REPORT

You Are Eating More Calories Than You Think

And What You Can Do to Protect Yourself

By Julius Goepp, MD

COMPELLING NEW EVIDENCE FOR ESTABLISHED CR MIMETICS

RESVERATROL

Resveratrol, the most widely known of the CR mimetics, is a polyphenol found most abundantly in red wine grape skins, as well as in many other darkly colored fruits, accounting in part for their known health-promoting effects.[59] Its ability to activate sirtuins has been thoroughly documented in the scientific literature.[26,59-64]

While a potent sirtuin activator and antioxidant in its own right, resveratrol also mobilizes a number of antioxidant processes internal to cells.[59,65-69] These combined effects are responsible for resveratrol's ability to prevent oxidative damage following heart attack or stroke, heading off many of its deadly consequences.[70] Similarly, resveratrol's antioxidant function is credited with prevention of the neuronal damage observed in Alzheimer's and other neurodegenerative diseases.[63,68,71,72]

Resveratrol also inhibits *advanced glycation end products* (AGEs) that arise from lifelong exposure to glucose in blood—both effects and causes of type 2 diabetes. Resveratrol inhibits AGE-induced smooth muscle cell overgrowth in blood vessel walls.[73] It protects laboratory animals from kidney damage in early-stage diabetes by switching on a protective enzyme system called adenosine monophosphate-activated serine/threonine kinase (AMPK).[74]

Resveratrol improves insulin sensitivity and regulates genetic expression of dangerous *adipokines,* cytokines produced by fat tissue, which are associated with development of diabetes and the consequences of the metabolic syndrome.[75] In early 2010 it was discovered that resveratrol reduces body weight and fat content in obese animals through its effects on gene expression and enzyme activities.[76]

PTEROSTILBENE

Pterostilbene is a polyphenol closely related to resveratrol, but with unique attributes, including potent cancer-preventing and lipid-lowering capabilities.[77,78] It has powerful antioxidant capabilities, scavenging destructive free radicals and inhibiting oxidant-induced electrolyte loss from cells.[79] Diabetic animals supplemented with pterostilbene demonstrate marked improvements in their damaged cellular antioxidant systems.[80] Supplemented rats experience remarkable reversal of age-related cognitive deficits.[81] Astonishingly, pterostilbene switches on genes governing the production of intracellular antioxidant enzymes such as ***superoxide dismutase (SOD).***[82]

Pterostilbene has been shown to directly lower blood glucose, which may help prevent the formation of AGEs. Remarkably, pterostilbene's ability to lower glucose was comparable to that of metformin, a pharmaceutical used in the management of diabetes.[83]

Pterostilbene displays potent cancer-preventing effects related to its ability to prevent or repair DNA damage, one of the first steps in cancer initiation. It inhibits development of pre-cancerous lesions in mouse models of breast cancer, similarly to resveratrol.[79] And pterostilbene can prevent expression of genes that otherwise promote cancer metastasis; it has also been shown to inhibit metastatic malignant melanoma growth and extend host survival.[84]

Like its close relative resveratrol, pterostilbene is perhaps best known for its potent inflammation-quenching effects, which it achieves, as usual, by several complementary mechanisms. Pterostilbene inhibits the ubiquitous COX-2 enzyme responsible for producing inflammatory prostaglandins, which are also involved in creating the pain sensation.[85] Pterostilbene also targets

inflammatory cells called macrophages, reducing their ability to multiply; this has enormous application to atherosclerosis, which requires activated macrophages to initiate deadly inflammatory plaques.[86,87]

GRAPE SEED EXTRACT

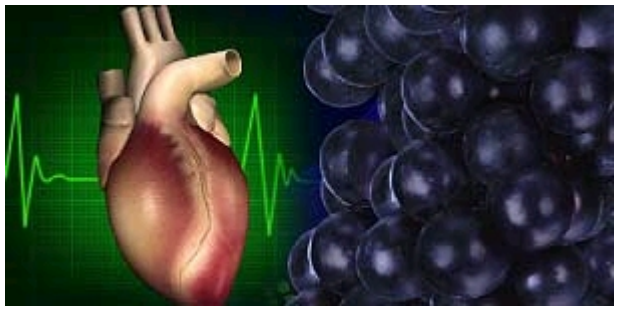
Grape seed extracts (GSE) favorably influence expression of genes involved in cellular aging, giving them a broad array of multitargeted benefits.[88,89]

GSE has been shown to enhance antioxidant status and decrease free radical-induced protein oxidation in aging rats' brains.[90] A 2009 study of type 2 diabetics at high risk of cardiovascular disease showed that GSE significantly improved markers of inflammation, oxidative stress, and blood sugar over a 4-week period.[91]

GSE's remarkable cardiovascular health benefits also derive from their ability to fight advanced glycation end products (AGEs) in endothelial tissue.[92,93]

GSE effectively combats inflammatory responses throughout the body by modifying gene expression. One early study found beneficial alterations in expression of 13 proteins in brain tissue alone.[88] GSE inhibited platelet inflammatory responses at doses easily attainable in humans, demonstrating an additional vascular protective effect.[94] And GSE switched off the inflammatory "master molecule" NF-kB in mice exposed to UV radiation, helping to mitigate oxidant-induced inflammation.[95]

QUERCETIN



The polyphenol quercetin protects endothelial tissue against oxidative damage by preventing oxidation of LDL cholesterol, one of the chief offenders in the atherosclerosis cascade.[96,97] It also reduces the new production of fats by liver cells.[98] Quercetin's antioxidant capacity prevents heart enlargement caused by blood pressure overload in laboratory animals.[99] By a different mechanism, quercetin prevents migration and proliferation of vessel wall muscle cells in response to oxidative stress and activated platelets.[100]

Quercetin sharply reduces genetic expression of major inflammatory cytokines, suggesting its use for treatment of allergic and other inflammatory conditions.[101,102] Inflammation plays a vital role in cancer development and cardiovascular disease as well, and quercetin's anti-inflammatory effects lead to reduced invasiveness of certain breast cancers and reduced production of adhesion molecules in vascular endothelia.[103,104]

BLACK TEA

Consumption of black tea is widely known to improve circulating antioxidant status in humans.[105,106] Black tea's polyphenols and other constituents are particularly notable for their cardiovascular protective effects.[107] These arise through a host of interlocking antioxidant-mediated mechanisms including reduced platelet aggregation, improved endothelial function, and reduced vascular inflammation.[108-110]

Components of black tea are powerful inhibitors of glycation and can prevent diabetic cataracts, further proving their calorie restriction mimetic credentials.[111] Unlike most of the other nutrients we've discussed, the black tea polyphenols don't directly reduce production of advanced glycation end products (AGEs); rather, they trap them as they are produced, reducing their concentrations in tissues.[112,113]

ACTIVATE YOUR LONGEVITY GENES <u>WITHOUT</u> HUNGER

Scientists estimate that 30 million Americans face the lethal risks of ***excessive energy intake,*** even though they *appear* thin and healthy.

These alarming findings underscore the enormous challenge of avoiding ***excess energy intake*** and the obstacles of undertaking a **caloric restriction** regimen.

Fortunately, *avant-garde* research has brought to light a handful of nutrients that can safely simulate many of the effects of caloric restriction. Each operates in a multitargeted and complementary fashion. These nutrients have been shown to limit oxidation, reduce glycation, restrict or even repair DNA damage, quell inflammation, support mitochondrial health, and enhance the function of the cellular sub-units called proteasomes and lysosomes.

In addition to the five natural CR mimetics ***Life Extension*** reviewed earlier this year, a sixth has been identified called ***fisetin.*** It optimizes levels of the endogenous antioxidant ***glutathione*** in cells, targets factors implicated in brain aging, and may even enhance the action of resveratrol.

To read an in-depth scientific report that describes all of the documented benefits of calorie restriction mimetic nutrients, log on to www.LifeExtension.com/Calorie-Restriction

If you have any questions on the scientific content of this article, please call a Life Extension® Health Advisor at 1-866-864-3027.

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