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Synthesis, cyclooxygenase inhibition, anti-inflammatoryevaluation and ulcerogenic liability of new 1-phenylpyrazolo[3,4-d]pyrimidine derivatives.

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Abstract

A new group of 1-phenylpyrazolo[3,4-d]pyrimidine derivatives 14a-d-21 were synthesized from 2-(6-methyl-1-phenyl-1H-pyrazolo[3,4-d]pyrimidin-4-yloxy)acetohydrazide (12). All the synthesized compounds were evaluated for their cyclooxygenase (COX) inhibition, anti-inflammatory activity and ulcerogenic liability. All the target compounds were more potential in inhibiting COX-2 than COX-1. Compounds having pyrazolyl moiety in a hybrid structure with pyrazolo[3,4-d]pyrimidine scaffold (14a-d, 16 and 17) showed higher edema inhibitionpercentage activities (34-68%) and the 5-aminopyrazole derivative (14c, ED_{50} = 87.9 µmol/kg) was the most potent one > celecoxib (ED_{50} = 91.9 µmol/kg). While, the in vivo potent compounds (14a-d, 16, 17 and 21) caused variable ulceration effect (ulcer index = 0.33-4.0) comparable to that of celecoxib (ulcer index = 0.33), the pyrazol-3-one derivative (16) and the acetohydrazide (21) were the least ulcerogenic derivatives showing the same ulcerogenicpotential of celecoxib.

KEYWORDS:

Anti-inflammatory; cyclooxygenase inhibition; pyrazolo [3,4-d] pyrimidine