The Fate of Pharmaceuticals After Wastewater Treatment

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Expanding cities are shortening the lapse between the release of treated wastewater into the environment and the uptake by water drinking facilities. Even though wastewater treatment plants usually exceed current discharge standards, the presence of unregulated pollutants in these effluents is of concern (Petrovic et al., 2003).

Unregulated contaminants, or emerging pollutants of concern (EPOCs), are defined as substances that were previously undetected or had not been considered as a risk (Daughton, 2001). The main sources of non-regulated contaminants in the environment are wastewater treatment plant effluents (Duaghton and Ternes, 1999), which are not designed to eliminate these compounds. They are present in treated wastewaters at trace levels (µg/l to ηg/l), and include personal care products, pharmaceuticals, surfactants, flame retardants, industrial chemicals, gasoline additives, and disinfection byproducts.

These contaminants do not need to be persistent in the environment to cause deleterious effects, since their high transformation and removal rates can be offset by their continuous introduction into the environment (Petrovic et al., 2003). Among the various substances that can be categorized as emerging pollutants, pharmaceutical active compounds (PhACs) are of special concern because of the volumes introduced to the environment, their endocrine disrupting activity, and a potential increase of bacterial resistance.

It is estimated that hundreds of tons of PhACs are produced and consumed in developed countries each year (Castiglioni et al., 2005, Kosjek et al., 2005, Daughton & Ternes, 1999, Tauxe et al., 2005). Most of them end up being excreted completely unchanged or only slightly transformed conjugated to polar molecules. These conjugates are often broken during sewage treatment, releasing the original PhAC, so they are constantly introduced into receiving waters (Heberer, 2002a). The following sections will describe the fate of the most characteristic PhACs during and after wastewater treatment.

PhACs in Wastewater Treatment Plant Effluents & Receiving Surface Waters

Some PhACs are easily removed and degraded during sewage treatment, mainly by adsorption and bio-degradation; however, they can still be detected at the low µg/l level in treated effluents and receiving waters. This is the case for the analgesics acetylsalicylic acid (ASA), fenofibrate, and acetaminophen.

Although ASA is easily degraded into its metabolites, which are effectively removed by secondary treatment, this analgesic has been detected at an average concentration of 0.22 µg/l in treated wastewaters (Ternes, 1998). Salicylic acid, ASA metabolite, has been detected at very low concentrations in sewage effluent and surface waters (Ternes et al., 1998; Quintana & Reemtsma, 2004).

Acetaminophen is also effectively degraded and removed by conventional sewage treatment. In Germany it was detected in less than 10 percent of sewage effluents and rivers (Ternes, 1998), and in the U.S. it was detected in only 17 percent of the affected surface waters analyzed in a National survey (Koplin et al., 2002).

Some antibiotics also exhibit high removal rates when exposed to conventional activated sludge treatment. During this process, penicillins are hydrolyzed and tetracyclines precipitate with cations (Heberer, 2002b). Amoxicillin is also removed efficiently by biological treatment (Morse and Jackson, 2004). These antibiotics are still found in receiving surface waters, however (Koplin et al., 2002).

High rates of oxic degradation for Ibuprofen during bench scale experiments resembling wastewater treatment conditions (Zweiner et al., 2003), and removals in the order of 96 to 99.9 percent during sewage treatment have been reported (Buser et al., 1999; Quintana and Reemtsma, 2004). In spite of these high removals, Ibuprofen is still detected in sewage effluents and surface waters at the µg/l level (Farre et al., 2002).

Synthetic estrogens such as 17a-ethinylestradiol (EE2) and mestranol (used as birth control drugs) are of special concern because of their potent endocrine disrupting activity. Activated sludge treatment was found to reduce influent concentrations of estrone (E1), 17-estradiol (E2), and 17-ethinylestradiol 93 percent, 93 percent, and 82 percent, respectively, but they are frequently found in wastewater treatment plant effluents at the ng/l level (Heberer, 2002a, Quanrud et al., 2004 Aguayo et al., 2004, Verstraeten et al., 2003; Koplin et al., 2002). These remaining low concentrations can still

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exhibit endocrine disrupting activity (Verstraeten et al., 2003).

Some drugs appear to degrade very little or none when treated with conventional activated sludge. That is the case for iodinated X-ray contrast media and the analgesic propyphenazone (Ternes et al., 2001).

Chemical structure seems to be a significant factor in determining removal rates. Medium polar drugs are removed on average between 60 and 90 percent (Ternes, 1998), while polar compounds exhibit lower removals during wastewater treatment, since they are less adsorbed onto activated sludge particles (Hirsch et al., 1999). Some of these polar drugs exhibit a maximum removal of only 7 to 10 percent, such as the antiepileptic carbamazepine (Ternes, 1998; Ternes et al., 2003; Heberer, 2002a; Stackelberg et al., 2004).

Not even extended retention times or tertiary treatment seems to be effective when treating this drug. Only micro-filtration followed by reverse osmosis has been reported effective in eliminating anti-epileptics from the effluents (Drewes et al., 2003b).

Another polar PhAC exhibiting low removal (17 percent) during sewage treatment is the analgesic Diclofenac. High percentages (up to 95 percent) have been recovered after treatment in traditional municipal plants (Zwiener et al., 2003, Koutsouba et al., 2003), and sometimes higher concentrations are found in the effluents because of desorption processes (Quintana and Reemtsma, 2004). Despite its poor removal during sewage treatment, diclofenac seems to be readily photodegraded (Heberer, 2002a; Buser et al., 1998).

Clofibric acid (the blood lipid regulator clofibrate polar metabolite) presents a very low to no removal under conventional sewage treatment conditions (Heberer, 2002a; Quintana & Reemstma, 2004, Koutsouba et al., 2003), and can also be found in surface waters affected by treated wastewater (Quintana & Reemstma, 2004).

Regardless of the removal efficiency of a conventional activated sludge treatment plant, it is evident that PhACs and their metabolites will be found in the effluents and receiving water bodies. Among these compounds, we have analgesics and anti-inflammatory drugs such as 4-aminoantirpryne, aminophenazone, codeine, fenoprofen, hydrocodone, indometacine, ketoprofen, ibuprofen, diclofenac, mefenamic acid, naproxen, phenazone, and propyphenazone (Ternes, 1998; Heberer, 2002b; Ternes et al., 2001, Drewes et al., 2002, Sedlak et al., 2005; Quintana & Reemtsma, 2004).

Also included are antibiotics such as macrolides (clarithromycin, dehydro-erythromycin (erythromycin metabolite), roxithromycin, and lincomycin), sulfonamides (sulfamethoxazole, sulfadimethoxine, sulfamethazine and sulfathiazole), fluoroquinolones (ofloxacin, ciprofloxacin, norfloxacin, end enrofloxacin), chloramphenicol, tylosin, and trimethoprim (Koplin et al., 2002; Heberer., 2002b; Gobel et al., 2004, Hirsch et al., 1999, Sedlak et al., 2005).

Other such compounds are beta-blockers such as atenolol, sotalol, celiprolol, metoprolol, propanolol, and bisoprolol (Ternes, 1998; Sacher et al., 1999; Ternes et al., 2003; Sedlak et al., 2005); the antiepileptic Primidone (Heberer, 2002b); the psychiatric drugs diazepam and carbamezapine; and the anti-angina drug nifedipine (Ternes et al., 2001, Ternes et al., 2003).

Blood lipid regulator compounds such as bezafibrate, gemfibrozil, fenofibric acid (fenofibrate metabolite), and clofibric acid (clofibrate metabolite) (Ternes, 1998; Ternes et al., 2003; Heberer, 2002b); the anti-diabetic drug glibenclamide (Ternes et al.,2001); the X-ray contrast media compounds diatrizoate, iopamidol, iopromide, and iomeprol (Ternes at al., 2003); and the antineoplastics (chemotherapy drugs) ifosfamide and cyclophosphamide (associated with hospital discharges) (Ternes, 1998) are all found in treated effluents at the low µg/l level, along with those listed in the preceding three paragraphs.

South Florida is no exception. Salbutamol, cimetidine, ranitidine, 1,7-dimethylxanthine, diltiazem, warfarin, dehydrodifedipine, thiabendazole, diphenhydramine, carbamezapine, and the antibiotics erythromycin, trimethroprim, ciprofloxacin, ofloxacin, sulfadiazine, sulfamethoxazole, and tetracycline have been detected at the low µg/l level in the South District Wastewater Treatment Plant effluent in the Miami-Dade area (Lietz and Meyer, 2006).

In general, wastewater treatment plants with higher retention times have a better performance in removing analgesic/anti-inflamatory drugs and lipid regulators. Tertiary treatment eliminates these drugs more efficiently than secondary treatment does. Granular activated carbon appears to be effective in removing PhACs completely, except for antibiotics (Sedlak et al., 2005), and none of the previously mentioned compounds (lipid regulators, antiepileptics, analgesics, antibiotics, and anti-inflamatories) can be detected after treating tertiary effluent with a micro-filtration/reverse osmosis combination (Drewes et al., 2003b).

PhACs in Groundwater

Indirect potable reuse through soil aquifer treatment (SAT) and bank filtration is a common practice in Europe and in some regions of the U.S. SAT consists of the application of treated wastewater into the ground (usually through infiltration from a pond) with aquifer recharge purposes. Bank filtration consists of the recharge of an aquifer with water infiltrated from a river bank before being used as a drinking water source.

These two approaches have been proved effective in reducing total organic carbon (TOC), pathogens, and disinfection byproducts (DBPs) precursors in recharged waters (Weiss et al., 2003). Adsorption to soil particles during infiltration seems to be a good barrier for non-polar compounds. This is the case for the lipid regulator bezafibrate, which

Continued on page 28

Continued from page 27
is readily adsorbed during bank filtration (Heberer, 2002a).

A period of six months of groundwater transport can completely eliminate acidic drugs, such as diclofenac, ibuprofen, ketoprofen, naproxen, fenoprofen, and gemfibrozil, from secondary effluent infiltrated using recharge basins (Drewes et al., 2002, Drewes et al., 2003a). Bank filtration has also proved to remove diclofenac efficiently through sorption (Heberer, 2002a). Even small distances (30.5m) of sub-soil transport can achieve complete removal of acidic drugs (Sedlak et al., 2005).

Synthetic and human hormones are also removed efficiently by SAT. Soil column experiments report 17b-estradiol, estriol, and testosterone removals in the order of 79 percent, 84.3 percent, and 97.5 percent, respectively, mainly due to sorption and bio-degradation (Mansell et al., 2004). These compounds exhibit low mobility in subsurface systems.

Estriol and testorone can be completely removed (<0.6 ng/l) only after 1.5m of transport through porous media; 17b-estradiol is somehow more mobile. None of these three compounds, however, is commonly detected in monitoring wells down gradient spreading operations (Mansell and Drewes, 2004).

Estrone is also efficiently removed through percolation. A minimum of 90 percent removal can be achieved by percolation ponds at a 10m depth, and complete removal has been reported down gradient infiltration operations (Verstraeten et al., 2003).

From this data, one can infer that groundwater is not significantly affected by non-polar to low-polarity compounds (e.g. estrogenic compounds and acidic drugs) because they are readily adsorbed onto sediments and subsoil particles preventing them from polluting drinking water sources; however, even drugs that are efficiently removed by SAT can be found in groundwater.

Analgesics such as diclofenac, ibuprofen, ketoprofen, phenazone, propyphenazone, and gentisic acid have been detected in groundwater samples (Sacher et al., 1999, Heberer, 2002b). The antibiotics trimethoprim, sulfadiazine, sulfadimidine, sulfamethoxazole, sulfamethazine, ronidazol, dapson, anhydro-erythromycin, roxithromycin and ciprofloxacin are partially removed by SAT (Sacher et al., 1999, Sedlak et al., 2005).

The blood lipid regulators fenofibrate, gemfibrozil, and its metabolite, clofibric acid, have been found in groundwater aquifers in Germany at the ng/l level (Heberer, 2002b). Beta-blockers are patially removed by SAT, and can also be found in groundwater samples (Sedlak et al., 2005, Sacher et al., 1999).

SAT seems to have little or no effect in the attenuation of polar PhACs. Polar compounds show low retardation and are not significantly adsorbed to soil particles leaching into groundwater. Soil column experiments have found that clofibric acid presents no significant adsorption to soil particles (Heberer, 2002a), and therefore it is frequently detected in groundwater. The anti-epileptics carbamazepine and primidone appear not be affected by SAT at any extent, since concentrations in samples obtained down-gradient recharge operations are very similar to those in the secondary effluent infiltrated even after six years of transport through the aquifer (Sacher et al., 1999, Drewes et al., 2002, Heberer et al., 2002).

X-ray contrast media easily percolates into groundwater aquifers (Sacher et al., 1999, Heberer, 2002a). Polar compounds such as clofibric acid and carbamazepine have been reported at depths ranging from 5 to 80 m at concentrations in the order of 100 to 180 ng/l (Verstraeten et al., 2003; Heberer, 2002a).

PhACs in Drinking Water

Eventually, some of the most polar and persistent PhACs can reach aquifers or surface waters used as drinking water sources, survive treatment, and go through water distribution systems.

Diatrizoate, iopromide, and iopamidol (X-ray contrast media) have been detected in

drinking water wells (Ternes et al., 2001). A study performed in the U.S. sampled raw and treated water at a drinking water treatment facility and found that caffeine, cotinine (nicotine metabolite), and the PhACs carbamazepine and dehydronifedipine (nifedipine metabolite) survived a coagulation, flocculation, activated carbon adsorption, filtration, and disinfection train, and these compounds were detected in drinking water samples at the low µg/l level (Stackelberg et al., 2004).

Analgesics such as diclofenac, ibuprofen, and phenazone, and the lipid regulator metabolite clofibric acid have been detected in drinking water samples in Germany (Heberer, 2002b). It must be pointed out that these sites extract water from aquifers recharged through bank filtration from rivers heavily loaded with wastewater treatment plant effluents, where municipal sewage can be 40 percent and 80 percent of the river flow during wet and dry season, respectively.

Especially in heavily populated areas, such as Europe, several pharmaceutical compounds are in a cycle from human application via human excretions, wastewater treatment plants, surface waters/groundwater recharge, and back to humans through drinking water (Heberer et al., 2002).

Effects

Health effects of the consumption of PhACs at low concentration levels are not fully understood (Kimura et al., 2004), and it hasn't been determined yet if levels of PhACs found in drinking water pose a human health risk (Richardson, 2003).

PhACs' effects are tested on humans before being released to the public. These studies are characterized by high doses and short terms; however, little is known of the possible effects of long-term exposure at very low dosages (e.g. drinking water).

Some research indicates that the low concentrations of PhACs and other contaminants present in drinking water are not harmful to humans from a toxicological point of view, but their presence is still not desirable as a precautionary principle (Heberer, 2002a). Others express their concern about the lifetime ingestion via drinking water of very low sub-therapeutic doses of several pharmaceuticals, which might pose a long-term risk for humans.

Not much is known, either, about the possible effects that the combination of several drugs can have in human health (Stackelberg et al., 2004). Even though drugs are present in aquatic environments at the low or sub ng/l level, there is concern that the presence of several drugs sharing a specific mode of action could lead to significant effects through additive exposures (Daughton & Ternes, 1999).

PhACs might also have an effect over environmental receptors. Drugs are designed to act over certain tissues, yet several side effects, not fully understood, might be present in non-target receptors. In the same manner, drugs that reach non-target species through wastewater discharges might have unpredictable effects (Daughton & Ternes, 1999; Gobel et al., 2004).

Also, pharmaceuticals that modulate endocrine and immune systems have a great potential of acting as endocrine disruptors (Daughton & Ternes, 1999). Antibiotics and antimicrobial agents (e.g. triclosan) are of concern because they could have direct effects over microbial populations, altering the community structure and increasing the resistance of human pathogens in the environment (Daughton & Ternes, 1999; Gobel et al., 2004; Hirsch et al., 1999).

Endocrine disrupting compounds (EDCs) are chemicals that can either mimic natural hormones or increase or decrease hormone production (Mansell et al., 2004). Compounds with estrogenic activity include a large number of natural and synthetic hormones, pharmaceuticals, pesticides, and industrial/household chemicals (Quanrud et al., 2004).

Estrogens (synthetic and natural) such as 17α-ethinylestradiol (EE2) and 17β-Estradiol (E2) have been proved to provoke feminization of some aquatic species at very low concentrations (<< 1nM) (Quanrud et al., 2004, Mansell & Drewes, 2004). Effects of human exposure to EDCs are uncertain, but some types of cancers (testicular and breast) are suspected to be product of exposure to estrogenic compounds (Conroy, et al., 2005; Quanrud et al., 2004).

Acute effects are not the only concern affecting aquatic species. The continuous introduction of these chemicals into the environment could elicit imperceptible effects that might accumulate over time, causing profound ecological changes such as adaptation or ecological succession (Daughton & Ternes, 1999).

Conclusions

It can be concluded that traditional wastewater treatment (activated sludge) does not eliminate most of the so-called "emerging pollutants" (they can be removed using advanced treatment, though). Their low concentrations and the abundance of other carbon sources prevent their complete removal. They are present in treated sewage generally at concentrations ranging from the low ng/l to the medium µg/l levels.

The same can be said about receiving waters, with the difference that several mechanisms tend to decrease these concentrations even more (e.g. biodegradation, sorption, photodegradation). Nevertheless, the continuous introduction of these chemicals in the environment makes them "persistent," regardless of their environmental half life.

Some PhACs reach drinking water supplies at trace levels, and some of these chemicals survive drinking water treatment to be introduced in potable water distribution systems. Although human exposure to PhACs has been verified by several studies, the effects of this exposure through drinking water consumption are far from being understood, and the fact that these chemicals are not present

Continued on page 30

Continued from page 29
alone makes even harder to understand their possible combined effects.

Further removal improvement of these contaminants from treated wastewater is required, particularly in cases where water is reused for aquifer recharge or released into sensitive ecosystems. In South Florida, there are several ongoing reuse projects, and many more are being considered. Whatever the intended use for the recycled water (golf course irrigation, aquifer recharge, or the Everglades Restoration Project), it is a necessity to address the issue of PhACs and EPOCs in general.

Some reuse facilities are achieving emerging pollutants removals below detection limits by using advanced oxidation processes or reverse osmosis filtration, but as long as regulations do not address their presence in treated effluents, it is expected that the use of these advanced technologies will remain relegated to certain specific reuse operations.

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