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# CEE 697z

# *Organic Compounds in Water and Wastewater*

PPCPs: Introduction

Lecture #16

For Background see:

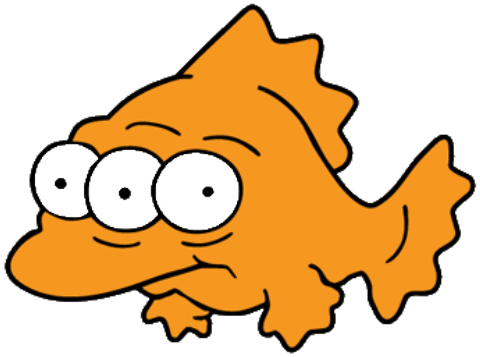
http://www.ecs.umass.edu/eve/background/chemicals/PPCPs/PPCP%20intro.html

# EDCs & PPCPs

- Endocrine Disrupting Compounds (EDCs)
  - Estrogens: regulate and sustain female sexual development and reproductive function
  - Androgen: male sex hormones
  - Mimics: *estrogenic* and *androgenic* compounds
  - Also anti-estrogenic and anti-androgenic
- Pharmaceuticals and Personal Care Products (PPCPs)
  - Non-steroidal anti-inflammatory
  - Anti-epileptic
  - Antibiotics
  - Anti-anxiety
  - Antioxidants
  - Pain reliever
  - Anti-cholesterol
  - Sun Screen

# What are EDCs and PPCPs and Why Study Them?

- EDC- Endocrine Disrupting Compounds
  - EDCs are a class of compounds which alter the hormonal system of an organism.
  - Eg: DDT, 17-alpha Ethinylestradiol, Bisphenol A,etc.



- PPCP- Pharmaceuticals and Personal Products
  - Any products used for personal health or cosmetic reasons
  - Includes prescription and non-prescription drugs, veterinary drugs, fragrances and cosmetics

# 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/ppcp/
- EWRE web site
  - http://www.ecs.umass.edu/eve/background/chemicals/PPCPs/
  - and especially
    - http://www.ecs.umass.edu/eve/background/chemicals/PPCPs/PPCP%20intro.html

# Estrogen lake study

PNAS PNAS PNAS PNAS

## Collapse of a fish population after exposure to a synthetic estrogen

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**Municipal wastewaters are a complex mixture containing estrogens and estrogen mimics that are known to affect the reproductive health of wild fishes. Male fishes downstream of some wastewater outfalls produce vitellogenin (VTG) (a protein normally synthesized by females during oocyte maturation) and early-stage eggs in their testes, and this feminization has been attributed to the presence of estrogenic substances such as natural estrogens [estrone or 17β-estradiol (E2)], the synthetic estrogen used in birth-control pills [17α-ethynylestradiol (EE2)], or weaker estrogen mimics such as nonylphenol in the water. Despite widespread evidence that male fishes are being feminized, it is not known whether these low-level, chronic exposures adversely impact the sustainability of wild populations. We conducted a 7-year, whole-lake experiment at the Experimental Lakes Area (ELA) in northwestern Ontario, Canada, and showed that chronic exposure of fathead minnow (*Pimephales promelas*) to low concentrations (5–6 ng·L$^{-1}$) of the potent 17α-ethynylestradiol led to feminization of males through the production of vitellogenin mRNA and protein, impacts on gonadal development as evidenced by intersex in males and altered oogenesis in females, and, ultimately, a near extinction of this species from the lake. Our observations demonstrate that the concentrations of estrogens and their mimics observed in freshwaters can impact the sustainability of wild fish populations.**

present (9) and has been linked to the feminization of male fishes in rivers receiving municipal wastewater (4, 6).

Despite growing documentation on the feminization of male fishes in waterways receiving municipal effluents, a critical question in the field of endocrine disruption research is whether these low-level, chronic exposures adversely impact wild populations (13). Although laboratory studies have shown decreased reproductive success of fish exposed to <1–5 ng·L$^{-1}$ of EE2 (14, 15), it is unknown whether this response would be observed in wild populations and whether it would result in a subsequent decline in abundances. To assess the ecological risk posed by this class of compounds, we must understand population-level effects of estrogens and their mimics on aquatic organisms.

The fathead minnow (*Pimephales promelas*) is a common species in North America, and its range extends from the southern United States to northern Canada (16). It is an important food source for numerous game fish species, such as lake trout (*Salvelinus namaycush*), walleye (*Sander vitreus*), and northern pike (*Esox lucius*). In the lakes used for this study, fathead minnow have a lifespan of ≈4 years, but few individuals live past 2 years of age (17). Asynchronous spawning starts in early summer and extends for a period of ≈2 months; multiple females will typically spawn in the nest of a single male, who will

# First to study PPCPs?

- Who are these people?

# 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

# 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

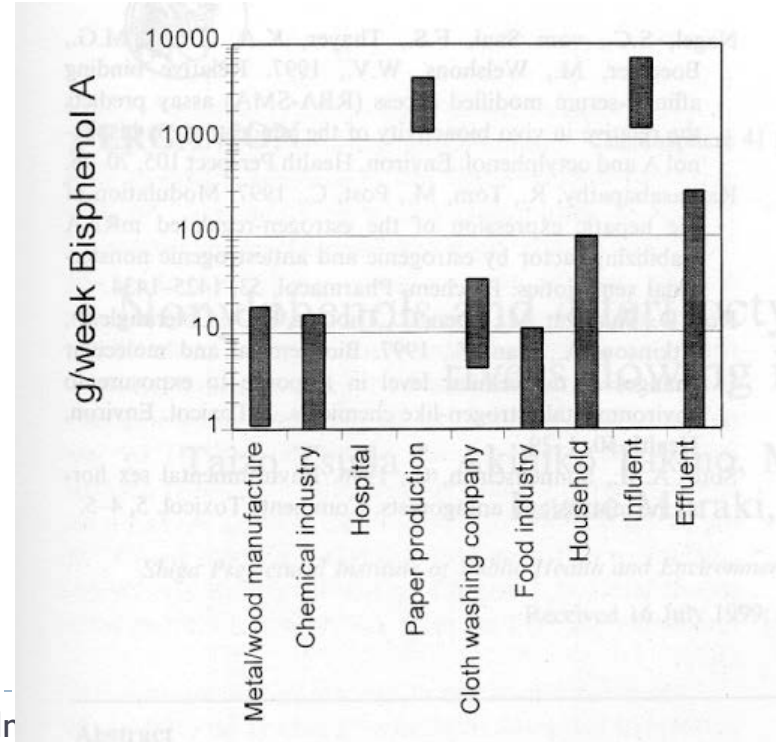

Fig. 3. Flux of Bisphenol A from different sample sites.

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

- To next lecture