

Mistra EviEM PS2 Pilot study

Publication date: 7 February, 2013

Please cite as: Land, M (2013): **What is the effect of pharmaceutical residues in water on aquatic biota?** Mistra EviEM, PS2 Pilot study. (www.eviem.se)

What is the effect of pharmaceutical residues in water on aquatic biota?

Pilot study

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Abstract

A systematic review on the effects of pharmaceutical residues in water on aquatic biota has been suggested by the Swedish Agency for Marine and Water Management, and has also been supported by the Swedish Chemicals Agency. The findings in this pilot review show that a systematic review question on this topic must be very specific regarding population, exposure (pharmaceutical substance) and outcome (critical effect). Furthermore, the scientific evidence is most probably not sufficiently abundant to allow for any systematic review on this topic.

Background

The worldwide consumption of pharmaceuticals has increased significantly since the 1950s as a direct result of factors including population growth, the fast development of medical science, ageing of the population, and practitioners' prescription habits (OECD, 2009). It is now well established that pharmaceuticals (and their metabolites) are present in the environment (Kümmerer, 2004).

Wastewater is considered the primary entry route and sources include households (Sanderson et al., 2004), agriculture and pharmaceutical industries (Kümmerer, 2004) and hospitals (Hawkshead, 2008; Ternes, 2006). Scientific and public concerns regarding their potential impact on the environment and human health are being raised (Le Corre et al., 2012).

Discharge of produced pharmaceuticals and their metabolites into wastewater occurs through excretion of consumed drugs as well as inappropriate disposal of unused drugs. The Swedish Medical Products Agency (Läkemedelsverket, 2012) has conducted an investigation regarding the latter discharge flow where the scope was to:

- Update and increase their knowledge about the reasons for the disposal through a review of Swedish and international scientific literature published during the last 20 years.
- Making an inventory of routines and services aimed at decreasing disposal of unused drugs.
- Making an inventory of routines for handling and measuring surplus pharmaceuticals among relevant operators.
- Develop information and probe the attitude among the public.

The purpose of the investigation was to identify additional measures that can be taken to minimize the disposal of unused pharmaceuticals.

Another Swedish initiative, MistraPharma, is a research programme which “works to identify human pharmaceuticals that are likely to be of concern to aquatic ecosystems and address the risk for antibiotic resistance promotion in the environment” (<http://www.mistrapharma.se/>). MistraPharma will also propose risk management strategies, in particular improved regulatory test requirements and wastewater treatment technologies. The programme started in 2008 and will end 2016.

One outcome of the MistraPharma research programme is the WikiPharma database (Molander et al., 2009). The database, which is freely available on the web (<http://www.wikipharma.org/welcome.asp>), contains environmental effect data for pharmaceuticals extracted from 222 scientific articles, encompassing approximately 155 active pharmaceutical ingredients (last updated 2012-11-07). Anyone is allowed to propose additional data to the database.

Identification of topic and stakeholders

The topic was suggested by the Swedish Agency for Marine and Water Management (SwAM). Another user that has shown interest in a review on this topic is the Swedish Chemicals Agency.

Key researchers in this field are active in the MistraPharma programme. The programme director Professor Christina Rudén, Stockholm University, has expressed doubts about the amount of scientific information to a systematic review.

Formulation of review question(s)

When the topic was suggested the review question was formulated as “What is the effect of pharmaceutical residues in water on aquatic biota?” The question contains the following elements:

Population/Subject: Aquatic biota
Exposure: Pharmaceutical residues
Comparator: No exposure
Outcome: Critical effects

Each element (except perhaps the comparator) needs to be better defined. The Population could be defined by species. The WikiPharma database contains data on more than 170 species. The exposure should also be more clearly defined. As already mentioned the WikiPharma database contain ecotoxicological data for approximately 155 substances. The outcomes, or critical effects, vary as well. In the Wikipharma database approximately 400 different critical effects are recorded, ranging from mortality to an array of sub-lethal defects and altered activity of various enzymes etc.

For a systematic review a more suitable structure of the question could be “At what exposure of substance X has critical effect Y been observed on species Z?” The PICO elements in this question are:

Population/Subject: Species Z
Exposure: Lowest Observed Effect Concentration (LOEC) of substance X
Comparator: No exposure
Outcome: Critical effects Y

The exposure can also be expressed by other means, e.g. LC50 (concentration level where 50 % of the population survives).

Looking outside the laboratory, an alternative question could be structured like “What is the effect of substance X on the biodiversity/species richness or abundance of species Z in aquatic environment Y?” The PICO elements in that question would be:

Population/Subject: Some specified species or group of species (e.g. fish or invertebrates)
Exposure: Substance X at some elevated concentration
Comparator: No exposure
Outcome: Changed biodiversity/species richness or abundance of species Z

Scientific basis

The literature on eco-toxicological effects of pharmaceutical substances on aquatic biota is fairly abundant. As discussed above, however, it may be difficult to find comparable data. Few studies report on the same species and critical effect when exposed to a certain substance. To illustrate the volume of the literature we can look at the following example:

One of the most studied species is *Daphnia magna*; in the WikiPharma database 337 experiments are recorded from 61 different sources. These studies report on 95 different substances and 47 different critical effects. In 19 experiments the exposure of acetylsalicylic acid metabolites has been studied. The most studied critical effect was immobilization (7 experiments from 6 different sources). None of these

experiments reported on LOEC but on EC50 (concentration level where the measured effect was observed on 50 % of the individuals). One study also reported on the No Observed Effect Concentration (NOEC). The purpose of this exercise is to show that when the question (by necessity) becomes very specific, very few comparable data exist. The WikiPharma database does probably not cover all the literature. However, a search in Web of knowledge (see search string 1) results in only 2 hits. Thus, a vast amount of additional data should not be expected to be found.

Search string 1

Topic=("Daphnia magna") AND (acetylsalicylic) AND (immobilization))

Timespan=All Years. Databases=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH.

Effect studies outside the laboratory are even scarcer. If the last question in section 3 is considered, search string 2 could be applied. In Web of Knowledge this results in just one hit. Adding the words "pharma*" and "medic*" in the exposure term in order to cover a wider range of substances results in 256 hits. However, very few of these are relevant to the question. It seems that the scientific evidence is too scarce to allow any systematic review on this topic. This view is also shared by the director of the MistraPharma programme Professor Christina Rudén (Pers. Comm.).

Search string 2

Topic=((Fish* OR invertebrate* OR *plankton) AND ("acetylsalicylic acid") AND (biodiversity OR richness OR abundance))

Timespan=All Years. Databases=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH.

Table 1.

Mandatory criterion	Y/N	Comments	Section
Deals with conditions in the natural environment	Y		
Relevant to the situation in Sweden	Y		
Well-defined, conceptually clear and reasonably limited in scope	N		

Deals with problem descriptions or countermeasures whose scientific support is insufficient, disputed or incompletely known	Y		
Covered in the scientific literature (or by other investigations) to such an extent that a systematic assessment can be implemented	N		

Optional criterion	Y/N	Comments	Section
Controversial and/or the subject of great public attention	Y		
Seen as environmental policy issues of high concern	Y		
Deals with new forms of environmental pressures, changes or actions	Y		
Deals with environmental disturbances or mitigation efforts that affect great natural values and/or extensive parts of the country	N		
Deals with measures that are particularly costly or resource-demanding in some other respect	N		
Deals with actions that in some respects are beneficial to the environment but may be unfavourable in other respects	N		
Deals with environmental problems currently treated by a variety of alternative measures.	N		

Conclusion

At present the scientific evidence is too scarce to allow any systematic review on this topic.

References

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Mistra EviEM Pilot studies

PS1 Pilot study: **How are fluxes of greenhouse gases between boreal forest ecosystems and the atmosphere affected by uneven-aged forestry?** (October 2012)

PS2 Pilot study: **What is the effect of pharmaceutical residues in water on aquatic biota?** (February 2013)

PS3 Pilot study: **Is thiamine deficiency a significant cause of declining bird populations in the Baltic Sea area?** (November 2013)



Mistra EviEM conducts systematic reviews of environmental issues identified as important by public agencies and other stakeholders. These provide an overall assessment of the state of scientific knowledge and help to improve the basis for environmental decision-making in Sweden.

All systematic reviews are preceded by a pilot study. If such a study indicates that the topic is not suitable for systematic review, the process ends with the pilot study being published in this series instead.

EviEM

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