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Design, synthesis and evaluation of a diphenylborinic dopa-derivative for Parkinson's disease in a murine model

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Boron containing compounds (BCC) are used as antiseptic and antineoplastic. Recently, they are introduced for treatment of multiple diseases. The knowledge about the mechanism of action, toxicology and pharmacokinetics profile for each BCC have let us to suggest the employment of some of these in several human maladies. Some of these BCC act by means of interaction with G-Protein coupled receptors such as adrenergic or dopamine receptors. The former receptors are involved in multiple pathologies, among these one is Parkinson's disease. The activation of some type of dopamine receptors (D2 family) is an attractive mechanism for inducing improvement in patients with Parkinson disease. In this work, we designed a boron-containing dopa-derivative (E-Levo) tested with high affinity on the D2 dopamine receptor and with a binding pose similar to that reached for some agonists on the dopamine receptors, involving interaction with residues well-known as key for receptor activation. Then, we synthesized E-Levo compound and tested it in a Parkinson's disease murine model induced for MPTP (80 mg/ Kg divided in 4 dosis) administration. The intra-peritoneal administration of this compound improves the performance of mice in motor (open field, rotarod and pole) tests, in similar mode as it was observed the improvement after levodopa administration, but an initial sedative effect was observed. On the basis of the current results, we hypothesized that E-levo interacts on dopamine receptors. However, additional studies are required in order to establish the mechanism(s) of biological action.

Biography

García-Ávila Ana K has completed his Bachelor-training from Escuela Superior de Medicina del Instituto Politécnico Nacional in Mexico City. She is working in Medicinal Chemistry Research projects from the last two years. She is particularly interested in the action of some molecules on Neurodegenerative Disease. Currently, she is enrolled in a program of social service in medical research and is starting a MD program for surgical training.

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