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Cyanidin-3-O-β-glucoside ameliorates lipopolysaccharide-induced acute lung injury by reducing TLR4 recruitment into lipid rafts

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Abstract

Cyanidin-3-O-β-glucoside (C3G), a typical anthocyanin pigment that exists in the human diet, has been reported to have anti-inflammatory properties. The aim of this study was to detect the effect of C3G on LPS-induced acute lung injury and to investigate the molecular mechanisms. Acute lung injury was induced by intratracheal administration of LPS in mice. Alveolar macrophages from mice were stimulated with LPS and were treated with C3G. Our results showed that C3G attenuated lung histopathologic changes, myeloperoxidase (MPO) activity, TNF-α, IL-1β and IL-6 production in LPS-induced acute lung injury model. In vitro, C3G dose-dependently inhibited TNF-α, IL-1β, IL-6, IL-10 and IFN-β production, as well as NF-κB and IRF3 activation in LPS-stimulated alveolar macrophages. Furthermore, C3G disrupted the formation of lipid rafts by depleting cholesterol and inhibited TLR4 translocation into lipid rafts. Moreover, C3G activated LXRα-ABCG1-dependent cholesterol efflux. Knockout of LXRα abrogated the anti-inflammatory effects of C3G. In conclusion, C3G has a protective effect on LPS-induced acute lung injury. The promising anti-inflammatory mechanisms of C3G is associated with up-regulation of the LXRα-ABCG1 pathway which result in disrupting lipid rafts by depleting cholesterol and reducing translocation of TLR4 to lipid rafts, thereby suppressing TLR4 mediated inflammatory response.

Keywords: Cyanidin-3-O-β-glucoside; TLR4; lipid raft; LXR; ABCG1

Abbreviations: LPS, lipopolysaccharide; TNF-α, tumor necrosis factor-α; IL-6, interleukin-6; IL-1β, interleukin-1β; NF-κB, nuclear factor-kappaB; IRF3, Interferon regulatory factor 3; ELISA, enzyme-linked immunosorbent assay

1. Introduction

Acute lung injury is a life-threatening syndrome characterized by overwhelming lung inflammation, which causes a high mortality rate worldwide [1, 2]. Lipopolysaccharide (LPS), a main component of the outer membrane of gram-negative bacteria, has been identified as an