Circular PhD mapping

Circular Pharmaceutical hospital Discharge

Towards circular human and veterinary hospitals:

mapping opportunities to reduce harmful pharmaceutical discharge

Final Report

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Highlights

- Concentrations of pharmaceutical compounds in hospital wastewater were tens to hundreds of µg/L. This is over an order of magnitude above concentrations commonly found in urban wastewaters.

- Concentrations of pharmaceutical compounds in urine sampled from ICU urine bags were thousands to tens of thousands of µg/L, with Vancomycin reaching 50 000 µg/L.

- Carbon based sorbents and ion exchange resins were tested for removal of pharmaceuticals from the ICU urine, showing a generally good removal performance for carbon based sorbents, which resulted in follow-up experiments and a related proposal which is currently in preparation (submission planned for Winter 2024)

- Horse manure was sampled at the Clinic for Horses, Utrecht University and selected veterinary medicinal products were analysed therein. A hazard screening indicated that some of the measured compounds may fulfill the criteria for the hazard class of persistent, mobile and toxic compounds. Therein, the leaching of these compounds, particularly sulfadiazine, which was found at relatively high concentrations, can be considered a potential hazard for receiving environments.

1.Introduction

Human and veterinary hospitals are potential hotspots for the emission of micropollutants such as pharmaceutical compounds and disinfectants, to the environment. The presence of these micropollutants in hospital waste streams is an obstacle to integrating hospitals into a circular economy. Previous research has shown that hospital wastewater contains a cocktail of pharmaceuticals; these micropollutants are insufficiently removed at existing wastewater treatment plants, thus contaminating surface waters with harmful compounds.

Researchers from Wageningen University, Wageningen Food Safety Research, Utrecht University and the University Medical Center Utrecht joined forces to map pharmaceutical compound discharge in human and veterinary hospitals. In this project we took first steps towards identifying suitable mitigation measures to attain zero discharge of pharmaceuticals of concern from hospitals to the environment in the future.

In 2022 the most relevant substances used in human and veterinary hospitals were identified and the inventory of used or supplied medicinal products was rated from an environmental protection and human health risk perspective. This included the distribution within the hospital waste system of both unused medication and medication that is excreted after treatment entering various waste streams. Opportunities for reducing the environmental risks associated to their use were also explored.

This follow-up project provides the basis for development of a more comprehensive intervention strategy using both technology and management strategies aiming at reducing pharmaceuticals entering circular water and food producing systems.

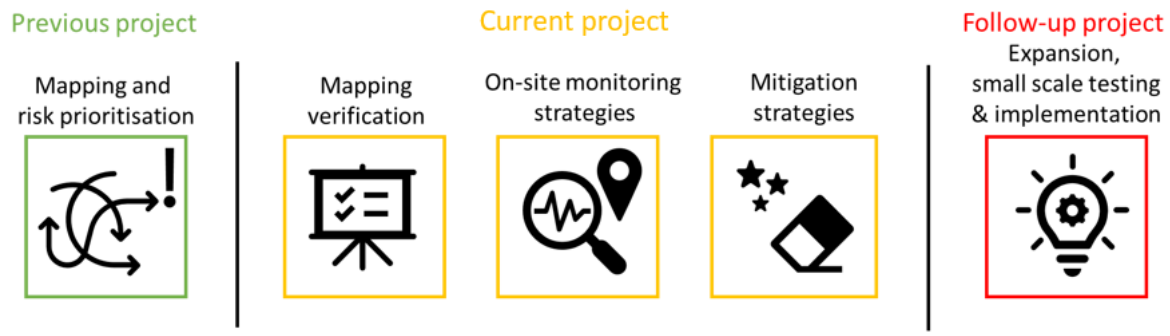

Figure 1. Overview of activities in the previous and current project and potential future collaborative efforts on pharmaceutical compounds discharge from hospitals.

Our first step was to experimentally verify our previous mapping results for the veterinary and human hospital. This was done by analysing the most relevant hospital waste (water) streams of the UMC and the veterinary hospital of Utrecht University. Also urine bags of intensive care (ICU) patients were analysed, as will be discussed later.

In a second step we applied a methodology to assess which residues in the veterinary hospital waste stream could be 'high' risk to human, environmental and ecological health by performing a hazard assessment. For this the data produced in the analyses of pharmaceuticals in the waste streams were used and related to environmental fate and exposure criteria.

Our third step was to identify technologies that can be implemented in a decentralized way to treat specific waste streams with high residue loads at their source in the hospitals. This study focussed on ICU urine bag waste streams.

A final part of this project is to search for additional funding to further and more extensively study all relevant pharmaceuticals and waste streams. This follow-up project should yield the first small scale implementation of new mitigation strategies to achieve discharge with no environmental impact.

2. Human Hospital Monitoring

2.1 Methods

Figure 2. Map of UMC Utrecht hospital, the arrow indicates the direction of wastewater flow and the red crosses represent sampling points.

Samples were collected from the UMC Utrecht. Based on the layout of the wastewater pipes, we selected four sampling points: upstream (wastewater inlet containing wastewater from the Princess Máxima Hospital), downstream (wastewater containing the totality of wastewaters from the UMC building complex), Normal station (inpatient area wastewater outlet), and ICU stream (ICU ward wastewater outlet).

We scheduled eight sampling time points for each of the four points. Sampling occurred over two consecutive weeks on Wednesdays and Sundays at 10:00 and 14:00 each day, resulting in a total of 32 samples. The samples were refrigerated and transported to the laboratory, where they were stored at -20°C for further experiments.

Extraction and analysis of Wastewater samples

Samples (10 mL, in two replicates) were pipetted into 14-mL plastic tubes and mixed with internal standards. Borate buffer and piperidine were combined and added to the samples, which were then incubated at 60°C for 1 hour. After cooling, n-hexane was added, and the samples were shaken and centrifuged. The aqueous layer was transferred to a new tube, the pH was adjusted, and the samples were centrifuged again. A Strata-X RP cartridge was conditioned, the extract was loaded and the cartridge washed and dried. Target compounds were eluted with a methanol/acetonitrile 50:50 v/v mixture, the eluate was evaporated, and the residue was reconstituted in 500 µL of piperidine solution for injection to a HPLC- MS/MS system for analysis.

Compounds were analysed within the following concentration ranges: 100 to 500 ng/mL for amoxicillin, benzylpenicillin, piperacillin, and ceftriaxone; 50 to 250 ng/mL for flucloxacillin; 10 to 50 ng/mL for cefazolin, ciprofloxacin, iopromide, meropenem, propofol, sulfamethoxazole, and vancomycin; 500 to 2500 ng/mL for ceftazidime; and 0.5 to 10 ng/mL for clindamycin and metronidazole.

The list of target substances measured on the HPLC- MS/MS consists of:

- Sulfamethoxazol
- Ciprofloxacin
- Clindamycin
- Metronidazole
- Meropenem
- Cefazolin
- Vancomycin
- Flucloxacillin
- Iopromide
- Piperacillin
- Ceftriaxone
- Ceftazidime
- Benzylpenicillin
- Amoxicillin
- Propofol

Due to challenging ionization behaviour in both ionization modes on the HPLC-MS/MS setup, propofol and its metabolites were additionally quantified via a GC-MS method at WFSR.

2.2 Monitoring Results in UMC Wastewater

We monitored 15 pharmaceuticals in the wastewater from UMCU, 11 of which were detected, with concentrations ranging from 0.34 to 1749.18 µg/L. Iopromide exhibited the highest single detection concentration and the highest average concentration across eight samples, with peak values exceeding 1500 µg/L. The average concentrations of the 11 pharmaceuticals across the four sampling points were 60 µg/L for the ICU stream, 110 µg/L for the upstream, 113 µg/L for the downstream, and 158 µg/L for the normal station.

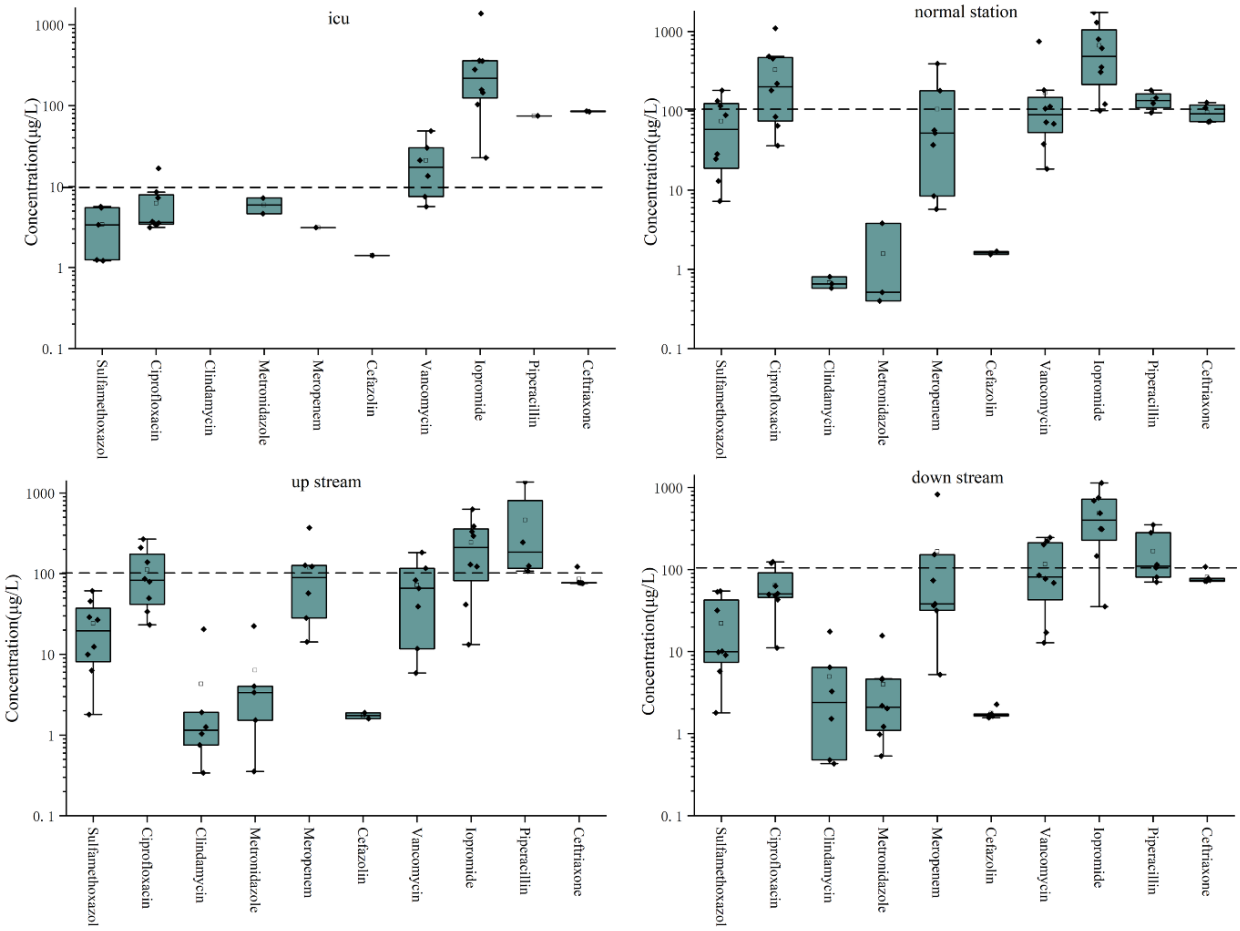

Figure 3. (a), (b), (c) and (d) represent the pharmaceutical concentration box plots of ICU stream, normal station, upstream and downstream.

Comparing the pharmaceutical concentrations upstream and downstream of the hospital, we found that the upstream and downstream had similar but not identical pharmaceutical profiles, indicating different use patterns between the Princess Máxima Hospital and the UMC. Even though concentrations were similar in both sampling points, the discharge at the downstream point was considerably higher than upstream. Thus, due to the higher volumes discharged, the pharmaceutical mass flux was considerably higher in the downstream sampling point. Unavailable more detailed discharge volume information at each sampling time point would be necessary for a more thorough analysis of exact mass fluxed.

The normal station exhibited the highest pharmaceutical concentrations, with average concentrations 2.59 times higher than those of the ICU stream, 1.43 times higher than those of the downstream, and 1.40 times higher than those of the upstream. This is likely because the normal station is closer to the source, with wastewater primarily originating from the inpatient area, whereas the overall hospital wastewater also includes other sources, such as visitors toilets ect. The wastewater stream from the ICU area was likely not driven by patient derived wastewater (see ICU Urine section below) and was thus not considered in the next discussion points.

To compare the pharmaceutical concentrations in the morning and afternoon wastewater at UMC, we averaged the data from four mornings and four afternoons at each sampling point (Figure 4). We found that for the downstream, 80% of the pharmaceuticals had higher concentrations in the morning. However, for the normal station, 70% of the pharmaceutical concentrations were higher in the afternoon. This discrepancy may be due to patients in the inpatient area (normal station) undergoing procedures and examinations in the morning and returning to the station in the afternoon.

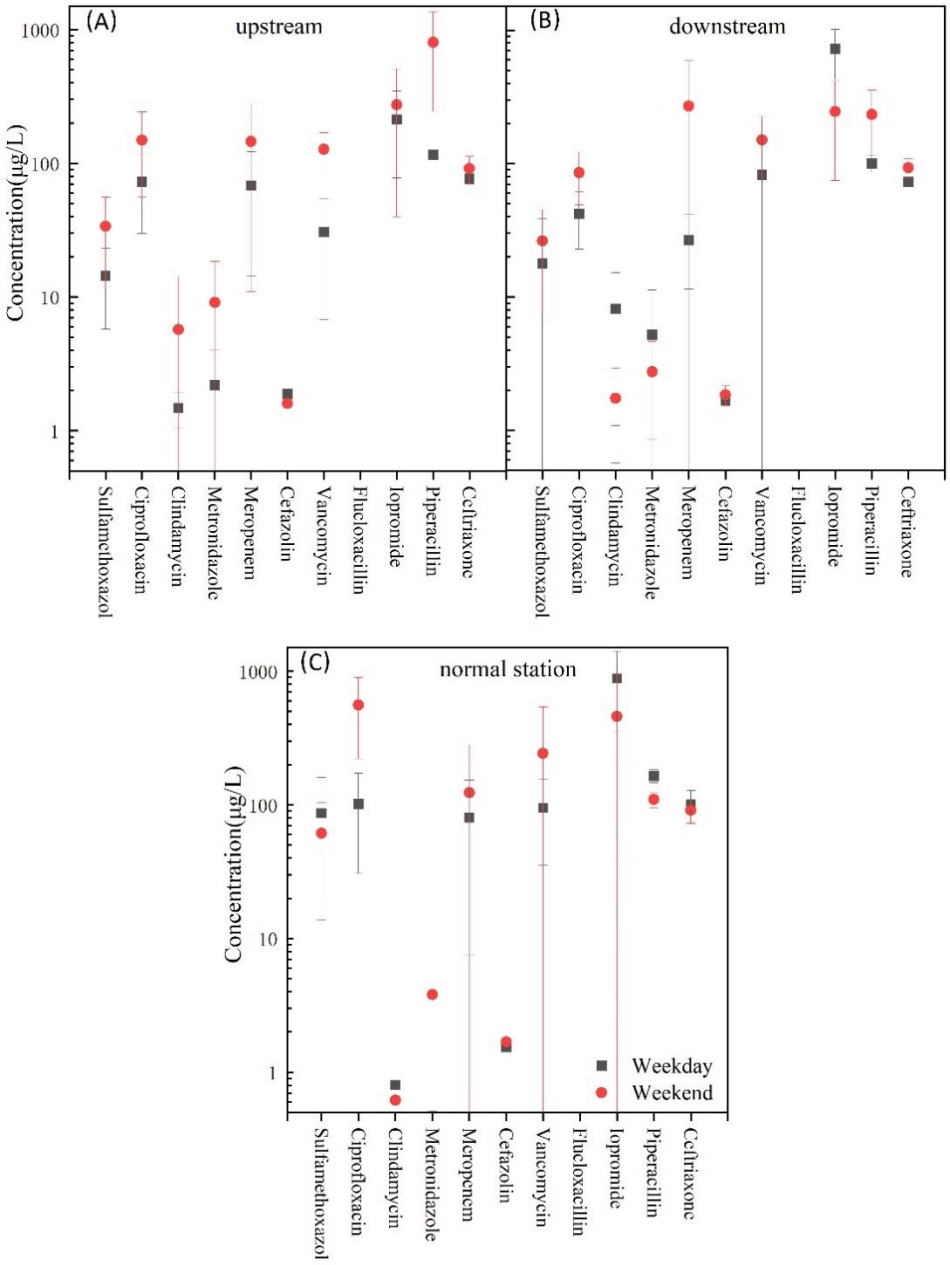

Figure 4. Average concentrations of 11 pharmaceuticals during the morning and afternoon in (A) the upstream (B) the downstream and (C) the normal station.

We also compared the pharmaceutical composition in UMC wastewater between weekdays and weekends (Figure 5). At the Normal station, 50% of pharmaceutical concentrations were higher on weekends. Similarly, for the upstream and downstream, 90% and 70% of the pharmaceuticals had higher concentrations on weekends. This was possibly due to the fact that on weekends, only essential patients visit or stay at the hospital, and there are fewer medical staff, resulting in higher concentrations of pharmaceuticals in the wastewater with a lower discharge volume.

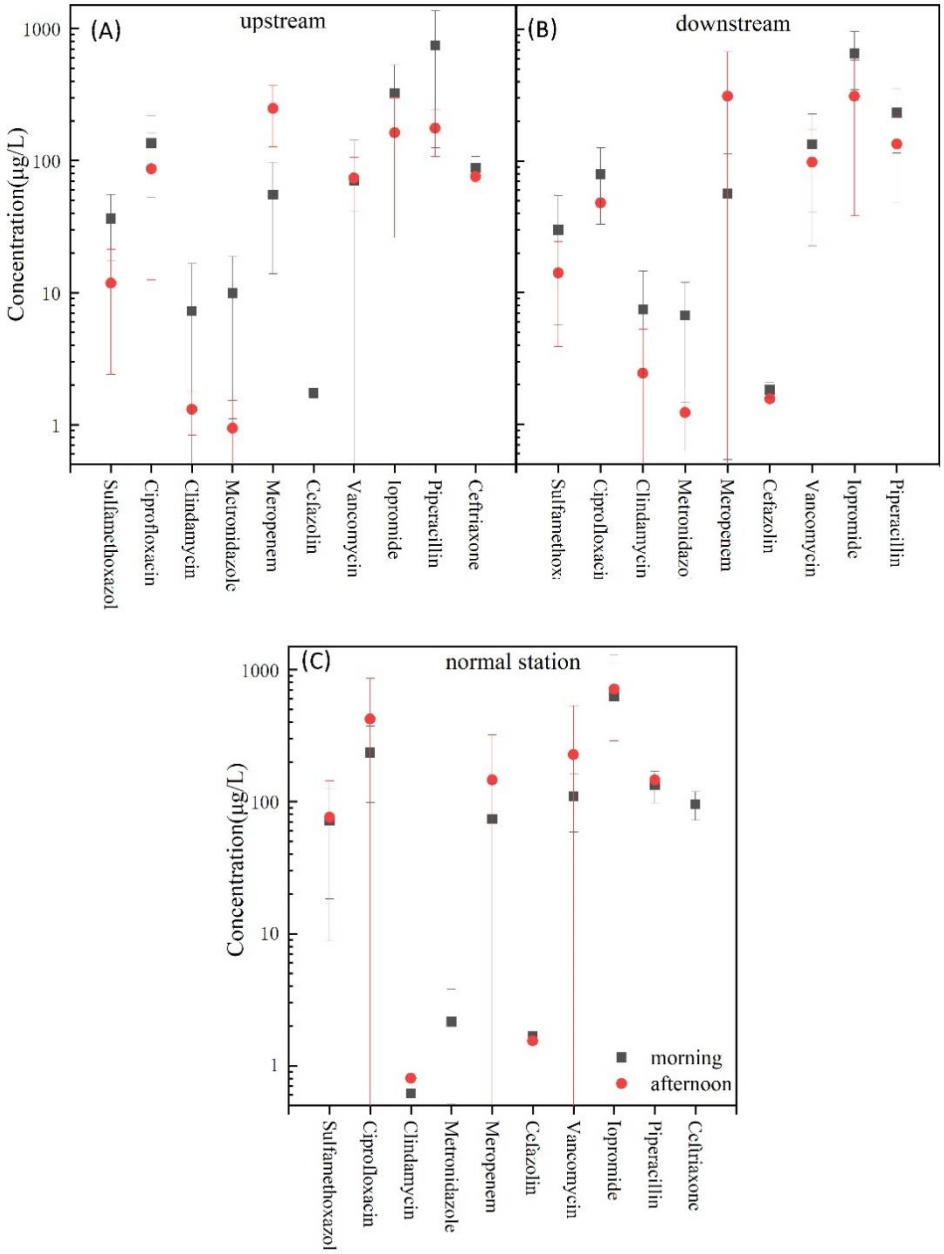

Figure 5. Average concentrations of 11 pharmaceuticals during weekdays and weekends in (A) the upstream (B) the downstream and (C) the normal station.

Overall, our measurements indicate that pharmaceutical concentrations in hospital wastewater streams are 10 to 100 fold higher than typically found in municipal wastewaters, with streams closer to the source (Normal Station) exhibiting even higher concentrations.

3. Pharmaceutical removal from ICU urine

We detected 11 pharmaceuticals in hospital wastewater, with concentrations ranging from 0.34 to 1749.18 μg/L. Pharmaceutical concentrations in ICU urine were 35 to 92 times higher than those in hospital wastewater (see 3.2). Literature reports indicate that urine contains 60% of the pharmaceutical residues discharged into municipal sewage, even though urine accounts for less than 1% of the total municipal sewage volume.[1] Therefore, managing ICU urine discharge from hospitals could be an effective upstream mitigation strategy, significantly reducing environmental risk and operational costs.

Currently, strategies for the rapid removal of organic pollutants from water include iron-activated persulfate, photodegradation, electro-Fenton, and adsorption. Due to the complex composition of urine, the effectiveness of these strategies is often compromised. For example, photodegradation studies found that the presence of urobilin significantly inhibited the removal of pharmaceuticals.[2] Additionally, the electro-Fenton method showed abnormally low degradation efficiency for antibiotics in urine.[3] Moreover, the processes of iron-activated persulfate, photodegradation, and electrochemical oxidation often require chemical additives, posing a risk of secondary environmental pollution, and/or are operationally complex, making them unsuitable for decentralized urine treatment.

Compared to oxidation techniques, adsorption has several advantages in terms of robustness and ease of use. It has low energy requirements and is simple to operate, making it suitable for decentralized treatment.[4] Second, adsorbents can be used in fixed-bed reactors and can be reactivated and reused.[5] Third, the adsorption process does not produce transformation products of pharmaceuticals, thus avoiding the environmental risks associated with such byproducts.[6] Common adsorbents include activated carbon, and ion exchange resins. However, there is no consensus on which material is best for removing pharmaceuticals from urine. Therefore, this study selected one laboratory-produced wood based steam activated carbon, one commercial activated carbon, and two commercial ion exchange resins. Batch and fixed-bed adsorption experiments were designed to investigate the removal efficiency of different materials and material combinations for pharmaceuticals in urine.

3.1 Materials

Sample Collection, extraction and analysis

Urine samples were collected from the ICU of UMC. Urine bags were obtained from two wards in the ICU station and transported under refrigeration to the laboratory. The samples were then mixed thoroughly and stored at -20°C until analysis. Subsequently samples were analysed using high resolution mass spectrometry (LC-HRMS) in positive and negative ionization mode.

The list of target substances measured on the LC-HRMS instrument consists of 27 compounds:

- Milrinone
- Acyclovir
- Clonidine
- Nordiazepam
- Diazepam
- Oxazepam
- Norquetiapine
- Temazepam
- Lorazepam
- Midazolam
- α-Hydroxy-midazolam
- Prednison

- Prednisolone
- Cortisol;
- 20α-Dihydro-prednisolon;
- 20β-Dihydro-prednisolon;
- Dihydro-prednisolon
- Methylprednisolone
- Meropenem
- Quetiapine
- Dexamethasone
- Flucloxacillin
- Rocuronium
- Ceftriaxone
- Vancomycin
- Tobramycin
- Voriconazole
- Fluconazol

Adsorbents

WBC is a laboratory-produced steam-activated carbon, derived from Beech wood through pyrolysis at 900 °C, with an specific surface area of 507 m^2/g. AquaSorb® CS is a granular activated carbon manufactured by steam activation from coconut shell charcoal. It has a specific surface area of 1050 m^2/g and was obtained from Jacobi. Purolite A400 is a polystyrenic gel, ammonium strong base anion resin with a Type I quaternary functional groupand was obtained from Purolite. Purolite® C100 is a polystyrenic gel, strong acid cation resin with a sulfonic acid functional group, also obtained from Purolite.

Batch Experiment

Adsorption experiments were performed in 50-mL brown glass bottles at room temperature (25 ± 2 ℃). 60 mg of adsorbent were weighed and added to 40 mL of collected, well-mixed urine. The mixture was then transferred to a shaker (120 rpm) to initiate the adsorption experiment. At specified time intervals (0, 20, 50, 100, 180, and 300 minutes), 1 mL samples were taken and stored at -20°C for further extraction and analysis. All adsorption experiments were performed in triplicate, and the average value was used for data analysis.

Column Adsorption Experiment

The adsorption columns were packed with sand as the filler. The sand was washed with water and then heated in a muffle furnace at 550°C for 12 hours. The ratio of adsorbent to filler was 20:80, with 1.6 g of adsorbent and 6.4 g of inert quartz sand. The mixture was packed into the adsorption column, with a small amount of glass wool at both ends to prevent particle loosening and blockage. The experiment was designed with WBC and C100 ion exchange resin as well as combination adsorption columns, filled with equal mass of each, and named WBC → C100 and C100 → WBC based on the sequence urine would get inContact with the sorbents.

Adsorption experiments were conducted using Watson-Marlow peristaltic pumps (Falmouth, Cornwall TR11 4RU, UK) at a flow rate of 0.24 mL/min, with the flow entering from the bottom and exiting from the top of the adsorption column. Samples were taken at specified time intervals (0, 2, 4, 6, 9, 23, 28, 48, 56 hours).

3.2 Pharmaceuticals in ICU Urine

A total of 27 pharmaceuticals were monitored in the urine samples, among which 19 were detected. The detected concentrations ranged from 2 µg/L to 50 000 µg/L. Vancomycin and Meropenem had the highest concentrations. The average concentration of the detected pharmaceuticals was up to 90 times higher than concentrations found in hospital wastewater.

3.3 Sorption Experiments

To elucidate the adsorption affinities of the four tested sorbent materials, we calculated the K_d (partition coefficient between solid and water) for each pharmaceutical to compare the sorption affinities of the adsorbents. The calculated average log K_d values were: WBC > C100 > AC > A400, with average values of 2.8, 1.8, 1.6, and 1.2, respectively. This indicates that WBC has the highest adsorption affinity.

Among the different pharmaceuticals, Milrinone had the highest sorption affinity, making it the most readily adsorbed by WBC. Over time the relative affinity between pharmaceuticals shifted somewhat, but overall trends for strongly adsorbing versus weakly adsorbing compounds were consistent across the tested contact times which ranged from 20 min to 300 min.

The adsorption affinities varied significantly among different sorbents and pharmaceuticals, and further analysis to disentangle these trends are ongoing. Nevertheless, it was evident that WBC exhibited the highest adsorption affinity and a rapid adsorption rate for most pharmaceuticals, making it suitable for use as an adsorber in column experiments.

Analysing the adsorption over time for each pharmaceutical, we observed that WBC could remove almost all pharmaceuticals within the first 0-4 hours, demonstrating its excellent adsorption capacity and broad applicability. We also found that the adsorption by C100 is selective. It effectively adsorbed Rocuronium and Clonidine, for prolonged times while showing almost no adsorption of Midazolam and 4-hydroxy Propofol Sulfate. A combination of the carbon based WBC with a cation exchange resin (C100) did not significantly increase removal or lifetime of the adsorbers, indicating that carbon based sorbents are the most promising material for further investigation.

Overall our data suggest that wood based steam activated carbon materials may be viable sorbent materials for on-site removal of pharmaceuticals from ICU urine. Follow-up experiments on carbon optimization and regeneration are ongoing.

3.4 References

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4. Risk assessment of veterinary medicinal products in horse manure from veterinary hospital

The previous project identified several 'hotspots' where veterinary medicinal products (VMPs) administered to patients in the veterinary hospital of Utrecht University, can enter the environment. Of these hotspots, the horse manure pile was ranked highest priority both because of the variety in VMP's administered to horses as well as the volumes involved. As the hospitals' horse manure is used in agriculture residues might end up in feed and food giving relevance to a risk assessment. A list of priority compounds was selected for analyses in the horse manure and subsequently a hazard assessment was conducted to determine on future mitigation steps.

VMP's are excreted by treated animals in the form of unchanged parent substances and/or metabolized compounds. These pharmaceutical residues can be released into the environment and consequently affect soil and water quality via manure application in agriculture. This pollution of soil and water is becoming an emerging environmental concern worldwide. Substances that are persistent, bioaccumulative and toxic (PBT), as well as substances that are persistent, mobile and toxic (PMT) are of particular concern.

In the European Union, environmental safety of VMPs is evaluated with a two-phase tier-based environmental risk assessment. The first phase (phase I) aims at identifying the environmental exposure of pharmaceuticals based on their potential for bioaccumulation and persistence in the environment, and determining the need for an ecotoxicological assessment. If environmental exposure is not negligible based on this phase I assessment, an ecotoxicological assessment (phase II) should be performed. Therein, the predicted environmental concentration should be calculated based on the guidance documents issued by the European Medicines Agency (EMA) (Figure 6) [1].

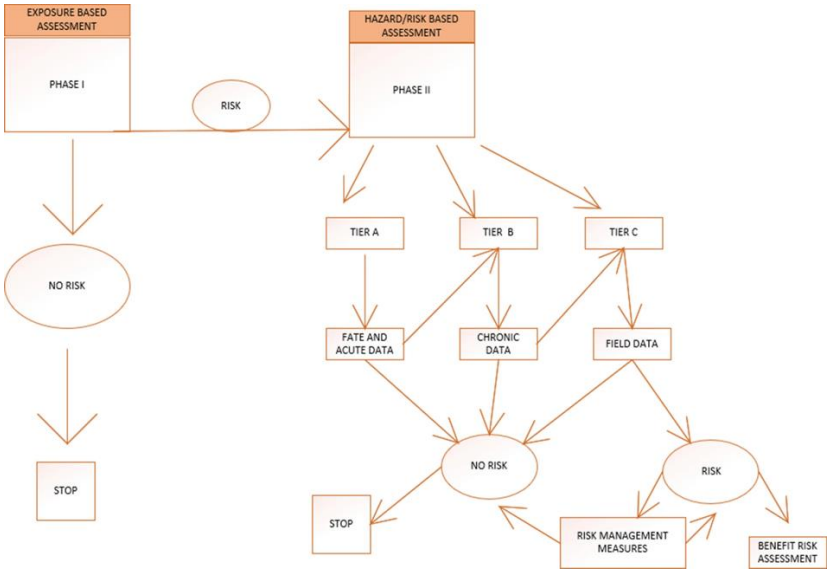

Figure 6. Schematic representation of the framework for the environmental risk assessment for veterinary medicinal products in the EU (Source: Fabrega, J. et al., 2020).

Risk assessments consist of a hazard assessment and an exposure assessment. Here we conducted a hazard-based PBT and PMT assessment, focusing on the intrinsic properties of substances. The goals were to identify and assess the potential environmental exposure to selected VMPs in horse manure from a university clinic and to provide a basis for a uniform risk assessment of VMPs.

4.1 Method

Selection of the VMPs

The selection of VMPs was based on a priority rank score, their physico-chemical characteristics, and administration route.

$$\text{Priority rank score} = \frac{\text{Total mass (g/y)}}{\text{ADI (µg/kg bw/day)}}$$

where ADI stands for Acceptable Daily Intake.

Data on total mass (g/y) of all pharmaceuticals used from July 2022 to June 2023 at the Clinic for Horses, Utrecht University (Universiteitskliniek voor Paarden, UKP) were collected. Databases from Joint FAO/WHO Expert Committee on Food Additives (JECFA) or EMA were used to gather information on ADI.

The list of selected pharmaceuticals includes 22 compounds:

- Acetylsalicylic acid (salicylic acid)
- Azithromycin
- Benzylpenicillin (penicillin G)
- Enrofloxacin
- Flunixin
- Gentamicin
- Hyoscine butyl bromide
- Ivermectin
- Levobupivacaine
- Meloxicam
- Metronidazole
- Moxidectin
- Paracetamol
- Phenylbutazone
- Phenytoin
- Praziquantel
- Prednisolone
- Propofol
- Rifampicin
- Sulfadiazine
- Trimethoprim
- Vedaprofen

These compounds span various classes, including antibiotics, corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs), antiparasitics, anesthetics, anticonvulsants, and antispasmodics. All compounds were monitored individually, except for acetylsalicylic acid. For acetylsalicylic acid, its primary active metabolite, salicylic acid, was monitored instead.

Sampling and analytical methods

Horse manure samples were collected at three moments (spring, summer and autumn) and analysed in December of the same year (2023). Between sampling and testing, the samples were stored in the freezer at -20°C. To address the analytical needs of various pharmaceutical classes and their specific requirements, three distinct extraction methods were employed:

1. For the detection and quantification of NSAIDs such as salicylic acid, flunixin, meloxicam, paracetamol, phenylbutazone, and vedaprofen, the following extraction procedure was used. Initially, 2 grams of each sample were diluted with water. The diluted samples were then extracted with acetonitrile. Following extraction, the samples were cleaned-up using Primary Secondary Amine (PSA) to remove matrix interferences. After centrifugation, the supernatant was evaporated and reconstituted in methanol. The final extracts were analyzed using LC-MS/MS.

2. The extraction procedure used for the detection and quantification of gentamicin involved starting with 2 grams of each sample, which were extracted using McIlvaine buffer. After centrifugation, the pH of the extracts was adjusted. A Solid Phase Extraction (SPE) clean-up was performed, with the eluate being collected using 10% glacial acetic acid in methanol. The eluate was then evaporated, and the residue was reconstituted in water containing 0.065% heptafluorobutyric acid. This final extracts were analyzed using LC-MS/MS.

3. For the detection of all other compounds, the extraction process began with 2 grams of each sample being extracted using a mixture of acetonitrile and McIlvaine buffer. Proteins present in the extract were precipitated with lead acetate, and the mixture was centrifuged to separate the precipitated proteins from the liquid phase. The supernatant was then dried, and to remove any remaining lead, it was treated with EDTA. A subsequent Solid Phase Extraction (SPE) clean-up was carried out, with the compounds eluted using methanol. After evaporation of the solvent, the residue was re-dissolved in Milli-Q water. The final extract underwent ultra-centrifugation before being analyzed using LC-MS/MS to ensure precise measurement of the analytes.

Calibration curves using matrix-fortified samples were utilized to quantify the analytes. For sulfadiazine and trimethoprim, the quantification range was 1.25-50 µg/kg, while for all other compounds, it ranged from 5-200 µg/kg.

Evaluation of VMPs compliance with PBT and PMT Criteria

Guidance on information requirements and chemical safety assessment was used to determine if the selected VMPs fulfil the criteria for PBT (Table 1 and Table 2). Data for this evaluation were collected from the US-EPA ECOTOX database (https://comptox.epa.gov/dashboard/) and the Veterinary Substances DataBase (http://sitem.herts.ac.uk/aeru/vsdb/). If a VMP does not meet the criteria for persistence and/or bioaccumulation, there is no obligation to assess the toxicity criterion within the PBT evaluation. Such a substance may still fulfill the new criteria for PMT.

Table 1: PBT and M criteria from the PBT and PMT substance classes[2,3]

Persistence	(a) the degradation half-life in marine water is higher than 60 days; (b) the degradation half-life in fresh or estuarine water is higher than 40 days; (c) the degradation half-life in marine sediment is higher than 180 days; (d) the degradation half-life in fresh or estuarine water sediment is higher than 120 days; (e) the degradation half-life in soil is higher than 120 days.	A substance fulfils the "very persistent" criterion (vP) in any of the following situations: (a) the degradation half-life in marine, fresh or estuarine water is higher than 60 days; (b) the degradation half-life in marine, fresh or estuarine water sediment is higher than 180 days; (c) the degradation half in soil is higher than 180 days.
Bioaccumulation	when the bioconcentration factor in aquatic species is higher than 2000.	A substance fulfils the "very bioaccumulative" criterion (vB) when the bioconcentration factor in aquatic species is higher than 5000.
Toxicity	(a) the long-term no-observed effect concentration (NOEC) or EC10 for marine or freshwater organisms is less than 0.01 mg/L; (b) substance meets the criteria for classification as carcinogenic (category 1A or 1B), germ cell mutagenic (category 1 or 1B), or toxic for reproduction (category 1A, 1B or 2) according to Regulation EC No 1272/2008 (c) there is other evidence of chronic toxicity, as identified by the substance meeting the criteria for classification: specific target organ toxicity after repeated exposure (STOT RE category 1 or 2) according to Regulation EC No 1272/2008.	
Mobility	when log Koc < 4.0	A substance fulfils the "very mobile" criterion (vM) when log Koc < 3.0

4.2 Results

Concentration levels of selected VMPs

Concentrations of the selected VMP's varied slightly over the seasons but were in general comparable, therefore it was decided to pool them. Average concentrations of the selected VMPs in horse manure at the three sampling moments are shown in Figure 7.

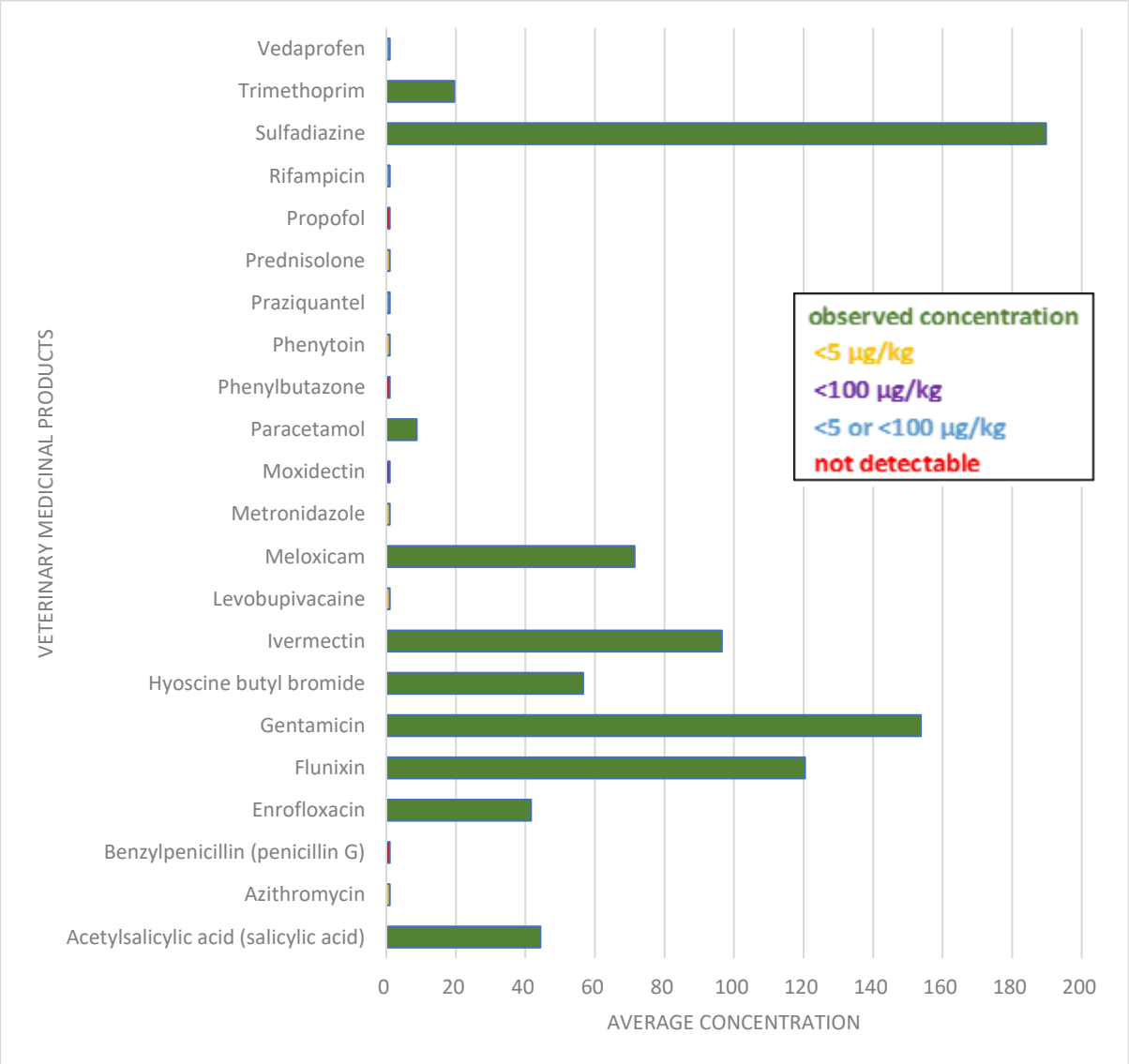

Figure 7. Average concentrations of the selected VMPs in horse manure at three sampling moments in µg/kg.

Evaluation of VMPs compliance with hazard class criteria (PBT and PMT)

None of the investigated VMPs fulfilled the criteria to be classified as PBT substance, which could be expected based on the fact that these compounds were developed for use with PBT regulations in place. In contrast some of the compounds did fulfill the criteria for PMT substances, a hazard class that has only recently been introduced into the regulatory framework. We used the assessments presented in Arp and Hale 2022[4] as a basis for the PMT categorization. Accordingly, sulfadiazine is considered a PMT and a very persistent, very

mobile (vPvM) substance based on ample evidence on all necessary criteria. In addition, meloxicam, enrofloxacin, trimethoprim and paracetamol may be considered PMT substances based on the partially available data for assessment. The categorization for these compounds must be considered as preliminary, with further evidence being necessary to confirm the categorization. Consequently, the leaching of these compounds, particularly sulfadiazine, which was found at relatively high concentrations, can be considered a potential hazard for the receiving environments.

The hospital's sawdust-based horse manure ends up in agriculture, but in general straw-based horse manure ends up as compost ingredient for mushroom growing. This might also be the case for horse manure of other veterinary clinics. Therefore we compared our results with analyses carried out by WFSR in 2010 and 2019 on behalf of the company CNC, which supplies compost for mushroom cultivation. 5 of our selected substances were also part of one of those studies: azithromycin, enrofloxacin, ivermectin, trimethoprim and sulfadiazine. Experiments showed that ivermectin was not detected in mushrooms grown on compost of which the raw materials were spiked[5]. Of the other substances only sulfadiazine was detected in manure supplied for composting, in levels between 13 and 70 µg/kg (limit of detection 2 µg/kg). After the composting process, sulfadiazine was no longer found, indicating a composting process is sufficient to degrade it to undetectable levels[6].

4.3 References

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5. Follow up Activities

Currently we are in the process to further analyse and follow up on the results obtained from the work on ICU urine. We are planning to use these results as a basis for a first proof of concept publication that we will follow up with a joint proposal between Wageningen University and the UMC Utrecht. In our vision these decentralized filters can be applied at emission hotspots of aqueous waste without disturbing patients. Thereby, we drastically decrease volumes that need treatment, and thus decrease pharmaceutical loadings of hospital wastewater that is introduced into the general sewer system. Ideally these sorbents can be regenerated on site using organic solvents and/or pH swing approaches. Consortia building and proposal writing activities are ongoing.