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ORIGINAL ARTICLE

Pharmacological and biochemical studies on protective effects of mangiferin and its interaction with nitric oxide (NO) modulators in adjuvant-induced changes in arthritic parameters, inflammatory, and oxidative biomarkers in rats

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Abstract

Current study was designed to evaluate protective effect of mangiferin and its interaction with low dose of nitric oxide (NO) modulators in complete Freund's adjuvant (CFA) inoculated rats. Male wistar rats (200–300 g, $n=8$ per group) were used in the study. On day ''0'' of study arthritis was induced in rats by injecting 0.2 ml CFA in sub-planter region of right hind paw of animals. Treatment with methotrexate (5 mg/kg), mangiferin (10–30 mg/kg) alone and in combination with NO modulators was given (i.p.) from days 14 to 28. After 28 days, blood and joint synovial fluid was collected for biochemical analysis and rat paws were excised to estimate MDA and SOD in tissue (paw) homogenates. CFA inoculation significantly increases (1) arthritic index, (2) ankle diameter, (3) paw volume, and (4) serum TNF-α, IL-6, IL-1β, and synovial TNF-α levels ($p<0.001$). The serum Th_1 (IFN-γ) and Th_2 (IL-4) cytokine levels, MDA levels in rat paw tissue homogenates and serum NF-κB levels were also found significantly increased. Significant decrease in serum IL-10 levels and SOD activity was found after CFA inoculation. These CFA-induced arthritic changes, cytokine profile, and oxidative stress markers were significantly reversed by mangiferin (10–30 mg/kg) treatment alone and in combination with L-arginine and L-NAME nitric oxide modulators ($p<0.05$). Treatment with methotrexate (5 mg/kg) also significantly reversed these adjuvant changes ($p<0.05$). However, effect of methotrexate was less marked as compared to mangiferin (30 mg/kg) alone and in combination with L-NAME (10 mg/kg), but was comparable or slightly better than mangiferin (10 and 20 mg/kg). Thus, on the basis of our findings, we can suggest that interaction of mangiferin with nitric oxide modulators may have therapeutic value for chronic inflammatory disease such as RA.

Keywords Inflammation · Cytokines · Mangiferin · Arthritis · NF-kB · Oxidative stress

Abbreviations

CFA	Complete Freund's adjuvant
TNF-α	Tumor necrosis factor alpha
IL	Interleukin
NEMO	NF-κB essential modulator
L-NAME	*N*ω-nitro-arginine methyl ester hydrochloride
TRAF	TNF-receptor-associated factor
TRADD	TNF-receptor-type 1-associated death domain
IFN	Interferon
IKK	Inhibitory kappa kinase

Introduction

Rheumatoid arthritis (RA) is an inflammatory autoimmune disorder; however, its aetiology is still largely unknown. It is a lifelong progressive disorder and significant morbidity and premature mortality are attributed to it. Worldwide prevalence of RA ranges from 0.3 to 1% and is widespread in developed countries. Prevalence of RA in India is reported to be 0.75% in the adult population (Mathew et al. 2009).

Although a large number of researches have been done to find out the mechanism of inflammation and tissue destruction in arthritis, its exact mechanism is yet to be elucidated

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