عنوان مقاله:

In silico study of dimethyltryptamine analogues against ۵-HT۱B receptor: Molecular docking, dynamic simulations and ADMET prediction

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خلاصه مقاله:

Introduction: The ۵-HT۱B receptor has a potential role in various psychiatric disorders such as depression, anxiety, and post-traumatic stress disorder. The objective of this study was to perform docking and molecular dynamics simulation to evaluate at atomic level the behavior of N,N-dimethyltryptamine (DMT) on ۵-HT۱B receptor.Methods: In this study, initially, a search for DMT was performed using the PubChem database. Subsequently, molecular docking was executed using AutoDock Vina based in PyRx ۰.۸ with a ۹۵% analogy. Additionally, ergotamine (ERG) and serotonin were used as control. Then, it ran a total of ۱۰۰ ns molecular dynamics simulations on ۵-HT۱B bound with DMT, serotonin, ۱۱۲۸۱۴۷۷۵, and ERG. Finally, pharmacokinetic prediction and IV acute toxicity for analogues and DMT were performed.Results: It was possible to show that ۱۱۲۸۱۴۷۷۵ had the lowest binding energy with the receptor. In addition, ۱۱۲۸۱۴۷۷۵ presented great conformational stability, low mobility, and stiffness compared to the control ligands: ERG, serotonin, and DMT subsequent dynamic analysis. With respect to the free energy calculation, contributions such as Van der Waals, electrostatics, and nonpolar interactions for all systems, were highlighted.Conclusion: ۱۱۲۸۱۴۷۷۵ showed affinities with ۵-HT۱B receptor and evidenced notable behavior by molecular dynamic simulation according to root-mean-square deviation (RMSD), root-mean-square fluctuation (RMSF), solvent-accessible surface area (SASA), the radius of gyration, number of hydrogen bond, and free energy calculated. These results established the possible relevance of in-silico studies in search of DMT analogues against the ۵-HT۱B receptor, which may be associated with alterations such as depression and anxiety, and may become future study molecules for the treatment of this type of disorder.

کلمات کلیدی: