Updated: 17 April 2013

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CEE 577: Surface Water Quality Modeling

Lecture #39

Special Topics: Pharmaceuticals & Endocrine Disruptors

(misc. current literature)

Biochemically-active Contaminants

- Pharmaceuticals
  - Prescription
    - Codeine, albuterol, cimetidine, digoxin, warfaren
  - 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)† (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
  - †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)

Pharmaceuticals and Personal Care Products in the Environment: Overarching Issues and Overview, by Christian G. Daughton, in *Pharmaceuticals and Personal Care Products in the Environment: Scientific and Regulatory Issues*, 2001 (ACS)

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/ eehome.

Pharmaceuticals and Personal Care Products in the Environment: Overarching Issues and Overview, by Christian G. Daughton, in *Pharmaceuticals and Personal Care Products in the Environment: Scientific and Regulatory Issues*, 2001 (ACS)

More information

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

Physiological Impact

- Some have LC_{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

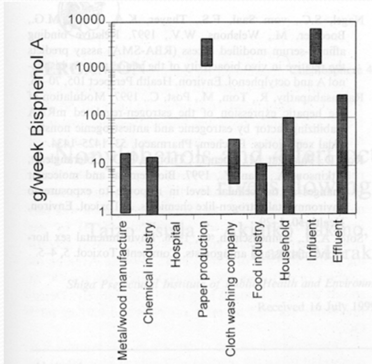
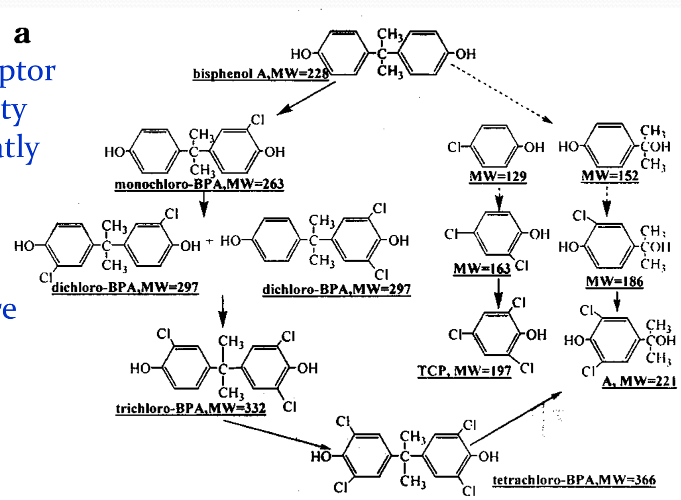


Fig. 3. Flux of Bisphenol A from different sample sites.

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.

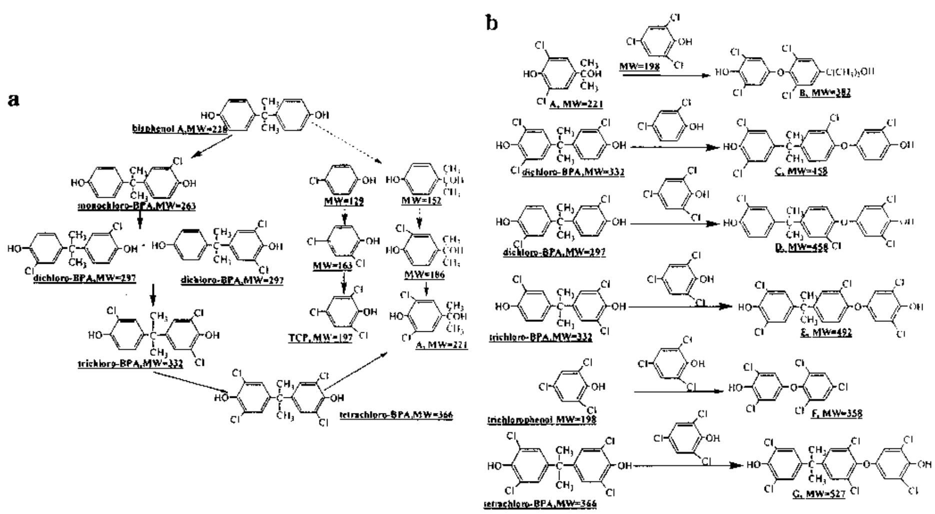


FIGURE 6. (a) Pathways of a chloro-substitution reaction between bisphenol A and HOCl. (b) Formation of polychlorinated phenoxyphenols.

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

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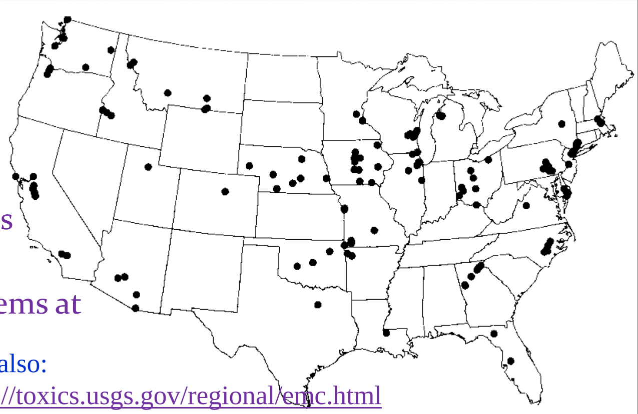
US National Reconnaissance

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



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

FIGURE 1. Location of 139 stream sampling sites.

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

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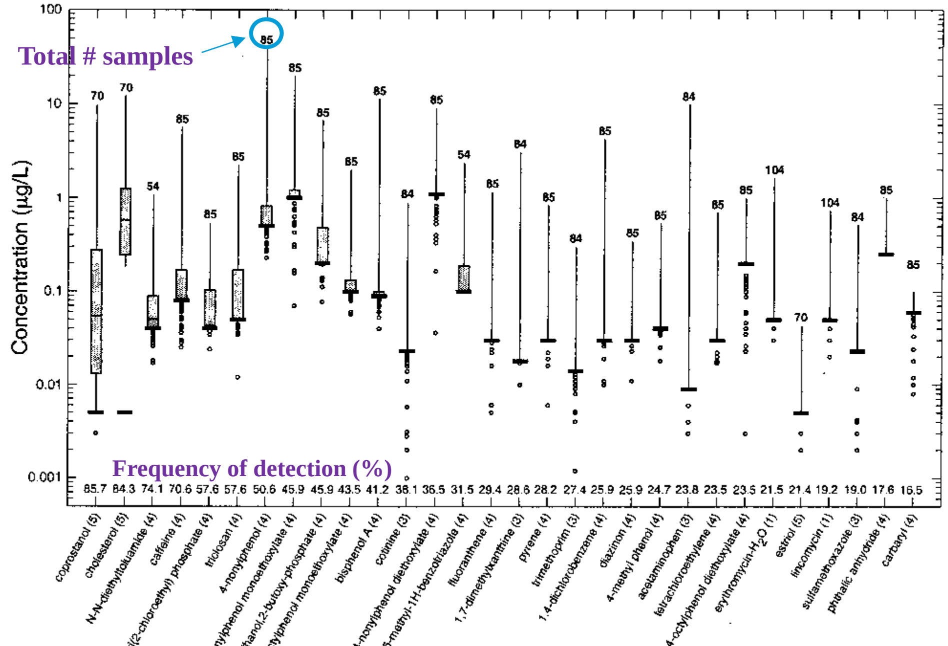
Total # samples



Frequency of detection (%)

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

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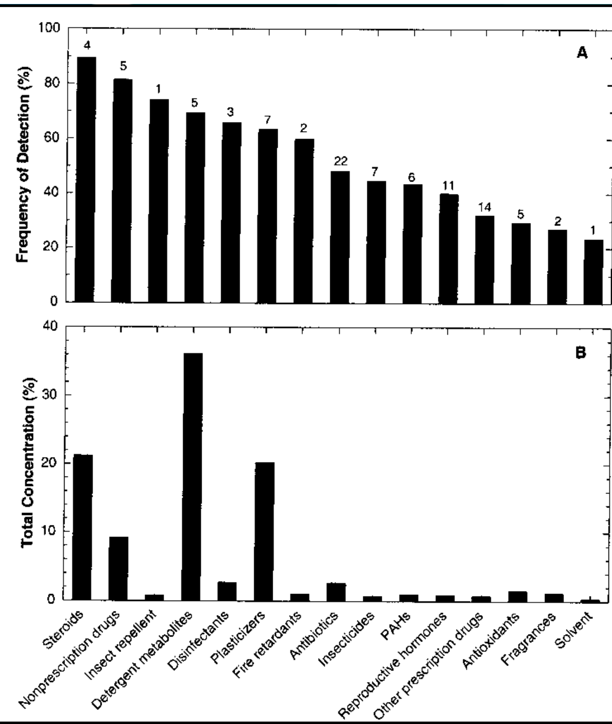
- Detection by category



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

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Removal by WW Treatment

- Biodegradation and washout during high flow?

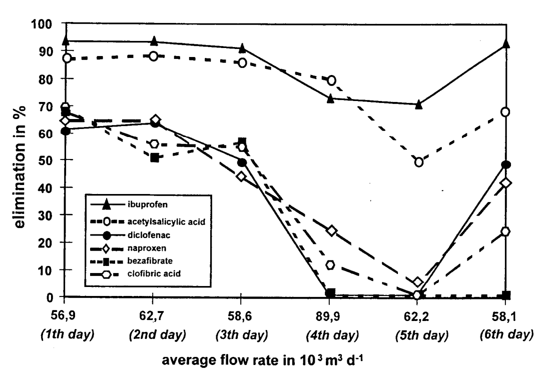
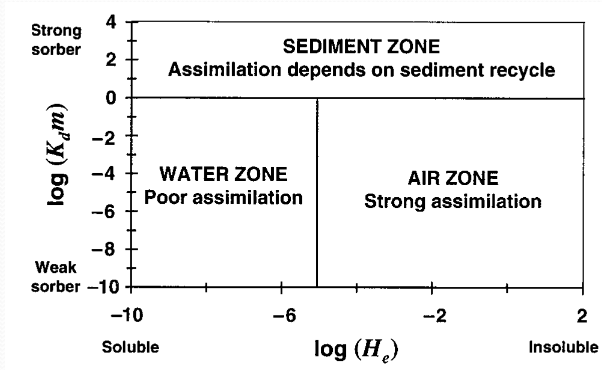


Fig. 2. Elimination of drugs during passage through a municipal sewage treatment plant near Frankfurt/Main over 6 d including a rainfall event: Sampling period, influents: May 24th to May 29th 1996, effluents: May 25th to May 30th 1996.

Ternes, 1998; Wat. 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 < 5L/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

$$K_d = f_{oc} K_{oc}$$

$$\left(\frac{mg-tox./g-C}{mg-tox./m^3}\right) or \left(\frac{m^3}{g-C}\right)$$

- and properties of organic fraction

$$K_{oc} = 6.17x10^{-7} K_{ow}$$

Octanol:water partition coefficient

$$\left(\frac{mg-tox./m^3-Oct.}{mg-tox./m^3-H_2O}\right)$$

- combining, we get:

$$K_d = 6.17x10^{-7} f_{oc} K_{ow}$$

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

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Other correlations

K_{oc} units

- Karickoff, 1979

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

$$K_{oc} = 6.17x10^{-7} K_{ow}$$

$$\left(\frac{mg-tox./g-C}{mg-tox./m^3}\right) or \left(\frac{m^3}{g-C}\right)$$

$$K_{oc} = 0.617 K_{ow}$$

$$\left(\frac{mg-tox./Kg-C}{mg-tox./L}\right) or \left(\frac{L}{Kg-C}\right)$$

- Karickoff, 1981

Karickhoff 1981; Chemosphere 10:833

$$K_{oc} = 2.57 K_{ow}^{0.84}$$

$$\left(\frac{mg-tox./Kg-C}{mg-tox./L}\right) or \left(\frac{L}{Kg-C}\right)$$

- Schwarzenbach

Schwarzenbach & Westall 1981; Env. Sci. Techn. 15:1630

$$K_{oc} = 3.09 K_{ow}^{0.72}$$

$$\left(\frac{mg-tox./Kg-C}{mg-tox./L}\right) or \left(\frac{L}{Kg-C}\right)$$

Based on neutral organic compounds

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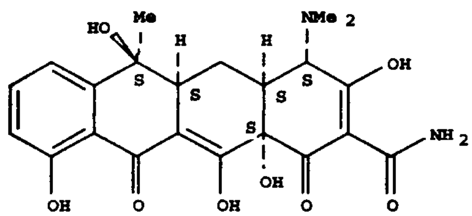
Tetracycline

Compound / CAS-Nr / MW	Structure	Physical-chemical properties:
Tetracycline 60-54-8 MW: 444.43		log K_{OW}: -1.19 [1] S: 1.7 g/L [2] $pK_{a,1}$: 3.30 [2] $pK_{a,2}$: 7.68 [2] $pK_{a,3}$: 9.69 [2] log K_f (Al^{3+}): $10^{12.5}$ [3] log K_f (Fe^{3+}): $10^{13.4}$ [3]

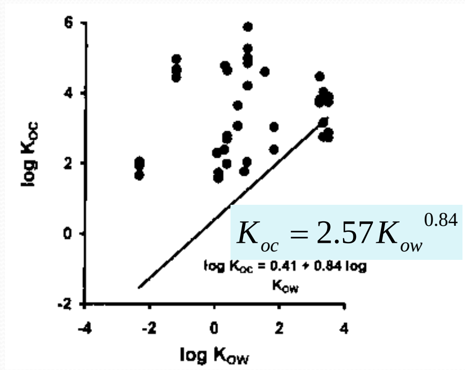
Tolls, 2001; Env. Sci. Technol., 35(17)3397

TABLE 2. Overview of Literature Data on Sorption of VPs to Soils or Soil Constituents[a]

compound/corollary information	$K_{d,solid}$ (L/kg)	K_{oc} (L/kg)	ref
Tetracycline			
pure Na-bentonite, Langmuir iso, pH dependency, $C_{s,max}$ at pH 6.1: 78 μmol/g, K_L not specified			30
pure Ca-bentonite, Langmuir iso, $C_{s,max}$ at pH 6.1: 200 μmol/g, K_L not specified			30
bentonite modified with cationic surfactant (C_{12}-trimethylammonium), Langmuir iso, $C_{s,max}$ at pH 6.1: 38 μmol/g, K_L not specified			30
bentonite modified with tannic acid, Langmuir iso, $C_{s,max}$ at pH 6.1: 210 μmol/g, K_L not specified			30
pure montmorillonite clay mineral, Langmuir iso, $C_{s,max}$ at pH 5.0: 540 μmol/g, K_L not specified			31
clay loam, Topeka, KS[b]	>400		57
soil organic matter (peat), Nova Scotia; pH 4.55	1 620		24
soil organic matter (peat), Nova Scotia; pH 6.14, iso's nonlinear	1 140		24

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

- Nearly all values fall above Karickoff's relationship

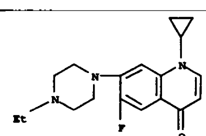
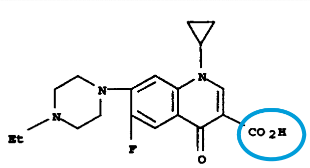


$$K_{oc} = 2.57 K_{ow}^{0.84}$$

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

Structure and sorption

- Enrofloxacin and Decarboxy Enro

Compound / CAS-Nr / MW	Structure	Physical-chemical properties:
Enro – CO_2 MW: 315.20 131775-99-0	 Enro – CO_2 =Decarboxylated enrofloxacin	log K_{OW}: n.a. S: n.a. $pK_{a,1}$: ca 8.3 [8]
Enrofloxacin 93106-60-6 MW: 359.40		log K_{OW}: 1.1 [6] 130 g/L [7] $pK_{a,1}$: 6.27 [7] $pK_{a,2}$: ca 8.3 [8] log K_f: n.a.

K_d (L/Kg)

7.7

500

Both based on same soil (8% clay fraction, montmorillonite)

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

- The End