“Development of Diarylpentadienone Analogues as Anti-inflammatory Agents”

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In an attempt to identify new potent anti-inflammatory molecules, a series of five 3-hydroxy-containing diarylpentadienones and twenty-four pyrrolylated-chalcone analogues were synthesized and assessed for their nitric oxide (NO) and prostaglandin E_2 (PGE_2) suppression on IFN-γ/LPS-induced RAW 264.7 macrophage cells. 3-(2,5-dimethoxyphenyl)-1-(1*H*-pyrrol-2-yl)prop-2-en-1-one (compound **16)** exhibited the most significant inhibition on PGE_2 and NO production with IC_{50} value of 0.5 ± 1.5 µM and 12.1 ± 1.5 µM, respectively, before further assayed for their *in vivo* acute toxicity and anti-inflammatory properties in LPS-induced zebrafish embryo. The obtained atomic coordinates for the single-crystal XRD of **16** was then applied in the docking simulation. Through molecular docking simulations, 1**6** was found to down-regulate the expression of cyclooxygenase-2 (COX-2) mRNA suggesting that this series of compounds could possibly target the mitogen-activated protein kinase (MAPK) signal transduction pathway. Therefore, we concluded that compound **16** could be used as a lead to further develop into anti-inflammatory agents as they displayed remarkable NO and PGE_2 inhibitory in *in vitro* and *in vivo* model.

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