Science of the Total Environment 746 (2020) 141134

Contents lists available at ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

How microbial community composition, sorption and simultaneous application of six pharmaceuticals affect their dissipation in soils

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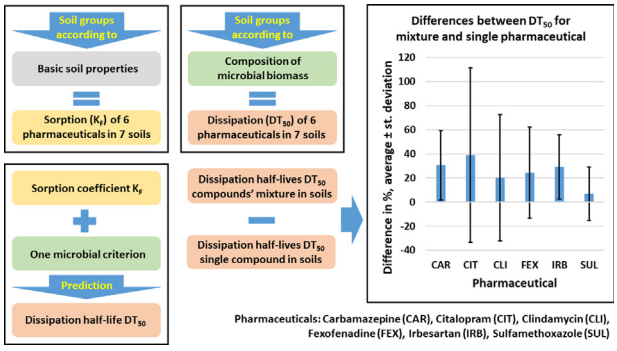
HIGHLIGHTS

- Soils groups according to basic soils properties and sorption of compounds matched.
- Soils groups according to microbial community structure and half-lives corresponded.
- Half-lives could be predicted using one microbial criterion and sorption coefficient.
- Simultaneous application of all compounds mostly reduced their dissipation in soils.
- The average increase in multiple-solute half-lives varied between 7 and 39%.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 5 June 2020
Received in revised form 17 July 2020
Accepted 19 July 2020
Available online 24 July 2020

Editor: Jose Julio Ortega-Calvo

Keywords:
Soil properties
Freundlich sorption equation
Half-life
Phospholipid fatty acids
Regression models for estimating half-lives

ABSTRACT

Pharmaceuticals 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. Standard laboratory batch degradation and sorption experiments were performed using soil samples obtained from the top horizons of seven different soil types and 6 pharmaceuticals (carbamazepine, irbesartan, fexofenadine, clindamycin and sulfamethoxazole), which were applied either as single-solute solutions or as mixtures (not for sorption). The highest dissipation half-lives were observed for citalopram (average $DT_{50,S}$ for a single compound of 152 ± 53.5 days) followed by carbamazepine (106.0 ± 17.5 days), irbesartan (24.4 ± 3.5 days), fexofenadine (23.5 ± 20.9 days), clindamycin (10.8 ± 4.2 days) and sulfamethoxazole (9.6 ± 2.0 days). The simultaneous application of all compounds increased the half-lives ($DT_{50,M}$) of all compounds (particularly carbamazepine, citalopram, fexofenadine and irbesartan), which is likely explained by the negative impact of antibiotics (sulfamethoxazole and clindamycin) on soil microbial community. However, this trend was not consistent in all soils. In several cases, the $DT_{50,S}$ values were even higher than the $DT_{50,M}$ values. Principal component analyses showed that while knowledge of basic soil properties determines grouping of soils according sorption behavior, knowledge of the microbial community structure could be used to group soils according to the dissipation behavior of tested compounds in these soils. The derived multiple linear regression models for estimating dissipation half-lives ($DT_{50,S}$) for citalopram, clindamycin, fexofenadine,

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https://doi.org/10.1016/j.scitotenv.2020.141134

irbesartan and sulfamethoxazole always included at least one microbial factor (either amount of phosphorus in microbial biomass or microbial biomarkers derived from phospholipid fatty acids) that deceased half-lives (i.e., enhanced dissipations). Equations for citalopram, clindamycin, fexofenadine and sulfamethoxazole included the Freundlich sorption coefficient, which likely increased half-lives (i.e., prolonged dissipations).

1. Introduction

Treated wastewater is often utilized to irrigate agricultural land in countries suffering from water deficiency that have a warm and dry climate, such as countries in the Middle East and Southern Europe (e.g., Carter et al., 2019; Lesser et al., 2018; Picó et al., 2020). Reclaimed wastewater is also increasingly utilized for irrigation in countries that have not previously suffered from a water shortage but face a change in a rainfall distribution throughout a year and a scarcity of water during vegetation seasons due to climate change (e.g., Helmecke et al., 2020). Another product of wastewater management is sewage sludge, which is frequently used as amendment to increase organic matter and nutrient content in soils (e.g., Ivanová et al., 2018; Verlicchi and Zambello, 2015). It has been documented that some pollutants of emerging concern, such as human pharmaceuticals, are not entirely removed from treated wastewater (e.g., Peña-Guzmán et al., 2019; Khan et al., 2020; Loos et al., 2013). Similarly, sewage sludge can contain a large number of pharmaceuticals, and some of them can occur in high concentrations (e.g., Ivanová et al., 2018; Kodešová et al., 2019b; Verlicchi and Zambello, 2015). The environment can also be polluted by veterinary pharmaceuticals from animal urine or farm waste (e.g., Charuaud et al., 2019). Pharmaceuticals that contaminate soils may subsequently leach to groundwater (e.g., Burri et al., 2019; Godfrey et al., 2007; Fram and Belitz, 2011; Lesser et al., 2018; Li, 2014; Loos et al., 2010) or can be taken up by plants (e.g., Ahmed et al., 2015; Al-Farsi et al., 2017; Christou et al., 2019; Goldstein et al., 2014; Klement et al., 2020; Kodešová et al., 2019a, 2019b; Li et al., 2018, 2019a, 2019b; Malchi et al., 2014; Montemurro et al., 2017; Mordechay et al., 2018; Shenker et al., 2011; Winker et al., 2010; Wu et al., 2013). Further propagation of pharmaceuticals in the environment depends on their sorption and dissipation in the vadose zone (e.g., Carter et al., 2019; Kümmerer, 2009a, 2009b; Zhi et al., 2019). The knowledge of the properties characterizing sorption and dissipation of various pharmaceuticals in this environment is crucial, for example, when using models simulating transport of these compounds in soils and their uptake by plants (e.g., Brunetti et al., 2019).

While sorption of pharmaceuticals in soils and sediments is increasingly studied (e.g., Li et al., 2020; Schaffer and Licha, 2015; Zhi et al., 2019), dissipation of these compounds is studied less frequently (e.g., Zhi et al., 2019). Studies have focused on the impacts of soil sterilization, incubation conditions (e.g., aerobic vs. anaerobic, diverse temperatures) and different amendments on the degradation of a specific compound. Compounds' dissipation rates are mostly due to biodegradation as demonstrated by comparing dissipation rates for sterile and nonsterile soils and sediments (e.g., Al-Khazrajy et al., 2018; Hurtado et al., 2017; Liu et al., 2010; Shen et al., 2018; Srinivasan and Sarmah, 2014; Wu et al., 2012; Yu et al., 2013; Zhang et al., 2017). Among others, Biel-Maeso et al. (2019) showed that dissipation of the most studied compounds was considerably increased under aerobic conditions compared with anaerobic conditions. Dissipation of some pharmaceuticals (e.g., antibiotics) may also be controlled by the initial compound concentration in soils, i.e., inhibition of degrading microorganisms in the context of higher concentrations (e.g., sulfadiazine and sulfamethoxazole studied by Shen et al., 2018; sulfamethoxazole tested by Srinivasan and Sarmah, 2014). On the other hand, Zhang et al. (2017) did not found significant differences in dissipation half-lives of the same compounds (sulfadiazine and sulfamethoxazole) at varying initial concentrations. Dissipation of compounds could also be enhanced by increased nutrient content and microbial biomass due to manure amendments (Zhang et al., 2017; Shen et al., 2018). In contrast, Albero et al. (2018) found that the amendment of soil with composted manure increased half-lives of six veterinary antibiotics (one fluoroquinolone, two tetracyclines, two sulfonamides and one lincosamide) between 6 and 53% likely due to higher sorption of compounds in manured soil and thus reduced availability. Similar effects of organic fertilization (e.g., a sewage sludge, green waste compost and farmyard manure, or composted sewage sludge, respectively) on sulfamethoxazole, its main metabolites N-ac-sulfamethoxazole and ciprofloxacin, or triclosan and carbamazepine was observed by Andriamalala et al. (2018) and Shao et al. (2018).

Whereas there have been developed several models for estimating sorption coefficients of pharmaceuticals in soils and sediments from sorbent and compound properties (e.g., Carter et al., 2020; Klement et al., 2018; Kodešová et al., 2015; Li et al., 2020), models for estimating dissipation half-lives has not been proposed. Previous studies only evaluated dissipation half-lives in few soils or sediments. Therefore, they could not correlate assessed half-lives to soil properties, parameters characterizing sorption of compound in soils or soil microbial community composition. Al-Khazrajy et al. (2018) attempted to estimate dissipation rates from selected freshwater sediment properties and microbial activity (assessed using 2,3,5-triphenyltetrazolium chloride solution, Monteiro and Boxall, 2009). They identified equations for predicting dissipation rates for 3 of 6 tested compounds: dissipation rates of diltiazem using clay content and logarithm of microbial activity, dissipation rates of ranitidine using organic carbon content and logarithm of microbial activity, and dissipation rates of cimetidine using silt content. All mentioned factors increased dissipation rates in tested sediments. No significant relationships were obtained for other compounds (amitriptyline, atenolol and mefenamic acid). Kodešová et al. (2016) documented that dissipation half-lives of 7 tested compounds (atenolol, metoprolol, trimethoprim, sulfamethoxazole, clindamycin, clarithromycin, carbamazepine) mostly did not depend on basic soil properties but on the overall soil type conditions. In general, for compounds that were degradable in the studied soils, lower average dissipation half-lives and variability were determined for better quality soils (soils with well-developed structure, high nutrition content and associated biological conditions as Chernozems) compared with lower quality soils (Cambisols). However, actual soil microbial properties were not evaluated.

Some pharmaceuticals may largely affect activity of the soil microbial community, i.e., antibiotics can inhibit the degradation of microorganisms (Caracciolo et al., 2015; D'Alessio et al., 2019; Grenni et al., 2018). As a result, dissipation of other compounds that occur in soils together with such compounds can be reduced. On the other hand, biodegradation of pharmaceuticals that simultaneously occur in soils might also be enhanced if these compounds interact with each other (Grenni et al., 2018). To date, degradation of a single compound in soils or sediments have been mostly studied, or studies were focused on behaviors of antibiotic mixtures and their influence on respective microbial community (e.g., Chen and Xie, 2018; Grenni et al., 2018; Thelusmond et al., 2019; Zhi et al., 2019).

Dissipation of many pharmaceuticals in soils is unknown. In addition, dissipation rates of pharmaceuticals in different soil types can be quite different. Therefore, the first goal of this study was to determine whether knowledge of soil properties and initial microbial composition of 7 diverse soils (samples were obtained from topsoils of 7 soil types)

can help to estimate probable trends in dissipation of 6 selected compounds in these soils. Although dissipation of 3 compounds (carbamazepine, clindamycin and sulfamethoxazole) under soil conditions have been evaluated in several studies (e.g., Kodešová et al., 2016; Koba et al., 2016, 2017), dissipation of 3 other compounds (citalopram, fexofenadine, irbesartan) in soils have not been explored to date. The influence of sorption of compounds in soils, which can reduce availability of compounds for microbial degradation, was also suggested. The second goal of this study was to determine whether and how two antibiotics (clindamycin and sulfamethoxazole) applied together with other four pharmaceuticals influence dissipation rates of all compounds in tested soils compared to applications as single compounds.

2. Materials and methods

2.1. Soils

The study was performed on the soil samples obtained from the 0- to 25-cm surface layer of 7 soil types (Table 1) that were previously used in studies by Kodešová et al. (2015, 2016) and Klement et al. (2018): SChS - Stagnic Chernozem Siltic developed on marlite, HCh - Haplic Chernozem on loess, GP - Greyic Phaeozem on loess, HL - Haplic Luvisol on loess, AE - Arenosol Epieutric on sand, HCa - Haplic Cambisol on paragneiss, and DCa - Dystric Cambisol on orthogneiss. The new samples were taken from the surface horizons (0–25 cm). A part of each sample was homogenized and stored at 4 °C prior measuring microbial activities; subsamples for biomarker analysis were freeze dried and stored at −80 °C until extraction. The remaining soils were air-dried, ground, and sifted through a 2-mm sieve. Standard laboratory procedures (see Appendix A part S2.1) were used to determine basic physical and chemical properties in Table 1 by Schmidtová et al. (2020): particle density (ϱ_s), particle size distribution (fractions of clay, silt, and sand), organic carbon content (C_{ox}), $CaCO_3$ content, pH (pH_{H2O}, pH_{KCl}, and pH_{CaCl2}), cation exchange capacity (CEC), hydrolytic acidity (i.e., sum of H+ cations) (HA), base cation saturation (BCS, the difference between CEC and HA), sorption complex saturation (SCS, the percentage of BCS in CEC), exchangeable acidity (EA), and salinity in water and ethanol. In addition, properties mainly affecting microbial conditions were measured: nitrogen content (N_{min}, N_{NO3}, N_{NH4}) (ISO, 11261:1995), total carbon (TC) and nitrogen (TN), and TC/TN ratio (C/N). Soil TC and TN concentrations were determined by dry combustion on an elemental analyzer (MicroCube, Elementar, Germany). The average values and standard deviations (Table 1) indicate large range of evaluated properties and thus suitability of these soil samples for this type of study.

2.2. Microbial analyses

Basal respiration (BR), substrate induced respiration (SIR), and microbial biomass C (C_{mic}), N (N_{mic}) and P (P_{mic}) (Table 1) were measured in soils after a preincubation period (see Section 2.4) in triplicate. BR and SIR were estimated from the headspace CO_2 accumulation rates (Anderson and Domsch, 1985). C_{mic}, N_{mic} and P_{mic} were determined using the chloroform fumigation extraction method (Brookes et al., 1982, 1985; Vance et al., 1987). The methods are in detail described in the Appendix A part S2.2.

The composition of soil microbial communities was determined using phospholipid fatty acid (PLFA) analysis. The method has been presented by Frková et al. (2020). The procedure is also explained in the Appendix A part S2.2. Briefly, PLFAs were extracted according to Bligh and Dyer (1959) with modifications by Frostegård et al. (2011). Phospholipids were eluted with 2 cm^3 methanol and subjected to mild alkaline metanolysis according to Dowling et al. (1986) and Oravecz et al. (2004). Samples were analyzed on an Agilent Trace 1310 GC (Agilent, Wilmington, Delaware, USA) equipped with a flame ionization detector and a 60 m × 0.32 mm BPX70 × 0.25 μm column (SGE Analytical Science) (Kotas et al., 2018). The results were processed using Chromeleon 7.2. PLFAs with <12 C and >20 C atoms were excluded from the analysis of soil microbial communities, as well as PLFAs with less than 0.5% of total in peak area. The responses from all the remaining PLFAs

Table 1
Basic soil and microbial characteristics: pH_{H2O}, pH_{KCl}, pH_{CaCl2}, organic carbon content (Cox), salinity in water and ethanol, exchangeable acidity (EA), cation exchange capacity (CEC), soil hydrolytic acidity (HA), basic cation saturation (BCS), sorption complex saturation (SCS), soil particle density, clay, silt and sand contents, nitrogen in nitrate (N_{NO3}) and ammonium (N_{NH4}), sum of mineral nitrogen (N_{min}), basal respiration (BR), substrate induced respiration (SIR), microbial biomass C (C_{mic}), N (N_{mic}) and P (P_{mic}), total carbon (TC) and nitrogen (TC), TC/TN ratio (C/N): SChS - Stagnic Chernozem Siltic developed on marlite, HCh - Haplic Chernozem on loess, GP - Greyic Phaeozem on loess, HL - Haplic Luvisol on loess, AE - Arenosol Epieutric on sand, HCa - Haplic Cambisol on paragneiss, DCa - Dystric Cambisol on orthogneiss.

		SChS	HCh	GP	HL	HCa	DCa	AE	Average	St. dev.
pH_{H2O}		8.06	8.08	7.45	7.29	5.84	5.77	5.41	6.84	1.14
pH_{KCl}		7.18	7.04	6.92	5.74	4.58	4.68	3.96	5.73	1.34
pH_{CaCl2}		7.41	7.35	7.14	6.29	5.36	5.26	4.35	6.17	1.20
Cox	%	2.89	1.75	1.36	1.06	1.85	2.23	0.55	1.67	0.77
Salinity H_2O	μS cm^{-1}	210.0	97.2	169.0	57.0	57.3	54.3	15.9	94.4	70.1
Salinity ethanol	μS cm^{-1}	33.1	9.1	37.3	10.8	14.5	11.9	2.3	17.0	13.0
EA	$mmol^+$ kg^{-1}	0.57	0.82	0.95	0.57	2.84	1.89	5.36	1.85	1.75
CEC	$mmol^+$ kg^{-1}	273.0	235.0	165.0	118.0	183.0	196.0	38.0	172.6	77.2
HA	$mmol^+$ kg^{-1}	3.61	4.21	6.61	16.8	51.7	61.3	30.9	25.0	23.7
BCS	$mmol^+$ kg^{-1}	269.4	230.8	158.4	101.2	131.3	134.7	7.1	147.6	85.8
SCS	%	98.7	98.2	96.0	85.7	71.8	68.7	18.6	76.8	28.5
ϱ_s	g cm^{-3}	2.48	2.53	2.54	2.59	2.55	2.49	2.61	2.54	0.05
Clay	%	20.7	36.5	17.0	12.4	18.3	19.4	7.6	18.8	9.0
Silt	%	52.2	58.1	66.5	72.9	41.3	57.7	7.0	50.8	21.8
Sand	%	27.2	5.4	16.5	14.7	40.4	22.9	85.4	30.4	26.6
N_{NO3}	mg kg^{-1}	52.12	6.78	23.82	11.54	24.79	6.99	1.21	18.2	17.4
N_{NH4}	mg kg^{-1}	3.58	1.47	1.11	1.07	0.89	2.03	2.10	1.8	0.9
N_{min}	mg kg^{-1}	55.70	8.58	24.72	13.85	25.52	9.92	4.03	20.33	17.57
BR	μg C g^{-1} h^{-1}	3.81	2.27	2.07	2.10	2.41	2.08	0.37	2.16	1.00
SIR	μg C g^{-1} h^{-1}	14.75	4.64	5.15	3.38	9.05	4.69	2.34	6.28	4.28
C_{mic}	μg C g^{-1}	670.5	363.9	298.0	195.6	283.5	218.1	120.0	307.1	178.1
N_{mic}	μg N g^{-1}	59.1	44.5	30.6	26.9	39.8	29.3	12.8	34.7	14.7
P_{mic}	μg P g^{-1}	24.3	19.0	12.5	24.4	26.6	16.7	24.9	21.19	5.22
TC	mg g^{-1}	64.1	25.0	15.7	10.9	18.8	24.9	4.1	23.4	19.5
TN	mg g^{-1}	3.29	1.82	1.53	1.19	1.93	2.49	0.36	1.8	0.9
C/N		19.5	13.8	10.3	9.19	9.77	10.0	11.4	12.0	3.63

(Table S2) were summed to obtain the total PLFA biomass ($PLFA_{tot}$, nmol g^{-1} of dry soil). Grouping according to main microbial taxa using indicative fatty acids was performed according to Johansen and Olsson (2005) and Willers et al. (2015) (Table 2). The average values and standard deviations (Tables 1 and 2) indicate large range of evaluated properties and thus suitability of these soil samples for this type of study.

2.3. Selected pharmaceuticals

Six compounds (Table S3) were selected based on results of our previous studies partly describing their behaviors in soil environment (Kodešová et al., 2015, 2016; Klement et al., 2018). Three compounds, including carbamazepine (CAR), clindamycin (CLI) and sulfamethoxazole (SUL), were selected from 7 compounds, for which sorption and dissipation of a single compound in 13 soils were evaluated by Kodešová et al. (2015, 2016). In this new study, SUL and CLI represented two antibiotics of low (4.7–15 days) and moderate (9.3–21.3 days) half-lives in topsoils, respectively, and CAR represented a compound that is very persistent in soils. The other 3 compounds citalopram (CIT), irbesartan (IRB) and fexofenadine (FEX) were used by Klement et al. (2018) to assess sorption of a single compound in 7 soils. Their degradation behavior in soils is unknown. Selected compounds have different properties and occur as different forms in the environment depending on soil pH (i.e., neutral, anion, cation, and zwitter-ion) (Table S3), which considerably affects their sorption in soils (Kodešová et al., 2015, 2016; Klement et al., 2018) and might influence their transformation in soils. All tested pharmaceuticals were purchased from TCI (Japan) and are of 97% (CAR) and 98% (CIT, CLI, FEX, IRB, and SUL) analytical grade purity. Isotope-labeled analogues of the native compounds (CAR-D_8, CIT-D_3, CLI-D_3, FEX-D_6, IRB-D_4, and SUL-D_4) were purchased from Toronto Research Chemicals (Canada) and used as internal standards for chemical analysis.

2.4. Degradation experiment

The batch degradation method (OECD, 2002) was used to evaluate degradation rates and half-lives of pharmaceuticals in soils. Twenty-four 100-mL high-density polyethylene bottles with soil mixed with pharmaceutical were prepared for each soil and compound. Fifty grams of air-dried soil (time needed for sample drying, grinding, and sieving did not exceed 5 days) was always placed into the bottle, and 6 cm^3 (3 cm^3 in the case of AE) of fresh water was added using VITLAB®Genius (5–50 mL) (VITLAB GmbH). The soils were incubated in the dark at a constant temperature of 20 °C. This initial incubation with water was chosen in order to guarantee optimal microbial conditions, which could be impaired even by very short drying in air (OECD, 2002). Next, 6 cm^3 (4 cm^3 in the case of Arenosol) of a solution of one pharmaceutical or mixture of all pharmaceuticals was added, and incubation continued. Both doses were designed to achieve approximately the one third (1st step) and two thirds (2nd step) of water holding capacity, respectively. Concentrations of solutions were calculated to reach similar compound loads per dry soil unit (1 μg g^{-1}), which corresponds to the concentration assumed for instance by Grossberger et al. (2014), Kodešová et al. (2016), Monteiro and Boxall (2009), and Srinivasan and Sarmah (2014). The following concentrations of applied solutions were assumed: 8.3 μg cm^{-3} (SChS, HCh, HL, GP, HCa, and DCa) and 12.5 μg cm^{-3} (AE). Precise water and solution volumes in each bottle were calculated from recorded masses of empty bottles, bottles with soil, bottles with soil and fresh water, and of bottles with soil, water and solution. During the incubation, the incubation bottles were regularly weighted at 2-week intervals to assess soil water contents, and water losses were compensated by adding water. After dosing of water or solution, each bottle was shaken for 30 s to achieve uniform water and compound distribution in a soil sample. Three bottles for each soil with each pharmaceutical were placed in the freezer immediately after applying compound solutions (time = 0 days). Three bottles for each pharmaceutical and soil were also removed from the incubator 1, 2, 5, 12, 23, 40 and 61 days after the pharmaceutical application and put in the freezer. Samples were stored at −20 °C until compound extraction, which was performed immediately after completing the degradation experiment. Such short-term storage in freezer should not affect compounds concentration (Fedorova et al., 2014). The approach (except 6 days preincubation with water) was the same as that applied by Kodešová et al. (2016) to obtain comparable results.

Compounds remaining in soils were extracted using the procedure that was adopted from the method validated for all 6 tested pharmaceuticals by Golovko et al. (2016). Briefly, the whole contents of the bottle were extracted with mixtures A (acetonitrile/water mixture - 1:1 v/v, with 0.1% of formic acid) and B (acetonitrile/2-propanol/water mixture

Table 2
Microbial biomass assessed using the phospholipid fatty acids (PLFAs): SChS - Stagnic Chernozem Siltic developed on marlite, HCh - Haplic Chernozem on loess, GP - Greyic Phaeozem on loess, HL - Haplic Luvisol on loess, AE - Arenosol Epieutric on sand, HCa - Haplic Cambisol on paragneiss, DCa - Dystric Cambisol on orthogneiss.

		SChS	HCh	GP	HL	HCa	DCa	AE	Average	St. dev.
$PLFA_{tot}$	nmol g^{-1}	175.28	116.62	148.67	136.26	173.62	171.44	46.72	138.37	45.97
PLFA origin										
Actinomycetes	nmol g^{-1}	12.08	11.13	11.24	9.30	11.05	9.91	1.98	9.53	3.45
Fungi	nmol g^{-1}	7.24	2.54	6.56	5.11	6.52	7.26	4.77	5.71	1.70
General bacteria	nmol g^{-1}	30.40	22.21	26.56	22.28	30.06	27.98	7.45	23.85	7.96
Gram-negative bacteria	nmol g^{-1}	50.01	32.65	43.89	33.83	42.77	45.09	8.67	36.70	13.82
Gram-positive bacteria	nmol g^{-1}	29.12	17.23	23.86	22.21	28.62	27.61	6.74	22.20	8.01
Microphototrophs/plants	nmol g^{-1}	2.00	1.12	1.91	1.18	2.01	2.15	1.25	1.66	0.45
Protozoa	nmol g^{-1}	0.82	0.64	0.91	1.45	0.99	1.44	0.87	1.02	0.31
Protozoa/fungi	nmol g^{-1}	11.46	6.52	9.65	8.17	15.76	11.39	4.87	9.69	3.61
Not-specific/NA	nmol g^{-1}	32.16	22.58	24.07	32.74	35.86	38.61	10.12	28.02	9.82
General marker										
Bacteria	nmol g^{-1}	121.60	83.22	105.55	87.61	112.50	110.59	24.84	92.27	32.74
Fungi	nmol g^{-1}	7.24	2.54	6.56	5.11	6.52	7.26	4.77	5.71	1.70
NA	nmol g^{-1}	46.44	30.87	36.55	43.54	54.61	53.59	17.11	40.39	13.35
Saturation										
Branched	nmol g^{-1}	41.20	28.36	35.10	31.50	39.68	37.52	8.72	31.73	11.09
Monounsaturated	nmol g^{-1}	70.15	47.78	61.73	48.60	63.44	64.98	14.52	53.03	18.93
OH-subs	nmol g^{-1}	2.03	1.41	1.80	1.92	1.77	1.67	0.28	1.55	0.60
Polyunsaturated	nmol g^{-1}	22.42	11.86	20.16	18.11	26.57	23.89	12.41	19.35	5.61
Saturated	nmol g^{-1}	31.92	21.16	23.37	30.72	35.63	37.98	7.33	26.87	10.54
NA	nmol g^{-1}	7.56	6.05	6.51	5.42	6.53	5.40	3.46	5.85	1.29

- 3:3:4 v/v/v, with 0.1% formic acid) in three consequent steps (A:B:B, 60:35:20 mL) using an ultrasonic bath (DT255, Bandelin electronic, Sonorex digitec, Berlin, Germany). After soil particle sedimentation, three supernatants from each bottle were mixed, and 10-cm^3 aliquots were filtered through a syringe filter (0.45 μm, regenerated cellulose, Labicom, Olomouc, Czech Republic) into 10-cm^3 vials. The possible impact (due to compound sorption) of the syringe filter material on the measured pharmaceuticals' concentrations was tested previously (Lindberg et al., 2014). No noticeable effect on the recovery of the studied compounds was found. Actual concentrations of studied compounds in applied solutions and extracts were determined using liquid chromatography with high-resolution mass spectrometry (LC-HRMS), which is described below.

Compound concentrations in soils (c, μg g^{-1}) were calculated based on the concentrations of soil extracts, their volumes and soil mass. Recoveries (Table S4) of each compound in each soil (3 bottles per treatment) were calculated from the initially applied compound load into the bottle (solute concentration (μg cm^{-3}) in solution multiplied by its volume (cm^3)) and recovered compound amount at day 0 (solute concentration in soil (μg g^{-1}) multiplied by soil mass (g)). Recoveries of compounds in all 7 soils (%) were: CAR 96 ± 26 (S) and 99 ± 25 (M), CIT 100 ± 21 (S) and 98 ± 24 (M), CLI 73 ± 6 (S) and 77 ± 13 (M), FEX 77 ± 5 and 78 ± 12 (M), IRB 87 ± 16 (S) and 92 ± 23 (M), and SUL 84 ± 14 (S) and 87 ± 15 (M). High variability in recovery is given by the measurement uncertainty that can be in this matrix (i.e., 7 soils of a high variability of soil properties) up to 30% (Golovko et al., 2016; Kodešová et al., 2016).

Since mathematical models for simulating transport of organic contaminants in soils usually assume the first-order kinetic model to describe compound dissipation in soils (e.g., Beulke et al., 2000; Šimůnek et al., 2016), the data points given by time (=0, 1, 2, 5, 12, 23, 40 and 61 days) and corresponding remaining compound's concentrations in soils were fitted with the first-order kinetic model:

$$\frac{c_t}{c_0} = e^{-k_R t} \tag{1}$$

where c_0 (μg g^{-1}) is the initial concentration, c_t (μg g^{-1}) is the concentration in time, t (day) is time, and k_R (day^{-1}) is the first-order rate constant (Table S5). Next, compound dissipation half-life DT_{50} (day) was calculated as follows (Table 3):

$$DT_{50} = \frac{\ln 2}{k_R} \tag{2}$$

It should be noted that coefficients of determinations (Table S5) expressing the correspondences between the measured remaining concentrations and those calculated using Eq. (1) calculated for CAR and CIT were low in some cases due to larger variability of measured values compared with the other compounds. The reason for this increased variability could be significant persistence of these two compounds in soils and greater sensitivity to actual conditions in the incubation bottle. The other reason for the low correlation values for CAR and CIT was, that while trends in dissipation of largely degradable compounds played a greater role than measurement inaccuracy (impact of which decreased with decreasing concentration in soils), in the case of the more persistent compounds the measurement uncertainty exceeded the effect of the dissipation trend. It should be noted that recently there have been developed new tools for a kinetic evaluation of a chemical degradation data (e.g., Ranke et al., 2018) using various functions, which could likely in few cases provide better fits of measured values for SUL, CLI, FEX and IRB and more accurate estimate of DT_{50} values. However, these tools would not help to provide better estimates of the dissipation half-lives of CAR and CIT. In addition, the resulting DT_{50} values could not be adopted in simulation models. Therefore, these tools were not utilized in this study. The medium uncertainty of the evaluated DT_{50} values for these two compounds could potentially influence the results of the following statistical analyses particularly when analyzing correlations between half-lives and various soil and microbial factors.

2.5. Sorption experiment

A batch equilibrium method (OECD, 2000) was used to evaluate sorption isotherms for single compound solutions and the same soils by Schmidtová et al. (2020), which were expressed using the Freundlich equation:

$$s = K_F c^{1/n} \tag{3}$$

where K_F ($cm^{3/n}$ $\mu g^{1-1/n}$ g^{-1}) and n are empirical coefficients. The methods are described in Schmidtová et al. (2020), Bořík et al. (2020) and the Appendix A part S2.5. Final values were presented by Schmidtová et al. (2020). In present study, to relate compounds' sorption affinities (which were described by K_F values that were n dependent) to their half-lives as well as soil and microbial characteristics, the same procedure proposed by Kodešová et al. (2015) and Klement et al. (2018) was applied. The average n coefficient (n_{avg}) was calculated for each pharmaceutical, and new $K_{F,navg}$ values were optimized assuming a fixed value of n_{avg} for all soils (Table 3).

2.6. Chemical analyses

One hundred-μL aliquots of extracted samples from degradation experiments were spiked with isotopically labeled internal standards and analyzed by LC-HRMS (HTS XT-CTC autosampler from CTC Analytics AG; LC pump Accela 1250 and Q-Exactive plus mass spectrometer, both from Thermo Fisher Scientific) in full scan and electrospray positive mode (scan range for mass was 100–700 *m/z*, resolution 70,000 FWHM) using the 16-minute method according to Koba et al. (2016). A Hypersil Gold aQ column (50 × 2.1 mm; 5 μm particles, Thermo Fisher Scientific) was used for chromatographic separation. More information about conditions of analysis, including gradient elution conditions, *m/z* values, retention time, and limits of quantification (LOQ), is provided in Table S5A. TraceFinder 3.3 software (Thermo Fisher Scientific) was used for data processing. Methods of internal and matrix matching standards were used for calculation of concentrations of chosen pharmaceuticals.

2.7. Statistical analyses

Simple correlations between measured physical, chemical and microbiological soil properties; Freundlich sorption coefficients; and dissipation half-lives were assessed using the Pearson product moment correlation coefficient and p-value, which tests the statistical significance of the estimated correlations. Multiple linear regressions were also used to obtain models for estimating dissipation half-lives resulting from single compound applications based on K_F values, PLFAs and soil properties related to microbial abundance and activity. It should be noted that DT_{50} values for FEX in AE were identified as outliers and excluded from all statistical analyses. Next, principal components analyses were used to evaluate the general behavior of compounds with respect to soil conditions. Analyses were performed using STAGRAPHICS Centurion XV Version 15.2.06.

3. Results and discussion

3.1. Dissipation of a single pharmaceutical in soils

The largest persistence (i.e., the largest dissipation half-lives in Table 3) of compounds in tested soils was observed for CIT (average $DT_{50,S}$, 152.1 days; range, 86.7–223.1 days) followed by CAR (105.6 days; 90.2–140.9 days). Considerably lower dissipation half-lives were obtained for IRB (average $DT_{50,S}$, 24.4 days; range, 19.0–29.2 days),

Table 3
The Freundlich sorption coefficient, K_F ($cm^{3/n}\ \mu g^{1-1/n}\ g^{-1}$), the half-lives $DT_{50,S}$ (days) resulted from the application of a single pharmaceutical and $DT_{50,M}$ (days) resulted from application of the mixture of all compounds: SChS - Stagnic Chernozem Siltic developed on marlite, HCh - Haplic Chernozem on loess, GP - Greyic Phaeozem on loess, HL - Haplic Luvisol on loess, AE - Arenosol Epieutric on sand, HCa - Haplic Cambisol on paragneiss, DCa - Dystric Cambisol on orthogneiss, CAR – carbamazepine, CIT – citalopram, CLI – clindamycin, FEX – fexofenadine, IRB – irbesartan, SUL – sulfamethoxazole.

			SChS	HCh	GP	HL	HCa	DCa	AE	Average	St. dev.
CAR	K_F for n = 1.02	$cm^{3/n}\ \mu g^{1-1/n}\ g^{-1}$	4.05	2.52	2.07	1.67	2.31	3.70	1.05	2.48	1.07
CIT	K_F for n = 0.92	$cm^{3/n}\ \mu g^{1-1/n}\ g^{-1}$	6.77 10^6	3.21 10^6	1.68 10^6	8.88 10^5	2.80 10^5	1.06 10^5	1.06 10^5	1.86 10^6	2.43 10^6
CLI	K_F for n = 0.91	$cm^{3/n}\ \mu g^{1-1/n}\ g^{-1}$	19.28	12.13	10.12	8.39	6.09	4.61	3.44	9.15	5.41
FEX	K_F for n = 1.05	$cm^{3/n}\ \mu g^{1-1/n}\ g^{-1}$	29.3	22.5	18.1	18.4	40.0	54.3	65.7	35.5	18.7
IRB	K_F for n = 0.51	$cm^{3/n}\ \mu g^{1-1/n}\ g^{-1}$	1.50	0.75	0.58	0.87	3.32	6.08	8.97	3.15	3.23
SUL	K_F for n = 1.25	$cm^{3/n}\ \mu g^{1-1/n}\ g^{-1}$	0.565	0.374	0.367	0.800	3.132	4.173	0.978	1.48	1.53
CAR	$DT_{50,S}$	days	140.9	100.7	101.2	93.7	99.9	91.7	90.2	102.6	17.5
	$DT_{50,M}$	days	160.6	145.6	170.9	85.1	128	146.9	97	133.4	32.1
	$DT_{50,M}$-$DT_{50,S}$	days	19.7	44.9	69.7	−8.6	28.1	55.2	6.8	30.8	27.6
	$DT_{50,M}$-$DT_{50,S}$	%	14.0	44.6	68.9	−9.2	28.1	60.2	7.5	30.6	28.7
CIT	$DT_{50,S}$	days	208.2	146.3	223.1	124.9	86.7	179.6	95.7	152.1	53.5
	$DT_{50,M}$	days	310.8	134.6	236.7	172.4	175	59	241.9	190.1	81.9
	$DT_{50,M}$-$DT_{50,S}$	days	102.6	−11.7	13.6	47.5	88.3	−120.6	146.2	38.0	88.2
	$DT_{50,M}$-$DT_{50,S}$	%	49.3	−8.0	6.1	38.0	101.8	−67.1	152.8	39.0	72.5
CLI	$DT_{50,S}$	days	14.7	18.4	9.1	8.6	7.4	7.4	10.3	10.8	4.2
	$DT_{50,M}$	days	8.2	17.5	9	13.5	10.3	15.6	8.7	11.8	3.7
	$DT_{50,M}$-$DT_{50,S}$	days	−6.5	−0.9	−0.1	4.9	2.9	8.2	−1.6	1.0	4.8
	$DT_{50,M}$-$DT_{50,S}$	%	−44.2	−4.9	−1.1	57.0	39.2	110.8	−15.5	20.2	52.3
FEX	$DT_{50,S}$	days	9	26	11.5	21.7	13.3	14.3	69	23.5	20.9
	$DT_{50,M}$	days	16.4	23.9	13.5	35.8	14.4	11.1	88.5	29.1	27.5
	$DT_{50,M}$-$DT_{50,S}$	days	7.4	−2.1	2	14.1	1.1	−3.2	19.5	5.5	8.6
	$DT_{50,M}$-$DT_{50,S}$	%	82.2	−8.1	17.4	65.0	8.3	−22.4	28.3	24.4	37.8
IRB	$DT_{50,S}$	days	24.2	29.2	26.4	23.1	19	21.8	27.2	24.4	3.5
	$DT_{50,M}$	days	25.7	34.1	31.4	28.1	20.4	37	45	31.7	8.0
	$DT_{50,M}$-$DT_{50,S}$	days	1.5	4.9	5	5	1.4	15.2	17.8	7.3	6.6
	$DT_{50,M}$-$DT_{50,S}$	%	6.2	16.8	18.9	21.6	7.4	69.7	65.4	29.4	26.7
SUL	$DT_{50,S}$	days	7.8	9.6	6.8	9.2	12.7	10.8	10.6	9.6	2.0
	$DT_{50,M}$	days	11.8	10.3	7.3	9.5	13.3	8.3	10.4	10.1	2.0
	$DT_{50,M}$-$DT_{50,S}$	days	4	0.7	0.5	0.3	0.6	−2.5	−0.2	0.5	1.9
	$DT_{50,M}$-$DT_{50,S}$	%	51.3	7.3	7.4	3.3	4.7	−23.1	−1.9	7.0	22.2

Table 4
The correlation coefficients describing relationship between the half-lives $DT_{50,S}$ (days) resulted from the application of a single pharmaceutical or $DT_{50,M}$ (days) resulted from application of the mixture of all compounds and the Freundlich sorption coefficient, K_F ($cm^{3/n}\ \mu g^{1-1/n}\ g^{-1}$), basal respiration, BR ($\mu g\ C\ g^{-1}\ h^{-1}$), substrate induced respiration, SIR ($\mu g\ C\ g^{-1}\ h^{-1}$), microbial biomass C, C_{mic} ($\mu g\ g^{-1}$), N, N_{mic} ($\mu g\ g^{-1}$) and P, P_{mic} ($\mu g\ g^{-1}$) and microbial biomass assessed using the phospholipid fatty acids, PLFAs (nmol g^{-1}): CAR – carbamazepine, CIT – citalopram, CLI – clindamycin, FEX – fexofenadine, IRB – irbesartan, SUL – sulfamethoxazole.

	$DT_{50,S}$ - Single compound application						$DT_{50,M}$ - Multiple compounds application					
	CAR	CIT	CLI	FEX[a]	IRB	SUL	CAR	CIT	CLI	FEX[a]	IRB	SUL
K_F	0.651	0.557	0.672	−0.323	−0.082	0.714	–	–	–	–	–	–
BR	0.819*	0.527	0.315	−0.494	−0.290	−0.321	0.563	0.211	−0.013	−0.164	−0.755*	0.289
SIR	0.922**	0.350	0.251	−0.659	−0.335	−0.162	0.504	0.511	−0.416	−0.372	−0.660	0.567
C_{mic}	0.971***	0.560	0.560	−0.416	0.043	−0.451	0.622	0.508	−0.219	−0.214	−0.503	0.345
N_{mic}	0.846*	0.420	0.557	−0.261	−0.101	−0.240	0.602	0.255	0.017	−0.196	−0.664	0.441
P_{mic}	0.172	−0.720	−0.017	0.038	−0.367	0.529	−0.645	0.286	−0.263	0.375	−0.273	0.847*
$PLFA_{tot}$	0.444	0.458	−0.192	−0.873*	−0.648	−0.068	0.545	−0.152	0.066	−0.663	−0.772*	0.101
PLFA origin												
Actinomycetes	0.496	0.540	0.198	−0.469	−0.270	−0.286	0.657	−0.095	0.226	−0.506	−0.761*	0.046
Fungi	0.344	0.409	−0.606	−0.924**	−0.677	−0.073	0.349	0.176	−0.512	−0.602	−0.344	−0.026
General bacteria	0.486	0.487	−0.076	−0.900*	−0.554	−0.116	0.624	−0.115	0.079	−0.777	−0.794*	0.120
Gram negative bacteria	0.533	0.625	−0.058	−0.961**	−0.475	−0.258	0.685	−0.063	0.045	−0.772	−0.718	−0.004
Gram positive bacteria	0.461	0.441	−0.231	−0.878*	−0.682	−0.065	0.513	−0.106	0.005	−0.595	−0.786*	0.126
Microphototrophs/plants	0.349	0.462	−0.425	−0.904*	−0.616	0.025	0.631	−0.001	−0.317	−0.883*	−0.384	0.025
Protozoa	−0.404	−0.056	−0.728	−0.008	−0.600	0.120	−0.387	−0.514	0.249	0.210	−0.044	−0.340
Protozoa/fungi	0.296	0.067	−0.419	−0.688	−0.853*	0.317	0.355	−0.084	−0.182	−0.592	−0.783*	0.416
General marker												
Bacteria	0.509	0.547	−0.078	−0.953**	−0.531	−0.183	0.636	−0.091	0.063	−0.753	−0.769*	0.063
Fungi	0.344	0.409	−0.606	−0.924**	−0.677	−0.073	0.349	0.176	−0.512	−0.602	−0.344	−0.026
Saturation												
Branched	0.488	0.487	−0.105	−0.918**	−0.577	−0.136	0.575	−0.106	0.074	−0.660	−0.804*	0.105
Monounsaturated	0.510	0.584	−0.074	−0.951**	−0.508	−0.203	0.673	−0.094	0.061	−0.808	−0.732	0.029
OH-subs	0.464	0.504	−0.061	−0.652	−0.466	−0.307	0.436	−0.049	0.112	0.066	−0.814*	−0.004
Polyunsaturated	0.271	0.195	−0.572	−0.800	−0.885**	0.205	0.331	−0.079	−0.242	−0.590	−0.673	0.221
Saturated	0.246	0.236	−0.319	−0.446	−0.779*	0.162	0.278	−0.368	0.236	−0.289	−0.702	0.133

[a] Half-lives values for FEX in AE were as outliers excluded from analyses.
* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.

FEX (23.5 days; 9.0–69 days), CLI (10.8 days; 7.4–18.4) and SUL (9.6 days; 6.8–12.7). A large persistence of CAR in soils has also been reported in previous studies. Our $DT_{50,S}$ values for CAR (Table 3) were lower than the DT_{50} values reported by Dalkmann et al. (2014) (355–1624 days), Shao et al. (2018) (108–1732 days), and Martinez-Hernandez et al. (2016) (194–326 days) as well as DT_{50} values evaluated in outdoor mesocosms by Walters et al. (2010) (462–533 days) and Grossberger et al. (2014) (147 and >200 days). Significant stability of CAR in tested soils (observed dissipation could not be fitted by the first-order kinetic model) was also documented by Biel-Maeso et al. (2019). Lower values, which were obtained under laboratory conditions, were reported by Monteiro and Boxall (2009) (60 days) and Yu et al. (2013) (28–39 days). Slightly lower values were found under field conditions (98 and 75 days for surface and subsurface soils, respectively) by Al-Rajab et al. (2015). Similar values were reported by Li et al. (2013) (46–173 days). Hurtado et al. (2017) reported $DT_{50} > 40$ days. Interestingly, considerably higher values of DT_{50} were obtained for the same soils in our previous study (Kodešová et al., 2016). In this former study, the DT_{50} values were generally greater than 1000 days except HL (329 days) and DCa (418 days). One possible reason for differences in half-lives obtained from our previous and present studies could be differences in soils sampling time, i.e., spring 2018 (present study) versus autumn 2014 (previous study). It has been assumed that the organic matter fraction can reduce carbamazepine bioavailability (e.g., Al-Rajab et al., 2015; Shao et al., 2018; Yu et al., 2013). Jirků et al. (2013) documented that organic content varied within the year and considerably differed in different years for 3 of the tested soils (i.e., GP, HL and HCa). However, basic soil properties (particularly organic carbon content) of soils sampled for our previous and present study did not considerably differ. Soil samples obtained in different seasons could exhibit different microbial biomass and activity with values higher during the spring compared with autumn. For instance, nitrification can have a moderately positive (Dawas-Massalha et al., 2014) or no (Kruglova et al., 2014) influence on CAR dissipation in soils, and soil bacteria, *Streptomycetes* in particular, can efficiently degrade carbamazepine under laboratory conditions (Popa et al., 2014; Ungureanu et al., 2015). Unfortunately, we do not have information about microbial conditions in previously studied soil samples; thus, we cannot compare those criteria. Another reason for observed differences in CAR half-lives between studies could be slightly different experimental procedures. In our previous study, we did not preincubate soils (i.e., 6 days of incubation of soils samples under 20 °C and soil water content corresponding to a half of the soil water capacity) before application of pharmaceuticals. Although soil sample processing followed the same method and was very fast in both experiments, bacterial activity could be suppressed. During the preincubation period, bacterial activity could be triggered that resulted in a better starting point for CAR degradation in soils compared with no preincubation.

The other two compounds that were assessed in our previous study (Kodešová et al., 2016) were CLI and SUL. Regarding CLI, the $DT_{50,S}$ values (Table 3) were again slightly lower than values (13–21 days) reported by Kodešová et al. (2016) in the same topsoils. Our results could also be compared with dissipation half-lives in biosolids presented by Wu et al. (2009) and Chenxi et al. (2008), who documented faster degradation in the first few days followed by stabilization afterwards. Both effects can be explained by better initial conditions for compound microbial degradation in preincubated soils (present study) and biosolids with large microbial abundance (Wu et al., 2009; Chenxi et al., 2008) compared with nonpreincubated soils (Kodešová et al., 2016).

In the case of SUL, the $DT_{50,S}$ values (Table 3) were similar those (5–15 days) reported by Kodešová et al. (2016). This finding indicates that different preincubation treatments (i.e., not and preincubated soil samples in our previous and present study, respectively) did not influence dissipation of SUL in the selected soils. The finding could potentially be explained by a very fast dissipation of this compound in the soil environment, which was also documented by other studies in different soils by Srinivasan and Sarmah (2014) (4–13 days) and Lin and Gan (2011) (9–11 days). On the other hand, higher dissipation half-lives in topsoils were published by Albero et al. (2018) (18–24 days), Shen et al. (2018) (29–36 days) and Wu et al. (2012) (38–55 days). Higher dissipation half-lives were also observed in subsoils by Kodešová et al. (2016) (66 and 152 days) and lake sediments by Zhang et al. (2013) (42–57 days). The biotic SUL transformation again appeared to be the major factor affecting compound dissipation (Srinivasan and Sarmah, 2014; Wu et al., 2012). At broad spectrum of soil bacteria or mixed microbial consortia may degrade SUL by metabolic or cometabolic pathways (reviewed in Wang and Wang, 2018). Thus, different half-lives found in the literature were results of different bioavailabilities of SUL dependent on its concentration together with presence of microbial members responsible for degradation in tested soils and sediments.

While dissipation of CAR and SUL (also partly CLI) in soils has been documented in several studies, dissipation of CIT in this environment has not been studied to date. The moderately lower persistence of CIT (DT_{50} of 41 days) compared to the $DT_{50,S}$ values in Table 3 was documented by Iranzo et al. (2018), who studied dissipation of CIT in composted sludge from a waste-water treatment plant. The large persistence of CIT could be partly explained by its very large sorption affinity to soils (e.g., Table 3 or Klement et al., 2018). Similar to CIT, our $DT_{50,S}$ values for IRB could be compared only with half-lives reported by Iranzo et al. (2018) in composted sludge from the wastewater treatment plant. Their values (9–27.7 days) were similar or slightly lower than our obtained values (Table 3). To the best of our knowledge, no study has addressed FEX dissipation in soils, sediments or in soils related materials.

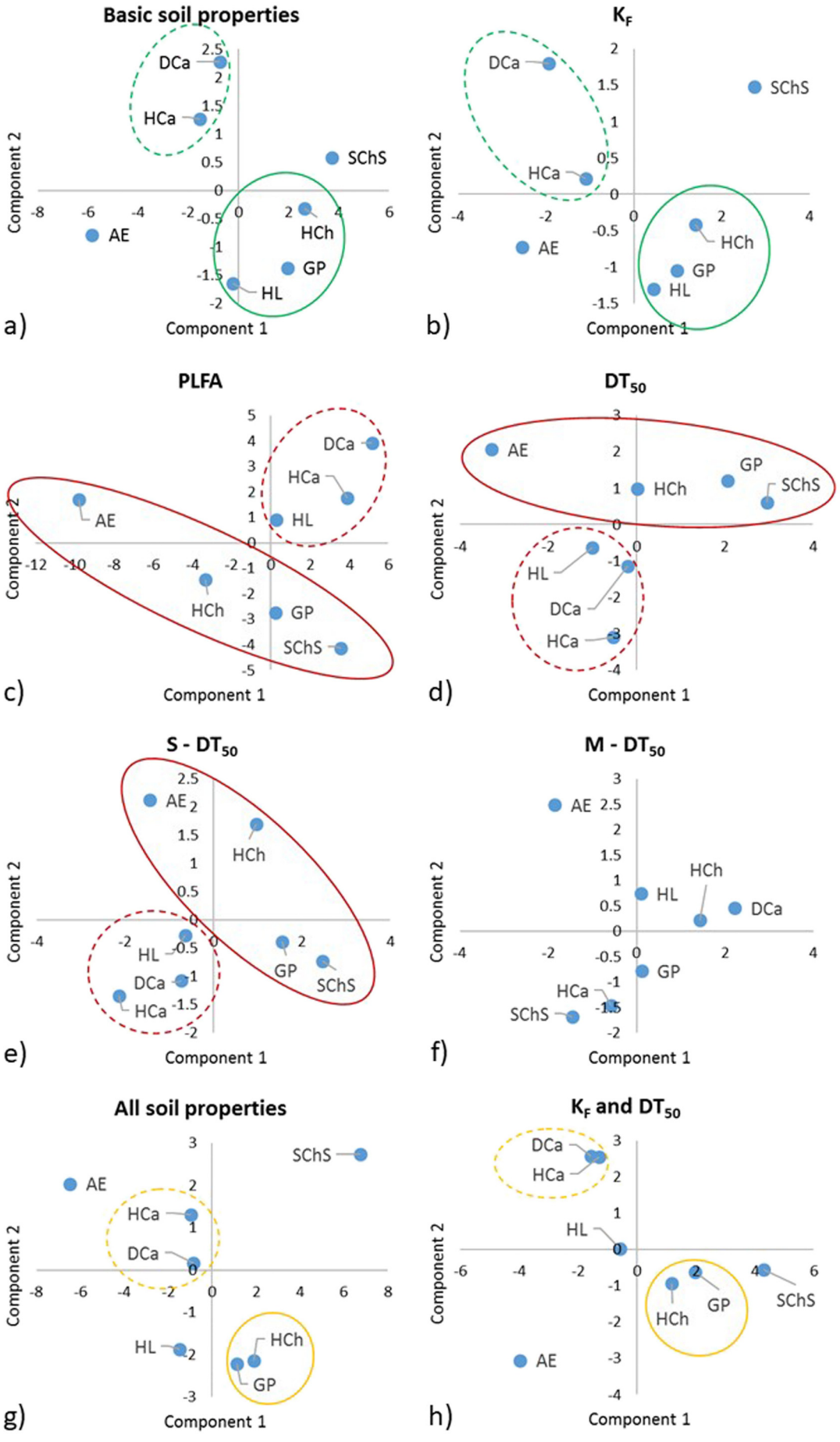
3.2. Simultaneous degradation of all pharmaceuticals in soils

The dissipation half-lives ($DT_{50,M}$) of compounds applied into soils simultaneously (Table 3) were mostly increased compared with values ($DT_{50,S}$) from a single compound application, which may indicate a negative impact of antibiotics on soil microbial communities (e.g., Caracciolo et al., 2015; Grenni et al., 2018). However, the impact

Table 5
Multiple linear regression models for estimating $DT_{50,S}$ values (days) from K_F ($cm^{3/n}\,\mu g^{1-1/n}\,g^{-1}$), microbial biomass P, P_{mic} ($\mu g\,g^{-1}$), microbial biomass assessed using the phospholipid fatty acids (nmol g^{-1}), i.e., total PLFA (PLFAtot), total fungal PLFA (Fungi), total bacterial PLFA (Bacteria), total Gram-negative bacterial PLFA (Gnegative), and total polyunsaturated PLFA (Poly): CAR – carbamazepine, CIT – citalopram, CLI – clindamycin, FEX – fexofenadine, IRB – irbesartan, SUL – sulfamethoxazole.

Pharmaceutical	Multiple linear regression models for estimating $DT_{50,S}$	R^2 (%)
CAR	$DT_{50,S} = 76.2^{**} + 0.10.6\ K_F$	42.3 ($p = 0.114$)
CIT	$DT_{50,S} = 290.2^{**} - 7.66\ P_{mic}{}^{*} + 0.0000130\ K_F{}^{*}$	86.7* ($p = 0.018$)
CLI	$DT_{50,S} = 14.9^{**} - 1.58$ Fungi$^{*} + 0.546\ K_F{}^{*}$	86.9* ($p = 0.017$)
FEX	$DT_{50,S} = 58.7^{***} - 0.413$ Bacteria**	90.8** ($p = 0.003$)[a]
	$DT_{50,S} = 61.0^{**} - 0.468$ Bacteria$^{**} + 0.109\ K_F$	95.0* ($p = 0.011$)[a]
	$DT_{50,S} = 69.4^{***} - 0.573$ Bacteria$^{***} + 0.197\ K_F{}^{*}$	99.2***($p = 0.0001$)
	$DT_{50,S} = 52.4^{**} - 0.237$ PLFAtot*	76.3* ($p = 0.023$)[a]
	$DT_{50,S} = 59.2^{**} - 0.325$ PLFAtot$^{*} + 0.219\ K_F$	89.0* ($p = 0.036$)[a]
	$DT_{50,S} = 65.9^{***} - 0.386$ PLFAtot$^{***} + 0.311\ K_F{}^{**}$	98.5*** ($p = 0.0001$)
IRB	$DT_{50,S} = 35.0^{***} - 0.549$ Poly**	78.4** ($p = 0.008$)
SUL	$DT_{50,S} = 8.28^{**} + 0.921\ K_F$	51.0 ($p = 0.072$)
	$DT_{50,S} = 11.4^{**} - 0.631$ Fungi $+ 1.26\ K_F{}^{*}$	73.8 ($p = 0.069$)
	$DT_{50,S} = 10.5^{**} - 0.0678$ Gnegative $+ 1.08\ K_F{}^{*}$	72.0 ($p = 0.078$)

[a] half-lives values for FEX in AE were excluded from analyses.
*** $p < 0.001$.
** $p < 0.01$.
* $p < 0.05$.


Basic soil properties
DCa
HCa
SChS
AE
HCh
GP
HL
Component 2
Component 1
a)
K_F
DCa
SChS
HCa
AE
HCh
GP
HL
Component 2
Component 1
b)
PLFA
DCa
HCa
HL
AE
HCh
GP
SChS
Component 2
Component 1
c)
DT_{50}
AE
GP
HCh
SChS
HL
DCa
HCa
Component 2
Component 1
d)
S - DT_{50}
AE
HCh
HL
GP
SChS
DCa
HCa
Component 2
Component 1
e)
M - DT_{50}
AE
HCh
HL
DCa
GP
HCa
SChS
Component 2
Component 1
f)
All soil properties
SChS
AE
HCa
DCa
HL
HCh
GP
Component 2
Component 1
g)
K_F and DT_{50}
DCa
HCa
HL
HCh
GP
SChS
AE
Component 2
Component 1
h)

of simultaneous application on the half-lives of selected pharmaceuticals was not consistent in all soils. The least influence on half-lives was observed for SUL (higher $DT_{50,M}$ in SChS, HCh, GP, HL, and HCa and lower $DT_{50,M}$ in DCa and AE). An ambiguous trend was observed for CLI (higher $DT_{50,M}$ in SChS, HCh, GP and AE and lower $DT_{50,M}$ in HL, HCa, and DCa). Dissipations of other non-antibiotic compounds were likely mostly decreased by the presence of antibiotics. However, lower $DT_{50,M}$ values compared with $DT_{50,S}$ values were also obtained for CIT and FEX in HCh and DCa and CAR in HL. The results of our study cannot confirm that enhanced dissipation of selected compounds in some soils was due to interactions with each other (e.g., Grenni et al., 2018). It can be hypothesized that compounds were less sorbed in some soils due to a competition of compounds for sorption sites and thus were more available for microbes. An inconsistent influence of simultaneous applications of compounds on their dissipations in different soils is also documented by insignificant positive correlations between $DT_{50,S}$ and $DT_{50,M}$ values (Table S7). Therefore, it is not possible to propose general relationships for estimating compounds half-lives in mixtures with other compounds from values obtained from single compound applications. The large persistence of some compounds in the mixture with other compounds increases their potential to migrate in the subsurface water environment and thus should be assumed in studies assessing potential threats related to the spread of pharmaceuticals in the environment. Despite the large variability of the percentage of increase/decrease in half-lives, average values that vary between 7 and 39% (Table 3) can be at least used to adjust half-lives resulting from single compound dissipation tests at diverse levels to simulate limit scenarios when assessing potential migration of these compounds in the soil environment.

3.3. Relationships among half-lives, K_F values and soil properties

Regarding K_F values, a significant positive relationship (Table S7) was found between the CAR K_F sorption coefficient and Cox ($R = 0.971$, $p < 0.05$ in all cases, when not different), CEC ($R = 0.862$) and BCS ($R = 0.756$) (Table S1). This finding indicates that the sorption affinity of organic compounds in neutral forms correlates positively to organic matter content, which was documented previously (Kodešová et al., 2015), and properties that correlate with C_{ox} (Table S7). A significant positive relationship ($R = 0.976$) was identified between the K_F sorption coefficients of the positively charged compounds CIT and CLI, and the K_F values of both compounds positively correlated with BCS ($R = 0.836$ and $R = 0.875$, for CIT and CLI, respectively). This finding can be explained by a sorption of cations on the negatively charged surface of soil components (Kodešová et al., 2015; Klement et al., 2018). The significant positive relationship ($R = 0.985$) was also identified between the K_F sorption coefficients of FEX and IRB, and a significantly negative correlation was observed between the K_F values for both compounds and SCS ($R = -0.889$, and $R = -0.942$, for FEX and IRB, respectively). These findings are again consistent with results of Klement et al. (2018) and associated with repulsion between the negative charges of their molecules and component surface. Finally, as observed by Kodešová et al. (2015), a strong positive relationship ($R = 0.957$) was found between the SUL K_F values and HA, which can be again explained by its negative charge in soils with higher pH and neutral form in soils with low pH and high HA (i.e., Cambisols), in which its sorption is less or not influenced by repulsion between negative charges.

While correlation analyses showed meaningful statistically significant relationships ($p < 0.05$) between some soil properties and the K_F values (Table S7), analyses for half-lives generally showed no relationships (Table S8). One exception is that the $DT_{50,S}$ values for SUL correlated with HA ($R = 0.806$, $p = 0.0285$). This finding may be associated with the positive correlation between the K_F values and HA (Table S7). Therefore, the dissipation half-live increased with increasing sorption affinity of SUL to soils, thus decreasing its availability. However, the positive correlations between the K_F and $DT_{50,S}$ values of SUL were not statistically significant (Table 4 or S8). Similar correlations (Table S8) between the $DT_{50,S}$ values for CAR and BCS ($R = 0.759$) can be partly explained by the positive relationship between K_F values and BCS (Table S7). However, the positive correlations between the K_F and $DT_{50,S}$ values of CAR were not statistically significant (Table 4 or S8). Nonsignificant positive correlations were also identified between the K_F and $DT_{50,S}$ values for CIT and CLI, and even negative correlations were obtained between the K_F and $DT_{50,S}$ values for FEX and IRB (Table 4 or S8). In general, as also found in our previous study (Kodešová et al., 2016), dissipation half-lives cannot be related to a single property of soils. In addition, although Kodešová et al. (2016) documented statistically significant positive relationships between the K_F values and half-lives of CLI and SUL measured in topsoils, a nonsignificant correlation was observed in the present study.

Sorption coefficients for mixture of all compounds were not measured. Since sorption coefficients of all or some compounds should be impacted by their competition for sorption sites or synergy (Kočárek et al., 2016; Fér et al., 2018; Schmidtová et al., 2020), correlations between $DT_{50,M}$ and evaluated K_F were not calculated.

3.4. Relationships between half-lives and soil microbial biomass/biomarkers

Half-lives of FEX and IRB negatively correlated with some of the microbial factors (Table 4), i.e., dissipation of these two compounds increased with some of the increasing microbial factors. For instance, significant and insignificant correlations were found between the $DT_{50,S}$ values and the overall microbial biomass ($PLFA_{tot}$) for FEX ($R = -0.873$, $p = 0.023$) and IRB ($R = -0.648$, $p = 0.116$), respectively, and between the $DT_{50,M}$ values and $PLFA_{tot}$ for IRB ($R = -0.772$, $p = 0.042$) and FEX ($R = -0.663$, $p = 0.152$), respectively. These findings suggest a scenario wherein "the higher the biomass, the faster the dissipation". However, in general, no meaningful correlations were found for CAR, CLI, SUL and CIT. The reason could be that CAR is mainly metabolized by enzymes in human, animal and plant bodies (e.g., Kodešová et al., 2019a; Malchi et al., 2014; Paltiel et al., 2016) that are generally not present in soils (e.g., Thelusmond et al., 2019), and microbial degradation is likely very slow and linked to specific microbial members of the community (Popa et al., 2014; Ungureanu et al., 2015). CIT is strongly sorbed in soils, thus being mostly unavailable for degradation. Therefore, microbial factors did not play a major role. Regarding CLI and SUL, these compounds could variably modify microbial activity (Frková et al., 2020). However, the $DT_{50,S}$ values of CLI negatively but insignificantly correlated with the total fungal PLFA (Fungi) ($R = -0.606$, $p = 0.149$ for $DT_{50,S}$ and $R = -0.512$, $p = 0.240$ for $DT_{50,M}$) and the total protozoal PLFA (Protozoa) ($R = -0.728$, $p = 0.064$ for $DT_{50,S}$).

3.5. Estimation of dissipation half-lives from K_F values, soil properties and microbial indicators

Results of multiple linear regressions were evaluated with respect to expected impacts of particular factors on the dissipation of compounds in soils, e.g., increased microbial biomass or specific microbial markers stimulate dissipation of biodegradable compounds, while the higher sorption of compounds in soils would inhibit it. This notion means that the equations showing the opposite effects were excluded. Resulting regression models for $DT_{50,S}$ of CIT, CLI, FEX, IRB and SUL in

Fig. 1. Grouping soils according: a) basic soil properties (first 15 lines in Table 1); b) Freundlich sorption coefficients, K_F (Table 3); c) phospholipid fatty acids, PLFAs (Table S2); d) half-lives DT_{50} resulted from both treatments, $DT_{50,S}$ and $DT_{50,M}$ (Table 3); e) half-lives resulted from the single compound applications, $DT_{50,S}$; f) half-lives resulted from multiple compound applications, $DT_{50,M}$; g) all soil properties in Table 1; f) half-lives resulted from both treatments, $DT_{50,S}$ and $DT_{50,M}$, and K_F values (Table 3). Weights of the components corresponding to the components related to different properties and datasets shown in this figure (i.e., in a, b, c, d, e and f) are shown in Fig. S1 and corresponding Figs. S1a, b, c, d, e and f.

Table 5 always included at least one microbial factor (either P_{mic} or PLFA-derived microbial markers). In the case of CAR, CIT, CLI, FEX and SUL equations included the K_F values. However, it should be mentioned that in the case of CAR and SUL, the resulting multiple linear regression models were not statistically significant at the 95% or greater confidence level. Despite this, the models for both antibiotics CLI and SUL (of the highest R^2 and lowest p-value) included the same factors (i.e., fungal PLFA content and K_F), which may indicate similar mechanisms (i.e., stimulation and inhibition, respectively) controlling their dissipation in soils. The potential of fungal members of the microbial community to degrade SUL in soils was documented by their enhanced activity (Chen et al., 2016) or increased proportion of fungal biomass in loamy sand soil (Gutiérrez et al., 2010) or in Chernozem Haplic and Phaeozem Greyic (Frková et al., 2020). Antibiotics are efficiently degraded by various soil microorganisms (Wang and Wang, 2018; Martin-Laurent et al., 2019), including resistant soil bacteria, which exhibit increased numbers due to environmental pollution (e.g., Fahrenfeld et al., 2014; Goodman and Gilman, 2011; Heuer et al., 2008). In our study, the second model for SUL includes K_F and biomass of Gram-negative bacteria (Table 5) likely because these bacteria are more likely to acquire and spread plasmid-mediated antibiotic resistance in the environment (Stokes and Gillings, 2011). A decreased G+/G- ratio, which indicates a stimulatory effect on Gram-negative bacteria after the application of SUL or CLI into some soils, was also observed by Frková et al. (2020).

Bacteria seemed to be the main factors controlling dissipation of FEX (Tables 4 and 5). An increased R^2 was achieved when the K_F values were also included (Table 5). However, the impact of the K_F values was statistically insignificant, and the statistical significance of the model decreased. Close correlations were observed between half-lives and other microbial indicators (Table 5), including $PLFA_{tot}$. Models derived either from $PLFA_{tot}$ or from $PLFA_{tot}$ and K_F (Table 5) were less significant than those derived for the total bacterial biomass (General bacteria). Statistical analyses (Table 4) and previous multiple linear regressions (Table 5) were performed without the $DT_{50,S}$ values for FEX in AE. Similar models (to those discussed above) of greater statistical significance were obtained when all the $DT_{50,S}$ values for FEX were included (Table 5). Resulting models showed an overall stimulation effect of the entire microbial community and the inhibitory influence of relatively high sorption of FEX in soils although the simple correlation between $DT_{50,S}$ and K_F was negative (Table 4). The sum of polyunsaturated PLFAs (e.g., fungi, protozoa, microphototrophs/plants and some of nonspecific organisms, i.e., microeukaryotes) was the only factor affecting $DT_{50,S}$ in the best model derived for IRB (Table 5). Inclusion of the K_F values did not improve model performance. However, Table 4 shows that all microbial PLFA markers negatively (not statistically significantly) correlated with the $DT_{50,S}$ values and correlations increased for the $DT_{50,M}$ values. Similar to FEX, these findings may illustrate the overall stimulation effect of the entire microbial community on IRB dissipation in soils but no considerable impact of K_F.

In the case of highly sorbed CIT, dissipation was negatively related to the amount of phosphorus in microbial biomass and positively related to the coefficient describing its sorption in soils. In fact, no reliable model was derived for CAR. It has been previously documented that dissipation of CAR in soils is very slow likely because the enzymes responsible for the transformation of carbamazepine are not common in agriculture soils (Thelusmond et al., 2016, 2018, 2019). It should also be mentioned that statistical analyses for CIT and CAR were affected by moderate uncertainty in the evaluated $DT_{50,S}$ values (as discussed in part 2.7). Thus, the model derived for CIT is also uncertain.

The presented models for predicting dissipation half-lives of tested pharmaceuticals are more difficult to use in practice compared with those proposed for instance by Al-Khazrajy et al. (2018) for diltiazem, ranitidine and cimetidine, who used more easily measured indicators (i.e., microbial activity, clay content, silt content and carbon content). Correlations between half-lives and easier to determine indicators of microbial abundance and activity (BR and SIR in Table 4) were weak or not meaningful (i.e., positive correlations). Multiple linear regressions also did not result in statistically significant models. Nevertheless, our results proved the main impact of microbial PLFA markers on half-lives of compounds rapidly dissipating from soils (i.e., CLI, SUL, FEX and IRB). In addition, our findings also confirmed that sorption of some compounds in soils could reduce their dissipation from soils.

3.6. Behavior of compounds with respect to soil type

Principal component analysis (Figs. 1 and S1) showed that separation of soil types first by two PC (Figs. 1b and S1b) derived from all K_F values in Table 3 corresponds to the distribution derived from the basic soil properties (Figs. 1a and S1a) in Table 1 (15 lines pH_{H2O} – Sand), i.e., Group 1: soils developed on loess HCh, GP, and HL; Group 2: both Cambisols HCa and DCa; Group 3: AE; Group 4: SChS. Division of soil types (Figs. 1e and S1e) based on $DT_{50,S}$ values in Table 3 closely corresponds to distributions (Figs. 1c and S1c) derived from the microbial community composition (PLFA) in Table S2, i.e., Group 1: HCa, Dca, and HL; Group 2: GP and SChS; Group 3: AE; Group 4: HCh. Similarity in soil distribution (Figs. 1d and S1d) derived from both DT_{50} values (i.e., $DT_{50,S}$ and $DT_{50,M}$) with that derived from the PLFA (Figs. 1c and S1c) was also documented. Similar correspondence was not found for the $DT_{50,M}$ values (Figs. 1f and S1f) likely due to the variable impact of simultaneous application in different soils. When assuming all soil properties (Table 1), both characteristics describing compounds' behavior in soil (i.e., K_F and DT_{50}) distributions (Fig. 1f, h) differ. However, two groups can be identified in both cases, i.e., Group 1: both Cambisols HCa and DCa; Group 2: two of soils developed on loess GP and HCh. These findings proved previously formulated hypothesis by Kodešová et al. (2016) for trimethoprim, sulfamethoxazole, clindamycin, atenolol and metoprolol. This hypothesis states that while sorption of pharmaceuticals in soils is related to basic soil properties, their dissipation is controlled by overall soil properties controlling microbial composition in soils. Of note, in a study by Koba et al. (2017) who studied transformation of 3 antibiotics (CLI, SUL and trimethoprim) in 12 soil materials (including 7 soils in present study), soils were grouped according their substrates and character as follows: Group 1: three soils developed on loess and one on marlite substrate; Group 2: two soils developed on sandy materials; Group 3: four Cambisols. The results (Fig. 1d, e) slightly differ from results in our previous paper (Koba et al., 2017). The difference can be explained by the fact that our present study did not only include antibiotics (i.e., antibiotic behaviors can follow similar patterns). In addition, the behaviors of some of compounds (e.g., CAR) considerably differ from behaviors of other compounds.

3.7. Potential environmental threat related to the occurrence of studied compounds in soils

Given its great persistency and low sorption affinity in soils (Table 3 or Kodešová et al., 2015, 2016), CAR is a highly mobile compound in the subsurface water environment. Thus, this compound frequently occurs in groundwater (e.g., Fram and Belitz, 2011; Godfrey et al., 2007; Li, 2014; Huntscha et al., 2012; Loos et al., 2010; Radovic et al., 2015). It has also been documented that CAR is freely taken up by plants (e.g., Goldstein et al., 2014; Hurtado et al., 2017; Klement et al., 2020; Kodešová et al., 2019a, 2019b; Malchi et al., 2014; Montemurro et al., 2017; Mordechay et al., 2018; Shenker et al., 2011; Winker et al., 2010; Wu et al., 2013).

On the other hand, due to its low dissipation half-lives and higher sorption (Table 3 or Kodešová et al., 2015, 2016) CLI should not extensively migrate in the vadose zone (e.g., de Jongh et al., 2012). Potential uptake of CLI by plants is likely very limited. For instance, Kodešová et al. (2019b) reported no uptake of CLI and very low uptake of its metabolite clindamycin sulfoxide from sewage sludge applied into 7 soils as a soil amendment.

Although SUL rapidly dissipates in topsoils, it can rapidly migrate though topsoils under particular conditions (e.g., under intensive irrigation with contaminated water) due to its very low sorption (Table 3 or Kodešová et al. (2015, 2016)). Subsequently, due to its high dissipation half-life in subsoils (Kodešová et al., 2016) and low sorption affinity to soils and sediments, SUL can easily migrate in the subsurface water environment (i.e., frequent SUL occurrences in groundwater have been published by Fram and Belitz (2011), Godfrey et al. (2007), Li (2014) and Loos et al. (2010)). Furthermore, it has been documented that SUL can also be taken up by plants (e.g., Ahmed et al. (2015); Klement et al., 2020; Kodešová et al., 2019a; Malchi et al., 2014; Wu et al., 2013).

Given its large sorption, CIT is less mobile in the subsurface water environment. However, CIT can be taken up by plants from sewage sludge incorporated into soils (e.g., Kodešová et al., 2019b).

The sorption of IRB in soil (Table 3 or Klement et al., 2018) is strongly soil-specific. It can be either very low (soils developed on loess) or high (DCa and AE). Since dissipation half-lives of IRB in different soils were relatively similar, IRB's potential to migrate in a subsurface water environment is moderate (soils developed on loess) or low (DCa and AE). No plant uptake of IRB from sewage sludge was reported by Kodešová et al. (2019b).

Finally, the stability of FEX is moderate ($DT_{50,S}$ values in Table 3), but its sorption affinity to soils (Table 3 or Klement et al., 2018) is relatively high. Thus, its mobility in the vadose zone seems to be very low. Negligible plant uptake of FEX from sewage sludge was reported by Kodešová et al. (2019b).

4. Conclusions

Results of our study (i.e., results from the principal component analysis of different data sets) showed that while knowledge of basic soil properties can be used to group soils according sorption behavior of studied compounds in these soils, the knowledge of microbial composition can be used to group soils according their dissipation potential. These findings confirmed the hypothesis suggested in our previous study (Kodešová et al., 2016) and can be used to properly design future experiments, e.g., selection of representative soils, and extrapolate obtained results to similar soils in a particular group. Our results from the multiple linear regressions relating the DT_{50} values to soil and microbiological properties also showed that knowledge of initial microbial community composition (or property related to microbial biomass) and sorption of compounds in soils could be used to estimate the dissipation half-lives ($DT_{50,S}$ – single solute application) of CIT, CLI, FEX and IRB in tested soils. No statistically significant relationships at the 95% or higher confidence level were found for CAR and SUL, but the derived model for SUL was similar to that obtained for the second antibiotic CLI. The dissipation half-lives ($DT_{50,M}$) generated from the applications of multiple solutes were generally increased compared with the $DT_{50,S}$ values, which could be attributed to the negative influence of antibiotics on microbial communities. However, this trend was not consistent in all soils. In several cases, $DT_{50,S}$ values were even higher than the $DT_{50,M}$ values. Further studies are needed to reveal actual mechanisms occurring during the transformations of various compounds in the soil environment. The experimental design can be improved, e.g., use less pharmaceuticals (starting with 2 compounds) for the multiple-compound applications and monitoring of microbial activity and composition in soils during the entire degradation experiment. DNA/RNA analysis in combination NGS techniques could give indication, how the various compounds affect microbial diversity etc. Despite some limitations discussed in this study, our results and findings can be adopted in environmental studies assessing transport and dissipation of tested compounds in the vadose zone and future experiments dealing with dissipations of organic compounds as pharmaceuticals in the soil environment.

CRediT authorship contribution statement

Radka Kodešová: Conceptualization, Methodology, Formal analysis, Writing - original draft. **Alica Chroňáková:** Writing - original draft. **Kateřina Grabicová:** Investigation, Writing - original draft. **Martin Kočárek:** Investigation, Data curation. **Zuzana Schmidtová:** Investigation, Data curation. **Zuzana Frková:** Investigation, Writing - original draft. **Andrea Vojs Staňová:** Investigation. **Antonín Nikodem:** Investigation. **Aleš Klement:** Investigation. **Miroslav Fér:** Investigation. **Roman Grabic:** Validation, Writing - original draft.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors acknowledge the financial support of the Czech Science Foundation project No. 17-08937S, Behavior of pharmaceuticals in soil-water-plant system. Pharmaceutical concentrations were analyzed using devices financially supported by the Ministry of Education, Youth and Sports of the Czech Republic - projects “CENAKVA” (LM2018099), “CENAKVA Centre Development” (No. CZ.1.05/2.1.00/19.0380). The work was also supported by the European Structural and Investment Funds projects NutRisk (No. CZ.02.1.01/0.0/0.0/16_019/0000845). Authors also thank Veronika Jílková, David Kahoun and Petr Kotas for access to the lab with GC and GC-FID and advice on PLFA analyses. Anna Koubová and Martina Petrlíková are thanked for help in experimental set up, sample processing, microbial analyses and PLFA extractions. Helena Švecová and Petra Nováková are thanked for analytical sample preparation. Tomáš Picek and Eva Kaštovská are thanked for providing data on TC, TN, and microbial C, N, and P.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2020.141134.

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