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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

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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

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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