Negative Ion Paper Spray for the

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Overview

- Negative ion ESI techniques have always been plagued by a susceptibility to corona discharge, which harms method reproducibility
- A semi-novel method was used to quantify and monitor discharge in negative ion paper spray MS
- Good paper spray MS/MS detection was achieved for barbiturates and organophosphonates by including CCl_4 in the spray solvent to inhibit discharge

Introduction

- Paper spray MS (PS-MS)[1] is an ESI-based technique that uses a pointed substrate and a high voltage to generate an electrospray
  - ✓ Small amounts of sample and solvent
  - ✓ Cheap materials with no chemical waste
  - ✓ Rapid sample testing (1-2 minutes)
  - ✓ Good for therapeutic drug monitoring[2,3]
  - ✓ When automated, it is easily translated to fieldable and clinical MS techniques

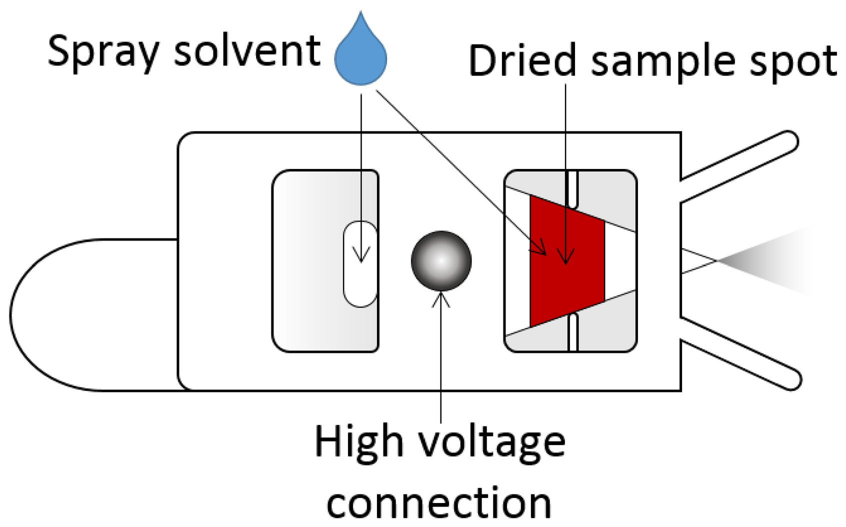

Figure 1. A Velox Sample Cartridge used for PS-MS.

- In negative ion mode, ESI techniques are highly susceptible to corona discharge because of the elevated electric field that exists around the tip
  - x Impairs method sensitivity and precision
  - x Harms attempted quantitation
  - x Is readily influenced by instrumental parameters such as the applied voltage and the tip-to-inlet distance

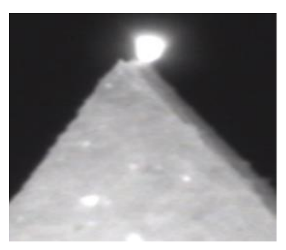

Figure 2. Corona discharge in PS-MS.

- The goal of this study was to investigate a means by which corona discharge could be prevented in negative ion PS-MS to allow for good quantitation of acidic compounds such as barbiturates and alkyl methylphosphonic acids (MPAs) from biological samples

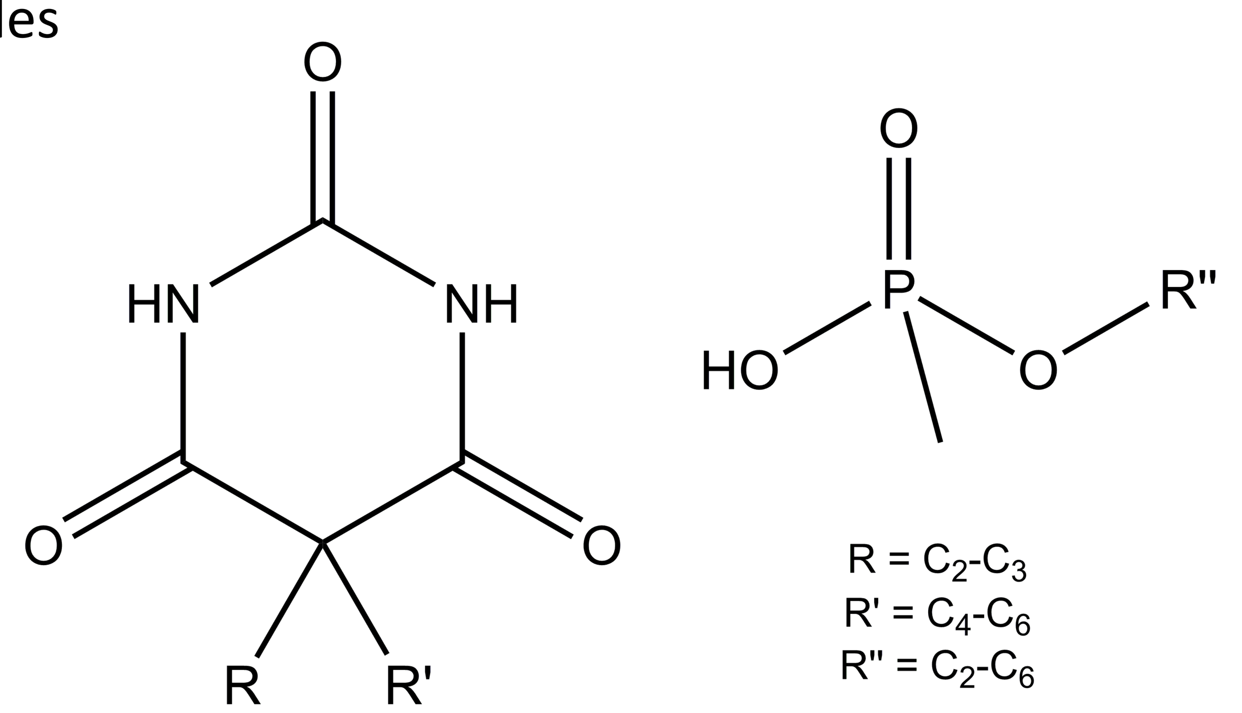

Figure 3. The general structures of barbiturates (left) and alkyl MPAs (right).

Methods

- Prosolia's automated Velox 360 PS source was used with a Thermo Q-Exactive Focus orbitrap MS, operating at 4.0 kV in negative ion mode and acquiring based on an MS/MS inclusion list
- The optimized solvent to avoid discharge was 90:10:0.01 methanol:CCl_4:NH_4OH, applied with a large delay in the pump programming to prevent excessive evaporation before spraying

Figure 4. The Velox 360 PS source attached to a Q-Exactive Focus MS.

- Eight barbiturates were quantitated down to 500 ng/mL in blood samples using phenobarbital-d5 as an internal standard (ISTD)
  - Butabarbital, butalbital, amobarbital, pentobarbital, phenobarbital, secobarbital, thiopental, and phenytoin
- Five alkyl MPAs were quantitated down to 1.25 ng/mL in blood and urine samples using their corresponding stable isotope labeled ISTDs
  - Ethyl MPA (EMPA), isopropyl MPA (IMPA), isobutyl MPA (iBuMPA), cyclohexyl MPA (CHMPA), and pinacolyl MPA (PinMPA)

Results

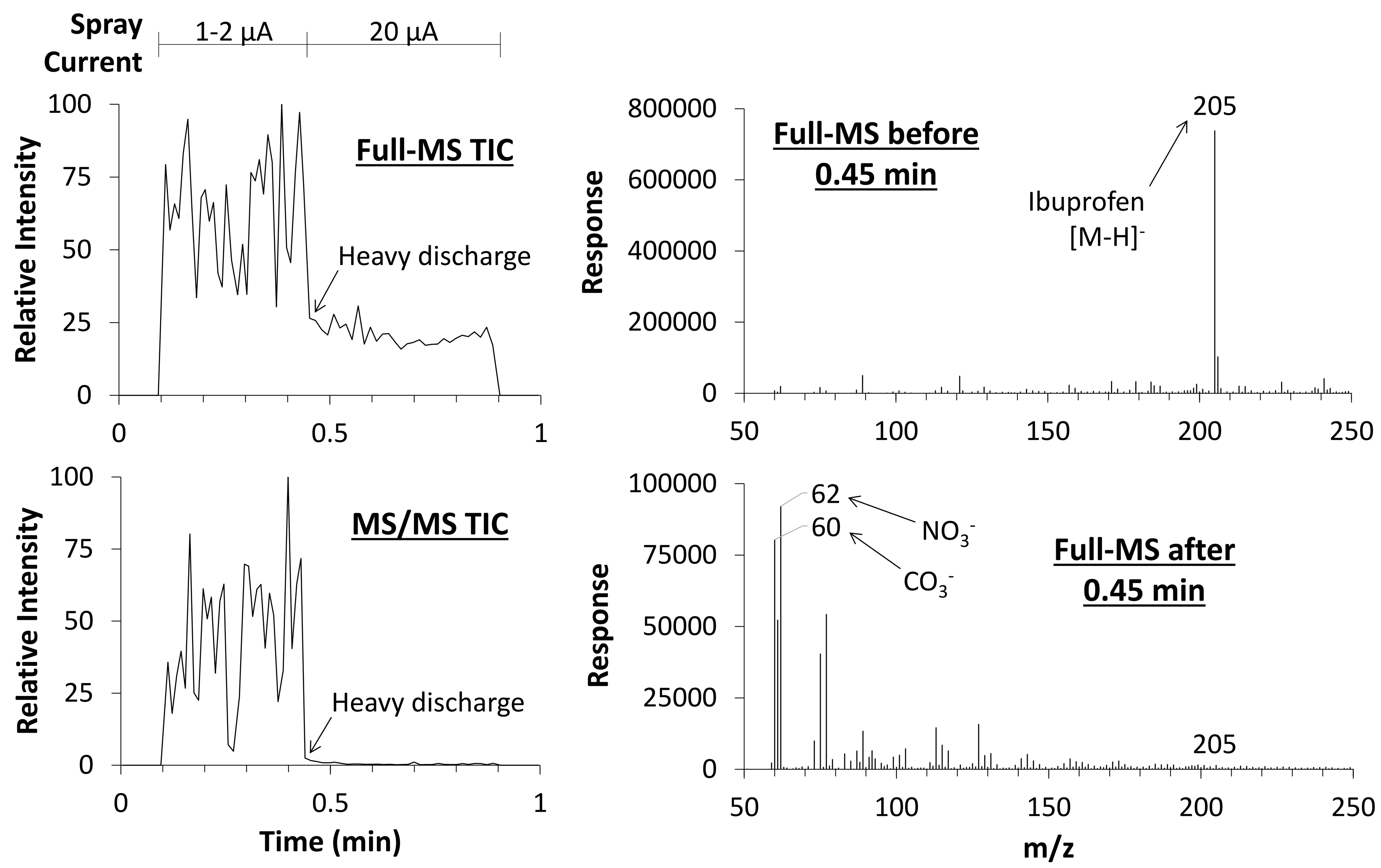

Figure 5. PS-MS and -MS/MS of a discharging sample of ibuprofen. At 0.45 min, the spray began to more intensely discharge, significantly decreasing the intensity of ibuprofen's precursor ion (thereby eliminating virtually all MS/MS signal from ibuprofen's fragment ion) and increasing the relative strength of CO_3^- and NO_3^-—two ions which are produced in negative corona.[4]

e Detection of Acidic Compounds

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Results

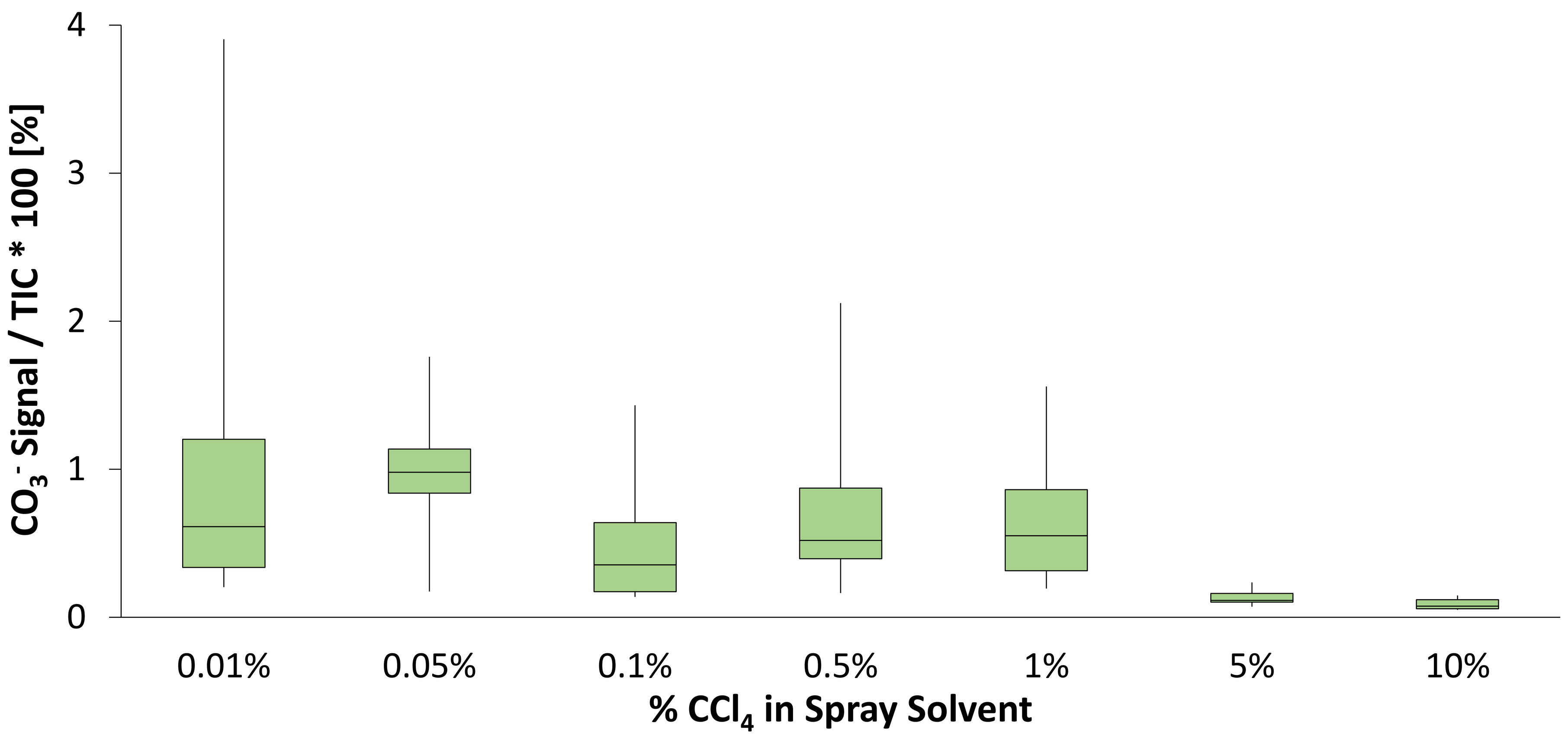


Figure 6. Full-MS discharge signal at m/z 60 (corresponding to CO_3^-) with methanol-based spray solvents containing differing amounts of CCl_4.

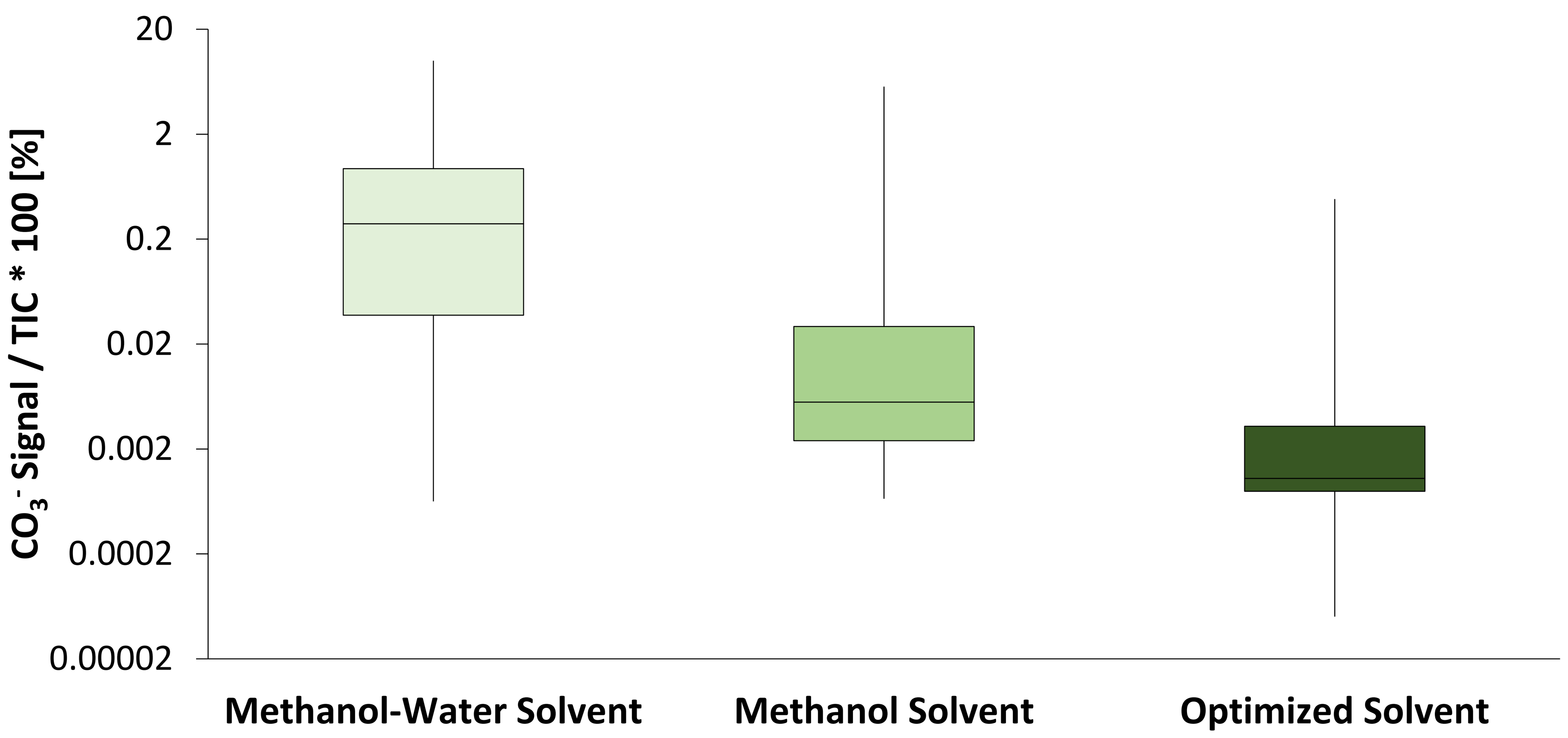


Figure 7. Full-MS discharge signal from CO_3^- for three separate solvents: a 95:5 methanol:water solvent, a pure methanol solvent, and a 90:10 methanol:CCl_4 solvent. Since the latter was able to demonstrably reduce the severity and frequency of discharge observed, it was used as the optimized solvent for PS-MS in negative ion mode.

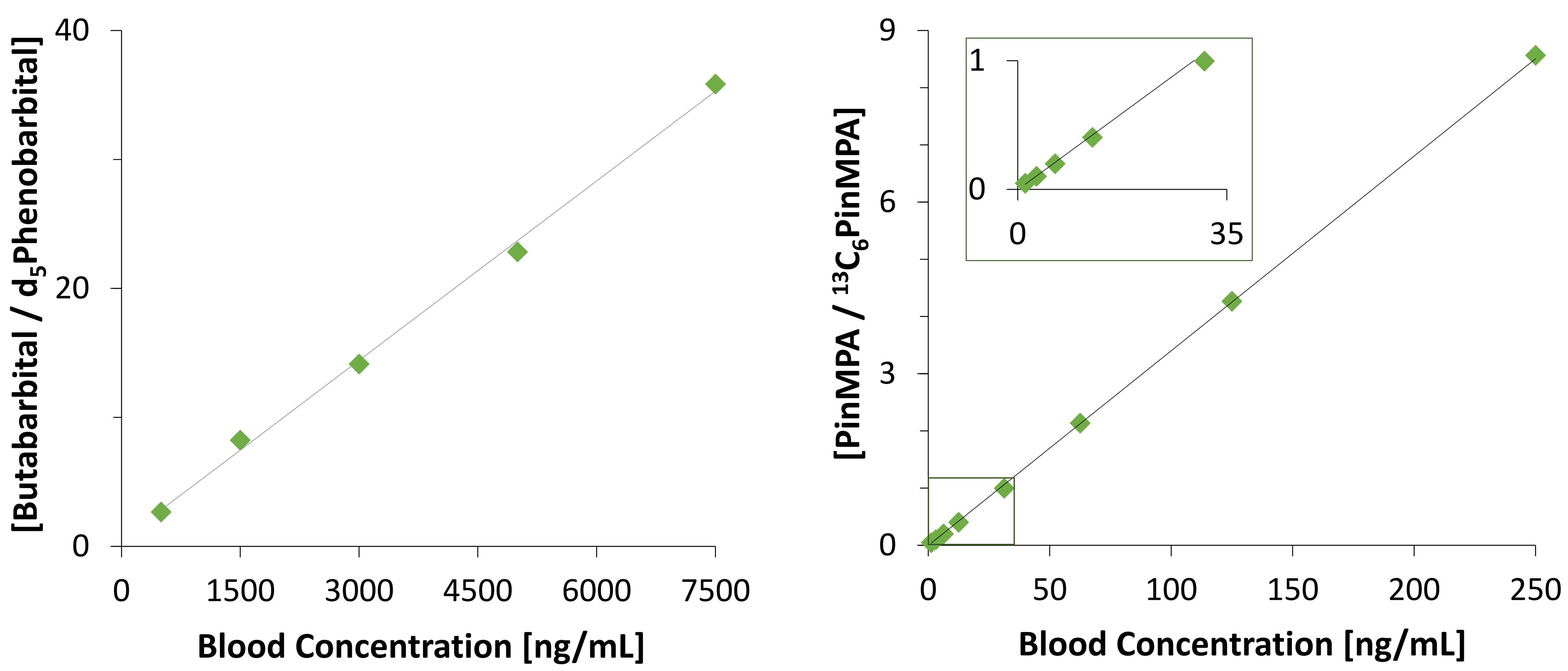


Figure 8. Representative calibration curves for barbiturates (butabarbital – left) and alkyl MPAs (PinMPA – right).

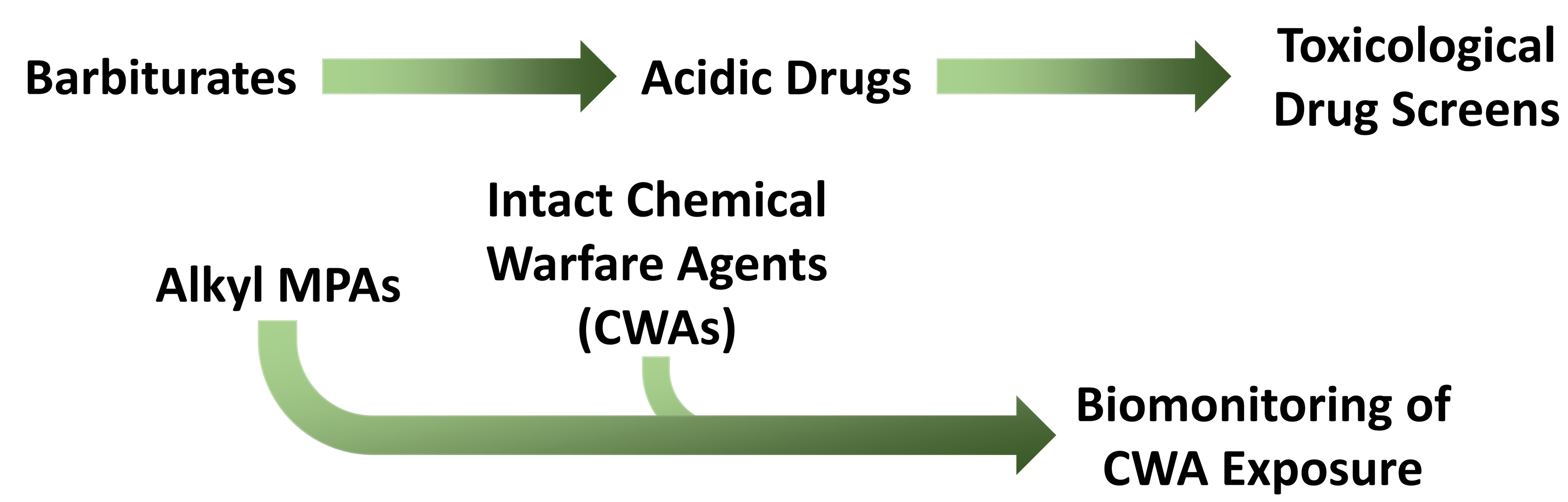
Results

Table 1. Quantitative summary of the calibration curves generated for each analyte.

	Compound	Lowest Cal. [ng/mL]	LOD [ng/mL]	Rel. Error in Slope [%]	R^2
Blood	Butabarbital	500	229	3	0.99
	Butalbital	500	263	4	0.98
	Amobarbital	500	321	5	0.97
	Pentobarbital	500	561	8	0.94
	Phenobarbital	1000	502	4	0.98
	Secobarbital	500	286	4	0.98
	Thiopental	2000	1100	4	0.98
	Phenytoin	1000	919	7	0.95
	EMPA	1.25	1.2	2	0.994
	IMPA	1.25	0.9	2	0.997
	iBuMPA	1.25	0.9	1	0.996
	CHMPA	1.25	0.8	1	0.998
	PinMPA	1.25	0.5	1	0.995
Urine	EMPA	1.25	1.2	3	0.982
	IMPA	1.25	1.2	2	0.994
	iBuMPA	1.25	1.1	2	0.996
	CHMPA	1.25	0.6	1	0.999
	PinMPA	1.25	0.4	1	0.998

Conclusion

- Discharge can be quantified using relative signals of CO_3^- and NO_3^- in full-MS
- Including 10% CCl_4 saw a drastic reduction in the frequency and severity of discharge, and it also allowed for more flexibility in setting the spray voltage
- Precise and reliable quantitation was achieved for eight barbiturates and five organophosphonates, establishing sub-ng/mL detection limits for the latter



References

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