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Applying Quantitative Structure Activity/Property Relationship (QSAR/QSPR) Models on Organic Compounds and its Investigation in Drug Design Chemistry

Dissertation to obtain Doctoral degree

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Summary:

This study is the application of Quantitative Structure/Property Activity Relationship (QSAR/QSPR) methods on several organic compounds. In chapter I, we are introducing the computational chemistry and its application in drug design and study of toxicology. Since a synthesis procedure in the laboratory is time consuming and expensive plus it releases a lot of chemicals to the environment, scientists nowadays try to predict models for different purposes before starting their work in the laboratory. QSAR/QSPR is one of the methods that chemists take advantages from it. In addition, in this chapter we talk about some principles such as graph theory, molecular descriptors, introducing a few matrices, etc. this principles are basically the fundamental knowledge of QSAR method.

In chapter II we discuss about the QSAR method in detail and the tools we need to apply it. For example, we talk about the function of linear regression briefly which is the base of this method; next we introduce the determination coefficient (R2) and standard error of estimate (S) that they are part of the regression method and the most important elements to value the QSAR models. This chapter also includes the definition and details about how the QSAR models should have been validated by different types of validation methods such as internal validation (Leave-One-Out), external validation method and similarity cluster validation along with their advantages and drawbacks.

Chapter III is actually introduces five organic compounds including thioxanthene, phenothiazine, serotonin, fluoxetine, and compounds with amine group which have been worked on in this study. We say that how and from where we collected a huge number of congeneric molecules that are derivatives of these four compounds. Also, we investigate two molecular properties (partition coefficient and topological polar surface area) and toxicity for every set of molecule to study their influence in the QSAR models. All the information about every single structure is included with figures and tables in this chapter. In the next step we explained how the hypermolecule is built for each set of molecule and we show the positions and atoms by figures. It should be mentioned that the general equations for each set of molecule along with the method of calculating SD (Sum Descriptors) have been investigated in this chapter. The next part is about building the QSAR models for each set of molecules and finally we validated our models with different validation methods such as Leave-One-Out (LOO) method, external validation method and similarity cluster validation method. Each set has its own plotted results and equations.

The last chapter (IV) belongs to the discussion and conclusion of the models we generated. In this chapter we show that the model predictions are reliable based on the method and the results we obtained.

Following parts are the published papers from this study and the references we used.

Keywords: QSAR models, External validation, Similarity cluster validation, Leave-One-Out validation method, LogP (partition coefficient), TPSA (Topological Polar Surface Area), toxicity, SD (Sum Descriptors), Hypermolecule.