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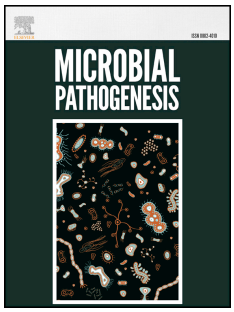

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Anti-inflammatory effects of isorhamnetin on LPS-stimulated human gingival fibroblasts by activating Nrf2 signaling pathway

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ABSTRACT

Periodontitis is a highly prevalent infective and inflammatory disease with an adverse impact on systemic health. Isorhamnetin, a flavonoid mainly isolated from Hippophae fhamnoides L. fruit, has been reported to have anti-inflammatory effect. This study aimed to investigate the anti-inflammatory effects and mechanism of isorhamnetin on lipopolysaccharide (LPS)-induced inflammatory response in human gingival fibroblasts (HGFs). The production of inflammatory mediators and the expression of proteins were measured by ELISA and western blot analysis. The results demonstrated that isorhamnetin attenuated LPS-induced release of PGE_2, NO, IL-6, and IL-8 in HGFs. Isorhamnetin also inhibited LPS-induced NF-κB activation. The expression of Nrf2 and HO-1 were up-regulated by treatment of isorhamnetin. Furthermore, knockdown of Nrf2 by siRNA reversed the anti-inflammatory effects of isorhamnetin. In conclusion, these results suggested that isorhamnetin inhibited LPS-induced inflammation in HGFs by activating Nrf2 signaling pathway.

Keywords: isorhamnetin; LPS; human gingival fibroblasts; IL-8; Nrf2

1.Introduction

Periodontal disease is a chronic inflammatory disease characterized by destruction of the alveolar bone and periodontal connective tissue [1]. Inflammatory response is critical to the pathogenesis of periodontal disease [2, 3]. Gingival fibroblasts are essential for the immune defense against oral bacteria infection. Stimulating of gingival fibroblasts with LPS could lead to the release of inflammatory mediators [4, 5]. These inflammatory mediators amplify the inflammatory response and lead to periodontal tissue destruction [6]. Previous studies suggested that inhibition of inflammatory response could attenuate periodontal diseases [7]. In recent years, many herbal medicines have been reported to have anti-inflammatory effects and have received considerable attention [8]. While, herbal rinses are traditionally used to clean the oral cavity [9]. Therefore, to seek herbal medicines that have the ability to attenuate inflammatory response is helpful for the treatment of periodontal diseases.