

P-32

## SUPPRESSIVE EFFECTS OF XANTHORRHIZOL ON INDUCIBLE CYCLOOXYGENASE (COX-2) AND NITRIC OXIDE SYNTHASE (iNOS) ACTIVITY IN MOUSE MACROPHAGE CELLS

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Prostaglandins and nitric oxide produced by inducible cyclooxygenase (COX-2) and nitric oxide synthase (iNOS), respectively, have been implicated as important mediators in the process of inflammation and carcinogenesis. On this line, the potential COX-2 or iNOS inhibitors have been considered as anti-inflammatory and cancer chemopreventive agents. In this study, we investigated the effect of natural sesquiterpenoid isolated from plants of Zingiberaceae family on the activities of COX-2 and iNOS in cultured lipopolysaccharide (LPS)-activated mouse macrophage cell RAW 264.7 for discovering new lead compounds as COX-2 or iNOS inhibitors. Xanthorrhizol, a sesquiterpenoid, isolated from the rhizome of *Curcuma xanthorrhiza* Roxb. (Zingiberaceae), exhibited a potent inhibition of COX-2 ( $IC_{50} = 0.2 \mu\text{g/ml}$ ) and iNOS activity ( $IC_{50} = 1.0 \mu\text{g/ml}$ ) in the assay system of prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) accumulation and nitric oxide production, respectively. Western blot analyses revealed that the inhibitory potential of xanthorrhizol on the COX-2 activity was well coincided with the suppression of COX-2 protein expression in LPS-induced macrophages. In addition, xanthorrhizol also suppressed the COX-2 mRNA expression in a dose-dependent manner. These results suggest that natural sesquiterpenoid from *C. xanthorrhiza* might be a potential lead candidate for further developing COX-2 or iNOS inhibitor possessing cancer chemopreventive or anti-inflammatory activities.