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Inhibitory effect of lotus seedpod oligomeric procyanidins on advanced glycation end product formation in a lactose–lysine model system

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ABSTRACT

Background: Industrial food processing induces protein glycation modifications and toxic advanced glycation end products (AGEs) which affect human health. Therefore, it is of interest to monitor AGEs in food processing. The present study was carried out to investigate the influence of lotus seedpod oligomeric procyanidin (LSOPC) concentrations, solution pH value and metal ions on AGE formation by heat treatment of lactose–lysine model solutions. Nε-(carboxymethyl) lysine (CML), as one of the common AGEs was also determined by HPLC–MS/MS in this experiment.
Results: The results showed that LSOPC can inhibit the formation of AGEs effectively at higher concentrations, lower temperature, and it can reverse the promotion function of metal ions because of its high inhibition activity. Also, LSOPC can inhibit CML formation in the Maillard reaction as well.
Conclusion: These results indicated that LSOPC could be used as functional food ingredients to inhibit AGE formation.

1. Introduction

Advanced glycation end-products (AGEs) are formed as a result of a non-enzymatic Maillard or 'browning' reaction in which glucose forms adducts with proteins, lipids and nucleic acids [1]. First, carbonyl group forms a reducing sugar and an unprotonated amine group forms a protein producing a nucleophilic addition reaction to form a freely reversible Schiff base. This is subsequently stabilized after rearrangement into Amadori products or Heyns products according to the type of sugar involved (aldoses or ketoses). With additional complex rearrangements such as oxidation, enolization, dehydration, condensation and fragmentation, early glycated products are formed [2]. Subsequent further reactions (cross-linkages and polymerization) lead to the formation of AGEs [3]. AGEs were originally characterized by a yellow-brown fluorescent color and by an ability to form cross-links with and between amino groups, but the term is now used for a broad range of advanced products of the glycation process (also called the "Maillard reaction"). Generally, these compounds can be divided into two types on the basis of chemical structure: one type is the fluorescent properties and crosslinking structure AGEs, such as crossline, 2-(2-furoyl)-4(5)-(2-furanyl)-1H-imidazole (FFI), glyoxal-lysine dimer (GOLD), methyl-glyoxal-lysine dimer (MOLD), fluorolink, pentosidine and vesperlysine, and the other type is the non-fluorescent and non-crosslinking AGEs, such as Nε-(carboxymethyl) lysine (CML), Nε-(carboxyethyl) lysine (CEL), pyrraline and argpyrimidine [4].

Recently, AGEs in vivo have been implicated in the pathogenesis of diabetic complications, including neuropathy, nephropathy, retinopathy, and cataract [5] and other health disorders such as atherosclerosis [6], Alzheimer's disease [7] and chronic kidney disease, as well as other phenotypes related to aging [8]. Other detrimental effects of the glycation process are their contribution to the functional properties of proteins such as their emulsifying, foaming and gelling capacities as well as their solubility [9,10] and the production of toxic and carcinogenic compounds such as the low-molecular weight products, keto-aldehydes, glyoxal, methylglyoxal, 3-deoxyglucosone, heterocyclic amines and acrylamide [11].

The two major sources of human exposure to AGEs are exogenous AGEs found in foods, and endogenous AGEs that are generatiod by abnormal glucose metabolism or as a byproduct of lipid peroxidation. The contribution of dietary AGEs to the total pool of AGEs in the body is likely to be much greater than the contribution from AGEs that are endogenously generated by abnormal glucose metabolism or lipid oxidation [12]. Since dietary AGEs are absorbed as free adducts after

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digestion they are likely to constitute a major source of intracellular and plasma AGEs [13]. Moreover, dietary AGEs are also a major environmental source of proinflammatory AGEs [14]. Industrial processing or cooking of food is rich in AGEs because of the high temperatures that are used in processing, such as deep frying, baking and broiling [15]. Thus, the role of dietary AGEs in human health remains highly controversial and the restriction of food-derived AGEs or the inhibition of absorption of dietary AGEs may be a novel target for therapeutic intervention in the above-mentioned AGE-related disorders.

Lotus seedpod is not an edible part of lotus, which is rich in B-type procyanidins. Lotus seedpod oligomeric procyanidins (LSOPC) (molecular structure; Fig. 1) is a kind of mixture, which doesn't have certain molecular weight. The mean degree of polymerization of LSOPC was 3.21, with 74.2% catechin and 25.8% epicatechin in the terminal units and 26.0%, 43.1%, 30.9% of catechin, epicatechin, epigallocatechin in the extensive units, respectively, which were detected by HPLC/MS. Our laboratory has established the proper extraction technology of LSOPC in recent years [16]. Furthermore, antioxidant properties, metal-chelation and free radical scavenging activity of oligomeric Procyanidins of lotus seedpod (LSOPC) have been extensively identified [17]. In recent years, much attention has been paid to the influence of LSOPC on insulin action and reactive carbonyl species (RCS) scavenging activities, which may provide benefits for diabetic patients [16,17]. Some researchers indicated that LSOPC may play a useful role in the treatment of cognitive impairment caused by Alzheimer's disease and aging due to their excellent performance in scavenging free radicals, antioxidation, anti-lipid peroxidation [18]. Moreover, our previous studies have showed that LSOPC could inhibit AGE formation effectively in simulated physiological environment and the corresponding inhibition mechanisms to scavenging reactive carbonyls by forming adducts with them [19]. However, there are few reports about LSOPC inhibiting AGE formation especially in food system. In this study, a model system was chosen consisting of lactose (as a reducing disaccharide) and lysine (as a very reactive amino acid) to monitor the AGE formation, and observed the effect of different LSOPC concentrations, solution pH values and metal ions on inhibiting AGE formation. This type of modeling system can be a powerful tool to improve our understanding of the evolution of AGEs during food processing with AGE inhibitor.

Table 1
MS/MS conditions for the compounds studied.

Analyte	Molecular weight	Parent ion (m/z)	Daughter ion (m/z)	tR (min)	DP (V)	CE (eV)	EP (V)	CXP (V)
CML	205	205.2	84.0 130.1	7.20	71 74	31 18	10	12

2. Materials and methods

2.1. Chemical and reagents

Lotus seedpods were obtained from local supermarket (Wu Zhi 2 hao). α-Lactose, L-lysine, phosphate buffer saline (PBS, pH 7.4), D-glucose and FeCl3 were purchased from Sinopharm (Shanghai, China). $FeCl_2 \cdot 4H_2O$, $CuCl_2 \cdot 2H_2O$, $MgCl_2 \cdot 6H_2O$, $ZnCl_2$, $CaCl_2 \cdot 2H_2O$, $SnCl_2 \cdot 2H_2O$ and $AlCl_3 \cdot 6H_2O$ were purchased from Sigma-Aldrich (St. Louis, MO). All other chemicals were of analytical grade.

2.2. Preparation of lotus seedpod oligomeric procyanidins

Fresh lotus seedpod fragments were extracted using 70% ethanol at 60°C for 1.5 h. The crude procyanidin aqueous solution was loaded onto an AB-8 resin (weak polarity macroporous resin, 0.3–1.25 mm particle size, Nankai Hecheng Science & Technology Co., Tianjin, China) column (15 × 3.5 cm, ID), and the fraction eluted by 70% ethanol was collected. The eluent was evaporated, and the procyanidin extract of lotus seedpod was obtained. Subsequently, they were extracted by ethyl acetate to get the oligomeric procyanidins of lotus seedpod (LSOPC), which included catechin monomers, B-type procyanidin dimers, trimers and a few tetramers by LC–MS analysis [20]. The yield of LSOPC was 0.8%. Its purity was 106.22 ± 0.46% compared to that of grape seed procyanidins measured by Butanol-HCl assay [21].

2.3. Preparation of model systems

In order to study the Maillard reaction in real food systems, in particular in milk and milk products, lactose was chosen as the model

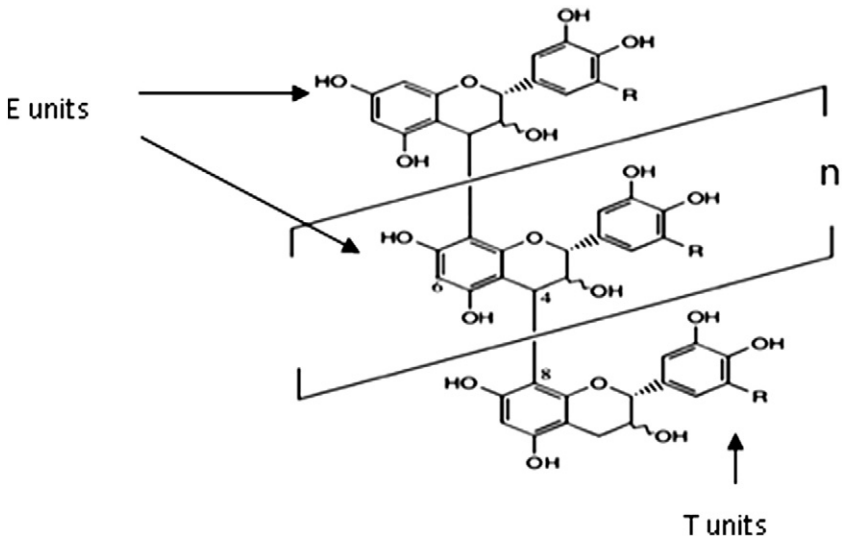

Fig. 1. Scheme of LSOPC: terminal Unit, T-units; extension units, E-units.