Keywords

SOD
Orally effective
Skin Health
Immune system

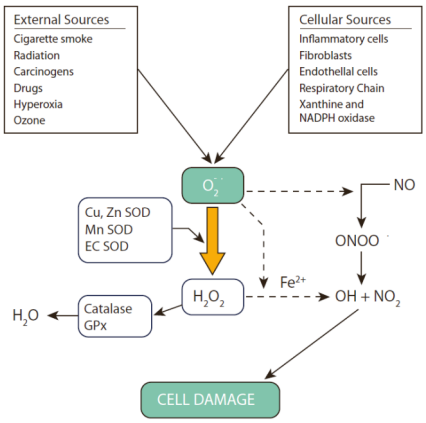
Summary

First orally effective SOD, GliSODin® is the new oral active for skin health, immune system and free radicals protection developed by Isocell and supported by more than 20 – mostly published - studies.

To get efficient SOD and related properties.

Thanks to its gliadin matrix, GliSODin® is orally effective unlike most existing SOD supplements. The gliadin is not an enteric protection – what should not be enough - but a real vehicle for the SOD, thanks to its specific bio-adhesive properties with the epithelial cells in the small intestine.

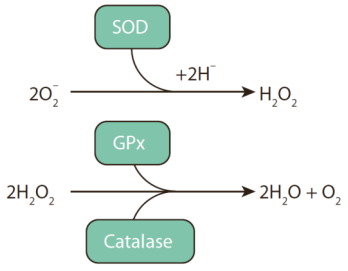
Production of reactive oxygen species (ROS) is a normal process in oxygen-breathing organisms. Under normal physiological conditions a balance between these species and the body's anti-oxidant defenses exists. However, certain conditions can increase the production of Reactive Oxygen



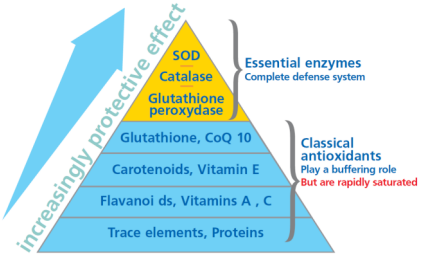
Species (ROS) such as the superoxide ion (O2-) and the hydroxyl ion (OH-).This can disrupt the natural balance and lead ultimately to oxidative stress.

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).



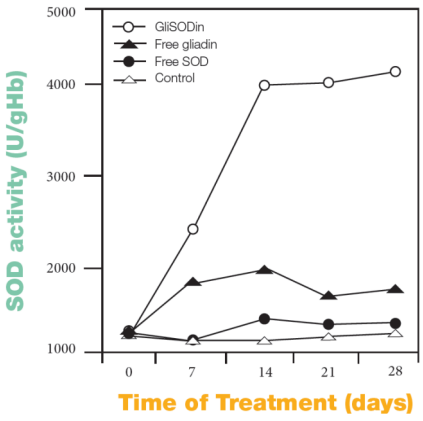
These antioxidant enzymes have a distinct advantage over the antioxidants consumed from the diet or nutritional supplements, like the vitamins A, C, and E, carotenoids, and thiols since the enzymes are biological catalysts, rapidly and repeatedly reducing reactive oxygen species without being consumed themselves. 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.



Oral administration

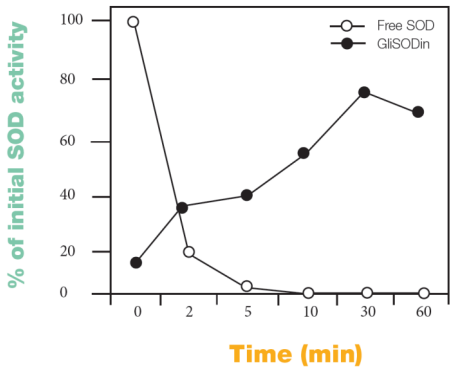
Oral administration of SOD and the other antioxidant enzymes present in many plant extracts is, under normal conditions, not effective. During passage through the gastrointestinal pathway the enzyme is denatured (deactivated) rendering it ineffective as an antioxidant. However, studies have shown that 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.

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 .



Vouldoukis et al. have shown ex vivo that prime activation of macrophages isolated from rodents with interferon-gamma (INF-gamma) subsequently challenged with IgGl/anti-lgG1 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.

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.
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.



The enzymatic activity of oral free SOD in the body is mainly to totally destroyed within few minutes, despite the source, and can so not promote the production of the SOD cascade by the cells (incl. endogenous SOD, gluthatione peroxidase and catalase) and the related expected optimal activities.
For this reason, usual studies based on free SOD cannot prove the efficacy, or at an incredibly high use (in-vivo).
GliSODin® multiple health benefits have been demonstrated in human clinical studies :

- Protection of cellular DNA subjected to intense oxidative stress induced by pure oxygen in a hyperbaric chamber, with comet assay cell nucleous damage control (20 patients study)
- Increase of the MED (resistance to UV induced erythema or redness), and redness resolved more quickly, Skin's protection against UV rays (50 patients study)
- Help prepare the skin for sun exposure and improved tanning speed and quality (150 patients study)
- Regulation of inflammation and decreases oxidative stress (35 patients)
- Significant decline in lactic acid levels (patients treated with GliSODin® for 4 weeks before strenuous exercise)

Dose : 250mg to 2 x 250mg a day

oxidative stress & DNA damages

GliSODin®'s protective benefits have been demonstrated in human interventional studies. GliSODin® was shown to protect against cellular oxidative stress damage in a dramatic human model. In this double-blind, placebo-controlled trial, twenty healthy volunteers were given pure oxygen in a hyperbaric chamber (HBO), which increased atmospheric pressure to 2.5 times normal, inducing intense oxidative stress. A measure of blood cell protection, looking at the integrity of the cellular DNA, was taken before and after exposure to measure the effect of oxidative stress. One group was given 1000 mg GliSODin® once daily for two weeks prior to the test, while the placebo group received 1000 mg of wheat gliadin alone. The GliSODin® group had significantly lower cellular DNA damage as evidenced by a test called "Comet Assay." Also, these findings coincided with reduced blood isoprostane levels, another marker of oxidative stress.

Significant protection GliSODin group | **DNA damage Placebo group**

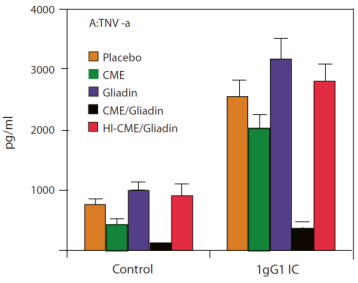
In the GliSODin group, the cell nucleus is intact, while the placebo group shows progressive nucleus damage with pronounced "comet tail".

Immune health

GliSODin® was studied for its ability to regulate the immune response. Supplementation 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, 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.
Rahman et al. investigated the effect of receiving GliSODin®-containing supplements on quality of life and performance of 23 AIDS patients on HAART (significant benefits for the millions of people infected with the HIV-1 virus and receiving anti-retroviral therapy).

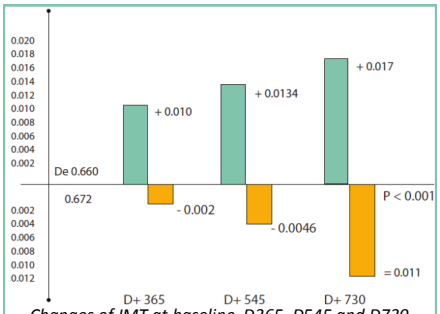
Supressing inflammation

In an in vivo study, Vouldoukis et al. compared the effects on production of pro- and anti-inflammatory cytokines with SOD, Gliadine, heat inactivated GliSODin® and GliSODin®.
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.
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. This result indicated that the antioxidant and anti-inflammatory properties of GliSODin® might have significant benefits for the prevention of tumor development and progression.



Cardiovascular health

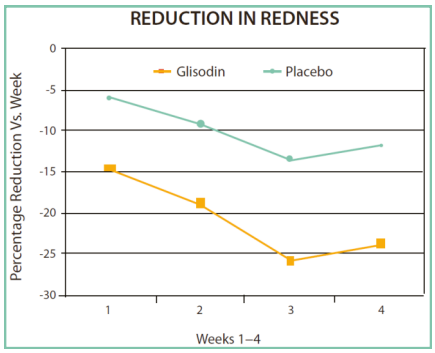
A newly published, three-year study with GliSODin® supplementation showed significant benefits for cardiovascular health.
Using ultrasound-B imaging to measure carotid artery intima thickness (IMT), a sign of hardening of the arteries (atherosclerosis), the researchers found a reduction in the progression of IMT in the SOD-supplemented group, compared to the group with the prescribed diet and lifestyle. 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.



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

GliSODin® promoted arterial health and function compared to the control group as measured by the thickness of the participants' carotid arteries. Further, GliSODin® significantly improved the antioxidant status and provided a reduction in measures of lipid oxidation. The researchers called the results "remarkable".

GliSODin® for skin health Photo oxidative stress



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. 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).
Supplementation with GliSODin® results 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.
In a later study of similar design with Type II (fair-skinned) participates, GliSODin significantly increased the MED in two weeks' time with a dose of just 250mg.

Why Gliadin and what dose ?

- Hydrophobic protein that can be made into films
- Used as carriers for conventional pharmaceuticals
- Protect proteins and peptides from GI digestion
- Optimize the uptake of SOD in the cells of the small intestine
- Promotes the immuno-modulating properties of heterologous SOD

GLISODIN contains 3.3% of Gliadin that correspond to 33mg per day based on the max. daily dose. A bread slice is about 40g (36g of flour at 15% gluten), what means 5,4g of gluten or 2,7g of gliadin, so close to 200 times what GliSODin® brings.

GliSODin® In Sport Nutrition

A double-blind study included 19 participants who were participating in a training camp (2 capsules (total 500 mg) of GliSODin®). SOD activity was significantly higher ($p < 0.01$) in the supplemented group at all measurement times, and post-exercise C-reactive protein was significantly lower in athletes receiving GliSODin®.
Supplementation with an extract rich in SOD activity promoted antioxidant status and protected against increased inflammation in the serum of professional rowers.
Hong et al. recruited 44 healthy individuals and assigned them to receive a daily GliSODin® dose of 1500 IU for four weeks. Healthy volunteers were then submitted to cycling or treadmill exercise but 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.

GliSODin® for Diabetes

(Naito et al.) 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. 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.

www.glisodin.org

Many other studies and research are available on GliSODin® (neuroprotection, spatial memory, Redox parameters, ...), mostly available on the dedicated website www.glisodin.org