ADME NTP Study K03021 Ionic liquid (1-Butyl-1-methylpyrrolidinium chloride) Toxicokinetics

The contractor used the abbreviation BmPy-Cl for the test article.
Sex/Species: male F344 rats.
Vehicle: intravenous, saline; oral, saline.

CASRN 479500-35-1, IONICLIQUIDS

Radiolabeled with carbon-14; N-[1-^{14}C]Butyl-1-methylpyrrolidinium chloride

Studies Performed:

- Single 5 mg/kg intravenous dose with blood sampling 7.5, 15, 30, 60, 90, 180, 360, 540, 720, 1440, 2160, and 2880 minutes postdose. (n=4 per group)

- Single 1, 10, or 100 mg/kg oral gavage dose with blood sampling 7.5, 15, 30, 60, 90, 180, 360, 540, 720, 1440, 2160, and 2880 minutes postdose. (n=4 per group)

Mean ± standard deviation values for total [^{14}C]BmPy-Cl in blood for the concentration-time curves were displayed in figures for intravenous and oral gavage dosed male rats and are not shown here. No individual animal data for toxicokinetic blood concentrations were available.

Toxicokinetics:

Concentration-time curves for total [^{14}C]BmPy-Cl in whole blood were modeled using the WinNonlin, Pharsight Corp., Mountain View, CA program. Samples below the limit of quantitation were not used in the best-fit oral and intravenous dose analyses. Predicted values for single intravenous dose parameters were calculated based on best-fit analyses using a two-compartment model fit. Blood data for time points less than 10 hours were used.

For the single oral gavage dose, BmPy-Cl was readily absorbed. [^{14}C]BmPy-Cl disappeared from blood in a biphasic manner following C_{max} (1.5 hours). The first phase appeared to be a distribution phase, followed by a slower elimination phase. The best fit analyses for the single oral gavage dose used a one-compartment model fit. Blood data for time points less than 5 hours were used for the oral dose modeling.

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Table 1: Toxicokinetic parameters for BmPy-Cl following IV (5 mg/kg) or oral (50 mg/kg) administration to male F-344 rats (N = 4 per dose route).

	Dose (µg)	AUC (min*µg/mL)	$t_{1/2\alpha}$ (min)	$t_{1/2\beta}$ (h)	CL_f (mL/min)	V_{ss} (mL)	C_{max} (µg/mL)	T_{max} (min)	*F* (%)
IV	907	274	33.3	6.8	3.3	1,495	-	-	-
Oral	8,157	1,069	20.9	5.6	7.6	-	1.8	89.1	43.4

$AUC_{[0-\infty]}$: area under the blood concentration-time curve from 0 to infinity. $t_{1/2\alpha}$: distribution half life. $t_{1/2\beta}$: terminal elimination half life. CL_f: total final systemic clearance from blood. V_{ss}: volume of distribution at steady-state. C_{max}: maximum concentration of analyte in blood T_{max}: time to maximal concentration. F: systemic bioavailability of BmPy-Cl. -: data not predicted for by pharmacokinetic models.