

## Conclusions

Protein glycation and the resultant formation of advanced glycation end-products (AGEs) increase with age leading to the deterioration of important structural proteins such as collagen as well as a sallow appearance of skin. Glycation inhibitors are compounds that interfere with the formation of AGEs, helping to prevent deleterious cross-linking and preserve the youthful integrity and functionality of essential proteins.

The results from this study show a new mechanism by which lactobionic acid, maltobionic acid and gluconolactone may help preserve skin elasticity and firmness. These ingredients significantly reduced non-enzymatic glycation comparably to the potent inhibitor, aminoguanidine. The antiaging compounds, lactobionic acid, maltobionic acid and gluconolactone, are cosmetic ingredients that can be used to help preserve skin's natural collagen and improve sallowness and tone via anti-glycation effects.

## References

1. Dyer D, Dunn J, Thorpe S, Bailie K, Lyons T, McCance D, Baynes J. Accumulation of maillard reaction products in skin collagen in diabetes and aging. *J Clin Invest*. 1993;91:2463-9.
2. Bucala R, Cerami A. Advanced glycosylation: chemistry, biology and implications for diabetes and aging. *Adv Pharmacol*. 1992;23:1-4.
3. Nomoto K, Masayuki Y, Seizaburo A, Mari O, Yoshikazu Y. Skin accumulation of advanced glycation end products and lifestyle behaviors in Japanese. *J Anti-Aging Med*. 2012;09:165-73.
4. Schmid D, Muggli R, Züllli F, Mibelle. Collagen glycation and skin aging. *Cosmetics and Toiletries Manufacture Worldwide*. 2002;1-6.
5. Ohshima H, Oyobikawa M, Tada A, Maeda T, Takiwaki H, Itoh M, Kanto H. Melanin and facial skin fluorescence as markers of yellowish discoloration with aging. *Skin Res and Tech*. 2009;15:496-502.
6. Fu M, Wells-Knecht K, Blackledge J, Lyons T, Thorpe S, Baynes J. Glycation, glycoxidation, and cross-linking of collagen by glucose: kinetics, mechanisms, and inhibition of late stages of the maillard reaction. *Diabetesjournals.org*. 1994;43:676-83.
7. Edelstein D, Brownlee M. Mechanistic studies of advanced glycosylation end product inhibition by aminoguanidine. *Diabetesjournals.org*. 1992;41:26-9.
8. Green BA, Edison BL, Sigler ML. Antiaging effects of topical lactobionic acid: results of a controlled usage study. *Cosmet Dermatol*. 2008;21(2):76-82.
9. Green BA, Van Scott EJ, Yu RJ. Clinical uses of hydroxyacids. In: Draelos ZD ed. *Cosmetic Dermatology: Products and Procedures*, 1st ed. West Sussex, UK: Wiley-Blackwell 2010;327-334.
10. Edison BL, Green BA, Wildnauer RH, Sigler ML. A polyhydroxy acid skin care regimen provides antiaging effects comparable to an alpha-hydroxyacid regimen. *Cutis*. 2004;73(suppl 2):14-17.
11. Suzuki YJ, Tsuchiya M, Packer L. Lipoate prevents glucose-induced protein modifications. *Free Radic Res Commun*. 1992;13(3):211-7.

# Antiaging Bionic and Polyhydroxy Acids Reduce Non-Enzymatic Protein Glycation and Skin Sallowness

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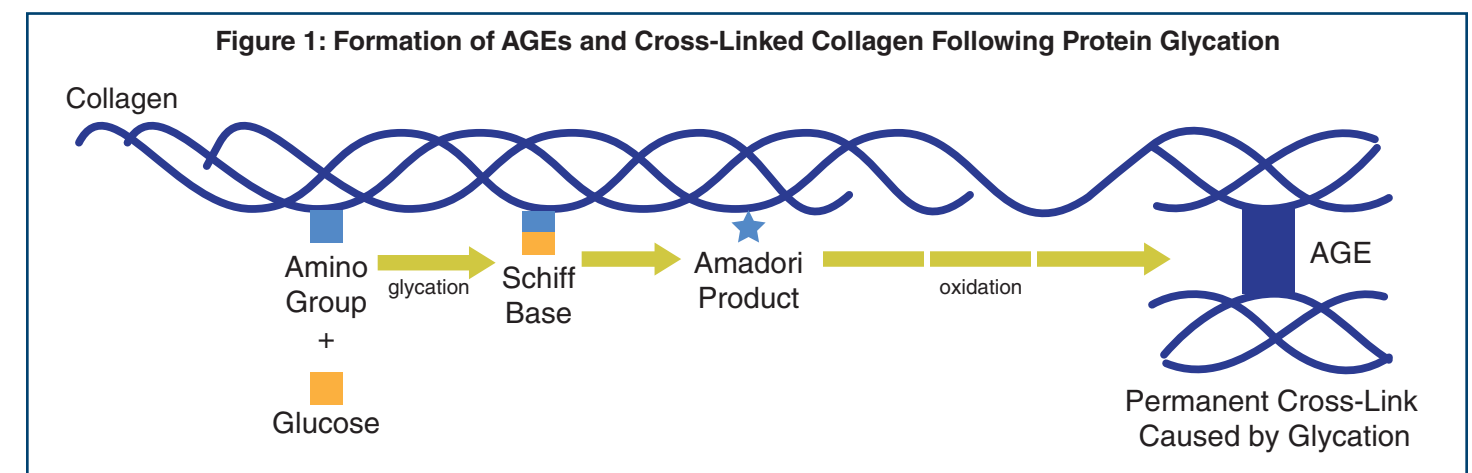
## Introduction

Protein glycation is one of many natural aging processes that occurs in skin. Glycation is caused by the non-enzymatic reaction between a reducing sugar (glucose) and primary amino group found on proteins such as collagen. This process yields glycation intermediates that are further oxidized to form irreversible and highly detrimental advanced glycation end-products (AGEs). An increase in AGEs leads to a gradual deterioration of collagen due to undesired cross-linking, causing dermal inflexibility and wrinkling. This damaged collagen is less susceptible to normal catabolism and thus accumulates over time (Figure 1).<sup>1-4</sup>

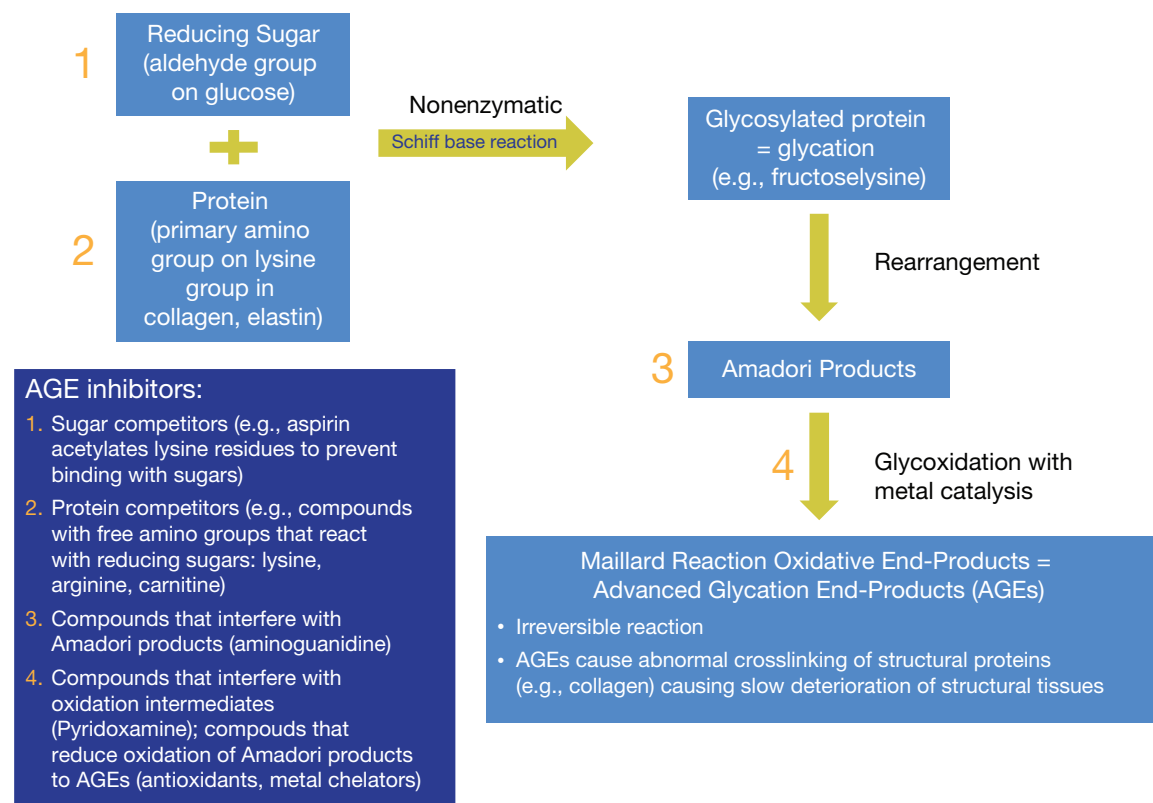
Glycation and AGEs are consequences of the Maillard reaction which, in food, causes the non-enzymatic browning that is important for flavor. In skin, AGEs form in the upper dermis imparting a yellow color and sallow appearance.<sup>5</sup>

Anti-glycation is considered an important treatment approach in the maintenance of healthy, youthful skin. Compounds that inhibit non-enzymatic glycation may interfere in various steps in the Maillard reaction pathway. (Figure 2) In order to prevent the formation of AGEs, cosmetic compounds may interfere in later steps by functioning as antioxidants and/or chelators of oxidation promoting metals (Figure 2, Step 4).<sup>1,4,6,7</sup>

The bionic acids, including lactobionic and maltobionic acids, and the polyhydroxy acid, gluconolactone, are oxidized sugar acids with antioxidant and metal chelation properties which may provide anti-glycation effects. Previous studies have demonstrated the ability of these compounds to improve the appearance of sallowness up to 36% when applied topically twice daily over 12 weeks,  $p < 0.05$ .<sup>8-10</sup> This antiaging benefit may in part be due to an anti-glycation effect.



**Figure 2: Reduction of Advanced Glycation End-Products (AGEs) by Targeting Specific Steps in the Maillard Reaction**



## Objective

An *in vitro* study was conducted to determine whether lactobionic acid, maltobionic acid and gluconolactone influence non-enzymatic protein glycation (NEG).

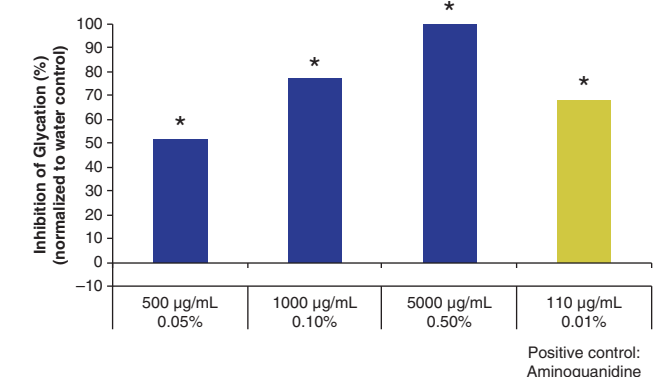
## Study Methodology

Study Parameter	Description
Test materials (dissolved in PBS)	<ul style="list-style-type: none"> <li>Gluconolactone: 0.05%, 0.10%, 0.50%</li> <li>Lactobionic Acid: 0.05%, 0.10%, 0.50%</li> <li>Maltobionic Acid: 0.05%, 0.10%, 0.50%</li> </ul>
Controls	<ul style="list-style-type: none"> <li>Positive: Aminoguanidine 0.01%, a well-known NEG inhibitor</li> <li>Negative: Water</li> </ul>
Protein substrate	<ul style="list-style-type: none"> <li>Serum albumin 1.0%</li> </ul>
Test material preparation	<ul style="list-style-type: none"> <li>24-day incubation period of test material plus albumin at 37°C in the presence and absence of 0.5M glucose. Sodium azide 0.025% was used as an antimicrobial agent.</li> </ul>
Non-enzymatic glycation measurement <sup>11</sup>	<ul style="list-style-type: none"> <li>Test materials were added to 96 black well plates containing albumin in the presence or absence of glucose. Initial non-tryptophan fluorescence was recorded at excitation/emission wavelengths 409/460nm with a microplate fluorometer. After 24 days of incubation, fluorescence measurements were collected. The experiment was performed in triplicate.</li> </ul>
Analysis	<ul style="list-style-type: none"> <li>Difference in signal intensity between baseline and 24 days for each sample condition was calculated and standardized to the water control. Significance was determined at <math>p &lt; 0.05</math> (with at least 20% variation from the water control).</li> </ul>

## Results

Gluconolactone showed a dose-dependent inhibitory effect on non-enzymatic glycation that was statistically significant ( $p < 0.05$ ) compared to water control and similar in efficacy to the positive control aminoguanidine (0.01%). Complete inhibition (100%) was achieved at the highest dose (0.50%). (Figure 3)

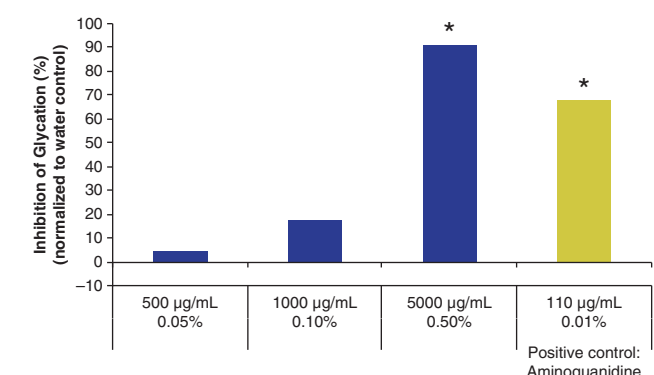
**Figure 3: Percent Inhibition of Non-Enzymatic Glycation by Gluconolactone**



\*Significant inhibition of non-enzymatic glycation expressed as a % of water control,  $p < 0.05$ .

Lactobionic acid showed a statistically significant, 91% inhibition of non-enzymatic glycation at the highest dose (0.05%),  $p < 0.05$ . The result was similar to the positive control aminoguanidine (0.01%). (Figure 4)

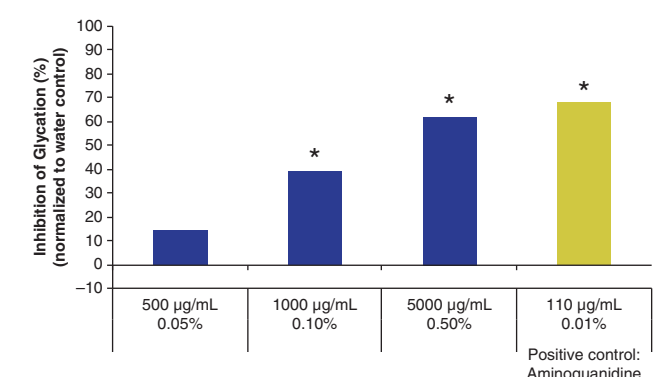
**Figure 4: Percent Inhibition of Non-Enzymatic Glycation by Lactobionic Acid**



\*Significant inhibition of non-enzymatic glycation expressed as a % of water control,  $p < 0.05$ .

Maltobionic acid showed a significant, dose-dependent inhibitory effect on non-enzymatic glycation at 0.10% and 0.50%,  $p < 0.05$ . The result was similar to the positive control aminoguanidine (0.01%). (Figure 5)

**Figure 5: Percent Inhibition of Non-Enzymatic Glycation by Maltobionic Acid**



\*Significant inhibition of non-enzymatic glycation expressed as a % of water control,  $p < 0.05$ .