Advances in Glycation Research Reverse AGE

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Introduction

Our stressful life style - less sleep, more stress, 'fast food' - is a major cause of skin ageing, as it raises the level of internal toxins, one of these being glycotoxins.

Glycation is an unspecific non-enzymatic reaction of sugars and their radical derivatives with proteins, leading to reticulation, AGEs (Advanced Glycation Endproducts) and other glycotoxins. Glycation of mitochondrial proteins reduces their ability to produce energy and long-lasting structural proteins such as collagen and elastin lose their ability to respond to mechanical stresses.

The objective of this article is to help understand further details of the glycation process in the skin as well as the mechanisms of action in inhibiting or even reversing the reactions.

Glycation and Glycotoxins - Description

AGE formation involves several successive stages (see Figure 1). In the early stages, the aldehyde group of a reducing sugar such as glucose forms an unstable bond with the protein amine, known as a Schiff's base, which rapidly rearranges to produce an Amadori compound. These two formations are reversible. The next, later stage leads to the formation of irreversible advanced glycation end-products which accumulate over time in tissues.

At the Amadori compound stage, the sugar can deprotonate and create several highly reactive compounds which themselves become glycotoxins: glyoxal (GO) or its methylglyoxal derivative (MGO), 3-deoxyglucosone (3-DG) and fructosamines [1].

Glyoxals and 3-DG can in turn bind to free protein amines and produce different AGEs such as carboxymethyl-lysine (CML), carboxymethyl-arginine (CMA), carboxymethylcysteine (CMC) and their ethyl equivalent or pyrraline[2].

These reactive chemical groups can also be formed by glucose auto-oxidation. Other sugars such as ribose or xylose, although present in smaller amounts, are far more reactive than glucose and fructose and also produce AGEs which have only been shown to be toxic *in vitro* in the absence of reliable *in vivo* demonstration methods.

Experimentally, these products are formed very quickly [3]. This leads to the formation of many altered proteins, whose functional, enzymatic and structural properties are also

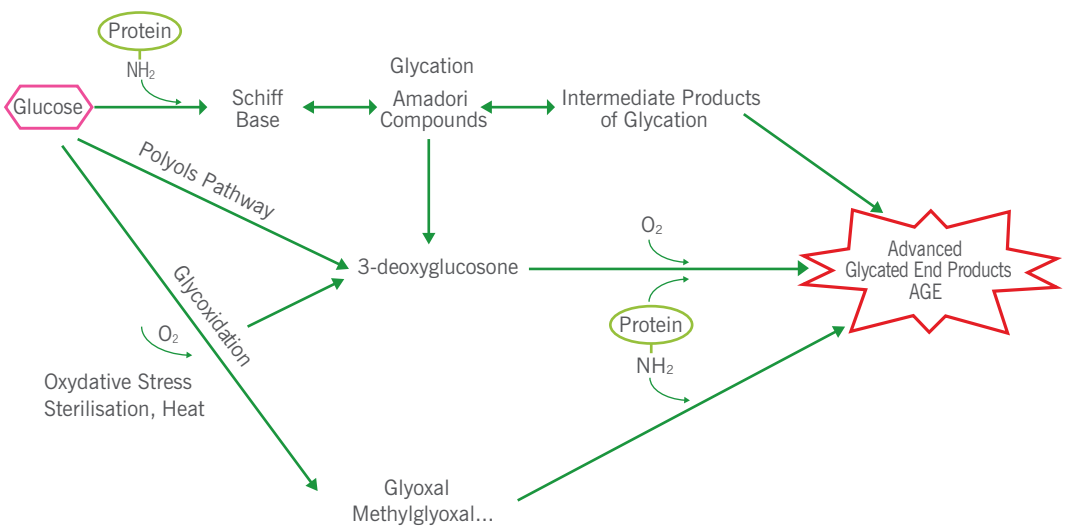

Figure 1. Mechanism of Formation of AGEs