Pharmaceuticals in the environment

Make ideas work!

Products of transformed pharmaceuticals: formation and occurrence in the urban water cycle

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Fate of pharmaceuticals in urban water cycle

- Pharmaceuticals
- Human body
  - Human metabolism
- Waterworks
  - Chlorination, ozonation
- Bank filtration
  - Microbial processes
- Surface water
  - Phototransformation, microbial processes
- WWTPs
  - Microbial processes, ozonation
- Sewer
  - Microbial processes
- Transformation products (TPs)
- Veterinary
  - Pharmaceuticals
Incomplete removal in wastewater treatment plants (WWTPs)

source: Ternes et al., Chemosphere 2007, 66(5), 894-904.
Formation of transformation products (TPs) in WWTPs

<table>
<thead>
<tr>
<th></th>
<th>ng/L</th>
<th>ACV</th>
<th>Carboxy-ACV</th>
<th>Sum</th>
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<tbody>
<tr>
<td>influent</td>
<td>1990</td>
<td>430</td>
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<td>2420</td>
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<td>effluent</td>
<td>140</td>
<td>2380</td>
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<tr>
<td>removal</td>
<td>93%</td>
<td>-453%</td>
<td></td>
<td>none</td>
</tr>
</tbody>
</table>

Source: Prasse et al., Environ. Sci. Technol. 2011, 45(7), 2761-2769
Fate of TPs in the urban water cycle

TPs are frequently present in groundwater and drinking water.

Carboxy-Acyclovir

Source: Prasse et al., Environ. Sci. Technol. 2011, 45(7), 2761-2769
Transformation in biological processes and during ozonation

Example: transformation of Acyclovir in lab-scale experiments

- Acyclovir (ACV)
- Carboxy-ACV
- COFA

COFA
N-(4-Carbamoyl-2-imino-5-oxoimidazolidin)formamido-N-methoxyacetic acid

source: Prasse et al., Environ. Sci. & Technol., 2012, 46(4), 2169-2178
Advanced wastewater treatment via ozone and GAC

German WWTP in Hessian

primary clarifier → denitrification/nitrification → secondary clarifier → Microfilter (10 µm) → Ozonation system (diffuser, ozone generator) → Sampling sites → GAC 1 (non aerated) → GAC 2 (aerated) → Biofilter 2 (aerated) → Biofilter 1 (non aerated)

source: Knopp et al., Water Research, 2016, 100, 580–592.
Fate of acyclovir in advanced wastewater treatment

(O$_3$/DOC: 0.84 ± 0.15)

Conc. µg/L

**Acyclovir**

**Carboxy-Acyclovir**

**COFA**

mass balance

Carboxy-ACV 64 %

mass balance

(COFA) 84 %

no further removal of COFA

source: Knopp et al., Water Research, 2016, 100, 580–592.
COFA inhibited the growth of green algae: DIN 201 (72h)

Activated sludge
(diluted 1:5 with eluent)

Ozonation
(ACV, Carboxy-ACV < 0.01 %)

Acyclovir
$c_0 = 100 \text{ mg L}^{-1}$

Carboxy-Acyclovir
$c = 100 \text{ mg L}^{-1}$

COFA
$c = 80 \text{ mg L}^{-1}$

Cell number
$*10^4$/mL

- Control
- ACV
- Control
- Carboxy
- Control
- Ozonation
- COFA

*** significant difference
Tuckey, $p < 0.01$

Source: Schlüter-Vorberg et al., ES&T letters, 23, 2015, 342–346

COFA
$(E_{rC_{10}}: 14.1 \text{ mg L}^{-1})$
Carbamazepine and Oxcarbazepine

- treatment of epilepsy and bipolar disorders
- Germany (2012): 47.3 t
- treatment of epilepsy and bipolar disorders
- Germany (2012): 12.8 t

Transformation by humans and excretion of metabolites

Anti-epileptics
Carbamazepine (CBZ)
Oxcarbazepine (OXC)

CBZ  ca. 30 %

OXC  ca. 4 %

OH-CBZ  ca. 20 %
ep-CBZ  ca. 1.4 %

10OHCZB  ca. 70 %

DiOHCBZ  ca. 7 %
ca. 32 %
Metabolites from CBZ and OXC in the urban water cycle

Transformation of CBZ/OXC metabolites in biological processes

DiOHCBZ \[\rightarrow\] TP223 \[\rightarrow\] 9-CA-ADIN

10OHCBZ \[\rightarrow\] TP268 \[\rightarrow\] TP207

Occurrence of TPs in the urban water cycle

**Predicted cancerogenicity via expert system Lazar**

**Lazar Home**  [http://www.in-silico.ch/](http://www.in-silico.ch/)

<table>
<thead>
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<th>Compound</th>
<th>Single Cells</th>
<th>Multiple Cells</th>
<th>Mouse</th>
<th>Rat</th>
<th>Hamster</th>
<th>ISSCAN Canc</th>
<th>Kazius-Bursi</th>
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</tr>
</tbody>
</table>

*blew*: detected in river water and/or drinking water

*source: Kaiser et al., Environ. Poll., submitted*
Conclusions

Due to their enhanced polarities, metabolites and transformation products of pharmaceuticals are present in surface water, ground water and drinking water in appreciable concentrations up to the µg/L range.

Transformation does not mean that always a detoxification occurs. We have examples that transformation products can have appreciable (eco)toxicological effects.

Expert systems such as Lazar can be used to prioritize for an extended testing of those TPs that have the highest (eco)toxicological potential.

9-CA-ADIN: Due to its occurrence in groundwater and drinking water, a full analysis of the genotoxicity should be carried out in future.
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Thank you for your attention
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