Optibrium – ADME Properties

BioSolveIT
expect actives!

The optional Optibrium module predicts key molecular parameters for absorption, distribution, metabolism, excretion (ADME). Assess these key parameters on-the-fly for your lead modification ideas, for database information augmentation, or prior to synthesis. The predictions are powered by Optibrium's highly renown and rigorously validated StarDrop® algorithms.

What is this module for?

Knowledge about the 'fate' of a compound after application is crucial during the drug design process. This involves molecular absorption, distribution, metabolism, and excretion properties (collectively referred to as 'ADME'). Every step during your design entails compound-specific, physicochemical property changes: You add a methoxy, and not only solubility will change, but this will also potentially affect the blood-brain-barrier penetration. Therefore, relia-ble predictions, processing, and interpretation of the data is a time-saver. Early and speedy assessment will save resources and help you make the best possible candidate selection for the next step.

SeeSAR and infiniSee feature a seamlessly integrated, optional Optibrium expansion to calculate important com-pound properties within the software's interface in no time. Everything is on display while you conduct your inter-active design work, changes in your molecules are visible instantaneously.

What properties are predicted?

The platforms spots the following parameters of molecules. Watch, filter, and optimize:

2C9 pK_i	Cytochrome P450 CYP2C9 pK_i prediction. Affinity estimates of the compound to bind at the enzyme involved in several metabolic drug pathways.
2D6 affinity category	Cytochrome P450 CYP2D6 classification. Compounds are predicted to be in one out of four categories: 'low' for compounds with a pK_i<5, 'medium' for compounds with a pK_i between 5 and 6, 'high' for compounds with a pK_i between 6 and 7, and *very high* for compounds with a pK_i>7.
BBB category	Blood-brain barrier classification of compounds. There will be a '+' annotation if log([brain]:[blood])≥–0.5 and a '–' category if log([brain]:[blood])<-0.5.
BBB log([brain]:[blood])	Logarithm of blood-brain partition coefficient of a compound. Use this as an indicator for CNS penetration properties of your in silico active compounds.
HIA category	Human intestinal absorption classification. Compounds that are predicted to be absorbed by ≥30% are classi-fied with a '+', compounds which are predicted to be ab-sorbed <30% are classified with a '–'.
P-gp category	P-glycoprotein 1 transport classification. Involvement of this protein, also known as multidrug resistance pro-tein 1 (MDR1) and ATP-binding cassette sub-family B member 1 (ABCB1)), is relevant for many unwanted ef-fects. The computed flag predicts whether a compound is likely to be a substrate of P-gp or not.
PPB90 category	Plasma protein binding classification. Predicts 'low' for compounds which are <90% bound and 'high' for com-pounds which are >90% bound.
hERG pIC_{50}	Prediction of pIC_{50} values for inhibition of human Ether-a-go-go Related Gene (hERG) potassium channels ex-pressed in mammalian cells. Highly relevant for drug effects on the heart.
logD	Logarithm of *n*-octanol-water partition coefficient at the physiological pH7.4. Used to describe the relationship between lipophilicity and hydrophilicity of an ionized compound.
logP	Logarithm of *n*-octanol-water partition coefficient. Used to describe the relationship between lipophilicity and hydrophilicity of a neutral compound.
logS	Logarithm of intrinsic aqueous solubility in µM for neutral compounds.
logS @ pH 7.4	Logarithm of intrinsic aqueous solubility at physiological pH 7.4 in µM for ionizable compounds.

Adding prediction models

You have your own models computed with StarDrop®? One of the big benefits of the Optibrium Mod-elRunner is the pos-sibility to be expanded with additional external or own in-house parameter calculations. Extended knowledge about the SAR of a compound series, toxicity findings, selectivity observations, and much more can be translated into a readable format for on-the-fly property calculations.

Create your own tailored set of compound properties to be calculated for strategy planning during compound evolution and hit assessment. Reviewed models submitted by the community can be downloaded and accessed here. Source and references for the model data are provided in the respective description.

To install a calculated model simply download the *.aim file, and copy it into the platform's installation directory, right into the folder *models*\, for example in `C:\BioSolveIT\SeeSAR_or_infiniSee-11.2.2\models\`. Restart the application, and your new properties shall be displayed in the tables and be ready for visualization and filtering.

References

A detailed explanation as well as references to the methods behind the calculation of the different Optibrium properties can be found the Optibrium Reference Guide here.

[1] Optibrium Ltd., StarDrop, 2022, www.optibrium.com