

Best Application of Dietary Supplementation with Collagen-derived peptide Sources and Protandim For Brain, Bone, Tendon and Skin Health

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Most of the general public are probably aware of collagen supplements. Scroll through any random fitness account on Facebook or Instagram, and you'll come across a collagen supplement being celebrated for supporting joints and strengthening muscles. It has also been of prime importance in the beauty world and has even been labeled as the fountain of youth.

But have you ever heard of using collagen to support brain health? The whole world is most interested in this unique benefit of collagen. It's intriguing to know that the latest research strongly agrees on the role of collagen in protecting brain cells against various issues, such as Alzheimer's disease. Although most of these studies are in early phases and it's too early to confirm anything, it is pretty clear that collagen does carry some brain-supporting benefits.

This article will shed light on collagen as a potential supplement for brain health, its uses, side effects, and how to choose a good collagen supplement for yourself.

What is Collagen: An Overview

Collagen is the most common protein in the body. As a primary component of the connective tissue, collagen provides functional and structural support to your skin, bones, tendons, muscles, and organs. It is also responsible for sending out important signals to your body cells to repair damage and fight inflammation.

The human body is naturally capable of producing collagen on its own. Unfortunately, this production process begins to decline as you age. With the plummeting stores of natural collagen come a host of issues, especially if you fail to compensate for it. To avoid these circumstances, I suggest relying on Collagen supplementation.

Collagen for Brain Health

Collagen, a hero ingredient in many beauty elixirs and fitness supplements, has so many amazing uses for our well-being. Its anti-aging properties make us look young and radiant, while its muscle-building effects help us put on mass and look and feel healthier. It can support us in exercise and even promote recovery after injury. It improves cardiovascular health and supports a healthy liver, too. But did you know that collagen can also positively affect brain health?

Your very own muscle-building supplement can improve your brain performance too. As a pure protein, our brain requires collagen to work adequately. In the absence of this protein, brain degeneration is likely to occur. Structurally speaking, one-third of collagen is made up of a non-essential amino acid called **glycine** that plays a primary role in regulating brain health. Research has even proven its role in enhancing cognitive performance and supporting the treatment of patients with mental disorders.

Collagen and Schizophrenia

Further studies have also established a strong connection between glycine and schizophrenia. These studies found that the use of glycine in psychiatric patients can improve their symptoms. Collagen peptide, a form of collagen, has interestingly been linked to protecting the brain from schizophrenia by improving neural synapses.

Collagen and Alzheimer's Disease

There is evidence that a specific type of collagen protects the brain from a specific type of protein called amyloid-beta protein. The incidence of these protein accumulations has been widely linked with Alzheimer's disease. The use of collagen for preventing these from collecting in the neural tissue, might protect you from acquiring this extremely distressing disease as you age.

Collagen and Cognition

Some scientists have even credited collagen for helping with brain fog. New research verifies it, suggesting that ingesting collagen hydrolysates may positively affect the structure of the brain and improve cognition.

Collagen and Sleep

Collagen has also been studied as an effective sleep aid. The onus of this effect is on glycine, an amino acid majorly found in this protein structure. Glycine not only helps the brain fall asleep faster but also ensures to keep you in a deeper and more restful state of sleep. A good night's sleep, in turn, also supports brain performance.

With all the benefits of collagen on the brain, it can easily be regarded as a super ingredient to add to daily life. With all its amazing benefits, collagen really may be a super ingredient.

Side Effects of Collagen

Collagen is generally well-tolerated in a supplement form with very few and mild side effects. However, it must be kept in mind that some collagen-based supplements contain common food allergens, such as eggs, shellfish, and fish. Individuals with allergies to these food groups should be extremely careful while using collagen supplements. While using a supplement, keep an eye out for the common symptoms of an allergic reaction. Excessive itching on the body

- Overall, collagen supplements appear to be safe on the whole.

Choosing the Best Collagen Supplements

From bone broths to powders and pills, consuming collagen is slowly popularizing among the masses. However, the concept of supplementing this protein is certainly not new. In fact, people have been relying on collagen to rejuvenate skin and achieve their beauty goals for years, and this decades-old remedy is catching the attention of beauty editors and celebrities just now.

With all sorts of powders, capsules, and liquid collagen stacked up on the shelves of a supermarket, it can be confusing for anyone wishing to try it out for a brain boost. While some of them can be amazing for your health, others can easily do more harm than good. Look for the following points in mind while choosing a collagen supplement for yourself:

Source of Collagen

Most collagen supplements are extracted from the connective tissue of animals, including skin, bones, and fish scales. Make sure you grab a supplement with high-

quality collagen made from pasture-raised, grass-fed animals or wild-caught fish for a more organic and wholesome experience.

Type of Collagen

Various supplements offer collagen in different forms, which include:

Collagen peptides: The skin contains type I and III collagen and the cartilage, type II and III collagen. Collagen fibers confer tensile strength to these tissues. Unlike collagen of animal origin, collagen obtained from marine sources is more easily absorbed, has low molecular weight and is preferable to industry due to low inflammatory reactions and low number of contaminants. Marine collagen is similar in terms of biocompatibility and amino acid content to that of animals of porcine or bovine origin. Also from marine organisms, type I collagen is abundant.

Fish (marine) collagen has superior bioavailability.

This is due to its smaller particle size compared to other types of collagen. The smaller particle size allows an easier and faster uptake and transportation of the collagen peptides to the skin, bones and joints for the synthesis of new collagen. Fish collagen is absorbed up to 1.5 times more efficiently into the body which means it has superior bioavailability.

Collagen is a tasteless, odorless form that is dissolved into water to form a drink.

Hydrolyzed collagen: This type of collagen has been broken down by enzymes through a process known as hydrolysis into smaller particles for faster absorbability.

Ingredients Label: Scrutinize the ingredients label of every supplement in detail and check for any added fillers, preservatives, or other types of additives

Authenticity

The Food and Drug Administration does not need to approve Collagen supplements before hitting the stores. When you decide to purchase one, consider a supplement with third-party validation, for example, USP. This is one way to ensure that you are consuming exactly what's listed on the label.

Conclusions

My research has Convinced me that the best application of collagen supplementation is with small packets that are individually sectioned to avoid the exposure of the collagen to excessive air that will oxidize the ingredients.

Fish Collagen is an excellent source of the Peptides used most by our bodies.

Adding the following enhance the effectiveness of the Collagen:

Ruby Quinoa Extract (*Chenopodium Formosanum*)

Proprietary Citrus and Berry blend: Blueberry Powder, Young Ponkan Fruit and Acerola berry supply Vitamin C and Antioxidants to promote Collagen and Elastin production and help your skin create more of its own natural moisture.

Touted as an effective remedy for healthier skin and stronger muscles, the use of collagen is not new. However, the latest evidence has unraveled its potential cognitive benefits only recently. With the potential to fight brain-related disorders like Alzheimer's disease, induce more restful sleep, and enhance cognition, it can be a great solution to enjoy a healthy life with an efficiently working brain. Even though the research is still preliminary and more evidence is required to confirm it, collagen can be easily predicted as a [nootropic](#) of the future for sure.

The Best source that I can recommend is **True Science Collagen** by Lifevantage. It is a liquid form in individual containers with the added above ingredients. Information will be at the conclusion of this document.

Further Considerations:

Chronic tendinopathy, ligament ruptures, and bone fractures are common injuries among athletes. The consequences can be severe for elite athletes, who may be forced to end their career, treatment in a majority of patients is incomplete and unsuccessful from the perspective of a return to play at the elite level Furthermore, osteoarthritis (OA) is a chronic condition affecting the joints, and the progressive degeneration of articular cartilage causes pain and functional disability. It is

estimated that more than 250 million people are affected by OA worldwide and to this day no curative treatments are available

Therefore, there is an obvious need to search for alternative treatment strategies to optimize rehabilitation. Bones, tendons, ligaments, and cartilage are constituted by a complex matrix but are characterized by a high content of collagen, and this structural protein is vital for the structure and biomechanical properties of these musculoskeletal tissues.

Collagen is an abundant structural protein present in connective tissue. Besides its nutritional value as a protein source, dietary supplementation with collagen-derived peptide sources has been suggested to provide beneficial effects in patients with tendinopathy chronic joint instability, osteoarthritis (OA)], and activity-related joint pain]. Thus, nutritional interventions focusing on increasing the amino acid (AA) components of collagen have been suggested to improve collagen synthesis of collagen-rich tissues such as ligaments and bones and potentially slow the degenerative process in OA affected joints. However, in order to exert any potential beneficial effects, **optimal digestion and absorption** of AA components of collagen is pivotal. Protein digestibility generally varies depending on dietary source and processing methods . **Enzymatic hydrolysis** of proteins has shown an enhanced postprandial AA absorption and bioavailability. Always use **Hydrolysed Collagen**.

Effects of Collagen Hydrolysates on Human Brain Structure and Cognitive Function: A Pilot Clinical Study

Seiko Koizumi , Naoki Inoue, Fumihito Sugihara , etal.

Abstract: This study investigated the effects of **collagen hydrolysates (CH)** on language cognitive function and brain structure. In this open-label study, 5 g CH was administered once a day for 4 weeks to 30 healthy participants aged 49–63 years. The primary outcome measures were the brain healthcare quotients based on gray matter volume (GM-BHQ) and fractional anisotropy (FA-BHQ). The secondary outcome measures were changes in scores between week 0 and week 4 for word list memory (WLM) and standard verbal paired associate learning (S-PA) tests as well as changes in the physical, mental, and role/social component summary scores of the Short Form-36(SF-36) quality of life instrument. CH ingestion resulted in significant improvements in FA-BHQ ($p = 0.0095$), a measure of brain structure, as well in scores for the WLM ($p = 0.0046$) and S-PA ($p = 0.0007$) tests, which measure cognitive function. There were moderate correlations between the change in WLM score and the change in GM-BHQ ($r = 0.4448$; Spearman's rank correlation) and between the change in S-PA score and the change in FA-BHQ ($r = 0.4645$). **Daily ingestion of CH changed brain structure and improved language cognitive function.**

Oral glycine administration increases brain glycine/creatine ratios in men: a proton magnetic resonance spectroscopy study

Psychiatry Res. 2009 August 30; 173(2): 143–149. doi:10.1016/j.psychresns.2009.03.004.

Marc J. Kaufmana,* , Andrew P. Prescott, Dost Ongura, et al.

Abstract Oral high-dose glycine administration has been used as an adjuvant treatment for schizophrenia to enhance glutamate neurotransmission and mitigate glutamate system hypofunction thought to contribute to the disorder. Prior studies in schizophrenia subjects documented clinical improvements after 2 weeks of oral glycine administration, suggesting that brain glycine levels are sufficiently elevated to evoke a clinical response within that time frame. However, no human study has reported on brain glycine changes induced by its administration. We utilized a noninvasive proton magnetic resonance spectroscopy (1H-MRS) technique termed echo time-averaged (TEAV) 1H-MRS, which permits noninvasive quantification of brain glycine in vivo, to determine whether 2 weeks of oral glycine administration (peak dose of 0.8g/kg/day) increased brain glycine/creatine (Gly/Cr) ratios in 11 healthy adult men. In scans obtained 17 hours after the last glycine dose, brain (Gly/Cr) ratios were significantly increased. The data indicate that it is possible to measure brain glycine changes with proton spectroscopy. Developing a more comprehensive understanding of human brain glycine dynamics may lead to optimized use of glycine site agonists and glycine transporter inhibitors to treat schizophrenia, and possibly to treat other disorders associated with glutamate system dysfunction.

Improvement of activity-related knee joint discomfort following supplementation of specific collagen peptides

Denise Zdzieblik, Steffen Oesser, Albert Gollhofer, and Daniel König Updated online 18 April 2017:

Appl. Physiol. Nutr. Metab. Vol. 42, 2017

Abstract: The aim of the study was to evaluate the use of specific collagen peptides in reducing pain in athletes with functional knee problems during sport. Athletic subjects (n = 139) with functional knee pain ingested 5 g of bioactive collagen peptides (BCP) or a placebo per day for 12 weeks. The primary outcome of the study was a change in pain intensity during activity, which was evaluated by the participants and the attending physicians using a visual analogue scale (VAS). As secondary endpoints, pain intensity under resting conditions, the range of motion of the knee joint, and the use of additional therapeutic options were assessed. The results revealed a statistically significant improvement in activity-related pain intensity in the

verum group compared with placebo. (VASBCP = 19.5 ± 2.4 ; VASPlacebo = 13.9 ± 2.1 ; $p = 0.046$). The results were confirmed by the physician's assessment. (VASBCP = 16.7 ± 1.8 ; VASPlacebo = 12.2 ± 1.8 ; $p = 0.021$). Pain under resting conditions was also improved, but no significance compared with placebo was detected (VASBCP = 10.2 ± 18.4 ; VASPlacebo = 7.4 ± 15.2 ; $p = 0.209$). Due to the high joint mobility at baseline, no significant changes of this parameter could be detected. The use of additional treatment options was significantly reduced after BCP intake. The study demonstrated that the supplementation of specific collagen peptides in young adults with functional knee problems led to a statistically **significant improvement of activity-related joint pain**.⁸

COLLAGEN SUPPLEMENTATION: THERAPY FOR THE PREVENTION AND TREATMENT OF OSTEOPOROSIS AND OSTEOARTHRITIS: A REVIEW Bharat Kwatra

ABSTRACT Introduction: Collagen hydrolysate is recognized as a safe nutraceutical, whose combination of amino acids stimulates the synthesis of collagen in the extracellular matrix of cartilage and other tissues. Objective: to conduct a systematic review of literature on the action of collagen hydrolysate in bone and cartilaginous tissue and its therapeutic use against osteoporosis and osteoarthritis. Method: a study of the PubMed, MEDLINE, LILACS, and SciELO databases was performed. Articles published in English and Portuguese in the period of 1994 to 2014 were considered. Results: the sample comprised nine experimental articles with in vivo (animals and humans) and in vitro (human cells) models, which found that the use of different doses of collagen hydrolysate were associated with the maintenance of bone composition and strength, and the proliferation and cell growth of cartilage. Conclusion: hydrolyzed collagen has a positive therapeutic effect on osteoporosis and osteoarthritis with a potential increase in bone mineral density, a protective effect on articular cartilage, and especially in the symptomatic relief of pain. **KEYWORDS:** MEDLINE, LILACS, and SciELO. **INTRODUCTION** The human body goes through several stages: childhood WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES SJIF Impact Factor 7.632 Volume 9, Issue 5, 589-604 Review Article ISSN 2278 – 4357

A Collagen Supplement Improves Skin Hydration, Elasticity, Roughness, and Density: Results of a Randomized, Placebo-Controlled, Blind Study Liane Bolke, Gerrit Schlippe, Joachim Gerß and Werner: *Nutrients* 2019, 11, 2494; doi:10.3390/nu11102494

Abstract: The purpose of this randomized, placebo-controlled, blind study was to investigate the effects of the drinkable nutraceutical ELASTEN® (QUIRIS Healthcare, Gütersloh, Germany) on skin aging and skin health. Drinking ampoules provides a blend of 2.5 g of collagen peptides,

acerola fruit extract, vitamin C, zinc, biotin, and a native vitamin E complex. This controlled interventional trial was performed on 72 healthy women aged 35 years or older. They received either the food supplement (n = 36) or a placebo (n = 36) for twelve weeks. A skin assessment was carried out and based on objective validated methods, including corneometry (skin hydration), cutometry (elasticity), the use of silicon skin replicas with optical 3D phase-shift rapid in-vivo measurements (PRIMOS) (roughness), and skin sonography (density). The verum group was followed for an additional four weeks (without intake of the test product) to evaluate the sustainability of the changes induced by the intake of the test product. The test product significantly improved skin hydration, elasticity, roughness, and density. The differences between the verum group and the placebo group were statistically significant for all test parameters. These positive effects were substantially retained during the follow-up. The measured effects were fully consistent with the subjective assessments of the study participants. The nutraceutical was well tolerated. Keywords: aging; beauty; bioavailability; collagen peptides; cutometry; corneometry; wrinkles

Enzymatic Hydrolysis of a Collagen Hydrolysate Enhances Postprandial Absorption Rate—A Randomized Controlled Trial

Kathrine Skov Mikkelsen, Rebekka Thøgersen, Mette Hansen and Hanne Christine Bertram:
Nutrients 2019, 11, 1064; doi:10.3390/nu11051064

Abstract: Collagen is characterized by its high content of glycine, proline and hydroxyproline, and is found to exert beneficial effects on joint pain related to activity and osteoarthritis. However, to exert any beneficial effects it is essential that collagen is optimally absorbed. This study aimed to investigate the postprandial absorption of collagen and elucidate the impact of an exogenous enzymatic hydrolysis on absorption rate and bioavailability. A randomized, blinded, cross-over study was conducted where ten healthy male subjects received either 35 g enzymatically hydrolyzed collagen protein (EHC), 35 g non-enzymatically hydrolyzed collagen protein (NC) or placebo (250 mL water) on three nonconsecutive days. Blood samples were drawn before, and up to 240 min following, ingestion and the blood metabolome was characterized by nuclear magnetic resonance (NMR)-based metabolomics. A significant increase in the plasma concentration of nearly all amino acids (AAs) was observed over a 240 min period for both EHC and NC. In addition, the absorption rate and bioavailability of glycine, proline and hydroxyproline were significantly higher for EHC ($p < 0.05$). In conclusion, ingestion of collagen hydrolysates increases postprandial plasma concentrations of AAs over a period of 240 min, and an enzymatic hydrolysis increases the absorption rate and bioavailability of the collagen-rich AAs glycine, proline and hydroxyproline. Keywords: collagen absorption; glycine; proline; hydroxyproline; nutrimental metabolomics; collagen nutraceuticals; sports nutrition; amino acid absorption; dietary protein; collagen uptake.

Ruby Quinoa Extract

Protective Effect of Djulis (*Chenopodium formosanum*) Extract against UV- and AGEs-Induced Skin Aging via Alleviating Oxidative Stress and Collagen Degradation

Jia-Ling Lyu, Yi-Jung Liu, Kuo-Ching Wen Chen-Yuan Chiu, Yung-Hsiang Lin and Hsiu-Mei Chiang

Abstract: Skin aging is a complex process involving photoaging and glycation stress, which share some fundamental pathways and have common mediators. They can cause skin damage and collagen degradation by inducing oxidative stress and the accumulation of reactive oxygen species (ROS). *Chenopodium formosanum* (CF), also known as Djulis, is a traditional cereal in Taiwan. This study investigated the protection mechanisms of CF extract against ultraviolet (UV) radiation and advanced glycation end products (AGEs)-induced stress. The results indicated that CF extract had strong antioxidant and free radical scavenging effects. It could reduce UV-induced intracellular ROS generation and initiate the antioxidant defense system by activating the nuclear factor erythroid 2-related factor 2 (Nrf2)/heme oxygenase-1 (HO-1) signaling pathway in human skin fibroblasts. CF extract modulated mitogen-activated protein kinase (MAPK) and transformed growth factor-beta (TGF- β) signaling pathways to alleviate oxidative stress-induced skin aging. Moreover, the results revealed that CF extract not only promoted collagen synthesis but also improved aging-induced collagen degradation. CF extract attenuated AGEs-induced ROS production and the upregulation of receptor for AGEs (RAGE). The overall results suggest that CF extract provides an effective anti-aging strategy by preventing skin damage from oxidative stress and collagen loss with potent antioxidant, anti-photoaging, and antiglycation activities. *Molecules* 2022, 27, 2332. <https://doi.org/10.3390/molecules27072332>

Chenopodium quinoa (Amaranthaceae) is the seed crop known as the “golden grain” by the native Andean people in South America, including 20-hydroxyecdysone, which has been shown to inhibit intracellular ROS production and MMPs activity [42]. In addition, 20-hydroxyecdysone isolated from *C. quinoa* seeds possess strong inhibition activity against collagenase and the DPPH free radicals, and a potent ability to chelate iron ions [43]. Many previous studies have reported that CF extract contains rutin and 20-hydroxyecdysone as its rich bioactive ingredient, other plants containing these compounds also possess similar activities and skin care potential. The primary advantage of botanicals is their complex composition and the synergistic effect of related compounds with multiple activities to obtain greater efficacy [44]. Plant extracts pose a promising future in skin care due to their appeal as natural products, perception as safe, and abundance and sustainability. ROS are byproduct

Blueberry consumption prevents loss of collagen in bone matrix and inhibits senescence pathways in osteoblastic cells

Jian Zhang & Oxana P. Lazarenko & Michael L. Blackburn & Thomas M. Badger & Martin J. J. Ronis & Jin-Ran Chen Received: 2 November 2011 / Accepted: 17 April 2012 / Published online: 4 May 2012 # American Aging Association 2012 *AGE* (2013) 35:807–82

Abstract Ovariectomy (OVX)-induced bone loss has been linked to increased bone turnover and higher bone matrix collagen degradation as the result of osteoclast activation. However, the role of degraded collagen matrix in the fate of resident bone-forming cells is unclear. In this report, we show that OVX-induced bone loss is associated with profound decreases in collagen 1 and Sirt1. This was accompanied by increases in expression and activity of the senescence marker collagenase and expression of p16/p21 in bone. Feeding a diet supplemented with blueberries (BB) to pre-pubertal rats throughout development or only prior to puberty [postnatal day 21 (PND21) to PND34] prevents OVX-induced effects on expression of these molecules at PND68. In order to provide more evidence and gain a better understanding on the association between bone collagen matrix and resident bone cell fate, in vitro studies on the cellular senescence pathway using primary calvarial cells and three cell lines (ST2 cells, OB6, and MLOY4) were conducted. We found that senescence was inhibited by collagen in a dose–response manner. Treatment of cells with serum from OVX rats accelerated osteoblastic cell senescence pathways, but serum from BB-fed OVX rats had no effect. In the presence of low collagen or treatment with OVX rat serum, ST2 cells exhibited higher potential to differentiate into adipocytes. Finally, we demonstrated that bone cell senescence is associated with decreased Sirt1 expression and activated p53, p16, and p21. These results suggest that (1) a significant prevention of OVX-induced bone cell senescence from adult rats can occur after only 14 days consumption of a BB-containing diet immediately prior to puberty, and (2) the molecular mechanisms underlying this effect involves, at least in part, prevention of collagen degradation.

Antioxidant capacity and mineral content of pulp and peel from commercial cultivars of citrus from Brazil

Helena Rudge de MoraesBarros^aTânia Aparecida Pinto de CastroFerreira^aMaria InésGenovese^b
Food Chemistry

[Volume 134, Issue 4](#), 15 October 2012, Pages 1892-1898

Abstract

Four *Citrus* species (*C. sinensis*, cvs. Pera and Lima; *C. latifolia* Tanaka cv. Tahiti; *C. limettioides* Tanaka cv. Sweet lime and *C. reticulata*, cv. Ponkan) grown in Brazil were characterised in relation to contents of minerals, ascorbic acid, total polyphenols and antioxidant capacity of pulps and peels. In general, the peels demonstrated significantly higher contents of all compounds than the pulps ($p < 0.05$), with the exception of the Pera orange pulp that presented the highest acid ascorbic content (68 mg/100 ml), while the Tahiti lime peel presented the lowest (8 mg/100 g). Citrus showed high levels of potassium, calcium and magnesium, and the peels were considered sources of these minerals. The Ponkan mandarin peel presented the highest antioxidant capacity. The antioxidant capacity of citrus was correlated both to vitamin C and phenolics. Aside from citrus pulps,

the peels are also good sources of bioactive compounds and minerals, and can be explored for their health promoting values in food products.

High-dose glycine inhibits the loudness dependence of the auditory evoked potential (LDAEP) in healthy humans Barry V. O'Neill & Rodney J. Croft & Sumie Leung & Chris Oliver & K. Luan Phan & Pradeep J. Natha

Glycine Suppresses AGE/RAGE Signaling Pathway and Subsequent Oxidative Stress by Restoring Glo1 Function in the Aorta of Diabetic Rats and in HUVECs Ziwei Wang, Junqing Zhang, Lei Chen, Jingjing Li, Hong Zhang, and Xiaohui Guo

Oxidative Medicine and Cellular Longevity Volume 2019, Article ID 4628962, 14 pages

<https://doi.org/10.1155/2019/4628962>

Oxidative stress plays a crucial role in the pathogenesis of diabetic vascular complications. It is known that the accumulation of advanced glycation end products (AGEs) and the activation of the receptor of AGEs (RAGE) induce sustained oxidative stress in the vascular tissue. Growing evidence indicates that glycine, the simplest amino acid, exerts antioxidant and antiglycation effects and also improves vascular function. However, the mechanism whereby glycine protects vascular tissue against oxidative stress in models with diabetes has not been investigated. In the present study, we evaluated whether glycine can attenuate oxidative stress by suppressing the AGE/RAGE signaling pathway in the aorta of streptozotocin-induced diabetic rats and in human umbilical vascular endothelial cells (HUVECs). Our results showed that oral glycine administration increased NO content and ameliorated oxidative stress in the serum and aorta of diabetic rats. The AGE/RAGE signaling pathway in the aorta of diabetic rats was significantly attenuated by glycine treatment as manifested by decreases in levels of AGEs, RAGE, Nox4, and NF- κ B p65. The suppressive effect of glycine on the formation of AGEs was associated with increased activity and expression of aortic glyoxalase-1 (Glo1), a crucial enzyme that degrades methylglyoxal (MG), the major precursor of AGEs. In MG-treated HUVECs, glycine restored the function of Glo1, suppressed the AGE/RAGE signaling pathway, and inhibited the generation

of reactive oxygen species. In addition, the reduction in the formation of AGEs in HUVECs caused by glycine treatment was inhibited by Glo1 inhibition. Taken together, our study provides evidence that glycine might inhibit the AGE/RAGE pathway and subsequent oxidative stress by improving Glo1 function, thus protecting against diabetic macrovascular complications.

Methylglyoxal (MG), a highly reactive dicarbonyl metabolite of glycolysis, has been increasingly recognized as the major precursor of intracellular AGEs [10]. MG is degraded by the glyoxalase system, an efficient enzymatic detoxification system, of which glyoxalase-1 (Glo1) is the rate-limiting enzyme [11]. With glutathione (GSH) as a cofactor, Glo1 converts MG into an intermediate product, which is further detoxified into lactate by glyoxalase-2. Under diabetic conditions, both Glo1 expression and GSH levels are decreased [12–14]. Therefore, the function of Glo1 is impaired, leading to uncontrolled AGE formation and oxidative stress [15, 16]. Hence, an enhancement of Glo1 function would play a valuable role in inhibiting this detrimental process.

Glycine is the simplest amino acid in mammals. Besides participating in synthesizing structural biomolecules, glycine serves as one of the predecessors of GSH, one of the most important antioxidants in the human body. In diabetic complications, glycine exerts suppressive effects on glycation, such as delaying cataract formation [17], although the mechanism for this has not been clearly established. Recent studies have reported some protective effects of glycine on vascular injuries, such as improving endothelial function [18] and restoring vascular reactivity [13], but the effects of glycine on large blood vessels exposed to diabetic conditions have not been investigated. The antiglycation and antioxidant effects of glycine leave open the possibility that glycine might work by suppressing AGE formation and inhibiting the activation of the AGE/RAGE axis, thus protecting against oxidative stress and diabetic vascular complications. Due to the effect of glycine in restoring vascular GSH levels [13], we speculated that glycine may exert beneficial effects on Glo1 function, thus restoring the ability of Glo1 to inhibit AGE formation.

Beneficial effects of food supplements based on hydrolyzed collagen for skin care (Review)

Mihaela-Adi Lupu¹, Gratiela Gradisteanu Pircalabioru,

Mariana-Carmen Chifiriuc, Radu Albulescu, and Cristiana Tanase

Abstract. Aging is a complex, multi-step process which involves, among others loss of collagen and elastin. Collagen is found in large amounts in the body, especially in the dermis layer. These fibers provide the skin's normal strength, hydration and mechanical properties. Collagen is largely available, as it can be extracted from many animal sources, it can be easily absorbed upon topical administration, hence it is largely used in the cosmetic and pharmaceutical industry for the treatment of premature aging. Bioactive peptides, such as collagen hydrolyzate, are among the most used ingredients for the development of nutraceuticals - food or food ingredients that have defined physiological effects. Numerous studies have demonstrated that peptides resulted from ingestion of hydrolysate collagen and detected in the blood stream have chemotactic properties for skin fibroblasts, helping the skin restoration process. The purpose of this minireview is to present an update on the use of hydrolyzed collagen for skin care.

The presence of aging is noticeable in the second decade of life and involves numerous and important changes. Although at the beginning the changes are hardly observable, towards the third decade, important structural and functional changes occur. The skin is a protection system of the body against undesired influences from the external environment having multiple key roles in the sensitivity and protection against physical, chemical and biological aggressors of the human body (2). Due to its large exposure to environmental factors, skin suffers alterations which affect not only this aspect, but ultimately human health conditions (3). This is one of the reasons for which food, cosmetic and pharmaceutical industry are preoccupied with developing novel and improved products to prevent, delay or minimize the signs of ageing and to protect and heal the skin (4). Nutraceuticals ('nutrition' + 'pharmaceutical') are foods, food ingredients or pharmaceutical/cosmetic products with defined physiological effects (5), but without adverse effects, administered with the purpose to improve health status (6). Due to population growth and diversified food requirements, the consumption of nutraceuticals has increased. Nutraceutical products obtained from plants contain antioxidants, polyunsaturated fatty acids, as well as pre and probiotics. Recently the treatment of collagen deficiency has been treated with bioactive peptides obtained by enzymatic hydrolysis of food proteins. Bioactive peptides, such as collagen hydrolyzate, are among the most used ingredients for the development of nutraceuticals. Collagen represents ~30% of the body's protein mass and plays an important role in the structure of different tissue types, giving rigidity and integrity to the bones and skin. Collagen fiber has a triple helical structure composed of α chains. Type I collagen is found in mammals and is made up of two $\alpha 1(I)$ and one $\alpha 2(I)$ chains. The skin contains type I and III collagen and the cartilage, type II and III collagen. Collagen fibers confer tensile strength to

these tissues. Hydrolyzed collagen is rich in amino acids such as glycine and proline, and after digestion it accumulates in the cartilage or skin and helps maintain stability or regeneration.

GeroScience 2017 Apr; 39(2) 176-186.

“Influence of Nrf2 activators on the subcellular skeletal muscle protein and DNA synthesis rates after 6 weeks of milk protein feeding in older adults”

Abstract

In older adults, chronic oxidative and inflammatory stresses are associated with an impaired increase in skeletal muscle protein synthesis after acute anabolic stimuli. Conjugated linoleic acid (CLA) and Protandim have been shown to activate nuclear factor erythroid-derived 2-like 2 (Nrf2), a transcription factor for the antioxidant response element and anti-inflammatory pathways. This study tested the hypothesis that compared to a placebo control (CON), CLA and Protandim would increase skeletal muscle subcellular protein (myofibrillar, mitochondrial, cytoplasmic) and DNA synthesis in older adults after 6 weeks of milk protein feeding. CLA decreased oxidative stress and skeletal muscle oxidative damage with a trend to increase messenger RNA (mRNA) expression of a Nrf2 target, NAD(P)H dehydrogenase quinone 1 (NQO1). However, CLA did not influence other Nrf2 targets (heme oxygenase-1 (HO-1), glutathione peroxidase 1 (Gpx1)) or protein or DNA synthesis. Conversely, Protandim increased HO-1 protein content but not the mRNA expression of downstream Nrf2 targets, oxidative stress, or skeletal muscle oxidative damage. Rates of myofibrillar protein synthesis were maintained despite lower mitochondrial and cytoplasmic protein syntheses after Protandim versus CON. Similarly, DNA synthesis was non-significantly lower after Protandim compared to CON. After Protandim, the ratio of protein to DNA synthesis tended to be greater in the myofibrillar fraction and maintained in the mitochondrial and cytoplasmic fractions, emphasizing the importance of measuring both protein and DNA synthesis to gain insight into proteostasis. Overall, these data suggest that Protandim may enhance proteostatic mechanisms of skeletal muscle contractile proteins after 6 weeks of milk protein feeding in older adults.

Protandim maintained the rates of myofibrillar protein synthesis Overall these data suggest that Protandim may enhance proteostatic mechanisms of skeletal muscle contractile proteins.

J Appl Physiol (1985)
. 2018 Aug 1;125(2):661-671.
doi: 10.1152/jappphysiol.00277.2018. Epub 2018 Jun 1.

Differential effects of vitamin C or protandim on skeletal muscle adaptation to exercise [Danielle R Bruns](#)¹, [Sarah E Ehrlicher](#)¹, [Shadi Khademi](#)¹, [Laurie M Biela](#)¹, et al. PMID: 29856263 **Abstract**

Maintaining proteostasis is a key mechanism for preserving cell function. Exercise-stimulated proteostasis is regulated, in part, by redox-sensitive signaling. Several studies suggest that supplementation with exogenous antioxidants blunts exercise-induced cellular adaptations, although this conclusion lacks consensus. Our group uses a fundamentally different approach to maintain redox balance by treatment with bioactive phytochemicals to activate the transcription factor nuclear factor (erythroid-derived 2)-like 2 and downstream endogenous antioxidant pathways. We hypothesized that vitamin C (VitC) would interfere with redox-sensitive proteostatic mechanisms in skeletal muscle, whereas phytochemical treatment would permit proteostatic maintenance. We measured protein and DNA synthesis in skeletal muscle from high-volume voluntary wheel-running rats. Whereas phytochemical treatment permitted mitochondrial and other proteostatic adaptations to exercise, VitC treatment did not. During an in vitro oxidative challenge, phytochemical treatment helped maintain proteostasis, including the mitochondrial fraction while VitC did not. Our findings support the conclusion that VitC can blunt some of the beneficial adaptations to exercise. We propose that regulation of endogenous antioxidants represents a novel approach to maintain redox balance while still permitting redox-sensitive proteostatic adaptations. **NEW & NOTEWORTHY** Whether vitamin C blocks aerobic exercise adaptations lacks consensus, perhaps because of approaches that only assess markers of mitochondrial biogenesis. By directly measuring mitochondrial biogenesis, we demonstrate that vitamin C blunts exercise-induced adaptations. Furthermore, we show that treatment with Protandim, a purported nuclear factor (erythroid-derived 2)-like 2 activator that upregulates endogenous antioxidants, permits mitochondrial biogenesis. We confirm that vitamin C blunts aerobic exercise adaptations, whereas Protandim does not, suggesting targeting the endogenous antioxidant network facilitates adaptations to exercise.

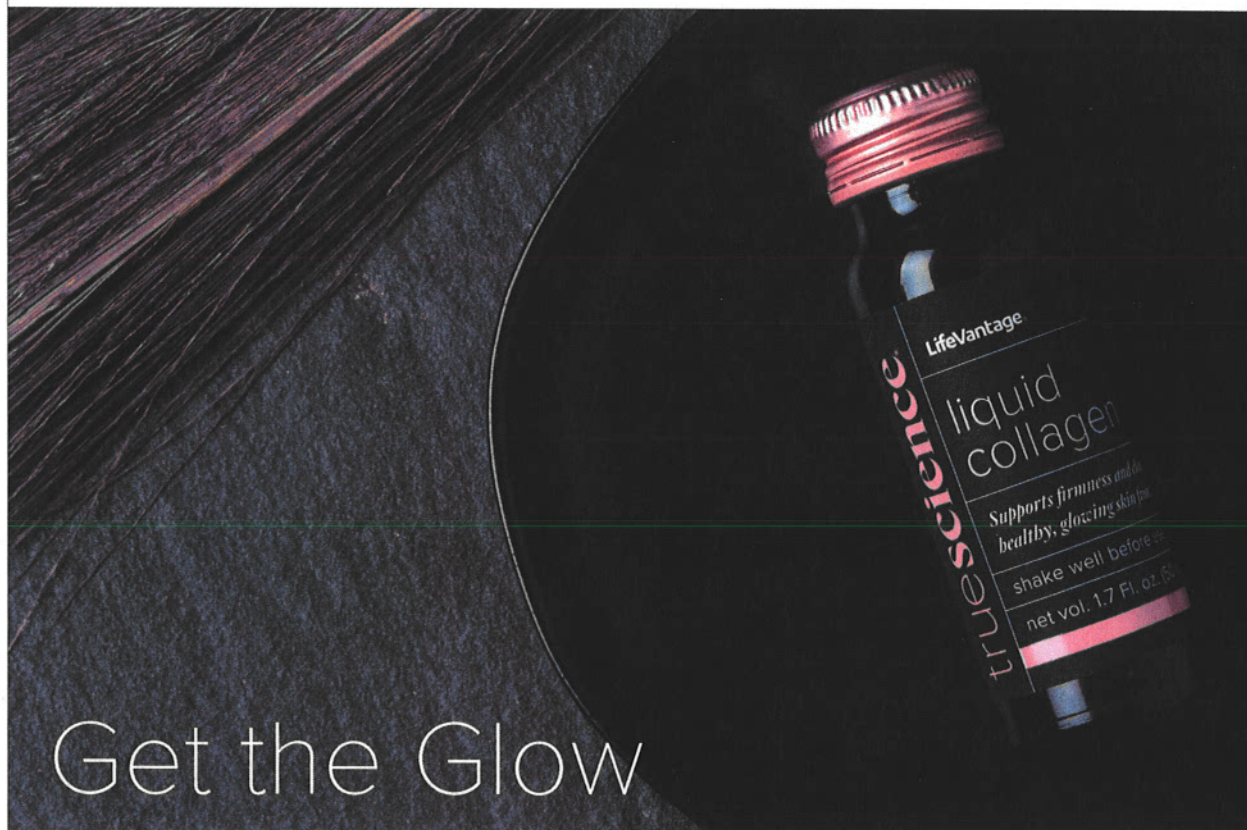
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liquid collagen

ACTIVATE, REPLENISH, MAINTAIN.

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Get the Glow

Get glowing, gorgeous skin with a daily boost of collagen and activating botanicals. The proprietary ingredients in this delicious Appleberry blend have been clinically shown to deliver visible support to skin health and hydration in 8 weeks or less. Your skin looks smoother, softer, and more even, while Liquid Collagen works from within to reduce collagen breakdown and improve skin elasticity. It also helps protect against the damaging effects of oxidative stress, caused by free radicals. With more youthful-looking skin, you'll glow with True Confidence. You get real results that you can see—and feel.*

Benefits



Reduce the appearance of fine lines and wrinkles*



Improves skin moisture, tone, and texture*



Helps protect against the damaging effects of oxidative stress*



Prevents collagen breakdown and improve skin elasticity*



Promotes a youthful appearance*



Supports healthy hair and nails*

*These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.

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product information sheet

liquid collagen

Directions

Shake well. Drink 1 bottle daily. Refrigerate after opening if not consumed at once. Chill if preferred, but refrigeration is not required.

WARNINGS: Not recommended for children or individuals under 18 years of age or women who are pregnant or nursing. Keep out of the reach of children.

Ingredients



Fish Collagen Peptides

Peptides from responsibly caught fish from 10 types of collagen plus amino acids to support collagen density, elasticity, and moisture for a youthful appearance.*



Ruby Quinoa Extract

(*Chenopodium formosanum*) Extract from this grain unlocks the cell's ability to absorb collagen as it activates natural collagen synthesis to reduce the appearance of fine lines and wrinkles.*



Proprietary Citrus + Berry Blend

Blueberry powder, young ponkan fruit and acerola berry supply vitamin C and antioxidants to promote collagen and elastin production and help your skin create more of its own natural moisture for a healthy, glowing complexion.*

Results



COLLAGEN DENSITY
INCREASED BY

42%



DEPTH OF CROW'S
FEET REDUCED BY

22%



SKIN ROUGHNESS
DECREASED BY

10%



BLOOD CATALASE (CAT)
LEVEL INCREASED BY

202%



SKIN ELASTICITY
INCREASED BY

8%

Results based on 8-week clinical trial on key ingredients in Liquid Collagen. Individual results may vary.

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PROTANDIM

Protandim is a one-a-day, all natural supplement that activates our body's internal defenses, our survival genes, to do what they were created to do – protect our cells from damage and disease.

Over time and around the age of 20, our genes, like the keys of a piano, get out of tune and no longer function at their peak performance: Aging and disease result from this disharmony.

Protandim activates NRF-2, the master tuner within our cells, and brings our genes back to the perfect harmony and powerful function of our youth. It also activates Nrf-1 to increase Mitochondrial production.

Independent research by Harvard, VCU, LSU and others, have validated this ability and measured Protandim's impact in tuning between 400 - 500 survival genes and what that means for our health and our battle against aging, cancer and heart disease. Additional studies are being conducted on osteoarthritis, diabetes, HIV/AIDS, periodontal disease, asthma, preserving muscle tissue, reduced injury recovery rates, and many others. Published peer-reviewed research demonstrates Protandim's ability to tune the following genes:

- Antioxidant - reducing oxidation/aging by over 40%
- Glutathione – increasing by 300%
- Anti-inflammatory
- Anti-fibrotic genes – reducing scarring of the heart
- P-53 - a tumor suppressor gene
- Osteopontin - levels reduced by over 50%. – High levels of osteopontin accompany critical diseases by creating the environment for diseases to thrive and grow.
- FABP-4 – associated with multiple pro-inflammatory responses - Protandim reduces by 85%
- FABP -5 - reduces by 66% which lowers likelihood of calcified arteries
- Akr1B10 - Promotes cell survival

Protandim unleashes the power within, which is both safe and our powerful and proven first line of defense.

Summary of Peer-Reviewed Science on Protandim

Complete studies available at www.Pubmed.gov – search Protandim

1. "Oxidative stress in health and disease: the therapeutic potential of Nrf2 activation", [Mol Aspects Med](#). 2011 Aug;32(4-6):234-46. Epub 2011 Oct 15.

- Protandim upregulates genes that encode anti-inflammatory and antioxidant proteins
- In colon carcinoma, analysis revealed 28 genes associated with the disease that were modulated by Protandim
- In Alzheimer disease, 66 genes were identified that are modulated by Protandim
- "The focus on Nrf2 will not only broaden our view, it will provide practical solutions

Nrf2 Science: Wellnessrevolutioncommunity.com

Products and additional Information: Biohackgenetics.lifevantage.com

2. "The Induction of Human Superoxide Dismutase and Catalase In Vivo: A fundamentally New Approach to Antioxidant Therapy, *Free Radical Biology and Medicine* (2006)

The results of a **University of Colorado** peer-reviewed study in men and women, young and old, showed:

- Protandim completely eliminates the age-related increase in cell aging factors, oxidative stress.
- Reduces oxidative stress by a minimum of 40 percent - to the progressive aging rate of a 20 year old.
- Significantly increases activity of SOD and CAT antioxidant enzymes by 54 percent - substantially increasing the body's antioxidant defenses.

3. "Synergistic Induction of Heme Oxygenase-1 by the Components of an Antioxidant Supplement Protandim", *Free Radical Biology and Medicine* (2008)

Results of a peer-reviewed study at the **University of Colorado, Denver** clearly demonstrate that:

- Protandim produces a 300 percent increase in glutathione, a key antioxidant and anti-aging factor.
- Protandim's synergistic formulation provides more antioxidant power than any food or supplement.

4. "Influence of Nrf2 activators on the **subcellular skeletal muscle protein** and DNA synthesis rates after 6 weeks of milk protein feeding in older adults", *GeroScience* 2017 Apr; 39(2) 176-186.

Protandim maintained the rates of myofibrillar protein synthesis Overall these data suggest that Protandim may enhance proteostatic mechanisms of skeletal muscle contractile proteins.

5. "Chronic Pulmonary Artery Pressure Elevation is Insufficient to Explain Right Heart Failure", *American Heart Association, Circulation* 2009

Researchers at **Virginia Commonwealth University** concluded that:

- Protandim prevented the formation of scar tissue in the heart
- Prevented capillary loss in the heart muscle; prevented death of heart cells.
- Osteopontin levels reduced by more than 50%.
- Heart output was preserved and cardiac fibrosis prevented.

6. "The Chemopreventive Effects of Protandim: Modulation of p53 Mitochondrial Translocation and Apoptosis during Skin Carcinogenesis", *PLoS ONE Journal* (2010)

Results of a peer reviewed study conducted by researchers at **Louisiana State University** reported:

- Protandim's ability to modulate relationship between superoxide dismutase and tumor suppressor p53 believed responsible for reduction of skin cancers.
- Protandim's ability to increase production of the body's Nrf2-regulated protective genes, sometimes referred to as "survival genes".

7. "The Dietary Supplement Protandim Decreases Plasma Osteopontin and Improves Markers of Oxidative Stress in Muscular Dystrophy Mdx Mice", *Journal of Dietary Supplements* (2010)

A peer reviewed study from **Harvard, Mass General Hospital and University of Colorado** documents:

- 48% decrease in plasma TBARS, a marker of lipid peroxidation and oxidative stress.
- 57% decrease in plasma Osteopontin, a fibrosis-promoting factor linked to heart failure,
- 35% increase in beneficial, protective plasma PON1 activity, an enzyme that protects against atherosclerosis by preventing the oxidation of low-density lipoprotein (LDL) cholesterol.

8. "Protandim Attenuates Intimal Hyperplasia in Human Saphenous Veins Cultured ex vivo via a Catalase-Dependent Pathway." *Free Radical Biology and Medicine* (2010)

The Ohio State University reported on:

- Protandim's prevents the proliferation of cells that can cause re-blockage of vessels following coronary artery bypass surgery, stenting, and carotid endarterectomy.
- Treatment with Protandim, reduced intimal proliferation to the level seen in a normal healthy saphenous vein.

Nrf2 Science: Wellnessrevolutioncommunity.com

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