Bio-amidation of (S)-ibuprofen with Benzylamine : *In silico and in vitro* anti-inflammatory Activity Evaluation

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Abstract:

Non-steroidal anti-inflammatory drugs (NSAIDs) are widely used for the management of pain and inflammation. Despite their therapeutic efficacy, conventional NSAIDs, like ibuprofen, are associated with notable gastrointestinal toxicity, which is partly attributed to the presence of a free carboxylic acid functional group in their chemical structure. To circumvent this problem by reducing some of their undesirable effects and improving their effi¬ciency, their transformation into amide or ester func¬tionalities, as well as their isosteres, seems the best solution, since these derivatives may retain the activity of the parent acids and lead to a decrease of their gastrointestinal toxicity. Here, we described an efficient preparation of (S)-N-benzyl-2-(4-isobutylphenyl)propanamide: (S)-AMD via direct condensation of (S)-IBU and benzylamine catalyzed by the immobilized Candida antarctica lipase fraction-B. This study is coupled with the evaluation of the inhibitory potency of the prodrug amide through docking simulations into the active sites of the human hCOX-2 (5KIR) enzymes. In addition, the potential anti-inflammatory activity of (S)-AMD compound was assessed using an albumin denaturation inhibition assay. The results demonstrated that the synthesized prodrug exhibits superior anti-inflammatory properties compared to the parent compound, (S)-ibuprofen, and may be considered a promising selective COX-2 inhibitor.

Keywords:

Ibuprofen, prodrug amide, CAL-b, enzymatic amidation, NSAIDs, hCOX2.