Cardamonin, inhibits pro-inflammatory mediators in activated RAW 264.7 cells and whole blood

ABSTRACT

Some chalcones, such as hydroxychalcones have been reported previously to inhibit major pro-inflammatory mediators such as nitric oxide (NO), prostaglandin E2 (PGE2), tumor necrosis factor-α (TNF-α) and reactive oxygen species production by suppressing inducible enzyme expression via inhibition of the mitogen-activated protein kinase (MAPK) pathway and nuclear translocation of critical transcription factors. In this report, the effects of cardamonin (2′,4′-dihydroxy-6′-methoxychalcone), a chalcone that we have previously isolated from Alpinia rafflesiana, was evaluated upon two cellular systems that are repeatedly used in the analysis of anti-inflammatory bioactive compounds namely RAW 264.7 cells and whole blood. Cardamonin inhibited NO and PGE2 production from lipopolysaccharide- and interferon-γ-induced RAW cells and whole blood with IC50 values of 11.4 μM and 26.8 μM, respectively. Analysis of thromboxane B2 (TxB2) secretion from whole blood either stimulated via the COX-1 or COX-2 pathway revealed that cardamonin inhibits the generation of TxB2 via both pathways with IC50 values of 2.9 and 1.1 μM, respectively. Analysis of IC50 ratios determined that cardamonin was more COX-2 selective in its inhibition of TxB2 with a ratio of 0.39. Cardamonin also inhibited the generation of intracellular reactive oxygen species and secretion of TNF-α from RAW 264.7 cells in a dose responsive manner with IC50 values of 12.8 μM and 4.6 μM, respectively. However, cardamonin was a moderate inhibitor of lipoxygenase activity when tested in an enzymatic assay system, in which not a single concentration tested was able to cause an inhibition of more than 50%. Our results suggest that cardamonin acts upon major pro-inflammatory mediators in a similar fashion as described by previous work on other closely related synthetic hydroxychalcones and strengthens the conclusion of the importance of the methoxyl moiety substitution on the 4′ or 6′ locations of the A benzene ring.

Keyword: Cardamonin, Alpinia rafflesiana, RAW 264.7, Whole blood, Inflammatory mediator