

Accepted Manuscript

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

Gina N. Tageldin, Salwa M. Fahmy, Hayam M. Ashour, Mounir A. Khalil, Rasha A. Nassra, Ibrahim M. Labouta

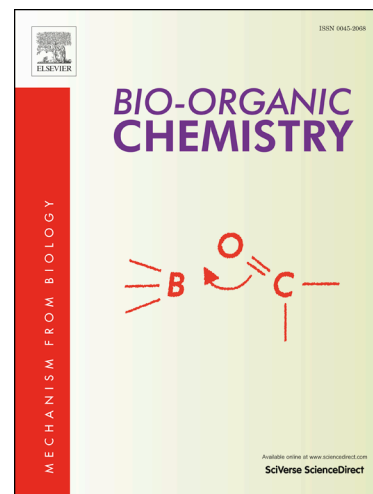
PII: S0045-2068(17)30874-X
DOI: <https://doi.org/10.1016/j.bioorg.2018.03.030>
Reference: YBIOO 2320

To appear in: *Bioorganic Chemistry*

Received Date: 19 November 2017
Revised Date: 25 March 2018
Accepted Date: 31 March 2018

Please cite this article as: G.N. Tageldin, S.M. Fahmy, H.M. Ashour, M.A. Khalil, R.A. Nassra, I.M. Labouta, Design, synthesis and evaluation of some pyrazolo[3,4-d]pyrimidines as anti-inflammatory agents, *Bioorganic Chemistry* (2018), doi: <https://doi.org/10.1016/j.bioorg.2018.03.030>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.



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

Download English Version:

<https://daneshyari.com/en/article/7771456>

Download Persian Version:

<https://daneshyari.com/article/7771456>

[Daneshyari.com](https://daneshyari.com)