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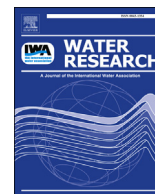
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Uptake of pharmaceuticals by sorbent-amended struvite fertilisers recovered from human urine and their bioaccumulation in tomato fruit

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ABSTRACT

Struvite precipitation is a well-documented method for recovering up to 98% of phosphorus from urine, which is one of the main nutrients in fertilizers besides nitrogen and potassium. Shortcomings of this process, however, are the low nitrogen recovery ratio and the possible uptake of pharmaceuticals from urine. In this work, the NH_4^+ adsorbent materials biochar and zeolite are coupled with struvite precipitation to increase the N-recovery of struvite from 5.7% to 9.8%. Since nitrogen is one of the main nutrients in fertilisers, this increase is of significance for its potential commercial use. In addition, urine is spiked with pharmaceuticals to measure the consequential uptake in struvite-based fertilisers and crops afterwards. Five fertilisers are prepared by nutrient recovery from spiked urine using: (1) struvite crystallisation, (2) struvite crystallisation combined with N adsorption on zeolite, (3) struvite crystallisation combined with N adsorption on biochar, (4) N adsorption on zeolite without struvite crystallisation, and (5) N adsorption on biochar without struvite crystallisation. The fertiliser with the highest purity product and the lowest uptake of pharmaceuticals was struvite combined with zeolite.

Next, the contaminated struvite-sorbent fertilisers are tested in a crop trial in which the bioaccumulation of pharmaceuticals in edible plant tissue (tomatoes) is measured. This bioaccumulation in tomato fruit biomass from each of the spiked fertilisers in the crop trial was found to be lower than 0.0003% in all cases, far below the acceptable daily intake (ADI) levels (750 kg of dry tomatoes should be consumed per day to reach the ADI limit). Consequently, the subsequent risk to human health from tomato fruit grown using urine derived struvite-sorbent fertilisers is found to be insignificant.

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1. Introduction

EU stakeholders identified efficient nutrient recycling from wastewater as an important step towards creating a circular phosphorus economy (EC, 2014). To date, phosphorus (P) is still a critical, irreplaceable raw material for soil fertilization that is not widely recovered (Egle et al., 2016). In addition, the agricultural industry relies heavily on nitrogen (N) in the form of ammonia that is currently produced via the energy intensive Haber-Bosch process, and is not recycled either. Recently, wastewater treatment plants are increasingly implementing P-/N- recovery technologies, primarily the struvite precipitation technology, which show great

promise (Egle et al., 2016). Two challenges remain, namely increasing the efficiency of nutrient recycling and securing the quality and safety of the recovered nutrients for subsequent reuse in food production.

In order to advance the efficiency of nutrient recovery, new technologies need to be developed to increase the recycling of nutrients from wastewater. The current implemented struvite recovery technologies only recover less than 3 percent of the N and up to 15 percent of the P found in wastewater. Since more than 90% of the N and more than 50% of the P found in domestic wastewater originates from urine, source separation of urine is considered an interesting method for simplifying nutrient recovery (Larsen et al., 2001). Even though the concentration of N in urine is significantly higher than that of P, struvite ($\text{MgNH}_4\text{PO}_4 \cdot 6\text{H}_2\text{O}$) precipitation only removes N and P in a 1:1 molar ratio, necessitating the combination with adsorbent materials to increase the N recovery. In hydrolysed urine, N is largely present in the form of ammonium (NH_4^+), which

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can undergo adsorption to negatively charged surfaces by ion exchange (Jorgensen and Weatherley, 2003). For example, natural clinoptilolite zeolites, which are composed of Al^{3+} substituted silica oxides, form a net-negative surface charge and a microporous framework of nanotube ion channels that result in a wide range of cation exchange capacities (Wang and Peng, 2010). Ban and Dave (2004) showed that it was possible to recover ~90% N and ~98% P by combining struvite precipitation with ammonium adsorption to clinoptilolite zeolite (15 g/L) over a 72 h period. The resulting nutrient enriched zeolite can be added directly to agricultural soil as a fertiliser, also improving water retention and reducing nutrient leaching (Hina et al., 2015). Another ion exchange material that can be used in combination with struvite precipitation is biochar, as it also meets several sustainability goals, such as energy production, carbon sequestration, soil enrichment and improvement of plant-growth (Marris, 2006). During biochar production via pyrolysis useful by-products, such as syngas and bio-oils are released, which could make the process self-sustainable (Xu et al., 2011). Biochar has a broad range of adsorption rates due to the variety of chemical compositions of biochar depending on the feedstock (Hina et al., 2015). Biochars with a negative surface charge have a higher affinity for NH_4^+ , whereas high intrinsic N or P levels can cause net release of these nutrients. Nutrient recovery by struvite precipitation combined with biochar adsorption increases the N uptake from 14% to 40%, indicating a promising N adsorption capacity (Xie and Reddy, 2013). Biochar is also a known adsorbent of micro-pollutants (Zhang et al., 2013) that can adsorb a broad range of organic chemicals, such as pesticides, polycyclic aromatic hydrocarbons (PAHs) and steroid hormones (Kookana et al., 2011). Conversely, the surface of zeolite is hydrophilic, limiting the affinity for organic micro-pollutants, although zeolite is an effective adsorbent of phenol (Yousef et al., 2011).

The combination of sorbent materials with struvite clearly increases the nutrient uptake, but the possible uptake of micro-pollutants found in human waste poses a barrier to the reuse of both phosphorus and nitrogen via urine-derived fertilisers (Lienert et al., 2007), but has never been quantified. Pharmaceutical residues are also predominantly excreted via urine (64% on average, with a maximum deviation of 27%) and the risk to human health from these contaminants must be assessed in order to unlock the commercial potential of urinary P and N (Lienert et al., 2007). Previous research on contamination of nutrients recovered from urine has focused on chemical precipitation of struvite as an efficient (~100%) P recovery technique (Liu et al., 2014; Rontelap et al., 2010), which produces high purity, crystalline material that is well within regulatory limits. Furthermore, struvite precipitation from urine that is spiked with pharmaceutical residues resulted in a product that excluded 98–99% of the organic micro-pollutants that were tested (Escher et al., 2006; Rontelap et al., 2007). Struvite precipitation from urine that contains pharmaceutical residues in combination with adsorbent materials, however, has not been investigated, as well as the possible health risks of using these recovered nutrients for food production. Besides analysing the

uptake of micro-pollutants into struvite when combined with adsorbent materials, it is also important to measure the uptake into edible parts of the crops since this might entail a risk to human health. However, there have been no previous studies that have examined the possible uptake of pharmaceutical micro pollutants from struvite into edible parts of the crops, the fruits.

The objective of this research is twofold: Firstly, to determine the uptake of pharmaceutical micro-pollutants by struvite recovered from contaminated human urine in combination with adsorbent materials and secondly, to determine the subsequent uptake of these micro-pollutants into edible parts of crops.

2. Material and methods

2.1. Urine, reagents, adsorbent materials, cuvettes and stock solutions

Pure urine, with an average pH of 9.5–9.7 (Fig. S1 in the supplementary information) was collected from a waterless men's urinal at Café de Ceuvel (Amsterdam, Netherlands) in two 100 L buffer tanks and pumped from the second tank to the struvite reactor. Magnesium chloride and all pharmaceuticals (>98% purity) were obtained from Sigma Aldrich (Netherlands) and used as received. Clinoptilolite zeolite and wheat husk biochar (pH 8.78–8.97) were purchased from Zeolite Products (Netherlands) and Sonnenerde (Austria), respectively, and their properties are listed in the supplementary information (Table S2). Ortho and Total-P cuvette tests, LCK350 (2.0–20.0 mg/L PO_4 -P), total N cuvette tests, LCK338 (20–100 mg/L N), and NH_4^+ cuvette tests, LCK302 (47–130 mg/L NH_4 -N) were obtained from Hach Lange (Netherlands).

Aqueous stock solutions of pharmaceuticals (carbamazepine, (\pm)-propranolol, diclofenac, sulfamethoxazole and ibuprofen) were prepared using distilled water and ethanol (96% purity), obtained from VWR. The five pharmaceuticals have been selected on the basis of their common occurrence in urine, their wide range of physiochemical properties (Table S1 in the supplementary information), different biological activities and previous appearance in literature. The pharmaceutical concentrations in urine were based on toxic potency and molar predicted urine concentrations (PUC), calculated according to Escher et al. (2006), to simulate an average population. Nutrients were recovered using struvite precipitation and adsorption of N onto zeolite and biochar. The change in nutrient and micro-pollutant concentration in the input and effluent urine was measured to determine the uptake using chemical analysis. The five fertilisers were then tested in a small crop trial using dwarf tomato plants, and the resulting tomato fruit biomass was tested for micro-pollutant content. The biomass concentrations were then used to assess the risk to human health using toxicity data. Solution concentrations and ethanol/water ratios are listed in Table 1. The relative molecular mass (RMM), acidity (pK_a) and hydrophobicity ($\log K_{ow}$) values for each pharmaceutical are shown in the supplementary information (Table S1), as these

Table 1
Aqueous micro-pollutant stock solutions spiked to human urine.

Micro-pollutant	EtOH:water ratio ^a %	Stock solution concentration mg/L	Spiked urine concentration ^b μ g/L
Carbamazepine	40:60	97.5	234
Propranolol-HCl	0:100	103	14
Diclofenac sodium	12:88	3570	640
Sulfamethoxazole	2:98	392	630
Ibuprofen	32:78	12700	2700

^a The ethanol:water ratio is adjusted to the water solubility of the pharmaceuticals.

^b Based on predicted urine concentration (PUC) values.

Source: Escher et al., 2006.

Table 2
Nutrient recovery experiments.

Fertiliser ID	Mg:P ratio in urine	Sorbent material	Nutrient recovery technique
Struvite	1.2:1	–	Struvite crystallisation
SZM	1.2:1	Zeolite	Struvite crystallisation & N adsorption onto zeolite
SB	5:1	Biochar	Struvite crystallisation & N adsorption onto biochar
Zeolite	0:1	Zeolite	N adsorption onto zeolite
Biochar	0:1	Biochar	N adsorption onto biochar

properties may influence the adsorption onto zeolite and biochar surfaces.

2.2. Nutrient recovery

Pharmaceutical solutions were added to human urine in final concentrations calculated according to Escher et al. (2006), as shown in Table 1. The spiked urine was used to generate fertilisers in an air agitated batch reactor using five different nutrient recovery techniques, listed in Table 2. The desired volume of the MgCl₂ solution, added in order to precipitate struvite, was based on the total-P concentration of the influent urine, and calculated using Equation S(1) in the supplementary information. The reactor was filled with urine to ~25 L, a sample of urine was removed for P content analysis, pharmaceutical stock solutions were added and aeration was switched on. An aqueous, 32% MgCl₂ solution was added to the struvite crystallisation experiments in the Mg:P ratio indicated in Table 2 and sorbent materials (300 g) were added to the N adsorption experiments, either subsequent to or instead of MgCl₂ addition. The resulting mixture was agitated by aeration for 2 h, during which nutrient recovery by struvite crystallisation and/or adsorption occurred. The reactor was drained through a food grade micron filter mesh (110 µm) to collect the sorbents, and through a smaller mesh filter (20 µm) to collect the precipitated struvite. A sample of the urine effluent was removed for analysis and the remaining supernatant was directed to the sewer. The filter cake was washed with tap water and left to air dry over several days. Five batches of each nutrient recovery technique were carried out.

2.3. Crop trial

The urine-fertilisers were used to grow dwarf tomato plants from seedlings in a crop trial over a 2 month period. The P content of urine-derived fertilisers was measured in order to accurately balance the mass of each struvite-based fertiliser by P (5.3 g, see the supplementary information, Table S3). The mass of the zeolite and biochar fertilisers (350 g) was equal to the mass used for the SZM and SB fertilisers (400 g), subtracting the approximate mass of struvite (50 g). The plant growth experiments were set up by planting a seedling in a mixture of sand, potting soil (500 mL) and the pre-weighed urine-derived fertilisers (using the approximate volume ratios shown in Table S3) in a 6 L pot. A cotton wick was placed from each pot to a water reservoir below, in order to maintain moisture levels by capillary action. After 63 days of growth, all tomato fruits were harvested and dried at 75 °C for 24 h in a drying oven.

2.4. Analytical methods

The influent and effluent urine were characterised for N and P content using colorimetric analysis in order to determine the N and P uptake into each fertiliser. When necessary, urine samples were first diluted with deionised water to an appropriate concentration for analysis using a Hach Lange DR laboratory VIS

Spectrophotometer, following the working procedures described in the Hach Lange DR 3900 User Manual and using the Total-N and Total-P test cuvettes (see Table 3).

The struvite fertiliser was characterised by X-ray powder diffraction (XRPD) and for P content by a colorimetric analysis, in order to determine the crystallinity and purity of the generated material, respectively. XRPD analysis of the solid, dry filter cake material was carried out with a Rigaku Miniflex II diffractometer, using Ni-filtered Cu-K α radiation (Universiteit van Amsterdam, Netherlands). The solid material was also observed through a Leica DMLS polarising light microscope (PLM) with 10x/0.22 PH1 magnification (Waternet, Amsterdam). The purity of the struvite was tested further by dissolving ~10 mg material in 500 mL deionised water and measuring the P concentration, using colorimetric analysis (as described above). The purity was then calculated as a percentage of the theoretical P concentration, based on the sample mass.

Micro-pollutant uptake from urine was tested by measuring the final concentrations of spiked pharmaceuticals in the effluent of each nutrient recovery experiment. Because pure human urine was used for these experiments, it was expected that there could be low-level concentrations of pharmaceutical micro-pollutants already present in the influent urine. Therefore, the measured influent urine concentrations, before spiking with pharmaceuticals, and the spiked concentrations were added together to give the total input urine concentration (shown in Table 4). Samples from each batch (20 mL) were combined so that a 100 mL mixed sample of each of the fertiliser effluents was submitted for micro-pollutant concentration analysis at Eurofins Omegam B.V. (Netherlands). Samples were diluted in several dilutions (x10 and x100) and analysed with HPLC-MS/MS with an Agilent 1260 infinity HPLC and an Agilent 6460 triple quadrupole mass spectrometer with jet stream technology by direct injection. The percentage uptake of pharmaceuticals into the fertilisers was then calculated from the difference in concentration in the urine effluent and input concentration. Since pharmaceuticals tend to be poorly degradable in urine (Richter, 2003), we believe that there is no significant degradation of the studied micropollutants in urine. Escher et al. (2006) confirm this, as they reported that there is no degradation of ibuprofen and propranolol in urine over time.

Dried tomato biomass samples were also submitted for analysis at Eurofins Omegam B.V. (Netherlands) to determine the micro-pollutant accumulation in the tomato fruits. Samples were extracted and analysed with HPLC-MS/MS by direct injection. The mass uptake of pharmaceuticals into the tomato biomass from urine-derived fertilisers was then calculated.

3. Results and discussion

3.1. Struvite characterisation

Higher purity struvite is less prone to the uptake of contaminants. Since the main goal of this research was the possible detection of pharmaceuticals in crops using struvite in combination with sorbent materials, we wanted to set an upper limit by

using low purity struvite (~84%_w) to maximise the possible uptake of contaminants in the fertilizers. This will provide an upper boundary for the quality and safety of the recovered nutrients for subsequent reuse in food production. The obtained struvite by struvite precipitation of the pure urine from the urinary of restaurant de Ceuvel, Amsterdam, was observed to be greyish white and powdery, with little odour. A crystallinity analysis by X-ray powder diffraction (XRPD; Fig. 1) indicated that the material was crystalline and comparable to literature values (Sinha et al., 2014). There were no extra peaks, qualitatively indicating just one polymorphic form and no trace crystalline impurities. The crystal size observed by polarised light microscopy (PLM) was very small, between 20 and 120 μm, with an X-shaped morphology which supports literature (Kemacheevakul et al., 2015). Crystallised material from struvite-zeolite-mineral with N adsorption from urine (SZM) and struvite-biochar with N adsorption from urine (SB) experiments were also analysed by PLM and the morphology observed was more rod shaped crystals in nature, likely caused by the presence of solid zeolite and biochar material during the crystallisation process.

3.2. Phosphorus recovery

The P recovery for struvite, struvite in combination with zeolite (SZM) and in combination with biochar (SB) fertilisers was in all cases high (96–98%) as confirmed in literature (Liu et al., 2014; Rontelap et al., 2010), whereas the P recovery for zeolite and biochar without struvite precipitation was substantially lower (<5%), which indicates that P recovery for SZM and SB was predominantly controlled by struvite precipitation, rather than adsorption into the sorbent materials. The mean measured P uptake of the solely zeolite fertiliser of 4.9% is in line with previous findings that report between 2.8 and 12.9% uptake from an average urine concentration (~200 mg P/L urine). The P (PO₄³⁻) adsorption capacity of zeolite is low, due to unfavourable electrostatic interaction, and was found to be 0.93 mg P/g zeolite. This is consistent with the previous reported findings, which varies from 0.46 mg P/g zeolite (Drizo et al., 1999) to 2.15 mg P/g zeolite (Sakadevan and Bavor, 1998). Zeolite P adsorption is known to be driven by the presence of hydrous metal oxides (such as Al-OH) on the surface, where phosphate anions replace OH⁻ and H₂O groups (Rajan, 1976). Phosphate adsorption onto zeolite can also occur via precipitation with native exchangeable zeolite cations (Ca²⁺, Na⁺ or K⁺) which are free to move in the channels of the zeolite framework (Wang and Peng, 2010). However, the average concentration of these cations in zeolite is low (Table S2 in the supplementary information). A combination of these mechanisms and varying availability of these metals accounted for the low P-recovery from urine into zeolite.

Table 3
Percentage nutrient recovery (%_{rec}) from urine into fertilisers.

Fertiliser batch	Struvite		SZM		SB		Zeolite		Biochar	
	% _{rec}		% _{rec}		% _{rec}		% _{rec}		% _{rec}	
	P	N	P	N	P	N	P	N	P	N
1	95.4	4.5	96.6	10.8	97.8	1.9	5.6	9.4	4.8	5.9
2	97.5	6.0	96.5	11.5	98.6	20.7	6.3	8.9	3.2	3.5
3	96.6	7.2	96.2	11.0	97.9	16.2	4.6	3.1	-2.5	5.8
4	97.4	6.8	97.3	9.8	98.0	8.7	3.4	5.6	-7.7	16.8
5	96.5	5.7	98.1	4.2	97.9	1.6	4.8	3.4	6.4	14.1
Mean:	96.7	6.0	96.9	9.5	98.1	9.8	4.9	6.1	0.8	9.2
Standard dev.:	0.76	0.94	0.8	3.0	0.3	8.5	1.1	3.0	5.8	5.8
Standard error:	0.87	0.97	0.3	1.4	0.1	3.8	0.5	1.3	2.6	2.6

We believe that the uptake for batch 3 and 4 (-2.5 and -7.7 respectively) is a result of the intrinsic P content of biochar (1.8%, Table S2 of the supplementary information) which could have released water soluble P. The soluble P content of biochar (500 mg P/kg), described in the supplementary information, could release ~150 mg P/batch, on average. Due to the irregular nature of biochar, this value may not be representative of the total amount of water soluble P in every batch, resulting in a positive uptake for batches 1, 2 and 5 and net release in 3 and 4. Zheng et al. (2010) showed that P adsorption by biochar is controlled by a precipitation reaction with Ca²⁺, producing Ca₃(PO₄)₂·xH₂O, and is therefore dependent on the intrinsic Ca²⁺ content of the biochar.

3.3. Nitrogen recovery

Besides P recovery, also the N recovery of each of the fertiliser streams has been analysed. The N recovery of struvite without the sorbent materials zeolite or biochar was on average 6.0% and almost doubled when combined with addition of the sorbent materials in both SZM and SB, reaching ~10% total N recovery. The N recovery into struvite was found to be 6.0 g_N per 25 L batch. This is greater than the N recovery by a 1:1 (N:P) molar ratio with recovered P, which would be 4.9 g_N. This indicates an excess N of 1.1 g_N per batch (Table S4 of the Supplementary Information), which is possibly adsorbed to the 16% amorphous struvite content. The N recovery into zeolite (1.52 mol NH₄⁺/kg zeolite) was equal to the cation exchange capacity (CEC) of the zeolite (Table S2 in the Supplementary Information), indicating that the main uptake mechanism was cation exchange (Hina et al., 2015). The SZM fertiliser did not contain the N impurity observed in the struvite experiments. This is because zeolite seeding enhances crystal growth, allowing agglomeration of struvite fines on the zeolite surface, which do not otherwise agglomerate in hydrolysed urine due to high struvite zeta-potentials at high pH (Le Corre et al., 2007).

Urine contains naturally competing cations, such as Mg²⁺ and Ca²⁺, which are most likely the reason for the high variability of N uptake. Since Mg²⁺ can compete with NH₄⁺ for adsorption sites a high 5:1 ratio of Mg:P is used in our SB experiments. The chemical composition and surface functionality of biochar is known to vary widely, which results in a number of different adsorption mechanisms. These account for the higher N uptake variability, relative to zeolite-based fertilisers (Spokas et al., 2012), where some of these uptake mechanisms, such as ammonium sulphate or amine formation in the biochar carbon lattice, can be irreversible (Hina et al., 2015; Spokas et al., 2012). The N uptake of biochar was therefore higher than zeolite, but the availability of N to plants may be lower.

3.4. Micro-pollutant uptake into fertilisers

A significant uptake of pharmaceuticals into the five fertilisers was found as the micro pollutant concentration in the effluent streams was reduced compared to the total input concentrations (Fig. 2). The pharmaceutical uptake is dependent on the type of fertilisers and pharmaceuticals (Table 4). The highest average uptake during the conditions and concentrations of this experiment was for propranolol, with an average uptake ranging between 34 and 87% and an average of 66.8%. On average 92% of the diclofenac of the input urine concentrations was found in the effluent, which means that only 8% of the diclofenac was taken up in the fertilisers. The fertiliser with on average the highest uptake was zeolite, with an uptake of ~50% of the micro-pollutants in the input stream. The lowest uptake was in the struvite and SZM fertilisers, both on average 26.6% uptake. A more extensive study with different concentrations of pharmaceuticals and amounts of struvite and sorbent materials is necessary to understand fully the sorption processes.

The ibuprofen concentration in the struvite effluent and diclofenac concentration in SB and biochar effluent streams have a slightly higher concentration than in the influent streams, which compares well with a study on pharmaceuticals in the influent and effluent of several wastewater treatment plants where also a slight increase of diclofenac in the effluent stream was found (Kasprzyk-Hordern et al., 2009). This increase can be a result of hydrolysis of pharmaceutical conjugates or other factors. Since human urine has been used instead of synthetic urine. In this study, there were no trends linking uptake to pharmaceutical properties such as $\log K_{ow}$ or pK_a (Table S1 in the supplementary information).

biochar's surface, allowing interaction with pharmaceuticals via several different mechanisms (Zhang et al., 2013). The pharmaceutical uptake was not affected by the addition of magnesium used in SB experiments compared to biochar, indicating that the additional Mg content was indeed sequestered by the biochar and not available to chelate with pharmaceutical molecules (Xie and Reddy, 2013; Kemacheevakul et al., 2015).

Unlike the similarity between SB and biochar, the uptake of micro-pollutants into zeolite was ~30% higher than SZM on average, with the exception of ibuprofen uptake. The sorption characteristics of zeolite are largely controlled by surface area, pore size and

Table 4

Micro-pollutant concentrations in input urine (average influent + spiked urine concentrations), effluent urine and percentage uptake (%_{up}) into fertilisers from nutrient recovery experiments.

Micro-pollutant	Input urine concentration		Nutrient recovery experiment effluent urine concentration				
	Average influent urine	Spiked urine	Struvite effluent	SZM effluent	SB effluent	Zeolite effluent	Biochar effluent
	µg/L	µg/L	µg/L (% _{up})	µg/L (% _{up})	µg/L (% _{up})	µg/L (% _{up})	µg/L (% _{up})
Carbamazepine	1.2	234	180 (24%)	200 (15%)	170 (27%)	140 (41%)	180 (24%)
Propranolol-HCl	0.5	14	6 (58%)	10 (34%)	3 (79%)	4 (76%)	2 (87%)
Diclofenac sodium	3.4	640	550 (14%)	620 (3%)	650 (-2%)	420 (34%)	680 (-6%)
Sulfamethoxazole	1.4	630	350 (44%)	400 (37%)	280 (56%)	260 (59%)	290 (54%)
Ibuprofen	280	2700	3200 (-7%)	1700 (44%)	1200 (60%)	1800 (40%)	1500 (51%)

Kemacheevakul et al. (2015) indicates that the Mg:P ratio has a direct influence on pharmaceuticals in struvite. Via using a low Mg:P ratio (1.2:1) for the precipitation of the struvite fertilisers, we succeeded in a high pharmaceutical uptake in the struvite based streams. By using a low Mg:P ratio, the micro-pollutants had the opportunity to be adsorbed to the 16% amorphous impurity content in the struvite. Consequently, if the purity is improved via increasing the Mg:P ratio, the micro-pollutant uptake will be lower. In combination with zeolite in SZM, the crystallisation of struvite improved, resulting in the lowest uptake of 4 out of 5 micro-pollutants (Table 4).

The uptake of all the micro-pollutants except diclofenac into SB and biochar fertilisers was relatively high, ranging between ~30% and 90% uptake. This is due to the organic composition of the biochar, as the hydrocarbon micro-pollutant molecules are able to form hydrophobic interactions that are not possible with inorganic zeolite and struvite (Spokas et al., 2012). The high $\log K_{ow}$ values (Table S1) indicate high hydrophobicity for the majority of the pharmaceuticals, with the exception of sulfamethoxazole ($\log K_{ow}$ 0.89). However, the uptake of sulfamethoxazole into biochar-based fertilisers was the second highest since there was no direct correlation between hydrophobicity and uptake. Therefore, in addition to hydrophobic interactions, pharmaceutical adsorption may also be controlled by the high amount of functional groups on the

electrostatic interaction with the surface charge (Anderson, 2000). In the basic environment of the urine (pH 9.4–9.8), the micro-pollutants with higher pK_a than NH_4^+ (pK_a 9.24, Table S1 in the supplementary information), carbamazepine (pK_a 13.9) and propranolol (pK_a 9.24) are more basic and could compete with NH_4^+ . The remaining micro-pollutants with lower pK_a values are more likely to be deprotonated by the more basic species in solution. The uptake of the remaining micro-pollutants is therefore more likely to be due to a different mechanism.

Yousef et al. (2011) found that phenol adsorption onto zeolite was enthalpy driven and physical in nature. Zeolites with less Al^{3+} substitution of Si^{4+} have a lower capacity for NH_4^+ uptake, but are more hydrophobic and could thus sorb the uncharged organic micro-pollutants (Anderson, 2000). The pharmaceutical micro-pollutants are also slightly polar, which strengthens dipole interactions with the zeolite surface. However, selectivity could arise from size exclusion by the zeolite micro-pore, which reduces the effective surface area for adsorption onto zeolite. The comparatively reduced uptake to SZM may be partially due the presence of struvite crystals, blocking the zeolite pores and reducing the number of adsorption sites.

Finally, the spiked micro-pollutant concentrations were based on predicted urine concentration (PUC) values calculated by Escher et al. (2006), which were representative for the selected

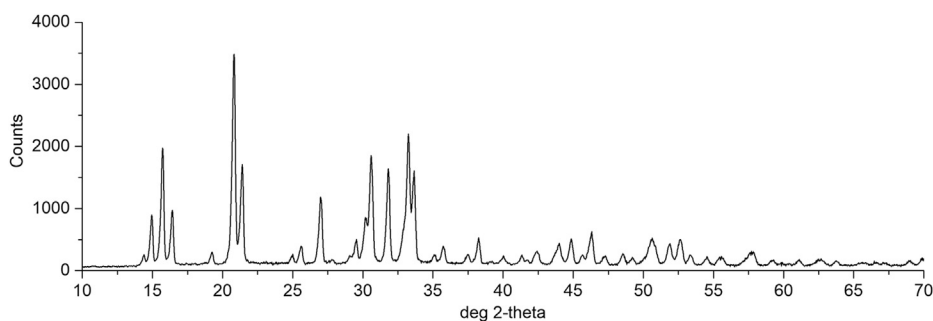


Fig. 1. XRPD analysis of struvite produced from human urine, exhibiting a crystalline structure consistent with literature.

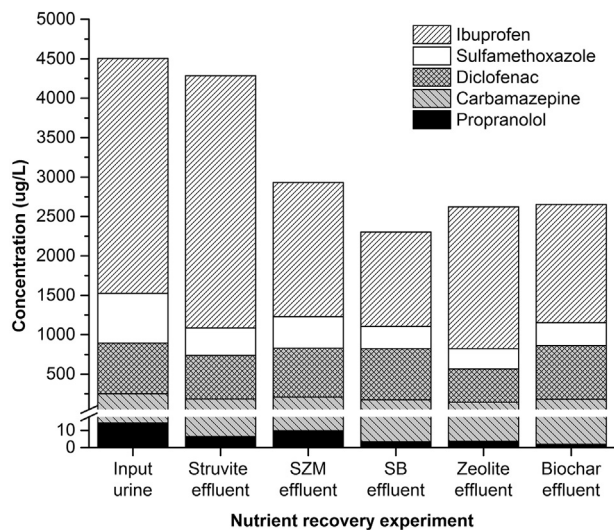


Fig. 2. Pharmaceutical micro-pollutant concentrations in the input urine/influent stream and the different effluent streams.

pharmaceutical micro-pollutants. Additional micro-pollutants are also often present in human urine, such as hormones and other pharmaceuticals. Indeed, the following chemicals, which were not spiked to urine, were detected by HPLC-MS/MS in trace amounts: salicylic acid, atenolol, caffeine, gabapentin and paracetamol, which can therefore have only a minor influence on the sorption results.

3.5. Micro-pollutant bioaccumulation in tomato fruit

Next, the bioaccumulation of five common pharmaceuticals (propranolol, diclofenac, sulfamethoxazole, ibuprofen and carbamazepine) was determined by harvesting the tomatoes fertilized with the various fertiliser streams and analyzing these with HPLC-MS/MS. No pharmaceuticals were detected in the tomatoes produced with the struvite, SB, SZM and Biochar fertilizers (detection limit 0.001 mg/kg). In the tomatoes fertilized with zeolite, only a minimal amount of carbamazepine (~0.003 mg per kg tomato fruit) was detected. Therefore, we can conclude that the bioaccumulation was at most $\leq 0.0003\%$ for the micro pollutant carbamazepine and for the others below 0.0001% under the circumstances of this study, which is the detection limit.

The harm to human health that could be caused by this micro-concentration of carbamazepine is assessed using toxicology data (Fig. 3). Several different limits are available in the literature: 3 mg/kg/day is the lowest dose of carbamazepine at which an adverse effect is observed (LOAEL), from which a toxicological reference value (TRV) or tolerable daily intake of 0.033 mg/kg/day can be derived (Houeto et al., 2012). With a mean uptake of 0.003 mg carbamazepine/kg DW tomato biomass, an adult weighing 67 kg would need to consume 220,000 kg of dried tomatoes per day in order to reach the LOAEL limit, which is 10 million times more than the average daily intake of a citizen of the United States (Fig. 3).

An alternative to using LOAEL and TRV values is to calculate an acceptable daily intake (ADI) value by applying a safety factor of 100 to the minimum therapeutic dose (Carter et al., 2014; shown in the Supporting Information). Since none of the other pharmaceuticals has been detected, the acceptable daily intake is based on the margin of error of the instrument, 0.001 mg/kg tomato DW (Table 5). The total dry tomato biomass calculated in each case of taking the detection limit as the value is at least a million times higher than what would reasonably be consumed per day for each

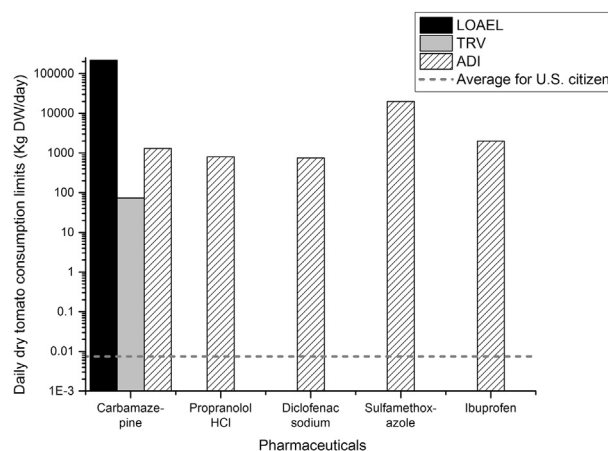


Fig. 3. The amount of tomato dry weight which has to be consumed daily to reach the LOAEL, TRV or ADI levels of the spiked pharmaceuticals (calculated in the Supporting Information) compared to the daily average consumption of a U.S. citizen.

pharmaceutical. It can therefore be concluded that levels of micro-pollutants detected in the tomatoes are not harmful to human health and the tomato fruit are safe for human consumption. From a health safety point of view, the struvite/sorbent fertilisers derived from spiked human urine are hence acceptable for use in tomato production.

The uptake of pharmaceutical micro-pollutants in the struvite is high due to the amorphous impurities and the low Mg:P ratio for the precipitation. When the crystallisation process is optimized, the amount of taken up pharmaceuticals will be reduced resulting in an even lower bioaccumulation in the fruits.

In addition to the uptake of pharmaceuticals in fruits and the roots, the accumulation of the pharmaceuticals in the soil and ground water has previously been studied. The uptake into plants could increase over time if there is an accumulation of micro-pollutants in soils, or that pharmaceutical concentrations could affect bacterial or mycorrhizal organisms in the soil (Hillis et al., 2008). A complex but important task for further research would be to carry out an analysis of the accumulation of the pharmaceuticals in other parts of the plant, roots and leaves, and the soil and aqueous environment. In this case, human urine is used, but struvite is currently mainly precipitated out of waste streams, such as wastewater. These sources increase the risk of contaminations with several types of micro-pollutants as other pharmaceuticals, personal care products, hormones, pesticides and industrial chemicals.

4. Concluding remarks

Struvite-based fertilisers resulted in effective P-recovery and combination with sorbent materials, zeolite and biochar, allowed the N-recovery to increase, which is related to the presence of competing ions. The bioaccumulation in tomato fruit biomass from each of the contaminated fertilisers in a crop trial was at most $\leq 0.0003\%$ and far below the acceptable daily intake (ADI) levels calculated from the literature. With an uptake of 0.003 mg carbamazepine/kg DW tomato biomass, an adult weighing 67 kg would need to consume 73 kg of dried tomatoes per day in order to reach the TRV limit (Table 5), which is 10 thousand times more than the average daily intake of a citizen of the United States. To reach the lowest toxicity limit (LOAEL₂) over 220,000 kg dried tomatoes would need to be consumed in one day.

Nutrient recovery into struvite-sorbent fertilisers therefore has

Table 5

Tomato biomass containing the acceptable daily intake (ADI), calculated as a factor of 100 of the minimum therapeutic dose for a 67 kg adult using the maximum biomass concentrations of all pharmaceutical micro-pollutants.

Micro-pollutant	Micro-pollutant tomato biomass concentration (mg/kg)	Tomato dry biomass to reach ADI limit (kg DW/day)
Carbamazepine	0.003 ± 0.001	1300
Propranolol-HCl	0.000 ± 0.001	800
Diclofenac sodium	0.000 ± 0.001	750
Sulfamethoxazole	0.000 ± 0.001	20,000
Ibuprofen	0.000 ± 0.001	2000

potential as a safe method to re-use N and P from human urine. As tomato plant leaves and roots are not consumed by humans, this is unlikely to affect human health, however it is advisable to carry out further research in order to determine the risk of using contaminated plant biomass for other purposes, such as compost or animal feed. Therefore, besides the uptake of pharmaceuticals in fruits, the accumulation of the pharmaceuticals in the roots, the soil and ground water should be investigated. This study has shown that the health risk from pharmaceutical micro-pollutants, transferred from human urine to struvite and sorbent-based fertilisers, into tomato crop fruit is insignificant.

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Nomenclature

ADI	Acceptable daily intake
Ca	Calcium
DW	Dry weight
HPLC-MS/MS	High-performance liquid chromatography (HPLC) with tandem mass spectrometric (MS/MS) detection
LOAEL	Lowest-observed-adverse-effect level
K_a	Acid dissociation constant
K_{ow}	The octanol/water partition coefficient
Mg	Magnesium
$MgCl_2$	Magnesium chloride
N	Nitrogen
NH_4^+	Ammonium
P	Phosphorus
PLM	Polarising light microscope
PUC	Predicted urine concentrations
SB	Fertiliser with struvite crystallisation & N adsorption onto biochar
SZM	Fertiliser with struvite crystallisation & N adsorption onto zeolite
TRV	Toxicological reference value
XRPD	X-ray powder diffraction

Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.watres.2018.01.017>.

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