cyprotex
AN EVOTEC COMPANY

Diverse Modalities

Our comprehensive range of ADME-Tox services are flexible and customizable allowing assessment of diverse modalities whose physicochemical properties may sit outside the typical rule of 5 (Ro5) chemical space. Such physicochemical properties may create some unique challenges in performing *in vitro* assays or analysing samples by mass spectroscopy. Our capabilities in diverse modalities are underpinned by state-of-the-art analytical capabilities combined with extensive experience in the design and execution of ADME-Tox studies for a range of diverse modalities.

General Characteristics

- **Peptides**
  - generally, low lipophilicity and high hydrogen bonding capacity
  - often demonstrate low permeability, chemical and enzymatic instability, high non-specific binding, transporter uptake, low DDI risk
  - analytical challenges
- **Targeted protein degraders**
  - large, flexible molecules
  - typically high MW, high PSA, high number of rotable bonds, high non-specific binding, high plasma protein binding, P-gp efflux, CYP-mediated metabolism
  - usually poor solubility and permeability
- **Oligonucleotides**
  - high MW, negatively charged polar molecules
  - typically, low permeability, high tissue distribution, high plasma protein binding (dependent on type of oligo), nuclease hydrolysis (CYP and Phase II metabolism not relevant), low DDI risk
  - analytical challenges

Bioanalysis of Diverse Modalities

Modality	Molecular Weight	Technique	Bioanalytical Challenges
Linear peptides	< 2 kDa	Protein precipitation TQMS	Formulation analysis. Sensitivity, selectivity, recovery in biological matrix.
Complex peptides e.g., bicyclic	2–6 kDa	SPE IMS-TQMS, SPE TOF MS	Formulation analysis. Sensitivity, selectivity, recovery.
ASOs, siRNAs or oligoconjugates	5–15 kDa	▸ SPE IPLC-TQMS ▸ SPE HILIC-TQMS	Ion pair chromatography, non-specific binding, recovery.
Proteins/mAbs	5–150 kDa	▸ Protein precipitation-Digestion-(SPE) (IMS)-TQMS ▸ Protein precipitation-Digestion-(SPE) TOFMS	Complex workflow.
Targeted protein degraders	< 1.5 kDa	Protein precipitation (SPE) TQMS	Non-specific binding, recovery, multiple charging, protein binding.
Very polar small molecules	< 1 kDa	Protein precipitation HILIC/ion exchange/ion pairing TQMS	Metal binding, chromatography, recovery.

Experience

- Dedicated study managers are assigned to your project
- Consultancy from experienced ADME-Tox and analytical experts
- High quality data using validated methods
- Comprehensive range of ADME-Tox services

Liquid Handling Platforms

- Rapid pipetting (96 and 384 well)
- ECHO acoustic liquid handling
- Tecan and Agilent liquid handling platforms
- Sample and plate barcoding
- Managed by LIMS
- Sample management tracked through Titian Mosaic software

Analytical Platforms

- LC-MS/MS, LC-MS, GC-MS
- High resolution mass spectrometry (HRMS)
- Radiochemical detection (^{3}H and ^{14}C)
- SelexION differential mobility separation
- Chromatography using different separation modes (HILIC, ion pair, ion exchange and chiral chromatography)

- **Experimental Considerations:** addition of protease inhibitor, low binding tips and plates, addition of BSA
- **Analytical Considerations:** detection method, column properties, solvent composition and ionic strength, temperature and pH, solid phase extraction

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2024/09 | V1