S1 - MODELACIÓN MOLECULAR Y COMPUTACIÓN APLICADA / *MOLECULAR MODELING AND APPLIED INFORMATICS*

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Introducción: La solubilidad es una propiedad fisicoquímica, esencial en los procesos biológicos de los fármacos. Su determinación experimental conlleva varias limitaciones, como el elevado tiempo invertido y el consumo de cantidades considerables de muestra, por lo cual en los últimos años han sido aplicados con este propósito distintos métodos de modelación molecular, como los estudios QSPR que buscan establecer relaciones cuantitativas entre la estructura química y alguna propiedad de la molécula de interés, a partir de la información que recogen sus descriptores moleculares. El objetivo del presente trabajo fue definir modelos matemáticos para la predicción de la solubilidad acuosa de compuestos orgánicos de interés farmacéutico de amplia variabilidad estructural, en rangos de pH ácidos (1−1,3; 1,4−1,7; 1,8−2,1; 2,2−2,5). **Materiales y Métodos:** Fueron empleados los programas computacionales ACDLabs, en la construcción de la serie de entrenamiento; MODESLAB, para calcular los descriptores moleculares; IBM SPSS Statistics, para la reducción de datos y BuildQSAR, para la obtención y optimización de los modelos. **Resultados:** Se obtuvieron cuatro modelos de regresión lineal múltiple, uno para cada rango de pH, relativamente sencillos, en función de dos descriptores moleculares representativos de la distancia de enlace y la hidrofobicidad respectivamente, como variables que influyen significativamente en la variación de la solubilidad de los 592 compuestos incluidos en la serie de entrenamiento. Los modelos resultaron eficientes, pues exhibieron coeficientes de correlación y determinación y errores estándar del estimado cercanos a la unidad. **Conclusiones:** Lo anterior sugiere que una vez validados, pudieran ser útiles en el diseño y desarrollo de medicamentos de administración oral.

PO-81: UN MÉTODO DE TOPS-MODE-QSAR PARA LA MODELACIÓN DE LA ACTIVIDAD INHIBITORIA SOBRE LA F1F0 ATP HIDROLASA DE NUEVOS DERIVADOS DE 1,4-DIHIDROPIRIDINA / A TOPS-MODE-QSAR APPROACH FOR MODELING THE F1FO ATP HYDROLASE INHIBITORY ACTIVITY OF NOVEL 1,4-DIHYDROPYRIDINE DERIVATIVES

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Introduction: The mitochondrial F1F0 ATP synthase is responsible for the majority of ATP production in mammals. Studies show that the F1F0 ATP synthase can switch to an ATP hydrolase, and this occurs under conditions seen during ischemia. This ATP hydrolysis causes wasting of ATP that does not produce work. **Materials and methods:** The mitochondrial ATP hydrolase inhibitory activity of a data set of 24 novel 1,4-dihydropyridine derivatives (DHPs), evaluated as potential anti-ischemic agent, was studied by using a TOPS-MODE-QSAR approach. The calculation of the TOPS-MODE descriptors was carried out with the software MODESLAB 1.0 and the QSAR models were obtained with MOBYDIGS 1.0. The QSAR model was transformed into a bond additive scheme in order to obtain sub-structural information. **Results:** According to the best-fit model found, the positive contribution of the spectral moments weighted with DM and vdW suggests that an increase of the volume and polar features on the structure causes an unfavourable effect on the inhibitory activity. Thereby, the greatest fragment contributions were obtained when both aromatic rings have no substituent, and with the ethyl group in the OR portion of the ester substituting the dihydropyridine ring. The nitro, F and methyl groups also show good values of fragment contribution. **Conclusion:** It has been identified the most important structural factors responsible for the ATP hydrolase inhibitory activity of a series of DHPs. The aforementioned groups elicit the better contributions to the IC_{50} values in 70% of the DHPs studied that contained at least two of these groups.

PO-82: ESTUDIO IN SILICO DE LAS INTERACCIONES ENTRE XANTANÓLIDOS Y LA CAVIDAD DE UNIÓN A COLCHICINA EN LA TUBULINA / IN SILICO STUDY OF INTERACTIONS BETWEEN XANTHANOLIDES AND THE DESESTIBILIZING BINDING POCKET COLCHICINE IN TUBULIN

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Introduction: Microtubules are dynamic assemblies of αβ-tubulin heterodimers that play a crucial role in the cellular division and have been recognized as highly attractive targets for cancer chemotherapy. To date two well characterized destabilizing-antimitotic binding domains in tubulin are known: Vinca and Colchicine. Xanthatine and 8-epi-xanthatine, derived from *Xanthium strumarium*, have antitumoral activity in vitro, related to the microtubule destabilizing properties of these vegetal compounds. The aim of this work is to predict the possible xantanolides binding modes to destabilizing-antimitotic binding pocket Colchicine in tubulin. **Materials and Methods**: A geometric optimization of xanthanolides was carried out using semiempiric methods and Density Functional Theory (DFT). Several conformations of the xanthanolides γ-lactamic ring were generated and docked, using Autodock/Vina, into the selected binding pocket conformation from available PDB files, considering flexible the ligand and some residues in the receptor. The residues involved in the xanthanolides-tubulin interactions were identified using Binana software. The obtained complexes were optimized by molecular dynamics and we performed an stability analysis of them to select the more probable binding modes. **Results:** In the obtained complex tubulin-xanthanolides, two preferential conformations in Colchicine Domain were observed. In both cases a well-defined pattern of interaction was observed with hydrophobic residues in the binding pocket. The molecular dynamics in vacuum and solvated showed a really good stabilization of these xanthanolides in this pocket getting rmsd values lower than two in all evaluated complexes. **Conclusion:** The Colchicine Domain seems to be a promising site for xantanolides to exert their destabilizing tubulin activity.

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Introduction: Cancer and cardiovascular diseases are the two leading causes of death in Cuba and in most of the countries over the world. Positron Emission Tomography (PET) has been used for diagnosis and monitoring of these diseases. Although more than 95% of PET studies are performed with [^{18}F]Fluorodeoxyglucose, current research focuses on finding new molecules with high affinity to a specific receptor. Angiotensin II Type 1 Receptor (AT_1R) is overexpressed in several cardiovascular and oncoproliferative diseases and losartan is an antagonist of this receptor. **Materials and Methods:** This work evaluated the stability, reactivity and coupling to the AT_1R of two new derivatives of losartan that are obtained from Cu-catalyzed 1,3-dipolar Huisgen cycloaddition reaction. Absorption, Distribution, Metabolism and Excretion properties (ADME) were obtained from the platform http://www.swissadme.ch/. **Results:** A stability and reactivity study was carried out by calculating: the area / volume ratio; dual descriptor; molecular electrostatic potential; Quantum Theory of Atoms In Molecules; enthalpy of formation and combustion and Gibbs's free energy with a level of theory DFT-M06-2X/6-311++G(2df,2p) and with the SMD solvation model using water as a solvent. The association with the AT_1R was investigated by Docking simulations. Molecular Dynamics (DM) simulations were performed to refine the calculation of the affinity constant of AutoDock, considering the membrane in the DM simulations. **Conclusion:** The two molecules showed good properties in comparison with other molecules proposed in previous theoretical works even respect to [^{18}F]FPyKYNE, the only PET radiopharmaceutical currently in use for AT_1R.

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Introduction: Laccases ligninolytic enzymes are phenols oxidase which due to their low specificity of substrate can catalyze the oxidation of some aromatic compounds with chemical structure similar to lignin. Some of these compounds are recalcitrant and therefore accumulate in the environment. The White Rot fungi produce these enzymes and have been studied exhaustively in this issue. **Materials and Methods:** In the present study, the production of laccase enzymes was evaluated by the *Ganoderma weberianum* B 18 strain in Solid State Fermentation (FES). The eighth day was the highest laccase activity in FES, both in enzymatic activity using 2.6 DMP as a specific substrate, as in native electrophoresis. **Results:** Seven peptides of laccase enzyme were identified at 8 days of culture and three of these were found in the same laccase enzyme of *G. weberianum* (Gene Bank: ANA53145.1 (Zhou *et al*., 2014)). This sequence was used in the Molecular Docking studies. In this analysis, different compounds of biotechnological interest were used as ligands, such as the antibiotics sulfisoxazole, trimethoprim and tetracycline and t xenobiotics benzidine and 2,4-dichlorophenol. The resulting affinity values were: -4.7, -6.5, kcal / mol for 2,4-dichlorophenol and benzidine respectively, and -6.8, -5.2 and -6.5 kcal / mol for sulfisoxazole, tetracycline and trimethoprim respectively. The controls showed strong interactions, DMP (-4.8 Kcal / mol) and ABTS (-7.1 kcal / mol). **Conclusion:** The laccase enzymes of *G. weberianum* B-18 showed *in silico* potentialities on the degradation of all the analyzed compounds, which constitute environmental pollutants