Prodrug synthesis and biological screening of cox2 inhibitors

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Non-steroidal anti-inflammatory drugs (NSAIDs) are most widely prescribed drugs for the treatment of various inflammatory disorders including rheumatoid arthritis. However, gastrointestinal, renal and cardiovascular toxicityassociated with common NSAIDs limits their usefulness. All NSAIDs are believed to inhibit the biosynthesis of prostaglandins by inhibiting the group of enzymes called cyclooxygenases (COX). In early 1990’s, two isoforms of COX were discovered, a constitutive COX-I and inducible COX-II. The COX-I enzyme is located in normal tissues and is cytoprotective, physiologically important for GI and renal functions. On other hand COX-II is pathological, found primarily in inflamed tissues. Thus, non-selective COX inhibitors cause inhibition of both the isoforms, producing GI and renal side effects due to inhibition of COX-I. While selective inhibition of COX-II could block the prostaglandin production at the site of inflammation without affecting the beneficial prostaglandin in normal tissues such as stomach andkidneys. This led to the development of selective COX-II inhibitors with improved pharmacological profile and reduced gastric toxicity.