PHARMACELSUS

GBAGROUP

In-vitro Services

ADME Studies

For more than a decade **Pharmacelsus**, Germany's market-leading preclinical CRO, offers high quality drug discovery and development solutions to the pharmaceutical and biotech industry.

GLP-certified since 2008, we are able to provide GLP and non-GLP studies. Our assays support exploratory research and meet regulatory demands.

Pharmacelsus' *in-vitro* ADME programs include all studies required to improve efficacy and prognostic profiling of drug candidates addressing the following issues:

Absorption	Physico-Chemical Parameters, Stability, membrane Permeability, transport, Protein binding
Distribution	
Metabolism	Drug Interaction, metabolism, Clearance
Excretion	

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Pharmacelsus provides reproducibly high quality data for basic and challenging compounds, performs metabolite identification without the need of radio-labelled substances, and applies cassette analysis for quantification, e.g. up to 8 CYP substrates in one measurement.

Our experienced bioanalytical team supports in house and external ADME studies with optimized analytical methods enabling the detection of 10pg to 10ng amounts in biological matrices with mass resolutions up to 280,000. High-end mass spectrometry instruments (Q Exactive LC-MS/MS system with Orbitrap™ technology) allow not only the quantification of small molecules but also the analysis of larger molecules e.g. small proteins or peptides and phyto-extracts.

Basic Druggability Screening Package for Lead Optimization

At the early stage of hit-to-lead validation, key *in-vitro* assays provide necessary data to select the most potent compounds for further drug development. Our competitive basic druggability package contains the following assays:

- Aqueous Solubility testing (Kinetic)
- Metabolic Stability testing in Liver microsomes (rodents, Dogs, monkeys and humans)
- Plasma Protein binding (Ultrafiltration, rodents, Dogs, monkeys and humans)
- Bidirectional Caco2 Permeation (a-b/b-a Direction)

In-Vitro ADME Service Portfolio

The *in-vitro* team at Pharmacelsus combines experience from the pharmaceutical industry with the flexibility to adapt standard assays to accommodate for the uniqueness of your project. We support you in setting up your studies meeting the applicable regulatory requirements. Access the "druggability" of your compounds with the below set of *in-vitro* ADME assays:

Physico-Chemical Parameters
Analysis: LC-MS, LC-UV
Readout: Solubility, Half-Life

Stability in Biological Matrices
Analysis: LC-mS
Readout: Stability, half-Life, metabolite Identification

Membrane Permeability: PAMPA
Analysis: LC-mS or LC-UV
Readout: Flux (%)

Membrane Permeability: Caco2
Analysis: LC-mS
Readout: P_{app} Value, efflux ratio, Pgp Substrate Identification

Interaction with Drug Transporters
Analysis: Scintillation Counting
Readout: IC_{50}, Ki, Vmax

Protein Binding Mechanisms
Analysis: LC-mS
Readout: PPb (% fb), Brain Tissue Binding
KrbC/plasma, % fu-microsomal, % fu-brain

[1] Unique method

Metabolic Stability
Analysis: LC-mS
Readout: Clint, half-Life, metabolite Identification

Reactive Metabolite Trapping
Analysis: LC-mS(-mS)
Readout: reactive metabolite Formation

Metabolic Pathway Identification
Analysis: LC-mS or LC-UV
Readout: Proposed metabolic Pathway, metabolite abundance

CYP Inhibition
Analysis: Fluorimetry , LC-mS
Readout: IC_{50}, Inhibition mode, time-Dependent Inhibition

CYP Phenotyping
Analysis: LC-mS
Readout: Loss of Parent Compound, Cl_{int}, half-Life, metabolite Identification

CYP Induction
Analysis: LC-mS
Readout: n-Fold Induction

[2] heparG®

[1] Highly suitable for strong binders [2] Also available

Further assays are available on request e.g. assays to analyse phase II metabolism. In addition to the standard setup, all assays are offered as a fit-for-screening format. Screening assay packages will be tailored to your needs.

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