Seminario de Química Orgánica

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AULA SEMINARIO DQO – 3º piso – PAB. II – CIUDAD UNIVERSITARIA
AULA VIRTUAL DQO: https://zoom.us/my/qo.aula01 - Clave: exactas20
YouTube: https://www.youtube.com/channel/UCyIYRdx196IH55Do6PVMzXA

"Unveiling and Leveraging the Neuroprotective Potential of Tetracyclines: A Journey from Biophysics to Pharmacology"

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The escalating prevalence of Parkinson's disease (PD) underscores the need for innovative therapeutic interventions since current palliative measures, including the standard L-Dopa formulations, face challenges of tolerance and side effects while failing to address the underlying neurodegenerative processes. Here, we introduce DAD9, a novel conjugate molecule that aims to combine symptomatic relief with disease-modifying strategies for PD. Here we introduce the rational design, synthesis, and biological properties of the concept drug DAD9, a novel dopaminergic agonist with neuroprotective effects that result from coupling a non-antibiotic TC with DA. This compound aims at simultaneously offering both symptomatic replacements of DA and neuroprotective effects attributed to TC, in the same molecular entity. Notably, the synthesis of DAD9 proved to be a straightforward process, providing a foundation for potential structural modifications aimed at enhancing desired pharmacological attributes. Through structure-based drug design, biophysics, cell culture, animal models, and computational biology, we showcase the potential of DAD9, which had no effects on PD-relevant off-targets tested, is structurally unable to be oxidized into toxic DA derivatives, and retained or improved anti-inflammatory, antioxidant, and -Syn antiaggregant and anti-seeding effects in vitro. Importantly, DAD9 also preserved the ability to bind and activate DRs, additionally highlighted by molecular docking. These findings position DAD9 as a potential neuroprotective dopaminergic agonist, promising advancements in PD therapeutics.