BIOCHEMISTRY VERSUS BIOBIMETRICS IN MODELLING OF BIOLOGICAL ACTIVE COMPOUNDS

Sorana D. BOLBOACĂ1 and Lorentz JÄNTSCHI2
1”Juliu Hatâeganu“ University of Medicine and Pharmacy Cluj-Napoca, 6 Louis Pasteur, 400349 Cluj-Napoca, Romania, http://sorana.academicdirect.ro
2Technical University of Cluj-Napoca, 103-105 Muncii Blvd, 400641 Cluj-Napoca, http://lori.academicdirect.org

ABSTRACT

A new mathematical approach that works at the level of molecular topology is proposed for characterization of structure-activity relationship of biological active compounds. A family of molecular descriptors is generated for a set of biologic active compounds and a genetic algorithm is used for identification of the best performing multivariate regression model. A series of statistical approaches are considered for model assessment (Bolboaca and Jäntschi, 2008 [8]). In order to validate the new method the performances of the obtained model will be compared through a correlated correlation analysis with other QSAR models.

INTRODUCTION

Development of information and computer technologies introduces changes towards research concept, leading to the development of many in silico analytical and experimental methods [1,2] used in determination and prediction of drug metabolism [3]. These methods have some advantage, from which the most important are: allows determination of metabolic profile in early stages of drug design; experiments are done in a shorter time and with fewer expenses [2].

Methodology

A mathematical approach developed starting with the information obtained from the 2D and 3D structure of a chemical compounds leads to introduction of Molecular Descriptors Family on the Structure-Activity Relationship method [7]. A family of molecular descriptors is generated for the set of biologic active compounds and a genetic algorithm is used for identification of the best performing multivariate regression model (see Figure 1 for the formal description of the approach). A series of statistical approaches [8] are considered for model assessment:

- Simple correlation analysis
- Leave-one-out cross-validation analysis
- Correlated with test experiment
- Correlated with other qSAR models
- Analysis of Amino Acids Hydrophobicity

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Examples: Biometrics in Modelling Biological Active Compounds

Amino Acids Modelling [9]

- Analysis bulletins [9]
- Models assessment [10]

Inhibitory Activity on Carbonic Anhydrase (Substituted 1,3,4-Thiadiazole- and 1,3,4-Thiadiazolinedisulfonamides)

- CA IV [11]
  - CA II [12]: $r^2 = 0.9859 + 4.5643 \times \log DSCG + 2.945 \times 10^{-3} \times IapDqG + 1.4832 \times IapMdsG$
  - CA I [13]: $r^2 = 0.8965 + 4.5463 \times \log DSCG + 2.945 \times 10^{-3} \times IapDqG + 1.4832 \times IapMdsG$

Conclusion

The proposed mathematical model proved to have abilities in prediction and estimation of property and activity of chemical compounds in terms of estimation as well prediction.

References