APPLICATION OF IN SILICO METHODS FOR ASSESSMENT OF PHARMACOLOGICAL POTENTIAL OF RUSSIAN MEDICINAL PLANTS

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Plants growing on the territory of the Russian Federation, which has many climatic zones, are characterized by high species diversity, which causes a varied set of structures of their secondary metabolites. This makes secondary metabolites of medicinal plants a promising starting point for the search for new pharmaceuticals. A special role is played by plants already used in folk medicine, for which methods of analysis and standardization of plant raw materials have been developed and validated.

Assessment of the phytochemical composition of natural products, isolation, purification of individual phytocomponents and experimental testing of biological activity are laboratory-intensive and expensive processes. *In silico* methods based on the analysis of structure-activity relationships are widely used to identify the most promising areas of natural products research.

One of the most widely-used software for estimation of pharmacological potential of natural compounds is PASS (Prediction of Activity Spectra for Substances) [1], which predicts several thousand biological activity on the basis of structural formulae of drug-like compounds with average accuracy about 93%. Another software, PharmaExpert allows selection of compounds with the desirable combination of pharmacotherapeutic effects and mechanisms of action based on PASS predictions. Freely available in the Internet web-service PASS Online (http://www.way2drug.com/passonline/) is used by more than 50 thousand researchers from 106 countries; based on the prediction results, the most promising molecules are synthesized and the particular assays for their studies are determined.

In order to assess the pharmacological potential of officinalis medicinal plants of the Russian Federation and to make these data available to a wide range of researchers, we have developed the Phyto4Health database (https://www.way2drug.com/p4h/) [3]. The database presents the structures of chemical compounds represented in the phytochemical composition of officinalis plants and the results of computer prediction of PASS.

We performed and analyzed the results of computer prediction using PASS and PharmaExpert for phytocomponents of Russian medicinal plants. In addition, the results of our analyses were confirmed by *in vitro* and *in vivo* experiments. These included detection and laboratory confirmation of the cytotoxicity of a phytocomposition consisting of 22 phytocomponents against bladder cancer cells, confirmation of the antitumor and antimetastatic effects of a pharmaceutical composition comprising 70 phytocomponents, and detection and laboratory confirmation of the induction of CYP450 and GST by oxycinnamic acids isolated from *Cichórium íntybus L.* [4].

Some other studies of biological activity estimation using PASS & PharmaExpert with the experimental confirmation of predictions are given in publications [5-10]. Also, PASS predictions are implemented in the database of Brazilian medicinal plants [11], to identify their hidden pharmacological potential and identify the most promising directions of studies.

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