
PPCPs in the Arctic and Their Effect on the Environment

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Abstract

Pharmaceuticals and personal care products (PPCPs) have been used for generations to cure, prevent and control conditions as well as for life improvement in general. With the increasing population and globalization both the need and overall want for these kind of products are increasing rapidly. While these products might be useful for maintaining the way of life we live today it also poses as a potential risk to the environment. Due to most PPCPs having a low volatility and are mostly disposed of through sewage systems it is the local aquatic environments that are the most common recipient; leading to this being the place most affected by these pollutants. This can affect smaller animals and organisms at sub-therapeutic concentrations, which in some cases can cause drastic changes in species that lives in or are in other ways in contact with these polluted environments.

The Arctic region differ from other places because of the its harsh climatic conditions, but also due to it largely consisting of smaller settlements. Waste water treatment in these settlement are often not prioritized because of practical and economical issues. Harsh climate and periodically extreme weather makes installing modern waste water treatment plants both expensive and challenging; both transport and installation of these kind of constructions. In addition to PPCPs not being entirely eliminated in the suboptimal waste water treatment plants, PPCPs degrade at a significantly slower pace in the Arctic region. This is, among other factors, due to lower temperatures and the absent of sunlight larger part of the year. This allows for the pollutants to accumulate in a different in the Arctic compared to lower latitude regions.

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1 Introduction

During the last decade there has been an increasing interest in researching the effects of pharmaceuticals and personal care products (PPCPs), more specifically their effect on the environment including human health issues. Pharmaceuticals in particular is a product group that differ from other pollutants because they are made to withstand degradation until they reach their target tissue in the body. This results in the product either being unchanged or being an active metabolite when excreted which can have negative irreversible effects on the environment, especially the aquatic environments since this is where most of the waste ends up^[1].

Microbial resistance develops naturally in the environment. When bacteria and other microorganisms are exposed to anthropogenic antibiotics they will adapt to these as well, leaving us with resistance to commonly used drugs in potential human pathogens^[2].

The biochemical mechanism of pharmaceuticals is still in need of further elucidation even for the ones where the effect is documented and understood. This is a challenge when trying to predict what these pollutants can do to smaller organisms and how small doses are required to see an effect at all^[3].

PPCPs mainly enter the environment through local wastewater disposal which is likely because of their low volatility^[3]. Siloxanes, for example, are an exception to this. They have a high volatility, and can thus travel far from their respective source. However, most of the PPCPs pollutants originates from local sources. Either way, improper treatment of these pollutants can be problematic for the local aquatic environment. The Arctic regions consist of more secluded smaller towns with few people as well as larger cities. Economically it does not make sense for smaller towns to invest in state of the science waste water treatment plants (WWTPs)^[4]. This imposes as a noteworthy risk to the local environment, in terms of pollutants not being properly degraded before released into the local seawater. Lately there has been an increase in population leading to more consumption of commercial produced goods creating a challenge for the already suboptimal WWTPs^[5].

PPCPs also appear to be harder to break down in these northern climates,^[4] both because of the lack of sufficient solar irradiation and because of the general low ambient temperatures year round. Both solar irradiation and higher temperatures have been observed to increase the degradation rate of other pollutants, and this is also true for PPCPs^[6]. All of the mentioned factors makes studying the concentration levels of PPCPs in the Arctic of great importance for the local environment, and that is what this literary review is going to focus on.

2 Theory

2.1 PPCPs effect on the environment

There has been an interest in researching the environmental impact of PPCPs and their potential risk since 1999^[7]. During the last decade there has been a rapid development of analytical techniques making modern instruments sensitive enough to detect the low concentrations of PPCPs in effluent and influent sewage water, ground water, and even drinking water so that they can be quantified^[1]. Although the expected concentration levels of PPCPs in seawater is still problematic for current instrumentation^[4].

Residues of pharmaceuticals are widespread in aquatic systems but their concentrations are relatively low; in the $\mu\text{g/L}$ to ng/L levels. Because of this an acute toxicity is unlikely and only really of concern in case of spills. However pharmaceuticals are made to have a specific physiological action and to resist inactivation before they have achieved their therapeutic effect. When pharmaceuticals enter the aquatic environment their mode of action can affect organisms in a similar way to how they impact humans if they share identical or alike target organs, tissues, cells or biomolecules. Unfortunately the mode of action of many drugs are not well understood. This makes it difficult to predict both how they might act and where they might occur in other organisms as well^[3]. In addition the metabolites of a compound can in some cases have higher toxicity than the compound itself^[8].

For small aquatic organisms this can have an irreversible effect even when they are exposed to sub-therapeutic doses because of their long exposure time that can last for several generations^[9]. Besides being introduced to the environment either unchanged or as metabolites the issue with pharmaceuticals in particular is their persistence and critical biological activity. Meaning that pharmaceuticals with these characteristics could have harmful effects on the environment even if they have lower production volumes. 17 α ethinylestradiol (EE2) is an example of this. EE2 is a synthetic steroid hormone in contraceptive pills that has shown great persistence and potency at 1-4 ng/L or even lower. At these concentrations there has been shown estrogenic activity in fish^[3]. Although the same drug only had minor effects on crustaceans where estrogen receptors have not been found^[10]. This supports the growing evidence that a pharmaceuticals effect is dependent on whether or not the recipient organisms have drug-target orthologs^[10].

Steroidal hormones regulate reproductive activities in a number of organisms. Only a small amount of a hormone is needed to induce drastic cellular and physiological effect, meaning that most organisms are sensitive to changes in the amount of steroidal hormones. The two basic ways a toxin to the endocrine system works is either by mimicking the hormone or by acting as a hormonal blockage. When the toxin mimic the hormone the structure of the receptor changes and initiates a response. This will either result in an increased response or activation at inappropriate times, and is what may cause feminizing of fish.

Or the toxin can act as a hormonal block by occupying the active site on the receptor and may cause the hormonal response to be blocked. This can cause masculinization in fish^[11].

2.2 PPCPs in the Arctic

As well-known pollutants like persistent organic pollutants and trace metals, PPCPs are also assumed to have a prolonged presence in northern environments due to low year round temperatures^[12]. A study done on Benzyl-penicillin showed that it indeed had a higher stability in colder temperatures. This was due to biodegradation being slowed down significantly at low temperatures, with the lowest in the study being 5°C. However, the study also mention that they did not use microbial communities adapted to the Arctic climate. These will presumably have activity and metabolic capacity that varies compared to bacteria from mid latitude environments around the freezingpoint. They also have a lower density presumably due to lower growth rates^[13].

Recent development of modern trace-analytical technology for quantification of anthropogenic pollutants at ultra-trace levels has allowed for the increasing discovery of priority pollutants in the Arctic. As of 2017 there had been identified 110 different PPCPs in Arctic samples^[4]. Lately there has been a rapid urbanization and population growth which has led to increased consumption of modern goods in the Arctic. This along with global climate change and increased tourism, resource extraction, and transportation is creating new challenges of wastewater handling^[5]. In the Arctic regions there has been observed that a lack of modern services within the water and sanitation department is considerable more common than compared to other regions^[14]. This is due to the small urban towns, that a sizable part of the arctic consist of, not having the economy to install new and improved WWTPs^[4]. Although, it is worth mentioning the vast size of the Arctic, as shown in Figure 2.1, which also includes larger cities.

Another problem in the Arctic region is that many centralized sewage and water infrastructures suffer from long-term failure because of age, defective infrastructure, harsh weather conditions, climate effect, and high costs of operation^[5]. Waste and wastewater treated in an unsatisfactory manner imposes a risk to the local environment due to the containment by various anthropogenic chemicals from commercial and household activities. This includes industrial chemicals, synthetic oil, grease, pesticides, flame-retardants, and residues of pharmaceuticals and personal care product^[5].

In Greenland there has been shown negative effects on the local ecological environment due to untreated wastewater. This led to the reduction in fertility of a benthic amphipod in comparison to the same species living in clean waters^[16]. One of the more concerning effect is the development of antibiotic resistance in the local microbial communities after being exposed to a variation of pharmaceutical residues in high concentrations^[17].



Figure 2.1: Arctic geographical coverage and the Arctic Circle demonstrating the Arctic area that the AMAP reports covers^[15]

Pharmaceuticals having a low degradation rate in form of slow microbial transformation in colder climates is not a new discovery. Already in 2004 there was a study conducted that detected surprisingly high concentrations of ibuprofen, its metabolites and caffeine in surface seawater outside Tromsø/Norway despite the strong sea currents that were thought to dilute the effluent water effectively. The sewage in Tromsø is either disposed of directly into the sea or after being processed in one of the treatment plants. Sewage treatment in one of these WWTPs consist only of mechanical filtration and not any biological treatment. In addition the hospital wastewater is discharged directly into the public sewage system without any prior treatment. To compare with samples from another region, samples were also taken from Hamburg/Germany after what was considered the equivalent of the filtration steps in Tromsø and after biological treatment. They found that the relative amounts of the compounds samples investigated had a similar pattern in Norwegian and German sewage but a very different behavior in limnic and marine waters. The two major metabolites of ibuprofen, ibu-OH and ibu-CX, was found to have significantly different concentration levels after entering the local aquatic environment. Ibu-OH was the major component in the River Elbe in Hamburg, whereas ibu-CX was the major component in the seawater in Tromsø. This support the assumption that local environmental conditions have a great impact on the degradation of PPCPs, and in this case ibuprofen^[18].

2.2.1 Potential resistance development

The release of antimicrobial substances could potentially lead to the evolution of resistance determinants developing in clinically relevant microbial pathogens^[6]. When isolating different layers of Arctic soil in the Canadian permafrost there is evidence to support this theory. The overlaying active layer showed resistance to the six different types of antibiotics tested in the study. At the same time the underlying ancient layers also showed clinical resistance to four of the antibiotics tested; one of which does not naturally occur in microorganisms^[2].

2.3 Pathways of pharmaceuticals to the environment

The main pathway of pharmaceutical to the environment is disposal via wastewater. Arguably because of their low volatility after excretion^[3]. Low volatility and generally an environmentally low mobility is a common factor for PPCPs meaning the highest concentrations of these products are expected to be closer to their respective anthropogenic source^{[3][4]}. However, volatile siloxanes have shown to be an exception and these have been found far away from their source^[19]. Nevertheless it is strongly suggested that the main source of PPCPs in the Arctic originates from direct release from waste water treatment plants (WWTPs) in addition to direct release from households, and diffuse seeping from disposal sites^{[20][17]}.

The two main ways to treat wastewater are adsorption to suspended solid and biodegradation. Acidic pharmaceuticals occurs as ions at a neutral pH and does not adsorb well to the sludge. These are therefore most often found in the dissolved phase in the wastewater. Pharmaceuticals that mainly occur in the dissolved phase seem to have biodegradation as the most important elimination process. On the other hand basic pharmaceuticals and zwitterions do show significant adsorption to the sludge. This is the case for the synthetic estrogen EE2. Treated effluent sewage water is being contaminated with pharmaceuticals not properly degraded in the sewage treatment plants (STPs) resulting in the pollutants ending up in river, lakes, estuaries and in some rare cases also groundwater and drinking water^[3].

2.4 Removal rate dependencies

Different pharmaceuticals have different removal rates because of their varied chemical properties. More surprising however is the dissimilar removal rates that have been observed for the same compound in different treatment plants due to their equipment and treatment steps in processing the wastewater. Even temperature and weather have been observed to have an impact on the elimination rates of a compound^[3].

Abiotic transformation is thought to be of more importance than biodegradation once the pharmaceuticals reaches the surface water. Hydrolysis only contributes in a minor fashion for environmentally relevant human drugs whereas

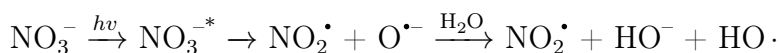
photodegradation have an important role of eliminating certain pharmaceuticals in surface waters^[3]. This is true for diclofenac^[21], and sulfamethoxazole, ofloxacin and propanol^[22]. In addition there has been observed slow photodegradation of carbamazepine and clofibrilic acid, neither of which are well eliminated in sewage treatment plants, in salt and organic-free water^[22]. How effective photodegradation is on a compound depends on its chemical properties, components in the water that can act as photosensitizers, and on solar irradiation^[3].

2.4.1 Photodegradation

Photodegradation or photolysis is the chemical bond breaking due to a product being exposed to light. Photodegradation is highly dependent on the duration of solar irradiation; intensity and spectrum of the solar irradiation; and on the presence of photosensitizer^[6]. Above the Arctic Circle there are periods during winter with no sunlight at all. For Tromsø/Norway this period lasts from November 25th to January 19th. To be able to induce photodegradation, the UV-light has to be of within certain wavelengths. In Tromsø, the period without UV-light in the range of these wavelengths exceeds the period without any sun, and lasts from October to March^[6].

In the atmosphere and surface waters photodegradation may be one of the more important removal mechanisms. This can either happen directly in the compound or indirectly via a photosensitizer. A photosensitizer is a chromophore that absorbs the light instead of the compound doing so itself. The extra energy gained from the light elevates an electron in the photosensitizer. This can be transferred to the compound as an electron, a hydrogen ion, or result in short-lived reactive oxygen species or photooxidants that can interact with the compound. Examples of this are: $\text{OH}\cdot$, $\text{NO}_3\cdot$, O_3 , and $\cdot\text{O}_2^-$. In natural waters common photosensitizer are nitrates and nitrites^[23].

Nitrate seemed to magnify the rate of phototransformation for a number of compounds investigated by a study conducted in 2002^[22]. This effect is believed to be due the formation of HO radicals during photolysis of nitrate. HO radicals can in turn react with the pollutant, enhancing its photodegradation^{[24][25]}.



2.4.2 Biotransformation

Biotransformation of a xenobiotic consist of two main phases; Phase I and Phase II. Reactions of Phase I are mainly oxidation, reduction, and hydrolysis whereas Phase II are synthetic or conjugated reactions. Many pollutants undergo both of these but some might only go through one of them depending on the compound and the environmental surroundings system. For these reactions to be able to occur efficiently good enzymatic activity is required^[26]. Pollutants may disrupt the enzymes activity and effect by: taking up the enzymes active site; inactivating the enzymes cofactor; inhibiting the enzymes itself; or by competing with

the cofactors active site^[27]. However, abiotic conditions impact the enzymatic activity as well. Temperature, pH level and the concentration of the substrate of which the enzyme binds to all contribute to the efficiency of the enzyme^[28].

2.4.3 Microbial degradation

Microbial degradation is biotransformation that takes place in different microorganisms. This occurs because a number of microorganisms are able to use xenobiotics as a source of carbon or other nutrients. Many organic xenobiotics are fully metabolized under aerobic conditions to carbon dioxide and water. This is possible if the xenobiotic metabolizes in a way that results in a material able to enter the citric acid cycle, also known as the Krebs cycle. Molecules that are essentially simple chains are easily degraded since they can enter the Krebs cycle with little modification. Aromatic compounds however, are metabolically more challenging, and the 3-ketoadipic acid pathway is generally the main pathway for the metabolism of aromatic compounds with this resulting in acetyl-CoA and succinic acid which can easily enter the Krebs cycle. The coding process for degradation of xenobiotics is often contained on the extrachromosomal DNA, the plasmid, and the chromosome^[26].

3 Discussion

There are a number of factors that contribute to the fate of a PPCP pollutant. Temperature, light, chemical properties, sea current and the different organisms present are all important components to consider when investigating how a compound breaks down and effect the local environment. This is tedious work because of the vast number of PPCPs. In addition the effect of their major metabolites have to be accounted for too. For the Arctic it is important to investigate which of these metabolites are stable in cold and dark conditions to be able to evaluate their environmental risk.

3.1 Environmental challenges of PPCPs in the Arctic

The Arctic with its generally low temperatures and dark conditions for larger parts of the year is quite optimal for preserving rather than degradation. This allows for PPCPs to accumulate in the local aquatic environment, since most of these pollutants eventually end up here due to them being disposed of via excretion and the sewage system. This can directly disturb the local ecological environment. It is unlikely to be a spontaneous effect, but the organisms living in the the aquatic ecosystems will be exposed to these pollutants for longer periods of time and even whole lifespans. This can lead to irreversible changes in the species that could potentially lead to a decrease in the populations if it the pollutant effect the reproductive system. Changes like this may happen over a longer period of time and could potentially lead to drastic changes in the population before it is understood what the actual cause is.

Tracing these changes to relatively low concentrations of a PPCP can be a difficult challenge since there are many pollutants present at the same time. Figuring out the pollutant that is causing the actual mutation in a species can be troublesome in itself, especially if the biomechanisms of the compound is somewhat unclear. This is a know problem in concern of pharmaceuticals. The detailed biochemical mechanisms are not always well understood for pharmaceutical even if the effect itself is documented and proven. Furthermore there is bound to be more than one type of PPCP existing at the same place and time, because of the increased use and therefor also disposal. Therefor elucidation of the potential risk of the combination of these compound and their metabolites are needed for a full evaluation of their environmental risk assessment. One example of the importance of the understanding of this is the potential antibiotic resistance. Organisms do have antibiotic resistance as a natural process of microbial defense but there is evidence supporting that pollution of anthropogenic antimicrobial leads to this occurring more often in clinically relevant human pathogens compared to environments where anthropogenic pollutants have yet to reach.

3.2 Degradation of PPCPs in northern climates as a potential challenge

Lately there are more and more studies that support the assumption that the degradation of PPCPs in the Arctic are significantly slower compared to warmer regions. This is, among already mentioned factors, due to the natural dilution of the compounds when entering the larger bodies of water, and the degradation that takes places in warmer regions more so than compared to the Arctic.

The concept of preserving compounds dark and cool to prolong their lifetime is well know and has been observed to also be true for PPCPs as well. This applies to environments with colder climates resulting in higher concentrations of pollutants than what is to be expected when considering normal degradation. There are multiple reasons that these concentration levels occur. The cold weather does not only work in a preservative manner itself, but also causes water to freeze decreasing the microbial activity in surface waters allowing the pollutant to accumulate. In some cases this can result in PPCPs having higher concentrations in effluent sewage water from smaller cities located at higher latitudes than compared to the effluent sewage waters from larger cities in lower latitudes.

The microbial activity is observed to be lower in colder climates but this is not necessarily true for all types of microbial communities. To be able to get a clear picture of how microbial degradation affect PPCPs there has to be conducted more studies that, not only applies the local environmental conditions to their analysis, but also uses cold adapted microbes. There are microbes in the Arctic that have adjusted to this harsh climate and are able to continue increasing in number in spite of this climate. These microbes will possibly be able to degrade PPCPs, even at temperatures close to the freezingpoint, at a higher rate than microbes that are not cold adapted. However, the microbes are still lower in

density in the Arctic. With fewer microbes to be able to degrade the pollutants they will potentially have a longer half life in the Arctic.

Not only is heat important for degrading PPCPs but also solar irradiation. Photodegradation naturally varies with the amount of light occurring, which changes with the latitude and the season. The Arctic, being on a high latitude, lacks light extensive portions of the year. During large parts of the winter season in the Arctic there is no sunlight at all. Photodegradation will therefore not be able to take place at all. Seeing as this is one of the major contributing factors to the degrading of PPCPs in surface water; this could potentially lead to an increasing concentration of PPCPs over the course of the winter. As mentioned earlier, the UV-light needs to be of high enough energy for photodegradation to happen. This extends the period of which little to no photodegradation occurs even more. On the other side, the Arctic region also experiences midnight sun during summer times. With the constant solar irradiation, photodegradation can then be more or less constant during the course of this time.

3.3 Wastewater handling as a major issue in smaller towns

The already slower degradation of PPCPs increases the importance of the handling of PPCPs in particular since the handling of wastewater in the Arctic in general is largely insufficient. When added the issue of the PPCPs being more stable in colder climates this should strongly indicate a need for continuously monitoring even with the low levels presented. If the pollutants do not break down properly these will continue to accumulate in the Arctic instead of being diluted. One of the most concerning problems is that the observed high concentrations of pollutants per person in colder regions. This can have negative effect on the local ecologically environment and even humans if they are allowed to bioaccumulate ending up in traditional food sources for Arctic indigenous people in particular, but also the more urbanized people could potentially be at risk.

Pharmaceuticals and personal care products have been used for treatment, control and prevention of a number of conditions worldwide in addition to making life in general easier for generations. With the increasing population and globalization the use of PPCPs have increased drastically as well, and subsequently have also the need for proper waste water treatment. Unfortunately what can be considered proper waste water treatment in concern of PPCPs is lacking for larger parts of the Arctic much because of their smaller settlements. Waste water treatment plants in these smaller towns do not treat the wastewater properly leading to the presence of both parent compound and active metabolites in effluent sewage water. This leads to the presence of these PPCPs in the nearby bodies of waters potentially disrupting the aquatic environment.

To decrease the amount of pollutants in the local environment the WWTPs will probably have to be improved. This seems to be one of the bigger problems at least in smaller settlements of the Arctic. If the WWTPs were highly modernized the concentrations levels of PPCPs would probably be lower but installing

this is costly and not always a viable option for smaller towns. Building a large construction like this is difficult in the rough climate of the Arctic. In addition the materials would have to be transported from a factory to these rural places and then there is the need for constant maintenance. All of these factor contribute to this being unlikely to happen in the nearest future.

4 Conclusion

In conclusion there is a lot of research still needed to understand PPCPs effects on the environment as a whole to be able to do an environmental risk assessment. Pharmaceuticals are particularly interesting due to them being synthesized to have the ability to resist degradation, so that they reach their target tissue and do their therapeutic effect. The countless modes of action and how they affect different organisms are still issues that need further elucidation, because of the many ways these pollutants can act on different organisms.

PPCPs concentration levels and how they break down in colder climates are shown to be significantly different compared to warmer climates. Two major factors stand out; the low temperatures; and less solar irradiation compared to lower latitudes. UV-light relevant for photodegradation are absent for many months in the Arctic leading little or no photodegradation, but during the summertime the opposite is true. Both the temperature and light conditions impacts the environments microbial activity and growth, which in turn is one of the probable causes that leads to PPCPs having longer half lives under these conditions.

How they affect each other and if there are any major metabolites that need to be of concern are also issues that still needs more understanding. When the understanding of the different environmental factors increases it is possible that this can begin to be used as an advantage when considering what treatment is needed, especially of the influent waters, but also for the effluent. The necessary waste water treatment needed will differ from region to region, because the stability of different PPCPs and their metabolites are going to vary with the local environmental factors. Their biochemical mechanisms, concentration levels of which they affect smaller organisms, potential metabolites, and the affect that they have on each other when in close approximating to each other, and how they degraded during the midnight sun are all potential research fields that needs further investigation.

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