Characterization of Non-steroidal Anti-inflammatory Compounds as Potential Induced Hypersensitivity: A Computational Study

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ABSTRACT

Non-steroidal anti-inflammatory drugs (NSAIDs), including ketoprofen, flurbiprofen, and ibuprofen, are widely used analgesic and anti-inflammatory agents but are also well-recognized triggers of hypersensitivity reactions. While many NSAID-induced reactions arise through non-immunological cyclooxygenase inhibition, increasing evidence suggests that a subset involves immune-mediated mechanisms associated with major histocompatibility complex (MHC) proteins. In this study, an integrated computational approach was employed to characterize the potential of selected arylpropionic acid NSAIDs to interact with MHC class I (PDB ID: 2XPG) and thereby contribute to hypersensitivity induction. Molecular docking was performed to evaluate binding affinity and interaction patterns, followed by molecular dynamics (MD) simulations and normal mode analysis (NMA) to assess the stability and conformational behavior of the most favorable complex. In addition, absorption, distribution, metabolism, and excretion (ADME) properties were predicted to evaluate pharmacokinetic suitability. Docking results revealed that ketoprofen exhibited the strongest binding affinity toward MHC (−8.3 kcal/mol), surpassing flurbiprofen and ibuprofen. MD simulations over 100 ns demonstrated that the ketoprofen–MHC complex was structurally stable, supported by low RMSD values, consistent hydrogen bonding, stable radius of gyration, and favorable solvent accessibility profiles. NMA further confirmed the rigidity and coordinated motions of the complex, indicating a stable binding mode. ADME profiling suggested acceptable drug-likeness and pharmacokinetic characteristics. Collectively, these findings suggest that ketoprofen may interact stably with MHC class I molecules, supporting a potential immunological contribution to NSAID-induced hypersensitivity. This study provides mechanistic insights and a computational framework for evaluating NSAID–MHC interactions, warranting further experimental validation.

Keywords: Non-steroidal; non-immunological; MHC; ketoprofen induced hypersensitivity; molecular docking; molecular dynamics; ADME profiling.

Bahrain Med Bull 2026; 48 (2): 3170-3176

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