방풍의 항염 효과 기전

노상일, 김상돈, 박성철, 서병윤, 임승룡, 권영달, 신병철, 송용선

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Mechanism of Anti-inflammatory Effect of Peucedanum japonicum Thunb

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목적: 방풍은 임상적으로 관점범을 포함한 다양한 염증성 질환 치료제로 사용되며, 본 연구에서는 인간 비만세포를 이용하여 세포 독성에 영향을 주지 않는 농도에서 방풍의 항염 효과 및 그 기전을 검토하였다.

방법: 인간의 HMC-1세포를 IMDM에 페니실린, 스톨로미cef라, 모노노글리세린을 첨가하여 배양하고 방풍추출액을 투여하였다. 그 다음 MTT, ELISA, RT-PCR, 세포내 활성계정, 백단백분석을 이용하여 TNF-α, IL-6, IL-8 각각의 생성과 mRNA발현, 세포내 활성계정을 수준, NFκB 발현에 대한 방풍추출액의 반응을 측정하고 통계처리 하였다.

결과: 방풍은 PMA의 calcium ionophore A23187으로 활성화된 비만세포에서 세포내 활성계정 수준과 NFκB, TNF-α와 IL-6의 발현을 억제하였고, RT-PCR를 이용한 mRNA 발현에서 TNF-α와 IL-6의 발현을 억제하였다.

결론: 방풍은 비만세포내 활성계정 수준 및 NFκB의 활성을 억제하고 염증성 세포 활성 물질인 TNF-α와 IL-6의 분비도 억제하여 항염 효과를 나타내는 것으로 있다.

중심어: 방풍, 항염효과, 비만세포
I. Introduction

Traditionally, Bang Poong (BP, Peucedanum japonicum Thunb.) has been used to treat several inflammatory diseases, such as arthritis. The reported biological activities of BP include anti-inflammatory and anti-nociceptive effects\(^1\). However, their effects on proper experimental models remains unknown.

Mast cells are important effector cells in allergic reactions and also in inflammatory processes due to their ability to secrete numerous cytokines\(^3\). The significant contribution of mast cells has become growing evident in pathogenesis of diverse inflammatory disease such as asthma, arthritis, fibrosis and malignancy\(^5\). In view of such findings, mast cells are now recognized to play a more versatile role\(^7\), especially in allergic inflammation\(^8\). In addition, inflammatory cytokine release from mast cells in response to an allergen challenge plays a crucial role in allergic ocular inflammation. Therefore, modulation of the secretion of these cytokines from mast cells can provide a useful therapeutic strategy for treating allergic inflammatory diseases.

Inflammatory cytokines are rapidly induced and expressed early in the disease or injury process in an antigen-independent manner\(^9\). The principal inflammatory cytokines are tumor necrosis factor (TNF)-α, interleukin (IL)-1 and , IL-6, and IL-8. TNF-α and IL-6 participate in the initiation of inflammation and acute phase reactions, while IL-8 is a potent neutrophil chemotactic molecule involved in inflammation\(^10\). TNF is a pleiotropic cytokine capable of altering physiological and immunological sequelae as well as mediating the pathophysiologic responses of various disease conditions\(^11\). IL-6 is thought to be involved in several diseases including autoimmune disorders and plasma cell neoplasms and especially in inflammatory processes of the skin as diverse as scleroderma, psoriasis, and delayed pressure urticaria\(^12,13\). Also, a primary in vivo role of IL-6 is the induction of the acute phase response, a striking alteration in plasma concentrations of a series of liver-derived serum proteins which is the hallmark of the acute inflammatory response\(^14\). Mast cells play an important role in immediate hypersensitivity responses, and their numbers are increased in a broad spectrum of pathologic conditions\(^5,16\). Human mast cell line (HMC-1) is also known to release pro-inflammatory cytokines such as TNF-α, IL-6 and IL-8\(^17\).

Calcium acts as a second messenger during cell activation\(^18\). An increase in the intra-cellular calcium level has been proposed as an essential trigger for mast cell activation\(^19\). Cross-linking of the IgE-binding protein (FcεRI) is known to increase intra-cellular Ca\(^{2+}\) ion levels\(^20\). However, the Ca\(^{2+}\) requirement for cytokine release has not been investigated sufficiently. In one study, TNF-α production in rat basophilic leukemia (RBL-2H3) cells was apparently Ca\(^{2+}\) independent, but the stimulus was the Calcium ionophore A23187 and phorbol esters\(^21\). In humans, IL-2, IL-6, IL-8 and TNF-α are regulated to some degree by NF-κB activation\(^22\). NF-κB is a ubiquitous protein transcription factor that enhances the transcription of a variety of genes. Many of these genes encode molecules im-