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2,3-dihydro-1H-isoindoline derivatives as novel drugs for Parkinson's disease: *In silico* and an *in vivo* evaluation

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Parkinson's disease is a chronic neurodegenerative disorder that eventually leads to progressive disability, this occurs as a result of the destruction of dopaminergic neurons of the substantia nigra. The purpose of the current treatment is to cover the deficiency of dopamine, but due to the high degree of homology between the D2 and D3 receptor, it has been difficult to obtain selective compounds for one of the two receptors. Therefore, the aim of the present study was to design and evaluate a series of 2,3-dihydro-1H-isoindoline to test their selectivity for the dopamine D2 receptor. Docking results showed that the ligands that have more affinity for the D2Hu receptor are molecules MD2m13-13S, MD2f13-6S and MD2g13-7S with a ΔG of -7.67, -7.18 and -6.99 Kcal/mol respectively and interact with 12 amino acid residues in the orthosteric site that are reported as important for recognition. In the study of the molecular and toxicological properties, the isoindolines showed that possess favorable characteristics as potential drugs. Taking into account the *in silico* results, it carried out the synthesis of the molecule MD2a13-1 and its structure was confirmed by IR, ¹H and ¹³C NMR and mass spectroscopy. The *in vivo* evaluation showed that this compound has effect on motor activity of male C57BL/6 mice in the MPTP model. These results allow us to try other candidates who might possess the same properties and also perform binding studies that can give us more evidence about the selectivity for the dopamine D2 receptor.

Biography

Erik Andrade Jorge is a Doctorate student in the Department of Biochemistry at Instituto Politecnico Nacional. He is a chemist-pharmaceutical-biologist and has a Master's degree in Pharmacology and is currently in the fifth semester of the Doctorate in research in medicine. Currently, he has three different research lines one of these is cancer cell proliferation, another one is in Parkinson's disease and the third one is in obesity. He has been focused on the rational drug design based on the molecular mechanisms of different pathologies.

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