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Bioaccumulation of five pharmaceuticals at multiple trophic levels in an aquatic food web - Insights from a field experiment

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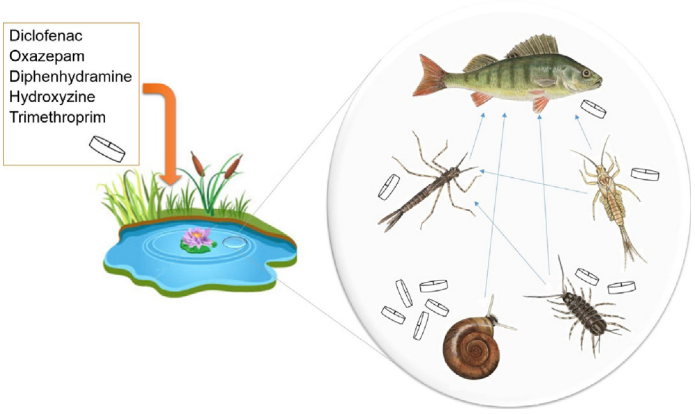
HIGHLIGHTS

- A study of uptake of five pharmaceuticals by fish and four aquatic invertebrates
- There are inter-specific differences in uptake of pharmaceuticals.
- Highest concentrations were found for the benthic species.
- Important to not only consider waterborne exposure in risk assessments
- Important to include organisms from different trophic levels in risk assessments

GRAPHICAL ABSTRACT



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ABSTRACT

Pharmaceuticals derived from manufacturing and human consumption contaminate surface waters worldwide. To what extent such pharmaceutical contamination accumulates and disperses over time in different compartments of aquatic food webs is not well known. In this study we assess to what extent five pharmaceuticals (diphenhydramine, oxazepam, trimethoprim, diclofenac, and hydroxyzine) are taken up by fish (European perch) and four aquatic invertebrate taxa (damselfly larvae, mayfly larvae, waterlouse, and ramshorn snail), by tracing their bioconcentrations over several months in a semi-natural large-scale (pond) system. The results suggest both significant differences among drugs in their capacity to bioaccumulate and differences among species in uptake. While no support for in situ uptake of diclofenac and trimethoprim was found, oxazepam, diphenhydramine, and hydroxyzine were detected in all analyzed species. Here, the highest bioaccumulation factor (tissue:water ratio) was found for hydroxyzine. In the food web, the highest concentrations were found in the benthic species ramshorn snail and waterlouse, indicating that bottom-living organism at lower trophic positions are the prime receivers of the pharmaceuticals. In general, concentrations in the biota decreased over time in response to decreasing water concentrations. However, two interesting exceptions to this trend were noted. First, mayfly larvae (primarily grazers) showed peak concentrations (a fourfold increase) of oxazepam, diphenhydramine, and hydroxyzine about 30 days after initial addition of pharmaceuticals. Second, perch (top-predator) showed an increase in concentrations of oxazepam throughout the study period. Our results show that drugs

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can remain bioavailable for aquatic organism for long time periods (weeks to months) and even re-enter the food web at a later time. As such, for an understanding of accumulation and dispersion of pharmaceuticals in aquatic food webs, detailed ecological knowledge is required.

1. Introduction

Many of the about 4000 pharmaceuticals currently used globally (Boxall et al., 2012) enter surface waters via manufacturing and human excretion, veterinarian use, and aquacultural and agricultural use (Arnold et al., 2014). Several pharmaceuticals have been identified as potent aquatic contaminants and as chemicals of emerging environmental concern (Brodin et al., 2014; Corcoran et al., 2010; Rosi-Marshall and Royer, 2012). In 2011, pharmaceutical contamination was listed by policymakers and scientists as one of the 40 most important issues of environmental concern in the US (Fleishman et al., 2011). Further, the EU Parliament has added several drugs to their watch list of water pollutants that could, in the future, be placed on their priority list of controlled chemicals (European Union, 2015). An environmental classification system for pharmaceuticals in Sweden has demonstrated that 92% of commonly used drugs with environmental data were not readily biodegradable, 23% had the potential for bioaccumulation, and 61% were toxic to aquatic organisms at concentrations below 1 mg/l (Wennmalm and Gunnarsson, 2009).Concentrations of pharmaceuticals measured in surface waters are usually low, ranging from ng/l to μg/l in developed countries (Larsson et al., 2007), but have been found up to mg/l in close proximity to pharmaceutical manufacturing and formulation facilities (Fick et al., 2009; Phillips et al., 2010). Even though concentrations found in natural systems are far from being lethal, several studies have demonstrated sub-lethal effects on aquatic organisms at concentrations near the range of concentrations that has been found in aquatic ecosystems. For example, estrogenic compounds can feminize male fish and subsequently cause cascading ecosystem effects (Kidd et al., 2007). Other effects include behavioural modifications in fish exposed to anxiolytics at concentrations below that found in effluent waters (Klaminder et al., 2014), antihistamines modifying behaviour of insect larvae (Jonsson et al., 2014) and nutrient recycling in streams (Jonsson et al., 2015), and nonsteroidal anti-inflammatory drugs affecting reproduction, hatching success, growth rate, and behaviour of aquatic organisms (Ericson et al., 2010; Lee et al., 2011; Nassef et al., 2010). Despite numerous studies indicating that pharmaceutical substances may be universal contaminants, little is known as to what extent they are taken up and redistributed among different types of organisms in natural aquatic food webs. For example, a recent global synthesis on trophic magnification of organic chemicals (including 1591 compounds) did not include any pharmaceuticals due to the limited knowledge about their fate in food webs (Walters et al., 2016).

Aquatic organisms in contaminated environments are exposed to bioactive pharmacological substances both via uptake from the water (bioconcentration) and via the diet, and the combined uptake, via all routes, is defined as bioaccumulation. In general, the former route is more studied than the latter, and few studies have measured uptake under natural conditions. Nevertheless, some experiments have assessed uptake of pharmaceuticals in organisms of different trophic positions. In artificial experimental food webs, aquatic organisms at lower trophic positions (e.g. algae) seem to bioaccumulate pharmaceuticals to a greater extent than organisms at higher tropic positions (e.g. water fleas and fish) (Ding et al., 2015; Vernouillet et al., 2010), and field studies support these findings (Du et al., 2014; Ruhi et al., 2016). However, other field studies have found low or no bioaccumulation and trophic biomagnification potential of pharmaceuticals in freshwater food webs (Xie et al., 2015). Such contradictory results could be due to short-term variation in pharmaceutical concentrations (and thus exposure of organisms) in the field, due to site- and/or taxon-specific differences in diets, and due to variation in movement propensity (i.e. moving in from less contaminated habitats). Therefore, to identify general patterns of pharmaceutical uptake and transfer in aquatic biota long-term studies of pharmaceutical uptake in controlled aquatic systems are highly warranted.

In this study, we conduct a full ecosystem experiment to assess the extent at which five commonly used pharmaceutical substances (trimethoprim, diclofenac, oxazepam, hydroxyzine, and diphenhydramine) are taken up by organisms in an aquatic food web over a monthly time-scale. The food web consisted of a vertebrate top consumer (European perch - *Perca fluviatilis*) and four invertebrate species positioned at different trophic levels in the food web (damselfly larvae – Zygoptera [predator], mayfly larvae – Ephemeroptera [primarily grazer], waterlouse – *Asellus aquaticus* [omnivore] and ramshorn snail – Planorbidae [primary grazer]) in a semi-natural pond ecosystem. As no additional inputs or losses of pharmaceuticals, to or out of the pond, occurred during the study we assess the trophic transfer of the pharmaceuticals solely as a result of their chemical properties (octanol-water partition coefficient, K_{ow}) and persistence (half-lives) in an environment that is much more similar, and thus more relevant, to natural systems than are laboratory studies. We hypothesized that: i) bioaccumulation in invertebrates and fish can be predicted from the K_{ow} value of the pharmaceuticals, according to previously quantified relationships (Arnot and Gobas, 2006); ii) bioaccumulation differs significantly among organisms due to their trophic position and habitat use; and iii) temporal changes (i.e. recovery rates) in bioaccumulation of the studied drugs differ among organisms. Based on our findings, we discuss how the ecology (diet and habitat) of different species influences bioaccumulation and the likelihood of significant biomagnification of pharmaceuticals in aquatic food webs.

2. Materials and methods

2.1. Pharmaceuticals used in this study

The substances examined in this study were chosen to represent a range of chemical properties and biodegradability, and have all been detected in natural aquatic ecosystems (Hughes et al., 2013). Despite their relatively rapid degradation (over weeks to months), compared to some classic organic contaminants (PBCs or DDes), all five pharmaceuticals can be considered pseudo-persistent due to near-continuous input to aquatic systems (Daughton, 2002). Specific information about their known fate in aquatic ecosystems is listed in Table 1 and described in detail below along with the original references (arranged in an order of increasing log K_{ow}-values).

Trimethoprim is an antibiotic mainly used to treat urinary tract infections (Wishart et al., 2006). The drug has demonstrated a high degree of persistence in aquatic environments (Alexy et al., 2004; Lunestad et al., 1995; Sirtori et al., 2010; Suarez et al., 2010) and has a reported half-life in water of 215 h in unfiltered river water exposed to UV-light (Blum, 2013) and 100–200 days in marine sediments (Hektoen et al., 1995). Trimethoprim has a low log K_{ow} value between 0.59 and 0.91 (Bendz et al., 2005; Dalkmann et al., 2014; Heidler and Halden, 2008) and is therefore predicted to show the lowest BAF of the studied pharmaceuticals (Table 1).

Diclofenac is a nonsteroidal anti-inflammatory drug used to reduce inflammation and as an analgesic reducing pain (Wishart et al., 2006). The half-life has been measured to be 8 h in water (unfiltered river