Prediction of sites of metabolism using information about structural formulae of xenobiotics

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Drug metabolism is an important process and prior knowledge about drug metabolism and metabolites is very important for the discovery and development of new pharmaceuticals. We have developed a novel method for prediction of sites of metabolism (SOM) of xenobiotics that used only information about 2D structural formulas of molecules on the basis of modified MNA descriptors and algorithms of program PASS [1].

We have prepared different training sets for each from five P450 isoforms (CYP3A4, CYP2C9, CYP2C19, CYP2D6, CYP1A2). The average Invariant Accuracy of Prediction (IAP) for five isoforms is about 92%.

For evaluation our method we have performed prediction for the test sets contained information about biotransformation of more than 50 cardiovascular drugs. The results have been compared with SMARTCyp [2] (Version 2.4) prediction results using IAP, Top-1, Top-2, Top-3 metrics [3].

The average accuracy (using all metrics) of SOMs prediction for five isoforms for the test sets is about 80%.

The work was supported by the RFBR grant No 12-04-31670.

References

[1] http://way2drug.com/passonline

[2] http://www.farma.ku.dk/smartcyp

[3] J. Zaretzki, C. Bergeron, P. Rydberg, T.W. Huang, K.P. Bennett, C.M. Breneman. Model. RS-predictor: a new tool for predicting sites of cytochrome P450-mediated metabolism applied to CYP 3A4 Chem Inf. 2011 Jul 25;51(7):1667-89.