



GlisODin[®]

TECHNICAL PUBLICATION

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

MAY 2009

TECHNICAL PUBLICATION
LITERATURE REVIEW OF A CANTALOUPE MELON CONCENTRATE NATURALLY RICH IN
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BENEFICIAL HEALTH ASPECTS.

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Summary

The purpose of this technical publication is to review and update the science and health benefits reported to date for the superoxide dismutase enzyme extracted from 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 disturbed by a number of different factors, including aging, smoking, pollution, exposure to sunlight, infection and the subsequent immune response, and high intensity exercise. Under such conditions the body experiences oxidative stress and this is linked with increased risk of chronic disease.

In the past, oral supplementation with the superoxide dismutase enzyme in order to boost the body's antioxidant defenses has been ineffective. This is due to the biochemical conditions experienced in the gastrointestinal tract, leading to degradation of the enzyme and subsequently 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. Science is presented to demonstrate that combination with gliadin protects the SOD during passage through the stomach and enhances absorption once inside the intestine.

An extensive section is dedicated to the proof of this concept, with presentation of results from in vitro, in vivo and human studies which show both the increase in antioxidant status as well as the reduction of markers of oxidative stress. It will also be shown that GliSODin's bioactivity in humans has been demonstrated with a daily dose of as little as 250 mg over a period of just 14 days.

Anti-inflammatory and immune system modulating effects for the SOD-gliadin combination have also been reported, and these are discussed in this publication, with particular attention paid to the mechanism(s) behind the effects.

Reducing the production of reactive oxygen species associated with oxidative stress has many important health implications. These benefits include improved recovery after strenuous exercise, reduction of inflammation (reddening) in the skin on exposure to sunlight (UV radiation), improvement in heart health, and complications arising from diabetes. Sections in the review are dedicated to each of these areas.

This publication is presented in such a way as to be accessible to both scientists and non-scientists, with the intention of providing a concise and accurate review of the science behind the GliSODin® ingredient. Key references are presented throughout the review.

Introduction

Reactive Oxygen Species and their role in Disease

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, like smoking, pollution, exposure to sunlight (UV radiation), infection and the subsequent immune response, metabolism of sugars related to high intensity exercise, and aging, can increase the production of Reactive Oxygen Species (ROS) such as the superoxide ion (O₂⁻) and the hydroxyl ion (OH⁻). This can disrupt the natural balance and lead ultimately to oxidative stress^[1]. **(Figure1)**^[2]

The detrimental health effects that can result from prolonged exposure to oxidative stress include: DNA damage that can ultimately produce cancer and atherosclerosis (hardening of the arteries) that leads to cardiovascular disease. Oxidative stress is known to significantly contribute to the process of inflammation, which underpins conditions like rheumatoid arthritis, inflammation, metabolic syndrome and diabetes, as well as to neurodegenerative diseases like Alzheimer's^[3].

GliSODin® – Definition and proof of concept/mechanism of action

How do cells defend themselves?

Superoxide dismutase (SOD), along with catalase and glutathione peroxidase, form the front line of the body's antioxidant enzyme defenses^[4]. The superoxide anion is the starting point of the cascade of reactions of free radical production.

SOD, dubbed the "enzyme of life" on discovery in 1968, is the first antioxidant mobilized by the cell as defense against oxidative stress. The enzyme reacts with the superoxide ion and turns it into hydrogen peroxide (H₂O₂). This is then catabolised by catalase and glutathione peroxidase to produce molecular oxygen (O₂) and water (H₂O).

Do Antioxidant Enzymes confer any advantage over Dietary Antioxidants?

These antioxidant enzymes have a distinct advantage over the antioxidants consumed from the diet or nutritional supplements, like the vitamins A, C, and E, carotenoids, and thiols since the enzymes are biological catalysts, rapidly and repeatedly reducing reactive oxygen species without being consumed themselves. By reacting early in the process, the antioxidant enzymes can minimize the potentially-harmful oxidation of a range of biological molecules. On the other hand, a non-catalytic or stoichiometric relationship exists for most vitamins, carotenoids and thiols, meaning a defined relationship exists – one vitamin C molecule, for example, quenches just one ROS. As vitamin stores can be readily depleted under extreme free radical burden, more vitamin C must be consumed to replace that which has been lost. Moreover, in this example, as Vitamin C is involved in many other essential activities within the cell, relying on Vitamin C to quench free radicals means that Vitamin

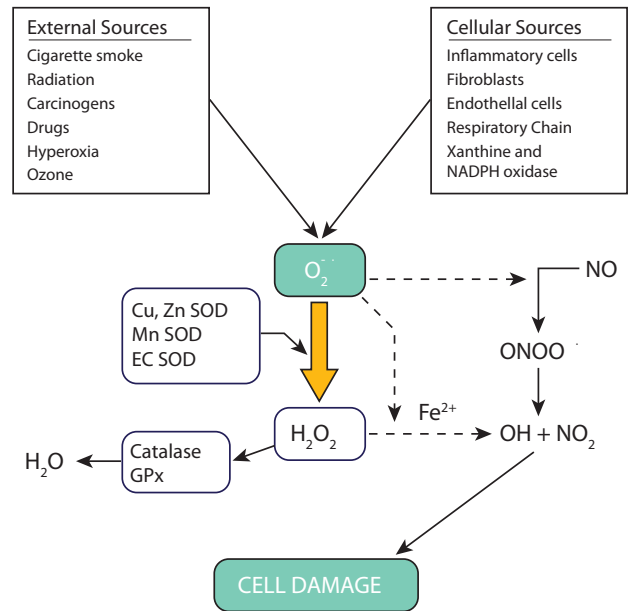


Figure 1: Cellular generation of reactive oxygen species and antioxidant defense system

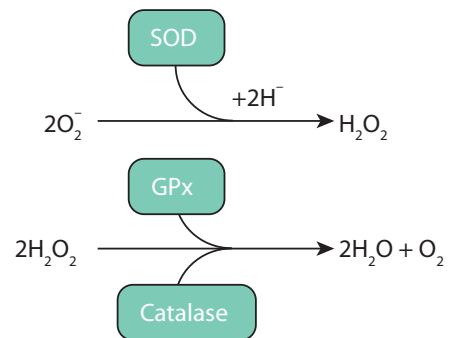


Figure 2: Role of antioxidant enzymes in the activation of the superoxide ion.

C is no longer available to perform its other essential tasks; these tasks include the production of collagen, and synthesis of certain neurotransmitters to name but two.

Like most other protective mechanisms in the body, the production of SOD decreases with age^[5], while a cell's susceptibility to oxidants increases, putting the cells under increasing oxidative stress.

Vitamin Depletion under Oxidative Stress

Oral administration of SOD and the other antioxidant enzymes present in many plant extracts is, under normal conditions, not effective. During passage through the gastrointestinal pathway the enzyme is denatured (deactivated) rendering it ineffective as an antioxidant. However, studies have shown that combining SOD with a wheat gliadin biopolymer system temporarily protects the SOD during its passage through the gastro-intestinal tract. One explanation of this efficiency was presented by Clemente et al. who showed that gliadin increases the permeability of the intestinal wall by promoting the release of a zonulin, thereby allowing the transport of the macromolecule SOD across the intestinal barrier^[6].

The combination of SOD extracted from cantaloupe melon (*Cucumis melo* L.C.) with the wheat gliadin biopolymer (GliSODin®) significantly improves the delayed release of SOD as evidenced *in vitro* by the progressive increase of its activity in a medium mimicking the digestive conditions (Figure 3)^[7].

Vouldoukis et al. have shown *ex vivo* that prime activation of macrophages isolated from rodents with interferon-gamma (INF-gamma) subsequently challenged with IgG/anti-IgG1 immune complexes leads 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 the potent *in vivo* activation of antioxidant activities made by the SOD-containing melon extract/gliadin biopolymer combination^[8]

Proof of Concept

An important proof of concept *in vivo* study by Vouldoukis et al. using Balb/c mice receiving the SOD melon extract orally, either alone or combined with wheat gliadin (GliSODin®) for 28 weeks showed that only the gliadin-SOD complex resulted in a significant increase in circulating antioxidant levels^[6].

Figure 4 illustrates circulating SOD activity in mice supplemented with free gliadin, free SOD, or GliSODin®, compared to control (no supplement).

Kick et al.^[9] used the aortic cross-clamping technique with 18 pigs to induce ischemia-reperfusion process (IR), a well-established model of oxidative stress. After two weeks of supplementation with GliSODin® (1250 mg, nine pigs) or placebo (nine pigs), the animals were subjected to aortic clamping to induce injury-related oxidative stress. Pigs were chosen to avoid confounding factors such as smoking and dietary habits, and because their tissue antioxidant profiles and susceptibility to oxidative stress are similar to that of humans.

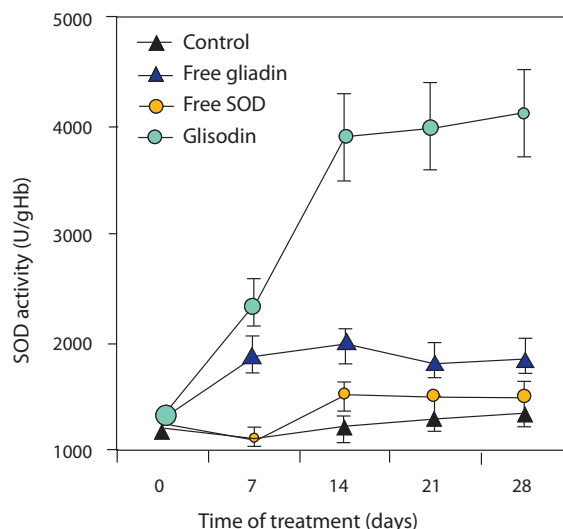


Figure 3: Effect of a supplementation with GliSODin® on circulating SOD activity. A. Mice were fed for 28 days with either a control diet or supplemented with (a) melon SOD extract (10 IU of non protected SOD), (b) gliadin (1 mg) or (c) GliSODin® (1 mg for 1IU)

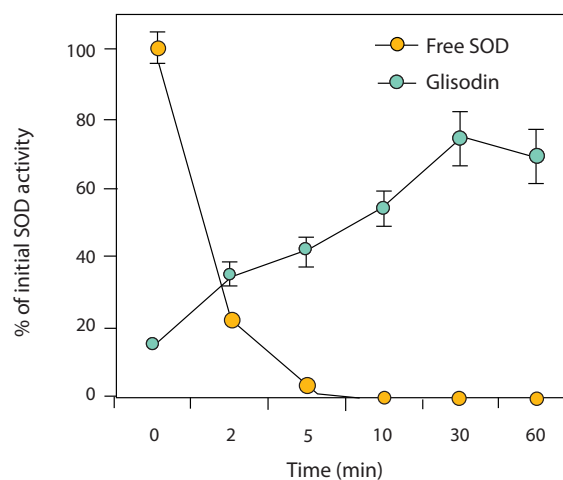


Figure 4: Gliadin polymers delay the release of the melon SOD activity in a medium mimicking the digestive process. An identical amount (100 units) of melon-SOD extract was submitted free or combined with gliadin (GliSODin®) to conditions mimicking the digestive process, for 1 h at 37 °C.

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

GliSODin® – Evidence from human studies

GliSODin® was studied in a trial utilizing induced oxidative stress, thereby establishing its efficacy in humans. Similar results to the swine study were obtained in a randomized, double-blind, placebo-controlled clinical trial involving 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 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, and found to have significantly increased in the placebo group, while no significant changes were observed for the SOD-supplemented group. (Figure 5)

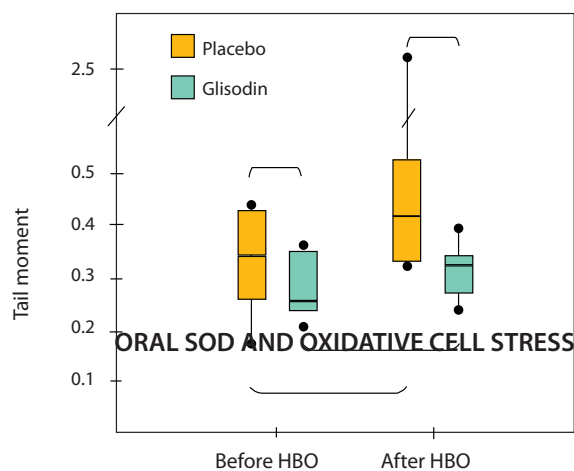


Figure 5: Results of the comet assay measuring human DNA damage that results from exposure to HBO. GliSODin was protective while damage significantly increased in the placebo group.

Protection observed by reduced F2- Isoprostane levels

Moreover, the levels of F2-isoprostanes, well-accepted markers for oxidative stress, 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 indicating significant protective benefit.

Muth et al. concluded that GliSODin® was able to protect against DNA damage induced by HBO and thereby confirmed 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 to receive placebo, non-protected SOD extracted from melon (*Cucumis melo*, 1000 IU SOD) or the SOD-gliadin combination (1000 IU SOD) every day^[11].

At the end of 21 days of supplementation, patients receiving GliSODin were found to have normalized circulating SOD1 activity and total antioxidant status, while no such effects were observed in the placebo or non-protected SOD groups. The researchers concluded that GliSODin could improve antioxidant defenses.

Bioavailability demonstrated

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

Benefits of the antioxidant GliSODin® for promoting 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 glutathione peroxidase indicate 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 type1 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 due to an activation of 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® since this polarization is a sign of the natural equilibrium of antioxidants in the cells^[11].

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 of 23 AIDS patients on HAART. Subjects received two daily supplements of Resurgex, a blend of GliSODin® (500 IU), co-enzyme 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. Such improvements were supported by improvements in measures of performance status.

On a biochemical level, Rahman et al reported clinically important 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.

Benefits of GliSODin® for physical performance & sport

High intensity aerobic exercise can increase oxygen consumption by up to 20 –fold, overwhelming our antioxidant defenses and resulting in increased oxidative stress^[14]. A study by Arent et al. at Rutgers University looked at the effects of pre-season training on performance capacity and oxidative stress responses of 22 Division 1 soccer players randomly assigned to receive a supplement of Resurgex, a blend of GliSODin® (500 IU), co-enzyme Q10 (75 mg), beta-glucans (100 mg) and other complementary nutrients, or an isocaloric equivalent daily for the duration of preseason.

The group receiving the GliSODin® supplement showed improvements in measures of lactic acid threshold and “time to exhaustion”, and significantly greater reductions in oxidative stress-inducing lipid hydroperoxide levels than the control group. The researchers concluded that the GliSODin® may have meaningful effects possibly including improved recovery for people exercising at a high intensity^[15].

Enhanced performance in soccer players

In another study with the GliSODin/ nutraceutical blend, various parameters were measured in the strength athlete using College Football players. The active group demonstrated an increase in peak power approximately 86% greater than the increase in the control group using a commercially available performance nutrition shake. Further, the active group showed significantly improved recovery parameters and inflammatory markers, including IL-6, Creatine Kinase and Isoprostanes levels as compared to control^[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 assigned

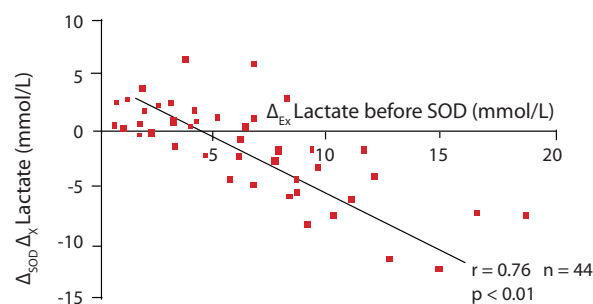


Figure 6: Effect of 4-week oral SOD administration on exercise increase in plasma lactate

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 6.)

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

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 significantly reducing vascular inflammation, and may even positively impact on previous damage.

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

Glisodin modifies hard clinical endpoints

Using ultrasound-B imaging to measure carotid artery intima media thickness (IMT), a sign of hardening of the arteries (atherosclerosis), the researchers found a reduction in the IMT in the SOD-supplemented group, compared to the diet and lifestyle only group. (Figure 7.) It is interesting to note that recent studies with statins have not shown a regression in IMT.

While no changes in antioxidant status were 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 antioxidant status and the inflammatory process, and had clear benefits against atherosclerosis, a major risk factor for cardiovascular disease^[18].

Benefits of GliSODin® for skin health

A randomized double-blind clinical trial by Mac-Mary et al. showed that GliSODin® supplementation reduced skin-reddening when healthy fair-skinned volunteers were exposed to UV radiation^[19]. Fifty subjects were randomly assigned to receive a daily dose of GliSODin® (500 mg) or placebo four weeks. Subjects were exposed to UV radiation to induce sunburn on the inner-forearms, and the susceptibility of the participants to sunburn (defined as the minimum erythematous dose – MED) and a measure of the resulting redness (actinic erythema).

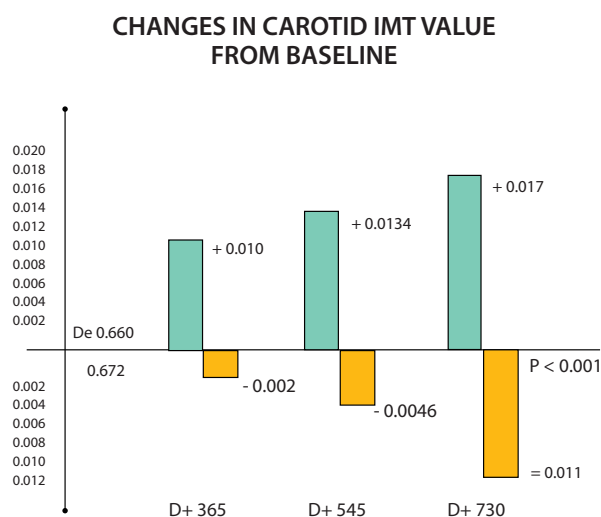


Figure 7: Changes of IMT at baseline, D365, D545 and D730. Upper columns: IMT in control group; lower columns: IMT in GliSODin group. While the control group experienced significant thickening of IMT, the GliSODin group experienced a significant reduction of IMT.

Figure 8 shows that supplementation with GliSODin® resulted in an increase in the minimum exposure to UV rays necessary to produce skin burn for fair-skinned people (phenotype II), compared to placebo. The induced redness also decreased quicker in the GliSODin®-supplemented group 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 in two weeks' time with a dose of just 250mg.^[19]

These studies were built on two older studies; a pilot study of 15 patients who were susceptible to sun-burn supplemented with a daily dose of 500 mg GliSODin® for three to eight weeks of normal sun exposure; and an open clinical trial with 150 volunteers taking a daily GliSODin® supplement (500 mg) for 60 days. 86% of participants reported significant relief.^[19,20]

The role of GliSODin® in suppressing inflammation

An in vivo study by Vouldoukis et al.^[7] 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 macrophages were harvested 24 hours later and challenged with IgG/anti-IgG1 immunocomplexes to amplify the inflammatory response. Only GliSODin® reduced the production of the pro-inflammatory cytokine, tumor necrosis factor-α (TNF-α) and promoted production of the anti-inflammatory cytokine interleukin-10 (IL-10), compared to the other treatments (**Figure 9**).

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.

Targeting inflammation at the level of oxidative stress

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

Moreover, Okada et al. reported that administration of the gliadin-SOD complex could prevent cancer progression, promoted by inflammation^[22]. The researchers used C57BL/6 female mice implanted with a gelatine 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, the superoxide ion. It was also proposed that the melon SOD extract-gliadin combination may also be affecting immune response.

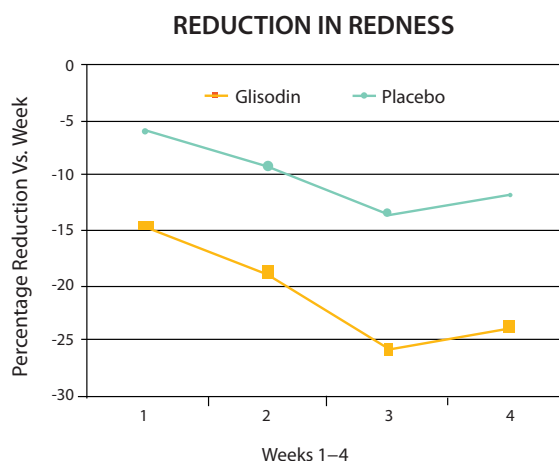


Figure 8: GliSODin induced in minimum erythematosedose (MED) compared to Placebo.

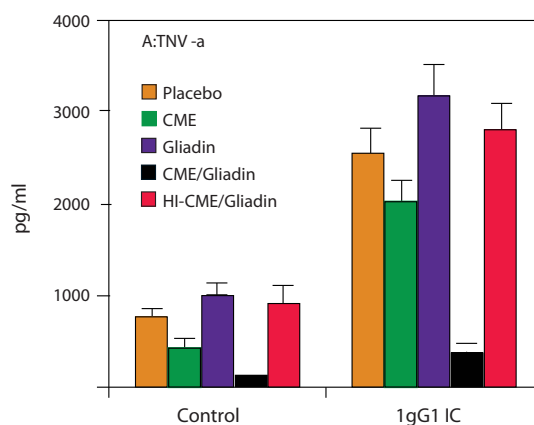


Figure 9: Effects of GliSODin® on production of pro- and anti-inflammatory cytokines.

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

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 and one group was supplemented with the cantaloupe melon extract-gliadin combination (0.08 per cent of the diet) for twelve weeks^[23].

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.

Attenuating the secondary complications of diabetes

In terms of kidney health, significant reductions in the levels of 8 hydroxydeoxyguanosine (8-OHdG), a marker of oxidative stress, were observed in the SOD-gliadin-supplemented group. Ha et al.^[24] have reported that 8-OHdG formation is closely related to the development of diabetic kidney disease in rodents, and reductions in 8-OHdG were associated with improvements in kidney health amongst the test animals used by Naito et al.

This study suggested that the cantaloupe melon extract-gliadin combination might be a novel approach for preventing diabetic kidney disease by reducing oxidative stress.

Potential benefits of GliSODin® for cognitive health

Aging is associated with a natural decline in cognitive function, and this decline precedes diseases such as Alzheimer's. Loss of cognitive function is related to a build-up of plaque from beta-amyloid deposits, which is associated with an increase in brain cell damage and death from oxidative stress.

An *in vivo* study by Nakajima et al.^[25] investigated if GliSODin® could protect against cognitive decline in male C57BL/6 mice. The animals were divided into four groups: normal diet and housed in normal cages (control); normal diet, but restrained in a case to induce

stress; restrained and diet supplemented with vitamin E (alpha-tocopherol acetate at 88mg per 100 g of diet); restrained and diet supplemented with GliSODin® (125mg 100 per 100 g of diet).

After five weeks, levels of 4-hydroxy-2-nonal (4-HNE), a marker of lipid peroxidation, and therefore oxidative stress, were significantly reduced in both vitamin E and SOD groups. The GliSODin®-supplemented mice showed greater spatial learning memory, related to a lower loss of certain cells linked to better brain function, related to new neuron development (Ki67-positive cells) in the hippocampal region of the brain (Figure 10).

This study indicated that the SOD-gliadin combination could prevent age-related cognitive decline by reducing oxidative stress.

Potential benefits of GliSODin® for eye health

Oxidative stress has been implicated in a number of age-related conditions, including age-related macular degeneration, the leading cause of blindness in the over-fifties.

Sicard et al.^[26] used senescence-accelerated mouse prone 8 (SAM P8) to evaluate the potential protective role of GliSODin® against light induced oxidative stress of the retina, and subsequent degeneration.

Animals were exposed to light (1900 lux for 7 hours) at one, two, and three months of age. Prior to the last exposure animals were administered water or GliSODin® for seven days (10.8 mg/kg/day). An increase of 30% in antioxidant capacity was recorded in SOD-supplemented animals, and SOD levels increased by 50% in the ganglion cell layer of the retina, and by 300% in the outer nuclear layer.

Furthermore, levels of the superoxide anion were significantly reduced. These results suggest that GliSODin® might limit oxidative stress in the retina by increasing the antioxidant capacity of the blood.

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, but certain conditions can increase the production of ROS like the superoxide ion (O₂⁻) and disrupt the natural balance and lead ultimately to oxidative stress.

The superoxide ion is the starting point of the cascade of reactions of free radical production. Superoxide dismutase (SOD), dubbed the "enzyme of life" on discovery in 1968, is the first antioxidant mobilized by the cell as 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, combination of SOD extracted from cantaloupe melon (*Cucumis melo* L.C.) with the wheat gliadin biopolymer (GliSODin®) can significantly and progressively increase SOD stability and delivery 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, reduction of inflammation (reddening) in the skin on exposure to sunlight (UV radiation), improvement in heart health, and complications arising from diabetes.

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

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