Ferulic acid inhibits AGEs formation

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Non-enzymatic glycation is a major factor responsible for complications of diabetes and aging (1). Both early and advanced glycation endproducts (AGEs) are involved in these complications. Thus, it follows that inhibitors of glycation pathways might be useful as therapeutic agents for their prevention. Several reports have indicated that ferulic acid, among other natural substances of plant origin, possesses antiglycating power (2-5). Also, related food components like feruloyl oligosaccharides (FOs) have been shown to inhibit fluorescent AGEs formation (4). Few and controversial data on the inhibitory effects of ferulic acid against protein glycation have been published so far.

The role of ferulic acid as an antiglycating agent depends on its concentration in the glycation mixture (2, 5). The effectiveness of this compound might also vary according to its concentration relative to that of compounds possessing either carbonyl groups or amino groups or both. The nature of the protein, availability of reactive amino acid residues and incubation conditions may also play a role. This might explain why some authors have reported ferulic acid to be an antiglycating agent and others have not observed such activity for this phytochemical compound. Studies performed by Wu et al. (6) indicated that, in an albumin-glucose model system, ferulic acid shows no antiglycating activity at concentrations as low as 50µg/ml (glucose:ferulic acid molar ratio = 1940:1; ferulic acid:protein molar ratio = 0.29-0.87:1) while other plant compounds like gallic acid, catechin and quercetin at the same concentration, inhibited glycation by 80%. In contrast, final concentrations of ferulic acid of 83 µg/ml (glucose:ferulic acid molar ratio = 388:1; ferulic acid:protein molar ratio = 8.6:1) clearly decreased the formation of fluorescent AGEs (4). Interestingly, very recently, we have found that ferulic acid at a final concentration of 2.5 mg/ml, exerts a selective inhibitory effect on the formation of AGEs (7). Incorporation of fructose into the protein backbone was not inhibited by ferulic while the level of formation of CML was reduced by nearly 90%. Moreover, fluorescence of the samples containing ferulic acid was greatly quenched. In summary, formation of AGEs (both fluorescent and non-fluorescent compounds, such as CML) can be selectively inhibited by adding ferulic acid to glycation mixtures. Our preliminary findings indicated that ferulic acid can be a feasible compound for controlling the production of novel glycopotreins preparations (7) and reducing AGEs formation during thermal processing of foods and it may be also used for health therapy (5,8).

The mechanism of antiglycation by ferulic acid requires further investigation. Some authors attribute this effect to the antioxidant activity of the antiglycating agent (4-5). However, the relationship between these two activities should be further investigated. Some typical dietary antioxidants show no or poor antiglycating capacity (2). It is believed that the mechanism of inhibition of glycation by ferulic acid is different from that of other phenolic compounds (5, 7).

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