KEY STRUCTURAL IDENTIFICATION OF CHITOOLIGOSACCHARIDES RESPONSIBLE FOR THEIR ANTI-INFLAMMATORY ACTIVITY

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Endotoxemia is mainly caused by a massive burst of inflammatory cytokines as a result of lipo-polysaccharide (LPS) invasion. Chitooligosaccharides (COS) has attracted wide attention for relieving endotoxemia due to its anti-inflammatory properties. However, the structural parameters of COS are often ambiguous, and the structural basis of COS for its anti-inflammatory remains unknown. In this study, some specific COSs with well-defined structure were successfully obtained. Their structures and sequences were confirmed by ^{1}H NMR and MS analysis. Then, the effect of DA and PA (degree and pattern of acetylation) on the anti-inflammatory activity and relieving endotoxemia potential of COS was researched. The results revealed that COS with a DA of 12% had better anti-inflammatory activity than COSs with other DAs, mainly in inhibiting LPS-induced inflammatory cytokines burst, down-regulating its mRNA expression and reducing phosphorylation of IκBα. The KEGG results showed that COS induces the pleiotropic modulation of classical inflammatory pathways and shows an obviously protective effect on endotoxemia mice, such as inhibiting the increase in inflammatory cytokines and transaminases, alleviating the injury of liver and intestinal tissue. Furthermore, the key sequence responsible for the anti-inflammatory activity of COS was identified. This study explored the relationship between the structure of chitooligosaccharides and their anti-inflammatory activity and lays the foundation for the development of COS as an anti-inflammatory drug against endotoxemia.