Novel Anti-arthritic Mechanisms of Polydatin in Complete Freund's Adjuvant-Induced Arthritis in Rats: Involvement of IL-6, STAT-3, IL-17, and NF-κB

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Abstract

Articular manifestations are the main hall mark for rheumatoid arthritis; inflammation and oxidative stress are involved in its pathogenesis. This study was designed to figure out the possible therapeutic potential of polydatin on experimentally induced arthritis in rats. Polydatin (POLY) was administered (200 mg/kg, p.o.) for 21 days to complete Freund's adjuvant (CFA; 0.1 ml, s.c.)-induced arthritic rats. Meanwhile, methotrexate (MTX; 0.75 mg/kg, i.p.) was given as a reference standard disease-modifying anti-rheumatic drug (DMARD). Both POLY and MTX significantly attenuated articular damage associated with CFA-induced arthritis. This was manifested by reducing levels of tumor necrosis factor alpha (TNF-α), interleukin-6 (IL-6), interleukin-17 (IL-17), and matrix metalloproteinase-3 (MMP-3), paralleled with marked decrease in hind paw and ankle diameters. Moreover, POLY and MTX downregulated gene expressions of receptor activator of nuclear factor kappa-B ligand (RANKL) as well as signal transducer and activator of transcription-3 (STAT3) besides hampering immunohistochemical staining of vascular endothelial growth factor (VEGF) and nuclear factor kappa-B (NF-κB). Furthermore, substantial decline in myeloperoxidase (MPO) activity and malondialdehyde (MDA) level associated with significant rise in reduced glutathione content (GSH) was observed. These findings provide an innovative therapeutic approach of POLY as a natural anti-arthritic drug through modulating IL-6/STAT-3/IL-17/NF-κB cascade.

Inflammation 2018, October