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## IMPACT OF PHARMACEUTICALS AND PERSONAL CARE PRODUCTS IN ENVIRONMENT

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### ABSTRACT

Tons of pharmaceutical substances are used in human medicine for diagnosis, treatment or prevention every year. The presence of pharmaceuticals and personal care products (PPCPs) in the ecosystem has emerged as a serious concern due to their rapid growing and unregulated disposal practices. These micro pollutants disturb the ecological balance and attracted the public as well as scientific community. As a result, a number of investigations have been reported on widespread occurrence of pharmaceuticals and personal care products in the environment. To date, more than 100 pharmaceutical compounds (anti-inflammatory, analgesics, beta-blockers, antiepileptic, lipid regulators, antibiotics, etc.) have been reported in sewage, rivers and creeks, seawater, surface water, groundwater and drinking water resources throughout the world. Although these emerging pollutants introduced into aquatic environment by discharges from sewage treatment plants, industrial and hospital wastewater, landfill leachates, disposal of unused drugs, effluents from aquaculture, agricultural use and so on, the occurrence of drugs in the environment was usually in low concentrations, where in rivers, lakes and seawater ranges from ng/L. Many pharmaceuticals are not completely degraded after application, upon entering to the aquatic ecosystem the metabolites and some unchanged form may interfere with molecules, cells and organs of aquatic organisms due to their lipophilic nature and may lead to biological effect. The present paper is an attempt to explore the pharmaceuticals and personal care products (PPCPs) as emerging contaminants. We hereby discussed the impact of pharmaceuticals and personal care products on environment.

**Keywords:** Emerging contaminants, Pharmaceuticals, Personal care products, Environment

### INTRODUCTION

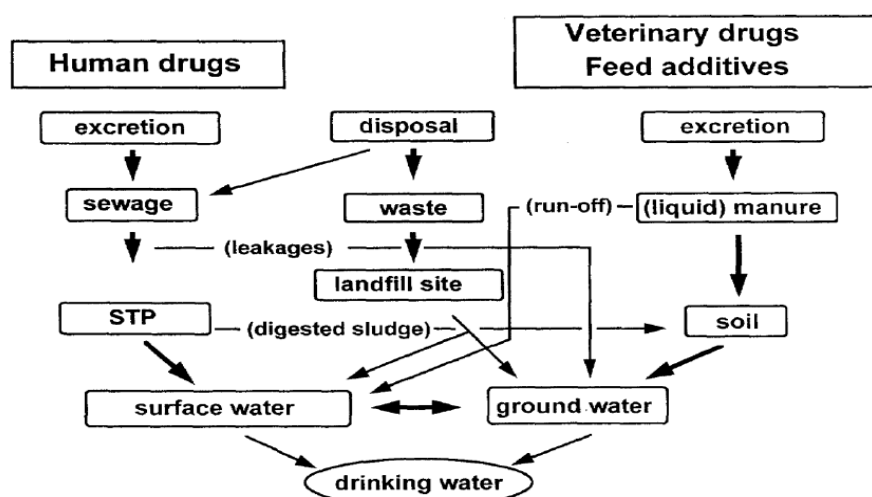
Pharmaceutical and personal care products (PPCPs) are a group of chemicals which are emerging contaminants, used as ingredients and components in products that are extensively used worldwide. They are used in human and veterinary therapeutic drugs, as growth promoting agents in animal husbandry, and in personal health, cosmetic and cleaning products. After the intended usage, therapeutic drugs, such as antibiotics, non-steroidal anti-inflammatory drugs, and other prescription or over the counter medicines can leave the human body unchanged or partially metabolized, inputting residues into the municipal waste stream<sup>[1]</sup>. Incomplete removal during wastewater treatment then allows discharge to deliver PPCPs residues to receiving waters<sup>[2]</sup>. Waste by-products, such as manures and sewage sludges, can also introduce a variety of veterinary pharmaceutical residues into the environment through their land-application<sup>[3][4]</sup>. PPCPs such as Sulfamethoxazole (Sulphonamide Antibiotic), Carbamazepine (Psychiatric Drug), Caffeine (Psychoactive drug),

Diclofenac, Ibuprofen, Naproxen, Ketoprofen (Anti-inflammatory drugs), Atenolol, Propranolol ( $\beta$  - Blockers) and Triclosan (Antiseptic) etc. are frequently detected in the aquatic environment as a result of the consistent input from both human and animal sources.

The occurrence of PPCP residues in the aquatic environment has been reported in both developed and developing countries. The United States Geological Survey has conducted a series of monitoring studies to characterize PPCPs and other anthropogenic organic contaminants in surface and groundwater<sup>[5-8]</sup> analyzed more than 100 river water samples from 27 European countries for polar organic pollutants including PPCPs. Terzić et al. 2008 reported the occurrence of PPCPs from the western Balkan Region<sup>[9]</sup>. Spongberg et al. (2011) studied PPCPs in both surface water and wastewater from Costa Rican waters<sup>[10]</sup>. Results from these studies suggested that PPCPs are ubiquitous in the aquatic environment worldwide. As a result of the high detection frequency and the increased concern over their potential adverse effects to non-target organisms, PPCPs are considered as "contaminants of emerging concern"<sup>[11][12]</sup>.

#### Source of Pharmaceuticals and personal care products

There are different possible pathways by which pharmaceutical compounds and other personal care products enter into the environment. After their release into the sewage system, they pass through wastewater treatment plants (WWTPs) and enter water systems, where a large variety of these compounds and their metabolites have been detected<sup>[13-16]</sup>, producing a complex mixture of compounds that may have synergetic effects. Some of these compounds are more bioactive than their metabolic precursor. Pharmaceuticals used in veterinary medicine are excreted onto the ground or directly into surface waters without passing through a WWTP, making their control and follow-up much more challenging. The ground can act as a major source of water contamination<sup>[17]</sup>, since most of these compounds and their metabolites are soluble in water, and they are excreted by urine and feces<sup>[18]</sup>. In intensive livestock farming, pharmaceuticals may in directly enter the environment through the application of manure and purines as fertilizers and can pass to humans through the food chain. Pharmaceuticals used in fish-farms are directly released into surface water<sup>[19]</sup>.



Pathways of Pharmaceuticals and personal care products

#### Effects of Pharmaceuticals and personal care products

Responses such as histological changes, behavioural effects, bio chemical responses, and up- or down-regulation of genes have been observed in organisms exposed to PPCPs<sup>[20-22]</sup>. Aquatic and terrestrial systems will be exposed to a complex mixture of PPCPs and other contaminants. Many pharmaceuticals, if consumed together at therapeutic doses, can cause severe adverse interactions in humans<sup>[23]</sup>. If aquatic

organisms respond to these compounds in the same way as humans, effects on the environment could be greater than predicted based on effects data for the single compounds. Antimicrobial PPCPs may also increase persistence of other PPCPs, thus affecting the overall risk<sup>[24]</sup>.

Because many human-use PPCPs will be emitted continuously into the environment, organisms in the environment will be exposed throughout their lifetime. However, no regulatory program for prospective environmental risk assessment of PPCPs (or other product classes) takes into account the long-term combined toxicity of mixtures of chemicals, so there is a need to develop new approaches for assessing the risks arising from long-term exposure to mixtures. The concept of mixture risk assessment is gathering momentum, particularly in the public health arena, and recent reports by the European Commission, the UK Committee on Toxicology, and the U.S. National Academy of Sciences have already started to consider this topic<sup>[25]</sup>.

For human medicines, it may be possible to use observed contra indications in humans to provide an indication of whether a particular combination of pharmaceuticals in the environment may be of concern. Mixture interactions could also be simulated by pharmacokinetic modeling, linking models at the interaction site<sup>[26]</sup>, although this will require extensive quantitative information on pharmacokinetics or toxicokinetics. Although the use of *in vitro* assays for relevant end points (e.g., carcinogenic, mutagenic, and reproductive effects) to assess the effects of mixtures of pharmaceuticals that typically occur in environmental systems may also provide useful information for use in risk assessment, these will need to be extensively validated before use.

For personal care products, there is regulatory pressure in some geographic regions to reduce the amount of animal testing used for human safety and environmental risk assessment in a 3Rs framework (reduce, refine, replace). It may be possible to reduce the amount of animal testing using nonanimal testing methods, such as *in vitro* approaches and *in silico* methods (e.g., quantitative structure–activity relationships, read-across and expert systems), by optimizing experimental designs, and by employing intelligent testing strategies<sup>[27-29]</sup>.

Although these approaches are being promoted (e.g., National Academy of Sciences 2007) and used for industrial chemicals [e.g., as part of the REACH (Registration, Evaluation, Authorisation and Restriction of Chemical substances) regulations in Europe and elsewhere<sup>[30]</sup>], additional approaches are needed to replace animal test methods with methods able to evaluate specific and nonspecific modes of action.

### **Risk and Relative Risks**

Risks of PPCPs in the environment in different geographic regions vary because of differences in the presence/absence and type of manufacturing sites, level of PPCP use, population demographics, cultural practices, environmental and climatic characteristics, dilution potential of receiving environments, and infrastructure related to wastewater and drinking water treatment. Risks may change in the long term due to factors such as increased urbanization and effluent-dominated instream flows<sup>[31]</sup>; increased disease pressures, demographic change, population increases, technological developments (e.g., move from small molecules to biologics, development of nano medicines, improvements in drug delivery), and climate change. By better understanding the drivers for PPCP exposure in different regions, it may be possible to identify those areas that are at greatest risk, meaning that control options can be focused to areas/regions where they will be most effective. By understanding how risks will change in the longer term, it may be possible to anticipate and preemptively mitigate against unacceptable changes in risks.

### **PPCPs relative to other chemicals and non-chemical stressors in terms of biological impacts in the natural environment**

PPCPs are released into the natural environment along with many other chemicals (e.g., nutrients, metals, industrial chemicals, pesticides, natural hormones). The natural environment is also exposed to nonchemical stressors such as changes in water flow and temperature. The effect of PPCPs could be small

compared with the many other chemical and nonchemical stressors present in the natural environment. To make informed management decisions, it is necessary to understand the relative impact of PPCPs compared with other pressures in a particular situation.

#### **PPCPs pose a risk to wildlife such as mammals, birds, reptiles, and amphibians**

Most studies have focused on effects of PPCPs on fish and invertebrates, but our knowledge of risks to other wildlife species, such as birds and small mammals, is less developed. Several case studies have highlighted the importance of understanding effects on birds and mammals. For example, the inappropriate use of diclofenac and associated cultural practices regarding disposal of animal carcasses, combined with the high sensitivity of vultures to diclofenac, were responsible for the decline in populations of three vulture species in Asia<sup>[32]</sup>, resulting in ecological, socio economic, cultural, and human health impacts<sup>[33]</sup>.

Indirect effects on top predators may also be important; for example, there is concern that anti-parasitic veterinary medicines may be indirectly affecting populations of insect-eating bats and birds by affecting the quantity of food available<sup>[34]</sup>. More work is needed to better understand the exposure of birds, mammals, and amphibians to PPCPs, as well as the potential toxicological effects of PPCPs on these species.

#### **The environmental risks of metabolites and environmental transformation products of PPCPs**

Pharmaceuticals may be metabolized in the treated human or animal so that a mixture of parent compound and metabolites will be released into the environment. Transformation of PPCPs will also occur in wastewater treatment processes, surface waters, sediments, manure, soils, and drinking water treatment processes. Although metabolites and transformation products are usually less hazardous than the parent compound. The environmental fate of these substances can also be different from the parent compound, meaning that environmental compartments that are not exposed to the parent may be exposed to a transformation product. Concerns have also been raised over the potential human health effects of selected transformation products of PPCPs, such as the halogenated and nitrosamine products resulting from transformation in wastewater and drinking water treatment processes<sup>[35]</sup>. We need to better understand the release and formation of transformation products of PPCPs in the environment and develop approaches for identifying transformation products that could pose a greater risk than the parent compound.

#### **Conclusion**

In the event that a Pharmaceuticals and personal care products poses an unacceptable risk to the environment, options exist for minimizing or removing emissions to the environment, including substitution of the compound with a more environmentally benign compound, development of better drug delivery systems so that smaller doses are needed, improvement of packaging and package sizes to extend shelf life and reduce the amount of the product that expires and must be discarded unused, changes in prescription and animal husbandry practices, introduction of improved wastewater treatment options. However, the efficacy and practicality of many of these solutions is poorly understood. A systematic study is needed to determine the benefits of different management and mitigation options and any societal and environmental costs associated with a particular option in different regions of the world. This will allow informed decisions to be made on the best mitigation strategy.

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