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XANTHINE OXIDASE INHIBITORY PROPERTIES OF 1,2,3,4-TETRAHYDROISOQUINOLINE DERIVATIVES

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Xanthine oxidase (XO) is a versatile metalloflavoprotein enzyme that is best known for its rate-limiting role in the purine degradation pathway. Therapeutic inhibition of XO is based on its role in a variety of diseases that is attributed either to the hyperproduction of uric acid, or the hyperproduction of reactive oxygen species. Herein, we report the assessment of XO inhibitory properties of 24 1,2,3,4-tetrahydroisoquinoline derivatives, among which compound 16 exhibited IC50 value of 135.72 ± 2.71 μM. The interaction of compound 16 with XO enzyme was simulated using the Site Finder module, molecular docking and molecular dynamics. Molecular modeling suggests that interactions with Met 1038, Gln 1040, Thr 1077, Gln 1194 and Val 1259 are an important factor for inhibitor affinity toward the XO enzyme. Our proposed binding model might be beneficial for the discovery of new active 1,2,3,4-tetrahydroisoquino-line-based inhibitors of XO enzyme.

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Key words: *xanthine oxidase inhibition, 1,2,3,4-tetrahydroisoquinolines, molecular docking, molecular dynamic simulation*