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Design, synthesis, biological evaluation, and molecular docking of chalcone derivatives as anti-inflammatory agents

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Abstract: In this study, two series of 35 new chalcone derivatives containing aryl-piperazine or aryl-sulfonyl-piperazine fragment were synthesized and their structures were characterized by ^{1}H, ^{13}C and ESI-MS. The *in vivo* and *in vitro* anti-inflammatory activities of target compounds were evaluated by using classical para-xylene-induced mice ear-swelling model and ELISA assays. Furthermore, docking studies were performed in COX-2 (4PH9). The *in vivo* anti-inflammatory assays indicated that most of the target compounds showed significant anti-inflammatory activities. Docking results revealed that the anti-inflammatory activities of compounds correlated with their docking results. Especially, compound **6o** exhibited the most potent anti-inflammatory activity *in vivo* with the lowest docking score of -17.4 Kcal/mol and could significantly inhibit the release of LPS-induced IL-6 and TNF-α in a dose-dependent manner *in vitro*.

Keywords: inflammation, chalcone, derivatives, anti-inflammatory activity, COX-2

Inflammation is a complex biological process which seriously threatens human health. Exaggerated and prolonged inflammation may cause various diseases, such as arthritis, sepsis, and even cancer.[1] At present, the most widely used drugs in treating