

Curcumin Derivatives as Potent Inhibitors of Inducible Nitric Oxide Synthase in Osteoarthritis: A Molecular Docking Study

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Abstract : Osteoarthritis (OA) is a degenerative disorder affecting millions of people worldwide. Nitric oxide (NO) was found to play a catabolic role in the development of osteoarthritis. It is a toxic free radical gas generated during the metabolism of L-arginine by the enzyme Nitric oxide synthase (NOS). Inducible Nitric Oxide Synthase (iNOS) is one of the isoform of NOS, and its overexpression leads to the excessive formation of NO that results in pathophysiological joint conditions. Several synthetic anti-inflammatory drugs and inhibitors are present to date, but all showed side effects and complications. Therefore, the pursuit of natural disease-modifying drugs remains a top priority. Curcumin is an active component of turmeric, and the past few decades have witnessed intense research devoted to the antioxidant and anti-inflammatory properties of curcumin. The present study focused on curcumin and its derivatives in the search for new iNOS inhibitors for the treatment of osteoarthritis. We conducted a molecular docking study on curcumin and its four derivatives; cyclocurcumin, tetrahydrocurcumin, demethoxycurcumin and curcumin monoglucoside with iNOS using CLC Drug discovery work bench 3.02. We selected two co-crystallized ligands for this study; tetrahydrobiopterin and N-omega-propyl-L-arginine present in complex with the enzyme iNOS. Results showed the best binding affinity of N-omega-propyl-L-arginine with cyclocurcumin and curcumin monoglucoside that exhibit binding energies of -65.2 kcal/mol and -68 kcal/mol respectively. Whereas with tetrahydrobiopterin, best binding scores of -64.7 kcal/mol and -62.2 kcal/mol were found with tetrahydrocurcumin and demethoxycurcumin respectively. This information could open doors of research for the designing of novel drugs using herbs such as curcumin for the treatment of inflammatory joint diseases.

Keywords : curcumin, iNOS, molecular docking, osteoarthritis

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