

Resveratrol



Introduction



Green grapes

Resveratrol is obtained from plants. The function of resveratrol in plants is thought to be protection since it is produced when the plant is under environmental stress, whether ultraviolet radiation, infection, or insect infestation. Resveratrol has been found in at least 72 plants¹. Many of these plants are part of our regular diet such as blueberries, muscadine grapes, blackberries, and cocoa².

Neurodegenerative diseases

The main cause for neurodegenerative diseases has been found to be oxidative damage that can cause neurons to be vulnerable to neurotoxins, injury and oxidative stress⁶. Many compounds from fruits and vegetables have been found to be neuroprotective due to their

antioxidant nature. In addition, they protect the neurons from plaque and other molecular damage. Resveratrol has been found to diminish plaque formation up to 90% in some regions of the brain¹. It has also been found to protect the spinal cord from injury by preserving the lipid

One of the best known sources of resveratrol is red wine. In grapes, resveratrol occurs only in the skin. Red wine has more resveratrol than white wine due to the inclusion of the skin of the red grapes in the wine making process for a longer time so the resveratrol has time to leach out in the wine. With white wine, the skins are removed sooner during the fermentation process and therefore there is less resveratrol in white wine¹. Another good source of resveratrol is peanuts. Both raw and boiled peanuts are good sources of resveratrol as is peanut butter.

Resveratrol is a strong antioxidant and acts in many chemical reactions in the cell³. It can also bind to an

estrogen receptor in the cell, therefore it can be considered as an estrogenic compound⁴. As an estrogenic compound, it could be effective against hormone related cancers.

Resveratrol enhances the internal functions of the cell, particularly mitochondria, which is the energy source for the cell⁵. Mitochondria converts food energy in to energy that the cell can use. Decreased mitochondrial function has been linked to insulin resistance, metabolic syndrome, and cardiovascular disease.

Resveratrol has been found to be linked to decreased incidence of many chronic diseases such as neurodegenerative diseases, cancer and heart disease¹.

layer around the nerves. Resveratrol increases the activity of cellular components that protect and improve cellular energy cycles⁶. This improves the cell function and retains healthy neuronal cells, delaying Alzheimers and other neuronal declines with aging.

Special points of interest:

- RESVERATROL IS A STRONG ANTIOXIDANT
- RESVERATROL REDUCES PLAQUE FORMATION IN THE BRAIN
- RESVERATROL REDUCES OXIDATIVE DAMAGE
- RESVERATROL HELPS TO REGULATE GLUCOSE LEVELS

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Resveratrol

Cancer



Purple grapes

RESVERATROL
INFLUENCES
CANCER
DEVELOPMENT
AT MANY
STAGES

Cancer is among the top 10 causes of death in the US⁷. It is a disease that progresses slowly through three stages: initiation, promotion and progression. Preventing the first stage, initiation, is one of the best ways to reduce the incidence of cancer. If cancer is initiated, there are ways to slow down the promotion process so that an initiated cell never develops into a cancerous mass. Resveratrol inhibits the initiation step by inhibiting an enzyme whose products are pro-inflammatory⁸. It also increases the activity of an enzyme that destroys carcinogens. Therefore it is very potent in the early stages in preventing cancer develop-

ment. The promotion process can take years, and it is during this time when diet and physical activity are very important part of keeping the process in check. Resveratrol is also powerful in the promotion stage in reducing the size of the tumorous growth. In animal models, those treated with resveratrol had smaller and less frequent cancerous masses than in the untreated. Progression is the growth of the cancerous cells and during this stage, medical treatment is more important than dietary or physical activity intervention.

There are several naturally occurring compounds that can slow down cancer development at all stages such as

resveratrol, quercetin, curcumin, carotenoids and sulforaphane⁹.

Resveratrol has been effective in inhibiting lung, colorectal, gastric, breast, prostate, and skin cancer development in animal models. It has also been effective against melanoma, neuroblastoma, fibrosarcoma and leukemia. In many of these cancers, resveratrol caused increased cancer cell deaths thereby reducing the size of the tumorous growths.

Resveratrol actually slows down cancer development at the genetic level. It inhibits an enzyme production system in the cell that is involved in inflammation and tumor growth.

Heart Disease

Heart disease develops due to oxidative stress when the arterial wall is inflamed and a lesion is produced that attracts platelets, lipids and proteins and results in increased smooth muscle cell and collagen build up³. Grape and wine polyphenols have been shown to have beneficial effects on the cardiovascular system based on many animal studies and large scale cohort studies both in the US and overseas¹.

Resveratrol, a phytochemical found in red wine has been found to reduce vascular ox-

idative damage in several ways³. It eliminates free radicals that damage cellular components such as proteins, lipids, carbohydrates and the DNA. Resveratrol increases nitric oxide production in the cell, a protective action that causes vasodilation among other things. It inhibits free radical release from platelets that could otherwise result in more free radical production, and it inhibits platelet aggregation, another hallmark of myocardial infarction and stroke. With less free radicals, the low density lipoprotein particles are less likely to

be oxidized and cause harm once taken inside the cell. Resveratrol also inhibits smooth muscle cell build up inside the vessel walls by several different mechanisms³. Overall there is a reduced inflammatory response in those that consume resveratrol. Many inflammatory factors are significantly reduced and those that are protective show an increase. One cup of red grapes has anywhere from 1 to 5 mg of resveratrol, while a glass of red wine has about 0.8 to 1.2 milligrams of resveratrol.



Green grapes

Diabetes

Type 1 Diabetes (T1D) is due to insulin deficiency due to failure of the pancreatic beta cells. In Type 2 Diabetes (T2D), an individual has elevated glucose and insulin levels, high blood lipids, is overweight or obese, and has low level of physical activity. They also have mitochondrial dysfunction¹⁰. Mitochondrial dysfunction can cause insulin resistance, altered fatty acid vs glucose metabolism, and fatigue due to lack of energy⁵. Fatty acids accumulate in the cells and cause free radical formation that in turn damage other cellular lipids, proteins and DNA.

Resveratrol may be effective in ameliorating the metabolic dysfunctions of T2D diabetes.

It has been found to be hypoglycemic and decrease blood glucose levels by increasing glucose use by the muscle, liver and adipose cells, and by increasing glycogen synthesis in the liver². Glycogen is a storage form of glucose.

Similarly, it is hypolipidemic and has been found to reduce blood fats. There is a decrease in circulating triglycerides and cholesterol with the inclusion of resveratrol in the diet.

One of the tests for maintaining glucose control in diabetes is the amount of circulating glycosylated hemoglobin. Resveratrol supplementation resulted in significant decrease in the level glycosy-

lated hemoglobin in mice. It also improved the activity of many enzymes in the liver.

Diabetic nephropathy is a serious complication and can lead to end-stage renal disease. Treatment with resveratrol was effective in reducing the incidence of end-stage renal disease in mice¹.

Exercise, lifestyle modifications and inclusion of strong anti-oxidants such as resveratrol in the diet can repair and improve cellular function and improve glucose, insulin and lipid metabolism in diabetes.



Fresh blueberries

Inflammation

The root of many of the common chronic diseases such as heart disease, cancer and diabetes is inflammation^{2,10}. Small molecules called proinflammatory cytokines are produced in the body due to a stressful event and cause an increase in many harmful molecules¹¹. Once the inflammatory state becomes chronic, negative changes take place that can cause plaque formation, cancerous growths, or tightening of arteries leading to high blood pressure. Resveratrol inhibits the activity of those

inflammatory molecules and even at the genetic level prevents the formation of them¹². Resveratrol also inhibits the formation of peroxide molecules in cells that can cause widespread damage such as protein and DNA damage and oxidative stress. It reduces inflammation by changing the chemical cascades in the cells from pro-inflammatory to non-inflammatory¹. This is done by activating and inactivating enzymes involved in inflammation and normal metabolism.

Individuals with higher blood levels of resveratrol have been linked to decreased incidence of many chronic diseases, decreased inflammation, and improved cognitive function.

**RESVERATROL IS
IMPORTANT IN
REDUCING
INFLAMMATION
IN THE BODY BY
REDUCING AND
ELIMINATING
FREE RADICALS**



Cocoa powder

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Pennington Biomedical Research Center

VISION

Our *vision* is to lead the world in eliminating chronic diseases.

MISSION

Our *mission* is to discover the triggers of chronic diseases through innovative research that improves human health across the lifespan. We are helping people live Well Beyond the Expected.

The Pennington Center has several research areas, including:

- Clinical Obesity Research
- Experimental Obesity
- Functional Foods
- Health and Performance Enhancement
- Nutrition and Chronic Diseases
- Nutrition and the Brain
- Dementia, Alzheimer's and healthy aging
- Diet, exercise, weight loss and weight loss maintenance

The research fostered in these areas can have a profound impact on healthy living and on the prevention of common chronic diseases, such as heart disease, cancer, diabetes, hypertension and osteoporosis.

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We invite people of all ages and backgrounds to participate in the exciting research studies being conducted at the Pennington Center in Baton Rouge, Louisiana. If you would like to take part, visit the clinical trials web page at www.pbrc.edu or call (225) 763-3000.

Longevity

One of the most effective ways of increasing life span is by food restriction¹³. Resveratrol induces the same kinds of changes in cells as food restriction, therefore it has been looked at as a potential treatment for treating various conditions that occur with aging and overeating. In several studies on mice, inclusion of resveratrol to a high fat diet reduced total body fat content and increased survival.

Mitochondria, a small organelle in cells that controls energy production is an important unit and its function can determine well being in humans. Mitochondrial function is reduced in aging, diabetes,

metabolic syndrome and was the result of high fat, high calorie diet¹⁴. Accumulation of high level of reactive oxygen species that occurs due to poor diet, lack of exercise, smoking or excess alcohol intake can damage the mitochondria. The mitochondria is a very elegant energy production machinery in the cell that relies on many enzymes and cofactors for it to operate optimally. Mitochondrial dysfunction causes many chronic and serious conditions but mitochondrial function can be improved by food restriction, increased exercise and certain dietary compounds such as resveratrol. It increases the

activity of certain enzymes that are involved in mitochondrial regeneration. Resveratrol improves the survival of mice that are fed a high-fat, high-calorie diet by negating the effects of the fat and excess calories and normalizing insulin and glucose values. Similar effects have been seen in humans. Resveratrol also removes excess free radicals that are produced in the cell and prevents damage to other lipids and cellular proteins¹⁰.