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Design and development of some novel esters of NSAIDs as prodrugs

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The discovery of the inducible isoform of cyclooxygenase enzyme (COX-2) spurred the search for anti-inflammatory agents devoid of the undesirable effects associated with classical NSAIDs (non-steroidal anti-inflammatory drugs). New Omeprazole ester (OM I-IV) and Rabeprazole ester (RH I-IV) prodrugs of some acidic NSAIDs (I-IV) were designed, synthesized and evaluated as mutual prodrugs with the aim of improving the therapeutic potency and retard the adverse effects of gastrointestinal origin. The structure of the synthesized mutual ester prodrugs were confirmed by melting point, IR, ¹H NMR, mass spectroscopy (MS) and their purity was ascertained by TLC and elemental analyses. The logP values of the NSAIDs (I-IV), omeprazole, rabeprazole, hydroxymethyl omeprazole (OM), hydroxymethyl rabeprazol (RH) and the target derivatives (OM I-IV & RH I-IV) were measured by routine shake flask method and computed for logP (ClogP) contained in a PC-software package. Hydrolysis study of synthesized prodrugs were also done by validated HPLC method to ensure that release of parent drugs. Ester prodrugs were evaluated for their *in-vitro* anti-inflammatory activity by inhibition of bovine serum albumin denaturation. Synthesized prodrugs showed satisfactory anti-inflammatory activity.

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