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Enzyme inhibitory activity of dihydroisoquinoline alkaloids derivatives in view of their physicochemical properties

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Dihydroisoquinoline alkaloids are well known in medicinal chemistry due to their wide spectrum of biological activities. They display antimicrobial, antiviral, antiparasitic, antioxidative, anticancer and antipsychotic properties (including D-amino acid oxidase (DAAO) inhibitory activity). DAAO is an enzyme that catalyzes oxidative deamination of D-amino acids. This flavoprotein is found in mammalian liver, kidney and brain. D-amino acids (e.g., D-serine, glycine) are involved in neuronal signaling being co-agonists of NMDA receptor. NMDA receptor is believed to play a major role in the pathophysiology of schizophrenia. Hypofunction of this receptor is thought to be related with behavioral and neurobiological deficits observed in this disease. Probably, DAAO inhibition and hence D-serine level increase may alleviate symptoms of schizophrenia. In our study, a series of 3, 4-dihydroisoquinoline-3-carboxylic acid derivatives were design, synthesized and tested for the DAAO inhibitory activity. Relationship between the activity and structure of the selected compounds was studied. An effect of halogen substituents on the inhibitory activity of tested dihydroisoquinoline alkaloids was examined. The physicochemical properties and druglikeness (like log P, ligand lipophilicity efficiency, molecular weight, number of rotatable bonds, hydrogen bond donors, hydrogen bond acceptors, polar surface area, etc.) of tested 3, 4-dihydroisoquinoline-3-carboxylic acid derivatives were calculated. Moreover, geometry of studied compounds was optimized with the help of HyperChem software (Hypercube, Inc.) to obtain some molecular descriptors. Docking studies of selected, one of the most potent inhibitor was performed.

Biography

Solecka J is Medical Researcher, Associate Professor. She completed her PhD in 1996, Faculty of Pharmacy, Medical Academy in Warsaw, Poland. Since 1983 until present she is employed at the NIPH-NIH, Poland. She is the head of the Laboratory of Biologically Active Compounds at NIPH-NIH. She has published more than 38 papers in reputed journals. She is conducting as a project manager within a POiG grant (co-financed from European Regional Development Fund within Operational Programme "Innovative Economy"). Her achievements include 4 patents.

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