SYNTHESIS AND BIOLOGICAL EVALUATION OF 4-[2-ALKYLTHIO-4(5)-(4-SUBSTITUTEDPHENYL) IMIDAZOLE-5(4)-YL] BENZENESUFONAMIDES AS SELECTIVE COX-2 INHIBITORS

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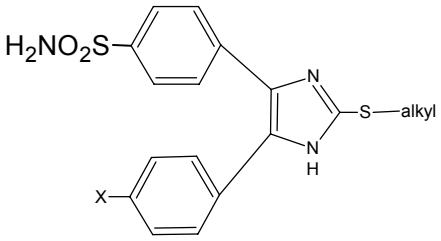
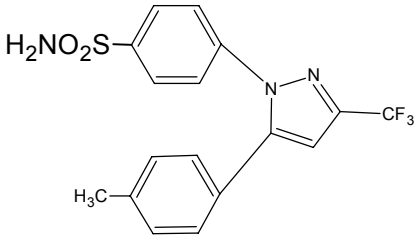
Selective COX-2 inhibitors currently provide effective treatment of inflammatory disease states such as rheumatoid arthritis and osteoarthritis[1,2].Diarylheterocycles constitute a major class of selective COX-2 inhibitors. In this regard celecoxib possesses a central five-membered pyrazole ring [3,4]. Structural-activity relationship (SAR) studies for the diarylheterocycles class have shown that SO_2NH_2 pharmacophore and SEt substituents provides optimum COX-2 selectivity and potency [5]. We designed, synthesized and evaluated biologically 4-[2-alkylthio-4 (5)-(4-substitutedphenyl) imidazole-5 (4)-yl] benzenesufonamides as selective COX-2 inhibitors. Conformational analysis and superimposition of energy minima conformers on celecoxib along with biological evaluation provided a good explanation that compounds with high COX-2 inhibitory potency and selectivity can obtain by placement of SO_2NH_2 at the *para*-position of one of the phenyl ring, thioalkyl group on the imidazole ring and various substituents at the *para*-position of the other phenyl ring. COX-2 inhibitory potency and selectivity of the synthesized compounds are equal or better than celecoxib as the reference drug.





Celecoxib

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