Poster Presentation

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Structural analysis of new ligands against Schistosoma mansoni

A. Mafud[1], Y. Mascarenhas[1]

[1]*Instituto de Física de São Carlos, USP, São Carlos, SP, BRAZIL*

Natural compounds have been an alternative to treat several diseases. In this sense, epiisopiloturine (EPI) [1] is an alkaloid found in Pilocarpus microphyllus (Rutaceae) leaves, with anthelmintic activity in vitro [2] and in vivo (To be publish). Unfortunately, EPI is slightly soluble in water. To solve this question, complexes and new derivatives were synthetized. Here, we present a x-ray structural analysis of the compounds: EPICu (CCDC 947608), C64H42N8O23Cl2Cu, P21, and EPIZn (CCDC 959718) C32H36N4O6Cl2Zn, P212121, both complexes with anthelmintic activity; EpiiHCl (CCDC 945616), C16H18N2O3Cl, P21, a derivative with reduce anthelmintic activity even high solubility; and epiisopilosine, EPIss C16H18N2O3, (CCDC 957103), P212121, a new active compound found in the same leaves but seasonally. The ligands conformational analysis were determined using Density Functional Theory calculations with the operator correlation of Lee–Yang–Parr (B3LYP), 6-31G++ base set, implementing two functions of polarization (d,p), to obtain the molecular electrostatic potential map. X-ray powder diffraction and thermogravimetry analysis were also performed to EPIss. The dihedral angle between the benzene and imidazole rings is feature common to such compounds, which range from 3 to 73 degrees. It is interesting to observe that the dihedral angle may be associated with the activity of these compounds, as well as other factors, since the smaller the dihedral angle, the activity is increased, even taking into consideration the EPI to this study. To compare the structures of the ligands, they were aligned and the overlay optimizer was the augmented Lagrangian method (local, no-derivative), shown in Figure 1, EPICl in green, EPI in blue and EPIss in yellow. Results showed that hydrophobic regions are conservative except for EPIss, due to its larger volume. And it may be understood through the occurrence of the CH/pi intramolecular interactions in the crystal stacking, which guarantee the EPIss larger globularity. Experimental parameters for TGA curve indicates that EPIss degradation occurs in two steps, associated with an endothermic DTA signal. XRD were performed in order to exclude the occurrence of isoforms in the crystalline powder.

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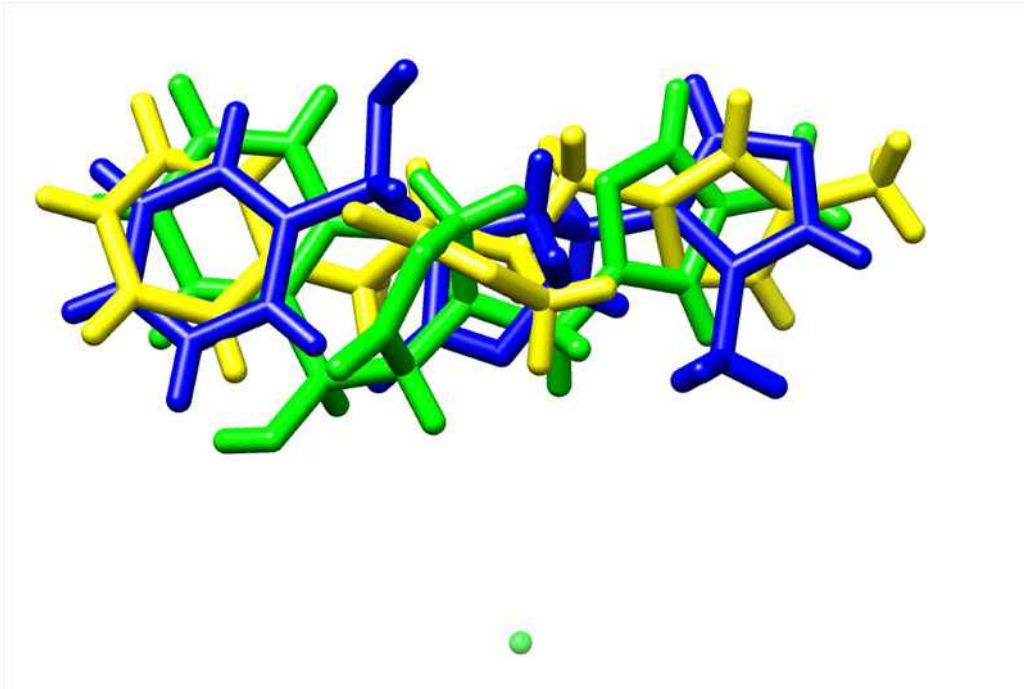

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