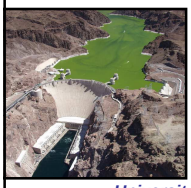
Exploring the Composition and Toxicity of Complex Environmental Mixtures



University of Tokyo, Japan: 26th November 2015

Shane Snyder, Ph.D.
Professor: Chem. & Env. Eng.
Co-Drector: WEST Center
University of Arizona

Editor in Chief
Chemosphere

azengineering

WEST CENTER
WATER & ENERGY SUSTAINABLE TECHNOLOGY

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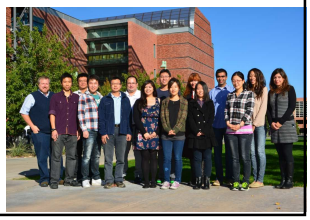
Weikang Ji: China Agricultural U.
Norma Villagomez-Marquez: UNC
Mojtaba Azadi: Sharif UT
Tharun Murali: SASTRA U

snyderlab.arizona.edu

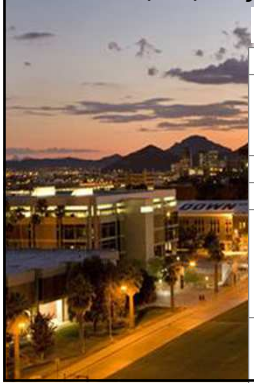



University of Arizona – Tucson, Arizona USA

"Leading Research Institution in the American Southwest"

University of Arizona – Tucson, Arizona USA

"Over $610,000,000/year in Research Expenditure"



Expenditures ($1,000's)	Institution Name
$656,967	Yale University
$655,375	Georgia Institute Of Technology
$649,774	Harvard University
$632,171	University of Texas
$618,980	Northwestern University
$610,565	University Of Arizona

University of Arizona ranked #1 among US Universities and #4 among institutions worldwide for top-cited environmental science publications

An article published recently in the peer-reviewed journal Science of the Total Environment found the University of Arizona to be the most productive university in the United States for top-cited publications pertaining to the field of "environmental science"—and the fourth most productive institution in this regard worldwide.

The authors employed the Thompson Reuters Web of Science database to measure institutional contributions to 181 environmental science journals listed in Journal Citation Reports (JCR). Productivity of the UA was exceeded worldwide only by the U.S. Geological Survey, Brunel University (UK), and the U.S. Environmental Protection Agency, which were ranked 1-3 respectively.

Science of the Total Environment 431 (2012) 122–127

Contents lists available at SciVerse ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

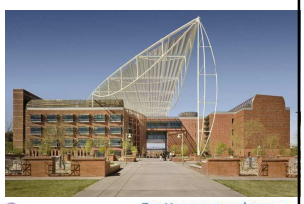
ELSEVIER

Top-cited articles in environmental sciences: Merits and demerits of citation analysis

Moonis Ali Khan [a], Yuh-Shan Ho [b,*]

[a] Chemistry Department, College of Science, King Saud University, Riyadh 11451, Saudi Arabia
[b] Trend Research Centre, Asia University, Taichung 41354, Taiwan



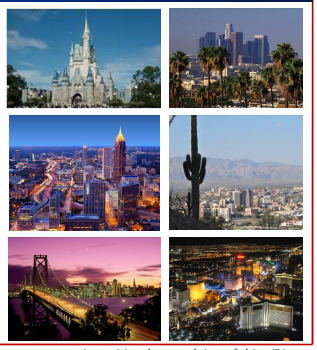
Institute of the Environment

WEST CENTER
WATER & ENERGY SUSTAINABLE TECHNOLOGY

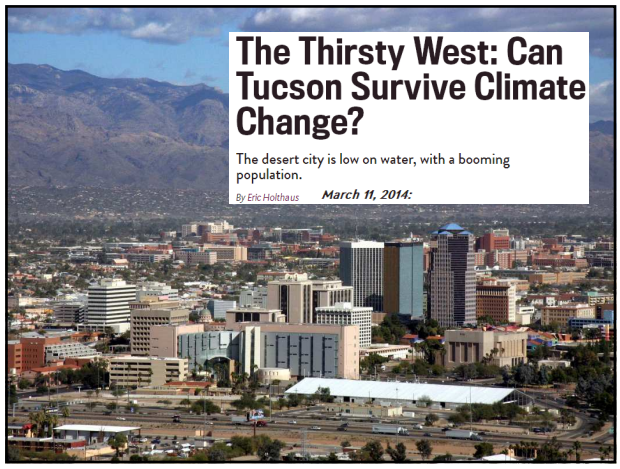
THE UNIVERSITY OF ARIZONA
BIO5 Institute
Science | Education | Jobs

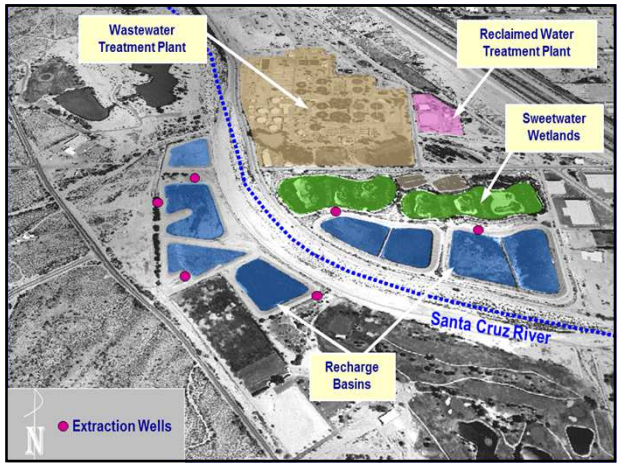
Water Scarce US Cities

10. Orlando
9. Atlanta
8. Tucson
7. Las Vegas
6. Fort Worth
5. San Francisco
4. San Antonio
3. Phoenix
2. Houston
1. Los Angeles



Source: http://247wallst.com/2010/10/29/the-ten-great-american-cities-that-are-dying-of-thirst/3/

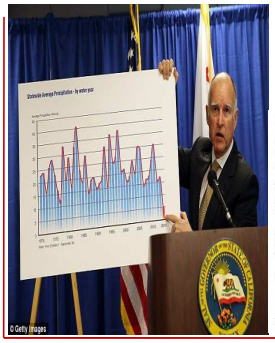




California 2011

California 2014

California Water Reuse Future



OCT 08 2013 OFFICE OF THE GOVERNOR

To the Members of the California State Senate:

I am signing SB 322 which requires the Department of Public Health in consultation with the State Water Resources Control Board, to investigate the feasibility of developing uniform water recycling criteria for direct potable reuse by September 2016.

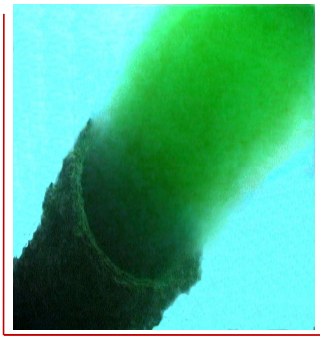
This information is past due. In an effort to enhance the use of recycled water, I have proposed the consolidation of the management of the drinking water program and all other water quality programs, including recycled water, under the State Water Board.

I am directing the Water Board to ensure that this work is completed expeditiously. The 3-year time frame mandated in this bill is too slow. California needs more high quality water and recycling is key to getting there.

Sincerely,

Edmund G. Brown Jr.

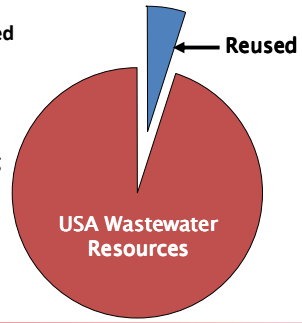
Restrictions on Ocean Outfalls



- South Florida
  - 2025 Ocean outfalls banned (except rain)
- Cape Cod
  - Moratorium on new outfalls and expanding existing
- California
  - Evidence of endocrine disruption at discharges

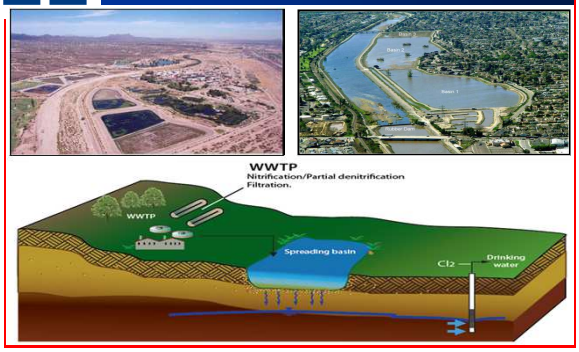
Potential for Water Reuse

- About 5-6% of US wastewater is reused
  - 1/3rd of all US wastewater discharged to oceans
- California is mandating increased reuse
- Arizona, Florida and Texas also high growth

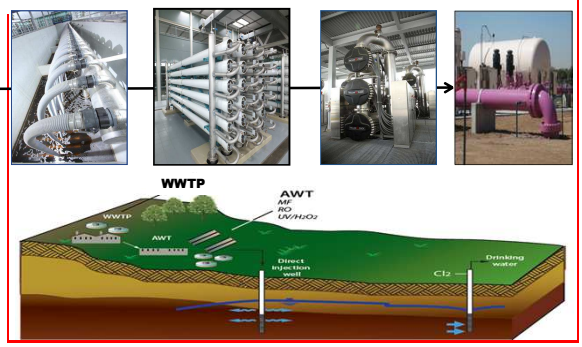


Source: Wade Miller – WateReuse Association

Water Reuse – Natural Systems



Water Reuse – Advanced Treat.



Water Reuse – Direct Potable

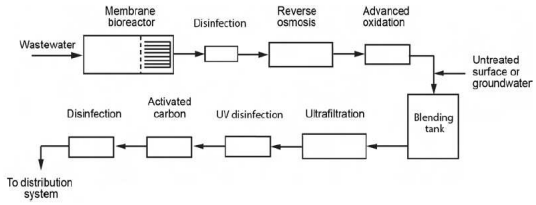
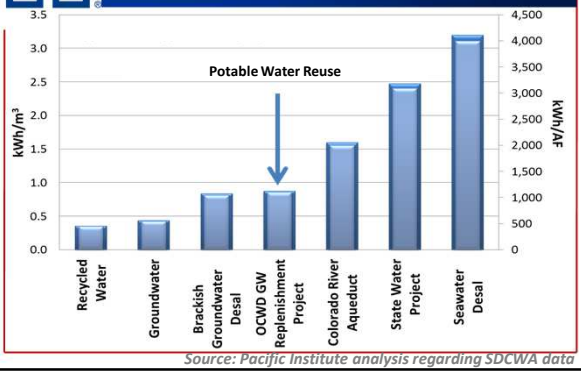


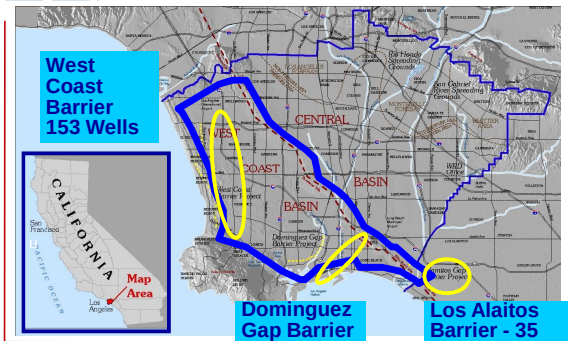
Figure 3-7
Schematic of Cloudcroft, NM DPR treatment process flow diagram (Adapted from Livingston, 2008).

Energy Intensity by Water Source



Source: Pacific Institute analysis regarding SDCWA data

Ground Water Replenishment



Facing the Yuck Factor

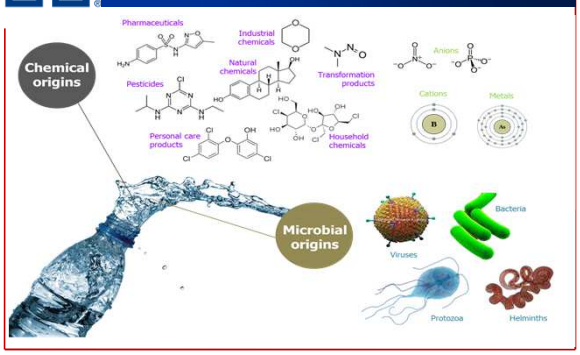
FEATURE ARTICLE - September 17, 2007 *by Peter Friederici*

Facing the yuck factor. PAUL LACHINE

How has the West embraced water recycling? Very (gulp) cautiously

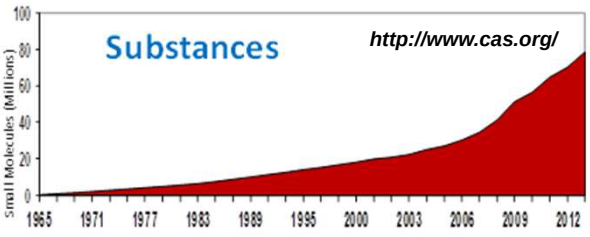
Source: http://www.hcn.org/issues/354/17227

Potential Contaminants



89,008,294 ORGANIC AND INORGANIC SUBSTANCES TO DATE

CHEMCATS 65,768,974 Commercially available chemicals



Snyder, S. A., Emerging Chemical Contaminants: Looking for Better Harmony. *J. Am. Water Works Assoc.* **2014,** *106* (8), 38-52.

Comprehensive Screening

Targeted quantification

Analysis of a small set of predefined target compounds

Standards → Isolation and separation of analytes from matrix → Identification by RT & MS → Calculation of surrogate recoveries → Comparison to target peak areas → Quantification of specific compounds in a sample

Samples

LC-MS Triple Quad
Polar and moderately polar compounds

GC-MS Triple Quad
Volatile and semi-volatile compounds

ICP-MS
Metals and targeted organic complexes

IC-MS
Anions, cations, oxyhalides

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Samples

LC-MS Triple Quad
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GC-MS Triple Quad
Volatile and semi-volatile compounds

ICP-MS
Metals and targeted organic complexes

IC-MS
Anions, cations, oxyhalides

Non-targeted screening

Characterization of broader/unknown compounds

Sample → QTOF analysis and sample comparisons → Data alignment and analysis → Validation with MS/MS from standards → Compound profile in a sample

LC-MS QTOF
Polar and moderately polar compounds

GC-MS QTOF
Volatile and semi-volatile compounds

Cell Bioassay
Quantifiable cellular responses from mixtures isolated from biological samples

LC/GC-ICP-MS
Untargeted organic-halogens/ metals

Surrogates and Indicators

Health-relevant CECs — Potential health risks at levels at/near occurrence

Performance indicator CECs — Provide information on treatment efficacy and/or represent broader classes

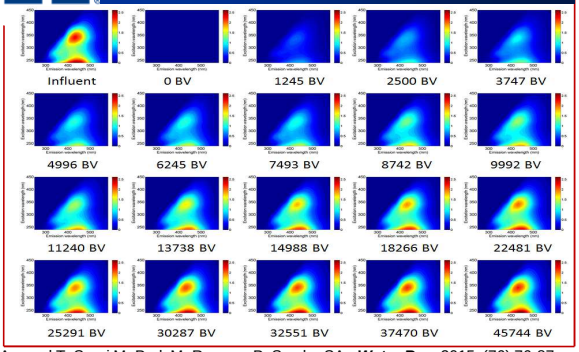
Surrogates — Bulk parameters that are indicative of occurrence and/or attenuation of substances/organisms

ftp://ftp.sccwrp.org/pub/download/DOCUMENTS/CECpanel/CECMonitoringInCARecycledWater_FinalReport.pdf

SURROGATES

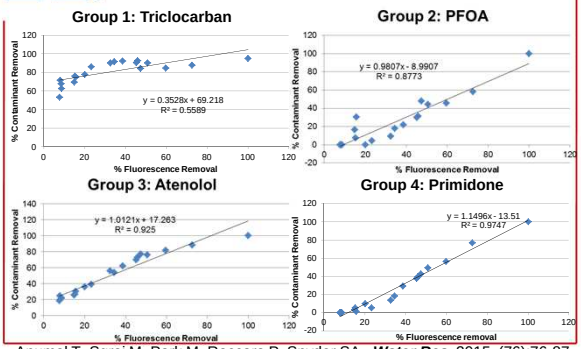
Granular Activated Carbon

Application of fluorescence as surrogate for water quality



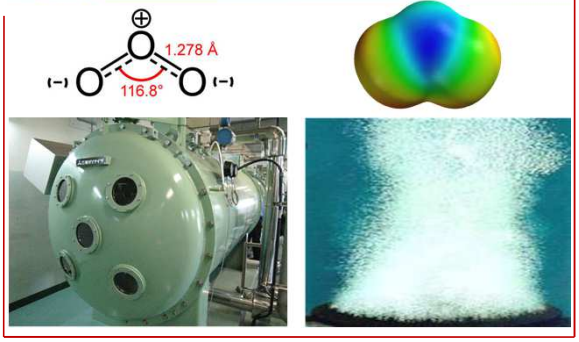
Anumol T, Sgroi M, Park M, Roccaro P, Snyder SA. ***Water Res.*** 2015 (76):76-87.

Fluorescence Surrogate Correlation to LC-MS/MS

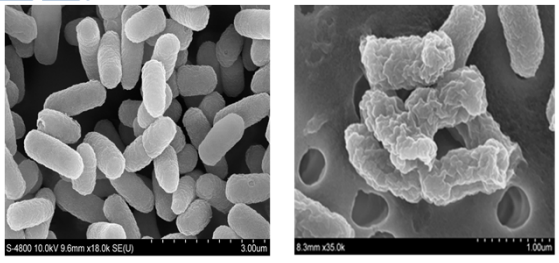


Anumol T, Sgroi M, Park M, Roccaro P, Snyder SA. ***Water Res.*** 2015 (76):76-87.

Ozonation Example



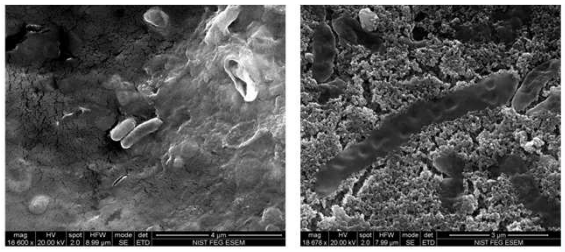
Disinfection



E. Coli - Healthy ***Post-AOP***

Sherchan, S. P.; Snyder, S. A.; Gerba, C. P.; Pepper, I. L. *J. Environ. Sci. Health Part A-Toxic/Hazard. Subst. Environ. Eng.* **2014,** *49* (4), 397-403.

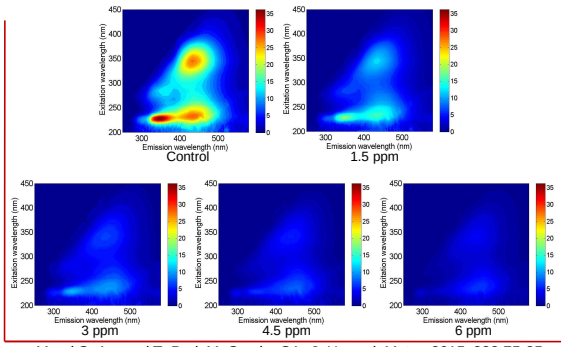
Membrane Fouling Reduction



MBR-RO control **MBR-Ozone-RO (3 mg/L)**

Stanford, B. D.; Pisarenko, A. N.; Holbrook, R. D.; Snyder, S. A., Preozonation Effects on the Reduction of Reverse Osmosis Membrane Fouling in Water Reuse. *Ozone-Sci. Eng.* **2011,** *33* (5), 379-388.

Fluorescence Surrogate Response



Merel S, Anumol T, Park M, Snyder SA. *J. Hazard. Mater.* 2015 282:75-85

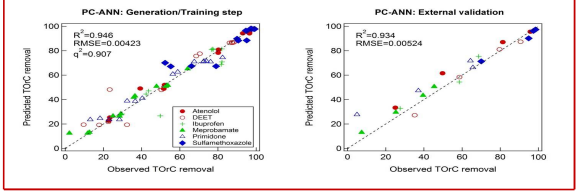
Surrogates

Environmental Science Water Research & Technology

PAPER

Modeling approaches to predict removal of trace organic compounds by ozone oxidation in potable reuse applications†

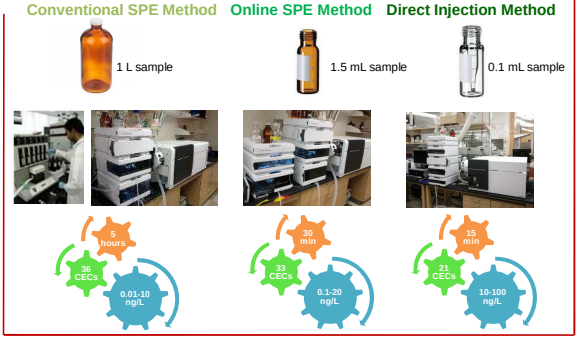
Minkyu Park,[a] Tarun Anumol[ab] and Shane A. Snyder*[ac]



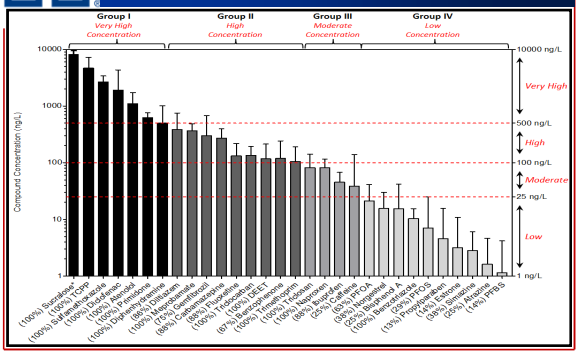
On-Line/Real-Time Sensor Network

INDICATORS

Targeted Indicator Analysis



Indicator Occurrence



Indicator Example – Secondary WWTP

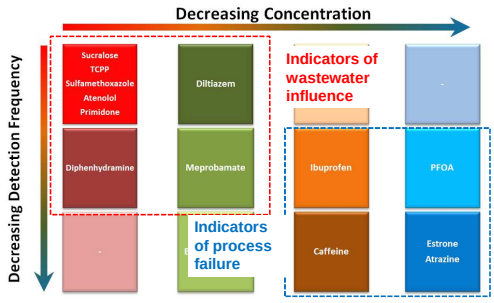
Faster transformation during secondary treatment

Higher sorption during secondary treatment

Sorption (log K_d)	Biotransformation (K_{bT} L/g-d) Recalcitrant <0.1	Moderate Slow 0.1-10	Rapid >10
Low <2.5	Carbamazepine, Meprobamate, Primidone, TCEP, Sucralose	DEET, Sulfamethoxazole, Gemfibrozil, Iopromide	Acetaminophen, Caffeine, Naproxen, Ibuprofen, Atenolol
Sorptive 2.5-3	TCPP	Cimetidine, Trimethoprim	Benzophenone, Diphenhydramine, Bisphenol A
Effective >3	Triclocarban		Triclosan, Fluoxetine

WERF CEC4R08 – Tanja Rauch-Williams *et al.* 2013

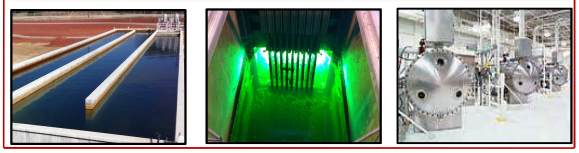
Indicator Priority List



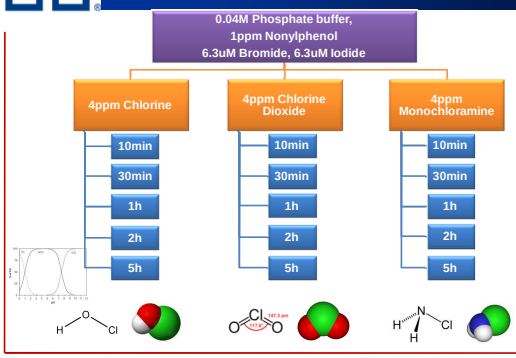
TRANSFORMATION PRODUCTS: CHLORINE

Oxidation/Disinfection

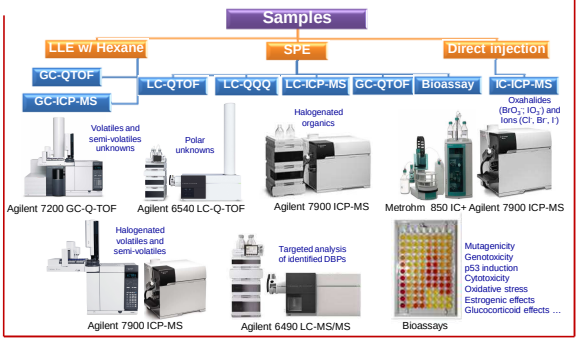
Disinfectant	Bacteria	Viruses	Parasites	DBPs
Free Chlorine	✓	✓	✗	THMs, HAAs
Chloramines	▭	✗	✗	NDMA
UV	✓	▭	✓	None???
Ozone	✓	✓	▭	Bromate, NDMA



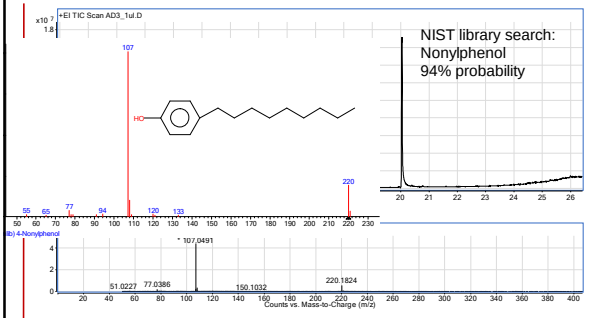
Nonylphenol Experiment



Sample Preparation and Analysis



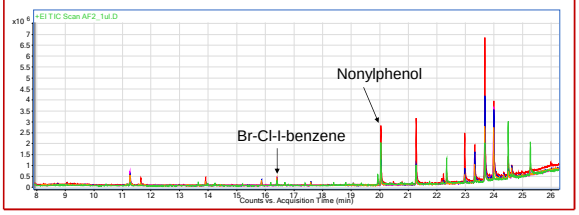
Nonylphenol – GC-QTOF



Oxidation with chlorine

DBP formation after oxidation with chlorine:

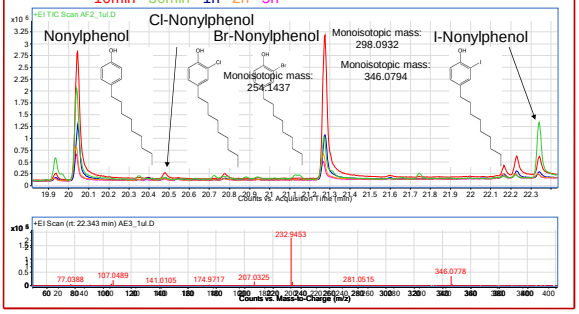
- 10min
- 30min
- 1h
- 2h
- 5h



Oxidation with chlorine

Monohalogenated DBPs:

10min 30min 1h 2h 5h

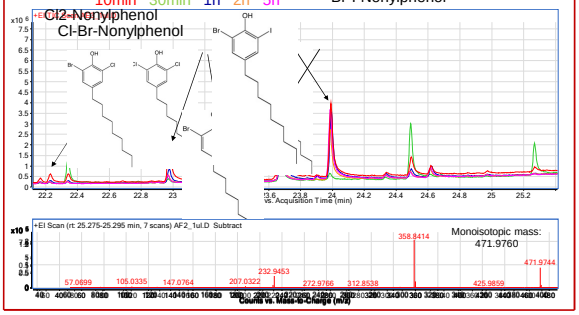


Oxidation with chlorine

Dihalogenated DBPs:

10min 30min 1h 2h 5h

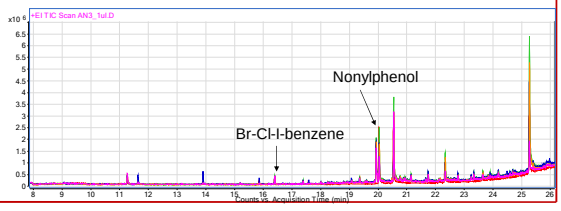
Cl2-Nonylphenol
Cl-Br-Nonylphenol
Br-I-Nonylphenol
I2-Nonylphenol



Oxidation with chlorine dioxide

DBP formation after oxidation with chlorine dioxide:

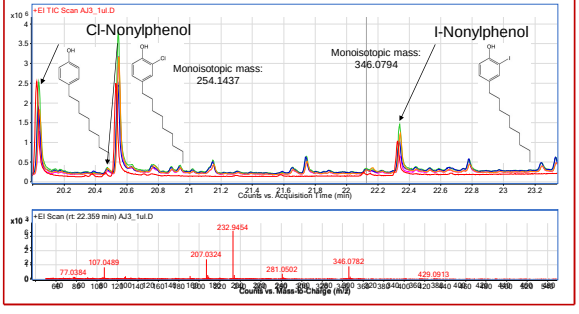
- 10min
- 30min
- 1h
- 2h
- 5h



Oxidation with chlorine dioxide

Monohalogenated DBPs:

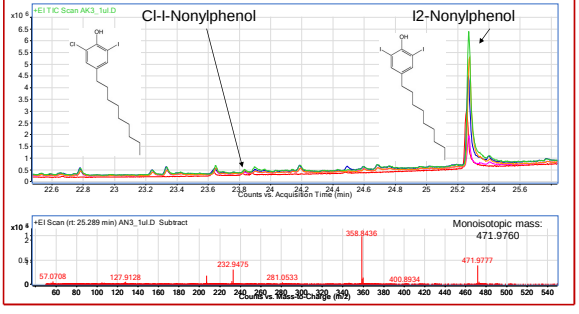
Nonylphenol 10min 30min 1h 2h 5h



Oxidation with chlorine dioxide

Dihalogenated DBPs:

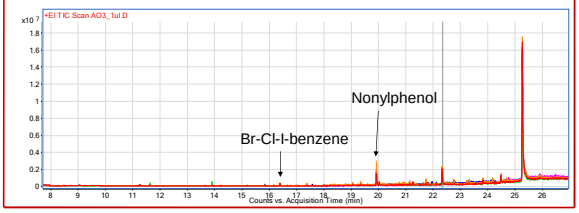
10min 30min 1h 2h 5h



Oxidation with monochloramine

DBP formation after oxidation with chlorine dioxide:

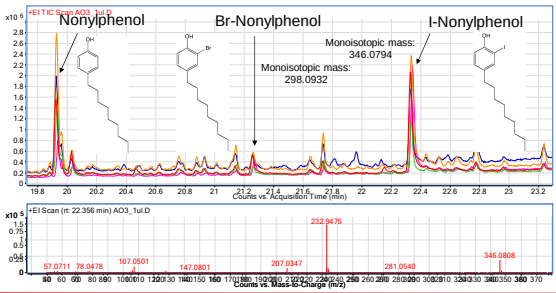
- 10min
- 30min
- 1h
- 2h
- 5h



Oxidation with monochloramine

Monohalogenated DBPs:

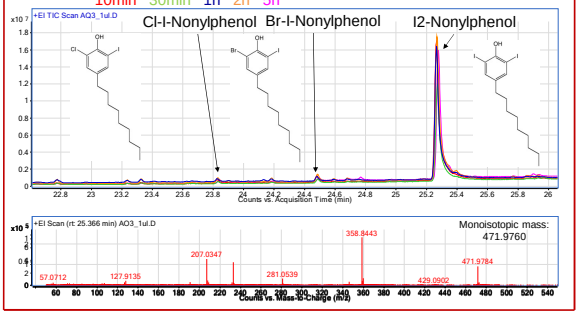
10min 30min 1h 2h 5h



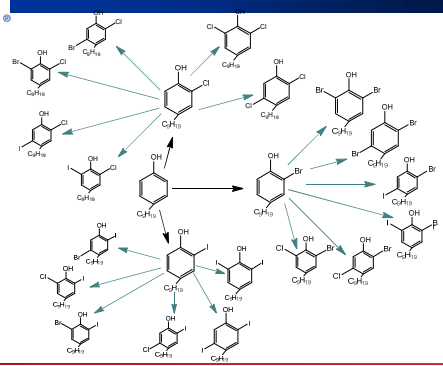
Oxidation with monochloramine

Dihalogenated DBPs:

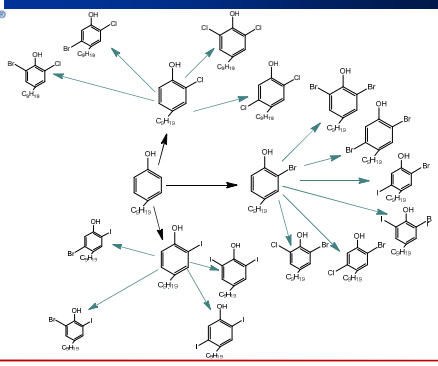
10min 30min 1h 2h 5h



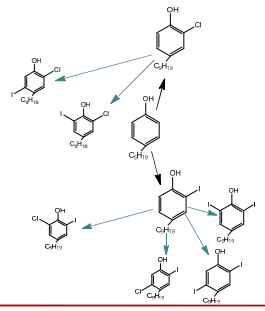
Transformation Pathways



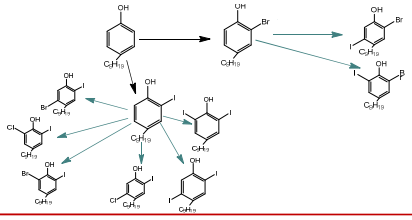
Identified DBPs after chlorination



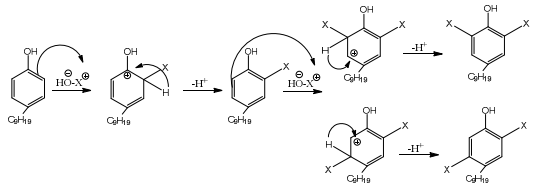
Identified DBPs after oxidation with chlorine dioxide



Identified DBPs after monochloramination



Mechanism of Formation



GC-ICP-MS

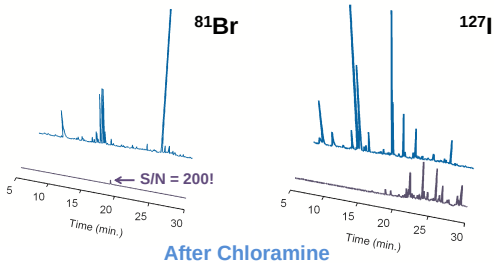
Advantages:

- **No water present → little/no oxide interferences**
- **No evaporative cooling of plasma → lower RF forward power**
- **Lower RF power → fewer Ar-based ions ($^{40}Ar^+$, $^{38}Ar^{40}Ar^+$, $^{38}Ar^{40}ArH^+$, etc.)**

∴ **Interference-free analysis without collision gas**

Model 7900 ICP-MS | Model 7890B GC | GC-ICP-MS

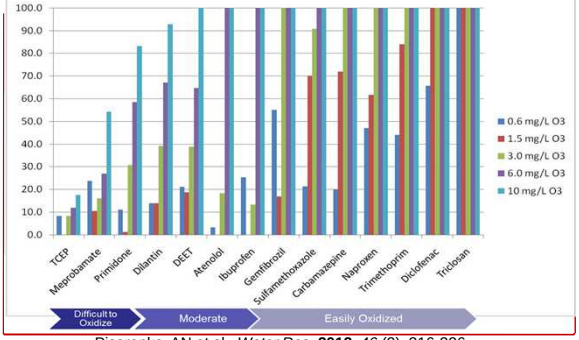
GC-ICP/MS: DBP Formation



After Chloramine
Before Chloramine

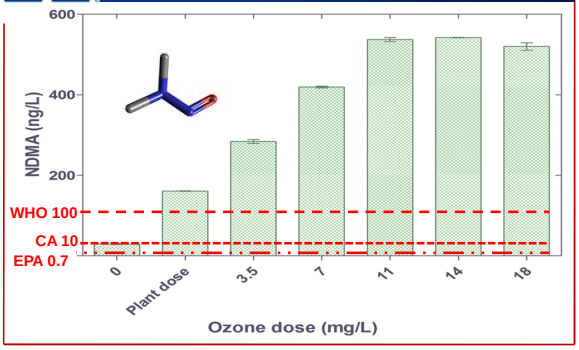
TRANSFORMATION PRODUCTS: OZONE

Indicator Oxidation



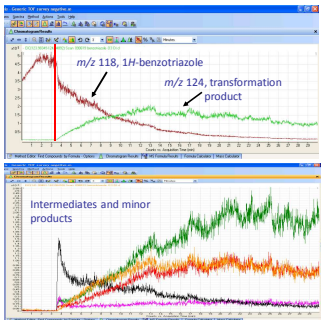
Pisarenko, AN et al.. *Water Res.* **2012,** *46* (2), 316-326.

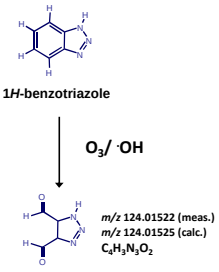
NDMA Formation w/ Ozone



Sgroi M, Roccaro P, Oelker GL, Snyder SA. ***ES&T*** 2014 48:10308-10315.

Benzotriazole Transformation Products

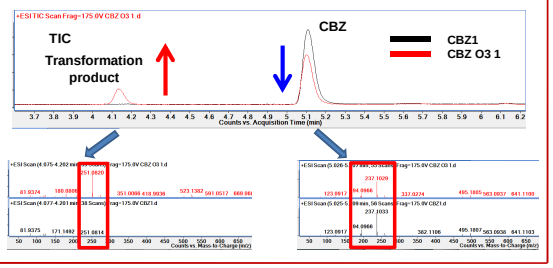




Mawhinney, DB, BJ Vanderford, SA Snyder. (2012). ***ES&T*** 46(13):7102-7111

Carbamazepine with/without ozonation

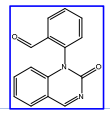
- CBZ (RT=5.1min) was degraded by ozone

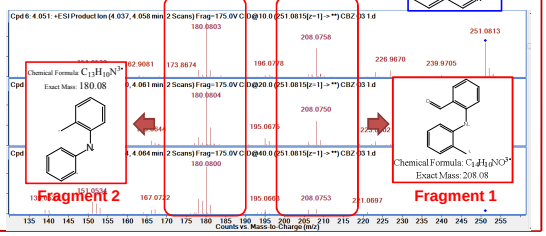


MS/MS spectra of transformation product (BQM)

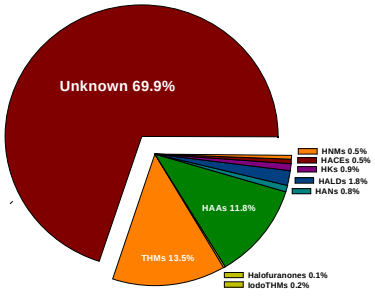
BQM

1-(2-benzaldhyde)-4-hydro-(1H,3H)-quinazoline-2-one





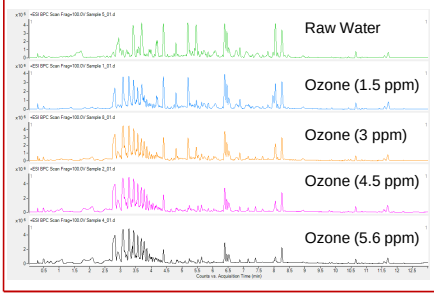
Most DBPs Not Identified



Nationwide Occurrence Study, Krasner et al., *Environ. Sci. Technol*. 2006, *40*, 7175-7185.

OZONE TREATMENT & QTOF ANALYSIS OF UNKNOWNS

Searching for unknown in water



Chromatograms Very Similar

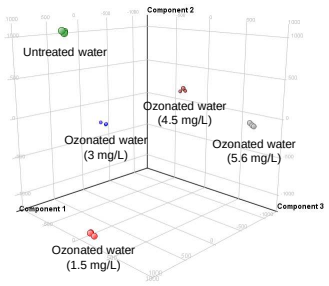
Extraction of Molecular Features Reveals thousands of compounds in each chromatogram

Further Data Processing Requires Specific Software

Merel, S.; Anumol, T.; Park, M.; **Snyder, S. A.**, *J. Hazard. Mater.* 2014 In Press

OZONE TREATMENT & QTOF ANALYSIS OF UNKNOWNS

PCA Plot for Different Ozone Doses



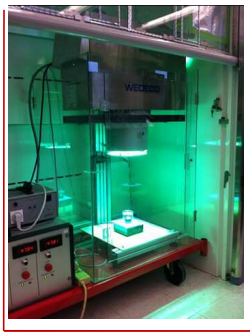
Although chromatograms were all similar for the analyst

Software identifies features able to discriminate the different water quality

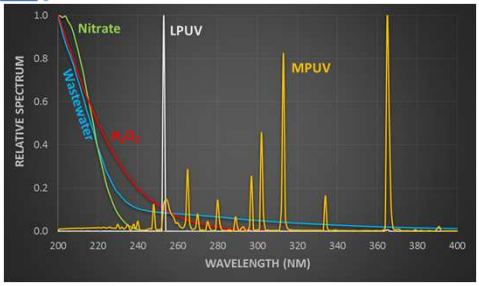
Merel, S.; Anumol, T.; Park, M.; **Snyder, S. A.** *J. Hazard. Mater.* 2014, In Press

TRANSFORMATION PRODUCTS FROM UV PHOTOLYSIS & OXIDATION

UV Transformation Products



Formation of nitrogenous byproduct by MPUV photolysis



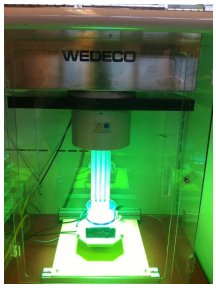
- Formation of nitrogenous byproducts (nitro- or nitroso aromatic compounds) through nitrate photolysis with organic precursors

Experimental matrix for UV AOP genotoxicity

- UV lamp type: low pressure (LP) and medium pressure (MP)
- Test water: Secondary treated wastewater (Ina Rd. WWTP)
- Oxidant: Hydrogen peroxide

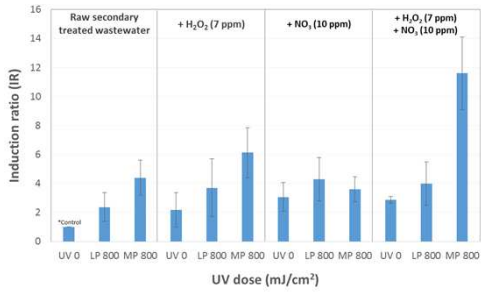
		Nitrate (0 mg/L)		Nitrate (10 mg/L)	
LP·MP UV /H_2O_2 AOP		H_2O_2 (mg/L)		H_2O_2 (mg/L)	
		0	**7**	**0**	**7**
UV dose (mJ/cm²)	**0**	X	X	X	X
	400	X	X	X	X
	800	X	X	X	X

UV collimated beam device



Ames mutagenicity test

- Mutagenicity strain: *Salmonella typhimurium* (TA98 w/o S9)
- Type of reversion mutation: Frameshift



Identification of Genotoxicant

Characterization of a larger set of unknown compounds

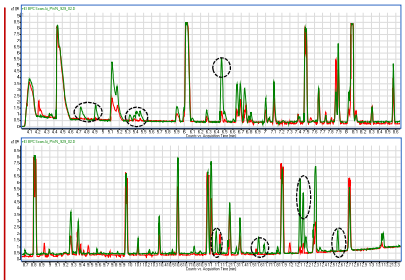
Sampl e → LC/MS of sample and overlayed extracted chromatograms → Data alignment and analysis → Validation with MS/MS from standards

Compound profile in a sample

LC/MS QTOF
Polar or moderately polar compounds

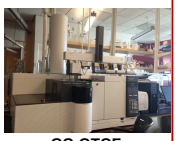
GC/MS QTOF
Volatile and semi-volatile compounds

Discovery of New DBPs



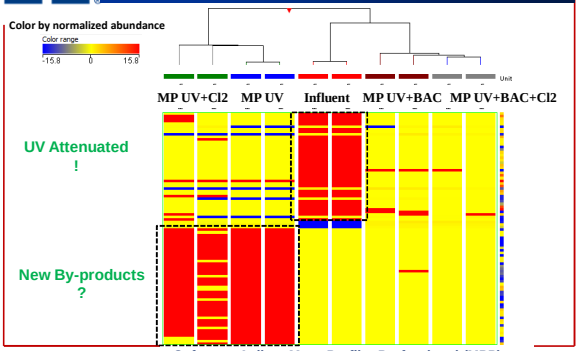
Red = Before MP UV
Green = After MP UV

LC-QTOF



GC-QTOF

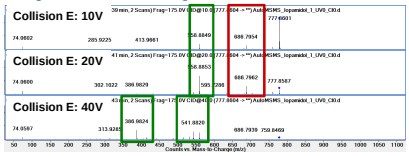
Discovery of Novel UV Transformation Products

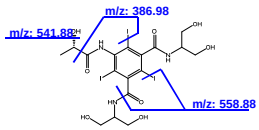


Software: Agilent Mass Profiler Professional (MPP)

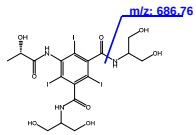
Fragmentation pattern of Iopamidol

MS/MS spectra of Iopamidol





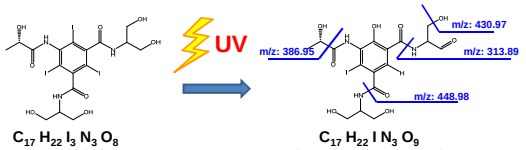
< Fragmentation pattern 1 >



< Fragmentation pattern 2 >

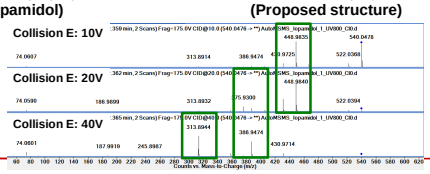
Transformation product of Iopamidol

$C_{17}H_{22}I N_3 O_9$ (Proposed structure)



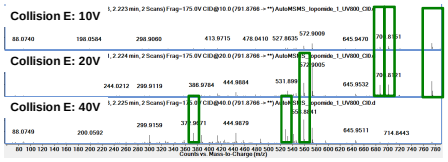
$C_{17}H_{22}I_3N_3O_8$ (Iopamidol)

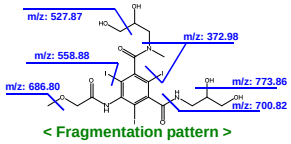
$C_{17}H_{22}IN_3O_9$ (Proposed structure)



Fragmentation pattern of Iopromide

MS/MS spectra of Iopromide

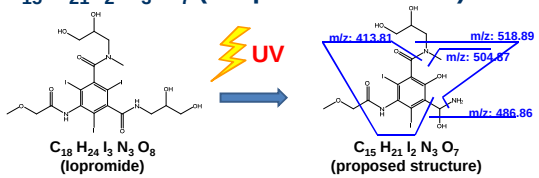




< Fragmentation pattern >

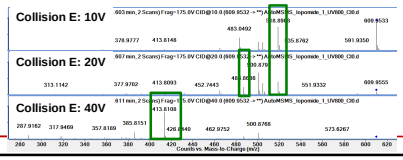
Transformation product of Iopromide

C_{15} H_{21} I_2 N_3 O_7 (Proposed structure)



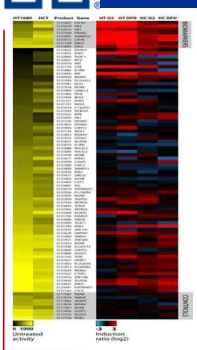
C_{18} H_{24} I_3 N_3 O_8
(Iopromide)

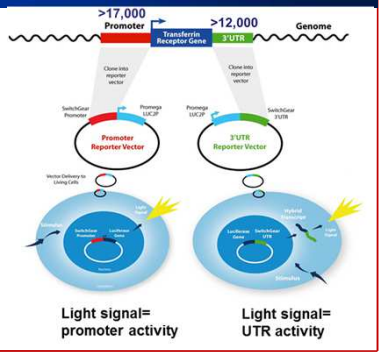
C_{15} H_{21} I_2 N_3 O_7
(proposed structure)



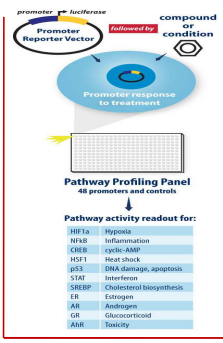
DISCOVERY & TREATMENT OF GLUCOCORTICOIDS

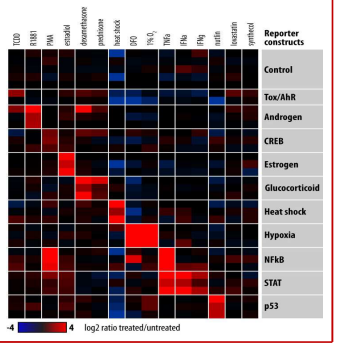
Transient Transfection Assay



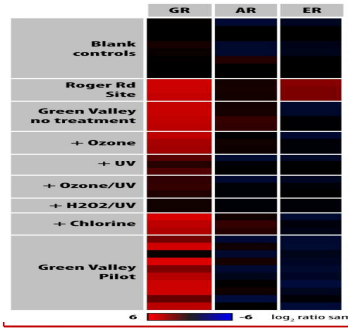


Multiple Endpoints Considered





Initial Recycled Water Screening



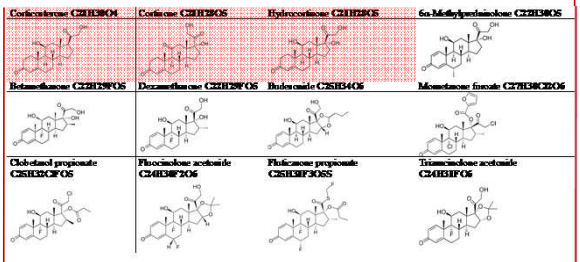
Receptors:

GR = glucocorticoid
AR = androgen
ER = estrogen

Glucocorticoids (GC)

- Natural & Synthetic
- Used for human diseases such as severe allergies, skin problems, asthma, and arthritis
- Used as veterinary medicine to restore muscle strength and as growth promoters to increase muscle size

Chemical structure of selected GCs



In most synthetic GCs, halogens are introduced to increase drug stability and potency/efficacy.

Glucocorticoids Among Most Widely Used Drugs

Amount prescribed in UK (2006)

Class	Prescribed (kg)
Estrogens	480
Androgens	307
Progestogens	1705
Glucocorticoids	4368

Human and Ecological Risk Assessment: An International Journal

Pharmaceuticals in the Aquatic Environment: Steroids and Anti-Steroids as High Priorities for Research

Medicare drugs USA (2013)

Source: The 2013 Drug Trend Report, Express Scripts Lab.

Recently approved as over-the-counter (OTC) drugs by the US FDA (2014)

Fluticasone propionate (Flonase)
Triamcinolone acetonide (Nasacort)

Glucocorticoids in environmental waters

Compared to estrogenic compounds, limited studies have investigated the occurrence and behavior of GCs in environmental waters.

Country	Number of investigated cpds	Concentration range (ng/L)	*In vitro* GR bioactivity (Dex-EQ, ng/L)	Mass Balance	Ref.
Australia	NA	NA	81	NA	*Water Res* **2014,** *49*, 300.
USA	NA	NA	16-90	NA	*Water Res* **2015,** *80*, 1. *Water Res* **2015,** *83*, 303.
China	7	<LOD-3.4	NA	NA	*Environ Sci Technol* **2007,** *41*, 3462. *Environ Sci Technol* **2011,** *45*, 2725.
France	9	3-229	NA	NA	*Talanta* **2008,** *74*, 1463.
Netherlands	18	ND-14	11-38	Maybe	*Environ Sci Technol* **2008,** *42*, 5814. *Environ Sci Technol* **2010,** *44*, 4766.
Japan	10	<LOD-7.6	<3-78	NO	*Sci Total Environ* **2015,** *527*, 328. *Environ Toxicol Chem* **2015,** doi: 10.1002/etc.3136.
Switzerland	~23	<LOD-29	30	NO	*Anal Bioanal Chem* **2014,** *406*, 7653. *Environ Sci Technol* **2014,** *48*, 12902.

Expose to GCs at low levels could potentially affect aquatic organisms

- GC at concentration of 0.1-1.0 µg/L can
  - Increase plasma glucose concentration as well as the related gene expression (PEPCK)
  - Increase the serum concentrations of free amino acids
  - female fathead minnows exhibit male secondary sexual characters, which suggest glucocorticoids may induce fish masculinization
- GCs crosstalk with other pathways and could enhance/depress xenobiotic metabolism related toxicity.
  - Glucocorticoids simulated aryl hydrocarbon receptor (AhR)-mediated transcription and the consequent CYP1A1 gene expression in rodents, however, suppress the AhR expression in human cells.


Fathead minnow


Rainbow trout


Carp

Environ. Sci. Tech. **2013,** *47*, 9487-9495.
Mar. Pollut. Bull. **2014,** *85*, 370-375.
Toxicol. Sci. **2007,** *99*, 455-469.

In Vivo Evaluation with GCs

Glucocorticoid activity detected by *in vivo* zebrafish assay and *in vitro* glucocorticoid receptor bioassay at environmental relevant concentrations

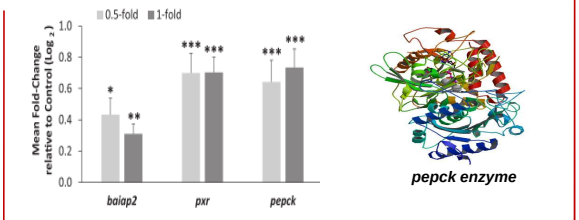
Chemosphere 144 (2016) 1162–1169

Qiyu Chen [a], Ai Jia [b], Shane A. Snyder [b], Zhiyuan Gong [c], Siew Hong Lam [a, c, *]

Treatment in Larvae / Gene	Dexamethasone (DEX)				Prednisolone (PRE)				Triamcinolone (TRI)			
	50 pM	500 pM	5 nM	50 nM	50 pM	500 pM	5 nM	50 nM	50 pM	500 pM	5 nM	50 nM
pepck	**	**	**	**	*	**	**	**	**	**	**	**
baiap2	**	**	**			**	**	**	**	**	**	**
pxr	**			**			**	**	**	**	**	**
mmp-13	**					**	**	*		**	**	**
cdkn1c				**	*				**	**		**
mmp-2							*			*	*	**
fkbp5				*								
cyp3a65						*						
sox9b		**		**			**					
gilz		*					*					
mmp-9						**	**	**				

Mean Fold-Change relative to Control (Log 2)
> 3
> 2 to 3
> 1 to 2 ** P < 0.01
> 0 to 1 * P < 0.05
Not significant (P > 0.05)
< 0 to -1
< -1 to -2
< -2

In Vivo Evaluation with GCs



pepck enzyme

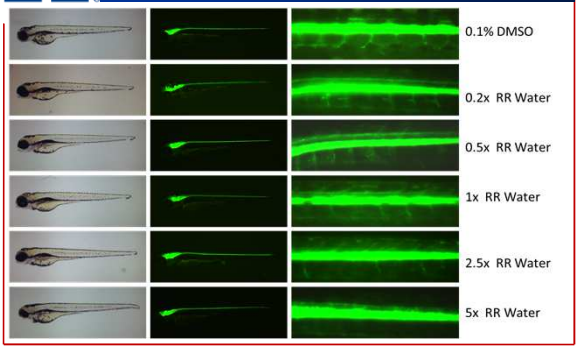
Brain-specific angiogenesis inhibitor 1-associated protein 2): insulin receptor

Pregnane X receptor (pxr): signals for detoxification

Phosphoenolpyruvate carboxykinase (pepck): gluconeogenesis

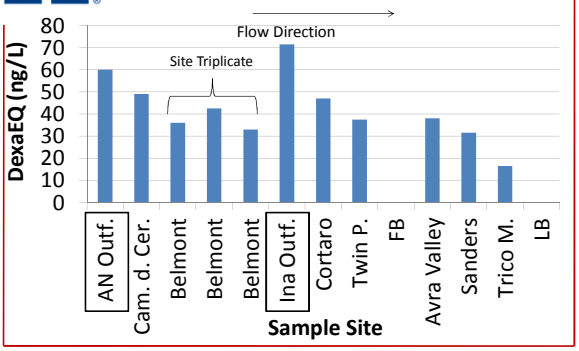
Chemosphere 144 (2016) 1162–1169

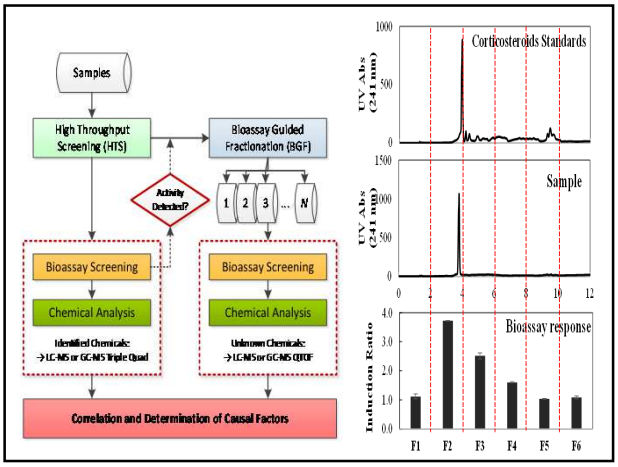
In Vivo Evaluation with GCs

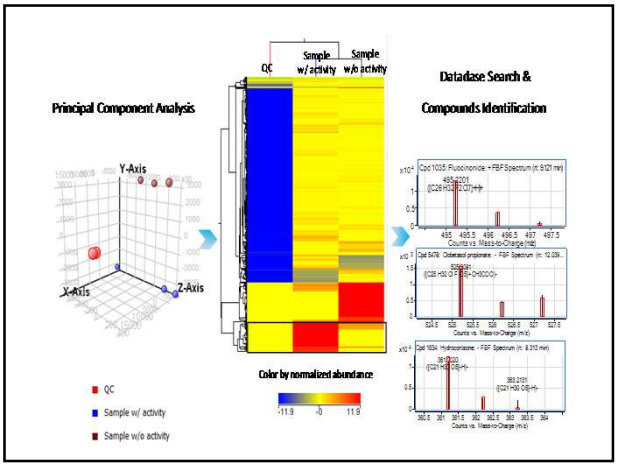


Santa Cruz River Sampling Sites

GR Cellular Activity

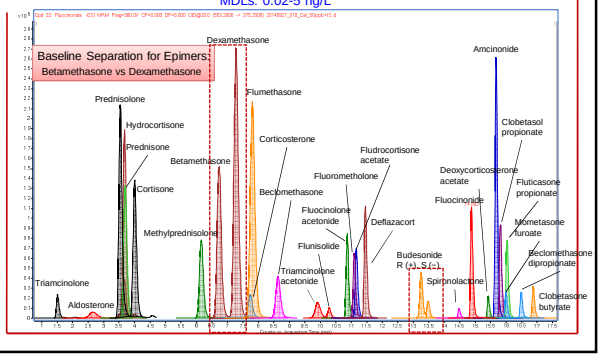




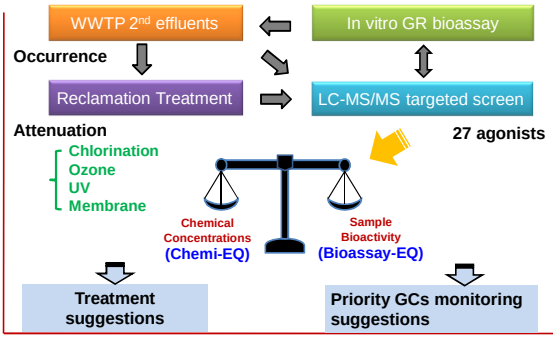


Sensitive LC-MS/MS analysis for targeted GR agonists

MDLs: 0.02-5 ng/L



Balancing the GC Budget



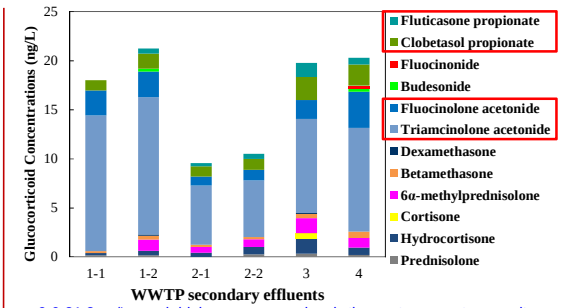
Sample Collection

- 2nd effluents from four WWTPs in Arizona and California.
- Full scale:
  - Chlorination
    - Pre-, Chlor-, De-chlor.
  - WWRF:
    - Effluent-MF-RO-UV
    - Effluent-ozone
- Bench/pilot scale:
  - Ozonation:
    - O_3: TOC 0.25, 0.5, 1.0
  - UV
    - 20, 40, 80, 100, 200, 400 mJ/cm^2
  - Reverse osmosis (RO)
    - RO permeate, RO brine
  - Chlorination

WWTP Effluent

AOP Pilot (Wedeco)

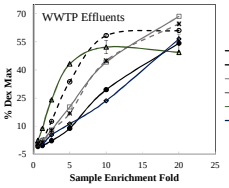
Glucocorticoid Concentrations in WWTP Effluents



9.6-21.2 ng/L, much higher occurrence levels than estrogens at same sites

The occurrence and attenuation of GR activity in water treatment processes

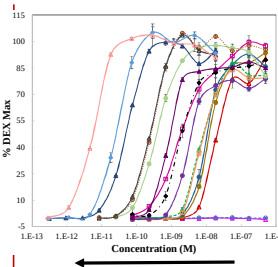
GR activity in four US WWTP effluents



Effluent	EC_{10}	EC_{50}	Dex-EQ (ng/L)
1-1	5.25	17.8	39.0
1-2	2.19	7.59	93.6
2-1	2.95	11.8	69.4
2-2	3.16	11.8	64.8
3	1.32	7.41	155
4	4.47	17.8	143

Comparable with reported levels (<3-90 ng Dex-EQ/L)

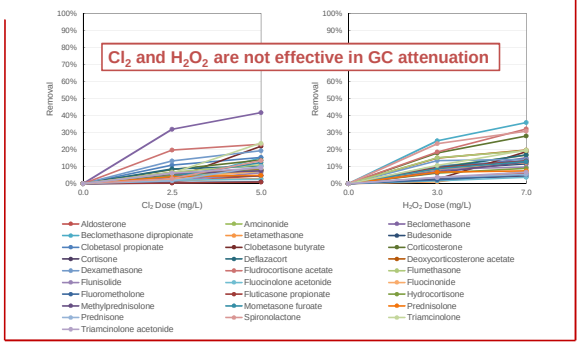
Relative potency of targeted GR agonists



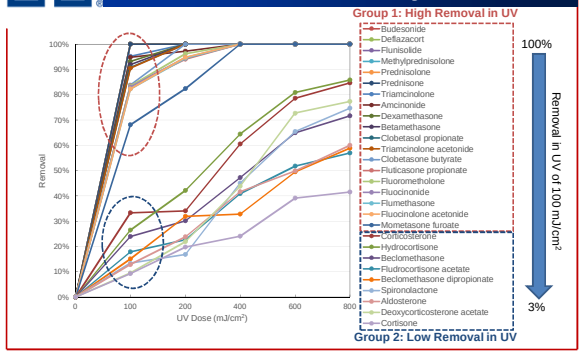
GCs	EC_{50} (nM)	REP
Prednisone	>500	<0.004
Cortisone	>500	<0.004
Prednisolone	17.7	0.101
Triamcinolone	11.8	0.152
Fludrocortisone acetate	9.67	0.185
Hydrocortisone	6.81	0.264
6α-methylprednisolone	6.79	0.264
Betamethasone	2.83	0.634
Fluocinonide	1.89	0.948
Dexamethasone	1.79	1.000
Triamcinolone acetonide	0.79	2.265
Flumethasone	0.36	5.032
Budesonide	0.26	6.895
Fluocinolone acetonide	0.24	7.398
Clobetasol propionate	0.048	37.04
Fluticasone propionate	0.025	70.88
GCs mixed standard	0.005	329

Most synthetic GCs have much higher activity than natural GCs

Removal of GCs in Cl_2 and H_2O_2 Only

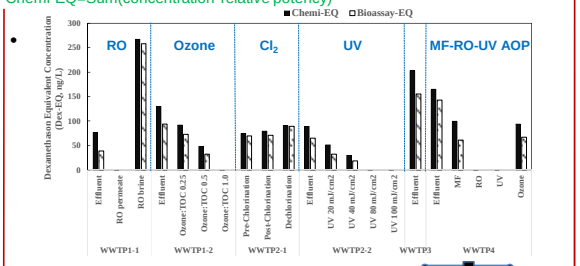


Removal of GCs in LPUV Only



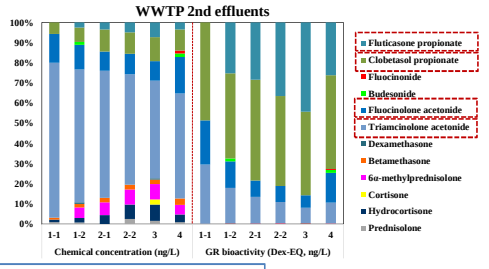
Targeted GCs derived GR activity in water

Chemi-EQ=Sum(concentration*relative potency)



The detected glucocorticoids can entirely explain the observed biological GR activity

GCs concentration and GR activity profiles in WWTP effluents

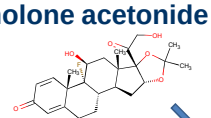


Fluticasone propionate, **clobetasol propionate**, **fluocinolone acetonide**, and **triamcinolone acetonide**, which have high contributions to GR activity in WWTP effluents, all within Group 1

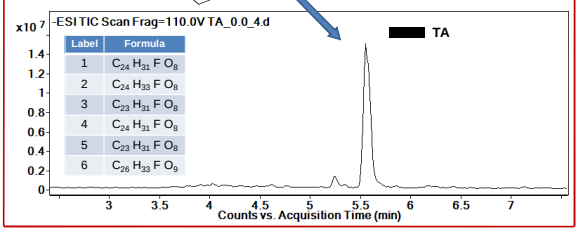
UV treatment is very effective in GR activity attenuation

GR Oxidation Products

Triamcinolone acetonide (TA)

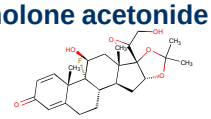


$C_{24}H_{31}FO_6$

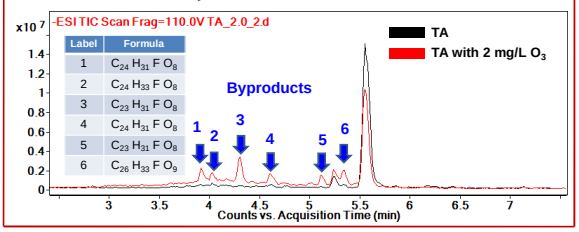


GR Oxidation Products

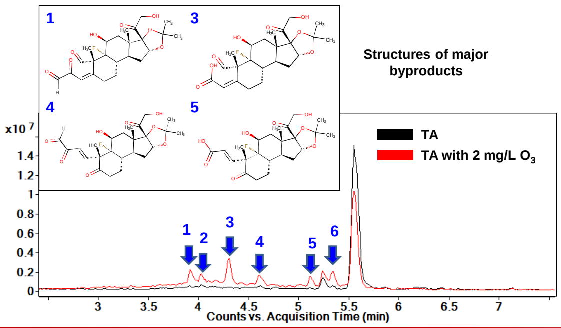
Triamcinolone acetonide (TA)



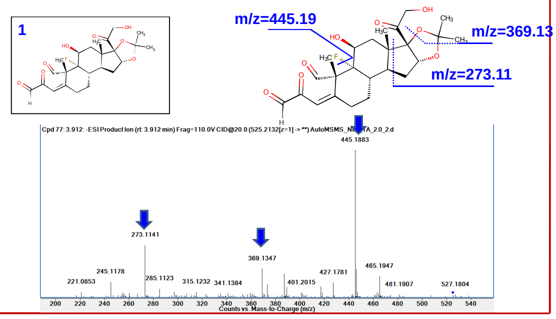
$C_{24}H_{31}FO_6$



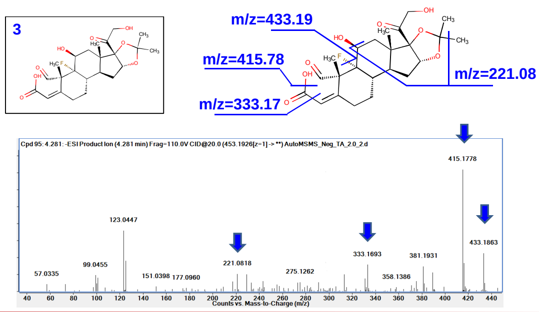
GR Oxidation Products



GR byproduct (MS/MS)



GR byproduct (MS/MS)



Public Acceptance is Growing

USA TODAY

THE NATIONAL ACADEMIES
Advisers to the Nation on Science, Engineering, and Medicine

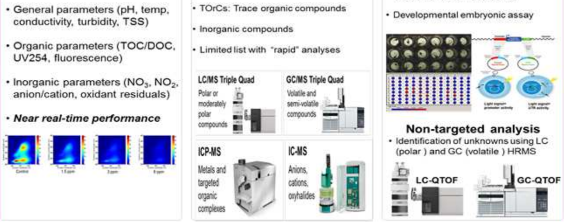
Report: Drinking wastewater preferable to wasting it

Council touts it as potable after treatment

"…distinction between *indirect* and *direct* potable reuse is not scientifically meaningful…"

Tiered Testing Strategy

Tier 1 Bulk Water Characteristics (Surrogates)	Tier 2 Targeted Chemical Analysis: (Indicators)	Tier 3 Bioassay & Non-targeted Analyses
On-line & off-line analysis • General parameters (pH, temp, conductivity, turbidity, TSS) • Organic parameters (TOC/DOC, UV254, fluorescence) • Inorganic parameters (NO_3, NO_2, anion/cation, oxidant residuals) • *Near real-time performance*	**Targeted chemical analysis** • TOrCs: Trace organic compounds • Inorganic compounds • Limited list with "rapid" analyses LC/MS Triple Quad: Polar or moderately polar compounds GC/MS Triple Quad: Volatile and semi-volatile compounds ICP-MS: Metals and targeted organic complexes IC-MS: Anions, cations, oxyhalides	**In Vitro Screening** • Battery of relevant bioassays • Developmental embryonic assay **Non-targeted analysis** • Identification of unknowns using LC (polar) and GC (volatile) HRMS LC-QTOF GC-QTOF



ftp://ftp.sccwrp.org/pub/download/DOCUMENTS/CECpanel/CECMonitoringInCARecycledWater_FinalReport.pdf

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