Research Project Proposal
Academic year 2019-2020

Project Nº 22

Title: Design, synthesis and biological evaluation of novel selenides as antitumoral agents

Department/ Laboratory.
Department of Pharmaceutical Technology and Chemistry

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Summary

Cancer is one of the most dangerous diseases and millions of people suffer or die from cancer each year. There are no particularly good medications available at present. Extensive studies of selenium compounds have demonstrated their antitumor and chemopreventive activities in a vast array of experimental models. In the present project, considering our experience in the field of antitumoral agents, we proposed by applying the molecular hybridization approach, the synthesis of new series of molecules containing selenium in different chemical entities such as selenide, which are linked through different nexus to carbo or heterocycles of confirmed efficacy as antitumoral agents. The potential anticancer activity of the synthesized selenocompounds will be tested in a preliminary screening against six cancer cell lines of different types of tumors. Depending on their cytotoxic activity and selectivity, hit compounds will be selected in order to unveil their mechanism of action, their capacity to induce programmed cell death, to modulate cell cycle and to affect proteins of certain signaling pathways. Furthermore, their possible effect over some selenoproteins involved in tumor processes (GPx, TXNRD, SelS y SePP) will be studied. Additionally toxicological and pharmacological properties for the hit compounds, as well as supramolecular associations and mutagenic/anti-mutagenic effects will be determined. After the fulfill of the above mentioned assays, molecular modeling techniques will be used to establish quantitative structure-activity relationships, allowing the re-design of the hit compounds, along with docking studies over the proteins involved in the signaling pathways affected by these hit compounds, which should allow us to optimize their pharmacological profile.

Material and Methods

Chemistry: Organic synthesis, infrared spectroscopy, NMR spectroscopy, mass spectrometry, HPLC etc

Biological evaluation: Cell culture, molecular biology (western blot, ELISA; flow cytometry etc)

This TFM can follow with the PhD degree.

yes	
no	**X**

Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?