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A NOVEL NON-STOCHASTIC QUADRATIC FINGERPRINTS-BASED APPROACH FOR THE "IN SILICO" DISCOVERY OF NEW ANTITRYPANOSOMAL COMPOUNDS

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Keywords: *Antitrypanosomal Compounds, Chagas'Disease, LDA-based-QSAR-Model, Non-Stochastic Quadratic Indices, QSAR, TOMOCOMD Software.*

A Non-Stochastic Quadratic Fingerprints-based approach is introduced to classify and design, in a rational way, new antitrypanosomal compounds. A data set of 153 organic-chemicals; 62 with antitrypanosomal activity and 91 having other clinical uses, was processed by a k-means cluster analysis in order to design training and predicting data sets. Afterwards, a linear classification function was derived allowing the discrimination between active and inactive compounds. The model classifies correctly more than 93% of chemicals in both training and external prediction groups. The predictability of this discriminant function was also assessed by a leave-group-out experiment, in which 10% of the compounds were removed at random at each time and their activity a posteriori predicted. Also a comparison with models generated using four well-known families of 2D molecular descriptors was carried out. As an experiment of virtual lead generation, the present TOMOCOMD approach was finally satisfactorily applied on the virtual evaluation of ten already synthesized compounds. The in vitro antitrypanosomal activity of this series against epimastigotes forms of T. cruzi was assayed. The model was able to predict correctly the behaviour of these compounds in 90% of the cases.