Report to Scientific Guidance Panel

Program Update
Environmental Health Laboratory

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BIOMONITORING CALIFORNIA

Overview

- ❑ Completed & ongoing projects
- ❑ Publications
- ❑ Semi-targeted analysis
- ❑ Ongoing method development

Completed projects: 2018

- ❑ Northern California Firefighters (NCFF) Study
  - Metals in blood and urine (n = 180)
- ❑ California Regional Exposure Study – Los Angeles (CARE-LA)
  - Metals in blood and urine (n = 430)
  - Phenols in urine (n = 60)

Completed projects: 2019-2020

- ❑ Camp Fire Firefighters
  - Metals in blood and urine (n = 66)
- ❑ Maternal Cotinine and Autism (MACOTA) Study
  - Cotinine in serum (n = 1000)
- ❑ CARE Study - Region 2
  - Metals in blood and urine (n = 359)
  - Phenols in urine (n = 151)

Ongoing projects

- Camp Fire Firefighters (n = 66)
  - PAH metabolites in urine
- CARE-3 Study (n = 90)
  - Metals in blood and urine
  - Phenols
- Pregnancy Exposure to Cannabis and Tobacco (PRECATO) (n = 1800 serum samples; 600 samples/year)
  - Cotinine

Recent publications

1. Fang Li, Qui F, Li Y, Wang S, DeGuzman J, Wang J, and She J (2019). Determination of carbazole and halogenated carbazoles in human blood samples using GC-MS/MS. Ecotox Environ Saf 30(184):109609. Abstract available at: https://www.sciencedirect.com/science/article/abs/pii/S0147651319309406.

2. Von Behren J , Liu R, Sellen J, Duffy CN, Gajek R, Choe KY, DeGuzman J, Janes MK, Hild J, and Reynolds P (2019). Heavy metals in California women living in a gold mining-impacted community. Int J Environ Res Public Health 16(13): 2252. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6651337/.

3. Jiang J, Sai H, Ip S, Zhou J, Guan Y, Zhang J, Liu G, Garrotto N, Lu Y, DeGuzman J, and She J (2019). Supported-liquid phase extraction in combination with isotope-dilution gas chromatography triple quadrupole tandem mass spectrometry for high-throughput quantitative analysis of polycyclic aromatic hydrocarbon metabolites in urine. Environ Pollut 248:301-311. Abstract available at: https://doi.org/10.1016/j.envpol.2019.01.125.

4. Berger K, Kogut KR, Bradman A, She J, Gavin Q, Zahedi R, Parra KL, and Harley KG (2018) Personal care product use as a predicator of urinary concentrations of certain phthalates, parabens, and phenols in the HERMOSA study. J Exp Sci Envi Epi 29(1):21-32. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6037613/.

Targeted, semi-targeted, and non-targeted data acquisitions

Targeted and semi-targeted (Data Dependent - DDMS)

SURVEY SCAN → MS/MS of Selected Precursor ions → MS^n Scan

Full Scan or SIM

- Criteria for selecting precursor ions
- Inclusion list
- Exclusion list

Non-targeted (Data Independent - DIA)

FULL SCAN → MS/MS , AIF, MS^E

Full Scan

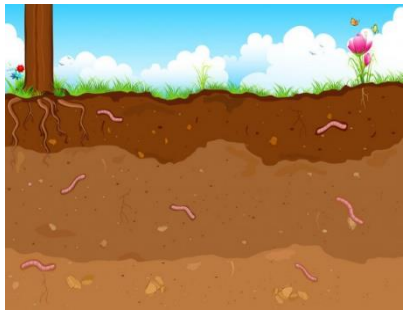
- Without pre-selection of precursor ions
- Selection of small m/z range.
- Exclusion list

Halogenated carbazoles in the environment

Possible origin

Naturally occurring
- Petroleum

Industrial sources
- Organic light-emitting diodes
- Flame retardants
- Chloralkali production
- Indigo dyes

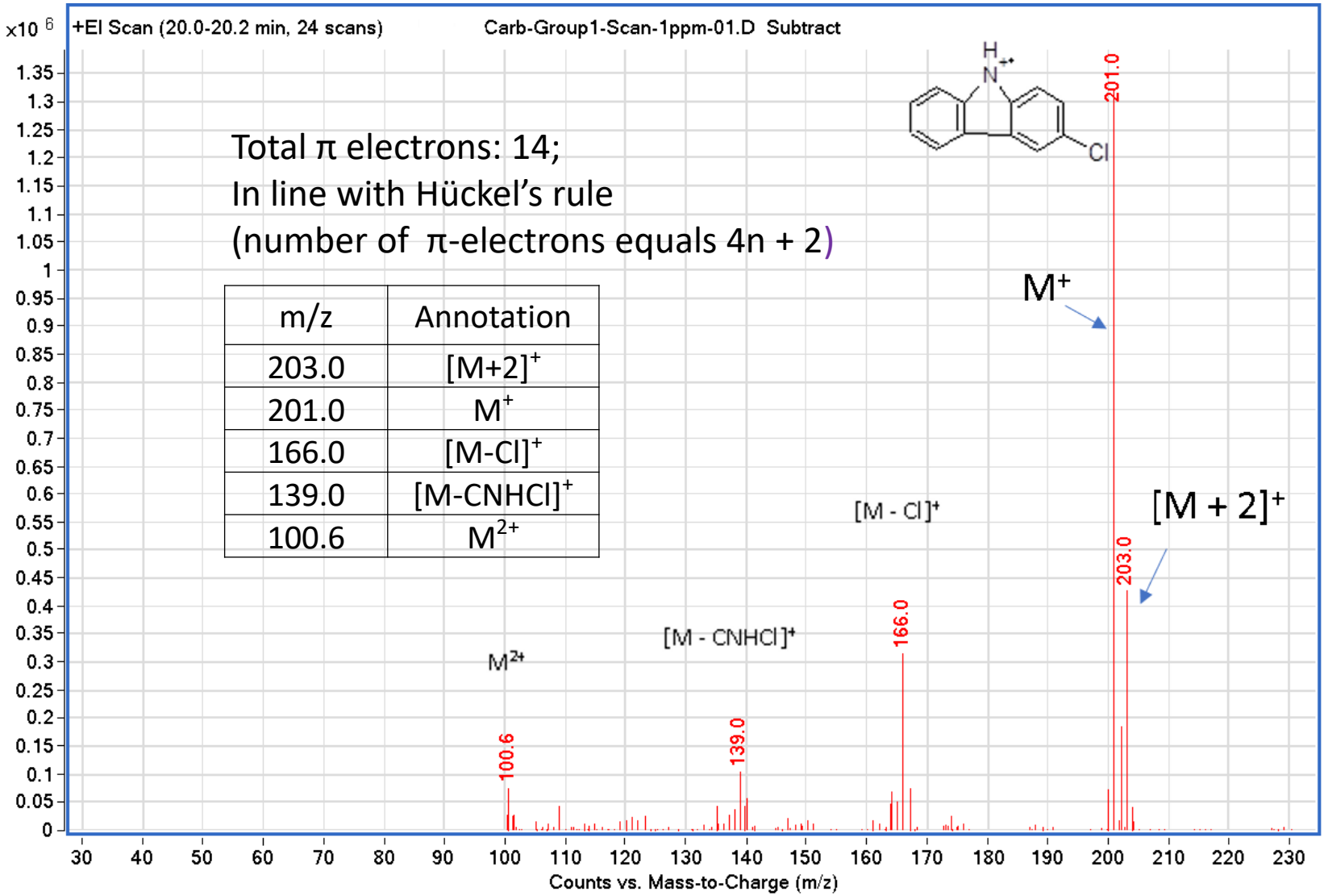


Inhalation; drinking water; dietary intake; skin contact; etc. ???

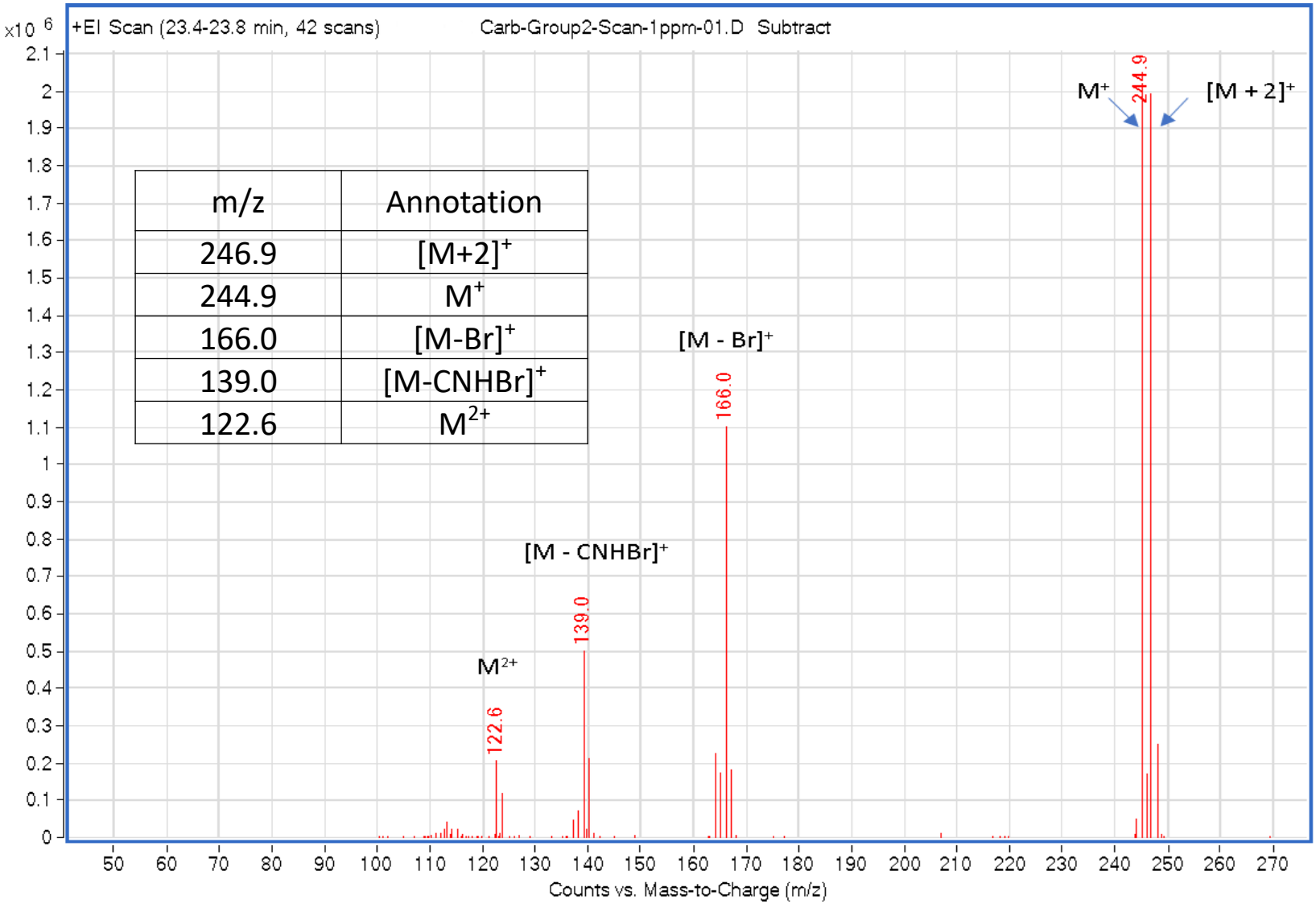
Carbazole and halogenated carbazoles are widely detected in the environment

Will they eventually enter the human body?

Mass spectrum of 3-chlorocarbazole by EI-MS

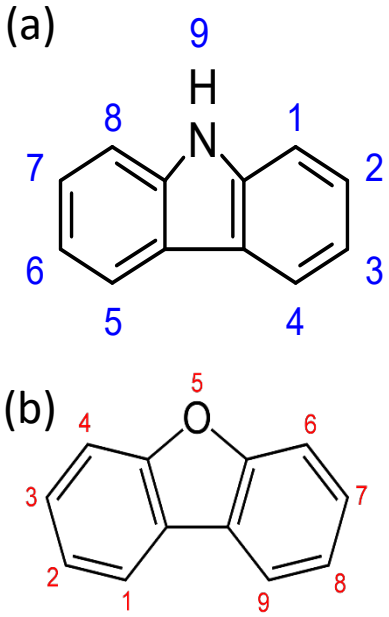


Mass spectrum of 3-bromocarbazole by EI-MS



m/z	Annotation
246.9	$[M+2]^+$
244.9	M^+
166.0	$[M-Br]^+$
139.0	$[M-CNHBr]^+$
122.6	M^{2+}

Characteristic fragmentation: PCDF vs 3-CCZ/3-BCZ



Molecular structures of:
(a) carbazole and (b) dibenzofuran

PCDF		3-CCZ/3-BCZ	
Relative intensity	Ion/Fragment	Ion/Fragment	Relative intensity
Highest	M^+	M^+	Highest
Low	$[M-Cl]^+$	$[M-X]^+$	Medium
Medium	$[M-COCl]^+$	$[M-CNHX]^+$	Medium
Medium	M^{2+}	M^{2+}	Medium

- Only one substituent of Cl (or Br) in the molecule(s)
- X stands for halogen (Cl or Br)

Targeted and semi-targeted approaches and references

Approach	Features	Reference
ASES/MS	Library search and spectra interpretation	Zhu D, She J, Hong Q et al. (1988). ASES/MS: an automatic structure elucidation system of organic compounds using mass spectrometric data. Analyst 113(8):1261 – 1265.
IsoCAL	Isotope profiles match	She J, McKinney M, Petreas M, and Stephens R (1995). Design and application of an isotope pattern calculator for Microsoft Windows. Organohalogen Compounds 23:171-174.
AMBIPR	Database and library search, plus metabolite predication	Lu D, Zhang S, Wang D et al. (2016). Identification of flurochloridone metabolites in rat urine using liquid chromatography/high resolution mass spectrometry. J Chromatogr A 1445:80-92.

Method development

- ❑ VOC metabolites in urine
- ❑ Add selected metabolites of benzophenone-1 (BP-1), a metabolite of BP-3, to phenols panel
- ❑ Investigate deconjugation step in bisphenol A assay
- ❑ Further work on semi-targeted analysis
  - Automation of data analysis
  - Investigation of fragmentation profiles for selected chemicals of interest to Biom CA