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CONCEPT LIFE SCIENCES

Concept Life Sciences:
Chemical stability

Introduction

Compounds that are unstable in aqueous media may not be able to be maintained at therapeutically effective concentrations in vivo, and therefore have reduced chances of becoming a successful drug candidate. In dosing solutions, drugs may be prone to chemical degradation which may be caused by a variety of mechanisms: hydrolysis, oxidation, light-catalyzed degradation and others. In the gastrointestinal tract drugs can also be subject to chemical degradation under different conditions. It is therefore important to determine the stability of a compound prior to its administration to animals for pharmacokinetic evaluation. Stability testing in buff er solutions at room temperature or 37ºC at acidic, neutral and basic pH's in early drug discovery allows timely identification of potentially weak candidates.

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.

Buffers

A variety of buffers are available upon request. The table below lists some popular buffers with recommended pH ranges. Client selects the exact pH and temperature at which the stability test is performed.

CYP	pH
Hydrochlorate Buffer	1.0 - 2.2
Citrate Buffer	3.0 - 6.2
Phosphate Buffer	5.8 - 8.0
Fasted-State Simulated Intestinal Fluid (FaSSIF)	6.5
Fed-State Simulated Intestinal Fluid (FeSSIF)	5

Test compound

Incubation concentration 5µM.

Format

96-well format, shaking incubator at chosen temperature.

Protocol

At each specified time-point, a sample aliquot (25µL) is removed from the test incubation mixture and immediately combined into a cassette of up to 4 compounds, in 300µL ice cold methanol containing internal standard, and mixing to stop degradation.

Positive controls

Eucatropine, Benfluorex, Chlorambucil and Omeprazole.

Quantitation

Solutions 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

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

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

Concept benfluorex chemical stability