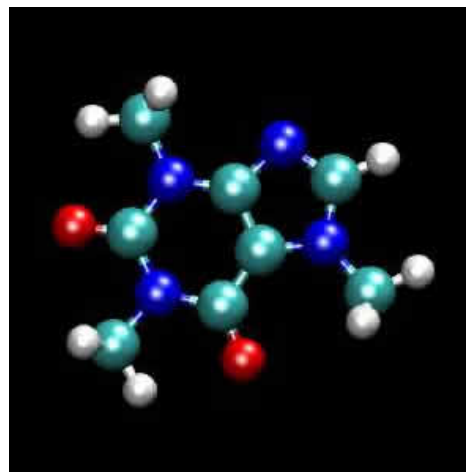
Occurrence, Environmental Fate and Exposure Assessment of SSRIs in Aquatic Environments

Kevin L. Armbrust, Ph.D.

and Jeong Wook-Kwon Ph.D.

State Chemical Lab of Mississippi

Office of the State Chemist



Overview of the State Chemical Laboratory

Four Divisions

- Chemical Regulatory
- Petroleum Products
- Industrial and Agricultural Services
- Research

MSCL Overview (Continued)

- *Chemical Regulatory Division*
  - Quality Control analysis to insure label compliance for feeds, fertilizers and pesticides sold in the state.
  - Conducts approximately 60,000 tests on 9,000 samples each year.
- *Petroleum Products Division*
  - Quality control analysis of gasoline, diesel and kerosene sold at retail establishments.
  - Conducts approximately 20,000 tests on 4,000 samples each year.

MSCL Overview (cont)

- *Industrial and Agricultural Services*
  - Fee for Service
  - Analyzes food, water, and soil samples for chemical contamination by pesticides and industrial chemicals. Samples are for regulatory enforcement for the Departments of Agriculture, Health Services, and Environmental Quality as well as local and state law enforcement.
  - Samples also are analyzed as a service to private industries, citizens and federal agencies.
  - Analyzes approximately 3000 samples/yr.

Research Division

- Conducts basic research similar to other University academic units.
- Conducts large-scale contract analytical services for federal and state agencies as well as other public and private groups.
- Develops methods for chemical analysis in preparation for state emergencies.
- Conducts chemical research important to state economic development and the welfare to the state’s citizens.

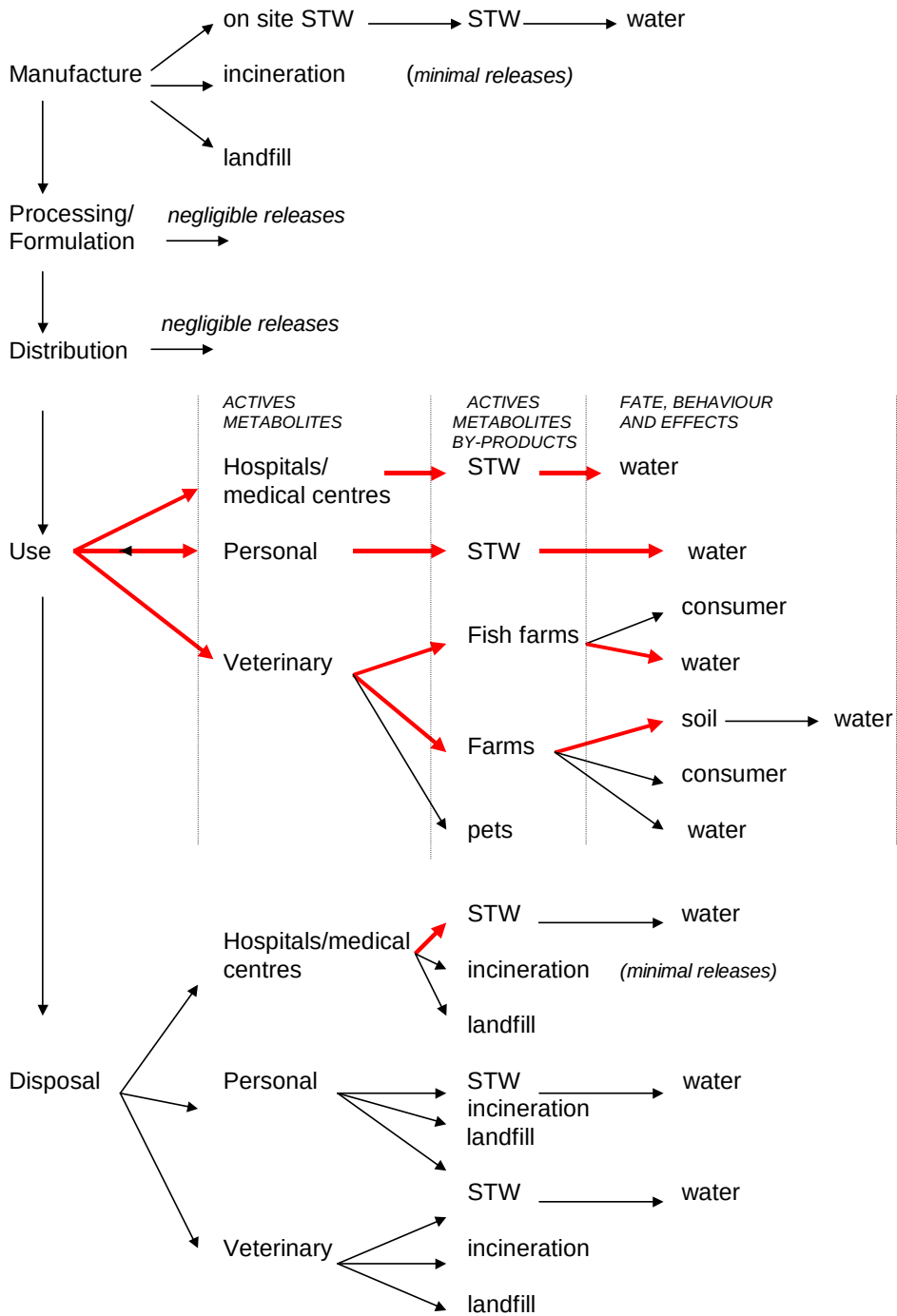
Research Division Projects

- Chemical Monitoring
  - Organic contaminants (pesticides, chlorinated organics, PAHs, etc) in biological tissue, sediment and water.
  - USDI, Misc. States, MSDEQ, EPA 319
  - 2000 – 3000 samples/year
- Environmental Fate of Antidepressants
  - EPA STAR
- Custom synthesis of PCB congener standards
  - Industry

Matrices Analyzed

- **Soil, Sediment and Water –** (freshwater and marine)
- **Insects** – bees, grasshoppers, crickets
- **Reptiles** – lizards, snakes
- **Amphibians** – salamanders, frogs (eggs, tadpoles, adults), turtles
- **Mammals** – Walrus blubber, manatee fat, seal teeth, bat skin (museum specimens), deer carcasses, dogs (including feces)
- **Avian (multiple species) –** Tissues, eggs, brains.
- **Fish -** (multiple species both freshwater and marine)
- **Aquatic Invertebrates -** shrimp, lobster, crayfish, oysters, clams.
- **Human –** adipose, serum, urine, breast milk.
- **Stomach contents –** human, dogs, cats, birds, possums, coyotes.
- **Field Crops -** many
- **Food Items** – (meats, vegetables, soups, snack foods)
- **Miscellaneous –** swab samples, air samples, and some limited field sampling.

Pathways for Entry of Pharmaceuticals into the Environment



major

minor

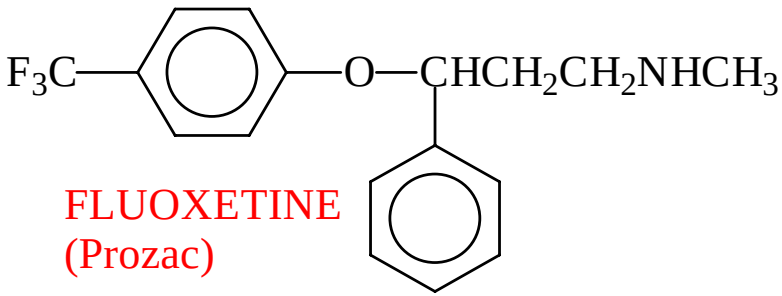
From Ayscough, et al. 2005

Research Plan…….

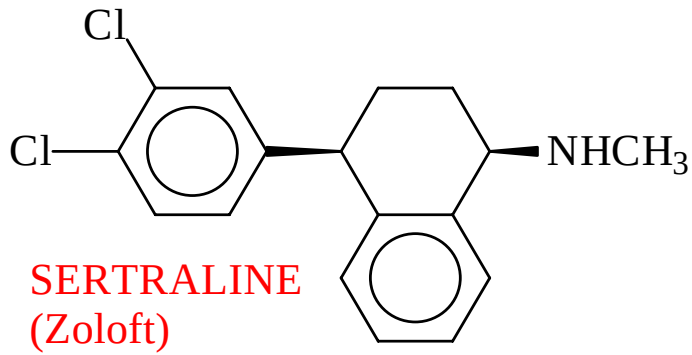
- Determine environmental fate in experiments similar to those required for pesticide registration (hydrolysis, photolysis, aquatic metabolism, etc).
- Measure parent and major degradation product occurrence in wastewater effluent and downstream receiving water.
- Determine acute and chronic impacts to *Ceriodaphnia* and reproductive impacts to *Gambusia*.

Why Pesticides?????

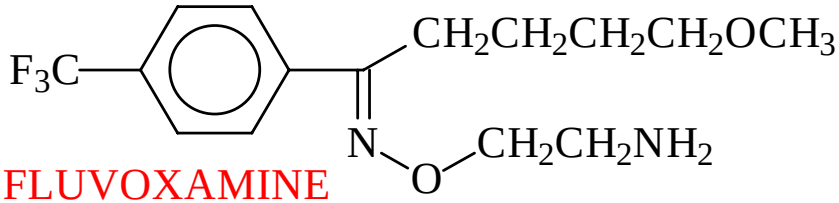
- Used on soil
- Used in Water
- Lessons Learned
  - Proactive vs Reactive approach (DDT)



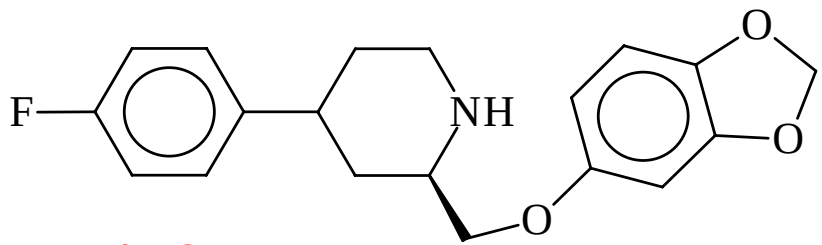
FLUOXETINE
(Prozac)



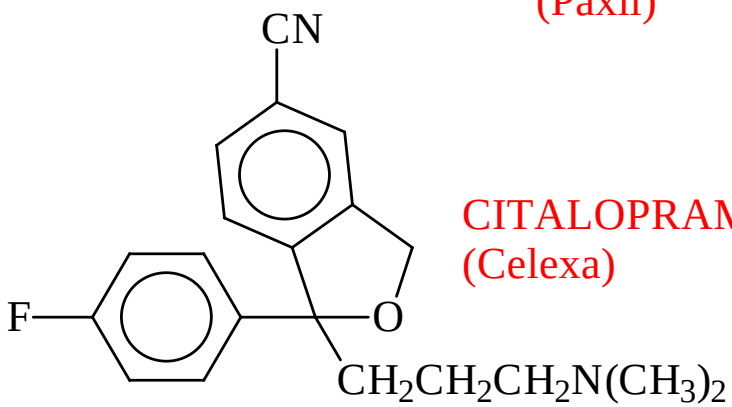
SERTRALINE
(Zoloft)



FLUVOXAMINE
(Luvox)



PAROXETINE
(Paxil)



CITALOPRAM
(Celexa)

Physical Properties

- Solubility in water
- Octanol-Water Partition Coefficient
- pKa
- Hydroxyl Radical Rate Constant
  - Measured by competition kinetics

Note: Assume volatility to be negligible

Soil Adsorption Coefficient

- Freundlich Isotherms measured on 3 soils and 2 sediments
- Soils selected according to EPA Subdivision N criteria.
- Soil properties

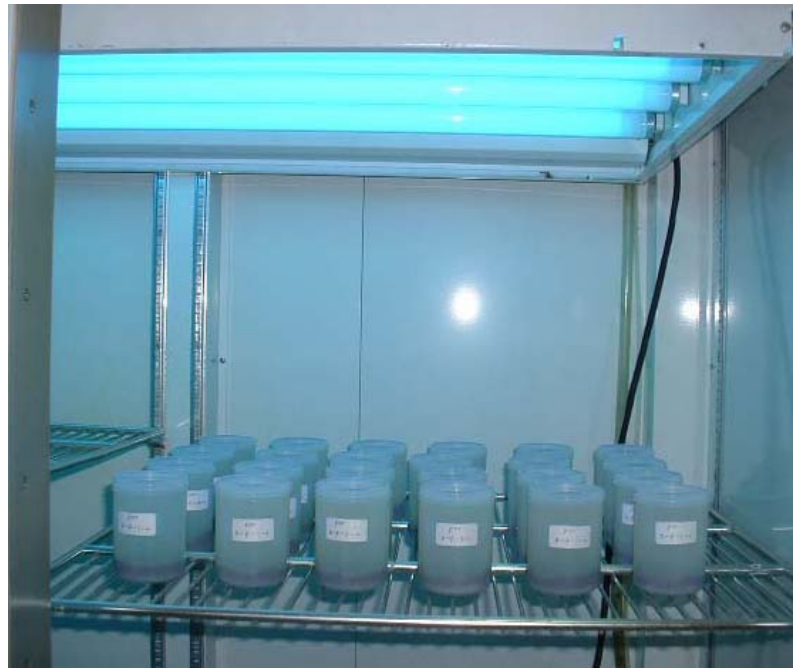
Sediment	Texture	Clay	Silt	Sand	OM	pH	CEC[a]
		---------- % ----------					Meq/100 g
Creek	Sand	0.00	92.75	7.25	0.16	6.7	0.90
Pond	silt loam	7.50	66.25	26.25	0.65	5.6	7.73
Dundee Soil	loamy sand	6.25	7.50	86.25	1.01	5.0	10.30
Leeper Soil	sandy loam	7.50	16.75	75.75	1.77	7.8	72.42
Marieta Soil	Loamy sand	5.00	8.50	86.50	0.93	7.8	34.97

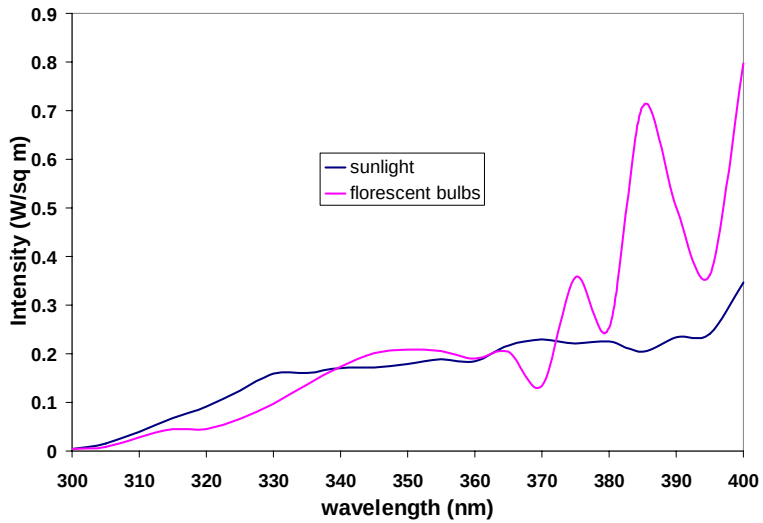
[a]Cation exchange capacity

Degradation Experiments

- Hydrolysis – pH 5, 7, and 9 buffered solutions;
  - 25°C and 40°C. 30 days.
  - Measure rate, products.
- Aqueous Photolysis – pH 5, 7 and 9. Natural Water, Synthetic Humic Water (SHW). 15 days.
  - Measure rate, quantum yield and products.
- Ready Biodegradability
  - Sludge from STP with appropriate dilutions
  - 28 day experiment
  - Measure rate and products.

Dissipation of SSRIs in Irradiated Water-Sediment Systems





System Set-up

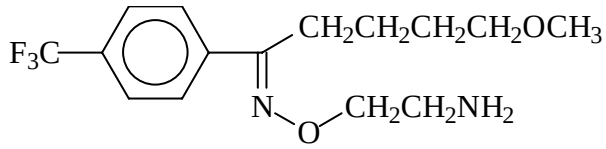
- Systems consist of 50 grams of sediment and 175 mls of water.
- Water-sediment systems allowed to equilibrate for 1 week
- Systems sampled at 1, 3, 7, 14, 22 and 30 days
- Dark controls equate to EPA aerobic-aquatic metabolism study or EU Water-sediment study.

Sediment Properties

Sediment	Texture	Clay	Silt	Sand	OM	pH	CEC[a]
		---------- % ----------					Meq/100 g
Creek	Sand	3.75	6.50	89.75	0.29	6.2	2.35
Pond	Loamy sand	5.00	15.50	79.50	0.74	5.5	8.40

[a]Cation exchange capacity

Fluvoxamine



<u>Hydrolysis</u> – stable

<u>Ready Biodegradability</u>

– stable 28 days

<u>Photolysis</u> – 3-5 days in buffer

0.5 days in natural waters

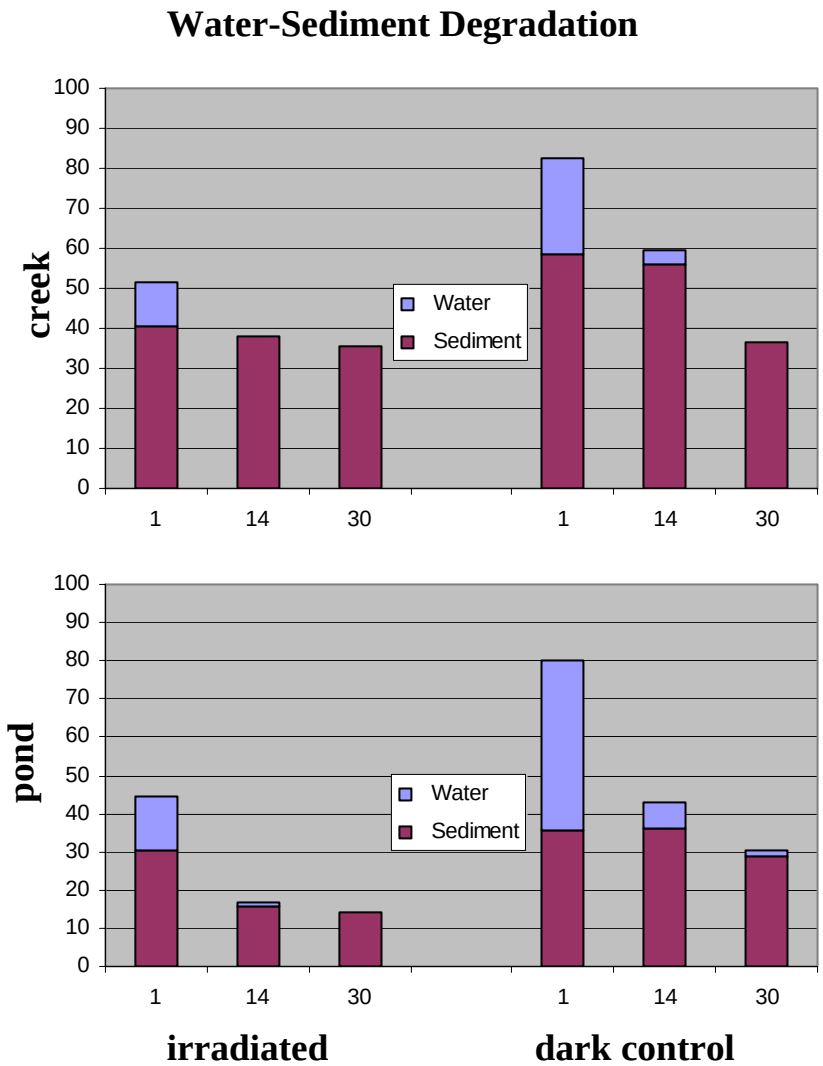
K_{ox} = 6.51 x 10^{12}/M-hr

K_{oc} = 9700 (average)

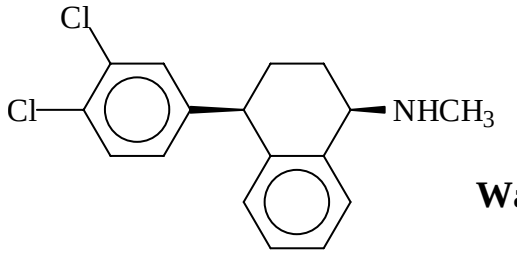
range (19,000 – 2,200)

<u>Primary degradation products</u>

- isomerization (E-Z)



Sertraline



Photolysis – 200 days (pH 5,7)

3 days (pH 9); 11 days natural waters

Stable (seawater and 0.5 M NaCl)

K_{ox} = 1.41 x 10^{12}/M-hr

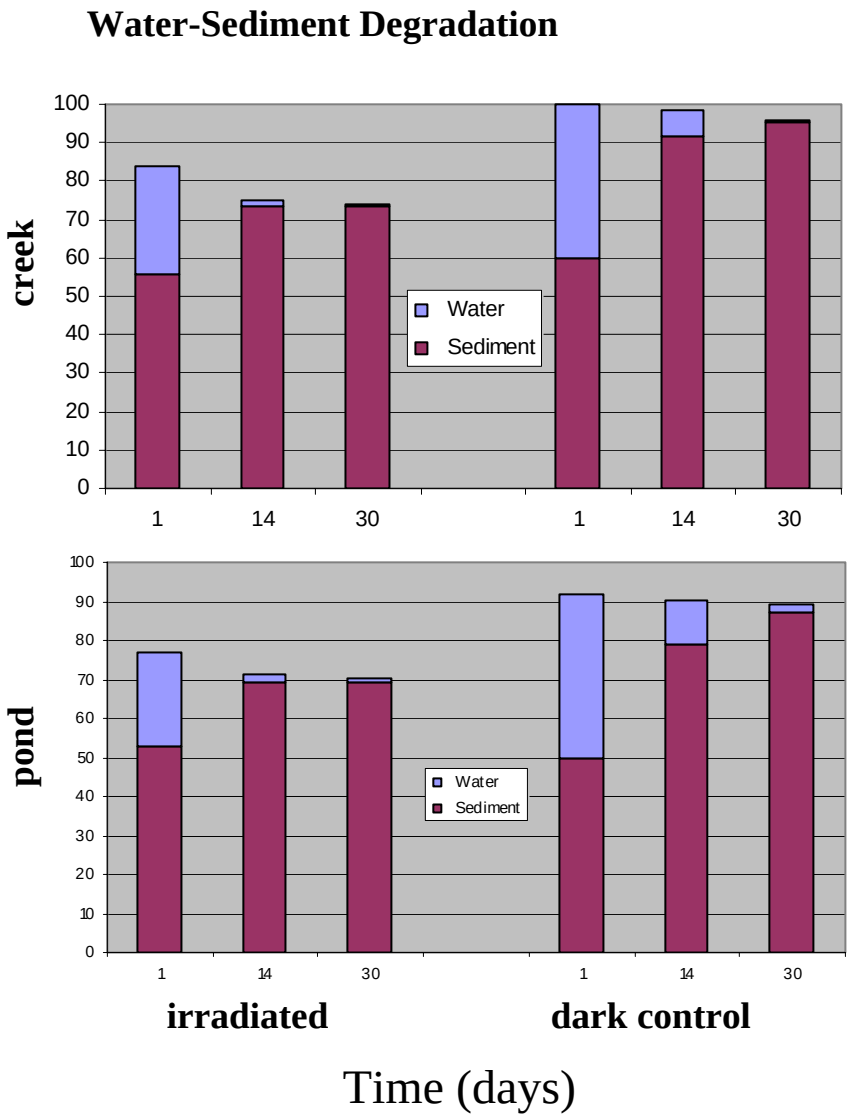
K_{oc} = 23,370 (average)

range (71,000 – 6,300)

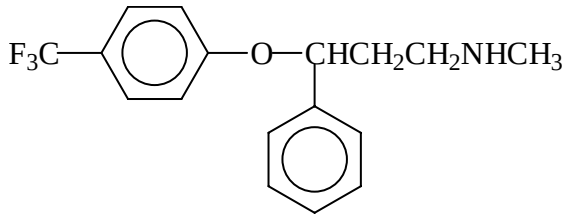
Primary degradation products

-N-desmethylsertraline (norsertraline)

-Others (unknown)



Fluoxetine



Photolysis – 100 - 200 days in natural waters and buffers. 10 days in SHW.

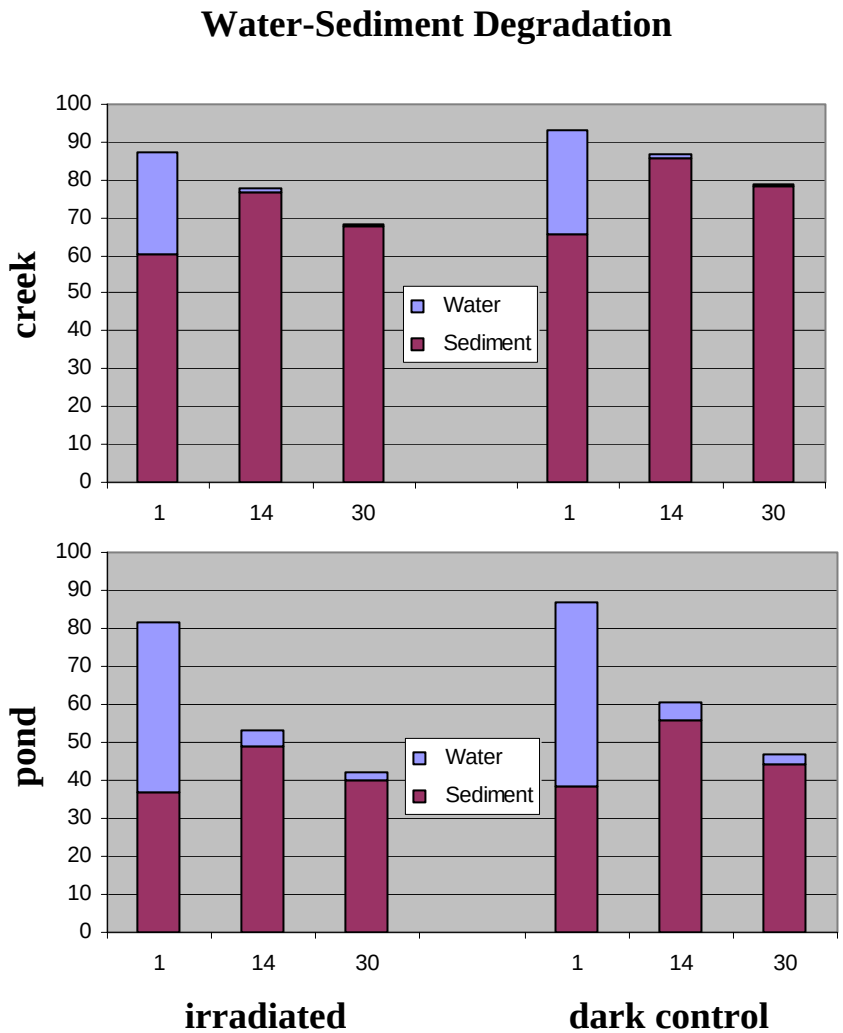
K_{ox} = 2.53 x 10^{12}/M-hr

K_{oc} = 102,000 (average)

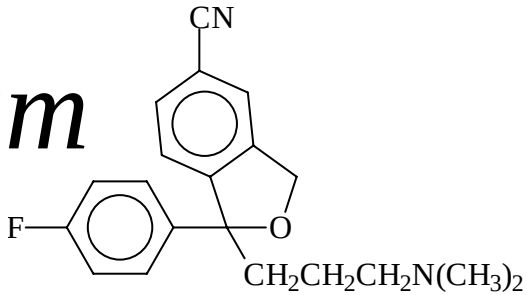
range (309,000 – 12,000)

Primary degradation products

-N-desmethylfluoxetine (norfluoxetine)



Citalopram



Photolysis – stable (pH 5,7);

65 days pH 9; 13 – 42 days in natural waters and SHW.

K_{ox} = 2.90 x 10^{12}/M-hr

K_{oc} = 522,000 (average)

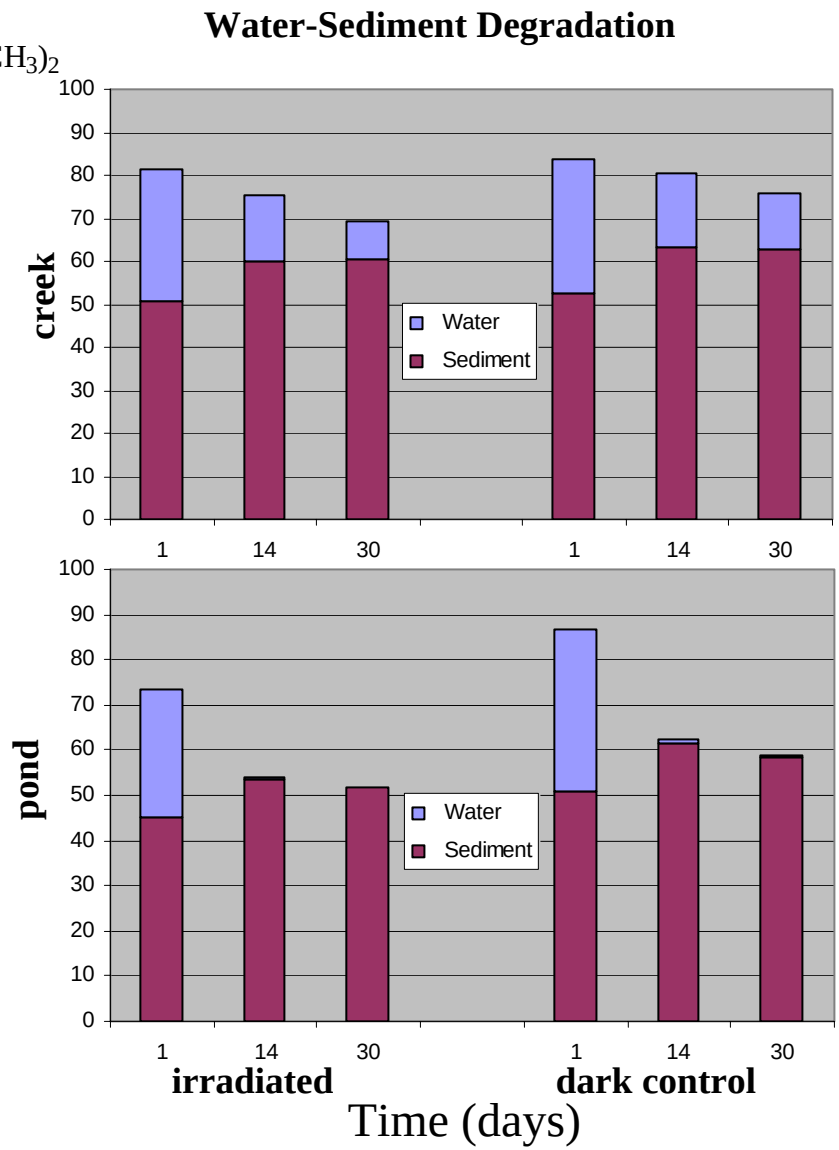
- range (1,000,000 – 208,000)

Primary degradation products

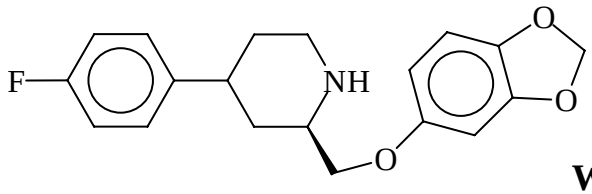
- citalopram N-oxide

-N-desmethylcitalopram

-Others (unknown)



Paroxetine



<u>Photolysis</u> – 11- 16 hours (0.5 days) in all solutions.

K_{ox} = 1.99 x 10^{13}/M-hr

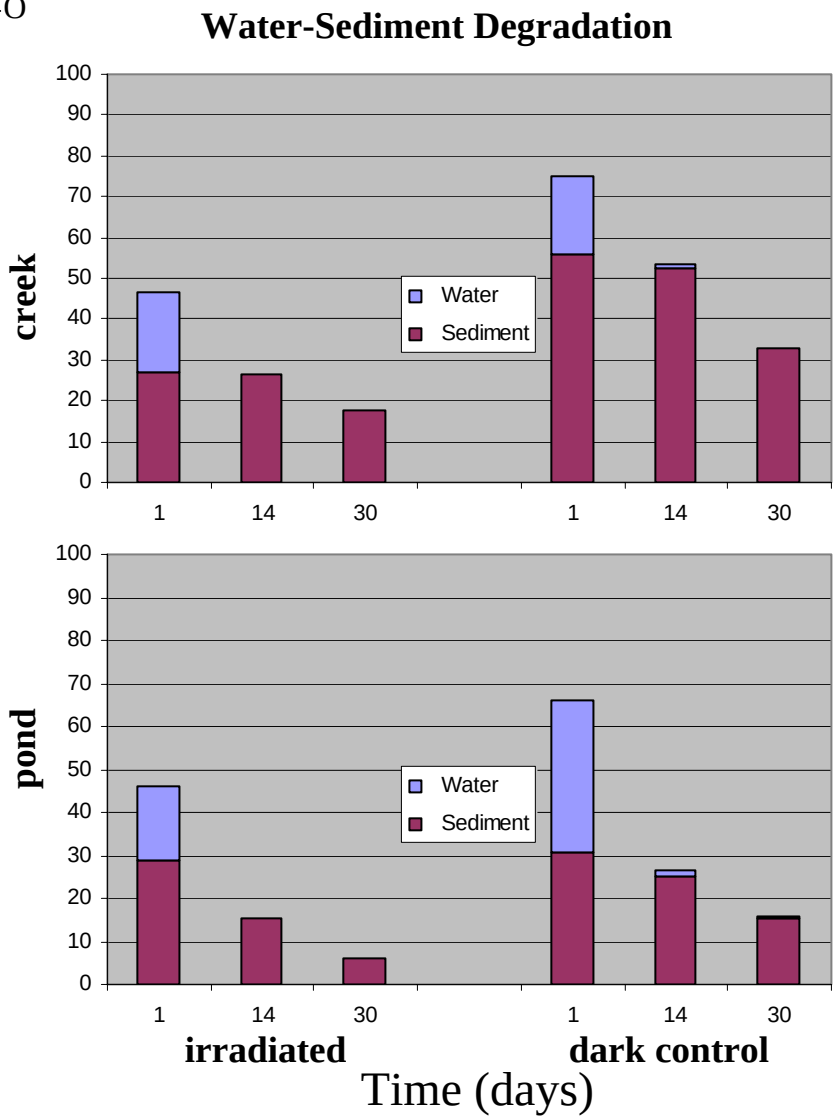
K_{oc} = 77,000 (average)

range (288,000 – 8,100)

<u>Primary degradation products</u>

-N-oxides

-Numerous small products



Environmental Fate – General Trends

- All strongly adsorb to soil/sediment
- All are hydrolytically stable
- All are relatively persistent, with the exception of paroxetine.
- Exposure Assessment models would be driven by sorption and stability.

Monitoring of SSRIs in Aquatic Systems

- Columbus Wastewater Treatment Plant, Columbus Mississippi
- Discharges to Tombigbie Waterway.
- Treats ten million gallons of wastewater daily
- Two storm lagoons totaling 80 acres, and the three 5-acre sludge lagoons are located on the 200-acre-site.
- 60 pumping stations.
- Process includes: pumping stations, grit chamber, aeration tanks, clarifiers, aerobic digesters, sludge thickeners, sludge lagoons and chloride contact chambers.
- Influent, Effluent, Upstream and Downstream water and sediment collected monthly starting April 2005.

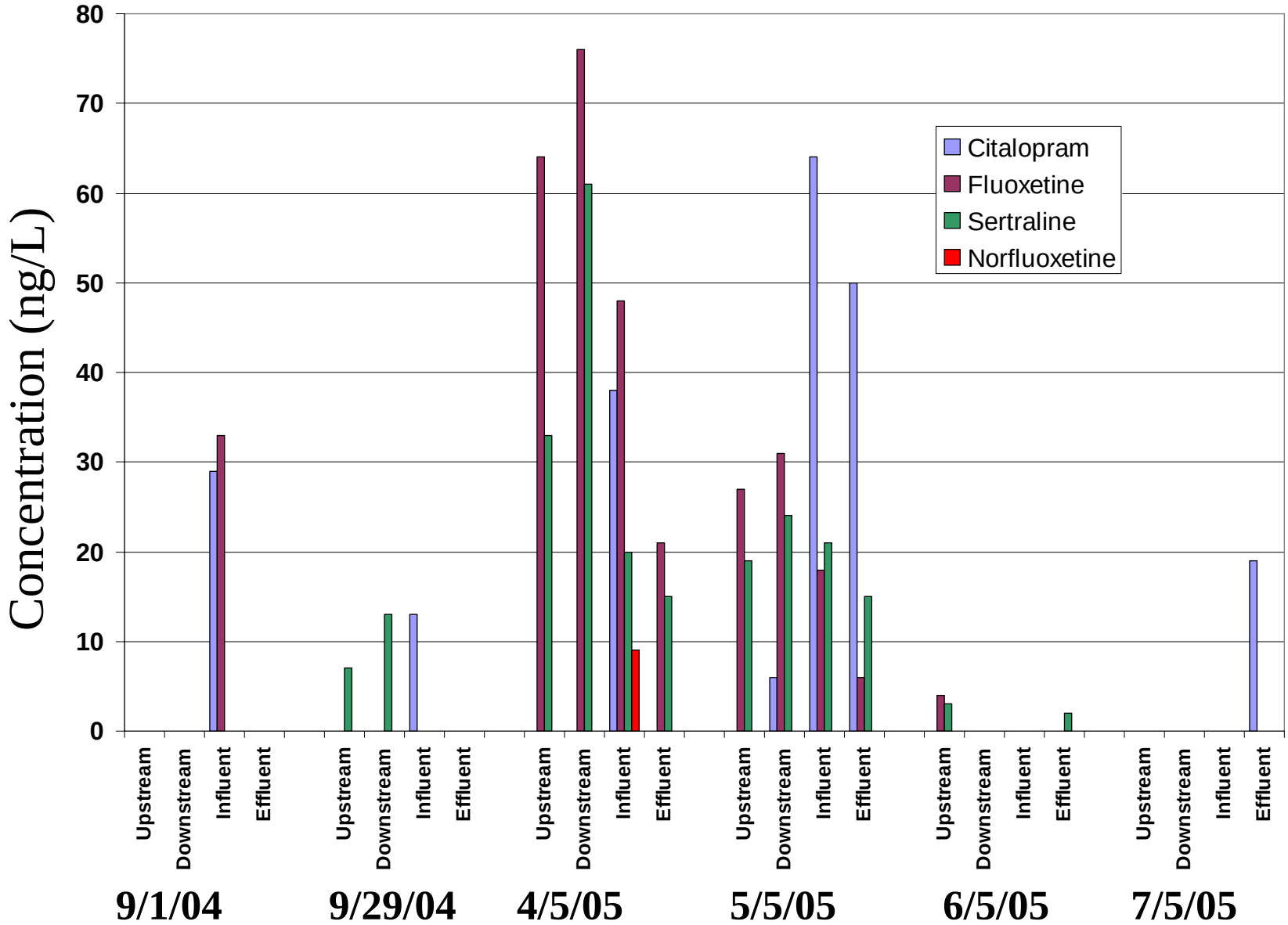
Methods and Detection Limits

- Pre-wash Oasis HLB SPE (500 mg/6mL) with 5 ml methanol and 5 ml water
- Load 500 ml of a pre-filtered (0.45 um) water sample at a speed of 8 ml/min.
- Elute with 7 (3+4) ml methanol
- Evaporating to dryness using N_2 gas
- Dissolve residue in 2 ml of a mixture of methanol:water (1:1, v/v)
- Analyze with LC/MS/MS

Mean (n=5) percent recoveries

Compound	Instrumental detection limit (ng)	Method detection limit (ng/L)	0.05 ug/L spike	0.5 ug/L spike
Fluoxetine	0.06	2.4	94	97
Norfluoxetine	0.04	1.6	97	95
Fluvoxamine	0.06	2.4	102	104
Citalopram	0.03	1.2	99	101
Paroxetine	0.04	1.6	99	102
Sertraline	0.01	0.4	84	88
N-desmethyl sertraline	0.03	1.2	85	87

SSRI's in STP Influent, Effluent and Receiving Water



Next Steps

- Complete pKa measurements
- Complete Exposure Assessment based upon phys/chem properties and degradability.
- Complete Analysis of Sediments
- Validate methods for fish and mussel tissue
  - Build into existing contracts

Continue working with all who have interest

http://www.mscl.msstate.edu