SWITCH

Sixth Framework Programme (2002-2006)

018530 - SWITCH

Sustainable Water Management in the City of the Future

Integrated Project
Global Change and Ecosystems

Deliverable D 4.1.4

Development of a bio-physical-chemical system for removal of micro pollutants from concentrated wastewater flows

Due date of deliverable: Month 39
Actual submission date: Month 45

Start date of project: 1 February 2006 Duration: 60 months

Organisation name of lead contractor for this deliverable
Wageningen University, The Netherlands

Katarzyna Kujawa-Roeleveld, Junhua Zhang, Joost Jacobi
Wageningen University Sub-department of Environmental Technology, Wageningen,

Final Version
Reviewer: Adriaan Mels

Project co-funded by the European Commission within the Sixth Framework Programme (2002-2006)		
Dissemination Level		
PU	Public	Pu
PP	Restricted to other programme participants (including the Commission Services)	
RE	Restricted to a group specified by the consortium (including the Commission Services)	
CO	Confidential, only for members of the consortium (including the Commission Services)	

SWITCH Deliverable Briefing Note

SWITCH Document 4.1.4 entitled **Chemical- physical treatment of concentrated wastewater for removal of pharmaceuticals; Treatment configurations for concentrated streams for removal of pharmaceuticals**
Audience This document is targeted mainly at engineers, scientists and technologists. To a lesser extent it addresses policy makers, the pharmaceutical industry (awareness) and the general public.
Purpose Earlier research (deliverable 4.1.3) showed that many (excreted) pharmaceuticals in wastewaters are biodegradable. However, it also showed that for persistent and semi-persistent compounds it is inevitable to develop more effective chemical-physical treatment methods. This research investigated the potential of advanced chemical-physical treatment techniques to remove pharmaceuticals from source separated concentrated wastewater (urine, black water). Based on the results a number of possible treatment scenarios for concentrated wastewater streams was formulated to achieve a high degree of elimination of pharmaceutical compounds.
Background In the implementation of new sanitation concepts based on source separation much attention is paid to the treatment of separated wastewater streams: urine, faeces, black water, grey water, etc. for elimination of harmful constituents and the recovery of resources. As part of Theme 4 the removal of human pharmaceuticals from urine, faeces black water) and personal care products (grey water) is investigated. The treatment of concentrated streams aiming at removal of pharmaceutical compounds, will usually require a chain of various technologies. The core technology will be biological treatment, however this will have to be complemented with physical-chemical treatment processes for the removal of persistent or semi persistent compounds. It is not yet clear which of the currently available technologies is the most appropriate, especially not for source domestic wastewater streams. The majority of pharmaceuticals administered by humans are excreted with urine – approximately 70%. As urine constitutes a relatively clean wastewater stream of a very small volume it is believed it can be treated efficiently to remove pharmaceutical compounds. In this study urine – as a representative of concentrated wastewater stream containing elevated concentrations of pharmaceuticals – was collected from a nursery house/service apartment in the Netherlands. The urine was exposed to a number of chemical-physical laboratory tests: oxidation with ozone and adsorption to activated carbon, as these technologies seem to have a high potential for removal of refractory compounds. Laboratory batch tests were conducted to determine the potential and efficiency of activated carbon sorption and oxidation with ozone for the selected number of pharmaceutical compounds. These were: Acetylsalicilic acid (aspirine) (ASA), Ibufrofen (IBU), Diclofenac (DCF), Metoprolol (MTP), Carbamazepine (CBZ), Clofibric acid

(CFA), Bezafibrate (BZF), Fenofibrate (FNF). For a selection of test compounds a number of criteria were taken into account: consumption, occurrence in aquatic environment, differences in physical-chemical properties (e.g. polarity, hydrophobicity) and suspected biological degradability (persistent, biodegradable), potential eco-toxicological effects and availability of analytical methods, to mention the most important (see also D 4.1.2). An attempt has been taken hereby to represent with this selection of eight compounds a broader group of PhACs.

Potential Impact The results of the conducted tests on advanced physical-chemical treatment of urine containing elevated concentration of (selected) pharmaceuticals contributes to knowledge development and our understanding on the application of these processes in new sanitation concepts and more generally in wastewater treatment process. The scientific knowledge on this issue is still very scarce.

Issues

A list of promising treatment configurations are given for treatment of concentrated wastewater streams within source oriented sanitations concepts with a special focus on removal of pharmaceutical compounds. These are based on the laboratory research on the potential of biological treatment (deliverable 4.1.3) and advanced chemical treatment (deliverable 4.1.4) of concentrated wastewater.

Only two techniques were researched for one wastewater stream and a restricted number of pharmaceutical compounds. More research is needed, both in a batch reactor systems as well as in continuous reactor configurations.

Recommendations

- From the restricted number of ozonation and activated carbon tests with human urine containing elevated concentrations of pharmaceuticals it is concluded that both tested techniques are able to remove pharmaceutical compounds from a concentrated (waste)water streams.
- In addition to abovementioned tested techniques a larger scale to advanced physical-chemical treatment methods should be tested for (pre-treated) concentrated wastewater;
- The proposed treatment trains for source separated wastewater should be demonstrated on a larger scale and tested for their efficiency and economic feasibility.

Table of content

Summary

In the implementation of new sanitation concepts (often referred to as source separation, sustainable sanitation or decentralised sanitation) much attention is paid to the treatment of separated wastewater streams: urine, faeces, black water, grey water, etc. for elimination of harmful constituents and recovery of resources. Emerging group of compounds present in these streams are human pharmaceuticals (urine, faeces, black water) and personal care products (grey water).

The majority of pharmaceuticals administered by humans are excreted with urine – approximately 70%. As urine constitutes a relatively clean wastewater stream of a very small volume it is believed it can be treated efficiently to remove pharmaceutical compounds.
In this study urine separately collected from a nursery house/service apartment in the Netherlands was subjected to a number of tests – oxidation with ozone and adsorption to activated carbon, as these technologies seem to have a high potential for removal of refractory compounds.

Wastewater, and specifically urine, from a location like an elderly home or a hospital, contains a lot pharmaceutical residues. It is considered that urine from these kinds of locations could be stored and treated periodically with advanced physical-chemical methods to deplete pharmaceutical compounds and lower their overall emissions to the environment.

The laboratory batch tests were conducted to determine the potential and efficiency of activated carbon sorption and oxidation with ozone for the selected number of pharmaceutical compounds. These were: Acetylsalicilic acid (aspirine) (ASA), Ibufrofen (IBU), Diclofenac (DCF), Metoprolol (MTP), Carbamazepine (CBZ), Clofibric acid (CFA), Bezafibrate (BZF), Fenofibrate (FNF). For a selection of test compounds a number of criteria were taken into account: consumption, occurrence in aquatic environment, differences in physical-chemical properties (e.g. polarity, hydrophobicity) and suspected biological degradability (persistent, biodegradable), potential eco-toxicological effects and availability of analytical methods, to mention the most important (see also D 4.1.2). An attempt has been taken hereby to represent with this selection of eight compounds a broader group of PhACs. Both tested techniques have potential to remove pharmaceutical compounds from a concentrated (waste)water streams. For concentrated streams, such as human urine, optimization of processes in terms of required pre-treatment, sequence of processes and operational parameters is required.

After the obtained results have been discussed, a list of promising treatment configurations are given for treatment of concentrated wastewater streams within source oriented sanitations concepts with a special focus on removal of pharmaceutical compounds.

1 Introduction

1.1 Urine separation

The urine samplse used here described tests originated from Sleen, The Netherlands, from a nursery house/service apartment *Leveste/ De Schoel* were no-mix toilets of Gustavsberg were installed. The flush water was expected to contribute to the dilution of urine with a factor of 2 a 3. The collected urine was stored in the underground storage tanks.

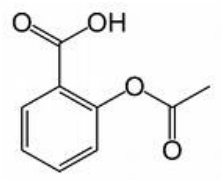
1.2 Pharmaceuticals consumption in nursery houses

The consumption of pharmaceuticals in nursery houses/hospital is generally very high. The list of all administered, by the residents of above mentioned nursery house *Leveste/ De Schoel*, pharmaceuticals and supplements is given in Table 1 in annex 1, together with the amounts taken daily, the therapeutic function a given compound and its excretion. For a new sanitation concept with objective to eliminate pharmaceutical compounds from source separated urine, only these compounds are of interest, which are partially or completely excreted with urine.

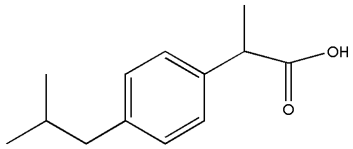
2 Pharmaceutical compounds

2.1 Selected test pharmaceuticals

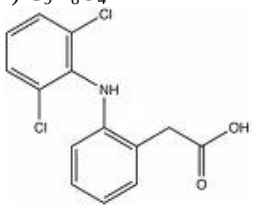
The selected compounds for the laboratory research were: Acetylsalicylic acid (aspirine) (ASA), Ibufrofen (IBU), Diclofenac (DCF), Metoprolol (MTP), Carbamazepine (CBZ), Clofibric acid (CFA), Bezafibrate (BZF), Fenofibrate (FNF). For a selection of test compounds a number of criteria were taken into account: consumption, occurrence in aquatic environment, differences in physical-chemical properties (e.g. polarity, hydrophobicity) and suspected biological degradability (persistent, biodegradable), potential eco-toxicological effects and availability of analytical methods, to mention the most important. An attempt is taken hereby to represent with this selection of eight compounds a broader group of PhACs.
This selection was decided as a continuation of earlier research (D 4.1.2 and 4.1.3). In future projects the list of tested pharmaceuticals can be further extended if necessary. The structural formulas of the selected compounds are given in Figure 2.1 while the physical-chemical-biological properties of the selected compounds are given in Table 2.1.



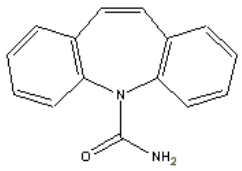
Aspirine (ASA) $C_9H_8O_4$



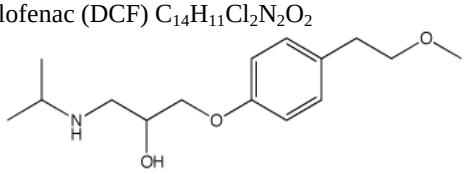
Ibuprofen (IBU) $C_{13}H_{18}O_2$



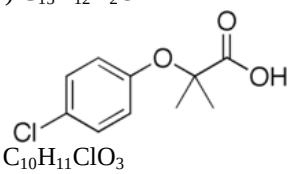
Diclofenac (DCF) $C_{14}H_{11}Cl_2N_2O_2$



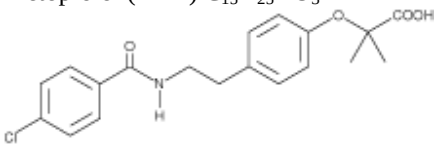
Carbamazepine (CBZ) $C_{15}H_{12}N_2O$



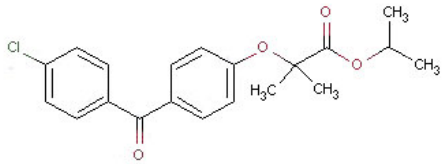
Metoprolol (MTP) $C_{15}H_{25}NO_3$



Clofibric acid (CFA) $C_{10}H_{11}ClO_3$



Bezafibrate (BZF)$C_{19}H_{20}ClNO_4$



Fenofibrate (FNF) $C_{20}H_{21}ClO_4$

Figure 2.1: Chemical and structural formulas of eight selected pharmaceutical compounds for sorption and oxidation experiments in Sleen project.

Table 2.1. Physical-chemical properties of the selected pharmaceuticals

Pharmaceutical	Therapeutic group	Log K_{ow} [2]	Hydrophilic / hydrophobic	pKa value at T = 20 °C [2]	k_{biol} for CAS (L/ gSS/d) [1]
Aspirin	anti-inflammatory	1.426	hydrophilic	3.5	n.a.
Ibuprofen	anti-inflammatory	3.481	Moderately hydrophobic	4.5-5.2	21–35
Diclofenac	anti-inflammatory	0.7-4.5 depending on pH	varying	4.15	<0.1
Metoprolol	β – blocker	1.9	hydrophilic	9.7	n.a.
Carbamazepine	anti-epileptic	2.69	Moderately hydrophobic	<1, 13.9	n.a.
Clofibric acid	lipid regulating	2.57	Moderately hydrophobic	3.0	0.3–0.8
Bezafibrate	lipid regulating	4.25	hydrophobic	3.6	2.1–3.0
Fenofibrate	lipid regulating	5.19 [3]	hydrophobic	n.a.	n.a.

[1](Joss 2006), , [2](Ternes 2006); [3] (van Beelen 2007)

3 Material and methods

3.1 Main reagents & media

The PhACs were obtained from Sigma-Aldrich (Steinheim, Germany): ASA ≥99.0% (CAS-nr: 50-78-2), BZF ≥98% (CAS-nr: 41859-67-0), CBZ (CAS-nr: 298-46-4), CFB 97% (CAS-nr: 882-09-7), DCF (diclofenac sodium salt) (CAS-nr: 15307-79-6), FNF ≥99% (CAS-nr 49562-28-9), IBU ≥98% (GC) (CAS-nr: 15687-27-1) and MTP as Metoprolol (+)-tartrate salt ≥98% (titration) (CAS-nr: 56392-17-7).
Six granular activated carbon (GAC) types were tested:

- NRS CARBON EA 0,5-1,5 is a thermally reactivated extruded carbon, especially developed for wastewater treatment and groundwater remediation. NRS CARBON EA 0,5-1,5 is a durable product with excellent adsorption properties for a range of organic compounds, like COD, colour and organic micropollutants (f.i. detergents, AOX, EOX). On condition that the exhausted carbon complies with the acceptance criteria, NRS CARBON EA 0,5-1,5 is suitable for intake by Norit Recycling Service. Following intake and quality checks the exhausted carbon is reactivated under controlled circumstances at high temperature.
- NORIT ROW 0,8 SUPRA is an extruded activated carbon, which offers superior adsorption properties in a wide range of applications such as purification of (potable) water. Its dedicated pore size distribution makes NORIT ROW 0,8 SUPRA highly suitable for the removal of taste and odour, organic micro pollutants such as pesticides, other dissolved organic substances, chlorine and ozone. Its superior hardness makes NORIT ROW 0,8 SUPRA particularly suited for thermal reactivation.
- ORGANOSORB 10-AA (DESOTEC Activated Carbon) The activated carbon ORGANOSORB 10 AA is an agglomerated carbon with an ideal porosity. This makes the carbon very suitable for decolourisation and purification of liquids.
- ORGANOSORB 11 (DESOTEC Activated Carbon) Standard acid washed coal based carbon for liquid applications.
- DARCO 12x20 (Norit) from lignite (biological source), granulated material, used in the purification of potable water and foods. It is frequently used for water purification because of its excellent adsorption capacity for taste and odour causing compounds, colours and algal toxins (more information see appendix 1).
- NORIT VAPURE 612 granular activated carbon is recommended for use in gaseous applications involving purification and separation processes. It is a premium grade product manufactured from select grades of coal. As the result of a unique, patented steam-activation process and stringent quality control, NORIT VAPURE 612 granular activated carbon offers superior adsorption properties and is recommended for removal of odors, toxic vapors, irritants, corrosive gases, and to recover solvents and hydrocarbons from various gas streams.

These subsequent types of GAC will be named further on as: GAC 0.5-1.5, GAC 0,8; GAC 10-AA, GAC 11, GAC 12×20, GAC 612 respectively.

3.2 Selection of optimal GAC type

The experiments were performed in 200 mL bottles (Figures 3.1-3.3). Two types of experiments were performed:

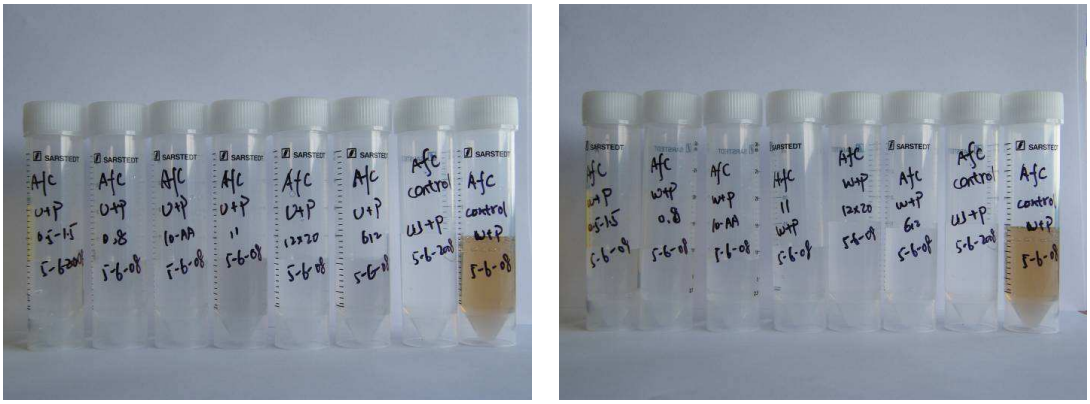
(1) Experiments with Millipore water, pharmaceuticals and GAC
To each bottle 99 mL millipore water, 1 mL pharmaceutical stock solution (1000mg/L), 1 g GAC were added. The mixture of water and activated carbon were shaken first for 24 h to get to equilibrium. After pharmaceuticals were spiked the mixtures were shaken for more 18 hours.

(2) Experiments with separately collected urine from a nursery home (preserved at 2°C), pharmaceuticals and GAC
To each bottle 99 mL urine sample, 1 mL pharmaceutical stock solution (1000mg/L), 1 g GAC were added. The mixture of water and activated carbon were shaken first for 24 h to get to equilibrium. After pharmaceuticals were spiked, the mixtures were shaken for more 18 hours.

Figure 3.1: Flasks containing urine or water, different types of GAC and the same concentrations of pharmaceuticals.

(1) urine+phar.+GAC (2) water+phar.+GAC

Figure 3.2: Urine and water samples after contact with GAC, taken after the settling took place ready to be put in centrifuge (GAC 11 and 612 being very fine type of activated carbon did not settle well)



(1) urine+phar.+GAC (2) water+phar.+GAC

Figure 3.3: Urine and water samples after contact with GAC, taken after the settling and centrifugation. All suspended GACs (GAC 11 and 612) seem to be separated. The colour of urine is eliminated (the last sample is control (urine) that was not in contact with GAC).

Table 3.1: Concentration of selected pharmaceuticals (µg/L), after contact with different types of GAC. The initial concentration in each bottle was approximately 10 mg/L for each pharmaceutical compound

	MTP	ASA	CBZ	CLF	BZF	DCF	IBU	FNF
				µg/l				
u+p 10-AA	0.2	<3	1.4	15	6.6	<1.7	<10	<0.3
u+p 0,8	<0.02	<3	0.7	45	2.7	<1.7	<10	3.8
u+p 12x20	<0.02	<3	0.3	<0.9	0.8	4.2	<10	<0.3
u+p 11	<0.02	<3	1.2	70	1.5	18	<10	7.9
u+p 0,5-1,5	0.1	<3	0.8	15	1.5	<1.7	<10	<0.3
u+p 612	0.4	22	0.9	46	3.1	25	50	123
w+p 10-AA	<0.02	<3	0.4	13	<0.06	4.3	<10	2.3
w+p 0,8	<0.02	<3	0.6	7.5	3.3	4.7	<10	2.1
w+p 12x20	<0.02	79	<0.09	34	1.2	7.8	<10	4.6
w+p 11	1.2	<3	0.9	<0.9	1.3	6.0	146	<0.3
w+p 0,5-1,5	<0.02	<3	0.2	3.2	0.9	2.4	<10	<0.3
w+p 612	<0.02	<3	<0.09	<0.9	<0.06	<1.7	<10	3.3

u+p = urine + pharmaceuticals, w+p = water + pharmaceuticals

In general the removal of all pharmaceuticals present in excess (10 mg/L each), with different types of GAC was very high. The removal efficiencies were always above 99% (the worst result for 612). The Norrit Vapure 612 performed the worst for the mixture with urine, but satisfactory for the mixture with water. Organosorb 11 performed worse than other types of GAC, for both urine and water.

Finally for the further research GAC 12x20 and GAC ROW 0.8 Supra were selected.

3.3 Sorption to granular activated carbon

The experiment to asses Freundlich isotherm for selected two types of GAC (Darko 12x20, ROW 0,8 Supra) were performed based on the procedure of Norit (Appendix 3) with source separated urine and water. Initial concentrations of all pharmaceuticals were approx. 1 mg/L each. Five increasing concentrations of GAC has been applied, viz. 0.5, 1, 2, 5, 10 g/L. The tests were performed in 200 mL flasks (serial method). The volume of liquid in the bottles was 100 mL (99 mL urine or water and 1 mL pharmaceutical stock solution).
The experiment was started by mixing a liquid medium (urine or water) with the required amount of GAC. The equilibrium was established within 24 h. After, the mixtures were spiked with pharmaceuticals and mixed again. The contact time was set to 4 h. After termination of this period, mixing stopped, GAC was allowed to settle. Subsequently the liquid samples were centrifuged, preserved in T = -20°C before sent to analysis for pharmaceutical compounds.

3.4 Ozonation of medium containing pharmaceuticals (water, urine)

Experimental set-up
From a gas bottle (4 bar) oxygen (O_2) was guided through an ozone generator. In this generator part of oxygen is converted into ozone (O_3). Via a spectrophotometer the ozonized air stream is directed to the bottom of the reaction vessel. The reactor contains a solution (either Millipore water or urine) which is spiked with 8 selected pharmaceuticals. By means of a magnet-stirrer the ozone gas bubbles are distributed throughout the reactor. The part of ozone in the reactor which does not react with organic substrate, leaves the reactor at the upper part. The spectrophotometer registers the outgoing concentration of ozone, which then is discharged to a gas -lock (filled with a solution of Sodiumthiosulfate) (Figure 3.4).

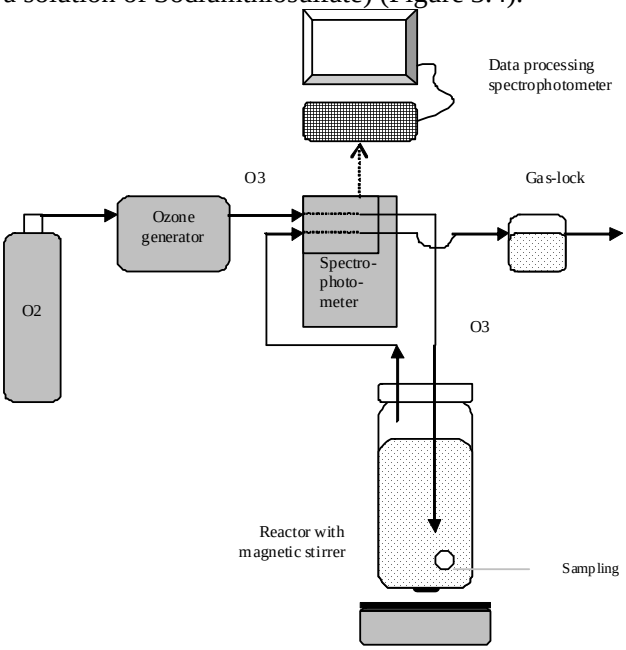


Figure 3.4: Scheme of experimental set-up (see also Figures 3.5 -3.6)

The spectrophotmeter measured the absorption (at λ = 254 nm) of ingoing and outgoing ozone. These absorption values were converted into ozone concentrations and then to total ozone consumption in the reactor.
During the experiments samples were taken by a needle from the bottom of the reactor. By adding 5 drops of chloroform the samples any biological activity was presumably stopped. Then the samples were frozen (- 20 °C) before sent to analysis at RIVM for determination of residual pharmaceuticals.

Figure 3.5: Experimental set-up for oxidation of liquid medium (water, urine) with ozone (oxygen bottle in the closet, computer for data reading, spectrophotometer for O_3 concentration, reactor, ozone generator (at the end, white box not to see), mass flow meter (also not shown).

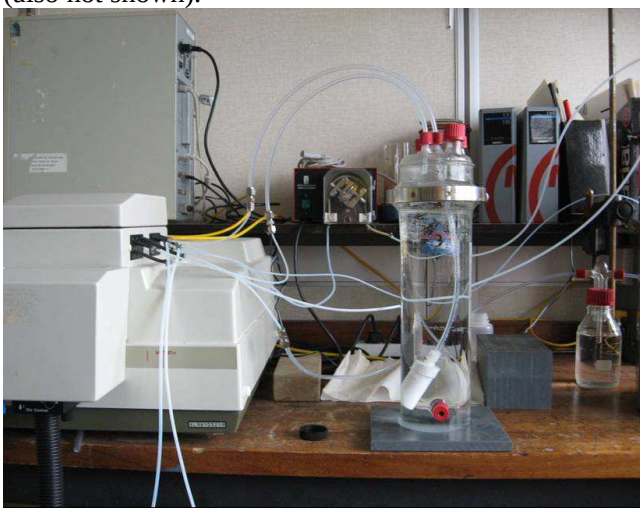


Figure 3.6: Empty reaction vessel for medium ozonation (still a magnetic stirrer need to be placed underneath for a better mixing).

Execution of the experiments
The aim of experiments was to get insight in the oxidation capacity of ozone to remove pharmaceuticals present in urine. For that purpose two tests were run:

Test 1: The ozone was brought to the reaction vessel filled with 2600 ml Millipore water and a solution of 8 selected pharmaceuticals. The initial concentration per pharmaceutical in the reactor was 1.0 mg/L.

Test 2: Ozone was discharged in the reactor filled with 2600 ml of urine originated from Sleen and a solution of 8 selected pharmaceuticals. The initial concentration of pharmaceuticals in the reactor was 1.0 mg/L each.
Both tests were performed in four runs: Run 1.1, 1.2, 2.1 and 2.2.

The reason to perform these two types of experiments was to get insight into the matrix effect of urine on the removal efficiency of pharmaceuticals. The experiment with Millipore water was expected to reveal a potential of ozone to remove pharmaceutical compounds only.

Stock solution of pharmaceuticals
To add the 8 selected pharmaceuticals to the required medium, a stock solution was first prepared made in methanol as the pharmaceuticals usually solve poorly in water. Per pharmaceutical 0.065 gram was solved in 50 ml methanol. The concentration of this stock solution is 1.3 g each pharmaceutical per L. The list below shows the exact amount of pharmaceuticals added to the 50 ml of methanol.

Table 3.2: Composition of stock solution

Pharmaceutical	**Amount (g) in 50 ml methanol**
Metoprolol	0.0665
Acetylsalicylic acid	0.0646
Carbamazepine	0.0657
Clofibric acid	0.0662
Bezafibrate	0.0667
Diclofenac	0.0650
Ibuprofen	0.0662
Fenofibrate	0.0670

For the actual experiments at the start of the test a quantity of 2.0 ml stock solution (of 1.3 g/L) was injected at the bottom of the reactor. As the volume of the reactor was 2600 ml, it resulted in the initial total concentration per pharmaceutical of 1.0 mg/L (2.0 ml * 1300 mg/2600 ml)

Ozone treatment of pharmaceuticals in Millipore Water (RUN 1.1 and 1.2)
Two runs were executed at similar conditions. The reactor was filled with 2600 ml Millipore water, to which 2.0 ml of pharmaceuticals' stock solution was added.
Calculations on ozone consumption were performed. The supply of oxygen to the ozone generator in this experiment was 80 ml O_2/min. The spectrophotometer registered the incoming and outgoing ozone in mol/min. Converted to (incoming) ozone supply per liter content of the reactor this is approximately 1,7 mg O_3/(L*min). The duration of the experiment was 4.5 hours. The samples were taken at the following time-intervals: 0, 20, 40, 60, 80, 100, 120, 180, 240 and 270 min.

Ozone treatment of pharmaceuticals present in urine (RUN 2.1 and 2.2)
Two runs are executed under similar conditions. The reactor was again filled with 2600 ml urine to which 2.0 ml stock solution was added. The concentration (per pharmaceutical) in the reactor was 1.0 mg/L.

A difference between the two runs is the concentration of organic compounds in the urine. This aspect will be further discussed in chapter 4.
For RUN 2.2 he supply of oxygen to the ozone generator was again 80 ml O_2/min. Converted to ozone supply this resulted in approximately 1,7 mg O_3/(L*min). The duration of the experiment was 8.0 hours.
In RUN 2.2 samples were taken at the following time-intervals: 0; 20; 40; 60; 80; 100; 120; 180; 240; 300; 360; 420 and 480 min.

3.5 Combined treatment of urine GAC followed by ozonation (partial simulation demonstration process in Sleen)

The laboratory test was performed with combined treatment: sorption on activated carbon followed by oxidation with ozone. Initial concentration of pharmaceuticals (before subjected to sorption) was 1 mg/L for each compound. Two types of GACs were tested: DARCO 12×20 and ROW 0,8. Concentration of GAC in bottles was: 2 g/L
Before addition of pharmaceuticals, urine sample was mixed with GAC for 24 h to establish equilibrium. Afterwards pharmaceuticals were added and the mixture was in contact for 24 h. Then the volume of urine was filtered (paper filter) and subjected to ozonation. The max concentration of ozone in the solution was approximately 53 mg/L. During ozonation 8 samples were taken for analysis of pharmaceuticals in the following time intervals: 20, 40, 60, 120, 180, 300, 420 and 600 min.
The experimental set-up for ozonation consisted basically of reaction vessel with an active volume of 2.6L, ozone generator, photo-spectrometer and computer as described earlier (§ 3.4). Unfortunately due to analytical errors the obtained results were not clear enough to be further interpreted.

3.6 Analysis of pharmaceuticals

Analyses of pharmaceuticals were performed at The National Institute for Public Health and the Environment (RIVM) Laboratory for Food and Residue analysis, European Union Community Reference Laboratory (ARO-CRL).

Materials

All chemicals and reagents were of high purity quality. Besides standard laboratory equipment the systems described below were used.

Apparatus

Liquid chromatography (LC): Waters Chromatography Acquity UPLC separation module. Column: Acquity UPLC BEH C18 1.7 µm (100 * 2.1 mm ID). Column temperature was 65°C. The LC mobile phase consisted of a mixture of 0.1 percent acetic acid (solution A) and 100% acetonitrile (solution B). The gradient used was linear, started at 10% B and progressed to 30% B in 3 minutes after which it was increased to 100% B in 6 minutes . After 9 min the mobile phase was kept for 2 min at 100% B, then the percentage B was decreased to 10 percent in 0.01 minute. The mobile phase flow was set at 0.4 ml min-1. The injection volume was 20 µl.
Mass-spectrometer (MS) analysis was carried out on a Waters-Micromass Ultima Platinum. Depending on compound the measurement was carried out in positive or negative electrospray ionisation (ESI) mode. In case of co-eluting compounds the ionisation alternates between positive and negative.

The following settings were used in positive ESI mode: capillary voltage was 3.5 kV. Cone voltage was 35 V. RF lens 1: 15, aperture: 0.1 and RF lens 2: 0.3. Source temperature was 120°C and desolvation temperature: 325°C. The cone gas flow was 116 L.h-1 and the desolvation gas flow was 701 L.h-1. LM1/HM1 resolution was 14, with ion energy: 0.8. LM2/HM2 resolution was 14.5, with ion energy: 1.0. For the collision cell the entrance was 7, with a CE gain of 2 and exit 0. Collision cell pressure 3.06e-03. See Table 3.11 for the measured MRM transitions.
In negative mode the following settings were used: capillary voltage was 1.2 kV. Cone voltage was 35 V. RF lens 1: 5, aperture: 0.5 and RF lens 2: 1.0. Source temperature was 120°C and desolvation temperature: 325°C. The cone gas flow was 116 L.h-1 and the desolvation gas flow was 701 L.h-1. LM1/HM1 resolution was 14, with ion energy: 0. LM2/HM2 resolution was 14.5, with ion energy: 1.0. Collision cell pressure 3.06e-03. For the collision cell the entrance was 10, with a CE gain of 1 and exit 0. See table 3.3 for the measured MRM (multiple reaction monitoring) transitions.

Table 3.3: Pharmaceuticals measured and their corresponding retention time, ionisation mode, MRM's, dwell time and corresponding collision energy.

Compound	Retention time (min)	Ionisation mode	MRM	Dwell time (msec)	Collision energy (V)
Acetylsalicylic acid	2.28	Negative	137.0>93.2	20	10
Bezafibrate	5.27	Positive	362.1>316.1	20	12
Carbamazepine	4.31	Positive	237.1>194.1	20	10
Clofibric acid	5.03	Negative	213.0>127.0	20	8
Diclofenac	6.03	Negative	294.0>250.0	20	8
Fenofibrate	7.66	Positive	361.1>233.0	20	10
Ibuprofen	6.23	Negative	205.0>161.1	20	5
Metoprolol	2.52	Positive	268.2>116.2	20	15

Sample clean-up

Sample clean-up of the liquids was straight forward. The samples were 10 times diluted in LC-eluens A after which they were vortexed for 10 seconds. For samples with lower concentrations the samples were acidified with 2µl 50% acetic acid. The samples were direct injected.
Sample clean-up of the soils was performed by a liquid liquid extraction. A portion of the sample (circa 0.5 gram) was weighted and five millilitres of acetonitrile was added. The samples were sonified by an ultrasonic finger for 20 seconds followed by rotating head over head for 10 minutes. After which the sample was centrifuged. The supernatant was transferred to a clean tube and evaporated under nitrogen at 55°C. The dried sample was reconstituted in one millilitre of eluens A, followed by 10 minutes ultrasonification.

Calibration curves

To correct for losses due to sample storage and to correct for signal suppression due to matrix compounds the calibration curves were prepared in reprehensive blank materials for each corresponding experiment. In figure 3.7 a chromatogram is shown of a spiked sample containing a mixture of all the pharmaceuticals. Each trace represents the measured transition for the given compounds.

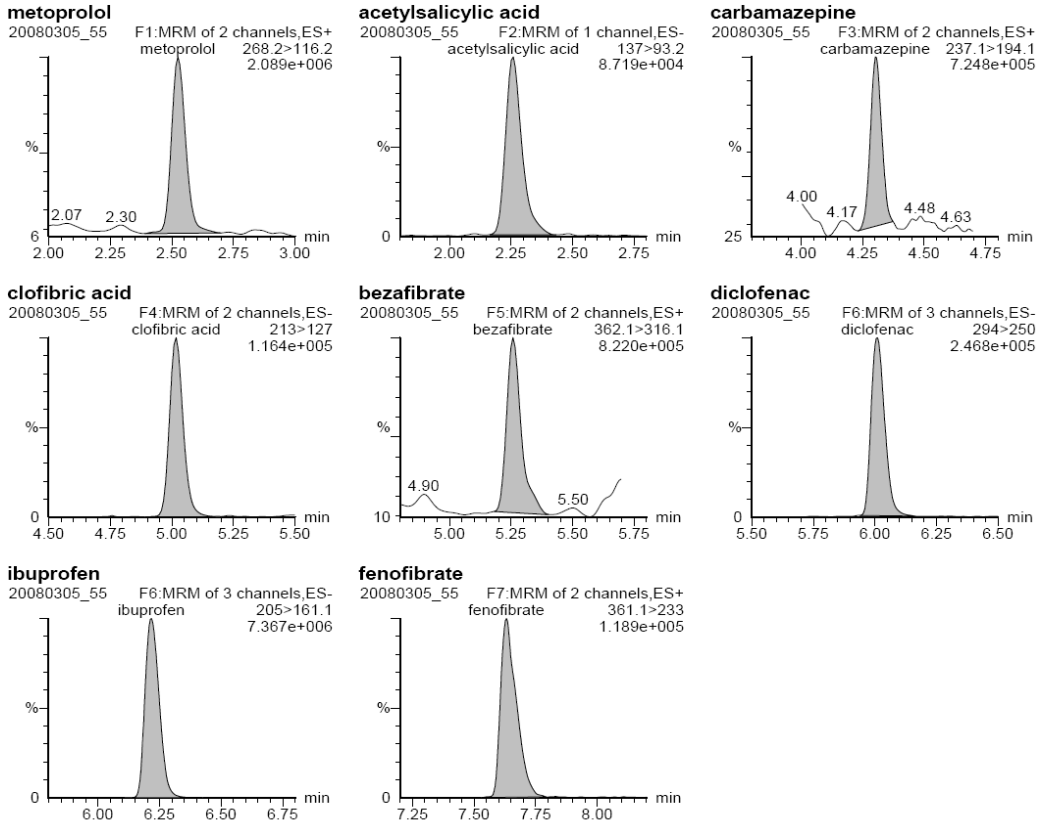


Figure 3.7: Reversed phase microbore LC-ESI MSMS profiles of an sample spiked (5 ng/ml) with a mixture of pharmaceuticals

4 Results

4.1 Urine composition in terms of macro-parameters

Few macro-parameters were determined for the used urine (Table 4.1). As it can be seen in the Table 4.1 a COD of urine was approximately 1 g/L. Undiluted urine is expected to be characterized by a COD as high as 8-10 g/L. In this term used urine seems to be 8-10 times diluted. Also concerning other parameters a similar dilution factor could be derived: for ammonia, chlorides, potassium.

Table 4.1: Some parameters measured in used urine

Parameters, unit	**Theoretical expected, undiluted urine**	**Used urine**
pH	8.8	8.71
COD_{total} , (mg/L)	8000-9600 8160[1)]	1005
N-Ammonia, mgN/L		716.4±47.7
N-total	5600 – 8800	
NO_2/NO_3-N		1.65±0.99
P-ortho P-total	 480-800	
Chloride, mgCl-/L	4757 (Grifith et al., 1976, after Wilsenach, 2006); 5600	640
Sulphate, $mgSO_4$/L	1550 (the same source as above)	245
Na		360
K	1826-2400	246

4.2 Qualitative analysis of used urine for the presence of pharmaceutical compounds

The used for the tests urine was 'screened for the presence of pharmaceuticals, other than the 8 primarily selected for laboratory research (see 2.1) based on the list of pharmaceuticals being currently administered at the location. Only the qualitative analysis was performed (Table 4.2). As it can be seen a broad spectrum of various pharmaceuticals has been consumed a nursing home.

Table 4.2: Pharmaceutical compounds quantitatively determined in the tested urine. As it can be seen there is a little overlap between previously selected 8 pharmaceuticals and pharmaceutical consumed from the location.

Pharmaceutical	**Chemical formula**
Acenocoumarol	$C_{19}H_{15}NO_6$
Acetylsal Car.	$C_7H_6O_3$
Ascal cardio Brisp	$C_7H_6O_3$
Atenolol	$C_{14}H_{22}N_2O_3$
Bisoprol fum. merc	$C_{18}H_{31}NO_4$

Carbasalaat ca. card.	$C_7H_6O_3$
Cetirizine dih	$C_{21}H_{25}ClN_2O_3$
Chloortalidon RP	$C_{14}H_{11}ClN_2O_4S$
Citolapram	$C_{20}H_{21}FN_2O$
Efexor XR	$C_{17}H_{27}NO_2$
Enalapril maleaat	$C_{20}H_{28}N_2O_5$
Exelon	$C_{14}H_{22}N_2O_2$
Furosemide	$C_{12}H_{11}ClN_2O_5S$
Hydrochloorthiazide	$C_7H_8ClN_3O_4S_2$
Isosorbide din. Ret.	$C_6H_{10}O_4$
Levomepromazine	$C_{19}H_{24}N_2OS$
Metoprolol ret	$C_{15}H_{25}NO_3$
Nitrazepam	$C_{15}H_{11}N_3O_3$
Omeprazol	$C_{17}H_{19}N_3O_3S$
Oxazepam	$C_{15}H_{11}ClN_2O_2$
Paracetamol	$C_8H_9NO_2$
Perindopr.tert.-Bu	$C_{17}H_{28}N_2O_5$
Temazepam	$C_{16}H_{13}ClN_2O_2$
Tildiem	$C_{22}H_{26}N_2O_4S$
Tolbutamide	$C_{12}H_{18}N_2O_3S$
Tramadol HCL	$C_{16}H_{25}NO_2$

4.3 Preliminary experiments ozonation of urine

The objective of this experiment was to test the ozonation set-up. A urine sample was subjected to oxidation with ozone. The O_2 flowrate was established at 80 mL/L, resulting in O_3 concentration of 0.028 mg/L. During this preliminary test COD of urine was determined in samples taken in time intervals and pH (Figure 4.1)

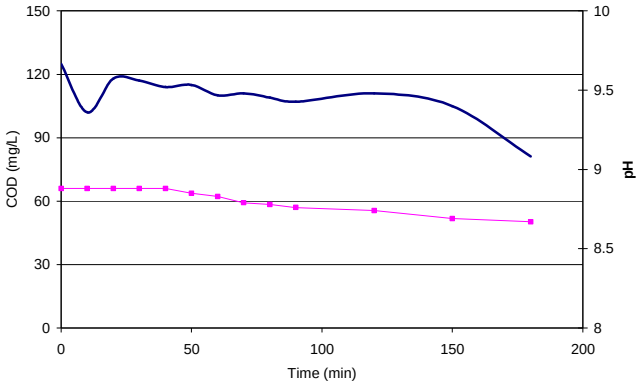


Figure 4.1: Oxidation of diluted urine from Meppel with ozone measured by depletion of COD (solid line)

Slight reduction of COD observed (35% in 3 hours) could be because of the low oxidation capacity of the used set-up and/or the nature of the remained COD in the old urine sample.

4.4 Ozone treatment of spiked Millipore Water

RUN 1.1

The results of RUN 1.1, in which the 8 selected pharmaceutical compounds have been solved in Millipore water at an initial concentration of 1 mg/L, are shown in Figure 4.2 and 4.3. Of the 8 represented pharmaceuticals it is noticeable that clofibric acid and ibuprofen take the longest before they are totally removed (respectively 420 and 480 minutes). The remaining pharmaceuticals are oxidised by ozone in an earlier stage. Acetylsalicylic acid is removed entirely after 250 minutes. Metoprolol, bezafibrate and fenofibrate are oxidized after 120 minutes. For the most persistent compounds, in traditional biological treatment, carbamazepine and diclofenac it takes only 40 minutes for their significant reduction (99.98 and 99.3 respectively).

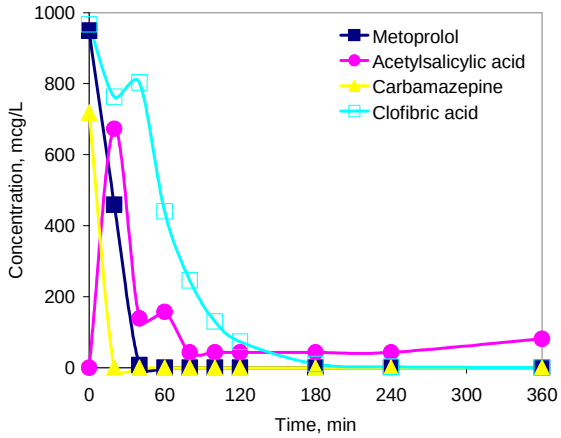


Figure 4.2: Depletion of original pharmaceutical compounds (metoprolol, acetyl salicylic acid, carbamazepine and clofibric acid) in Millipore water subjected to oxidation with ozone in RUN 1.1.

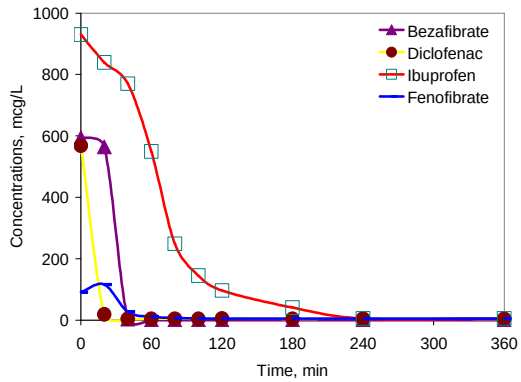


Figure 4.3: Depletion of original pharmaceutical compounds (bezafibrate, diclofenac, ibuprofen and fenofibrate) in Millipore water subjected to oxidation with ozone in RUN 1.1.

RUN 1.2

The results of RUN 1.2, in which Millipore water was again spiked with the selected 8 pharmaceuticals at an initial concentration of 1 mg/L are shown in Figure 4.4 and 4.5. Data from fenofibrate in this run is lacking because of an analytical error. Of the 7 represented pharmaceuticals it is notable that acetylsalicylic acid is hardly decreasing in time. Also in the previous run (RUN 1.1) acetylsalicylic acid was exposing irregular pattern. This could be also because of analytical difficulties to analyse this specific compound). The remaining pharmaceuticals are, however, well oxidised by ozone. Carbamazepine and diclofenac were again very quickly oxidised with ozone, already within first 20 minutes of the test (99 and 96% reduction). Also metoprolol and bezafibrate were quickly removed (after 40 minutes 98 and 95% respectively were reduced). After 180 minutes clofibric acid and ibuprofen are also far removed.

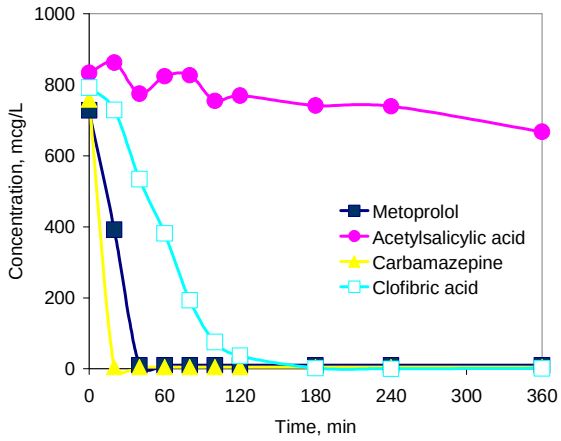


Figure 4.4: Depletion of original pharmaceutical compounds (metoprolol, acetylsalicylic acid, carbamazepine, clofibric acid) in Millipore water subjected to oxidation with ozone in RUN 1.2.

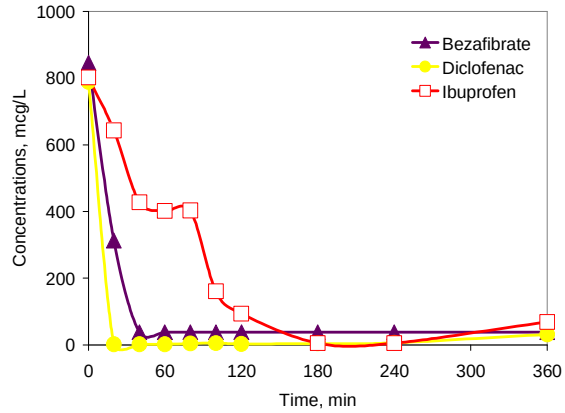


Figure 4.5: Depletion of original pharmaceutical compounds (bezafibrate, diclofenac, ibuprofen) in Millipore water subjected to oxidation with ozone in RUN 1.2.

Ozone consumption during the tests

In Figure 4.6 the data of the spectrophotometer revealing ozone consumption of RUN 1.2 were processed.

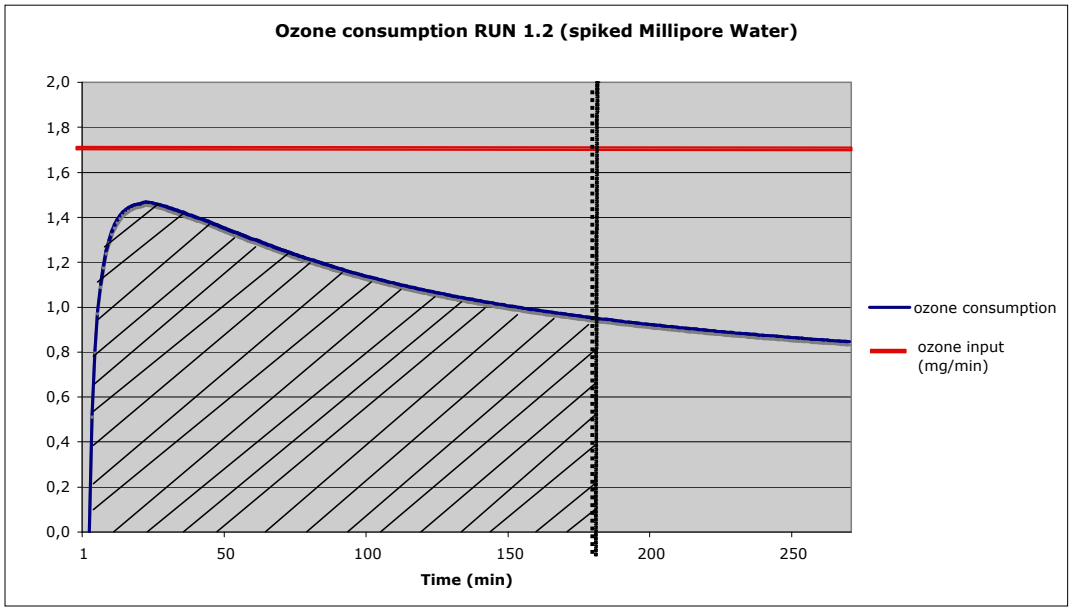


Figure 4.6: Ozone input (upper line) and ozone consumption (curve) during RUN 1.2 (spiked Millipore Water)

After 180 minutes 6 of the 7 analysed pharmaceuticals (only not Acetylsalicylic acid) are entirely removed by ozone. The marked surface in Figure 4.6 represents the total amount of ozone consumed after this 180 minutes period. The marked surface corresponds with 203 mg O_3/L. The concentration of each pharmaceutical at the beginning of the experiments is 1 mg/L. This means for the total removal of the 6 mentioned pharmaceuticals (6 x 1 mg/L, 203 mg O_3/L was needed in situation when there is any matrix disturbance. Simplifying, on average 34 mg O_3 was needed to oxidise 1 mg of given pharmaceutical.
Of the total amount of 306 mg/L of incoming ozone, 103 mg O_3 (306-203) was not used for the oxidation process and left the reactor.

4.5 Ozone treatment of spiked urine (RUN 2.1)

RUN 2.1
The results of RUN 2.1, in which urine was spiked with 8 pharmaceuticals at an initial concentration of 1 mg/L of each, are shown in Figure 4.7 and 4.8. All 8 pharmaceuticals were reduced at varying degree over a time period of 600 minutes. This reduction was significantly slower and lower than in the test with Millipore water. The following reduction degrees were measured: 22 % (clofibric acid), 25% (bezafibrate), 32% (metoprolol), 42% (ibuprofen), 43% (carbamazepine), 65% (diclofenac), 88% (acetylsalicylic acid) and 99% (fenofibrate).
(Trace) organic compounds, with concentration ranging from mg/L to µg/L are ozone-consumed substances in urine. This could be the reason that a longer reaction time and a higher total ozone supply are necessary for the removal of the pharmaceuticals in a more complex matrix of urine. This suggests that for efficient process performance urine could be first pre-treated to remove a major fraction of lowering the ozonation efficiency organic matter. The possible processes could be for instance a pre-aeration or filtration on a (coarse) granular activated carbon.

This complex matrix of urine could be also the reason of insufficient extraction of the compounds revealing in lower than expected initial concentration of the compounds (at t=0, each pharmaceutical compound should be around 1000 µg/L) and irregular pattern of the depletion curves.

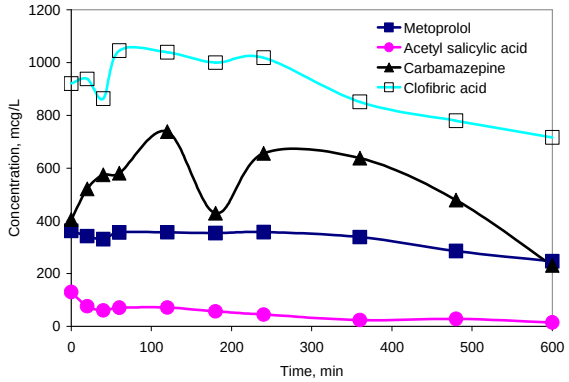


Figure 4.7: Depletion of original pharmaceutical compounds (metoprolol, acetylsalicylic acid, carbamazepine, clofibric acid) in spiked Sleen urine subjected to oxidation with ozone in RUN 2.1

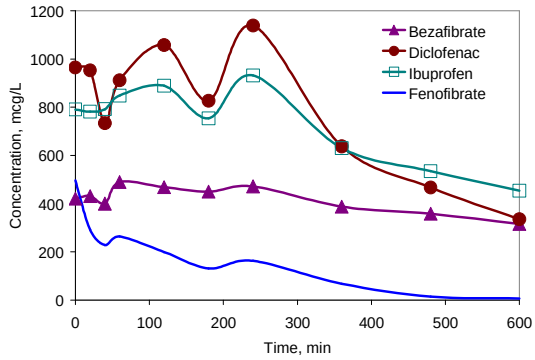


Figure 4.8: Depletion of original pharmaceutical compounds (bezafibrate, diclofenac, ibuprofen, fenofibrate) in spiked Sleen urine subjected to oxidation with ozone in RUN 2.1.

RUN 2.2

The results of RUN 2, in which the 8 pharmaceuticals were spiked to urine with a concentration of 1 mg/L, are shown in Figure 4.9 and 4.10. Besides from fenofibrate (Figure 4.7) no significant decrease of the concentration of pharmaceuticals in time was observed. The difference between RUN 2.1 and RUN 2.2 can be explained by the urine characteristics used for this test. Urine used in RUN 2.2 was much more concentrated that that one used in RUN 2.1, as it concerned last available sample containing elevated amounts of suspended material. This might be the reason that the detection of the pharmaceuticals during the analyses was quite difficult and their oxidation was poor as other organic compounds were utilizing O_3. These results suggest that to remove pharmaceutical compounds from pure urine much higher O_3 dosages should be used or the urine should be first pre-treated. Another option could be implementation of advanced oxidation, in which more oxidation techniques are combined in one process. This however could not be validated within these tests.

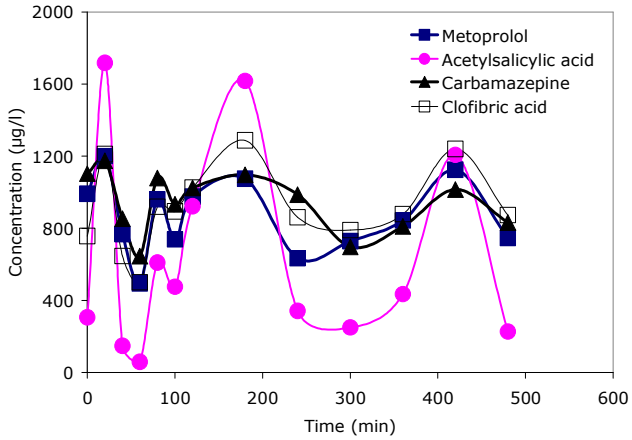


Figure 4.9: Depletion of original pharmaceutical compounds (metoprolol, acetylsalicylic acid, carbamazepine, clofibric acid) in spiked Sleen urine (more concentrated than in RUN 2.1 regarding organic matter content) subjected to oxidation with ozone in RUN 2.2.

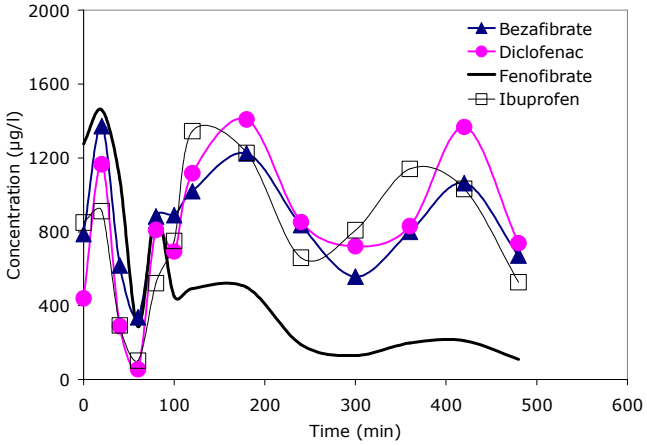


Figure 4.10: Depletion of original pharmaceutical compounds (bezafibrate, diclofenac, ibuprofen, fenofibrate) in spiked urine ((more concentrated than in RUN 2.1 regarding organic matter content) subjected to oxidation with ozone in RUN 2.2.

Ozone consumption during RUN 2.2

In Figure 4.11 the data from the spectrophotometer of RUN 2.2 is processed. The upper line reflects ozone supply and the curve ozone consumption in the reactor during the experiment. As it can be seen ozone consumption in that test was of 100% of the total input. This was probably caused by a higher concentration of organic compounds in the urine used causing consumption of all available ozone.

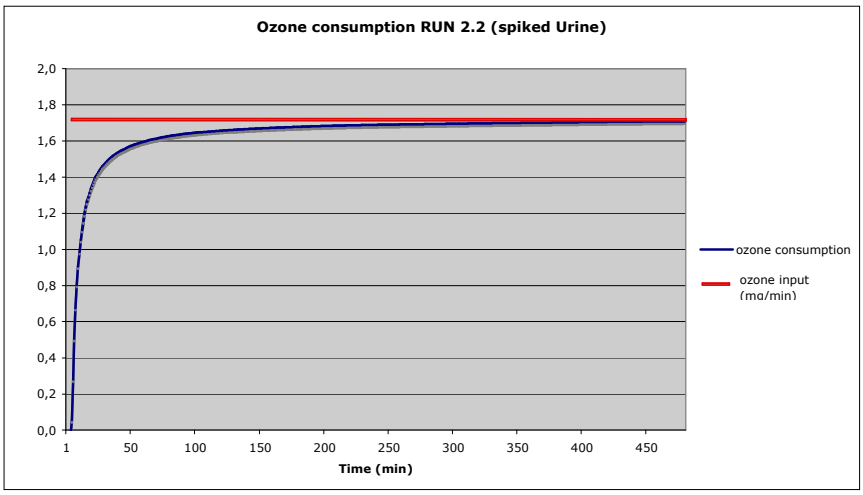


Figure 4.11 Ozone input and ozone consumption during RUN 2.2 (spiked urine)

4.6 GAC treatment of spiked urine

In Figures 4.12-4.15 adsorption of pharmaceuticals in function of a GAC dose is shown. Two granular activated carbon types were used in this research: DARCO 12x20 and SUPRA 0.8. The initial concentration of pharmaceuticals was approximately 1 mg/L. As the sorption took place immediately, rarely this initial concentration could be revealed from the first measurement. From Figures it can be seen that at the concentration of DARCO 12x20 GAC type of 2 g/L, all pharmaceuticals except clofibric acid are absorbed from a spiked urine solution. For metoprolol, acetylsalicylic acid and fenofibrate this was even less (around 0.5 g GAC/L). Clofibric acid required somewhat higher dose of GAC. For GAC DARCO 12x20 on average 250 mg GAC (2000mg/L/(8* 1 mg/L) was needed to absorb 1 mg of pharmaceutical.

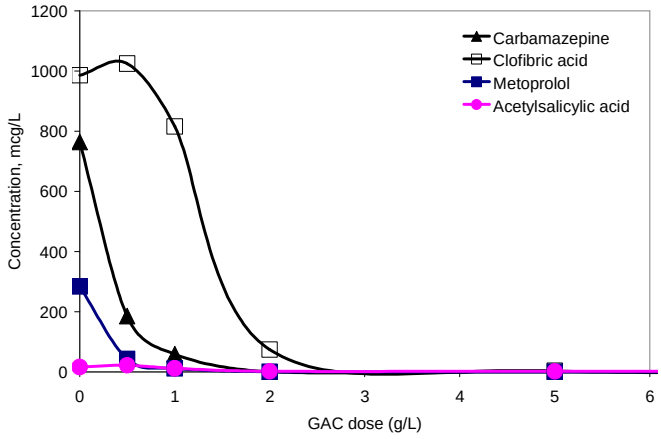


Figure 4.12: Sorption of pharmaceutical compounds (metoprolol, acetylsalicylic acid, carbamazepine, clofibric acid), shown as depletion of a given compound from a liquid phase, from spiked Sleen urine onto granular activated carbon DARCO 12x20 as a function of GAC dose.

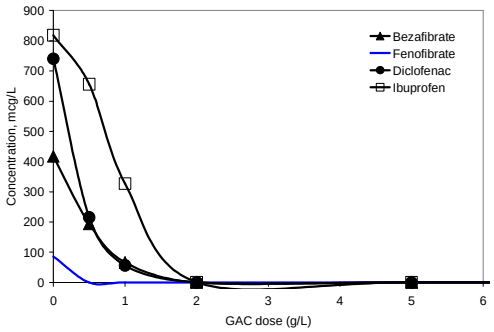


Figure 4.13: Sorption of pharmaceutical compounds (bezafibrate, diclofenac, ibuprofen, fenofibrate), shown as depletion of a given compound from a liquid phase, from spiked urine onto granular activated carbon DARCO 12x20 as a function of GAC dose.

For SUPRA 0.8 similar results were obtained. Majority of pharmaceuticals at initial concentration of 1 mg/L 'disappeared' from the liquid phase already at GAC dose of 2 or less g/L. Exception was again clofibric acid (more than 5 g/L) and ibuprofen (> 4 g/L).

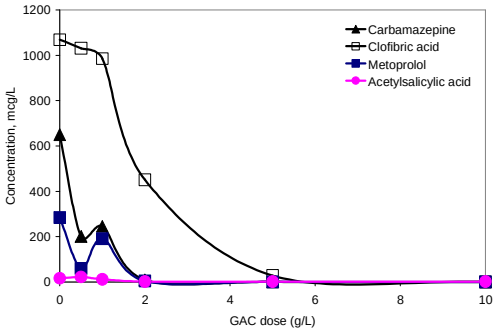


Figure 4.14: Sorption of pharmaceutical compounds (metoprolol, acetylsalicylic acid, carbamazepine, clofibric acid) shown as depletion of a given compound from a liquid phase, from spiked Sleen urine onto granular activated carbon SUPRA 0.8 as a function of the GAC dose.

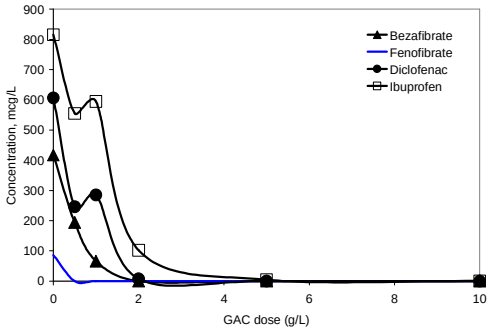


Figure 4.15: Sorption of pharmaceutical compounds (bezafibrate, diclofenac, ibuprofen, fenofibrate), shown as depletion of a given compound from a liquid phase, from spiked Sleen urine onto granular activated carbon SUPRA 0.8 as a function of the GAC dose.

In addition sorption tests were performed with two types of GAC (DARCO 12x20 and SUPRA 0.8) and Millipore water containing pharmaceuticals at the initial concentration of 1 mm/L each. The results are shown in Figure 4.16. The patterns of compounds depletion are quite similar, although the

considered compounds 'disappear' from the liquid phase at a lower GAC dose. The absence of other organic matter competing for available adsorption sites, seems to have a positive effect on the removal of more polar compounds such as clofibric acid and ibuprofen.

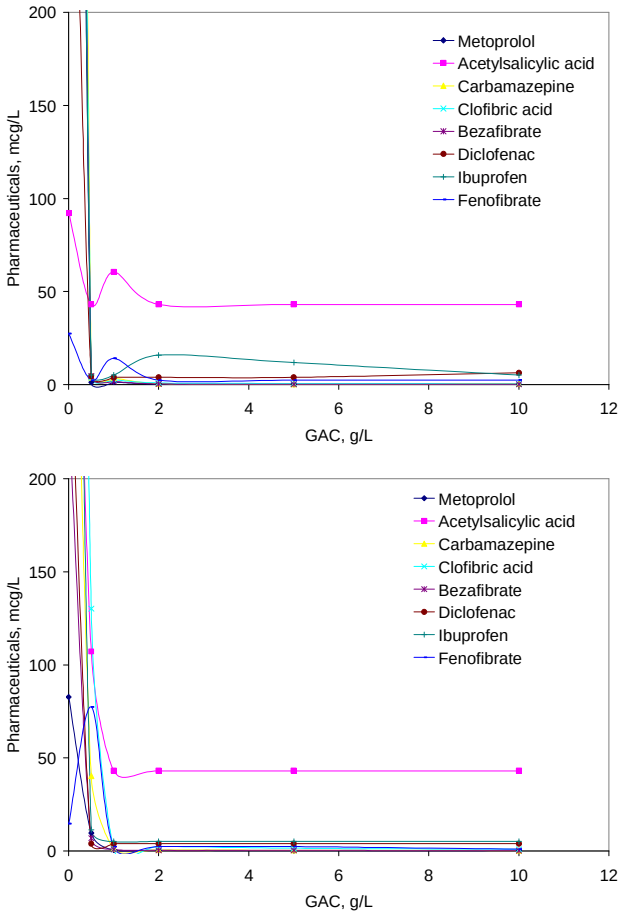


Figure 4.16: Sorption of all pharmaceutical compounds, shown as depletion of a given compound from a liquid phase, from spiked Millipore water urine onto two types of granular activated carbon: DARCO 12x20 (above) and SUPRA 0.8 (below) as a function of the GAC dose.

5. Discussion and Conclusions

The eight selected pharmaceuticals: acetylsalicylic acid (aspirine) (ASA), ibufrofen (IBU), diclofenac (DCF), metoprolol (MTP), carbamazepine (CBZ), clofibric acid (CFA), bezafibrate (BZF), fenofibrate (FNF)are all potentially well oxidized by ozone. Presence of, other than pharmaceuticals, organic compounds in treated matrix slowed down or even inhibited process of oxidation of most of pharmaceuticals at applied low O_3 dose. An ozone input in the ozonation tests described in this report was 1.7 mg/L/min. (Nguyen) in their tests on ozonation of elevated concentrations of a cocktail of pharmaceuticals (60 mg/L level) dissolved in a synthetic urine applied O_3 input of 10 mg/L/min. From the investigated PhACs, 6 PhACs were sufficiently degraded after 2h by using the selective oxidant alone at a mentioned dosage, some pharmaceuticals were only removed partially.

Various organic compounds that are present in urine matrix seem to have significant effects on the reactions. To lower the matrix effect and optimise ozonation a pre-treatment (e.g. biological, filtration) could be considered. The effect of applying combined oxidation techniques (advanced oxidation processes, AOP) on enhancement of oxidation of pharmaceuticals was not investigated in this study.
For biologically treated wastewater with dissolved organic carbon (DOC) between 8 and 23 mgDOC/L, an ozone dose of 2 to 10 mgO_3/L should be sufficient to remove majority of pharmaceuticals to 90-99% (Huber 2003) (Ternes 2003). From recent investigations with urine, it was concluded that complete oxidation of a representative set of micropollutants including pharmaceuticals and synthetic hormones may be achieved. Despite the quenching of oxidants by the organic matrix in urine, it was shown that all the tested compounds could be transformed completely. At an ozone dose of 1.1 gO_3/l, fast-reacting compounds such as ethinylestradiol were completely removed, while removal of more recalcitrant compound such as ibuprofen was 80% (Pronk 2006). Analysis of the results showed that oxidation took place directly by ozone as well as by OH radicals. Considering the high reactivity of the OH radicals with most organic micropollutants, ozonation can be regarded as a suitable method for removing a wide range of micropollutants from urine.

With respect to the analyses and detection of pharmaceuticals we can assume that the higher the concentration of organic compound (in urine), the more difficult it is to get accurate results and better extraction techniques are needed.
Sorption of pharmaceuticals on granular activated carbon (GAC) occurred for all tested pharmaceuticals. For more polar compounds such as clofibric acid a higher dosis of GAC was required.
Both tested techniques, activated carbon sorption and ozonation, are appropriate to remove pharmaceutical compounds from various water matrixes. For economical reasons the sequence of the processes and implementation of pre-treatment techniques should be considered for more concentrated wastewater streams such as urine or black water.

6 Treatment configurations for concentrated wastewater streams to remove pharmaceuticals

6.1 Black water

Black water (feaces, urine, flush water), especially when collected with a minimum amount of flush water, constitutes a concentrated medium in terms of organic material, solids, nutrients and pharmaceuticals. Organic material can be removed and converted to biogas (energy carrier) by means of anaerobic digestion. As anaerobic digestion is not efficient towards removal of nutrients and micro-pollutants an additional step has to follow. In simplified application the content of the digestors (sludge, effluent) could be used in agriculture. The caution has to be taken however as both media are not stabilised. The fate of pharmaceuticals 'on the fields' and its effects on the crops is not completely clear yet. Most probably sorption and in the course of time degradation of many pharmaceuticals would take place.
In order to polish the anaerobic effluent an aerobic step could be added in form of:

- suspended activated sludge;
- suspended activated sludge with membrane filtration (MBR);
- fixed activated sludge – biofilm (trickling filter, rotating biological contactor (RBC), submerged filter, downflow hanging sponge (DHS);
- natural and semi-natural systems (facultative and maturation ponds, (constructed) wetland systems, aquatic plants).

In all of these systems removal of nutrients can be accomplished and further removal of organic material. Also further degradation of pharmaceuticals will take place; the degree will depend on the system used and process conditions.
The complete removal of all pharmaceutical compounds cannot be assured in aerobic treatment systems. If the objective is to eliminate the pharmaceuticals compounds to a low level, only advanced physical-chemical techniques can assure it. In order to optimise efficiency of these systems one has to take sure that the influent has a very good quality, especially in terms of organic material and suspended material (as low as possible).
Advanced physical techniques, which could be potentially applied and good results have been attained so far are:

- oxidation techniques (ozone, advanced oxidation processes: combinations of O_3, UV, H_2O_2, TiO_2);
- sorption on activated carbon, and
- tight filtrations: nanofiltration and reverse osmosis.

As much experience have been gained already with above mentioned techniques in production of drinking water, their application in wastewater treatment is quite limited. Very little experience, if any, has been gained with application of advanced physical-chemical techniques for treated black water in order to remove pharmaceutical compounds.
A general scheme for a recommended treatment of source separated black water has been presented schematically in Figure 6.1.

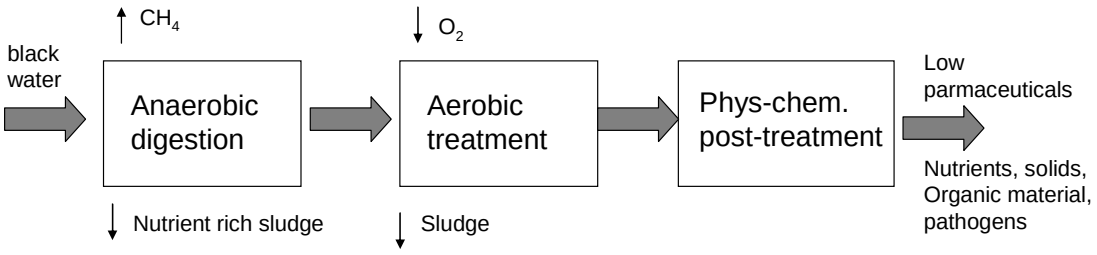


Figure 6.1: A sequence of processes to apply for black water treatment in order to eliminate human pharmaceuticals emissions into the environment.

6.2 Urine

Urine is produced in small quantities (1-1.5 L/person/day) and can be collected undiluted. Although considered as a relatively clean it still contains a significant load of organic material, nutrients, pathogens and pharmaceuticals. Regarding the small volume of the urine in certain situation it could be treated separately using advanced physical-treatment at a relative high costs. Such a solution could be applied in situation when point sources emit elevated concentration of pharmaceuticals into the environment (hospitals and other health care centres, pharmaceutical industries).

A train of processes applying aerobic biological degradation followed by advanced physical-chemical treatment could be applied as well. It has an advantage that a bulk of organic material is for a large part eliminated, allowing for optimisation of a post-treatment in terms of lower doses of reagents, contact times, energy consumption, etc.

When urine is used, after a storage, as a fertiliser in agriculture, the pharmaceuticals will be removed, at least partially, as a consequence of the spectrum of (natural) processes in the course of time:

- sorption on soil particles, roots,
- filtration
- biodegration in soil;
- exposure to sun – photolytic degradation.

The possible treatment configuration for separated collected urine are scetched in Figure 6.2.

-

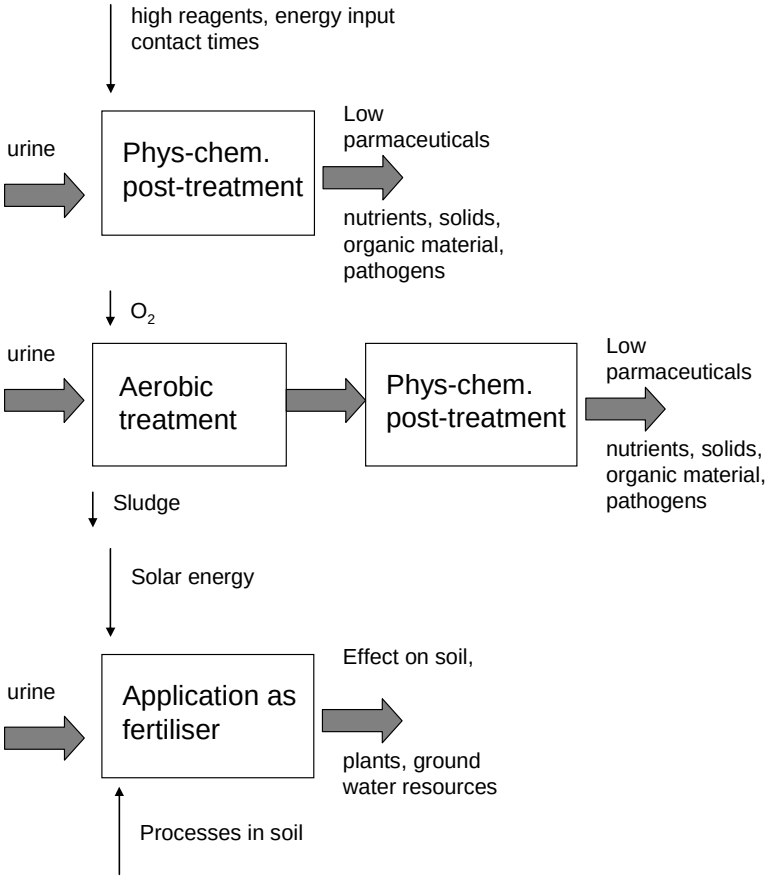


Figure 6.2: Possible solutions for source separated urine for elimination/reduction of human pharmaceuticals emissions into the environment.

Literature

Huber, M. M., Canonica, S., Park , G.Y. and Gunten, von, U. (2003). "Oxidation of Pharmaceuticals during Ozonation and Advanced Oxidation Processes." Environ. Sci. Technol. 37: 1016-1024.

Joss, A., Zabczynski, S., Goebel, A., Hoffman, B., Loeffler, D., McArdell, Ch.S., Ternes, Th.A., Thomsen, A. and Siegrist, H. (2006). "Biological degradation of pharmaceuticals in municipal wastewater treatment: proposing a classification scheme." Water Research 40(1686-1696).

Nguyen, L. V. Treatment of high concentration of pharmaceuticals in urine by ozonation processes, Hokkaido University.

Pronk, W., Biebow, M. and Boller, M. (2006). "Treatment of source-separated urine by a combination of bipolar electrodialysis and a gas transfer membrane." Water Science and Technology 53(3): 139–146.

Ternes, T., A., Joss, A. (2006). Human pharmaceuticals, hormones and fragrances. The challenge of micropollutants in urban water management., IWA Publishing.

Ternes, T. A., Jeannette Stuber, Nadine Herrmann, Derek McDowell, Achim Ried, Martin Kampmann, Bernhard Teiser (2003). "Ozonation: a tool for removal of pharmaceuticals, contrast media and musk fragrances from wastewater? Rapid communication." Water Research 37: 1976–1982.

van Beelen, E. S. E. (2007). Municipal Waste Water Treatment Plant (WWTP) Effluents a Concise Overview of the Occurrence of Organic Substances. A. o. R. W. RIWA.

Appendix 1 List of pharmaceuticals prescribed and administered in nursery home in Sleen, The Netherlands (2008)

Type pharmaceutical	Use in gram/day	No of residents	Function of pharmaceutical	Excretion
Mealatonine	1 mg	1		Volledig omgezet
Zapicolon	3.75 mg	1		
Temazepam	30 mg	3	Slapeloosheid en hypnotica	Eliminatie: 80% met de urine (als metaboliet), 12% met de feces
Fentanyl pleister	25 mcg elke 3 dagen = 8.33mcg	1	Opioïd	Eliminatie: vnl. met de urine, als metabolieten en ca. 10% onveranderd
Perindopr.tert.-Bu	2 mg	1	hartfalen, hypertensie en na een myocardinfarct	via de nieren als perindoprilaat
Bisoprol fum. merc	3.75 mg	2	ß-Receptorblokkerende sympathicolytica	95% via de nieren, 50% onveranderd, 50% als inactieve metabolieten
Simvastatine	40 mg	2	Lipidenverlagende middelen	vnl. met de feces als actieve en non actieve metabolieten
Metformine	1500 mg	1	Orale bloedglucoseverlagende middelen	met de urine onveranderd
Tildiem	300 mg	1	Overige calciumantagonisten	65% met de feces binnen 72 uur, 35% met de urine
Persantin ret.	200 mg	1	Trombocytenaggregatieremmers	vnl. met de feces (ca. 95%), in de vorm van metabolieten
Chloortalidon RP	25 mg	1	Diuretica, hypertensie	vnl. met de urine grotendeels onveranderd
Amlodipine	5 mg	1	Bij stabiele angina pectoris wanner met β-blokkers en/of nitraten onvoldoende resultaat wordt verkregen	Eliminatie: 60% met de urine, waarvan 10% onveranderd
Citolapram	20 mg	1	Depressie en antidepressiva	85% via de lever, 15% via de nier, 12–23% onveranderd met de urine
Lactulose 50%	15 ml	1	Laxantia	2 % slechts uitgescheiden met urine,
Flixtide disk	1500 mcg	2	Corticosteroïden, astma	(Absorptie in longen)
Acetylsal. Card. KTW	80 mg	1	Trombocytenaggregatieremmers	salicylzuur en metabolieten worden tezamen met onveranderd acetylsalicylzuur (1%) uitgescheiden met de urine
Bumetanide	3 mg	2	Diuretica	ca. 80% met de urine, de helft als inactieve metabolieten
Captopril	50 mg	2	ACE-remmers (hart)	vnl. met de urine, 50% ongewijzigd, de rest geconjugeerd
Flucloxacil	4000 mg	1	Smal-spectrum penicillinen	vnl. met de urine, 55% onveranderd
Oxycontin	5 – 15 mg	1	Opioïd	Uitgescheiden met urine als metabolieten
Tramadol HCL	150 mg	1	Opioïd	met de urine vnl. als

				metabolieten
Ioperamide	2 mg	1	Antidiarrhoica	vnl. met de feces, 25% onveranderd binnen 3 dagen
Ranitidine	300 mg	1	H2-receptorantagonisten gastro-oesophageale refluxziekte	oraal 60–70% via de nieren, i.v. 90%; 25% via de lever
Efexor XR	150 mg	1	Depressie en antidepressiva	vnl. via de nieren (87% onveranderd of metabolieten)
Levomepromazine	37.5 mg	1	Overige niet-opioïden, antipsychotische, analgetische en duidelijk sederende werking	Metabolisering: tot levomepromazinesulfoxide en antipsychotisch actief N-desmethyl-levomepromazinesulfoxide; uitgescheiden met urine en feces
Ascal cardio Brisp	100	1	Trombocytenaggregatieremmers	met de urine als salicylzuur en metabolieten tezamen met onveranderd acetylsalicylzuur (1%).
Dipyridamol drag.	300 mg	1	Trombocytenaggregatieremmers	vnl. met de feces (ca. 95%), in de vorm van metabolieten
Cetirizine dih	10 mg	1	Antihistaminica (H1-receptorantagonisten) allergische aandoeningen	vnl. met de urine, vnl. onveranderd
Nitrazepam	5 mg	1	Slapeloosheid en hypnotica	Metabolisering: in de lever tot inactieve metaboliet
Fragmin inj.	2500IE/0.2ml 19/3 t/m 14/4	1	Heparinegroep, trombo-embolische aandoeningen óf bij acuut coronair syndroom	vnl. met de urine
Combivent aerosol	Vlgs. Voorschrift	1	inhalatievloeistof	
Calci chew	500mg/400 IB	1	Calciumsupplement	
Furosemide	40 mg	2	Diuretica, chronisch hartfalen	met de urine, vnl. onveranderd; bij hoge doseringen 2/3 met de urine en 1/3 met de feces.
Micardisplus	80/12.5 mg	1	AT_1-antagonist en een thiazidediureticum	Grotendeels met urine, onveranderd
Micardisplus	40/12.5 mg	1	idem	
Acetylsal Car.	160 mg	2	Trombocytenaggregatieremmers	met de urine als salicylzuur en metabolieten tezamen met onveranderd acetylsalicylzuur (1%).**
Atenolol	100 mg	1	ß-Receptorblokkerende sympathicolytica	Metabolisering: weinig tot geen. Eliminatie: i.v. voor 95%, oraal 40–50% vrijwel onveranderd via de nieren
Paracetamol	2000 – 3000 mg	1	Overige niet-opioïden	met de urine, vnl. als glucuronide en sulfaatconjugaat, < 5% onveranderd; bij nierfunctiestoornissen cumulatie geconjugeerde metabolieten
Zolpidem(tart)	10 mg	1	Slapeloosheid en hypnotica	Eliminatie: 56% met de urine, 37% met de feces*

Plaquenil	400 mg	1	Malariamiddelen	langzaam, vnl. met de urine als metabolieten en voor 23–25% onveranderd, ca. 20% met de feces
Pantozol	40 mg	2	Protonpompremmers (maag klachten)	80% als metabolieten met de urine, 20% met de feces
Betahistini 2 HCL	24 mg	1	syndroom van Ménière	Metabolisering: volledig. Eliminatie: via de nieren
Nebilet	5 mg	1	ß-Receptorblokkerende sympathicolytica	38% met de urine, 48% met de feces, vnl. als metaboliet
Movicolon poeder		2	Laxantia	Niet met urine
Bisacadyl	5 mg (1 x 2 in 3 dagen)	1	Laxantia	Niet met urine
Omeprazol	40 mg	2	Protonpompremmers, gastro-oesophageale refluxziekte	80% via de nieren als metaboliet, 20% via de lever
Exelon	9 mg	1	Middelen bij dementie	> 90% binnen 24 uur met de urine als metabolieten.
Oxazepam	95 mg	3	Benzodiazepinen, toegepast als anxiolyticum	via de nieren als glucuronide
Enalapril maleaat	60 mg	5	ACE-remmers, hartfalen, hypertensie en na een myocardinfarct	volledig via de nieren, als enalapril en enalaprilaat
Hydrochloorthiazide	25 mg	1	Diuretica	vrijwel onveranderd, vnl. met de urine (hydrochloorthiazide); met urine 20–50% en feces 40% (amiloride).
Asasantin ret	25/200 2x	1	Trombocytenaggregatieremmers	o.a. met de urine als salicylzuur en metabolieten tezamen met onveranderd acetylsalicylzuur (1%).**
Acenocoumarol	1 Volgens schema	7	Coumarinederivaten, Remt de bloedstolling (dus Trombocytenaggregatieremmers	na 1 week ca. 60% met de urine en ca. 29% met de feces as inactieve metabolieten
Lanoxin	0.75 mg	4	Hartglycosiden	60-75% onveranderd met de urine
Tolbutamide	3000 mg	2	Orale bloedglucoseverlagende middelen	met de urine als metabolieten
Actonnel	35 mg	1	Calciumregulerende middelen	ca. 50% wordt binnen 24 uur met de urine uitgescheiden. Niet geresorbeerd risedroninezuur wordt uitgescheiden met de feces
Metoprolol ret	100 mg	1	ß-Receptorblokkerende sympathicolytica	via de nieren bijna volledig, 5% onveranderd
Isosorbide din. Ret.	40 mg	1	Nitraten	via de nieren, vnl. als metabolieten
Spironolacton	25 mg	2	Diuretica	grotendeels tot actieve metabolieten (o.a. canrenon). Eliminatie: vnl. met urine en feces
Acetylsal. Car. disp.	400 mg	5	Trombocytenaggregatieremmers	met de urine als salicylzuur en metabolieten tezamen met onveranderd acetylsalicylzuur (1%).**
Novomix flexpen	300IE/3 ml	2	Insulinen	

	volgens voorschrift			
Carbasalaat ca. card.	100 mg (poeder)	1	Trombocytenaggregatieremmers	Metabolisering: in de lever (salicylzuur) tot inactieve metabolieten. Eliminatie: met de urine als salicylzuur en metabolieten tezamen met onveranderd acetylsalicylzuur (1%)
Ferrogradumet	105 mg	1	ijzerpreparaat	
Actrapid penfill	300IE/3 ml volgens voorschrift	1	insulinen	
Selokeen zoc	50 mg	1	= metoprolol	via de nieren bijna volledig, 5% onveranderd
Mono cedoc. Ret.	100 mg	1	Angina pectoris	
Lipitor	40 mg	1	Lipidenverlagende middelen	Metabolisering: Door CYP3A4 tot actieve ortho- en paragehydroxyleerde metabolieten en tot diverse β-oxidatiemetabolieten. Eliminatie: vnl. via de lever
Thyrax	0,1 mg	1	Thyreomimetica, hypothyroïdie, schieldklierhormoon disfunctie	de metabolieten worden uitgescheiden in de urine en feces
Amlodipine	10 mg	1	Dihydropyridinen, Bij stabiele angina pectoris	60% met de urine, waarvan 10% onveranderd
Ceranesp	60 mcg/o.3 ml 1 x 2 wkn	1	?	

* Not known in each form excreted: unchanged vs. metabolites and in which ratio

Appendix 2 Data sheets of 6 tested GAC types:

- **DARCO 12x20**
- **Norit Vapure 612**
- **Norit ROW 0.8 Supra**
- **NRS CARBON EA 0,5-1,5**
- **ORGANOSORB 10-AA (DESOTEC Activated Carbon)**
- **ORGANOSORB 11**

DARCO 12x20

DARCO 12x20 is a granular activated carbon used in the purification of potable water and foods. DARCO 12x20 is frequently used for water purification because of its excellent adsorption capacity for taste & odour causing compounds, colours and algal toxins. The dedicated particle size distribution includes a low uniformity coefficient. DARCO 12x20 is an acid washed granular activated carbon, produced by steam activation.

DARCO 12x20 meets the requirements of the US Food Chemicals Codex (5th edition, 2004).

SPECIFICATIONS

Particle size > 12 mesh (1.70 mm)	**max. 10**	**mass-%**
Particle size < 20 mesh (0.85 mm)	**max. 5**	**mass-%**
Moisture (as packed)	**max. 12**	**mass-%**

GENERAL CHARACTERISTICS

Iodine number	650	-
Methylene blue adsorption	14	g/100 g
Tannin value	150	mg/l
Total surface area (B.E.T.)	725	m^2/g
Apparent density	380	kg/m^3
Density backwashed and drained	335	kg/m^3
Effective Size D_{10}	1.0	mm
Uniformity coefficient	1.5	-
pH	neutral	-

Norit VAPURE 612

Norit VAPURE 612 granular activated carbon is recommended for use in gaseous applications involving purification and separation processes. It is a premium grade product manufactured from select grades of coal. As the result of an unique, patented steam-activation process and stringent quality control, Norit VAPURE 612 granular activated carbon offers superior adsorption properties and is recommended for removal of odours, toxic vapours, irritants, corrosive gases, and to recover solvents and hydrocarbons from various gas streams.

SPECIFICATIONS

Iodine number	**min. 920**	**-**
Carbon tetrachloride activity	**min. 60**	**mass-%**
Abrasion number (AWWA method)	**min. 90**	**-**
Particle size > 6 mesh (3.35 mm)	**max. 5**	**mass-%**
Particle size < 12 mesh (1.70 mm)	**max. 5**	**mass-%**
Moisture (as packed)	**max. 3**	**mass-%**

GENERAL CHARACTERISTICS

Total surface area (B.E.T.)	900-1000	m^2/g
Apparent density	510	kg/m^3
Ignition temperature, above	450	°C

NORIT ROW 0,8 SUPRA

NORIT ROW 0,8 SUPRA is an extruded activated carbon, which offers superior adsorption properties in a wide range of applications such as purification of (potable) water. Its dedicated pore size distribution makes NORIT ROW 0,8 SUPRA highly suitable for the removal of taste and odour, organic micro pollutants such as pesticides, other dissolved organic substances, chlorine and ozone. Its superior hardness makes NORIT ROW 0,8 SUPRA particularly suited for thermal reactivation.

NORIT ROW 0,8 SUPRA meets the requirements of the US Food Chemicals Codex (5th edition, 2004) and the Drinking Water Standard EN 12915 (European Normalisation, 2003).

SPECIFICATIONS

Iodine number	**min. 1000**	**-**
Ball-pan hardness	**min. 90**	**-**
Particle size < 0.60 mm	**max. 0.5**	**mass-%**
Moisture (as packed)	**max. 5**	**mass-%**

GENERAL CHARACTERISTICS

Iodine number	1050	-
Methylene blue adsorption	22	g/100 g
Micropollutant loading:		
* atrazine at 1 µg/l	50	mg/g
* DBS at 1 mg/l	145	mg/g
* phenol at 1 mg/l	65	mg/g
Total surface area (B.E.T.)	1150	m^2/g
Apparent density	390	kg/m^3
Density backwashed and drained	345	kg/m^3
Ball-pan hardness	97	-
Particle size < 0.60 mm	0.1	mass-%
Ash content	7	mass-%
pH	alkaline	-
Moisture (as packed)	2	mass-%
Dechlorination halving value	4	cm

NRS CARBON EA 0,5-1,5

NRS CARBON EA 0,5-1,5 is a thermally reactivated extruded carbon, especially developed for wastewater treatment and groundwater remediation.
NRS CARBON EA 0,5-1,5 is a durable product with excellent adsorption properties for a range of organic compounds, like COD, colour and organic micropollutants (f.i. detergents, AOX, EOX). On condition that the exhausted carbon complies with the acceptance criteria, NRS CARBON EA 0,5-1,5 is suitable for intake by Norit Recycling Service. Following intake and quality checks the exhausted carbon is reactivated under controlled circumstances at high temperature.
For drinking water and food grade applications, other dedicated Norit grades are recommended.

SPECIFICATIONS

Iodine number	**min. 800**	**-**
Molasses number (EUR)	**max. 400**	**-**
Particle size < 0.50 mm	**max. 2**	**mass-%**
Moisture (as packed)	**max. 5**	**mass-%**

GENERAL CHARACTERISTICS

Iodine number	850	-
Total surface area (B.E.T.)	950	m^2/g
Apparent density	410	kg/m^3
Density backwashed and drained	360	kg/m^3

ORGANOSORB 10-AA

ORGANOSORB 10-AA is een gereactiveerde geagglomereerde actief kool met een uitstekende porositeit. Hierdoor is deze kool geschikt voor het ontkleuren en zuiveren van organische en waterige vloeistoffen.

type	steenkool –granulair	
Parameter	Kwaliteit	Typische waarden
Totaal BET oppervlak (m^2/g)	min 950	1000
Joodgetal (mg/g)	min 950	1040
Methyleenblauw getal (mg/g)	min 240	270
Melassegetal (mg/g)	min 230	290
Watergehalte (%)	max 5	4
pH	8 - 9	8,6
Hardheid (%)	min 90	96
Dichtheid (schudgewicht) (g/l)	430 ± 30	
Partikelgrootte (mesh)	8*30 (2,36–0,6 mm)	

ORGANOSORB 11

ORGANOSORB 11 is een zuurgewassen granulaire actieve kool en wordt gebruikt voor de zuivering van water met lage zoutgehaltes en een lage geleidbaarheid en chemicaliën.

type	steenkool –granulair	
Parameter	Kwaliteit	Typische waarden
Totaal BET oppervlak (m²/g)	min 1000	1040
Joodgetal (mg/g)	min 1000	1020
Methyleenblauw getal (mg/g)	min 190	195
Watergehalte (%)	max 5	2,6
Asgehalte (%)	max 6	5,5
pH	6 - 8	7
Hardheid (%)	min 90	96
Dichtheid (schudgewicht) (g/l)	470 ± 30	
Partikelgrootte (mesh)	8*30 (2,36–0,6 mm)	

Appendix 3 Norit procedure to determine adsorption isotherms onto activated carbon

Norit Electronic Version

Technical Bulletin

AQUEOUS PHASE SINGLE SOLUTE ADSORPTION ISOTHERMS ONTO Norit ACTIVATED CARBON

1. INTRODUCTION

Activated carbon is a key adsorbent applied in many water treatment processes for the removal of dissolved organic pollutants. Target compounds are usually poorly or non-biodegradable organics, including organic micropollutants such as: chlorinated solvents, detergents, pesticides, oil and petrol residuals. Activated carbon is used as a powder (PAC, powdered activated carbon) or in granular form (GAC, granular activated carbon). How to get information regarding the adsorptivity of a specific organic compound is described below.

Generation of isotherm data at Norit's R&D lab

2. SINGLE SOLUTE ISOTHERMS, THE METHODOLOGY

Isotherms, measured under defined conditions, represent the maximally achievable adsorption by an activated carbon under equilibrium conditions. The adsorptivity of a single organic compound measured in a clean water matrix (ultrapure or deionised water) yields a "single solute isotherm". Norit's R&D lab determines the single solute isotherms according to Norit Standard Testing Method (NSTM) 2.33 Essentially the isotherm data are generated as follows. A buffered (pH =7.0) stock solution of the target compound is made in ultra pure or deionised water. Using this stock solution ("adsorbate solution") typically 5-10 batches are prepared containing different amounts of activated carbon (PAC or ground GAC).

A blank (stock solution without activated carbon addition) is included as well. Equilibrium is obtained b stirring the batches at constant temperature for 1-4 days, depending on the target compound. The acti carbon is separated from the solutions through pressure filtration over glass fiber filters. After filtration (including the blank) all obtained solutions are analysed for the target compound.

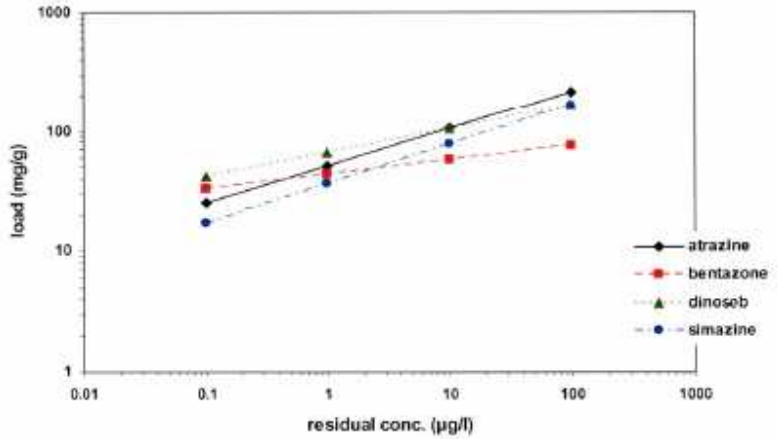


Fig. 1: Single solute isotherms of pesticides

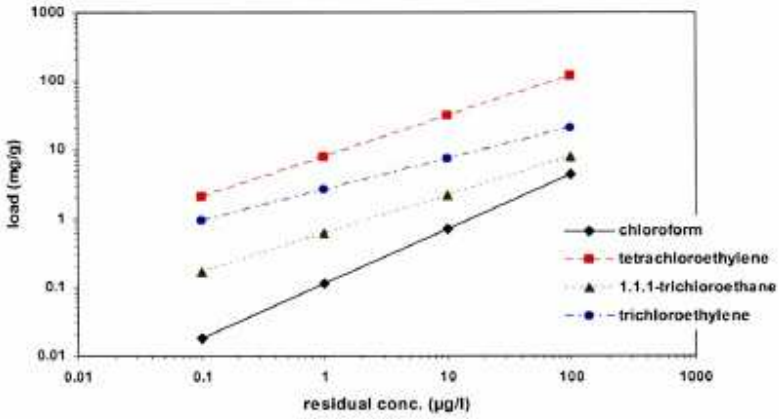


Fig. 2: Single solute isotherms of chlorinated solvents

The carbon load (q) is calculated from the aqueous phase concentrations:

$$q = \frac{C_0 - C_e}{m}$$

If the empirical data are plotted on log/log scale, the relationship becomes linear. The parameters of to the empirical Freundlich equation can be calculated as follows:

$$q = K * C^{\left(\frac{1}{n}\right)}$$
$$\log(q) = \log(K) + \frac{1}{n} * \log(C)$$

q = loading on the GAC (mg/g)
C = equilibrium concentration
K, $\frac{1}{n}$ = Freundlich parameters

3. WHAT DOES A SINGLE SOLUTE ISOTHERM TELL YOU?

Single solute isotherms do yield valuable information, especially regarding the compound of interest: to which degree is it adsorbable. Isotherms for a number of compounds are given in fig. 1-4 (activated carbon grade: Norit ROW 0.8 SUPRA). Referring to the examples given, adsorptivities can be ranked (see table below).

Adsorptivities of compounds based on single solute isotherms.

Adsorbability	Examples of compounds
very good	atrazine
good	benzene, phenol
moderate	chloroform
very poor*	acetone, methanol

* not included in graphs

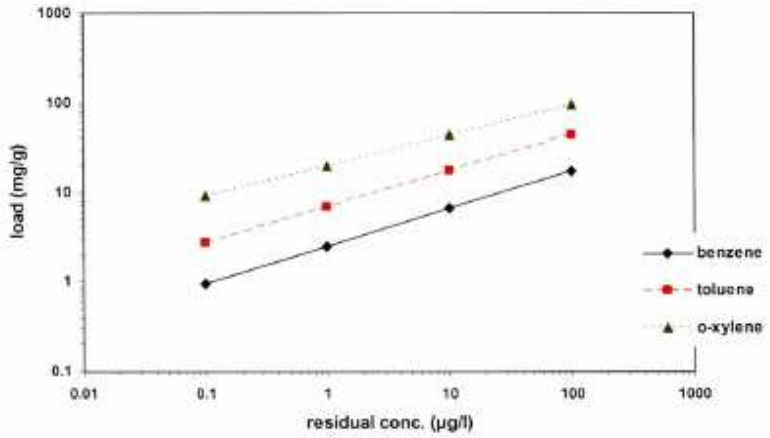


Fig. 3: Single solute isotherms of BTX

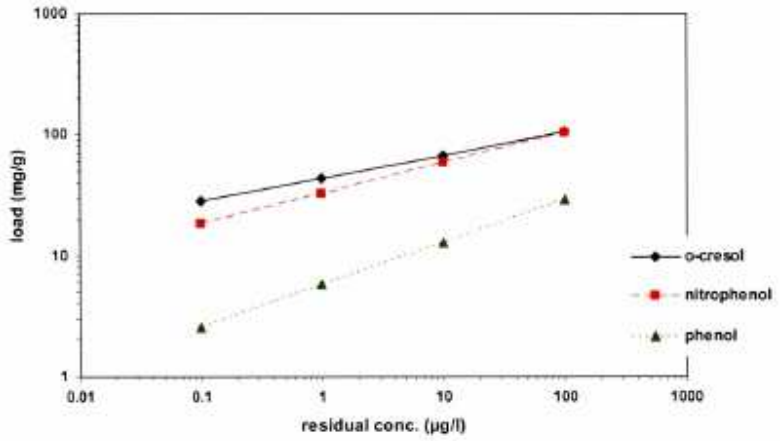


Fig. 4: Single solute isotherms of phenols

4. WATER TREATMENT IN PRACTICE

For specific compounds, data from single solute isotherms can give valuable information. However, the single solute loadings achieved represent best case scenario and cannot be quantitatively used in practice, due to:

- kinetic effects
- competitive adsorption by other compounds present in the water to be treated

In most cases where GAC or PAC is considered, the water to be treated is a complex mixture of numerous, unidentified compounds. Usually, the feasibility of activated carbon treatment can be assessed based on experience from comparable cases or from dedicated testing on the actual water to be treated.