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Advanced LC/MS/MS Methods for CECs in Waters

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Presentation Outline

- CECs and Water Reuse Introduction
- CEC Monitoring and Analytical Methods
- Direct Injection LC/MS/MS Validation and Results
- Conclusions

What are CECs?

Pharmaceuticals and Personal Care Products (PPCPs)
Veterinary Drugs
Steroids and Hormones
Alkylphenols
Household Cleaning Products
Flame Retardants
Explosives

Persistent Organic Pollutants (POPs)
Per- and Polyfluoroalkyl Substances (PFAS)
Polybrominated Diphenyl Ethers (PBDEs)
Polybrominated Biphenyls (PBBs)

Endocrine Disrupting Chemicals (EDCs)
Steroids and Hormones
Alkylphenols
Bisphenol A (BPA)
Organochlorine Pesticides

Cyanotoxins, Perchlorate, 1,4-Dioxane
N-nitroso-dimethylamine (NDMA)
1,2,3-Trichloropropane (TCP)
Trichloroethylene (TCE)
Tungsten, Nanomaterials, etc.

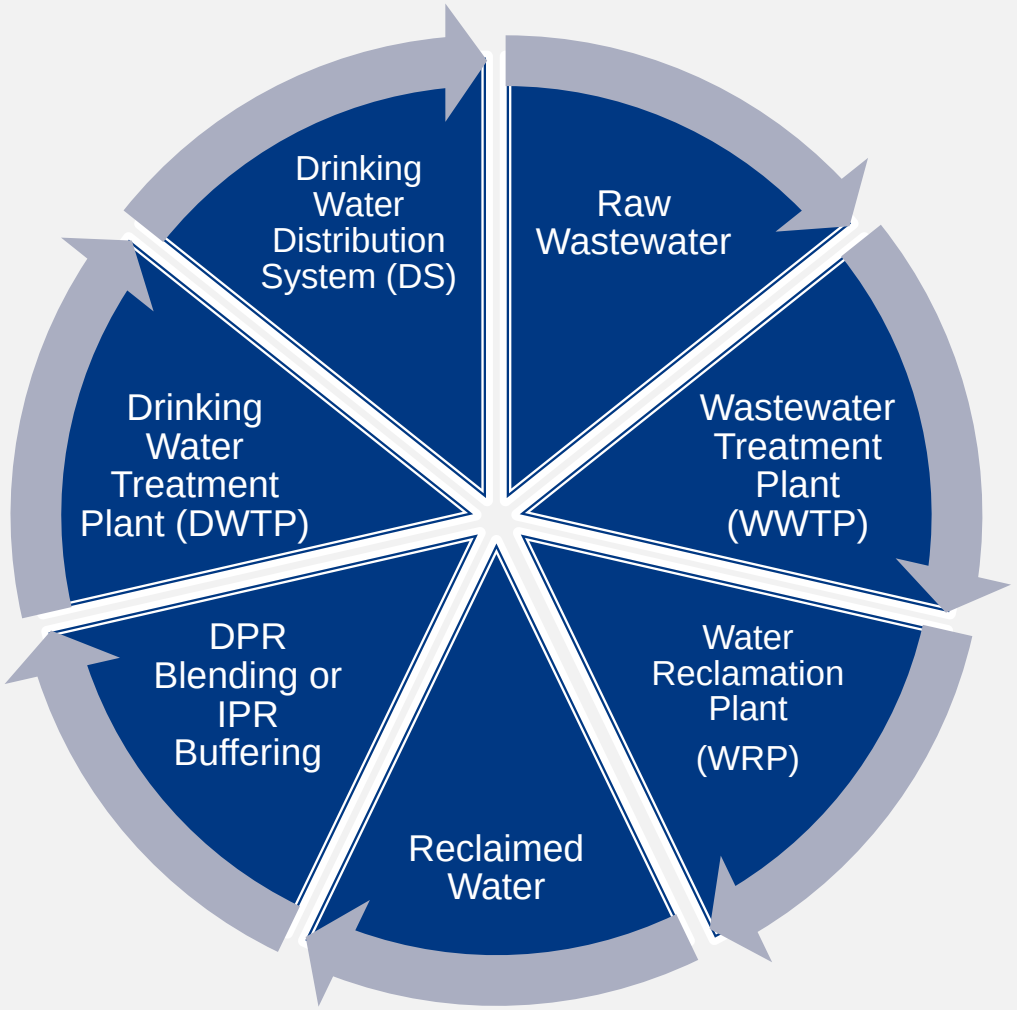
Where do they come from?

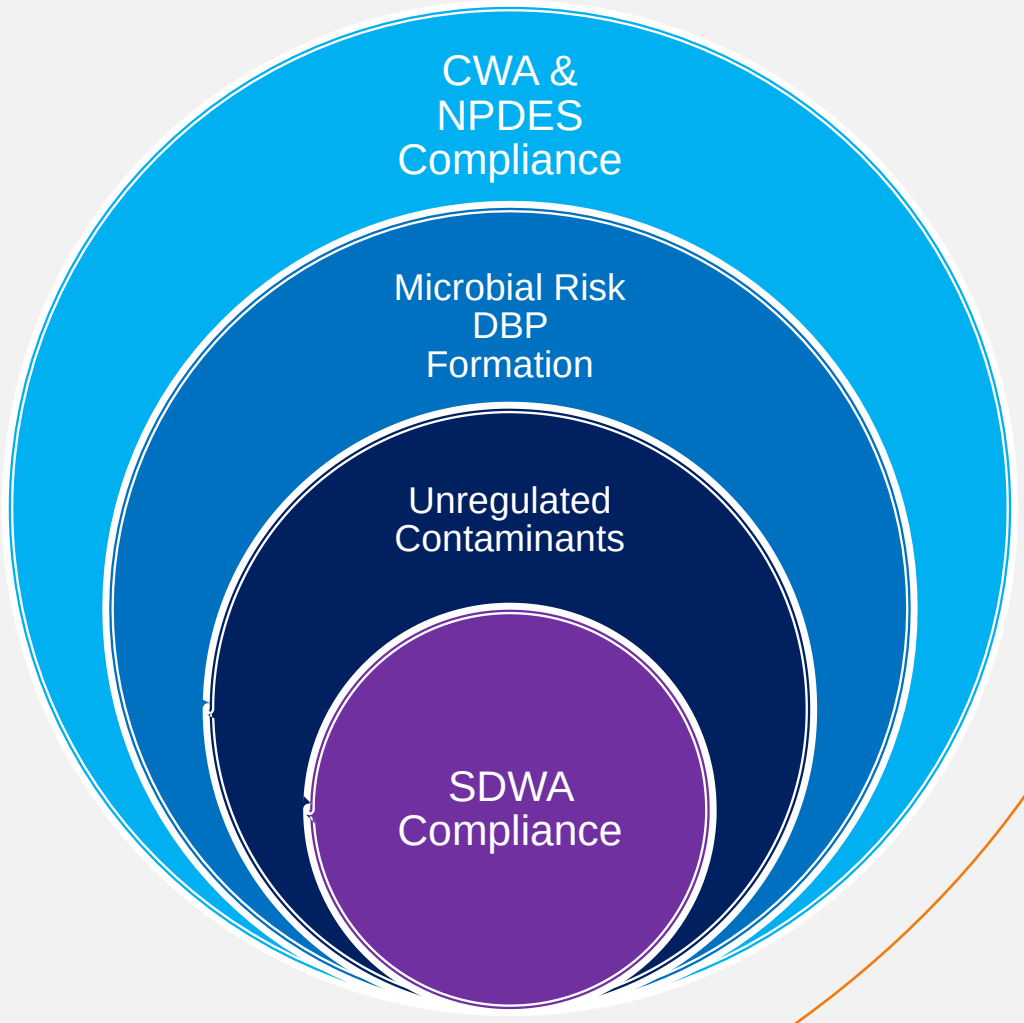
- CECs can enter water through wastewater treatment plants (WWTPs) and septic systems.
  - Direct disposal of products
  - Indirect disposal or contact with substances
  - People and livestock excretion
- CECs can also enter ambient water through agricultural, landfill, and stormwater runoff.

What are concerns with CECs?

- Little is known about the environmental occurrence, fate, and transport of CECs.
- The potential impacts of CECs on aquatic life and humans are largely unknown.
- Water resource scarcity has made wastewater reclamation for potable reuse become a viable option in certain geographical areas.
- Monitoring CECs is essential in wastewater reclamation, particularly in potable water reuse.

Wastewater Reclamation and Monitoring





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Analytical Methods for Common CECs

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LC/MS/MS

- PPCPs, veterinary drugs & household cleaning products
- Steroids & hormones
- Alkylphenols & bisphenol A
- Organochlorine pesticides
- Phosphate esters
- PFAS
- Cyanotoxins
- Perchlorate

GC/MS or HRGC/HRMS

- Steroids & hormones
- Alkylphenols
- Organochlorine pesticides
- PBDEs & PBBs
- Explosives
- 1,4-Dioxane
- NDMA
- 1,2,3-TCP
- TCE

LC/MS/MS Methods for CECs

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CECs	Available Methods	Eurofins Online SPE-LC/MS/MS	Eurofins DI-LC/MS/MS
PPCPs, veterinary drugs, and house cleaning products	EPA 1694 (4 extracts) EPA 542 In-house LC/MS/MS	Positive mode ESI	Positive mode ESI
		Negative mode ESI	Negative mode ESI
Steroids and hormones	EPA 1698 EPA 539 In-house LC/MS/MS	Positive mode ESI	Positive mode ESI
		Negative mode ESI	Negative mode ESI
Alkylphenols and bisphenol A	ASTM D7065-06 ASTM D7485-09 ASTM D7574-09 In-house LC/MS/MS	Negative mode ESI	Negative mode ESI
Phosphate esters	In-house LC/MS/MS	Positive mode ESI	Positive mode ESI
Organochlorine pesticides	EPA 500s EPA 800s In-house LC/MS/MS	Positive mode ESI	
		Negative mode ESI	

DI-LC/MS/MS Method Summary

- Waters Acquity–H Class UPLC & Xevo TQ–Absolute in the MRM mode
- 40 mL amber glass VOA vials for sampling
- 50–100 µL of injection volumes
- Internal standard calibration with the use of isotope dilution analogs (IDAs)
- 49 CECs with 33 IDAs analyzed in the positive ESI mode
- 34 CECs with 23 IDAs analyzed in the negative ESI mode

ESI- 34 Analytes & Sensitivity

CECs	MRL (ng/L)	MDL (ng/L)	CECs	MRL (ng/L)	MDL (ng/L)
17 alpha-Estradiol	5.0	1.6	17 beta-Estradiol	10	2.1
Bezafibrate	5.0	1.1	Diethylstilbestrol (DES)	10	1.7
Chloramphenicol	5.0	1.1	Dilantin	10	2.5
Clofibric acid	5.0	1.5	Equilin	10	3.0
Diclofenac	5.0	2.4	Estriol	10	2.9
Estrone	5.0	1.2	Iopromide	10	5.0
Gemfibrizol	5.0	0.6	Penicillin G	10	1.0
Prednisone	5.0	1.4	Penicillin V	10	1.3
17 alpha-Ethynylestradiol	10	2.7			

ESI- 34 Analytes & Sensitivity (Cont'd)

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CECs	MRL (ng/L)	MDL (ng/L)	CECs	MRL (ng/L)	MDL (ng/L)
4-tert-Octylphenol	20	12	Phenylphenol	50	7.7
Acesulfame-K	20	2.0	Tetrabromobisphenol A	50	13
Bisphenol A (BPA)	20	7.4	Triclocarban	50	19
Ibuprofen	20	3.5	Triclosan	50	20
Levothyroxine	20	7.9	Sucralose	100	14
Naproxen	20	8.4	Trichlorophenol	100	27
Theophylline	20	2.0	Nonylphenol	200	86
Iohexol	50	8.7	Salicylic acid	200	120
Pentachlorophenol	50	19			

ESI- Accuracy & Precision

CECs	Rec (%)	RSD (%)	CECs	Rec (%L)	RSD (%)
17 alpha-Estradiol	100	6.2	Diclofenac Acid	92	6.1
17 alpha-Ethynylestradiol	91	5.8	Diethylstilbestrol	95	4.7
17 beta-Estradiol	95	3.6	Dilantin	94	4.7
4-tert-Octylphenol	94	4.1	Equilin	94	5.4
Acesulfame K	93	4.6	Estriol	101	4.3
Bezafibrate	94	4.6	Estrone	95	5.1
Bisphenol A	98	3.2	Gemfibrozil	95	5.4
Chloramphenicol	91	4.2	Ibuprofen	96	2.4
Clofibric Acid	93	6.6	Iohexol	95	3.0

ESI- Accuracy & Precision (Cont'd)

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CECs	Rec (%)	RSD (%)	CECs	Rec (%L)	RSD (%)
Iopromide	95	4.0	Prednisone	90	4.0
Levothyroxine	90	7.2	Salicylic Acid	115	5.8
Naproxen	93	3.6	Sucralose	91	2.1
Nonylphenol	95	2.7	Tetrabromobisphenol A	89	5.5
Penicillin G	90	4.1	Theophylline	92	4.3
Penicillin V	91	5.6	Trichlorophenol	100	5.5
Pentachlorophenol	93	4.6	Triclocarban	83	10.0
Phenylphenol	102	2.9	Triclosan	80	1.1

ESI+ 49 Analytes, MRLs, and MDLs

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CECs	MRL (ng/L)	MDL (ng/L)	CECs	MRL (ng/L)	MDL (ng/L)
Androstenedione	5.0	3.9	Meprobamate	5.0	4.1
Antipyrine	5.0	1.4	Monensin	5.0	3.4
Atenolol	5.0	1.7	Oleandomycin	5.0	1.5
Carbadox	5.0	2.6	Primidone	5.0	3.2
Carbamazepine	5.0	1.9	Progesterone	5.0	2.7
Cimetidine	5.0	1.3	Roxithromycin	5.0	2.2
cis-Testosterone	5.0	2.0	Sulfadiazine	5.0	2.5
Codeine	5.0	3.4	Sulfadimethoxine	5.0	2.5
Cotinine	5.0	4.5	Sulfamethazine	5.0	2.4
Diazepam	5.0	1.6	Sulfathiazole	5.0	2.9
Diphenhydramine	5.0	2.7	trans-Testosterone	5.0	4.2
Fluoxetine	5.0	1.7	Trimethoprim	5.0	1.0
Lincomycin	5.0	2.7	Tylosin	5.0	4.1

ESI+ 49 Analytes, MRLs, and MDLs (Cont'd)

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CECs	MRL (ng/L)	MDL (ng/L)	CECs	MRL (ng/L)	MDL (ng/L)
Virginiamycin M1	5.0	3.9	Metformin	20	5.3
Azithromycin	10	8.1	Narasin	20	12
Caffeine	10	5.2	Paraxanthine	20	17
Dexamethasone	10	4.0	Salinomycin	20	8.5
DEET	10	3.4	Quinoline	50	23
Diltiazem	10	5.2	Sulfasalazine	50	11
Sulfamerazine	10	4.5	Nicotine	400	267
Sulfamethizole	10	3.0	Theobromine	400	254
Sulfamethoxazole	10	7.0	TDCPP	400	346
TCEP	10	3.4	TCPP	400	245
Acetaminophen	20	15	Amoxicillin	1000	534
Erythromycin	20	13			

ESI+ Accuracy & Precision

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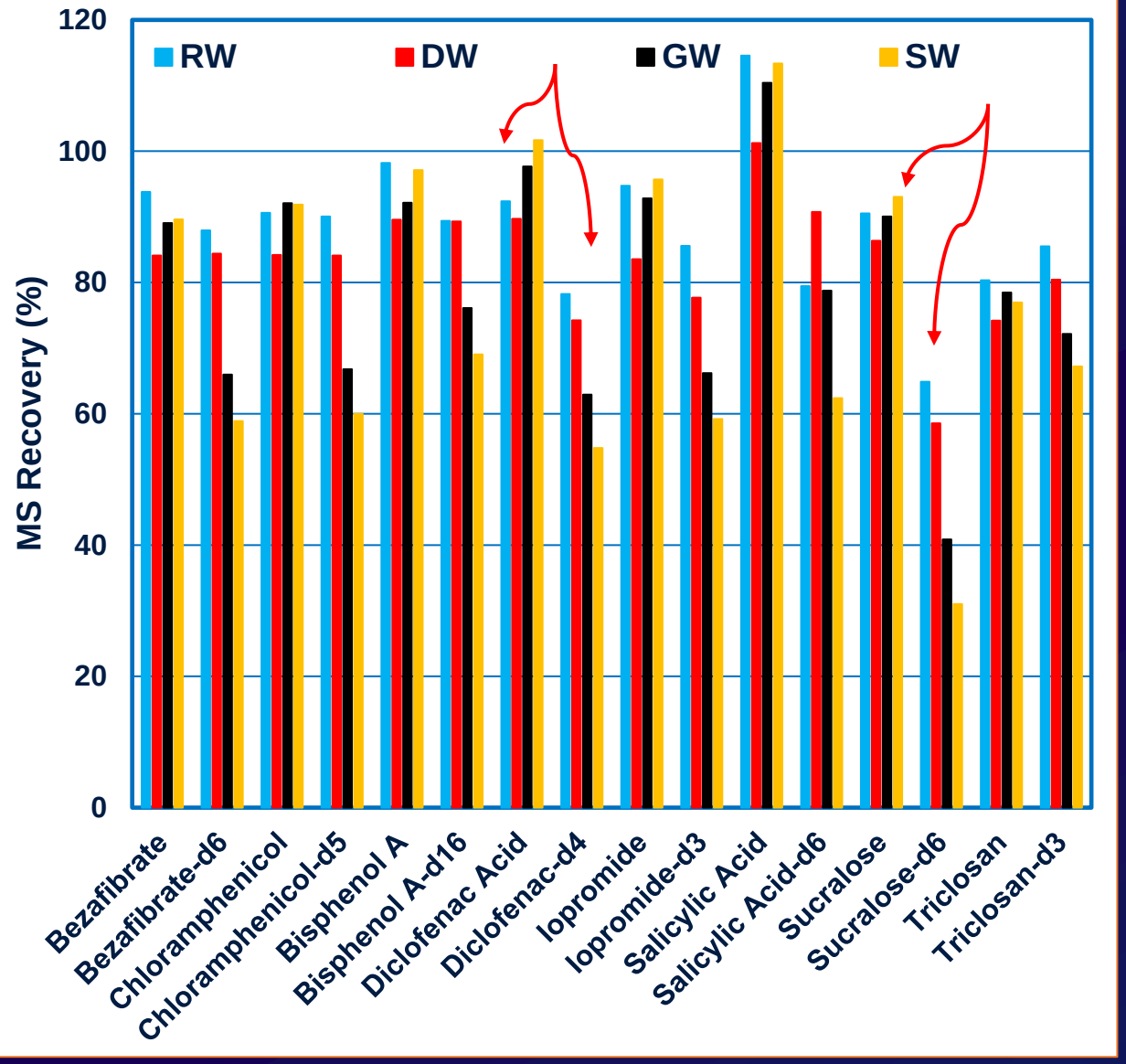
CECs	Rec (%)	RSD (%)	CECs	Rec (%)	RSD (%)
Acetaminophen	105	5.2	DEET	103	5.9
Amoxicillin	100	4.1	Dexamethasone	94	5.8
Androstenedione	99	6.8	Diazepam	101	6.8
Antipyrine	102	4.5	Diltiazem	104	4.0
Atenolol	102	6.9	Diphenhydramine	101	5.9
Azithromycin	85	5.3	Erythromycin	98	19.0
Caffeine	99	3.9	Fluoxetine	100	7.0
Carbadox	100	8.0	Lincomycin	90	5.9
Carbamazepine	97	4.7	Meprobamate	102	5.5
Cimetidine	102	6.7	Metformin	106	4.9
cis-testosterone	97	6.6	Monensin	84	4.9
Codeine	98	4.4	Narasin	69	10.2
Cotinine	98	3.4	Nicotine	103	7.2

ESI+ Accuracy & Precision (Cont'd)

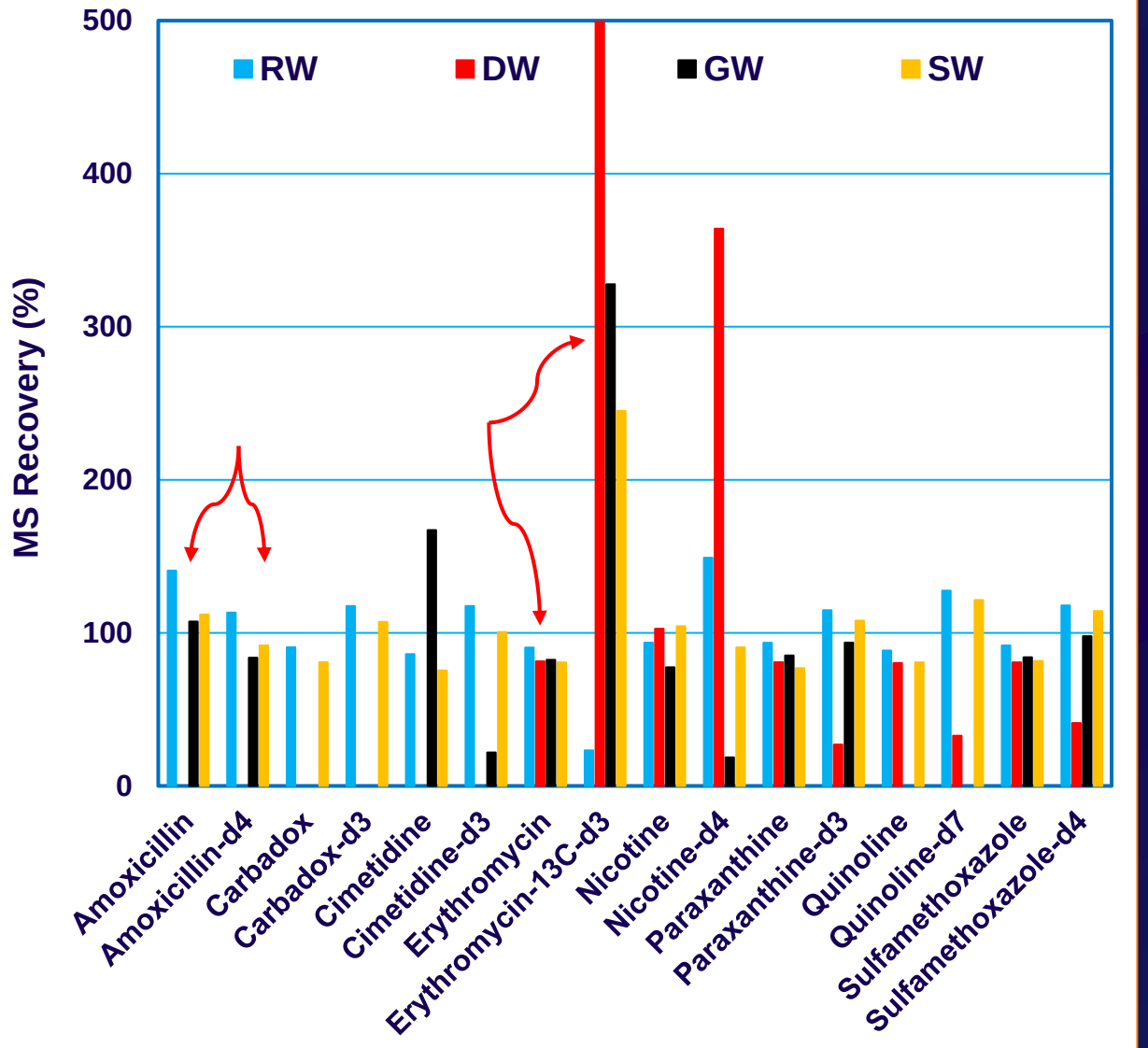
CECs	Rec (%)	RSD (%)	CECs	Rec (%)	RSD (%)
Oleandomycin	88	7.2	Sulfamethoxazole	99	7.5
Paraxanthine	109	7.4	Sulfasalazine	100	7.6
Primidone	101	7.9	Sulfathiazole	102	3.3
Progesterone	100	6.4	TCEP	96	8.6
Quinoline	93	6.4	TCPP	102	4.0
Roxithromycin	98	3.3	TDCPP	99	5.5
Salinomycin	28	10.9	Theobromine	97	7.2
Sulfadiazine	103	7.8	trans-testosterone	101	7.5
Sulfadimethoxine	98	7.4	Trimethoprim	92	8.0
Sulfamerazine	93	11.4	Tylosin	88	4.8
Sulfamethazine	102	9.8	Virginiamycin M1	89	6.1
Sulfamethizole	108	11.5			

ESI- Matrix Interferences (n = 4)



CECs	RW (%)	DW (%)	GW (%)	SW (%)
Bezafibrate	94	84	89	90
Bezafibrate-d6	88	84	66	59
Chloramphenicol	91	84	92	92
Chloramphenicol-d5	90	84	67	60
Bisphenol A	98	90	92	97
Bisphenol A-d16	89	89	76	69
Diclofenac Acid	92	90	98	102
Diclofenac-d4	78	74	63	55
Iopromide	95	84	93	96
Iopromide-d3	86	78	66	59
Salicylic Acid	115	101	110	113
Salicylic Acid-d6	79	91	79	62
Sucralose	91	86	90	93
Sucralose-d6	65	59	41	31
Triclosan	80	74	78	77
Triclosan-d3	86	80	72	67

ESI+ Matrix Interferences (n = 4)



CECs	RW (%)	DW (%)	GW (%)	SW (%)
Amoxicillin	141	0	107	112
Amoxicillin-d4	113	0	84	92
Carbadox	91	0	0	81
Carbadox-d3	118	0	0	107
Cimetidine	86	0	167	75
Cimetidine-d3	118	0	22	101
Erythromycin	90	81	82	81
Erythromycin-13C-d3	23	821	328	245
Nicotine	94	103	77	104
Nicotine-d4	149	364	19	91
Paraxanthine	94	81	85	77
Paraxanthine-d3	115	27	94	108
Quinoline	88	80	0	81
Quinoline-d7	128	33	0	121
Sulfamethoxazole	92	81	84	82
Sulfamethoxazole-d4	118	41	98	114

Conclusions

- Two direct injection LC/MS/MS methods were demonstrated for analysis of 83 CECs in drinking water supplies.
- Advanced LC/MS/MS could provide low ng/L-level detection of suitable CECs.
  - The advantage of DI-LC/MS/MS was to remove sample extraction and its associated challenges as well. So all CECs could be analyzed.
  - The disadvantage of DI-LC/MS/MS was to have potential matrix interferences. Certain sample matrices might cause signal suppression or enhancement, which could be compensated by isotope dilution.
- Several CECs and IDAs demonstrated relatively low stability in some water matrices. Semi-quantitation might be applied to amoxicillin, carbadox, cimetidine, erythromycin, iohexol, iopromide, levothyroxine, narasin, nicotine, quinoline, and salinomycin.

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THANK YOU

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