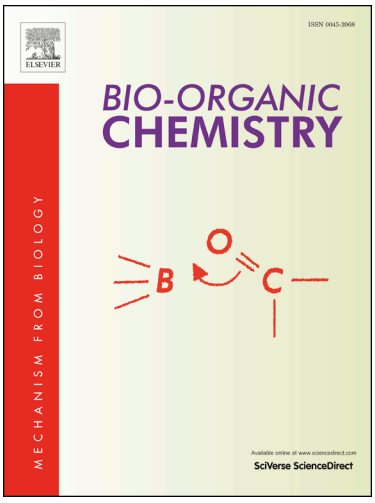

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Abstract

Inflammation is a fundamental physiological process that is essential for survival of human being but at the same time is one of the major causes of human morbidity and mortality. In the past decade, numerous advances have taken place in the understanding and development of novel anti-inflammatory drugs. Therefore, investigation of newest anti-inflammatory agents is still a major challenge. In this study, novel and successfully synthesized naproxen-derivatives indicated powerful anti-inflammatory properties as potent of COX-1 and/or COX-2 inhibitors are reported. Results obtained revealed the presence of very potent derivatives with % inhibition of the oedema by 100% in addition to enzyme inhibition values that can reach 92%. The molecular docking and molecular dynamic calculations have been studied. Thus, new potent candidates for further investigation as prospective non-steroidal anti-inflammatory drug were proposed. Furthermore, twenty of the synthesized derivatives have been selected by the NCI, USA for anti-cancer screening and some of the tested compounds showed good % growth inhibition and some selectivity against some cell lines such as melanoma, non-small cell lung and colon cancer with GI% values ranging from 60.9-82.8%. Structure activity relationship has been performed and molecular modeling studies and molecular dynamic simulations have been performed for more explanation of the action of the synthesized compounds.

Key words: Synthesis, Naprosyn analogs, COX-1, COX-2, anti-inflammatory activity, antitumor screening, Docking studies, Dynamic simulations study, NCI cancer screening.