World Academy of Science, Engineering and Technology
International Journal of Bioengineering and Life Sciences
Vol:17, No:09, 2023

Design, Synthesis, and Evaluation of Small Peptides for Managing Inflammation: Inhibition to Substrate Approach

Authors : Palwinder Singh, Baljit Kaur, Sukhmeet Kaur

Abstract : Amongst a library of rationally designed small peptides, (H)Gly-Gly-Phe-Leu(OMe) was identified, reducing prostaglandin production of COX-2 with IC50 60 nM vs. 6000 nM for COX-1. The 5 mg Kg-1 dose of this compound rescued albino mice by 80% from capsaicin-induced paw licking and recovered it by 60% from carrageenan-induced inflammation. The mode of action of the compound for targeting COX-2, iNOS, and VGSC was investigated by using substances P, L-arginine, and veratrine, respectively, as the biomarkers. The interactions of the potent compound with COX-2 were supported by the isothermal calorimetry experiments showing Ka 6.10±1.10x104 mol-1 and ΔG -100.3 k J mol-1 in comparison to Ka 0.41x103 ±0.09 mol-1 and ΔG -19.2±0.06 k J mol-1 for COX-1. This compound did not show toxicity up to 2000 mg Kg-1 dose. Furthermore, beyond the conventional mode of working with anti-inflammatory agents through enzyme inhibition, COX-2 was provided with a peptide-based alternate substrate. Proline-centered pentapeptide iso-conformational to arachidonic acid exhibited appreciable selectivity for COX-2 overcoming acetic acid and formalin-induced pain in rats to almost 80% and was treated as a substrate by the enzyme. Hence, we suggest small peptides as highly potent and promising candidates for their further development into an anti-inflammatory drug.

Keywords : small peptides, cyclooxygenase, inflammation, substrate
Conference Title : ICBCMCCB 2023 : International Conference on Bioorganic Chemistry, Medicinal Chemistry and Chemical Biology
Conference Location : Vancouver, Canada
Conference Dates : September 25-26, 2023