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).

Noha H Amin*[,1], Mohammed T El-Saadi[1], Ahmed A Hefny[1], Ahmed H Abdelazeem[1,2], Heba AH Elshemy[3] & Khaled RA Abdellatif[3,4]

[1]Department of Medicinal Chemistry, Faculty of Pharmacy, Beni-Suef University, Beni-Suef 62514, Egypt

[2]College of Medicine, Al-Rayyan Colleges, Al Madinah Al Munawarah, 41411, Kingdom of Saudi Arabia

[3]Department of Pharmaceutical Organic Chemistry, Faculty of Pharmacy, Beni-Suef University, Beni-Suef 62514, Egypt

[4]Pharmaceutical Sciences Department, Ibn Sina National College for Medical Studies, Jeddah 21418, Kingdom of Saudi Arabia