MODERN ASPECTS OF CREATING OF NEW POTENTIAL DRUGS BASED ON *QuS*-PROGRAM DEVELOPMENT

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Development of drugs – is a unique multidisciplinary process aimed at creating of a new therapeutic agent with the most useful and safe properties. In the world practice development of original drug includes two functionally related stages: 1 – Study and 2 – The introduction or creation. In the first stage there is a discovery or synthesis of the new molecule of potential drug. Most of the new potential drugs (lead compounds) are discovered with using of one of three approaches: 1) chemical modification of known molecules; 2) screening of biological activity of a large number of natural compounds or their modifications; 3) direct synthesis based on the understanding of biological mechanisms, chemical structure and physical-and-chemical properties of the substance. Expenditures for the synthesis, screening and further preclinical and clinical studies of potential drug, amount up to 800-1000 millions of dollars. The duration of such studies 7–10 years.

The recent decades became critical in the studying and testing of new drugs. Intuitive (random) approach was replaced with the rational drug design that ensures the creation of the drug molecular structure based on information on the receptor structure. New domains of scientific research have developed: cheminformatics, which includes a variety of chemical libraries, computer design, combinatorial chemistry etc. Part of Combinatorial Chemistry is computer chemistry (Computer drug design: CADD). Thus, by using database of relevant substances, combining their construction with the help of proper computer software it becomes possible to design potential drugs. Having a number of compounds with known activity, QSAR method provides an opportunity to forecast the necessary structure or to specify a direction for its modification and thus significantly restrict the search. However among existing software tools for solving problems of QSAR there is no readymade software packages in free access, which would be universal with an understandable and intuitive interface. Based on these requirements, scientists from biology department of ZNU have developed a new software tool called QuS (short form of QSAR Server). The task of this tool is to integrate and coordinate the work of other software that performs specific stages.

The relevance of QuS tool is determined by using the latest in silico technologies for drug searching. For determining of the SAR / QSAR regularities significant role plays formation of database that will help to solve the problem of forecasting activity and toxicity of chemical compounds. Nitrogen-containing heterocycles are of exclusive value for the formation of databases, studying of "structure – activity – toxicity" relationships and searching for new highly efficient and low-toxic bioregulators. Pride of place among these heterocyclic systems goes to six-membered aromatic heterocycle – quinoline. Various quinoline derivatives are used both as synthons in organic synthesis and molecular design and as effective biologically active compounds. Quinoline-based drugs take an important place in the modern arsenal of antibacterial chemotherapeutic drugs.

In addition, for a number of biologically active derivatives of nitrogen-containing heterocycles there is limited or completely absent systematic study of "structure – activity – toxicity". This was the main reason for the studying of quinoline derivatives database and searching descriptors of their structure, which are important for development of QSAR models as a system for evaluation of compounds' biological effects. Received dependence equations of toxicity and activity of the studied types of quinoline derivative from 2D- and 3D- descriptors allow forecasting the levels of activity for new biologically active substances at pre-experimental stage.