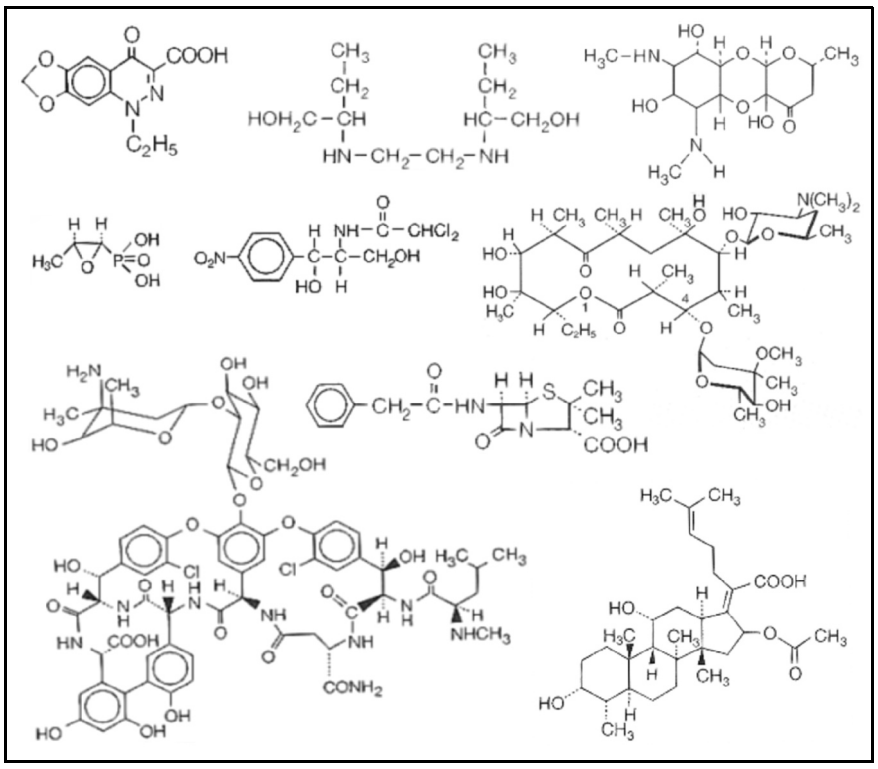
MolScore Antibiotics

Expert system for antibacterial research

==> Hit detection & validation

==> Lead selection & prioritisation

MolScore-Antibiotics discriminates between antibiotics and non-antibiotics. The expert system identifies novel antibiotic substances at the earliest stage through analysing the chemical structure of a drug candidate, its ADMET characteristics and its molecular targets.



Examples of identified molecular patterns by MolScore-Antibiotics

MolScore-Antibiotics detects all types of antibiotics, regardless of mechanism of action or molecular weight.

All antibiotic classes can be identified, including:

- macrolides, lincosamides
- penicillines, beta-lactams
- aminoglycosides
- glycopeptides
- cephalosporins
- sulfonamides
- fluoroquinolones
- streptogramins
- tetracyclines and others

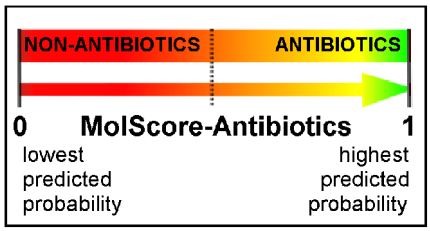
MolScore-Antibiotics has been proven to detect novel antibiotic substances with unknown mechanism of action and which are now in clinical trials.

The chemical space of antibiotics is different to that of common drugs. Extremely large structure-activity relationships (SAR) and structure-property relationships (SPR) with up to tens of thousands compounds allow the estimation of useful antibacterial chemical space.

Application & Advantages

- Ranking and selecting compounds from external suppliers before purchase or synthesis
- Selection of compounds to focus screening campaigns against bacterial diseases
- Validation of hits from primary screening
- Selects and prioritises promising antibacterial drug candidates for further development
- Prioritises derivatives even of different lead structures
- Simple usage and integration of results

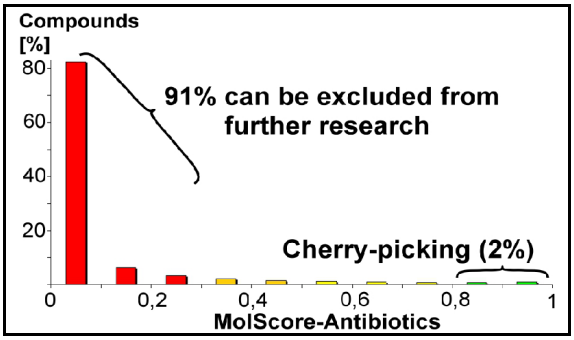
MolScore-Antibiotics calculates the probability of having antibiotic activity and is defined as a value between 0 and 1. This value correlates with the predicted probability of a substance becoming a successful antibiotic drug.



MolScore-Antibiotics uses a number of different strategies to discover novel antibiotics. It is complicated to calculate but easy to use!

Hit detection & validation

The expert system identifies compounds which are not useful for further development. To provide an example we have analysed a commercial available library composed of 200.000 compounds.



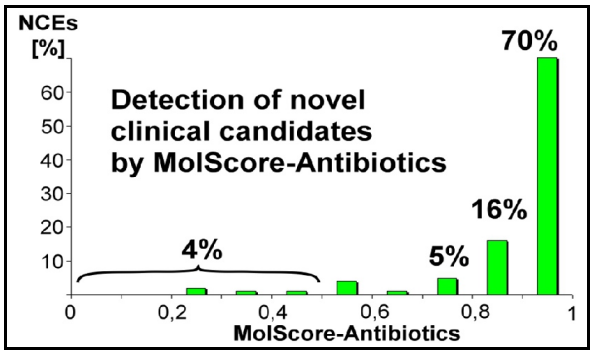
More than 91% of the examined compounds don´t fit into the chemical space of antibiotics and can be filtered out. Only 2% of the compounds had a MolScore-Antibiotics result higher than 0,8 and can be selected for further research ("cherry-picking").

In general about 60-95% of molecules can be filtered out by MolScores-Antibiotics depending on molecular patterns and properties of each molecule.

MolScores-Antibiotics focuses screening campaigns (increase of hit-rate) and validates hits from primary screening.

Lead selection & prioritisation

MolScores-Antibiotics detects and prioritises candidates for clinical development. The expert system has been validated with novel antibacterials which are now in clinical trials.



96% of diverse clinical candidates have been correctly classified as antibacterial molecules, which are suitable for further development into drugs.

This validation demonstrates the excellent prediction capability of MolScore-Antibiotics to detect clinical candidates. These results are in accordance with previous obtained results (quality of prediction in the range of 90-95%).

Oral bioavailability knowledge base and prediction

Oral bioavailability is one of the most important properties in drug development. Low oral bioavailability in clinical trials is a major reason for drug candidates failing to reach the market.

PharmaInformatic develops and licenses PACT-F, the largest knowledge base on bioavailability worldwide. PACT-F contains experimental bioavailability results of clinical trials in humans and preclinical trials in animals. The results and conditions of those trials have been taken manually from more than 5000 scientific research articles related to bioavailability.

The knowledge base has been used to develop the expert system IMPACT-F, which estimates oral bioavailability in humans much more precisely compared to animal trials. Predictions of IMPACT-F were as accurate as the common deviation between individual humans taking part in the same clinical trial (inter-subject variability in humans).

About PharmaInformatic

PharmaInformatic is a German biotech company, which provides ADME/Tox knowledge bases and expert systems to improve drug discovery and development. The company was founded in 2004 by Dr Wolfgang Boomgaarden. Before he founded the company, he worked as a professor in bioinformatics in Emden, Germany.

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