

## Inhibitory Effect of Coumaroyl Lupendioic Acid on Inflammation Mediator Generation in Complete Freund's Adjuvant-Induced Arthritis

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**Abstract :** *Careya arborea* Roxb. belongs to the Lecythidaceae family, is traditionally used in tumors, anthelmintic, bronchitis, epileptic fits, astringents, inflammation, an antidote to snake-venom, skin disease, diarrhea, dysentery with bloody stools, dyspepsia, ulcer, toothache, and ear pain. The present study was focused on investigating the anti-arthritic effect of coumaroyl lupendioic acid, a new lupane-type triterpene from *Careya arborea* stem bark in the chronic inflammatory model and further assessing its possible mechanism on the modulation of inflammatory biomarkers. Arthritis was induced by injecting 0.1 ml of Complete Freund's Adjuvant (5 mg/ml of heat killed *Mycobacterium tuberculosis*) into the subplantar region of the left hind paw. Treatment with coumaroyl lupendioic acid (10 and 20 mg/kg, p.o.) and reference drugs (indomethacin and dexamethasone at the dose of 5 mg/kg, p.o.) were started on the day of induction and continued up to 28 days. The progression of arthritis was evaluated by measuring paw volume, tibio tarsal joint diameters, and arthritic index. The effect of coumaroyl lupendioic acid (CLA) on the production PGE<sub>2</sub>, NO, MPO, NF-κB, TNF-α, IL-1β, and IL-6 on serum level as well as inflamed paw tissue were also assessed. In addition, ankle joints and spleen were collected and prepared for histological examination. CLA in inflamed rats resulted in significant amelioration of paw edema, tibio-tarsal joint swelling and arthritic score as compared to CFA control group. The results indicated that CLA treated groups markedly decreased the levels of inflammatory mediators (PGE<sub>2</sub>, NO, MPO and NF-κB levels) and down-regulated the production of pro-inflammatory cytokines (TNF-α, IL-1β, and IL-6) in paw tissue homogenates as well as in serum. However, the more pronounced effect was observed in the inflamed paw tissue homogenates. CLA also revealed a protective effect to the tibio-tarsal joint cartilage and spleen. These results suggest that coumaroyl lupendioic acid inhibits inflammation may be through the suppression of the cascade of proinflammatory mediators via the down-regulation of NF-κB.

**Keywords :** complete Freund's adjuvant, Coumaroyl lupendioic acid, pro-inflammatory cytokines, prostaglandin E2

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