

# **Resveratrol:** *What the Research Shows*

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Resveratrol is a natural substance found in many plants, including grapes, peanuts<sup>1</sup> and Japanese Knotweed (*Polygonum cuspidatum*).<sup>2</sup> Resveratrol's introduction into the dietary supplement market a few years back was based upon the consideration that intake of it and other polyphenol compounds from red wine may contribute to the "French paradox", the unexpectedly low rate of death from cardiovascular disease in the Mediterranean population, despite a diet that is relatively high in saturated fat.<sup>3</sup> Since then, interest in resveratrol has increased due to research suggesting additional antioxidant, antiinflammatory anti-cancer, antiviral, and anti-aging effects; as well as possibly playing a role in weight loss and athletic performance. This article will review the research on resveratrol.

## Cardiovascular health

Resveratrol has been found to exert a number of effects that may have protective effects on the cardiovascular system. In both test-tube and animal research, resveratrol has been shown to inhibit platelet aggregation (i.e., the clumping together of blood platelets). This has value since excessive or inappropriate aggregation of platelets can lead to formation of blood clots and subsequent blockages in blood vessels that result in insufficient blood flow, heart attack or stroke.<sup>4</sup> Resveratrol can also promote vasodilation (a relaxed and expanded state of the artery that accommodates increased blood flow) by enhancing the production of a naturally occurring substance in the body called nitric oxide.<sup>5</sup> Some animal studies suggest that high oral doses of resveratrol could decrease the risk of thrombosis (clot formation) and atherosclerosis.67

#### Antioxidant properties

Resveratrol has demonstrated antioxidant properties in animal research.<sup>8</sup> It is not clear, however, whether the antioxidant effects are direct, or the result of increasing the production of antioxidant enzymes made by the body. Test tube research has shown that resveratrol prevents the oxidation of LDL particles (the "bad cholesterol") by chelating copper and by directly scavenging free radicals.<sup>9</sup>

# Anti-inflammatory activity

Our bodies manufacture cyclooxygenase (COX) enzymes, which perform various functions. One such function, inflammation, is necessary as a normal, healthy attempt by the body to heal itself. However, when inflammation gets out of control (such as in the case of arthritis, or other chronic inflammatory disorders) ongoing pain and discomfort is the result. Resveratrol has anti-inflammatory activity, due to inhibition of the COX enzymes, as well as other inflammatory substances including hydroperoxidases, and 5-lipoxygenase  $^{10\ 11\ 12\ 13}$  and inflammatory cytokines.<sup>14</sup> Some evidence suggests that resveratrol is a more potent anti-inflammatory agent than NSAIDs such as aspirin, ibuprofen, or indomethacin.<sup>15</sup><sup>16</sup> Animal research has even shown that injections of resveratrol decreases inflammation and reduces cartilage destruction.<sup>17</sup>

# Anti-cancer effects

In test-tube research, resveratrol has been found to inhibit the proliferation of various human cancer cell lines, including those from breast, prostate, stomach, colon, pancreatic and thyroid cancers.<sup>18</sup> In animal research, resveratrol was shown to inhibit the development of chemical induced cancers of the breast<sup>19</sup>, esophagus<sup>20</sup> and intestine.<sup>21</sup> One mechanism by which resveratrol exerts this effect is by inhibiting angiogenesis (the growth of new blood vessels).<sup>22</sup> For tumors to grow, angiogenesis must take place so that blood vessels can develop in order to feed the tumor. Another mechanism is by inhibiting the enzymatic activity of both forms of the cyclooxygenase enzymes. Research shows that long-term inhibition of cyclooxygenase significantly reduces the risk of developing many cancers.<sup>23</sup>

# Antiviral activity

In test-tube research, resveratrol seems to have some antiviral benefits. For example, it was found to block the influenza virus from transporting certain proteins, thereby restricting the ability of the virus to replicate.<sup>24</sup> Likewise, resveratrol suppressed the activation of herpes simplex virus proteins, and reduced the production of viral DNA.<sup>25</sup> In addition, resveratrol has also increased the potency of some antiretroviral drugs against HIV.<sup>26</sup>

# Anti-aging

Research has shown that resveratrol significantly extends the lifespan of lower organisms such as the yeast *Saccharomyces cerevisiae*<sup>27</sup>, the worm *Caenorhabditis elegans* and the fruit fly *Drosophila melanogaster*.<sup>28</sup> Other research demonstrated that resveratrol had similar life extension effects on the short-lived fish, *Nothobranchius furzeri*,<sup>29</sup> also increasing swimming performance, and cognitive performance. Another study has shown that resveratrol improved the health and survival of mice that were on a high-calorie diet.<sup>30</sup> The reason that resveratrol has these anti-aging effects is unknown, but may be related to the production of proteins by the *SIR2* gene.

#### Weight loss potential and athletic performance

Obesity is biologically characterized at the cellular level by an increase in the number and size of adipocytes (fat cells) that develop from preadipocytes in adipose tissue. Resveratrol has been shown to inhibit pre-adipocytes<sup>31</sup>, which may translate into reducing the production of new fat cells.

In addition, the *SIR2* gene in the body of animals and humans produces the protein sirtuin 1 or *Sirt 1*. *Sirt 1* promotes fat mobilization in adipose (fat) tissue.<sup>32</sup> Resveratrol is also a known an activator of *Sirt 1*, and was shown in research to protect mice against dietinduced-obesity and insulin resistance.<sup>33</sup> By means of stimulating *Sirt 1* in mice, resveratrol was further shown to improve glucose balance.<sup>34</sup> The question of whether resveratrol will have a similar effect on humans is an intriguing one. More research needs to be done to answer this question. Meanwhile, resveratrol remains an intriguing natural substance with potential to promote weight loss.

In another study, Mice fed resveratrol for 15 weeks had better treadmill endurance than controls. This study also supports the role that resveratrol has on the activation of *Sirt 1*.<sup>35</sup> Can it have similar effects for athletic performance in humans? Future research will also have to answer this question.

#### Resveratrol dosing, safety and availability

Since most of the research conducted on resveratrol has in been test-tubes or animals, it is difficult to determine an appropriate dose for humans. In an interview with Dr. Johan Auwerx<sup>36</sup>, one of the resveratrol researchers, he indicated that he personally takes 40 mg of resveratrol daily. In any case, resveratrol has been shown to be free of adverse effects in humans in doses up to 5,000 mg.<sup>37</sup> Animal research has shown a similar safety profile.<sup>38</sup>

A certain amount of resveratrol can be consumed in the diet. The richest sources of it are as follows:

- A 5-ounce glass of red wine provides about 0.30-1.07 mg of resveratrol
- A cup of peanuts (raw) provides about 0.01-0.26 mg of resveratrol
- A cup of red grapes provides about 0.24-1.25 mg of resveratrol

By comparison, a dietary supplement can provide 100 mg of resveratrol per capsule. It would take up to 100 glasses of red wine to provide the same amount.

## Conclusions

More research, particularly human research, needs to be conducted on resveratrol. Meanwhile, its potential health benefits are many, and individuals who wish to try resveratrol can be assured of a good safety profile.

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