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## REPORT

### Replenishing the Aging Body's Antioxidant Defenses

By Laurie Barclay, MD



One of the most important ways to protect against premature aging is maintaining the integrity of the cell's lipid membrane and DNA. Maintaining these vital cellular structures enhances the body's ability to guard against age-related disease, including the well-known destructive effects inflicted by free radicals.<sup>1,2</sup>

A critical defense against free-radical damage is the body's own internally generated antioxidant enzyme known as superoxide dismutase (SOD). This powerful enzyme, which functions both within and outside of cell membranes, greatly reduces oxidative stress and inflammation that can lead to atherosclerosis, arthritis, cognitive impairment, and other age-related afflictions.<sup>3-5</sup> Unfortunately, levels of SOD dramatically decrease with advancing age, thereby limiting our natural ability to ward off degenerative disease.

Intriguing new research suggests that a Chinese herb known as wolfberry can enhance the activity of superoxide dismutase throughout the body.<sup>6,7</sup> Combined with other proven SOD-boosting nutrients, wolfberry, an edible fruit, can help restore youthful SOD levels and optimal antioxidant defenses.

In this article, we reveal how to supercharge the production of powerful internal antioxidants (like SOD) to help you guard against oxidative stress and inflammation, while enhancing strength, vigor, and longevity.

#### SOD DISARMS DANGEROUS SUPEROXIDE RADICALS

While essential to life, oxygen also generates toxic byproducts known as reactive oxygen species, or free radicals. Both normal aging and chronic disease dramatically increase the production of free radicals,<sup>8,9</sup> which can severely damage DNA, proteins, and lipids needed for cell growth, reproduction, metabolism, and repair.<sup>1</sup> The result of all this cellular damage can range from atherosclerosis to cancer and even Alzheimer's.<sup>10,11</sup>

Each day, our bodies fight off these damaging free radicals with the help of superoxide dismutase (SOD), which helps break down free radicals so that they are eventually converted into harmless water and oxygen.<sup>12</sup>

#### IMPROVED BIOAVAILABILITY ENHANCES SOD'S EFFECTIVENESS

Until recently, supplementing with SOD from food sources has been almost impossible. Digestive enzymes in the stomach quickly break down and deactivate orally ingested SOD. To create a more bioavailable form of SOD, researchers have coupled the SOD protein molecule to a carrier protein known as gliadin, derived from plant sources. Like a protective convoy, gliadin ushers SOD past the destructive stomach enzymes and delivers it to the intestines, where it is then absorbed directly into the bloodstream.<sup>13</sup>

Scientists began experiments with this new form of SOD coupled with gliadin (GliSODin®) to measure its absorption and utilization in the body. In one study, GliSODin® was associated with significantly increased activity of circulating antioxidant enzymes. Additionally, researchers noted that GliSODin® enhanced anti-inflammatory activity and improved the resistance of red blood cells to rupture induced by oxidative stress. This led scientists to conclude that supplementation with GliSODin® improves cellular antioxidant status while protecting against cell death induced by oxidative stress.<sup>13,14</sup>

The SOD-gliadin combination was shown to exert beneficial effects in cancer prevention as well. In an experimental model of tumor development, about 80% of laboratory animals given oral gliadin alone developed cancer, compared to only 40% of those given an oral SOD-gliadin compound. Moreover, cancer cells from subjects given SOD-gliadin were much less likely to spread (metastasize) than were cancer cells from those given gliadin alone. The researchers attributed the SOD-gliadin combination's remarkable anti-cancer effects to SOD's ability to scavenge the inflammatory superoxide radical.<sup>15</sup>

## CLINICAL STUDIES CONFIRM BENEFITS OF SOD-BOOSTING SUPPLEMENTS

In clinical as well as laboratory studies, supplements that boost SOD activity in the body show tremendous therapeutic potential.

Two studies sponsored by Life Extension examined SOD's benefits in humans using SODzyme™, an extract derived from the sprouts of corn, soy, and wheat.<sup>17</sup> In an open-label study, 12 middle-aged volunteers given 2000 mg of SODzyme™ daily for two weeks had a 30% increase in serum SOD levels and a 47% decrease in blood levels of hydrogen peroxide, a compound that aggravates inflammation associated with arthritis. These volunteers not only experienced a restoration of SOD to levels typically seen in much younger adults, but also had a 47% increase in the activity of a vital antioxidant enzyme known as catalase.<sup>16</sup>



In the second pilot study, 30 adults with arthritis or other inflammatory conditions received placebo or SODzyme™ for four weeks. A validated test designed to evaluate pain showed an impressive 71% decrease in pain in the SODzyme™ group and no change in the placebo group. Interestingly, patients who had the most pain when the study began achieved the greatest pain relief with SODzyme™. Several patients with various forms of painful arthritis or joint injury reported dramatic improvements in (and even absence of) pain within one to two weeks of starting SODzyme™, with no return in pain at the three-month follow-up and an improved ability to return to usual activities.<sup>17</sup>

SODzyme™ also demonstrates an impressive safety record. Unlike conventional nonsteroidal anti-inflammatory drugs (NSAIDs) or COX-2 inhibitors such as Celebrex® that are used to treat arthritis and inflammatory pain, SOD-boosting supplements have no adverse gastrointestinal or cardiovascular effects, due to their different mechanism of action.<sup>18</sup>

SOD's versatility is demonstrated by its ability to protect the skin against damage caused by ultraviolet light. In a randomized, double-blind, placebo-controlled study, scientists exposed the forearms of 50 volunteers to ultraviolet light once a week for four weeks. Starting two to three days before the first exposure, the participants took a daily supplement containing either GliSODin® or placebo. Individuals receiving GliSODin®, even those with fair skin, were able to withstand eight times more ultraviolet light exposure before they developed sunburn compared to those who received placebo. Other benefits of GliSODin® were less skin inflammation and more rapid healing of redness after burning occurred. The scientists concluded that GliSODin® effectively prevents the consequences of oxidative stress resulting from excessive sun exposure, and that this effect is particularly important for fair-skinned individuals.<sup>19</sup>

For many patients suffering from burns or diabetic wounds, hyperbaric (high-pressure) oxygen can significantly contribute to faster healing. However, such treatment with high-pressure oxygen can result in breaks in DNA strands while increasing levels of isoprostanes, which reflect oxidative damage to cellular membranes. Studies show that oral antioxidants such as vitamin E and N-acetylcysteine do not protect against the unique type of oxidative damage associated with hyperbaric oxygen treatment.<sup>20</sup> The combination of SOD and gliadin, however, offers effective protection against the oxidative stress of hyperbaric oxygen.

In a randomized, double-blind, placebo-controlled study, 20 volunteers each received an hour of hyperbaric oxygen treatment. Those who supplemented with SOD-gliadin had significantly decreased oxidative damage and fewer DNA breaks, as well as less elevation of isoprostane levels. SOD thus appears to have great therapeutic value for people exposed to extreme oxidative stress.<sup>21</sup> Since other antioxidants did not protect against the damage induced by hyperbaric oxygen, researchers have proposed that SOD's beneficial effects are specific and not related solely to its antioxidant activity.<sup>20</sup>

These studies offer powerful evidence that supplements that boost SOD levels and activity in the body confer significant protection against damage to DNA, lipids, and skin, while relieving pain and inflammation.

### SOD AND WOLFBERRY: WHAT YOU NEED TO KNOW

- The antioxidant superoxide dismutase (SOD) works at the molecular level to disarm the superoxide radical and protect against cellular damage.
- Although SOD was previously unavailable as dietary supplement, scientists have recently developed an orally bioavailable SOD formulation that boosts blood levels of SOD.
- Potential benefits of orally available SOD include relieving inflammation and pain, enhancing cellular life span, and protecting against conditions ranging from diabetes and cancer to cardiovascular and neurodegenerative disorders.
- The Chinese herbal remedy wolfberry is rich in potent antioxidants and enhances SOD activity in the body.
- Wolfberry's therapeutic applications include relieving fatigue, promoting visual health, protecting against diabetes, enhancing male sexual function, and supporting a healthy life span.
- Combining orally available SOD with wolfberry is an effective way to boost the body's SOD levels and activity, with benefits for disease protection, youthful energy, and longevity.



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### WOLFBERRY BOOSTS SOD ACTIVITY TO FIGHT BIOLOGICAL AGING

Laboratory analysis has shown that an exotic fruit known as wolfberry is one of nature's most concentrated sources of antioxidants. Moreover, emerging research suggests that wolfberry's antioxidant properties may be attributable to its ability to increase the availability of SOD throughout the body.



For nearly 2,000 years, wolfberry has been used in traditional Chinese medicine to improve immune system function, vision, circulation, and sperm production, as well as to detoxify and protect the liver. Traditional Chinese medicine holds that wolfberry may also improve life span, sexual energy, vigor, and muscular strength, while reducing pain and protecting against cancer, inflammation, and viral infection.<sup>6</sup>

The abundance of nutrients and antioxidants packed into the tiny wolfberry include plant-derived polyphenolic antioxidants; carotenoids such as beta-carotene, zeaxanthin, lutein, beta-cryptoxanthin, and lycopene; vitamins C, B1, B2, and niacin; more than 30 essential and trace minerals, including zinc, iron, copper, calcium, selenium, and phosphorus; polysaccharides; and 18 amino acids such as isoleucine, tryptophan, leucine, and arginine.

Wolfberry's antioxidant activity is likely attributable in part to its carotenoids, phenolics, and vitamin C.<sup>44</sup> Compared to other highly potent antioxidants derived from traditional Chinese herbs, wolfberry is even more effective in scavenging superoxide radicals and preventing their formation. Based on these observations, scientists believe that wolfberry dietary supplements represent an important source of daily antioxidant intake.<sup>45</sup>

Wolfberry's powerful antioxidant effects, however, may also arise from its ability to boost SOD's activity in the body. Wolfberry accelerates the rate of biochemical reactions that enable SOD to carry out its essential function of quenching oxidative stress. Since SOD disarms the dangerous superoxide radical to fight inflammation and degenerative diseases, wolfberry may have similar therapeutic effects, protecting against diabetes, sexual dysfunction, and the effects of aging.

One research team tested wolfberry's effects in oxygen-deprived subjects. Those who received wolfberry demonstrated higher SOD activity and antioxidant capacity than did those deprived of oxygen in the absence of wolfberry.<sup>7</sup> Wolfberry thus appears to protect against the damaging effects of ischemia (insufficient oxygen supply).

### SOD PROTECTS AGAINST A HOST OF DEGENERATIVE DISEASES

While SOD has been linked to youthfulness, longevity, and protection against chronic illnesses, the body's production of SOD drops dramatically with advancing age.<sup>2</sup> Conditions associated with free-radical damage that may benefit from increased SOD levels include a host of inflammatory and degenerative diseases:

- Nowhere are the signs of aging more visible than in the skin, where the effects of free-radical damage accumulate and produce visible signs of skin aging. SOD may help to protect against age-related skin wrinkling by arresting the breakdown of collagen, an essential protein that tones and strengthens the skin.<sup>22</sup>
- A chronic illness with many serious complications, diabetes is associated with increased oxidative stress. Increasing SOD levels may help fight the onset and progression of diabetes.<sup>23</sup>
- SOD's powerful antioxidant properties could have important therapeutic applications in preventing and managing cancer.<sup>24-26</sup> Scientists now believe that genetically based deficiencies of SOD are linked to an increased susceptibility of certain people to breast and pancreatic cancers.<sup>24,25</sup> Ensuring adequate SOD levels may help protect against these potentially deadly malignancies.
- By shielding the body from superoxide radicals, SOD may help prevent the cellular and tissue damage associated with cardiovascular disease.<sup>27-29</sup> While mainstream medicine promotes high cholesterol as the primary culprit in atherosclerosis and cardiovascular disease, low levels of SOD and other antioxidants may be even more important factors in elevating cardiovascular risk.<sup>30</sup> Providing the body with optimal antioxidant support could protect against America's leading cause of premature death.
- The nervous system is highly susceptible to oxidative stress. Because of its ability to protect against superoxide

radicals, SOD may guard against the cellular and tissue damage tied to neurological disease.<sup>27</sup> Specific neurological diseases linked to abnormalities in SOD include multiple sclerosis<sup>31</sup> and Alzheimer's and Parkinson's diseases.<sup>32-34</sup>

- Superoxide radicals help perpetuate the chronic pain associated with inflammation. SOD's ability to neutralize superoxide radicals is associated with pain relief,<sup>35</sup> with potential benefits for numerous conditions, including fibromyalgia, a chronic source of muscle pain.<sup>36</sup>
- Superoxide radicals also underlie the pain and inflammation of arthritis. Research demonstrates that patients with rheumatoid arthritis have lower dietary levels and reduced activity of SOD and glutathione peroxidase (a related antioxidant enzyme) than do healthy subjects.<sup>37</sup> Rheumatoid arthritis sufferers also exhibit lower levels of SOD in joint-cushioning cartilage cells known as chondrocytes, leaving these cells vulnerable to the damaging effects of nitric oxide and oxygen radicals.<sup>38,39</sup> These findings suggest that depleted levels of critical antioxidants such as SOD perpetuate crippling rheumatoid arthritis.
- Scientists have linked inflammation to many chronic diseases that accompany aging. Both in cells grown in the laboratory and in live animals, SOD improved the function of white blood cells of the immune system known as macrophages. Although macrophages subjected to oxidative stress release the inflammatory compound called tumor necrosis factor, those treated with SOD release the anti-inflammatory cytokine interleukin-10 (IL-10) instead.<sup>14</sup>
- Studies have shown that people who reach the age of 90 or 100 have high blood levels of IL-10, which may protect them from the ravages of aging and from developing cancer by reducing inflammation.<sup>40</sup> By promoting the release of IL-10, SOD may help the body ward off inflammation, in a manner similar to that seen in individuals who survive to a very old age.
- Other studies similarly suggest that SOD may be an important determinant of life span and longevity. Among various mammal species, those that produce higher tissue and serum levels of SOD live longer than those who do not.<sup>41,42</sup> This findings suggests that boosting SOD levels may be an important strategy for extending the healthy human life span.

In sum, a wealth of scientific evidence indicates that optimizing SOD levels may help to avert the many diseases associated with inflammation and aging,<sup>43</sup> including diabetes, heart disease, neurological conditions, cancer, skin aging, and arthritis.

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Wolfberry's capacity to boost SOD activity may benefit the pancreas, the insulin-producing organ that malfunctions in diabetes. When pancreatic cells were exposed to alloxan (a drug that instigates diabetes by generating superoxide radicals), their protective SOD activity declined dramatically. Adding wolfberry polysaccharides to the oxidative stress-damaged pancreatic cells helped to preserve the cells' essential SOD activity, thus conferring protection against damaging agents that may contribute to the development of diabetes.<sup>46</sup>

Wolfberry's effects in neutralizing oxidative stress may offer additional benefits for diabetes management. Scientists induced diabetes and high cholesterol in test animals by exposing them to alloxan. After the subjects were treated with wolfberry juice or polysaccharides for 10 days, they demonstrated several beneficial changes in blood chemistry markers, including reductions in blood sugar, serum total cholesterol, and triglycerides, and marked increases in beneficial high-density lipoprotein (HDL).<sup>47</sup> In this study, wolfberry polysaccharides and amino acids had the greatest effect on blood sugar, whereas wolfberry polysaccharides and antioxidants showed the most benefit on blood lipids.<sup>47</sup> Previous studies have shown that wolfberry polysaccharides produce beneficial reductions in potentially dangerous low-density lipoprotein (LDL),<sup>48</sup> and that wolfberry flavonoids help limit lipid peroxidation caused by oxygen radicals.<sup>49</sup> These studies suggest that wolfberry provides a host of protective benefits against biochemical agents that instigate diabetes and contribute to its damaging effects in the body.

To assess whether wolfberry enhances male sexual performance and fertility, Chinese scientists administered wolfberry extract to partially castrated male rats and mouse testicular cells in the laboratory. Compared to control animals, the partially castrated male rats treated with wolfberry demonstrated higher SOD activity, enhanced secretion of sex hormones, increased testicular weight, and improved sperm quantity and quality. Wolfberry boosted their sexual performance and reproductive function, and also protected the DNA of mouse testicular cells against oxidative damage caused by hydrogen peroxide, with higher doses proportionately more effective than lower doses.<sup>50</sup> These findings support wolfberry's reputation as an aphrodisiac and fertility-facilitating agent, providing a modern scientific rationale for wolfberry's centuries-old use in managing infertility and promoting sexual health in males.

Wolfberry's ability to boost SOD activity may even help prevent visible signs of aging. In a research model of skin aging, an extract of wolfberry and bergamot (sour orange) significantly increased both SOD activity and collagen content in the skin. This same botanical combination also promoted hair growth.<sup>51</sup> Other studies of aging subjects have shown that treatment with wolfberry increased SOD activity in red blood cells while decreasing levels of harmful compounds in the skin.<sup>52</sup> In human skin cells, wolfberry extract has displayed important skin-protective properties.<sup>53</sup> These studies indicate that extracts of wolfberry contribute to healthy skin and hair.

### MODERN SCIENCE CONFIRMS WOLFERRY'S HEALTH BENEFITS

Scientific studies have confirmed that wolfberry offers a wealth of health-enhancing benefits: promoting youthful energy, preserving vision, optimizing brain health, increasing longevity, and protecting against conditions related to oxidative stress.

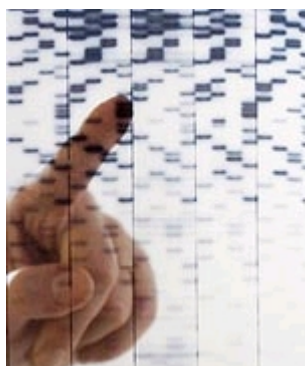


- All too many people suffer from waning energy levels as they grow older. New evidence suggests that wolfberry extract may help aging adults restore youthful energy levels. When test subjects consumed wolfberry, they became highly resistant to fatigue and were able to endure a greater exercise load. When the subjects did become fatigued, they recovered much more quickly. Scientists determined that this greater resilience was related to an increased ability to store glycogen (a form of glucose energy) in the muscles and liver. Glycogen helps provide the energy required for exercise and strenuous activity, and supports the elimination of metabolic wastes following exercise. Wolfberry thus helps the body to fuel itself for high-energy activity.<sup>54</sup>
- As a rich source of the nutrients known to support eye health, wolfberry may offer powerful protection for healthy vision. People seeking to maintain healthy visual function with aging often supplement with zinc and other minerals, carotenoids, and vitamin C, all of which are found in naturally high concentrations in wolfberry. Compared to other plant foods thought to help prevent age-related vision loss, wolfberry has the highest concentration of the dietary carotenoid zeaxanthin.<sup>55</sup> Along with lutein, zeaxanthin accumulates in the macula, the region of the eye's retina responsible for detailed vision. Zeaxanthin is believed to protect against oxidative damage caused by exposure to ultraviolet light. This photoexposure is a major culprit in age-related macular degeneration, one of the most common causes of irreversible

vision loss with aging. When 14 volunteers consumed 15 grams of wolfberry daily for 28 days, they demonstrated dramatically increased blood levels of zeaxanthin, about 2.5-fold higher.<sup>56</sup> Scientists believe that increased intake of foods containing zeaxanthin may be effective in preventing age-related macular degeneration. Wolfberry may be an ideal choice, since a modest daily intake provides bioavailable zeaxanthin that markedly increases plasma zeaxanthin levels.

- In addition to its benefits for the body, wolfberry may help keep the mind young. In a research model of cognitive aging, treatment with wolfberry was associated with enhanced learning ability and improved memory capacity.<sup>52</sup> Wolfberry may also protect against Alzheimer's disease, the most common cause of memory-robbing dementia. Using a laboratory model of Alzheimer's, scientists found that wolfberry protected brain cells from the harmful effects of amyloid beta peptides, damaging agents that are linked to the pathological changes seen in the brains of Alzheimer's patients. These findings suggest that wolfberry may hold value in preventive or therapeutic strategies for Alzheimer's disease.<sup>57</sup>
- Preliminary laboratory studies suggest other health-promoting applications of wolfberry. Utilizing a model of aging, researchers found that wolfberry increased the rate at which cells produced the genetic material DNA, while prolonging the cells' life span. Agents that extend the lives of cells could one day find applications in lengthening human life spans.<sup>58</sup>
- Evidence from the laboratory and early clinical studies suggests a potential therapeutic role for wolfberry in preventing and managing diseases associated with oxidative stress. Since oxidative stress plays a role in a vast array of illnesses, this suggests possible applications for wolfberry in averting heart disease, arthritis and other inflammatory diseases, some types of cancer, and premature aging, among other disorders.<sup>6,44</sup>

## CONCLUSION



Scientists and aging adults increasingly recognize that optimizing the body's antioxidant defenses is critical to fighting disease and avoiding the effects of biological aging. Superoxide dismutase (SOD) is one of the most powerful antioxidants for fighting inflammation, disease, pain, and the effects of aging. By quenching the dangerous superoxide radical, SOD works at the cellular level to prevent damage to crucial proteins, DNA, and lipids that support essential cellular activities.

Breakthroughs in nutritional science have led to the development of orally ingested, highly bioavailable forms of SOD. Combining orally available SOD with wolfberry offers a highly effective strategy to boost SOD levels and activity in the body. This novel combination protects against pain and inflammation, helps prevent a host of degenerative diseases, restores youthful energy and vitality, and promotes a long and healthy life span.

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