Pharmaceuticals in the environment
– an environmental hazard?

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## Public interest in the topic


YMPÄRISTÖ

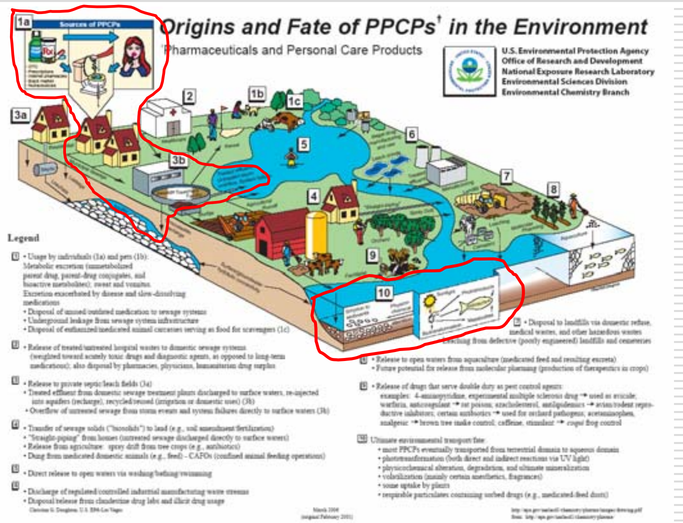
Jätevesien e-pillerijäämät muuttavat koiraskaloja naaraiksi

Lääkejäte ei kuulu luontoon

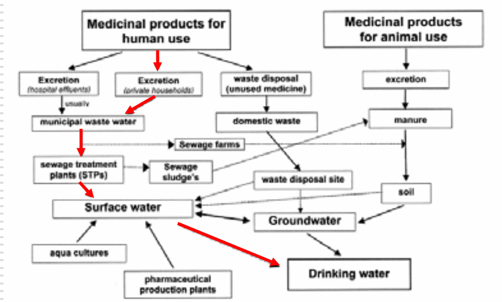
Syntetiskt östrogen påverkar fiskar

Lääkkeitä ja hajusteita päätyy juomaveteen






## Sources and pathways of pharmaceuticals to the aquatic environment




**Source:** Heberer, *Toxicol Let*, 2002 (131), 5-17

## Why should we study pharmaceuticals in the environment?

- The compounds are continuously discharged to the environment from sewage treatment plants
  ⇒ THE COMPOUNDS ARE PSEUDOPERSISTENT
- The compounds are biologically active and there are thousands of different substances (the parent compounds and the metabolites)
  ⇒ A PHARMACEUTICAL COCKTAIL
- In recent studies, already concentrations of < 10 ng/L of a certain pharmaceutical have been showed to caused behavioral disturbances in aquatic organisms.
- It is known that additive effects of mixtures of pharmaceuticals have to be considered when risk assessments are made
  ⇒ RISK FOR THE AQUATIC ENVIRONMENT IS EVIDENT



## Factors (determinants) affecting the occurrence and the impact of pharmaceuticals in the environment

- Consumption
  - High/low
- Metabolism
  - Phase 1 ⇒ inactivation
  - Conjugation of parent compound ⇒ may not be important
- Sewage treatment
  - Biodegradation/biotransformation/deconjugation
  - Sorption
- Surface water (aquatic environment)
  - Dilution
  - Phototransformation
  - Reactions at surfaces of particles?
  - (Biodegradation/biotransformation)
  - Sorption & sedimentation
- Biota
  - Uptake
  - Metabolism
  - Distribution
  - Excretion



## Waste water discharges

- The cmpds not removed to 100% in the STP are found in the effluent and consequently discharged to the aquatic environment
  - the concentrations in the effluent are usually much lower than in the influent
  - the concentration profile is different from that in the influent
  - the cmpds are further diluted in the recipient waters



## Fate in the aquatic environment

- A very complex issue – the environmental conditions play an important role and these vary from location to location
  - Cmpds that absorb light at 290 – 800 nm may undergo phototransformation
    - environmental fate of transformation products?
  - Sorption and sedimentation
    - not a degradation process but may offer surfaces for catalytic transformations?
  - The impact of humic substances (NOM)
    - act as a ”sink” for the compounds?
  - Biotransformation/biodegradation
    - it is not likely that compounds not undergoing biotransformation in the sewage plant would undergo transformation in the aquatic environment
  - A steady discharge of ”new” compounds
    - pseudopersistence!

## Risk for the Aquatic Environment (1)

- Highest risk of contamination: lakes, rivers and the ground water
- We have to consider the risk of the:
  - parent compound
  - the mixture of compounds
  - the transformation products
    - some transformation products may be of higher risk than the parent compounds



## Risk for the Aquatic Environment (2)

- Established risks
  - Ethinyl estradiol cause infertility in fish at concentration < 5 ng/L
  - A mixture of estrogenic compounds is a much more potent endocrine disruptor than the single compounds.
- Assumed effects
  - Spreading of drug resistant pathogens
  - Bioconcentration and biomagnification
  - Risks in conjuction with the sediments



## Human risk

- Mainly through drinking water (a risk?)
- Or through disturbance of the ecological integrity



## Disruption of Environmental Integrity

- Decline in the vulture population in India due to vetenary use of diclofenac (Oaks et al. *Nature*, 2004, 427, 630)

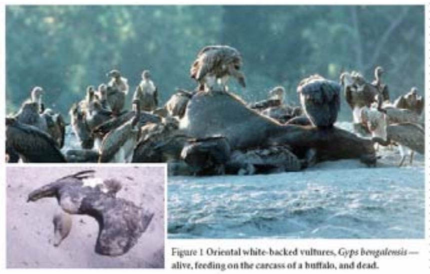


Figure 1 Oriental white-backed vultures, *Gyps bengalensis* — alive, feeding on the carcass of a buffalo, and dead.

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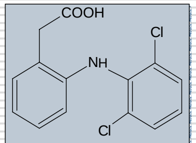



Diclofenac

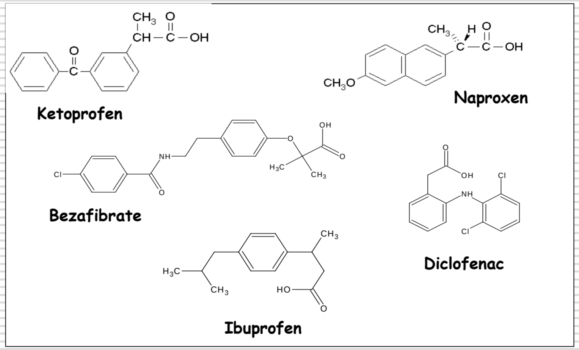
## Pharmaceuticals in waste water and in the environment in Finland

## Some results of our studies

(Our = Niina Vieno, Tuula Tuhkanen and Leif Kronberg)



## Some of the Studied Pharmaceuticals





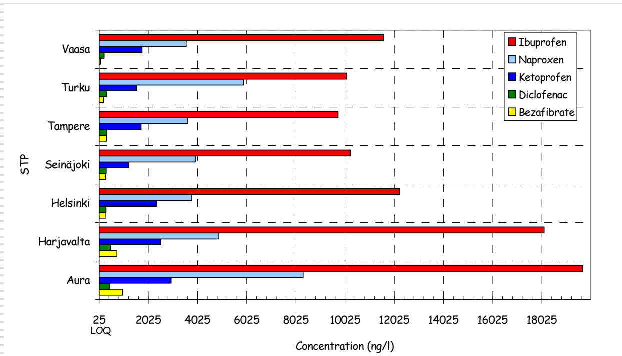

## CONSUMPTION OF STUDIED PHARMACEUTICALS IN FINLAND

| SUBSTANCE | USE (kg/year) | USE (mg/inh/year)* |
|---|---|---|
| Ibuprofen | 70 200 | 13 500 |
| Naproxen | 6 700 | 1 300 |
| Ketoprofen | 1 400 | 270 |
| Diclofenac | 965 | 190 |
| Bezafibrate | 510 | 100 |

* Population of Finland= 5 212 000



## Concentrations in the Influent of WWTPs




The same concentration profile as the consumption profile

## Theoretical Calculation of the Concentration of Pharmaceuticals in Waste Water Influents

$$C_{calc} = \frac{A \times P \times e\% \times 10}{365 \times Q}$$

$C_{calc}$ = theoretically calculated concentration of a pharmaceutical in STP influent ($\mu g\ l^{-1}$)

$A$ = the amount of a pharmaceutical used per year per capita (in grams per inhabitant per year)

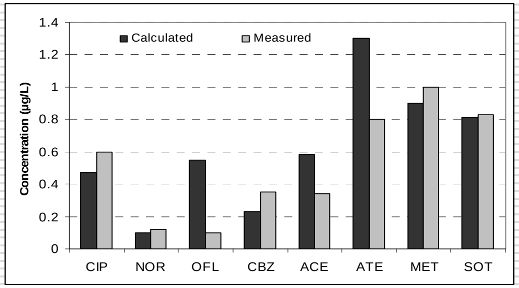
$P$ = the number of inhabitants serviced by the STP

$e\%$ = the amount of a pharmaceuticals excreted unchanged by humans (in %)

$Q_{inf}$ = the influent flow ($m^3 d^{-1}$)



## Comparison of Calculated and Measured Concentrations




CIP = Ciprofloxacin
NOR = Norfloxacin
OFL = Ofloxacin
CBZ = Carbamazepine

ACE = Acebutolol
ATE = Atenolol
MET = Metoprolol
SOT = Sotalol



## Vice versa: The Consumption Can be Determined from the Measured Influent Concentrations

Example: ibuprofen in Helsinki

c(ibuprofen) in STP influent = 12.2 µg/l

influent flow= 206 000 $m^3$/d

→2.5 kg of ibuprofen per day to the STP

About 90% metabolized in humans

→Use of ibuprofen in Helsinki per day is about 25 kg.

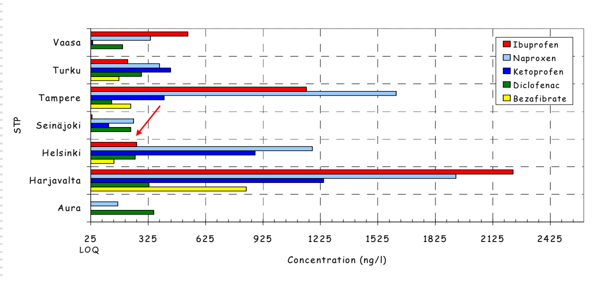
→Which makes about 12 500 mg of ibuprofen/inh/year.

→National Agency of Medicine reports: 13 500 mg IBU/inh/year

This example shows that our analytical method is reliable



## Concentrations in the Effluent of WWTPs




*Example:* * ibuprofen load to the environment in Helsinki ≈ 20 kg/yr

* Load of all the studied pharmaceuticals ≈ 200 kg/yr

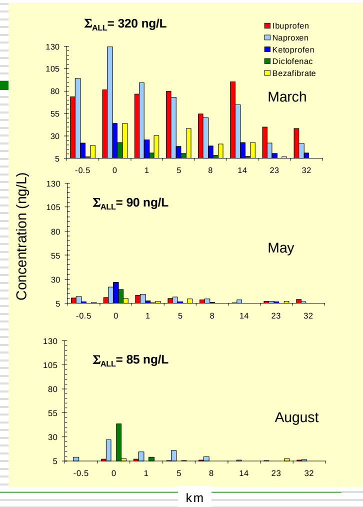
## Summary of Elimination Rates in WWTPs

| | |
|---|---|
| (I) Efficient elimination (>80%): | ciprofloxacin, norfloxacin, ofloxacin, ibuprofen, ketoprofen and naproxen |
| (II) Moderate elimination (40–80%): | acebutolol, atenolol, sotalol and bezafibrate |
| (II) Poor elimination (<40%): | diclofenac and metoprolol |
| (IV) No elimination: | carbamazepine |



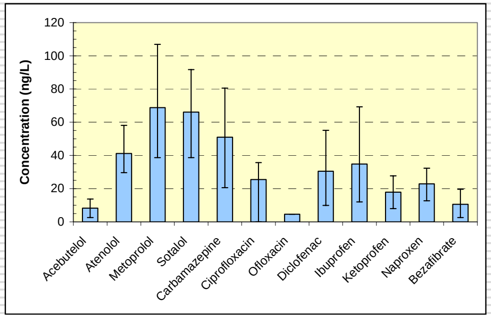
## Concentration of Pharmaceuticals in River Water (River Aura)

Samples collected upstream (-0.5 km), at the discharge point ( 0 km) and downstream (1, 5, 8, 14, 23 and 32 km) from a waste water treatment plant






## Concentration of Pharmaceuticals in River Water (River Vantaa)

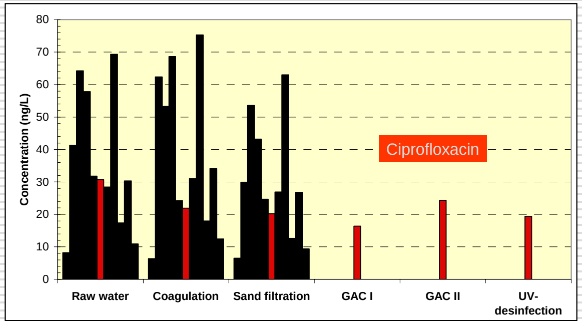



The compounds are abundant in the River Vantaa!



## RESULTS – Drinking water treatment (4)

The ozonation step is by-passed (no ozonation)

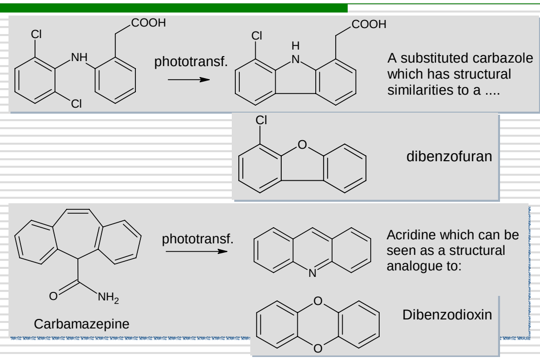


## Further work

- The environmental fate of pharmaceuticals
  - How stable are the compounds
  - Bioavailability?
  - Phototransformation
  - The significance of transformation products



## Phototransformation of diclofenac

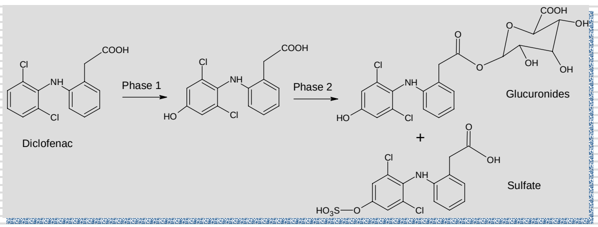



Some chlorinated dibenzofuranes are known to be very toxic, but do we know anything about the toxicity of chlorinated carbazoles?



## Bioavailability

- We have found diclofenac and naproxen metabolites in bile of fish exposed to the compounds.






## Conclusions

- The pharmaceuticals are not fully eliminated in WWTPs and consequently they are discharged to the aquatic environment
- They are detected in river waters downstream WWTPs at concentrations up to 100 ng/L
- The environmental impact and fate are largely unkown, but recent studies have shown that some of the compounds may have deleterious effects on certain organisms
- It is obvious that we have to find means to minimize the discharge of pharmaceuticals to the environment

## Coworkers

- Dr. Niina Vieno,
- Prof. Tuula Tuhkanen
- Prof. Aimo Oikari
- Doctorals students Jesper Svanfelt, Jenny-Maria Kallio, Jussi Kosonen, Marja Lahti

Thank you for your attention