Plasma Stability Assay (human, dog, rat or mouse)

Background: Determination of stability of the potential drugs in plasma is indispensable in early stages of the drug discovery process, as it is crucial for pharmacokinetic readouts and has direct impact on in vivo efficacy. Certain classes of drug molecules, such as those containing ester or amide-linked groups are prone to enzymatic hydrolysis by plasma esterases, amidases or proteases. On the other hand, enzymatic activation of some prodrugs that takes place in plasma is essential for their function. Hence, plasma enzymes can significantly alter the bioavailability of the active compounds, and therefore determination of the compound stability in plasma has both pharmacokinetic and clinical significance.

Service Details: Incubations are carried out in 96-well polypropylene plates in 5 aliquots of 70 µL each (one for each time point). Test compounds (1 µM, final solvent concentration 1 %) and reference compounds Verapamil and Propantheline are incubated at 37°C. Five time points over 120 minutes are analyzed (0, 20, 40, 60 and 120 min). All tests are performed in duplicates. The samples are analyzed by HPLC-MS (API3000, AB Sciex).

Deliverable: The percentage of parent compound remaining in plasma after incubation is plotted versus incubation time; plasma half-life ($T_{½}$) is calculated from the obtained curve. Full study report is provided.

Sample Submission: A minimal accurately weighable quantity of dry compound (~1 mg or 2 µmol) or 50 µL of 10-20 mM stock DMSO solution is required for this assay. For multiple assays, lesser amount of compound per assay may be sufficient, depending on the particular project. We do not need to know structures of the molecules for ADME testing. However, brutto formulas have to be provided for all studies involving MS detection.