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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