DRUGS IN THE ENVIRONMENT
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Pharmaceuticals and Personal Care Products

We have all heard discussions about the impact of sewage effluents on nutrients in the Bay, but there are many more chemicals in sewage that are of concern. Consider all the pharmaceutical products and personal care products (PPCP) that end up going down the toilet or drains in households all around the world. Products in sewage may end up in receiving waters or they may be deposited on land via sludge application. Many prescriptions for medications that have expired end up going down the drain, although there are now specified take-back days for turning in expired drugs sponsored by local governments. The Food and Drug Administration requires not only that drugs be tested for safety to humans, but they also require an environmental assessment be submitted as part of a new drug application if the expected concentration of the drug into the aquatic environment is at least one part per billion. The amount of the drug expected to be produced over the next five years determines whether this threshold is reached (Sherer, 2006). This article focuses on the effect of PPCPs in the environment rather than on humans.

What are the most significant compounds classified as PPCPs that are of concern to ecotoxicologists? Since there are more than 4,000 such compounds, ranking them for priority for research is essential. At a recent international conference, ecotoxicologists developed a list of twelve PPCPs of greatest concern (Donnache et al., 2015). Ranking is based on prescription data, concentration in the environment, the predicted concentration at which they may be toxic, their persistence, and their ability to be bioaccumulated or concentrated up the food chain. The top priority compounds are the estradiols, which are used for hormone replacement therapy and birth control. These tend to travel through the human gut unchanged so they are excreted at a fairly high rate by any woman who is taking them. Estradiols are classified as endocrine-disruptors, meaning that they have a profound impact on the reproductive function of animals. Male smallmouth bass exposed to environmental concentrations of estradiol have been shown to have immature eggs in their testes, becoming so-called intersex fish. In an experimental lake in Canada, estradiol addition caused the population of fathead minnows to crash while the population of prey species increased. Upsets at the ecosystem level are not generally considered when assessing the impact of a toxic substance.

Other compounds besides PPCPs, including pesticides, have also been shown to be endocrine disruptors, including the most widely prescribed anti-diabetic drug, metformin. This drug is not metabolized by humans so, within 24 hours of ingestion, it is excreted essentially unchanged.

In a 2014 study of pharmaceuticals in Lake Michigan, the ecotoxicologist Rebecca Klaper found evidence of 32 PPCPs in the water and 30 in lake sediment. Fourteen of them were found to be of medium or high risk to the ecosystem, based on data from EPA. Metformin is at the top of the list of concerns from EPA, and it is found at concentrations of concern even 3 kilometers off the shores of Milwaukee (Scudellari, 2015).

Other drugs of concern are propanolol, a beta blocker used to treat cardiovascular disease and paracetomal, an anlagesic and antipyretic, similar to aspirin. Others include ibuprofen, several anti-inflamatory drugs including aspirin and carbamazepine, used to treat epilepsy. A key aspect of all of these compounds is that they are designed to be biologically active and therefore, even at low concentrations, they tend to have an impact on animal metabolism. Effects of exposure to low concentrations on marine animals such as shellfish, crabs and fish include damage to muscle tissue and gills, damage to liver and pancreactic tissue, decline in metabolic enzymes, and damage to regulatory systems affecting growth and reproduction. Many of the studies that show these effects were conducted in a lab with a single compound for a short time, ranging from 96 hours to 28 days. (Fabri and Franzellitti, 2016). Imagine what the impact will be when they are exposed to a combination of substances throughout their lifetime.

Effects of PPCPs in the Environment

Some PPCPs can be outright lethal to wildlife if a sensitive population comes in contact with them. One example of unexpected lethality was seen in India and Pakistan starting in the 1990's when tens of millions of vultures began dropping dead. At first it was thought to be due to an infectious agent but in 2004 it was discovered that they were dying of kidney failure after eating discarded domestic animals treated with the anti-inflammatory compound diclofenac (Scudellari, 2015).

Not included in the top twelve pollutants of concern are micro-plastic materials which have recently received attention. In addition to being consumed by wildlife, toxins leach from these particles. These are discussed more in the next article.

There is one antibiotic in the list of 12 PPCPs of concern: sulfamethoxazole, a common sulfa drug. The primary concern with antibiotics in the environment is that some bacteria in nature possess genetic elements that resist the antibiotic and their genes may be passed on to bacteria that have not even been exposed to the sulfa drug. Indeed, microbiologists have found plasmids, which are extra-chromosomal DNA, that contain genes for resistance to eight different antibiotics. Such bacteria end up as the "super bugs" that resist our best antibiotics, causing serious and life-threatening infections.

Effects of PCPPs on Animal Behavior

In addition to all of these impacts at the biochemical and physiological level, there has also been work done recently on the impacts of PPCPs on animal behavior. For example, when predatory perch are exposed to a psychoactive drug, they become more active while their damselfly prey are not affected by the same drug, illustrating that the same compound can effect members of different trophic levels differently.

This same study found that 46% of the drug that was in the prey accumulated in the predator; thus measuring environmental concentrations alone will not necessarily tell us the true exposure of predators in nature. Anti-depressants have been shown to reduce territorial aggression in coral reef fish, and both locomotion and agression in Siamese fighting fish. Rainbow trout, however, were unaffected by very high concentrations of the same drugs. The anti-depressant drug fluoxetine (Prozac) is the number 2 ranked PPCP. Side effects of this drug in humans are loss of libido and loss of appetite. When white bass and striped bass and goldfish are exposed to this drug, their feeding rate declines. Similarly, wild-caught starlings given fluoxetine ate less and at the wrong times. They fed throughout the day rather than at dawn and dusk. Not feeding heavily at dusk in the winter could result in death.

Exposure to the psychiatric drug diazepam caused increased activity in zebrafish and pumpkinseed. Antihistimines and the anti-epileptic drug carbamazepine caused fathead minnows to feed at a slower rate. Responses to drugs such as these are likely to be significant in wildlife, perhaps resulting in changes in population dynamics and food webs (Brodin et al., 2014).

Environmental Fate

What is the environmental fate of all these compounds once they leave our hands? Of course we don't really know the answer, but we are beginning to learn about some of the fates of PPCPs in the environment. They are ubiquitous and although their concentrations are generally quite low, they are persistent. Wastewater treatment plants (WWTPs) are not designed to reduce the concentrations of PPCPs, and they vary greatly in their ability to do so. In Germany, the removal of 14 drugs by a WWTP was quantified. For most of the drugs tested, the facility removed overall about half of the original concentration, but this ranged from only 7% for carbamazepine to 96% for propranolol. It is important to note that the metabolic breakdown products of drugs can be as or more toxic than the parent compound (Scherer, 2006).

Samples taken from sediment cores have shown that the anti-anxiety drug oxazepam has been accumulating in sediment layers for over 30 years. Based on the samples, researchers were able to determine the year that the drug went on the market and they can correlate the concentration in the sediment with the number of prescriptions written each year. No degradation of the drug had occurred over that time. In general, environmental conditions such as temperature, salinity, pH, and organic content will certainly affect the rate at which a chemical is degraded. In the case of the water-sediment-interface, where many compounds end up, it is tremendously complex and very hard to predict the true fate of the myriad chemicals that we dump into our waterways every day. Although the concentrations of PPCPs are low in natural systems, they are predictably higher in the vicinity of WWTPs, and this is the area often studied to determine ecological impacts. Clams, sea urchins and fish that live in the Antarctic Ocean in the vicinity of the Scott and McMurdo stations have shown elevated concentrations of estradiols and anti-anxiety medications in their tissue (Fabri and Franzellitti, 2016).

How We Can Reduce These Compounds in our Waterways

Once they are in sewage, there is some decomposition by the bacteria in sewage, but, again, some breakdown products may be just as or more toxic than the original compound. Treatment of secondary effluents by UV or ozonation or nanofiltration may also reduce concentrations, but at a high cost. None of these treatments work for all contaminants and, in the case of ozonation, there is the possibility of making a drug more toxic. It is preferable to prevent their presence in sewage to begin with. One suggestion is to design drugs that degrade quickly but this would decrease their stability. Drugs could also be designed with a more efficient delivery system so that the dose could be decreased. Encouraging collection of expired drugs at take-back events is a natural solution. Collected drugs are generally disposed of by incineration. Also, drugs and their packaging could be designed with a longer shelf life. (Boxall et al., 2012)

Concentrations of PPCPs in nature is generally quite low, so humans are not considered to be at risk from these, but the development of antibiotic-resistant bacteria is of concern and calls for careful disposal of expired drugs.

Pharmaceuticals affect specific aspects of animal metabolism and we need to do our best to reduce the presence of these drugs in nature. Even at part per billion concentrations, the impact on the environment can range from changes in gene expression to changes in population structure and ecosystem function (Rodriguez-Moza and Weinberg, 2010).

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