Fluoxetine (Prozac)

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Pharmaceuticals and Personal Care Products (PPCPs):

Abstract

Pharmaceutical and Personal Care Products (PPCPs) are a diverse collection of thousands of chemical substances, including prescription drugs.1 Fluoxetine (FLX) is a commonly prescribed antidepressant (trade name – Prozac). FLX and its metabolites reach the aquatic environment via excretion after human consumption or through improper disposal of unused pharmaceuticals.2 This report builds on the existing literature of FLX and its primary metabolite, norfluoxetine, to evaluate their possible environmental health impacts at low concentrations and chronic exposure. Emphasis was placed on mechanisms that suggest the potential for interactions with other environmental chemicals or hormones.

Introduction

PPCPs are increasingly identified in aquatic systems in numerous countries.1 "Increasing populations increase the demand for Earth’s limited supply of freshwater. Thus, protecting the integrity of our water resources is one of the most essential environmental issues of the 21st century."2 FLX is an antidepressant in a class of drugs called selective serotonin reuptake inhibitors (SSRIs). FLX affects chemicals in the brain that may become unbalanced causing depression, panic, anxiety, or obsessive compulsive symptoms.3,4

FDA approved FLX in December 1987.5 In 2001, Prozac’s Patent expired; FLX generics are now common. FLX is one of the most widely used antidepressants and most prescribed active ingredients of SSRIs.6, 7, 8 In 90 countries and globally prescribed to 40 million people in 2001.9

FLX, its active metabolite, norfluoxetine (N-FLX), and other metabolites (of unknown activity) are frequently identified in water and soil samples.9

Fluoxetine (FLX)

Norfluoxetine (N-FLX)

Distribution and Biotransformation

FLX and its metabolites are continually introduced into aquatic environments and are present at detectable concentrations.10 Recent improvements in analytical methods permit the detection of FLX and N-FLX at environmentally relevant concentrations in aquatic systems.11,12

Fluoxetine and its metabolites are chemicals that reach the aquatic environment via excretion after human consumption or through improper disposal of unused pharmaceuticals.1,12

FLX and N-FLX readily sorbs into soil and sediment. FLX only partially desorbs to sludge.13,14

Fluoxetine and its metabolites are chemical contaminants that reach the aquatic environment via excretion after human consumption or the improper disposal of unused pharmaceuticals.1,12

Reports of removal in sewage treatment plants compared to the removal of human pharmaceuticals. STP influent Surface water Bivalves reduce the uptake of FLX and N-FLX by competitive inhibition for serotonin reuptake inhibitors.15

Fluoxetine absorbs to lipophilic Cross cell membranes Accumulate in tissues.

Notes:
1. Pharmaceuticals and Personal Care Products (PPCPs) - Environmental Protection Agency (EPA) 2009.
2. "Increasing populations increase the demand for Earth’s limited supply of freshwater. Thus, protecting the integrity of our water resources is one of the most essential environmental issues of the 21st century.
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Fate & Transport

Fluoxetine Human Medicine

Environmental and Ecological Effects of FLX and N-FLX

Table: Detection of FLX and N-FLX in Water Sources Globally

<table>
<thead>
<tr>
<th>Drug</th>
<th>Sample (μg/L)</th>
<th>Source</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>FLX</td>
<td>1.1-18</td>
<td>STP influent</td>
<td>Norway</td>
</tr>
<tr>
<td>FLX</td>
<td>3.1-18</td>
<td>STP influent</td>
<td>Canada</td>
</tr>
<tr>
<td>FLX</td>
<td>2.0-37</td>
<td>STP influent</td>
<td>Canada</td>
</tr>
<tr>
<td>FLX</td>
<td>0.6-6.4</td>
<td>STP influent</td>
<td>Norway</td>
</tr>
<tr>
<td>FLX</td>
<td>1.7</td>
<td>STP influent</td>
<td>South Korea</td>
</tr>
<tr>
<td>FLX</td>
<td>&lt;1.0</td>
<td>Surface water</td>
<td>South Korea</td>
</tr>
<tr>
<td>FLX</td>
<td>0.42-1.3</td>
<td>Surface water</td>
<td>Canada</td>
</tr>
<tr>
<td>FLX</td>
<td>21.4</td>
<td>Surface water</td>
<td>Spain</td>
</tr>
<tr>
<td>FLX</td>
<td>12</td>
<td>Surface water</td>
<td>USA</td>
</tr>
<tr>
<td>FLX</td>
<td>56</td>
<td>Ground water</td>
<td>USA</td>
</tr>
<tr>
<td>FLX</td>
<td>0.64</td>
<td>Drinking water</td>
<td>USA</td>
</tr>
<tr>
<td>N-FLX</td>
<td>1.84-41</td>
<td>STP influent</td>
<td>Canada</td>
</tr>
<tr>
<td>N-FLX</td>
<td>0.7-4.3</td>
<td>STP influent</td>
<td>Canada</td>
</tr>
<tr>
<td>N-FLX</td>
<td>&lt;0.54-2.4</td>
<td>STP influent</td>
<td>Norway</td>
</tr>
<tr>
<td>N-FLX</td>
<td>1.71-18</td>
<td>STP influent</td>
<td>Canada</td>
</tr>
<tr>
<td>N-FLX</td>
<td>1.2-1.3</td>
<td>Surface water</td>
<td>Canada</td>
</tr>
<tr>
<td>N-FLX</td>
<td>0.37</td>
<td>Drinking water</td>
<td>USA</td>
</tr>
</tbody>
</table>

FLX and N-FLX most commonly caused reproduction and growth effects with LOECs as low as 0.5 μg/L.14,15

Biocatalytic and Clotricic Acid on D. Magna16

Conclusion

The excessive production, use, and disposal of human antidepressants, especially SSRIs, raise concerns for potential adverse human and ecological health effects. Research shows that FLX and N-FLX can enter the environment, disperse, and persist to a greater extent than initially anticipated.14

More studies are needed to understand the mechanisms by which environmentally relevant levels of FLX and N-FLX impact biological systems. Environmental levels of FLX and N-FLX can be dramatically lowered by proper disposal. The key to accomplishing this is public awareness and education.

References

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