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ORIGINAL ARTICLE

Anti-inflammatory effects of *Clematis chinensis Osbeck* extract(AR-6) may be associated with NF-κB, TNF-α, and COX-2 in collagen-induced arthritis in rat

Cheng Peng · Pathirage Kamal Perera · Yun-man Li · Wei-rong Fang · Li-fang Liu · Feng-wen Li

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Abstract The root of *Clematis chinensis Osbeck* has been used widely in rheumatoid arthritis in Chinese traditional medicine, and AR-6 is a triterpene saponin isolated from it. In this present study, we investigated the in vivo effects of oral AR-6 in chronic rat with collagen-induced arthritis (CIA) and possible molecular mechanism. CIA was induced by immunizing 56 female Sprague-Dawley (SD) rats with chicken typeIIcollagen (CII). Following eighteen days, the immunization rats with CIA were treated with AR-6 (32, 16, 8 mg/kg), cyclophosphamide (7 mg/kg), and TGP (Total Glucosides of Paeonia) (180 mg/kg) for 7 days, and rats without CIA were given the same volume of purified water. TNF-α and IL-1β levels in peripheral blood will be measured by ELISA, and Western blot analysis will be used to detect the expression of NF-κB p65 subunits, TNF-α and COX-2, in synovial membrane. We found that therapeutic treatment with AR-6 markedly improves the paw swelling and histopathological changes. Moreover, the serum levels of pro-inflammatory cytokines TNF-α and IL-1β were markedly lowered, and the expression of NF-κB p65 subunits, TNF-α and COX-2, in the synovial membrane of CIA rats was significantly inhibited in the AR-6-treated groups. These results enable to prove that AR-6 has a potential anti-inflammatory effect in CIA rats, and its mechanism may relate to the inhibition of the expression of NF-κB p65 subunits, TNF-α and COX-2.

Keywords *Clematis chinensis Osbeck* · Collagen-induced arthritis · NF-κB · TNF-α · COX-2

C. Peng · P. K. Perera · Y. Li (✉) · W. Fang
Department of Physiology, China Pharmaceutical University, Nanjing 210009, China
e-mail: yucaoren@sina.com

L. Liu
Department of Pharmacognosy and the Key Laboratory of Modern Chinese Medicines, Ministry of Education, China Pharmaceutical University, Nanjing 210009, China

F. Li
Department of Traditional Chinese Pharmacy, China Pharmaceutical University, Nanjing 210009, China

Introduction

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disease with unknown etiology [1]. The main pathological changes of RA include hyperplasia of synovial membrane, infiltration of inflammatory cells, and neovascularization, which ultimately lead to cartilage erosion and articular destruction [2].

The transcription factor NF-κB has been well recognized as a pivotal regulator of inflammation in rheumatoid arthritis [3]. On one hand, NF-κB controls the expression of the pro-inflammatory cytokines such as tumor necrosis factor alpha (TNF-α) and interleukin-1β (IL-1β), which are expressed at very high levels in peripheral blood and synovial membrane [4]. On the other hand, cytokines TNF-α and IL-1β, which are considered to be the important participants in the histopathology of RA, are potent inducers of NF-κB activation, suggesting an interdependence of persistent NF-κB activation and sustained levels of TNF-α and IL-1β [5]. Active forms of NF-κB, commonly composed of p50/NFKB1 and p65/RelA subunits, are detected in the synovial membrane of rheumatoid arthritis patients, suggesting that NF-κB is involved in the expression of inflammatory genes in the rheumatoid arthritis synovial membrane [6]. Furthermore, NF-κB activation is necessary for the induction of cyclooxygenase-2 and inducible nitric oxide synthetase (iNOS), the

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