COMPUTER-AIDED PREDICTION OF BIOLOGICAL ACTIVITY OF PHYTOCONSTITUENTS FROM TRADITIONAL INDIAN MEDICINE AYURVEDA

Vladimir Poroikov, Alexey Lagunin, Dmitry Druzhilovsky, Anastassia Rudik, Dmitry Filimonov, Dinesh Gawande and Rajesh Kumar Goel

Orekhovich Institute of Biomedical Chemistry of Rus. Acad. Med. Sci., 10, Pogodinskaya Str., Moscow, 119121, Russia; Department of Pharmaceutical Sciences and Drug Research, Punjabi University, Patiala-147002, India; E-mail: vladimir.poroikov@ibmc.msk.ru;

A lot of empirical knowledge about pharmacotherapeutic properties of natural products (NP) is accumulated in Traditional Indian Medicine (TIM) Ayurveda, which is known earlier than 1000 years BC. This knowledge can be currently analyzed using modern computational approaches. Such studies may shed light on the basic mechanisms of TIM actions, providing the basis for rational design of new medicinal plant combinations, and identification of novel lead compounds for future pharmaceuticals.

In this work we used computer program PASS [1], which predicts over 6000 kinds of biological activity on the basis of structure-activity relationships established for more than 300,000 biologically active compounds. PASS predictions were analyzed with computer program PharmaExpert, which provides the means for analysis of PASS predictions and, in particular, integration of biological action of phytoconstituents mixtures based on analysis of drug-drug interaction. To increase the accuracy of prediction, the current PASS training set was enriched by addition of information about natural compounds with known biological activities collected from literature. The average value of the prediction error for 20-fold cross-validation is almost the same as the average value obtained with leave-one out cross-validation procedure (5.533% and 5.395%, respectively).

We selected fifty medicinal plants of TIM based on the following criteria: (1) Ayurvedic /traditional medicinal use; (2) adequately explored for phytochemical analysis, (3) unexplored for pleiotropic pharmacological studies. In order to retrieve the information about the studied medicinal plants from TIM, a web resource [2] was created. Information about 50 medicinal plants, their applications in TIM, structural formulae of their 1906 phytochemicals, as well as information about known biological activity of 288 phytoconstituents was added to the centralized relational database. Using the specialized version of PASS, predictions of biological activity spectra for all phytoconstituents of the selected medicinal plants of TIM were obtained. The results of prediction were analyzed using computer program PharmaExpert.

We will present a comparison of computational predictions with known therapeutic use of extracts from medicinal plants of TIM, new pharmacological effects predicted for a number of phytoconstituents, as well as some results of experimental pharmacological validation of the discovered hidden potential of TIM.

References

[1] http://www.way2drug.com/PASSOnline
[2] http://ayurveda.pharmaexpert.ru