INTEGRATIVE METABOLIC™

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GLYCATION MANAGER™
AGE CONTROL COMPLEX

Sugar and AGEing

Glycation is a biochemical process that involves reactions between simple sugars and proteins or lipids. The reactions result in the formation of substances known as advanced glycation end-products, or AGEs. AGEs amass in the cells and tissues of the body, and the deposition is irreversible. While glycation is a normal part of the aging process, dietary and lifestyle choices are of particular importance in influencing the speed at which glycation reactions occur. Reduction of glycation and the formation of AGEs can help support:

- Healthy blood glucose metabolism.*
- Nerve structure and function.*
- Healthy cellular aging.*

A Revolution in AGE Control

Glycation Manager is designed to slow the formation of advanced glycation end-products (AGEs) associated with normal metabolism and aging.* The unique formulation features clinically-studied levels of benfotiamine, a form of thiamine, chromium, and biotin, which have been shown to support healthy levels of hemoglobin A1c (HbA1c) and fructosamine,† two important indicators of glycation.* It also contains Theracurmin®, a novel preparation of turmeric with enhanced bioavailability. By helping promote optimal blood lipid, glucose, and protein metabolism, the ingredients in Glycation Manager support healthy metabolic function, circulatory health, and tissue health.*

wheat free · gluten free · dairy free · vegetarian

†Already within normal limits

Theracurmin® is a registered trademark of Theravalues.

Introduction

Almost all measures of physiological function decline as we age. The extent to which these declines occur depends on many factors, including numerous chemical processes occurring at the level of cells, tissues, and organs. A fundamental part of aging and decline in organ function may simply be the result of unwanted chemical processes causing the spontaneous appearance of side products of normal metabolism—the formation of mutated, less active, otherwise undesirable species of DNA, RNA, proteins, lipids, and small molecules. To the extent that humans can minimize the accumulation of these altered biomolecules, we can thrive and remain healthy. Several main biochemical processes occur as a normal part of human metabolism, but are modifiable to enhance health and longevity.

Glycation is one of these processes increasingly understood as a modifiable lifestyle factor that improves glucose metabolism and metabolic health, as well as slows the physical signs of aging. However, managing blood sugar levels is only part of the story. Even patients with normal blood sugar can benefit from slowing glycation in the body.

Advanced Glycation End-products (AGEs)

AGEs are formed exogenously in food and endogenously in the body as a result of glycation reactions. They form at a constant but slow rate in the body, starting in early embryonic development, and accumulate with time. Their formation is responsive to availability of glucose in the blood.

AGEs are a heterogeneous group of molecules formed from the non-enzymatic reaction of reducing sugars with free amino groups of proteins, lipids, and nucleic acids. The initial product of this reaction is called a Schiff base, which spontaneously rearranges itself into an Amadori product, as is the case of the well-known hemoglobin A1c (HbA1c).

Initial glycation reactions are reversible depending on the concentration of the reactants. A lowered glucose concentration can unhook the sugars from the amino groups to which they are attached; conversely, as glucose concentrations rise, the opposite effect may occur. A series of subsequent reactions lead to the formation of AGEs.

One key feature of certain reactive or precursor AGEs is their ability to form covalent crosslinks between proteins, which alters their structure and function, as in cellular matrix, basement membranes, and vessel-wall components. AGEs also interact with a variety of cell-surface AGE-binding receptors, leading either to their endocytosis and degradation, or to cellular activation, pro-oxidant, and cytokine-related events.

These are normal processes occurring in everyone all the time. However, certain dietary ingredients and supplements have been shown to support more optimal function and structure by maintaining glycation levels within a more optimal range for enhanced health and longevity.*

Glycation Manager™

Glycation Manager AGE control complex is a nutritional supplement designed to slow the formation of AGEs associated with normal metabolism and aging.* The ingredients in this unique formulation have been shown to exhibit several benifits for slowing the formation of AGEs.

Benfotiamine

Benfotiamine (S-benzoylthiamine O-monophosphate) is a fat-soluble, biologically active form of thiamine with unique effects on glycation that ordinary thiamine lacks.[1] Once absorbed, benfotiamine increases intracellular thiamine diphosphate, a cofactor needed to activate transketolase, which in turn reduces tissue levels of AGEs.* Benfotiamine also affects alternative pathways induced by glucose, while increasing pentose phosphate shunt.* Many more glycation-related mechanisms have been described.

GLYCATION MANAGER:

- Provides clinically-studied levels of chromium, biotin, and benfotiamine
- Supports healthy HbA1c and fructosamine levels*†
- Is appropriate for vegans

Each of the clinical trials below have confirmed the effects of benfotiamine—alone and in combination with lipoic acid, vitamin B6, and/or vitamin B12—on glycosylated hemoglobin (HbA1c) levels and/or nerve function.*

- In a study of 22 patients, treatment with benfotiamine and vitamin B6 for 45 days led to an HbA1C response rate of 63.6%. Of those who took the combination, 86.4% rated their overall condition as improved.[2]
- 40 patients received 400 mg benfotiamine per day and experienced significant support of normal sensation and nerve function ($P = 0.0287$) as compared to controls.*[3]
- Treatment with benfotiamine (300 mg BID) plus lipoic acid (600 mg BID) supported normal levels of AGE formation and reduced monocyte hexosamine-modified proteins by 40%.*[4]
- 45 patients took 100 mg benfotiamine plus 500 mcg B12 QID for 3 weeks; then reduced to 50 mg benfotiamine and 0.25 mg B12 TID for 9 weeks. The combination significantly supported normal nerve function with "dramatic" benefit to sensory function, according to the researchers, as compared to standard B complex.* Significant benefit to metabolic control was observed.*[5]
- Three groups of patients took various combinations of benfotiamine, B6, and B12 for 6 weeks. 320 mg of benfotiamine per day, in combination with B6 and B12, led to significant effects.*[6]

Chromium

Chromium is an important nutrient involved in the healthy metabolism of carbohydrates and lipids, playing a role in cellular transduction of insulin signals.*[7] Chromium may inhibit the glycosylation of protein in erythrocytes.*

A placebo-controlled single blind, prospective study was carried out to investigate the effect of chromium supplementation on various metabolic parameters.[8] Forty patients, after 1 month of stabilization, were randomly divided into two groups, a study group and placebo group. The study group received 9 g brewer's yeast (providing just 42 mcg Cr) daily and the other placebo group received yeast devoid of chromium for 3 months. Subjects were instructed not to change their normal eating and living habits. Outcomes were analyzed at beginning and completion of the study. Subjects consuming chromium-containing yeast had significant support of healthy glucose metabolism.*

Chromium and Biotin

Forty-three subjects seeking glycemic support were randomized to receive 600 mcg/day of chromium (as chromium picolinate) and 2 mg/day of biotin in addition to their current management regimen.[9] Measurements of glycemic support and blood lipids were taken at baseline and after 4 weeks. After 4 weeks, there was a significantly greater support of glucose metabolism during the 2-h oral glucose tolerance test for the treatment group (mean change -9.7%) compared with the placebo group (mean change +5.1%, $P < 0.03$).* There was also significantly greater support of fructosamine and lipid metabolism.* No significant adverse events were attributed to chromium picolinate and biotin supplementation.

In another study, 36 subjects seeking glycemic support were randomized to receive chromium picolinate and biotin or placebo in addition to their current regimen for 4 weeks. In addition to significant support of healthy blood lipid metabolism compared to the placebo group ($P < 0.05$), the treatment group also exhibited improvements in glucose and fructosamine metabolism.*[10]

GLYCATION MANAGER™

Theracurmin® (*Curcuma longa*)
Animal and in vitro studies have demonstrated that curcuminoids in general, and curcumin in particular, have the ability to interfere with protein cross-linking,[11] and thus attenuate the development of AGEs.*[12,13] Curcumin beneficially interacts directly with Receptors for Advanced Glycation End-products (RAGE),[14] protects Islet cells,[15] and holds the potential to protect other critical structures that are sensitive to glycation-related changes, including the arteries.*[16]

Alpha-Lipoic Acid
Alpha-lipoic acid is a broad-acting antioxidant due to its dual fat and water solubility.[17] It is among the best validated nutrients for supporting healthy nerve function.* Lipoic acid has pronounced anti-aging effects because it can reverse the age-associated decline in mitochondrial enzymes.*[18] Both intravenous and oral alpha-lipoic acid have been shown support healthy peripheral, autonomic, and cranial nerves *[19] Researchers have proposed benefits due to both the ability to reduce oxidative stress as well as support a healthy insulin response at cellular receptors.*[20]

Carnosine
L-Carnosine (beta-alanyl-L-histidine) is a small dipeptide composed of histidine and alanine. In humans, carnosine is concentrated in heart muscle, skeletal muscle, and the brain. It has been shown in animals and in vitro to exert carbonyl-quenching effects that attenuate the development of AGEs,[21] reduce age-related mitochondrial dysfunction,[22] and support healthy anti-oxidation and anti-glycation tissue responses.*[23-27] Its antioxidant and anti-glycation properties are attributed to carnosine's ability to scavenge radicals and sugar aldehydes. Carnosine protects against glycation-induced loss of enzyme activity and prevents glycation-induced changes in protein structure.*[28]

Thiamine and Vitamin B6
Thiamine (vitamin B1) and Pyridoxine/Pyridoxal-5'-phosphate (vitamin B6) serve many important roles in the body including supporting numerous metabolic enzyme systems, glucose metabolism, and supporting nerve health.*[29] Correction of thiamine deficiency restores disposal of triosephosphates by the reductive pentose phosphate pathway.* This prevents activation of protein kinase C, activation of the hexosamine pathway, increased glycation, and oxidative stress. Consequently, thiamine supplementation can support healthy kidney, nerve, and retinal structure and function.* Pyridoxine may help support healthy oxygen transport by erythrocytes by reducing glycosylation.*[30]

Grape Seed Phytosome™
Grape Seed is a potent inhibitor of AGEs due to its content of flavonoids such as catechin, epicatechin, and procyanidins.*[31] These flavonoids have been shown to inhibit the glycosylation of hemoglobin more significantly than aminoguanidine, as well as reduce the glycosylation of proteins and aberrant cross-linking of proteins.*[32]

Supplement Facts

Serving Size 2 capsules	Servings per container 30	
Amount per 2 capsules		%DV**
Vitamin C	18 mg	30%
Thiamin (as thiamin HCl) (Vitamin B1)	25 mg	1,667%
Vitamin B6 (as pyridoxine HCl, pyridoxal-5'-phosphate)	50 mg	2,500%
Biotin	2 mg	667%
Calcium	63 mg	6%
Chromium (as chromium picolinate)	600 mcg	500%
Proprietary AGE Blend: Alpha-Lipoic Acid; Theracurmin® (water-dispersible turmeric (Curcuma longa) rhizome); L-Carnosine; Grape (Vitis vinifera) Seed Phytosome™ One part Grape Seed Extract, standardized to contain 95% polyphenols including procyanidolic oligomers (PCOs), bound to two parts phosphatidylcholine (soy) using a proprietary process for improved absorption	700 mg	**
Benfotiamine	300 mg	**

**Daily Value not established.

Other ingredients: vegetable capsule (modified cellulose), dextrin, maltose, ascorbyl palmitate, silicon dioxide, gum ghatti, and citric acid.

Recommendations: Take 2 capsules daily. May be taken as 1 capsule twice daily or as recommended by your healthcare practitioner.

If pregnant, nursing, or taking prescription drugs, consult your healthcare practitioner prior to use.

Contains no sugar, salt, yeast, wheat, gluten, dairy products, artificial coloring, artificial flavoring, preservatives, or ingredients of animal origin. This product contains natural ingredients; color variations are normal.

Theracurmin® is a registered trademark of Theravalues.

Integrative Therapeutics	Natural Partners	Emerson Ecologics
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