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Design and synthesis of New Methyl4-Hydroxy-1-Alkyl-2-aryl 5-Oxo 2,5-Dihydropyrrole-3-Carboxylate Derivatives as Selective COX-2 Inhibitors

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Abstract:
The non-steroidal anti-inflammatory drugs (NSAIDs) are among the most commonly medications in the world. The mechanism of action of these drugs is the inhibition of cyclooxygenase (COX) enzyme, which catalyzes the first step of the biosynthesis of PGG2 from arachidonic acid. COX isozymes exist at least in two isoforms, COX-1 and COX-2.The constitutive COX-1 isozyme is found in plateletes, kidneys, and the gastrointestinal tract and is believed to be responsible for the maintenance of physiological functions such as gastro protection and vascular homeostasis. In contrast, the COX-2 enzyme is the inducible isoform that is produced by various cell types upon exposure to cytokines, mitogens, and endotoxins released during injury and therefore molecules that inhibit its enzymatic activity would be of therapeutic value. The gastrointestinal side effects associated with NSAIDs are due to the inhibition of gastroprotective PGs synthesized through the COX-1 pathway. Thus, selective inhibition of COX-2 over COX-1 is useful for the treatment of inflammation and inflammation-associated disorders with reduced gastrointestinal toxicities when compared with NSAIDs. The recent market withdrawal of some coxibs such as rofecoxib and valdecoxib due to their adverse cardiovascular side effects clearly delineates the need to develop alternative structures with COX-2 inhibitory activity. For this reason novel scaffolds with high selectivity for COX-2 inhibition need to be found and evaluated for their anti-inflammatory effects. As a result, in this study, new methyl4-hydroxy-1-alkyl-2-aryl 5-oxo 2,5-dihydropyrrole-3-carboxylate derivatives were designed and sythesized based on the structure-activity relationship of selective COX-2 inhibitors. A mixture of 4-methylthiobenzaldehyde, arylamine derivatives and para-toluene sulfonic acid (PTSA) as a catalyst in ethanol was stirred at room temperature for 1 hour until a white precipitate appeared. Then, dimethylacetylenedicarboxylate (DMAD) was added. The reaction was stirred at room temperature until a new precipitate appeared. Finally, the resulting precipitate was recrystallized with ethanol. In the next step, a solution of Oxone in water was added to a well-stirred solution of the resulting product and diethyamine as a catalyst in acetonitrile. After the completion of the reaction, the precipitates were filtered and recrystallized with ethanol. All the target compounds were synthesized in good to high yields and the chemical structures were confirmed by IR, 1HNMR and Mass spectra. A novel series of methyl4-hydroxy-1-alkyl-2-aryl 5-oxo 2,5-dihydropyrrole-3-carboxylate derivatives was designed and synthesized as selective COX-2 inhibitors in good yields. The target compounds were characterized via IR, 1HNMR and Mass spectroscopies. The COX-2 inhibitory activity of the target compouds is under investigation.

Keywords: Design , Synthesis, COX-2 Inhibtors, Dihydroprrole

References:
1. Zarghi, A., & Arfaei, S. (2011). Selective COX-2 inhibitors: a review of their structure-activity .1 relationships. Iranian journal of pharmaceutical research: IJPR, 10(4), 655