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SIRTUINS AND CARDIOVASCULAR HEALTH

Sirtuins appear to possess cardiovascular protective properties.

Research appearing in *Cardiovascular Research* (December 22, 2010 epub ahead of print) showed that SIRT1 acts in association with PPAR-[alpha]

to protect the heart from hypertrophy, metabolic dysregulation and inflammations in transgenic mice. Other studies (*Biophys Sin [shanghai]*

2011;43:103-9 and *Arterioscler Thromb Vasc Biol* 2008;28:1263-9) showed that Sirt1 acts to inhibit angiotensin II-induced vascular smooth muscle cell hypertrophy.

Sirtuins may also have a desirable effect on high blood pressure. According to research appearing in the journal *Science* (2005;310:314-7) SIRT1 deacetylates and activates endothelial nitric oxide synthase. Nitric oxide will thereby help lower blood

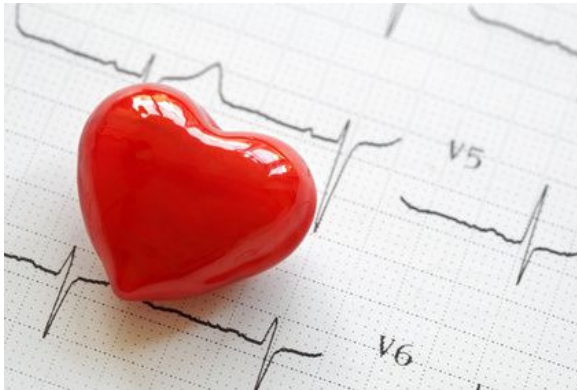
pressure. SIRT1 also protects the tubular epithelium, according to research appearing in the *Journal of Biologic Chemistry* (210;120:1056-68). Other research shows it to protect the renal medula from oxidative injury

(*Journal of Clinical Investigation* 2010;120:1043-55).

Sirtuins also have 'anti-aging' properties. The effect is most

notable in the cells lining the arteries. SIRT1 has been shown to facilitate the favorable effect of calorie restriction as well as improve the regulation of fat and cholesterol homeostasis. SIRT1 has the potential to increase the production of HDL cholesterol and protects against atherosclerosis by facilitating cholesterol removal.

Biotics Research has created a number of products for cardiovascular health that contain STACS, which are sirtuin activating compounds. An overview of these products are on page 6.



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RESVERATROL

Resveratrol (3,5,4'-trihydroxy-trans-stilbene) is a stilbenoid, a type of natural phenol, and a phytoalexin produced naturally by several plants in response to injury or when the plant is under attack by pathogens such as bacteria or fungi. Resveratrol is the first natural compound described to positively regulate the activity of sirtuins. Food sources of resveratrol include the skin of grapes, blueberries, raspberries, mulberries, and (famously) red wine. It has shown anti-inflammatory and antioxidant properties in animal studies. One study, published in the journal *Inflammation* (2015 Jan 15. [Epub ahead of print]), looked at the effect resveratrol treatment had on burned mice. The results of the simulation experiment *in vivo* on burned mice manifested that the survival rate of the mice in the resveratrol-treated group was markedly higher than that of controls.

In another animal study found in *Biologic Trace Element Research* (2007; 118(3): 244-9), one group (n=10, control group) was administered streptozotocin to

induce diabetes, while the other group (n=15, experimental group) was first administered resveratrol (0.5 ml/day), 10 days later the latter group was administered streptozotocin. Results found that compared to rats in the control group, rats pre-treated with resveratrol experienced increases in catalase activity, nitric oxide level, and zinc concentrations, as well as decreases in the lipid peroxidation product malonaldehyde and copper concentrations. These results suggest that resveratrol holds potential as a compound that may help in the prevention and/or treatment of diabetes.

Beyond cell protection, resveratrol may actually help with glycemic control. A study appearing in *Cell* (2006; 127(6): 1109-22), looked at glycemic control and weight in overfed mice. Compared to controls that were not fed resveratrol, mice who received resveratrol gained less weight, which was significant in mice fed the high-fat diet. Resveratrol was also found to increase resistance to muscle fatigue, increase muscle strength, and improve motor



Resveratrol is found in red wine

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coordination and traction force - suggesting a beneficial effect on neuromuscular function. Fasting insulin levels were significantly reduced in resveratrol-fed mice. Glucose tolerance was also found to improve in a genetic mouse model of diabetes whereby the mice were fed resveratrol 400 mpk for 10 weeks, as compared to the same such mice not fed resveratrol. These results suggest that resveratrol may have potential to protect against weight gain and metabolic disorders.

Of course this newsletter format does not allow for in-depth articles. This article is only the tip of the iceberg with respect to resveratrol and its uses. Check out the article by Rachel Olivier, MS, ND, PhD; it appears in the September, 2008 issue of the *Original Internist*. It is a great overview of the research behind resveratrol and its potential uses. Contact Biotics Research for a reprint of the article.



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SIRTUINS

Sirtuins are nicotinamide adenine dinucleotide (NAD)-dependent deacetylases (removes an acetyl group), Sirtuins, have been presented as "the fountain of youth". Their role in longevity control and prevention of age-associated disease has demonstrated promising options. This enzyme family resides in different subcellular compartments, and acts on a number of different targets in the nucleus, cytoplasm and in the mitochondria of the cell.

Sirtuins play a key role in DNA damage repair mechanisms in yeast as well as mammalian cells, according to research appearing in *Experimental Cell Research* (2014 Nov 12. pii: S0014-4827(14)00489-3. doi: 10.1016/j.yexcr.2014.11.001. [Epub ahead of print]). In this *in vitro* study, researchers examined the role of one of the least explored Sirtuin viz., SIRT7, under conditions of genomic stress when treated with doxorubicin. They found out that it promotes cellular survival under these conditions of genomic stress.

One area where this type of activity is important is in cardiovascular aging. Akt1 is involved in cellular survival pathways, by inhibiting apoptotic processes. Akt1 is also able to induce protein synthesis pathways, and is

therefore a key signaling protein in the cellular pathways that lead to skeletal muscle hypertrophy, and general tissue growth. Recent studies have shown that sirtuin isoforms, silent information regulator (SIRT) 1, SIRT3, and SIRT6, play an essential role in the regulation of Akt activation.

During aging the cardiovascular system is attacked by a variety of environmental stresses, including those encountered as a result of high blood glucose and lipids level, or by the presence of oxidized lipoproteins which, among others, determine important oxidative stress signals. In such a milieu, heart and vessels develop a functional impairment leading to atherosclerosis, ischemia, heart insufficiency and failure. Sirtuins, which are believed to have a positive impact on cardiovascular physiology and physiopathology, are distributed in different subcellular compartments including the nucleus, the cytoplasm and the mitochondria, where they regulate expression and function of a large variety of target genes and proteins. Remarkably, experimental animal models indicate resveratrol, the first natural compound described to positively regulate the activity of sirtuins, as able to protect the endothelium and the heart exposed to a variety of stress agents.

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PRODUCTS WITH SIRTUIN ACTIVATING COMPOUNDS

Lipid-Sirt™ provides support for vascular integrity and healthy aging by supporting and stimulating sirtuin activity. Specific nutritional compounds have been demonstrated to have a positive impact on cholesterol levels. **Lipid-Sirt™** supplies some of these specific nutrients, which have been demonstrated to: 1) modify the production of cholesterol in the liver by reacting with hepatic enzymes, 2) increase cholesterol excretion via the bile, 3) inhibit cholesterol uptake from the intestine, and 4) support increased levels of HDL.

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