Contact us for more information
cls-admet.services@conceptlifesciences.com

CONCEPT LIFE SCIENCES

Concept Life Sciences: **Plasma stability**

Introduction

Plasma stability plays an important role in drug discovery and development. Rapid metabolism lowers drug exposure at the therapeutic target. Furthermore unstable compounds cause difficulties for in vitro plasma protein binding studies, and in vivo PK studies since they continue to degrade after blood samples are taken from the animals. Plasma stability is also very useful for screening prodrugs where rapid conversion is desirable. Certain functional groups such as amides, esters or lactones make compounds favorable targets for plasma enzymes such as hydrolases and esterases.

Deliverable: % test compound remaining at each time-point.

Customer provides

Compound identifier and molecular formula.
Test: 25µL of 10mM in DMSO or 0.5mg solid.

Plasma

Pooled heparinised available in a range of species e.g. human, dog, rat, mouse and monkey.

Test compound

Incubation concentration 1µM.

Format

96-well plate, shaking incubator at 37ºC.

Protocol

Plasma is warmed to 37ºC for 10 min, mixed and centrifuged to pellet any aggregated protein. The clear supernatant is aliquoted into the assay plate. Plasma is equilibrated to 37ºC and biotransformation is initiated by addition of compound solution, and mixing. 300µL final incubation volume. Standard time-points 0, 5, 15, 30, 60, 120 min (or client specific). The final solvent concentrations are 0.99% acetonitrile and 0.01%DMSO.

Positive controls

Two standard compounds benfluorex and eucatropine are used in each assay run.

Quantitation

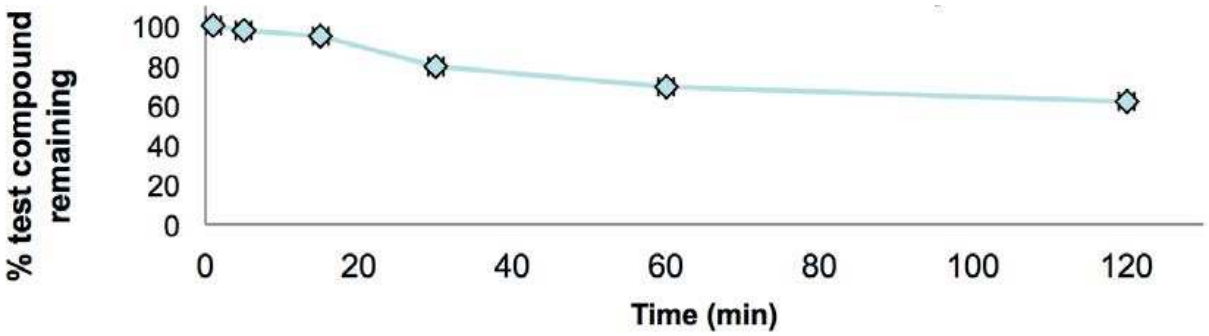
The supernatants are analyzed by LC-MS/MS using Concept Life Sciences generic analytical methods to measure the test parent compound % remaining at each time-point.

Data analysis and results

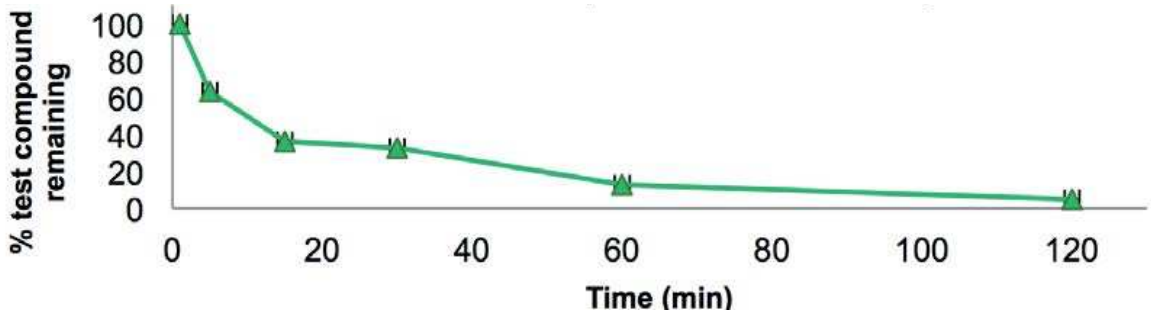
$$\text{For each test compound injection, response ratio} = \frac{\text{Test peak area}}{\text{Internal standard peak area in test}}$$

The response ratio is converted to % test compound remaining. The % test compound remaining is plotted versus time.

Benfluorex Human Plasma Stability



Eucatropine Human Plasma Stability



Eucatropine Rat Plasma Stability