

## **$\beta$ Mangostin suppress LPS-induced inflammatory response in RAW 264.7 macrophages in vitro and carrageenan-induced peritonitis in vivo**

### **Abstract**

Ethnopharmacological relevance: The fruit hull of *Garcinia mangostana* Linn. has been used in traditional medicine for treatment of various inflammatory diseases. Hence, this study aims to investigate the in vitro and in vivo anti-inflammatory effect of  $\beta$  mangostin ( $\beta$ M), a major compound present in *Garcinia mangostana*. Materials and methods: The in silico analysis of inflammatory mediators such as cyclooxygenase (COX) and nuclear factor-kappa B (NF-kB) were performed via molecular docking. Further evaluation of anti-inflammatory effect was conducted in lipopolysaccharide (LPS) induced RAW 264.7 macrophages. Suppression of activated NF-kB was analyzed by high content screening.  $\beta$ M triggered inhibition of COX-1 and COX-2 in vitro were studied using biochemical kit. The in vivo model used in this study was carrageenan-induced peritonitis model, where reduction in carrageenan-induced peritonitis is measured by leukocyte migration and vascular permeability. In addition, the evaluation of  $\beta$ M's effect on carrageenan induced TNF- $\alpha$  and IL-1 $\beta$  release on peritoneal fluid was also carried out. Results: Treatment with  $\beta$ M could inhibit the LPS-induced NO production but not the viability of RAW 264.7. Similarly,  $\beta$ M inhibited PGE2 production and the cytokines: TNF- $\alpha$  and IL-6. The COX catalyzed prostaglandin biosynthesis assay had showed selective COX-2 inhibition with a  $53.0 \pm 6.01\%$  inhibition at 20  $\mu$ g/ml. Apart from this,  $\beta$ M was capable in repressing translocation of NF-kB into the nucleus. These results were concurrent with molecular docking which revealed COX-2 selectivity and NF-kB inhibition. The in vivo analysis showed that after four hours of peritonitis,  $\beta$ M was unable to reduce vascular permeability, yet could decrease the total leukocyte migration; particularly, neutrophils. Meanwhile, dexamethasone 0.5 mg/kg, successfully reduced vascular permeability. The levels of TNF- $\alpha$  and IL-1 $\beta$  in peritoneal fluid was reduced significantly by  $\beta$ M treatment. Conclusion: The current study supports the traditional use of *Garcinia mangostana* fruit hull for treatment of inflammatory conditions. In addition, it is clear that the anti-inflammatory efficacy of this plant is not limited to the presence of  $\alpha$  and  $\gamma$ , but  $\beta$  also with significant activity.

**Keyword:**  $\beta$  Mangostin; *Garcinia mangostana*; iNOS; NF-kB; COX-2; Cytokines