**Background Information**

- Determination of the stability of new chemical entities in plasma is important as compounds (with the exception of pro-drugs) which rapidly degrade in plasma generally show poor in vivo efficacy.

- Instability in plasma can result in misleading in vitro data which can be difficult to interpret (e.g., plasma protein binding data). Storing and analysing clinical samples from in vivo pharmacokinetic studies may also prove challenging.

- Compounds with the following functional groups tend to be more susceptible to hydrolysis in plasma: esters, amides, lactones, lactams, carbamides, sulphonamides, and peptic mimetics.

- Compounds may exhibit interspecies differences in their stability in plasma.

- Plasma stability is very useful for screening of prodrugs and antedrugs, where rapid conversion in plasma is desirable.

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**Protocol**

- **Test Article Concentration**: 1 µM (different concentrations available)
- **DMSO Concentration**: 2.5%
- **Incubation Time**: 0, 15, 60 and 120 min
- **Test Article Requirements**: 30 µL of 10 mM DMSO solution
- **Analysis Method**: LC-MS/MS quantification
- **Assay Controls**: Positive control compound which undergoes degradation in plasma
- **Data Delivery**: Percent parent compound remaining at each time point

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**Follow on metabolite profiling studies**

Cyprotex’s Plasma Stability assay can be extended to profile the main breakdown product that is formed. Options include a low resolution analysis to identify whether a metabolite is formed, or a cross species comparison to identify potential differences in metabolism which could in turn help to interpret pharmacology and toxicity data. We can also perform ion-transition analysis in order to understand the derivation of metabolites.

Please refer to Cyprotex’s Metabolite Profiling and Identification section for further details.

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To find out more contact [enquiries@cyprotex.com](mailto:enquiries@cyprotex.com)
Plasma stability has several applications: to understand data where compounds are unexpectedly rapidly cleared; to screen for prodrugs and antedrugs; and to determine the liability of drugs with susceptible structural motifs.

Plasma Stability

4 compounds were incubated with human liver and rat plasma over 120 min. These compounds show clear differences in stability following incubations with human and rat plasma (Figure 1). These data may be useful in interpreting *in vivo* efficacy, toxicity and pharmacokinetic studies.

Figure 1

Cyprotex’s Plasma Stability data for diltiazem, enalapril, eucatropine, and procaine in human and rat plasma (mean ± sd, n=3).

References