عنوان مقاله:

Designing and Synthesis of Novel Celecoxib Derivatives with Aminosulfonylmethyl and Azidomethyl Substituents as Selective Cyclooxygenase-۲ Inhibitors

محل انتشار:

مجله دانشگاه علوم پزشکی کرمان, دوره 14, شماره 1 (سال: 1387)

تعداد صفحات اصل مقاله: 10

نویسندگان:

A.H Ebrahimabadi - Assistant Professor of Medicinal Chemistry, School of Pharmacy, Kerman University of Medical Sciences and Health Services, Kerman, Iran

.H Irannejad - Medicinal Chemistry Ph.D. Student, School of Pharmacy, Tehran University of Medical Sciences and Health Services, Tehran, Iran

خلاصه مقاله:

Introduction: Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) are used in treating pathologic conditions such as fever, pain and inflammation by inhibiting cyclooxygenase and consequently prostaglandin production. Recently , the discovery of different isoforms of this enzyme, Cyclooxygenase-۱ (COX-۱) and Cyclooxygense-۲ (COX-۲), has led to the synthesis and introduction of novel drugs with selective inhibitory effect on COX-۲, the isoform produced in pathologic conditions (celecoxib in ۱۹۹۷ and rofecoxib in ۱۹۹۹). This study was carried out to design and synthesize two novel celecoxib derivatives with potential selective COX-۲ inhibitory activity. Method: The derivatives were designed according to the Structure-Activity Relationship (SAR) data of selective COX-۲ inhibitors. The condensation reaction of ۴-hydrazinobenzoic acid and ۴,۴,۴-triflouro-۱-ptolylbutane-۱,۳-dione led to the formation of ۴-(۵-p-tolyl-۳-(trifluoromethyl)-۱H-pyrazol-۱-yl)benzoic acid [۸]. The carboxyl group of this acid was reduced to hydroxyl and then converted to chloride by freshly distilled thyonyl chloride. Successive reaction of chloride derivative with sodium sulfite, phosphrous pentachloride and ammonia led to the formation of sulfonamide derivative and reaction of it with sodium azide led to the azide analogue. Results: About ۴ grams of each derivative has been synthesized (total yield ۶۰-۷۰%) and their chemical structures have been verified using appropriate spectroscopic methods. Conclusion: In this study, two novel celecoxib analogues with a methylene bridge distance between sulfonamide and azide functional groups and the rest of the molecule were designed and synthesized according to the SAR data of selective COX-۲ inhibitors. This methylene group brings the pharmacophoric sulfonamide and azide functional groups closer to the binding site and leads to better binding. Furthermore, this methylene group provides free rotation to pharmacophore to attain appropriate conformation for better binding. Hopefully, pharmacological evaluation of derivatives, which is currently in progress, .will confirm these assumptions

کلمات کلیدی:

Synthesis, Design, Nonsteroidal anti-inflammatory drugs (NSAIDs), Cyclooxygenase, Rofecoxib, Celecoxib