Low removal of acidic and hydrophilic pharmaceutical products by various types of municipal wastewater treatment plants

Christian Gagnon, André Lajeunesse
Science & Technology Branch, Environment Canada, Montreal, Quebec, Canada

Abstract

Pharmaceutical substances represent a risk for aquatic environments and their potential impacts on the receiving environment are poorly understood. Municipal effluents are important sources of contaminants including common pharmaceuticals like anti-inflammatory and anti-convulsive substances. The removal of pharmaceuticals, particularly those highly soluble can represent a great challenge to conventional wastewater treatment processes. Hydrophilic drugs (e.g. acidic drugs) have properties that can highly influence removal efficiencies of treatment plants. The performance of different wastewater treatment processes for the removal of specific pharmaceutical products that are expected to be poorly removed was investigated. The obtained results were compared to inherent properties of the studied substances. Clofibric acid, carbamazepine, diclofenac, ibuprofen and naproxen were largely found in physicochemical primary-treated effluents at concentrations ranging from 77 to 2384 ng/L. This treatment type showed removal yields lower than 30%. On the other hand, biological treatments with activated sludge under aerobic conditions resulted in much better removal rates (>50% for 5 of the 8 studied substances). Interestingly, this latter type of process showed evidence of selectivity with respect to the size (R²=0.7388), solubility (R²=0.6812), and partitioning (R²=0.9999) of the removed substances; the smallest and least sorbed substances seemed to be removed at better rates, while the persistent carbamazepine (392 ng/L) and diclofenac (66 ng/L) were poorly removed (<10%) after biological treatment. In the case of treatment by aerated lagoons, the most abundant substances were the highly soluble hydroxy-ibuprofen (350-3321 ng/L), followed by naproxen (42-413 ng/L) and carbamazepine (254-386 ng/L). In order to assess the impacts of all these contaminants of various properties on the environment and human health, we need to better understand the chemical and physical transformations occurring at the treatment plant and in the receiving waters.

Introduction

Pharmaceutical and personal care products (PPCPs) are introduced into the environment via a number of routes, the primary one being the discharge of treated and poorly treated wastewater to surface water.¹ The presence of these substances and their metabolites in municipal wastewaters and receiving aquatic ecosystems raises growing concerns about environmental and human health.²,³

Nowadays, certain major treatment plants are still using limited physicochemical processes that unfortunately generate low removal efficiencies for emergent contaminants such as pharmaceutical substances. Physicochemical treatment processes are renowned for their higher values of water quality parameters than are observed with biological treatments.⁴ As a result, physicochemical treatments typically present poorly improved values for key parameters like total organic carbon (TOC), biological oxygen demand (BOD) and coliforms. Besides the improved biological quality of the treated wastewater, information on the removal of chemical contaminants like the ubiquitous pharmaceutical products found especially in poorly treated wastewaters is required. The information could be used to evaluate the sources of pharmaceuticals into the receiving environment, and therefore contribute to global environmental risk assessments of discharges of effluents treated with various wastewater treatment processes.

Recent studies have clearly shown that the elimination of PPCPs in municipal sewage treatment plants (STPs) is often incomplete with efficiencies averaging 75%, but in many cases less than 20% depending on the treatment process used, the environmental temperature, light and matrix effects, and substance’s properties as well.⁵-⁷ Hence, the removal rate of acidic and hydrophilic drugs is expected to be low, due to their high water-solubility and relatively poor degradability. The group of acidic pharmaceuticals is mainly defined by the fact they possess a carboxylic acid moiety (pKₐ ~ 4) and are extractable at acid pH.⁸ Among acidic pharmaceuticals are listed the lipid regulator clofibric acid and the non-steroidal anti-inflammatory drug (NSAIDs) family.

An important consideration when assessing the environmental fate of PPCPs is that, as a specific class compounds, they generally possess characteristics that make them different than conventional industrial chemical pollutants.⁹ Owing to their hydrophilic properties and stability, PPCPs generally tend to remain in the aqueous phase and are not totally eliminated by STPs; as a consequence they and their metabolites are still frequently detected in surface waters.¹⁰-¹¹

A major factor influencing the efficiency of pollutants removal from raw sewage water is their ability to interact with solid particles, either natural (clay, sediments, microorganisms) or chemical additive mixtures to the medium (e.g., active carbon, coagulants). This action tends to facilitate the removal or biodegradation of pollutants by physicochemical (precipitation, floation) or biological (activated sludge) processes.¹² However, as reported by Carballa et al.¹³ and Loffler et al.,¹⁴ compounds with low partitioning coefficient (Kd) or low Kᵦₐ values tend to remain in the aqueous phase, which favor their mobility through the STP and in the receiving environment.

Among the studied substances (Figure 1), the heteroatom content and the chemical functionalities revealed by the hydroxyl and carboxylic acid moieties make them polar, ionic molecules with physicochemical properties that could largely explain their occurrence in surface water samples taken from sewage treatment plants.¹⁵-¹⁷ For practical reasons, acidic drugs are usually selected among pharmaceuticals on the basis of levels of use and the abundance in municipal effluents.⁸ Acidic drugs, especially analgesic/anti-inflammatory drugs such ibuprofen, diclofenac, naproxen and ketoprofen are found to be the most detected pharmaceuticals in municipal wastewater effluents.¹⁸ In addition to the previous list of substances, the persistent neutral anti-convulsive drug carbamazepine is also frequently detected in wastewater-impacted waters.¹⁹-²⁰ The reported properties (Table 1), coupled with trace quantities, create unique challenges for both removal processes and...
analytical detection. As such, the lack of information about removal efficiency of pharmaceutical residues in municipal sewage has forced the scientific community in the last decade to rapidly investigate on the capacity of existing STPs to remove these emergent contaminants. Therefore, more studies are needed to better understand the environmental fate of PPCPs following different STP processes.

In this paper, the removal efficiency for target pharmaceuticals by physicochemical and biological municipal wastewater treatment technologies is studied. The main objectives of this work were as follow: i) to report on the occurrence of selected acidic and neutral compounds detected in various treated effluent sources (aerated lagoons, physicochemical and biological plants), ii) to establish some possible correlations between their removal and key physicochemical parameters such $K_d$, log $K_{ow}$, solubility, and molecular weight.

**Material and Methods**

**Wastewater treatment**

The treatment processes investigated were of various types, from physicochemical to biological processes, as well as simple aerated lagoons. Information on visited treatment plants is given in Table 2. The investigated physicochemical wastewater treatment plant, located in Montreal, Canada, is the largest one in North America and processes 1.3 million m$^3$ of raw sewage daily (Table 2). This primary-treated wastewater results from a physical and chemical treatment (screening and suspended matter removal by the addition of flocculants (alum 10 mg/L, FeCl$_3$ 10-20 mg/L) that removes suspended materials and associated contaminants. The lightly treated effluent generally contains less than 5 mg/L of suspended solids but has relatively high coliform bacteria counts (concentrations greater than 1 million cells / 100 mL). Dissolved organic carbon (DOC) concentrations and pH values ranged from 90 to 110 mg/L and 8.1 to 8.2, respectively.

Municipal STP of Granby consists of mechanical pre-treatment (grid removal set-up and sand filtration), followed by a secondary treatment process involving the formation of aerobic activated sludge. Regarding aerated lagoons, three municipal sewage treatment plants located in the cities of Chambly, St-Basile-le-Grand and Mascouche were each visited in triplicate. These STPs are connected to a sewage system servicing about 17,000-43,000 population equivalents with a mean flow rate of 21,000 m$^3$/d. The Mascouche STP which receives mostly urban wastewaters from about 42,320 population equivalent is, in addition, directly connected to a hospital complex.

**Pharmaceutical sampling and analysis**

The PPCPs selected for the study are listed in Figure 1 alongside their respective chemical structures. Except the neutral carbamazepine, all investigated substances were acidic pharmaceuticals and their metabolites.

For the physicochemical and the biological sewage treatment plants (STPs), waters samples were taken as 24 h flow-proportional composite samples from mechanical devices. Regarding the aerated lagoons, rapid snapshot samples were taken around noon at each STP. Mean pH values for all visited STP ranged from 8.1 to 8.3. Samples of treated and, in some cases, untreated effluents (or influents) were taken three times (from spring to fall) directly at the plant and transported to the laboratory in Spartanburg™ stainless steel containers and stored in the dark at 4°C for less than 24 h until the extraction step. Prior to extraction, each wastewater sample was filtered under a nitrogen flow from the Spartanburg™ container through a 142-mm glass fiber filter (0.7 μm) and then on a 90-mm GF/F glass microfiber filter (0.7 μm) with a fritted, all-glass filtration device and Celite 545 under tab vacuum. Pharmaceutical residues were then extracted from wastewater samples following the

![Figure 1. Molecular structures of studied pharmaceutical substances.](image)

### Table 1. Properties of the studied substances: molecular weight, octanol-water coefficient, partitioning coefficient and water solubility.

<table>
<thead>
<tr>
<th>Substance</th>
<th>M.W.</th>
<th>Log $K_{ow}$</th>
<th>$K_d$ (L.kg$^{-1}$)</th>
<th>Solubility (mg.L$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibuprofen</td>
<td>206.3</td>
<td>3.8</td>
<td>10 (Joss et al. 20)</td>
<td>21 (Bui and Choi 21)</td>
</tr>
<tr>
<td>2-Hydroxy-ibuprofen</td>
<td>222.3</td>
<td>n/d</td>
<td>n/d</td>
<td>n/d</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>296.2</td>
<td>4.0</td>
<td>460 (Joss et al. 23)</td>
<td>2 (Bui and Choi 21)</td>
</tr>
<tr>
<td>Fenoprofen</td>
<td>242.3</td>
<td>4.0</td>
<td>(Brun et al. 23)</td>
<td>n/d</td>
</tr>
<tr>
<td>Ketoprofen</td>
<td>254.3</td>
<td>3.0</td>
<td>n/d</td>
<td>51 (Bui and Choi 21)</td>
</tr>
<tr>
<td>Naproxen</td>
<td>230.3</td>
<td>3.1</td>
<td>217 (Joss et al. 23)</td>
<td>16 (Kern and Dir 20)</td>
</tr>
<tr>
<td>Salicylic acid</td>
<td>138.1</td>
<td>2.2</td>
<td>(Brun et al. 23)</td>
<td>1933 (Yalkowsky et al. 20)</td>
</tr>
<tr>
<td>Clofibric acid</td>
<td>214.7</td>
<td>2.6</td>
<td>(Bui and Choi 21)</td>
<td>583 (Bui and Choi 21)</td>
</tr>
<tr>
<td>Triclosan</td>
<td>289.5</td>
<td>4.8</td>
<td>(Thompson et al. 22)</td>
<td>n/d</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>236.3</td>
<td>2.3</td>
<td>(Brun et al. 23)</td>
<td>10 (Joss et al. 23)</td>
</tr>
</tbody>
</table>

M.W., molecular weight; $K_{ow}$, octanol-water coefficient; partitioning coefficient; $K_d$, water solubility.

### Table 2. Characteristics of the visited sewage treatment plants.

<table>
<thead>
<tr>
<th>STP (Gagnon and Lajeunesse 28)</th>
<th>Treatment processes</th>
<th>Population</th>
<th>Flow rate (m$^3$/d)</th>
<th>$DBO_5$ (Kg/d)</th>
<th>DOC (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Montreal</td>
<td>Physicochemical</td>
<td>1,780,000</td>
<td>1,300,000</td>
<td>144,000</td>
<td>102</td>
</tr>
<tr>
<td>Granby</td>
<td>Activated sludge</td>
<td>44,000</td>
<td>56,000</td>
<td>6,800</td>
<td>44</td>
</tr>
<tr>
<td>St-Basile-le-Grand</td>
<td>Aerated lagoon²</td>
<td>43,112</td>
<td>25,595</td>
<td>2,715</td>
<td>n/a</td>
</tr>
<tr>
<td>Mascouche</td>
<td>Aerated lagoon³</td>
<td>42,320</td>
<td>18,836</td>
<td>2,308</td>
<td>35</td>
</tr>
<tr>
<td>Chambly</td>
<td>Aerated lagoon³</td>
<td>17,155</td>
<td>18,640</td>
<td>1,443</td>
<td>n/a</td>
</tr>
</tbody>
</table>

STPs, sewage treatment plants.
pharmaceutical substance concentrations were typically lower in biological-treated effluents (Table 3). With the exception of the metabolite 2-hydroxy-ibuprofen, the highest concentration observed was for naproxen with a maximum concentration of 637 ng/L. Relatively high concentrations (<900 ng/L) of 2-hydroxy-ibuprofen could be explained by lower removal efficiency for the metabolite compared to its parent compounds.

**Treatments using aerated lagoons**

Concentrations of pharmaceuticals measured in effluents from aerated lagoons were comparable, in several cases, to those from activated sludge (Table 3). The substances hydroxy-ibuprofen (350-3321 ng/L), ibuprofen (93-981 ng/L), naproxen (42-462 ng/L) and carbamazepine (254-386 ng/L) were the most abundant in lagoon-treated wastewaters (Table 3). The metabolite 2-hydroxy-ibuprofen appeared in relatively high concentrations in comparison to its parent molecule ibuprofen. This observation could be explained by an extended aeration stage under bacterial activity, as reported by Lishman et al. This type of increase in metabolite forms was also observed with biological treatment processes using activated sludge (Table 3).

**Results and Discussion**

**Occurrence of pharmaceutical products in treated wastewater**

**Physicochemical treatments**

The most abundant pharmaceuticals were found in physicochemical-treated effluents. Concentrations of the target pharmaceutical products in the primary-treated Montreal effluent ranged from 77 ng/L to 2384 ng/L (Table 3). Salicylic acid, 2-hydroxy-ibuprofen, ibuprofen, and naproxen were most abundant (>800 ng/L); indeed, these substances seem to resist physicochemical wastewater treatments, which are relatively ineffective in removing pharmaceuticals in general at the plant.15,29,31

**Biological treatments**

Compared to physicochemical treatments, removal of pharmaceuticals from wastewaters was calculated as ([Influent] - [Effluent]) / [Influent] x 100. Results in Figure 2 clearly depict low removal of pharmaceuticals in physicochemical-treated effluents. Best removal efficiencies were about 30% only. No significant removal was even observed for salicylic acid and carbamazepine. Based on a published database for hundreds substances, primary treatments generally remove pharmaceuticals with low efficiency (0-40%) compared to biological treatments with removal efficiencies of 50-90%. As this type of treatment is based on accelerated (forced) flocculation of matter, sorption onto suspended particles does not appear to be of relevance to these types of hydrophilic substances. Due to their polar structure (Figure 1), most PPCPs are not removed in any significant way by treatment plants. As an example, carbamazepine displays a moderated affinity for solid phase, explaining the low removal efficiency observed at the physicochemical plant (Figure 2). Another similar case

![Figure 2. Removal of pharmaceuticals from physicochemical and biologically treated wastewater effluents. SALY, salicylic acid; CLO, clofibric acid; IBU, ibuprofen; IBU-OH, 2-hydroxy-ibuprofen; NAP, naproxen; TRI, triclosan; CAR, carbamazepine; DIC, diclofenac.](https://example.com/figure2.png)

**Table 3. Concentrations of pharmaceutical and personal care products in wastewater influent (1) and effluent (2) at different sewage treatment plants.**

<table>
<thead>
<tr>
<th>STPs</th>
<th>Wastewater type</th>
<th>SALY</th>
<th>IBU</th>
<th>IBU-OH</th>
<th>NAP</th>
<th>TRI</th>
<th>CAR</th>
<th>DIC</th>
<th>CLO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Montreal (n=8)</td>
<td>1 2183±108</td>
<td>104±59</td>
<td>1369±82</td>
<td>157±141</td>
<td>346±21</td>
<td>299±19</td>
<td>87±3</td>
<td>115±5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 2384±114</td>
<td>84±35</td>
<td>1043±49</td>
<td>1059±133</td>
<td>277±36</td>
<td>232±24</td>
<td>82±4</td>
<td>77±7</td>
<td></td>
</tr>
<tr>
<td>Granby (n=9)</td>
<td>1 688±417</td>
<td>2179±232</td>
<td>1738±164</td>
<td>507±12</td>
<td>341±17</td>
<td>445±17</td>
<td>65±1</td>
<td>n/d</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 145±27</td>
<td>83±7</td>
<td>624±9</td>
<td>183±6</td>
<td>129±2</td>
<td>403±6</td>
<td>62±2</td>
<td>n/d</td>
<td></td>
</tr>
<tr>
<td>St-Basile (n=8)</td>
<td>1 75±8</td>
<td>981±92</td>
<td>3321±180</td>
<td>413±25</td>
<td>67±6</td>
<td>254±16</td>
<td>27±3</td>
<td>n/d</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 87±9</td>
<td>95±2</td>
<td>1105±43</td>
<td>462±26</td>
<td>85±18</td>
<td>386±30</td>
<td>36±2</td>
<td>n/d</td>
<td></td>
</tr>
<tr>
<td>Mascouche (n=9)</td>
<td>2 86±4</td>
<td>n/d</td>
<td>350±19</td>
<td>42±2</td>
<td>22±2</td>
<td>307±24</td>
<td>34±3</td>
<td>67±5</td>
<td></td>
</tr>
</tbody>
</table>

1Primary treatment (physicochemical, alim and FeCl₃ addition); Secondary treatment (biological, aerobic activated sludge); 3Primary treatment ( aerated lagoons). STPs, sewage treatment plants; SALY, salicylic acid; CLO, clofibric acid; IBU, ibuprofen; IBU-OH, 2-hydroxy-ibuprofen; NAP, naproxen; TRI, triclosan; CAR, carbamazepine; DIC, diclofenac.
was clofibric acid which also displays a low affinity for solid phase where the negligible sorption would be due to its dissociated form (pKa=2.84). An extreme case was ibuprofen and its metabolite hydroxyl-ibuprofen. Relatively low affinity for sorption onto particles for ibuprofen, and even practically no sorption for its metabolites, was reported for physicochemical treatments. However, among the acidic pharmaceuticals, naproxen was the most removed (29%) by this treatment type (Figure 2) and this could be explained by its sorption onto particles, a potential reduction process.

**Biological treatments**

Biological treatment with activated sludge was found to be the most efficient (>50% for 5 of the 7 detected compounds) among all treatment types investigated (Figure 2). Salicylic acid and ibuprofen were practically eliminated (>98%). High removal efficiencies (>70%) were reported for these substances as the result of a rapid degradation. Ibuprofen and naproxen as well were reported as pharmaceuticals that have high reduction (78-98%) in biological treatments. At such high removal efficiency, treatment types were reported as of little importance despite we observed in this study quite low removal for the physicochemical treatment. This non-biological treatment is more based on sorption process than degradation. High removal efficiencies observed for the antibacterial triclosan (74-98%) by biological treatments were already reported by Lishman et al. and Singer et al. Removed triclosan would be mostly (∼80%) biologically degraded while 15% of the removed fraction would be sorbed onto waste sludge. Biodegradation was thus identified as the main removal mechanism for triclosan.

Despite triclosan is very hydrophilic, more than 95% of triclosan would be removed by activated sludge treatment. While most substances were highly affected by this type of treatment, carbamazepine and diclofenac remained slightly removed (4-9%). Similar removal efficiencies were also reported by Lee et al. Extremely low degradability of carbamazepine in biological treatment plants (<10%) is typically reported in the literature (e.g., ). Interestingly, this treatment seemed to indicate selectivity with respect to the size and solubility of the removed substances (Table 1). This observation could point out certain influence of the inherent properties of the studied substances on their fate in wastewater treatment plants. Despite the reported persistence of carbamazepine and diclofenac, the smallest molecules were typically more removed than the largest ones. In this study, the size of the molecules was significantly correlated (R²=0.7388) to its removal by biological treatments (Figure 3A). While the molecular weight of the substance seems to influence its removal at biological plants, no significant relationships were observed for physicochemical plants (Figure 3A). With their low Kd values (Table 1), sorption onto sludge particles would not be significant.

The reported partitioning coefficients (Kd) were quite variable with values from less than 0.05 to 460 among the studied substances (Table 1). Great relationships (R²=0.9999), with the exception of the neutral carbamazepine, were observed between Kd values and removal efficiencies at biological treatment plants (Figure 3C). Pharmaceuticals having high affinity to particles were poorly (lower than 6%) removed by biological treatments. In the same way, the most soluble pharmaceuticals were the most degraded ones by biological treatments (R²=0.6812, Figure 3D). On the other hand, no relationships were observed in the case of physico-chemical treatments (Figure 3D). Removal at this type of treatment plants was typically low (<30%) for all studied substances, especially when compared to efficiency values at biological treatment plants (Figure 2). Their high solubility combined with their relatively low affinity for the particulate phase likely result in low removal, particularly by physicochemical treatment plants.

Treatments by aerated lagoons typically seemed to result in mitigated rates of removal efficiency for several studied substances. Despite it is practically impossible to sample the exact water mass upstream the plant (due to variable flows over long residence period, 18 to 21 days) for purpose of comparison between concentrations after and before treatment, wastewater treatment using lagoons cannot be entirely considered with respect to the resilience of all substances studied here. Although no removal efficiency rates were therefore calculated for the long residence time treatment plants, the resulting concentrations after treatment could provide some insights on their removal efficiency. These final concentrations, in some cases, were not significantly lower (Table 3) than ones in effluents of comparable size and type of plant (e.g., Granby). Removal rates could be expected to be low for substances such as ibuprofen or carbamazepine, which are either highly hydrophilic or biologically persistent. Better removal results seem to be observed for substances such as triclosan and diclofenac, which had low concentrations (<88 ng/L) in treated wastewater effluents. In fact, diclofenac was proved to be a light sensitive compound: rapid degradation of this molecule was reported in the literature after sunlight exposition in natural environment. As reported elsewhere, lagoon treatment was found as one of the best treatment process for the elimination of triclosan, a well-known antibacterial substance used in many household products.

**Conclusions**

The results of the present study clearly point out quite low removal efficiency of the hydrophilic pharmaceuticals from physicochemical treatments. Much higher removal efficiencies were observed at aerated lagoons, and even better with biological processes like activated sludge. The removal efficiency was significantly influenced by the molecular size and partitioning of the substances. Certain substances such as carbamazepine, diclofenac and hydroxy-ibuprofen typically remained persistent in the investigated treatment plants.
References


