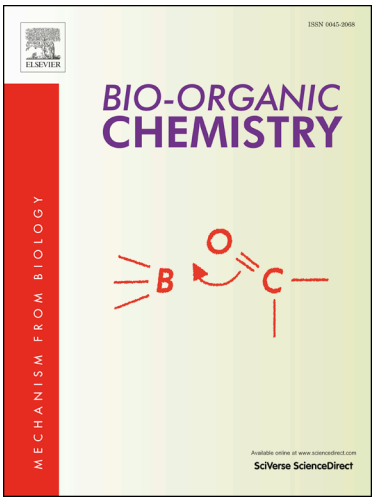

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Design, synthesis and evaluation of some pyrazolo[3,4-d]pyrimidines as anti-inflammatory agents

Gina N. Tageldin[a*], Salwa M. Fahmy[a], Hayam M. Ashour[a], Mounir A. Khalil[a], Rasha A. Nassra[b], Ibrahim M. Labouta[a]

[a] Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Alexandria, Alexandria 21521, Egypt
[b] Department of Medical Biochemistry, Faculty of Medicine, University of Alexandria, Alexandria, Egypt

*Author for correspondence:
Tel.: +20 34 871 317
Fax: +20 34 873 273

ginatageldin@yahoo.com

Abstract:

New pyrazolo[3,4-d]pyrimidines substituted with various functionalities or attached to a substituted pyrazole ring through different linkages were synthesized. The synthesized compounds were evaluated for their anti-inflammatory activity using *in vitro* COX-1/COX-2 inhibition assay and *in vivo* formalin induced paw edema and cotton pellet-induced granuloma assays. Results revealed that compounds **17b** and **18** possessed COX-1/COX-2 selectivity indices higher than diclofenac sodium and celecoxib. However, compounds **16a,b** exhibited selectivity indices higher than diclofenac sodium and nearly equivalent to celecoxib, whereas, **9b** displayed selectivity index comparable to diclofenac sodium. *In vivo* anti-inflammatory data showed that compounds **9b, 16a, 18** displayed anti-inflammatory activity higher than both references in the formalin induced paw edema model. On the other hand, the pyrazolyl derivatives **9b, 16b** and **17b** displayed anti-inflammatory activity about 2-2.5 fold that of diclofenac sodium and nearly 8-10.5 fold that of celecoxib in the cotton pellet-induced granuloma assay. The ulcerogenic effect of the active compounds was also investigated and results revealed that compounds **16a, 17a,b** and **18** showed good gastrointestinal safety profile. Based on this, compounds **16a** and **18** were considered as safe and effective leads in managing acute inflammation, while, **17b** was prominent in controlling chronic inflammation.

Keywords:

Pyrazolo[3,4-d]pyrimidines, Pyrazoles, Anti-inflammatory activity, Ulcerogenic effect, COX-1/COX-2 selectivity index