Enhancement of anti-inflammatory activity of fish myofibrillar protein by Maillard-type glycation and its molecular mechanism

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[Objective] Myofibrillar protein (Mf) from spawned-out chum salmon gained strong anti-inflammatory activity *in vitro* and *in vivo* by the glycation with alginate oligosaccharide (AO) through the Maillard reaction. Considering that alginate oligosaccharide is a copolymer linked by two types of uronic acid possessing one carboxyl group in each molecule, the role of carboxyl group of the attached sugars in enhancing the anti-inflammatory activity of Mf was investigated in this study.

[Methods] The lyophilized Mf was glycated with monosaccharides and their oxidized derivatives (uronic acid) at 60 °C and 35% relative humidity through the Maillard reaction. The glycated Mfs were digested by pepsin-trypsin and evaluated the anti-inflammatory activity by measuring the secretions of inflammatory mediators in lipopolysaccharide (LPS)-stimulated RAW 264.7 macrophages. In addition, the effect on gene expression related to LPS-stimulated signaling pathways was also examined to discuss the molecular mechanism of the enhanced anti-inflammatory activity.

[Results] The anti-inflammatory activity of Mf was not affected by glucose and galactose, whereas carboxyl-containing glucuronic acid and galacturonic acid conferred strong anti-inflammatory activity upon addition to Mf, as the same as alginate oligosaccharide. These results indicate that the presence of carboxyl group in reducing sugar is an important factor enhancing the anti-inflammatory activity of Mf in the Maillard type glycation. In the gene expression analysis, the uronic acid-glycation suppressed LPS-stimulated inflammation by inhibiting the ability of CD14 recognizing LPS, thereby enhancing the suppressive effect of Mf in TLR4-MyD88-dependent inflammatory signaling pathway. In conclusion, the uronic acid-glycation, which modulates cell signaling and enhances anti-inflammatory function, would be a useful method for developing food-functional materials from the Mf.

Keywords: Fish myofibrillar protein, Anti-inflammatory activity, Maillard reaction, Uronic acid, Carboxyl group, Macrophage