Diet, Skin Aging, and Glycation

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For years, dermatologic researchers have been postulating the effects of diet on the skin. Many familiar sayings regarding diet and health abound, such as "you are what you eat," "eat your way young," and "junk food in and bad health out." As a whole, physicians recognize that healthy skin, hair, and nails are an indication of general good health, and the first signs of illness can be visualized in the eyes and the facial skin. When an ill child is examined, the first comment may be that the child looks sick. What does it mean to look sick? In part, it means the patient's skin does not look good, which begs the question, how does a patient's health relate to attractive-looking skin? Furthermore, can a certain diet help patients achieve more beautiful skin and a younger appearance?

Diet supplements claiming to improve skin health abound. Everything from skin vitamins to vitamin drinks to exotic foods are sold in grocery stores, health food stores, and on the Internet, but there is little evidence to validate their value. One diet-related process that affects the skin and has a growing scientific knowledge base is glycation. Glycation commonly is observed in diabetics who experience premature skin aging because of high circulating serum glucose levels. Glycation and the production of advanced glycation end products (AGEs) are 2 diet-related processes that can affect skin health and aging. This article examines both exogenous and endogenous glycation and their effects on the body; it also assesses the premature aging effects of AGEs.

What is glycation?

Glycation occurs when a sugar molecule, such as glucose or fructose, covalently bonds with a protein or lipid. It also is known as nonenzymatic glycosylation because the controlling action of an enzyme is not required. Glycation can occur both outside (exogenous) and inside (endogenous) the body, both inducing detrimental effects.

What is exogenous glycation and how does it affect the body?

Exogenous glycation occurs when foods containing glycated proteins are consumed. At temperatures over 248°F, sugars readily bind to proteins to form advanced AGEs. When it occurs in foods, this process is known as the Maillard reaction. Glycated proteins that commonly are consumed in the human diet manifest as grill marks on grilled meat, brown crust on bread, the brown color of malted barley, and the browning of toasted bread. The Maillard reaction results when the reactive carbonyl group of the sugar reacts with the nucleophilic amino group of the amino acid to create molecules that impart flavor and odor to foods. Foods with high levels of AGEs include donuts, barbecued meats, and dark-colored soft drinks.[1]

When glycated proteins are consumed, they are absorbed in the gut with approximately 30% efficiency and begin to circulate through the bloodstream. Why is this detrimental? It is important because orally consumed AGEs are proinflammatory and accumulate on nucleic acids, proteins, and lipids, promoting such widely diverse diseases as diabetic sequelae, pulmonary fibrosis, and neurodegeneration.

Exogenous glycation occurs when sunless tanning creams are applied to the skin. These products contain dihydroxyacetone, a sugar that binds to protein-rich corneocytes to create a brown substance known as a melanoidin. These melanoidins stain the skin brown, simulating a tan. Are these exogenous glycation products harmful to the body? Probably not, but there is some preliminary discussion regarding the effects of absorption of these AGEs into the body.

What is endogenous glycation and how does it affect the body?

Endogenous glycation is more common and pervasive than exogenous glycation. It mainly occurs in the bloodstream when glucose, fructose, and galactose bind to structures such as red blood cells. Glycated hemoglobin

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(hemoglobin A_{1c}) is used to monitor the history of serum glucose in patients with diabetes mellitus. Because red blood cells are short lived with a lifespan of approximately 120 days, the effect of serum glucose over a 3-month period can be monitored and used to assess the precision of diabetic control. Longer-lived structures such as nerves, brain tissue, retina cells, and pancreatic beta cells also are easily glycated, but the amount of glycated protein is difficult to assess. High serum glucose levels lead to increased glycation, resulting in tissue damage. Tighter glycemic control can reduce glycated collagen by 25% in 4 months.

Advanced glycation proteins resulting from high serum glucose levels interfere with molecular and cellular functioning and promote the release of damaging by-products such as hydrogen peroxide. Glycation stiffens the collagen in blood vessel walls, leading to high blood pressure that is commonly seen with advanced age; it also weakens blood vessel collagen, leading to aneurysms that cause cerebral hemorrhage.[2] The effects of glycation are most pronounced in the eyes where the proteins deposit in the lenses, corneas, and retinal cells.

Why are AGEs damaging to the body?

Advanced glycation end products are highly stable and are almost impossible to eradicate from the body. Elastin and collagen cross-linked in glycation cannot be repaired in the same manner as normal elastin and collagen.[3] It is said that glycation collagen accumulates at a rate of 3.7% annually.[4] This rate is accelerated with UV exposure.[5]

Although there are foods that contain high levels of AGEs, there also are foods that inhibit the production of AGEs, such as cinnamon, cloves, oregano, and allspice.[6] It also has been suggested that systems in the human body have evolved to remove AGEs and mitigate their damaging effects. These AGE receptors include AGE receptor 1, galectin-3, CD36, and receptor for AGE.[7] Corneal cells express both receptor for AGE and galectin-3 because the accumulation of AGEs results in thickened corneal stroma and corneal edema that are especially pronounced in diabetics. Receptor for AGE also is found on lung, liver, kidney, endothelial, and smooth muscle cells.

Advanced glycation end products are found in high amounts in diabetics, especially in cells that are unable to reduce glucose intake during times of hyperglycemia (eg, endothelial cells). The increased glucose results in increased levels of nicotinamide adenine dinucleotide (NAD), increasing the proton gradient; complex III prevents further increase by stopping the mitochondrial electron transport chain, which results in the production of reaction oxygen species by the mitochondria damaging the DNA.[8]

How do AGEs affect aging?

It is difficult for the human body to excrete AGEs; however, some are removed in the urine as breakdown products of AGEs. There are several ways to manage the damaging effects of glycation: eat a low glycemic diet to reduce serum glucose levels; break AGE sugar/protein cross-links; and inhibit the formation of AGEs. There also are compounds that may prevent the negative effects of AGEs, such as resveratrol, a substance derived from the fermented red grape skins abundant in red wine.[9] Resveratrol is a potent antioxidant and also has been shown to have additional antiaging effects by modulating sirtuins. Other substances that may inhibit AGE formation include aspirin, carnosine, metformin, and α-lipoic acid. Some manufacturers of antiaging cosmeceuticals are incorporating carnosine and α-lipoic acid into their formulations and are making appearance claims related to skin glycation. It is unclear if topical application has an effect on existing skin glycation or preventative effects against future skin glycation.

Summary

Advanced glycation end products accumulate in the aging body and interfere with the function of many protein structures, including the skin. Diet plays an important role in skin glycation. High circulating serum glucose levels increase protein glycation, and the consumption of AGEs contributes to the total body load of these substances. Foods that are fried or have high sugar content are modern inventions. Are these foods prematurely aging the population? The answer probably is yet to come, but there are some observations that may support this contention. Notably, Asian countries where people eat a lower glycemic diet and boil and poach foods as a preferred preparation method tend to have older inhabitants. Is it possible to eat yourself young? I am not sure.

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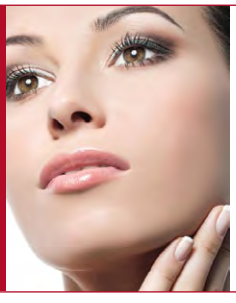

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