

β 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 β mangostin (βM), 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-κB) 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-κB was analyzed by high content screening. βM 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 βM's effect on carrageenan induced TNF-α and IL-1β release on peritoneal fluid was also carried out. Results: Treatment with βM could inhibit the LPS-induced NO production but not the viability of RAW 264.7. Similarly, βM inhibited PGE2 production and the cytokines: TNF-α and IL-6. The COX catalyzed prostaglandin biosynthesis assay had showed selective COX-2 inhibition with a 53.0±6.01% inhibition at 20 μg/ml. Apart from this, βM was capable in repressing translocation of NF-κB into the nucleus. These results were concurrent with molecular docking which revealed COX-2 selectivity and NF-κB inhibition. The in vivo analysis showed that after four hours of peritonitis, βM 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-α and IL-1β in peritoneal fluid was reduced significantly by βM 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 α and γ, but β also with significant activity.

Keyword: β Mangostin; *Garcinia mangostana*; iNOS; NF-κB; COX-2; Cytokines