Host-Guest Complexation Behaviour of NSAIDs with β-Cyclodextrin: A Molecular Dynamics Study

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Cyclodextrins (CDs) are cyclic oligosaccharides that are used as functional excipients to modify the physical, chemical, and biological properties of drugs via forming inclusion complexes. The outer surface of CDs is more hydrophilic than the interior and hence entrap guest molecules in the cavity. Among three natural CDs (α, β, and γ), β-CD is widely used due to its favourable pharmaceutical and toxicological properties. A series of docking inspired Molecular Dynamics (MD) simulations were carried out using NAMD 2.1; MD code with CHARMM-36 force field to examine the host-guest inclusion behaviour of β-CD and selected Non-Steroidal Anti-inflammatory drugs (NSAIDs); Aspirin, Ibuprofen, Piroxicam, Meloxicam, Ketoprofen, Indomethacin, Naproxen, Diclofenac and Acetaminophen. Resulted trajectories were analyzed to find out the energy and Solvent Accessible Surface Area (SASA) changes during the complexation and to identify the inclusion parts of the guest molecules. The result revealed that the inclusion complex formation is possible even with electronegative functional groups of drug molecules, especially when they have oxygen, particularly through carboxylic functional groups and other heteroatoms, confirming that the β-CD-cavity is not strongly hydrophobic. Molecules are in contact with β-CD molecule probably by making hydrogen bonds, and they further stabilize the complex. Drugs can freely move within the β-CD cavity and the complexes are dynamic and are predominantly found around an average energy conformation, which is not the lowest energy state. Naproxen, indomethacin, ibuprofen, and ketoprofen are indicated to form the most stable complexes with β-CD.

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