

# Plant Derived Phenolic Compounds as the Natural Antiglycating Agents

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## ABSTRACT

Glycation of biomolecules like proteins, nucleic acids and lipids involves non enzymatic addition of sugar and carbonyl compounds that results in formation of advanced glycation end products (AGEs). Accumulation of AGEs promote the progression of several diseases like diabetes, ageing and neurodegenerative disease. In order to prevent ageing and diabetic complications, there is a need to protect biomolecules from sugar induced glycation. Polyphenolic compounds possess significant in vitro anti-glycation activity. Polyphenols may inhibit the formation of AGEs either by scavenging ROS production during the glycation reaction or provides physical protection against glycating agents. The physical protection mechanism by polyphenols involves hydrogen bonding and non covalent interactions which acts as a sort of shield and prevents the accessibility of glycating agents on their target site. In this review, antiglycating activity of different polyphenolic compounds will be discussed.

**Keywords :** Glycation, Polyphenols, Scavenging, AGEs,

## I. INTRODUCTION

Protein glycation involves the adduct formation between amino groups ( $\epsilon$ -amino group of lysine and the guanidine group of arginine) of protein and carbonyl groups of reducing sugars and leads to complex heterogeneous advanced glycation end products formation (AGEs) [1,2]. These AGEs are responsible for promotion of ageing, diabetic complications and neurodegenerative disorders etc., and thus increases human sufferings and misery. The process of glycation, in diabetes, is mainly driven by the elevated blood glucose concentration through non-enzymatic condensation of a sugar molecule on a protein, lipid or DNA molecule. During diabetes prolonged hyperglycemia elevates glycated protein content which leads to advanced glycation endproduct (AGEs) formation and promotes development of diabetic complications and atherosclerosis [3-5]. Measurement of glycated proteins like glycated hemoglobin directly correlates with tissue damage. Carbonyl compounds which are excessively produced during chronic hyperglycemia condition are highly reactive species and are majorly responsible for protein glycation. Upon

glycation, protein loses its secondary structural properties which make them aggregation prone species.

Protein damage by glycation leads lot of pathophysiological conditions like aging, diabetic complications, neurodegenerative diseases [1, 5-10].

Thus there is a need to find an effective inhibitor against glycating agents that can delay ageing, diabetic complications and neurodegenerative disorders. Studies have reported that polyphenolic compounds possess significant in vitro anti-glycation activity. Polyphenols may inhibit the formation of AGEs either by scavenging ROS production during the glycation reaction or provides physical protection against glycating agents [11, 12]. The physical protection mechanism by polyphenols involves hydrogen bonding and non-covalent interactions which acts as a sort of shield and prevents the accessibility of glycating agents on their target site [13, 14]. In this review, antiglycating activity of different polyphenolic compounds will be discussed.

## II. QUERCETIN

Quercetin, a common polyphenolic compound has been reported to be an effective radical scavenging

compound in several in vitro systems [15]. It plays a vital role in the inhibition of AGEs formation at the very early stage, and it is antioxidant activity of quercetin which attributes its enhanced antiglycating activity [16].

Quercetin being rich in hydroxyl groups may interact with protein molecules by hydrogen bonding and non-covalent interactions and may prevent glycation agents like glucose, glyoxal and methylglyoxal to act on their glycation target sites [15, 17]. Thus quercetin may act as a sort of shield against glycation agents.

### III. CURCUMIN

Curcumin (diferuloylmethane) is a most potent antioxidant and anti-inflammatory phenolic compound [18]. It has been repeatedly claimed that curcumin is safe and natural curative agent of several number of diseases. Studies have reported that curcumin reduces blood glucose level in type 2 diabetic KK-Ay mice and chemically induced diabetic animals. In high glucose treated erythrocyte model, free radical generation as well as glycation of proteins was prevented by curcumin [19, 20]. Another study reported that accumulation of advanced glycation end products (AGEs) of collagen in skin and tail tendon of diabetic animal models were efficiently prevented by curcumin [21].

### IV. FERULIC ACID

Ferulic acid (4-hydroxy-3-methoxycinnamic acid), a cinnamic acid derivative is a biologically active phenolic compound [22,23]. It is an efficient antidiabetic and antiglycation agent as it reduces plasma glucose concentration as well as glycation and oxidation of albumin in animal models. Ferulic acid has been reported to prevent initial and intermediate stages of protein glycation, thus reduces the processes of AGEs formation [24-26].

### V. ELLAGIC ACID

Ellagic acid (ellagic acid; 2,3,7,8-tetrahydroxychromeno[5,4,3-cde]chromene-5,10-dione) is an important antioxidant, anticarcinogenic and anti-inflammatory phytochemical compound [27]. Dietary sources such as pomegranate, apples, guava and grapes are rich in ellagic acid which possesses efficient antiglycating potential [28, 29]. It prevents advanced glycation end product formation like carboxymethyl

lysine (CML) and other fluorescent AGEs. Both in vitro and in vivo antiglycation potential of ellagic acid has been experimentally evaluated [30].

### VI. RUTIN

Rutin is a well-known antioxidant phenolic compound present in various dietary sources fruits, tomatoes and vegetables [31]. Oral administration of high doses of rutin prevent development of protein adduct formation in diabetic rat skin [32]. Studies have reported that rutin metabolites suppresses the ADP-ribose induce glycation of histone H1 protein. Rutin metabolites containing vicinal hydroxyl groups in their structure are effective in inhibition of methylglyoxal and glyoxal induced histone glycation [33]. These vicinal hydroxyl groups involve condensation with dicarbonyl intermediates which further reacts to form acetal. Thus rutin involves inactivation of carbonyl compounds like glyoxal and methylglyoxal and protects proteins from glycation [33].

### VII. IRIDOIDS

Iridoids are monoterpenes and most of the medicinal plants are enriched with these terpenes. Asperuloside, aucubin, geniposide, harpagoside and oleuropein are well known iridoids. Oleuropein under physiological conditions gets converted into hydroxytyrosol which scavenges methylglyoxal and reduces carbonyl stress. Deacetylasperulosidic acid and loganic acid protects bovine serum albumin from in vitro glycation [34-36].

### VIII. CONCLUSION

Phenolic compounds have the potential to prevent glycation of proteins, lipids and nucleic acid either by scavenging or preventing the access of glycation agents like ribose, Methylglyoxal, and glyoxal etc. on their target site. Characterization of more polyphenolic compounds will be helpful for preventing glycation induced ageing, diabetic complications and neurodegenerative disorders.

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All the authors contributed equally.

## X. REFERENCES

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