Computer-aided estimation of pleiotropic effects of drugs

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The study of the activity of many effective drugs revealed their influence on several targets, and identifying the mechanisms of the pathogenesis of a number of social diseases led to the realization of the need to develop drugs with pleiotropic actions. We have developed and validated methodology for computational assessment of pleiotropic action of biologically active substances on the basis of the analysis of "structure-activity" and "active-active" relationships. Computer program PASS is used for prediction of biological activity spectrum of chemical compounds based on their structural formula [1]. Computer program PharmaExpert [2], which provides an analysis of PASS prediction results based on the knowledge of "mechanism-effect" relationships, is used to assess the potential pleiotropic actions of chemical compounds. In the case studies we identified: anxiolytics, anticonvulsants and nootropic compounds belonging to new chemical classes; new dual inhibitors of angiotensin-converting enzyme / neutral endopeptidase and lipoxygenase / cyclooxygenase 1; nootropic effect in perindopril, quinapril and monopril; preferred clinically relevant combinations of antihypertensive drugs of different classes; components of Hypericum extracts, potentially responsible for the manifestation of asthma and drug-drug interactions. It is shown that the developed methodology is significantly more effective than the traditional methods of virtual screening.

1. Lagunin A., et al. *Bioinformatics*, 2000, **16** (8), 747-748.
2. Lagunin A., et al. *Cur. Pharm. Design*, 2010, **16** (15), 1703-1717.