Abstract

This work aimed at improving efficacy and reducing toxicity of non-steroidal anti-inflammatory (NSAIDs) and anti-bacterial drugs by designing and synthesizing mutual prodrugs with dual activities. The NSAIDs were ibuprofen, flurbiprofen and aspirin, which contained a carboxylic group as part of their structure. The antibacterial included ampicillin, metronidazole, isoniazid, sulfamethoxazole, sulfamerazine, sulfamethazine, sulfanilamide, 7-ADCA and 7-AVCA, which contained an amino group as part of their structure. In the prodrugs of these compounds the two drugs were covalently linked together forming an amide linkage. In addition to these a prodrug from benzydamine, containing amino group, and cefazoline, containing carboxylic group was synthesized, in which the two drugs formed a quaternary ammonium salt. All the synthesized compounds were characterized by use of diverse analytical techniques including elemental analysis, FT-IR, electronic spectra, ^{1}H and ^{13}C NMR, ESI-MS and single crystal XRD techniques.

The new compounds were subjected to anti-bacterial, anti-inflammatory, enzyme inhibition and toxicity tests in order to evaluate them as more effective and safe drugs with dual activities. Some of the activity related properties, which could not be determined experimentally, were determined through computational analysis. The results showed that aspirin, flurbiprofen and ibuprofen prodrugs perform better (having moderate to significant difference) than the parent drugs in anti-bacterial and anti-inflammatory tests. The computational analysis also suggests that the prodrugs possess better druglike properties and bioavailability with slight variations. Thus this study clearly indicates that mutual prodrug is an advantageous option where a concomitant treatment is required.