I use ChoLeast from Thorne when patients who need statins are dead-set against using a "synthetic" pharmaceutical, even when I tell them that RYR is merely a watered down, less-standardized version of the cholesterol meds you get from the drugstore.

Finally, the question arises: If Bergamot, like statins and RYR, blocks HMGCR, which is the pathway to, not just cholesterol, but coenzyme Q10 synthesis, should patients take CoQ10 when using it? While that's not been completely worked out as yet, I would recommend that they take at least 200 mg of CoQ10, or 100 mg of Ubiquinol daily. Both support heart function anyway, and patients at risk for heart disease should be taking one or the other.

In conclusion, I think Bergamot will join the ranks of other heart-protective nutrients as a natural alternative, or as an adjunct to standard medical management. It possesses the advantage that it works not merely to lower cholesterol, but also to specifically protect the endothelium due to its rich endowment with beneficial plant polyphenols demonstrated to reduce inflammation.

Of course, we'll need more large, well-funded long-term studies of at-risk patients taking Bergamot before we assert with confidence that it protects people from actual heart attacks and strokes. That will be expensive, and there's less incentive to do a multi-million dollar study for a natural product that can't be patented. Even with statins, it has taken a long time to prove their (albeit limited) effectiveness, and many studies are still challenged for stacking the statistical deck in favor of unnecessarily widespread statin prescribing, or for minimizing side effects. Since Bergamot is safer and more natural, it's sure to become part of my armamentarium against cardiovascular disease.