Nutrition and aging skin: sugar and glycation

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Abstract The effect of sugars on aging skin is governed by the simple act of covalently cross-linking two collagen fibers, which renders both of them incapable of easy repair. Glucose and fructose link the amino acids present in the collagen and elastin that support the dermis, producing advanced glycation end products or “AGEs.” This process is accelerated in all body tissues when sugar is elevated and is further stimulated by ultraviolet light in the skin. The effect on vascular, renal, retinal, coronary, and cutaneous tissues is being defined, as are methods of reducing the glycation load through careful diet and use of supplements.

Introduction

The processes that support life require nutrients. Appropriate amounts of carbohydrate, fat, and protein, plus vitamins and minerals, are essential. Despite present guidelines, there remain doubts about the amounts of each that ought to be input to achieve the optimal effects upon the organism. The important side of the equation deals with output, or clinically, the outcome, whether dealing with clinical dermatology, surgery, or cosmetics.

Outcome analysis is a swiftly evolving field, and much of what is known about outcome from diet and dietary manipulation is inadequate, inaccurate, outdated, or rapidly being rethought. Consider the swiftly evolving recommendations for vitamin D3 dosing that have ramped up from 400 IU to more than 5000 IU in less than 2 years.1

Fortunately, publications continue to appear that address subjects that arise daily in office practice. The subject was recently reviewed by Logan, Rubin, and Levy,2 to whom I owe a debt of gratitude for putting their spotlight on the effect of sugars on aging skin, a presently evolving area of concern.

Glycation: the concept

The most important concept in understanding the relationship of sugars to aging is that the simple act of cross-linking two collagen fibers will render both of them incapable of being repaired through the usual process of remodeling. The more cross-linking that occurs, from whatever cause, the greater the limit on the potential for repair and maintenance. Because the appearance of youth depends on maintenance of youthful, flexible, and repairable collagen fibers, cross-linking should be avoided whenever possible. It is not just external appearance that suffers from cross-linking, however, which is why all of us should be aware of the overall affect of sugar on our lifespans as well as on our aging skins.

The problem derives from a process called glycation. This is a covalent bonding process that links, using glucose and fructose, the amino acids present in the collagen and elastin that support the dermis. Whereas collagen and elastin are normally linked in a pattern and a manner that allows them to be repaired, glycation adds cross-links that interfere with the repair mechanism.

Elevated amounts of sugar in the North American diet were noted as early as 1942. Urbach and Lentz in 1945 showed a correlation between a diet high in sugar and elevated levels of sugar in the blood and skin, and also
illustrated that a low-sugar diet lowered the sugar level within the skin. More importantly, they discovered that a large percentage of the sugar was protein-bound. It is this protein-bound sugar that is involved in glycation, the result being a complex referred to as an advanced glycation end product or an AGE.

Glycation: the science

The process of glycation likely starts quite early in life and is well established by our late 20s. Glycated collagen accumulates at a rate of 3.7% yearly, a percentage that will vary according to diet. Ultraviolet exposure also increases cross-linking in the skin, and cross-links of the proteins of antioxidant enzymes further decrease our natural defenses against free radicals.

The model for the damage done to dermis is, not unexpectedly, diabetes. The development of glycated collagen is accelerated in diabetes, but tight glycemic control can drop glycated collagen formation by 25% in 4 months.

Because it is almost impossible to repair glycated collagen cross-links, prevention is the prime defense, and the earlier preventive activity is begun, the better. The problem is that diet is the major source not only of sugars such as glucose and fructose but also of pre-formed AGEs, such as those produced by heat. The golden brown on a crust of bread and the skin on the Thanksgiving turkey contain AGEs, which tend to be formed at high temperatures in the absence of water. Grilling, frying, deep-fat frying, or roasting produce high levels of AGEs, whereas cooking processes involving water produce orders of less magnitude (Table 1). Preformed dietary AGEs are now known to be absorbed and capable of entering the circulation where they may react with cellular and extracellular components, thereby increasing the AGE burden of aging. Food-derived AGEs can induce protein cross-linking, inflammation, and intracellular oxidative stress, just as surely as the damaging reactions brought on by excess dietary sugar.

For a clinical illustration, one has only to look at the smooth skin of an elderly Japanese person and consider that this represents 70 to 80 years of eating poached, boiled, stewed, and steamed food, prepared using these predominantly water-based Asian cooking practices.

Glycation: the impact

Consider that the long-term results obtained with cosmetic procedures are likely to be much better if healing is not compromised by a diet high in preformed AGEs and dietary sugar. This is something to suggest when advising patients of their responsibility for postoperative care, a complementary adjunct to the admonition to use truly effective broadspectrum sunscreens.

In addition to their effect on collagen, enzymes, and other proteins, AGEs also interfere with the normal human intestinal microflora. Glycated food components in the gut can translate, it is believed, into lower levels of the “good bacteria” in the gut. This, in turn, leads to compromised absorption of nutrients and phytochemicals that have AGE-inhibiting properties. Further, lowering AGEs in the diet can help by reducing systemic oxidative stress and inflammation.

The other side of the question looks at diet as prevention of AGE-induced problems (Table 1). So far, nothing dietary has been found to break up, extract, unhitch, or eliminate the AGE-induced adducts. Some compounds, however, can actually inhibit the production of AGE; in particular, cinnamon, cloves, oregano, and allspice help protect against fructose-induced AGE formation. Ginger, garlic, α-lipoic acid, carnitine, taurine, carmosine, some flavonoids, and benfotiamine have also made the list, each working through one or more of several different mechanisms. Expect to see these compounds marketed as supplements and topical cosmeceuticals with a view towards enhancing and maintaining the benefits of cosmetic procedures or preventing (or just slowing) the effects of AGEs on our aging skin, and that of our patients.

Glycation: at depth

One last consideration is that glycation does not affect just the superficial areas of the body (i.e., the skin). In a series of reports during the past several years, a team from the Netherlands has outlined the threat posed by increased levels of glycation to patients with diabetic polyneuropathy, renal failure, atherosclerotic heart disease, macular degeneration of the retina, and lupus erythematosus.

They have shown that relative risks of future adverse events can be estimated by measuring the AGEs in the skin. This can be quantified by measuring the fluorescence induced from the AGEs in the skin in response to a single pulse of light of a known wavelength. This completely noninvasive technique works on Fitzpatrick I to IV skin types and shows promise of being integrated into clinical medicine.

Where from here?

Epidemic obesity, diabetes, acne, hidradenitis suppurativa, and the numerous cutaneous abnormalities associated

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Low vs high glycation end-products (AGE) cooking</th>
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<tbody>
<tr>
<td>Food</td>
<td>Low AGE cooking</td>
</tr>
<tr>
<td>Rice</td>
<td>Boiled 1</td>
</tr>
<tr>
<td>Potato</td>
<td>Boiled 1</td>
</tr>
<tr>
<td>Egg</td>
<td>Boiled 1</td>
</tr>
<tr>
<td>Fish</td>
<td>Salmon 1</td>
</tr>
<tr>
<td></td>
<td>Baked goods Toasted bagel</td>
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with cardiometabolic syndrome X—all are sugar and insulin-resistance related. They are also rooted, quite often, in low-grade systemic inflammation and oxidative stress. By reducing inflammation and the burden of oxidative stress, the potential collateral health benefits of a diet low in simple sugars and dietary AGEs are many; therefore, dietary advice needs to be part of our everyday discussion with our patients, whether medical, surgical, or cosmetic.

References