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Assessment of correlation between thiosemicarbazones' structures and their antitubercular activities by QSAR method

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Background and Aims: Tuberculosis is the main cause of death from a single infectious disease in human. The emergence of multi-drug resistant (MDR) strains of tuberculosis and the continuing pandemic of tuberculosis emphasizes the urgent need for the development of new and potent anti-tubercular agents. An effort was focused on quantification of structure activity relationship of thiosemicarbazone derivatives.
Methods: QSAR methodology was used to develop a mathematical model to calculated MIC of thiosemicarbazone inhibiting of tuberculosis. In the first step a set of thiosemicarbazone were chosen as data set, then the data set was divided into two sets, training and prediction sets. In the second step a set of 1497 structural descriptors were calculated for each structure in training set. In analyzing the descriptors, 1170 out of 1497 showed high autocorrelation or constant value, so they were excluded from modeling procedure. In the third step, multiple linear regression (MLR) was used as a selection method to choose the most informative descriptors.
Results: According to MLR calculations, 6 descriptors were shown to be the most important. The latest model was: Log MIC = 2.592 + 0.067±(0.018) PMIX – 0.066±(0.017) PMIZ – 1.706±(1.6) qneg – 0.235±(0.039) RDF030p + 0.118±(0.026) RDF140u – 0.064±(0.021) RDF060p Statistical parameters of the result of modeling for training set are r= 0.942, standard error= 0.232 and F=290 and that of prediction set are r=0.884, standard error=0.28 and F=39. The correlation coefficient of cross-validation (Q2) is equal to 0.8186, which means that the result model can reproduce 81.86% of variances.
Conclusions: These properties shall be helpful in the development of more potent analogs.

Keywords: Tuberculosis; Structure activity relationship (QSAR); Thiosemicarbazone