Anti-inflammatory and immunomodulatory activity of *Mangifera indica* L. in a mouse model of gouty arthritis

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In the context of inflammation and immunity, there are fragmented and observational studies relating to the pharmacological activity of *Mangifera indica* L. and its main active component mangiferin. Here, we aimed to evaluate the potential beneficial effects of this plant extract (MIE, 90% in mangiferin) in a mouse model of gouty arthritis, dissecting the cellular immune phenotypes and the biochemical mechanism/s beyond its activity.

Gouty arthritis was induced in mice by the intra-articular (i.a.) administration of MSU crystals (200 μg 20 μl⁻¹). MIE (0.1-10 mg kg⁻¹; p.o.) or corresponding vehicle (DMSO/saline 1:3; p.o. gavage) were administrated concomitantly to MSU (time 0), 6 and 12 h after the stimulus. Thereafter, knee joint score and oedema were evaluated in addition to western blot analysis for several components of the mPGES-1/PPARγ pathway. Moreover, the analysis of pro/anti-inflammatory cytokines coupled to the assessment of the cellular infiltrate’s phenotype was investigated.

Treatment with MIE revealed a dose-dependent reduction in joint inflammatory scores with maximal inhibition observed at 10 mg kg⁻¹. MIE significantly reduced leukocyte infiltration, activation, and the expression of different pro-inflammatory cytokines in inflamed tissues. Furthermore, biochemical analysis revealed that MIE modulated COX-2/mPGES-1 and mPGDS-1/PPARγ pathways. Flow cytometry analysis also highlighted a prominent modulation of infiltrating inflammatory monocytes (CD11b⁺ve/CD115⁺ve/LY6Chi), and (both infiltrated and circulating) Treg cells (CD4⁺ve/CD25⁺ve/FOXP3⁺ve) following MIE treatment.

Collectively, the results presented in this study demonstrate a beneficial action of MIE in the local and systemic inflammatory/immunological perturbation in the onset and progression of gouty arthritis.