QSARSOFT© WIZARD SERVICE ON DRUGS AND CHEMICALS

Subject

The Molcode's exclusive proprietary software solution encompasses the field of the fast and robust delivery and prediction of the physical, chemical, biomedical and molecular data on chemicals, drugs and other molecular materials. An accurate assessment of these properties is extremely important for chemical and pharmaceutical industry and in health, safety and environmental sectors.

Technology

The technological solution comprises unique combination of the data of very different formats and complexity as well as the engines for the generation of computational data. The data include:

- computationally predicted and experimental data on the physical, chemical, and biomedical (PCB) properties of chemical compounds;
- computationally predicted and experimental data on the environmental fate of chemicals and drugs;
- molecular characteristics (descriptors) of the chemical compounds calculated by using the theoretical physical methods;
- clinical test data (Phases I-IV) of drugs and drug candidates;
- data on the complex statistical and artificial intelligence models for the robust prediction of PCB properties of chemicals and other molecular systems.

The following software drivers are integrated for the computational data generation:

- driver for the calculation of molecular characteristics (descriptors);
- driver for the generation of complex statistical and artificial intelligence models used in the prediction of PCB properties of chemicals;
- driver for the prediction of data on the physical, chemical, and biomedical (PCB) properties and environmental fate of chemical compounds;
- driver for the prediction of chemical compounds and molecular structures with predetermined properties.

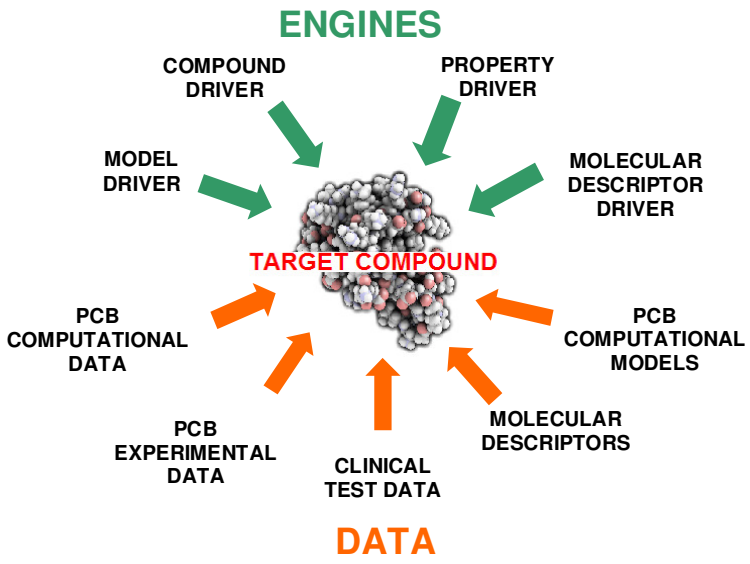
The amount of data handled with the technology is very large. The number of individual chemical compounds is in the order of millions, each compound can be characterized by hundreds of different PCB properties and up to tens of thousands molecular descriptors.

Molcode, Ltd. has developed unique specific software for each above listed driver. The most advanced theoretical methodology for problem solving has been applied in the development of this software. In addition, extensive data on all above given data types have been collected and stored in computers.

The new technology amalgamates all necessary data and computational drivers for the fast and accurate prediction of the properties of chemicals, drugs and other molecular structures (Figure 1).

For any target compound, thousands of data points on individual properties and molecular descriptors can be quickly recovered and analyzed by using the appropriate internal software drivers.

Figure 1.



The **molecular descriptor driver** enables to calculate thousands of theoretical characteristics of compounds reflecting their chemical constitution, topological and geometrical structure, electrostatic intra- and intermolecular interactions and a large variety of physical features derived from either *ab initio* or semiempirical quantum-chemical molecular wavefunctions.

The **model driver** encodes a wide diversity of mathematical models for the derivation of the relationship between the experimentally observable properties of compounds including statistical methods such as multi- and nonlinear regression, multivariate methods such as principal component analysis, partial least squares and linear discriminant analysis, and machine learning methods such as artificial neural networks, projection pursuit regression, support vector machines and others.

The **property driver** generates fast and dependably the data for any chemical compound belonging to an applicable class of structures from the menu of 250+ physical, chemical and biomedically or environmentally important properties. The driver gives also a detailed report on the computational model and the descriptors used together with the statistical evaluation of the reliability of the predicted data.

The **compound driver** is unique proprietary software for the fast construction of new compounds from large and diverse libraries of molecular fragments using the original genetic algorithms, pattern recognition techniques and predictive analytics. The new compounds integrate the best (optimum) property values for the given molecular design task.

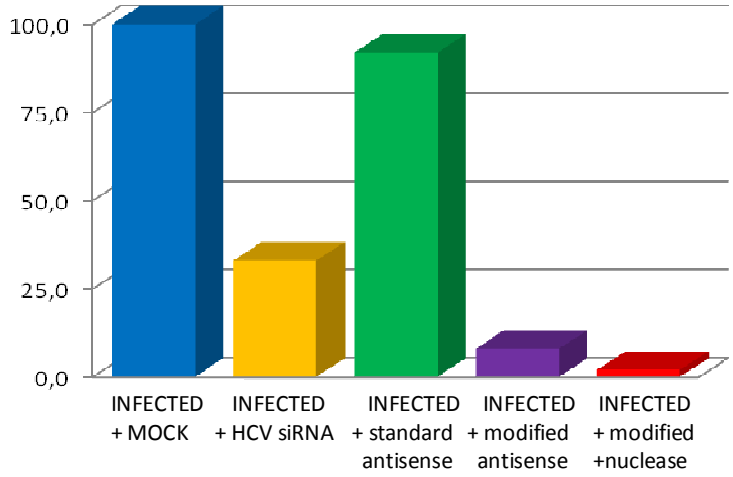
The **various data** are presented and stored in formats easily transferable between the different drivers and/ or external physicochemical and quantum chemical software.

Applications of QSARSOFT© Wizard in Drug Design

QSARSOFT© Wizard has been applied for the numerous successful predictions of the novel molecular entities including various drug candidates as a contract service. The predictions are very fast and of high efficiency.

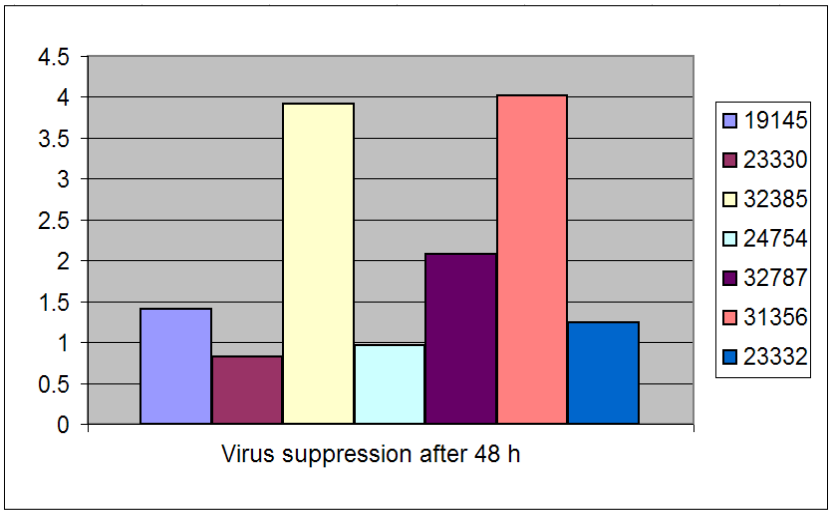
Novel oligonucleotide-artificial nuclease conjugates as efficient antivirals. The efficiency of modified antisense oligonucleotides against virus containing hepatitis C virus target sequence is demonstrated by data in Figure 2.

Figure 2. Suppression of the hepatitis C viral genomes in cell assays 24h after infection.



Novel small-molecule hepatitis C protease inhibitors. Unlike most of HCV protease inhibitors currently in development they do not mimic the structure of HCV protease substrate and thus represent novel class of inhibitors. All 7 compounds predicted by using QSARSOFT© Wizard from a diverse compound library exhibited significant antiviral activity, some at nanomolar level (see data from Figure 3).

Figure 3. Suppression of hepatitis C viral genomes in cell assays by novel HCV protease inhibitors. The compounds have code numbers.



Other novel compounds and drug candidates predicted with the help of QSARSOFT© Wizard include the following:

- novel small-molecule mimetics of the glial cell line-derived neurotrophic factor (GDNF) as possible drug candidates against Parkinson's disease, ALS and depression;
- novel small-molecule mimetics of neurotrophic factor artemin (ARTN) as possible drug candidates against neuropathic pain;
- novel small-molecule drug candidates against respiratory syncytial virus (RSV);
- others (confidential)

Market perspective

The accurate and reliable prediction of various properties of chemical compounds has become of extremely large importance. First, the national and international (European Union, OECD) regulatory initiatives require a very thorough characterization of each chemical, drug or material traded and used. The price of alone the laboratory experiments necessary for the registration of up to 150,000 chemicals according to European Union REACH directive is expected to exceed 10 billion euros and costs the lives of millions of test animals. This directive foresees, however, the possibility of an alternative generation of required data by using computational models. On the basis of QSARSOFT© software solution, Molcode has generated validated models for many properties of chemicals and offers the generation of necessary data sheets at much higher speed and lower cost as compared to the wet laboratory experiments.

Secondly, due to the more strict requirements on drugs imposed by regulatory agencies such as U.S. Food and Drug Administration (FDA), the expenses on the drug development have been rocketed up during the last decade. The main reason is the inability of researchers to predict reliably the possible clinical effects of the drug candidates that are directly related to their PCB properties. Therefore, the QSARSOFT© software will be extremely helpful as enabling early distinction of possibly hazardous or ineffective drug candidates.

The following segments of the market for the proposed QSARSOFT© Wizard on Drugs and Chemicals can be distinguished:

- chemical industry
- pharmaceutical and biotech industry
- traders of chemicals and materials
- governmental and public regulatory institutions
- universities and research institutes

The potential market of applications is huge, as each segment incorporates thousands of individual enterprises or institutions.

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