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DIPLOMA THESIS

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## **Diploma Thesis**

**Behaviour of selected micropollutants in the soil  
environment**

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**CZECH UNIVERSITY OF LIFE SCIENCES PRAGUE**

Faculty of Environmental Sciences

# **DIPLOMA THESIS ASSIGNMENT**

Oleksandra Rieznyk

Nature Conservation

Thesis title

**Behavior of selected micropollutants in the soil environment**

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## **Objectives of thesis**

Pharmaceuticals as one of the micropollutant type may enter soils due to the application of treated wastewater or biosolids. Their leakage from soils towards the groundwater, and their uptake by plants is largely controlled by sorption and degradation of those compounds in soils. The aim of this work is therefore to evaluate the sorption of selected pharmaceuticals in seven soils, to quantify the parameters of sorption isotherms and to evaluate the influence of the soil environment on the sorption of selected compound.

Hypothesis: Parameters describing the sorption of pharmaceuticals in soil can be estimated based on knowledge of basic soil properties.

## **Methodology**

Literature review will focus on both sorption and degradation behavior of these compounds in the soil environment. The practical part of the work will only concern the sorption of substances in the soil. A batch equilibrium method will be used to evaluate sorption isotherms for six pharmaceuticals and seven soils. Sorption isotherms will be described using the Freundlich equation. Multiple linear regressions will be applied to develop pedotransfer functions to estimate sorption parameter using basic soil properties. If applicable, previously developed models to estimate sorption parameters will be also tested. If necessary, the models will be further modified to best describe both new and old data.

## The proposed extent of the thesis

50

## Keywords

Soil, micropollutants, pharmaceuticals, sorption, degradation, pedotransfer functions, multiple linear regression

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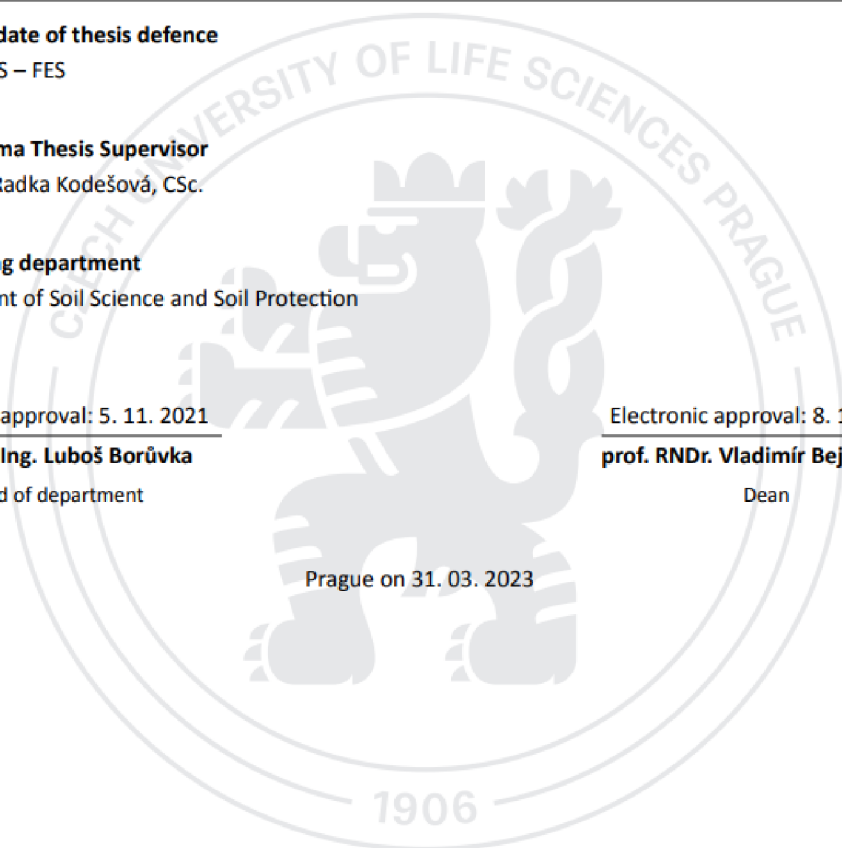
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Dean

Prague on 31. 03. 2023



### **Declaration**

I declare that I have worked on my master's thesis titled " **Behavior of selected micropollutants in the soil environment** " by myself and I have used only the sources mentioned at the end of the thesis. As the author of the master's thesis, I declare that the thesis does not break any copyrights.

In Prague on 31.03.2023

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I would like to thank Professor Ing. Radka Kodešová, CSc., PhD Miroslav Fer, PhD Ales Klement, PhD Antonin Nikodem for their advice and support during my work on this thesis.

# Chování vybraných mikropolutantů v půdním prostředí

## Abstrakt

Léčiva jsou jedním z druhů mikropolutantů, které kontaminují životní prostředí a mohou být toxické pro živé organismy. S vyčištěnými odpadními vodami nebo čistírenskými kaly se tyto látky mohou dostat do půdy, kde se mohou zdržovat a hromadit, nebo jít s dešťovým proudem a kontaminovat spodní vodu nebo se hromadit v plodině v důsledku příjmu rostlin. Cílem této práce je studovat sorpci šesti léčiv – atorvastatinu, lamotriginu, memantinu, sertralínu, telmisartanu a venlafaxinu v 8 různých půdách. Pro každou sloučeninu byly vyhodnoceny Freundlichovy sorpční izotermy a také korelace vlastností půdy se sorpčními koeficienty  $K_F$ . Na základě lineární regrese byly navrženy rovnice pro predikci sorpčního koeficientu pro každou látku.

**Klíčová slova:** Půda, mikropolutanty, léčiva, sorpce, pedotransferové funkce, vícenásobná lineární regrese

## Abstract

The pharmaceuticals are one of the kinds of micropollutants that contaminate the environment and may be toxic for the living organisms. With treated wastewater or sewage sludge these substances may get to the soil where they may stay and accumulate, or go with the rainflow and contaminate the groundwater or accumulate in the crop due to the plant uptake. The aim of this work is to study the sorption of six pharmaceuticals – atorvastatin, lamotrigine, memantine, sertraline, telmisartan and venlafaxine in 8 different soils. The Freundlich sorption isotherms were evaluated for each compound as well as the correlation of soil properties with the sorption coefficients  $K_F$ . Based on linear regression the equations for prediction of the sorption coefficient for each substance were suggested.

**Key words:** soil, micropollutants, pharmaceuticals, sorption, pedotransfer function, multiple linear regression

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# 1. Introduction

## Micropollutants in Environment and their sources

Micropollutants are defined as chemical substances produced by people that occur in the environment or in living organisms in low, sometimes trace concentrations. However, they may obtain different level of toxicity and cause negative effect on the environment and living organisms including humans. These substances may be pharmaceuticals, personal care products, stimulants, hormones, artificial sweeteners, pesticides, detergents, industrial chemicals, trace metals, microplastic, etc [Yang et al., 2022, Abbasi et al., 2022, Chavoshani et al., 2020, Petrie et al. 2015]

At the beginning of the millennium three common vulture species showed a catastrophic decline in India and Pakistan. Started in the late 1990 and early 2000 the death rate led to the disappearance of over 95% of the birds' population. The result of the research showed that there was a correlation of the death rate of the birds and the level of *Diclofenac*, anti-inflammatory pharmaceutical residuals in the livestock, which were scavenged by the vultures. [Oaks et al. 2004] This case showed how the population of high abundance can be practically eliminated on the vast territories in a short period of time with a common drug that is vastly used in veterinary and medicine in many countries. Such case can be compared with the DDT pesticide impact on birds that has been studied for many decades and which caused the significant shrinkage of some birds' populations. [Watson et at., 2004; Padayachee et al., 2023] These two global events are the evidence that the exposure to even a low concentration (less than 1 mg kg<sup>-1</sup> of living organism body mass) of chemical micropollutants that are released to the environment without proper study of their probable toxicity for wildlife, is able to have a strong negative impact on the ecosystems.

The rising concern stimulated the research of the issue. The publications about pharmaceutical micropollutants date back to the end of the 20<sup>th</sup> century. Every year more works, studying the behavior of different medical chemicals in the natural environment appear. However, the more the study goes the more obvious it is that there is a great variety of substances and their metabolites that may occur in different concentrations in every possible physical condition in the environment so

the studies of the behavior of chemical micropollutants are still up to date. Many authors still address the problem as the “recent” or “new”.

The sources of contaminants are multiple, various and differ from country to country. The chemical micropollutants come mainly from the municipal and industrial wastewater and water treatment plants. Thus, much research is focused on the micropollutants in water. This work is focused on pharmaceutical micropollutants. Treated and untreated wastewater (especially from the hospitals and field hospitals) that includes excretions of patients is considered to be the main source of pharmaceutical contaminants [Cardoso O., 2014; Khan et al., 2019]. In study of 164 substances (including 96 pharmaceuticals) 119 were detected in every sample of water from wastewater treatment plant. The most common were anti-inflammation, antiepileptic and antidepressant medicines [Golovko et al. 2021]

These pharmaceutical substances are widely used everywhere and are ubiquitous. They are commonly divided into two groups: the pharmaceutically active compounds, like antibiotics, anti-inflammatories, analgesics and other therapeutics medicines; and endocrine disrupting compounds, which include hormones (natural and synthetic), steroids, and other medicines that influence the human endocrine system [Luis et al., 2018].

Another important group of pharmaceutical micropollutants are antibiotics. Their presence in soil is not only toxic for microbiota and influences directly the composition of such communities but also causes the development of resistance genes to antibiotics in bacteria. With the gene flow such genes may spread to other bacterial populations making them not sensitive towards the antibiotic medicines. This threatens indirectly the effectiveness of medical treatment of animals and humans. [Liu et al. 2018] The impact of antibiotics on microbiota depends on the kind of antibiotic, properties of soil and the exposure time. [Zhi et al. 2019] Inducing of antibiotic resistance genes in soil bacteria communities is also considered a kind of pollution. This not only may affect negatively the human

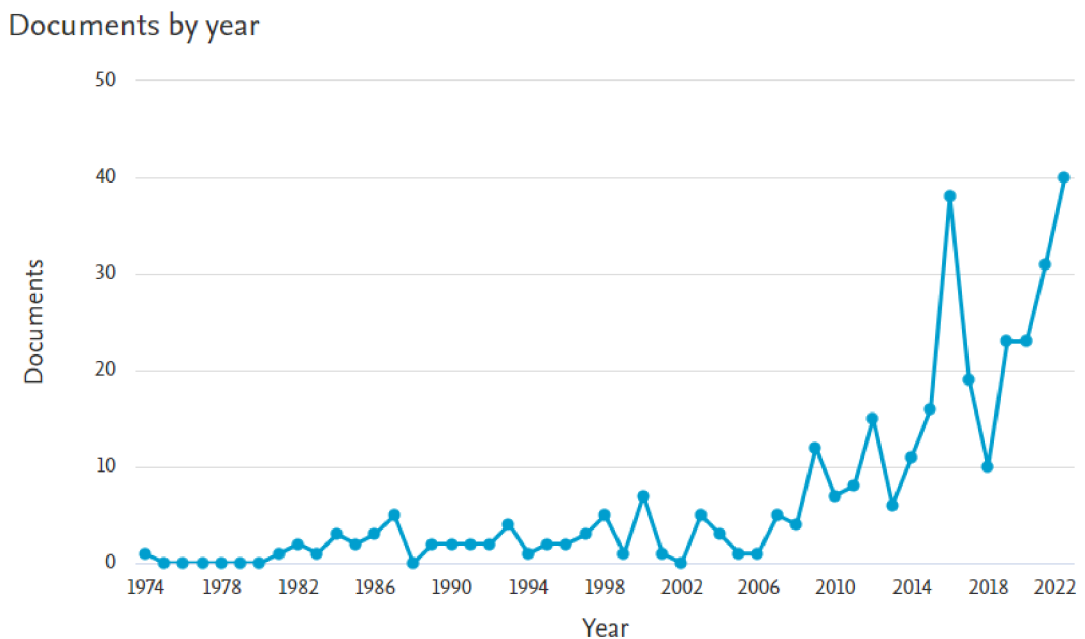


healthcare system but also decrease the level of biodegradation of antibiotics in soil [Grenni et al., 2018]

The pharmaceutical chemicals may accumulate in significantly high concentration and stay in soils for many years. These substances were designed to be biologically active so they may be a threat to different living organisms including humans. Pharmaceuticals may occur in food with agricultural plants uptake. Thus, it is essential to understand how these micropollutants behave in different soils under different conditions.

The number of publications devoted to micropollutants in soil is increasing every year starting from 2010 (Figure 1). This shows the growing interest of scientists in this topic.

Figure 1. Number of documents published in Scopus per year with the key words “micropollutants” and “soil”.



However, the number of publications focused on soils for the last 5 years is still relatively lower than of the pollutants in water (Figure 2, Figure 3). Combined with the growing interest to the topic this allows to assume that this area requires more attention and research nowadays.

Figure 2. VOSviewer visualization of the frequency and co-occurrence of publications (with minimal citation frequency 3) based on the search on Scopus for “micropollutants” key word, limited to 2019-2023 years and Environmental Sciences subject. The frequency and network for “water”, “soil” and “sorption” are zoomed in.

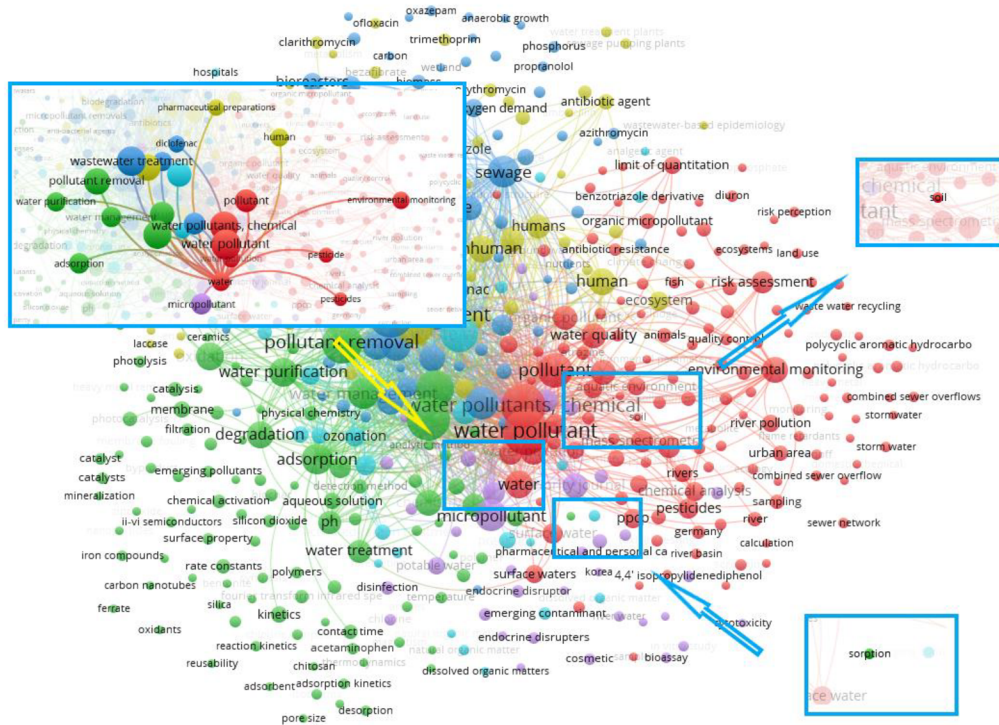
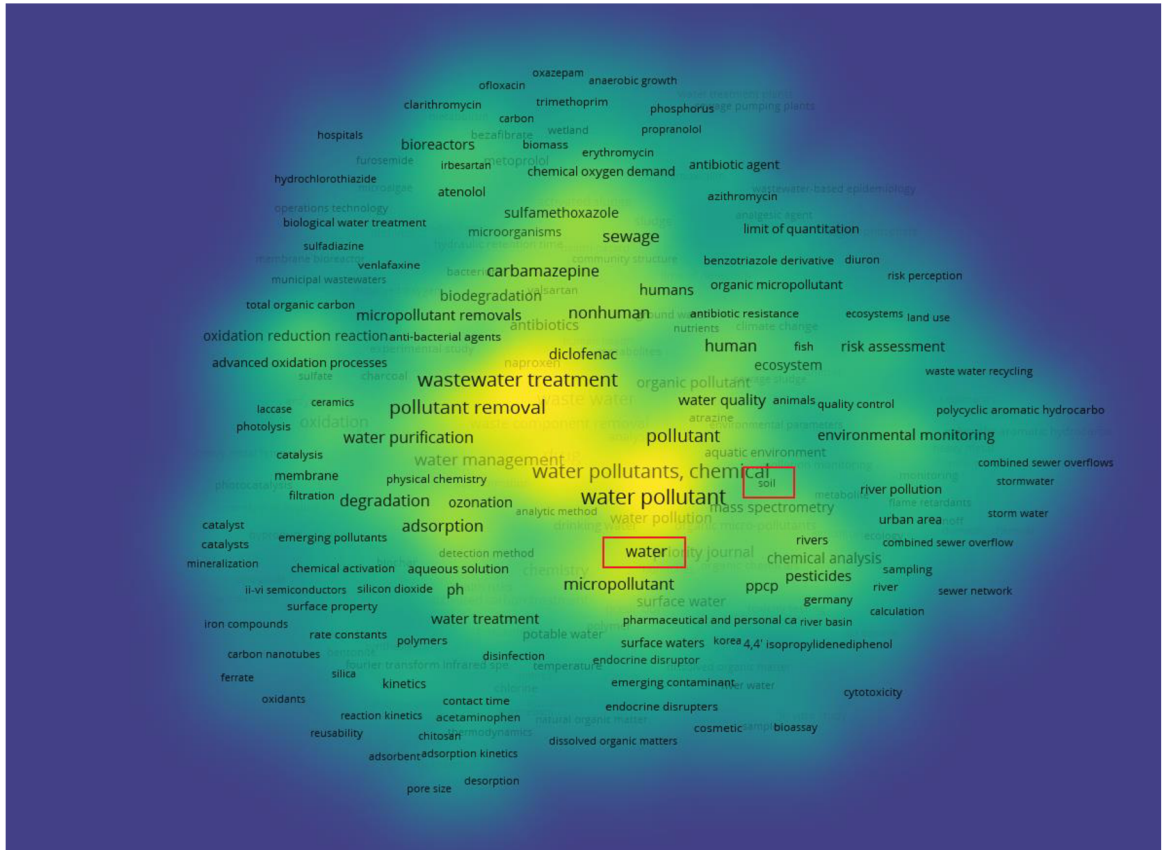


Figure 3. VOSviewer visualization of the density of key words occurrence based on the Scopus search for “micropollutants” limited to 2019-2023 years and Environmental Sciences subject.



This work is focused on experimental study of the behavior of the chosen pharmaceutical micropollutants in different types of soil. The sorption will be measured for each substance in each soil. This will help to understand which parameters of soil correlate with sorption of pollutants' molecules. At the end the equations for prediction of the sorption coefficient will be developed.

## **2 Literature Review**

### **2.1 Contaminants from Wastewater**

Pharmaceuticals are substances that are used on an everyday basis for humans and animals. They are not fully processed in the organisms and are excreted to sewage systems or directly to the environment, becoming the source of anthropogenic pollution. Wastewater treatment may not completely remove them so the pharmaceutical chemicals or their metabolites can get to the soil from the wastewater that is used for irrigation. In some countries the reclaimed wastewater that is used for the agricultural fields is not treated at all. One of the largest untreated wastewater irrigation systems is in Mexico where 65 pharmaceutically active compounds were found [Luis et al., 2018; Lesser et al., 2018].

Another study took place in Saudi Arabia and included research on the wetlands influenced by treated and untreated wastewater near the city situated next to the oil mining site with population over 1 million people. The irrigation with reclaimed water in the country is unavoidable due to the water shortage in the arid zone. The residues of 24 pharmaceuticals were found in the lakes and irrigation canals which get wastewater from farms, factories and residential areas. Atorvastatin, caffeine, etoricoxib, lorazepam, metformine, ofloxacin, paracetamol, salicylic acid and tramadol were in every sample of water. [Picóa 2019].

A large scale research that took place in Sweden in 2019 year studied the occurrence of 164 pollutants in wastewater samples including 96 pharmaceuticals. The most common ones with the highest concentration were 15 pharmaceuticals: salicylic acid, diclofenac, losartan, valsartan, venlafaxine, oxazepam, lamotrigine, carbamazepine, tramadol, hydrochlorothiazide, theophylline, furosemide, ranitidine, bicalutamide, and metformin). Some wastewater treatment plants were more efficient in removing the pharmaceuticals than the others. The new technology of waste water treatment was recommended for the area. [Golovko et. al., 2021]

Although the risk of using wastewater for agricultural irrigation seems to be high after so much research in the occurrence of the large number of pharmaceuticals, overpopulation, urbanization and climate change lead to water resources shortage that makes more and more regions consider reclaimed wastewater for irrigation in agriculture. In European Union for countries with the Mediterranean climate like Spain a significant amount of reclaimed water using for irrigation is predicted by 2025 [Beltran et al, 2020].

## **2.2 Contaminants from sewage sludge**

Sewage sludge is a kind of solid or semi-solid substance that is left after wastewater treatment. This is a by-product of the process, and it is now being produced in large quantities all over the world. Only in China the amount of raw sewage sludge (containing up to 80% water) will have gone up over 90 megatons by 2025 [Guo et al. 2021]. In the European Union this amount is expected to reach 60 megatons per year in the nearest future [Ivanova et. al., 2018]. In the context of circular economy and sustainable development this substance is being used not only for agriculture but also in other spheres of human activity. For example, to improve the concrete mixtures characteristics for non-heavy concrete constructions [Singh et al. 2021]

To be used as an organic amendment in agriculture the sewage sludge should be processed or stabilized as the raw material contains pharmaceutical micropollutants and pathogenic germs (including antibiotic resistant bacteria) which if got to the agricultural soil and further got uptaken by plants may cause health problem in humans and animals. [Laternus et al., 2007]. Even after treatment sewage sludge contains some organic and non-organic elements that are good for plants growing. It is widely used in agriculture for high concentration of phosphorus and organic matter. Moreover, this method of sewage sludge management fits perfectly with the circular economy implementation. There is a patent issued in Poland in 2019 [Głodniok et al., 2019] to produce the granulated fertilizer for the agricultural use where stabilized sewage sludge is mixed with lime, dolomite, gypsum cellulose and dried, which prevents the presence of parasites in the granules. However, there is still not enough information about the presence of pharmaceutical micropollutants

and the ways of their spreading to the soil from such fertilizer. [Rehman et al. 2018; Bolesta W, et al., 2022; Kaszycki P. et al., 2021]

Apart from being used in agriculture, the treated or stabilized sewage sludge is also spread on the soil as a fertilizer in gardens and in the forests. However, together with the substances that are beneficial for the plants' growth, even the treated sewage sludge includes a lot of pharmaceutical contaminants. They are due to their ecotoxic threat and emission to environment cause high interest among the researchers since the 80s [Ivanova et. al., 2018]

### **2.3 Plants uptake of the micropollutants**

Micropollutants from soil may get to the human and animals food chain via plants. This way is considered to be one of the most possible one. Among the detected plants pollutants there were some pesticides, pharmaceuticals and personal care products, stimulators. Fenthion sulfone, Salicylic acid, Methylparaben, Bisphenol-A were among the most common according to Picó et al. in 2020.

The pharmaceutical micropollutants can contaminate crops and may accumulate in different parts of plants. The sewage sludge from two wastewater treatment plants (A and B) with different treatment capacity in the Czech Republic was used as a soil amendment in a greenhouse where Spinach (*Spinacea oleracea L.*) was planted with stable temperature and humidity. Out of 69 micropollutants tested there were 45 found in sewage sludge and soil. The plants showed the selective uptake of the substances and their different distribution in plants parts. The most common was carbamazepine that accumulated in leaves of the plants and was included in the plants' metabolism. The properties of soils influenced the uptake of some substances, so in soils with higher pH and basic cation saturation the main substance that was accumulated was sertraline, which was accumulated mainly in roots and leaves. The further study of sources of micropollutants in soils and plants is necessary as well as deeper research in behaviour of the chemicals in soil-water-

plant systems that include more different kinds of soils and plants. [Kodesova et al., 2019]

The lettuce (*Lactuca sativa var. Tizian*) was planted in pots and irrigated with clean water, wastewater, water with a known mixture of pharmaceuticals and personal care products in low and high concentrations and wastewater with the same mixtures. The study showed that pharmaceuticals that accumulated the most in the plants were sulfamethoxazole (antibiotic) and citalopram (antidepressant). The concentration of micropollutants in leaves was significantly higher than in roots. The highest concentration of micropollutants was detected in plants irrigated with wastewater with the highest concentration of chemicals. During the second year of the experiment new lettuce was planted in the same soil in the pots to study the impact of the micropollutants accumulation in soil. Regardless the irrigation conditions the biomass of plants of the second year was significantly smaller than of the first year [Bigott et al., 2022].

The behavior of pharmaceutical micropollutants in soil-plant environment is complex. The chemicals can be sorbed by soil, get degraded and change their properties under the influence of biological or climatic factors, they may react with each other and change their properties and toxicity. Recently new mathematical models for predicting the contaminants behavior in soil-plant complex were created. These models not only take into consideration the pollutants properties but also the properties and functions of the plants' membranes, active transport of solutions in the plants and the chemical dissociation [Brunetti et al. 2022] Open for the further improvement, more factors describing the soil properties, (especially the pH), plants mechanics (plants hydraulic properties) and the micropollutants' behavior may be included to the model which is going to predict the pollution of the plants and thus the level of threat to human health with the high level of accuracy.



## **2.4 Behavior of contaminants in soil**

When the micropollutants get into the environment they can be sorbed by the soil particles, transported to groundwater from soil or to other water bodies or they can dissipate. The degradation often happens due to the activity of the soil microorganisms. The molecules of substances or their products of degradation can also be absorbed by plants and thus get included into the food chain of animals and people.

### **Sorption**

Sorption is the ability of soil to attract and keep the molecules of micropollutants in soil-aqueous systems. The process can be described as an accumulation of the compound that was dissolved in liquid on the surface or inside the solid. Sorption is a general term for adsorption and absorption. The adsorption is the adhesion of the particles on the surface of the soil substrate. The absorption is the intake of the particles in the soil substrate. The process opposite to sorption is desorption, when the chemical substance is released from the substrate it was sorped or absorbed to.

The micropollutants may occur in several types: non-ionic molecules, cations (positively charged molecules), anions (negatively charged molecules) and zwitterions (the molecules with positive and negative charge) [Schaffer et al., 2015]. Depending on the ionic properties of the pollutants, sorption may occur due to the weak Van der Waals interaction, hydrogen bonds, hydrophobic interactions or stronger electrostatic interactions. The charge of the soil is also important (i.e., clay is negatively charged, as well as the organic matter, abundance of which defines the general charge of the soil type). The sorption product is also affected by pH, temperature, concentration of the substance, time of exposure. This makes a variety of sorption complexes in soil [Sparks 2019] and prediction of the behavior of micropollutants more complex. Thus, the sorption research is often evaluated for several soils with different properties, as for example with thirteen different soils in the research of Kodesova et al, 2015.

Some pharmaceutical micropollutants like irbesartan, citalopram, fexofenadine may change their type from non-charged to ionic and zwitter ionic depending on the pH of the soil and the constant of dissociation pKa of the substance. Such substances need specific research including modeling of different conditions to observe the sorption rate of all their forms. [Klement et al., 2018]

The adsorption of some micropollutants is highly influenced by the abundance of soil organic matter (SOM). It is a highly variable group of compounds that influence the behavior of mainly charged microelements. The sorption of sulfonamides, the highly polar antibiotic, was reported to depend significantly on the abundance of SOM in soil [Ahmed et al., 2016]. Higher nutrition content, more developed structure of the soil like in the Chernozem are characterized with higher dissipation rate of some antibiotics (trimethoprim, sulfamethoxazole, clindamycin, clarithromycin) as shown in the study by Kodešová et al. in 2016.

### **Transportation**

The ability of the pollutants' molecules to be carried in soil shows how the substance can get from the surface layers of soil deeper to the ground and the possibility of the pollutants to get to groundwater or to be carried with the runoff or with a subsurface flow to the rivers and lakes.

The studies carried by Park et al. in 2016 showed how the sulfonamide antibiotics can be transported in the field during the rain events. The field study combined with the statistical models showed that during the dry season they stayed in the upper layer of the soil but during the rain the antibiotics can be transported deeper to the soil very fast which rises the chances of them getting to the groundwater.

## **2.5 Models and methods**

To understand and fully assess the environmental risk of micropollutants it is essential to know and predict the behavior of the substances in the environment. Multiple regression models where the soil properties are the independent values and

the sorption coefficient is a dependent one are used to predict the sorption of the substance in the soils [Kodesova et al., 2015]

To understand and predict the behavior of the exact substance in some physical and chemical conditions mathematical models that apply the information on the studied substance from the database are used. Aside from the sorption coefficients the models require the input of soil parameters (pH, organic matter proportion) and the characteristics of the substances. The estimation is made on the QSAR (Quantitative Structure-Activity Relationship) equations. [Binetin and Devillers, 1994; Hodges et al. 2019]

Choosing the right model that would predict precisely the behavior of micropollutants in soil could save time and cost less than experimental calculation of the sorption coefficient in each case. This is a difficult task as many parameters should be considered. The presence of ionizable substance requires including additional parameters to the model. Thus, with all the modern understanding of the factors that influence the behavior of the pharmaceutical polluting substances in soil. More studies should be conducted to create more precise models, especially for the variety of ionizable pharmaceutical pollutants. [Carter et al., 2020]

In case when the uptake of micropollutants by plants is studied more complex models are developed. Such models may not only describe the properties of soil that influence the behavior of micropollutants it also reflects the properties of different plant tissues (phloem, xylem) and transport or accumulation of water, neutral and electrolyte molecules of micropollutants in roots, stems, leaves and fruits of the plants. In 2022 Brunetti et al. worked on such a mathematical model that described transfer of five ionizable pharmaceutical micropollutants in soil and pea plants. The predictions of the model were compared with the experimental measurements and showed a high accuracy except a few measurements. The study also revealed that pH plays crucial role in uptake of micropollutants by plants. The further development of the model will include more precise measurement of the most

important parameters like soil pH, plants hydraulics, etc. and the influence of other components on the micropollutants' behavior. [Brunetti et al., 2022]

Table 1. Selected sorption models from Carter et al., 2020

Reference	Model	Specified Chemical Range of Applicability	Model Training Set
Bintein and Devillers, 1994	$\log K_d = 0.93 \log K_{ow} + 1.09 \log f_{oc} + 0.32 CFa - 0.55 CFb' + 0.25$	$3.07 \leq pKa \leq 8.85$ b	Organic chemicals (not including pharmaceuticals)
	Where:	$0.12 \leq \log K_{ow} \leq 6.42$ b	( $n = 229, r^2 = 0.96$ )
	$CFa = \log(1/(1 + 10^{pH-pKa}))$		
	$CFb' = \log(1/(1 + 10^{pKa-(pH-2)}))$		
Sabljić et al., 1995	$\log K_{OC} = 0.10 + (0.81) \log K_{ow}$	$1 \leq \log K_{ow} \leq 7.5$	Hydrophobic chemicals ( $n = 81, r^2 = 0.94$ )
Sabljić et al., 1995	$\log K_{OC} = 0.32 + (0.60) \log K_{ow}$	$1 \leq \log K_{ow} \leq 7.5$	Organic acids ( $n = 23, r^2 = 0.87$ )
Kah and Brown, 2007	$\log K_d = 0.13 \log D + 1.02 \log OC - 1.51$	$1.97 \leq pKa \leq 4.94$ b	Ionisable pesticides
		$1.2 \leq \log K_{ow} \leq 4.3$ b	( $n = 90, r^2 = 0.39$ )
Franco and Trapp, 2008	$\log K_{OC} = \log(f_{neutral} 100.54 \cdot \log P_n + 1.11 + f_{ion} 100.11 \cdot \log P_n + 1.54)$	$0 < pKa < 12$	Organic acids (including 5 basic pharmaceuticals)
		$-2.18 < \log P_n < 8.50$	( $n = 62, r^2 = 0.54$ )
Franco and Trapp, 2008	$\log K_{OC} = \log(f_{neutral} 100.37 \cdot \log P_n + 1.70 + f_{ion} 10^{pKa} 0.65 \cdot f_{ion} 0.14)$	$2 < pKa < 12$	Organic bases (including 5 basic pharmaceuticals)
		$-1.66 < \log P_n < 7.03$	( $n = 43, r^2 = 0.76$ )
Franco et al., 2009	$K_{OC} = \frac{(100.54 \cdot \log P_n + 1.11)}{(1 + 10^{(pH_{soil} - 0.6 - pKa)})} + \frac{(100.11 \cdot \log P_n + 1.54)}{(1 + 10^{(pKa - pH_{soil} + 0.6)})}$	Monovalent acids $pKa < 12$	Organic acids
		$-2.18 < \log P_n < 8.50$	( $r^2 = 0.70$ )
Droge and Gross, 2013	$K_d = K_{CEC,CLAY} \cdot CEC_{CLAY} + f_{OC} \cdot DOC_{IE}$	Strong bases (monovalent)	Organic cations
	$= K_{CEC,CLAY} \cdot (CEC_{SOIL} - 3.4 \cdot f_{OC}) + f_{OC} \cdot DOC_{IE}$		(including pharmaceuticals) c
	Where:		
	$\log K_{CEC,CLAY} = 1.22 (\pm 0.15) V_x - 0.22 (\pm 0.05) N_{Ai} + 2.09 (\pm 0.05)$		

<sup>a</sup> Model presented in paper calculates  $\log K_p$ . As this is defined as the soil sorption coefficient, which is what  $\log K_d$  has been reported as in this analysis,  $\log K_p$  has been changed to  $\log K_d$  for consistency; <sup>b</sup> Applicability domain not specified, calculated from information provided on physicochemical properties of training set chemicals; <sup>c</sup> Not a training set, model was developed using sorption data for a range of organic cations;  $\log K_d$ , (log) soil sorption coefficient;  $\log K_{OC}$ , (log) soil sorption coefficient normalised to organic carbon;  $\log K_{ow}$ , (log) octanol-water partition coefficient;  $pKa$ , negative log of the acid dissociation constant;  $f_{oc}$ , fraction organic carbon in soil;  $CFa$ , concentration of anionic species in relation to pH;  $CFb'$ , protonated species concentration in relation to pH;  $f_{neutral}/f_{ion}$ , fraction of nonionised and ionic species, respectively calculated according to Franco and Trapp 2008;  $\log P_n$  and  $\log P_{ion}$ , (log) octanol-water partition coefficient of the nonionised molecule and of the ionic species, respectively, calculated according to Franco and Trapp, 2008;  $\log D$ , (log) lipophilicity corrected to soil pH;  $K_{CEC,CLAY}$  and  $DOC_{IE}$  are the reference sorption coefficient for the clay and organic content fraction in soil, respectively.  $\log K_{CEC,CLAY} = 1.22V_x - 0.22N_{Ai} + 1.09$ ;  $\log K_{CEC,CLAY} = 1.53V_x + 0.32N_{Ai} - 0.27$ .  $V_x$ , molecular volume (L mol<sup>-1</sup>);  $N_{Ai}$ , number of hydrogens bound by the charged nitrogen.

### 3. Objectives and Methodology

#### 3.1 Objectives

Pharmaceuticals as one of the micropollutant types may enter soils due to the application of treated wastewater or biosolids. Their leakage from soils towards the groundwater, and their uptake by plants is largely controlled by sorption and degradation of those compounds in soils. The aim of this work is therefore to evaluate the sorption of selected pharmaceuticals in seven soils, to quantify the parameters of sorption isotherms and to evaluate the influence of the soil environment on the sorption of selected compound. Hypothesis: Parameters describing the sorption of pharmaceuticals in soil can be estimated based on knowledge of basic soil properties.

#### 3.2 Methodology

##### Chemicals

6 Substances (Table 2) were selected among the most frequently found in the studies with the negative impact on the environment described [Golovko et. al., 2021, Kodesova et al., 2015, Kodesova et al., 2019b].

**Atorvastatin** (Lipitor<sup>®</sup>) – is a synthetic medicine, a lipid-lowering agent. It is a dihydroxy monocarboxylic acid of statins group that lowers the lipids production in the organism, reduces the cholesterol synthesis, enhances the metabolism of low-density lipoproteins. In medicine the calcium salt of the substance is used.

It helps to prevent cardiovascular disease and to treat different types of dyslipidemias (hyperlipidemia, hypertriglyceridemia, hypercholesterolemia. It is a standard practice to proscribe this medicine to patients with any cardiovascular event. It is mainly metabolized in the liver and intestine. It causes skin, eye and respiratory system irritation. May cause harm to the fetus and breast-fed children in humans. In high doses it was shown to be carcinogenic in study on animals. However, it is considered to be not mutagenic. A lethal dose for LD50 for mice was reported to be 5000 mg/kg. [DrugBank, PubChem , 2022]

In Krakow, Poland 68 chemicals of emerging concern including pharmaceuticals of different groups and their metabolites were studied in wastewater and sewage sludge at the water treatment plants and in the related rivers. Although the efficiency of water treatment plants was considered to be over 95% the residues of the substances were found in both rivers studied with Atorvastatin among them, which also was described as a substance with the high ability to bioaccumulation and a substance of a high environmental risk [Styszko et al., 2020] The substance was also found and described as one with the highest risk quotients in the study in Lyon, France, where 10 waste water plants were monitored. Atorvastatin in this study was described as the substance that was one of five compounds that contributed the most to the mixed risk quotient of the pollutants in wastewater [Gosset et al., 2021] In China Atorvastatin was found in one third of samples from two rivers where the research took place. Its potential risk to algae in the monitors rivers was assessed as medium. The potential risk of the substance was considered bigger in Lu River than in Zhangxi River. It might be due to Lu River is situated in a more urbanized area than Zhangxi River. Thus, it supports the idea of the city sewage system as the source of the substance in the environment [Tang et al., 2021] In India the substance was first reported to be found in 2016 in wastewater from two water treatment plants in concentration of 395 ng/L. It was one of the most abundant pharmaceuticals and personal care products pollutant found on the two water treatment plants in the study [Subedi et al., 2016] Atorvastatin was also reported to be found in high concentrations in Sri Lanka and it made up 14,620 ng/L. However, it's risk to crustaceans in the wastewater was considered to be medium to low [Goswami et al., 2021]

The ability of Atorvastatin to change its neutral form to negatively charged and its tendency to repel from the negatively charged particles in soil may lead to leaching of the substance to water. This way the pharmaceutical may get to water bodies where its toxic effect has been studied. In studies on fish atorvastatin caused DNA damage after 5 days of exposure at the concentration of 13.00 ng/L [Rocco et al., 2012] Also the abnormal intestine development in amphibians due to the influence of the substance was revealed in 2006. Atorvastatin in EC10 17.8 mg/l (EC50 = 23.1 mg/l) caused abnormal gut colling in *Xenopus Laevis* larvae [Richards and Cole,



2006] Atorvastatin in chronic test applied for 7 days in concentration 5000  $\mu\text{g L}^{-1}$  caused death in *Daphnia magna*. Moreover, heart rate, swimming and reproduction behavior were also affected in a long-term exposure to the Atorvastatin (for 21 days) [Limei Hu et al., 2021] Atorvastatin was shown to be toxic for the *Mugilogobius abei* fish liver in studies where they were exposed to several concentrations of the substance up to 50  $\mu\text{g L}^{-1}$  during 1,3, and 7 days [Wang et al., 2021]

The ability of the molecule to change from neutral to anion at different pH of the environment gives it a possibility to be transported by microplastic. In the form of anion, atorvastatin gets adsorbed to the microplastic from the wastewater. The level of such adsorption is significant for the substance but in river water and in the intestinal liquid of living organisms with high acidity it desorbs into the environment [McDougall et al., 2021]. This way of bioaccumulation is more intense in the case of old microplastic in the sea. Aged plastic particles adsorbed Atorvastatin better and later desorbed it inside the living organisms, that might have swallowed the microplastic with food (sea fish, sea gulls). In such conditions, inside the organism of sea animals, Atorvastatin's bioaccessibility was up to 37.9% at the temperature of 37° C which made warm-blooded animals more vulnerable [Liu et al., 2022]

**Lamotrigine** – an antiepileptic medicine. It's a phenyl triazine (6-(2,3-Dichlorophenyl)-1,2,4-triazine-3,5-diamine) anticonvulsant used to jugulate epileptic seizures and against bipolar disorder. It stabilizes the presynaptic membrane and does not allow the excitation neuromediators to be released. It has a high bioavailability (about 98%) in human organism and is excreted with urine to the environment. Only 10% of the substance gets to the environment as Lamotrigine, 76% Lamotrigine-2-N- glucuronide (conjugation with a glucuronic acid). The lethal oral dose in mice LD50 is 205 mg/kg. The side effects may include severe rash, depression, meningitis and are associated with high doses of the medicine (go.drugbank.com, drugs.com).

In the study of small streams pharmaceutical micropollutants in Hungary Lamotrigine was reported to be one of the most abundant and was found in 76% of

samples from 26 streams. It was also on the list of the substances with the highest environmental risk with the risk quotient  $> 1$  [Kondor et al., 2021]

In study of water contaminants at 15 wastewater plants in Sweden the occurrence of Lamotrigine was also very high, it was found in high concentration with more than 95% of detection frequency [Golovko et al., 2020]. As many as 79% of the ground water samples contained Lamotrigine, concentration of which increased during the stormwater runoff infiltration [Pinasseau et al., 2020]. It was detected in 94% of wastewater samples and 75% of soil samples from the commercial fields in Israel, irrigated with wastewater. In this study Lamotrigine was found in tangerine, orange, leaves of herbs, potato, and carrots. At the same time, it was not detected in tomato, banana, and the fruits of avocado from the fields. These products were going to be sold for food and the authors insisted on routine testing of wastewater used for irrigation of the fields for the presence of micropollutants including Lamotrigine among the most common ones [Mordechay et al., 2021].

The ability of Lamotrigine molecules to ionize at the low pH as well as a small size of the molecule may lead to the sorption of the substance to the soil organisms and plants. The study on lettuce showed that Lamotrigine can be absorbed and accumulated in the roots of the plant and in the leaves of the lettuce. The comparatively small size of the molecules plays the main role in the process [Chuang et al., 2019]. The study of Lamotrigine in soil showed no effect of the substance on the earthworms after 48 hours of exposure. However, the substance was reported to get included to the worms' organism metabolism [Solé et al., 2021]

**Memantine** (*Namenda*) – memantine hydrochloride, a medicine that is used against the Alzheimer's disease. It decreases the excessive excitability of the neurons in brain. According to the World Alzheimer Report 2009 the number of people who suffer this disease doubles every 20 years and may make 115 million by 2050, thus the medicine application may grow responsively. LD50 in mice 437-498 mg/kg (drugbank.com)

Memantine was shown to be stable in the wastewater samples stored for 120 days in -180C. Moreover, the substance was detected in the effluent water from the wastewater treatment plant [Fedorova et al, 2014]. The frequency of detection in wastewater of the substance was 54% in influent and 78% in effluent wastewater from Ceske Budejovice. The origin of wastewater was mainly from the households, only 5% of it was from industrial area with one regional hospital in the town. [Golovko et al., 2014] There was a measurable concentration of Memantine detected near the shores of one of the Fiji Islands in the Pacific Ocean. Its frequency of occurrence there was 7% [Dehm et al., 2021] At the same time there are not many publications concerning the Memantine pollution/ Scopus search returns 12 results starting from 2014 year for “Memantine AND Wastewater” and only 4 results for “Memantine AND Soil”.

Though the cations should have a good affinity to the negatively charged soils, memantine in the study showed the lowest coefficients of sorption of all the substances. Thus, it may be easily desorbed and leached in water where it may have toxic effect on water organisms. The study on *Daphnia magna*, one of the most common model organisms to study the toxic effect of different substances in water, showed that under the influence of memantine the young animals do not perform the phototaxis so actively. This means that the neurotransmitter decreases their locomotion activity in response to a multiple stimulus. The same study also showed that the effect stays even after the memantine has degraded, which means the products of the degradation are still toxic and affect the water organisms [Bedrossiantz, et al., 2020; Bellot, et al., 2021].

**Sertraline** (*Zoloft*) – a selective serotonin reuptake inhibitor, a popular antidepressant; used against anxiety and other psychiatric conditions. The substance has a small molecule. Its LD50 for mice is 419 - 548 mg/kg (drugbank.com)

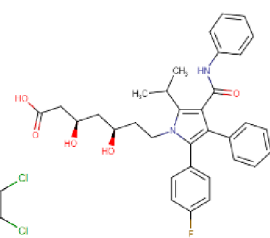
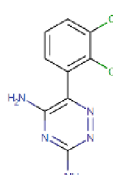
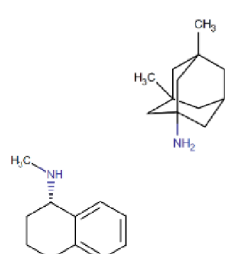
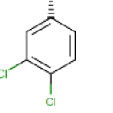
The frequency of detection was 70% for influent and 37% for the effluent wastewater in studies on the wastewater treatment plant [Golovko et al., 2014]. Sertraline was found sporadically in the River Foss during the study where 33 pharmaceuticals were monitored [Burns et al., 2018]

Although sertraline has the highest sorption coefficient in the study, and should stay sorpted in soil, it still can get to the environment on the quantities that can be detected. Sertraline was found in 12,8% of samples of sea birds' feather collected in the basin of the Adriatic Sea [Distefano et al., 2022]

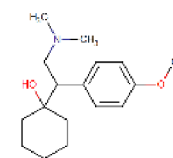
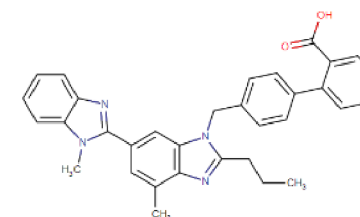
**Telmisartan** – antihypertensive, angiotensin II receptor antagonist. Was found in the wastewater treatment plants and reported to have toxic effect on algae and invertebrates and fish in study in Greece [Papageorgiou et al., 2019]. It was also detected in 56% of samples from the wastewater treatment plants in Spain where it was one of the substances with the highest individual concentration ( $534.7 \text{ ng L}^{-1}$ ) though it is considered to be less monitored than other pharmaceuticals. In the study it was considered to be also one of the substances of the highest ecotoxicological risk for the sea organisms [Celic et al., 2021] Telmisartan was also one of the most abundant pharmaceuticals in sewage sludge (max  $920 \text{ ng g}^{-1}$ ). During the plant uptake it accumulated mainly in roots of spinach [Kodesova et al., 2019b]

**Venlafaxine**, the antidepressant, was reported to be toxic for fish and some invertebrates. However, in the concentrations it is available in the water environment it causes no toxic effect. [Sehonova et al., 2018]. In the study of the plant uptake the substance was accumulating mainly in roots. It was detected in the sewage sludge where its highest concentration made up  $115 \text{ ng g}^{-1}$  [Kodesova et al., 2019b] It was found in 41% of samples from wastewater treatment plants with one of the highest individual concentrations of all the pharmaceuticals monitored ( $144.1 \text{ ng L}^{-1}$ ). It also was one of five pharmaceuticals found in the seawater and considered one of the substances that may cause ecotoxicological risk for the sea water organisms [Celic et al., 2021]

Table 2. The pharmaceutical micropollutants and their characteristics (drugbank.com)

Substance	Application	MW (g mol <sup>-1</sup> )	Water solubility (mg L <sup>-1</sup> )	pKa,	Log Kow	Structure
Atorvastatin (ATO)	Cardiovascular, cholesterol-lowering medicine.	558.64	0.63	pKa (basic) = -2.7 pKa (acidic) = 4.31	6.36 <sup>(1)</sup>	
Lamotrigine (LAM)	Antiepileptic medicine	256.09	170	pKa (basic) 5.89 pKa (acidic) 14.98	2.57 <sup>(2)</sup>	
Memantine (MEM)	Alzheimer's disease medicine	179.30	45.5	pKa (basic) 10.7	3.28 <sup>(3)</sup>	
Sertraline (SER)	Antidepressant	306.23	0.145	pKa (basic) 9.16	5.1 <sup>(4)</sup>	

Telmisartan (TEL)	Hypertension medicine	514.67	0.0009	pKa (acidic) 3.62 pKa (basic) 5.86	8.42 <sup>(5)</sup>
Venlafaxine (VEN)	Antidepressant	277.40	572000	pKa (acidic) 14.42 pKa (basic) 8.91	2.8 <sup>(6)</sup>



<sup>(1)</sup> [pubchem.ncbi.nlm.nih.gov](https://pubchem.ncbi.nlm.nih.gov)

<sup>(2)</sup> [pubchem.ncbi.nlm.nih.gov](https://pubchem.ncbi.nlm.nih.gov)

<sup>(3)</sup> (Pavlović, et al., 2022)

<sup>(4)</sup> (Minguez, et al., 2014)

<sup>(5)</sup> [pubchem.ncbi.nlm.nih.gov](https://pubchem.ncbi.nlm.nih.gov)

<sup>(6)</sup> (Minguez, et al., 2014)

## Soils and their properties

Eight types of soils that were used in experiments before were chosen for the study [Kodesova et.al., 2015, Klement et al., 2018, Schmidtova t al., 2021]. The samples were collected from the topsoil (0-25cm depth) The soils are Haplic Arenosol, Haplic Cambisol (A), Greyic Phaeozem, Haplic Chernozem, Haplic Cambisol (B), Haplic Luvisol, Dystric Cambisol, Stagnic Chernozem siltic. These soils represent the vast range of the soil conditions in the central Europe.

Haplic Cambisol was samples twice but in different locations which lead to different parameters of the soils. Haplic Cambisol (B) form Humpolec has higher CEC, acidity,  $C_{ox}$ , slit content and lower salinity and content of sand than the Haplic Cambisol (A) from Ceske Budejovice.

All soils have  $pH_{H_2O}$  higher than 6. Chernozem soils have the highest salinity, whereas Haplic Cambisol (Humpolec) and Haplic Arenosol have the lowest one. The highest cation exchange capacity (CEC) characterises the Chernozem soils and the lowest is in Haplic Arenosol.

After the sampling, the samples were air-dried, disintegrated, and any particles larger than 2 mm in diameter were removed by sieving. The selected chemical and physical soil properties were measured under the laboratory conditions and  $t = 20\text{ }^{\circ}\text{C}$ . The parameters measured: active soil reaction ( $pH_{H_2O}$ ) and potential soil reactions ( $pH_{CaCl_2}$ ) [ISO, 10390:2005], oxidizable organic carbon content ( $C_{ox}$ ) [Skjemstad and Baldock, 2008], soil salinity in water [Rhoades, 1996], particle density ( $\rho_s$ ) [Flint and Flint, 2002], exchangeable acidity (EA) [Hendershot et al., 1993], cation exchange capacity (CEC) [Bower and Hatcher, 1966], hydrolytic acidity (HA) [Klute, 1996], base cation saturation (BCS) was calculated as the difference between CEC and HA, and sorption complex saturation (SCS) was calculated as the percentage of BCS in CEC. The correlation between the soil parameters is presented in Table 3.



Table 3 Correlation coefficient for soil properties

	clay	slit	sand	$\rho_z$	$C_{OX}$	$PH_{H_2O}$	$PH_{CaCl_2}$	Salinity	EA	HA	$CaCO_3$	CEC	BCS	SCS
clay	1													
slit	0.811*	1												
sand	-0.868**	-0.995***	1											
$\rho_z$	-0.878**	-0.718*	0.767*	1										
$C_{OX}$	0.434	0.040	-0.112	-0.621	1									
$PH_{H_2O}$	0.850**	0.660	-0.712*	-0.615	0.437	1								
$PH_{CaCl_2}$	0.501	0.478	-0.496	-0.296	0.250	0.786*	1							
Salinity	0.668	0.435	-0.489	-0.660	0.805*	0.825*	0.673	1						
EA	-0.632	-0.755*	0.754*	0.434	0.002	-0.672	-0.751*	-0.491	1					
HA	-0.432	-0.253	0.292	0.044	-0.130	-0.789	-0.685	-0.569	0.543	1				
$CaCO_3$	0.647	0.134	-0.229	-0.633	0.874**	0.650	0.316	0.795*	-0.162	-0.437	1			
CEC	0.840**	0.692	-0.737*	-0.910**	0.725*	0.758*	0.514	0.837**	-0.428	-0.235	0.677	1		
BCS	0.874**	0.691	-0.743*	-0.829*	0.686	0.899**	0.652	0.910**	-0.535	-0.489	0.730*	0.963***	1	
SCS	0.828*	0.823*	-0.847**	-0.655	0.304	0.878**	0.859**	0.712*	-0.849**	-0.560	0.414	0.766*	0.843**	1

\*  $p < 0.05$

\*\*  $p < 0.01$

\*\*\*  $p < 0.001$

## Sorption

The sorption was evaluated by equilibrium batch method. The samples of 8 different soils were dried, sieved and placed into the centrifuge plastic tubes (10g of each soil per tube). The solutions of micropollutants were prepared with the adding of calcium chloride (0.01 M  $CaCl_2$ ) for better centrifugation and less cation exchange in solution. The 20ml of solution was added to the tube with soil. The solutions had 5 concentrations of the same substance: 0.5, 1, 2.5, 5, and 10  $\mu g mL^{-1}$ . The experiment was repeated twice for each concentration. After that, the solution with the soil was shaken on a reciprocal analog shaker at room temperature for 24 hours. Then the suspension was centrifuged for 10 min at 6000 rpm and filtered through a cellulose syringe filter to the glass vials. The aqueous part of the solution was analyzed. [Kodešová et al. 2015; OECD 2000; Doretto, Peruchi, and Rath 2014]

The liquid chromatography-tandem mass spectrometry and isotope dilution or an internal standard (IS) method was used to measure the actual initial and equilibrium concentrations  $c_{ini}$  and  $c_{eq}$  of micropollutants in the solution. [Fedorova et al., 2014; Grabic et al., 2012]

### **The sorption isotherms**

The concentration of the substance sorbed onto the soil particles ( $s$ ,  $\mu\text{g g}^{-1}$ ) was calculated with the equation:

$$s=2(C_{\text{ini},a}-C_{\text{eq}}) \quad (1)$$

To calculate the points for the sorption isotherms the Freundlich equation was used. The data points were the final micropollutants' concentration  $c=c_{\text{eq}}$  ( $\mu\text{g cm}^{-3}$ ) and  $s$  ( $\mu\text{g g}^{-1}$ ):

$$s=K_{\text{F}}C^{1/n} \quad (2)$$

where  $K_{\text{F}}$  ( $\text{cm}^{3/n}\mu\text{g}^{1-1/n}\text{g}^{-1}$ ) and  $n$  are empirical coefficients. For the statistical analysis of impact of the soil parameters on the  $K_{\text{F}}$  values the average  $n$  coefficient for each compound was calculated from all  $n$  coefficient for each substance. After that the Freundlich equation with the average  $n$  was applied to find the experimental data points ( $c^{1/n_{\text{avg},1}}$  and  $s$ ) and to calculate  $K_{\text{F}}$  by the least squares method. These  $K_{\text{F}}$  coefficients (Figure S1) were used later for the statistical analysis [Kodešová et al. 2015]

### **Statistical analyses**

The Pearson product-moment coefficient was used to find the correlation among the soil properties and between the soil properties and sorption coefficients  $K_{\text{F}}$  (for  $n_{\text{avg}}$ ) for pharmaceutical substances. The p-value was used to assess the statistical significance of the correlation coefficients. To obtain the equations for prediction of the sorption coefficients  $K_{\text{F}}$  for different substances the linear regression models were used where  $K_{\text{F}}$  was the dependent variable and soil properties the independent. The created models were evaluated according to the diagnostic plots, residual distribution histograms, p-values of the independent variables and the coefficient of determination  $R^2$ . Then the best model for each substance was chosen. As some of the soil properties showed strong

correlation between each other the variance inflation factor (VIF) was used to avoid the collinearity. The models with low VIF (1-5) were chosen.

The statistical analysis was performed in R-Studio (version 4.2.2 ) and JASP (version 0.17.1.).

## 4. Results

The highest sorption coefficient was for sertraline in the Chernozem  $K_F=273.4 \text{ cm}^{3/n} \mu\text{g}^{1-1/n} \text{ g}^{-1}$ . And the least one was for memantine in the Arenosol soil  $K_F=0.9 \text{ cm}^{3/n} \mu\text{g}^{1-1/n} \text{ g}^{-1}$  (Table 5). The level of sorption decreased (according to the average values of Freundlich sorption coefficient,  $K_F$ ) in this sequence: Sertraline>Venlafaxine>Telmisartan>Atorvastatin>Lamotrigine>Memantine

Table 4. Studied soils and their properties: pH<sub>H2O</sub>, pH<sub>CaCl2</sub>, cation exchange capacity (CEC), hydrolytic acidity (HA), exchangeable acidity (EA), basic cation saturation (BCS), sorption complex saturation (SCS), organic carbon content (C<sub>ox</sub>), CaCO<sub>3</sub> content, particle density (ρ<sub>s</sub>), clay, silt and sand contents (%).

Soil type	pH <sub>H2O</sub>	pH <sub>CaCl2</sub>	Salinity (μS cm <sup>-1</sup> )	CEC (mmol <sup>+</sup> kg <sup>-1</sup> )	EA (mmol <sup>+</sup> kg <sup>-1</sup> )	HA (mmol <sup>+</sup> kg <sup>-1</sup> )	BCS (mmol <sup>+</sup> kg <sup>-1</sup> )
Haplic Arenosol	6.29	5.01	21.2	35.23	3.79	26.34	8.9
Haplic Cambisol (A)	6.91	6.92	56.6	95.35	1.18	20.03	75.3
Greyic Phaeozem	7.65	6.44	66.1	166.21	0.96	6.49	159.7
Haplic Chernozem	8.08	7.13	104.3	213.22	1.25	4.75	208.5
Haplic Cambisol (B)	6.53	5.48	26.9	164.17	3.28	61.80	102.4
Haplic Luvisol	7.50	6.27	35.4	121.34	0.39	14.82	106.5
Dystric Cambisol	6.73	5.73	70.0	169.69	1.18	47.22	122.5
Stagnic Chernozem	8.25	6.60	131.7	254.80	1.28	3.86	250.9
Average	7.24	6.20	64.04	152.50	1.66	23.16	129.34
Standard deviation	0.73	0.73	38.42	68.41	1.20	21.22	76.24
Soil type	SCS (%)	C <sub>ox</sub> (%)	CaCO <sub>3</sub> (%)	ρ <sub>s</sub> (g cm <sup>-3</sup> )	clay (%)	silt (%)	sand (%)
Haplic Arenosol	25.3	1.230	0.00	2.662	5.29	6.68	88.01
Haplic Cambisol (A)	79.0	1.460	0.00	2.624	8.54	29.7	61.74
Greyic Phaeozem	96.1	1.204	0.62	2.566	15.77	76.06	8.15
Haplic Chernozem	97.8	1.774	4.40	2.528	15.47	68.47	16.05
Haplic Cambisol (B)	62.4	1.600	0.05	2.527	12.55	47.66	39.76
Haplic Luvisol	87.8	0.751	0.06	2.533	17.64	74.1	8.24
Dystric Cambisol	72.2	1.729	0.10	2.508	12.7	65.91	21.37
Stagnic Chernozem	98.5	2.894	25.90	2.450	21.3	58.05	20.63
Average	77.36	1.58	3.89	2.55	13.66	53.33	32.99
Standard deviation	24.76	0.63	9.02	0.07	5.08	24.27	28.55

Table 5. The Freundlich coefficients ( $K_F$ ) calculated with the  $n_{avg}$  for sorption of 6 target pharmaceuticals in 8 soils, with the coefficients of determination  $R^2$ , including coefficients  $K_F$  from other publications.

	Atorvastatin		Lamotrigine		Memantine	
	$K_F$	$R^2$	$K_F$	$R^2$	$K_F$	$R^2$
Haplic Arenosol	11.85	0.902	5.26	0.994	0.90	0.942
Haplic Cambisol (A)	6.37	0.976	7.24	0.993	2.65	0.98
Greyic Phaeozem	4.94	0.961	4.07	0.994	3.65	0.988
Haplic Chernozem	5.01	0.984	4.56	0.989	4.60	0.992
Haplic Cambisol (B)	17.77	0.993	13.28	0.998	2.69	0.993
Haplic Luvisol	3.17	0.879	5.59	0.988	2.53	0.996
Dystric Cambisol	10.38	0.994	9.05	0.985	3.96	0.994
Stagnic Chernozem siltic	9.80	0.986	6.34	0.984	6.40	0.984
Mean	8.66		6.92		3.42	
Standard Deviation	4.78		3.02		1.64	
	Sertraline		Telmisartan		Venlafaxine	
	$K_F$	$R^2$	$K_F$	$R^2$	$K_F$	$R^2$
Haplic Arenosol	24.1	0.998	51.0	0.935	21.4	0.999
Haplic Cambisol (A)	100.7	0.997	30.8	0.974	68.2	0.994
Greyic Phaeozem	120.9	0.974	21.5	0.873	98.4	0.998
Haplic Chernozem	143.8	0.998	18.3	0.899	96.2	0.999
Haplic Cambisol (B)	70.1	0.997	54.1	0.976	40.7	0.993
Haplic Luvisol	82.0	0.994	28.5	0.938	83.2	0.999
Dystric Cambisol	142.2	0.998	39.8	0.925	37.9	0.996
Stagnic Chernozem siltic	273.4	0.995	22.5	0.855	148.1	0.999
Mean	119.64		33.31		74.26	
Standard Deviation	73.8		13.6		41.2	

a [Ottmar et al., 2010]

b [Filep et al., 2021]

c [Paz et al., 2016]

d [Pavlović et al., 2022]

e [Costa Junior et al., 2022]

Table 6. Correlation coefficients between the properties of soils and the sorption coefficients  $K_F$  of the pharmaceuticals.

	Atorvastatin	Lamotrigine	Memantine	Sertraline	Telmisartan	Venlafaxine
<b>PH<sub>H2O</sub></b>	-0.59	-0.53	0.80*	0.76*	-0.91**	0.95***
<b>PH<sub>CaCl2</sub></b>	-0.69	-0.43	0.59	0.55	-0.89**	0.74
<b>Salinity</b>	-0.29	-0.32	0.95***	0.94***	-0.74*	0.81*
<b>CEC</b>	-0.04	0.06	0.95***	0.86**	-0.55	0.73*
<b>EA</b>	0.81**	0.41	-0.51	-0.5	0.82**	-0.61
<b>HA</b>	0.79*	0.90**	-0.4	-0.43	0.86**	-0.76*
<b>BCS</b>	-0.26	-0.2	0.96***	0.89**	-0.74*	0.87**
<b>SCS</b>	-0.59	-0.28	0.77*	0.7	-0.88**	0.84**
<b>C<sub>ox</sub></b>	0.3	0.15	0.81*	0.85**	-0.22	0.54
<b>carbonates</b>	0.04	-0.14	0.79*	0.88**	-0.41	0.78*
<b>clay</b>	-0.32	-0.16	0.81*	0.76*	-0.66	0.84**
<b>slit</b>	-0.46	-0.14	0.59	0.46	-0.63	0.54
<b>sand</b>	0.45	0.14	-0.65	-0.53	0.65	-0.61
<b>p<sub>z</sub></b>	-0.04	-0.22	-0.85**	-0.79*	0.37	-0.61

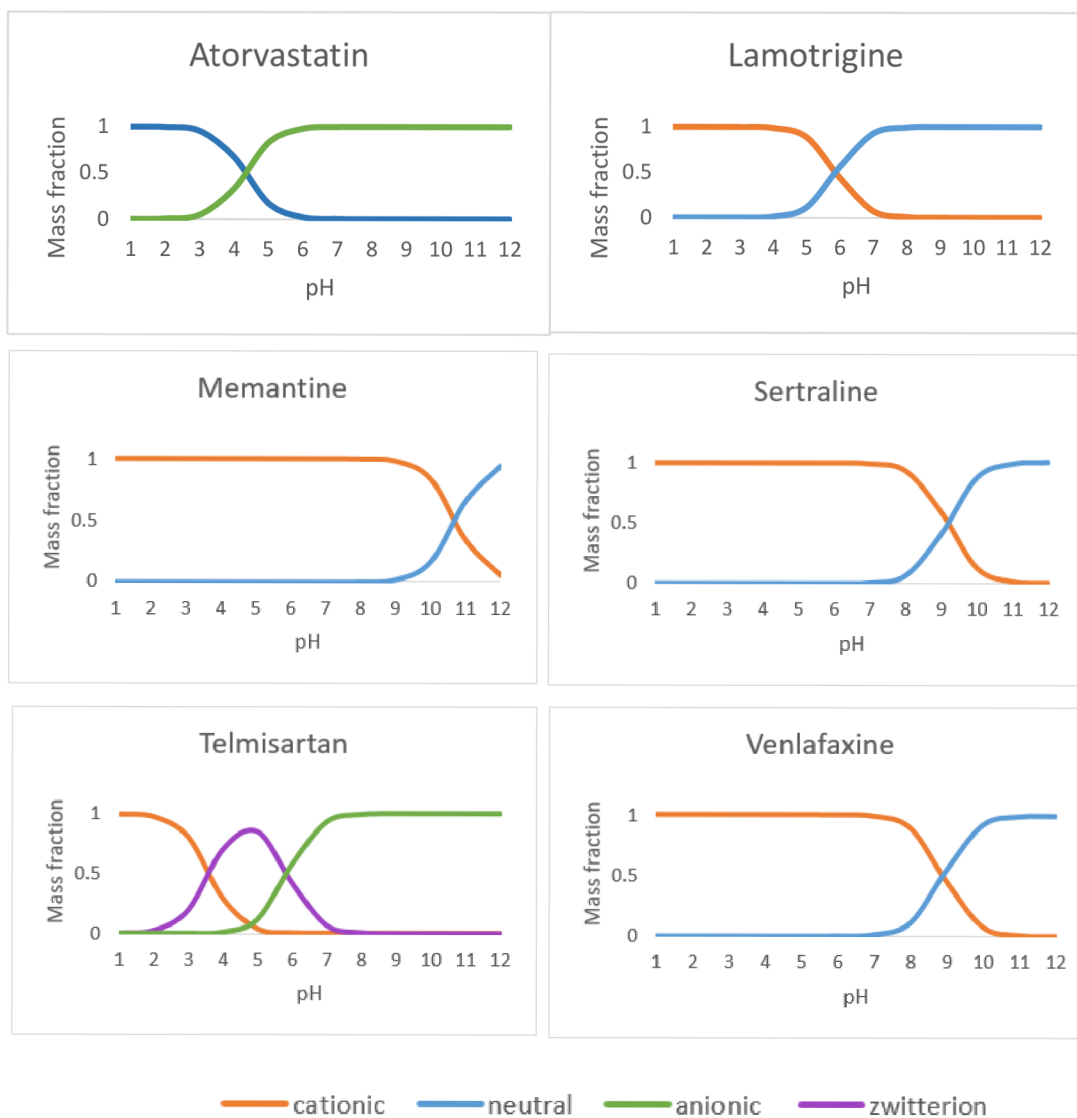
\* p<0.05

\*\* p<0.01

\*\*\* p<0.001

The soils pH varied from 6.29 to 8.25 (Table 4) which determined the main mass fraction of the pharmaceutical substances in soils. They occurred in neutral (lamotrigine), anionic (atorvastatin, telmisartan) and cationic (memantine, sertraline, venlafaxine) forms (Figures 4,5).

Figure 4. Mass fractions of the studied pharmaceuticals (neutral, cationic, anionic) depending on the pH of the soil.



The mass fraction of *memantine* and *sertraline* were calculated using pKa from Table 1 and formulas:

$$\alpha_{\text{cationic}} = 1/(1 + 10^{(pH-pKa)}) \quad (3)$$

$$\alpha_{\text{neutral}} = 1/(1 + 10^{(pKa-pH)}) \quad (4)$$

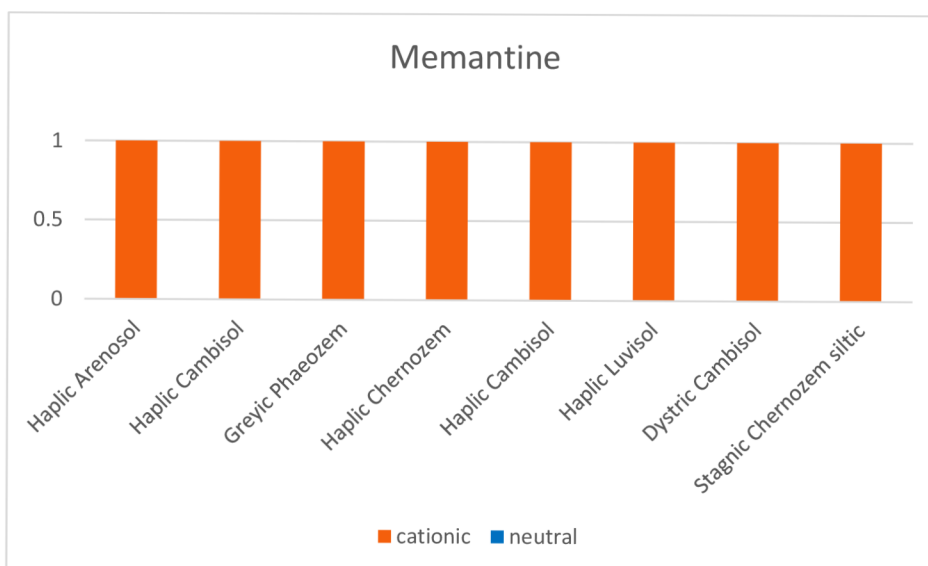
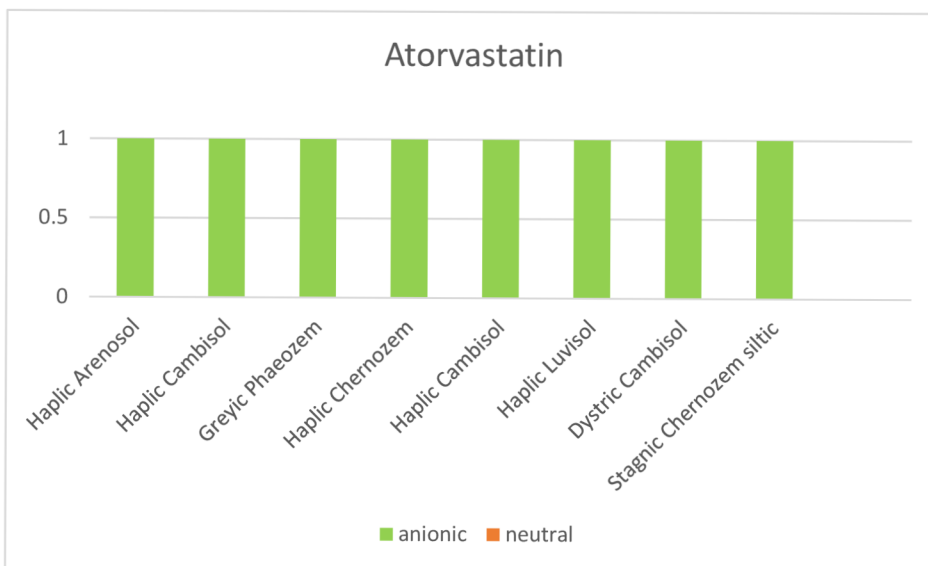
The mass fraction of atorvastatin, lamotrigine, telmisartan and venlafaxine was calculated using pKa from Table 1 and formulas:

$$\alpha_{\text{cationic}} = 1 / (1 + 10^{(pH-pKa1)} + 10^{(2pH-pKa1-pKa2)}) \quad (5)$$

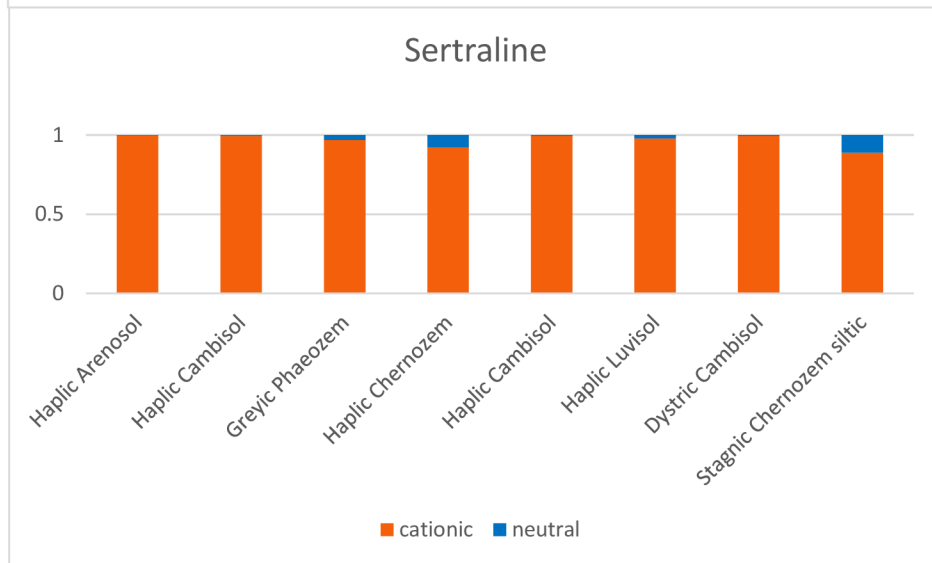
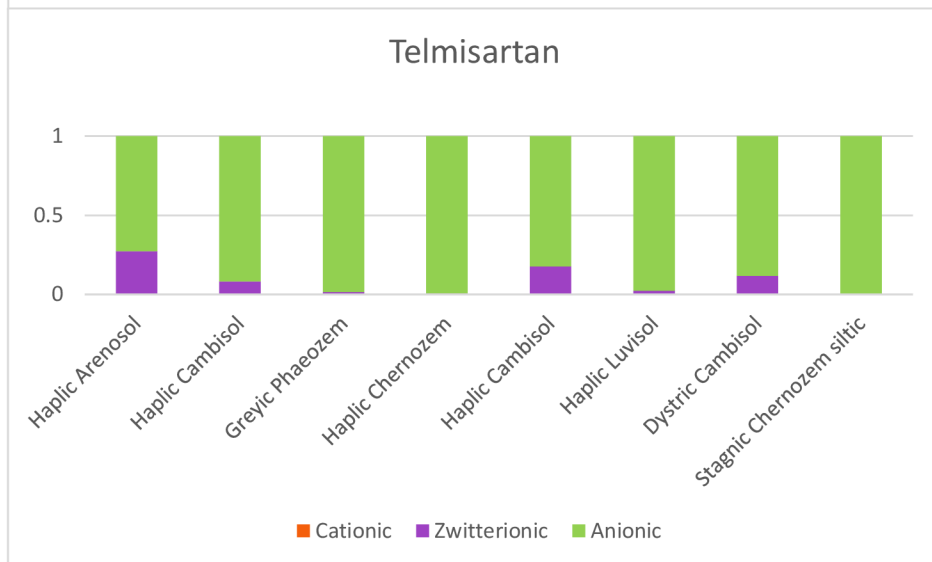
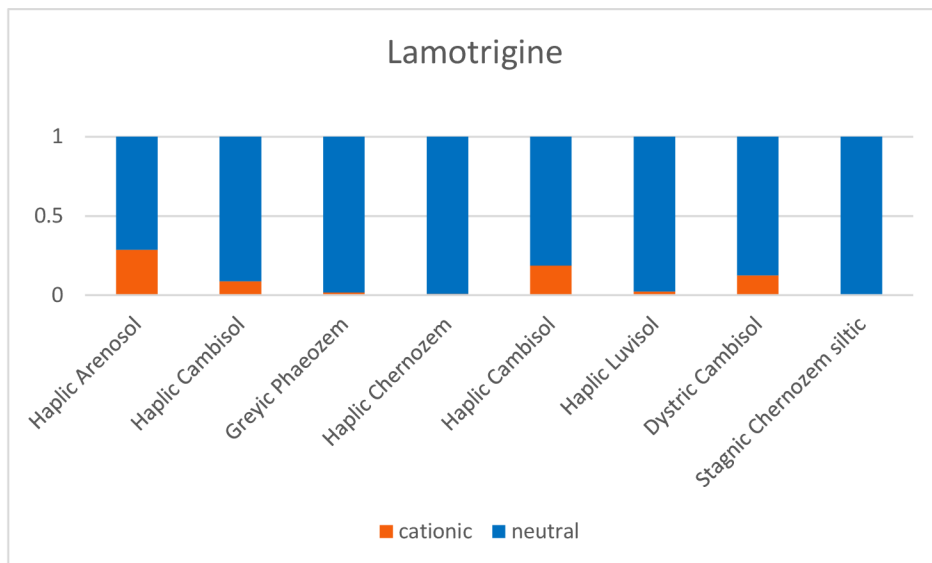
$$\alpha_{\text{neutral}} = 1 / (1 + 10^{(pKa1-pH)} + 10^{(pH-pKa2)}) \quad (6)$$

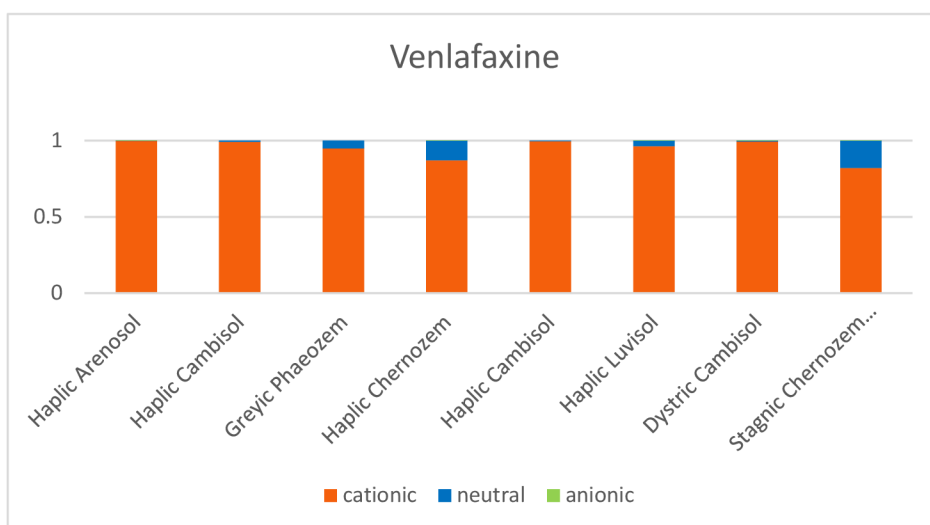
$$\alpha_{\text{anionic}} = 1 / (1 + 10^{(pKa2-pH)} + 10^{(pKa1+pKa2-2pH)}) \quad (7)$$

Figure 5. The mass fraction of the pharmaceutical substances in the pH values of the soils that were studied.









#### *Sorption of neutral pharmaceutical.*

**Lamotrigine** can become cationic at the low pH level but it was mainly in neutral form in the soils (Figures 4,5). As a neutral molecule it could not be sorpted to the soil by ionic forces. So its sorption could be driven by hydrogen bonds and Van der Waals forces [Strawn et al, 2020]. The only significant positive correlation of its sorption coefficient was with the hydrolytic acidity (HA) (Table 6). This soil characteristic showed negative correlation with carbon content ( $C_{ox}$ ), pH, cation exchange capacity (CEC) which though was not statistically significant. The sorption coefficient was one of the lowest among all the substances studied and it was even lower in studies of Filep et al., 2021 and Paz et al., 2016 (Table 5). The highest sorption of lamotrigine was observed in Haplic Cambisol (Humpolec)  $13.28 \text{ cm}^{3/n} \mu\text{g}^{1-1/n} \text{ g}^{-1}$  and the lowest in Greyic Phaeozem  $4.07 \text{ cm}^{3/n} \mu\text{g}^{1-1/n} \text{ g}^{-1}$ .

#### *Sorption of pharmaceutical anions.*

**Atorvastatin** a neutral compound at the low levels of pH (<5), was mainly in anionic form in all soils due to their pH level (>6). **Telmisartan** at low level of pH is a cation but closer to the neutral pH the main mass fraction becomes zwitterionic. In soils, at the pH level above 6, it occurred in the anionic form (Figures 4, 5). Being negatively

charged, the molecules of the substances must be repelled from the negatively charged particles of soil.

The sorption coefficient ( $K_F$ ) of both substances had statistically significant positive correlation with hydrolytic (HA) and exchangeable acidity (EA). Telmisartan was also negatively related to  $pH_{H_2O}$ ,  $pH_{CaCl_2}$ , salinity, basic cation saturation (BSC) and sorption complex saturation (SCS) (Table 6). EA and HA negatively correlated with sorption complex saturation (SCS) (Table 3) that together with BSC show the amount of the positively charged cations in the soil that may attract the molecules of pharmaceutical anions.

The highest sorption for both substances was observed in the Haplic Cambisol (B) soil which had the highest level of HA and second highest level of EA (Table 4), where atorvastatin had  $K_F = 17.77 \text{ cm}^{3/n} \mu\text{g}^{1-1/n} \text{ g}^{-1}$ , and telmisartan  $K_F=54.1 \text{ cm}^{3/n} \mu\text{g}^{1-1/n} \text{ g}^{-1}$  (Table 5). The lowest sorption for atorvastatin was in the Haplic Luvisol, where  $K_F = 3.17 \text{ cm}^{3/n} \mu\text{g}^{1-1/n} \text{ g}^{-1}$  and for telmisartan – in the Haplic Chernozem where  $K_F=18.3 \text{ cm}^{3/n} \mu\text{g}^{1-1/n} \text{ g}^{-1}$  (Table 5). The close results of level of sorption of atorvastatin were obtained by Ottmar et al. in 2010 for Silty sand  $K_d = 7.6\pm 0.1 \text{ L/kg}$  and sediment  $K_d = 15.7\pm 0.2 \text{ L/kg}$ . No data for telmisartan was found.

#### *Sorption of pharmaceutical cations.*

Although **memantine**, **sertraline** and **venlafaxin** occurred as a cation in all the soils, the molecules of these substance may become neutral at the higher levels of pH (>9-10) (Figures 4,5). The sorption of the substances can be described as the ionic interaction between the cations and the negatively charged particles of soil. The positively charged particles of the pharmaceuticals were bond to the sorption sites available in soil. There was a positive, statistically significant correlation between the sorption coefficients of the substances and several soil characteristics. The most significant among them were cation exchange capacity (CEC) and basic cation saturation (BCS) (Table 6). The same parameters were described in previous studies by Kodesova et al., 2015, 2020, Schmidtova et al., 2020, Klement et al., 2018. The other soil characteristics the sorption coefficient of the cationic forms of pharmaceuticals correlated with were  $pH_{H_2O}$ , salinity, SCS (except sertraline),  $C_{OX}$  (except venlafaxine), carbonates and clay content.

They were related to the CEC, BSC and salinity (Table 3). Memantine and sertraline sorption coefficients negatively correlated with particle density, and venlafaxine to hydrolytic acidity (HA).

The highest sorption of the cationic forms of the pharmaceuticals was observed in the Stagnic Chernozem siltic with  $K_F$  6.40  $\text{cm}^{3/n} \mu\text{g}^{1-1/n} \text{g}^{-1}$ , 273.4  $\text{cm}^{3/n} \mu\text{g}^{1-1/n} \text{g}^{-1}$ , 148.1  $\text{cm}^{3/n} \mu\text{g}^{1-1/n} \text{g}^{-1}$  (Table 5) for memantine, sertraline and venlafaxine respectively. The least sorption was in the Arenosol, with  $K_F$  0.90  $\text{cm}^{3/n} \mu\text{g}^{1-1/n} \text{g}^{-1}$ , 24.1  $\text{cm}^{3/n} \mu\text{g}^{1-1/n} \text{g}^{-1}$ , 21.4  $\text{cm}^{3/n} \mu\text{g}^{1-1/n} \text{g}^{-1}$  respectively (Table 5). The similar results were obtained for memantine by Pavlovic et al (2022); but for sertraline and venlafaxine the sorption coefficients in sediments and sewage sludge were lower in the studies of Costa Junior et al. (2022).

#### *Prediction of the pharmaceuticals behavior in soils.*

In order to predict the sorption of the pharmaceuticals in soils the linear regression models were created using sorption coefficients as the dependent variables and soil properties as the independent. The result is the equations that are presented in Table 7. The soils parameters included in the equations also showed the strong correlation with the corresponding sorption coefficients. The pharmaceuticals that were mainly in the form of anions (atorvastatin, telmisartan) or neutral (lamotrigine) contain hydrolytic and exchangeable acidity (HA and EA) in the equations. The cationic substances (memantine, sertraline, venlafaxine) contain cation exchange capacity (CEC), basic cation saturation (BCS), clay or carbon content (Cox). The independent variables had the level of statistical significance at no less than 95% confidence level. The coefficient of determination  $R^2$  for each equation also had high level of significance over 99% except one of the models for venlafaxine where  $R^2$  significance was at 95% confidence level. The high level of statistical significance and the values of the determination coefficients  $R^2$  show that it is possible to predict the sorption coefficients with the equations with the high reliability for all the pharmaceutical compounds except venlafaxine, which has quite low  $R^2$ .

Table 7.

Pharmaceutical compound	R <sup>2</sup>	Equation
Atorvastatin	0.972**	$K_F \text{ ATO} = 1.992EA^{**} + 0.129HA^{**} + 2.863Cox^* - 2.165$
Lamotrigine	0.814**	$K_F \text{ LAM} = 3.95^{**} + 0.13HA^{**}$
Memantine	0.904***	$K_F \text{ MEM} = 0.023CEC^{***} - 0.058$
	0.927***	$K_F \text{ MEM} = 0.739 + 0.02BCS^{***}$
Sertraline	0.915**	$K_F \text{ SER} = 75.3Cox^{**} + 7.06clay^* - 95.7^*$
Telmisartan	0.915**	$K_F \text{ TEL} = 91.5^{**} + 0.305HA^* - 10.53pHCaCl_2^*$
Venlafaxine	0.754**	$K_F \text{ VEN} = 13.58 + 0.47BCS^{**}$
	0.538*	$K_F \text{ VEN} = 6.92 + 0.44CEC^*$

\* p < 0.05

\*\* p < 0.01

\*\*\* p < 0.001

## 5. Conclusion

The sorption of the pharmaceutical micropollutants in soil depends on the mass fraction the molecules of these substances which in its turn depend on pH of the soils. Moreover, the sorption of the pharmaceuticals also depends on the soil parameters such as CEC, BSC, SCS and soil texture. The more the substance is sorpted in the soil the less mobile its molecules become, and less easily it will get washed to the ground water and contaminate it. The most sorpted substance among all the studied is sertraline. The least sorpted is memantine. Both pharmaceuticals were in cationic form and their sorption was influenced with the same soil characteristics. The correlation analysis between the Freundlich sorption coefficient of the substances and soil characteristics that sorption is related both positively and negatively to several parameters, such as

cation exchange capacity (CEC), pH<sub>H2O</sub>, pH CaCl<sub>2</sub>, cation exchange capacity (CEC), hydrolytic acidity (HA), exchangeable acidity (EA), basic cation saturation (BSC), sorption complex saturation (SCS), organic carbon content (C<sub>ox</sub>), CaCO<sub>3</sub> content, particle density ( $\rho_s$ ), clay, silt and sand contents (%). Moreover, these parameters correlate to each other. Including these parameters to the linear regression model the equations that predict the sorption coefficient of pharmaceutical compounds in the soils with the similar parameters with high reliability were obtained. However, there are also other factors that may influence sorption of the pharmaceutical micropollutants: interaction between the substances, dissipation or biodegradation of the parent substances, interaction with other micropollutants (sorption and desorption on the microplastic), etc. The issue requires further detailed study.

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