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Spectroscopic Studies of Human Serum Albumin Upon Interaction with An Anti-Tumor Pd(II) Complex

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Protein is an important chemical substance in our life and one of the main targets of all medicines in organism. Serum albumin, the most abundant protein in the circulatory system, is one of the most extensively studied proteins because it can interact with many endogenous and exogenous substances [1]. Binding of drugs to plasma protein is an important pharmacological parameter, since it frequently affects the distribution and elimination of a drug as well as the duration and intensity of its physiological action. The studies on this aspect can provide information of the structural features that determine the therapeutic effectivity of drugs, and have been an interesting research field in life science, chemistry, biochemistry and clinical medicine [2]. Therefore, in this investigations, we present our results on the interaction studies of HSA with an antitumoral water-soluble palladium(II) complex, which possesses dithiocarbamate and 1,10-phenanthroline ligands because of modulating activity and toxicity of platinum based drugs. The binding properties of this complex to Human serum albumin were studied using absorption spectroscopy and Circular dichroism techniques under physiological condition at 300 K and 310 K.Spectroscopic data would be used to quantify binding parameters, number of binding site and the binding constants of Pd(II) complex to HSA and thermodynamic parameters, , molar Gibbs free energy of binding, , molar enthalpy of binding and, molar entropy of binding. In addition, the experimental result indicated that this complex interacted with HSA. In general, we can assert that promising results obtained for the antitumor agent presented in this work make it possible candidates for the treatment of cancer and encourage us to design new complexes, which have better antitumor activity and helpful in the development of their potential biological, pharmaceutical and physiological implications in the future.

Keywords: HSA, Pd(II) complex, Thermodynamic Parameters, Circular Dichroism, Dithiocarbamate.

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4D-QSAR and Docking Study on the Pan Class I Phosphoinositide-3-Kinase (PI3K) Inhibitors: A Comparison to CoMFA Modeling

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At least one Holy Grail for many academic researchers and pharmaceutical research divisions alike has been to identify therapeutically useful selective PI3K inhibitors. The class I PI3Ks is currently investigated and attracted as a promising target toward anticancer therapies. A 4D-QSAR has been carried out on a series (42 compounds) of PI3Ks inhibitors. This approach makes use of the molecular dynamics (MD) trajectories and topology information retrieved from the GROMACS package. This new methodology is based on the generation of a conformational ensemble profile, CEP, for each compound instead of only one conformation, followed by the calculation intermolecular interaction energies at each grid point considering probes and all aligned conformations resulting from MD simulations. These interaction energies are independent variables or descriptors employed in a QSAR analysis. We developed the method by using docked multiple reference compounds as bioactive conformations in alignment step for building several regression models. The comparison of the proposed methodology to comparative molecular field analysis (CoMFA) formalism was performed. This methodology explores jointly the main features of CoMFA and 4D-QSAR models. Leave-N-out cross-validation (LNO), Y-randomization and application domain analysis (AD) of the obtained model were performed in order to confirm the robustness of the model in addition to analysis of the independent test set. Statistical parameters of the best 4D-QSAR model are (R2 = 0.941, q2LOO = 0.691, R2Pred = 0.751). Docking study was applied to investigate the major interactions in protein-ligand complex with CDOCKER algorithm. Visualization of the descriptors of the best model helps us to interpret the model from the chemical point of view, supporting the applicability of this new approach in rational drug design. Excellent statistical parameters and the suitable predictive ability of the results explain that this model can