# MOLECULAR DOCKING STUDIES OF NEW 2-ARYL-QUINAZOLIN-4(3H)-ONES AS NOVEL XANTHINE OXIDASE INHIBITORS

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**RESUMO**

INTRODUCTION: Many patients undergoing chemotherapy are affected by hyperuricemia, due to the accumulation of uric acid. It is formed as the final product of the catabolism of purines. The final pathway is the metabolism of hypoxanthine into xanthine and xanthine into uric acid, both of which are converted by enzyme xanthine oxidase. A drug that acts a competitive inhibitor of this enzyme is allopurinol, where the inhibited enzyme starts to accumulate both xanthine and hypoxanthin, which are more soluble and easier to be eliminated by urine [1]. Currently, febuxostat is an option in the European market, in case of allopurinol intolerance [2]. OBJECTIVE: Based on evidence of potential antitumor effect, a new series of previously synthesized quinazolin-4(3*H*)-ones were evaluated by molecular docking with xanthine oxidase. MATERIALS AND METHODS: The crystalline structure of xanthine oxidase from *Bos taurus* is available in PDB with the code 3BDJ (resolution: 2.0 Å). The study was conducted using the AutoDock Vina program [3]. The structure of the binders were built in the ChemDraw Ultra 16.0 program and the Chem 3D program built the optimal conformations with energy minimization. The Pymol Molecular Graphics System, Version 2.0.7 and the Discovery Studio Visualizer 21.1.0.20298 analyzed the results. The size of the box used was 30x30x30 and with spacing of 0.375 Å. RESULTS AND DISCUSSIONS: Compounds 01-06 were previously synthesized. The dock score values obtained for the analyzed compounds range from -10.3 to -8.4 kcal.mol$^{-1}$. The quinazolin-4(3*H*)-one 06 interacts with the active site of xanthine oxidase with energy of -10.3 kcal.mol$^{-1}$ through hydrogen bond formation involving Ala1079 (1.66 Å). It is also possible to observe pi-pi stacking interactions involving Phe914 (3.68 and 3.62 Å) and Phe1009 (4.68 Å). CONCLUSION: Based on studies of molecular docking, it is suggested that target compounds 03 and 06 are potential candidates for xanthine oxidase inhibitors, considering that the affinity energies are higher than that of the drug allopurinol. REFERENCES [1] Seth, R.; Kydd, A. S.; Buchbinder, R.; Bombardier, C.; Edwards, C. J. Allopurinol for chronic gout. *Cochrane Database Syst Rev.*, 2014, *2014*(10), CD006077. [2] Frampton, J. E. Febuxostat: a review of its use in the treatment of hyperuricaemia in patients with gout. *Drugs*, 2015, *75*(4), 427-438. [3] Trott, O., Olson, A. AutoDock Vina: improving the speed and accuracy of docking with a new scoring function, efficient optimization, and multithreading. *J Comput Chem*, 2010, *31*, 455-461. Sponsorship: CAPES and FAPESP. Resumo sem apresentação.

**PALAVRAS-CHAVE**: molecular docking, quinazolin-4(3H)-one, xanthine oxidase

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