Anti-inflammatory indomethacin analogs endowed with preferential COX-2 inhibitory activity

Aim: The undeniable indomethacin potency has always suffered serious obstacles such as gastric damage.
Continuous attempts to develop potent yet safe indomethacin analogs have never ceased. **Results:**
Herein are new indole derivatives **4a–h** and **5a–c**, which were synthesized via Fisher indole reaction, evaluated
for both their *in vivo* anti-inflammatory activities using rat paw edema method and their *in vitro*
cyclooxygenase inhibitory activities. Then ulcerogenic liability, physicochemical parameters and molecular
docking modeling were performed for the most potent ones. **Conclusion:** Promising results were
obtained, where compound **4f** was the best anti-inflammatory agent and preferential COX-2/COX-1 inhibitor
(90.5% edema inhibition, selective index = 65.71, ulcer index = 7.3), if compared with indomethacin
(86.7% edema inhibition, selective index = 0.079, ulcer index = 20.20).

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