THE ROLE OF GLYCATION PROCESSES IN AGING

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Background. Glycation is a non-enzymatic reaction in which reducing sugars react with free amino groups in proteins, lipids, or nucleic acids, leading to the formation of advanced glycation end products (AGEs). AGE accumulation leads to structural and functional alterations in proteins, contributing to aging.
Objective of the study. To elucidate the biochemical mechanisms of glycation, its impact on aging, and potential therapeutic strategies to mitigate its effects.
Materials and methods. A literature review covering the years 2019–2024 was conducted, analyzing 15 peer-reviewed articles from PubMed, ScienceDirect, Wiley Online Library, and MDPI.
Results. The glycation process begins when a reducing sugar, such as glucose or fructose, reacts with the free amino group of lysine or arginine residues in proteins. Over time, these intermediate compounds undergo glycoxidation and dehydration, forming irreversible AGEs such as Nε-(carboxymethyl)lysine, pentosidine, and pyrraline. AGEs interact with the receptor for advanced glycation end products (RAGE), a transmembrane receptor highly expressed in endothelial cells, macrophages, and neurons. AGE-RAGE binding triggers activation of nuclear factor kappa b (NF-κB), a transcription factor that upregulates the expression of pro-inflammatory cytokines such as TNF-α, IL-6, and IL-1β, promoting chronic inflammation and cellular dysfunction. Mitochondrial dysfunction is exacerbated by AGEs through oxidative phosphorylation impairment, increasing reactive oxygen species (ROS) production. This oxidative stress further amplifies AGE formation in a vicious cycle, accelerating cellular senescence via activation of the p53/p21 and p16INK4a pathways. Additionally, glycation disrupts the ubiquitin-proteasome system and autophagy, preventing the clearance of damaged proteins and contributing to intracellular toxicity. Therapeutic strategies to counteract glycation include AGE inhibitors (aminoguanidine, pyridoxamine), RAGE antagonists, and antioxidants (vitamin C, resveratrol, polyphenols), which scavenge ROS and reduce AGE formation. Dietary interventions, such as caloric restriction and a low-glycemic diet, have also been shown to limit AGE accumulation and mitigate aging-related damage.
Conclusions. Glycation is a key driver of aging through its impact on protein function, oxidative stress, and chronic inflammation. Understanding the biochemical processes underlying glycation opens avenues for therapeutic interventions aimed at reducing AGE accumulation and mitigating age-related diseases.
Keywords. Glycation, advanced glycation end products, oxidative stress, receptor for AGE, inflammation, aging, mitochondrial dysfunction, protein crosslinking, anti-aging strategies.