Insight into antiglycation mechanism of phenolic acid derivatives in model and food systems

The protein glycation reaction can initiate extensive structural and functional modifications in protein to form irreversible and harmful advanced glycation end products (AGEs) accompanied with the generation of a variety of reactive dicarbonyl species, like methyl glyoxal, glyoxal, and 3-deoxyglucosones. Apart from being formed endogenously, AGEs are also formed in foods. Excessive AGEs in food have been confirmed to cause many chronic diseases, including diabetes mellitus and kidney disease, Alzheimer's disease, and are also among the causes of the development and malignancy of tumors.

Therefore, various strategies for controlling protein glycation have been investigated over the years. Antioxidants have been proposed as effective inhibitors of AGE formation in thermally treated systems. Their antiglycation effect may involve a range of different mechanisms, including reactive carbonyl trapping, antioxidant activity, sugar autoxidation inhibition, and amino-group binding inhibition and competition However, among the parameters affecting the level of AGEs in foods, the effects of antioxidants have not yet been satisfactorily elucidated. Thus, the mechanism of action still remains unclear.

Phenolic acids are widely distributed in plants and are known natural antioxidants of various food products. Phenolic acids can be found naturally as free or in combination with other compounds, usually in the form of esters with polysaccharides, sterols, fatty alcohols and glycerol. To the best of our knowledge, this will be the first study to document the role of the structure of phenolic acids derivatives on the AGE formation mechanism and mitigation strategies.

The aim of the proposed project is to investigate the reactivity of phenolic acids derivatives, i.e. vinyl derivatives as well as alkyl and sterol esters of phenolic acids upon the formation of endogenous AGEs in glycated bovine serum albumins (BSA) and the formation of exogenous AGEs in model and food systems. Moreover, studies will be carried out exploring the protective effects of phenolic acids derivatives against dietary AGEs-induced oxidative stress and inflammation examined in RAW267.4 macrophages. In order to further explore the antiglycation mechanism, the free radical scavenging and direct methylglyoxal and glyoxal trapping capacities of phenolic acids derivatives will also be evaluated. The stability of phenolic acids derivatives during the thermal treatment, the lysine content available in food matrices, the formation and elimination of Maillard-type volatile compounds and sensory profile will be also studied. Since antioxidant activity has been proposed as one highly possible antiglycation mechanism, the aim of this study is also to evaluate the correlation between AGE content and antioxidant activity.

This project is expected to provide answers to the following questions:

- Do phenolic acids derivatives inhibit AGEs formation and protein oxidation in BSA-reducing sugar systems by blocking the cross-linking between proteins and dicarbonyl compounds?
- Is there a linear relationship between antioxidant activity and the antiglycative activity of phenolic acids derivatives?
- Is there a structure-activity relationship of phenolic acids derivatives in the trapping abilities of reactive carbonyl species?
- Do phenolic acids derivatives display anti-inflammatory activities by down-regulating the expression of pro-inflammatory mediators?
- Does the thermal stability of phenolic acids derivatives depend on their chemical structures and affect the final levels of AGEs?
- Do the differences in affinities for the nonpolar phase determine the antioxidant activity of phenolic acids derivatives towards AGE mitigation in a heterogeneous system, more than differences in radical scavenging activities do?
- Does the chemical structure of phenolic acids derivatives determine their reactivity towards the ε-lysine side chains?

The comprehensive character of these studies will contribute to a better understanding of the antiglycation mechanisms of phenolic acids derivatives. Studies concerning prevention strategies for autoimmune and neurodegenerative diseases are currently considered to be priority research and this project will contribute both to their development and to biology and food chemistry.