IN SILICO STUDIES ON TYROSINASE INHIBITORS AS POSSIBLE MULTITARGET AGENTS FOR TOPICAL TREATMENT OF INFLAMMATORY DERMAL DISEASE

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Our research is focused on multitarget molecules acting as inhibitors of two enzymes implicated in dermal conditions such as psoriasis and hyperpigmentation. Our molecular targets include lipoxygenases, a family of enzymes that are involved in many inflammatory diseases as well as tyrosinase which is responsible for the production of melanin and it is common to be induced by inflammation causing post inflammatory hyperpigmentation. As a result we focused on molecules that inhibit the action of these enzymes and could be used to treat topically dermal conditions like psoriasis. Reviewing the literature we collected several different groups of tyrosinases inhibitors and we examined *in silico* their drug-likeness and ADMET properties in order to define their route of administration, their safety, their carcinogenicity, mutagenesis and their metabolism.

In order to succeed our goal, we used several in silico programs such as Molinspirations, Molsoft, Swiss-Admet and others. Among the tested molecules were included Coumarine derivatives, Chalcone derivatives, Thiosemicarbazones, and Kojic Acid derivatives. *In silico* platforms offer an easy, fast and reliable tool to work with a large amount of new molecules and to examine their druglikeness in terms of safety, ways of administrations and stability.

The results from our analysis reveal that Chalcone derivatives present drug ability, better physicochemical profile and ADMET characteristics and are expected to be more appropriate for topical treatment compared to other chemical categories. The three most potent derivatives are nontoxic. The values LogP, LogKp and MW which are the most important to predict the abililty of a molecule to penetrate the dermal barrier and to be active for topical treatment, are very promising for them. These derivatives are subjected to QSARs analysis. A QSAR model was applied to predict their possible lipoxygenase inhibition. These results will help in vitro experiments, the design and the synthesis of new potent multitarget candidates for treating inflammatory dermal diseases.