

Synthesis, biological evaluation and QSAR studies of diarylpentanoid analogues as potential nitric oxide inhibitors

ABSTRACT

A series of forty-five 1,5-diphenylpenta-2,4-dien-1-one analogues were synthesized and evaluated for their nitric oxide (NO) inhibition activity in IFN- γ /LPS-activated RAW 264.7 cells. Compounds 3h, 7a, 7d and 7e exhibited comparable or significantly higher activity than the standard, curcumin ($IC_{50} = 14.69 \pm 0.24 \mu M$). Compound 7d, a 5-methylthiophenyl-bearing analogue, displayed the most promising NO-inhibitory activity with an IC_{50} value of $10.24 \pm 0.62 \mu M$. The 2D and 3D QSAR analyses performed revealed that a para-hydroxyl group on ring B and an α,β -unsaturated ketone moiety on the linker are crucial for a remarkable anti-inflammatory activity. Based on ADMET and TOPKAT analyses, compounds 3h, 7a and 7d are predicted to be nonmutagenic and to exhibit high blood–brain barrier (BBB) penetration, which indicates that they are potentially effective drug candidates for treating central nervous system (CNS) related disorders.