

PHARMACEUTICALS IN THE WATER CYCLE: moving from a problem to a solution

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The problem(s)

1. Many pharmaceuticals are present in the environment
2. Some pharmaceuticals have been shown to have adverse effects on wildlife
3. Drinking water may be contaminated with pharmaceuticals

Problem 1

Many pharmaceuticals are present in the environment

- About 100 different pharmaceuticals have, so far, been detected in the aquatic environment.
- They primarily enter in effluent from sewage treatment works (STWs).
- Some are also present in the terrestrial environment.
- These pharmaceuticals cover many different groups (e.g. steroids, beta-blockers, SSRIs, fibrates).

How did they get there?

- They were excreted by people taking the drugs.

OR

- Disposed of down toilets as unused drugs.
- They were not completely removed at the STW

Major unresolved issues about the presence of pharmaceuticals in the environment.

- Relatively little is known about the degradation rates of pharmaceuticals in the environment (or even in STWs).
- Very little is known about their concentrations in rivers, or other bodies of water that receive STW effluents.

100 ng/litre in effluent = ? in river water

Problem 2

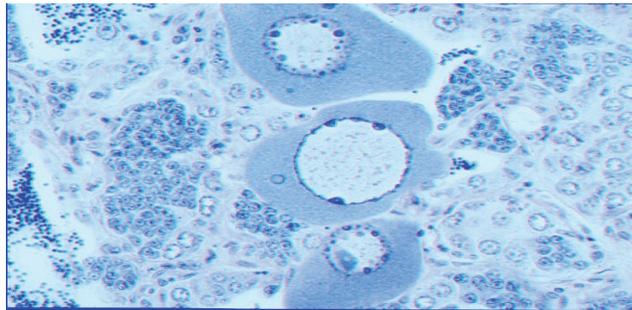
Some pharmaceuticals have been shown to have adverse effects on wildlife

- **Ethinyl Estradiol (EE2)** 'feminizes' male fish, preventing them from reproducing
- **Diclofenac** kills vultures (nothing to do with the 'water cycle', I realise!)

EE2 'feminizes' male fish

I: Historical Perspective

- Intersex fish found in U.K. rivers, then in many other developed countries



- These fish also had elevated plasma vitellogenin levels (a biomarker of estrogen exposure)
- EE2 identified as a major (but not the only) cause.

EE2 'feminizes' male fish

II: Results from Laboratory Experiments

- Fish full life-cycle study conducted.
- 205 days of continuous exposure
- Males exposed to >4 ng/litre failed to become sexually mature
- At 4 ng/litre, many males completely feminized. Others intersex.
- No observed adverse effect concentration (NOEC) was 1ng/litre

Data from Länge et al., 2001

EE2 'feminizes' male fish

III: Current Understanding

- Concentrations of about 5 ng/litre or above prevent fish reproducing. Fish populations crash.
- Concentrations above about 0.5 ng/litre will cause effects.
- It is unclear if EE2 adversely affects invertebrates at concentrations that could be present in the environment.

Diclofenac Kills Vultures

I: Field Observations



- 10 to 20 million vultures have died across the Indian subcontinent in the last 10 years
- Populations of 3 species have decline by more than 95%
- All 3 species are now considered **CRITICALLY ENDANGERED** (likely to become extinct very soon)

Diclofenac Kills Vultures

II: The Cause

- The birds died of acute renal failure.
- Diclofenac was the cause.
- The birds ingested diclofenac by feeding on dead domestic livestock that had been treated with this NSAID.
- Experimental (laboratory) research confirmed that diclofenac caused acute renal failure.

Diclofenac Kills Vultures

III: Some Lessons

- Pharmaceuticals can reach the environment in unexpected ways.
- Predicting what animals will receive exposure to pharmaceuticals is not easy.
- Some species (or groups of species) may be very sensitive to a particular pharmaceutical.
- A side effect in humans may be the dominant effect in other species.

CONCLUSION: We have a lot to learn about protecting wildlife from pharmaceuticals.

Summary

It is unclear presently whether these two examples will prove to be atypical – perhaps even the only examples of human pharmaceuticals adversely affecting wildlife – or whether many more examples will be discovered.

Other reported effects of low concentrations of pharmaceuticals on aquatic organisms

- A beta-blocker, **propranolol**, inhibits egg production in fish.



- A SSRI, **fluoxetine**, stimulates egg release from molluscs.



But, how reliable are these apparent effects?

- Most are based on the results of one, often preliminary, laboratory experiment.
- They have not been repeated by other researchers.
- The effects were not always concentration-related.

My personal opinion:-

The quality of the research needs to improve, and experiments need to be replicated. We want to go forward on good science.

Problem 3

Drinking water may be contaminated with pharmaceuticals



Duane Moser sampling in Nevada. *Jae C.Hong*
Figure from report from Associated Press

What the article said

“A vast array of pharmaceuticals – including antibiotics, anti-convulsants, mood stabilizers and sex hormones – have been found in the drinking water supplies of at least 41 million Americans, an Associated Press investigation shows”.

Articles based on the A.P. investigation appeared in over 100 U.S. newspapers, and on T.V. (e.g. CNN) on 10 and 11 March, 2008. **There is a problem!**

But what exactly is the problem?

- People will not want pharmaceuticals in their drinking water, **however low the concentrations are.**



- There is probably **not** a public health issue here, because concentrations are far, far below therapeutic levels.
- However, there **is** a public perception problem here. People will not like drugs excreted by their neighbour turning up in their drinking water.



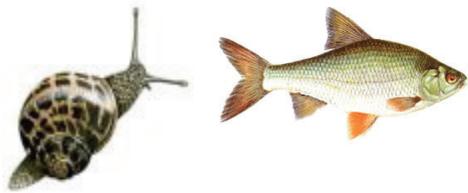
My views on these problems

Problem 1: Pharmaceuticals are present
 in the environment.

Unsurprising. Not of concern unless they
cause effects on aquatic organisms.



Problem 2: Pharmaceuticals can adversely affect wildlife.



Yes, they can, but probably only a small number. But which ones, and what are their effects. There is a lot yet to learn here.

Problem 3: Drinking water contaminated.



Yes, it probably is. But concentrations **EXTREMELY** low. No public health issue, but nevertheless public not reassured.

Possible Solutions

1. Use 'greener' pharmaceuticals.
2. Prevent pharmaceuticals reaching the environment.
3. Improve efficiency of STWs.

Solution 1

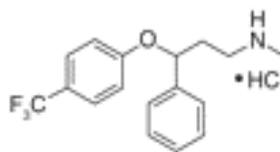
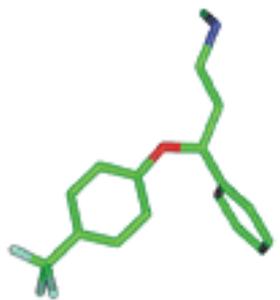
Greener Pharmaceuticals

- Use 'greener' pharmaceuticals that are more fully metabolized in people, and/or more easily degraded in the environment.
- But, there could be a conflict between developing 'greener' pharmaceuticals and desirable properties of pharmaceuticals (those that make them good pharmaceuticals).

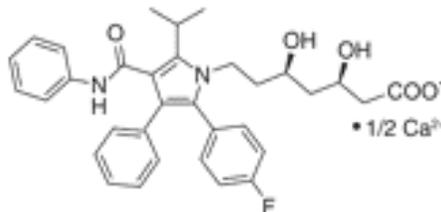
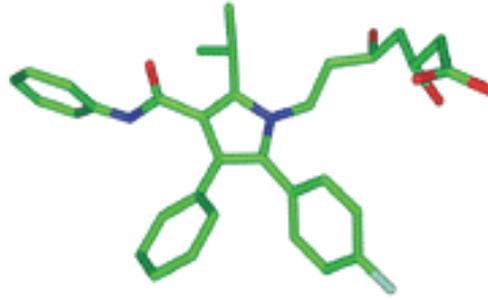
The conflict

Fluorine in Pharmaceuticals: looking beyond intuition.

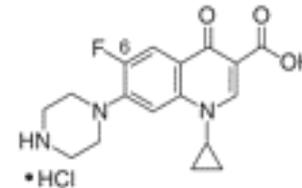
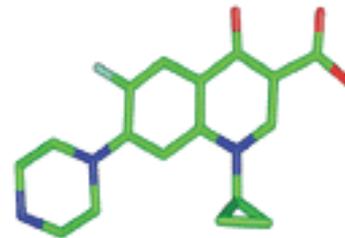
Müller, K. Faeh, C. and Diederich, F. *Science*, Volume 317, 28 September, 2007



Prozac



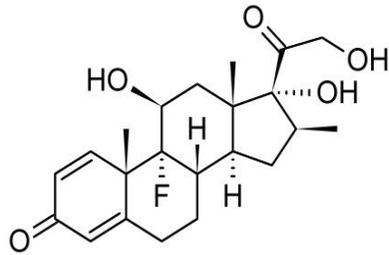
Lipitor



Ciprobay

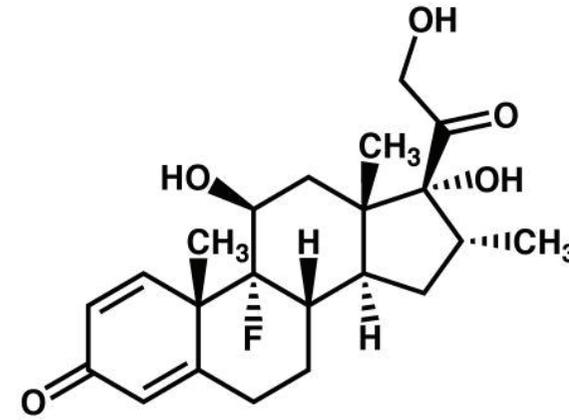
Glucocorticoids

Betamethasone



Mostly topical and sometimes injections for skin diseases

Dexamethasone



Anti-inflammatory, immunosuppressive. Some use in oncology and veterinary

With F, potency and stability increased up to 25 to 40 times compared to cortisol

Possible Compromise?

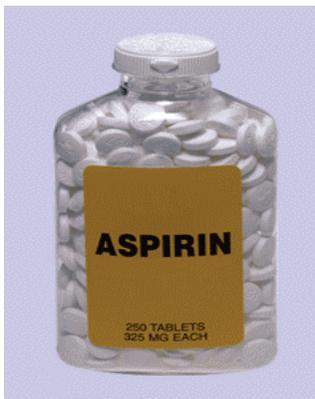
- Think about possible environmental stability **and** effects **early** in any drug development.
- Don't add lots of chlorine and fluorine atoms to new pharmaceuticals. If you do, your new drug will probably fail its environmental risk assessment.

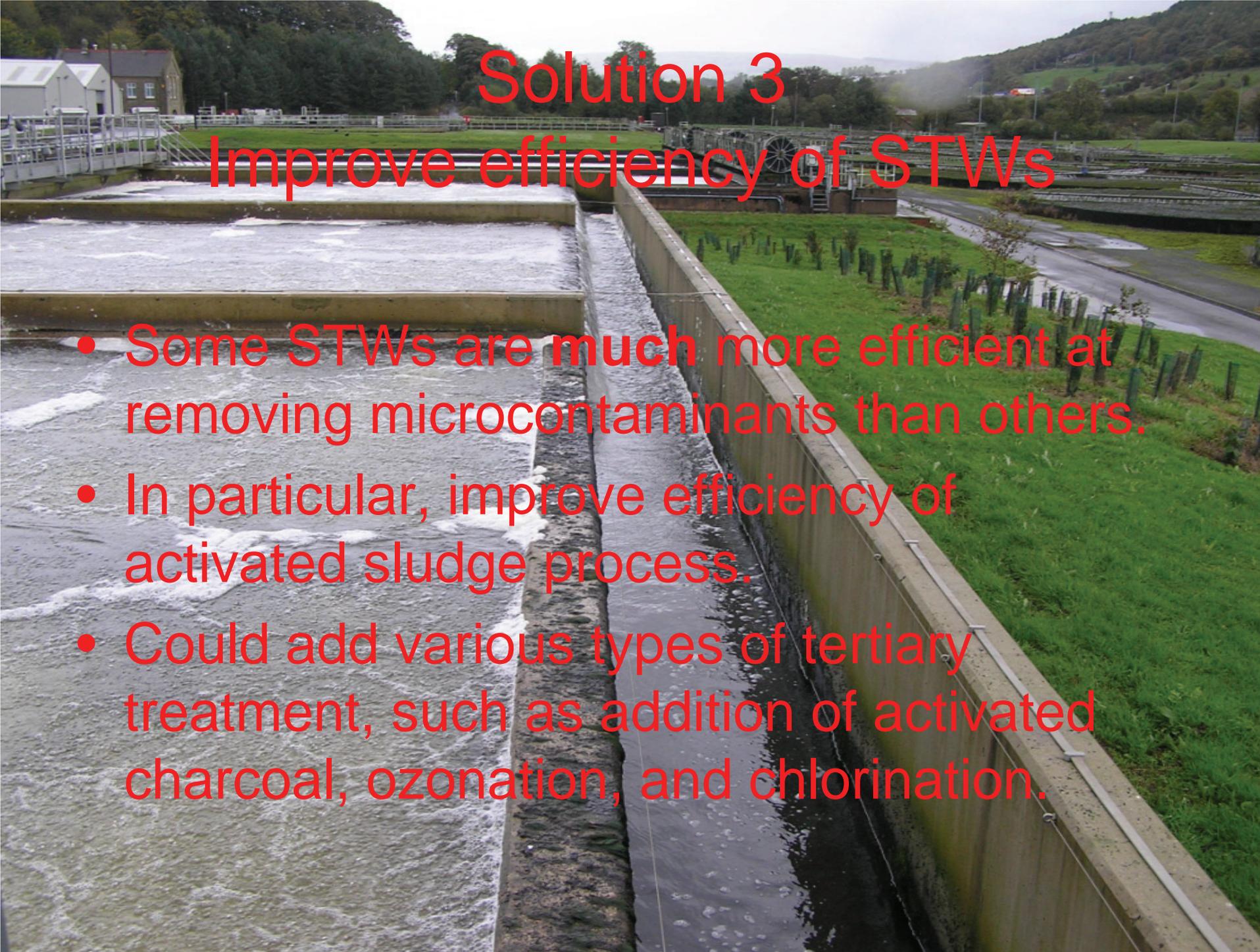


Solution 2

Prevent pharmaceuticals reaching the environment

- Redesign toilets, so that urine does not enter the sewer system.
- Improve collection of unused pharmaceuticals.





Solution 3

Improve efficiency of STWs

- Some STWs are **much** more efficient at removing microcontaminants than others.
- In particular, improve efficiency of activated sludge process.
- Could add various types of tertiary treatment, such as addition of activated charcoal, ozonation, and chlorination.

The conflict

- Additional costs, which could be very significant, and permanent.



- Increased energy use – bad for the environment.



(c) Ian Britton - FreeFoto.com

Enough from me. I have tried to set the scene. I do not know much about many of these issues: my expertise is confined to ecotoxicology. And even here the challenge is formidable, as the following slide will demonstrate.

The task: Protecting U.K. Biodiversity



Plants

Mammals

Birds (breeding)

Reptiles

Amphibians

Fish

Invertebrates

e.g. Spiders

e.g. Beetles

e.g. Moths

e.g. Butterflies

Native species

1,403

96

221

7

7

441

20,000 plus

600

3,700

2,500

59



An enormous task!

Thank you for
listening