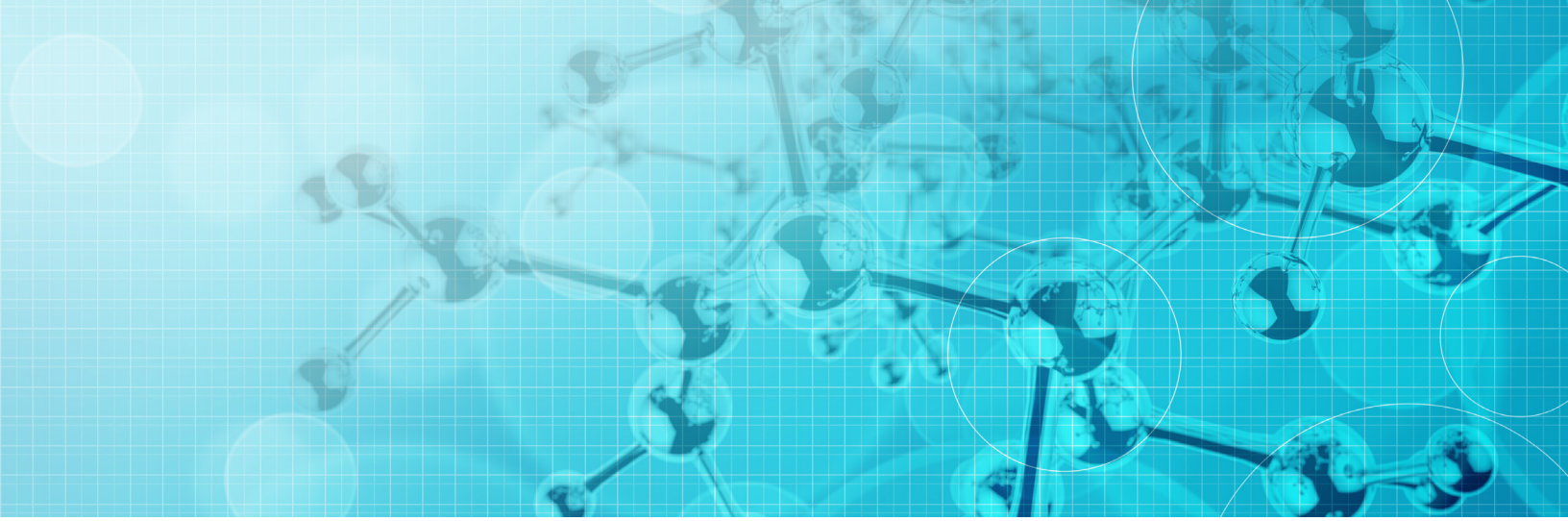


PK/PD Analysis in Rats using LC-MS

Small molecule drugs have defined chemical structures that are analyzed using mass spectrometry-based methods such as LC-MS (liquid chromatography-mass spectrometry). LC-MS is an analytical method that is widely used to analyze PK/PD profiles of small molecules that include drug product and intermediate metabolites. The combined methods of liquid chromatography (LC) and mass spectrometry (MS) allow for separation and identification of individual chemical entities in a given sample. JOINN/Biomere has expanded its services portfolio to include PK studies performed in Sprague Dawley (SD) rats.

Dexamethasone Clearance in SD Rats:
Validation studies were performed using three groups of male SD rats that were dosed with control or 2 doses of dexamethasone (0.5 or 2 mg/kg). Blood samples collected at specific times post dosing were processed to plasma and frozen at -80oC. The concentration of dexamethasone in the plasma samples was quantified using the Orbitrap Exploris 240 Mass Spectrometer (ThermoFisher Scientific).

Figure 1: Table summarizing the dexamethasone concentration detected by LC-MS from plasma samples collected from rats dosed with either vehicle control or dexamethasone.

					Time (h)								
					0	0.25	0.5	1	2	4	6	8	24
Day	Group	Dose_Level (mg/kg)	Gender	Animal ID	Concentration (ng/mL)								
D1	1	0	Male	1590	BQL				BQL				
				1591	BQL				BQL				
				1592	BQL				BQL				
	2	0.5	Male	1593	BQL	466.0	532.6	472.1	401.9	235.6	169.0	114.0	BQL
				1594	BQL	580.3	647.4	543.2	399.0	232.5	142.9	95.2	BQL
				1595	BQL	491.1	613.7	541.5	409.7	266.6	174.6	119.1	BQL
	3	2	Male	1596	BQL	1935.1	2403.6	1990.3	1434.5	792.5	446.8	234.8	BQL
				1597	BQL	2171.8	2137.3	2047.7	1381.9	713.6	384.7	208.3	BQL
				1598	BQL	1925.2	2440.3	2364.8	1760.1	1208.5	785.2	482.4	16.2

BQL: Below Lower Limit of Quantitation

Figure 2: Standard curve of dexamethasone concentration (left) and PK curves of SD rats dosed with either 0.5 or 2 mg/kg dexamethasone. Dexamethasone was undetectable in samples collected 10-12 hours after dosing.

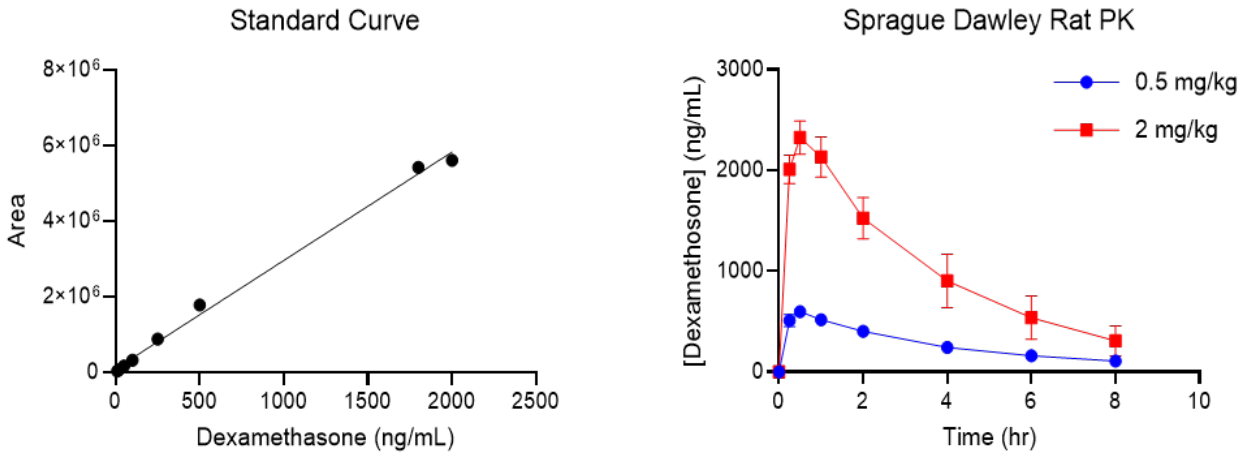
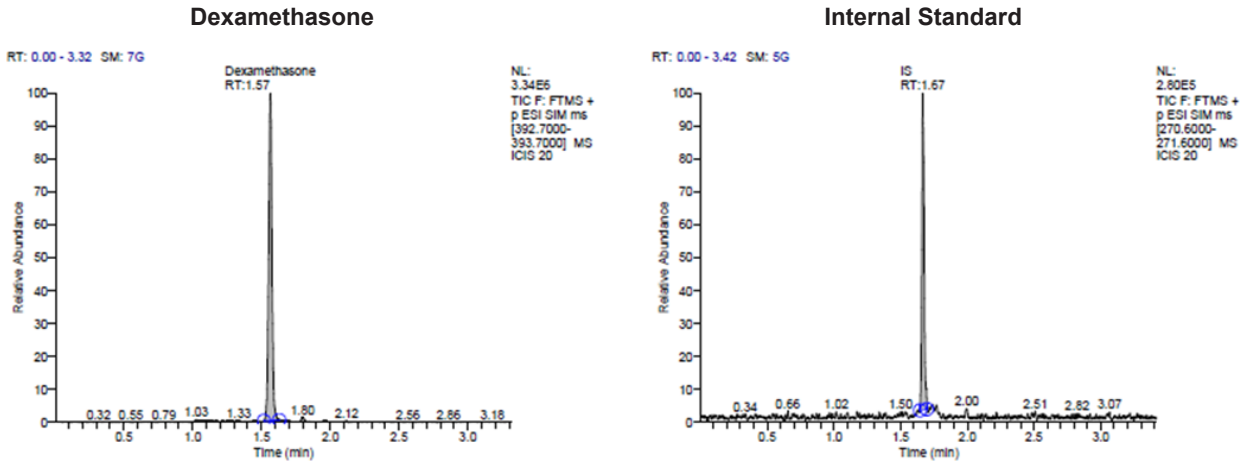


Figure 3: Sample MS data showing the internal standard peak at 270 m/z (mass to charge) ratio and the dexamethasone peak at the expected 393 m/z ratio.



Key Considerations to use LC-MS for Small Molecule PK/PD Studies:

- Analyte size and structure: smaller analytes (less than 1,000 MW) are more straightforward to quantify and larger analytes will require method development.
- Analyte stability in frozen samples: ideally the analytes should be stable at -80oC plasma samples to facilitate collection and shipping of samples prior to analysis.
- LC-MS method availability: the JOINN/Biomere team can develop new protocols for LC-MS analysis if a protocol is not available.

Learn more at: https://biomere.com/pk-pd/
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