Biochemically-active Contaminants

- **Pharmaceuticals**
  - Prescription
    - Codeine, albuterol, cimetidine, digoxin, warfarin
  - Non-prescription
    - Acetaminophen, caffeine, ibuprofen
- **Antibiotics (veterinary & human)**
  - Erythromycin, tetracycline, sulfadimethoxine, sulfathiazole
- **Steroids**
  - Cholesterol, coprostanol - not hormonally active
  - Androsterone - hormonally active
- **Reproductive hormones**
  - Estradiols, progesterone, estriol, testosterone
- **Other hormonally active compounds**
  - Nonylphenol, bisphenol A - household products
  - Carbaryl, chloropyrifos, diazinon, dieldrin - insecticides

Must also consider metabolites
Classifications

As a result of various science planning activities (within and outside government), confusion often develops with regard to the relationship between PPCPs and "endocrine disrupting compounds". Only a small subset of PPCPs are known or suspected of being direct-acting endocrine disrupting compounds (EDCs)\(^1\) (primarily synthetic steroids and other synthetic hormones, acting as hormone or anti-hormone modulating mimics -- agonists or antagonists, respectively). While many xenobiotics can have a wide range of ultimate, indirect effects on the endocrine system, few have direct effects (i.e., serve as immediate endocrine agonists/antagonists at the hormone-receptor level). As an example, the inhibition or induction (such as by triazine herbicides) of P450 aromatase can effect changes in androgen/estrogen ratios; this effect is not at the receptor level. It is important to note that PPCPs and direct-acting EDCs are NOT synonymous, and the toxicological concerns are usually totally different.

Classifications (cont.)

Furthermore, the endocrine system (and its interconnected signaling pathways) is extraordinarily complex and cannot be easily distilled to a simple issue of "disruption" or "modulation". While "disruptors" can act directly at the hormone-receptor level, they can also act indirectly via a plethora of alternative routes (e.g., nervous system, immune system, specific cellular transporter systems), most of which are not always considered in the scope of many of the current definitions of EDCs. Endocrine disruption, in general, is narrowly viewed as a reproductive/developmental issue. An excellent overview of EDCs can be found at the "Environmental Estrogens and other Hormones" web site (Bioenvironmental Research at Tulane and Xavier Universities): http://www.tmc.tulane.edu/ECME/eohome.

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\(^1\)a.k.a: environmental estrogens, endocrine-disruptors, endocrine-modulators, estrogenic mimics, ecoestrogens, environmental hormones, xenoestrogens, hormone-related toxicants, hormonally active agents (phytoestrogens being a subset)
More information

- EPA web site
  - [http://www.epa.gov/nerlesd1/chemistry/pharma/index.htm](http://www.epa.gov/nerlesd1/chemistry/pharma/index.htm)

Physiological Impact

- Some have LC\textsubscript{50} values below 1 µg/L
- Must consider synergistic effects
  - Shown to be significant
    - Silva et al., 2002 [ES&T 36:8:1751]
Risk to drinking water

- Many will not be removed by treatment
- Some will be altered by treatment
  - Possible increase in potency

Furhacker et al., 2000; Chemosphere, 41(5)751.

Chlorination of Bisphenol A

- Estrogen receptor binding affinity increases greatly upon chlorination
- Which byproducts are responsible?

Hu et al., 2002; Env. Sci. Technol., 36(9)1980.
US National Reconnaissance

- USGS Study
  - 1999-2000
  - 95 compounds
  - 139 streams
  - Focus on systems at risk

See also:
http://toxics.usgs.gov/regional/erfc.html

Kolpin et al., 2002; Env. Sci. Technol., 36(6)1203

David Reckhow
CEE 577 #39
Most often detected

Detection by category

Kolpin et al., 2002; Env. Sci. Technol., 36(6)1203
Removal by WW Treatment

- Biodegradation and washout during high flow?

Ternes, 1998; Water Res., 32(11)3245
Summary of sorption & volatilization effects

- Assume
  - $T_a = 283$ K
  - $M = 200$ g/mole
  - $U_w = 5$ mph
  - $v_s = 91$ m/yr

Classification based on partitioning

- In terrestrial (soil) systems
  - $m = 10^5$ to $10^6$ mg/L
  - Immobile: $K_d > 50$ L/kg
  - Slightly mobile: $K_d = 5$-50 L/kg
  - Medium to highly mobile: $K_d < 5$L/kg

- In aqueous systems
  - $@m = 100$ mg/L
  - Particulate based: $K_d > 10,000$ L/kg
  - Solution based: $K_d < 10,000$ L/kg
Estimation of partition coefficients

- Relationship to organic fraction
  \[ K_d = f_{oc} K_{oc} \]
  \( \text{mg tox.} / \text{g-C} \rangle \text{mg tox.} / \text{m}^3 \) \( \text{g-C} \)

- and properties of organic fraction
  \[ K_{oc} = 6.17 \times 10^{-7} K_{ow} \]

- combining, we get:
  \[ K_d = 6.17 \times 10^{-7} f_{oc} K_{ow} \]

Karickhoff et al., 1979; Wat. Res. 13:241

Other correlations

- Karickoff, 1979
  \[ K_{oc} = 6.17 \times 10^{-7} K_{ow} \]
  \[ K_{oc} = 0.617 K_{ow} \]

- Karickoff, 1981
  \[ K_{oc} = 2.57 K_{ow}^{0.84} \]

- Schwarzenbach
  \[ K_{oc} = 3.09 K_{ow}^{0.72} \]

Based on neutral organic compounds

Karickhoff 1981; Chemosphere 10:833
Schwarzenbach & Westall 1981; Env. Sci. Techn. 15:1630
Tetracycline

**Compound / Structure**

<table>
<thead>
<tr>
<th>Compound</th>
<th>CAS-Nr</th>
<th>MW</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetracycline</td>
<td>60-54-8</td>
<td>444.43</td>
</tr>
</tbody>
</table>

**Physical-chemical properties:**

- $\log K_{ow} = -1.19$
- $S = 1.7 \text{ g/L}$
- $pK_{a,1} = 3.30$
- $pK_{a,2} = 7.68$
- $pK_{a,3} = 9.69$
- $\log K_f (Al^{3+}) = 10^{12.5}$
- $\log K_f (Fe^{3+}) = 10^{13.4}$

*Tolls, 2001; Env. Sci. Technol., 35(17)3397*

<table>
<thead>
<tr>
<th>Compound/Corollary Information</th>
<th>$K_{ow}$ (LAQ)</th>
<th>$K_f$ (LAQ)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetracycline</td>
<td>pure Na-bentonite, Langmuir Iso, pH dependence, $C_{max}$ at pH 6.1: 78 µmol/L, $K_r$ not specified</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>pure Ca-bentonite, Langmuir Iso, $C_{max}$ at pH 6.1: 200 µmol/L, $K_r$ not specified</td>
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<td>30</td>
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<tr>
<td></td>
<td>bentonite modified with cationic surfactant (Cetyltrimethylammonium), Langmuir Iso, $C_{max}$ at pH 6.1: 38 µmol/L, $K_r$ not specified</td>
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<td>30</td>
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<tr>
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<td>bentonite modified with tannic acid, Langmuir Iso, $C_{max}$ at pH 6.1: 210 µmol/L, $K_r$ not specified</td>
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<td>30</td>
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<tr>
<td></td>
<td>pure montmorillonite clay mineral, Langmuir Iso, $C_{max}$ at pH 5.0: 540 µmol/L, $K_r$ not specified</td>
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<td>30</td>
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<tr>
<td></td>
<td>clay loam, Teske, KS</td>
<td>$&gt; 600$</td>
<td>37</td>
</tr>
<tr>
<td></td>
<td>soil organic matter (peats, Nova Scotia; pH 4.55)</td>
<td>1 620</td>
<td>24</td>
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<tr>
<td></td>
<td>soil organic matter (peats, Nova Scotia; pH 6.14, iso's non-linear</td>
<td>1 140</td>
<td>24</td>
</tr>
</tbody>
</table>

*Tolls, 2001; Env. Sci. Technol., 35(17)3397*
Nearly all values fall above Karickoff’s relationship

\[ K_{oc} = 2.57 K_{ow}^{0.84} \]

Structure and sorption

- Enrofloxacin and Decarboxy Enro

<table>
<thead>
<tr>
<th>Compound / CAS-Nr / MW</th>
<th>Structure</th>
<th>Physical-chemical properties:</th>
<th>( K_d ) (L/Kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enro - CO₂</td>
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<td>7.7</td>
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<td>MW: 315.20 131775-99-0</td>
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<td>Enro - CO₂ = Decarboxylated enrofloxacin</td>
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<tr>
<td>Enrofloxacin</td>
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<tr>
<td>93106-60-6</td>
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<tr>
<td>MW: 359.40</td>
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<tr>
<td>Tolls, 2001; Env. Sci. Technol., 35(17)3397</td>
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• The End