The Next Generation of Drinking Water Disinfection By-Products

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Drinking Water DBPs: How are they formed?
Fig. 12.7 Chemical network structure of humic acids according to Schulten and Schnitzer. Reproduced by permission of Springer-Verlag.
Drinking Water DBPs—What are the Issues?

Concern over possible human health risk:

• Epidemiologic studies: risk of bladder cancer; some cause cancer in laboratory animals

• Recent concerns about possible reproductive & developmental effects (from epi studies)

Goal: Comprehensively identify DBPs formed from different disinfectants, test for toxicity, understand their formation, minimize or eliminate in drinking water
Only 11 DBPs Regulated in U.S.

<table>
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<tr>
<th>DBP</th>
<th>MCL (µg/L)</th>
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<td>Total THMs</td>
<td>80</td>
</tr>
<tr>
<td>5 Haloacetic acids</td>
<td>60</td>
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<td>Bromate</td>
<td>10</td>
</tr>
<tr>
<td>Chlorite</td>
<td>1000</td>
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- Little known about occurrence, toxicity of unregulated DBPs
- Regulated DBPs do not cause bladder cancer in animals
- Two unregulated DBPs are carcinogens
- Many unregulated DBPs more genotoxic than regulated ones
>600 DBPs identified, but more than 50% still not known....


~50% of TOX >1000 Da: Khiari, et al., Proc. 1996 AWWA Water Quality Technology Conference
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- Two unregulated DBPs are carcinogens
- Many unregulated DBPs more genotoxic than regulated ones
Unlike other contaminants that may or may not be present in drinking water…

DBPs are ubiquitous
Iodo-THMs

New Iodo-Acids

Iodoacetic acid

Bromoiodoacetic acid

(Z)-3-Bromo-3-iodopropenoic acid

(E)-3-Bromo-3-iodopropenoic acid

(E)-2-Iodo-3-methylbutenedioic acid

Initially discovered using GC/MS
Highly genotoxic
Increase in formation with NH₂Cl vs. Cl₂
Occurrence Study published in Nov. 2008 (23 cities in U.S. & Canada)

Genotoxicity of Iodoacetic acid


IA also caused developmental effects in mouse embryos (Hunter et al., 1995)
Genotoxicity of Emerging DBPs

DBP Chemical Class

- Other DBPs
- Haloacetamides
- Haloacetonitriles
- Halonitromethanes
- Halo Acids
- Haloacetic Acids

Not Genotoxic: DCAA, TCAA, BDCAA, Dichloroacetamide, Chloroform
Chlorodibromomethane, 3,3-Dibromopropenoic Acid,
3-Iodo-3-bromopropenoic Acid, 2,3,3-Tribromopropenoic Acid

Data courtesy of Michael Plewa, University of Illinois
Genotoxicity of Other DBPs

Not Genotoxic: DCAA, TCAA, BDCAA, Dichloroacetamide, Chloroform, Chlorodibromomethane, 3,3-Dibromopropenoic Acid, 3-Iodo-3-bromopropenoic Acid, 2,3,3-Tribromopropenoic Acid

Data courtesy of Michael Plewa, University of Illinois
But, all of this toxicity testing is for separate, individual DBPs…

**DBPs are really present as MIXTURES**

>300 DBPs probably present in glass of water
Integrated Disinfection By-products Mixtures Research: Toxicological and Chemical Evaluation of Alternative Disinfection Treatment Scenarios

A collaborative effort between:
NHEERL (National Health and Environmental Effects Research Laboratory), RTP
NERL (National Exposure Research Laboratory), Athens
NRMRL (National Risk Management Research Laboratory), Cincinnati
NCEA (National Center for Environmental Assessment), Cincinnati

Purpose:
To address concerns related to potential health effects from exposure to DBPs that cannot be addressed directly from toxicological studies of individual DBPs or simple DBP mixtures
*In Vitro* and *In Vivo* Toxicological Assays

**In vitro:**
- Reproductive/developmental
- Mutagenicity
- Carcinogenicity
- Neurotoxicity
- Metabolism

**In vivo:**
- Reproductive/developmental
- Mutagenicity/carcinogenicity
- Immunotoxicity
- Hepatic/renal toxicity
- Neurotoxicity/developmental neurotoxicity
- Kinetics/metabolism
**RO Concentration of DBPs**

From Plant (0.5 gpm)

- 600 gal. CW
- Ion Exchange

1st Phase (1999-2001):
Cl₂ & O₃; treated water first
Concentrated after

Permeate to Waste

500 gal.

200 gal.

100 gal.

14 gal.

**Full Study Concentration**

- RAW SURFACE WATER
- FLOW EQUALIZATION
- ULTRAFILTRATION MEMBRANES
- BAG FILTER
- REVERSE OSMOSIS MEMBRANES
- ION EXCHANGE COLUMNS


Full Study (2006-2008):
Concentrated NOM first
Treated with Cl₂ after
Results

- Good mix of Cl/Br DBPs produced
- 75 Priority and regulated DBPs quantified
- >100 DBPs comprehensively identified
- Most DBPs fairly consistently produced among chlorination events
- Concentration offered by RO a bonus for detecting DBPs present at very low levels (e.g., MX, which is present in drinking water at ng/L levels)
- Most DBPs are stable over time on the rats’ cages
- No major repro/developmental effects observed, but some subtle effects (decreased sperm count, etc.)
Conclusions

• A thorough examination of reproductive/developmental and other endpoints was predominantly negative

• Some small, subtle effects for chlorinated water concentrate (136x concentration factor may be “on the edge” of ability to see effects)

• Concentration offered by RO a bonus for detecting DBPs present at very low levels (e.g., MX, which is present in drinking water at ng/L levels)

• Combination of comprehensive, qualitative identification work and quantification of 75 DBPs allowed comprehensive assessment of DBPs present in water

• Most DBPs stable on rats’ cages and chlorination events were reproducible

Planning a follow-up study that includes Chlorine vs. Chloramines
Formation of iodo-DBPs from X-ray contrast media

Iopamidol + NOM $\xrightarrow{\text{HOCl, } \text{NH}_2\text{Cl}}$ Iodo-DBPs
## Iodo-DBP Occurrence Study

<table>
<thead>
<tr>
<th>Plant</th>
<th>Iodide (µg/L)</th>
<th>Sum iodo-acids (µg/L)</th>
<th>Sum iodo-THMs (µg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plant 2</td>
<td>1.0</td>
<td>0.37</td>
<td>4.9</td>
</tr>
<tr>
<td>Plant 4</td>
<td>ND</td>
<td>0.10</td>
<td>1.2</td>
</tr>
<tr>
<td>Plant 11</td>
<td>1.5</td>
<td>0.21</td>
<td>2.3</td>
</tr>
<tr>
<td>Plant 15</td>
<td>ND</td>
<td>0.17</td>
<td>2.4</td>
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Detection limit = 0.13 µg/L

## ICM in U.S. Drinking Water Sources (ng/L)

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<tr>
<th>Plant</th>
<th>Iopamidol</th>
<th>Iomeprol</th>
<th>Iopromide</th>
<th>Iohexol</th>
<th>Diatrizoate</th>
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<tr>
<td>Plant 1</td>
<td>11</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
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<tr>
<td>Plant 2</td>
<td>510</td>
<td>ND</td>
<td>24</td>
<td>120</td>
<td>93</td>
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<tr>
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<td>110</td>
<td>ND</td>
<td>6</td>
<td>49</td>
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<td>ND</td>
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<tr>
<td>Plant 17</td>
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<td>ND</td>
<td>ND</td>
<td>ND</td>
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<td>Plant 19</td>
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Courtesy of Thomas Ternes, Federal Institute of Hydrology, Germany
ICM measured using LC/ESI-MS/MS; DLs = 5-20 ng/L
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ICM measured using LC/ESI-MS/MS; DLs = 5-20 ng/L
Controlled Laboratory Reactions

Experiments
• React ICM with HOCl, NH$_2$Cl (with and without NOM)
• 3 pHs
• Follow formation of iodo-DBPs
• Identify reaction products and intermediates
• Measure genotoxicity

Methods
• Iodo-THMs: GC/EI-MS
• Iodo-Acids: GC/NCl-MS (with derivatization)
• Iopamidol (and other ICM): LC, LC/MS/MS
• Larger MW products and intermediates: LC/MS/MS
• Genotoxicity: Chinese hamster ovary cells, single cell gel electrophoresis
Results

Iopamidol

\[
\text{HOCl} \quad \text{NH}_2\text{Cl} \quad \text{Iodo-DBPs}
\]

Only trace levels

NOM

Iodo-DBPs

Iodo-THMs

Iodo-Acids

[Chemical structures and reactions shown]

\[
\text{HOCl} \quad \text{NH}_2\text{Cl} \quad \text{Iodo-DBPs}
\]

Only trace levels

NOM

Iodo-DBPs

Iodo-THMs & Iodo-Acids

[Chemical structures and reactions shown]
Genotoxicity of Chlorinated Waters Containing Iopamidol

Organic Extracts from Water Samples (Concentration Fold)
Acknowledgments

A few fabulous toxicologists who have helped push this field forward....

Also, Mike Narotsky, Sid Hunter, Rex Pegram, ....