GliSODin®

Technical Monograph

LITERATURE REVIEW OF CANTALOUPE MELON SOD EXTRACT/ WHEAT GLIADIN BIOPOLYMER (GLISODIN®) AND ITS BENEFICIAL HEALTH ASPECTS

July 2012
## Index

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Summary</td>
<td>1</td>
</tr>
<tr>
<td>Introduction</td>
<td>2</td>
</tr>
<tr>
<td>GliSODin® - Definition and proof of concept/mechanism of action</td>
<td>3</td>
</tr>
<tr>
<td>GliSODin® - Definition and proof of concept/mechanism of action (continued)</td>
<td>4</td>
</tr>
<tr>
<td>GliSODin® - Evidence from human studies</td>
<td>5</td>
</tr>
<tr>
<td>Benefits of the antioxidant GliSODin® to promote immune health</td>
<td>6</td>
</tr>
<tr>
<td>GliSODin® in neuroprotection</td>
<td>7</td>
</tr>
<tr>
<td>Benefits of GliSODin® for physical performance &amp; sport</td>
<td>8</td>
</tr>
<tr>
<td>Benefits of GliSODin® for Cardiovascular Health</td>
<td>9</td>
</tr>
<tr>
<td>Alleviation of Reperfusion injury with oral administration of GliSODin®</td>
<td>10</td>
</tr>
<tr>
<td>Alleviation of Reperfusion injury with oral administration of GliSODin® (continued)</td>
<td>11</td>
</tr>
<tr>
<td>Benefits of GliSODin® on skin health</td>
<td>12</td>
</tr>
<tr>
<td>The role of GliSODin® in suppressing inflammation</td>
<td>13</td>
</tr>
<tr>
<td>Potential benefits of GliSODin® for diabetes</td>
<td>14</td>
</tr>
<tr>
<td>Benefits of GliSODin® in sports nutrition</td>
<td>15</td>
</tr>
<tr>
<td>Conclusions</td>
<td>16</td>
</tr>
</tbody>
</table>
Summary

The purpose of this technical publication is to review and update the scientific health benefits reported, for the enzyme Superoxide Dismutase, which is extracted from a cantaloupe melon and delivered in combination with wheat gliadin known as GliSODin®.

Superoxide Dismutase (SOD) constitutes part of the body’s front line in antioxidant defenses, helping to maintain the physiological oxidant-antioxidant balance. However, this balance can be disrupted by a number of factors that include aging, smoking, pollution, exposure to sunlight, high intensity exercise, infection and the subsequent immune response. The body experiences oxidative stress under these types of conditions, which has been linked to the increased risk of chronic disease.

Oral supplementation of the enzyme, in order to boost the body’s antioxidant defense system, has been ineffective due to the biochemical conditions experienced as the enzyme passes through the gastrointestinal tract. This passage degrades the enzyme, rendering it useless. This technical publication reviews the science related to GliSODin®, a trade name for SOD extracted from cantaloupe melon and combined with wheat gliadin. Clinical research and scientific evidence is presented to demonstrate that gliadin protects SOD during passage through the stomach, thus allowing absorption of the SOD enzyme once inside the intestine.

An extensive section is dedicated to the proof of this concept, with results from in vitro, in vivo and human studies presented. These studies show an increase in antioxidant status and a reduction in markers of oxidative stress. Evidence will also be presented regarding GliSODin’s bioactivity in humans. This evidence has been demonstrated using a dose of 500 mg, over a 14 day period.

Anti-inflammatory and immune system modulating effects of GliSODin® have been reported. These reports and effects are discussed in this publication, with particular attention focused on the mechanism(s) of action, behind the effects.

Neutralization of reactive oxygen species associated with oxidative stress has many important health implications, with potential benefits for improved recovery after strenuous exercise, reduction of inflammation (reddening) of the skin during exposure to sunlight (UV radiation), improvement in heart health, and complications arising from diabetes. Various sections throughout this Technical Publication are dedicated to exploring each of these areas.

This publication is presented in order to make the research and findings easily accessible to both scientists and non-scientists. The intention of this review is to provide a concise and accurate overview of the science behind GliSODin®. Key references can be found throughout the publication.
Production of reactive oxygen species (ROS) is a normal process in oxygen-breathing organisms. Under normal physiological conditions, a balance between these species and the body’s anti-oxidant defenses exists (Figure 1); however, certain conditions, such as smoking, pollution, exposure to sunlight (UV radiation), metabolism of sugars related to high intensity exercise, the natural progression of aging infection and the subsequent immune response, can increase the production of ROS like the superoxide ion (O2-) and the hydroxyl ion (OH-). This will disrupt the natural balance and ultimately lead to oxidative stress.1 (Figure 1).2

The detrimental health effects that can result from prolonged exposure to oxidative stress include: DNA damage that can cause cancer, atherosclerosis (hardening of the arteries) leading to cardiovascular disease, inflammation, rheumatoid arthritis, metabolic syndrome, diabetes and neurodegenerative diseases like Alzheimer’s.3

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GliSODin®

Definition and proof of concept/mechanism of action

Superoxide dismutase (SOD), catalase, and glutathione peroxidase work in conjunction with each other. This is essential in creating the front line in the body’s natural antioxidant enzyme defense system. Superoxide anion is the starting point of cascade reactions in free radical production.

SOD was dubbed the “enzyme of life” upon its discovery in 1968. Superoxide Dismutase is the first antioxidant mobilized by the cell and used as a defense mechanism against oxidative stress. The enzyme reacts with the superoxide ion and turns it into hydrogen peroxide ($H_2O_2$). This is then catabolised by catalase and glutathione peroxidase to produce molecular oxygen ($O_2$) and water ($H_2O$) (Figure 2).

These antioxidant enzymes have a distinct advantage over other antioxidants consumed from diet or nutritional supplements, like vitamins A, C, E, carotenoids, and thiols. These enzymes are biological catalysts, reducing many times and more rapidly reactive oxygen species, without being consumed themselves. By reacting at the beginning of the process, enzymes avoid the later occurrence of oxidized biological molecules. On the other hand, a non-catalytic or stoichiometric relationship exists for most vitamins, carotenoids and thiols. In other words, a defined relationship exists. For example: once Vitamin C removes an ROS, more Vitamin C must be supplemented and consumed in order to replenish any depleted Vitamin C stores that had been used during the ROS removal process.

Like most other protective mechanisms in the body, the production of SOD decreases with age, leaving it increasingly susceptible to oxidative damage.

Oral administration of SOD and other antioxidant enzymes contained in a variety of plant extracts is ineffective under normal conditions. During passage through the gastrointestinal pathway the enzyme is deactivated, rendering it ineffective as an antioxidant; however, studies have shown that when combining SOD with a wheat gliadin biopolymer, this system temporarily protects the SOD during passage through the gastrointestinal tract. One explanation of this efficiency, presented by Clemente et al., showed that gliadin increases the permeability of the intestine by promoting the release of a zonulin, thereby allowing the macromolecule SOD to be transported through the intestinal barrier.

The combination of SOD extracted from cantaloupe melon (Cucumis melo L.C.) combined with wheat gliadin biopolymer (GliSODin®) significantly improves the delayed release of SOD as evidenced in vitro by the progressive

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increase of its activity in a medium mimicking digestive conditions (Figure 4).[7]

Vouldoukis et al. demonstrated ex vivo that prime activation of macrophages isolated from rodents with interferon-gamma (INF-gamma), subsequently challenged with IgG1/anti-IgG1 immune complexes, will lead to the significant production of superoxide anions. This production may be regulated, in a dose-dependent manner, in macrophages originating from rodents previously supplemented with GliSODin®. These results prove potent in vivo activation of antioxidant gliadin biopolymer combination.[8]

An important proof of concept in vivo study by et al. using balb/c mice, demonstrates a significant increase in circulating antioxidant levels in mice that were supplemented with the gliadin-SOD complex. For 28 weeks the mice were supplemented orally with either SOD alone, or with the combined gliadin-SOD complex. The mice supplemented with the gliadin-SOD complex showed almost 4 times the antioxidant activity than those supplemented with the SOD alone.

Figure 3 illustrates circulating SOD activity in mice supplemented with free gliadin, free SOD, or GliSODin (no supplement).

Kick et al.[9] used the aortic cross-clamping technique on 18 pigs in order to induce ischemia-reperfusion process (HR), a well-established model of oxidative stress. After two weeks of supplementation with GliSODin® (1250 mg, nine pigs) and a placebo group (nine pigs), the animals were subjected to aortic clamping to induce injury-related oxidative stress. Pigs were chosen for this study to avoid confounding factors such as smoking and dietary habits. As well, their tissue antioxidant profiles and susceptibility to oxidative-stress is very similar to humans.

At the end of the study, the animals supplemented with GliSODin® had significantly lower levels of oxidative-stress induced DNA damage. Furthermore, the researchers found lower levels of apoptotic (dead) cells in the spinal fluid of the swine, thus showing a marked protective benefit.

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1 Vouldoukis I., Conti M., Krauss P., Kamaté C., Blazquez S., Teft M., Mazier D., Calenda A., Dugas B., "Supplementation with gliadin-combined plant superoxide dismutase extract promotes antioxidant defences and protects against oxidative stress" Phytotherapy Research 2004, Volume 18, Pages 957-962
GliSODin® Evidence from human studies

GliSODin® was studied in a trial utilizing induced oxidative stress, in order to demonstrate its efficacy in humans. Similar results were obtained from the study using pigs in a randomized, double-blind, placebo-controlled clinical trial. This particular study involved 20 men. Trials with such a design are considered the “gold-standard” for scientific evaluation. Muth et al. assigned the volunteers (average age 31) to receive a daily dose of 1000 International Units (IU) of SOD (GliSODin®) or a placebo for 14 days prior to being exposed to hyperbaric oxygen (HBO) – pure oxygen at a pressure of 2.5 atmospheres – for 60 minutes. DNA damage that results in exposure to HBO was measured using the comet assay technique. The DNA results were found to have significantly increased in the placebo group, while no significant changes were observed for the SOD-supplemented group (Figure 5).

Moreover, the levels of F2-isoprostanes, which are well-accepted markers for oxidative stress, had increased significantly in the placebo group (22.3 picograms per milliliter of plasma from the start of the study). No significant increases were observed in the SOD-supplemented group, which indicates significant protective benefits.

Muth et al. concluded that GliSODin® was able to protect against DNA damage induced by HBO and thereby proved the antioxidant activity of the supplement.[10]

Improvements in antioxidant status have also been observed in patients with HIV and AIDS, a population with reduced circulating antioxidant levels. Chenal et al. performed a double-blind clinical trial with 35 AIDS patients not receiving anti-retroviral therapy. These patients were broken up into three groups. One group received a placebo, the second group received the non-protected SOD and the third group received the SOD extracted from melon (Cucumis melo, 1000 IU SOD) gliadin combination (1000 IU SOD) every day.[11] At the end of 21 days of supplementation, the patients receiving GliSODin® were found to have normalized circulating SOD1 activity and total antioxidant status. No such effects were observed in the placebo or non-protected SOD groups. The researchers concluded that GliSODin® could improve antioxidant defenses.

Taken together these results from in vitro, in vivo and human studies show that GliSODin® is bio-available when taken orally and can significantly improve the antioxidant status of an individual.

Figure 5: Results of the comet assay measuring human DNA damage that results from exposure to HBO. GliSODin® was protective while damage significantly increased in the placebo group.

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Benefits of the antioxidant GliSODin®
to promote immune health

The combination of superoxide dismutase and gliadin (GliSODin®) was studied for its ability to regulate the immune response. Balb/c mice were fed a control diet supplemented with either free vegetal SOD (10 IU) or the SOD-gliadin combination (GliSODin®, 10 IU) for 28 days. Blood samples were taken every seven days and measures of circulating SOD, catalase or glutathion peroxidase indicated that their respective level only increased in the group receiving the GliSODin® combination.

Additionally, spleen cells isolated from mice in each of the groups showed that the mice supplemented with GliSODin® had increased production of type 1 helper T lymphocytes (Th1) and INF-γ and IL-4. The immunoglobulin G (IgG) response – the predominant antibody used by the body to identify and neutralize foreign objects – was stimulated, while the response of IgE, the immunoglobulin associated with an allergic response, was only marginally affected.

Vouldoukis et al. proposed that the mechanism behind these effects was because of an activation in antigen presenting cells (APC), which results in the production of hydrogen peroxide (H2O2) and nitric oxide (NO), both of which are reactive oxygen species and upset the oxidant-antioxidant balance. In response to this production of the antioxidant enzymes catalase and glutathione peroxidase is induced. This results in a polarized adaptive immune system, highlighting the benefits of GliSODin®. This polarization is a sign of the natural equilibrium of antioxidants in the cells.[12]

Quality of life, a measure of overall health, daily activities, tiredness, and energy levels, is an important issue for people infected with HIV and receiving highly active anti-retroviral therapy (HAART). Rahman et al. investigated the effect of receiving GliSODin®-containing supplements on quality of life and performance in 23 patients who were diagnosed with AIDS and treated with HAART.[13] Subjects received two daily supplements of Resurgex, a blend of GliSODin® (500 IU), coenzyme Q10 (75 mg), and beta-glucans (100 mg) for up to 24 weeks.

Measures of Quality of Life (QoL) significantly improved in the patients, particularly for measure of overall health, daily activities, tiredness, and energy levels. These types of progression were supported by improvements in measures of performance status.

On a biochemical level, Rahman et al. reported important clinical improvements in a number of metabolic and immunological functions, which would be tied to the improvements observed in performance and QoL.

These results indicated that supplements of GliSODin® could have significant benefits for the millions of people infected with the HIV-1 virus and receiving anti-retroviral therapy.

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GliSODin® in neuroprotection

Aging leads to a decrease in brain functions such as learning and memory. The aging effect is accelerated by chronic stress. As well, psychological stress plays a prominent role in accelerated aging. An experimental animal model using chronic immobilization stress significantly impairs spatial memory performance in immobilized animals. The effects of GliSODin® on stress-induced lipid peroxidation and impairment of spatial memory was investigated in rodents. Experimental mice were divided into four groups, as follows: (1) control mice (C mice) fed in a normal cage without immobilization; (2) restraint-stressed mice (RS mice) fed in a small cage; (3) vitamin E mice (VE mice) fed in a small cage with a diet supplemented with vitamin E; (4) GliSODin® mice (GS mice) fed in a small cage with a diet supplemented with GliSODin® (Figure 6). In the experimental model, mice were fed in narrow cages with 12 hour immobilization to generate psychological stress. Both GliSODin® and tocopherol protected against neuronal cell lipid peroxidation; however, GliSODin® also prevented impairment of spatial memory and significantly decreased latency of escape in the animals, compared to other experimental groups. The authors hypothesize that the GliSODin® treatment may upregulate Neurotrophic factors such as nerve growth factor (NGF) and insulin-like growth factor 1 (IGF-1) in the brain, enhance hippocampal neurogenesis and protect against stress-induced impairment of spatial memory induced by psychological stress.14

Figure 6: Spatial learning and memory in mice. The escape latency of GliSODin® (GS) receiving mice was significantly shorter than in the control groups (C, RS, VE).

Benefits of GliSODin® for physical performance & sport

High intensity aerobic exercise can increase oxygen consumption by up to 20 times the normal rate, which overwhelms our antioxidant defenses and results in increased oxidative stress.[15] A study by Arent et al. at Rutgers University looked at the effects of pre-season training on performance capacity and the oxidative stress response in 22 soccer players. These athletes were randomly assigned to receive a supplement of Resurgex, a blend of GliSODin® (500 IU), co-enzyme Q10 (75 mg), beta-glucans (100 mg), or an isocalorific equivalent, every day for the duration of preseason.

The group receiving the GliSODin® supplement showed greater improvements in measures of lactate production, "time to exhaustion" and showed significant reductions in oxidative stress-inducing lipid hydroperoxide levels than the control group. The researchers concluded that the GliSODin® may have meaningful effects, such as improved recovery, for people exercising at a high intensity.[16]

Hong et al. recruited 44 healthy individuals and assigned them to receive a daily SOD (GliSODin®) dose of 1500 IU for four weeks. Healthy volunteers were then submitted to cycling or treadmill exercise, but were assigned into two distinctive groups: the severe exercise group (27 subjects) or the moderate exercise group (17 subjects). Only volunteers ranging from the severe exercise group showed a significant reduction in the exercise-induced lactate production after the four-weeks of SOD supplementation[17] (Figure 7).

These studies indicate that supplementation with the gliadin-SOD complex could allow for quicker recovery in people undertaking strenuous exercise.

Figure 7: Effect of 4-week oral SOD administration on exercise-induced increase in plasma lactate

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Benefits of GliSODin® for Cardiovascular Health

Researchers from France’s National Association of Medical Prevention reported that supplementation with GliSODin®, in combination with diet and lifestyle changes, should significantly reduce the risk of cardiovascular disease by substantially reducing vascular inflammation, and may even have a positive impact on any previous damage.

Cloarec et al. recruited 76 patients considered to be at risk of cardiovascular disease, but free of any clinical symptoms associated with the illness. These patients were assigned diet and lifestyle changes over a period of 12 months. Minor improvements in blood pressure, LDL-cholesterol (so-called “bad” cholesterol) and body mass index (BMI) were reported. Due to stringent conditions of the study, 42 volunteers dropped out. The remaining 34 subjects, were randomly divided into two groups. One group would continue with the prescribed diet and lifestyle recommendations only and the second group received a daily supplement of GliSODin® (500 IU) for two more years.

Using ultrasound-B imaging to measure carotid artery intima thickness (IMT), a sign of hardening of the arteries (atherosclerosis), the researchers found a reduction in the progression of IMT in the SOD-supplemented group, compared to the group with the prescribed diet and lifestyle (Figure 8).

While no changes in antioxidant status had been observed in the control group, significant improvements in antioxidant status as a result of SOD supplementation were observed. Furthermore, GliSODin® supplementation produced a 34 per cent reduction in malondialdehyde (MDA) levels – MDA is a reactive carbonyl compound and a major end product of lipid oxidation. A major part of the pathogenesis of atherosclerosis, and subsequently cardiovascular disease, is the oxidative modification of LDL-cholesterol.

This study showed that supplementation with GliSODin® could impact the antioxidant status and the inflammatory process. The study also showed clear benefits against atherosclerosis, which is a major risk factor for cardiovascular disease.[18]

![Changes of IMT at baseline, D365, D545 and D730. Upper columns: IMT in control group; lower columns: IMT in GliSODin® group. While the control group experienced significant thickening of IMT, the GliSODin® group experienced a significant reduction of IMT.](image-url)

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18 Cloarec M., Caillard P., Provost J.-C., Dever J.-M., Elbeze Y., Zamaria N., “GliSODin®”, a vegetal SOD with gliadin, a preventative agents vs. atherosclerosis, as confirmed with carotid ultrasound-B imaging” European Annals of Allergy & Clinical Immunology, 2007, Volume 39, Number 2, Pages 2-7
**Alleviation of Reperfusion injury**

**with oral administration of GliSODin®**

In the in vivo experiment with ICR mice, the cardiovascular effect of oral GliSODin® on gastrointestinal arterial blood circulation was evaluated. After 9 days of gavage supplementation with GliSODin® in a dose of 1.6 mg/kg of body weight, the anesthetized animals were subject to a ischemia-reperfusion injury of superior mesenteric artery by clamping the blood vessel for 15 minutes and then opening the clamp and restoring blood flow. By opening the clamp and restoring blood flow, the blood vessel was subject to so-called reperfusion injury.

Reperfusion injury is the tissue damage caused when blood supply returns to the tissue after a period of ischemia or lack of oxygen due to, e.g., artery clamping or blockage by blood clot. The absence of blood flow and oxygen during the ischemic period creates a condition in which the restoration of circulation results in a massive formation of free radicals. This will produce oxidative damage and inflammation of the affected vessel, i.e. mesenteric artery. The blood flow in a reperfused damaged artery is compromised and the white cells tend to adhere to the damaged epithelium. This will impede blood flow and tissue oxygenation. During the in vivo experiment, a microscopic evaluation via camera of blood flow in the reperfusion-injury site with (A) and without (B) GliSODin® supplementation is presented in the attached photographs.

The reperfusion-injury site from the animals receiving GliSODin® for 9 days, (A) showed better passage of white blood cells through the damaged vessel in comparison to control mice with mesenteric artery showing attachment and aggregation of white blood cells to the epithelial cells lining the artery (B). The results of this experiment demonstrate that a short term regimen of oral GliSODin® may alleviate tissue oxygen deprivation, produced in the experimental model of a cardiovascular event, simulating the effects that occur during stroke or cardiac arrest.

![Picture A](image1)

![Picture B](image2)
Reperfusion-injury and management of this specific injury play a critical role, in recovering from stroke and cardiac arrest. Repeated bouts of ischemia and reperfusion injury are also thought to be a factor leading to the formation and failure to heal chronic wounds, including pressure sores and diabetic foot ulcers.

Picture (A) shows a lack of attachment and aggregation of white blood cells in reperfusion-injury of mesenteric artery from animals which were pretreated with GliSODin® 1.6 mg/kg BW for nine days. Picture (B) shows attachment and aggregation of white blood cells in reperfusion-injury of the mesenteric artery in the control animals not pretreated with GliSODin®.[19]
Benefits of GliSODin® on skin health

A randomized double-blind clinical trial by Mac-Mary et al. indicates that supplementing GliSODin® reduced skin-reddening when healthy fair-skinned volunteers were exposed to UV radiation. [20] 50 subjects were randomly assigned to receive a daily dose of GliSODin® (500 mg) or a placebo for a duration of 4 weeks. Subjects were exposed to UV radiation, in order to induce sunburn on their inner-forearms and to display the susceptibility of sunburn in participants (defined as the minimum erythematous dose – MED) and a measure of the resulting redness (actinic erythema).

Figure 9 shows that supplementation with GliSODin® resulted in an increase in the minimum exposure to UV rays necessary to produce a skin burn in fair-skinned people (phenotype II), compared to the placebo. The induced redness also decreased quicker in the group supplemented with GliSODin® over the four week period. These results confirmed the efficacy of the SOD-gliadin combination against the consequences of oxidative stress produced by exposure to UV radiation.

However, in a later study of similar design with Type II (fair-skinned) participants, GliSODin® significantly increased the MED within two weeks’ time (half the time of the first UV study), using a 250 mg dose. [21]

These studies were built on two older studies: a pilot study of 15 patients who were susceptible to sunburn and supplemented with a daily dose of 500 mg GliSODin® for three to eight weeks during normal sun exposure; and an open clinical trial, with 150 volunteers taking a daily GliSODin® supplement (500 mg) for 60 days. 86% of the participants reported significant relief. [22]

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[22] Laverdet C., Pomarede N., Oliveres-Ghouti C., “GliSODin® and Exposure to the Sun,” an open study conducted in France on 150 patients by 40 dermatologists. Sponsored by ISOCELL Nutra, France. March 2005
The role of GliSODin®
in supressing inflammation

An in vivo study by Vouldoukis et al.[23] submitted C57BL/6 mice groups to various supplements for 28 days: placebo, gliadin only (1 mg), SOD only (5 IU), the SOD-gliadin combination (5 mg equivalent to 5 IU of SOD, GliSODin®), or heat-inactivated SOD-gliadin combination (5 mg) for 28 days and then given an intra-peritoneal INF-γ injection (300 IU).

Peritoneal microphages were harvested 24 hours later and challenged with IgGl/anti-IgG1 immunocomplexes to amplify the inflammatory response. Only GliSODin® reduced the production of the pro-inflammatory cytokine, tumor necrosis factor-alpha (TNF-α) and promoted production of the anti-inflammatory cytokine interleukin-10 (IL-10), compared to the other treatments (Figure 10).

This result also showed that it is necessary to preserve the enzymatic activity of the administered-SOD to retain the anti-inflammatory effect of GliSODin® since IL-10 production was not observed when GliSODin® was previously heat inactivated.

The anti-inflammatory effects of GliSODin® are significant since chronic inflammation is associated with the onset and progression of many chronic diseases.

Okada et al. reported that administration of the gliadin-SOD complex could prevent cancer progression, promoted by inflammation.[24] The researchers used C57BL/6 female mice implanted with a gelatin sponge (to promote inflammation) and injected with QR-32 tumor cells. The mice were then randomly supplemented with GliSODin®, SOD-only, or gliadin only at a dose of 10 mg per kg of body weight. While tumor growth was suppressed in the GliSODin® group, the tumors in the mice supplemented with only SOD or gliadin were found to have significantly increased. The mechanism behind these effects was proposed to be related to reducing levels of the reactive oxygen species, superoxide ion. It was also proposed that the melon SOD extract-gliadin combination may also have an effect on immune response.

This result indicated that the antioxidant and anti-inflammatory properties of GliSODin® might have significant benefits for the prevention of tumor development and progression.

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Potential benefits of GliSODin®

for diabetes

Diabetes is on the rise worldwide, with diabetic kidney disease just one of the many complications of the disease. It has been suggested that high glucose levels may result in increased oxidative stress, and thereby promote the development of diabetic kidney disease (diabetic nephropathy). To test whether oral administration of GliSODin® could positively impact on the pathogenesis of diabetic nephropathy, Naito et al. assigned diabetic and non-diabetic mice to receive a standard rodent diet. One group was supplemented with the cantaloupe melon extract-gliadin combination (0.08 per cent of the diet) for twelve weeks.²⁵

No significant differences in blood glucose levels or body weight were observed between the diabetic mice in the SOD-gliadin-supplemented group and the control group. Both diabetic mice groups had higher blood glucose levels and body weights than non-diabetics.

In terms of kidney health, significant reductions in the levels of 8-hydroxydeoxyguanosin (8-OHdG), a marker of oxidative stress, had been observed in the SOD-gliadin-supplemented group. Ha et al.²⁶ reported that 8-OHdG formation is closely related to the development of diabetic kidney disease in rodents. Reductions in 8-OHdG were associated with improvements in kidney health amongst the test animals used by Naito et al.

Benefits of GliSODin®

in sports nutrition

A double-blind study included 19 members of the Polish National Rowing Team, who were participating in a training camp. Subjects were randomly assigned to the supplemented group (n = 10), which received 2 capsules (total 500 mg) of GliSODin® extract once daily for 6 weeks, and the placebo group (n = 9). At the beginning and end of the study, subjects performed a 2,000-meter maximum effort test on a rowing ergometer.

Blood samples were taken before each test, 1 minute after completing the test, and after a 24-hr rest period.

SOD activity was significantly higher (p = .0037) in the supplemented group at all measurement times, and post-exercise C-reactive protein was significantly lower (p = .00001) in athletes receiving GliSODin® than those in the placebo group (Table 1). In conclusion, supplementation with an extract rich in SOD activity promoted antioxidant status and protected against increased inflammation in the serum of professional rowers. [27]

Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before Supplementation</th>
<th>After Supplementation</th>
<th>Exercise</th>
<th>GliSODin</th>
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<tr>
<td></td>
<td>Preexercise</td>
<td>Postexercise</td>
<td>Recovery</td>
<td>Preexercise</td>
<td>Postexercise</td>
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<tr>
<td>CRP (μg/L)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sup</td>
<td>0.46 ± 0.31</td>
<td>0.49 ± 0.39</td>
<td>0.50 ± 0.37</td>
<td>0.18 ± 0.08*</td>
<td>0.21 ± 0.10*</td>
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<tr>
<td>Pla</td>
<td>0.28 ± 0.26</td>
<td>0.54 ± 0.50</td>
<td>0.41 ± 0.39</td>
<td>0.61 ± 0.56</td>
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<td></td>
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<td>Sup</td>
<td>1.77 ± 0.56</td>
<td>2.78 ± 1.11†</td>
<td>3.08 ± 0.89†</td>
<td>1.19 ± 0.31</td>
<td>1.89 ± 0.24†</td>
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<td>Pla</td>
<td>1.51 ± 0.69</td>
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<td>2.61 ± 0.78†</td>
<td>1.45 ± 0.59</td>
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<td>CK (U/L)</td>
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<td></td>
<td></td>
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<tr>
<td>Sup</td>
<td>166 ± 86</td>
<td>204 ± 100</td>
<td>167 ± 79</td>
<td>75 ± 41</td>
<td>92 ± 46</td>
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<tr>
<td>Pla</td>
<td>210 ± 163</td>
<td>259 ± 177</td>
<td>224 ± 120</td>
<td>110 ± 88</td>
<td>130 ± 117</td>
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<td>LDH (U/L)</td>
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<td>Sup</td>
<td>153 ± 68</td>
<td>242 ± 64†</td>
<td>195 ± 49</td>
<td>182 ± 51</td>
<td>262 ± 50†</td>
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<tr>
<td>Pla</td>
<td>128 ± 45</td>
<td>270 ± 43†</td>
<td>209 ± 37†</td>
<td>192 ± 78</td>
<td>279 ± 23†</td>
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</table>

Note. CRP = C-reactive protein; Sup = supplemented group; Pla = placebo group; TBARS = thiobarbituric-acid-reactive substances; CK = creatine kinase; LDH = lactate dehydrogenase.

*p < .05 relative to Pla group. †p < .05 relative to preexercise.

Conclusions

Production of reactive oxygen species (ROS) is a normal process in oxygen-breathing organisms. Under normal physiological conditions, a balance between these species and the body’s anti-oxidant defenses exists; however, certain conditions can increase the production of ROS like the superoxide ion (O2-) and this disrupts the natural balance and ultimately leads to oxidative stress.

The superoxide ion is the starting point of cascade reactions of free radical production. Superoxide dismutase (SOD), dubbed the “enzyme of life” upon discovery in 1968, is the first antioxidant mobilized by the cell as the primary defense against oxidative stress.

Oral delivery of the pure enzyme to boost the body’s natural antioxidant defenses has been limited by the harsh conditions experienced in the gastrointestinal (GI) passage. However, a combination of SOD extracted from cantaloupe melon (Cucumis melo L.C.) combined with wheat gliadin biopolymer (GliSODin®) can significantly and progressively increase SOD stability during passage through the GI tract, as shown by results from in vitro, in vivo and human studies.

The anti-inflammatory and immune system modulating effects for the SOD-gliadin combination have also been discussed, with the results showing that, while no such effects are observed when SOD or gliadin alone are administered, the SOD-gliadin combination is effective.

Such benefits can also be related to other conditions associated with oxidative stress, with significant health implications for improved recovery after strenuous exercise, reducing inflammation or reddening of the skin after exposure to sunlight (UV radiation), improvement in heart health, and complications arising from diabetes.

As scientific strategies are discovered in reducing oxidative stress, contributing towards healthy aging, oral supplementation with GliSODin® has been shown to scientifically offer a therapeutic means for the prevention and treatment of many conditions associated with increased oxidative stress and inflammation.

In summary, GliSODin® may offer important health benefits that go beyond the obvious internal anti-oxidant capabilities, in particular:

1. Cardiovascular effect preventing inflammatory damage to the lining of blood vessels;  
2. Lowering circulating pro-inflammatory markers contributing to chronic degenerative conditions; and  
3. Improving response to psychological stress and its detrimental effects on cognition and memory.