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Personalised services in drug discovery

Kinetic solubility and stability

Determination of kinetic solubility and stability in specific bioassay conditions

Solubility is a key physicochemical property which may cause many problems in different screening bioassay. An insufficient solubility can lead to discrepancies between bioassay, underestimated activity and toxicity, reduced hit rates and inaccurate structure activity relationship.

Moreover, in bioassay media, compounds can be subjected to degradations by several mechanisms like hydrolysis or oxidation. It is therefore of great importance to assess the kinetic solubility and stability of compounds in the specific assay conditions to avoid artefactual results.

Other early ADMET assays available

- *In vitro* cytotoxicity assay
- Spheroid Model for hepatotoxicity Study
- Kinetic solubility and stability
- CYP450 inhibition
- Permeability
- Metabolic assay

Kinetic solubility and stability

Method

Solubility:

Compound stock solutions are prepared in DMSO at a concentration depending on the final concentration in the assay. Compounds are then diluted in the buffer of interest and dispensed in triplicate in a 96-well filter plate. Plates are then incubated in the temperature, time and shaking conditions of the biological assay. At the end of the incubation, microplate's content is filtered under vacuum and collected. The concentration of compound in the filtrate is quantified by spectrophotometry.

Stability:

Compounds are incubated in the specific assay conditions. Serial samples are taken at different times and are analysed by LC-MS.

The compound stability is expressed as the percentage of remaining peak area related to the starting concentration peak area.

Method Validation

LogS measured at pH 6,5

Compounds	Shake flask	96-well filter plates
Diclofenac	-2.99	-2.47
Estradiol	-4.88	-4.74
Ibuprofen	-2.24	-2.07
Ketoconazole	-4.96	-4.71

Classification for kinetic solubility

High solubility: 60 µg/mL ; logS > - 3,92

Moderate solubility: 10-60 µg/mL ; -4,7 < logS < -3,92

Low solubility < 10 µg/mL ; logS < - 4,7

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