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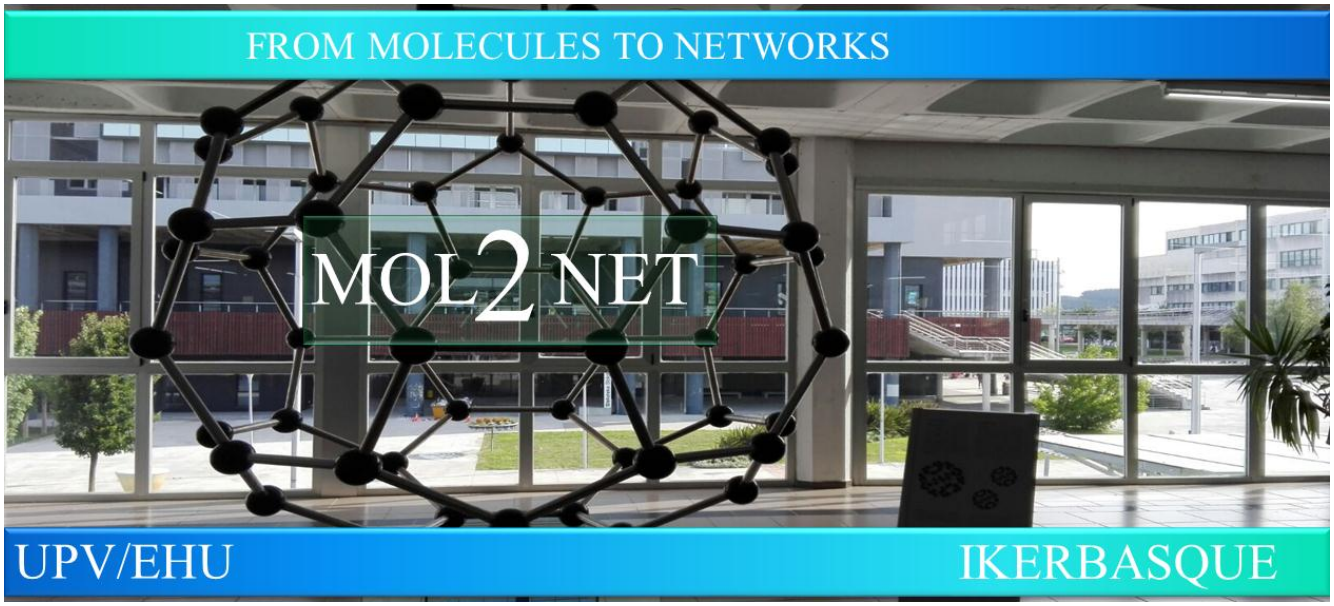

Prediction of antihistamine activity using QSAR methods

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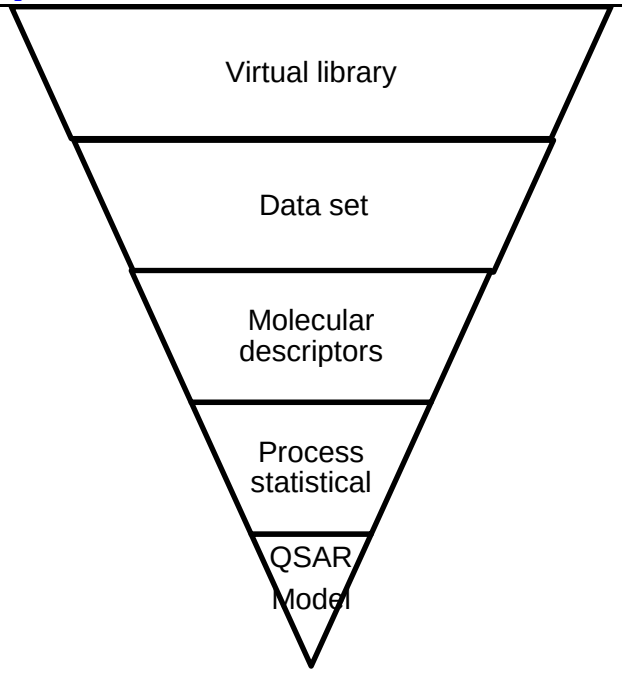
Graphical Abstract	**Abstract.**
	Antihistamines are responsible for blocking histamine receptors, thus reducing the effects of this amine on the body. However, the experimental classification of these compounds is accompanied by several limitations such as the high time invested and the consumption of large amounts of resources. QSAR methods reduce the cost and time spent discovering new drugs. The objective of the present study was to model the antihistamine activity of a series of



compounds reported in the literature for the identification of new therapeutic candidates. For this, the calculation of the spectral moments of the adjacency matrix between edges of the molecular graph with different parameters that characterize the molecules of 90 active and 250 inactive compounds was carried out. using the MODESLAB methodology. 91 descriptors related to the activity of these drugs were calculated,. The functions obtained present a Wilks Lambda of (0.421) and a high canonical correlation of (0.8351), which shows its discriminating power,.

Introduction

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. Computer-aided drug molecular design techniques can not only provide reasonable guidance for drug discovery processes, but also increase their effectiveness and efficiency by reducing costs. Quantitative structure-activity relationship (QSAR) is one of these design techniques, essential to help medicinal chemists understand how the modification of substituents at different positions of a molecular structure exerts its influence. on biological activity and physicochemical properties, so it receives great attention due to its predictive ability.

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Results and Discussion

. For the training and prediction series used in the work, 91 molecular descriptors (independent variables) were obtained. Such a number of variables would complicate any predictive study of the activity of compounds of pharmaceutical interest, making it practically impossible to find a model capable of efficiently describing the behavior of the activity based on the chemical structure. A large number of these in a function can make it difficult to explain and interpret it.

In the process of reducing variables using the general discriminant analysis, their significance was considered; As a result of this analysis, 26 variables were selected from the initial 91 (molecular descriptors previously calculated for the training series) with which the ADL was carried out in order to identify the set of descriptors with a high capacity to classify compounds into study, according to their activity. Since there are two groups, there is only one discriminant function (FD)

. **(FD)** = *5,5908* $\boldsymbol{\mu_0}$ *+1,6641* $\boldsymbol{STD_1}$*- 0,3676* $\boldsymbol{DIP_1}$*-1,4587* $\boldsymbol{DIP_2}$ *- 1.0763* $\boldsymbol{HYD_1}$ *-1,9615* $\boldsymbol{HYD_3}$*– 1,0368* $\boldsymbol{POL_1}$*-1,506* $\boldsymbol{VAN_2}$*+3,0251*

For the selection of the model, its quality and predictive capacity were taken into account, which is defined by the values in Table III, which contains the multivariate descriptive statistics necessary to globally compare the discriminative power of the function, and is given by the indices statistics λ (Wilk's lambda), D2 (squared Mahalanobis distance), F (Fischer's coefficient), CHi-squared, the corresponding p-value, the canonical correlation and the percentage of classification within each group (for each case).

. **Analysis of the effectiveness of the antihistaminic activity prediction model depending on the structure.**

An assessment of the effectiveness of the classification process was made. For this, the results of the classification matrix were analyzed. It was taken into account that the percentage of well-classified cases for the group of inactive substances was high, to avoid the appearance of "false assets" at the time of prediction, which shows the quality of the models since it avoids poor selection. of a compound at the time of rational drug design. In addition to this, special attention was paid as a final selection criterion, to the predictive capacity of the models, characterized by the percentage of good classification in the prediction series.

An increase in the number of C in the structure increases the number of atoms in the molecule and according to the equation of the mathematical model, the compound would be classified as active. If the number of atoms increases, it affects the other descriptor that also contributes positively, because as the chain increases, it becomes a more fat-soluble compound, but to a certain extent, since the increase in hydrophobicity decreases the antihistamine activity. A highly lipid-soluble drug can be more easily absorbed into the lipid tissue, reducing its arrival at the cell receptor; therefore, there must be a balance between the hydrophilicity and the lipophilicity of a molecule..

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