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## **INSTITUTE OF PHYSICAL AND APPLIED CHEMISTRY**

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# **INTERACTION OF IBUPROFEN WITH DIFFERENT SOIL TYPES**

INTERAKCE IBUPROFENU S RŮZNÝMI TYPY PŮD

## **MASTER'S THESIS**

DIPLOMOVÁ PRÁCE

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## Title of Master's Thesis:

Interaction of Ibuprofen with Different Soil Types

## Master's Thesis:

1. Get acquainted with the problem of ibuprofen occurrence in soil, wastewater as a source of soil and environmental pollution.
2. Get acquainted with the possible interactions of ibuprofen with the soil organic matter based on the type of soil and methods used for its detection in soil.
3. Based on the information gathered in the previous points, design a method suitable for the study of ibuprofen and carry out the experiments.
4. Evaluate the results of the experiments and formulate a conclusion.

## Deadline for Master's Thesis delivery: 30.7.2021:

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## **ABSTRAKT**

Táto práca sa zameriava na problematiku interakcie ibuprofenu s pôdnym systémom. Popísané sú jeho základné vlastnosti, správanie a faktory ovplyvňujúce toto správanie. Vo všeobecnosti najvplyvnejšími faktormi je prítomnosť pôdnej organickej hmoty v pôde a pH.

Ibuprofén patrí do skupiny nesteroidných protizápalových liečiv. Patrí medzi ľahko dostupné a vysoko konzumované liečivá. Toto prispieva k jeho narastajúcemu transportu a kontaminácii životného prostredia. Jeho prítomnosť v životnom prostredí môže pôsobiť negatívne na živé organizmy.

V experimentálnej časti bol preskúmaný vplyv pôdnej organickej hmoty a pH na sorpciu a desorpciu ibuprofenu. Použité boli tri pôdy získané z odlišných regiónov Českej republiky. V rámci procesu sorpcie a desorpcie boli použité koncentrácie v rozmedzí 1 až 10 mg/l. Vplyv pH na sorpciu a desorpciu bol preskúmaný použitím koncentrácie ibuprofenu 10 mg/l a Britton-Robinsonovho pufru s pH 3, 7 a 10. Detekcia ibuprofenu v jednotlivých vzorkách bola uskutočnená pomocou UV-VIS spektrometrie a kvapalinovej chromatografie s hmotnostne spektrometrickou detekciou.

## **ABSTRACT**

This thesis focuses on the problem of interaction of ibuprofen with soil system. Described are basic properties, behaviour of ibuprofen and factors influencing this behaviour. In general, the most influential factors are soil organic matter content and pH.

Ibuprofen belongs in group of non-steroidal anti-inflammatory drugs. It is highly available drug consumed in high amounts each year. This contributes to its increasing transport and contamination of the environment. Its presence in the environment can have negative effects on the living organisms.

In the experimental part studied was an influence of organic matter content in soil and pH on sorption and desorption of ibuprofen. Used were three soils acquired from different regions in the Czech Republic. The experiment was conducted with ibuprofen concentrations from 1 to 10 mg/l. The influence of pH was carried out using ibuprofen concentration 10 mg/l and Britton-Robinson buffer with pH of 3, 7 and 10. Recorded was the concentration of Ibuprofen after each cycle using UV-VIS spectrophotometry and liquid chromatography coupled with mass spectrometry detection.

## **KLÚČOVÉ SLOVÁ**

Sorpcia, desorpcia, ibuprofen, pôda

## **KEYWORDS**

Sorption, desorption, ibuprofen, soil

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## **DECLARATION**

*I declare that the diploma thesis has been worked out by myself and that all the quotations from the used literary sources are accurate and complete. The content of the diploma thesis is the property of the Faculty of Chemistry of Brno University of Technology and all commercial users are allowed only if approved by both the supervisor and the dean of the Faculty of Chemistry, BUT.*

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student's signature

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# THEORETICAL PART

## 1. Introduction

Pharmaceuticals are compounds defined as synthetic or natural chemical compounds that can be found in drugs for human or animal use. They contain active pharmaceutical ingredients (API) that are designed to have a positive effect on the human body [1]. Their specific chemical properties enable safe and successful modification, restoration, and influence over physiological functions. Therefore, they are consumed and sold in high quantities.

Many pharmaceutical compounds undergo metabolic reaction in human organism resulting in various products. These metabolic products are afterwards excreted and transformed by chemical and physicochemical factors in water. However, unchanged compounds may also be excreted from the human body in an active form [2].

Wastewater treatment plants (WWTP) are not effective enough to ensure complete elimination of these compounds. Unproper disposal of pharmaceuticals is one of the main factors leading to contamination [1]. The release into the environment and contamination of water and soil ecosystem [2]. Furthermore, in some countries, irrigation with treated wastewater contributes to dissemination of a variety of pharmaceuticals in agricultural soils with concentrations up to mg/kg [3]. Multiple studies have highlighted the presence of these contaminants in groundwater, surface waters, and drinking water due to process of leaching [2][4].

Consequently, their presence in water bodies has adverse effects on both aquatic and non-aquatic organisms.

Upon release from WWTP pharmaceutical compounds are considered to be pseudo-persistent contaminants that can be transported into the soil. For instance, carbamazepine and its metabolites were detected in human urine after consumption of a fresh product from the field irrigated with treated wastewater [3].

Soil and sediments are the ultimate repositories of pharmaceutical compounds from which they are discharged into the environment. Their fate in the soil environment is determined by sorption, which can be influenced by several factors such as texture of the soil, structure of the contaminant, organic matter (OM), mineral surfaces, and more [5].

In general, non-steroidal anti-inflammatory drugs (NSAIDs) are the most frequently detected pharmaceuticals in soil, sediments, surface, ground or drinking water. This can be attributed mainly to their high availability as they are sold as over-the-counter drugs. Recently, their production and consumption has been steadily increasing. More than 50 NSAIDs can currently be found on the world market. The most sought-after are ibuprofen (IBF), naproxen (NPX), diclofenac (DCF), ketoprofen (KTF), and paracetamol (PRC) [1].

IBF is the third most popular and stable over-the-counter pharmaceutical in the world. Due to its high rate of consumption its concentration in WWTP and water bodies has been continuously increasing throughout the years [4].

## 2. Non-steroidal anti-inflammatory drugs

Use of pharmaceutical has increased in recent years and will continue to do so in the future, as development of new medicine is crucial for treatment of diseases and previously untreatable conditions [6].

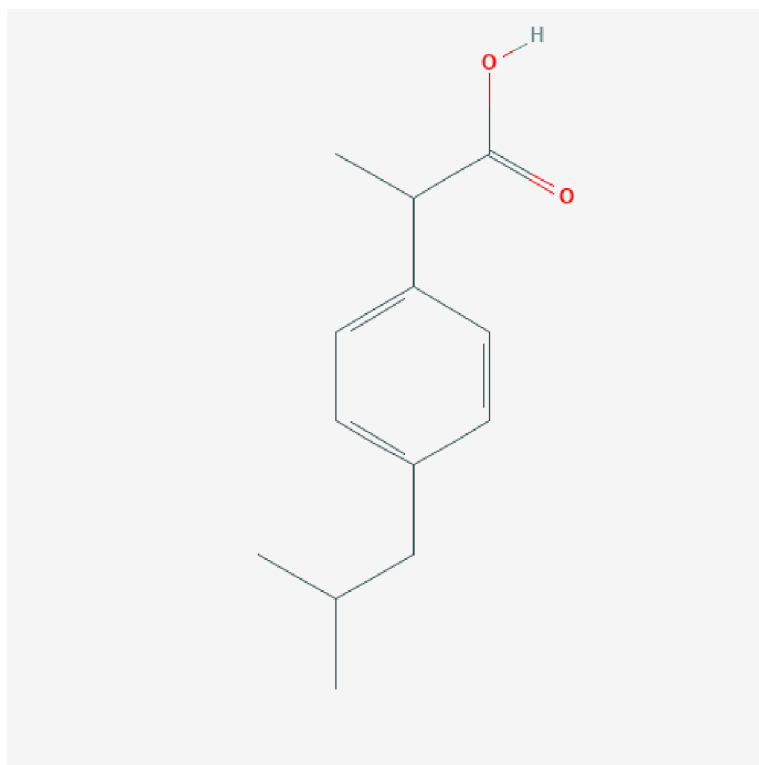
Multiple studies have confirmed the presence of NSAIDs in soil, wastewater, ground water, and surface water. These pharmaceuticals are used in large amounts, as they offer a way of treating the most common symptom of any disease, pain [7]. NSAIDs are organic acids which possess various chemical structures with anti-inflammatory, antipyretic, and analgetic effects. Due to the presence of certain group molecules (hydroxyl, amide), NSAIDs are highly reactive [7][8].

Among this group of drugs, IBF is the third most consumed pharmaceutical compound in the world.

### 2.1 Ibuprofen

IUPAC defines IBF as (RS)-2-(4-(2-methylpropyl)phenyl) propanoic acid [9]. As it belongs to the group of NSAIDs, it is known for its treatment of rheumatic diseases, fever, and pain [10]. Chemically, it is characterized as an amphiphilic molecule, which contains carboxyl group and aromatic ring, as shown in *Figure 1* [5].

Its worldwide consumption is estimated at several kilotons per year [11]. For example, the annual intake of IBF is 300 t in Germany, 58 t in Poland, and 162 t in England [12].



*Figure 1: Chemical structure of Ibuprofen [9]*



The recommended dosage differs based on the required treatment and the age of the patient. The usual oral dosage in the form of tablets for the treatment of short-term inflammation and pain is 600 to 1200 mg/day. On the contrary, the recommended dosage for rheumatic and musculoskeletal disorders is up to 2400 mg/day [13].

Its overall effect is the inhibition of prostaglandin synthesis by competitive inhibition of cyclooxygenases. These inhibitory properties are ensured by carboxyl group present in its structure.

In the human body, orally administered IBF is well and quickly absorbed from the gastrointestinal tract into the blood, where 99% of it binds to albumin [14]. Approximately 40-60% of bound IBF undergoes irreversible isomerisation in the liver or gut. The result of this process is the active form of S(+)-ibuprofen, which is then subjected to xenobiotic detoxification. This process consists of two phases.

The metabolites from the first phase (2-hydroxyibuprofen and 3-hydroxyibuprofen), subsequently undergo conjugation in the second phase. The final products are glucuronide and thiol conjugates [13]. The entire detoxification process ends with both the parent form and the active metabolites of IBF being excreted into the environment [13]. Once in the environment, the conjugated molecules of ibuprofen may be hydrolysed [15].

The excretion of the total ibuprofen dose is 15% in the form of unchanged molecule, glucuronide and thiol conjugates or as metabolites (hydroxy metabolites, carboxyibuprofen, carboxyhydratropic acid). Upon ingestion into the human body, the metabolites 2-hydroxyibuprofen and carboxyibuprofen account for 26% and 43% of the total dose, respectively. [15]

However, the concentration of certain metabolites present in wastewater varies compared to the excreted amount. This is the result of the microbial activity of the organisms present in WWTP. This particularly concerns hydroxylated metabolites and carboxyibuprofen, which were present in higher concentration than was their measured excreted amount [15].

For example, high concentrations of up to 36.230 ng/l were detected for carboxyibuprofen in WWTP influent. However, this amount does not correspond to the expected amount excreted by the human organism, as it is more abundant compared to 2-hydroxyibuprofen. Furthermore, *Ferrando-Climent et al.* reported in their studies that 2-hydroxyibuprofen is the dominant metabolite in influent wastewater samples in biodegradation studies. This highlights the fact that the presence of these metabolites in influent wastewater can be attributed not only to an input from the human organism, but also to activity of microorganisms in wastewater [16]. On the other hand, lower amounts of metabolites were detected in WWTP effluent. Reported removal rates for carboxyibuprofen, 2-hydroxyibuprofen, and 2-hydroxyibuprofen were 72-100%, 77-100%, and 58-100%, respectively. The metabolite 1-hydroxyibuprofen was even less biodegradable than IBF itself [16].

## 2.2 Physicochemical Properties of Ibuprofen

The pharmaceutical compound IBF is soluble in water, at neutral and acidic pH. It is also readily soluble in organic solvents and exhibits high mobility in the aquatic environment [9].

Octanol-water partitioning coefficient ( $K_{OW}$ ) represents the distribution of a chemical compound between an oil and water phase. In general, it describes how a chemical compound can partition from water into biomass of soil, sediments or sludge [17].

The hydrophobicity of IBF can be determined through its  $\log K_{OW}^1$  [5]. Compounds that have low or negative  $\log K_{OW}$  are typically hydrophilic with a higher solubility in water.

Chemical compounds with a high  $\log K_{OW}$  are hydrophobic with a low water solubility [17]. Therefore, drugs with a high value of  $\log K_{OW}$  or/and total positive charge at natural pH are capable of bonding to soil.

This contributes to lower degradation in the system. Consequently, due to specific interactions, the retention and persistence of IBF in the soil is ensured. [18] However, this partitioning coefficient is not reliable in the case of pharmaceuticals, especially IBF, as it does not consider the ionic species and overestimates the partitioning [17].

Presence of the neutral, cationic, anionic and zwitter-ionic form in the environment can be determined by the surrounding pH and by  $pK_a$  value of the pharmaceutical compound [19].

This can be applied in the case of IBF where its de/protonation is determined by the value of  $pK_a$  [5]. Thus, at environmentally relevant pH values (5-8), IBF is present in anionic form as its carboxyl group is deprotonated [5].

The influence of the pH value is also considered by  $\log D_{OW}^2$ . This unit indicates that the deprotonated structure of IBF retains its non-polar state despite its low hydrophobicity. Due to this amphiphilic character, IBF is capable of interacting with natural matrices such as soil organic matter (SOM), mineral surface and tissue [5]. Detailed data regarding the physicochemical properties of IBF can be found in *Table 1*.

*Table 1: Physicochemical properties of Iburpofen [9]*

NSAID	Mw (g/mol)	$pK_a$	Solubility (mg/l at °C)	Log Kow	Log Dow
Ibuprofen	206.3	4.91	21	4.5	2.55

### 3. Occurrence of Pharmaceuticals in the World

The high consumption and production of pharmaceutical compounds is reflected in their presence in the environment. To demonstrate this occurrence of pharmaceuticals, *Beek et al.* conducted a study in which they reviewed multiple publications and articles.

Globally 559 different pharmaceuticals have been detected in WWTP influent, effluent and sludge with highest number found in China, Canada, Europe and USA. In Europe, North America, and China, between 30 to 100 pharmaceuticals substances were detected in manure and soil. However, not much data regarding this particular occurrence of pharmaceuticals was available. Their illustration of the occurrence can be seen in *Figure 2* and *Figure 3* [20].

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<sup>1</sup>  $\log K_{OW}$  – Logarithm of partition coefficient n-octanol/water

<sup>2</sup>  $\log D_{OW}$  . Logarithm of distribution ratio n-octanol/water

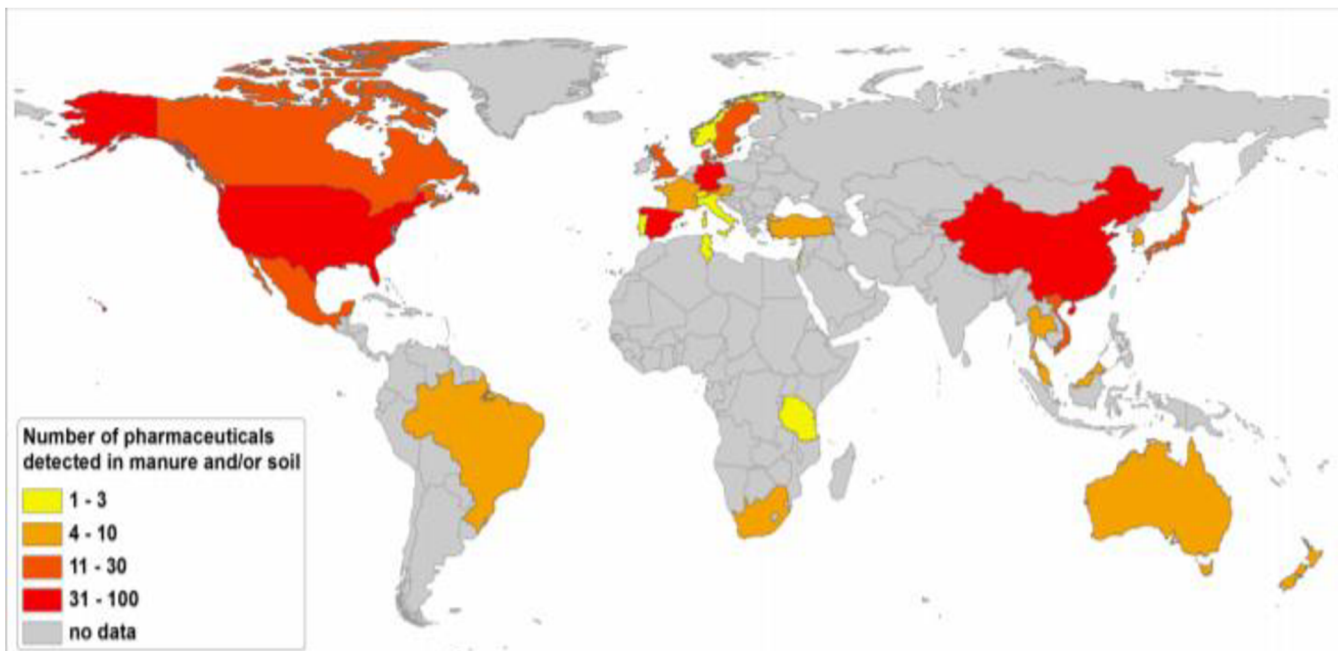


Figure 2: Number of pharmaceuticals in manure and/or soil by country [20]

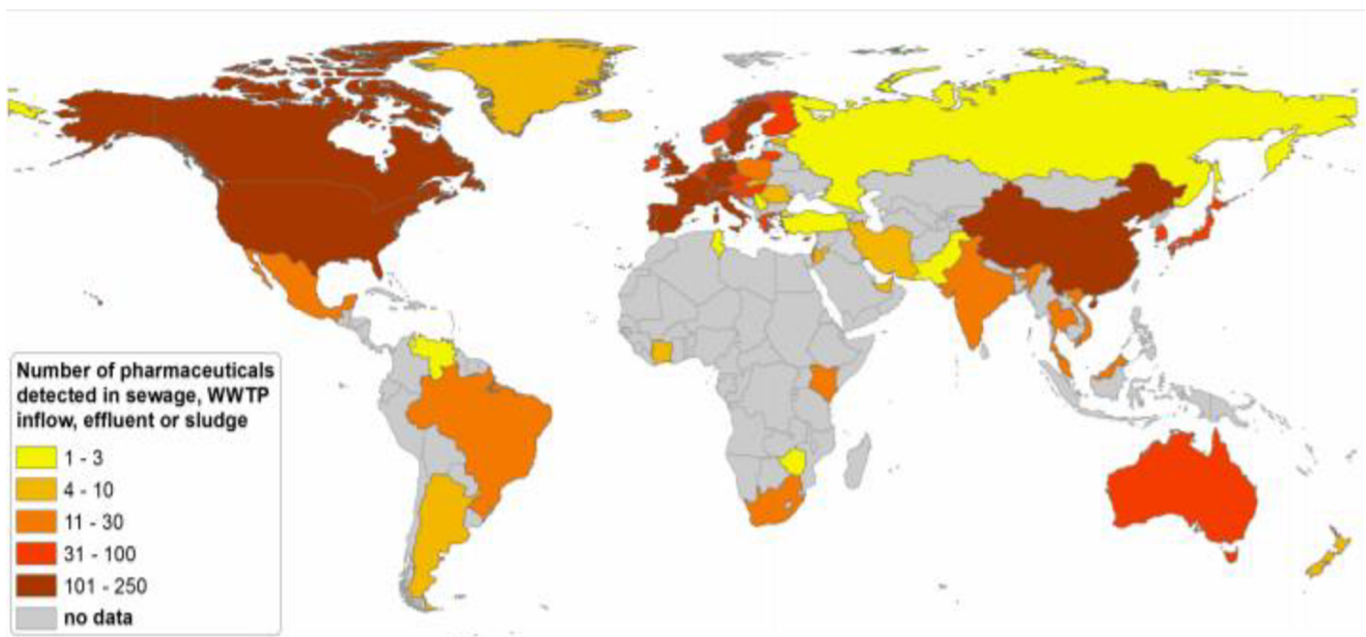


Figure 3: Number of pharmaceuticals in sewage, wastewater treatment plants inflow / effluent / sludge by country [20]

Regarding NSAIDs, concentration in the environment range from a few nanograms to hundreds of micrograms per litre [21]. The highest amount detected so far was 1.407 mg/l of acetylsalicylic acid recorded in untreated municipal wastewater in Korea [22]. In 2020 the most commonly detected NSAIDs were diclofenac (35 countries), ibuprofen (28 countries), naproxen (21 countries) and ketoprofen (19 countries) [21].

In their research, *Tyumina et al.* presented data showing the presence of NSAIDs in wastewater and surface waters in the world. The highest amount was attributed to IBF with a concentration of up to 70 µg/l. In the case of KTF and NPX, the highest amounts were

recorded in Latin America, Africa (9-10 µg/l) and Canadian wastewater (29 µg/l). Similarly, significant concentrations of diclofenac (20 µg/l) have been detected in WWTP effluents in Africa and Europe [21].

On the other hand, there is no study that summarises the occurrence of pharmaceuticals in soil in greater detail. The collected data in *Table 2* indicates that so far, the highest amount of NSAIDs was found in Lahore, Pakistan.

In general, high concentrations of NSAIDs and other pharmaceuticals in the environment pose a high risk for the environment and are a source of adverse environmental effects [21].

The most well-known recorded adverse effect of NSAIDs is the reduction in population of three vulture species in the Indian subcontinent. This was a result of intoxication and kidney failure of birds due to their feeding on carcasses of cattle treated with diclofenac [21].

Furthermore, several studies have shown that NSAIDs migrate into the food chain. For example, IBF and DCF have been found in otter wool in the United Kingdom indicating contamination of fish fauna and aquatic ecosystem [21].

Table 2: Occurrence of NSAIDs in soil and wastewater [20]

Soil				Wastewater Effluent			
NSAIDs	Concentration (µg/kg)	Area of study	S <sup>3</sup>	NSAIDs	Concentration (µg/l)	Area of study	S
Naproxen	30-199	Lahore, Pakistan	[23]	Diclofenac	58-599	United Kingdom	[20]
	0.7	Agricultural soil, Spain	[24]		10-100	Taiwan	[20]
	0.51-3.06	Mexico	[25]		4	Canada	[20]
	0.73	Mexico	[26]		0.038-1.02	Spain	[18]
	0.55	Mexico	[26]	Ketoprofen	16-23	United Kingdom	[20]
Ketoprofen	ND	Agricultural soil, Spain	[24]		0.210-5.48	Spain	[18]
Paracetamol	0.4	Agricultural soil, Spain	[24]	Naproxen	12.5	Canada	[20]
Salicylic acid	4.4	Agricultural soil, Spain	[24]		170-370	United Kingdom	[20]
Diclofenac	ND <sup>4</sup>	Mexico	[27]		0.040-1.630	Spain	[18]
	0.35-1.16	Hebei, China	[27]		0.07	Poland	[20]
	101-257	Laore, Pakistan	[23]	Ibuprofen	0.110-2.170	Canada	[20]
	ND-5.06	Jerez de la Frontera, Spain	[18]		2.203	UK	[20]
	N.D.	Spain	[24]		3.400	Germany	[20]
Ibuprofen	ND – 0.1	Mexico	[27]		0.0177-0.219	France	[20]
	1.51 – 5.03	Hebei, China	[27]		1.003	Italy	[20]
	321 – 610	Lahore, Pakistan	[23]		0.0141	Sweden	[20]
	0.213	Pego-Olive, Spain	[18]		0.095-0.751	Spain	[18]
	< LOQ <sup>5</sup>	Jerez de la Frontera, Spain	[18]		0.11	Poland	[20]

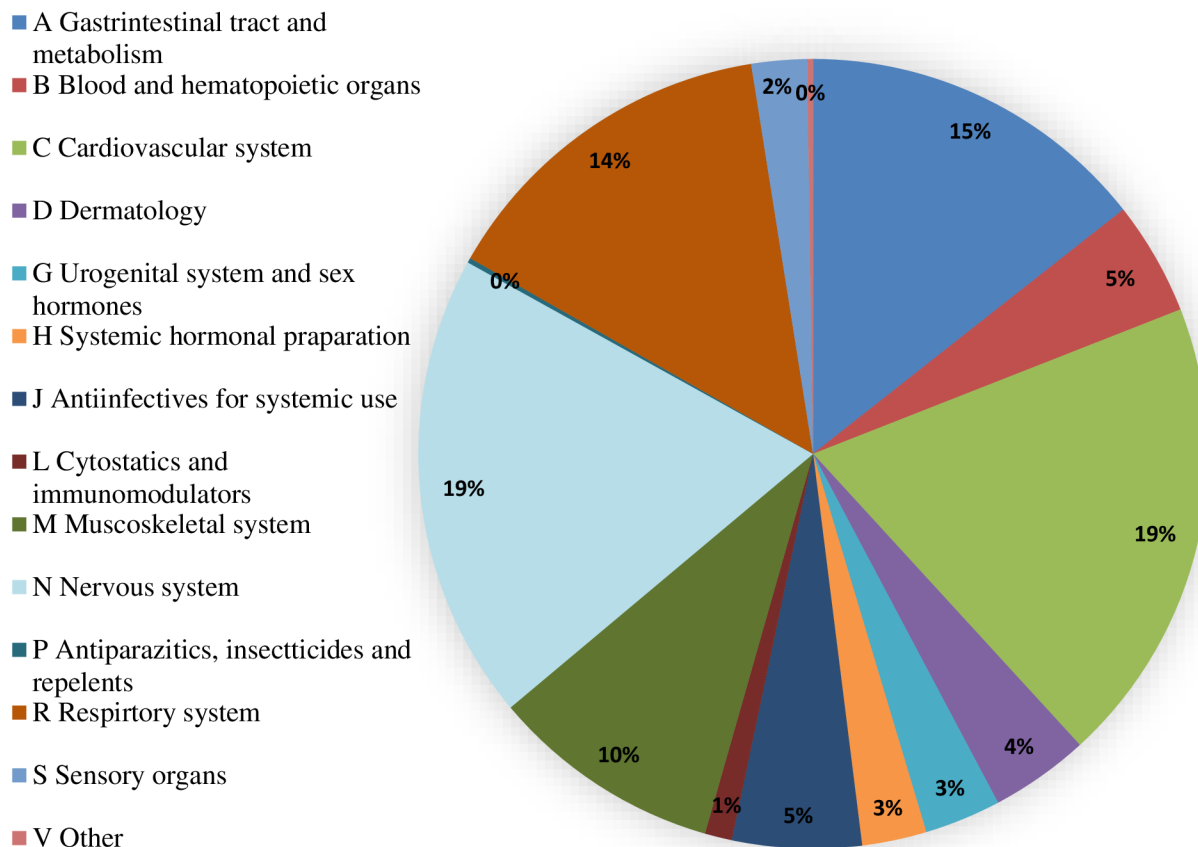
<sup>3</sup> S – source in literature

<sup>4</sup> ND – not detected

<sup>5</sup> LOQ – limit of quantification

### 3.1 Consumption of Pharmaceuticals in the Czech Republic and Slovakia

The occurrence of pharmaceuticals is closely linked with their consumption in individual countries across the world. In the Czech Republic, 236 million packs of pharmaceuticals were sold in 2019. Pharmaceuticals for the nervous system and the cardiovascular system sold the most (both 44.8 million packs). Among over-the-counter drugs PARALEN 500 (3.9 million packs) and IBALGIN (2.5 million packs) sold the most. A detailed overview can be found in *Figure 4*.



*Figure 4: Percentage of over-the-counter pharmaceuticals sold in the Czech Republic in 2019 [28]*

In Slovakia, around 156 million packs of pharmaceuticals were sold in 2019. The largest amount was represented by prescribed pharmaceuticals with 51.3%.

Over-the-counter pharmaceuticals made up 25.3% of all packs sold (39.6 million packs). The most sold pharmaceuticals were for the respiratory system (10.1 million packs), the gastrointestinal tract (8.4 million packs), and the nervous system (6.5 million packs) [29]. Detailed overview can be found in *Figure 5*.

The most sold over-the-counter drug was PARALEN (2.3 million packs) followed by MUCONASAL PLUS (1.1 million packs).

Pharmaceuticals intended for use in hospitals accounted for 8.5% of the total amount sold [29].

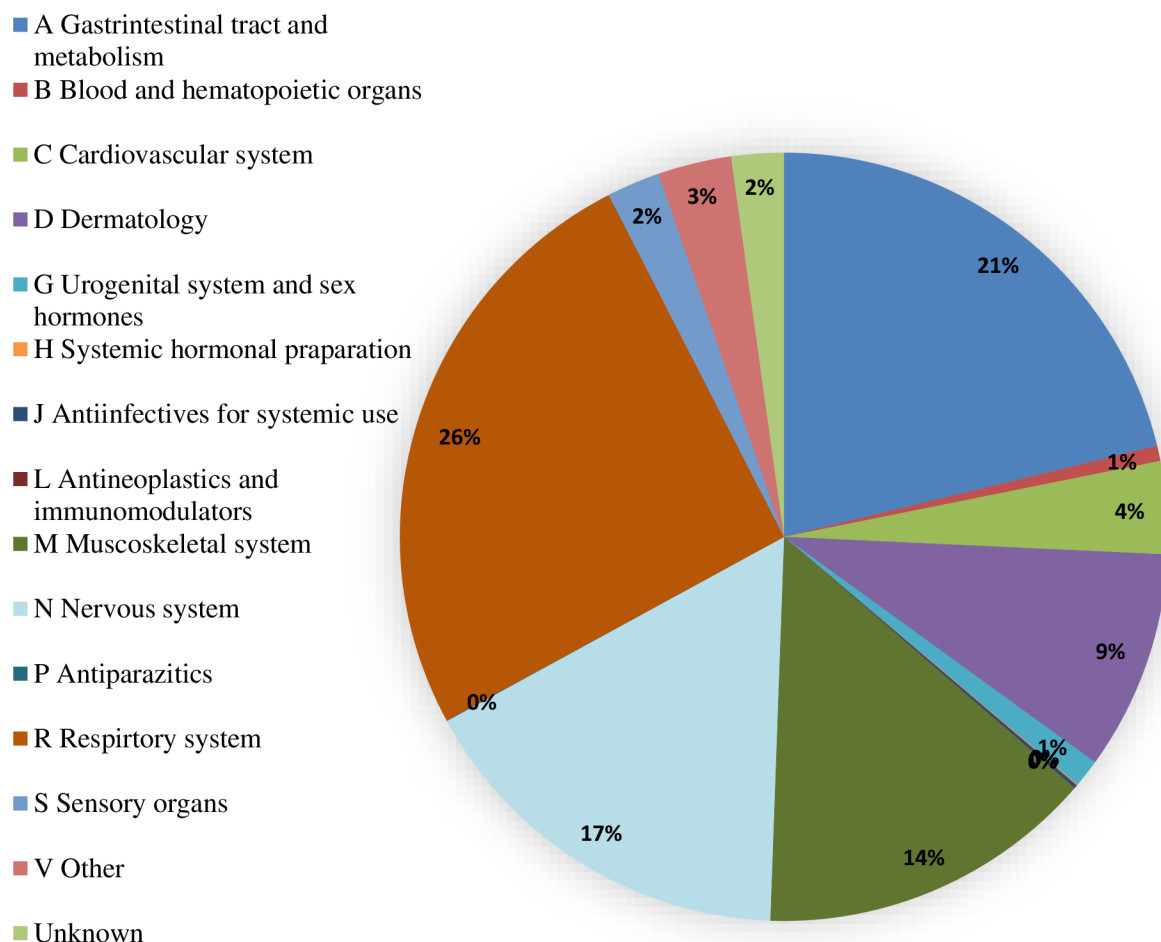


Figure 5: Percentage of over-the-counter pharmaceuticals sold in Slovakia in 2019 [29]

#### 4. Transport of Pharmaceuticals into The Environment

There are two main entry pathways for pharmaceuticals:

- Point source pollution
- Diffuse pollution

Point source pollution is a single specific source that can be easily determined. This includes hospital effluent, industrial effluent, septic tanks, and wastewater treatment plant discharge. Diffuse pollution is more complex as it cannot be identified and includes agricultural and urban runoff, leaching of septic tanks and waste treatment systems.

Point source pollution has three main sources of pharmaceutical compounds:

- Municipal landfills
- Wastewater tanks
- Septic tanks

Studies have shown that environment surrounding the municipal landfills contains a high concentration of pharmaceuticals. This is mostly the result of improper disposal of unused pharmaceuticals [30].

Municipal wastewater can be generated by sources such as hospitals, aquaculture, industries or households [4]. Incomplete metabolization and excretion contributes to the

presence of pharmaceuticals in wastewater. A similar entry pathway can be the disposal of unused pharmaceuticals into sinks or toilets [30].

Furthermore, *Daughton et al.* presented data concerning the release of API into the environment via secondary routes. They emphasised that, traces of pharmaceuticals can be found in sweat after consumption, which together with topically administered medication may leave residues on the skin. Consequently, in such instances, these pharmaceuticals can enter wastewater after bathing, washing or even laundering.

Wastewater that passes through the sewage treatment plant is not treated properly. This results in contamination not only of water but also of the soil environment. [4] For instance, pharmaceutical and hospital wastewater contains tens of  $\mu\text{g/l}$  of NSAIDs [21].

In their study, *Comber et al.* presented data showing efficiency of WWTP. This included the detection of 19 API and 4 metabolites in wastewater samples collected over two-year period. Results showed that the majority of the substances were removed with 80% efficiency. Poor removal (>40%) efficiency was recorded for ethinyloestrol, diclofenac, propranolol, the macrolide antibiotics, fluoxetine, tamoxifen, and carbamazepine [30].

However, the efficiency of a WWTP can vary depending on the unit processes (e.g., secondary treatment, filtration, and disinfection) and the operational variables of the particular plant. Even at a specific WWTP, the concentrations contained in effluent can differ based on influent concentrations, temperature, and weather. Furthermore, the operational conditions and the specific process applied can result in different concentrations in the finished effluent [17].

Overall, the main factor that determines the elimination of pharmaceuticals in WWTP are their physicochemical properties, in particular their acidity and solubility in water with very low solid-liquid partition. These factors, especially the last one, lead to a poor sorption onto sludge and consequently make them soluble in aqueous phase. Additionally, some pharmaceuticals detected in wastewater are also present in the sludge of the WWTP due to their low solubility [31].

In countries with water shortages, wastewater is reused for irrigation in agriculture. This leads to the presence of pharmaceuticals in soil, their leaching into deeper parts of soil and into groundwater.[18]. For instance, *Xu et al.* showed that the presence of dissolved organic matter in the form of reclaimed water or biosolids had no influence on the mobility of NSAIDs – IBF, KTF, NPX and diclofenac sodium. Only the amount of water passing through the soil profile had an influence on the leaching process of the studied NSAIDs. However, the solution of 10 mM  $\text{CaCl}_2$  significantly reduced the leaching potential of these contaminants. They concluded that increasing the salinity in irrigation water could reduce groundwater contamination [32].

Contamination of agricultural soil by irrigation was highlighted in the study conducted by *Biel-Maeso M. et al.* Wastewater and soil in depth of 20-150 cm was sampled over a two-year period in Jerez de la Frontera, Spain. The sampled soil was regularly irrigated with local recycled wastewater.

The target compounds were selected based on the agricultural, urban, and industrial activity of the area.



The results showed concentrations of pharmaceuticals between 73-372 µg/l in the wastewater influent samples and 3-41 µg/l in the wastewater effluent samples. The most frequently detected compounds in effluent samples were the NSAID diclofenac and the diuretic drug hydrochlorothiazide.

In soil samples at a depth of 0-20 cm, among the most frequently detected compounds were analgesics and anti-inflammatory drugs with a concentration of 10,05 ng/g, followed by antibiotics and psychiatric drugs with a maximum concentration of 5,45 ng/g. The most frequently detected anti-inflammatory drugs were ibuprofen and mefenamic acid. [18].

Due to inadequacy of some facilities to treat incoming wastewater, the removal efficiency of NSAIDs in some cases does not exceed 30%. In addition, during wastewater treatment, the release of conjugates can cause increase of NSAID concentration. Seasonal dynamics also influence the concentration of NSAIDs in aquatic ecosystems. For instance, their concentration is significantly higher in winter than in spring and summer. This is a result of low mixing of water masses and low temperatures, combined with weak biodegradation activity of microorganisms [21].

IBF can contribute to groundwater contamination in the soil environment. This is due to its transport to the surface of the soil, where aerobic conditions prevail and it is subjected to microbial degradation. Poor absorption and short residence time ensure its swift movement downwards [31].

The presence of these compounds in soil and aquatic ecosystems can have adverse effect on living organisms [30]. Even though some pharmaceuticals are present in low concentrations, prolonged exposure to multiple pharmaceuticals can have consequences [31]. Besides animals and plants, humans can also be exposed to these contaminants through drinking water, crops, fish, meat, or dairy products [30].

A detailed overview of the transport of pharmaceuticals into the environment can be seen in *Figure 6*.

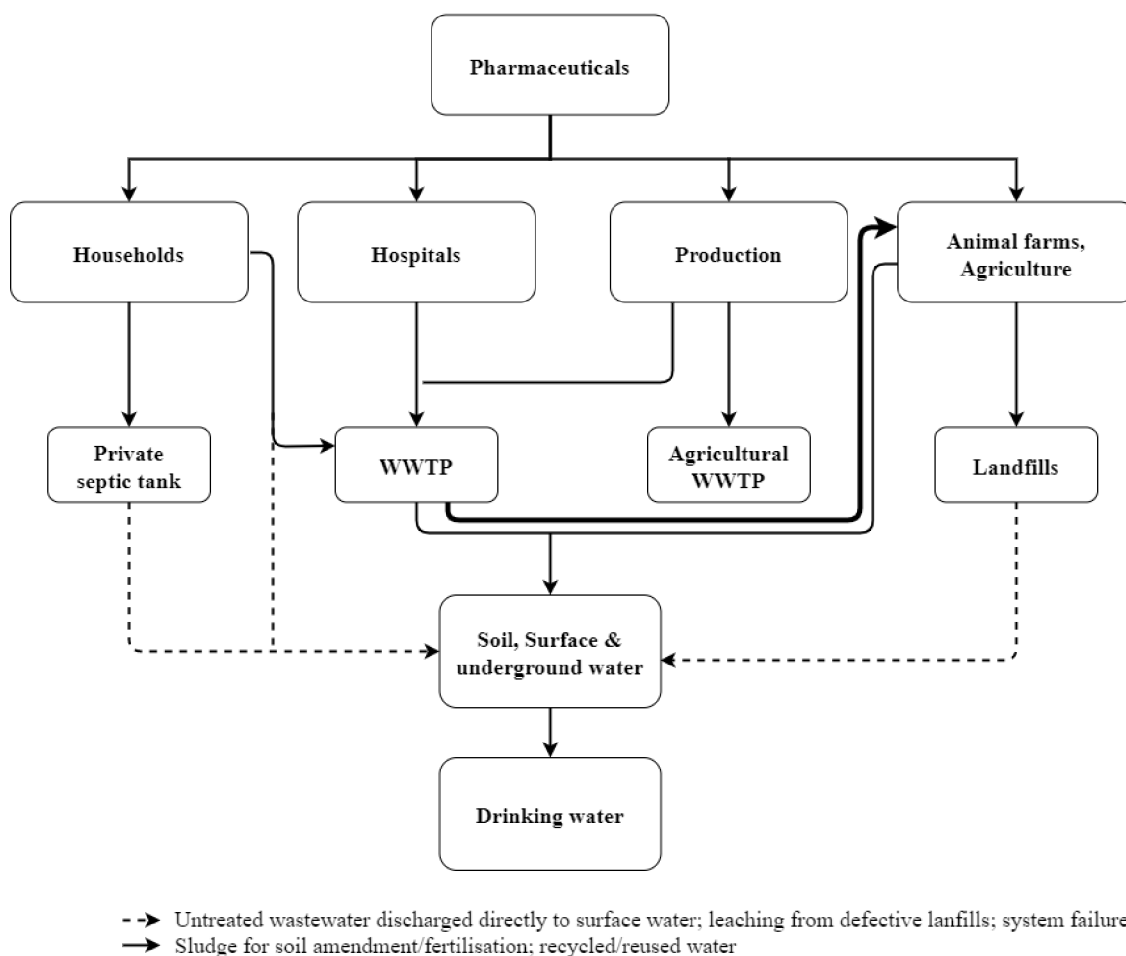


Figure 6: Transport of pharmaceuticals into the environment [34]

## 5. Fate of Pharmaceuticals in Soil

The fate of pharmaceuticals in the soil environment is determined by the process of sorption. It is assumed that the process of sorption of pharmaceuticals onto soil occurs in two steps. The first step is adsorption onto the soil surface, followed by a slower diffusion into the interlayers of micropores and clays [35]. Previous studies have shown that this process can occur within a time frame of one hour or one day. In some cases, however, it can take several days, months, or even years [35].

### 5.1 Sorption

The sorption mechanism is influenced by the form in which the compound is present. The process of sorption onto the solid matrix is influenced either positively or negatively by competition for the sorption sites or synergy [17]. Furthermore, the presence of more than one type of pharmaceutical compound in soil can cause different sorption onto various matrices [17].

The sorption of neutral pharmaceutical compounds is controlled by hydrophobic partitioning to the SOM through Van der Waals and electron donor-acceptor interactions. The existence of hydrogen bonds between hydroxyl groups of the compound and the surface of the sorbate is also an important contribution to the sorption of neutral molecules [17]. In

the case of ciprofloxacin, for example, hydrogen bond is the most prominent mechanism contributing to its sorption process on SOM. These bonds also occur during the interaction of norfloxacin (NOR), ofloxacin and soil sorbents [36]. Their presence was even found for IBF with between 14% of its undissolved cationic acid moieties and soil surface moieties [37].

However, only approximately 5-10% of pharmaceuticals are either neutral or hydrophobic. The more neutral a compound is, the greater the extent of its distribution into lipids in the biomass of WWTP and/or in living organisms.

On the other hand, the more ionized a compound is, the greater the extent of ionic complexation to minerals and clays is observed [17]. This interaction is observed in the case of IBF, which is capable of binding to the SOM, clay, and Fe/Al hydr(oxides). The sorption of ionic compounds is also strongly influenced by the pH of the environment. Therefore, a stronger electrostatic mechanism will contribute to their interaction, such as complexation, cation-exchange, and cation-bridging [17]. For example, the formation of a ternary surface complex between sulfamethazine (SMZ) and  $\text{Cu}^{2+}$  significantly strengthens the process of sorption [36]. The presence of surface complexation contributes to the sorption of NOR onto soil. Further experiments showed that the higher the cation exchange charge and clay content, the higher is the enhancement in NOR sorption [36].

On the other hand, the cationic molecules prefer interaction with negatively charged clay mineral surfaces. This can cause competition for adsorption sites between cationic organic contaminants and mineral ions.

In general, highly mobile organic compounds tend to leach into groundwater, whereas highly sorptive contaminants can accumulate in the top layer of the soil.

At low pH, cationic molecules can absorb more firmly to the solid phase than mineral ions with the same valence. At the moderate pH, mineral ions are favoured over cationic molecules [17].

The determining factor for the adsorption of cationic molecules is the charge density. However, this process is also influenced by the configuration of these compounds.

The cation-exchange assumes that the process of sorption of cationic organic contaminants is determined by negatively charged sorption sites. It defines the sorption of organic cations to soil as a contribution of sorption to organic matter and to phyllosilicate clay minerals. The mechanism of cation exchange was observed in the case of NOR, with its sorption to humic acid (HA) in particular reaching a maximum value at pH 6. The influence of pH and ionic strength (IS) are main indicators that cation exchange occurs [36].

Sorption of anionic organic contaminants is controlled by the attraction to positive charges on the solid surface, via cation bridging. This sorption mechanism is the result of an inner-sphere complexation between an exchangeable cation situated on the surface of the sorbate and an anionic functional group on the sorbate. This offers an opportunity for natural sorbents to absorb anions. The negatively charged solid surface enables the sorption of cationic molecules [36].

Finally, by cation bridging, the anion molecules can bind to the surface of the soil component. For example, tetracycline exhibits stronger sorption in the presence of bivalent metal cation on montmorillonite due to cation bridging. Experiments even showed that the metal oxides in soil minerals can also serve as a cation bridge between the carboxyl group of

ciprofloxacin and the interlayer cations in minerals. The same attraction was observed in the sorption experiment conducted with ofloxacin and enrofloxacin on organic soil [36].

However, in the case of zwitter-ionic molecules the charge distribution allows the orientation to change. This grants an optimal interaction with the sorption sites. Additionally, this

zwitter-ionic form can be affected by:

- The charge/area of the cationic amine group
- The delocalisation of the charge of heterocyclic amine in the ring,
- The positioning of the carboxyl and hydroxyl group
- The position of the cationic and anionic group within the zwitter-ionic form
- The orientation of the molecules within mineral interlayers [17]

*Kodešová et al.* studied the sorption of pharmaceuticals trimethoprim (TRM), clindamycin (CLN), clarymycin (CLR), metoprolol (MET), atenolol (ATN), sulfamethoxazole (SMX) and carbamazepine (CBZ) onto soil. This study was conducted with 13 soils that varied in their properties. They concluded that in some cases the process of sorption was highly influenced by pH of the soil. This was observed for TRM, CLN, CLR, MET, and ATN, where sorption was related to the base cation saturation and cation exchange capacity (CEC). On the other hand, the sorption of CBZ and SMX was influenced by organic matter content and hydrolytic acidity, respectively [38].

Overall, the mobility of pharmaceuticals in the environment and their bonding to soil is influenced by numerous factors, such as the texture of the soil, the exchange capacity, soil solution pH, the retention in the soil, and the presence of reactive groups in the soil compounds – organic matter and mineral oxide surfaces [1].

Studies have also shown that chiral soil matrices prefer connection to some enantiomers of chiral pharmaceuticals. Furthermore, acidic NSAIDs (IBF, NPX) are ionised at environmental pH and can undergo conjugation. The resulting complexes can subsequently interact with SOM and mineral surfaces [1].

In the soil environment, a process of reversible adsorption occurs. This adsorption can affect bioavailability of NSAIDs for soil microorganisms and influence their biodegradation. Moreover, the application of biosolids to soil causes decrease in the bound NSAIDs, leading to their increased biodegradability [1].

However, some pharmaceuticals can be part of non-equilibrium processes where they can become irreversibly bound to soil and sediments. This occurs mostly in the case of pharmaceuticals, where their residues are either potentially depleted and/or inactivated as they become incorporated into the humic acid cycle. There is also evidence that such irreversibly bound pharmaceuticals are no longer bioavailable and are removed [17].

## 5.2 Soil Organic Matter

Organic matter (OM) is characterized as a heterogenous mixture of organic compounds [39]. Although the carbon content of OM varies, the average amount is around 50%. Besides non-metallic elements, it also contains metals, either in exchangeable form or firmly bound in the form of complexes. Studies have shown that OM is comprised of various collections of humic substances and can be variable in the same soil [5].

The properties of soil OM are influenced by the origin of the constituent materials. OM in sediment contains biomolecules such as lipids, carbohydrates, proteins, and other organic debris from organisms. However, this composition changes during the process of decomposition. Due to polymerisation and condensation effect the OM content is increased, and the ratio of hydrogen/carbon and oxygen/carbon decreased. The result is a humification of OM, which consequently causes an increase in the hydrophobicity. In addition, the hydrophobicity in soil OM can be higher than in dissolved organic matter. This is mainly attributed to the presence of microorganisms and their processes [39].

In general, the amount of OM is determined by the soil type, the bulk density, the content of stones and coarse fragments. For instance, soils with finer textures have higher amount of OM than coarse-grained soils. Furthermore, the highest amount and turnover of OM is found in the uppermost horizons of permanent grassland soils [40].

OM is a sorption medium for organic contaminants that determines their retention and transport into the subsurface environment. Retention and transport can be influenced by the properties of the soil OM. The modification of surface chemistry i.e., polarity, aromaticity, aliphaticity of the soil OM affect the retention of the soil OM, and the soil pore system affects the transport [41].

Soil OM can increase the negative charge on the surface of iron oxides present in soil, leading to enhancement of electrostatic attraction and sorption of positively charged pharmaceuticals. Moreover, OM can also promote sorption by improving the stability of iron oxide colloids, resulting more surface area being exposed [17].

For example, in case of sulfamethazine, sorption can be improved by formation of compounds. This can occur when proteins dissolve in OM. In this state, they can be used as bridges to form compounds with goethite and SMZ molecules [17].

The surface of soil OM is known to contain carboxyl groups that causes electrostatic attraction between negatively charged humic molecules and positively charged solute molecules. The carboxyl and phenolic functional groups are part of soil OM as they are biosynthetic building blocks in plants [39]. Therefore, the acidity of different types of soil OM varies due to their different origins.

The sorption of pharmaceuticals can be also inhibited by soil OM. This applies in the case of oxytetracycline, where its sorption affinity to montmorillonite is reduced in the presence of humic acid (10 mg/l). Soil OM is known to be a critical factor affecting the sorption of only hydrophobic compounds. For polar compounds, the presence of soil OM is negligible [17].

*Park et al.* conducted a study focusing on the sorption of ATN, IBF, and CBZ onto two types of soil OM. The main focus of the study was to investigate electrostatic interactions of soil OM and pharmaceuticals at pH 7. The soil OM used was acquired from soils under different aquatic plants (*Acorus*, *Typha*) [39].

The analysis showed that *Acorus* soil OM had a higher hydrophobicity and electrical charge density than that acquired from *Typha*. Therefore, *Acorus* OM was able to absorb higher amounts of pharmaceuticals. Among the pharmaceuticals used, the highest sorption efficiency was observed for ATN (60 %), followed by CBZ (40 %), and IBF (30 %). The low sorption efficiency of IBF results from the electrical repulsion caused by the negative

charges of IBF and soil OM. The higher sorption efficiency of neutrally charged CBZ was attributed to its partitioning coefficient (2,77). Overall, both soil OM were highly hydrophobic, therefore a high value of log  $K_{ow}$  induced strong sorption. However, the sorption mechanism of CBZ and ATN was strongly influenced by electrical interaction [39].

Because of the high concentration of carboxyl and phenolic groups, the electrical density of *Acorus* soil OM was noticeably higher than that of *Typha* soil OM. Consequently, a higher absorption of pharmaceuticals was observed in *Acorus* soil OM [39].

The opposite course of sorption was observed for IBF in the study conducted by *Vulava et al.* in which the influence of OM on the sorption of two NSAIDs - IBF and NPX - was investigated. During the study, it was assumed that the presence of OM in the soil has a significant effect on the process of sorption of the aforementioned pharmaceuticals. The matrices used for this study were soils acquired from Charleston, USA. The soil was sampled from different depths ranging from 15 to 40 cm and differed in the amount of OM and clay mineral. The soil acquired from near the surface to a depth of 15 cm had the highest OM content.

Because of the non-polar moieties present in NPX and IBF, it was expected that strong sorption would be observed in the presence of a higher organic content [6].

Stronger sorption was observed onto soil with higher OM content, with stronger sorption observed at lower concentrations of NSAIDs and weaker sorption at higher concentrations. In general, in all cases the sorption was significantly stronger in soil with higher OM content.

The sorption was attributed to deprotonation of carboxyl group of both NSAIDs, the protonation of the amines contained in the OM as well as some amphoteric mineral oxide surfaces.

The presence of inorganic mineral components in soil with lower OM content in sorption of both pharmaceuticals was also highlighted. The deprotonation of IBF and NPX enabled bonding with the charged inorganic surfaces by electrostatic attraction or stronger chemisorption. The Freundlich isotherm model showed that with increase of sorbate concentrations, the sorbates sorbed to the soil components with weaker free energies. This course of sorption is generally more common in the case of polar organic solutes and charged surfaces. On the other hand, constant sorption of solutes is mainly observed between uncharged sorbent surface or non-polar organic compounds [6].

The authors also found that at pH 5, dominant deprotonation of IBF and NPX ensured strong sorption, especially onto amphoteric iron oxide surfaces rather than onto negatively charged clay mineral surfaces [6].

Based on the acquired data, IBF and NPX showed some preference in sorption to specific soil components in the following order: soil OM >> iron oxides > clay minerals [6].

Furthermore, the sorption and desorption of NSAIDs (IBF, DCF, KTF and NPX) was also investigated by *Zhang et al.* in their study. The main objective was to investigate the course of these processes onto loam textured soil in the individual system and in the mixture compound system. Soil OM content and ionisation of all NSAIDs at environmental pH were also considered, where the degree of deprotonation for NPX, DCF, IBF, and KTF was 97%, 97%, 86%, and 95% respectively [37].

High sorption affinity for IBF was observed in both the individual and the mixture compound systems. However, the comparison of the acquired  $K_D$  values showed different course of absorption. The order for all NSAIDs in the individual system and the mixture compound system was: DCF > NPX > KTF > IBF [37].

Due to its high hydrophobicity, IBF shows a stronger partitioning into soil OM. Furthermore, the presence of  $Al^{3+}$ ,  $Ca^{2+}$  and  $Mg^{2+}$  under acidic conditions contributes to the sorption of IBF. This is due to the ability of these cations to lower the negative potential of the soil surface through complexation. The sorption of IBF also increased with the concentration of IBF. The sorption was stronger in the mixture compound system indicating the presence of competitive interactions with NPX [37].

Overall, there was cooperative low to moderate sorption of NSAIDs observed in loam textured soil. In addition, the hydrophobicity of NSAIDs also contributed to the sorption of their anionic forms onto the soil. Due to its low hydrophobicity, KTF did not interact significantly with soil OM. However, the determined  $K_D$  values of NPX and KTF were higher in the individual compound system than in the mixture compound system. However, opposite was recorded for IBF and DCF. This indicates that hydrophobic compounds show stronger competition in partitioning onto soil OM. Furthermore, other studies suggested that sorption of IBF onto Ca-saturated components of soil may be increased by the presence of  $Ca^{2+}$  ions [37].

However, the study conducted by *Sanghwa et al.* shows that the presence of dissolved OM might have an opposite effect on the sorption of IBF. The experiment was carried out using 0.01, 0.1, and 1 M citrate and urea solution. Sediment was acquired from the surface layer of wetland in Changnyung, Republic of Korea [43].

The sorption of IBF to the sediment was studied in the presence of urea and citrate solutions. The experiment was carried out at different pH values (4, 5.3, and 7). Results showed that citrate with concentration ranging from 0.01 to 1 M interrupted the sorption of IBF onto the sediment. The sorption decreased with increasing citrate concentration. The reason for this could be the presence of carboxyl groups in citrate, which could bind to carboxyl groups of IBF. This complex could then exist in an anionic and soluble form and cause a decrease in sorption. This interruption was highest at pH 5.3, as half of IBF was negatively charged. On the other hand, urea increased the sorption of IBF. This was also proved by rising  $K_D$  values that were recorded at each concentration [43].

*Zhang J. et al.* focused on the influence of OM on the sorption of NOR. The soils used for the experiments were from different provinces in China - black soil (soil B), fluvo-aquatic soil (F), and red soil (soil R). The content of OM was as follows:

- 3.28% in soil B
- 1.73% in soil F
- 1.91% in soil R

The soil used for the experiment was additionally modified. It was first treated with a 30% solution of 50°C  $H_2O_2$ , followed by washing with 1 l of deionized water. This cycle was repeated until the conductivity of the solution was < 50  $\mu$ S. Afterwards, drying, sieving, and sterilisation was carried out. This entire process ensured the complete removal of OM [42].

NOR applied on individual soils was ranged in concentration from 5 to 200 mg/l. Overall, the sorption of NOR in bulk soils and in OM-removed soils increased with rising NOR concentrations. However, the sorption capacity of OM-removed soils was higher than in the corresponding bulk soils. Therefore, the sorption process of NOR was also influenced by soil properties [42].

The sorption process of NOR at a concentration 200 mg/l was more efficient than that of concentration 1 mg/l in soils B, F, and R. At the low concentrations (1 to 50 mg/l) the sorption was similar in soil R and B at the same initial concentrations. However, the sorption of NOR was much more efficient at concentrations 100 and 200 mg/l in soil B compared to soil R. Furthermore, the sorption amounts in soil B were significantly higher than in soil F. As the NOR concentrations increased, the sorption amounts in soil F and R were quite similar.

In OM-removed soils, the sorption of NOR increased rapidly with the increase of NOR concentrations. Despite similar sorption capacities, the amount of NOR sorbed to OM-removed B or OM-removed R was higher than the amount in OM-removed F. For example, at concentration of 5 mg/l, the sorption efficiency in OM-removed soils B and R was 102% and 99% higher than the efficiency in OM-removed F. In comparison, at a concentration of 50 mg/l, the efficiency of NOR in OM-removed soils B and R was 76% and 79%, respectively [42].

In general, NOR had a higher tendency to be sorbed onto OM-removed soils. The exception was soil R and OM-removed soil R. This process was attributed to the larger sorption area available in OM-removed soil due to the presence of clay particles. Negatively charged areas of OM in the soil could be responsible for this reduced tendency of sorption. Their presence could prevent NOR from sorption in the soil. The highest sorption in SOM-removed soil was observed in soil B, which was attributed to the presence of clay minerals and the soil pH [42].

Finally, it is also important to note that in reality pharmaceuticals do not enter the soil environment individually, but simultaneously with other pharmaceutical compounds. This could contribute to competitive adsorption leading to saturation, lower retention, and greater mobility of these contaminants. This was highlighted by *Conde-Cid et al.* in their study. The main objective was the competitive sorption of sulfonamides sulfadiazine (SDZ), sulfamethazine (SMT), and sulfachlorpyridazine (SCP) in agricultural soils. Agricultural soils from A Limia (S1, S2, S3) and Sarria (S4, S5, S6) located in Galicia, Spain were used. Each sample was sampled from depth of 0-20 cm and differed in soil organic carbon (SOC) in the following order from the lowest to the highest value: S1 < S5 < S4 < S2 < S6 < S3 [44].

Ternary competitive and individual adsorption tests were performed. The following total concentrations of sulfonamides were used: 15, 30, 60, 90, and 120  $\mu\text{mol/l}$  for the ternary competitive test and 5, 10, 15, 20, 30, 40, 60, 90, and 120  $\mu\text{mol/l}$  for the individual adsorption test. The highest adsorption capacity for all three sulfonamides was observed for soil S3 in ternary competitive tests. Soil S3 had the highest SOC and soil nitrogen content (TSN). On the other hand, soil S5 had the lowest adsorption capacity for SDZ and SCP. In the case of SMT, the lowest adsorption capacity was observed in soil S1. Moreover, soil S1



and S5 were the ones with the lowest OM content. The adsorption did not change when increased concentrations of antibiotics were applied on soil S2 and S3. However, in the case of soil S4 and S5 the adsorption percentage slightly decreased for all antibiotics with increase of initial concentrations of applied sulfonamides. This indicates slight and progressive saturation of the adsorption sites. The same course was observed in soil S1 and S6 for SDZ and SMT [44].

The average values of adsorption percentages were 40%, 44%, and 54% for SDZ, SMT, and SCP, respectively. SCP had the highest affinity for adsorption sites in soils S1, S2, S3, and S6, while SMT had the highest affinity in soil S5. However, the same affinity was attributed to all sulfonamides in soil S4. Based on the values  $K_D$  and  $K_F$ , the affinity order of the antibiotics in soils S1, S2, S3 and S6 was  $SCP \gg SMT \sim SDZ$ . It was  $SMT > SDZ \sim SCP$  for soil S5 and  $SMT \sim SCP > SDZ$  for soil S4. The authors concluded that the adsorption affinity of three sulfonamides was strongly influenced by OM [44].

In the ternary systems, the acquired values of  $K_D$  and  $K_F$  also varied. Based on the values of  $K_D$ , the adsorption affinity for three antibiotics on the soils was:  $S3 > S6 > S2 > S4 \sim S4 \sim S1 \sim S5$ . The contrary was observed when  $K_F$  was considered:  $S3 > S6 > S2 \sim S4 \sim S1 \sim S5$ . This suggests that the properties of the soils S1, S3, S5, and S6 have an influence on the adsorption of the three antibiotics [44].

Desorption was also focus of this study. In the case of the ternary system and the individual system the recorded desorbed amount increased with the initial concentration of the antibiotic. The lowest amount of desorbed antibiotics was recorded in soil S5. On the other hand, the highest desorbed amount of SDZ and SMT was recorded in soil S6, while the least desorbed amount of SCP was recorded in soil S2 [44].

When considering the values of  $K_D$ , the order of the desorption for three antibiotics for the soil was:  $S3 < S6 \sim S5 < S2 \sim S1 \sim S4$ . Different order emerges when considering the values of  $K_F$ :  $S3 \sim S6 \sim S5 < S4 \sim S2 \sim S1$ . In both cases, the lowest desorption was recorded for soil S3, which contained the highest amount of OM.

Comparison of data obtained from the ternary and the individual systems indicated that there was no difference between the two systems in the adsorption of three antibiotics in any of the soils [44].

### 5.3 Desorption

The mobility of pharmaceutical compounds depends not only on their sorption but also on their desorption from sediments. Once sorbed onto soil, pharmaceutical compounds can desorb by water carrying dissolved ions (reclaimed irrigation water) or by water carrying few inorganic ions (rainwater).

There are numerous factors that have been studied and have correlation with the sorption of pharmaceutical compounds. However, only a few studies include desorption.

One of these is study by *Zhang et al.* which focused on sorption and desorption of NSAIDs in soil. The goal of the study was to determine the distribution of IBF, DCF, ketoprofen, and NPX in the environment. The experiments were conducted with individual NSAIDs and their mixture. The matrix used in the experiment was loam textured soil from Mt. Hope, Ontario, USA sampled from a depth of 0-15 cm [37].

High sorption of NSAIDs onto the soil was observed. Maximisation of binding affinity between NSAIDs and soil components was ensured via covalent and non-covalent interactions. In the case of DCF, multilayer cooperative adsorption secured its chemical adsorption to the limited binding sites. However, IBF, KTF and NPX synergically saturated the weaker binding sites on the first layer of the soil. This way, adsorbable layers were formed that could accommodate more molecules. Conversely, the outer layers were not as attractive for such molecules and prevented the desorption of compounds [37].

This effect could explain low desorption of DCF that was observed in this study, where only 8-13% of the adsorbed DCF was actually desorbed. Furthermore, chemical sorption ensures the formation of stronger bonds than physical sorption. Therefore, a higher energy is needed to break these bonds and ensure desorption of DCF [37].

The compounds studied desorbed in the following order: DCF < NPX < KTF < IBF. Stronger retention was observed during desorption than in sorption [37].

The sorption-desorption hysteresis determines whether stronger retention of NSAID occurs during desorption or sorption. The higher the values of the hysteresis index (HI), the stronger the retention of the adsorbed compounds. This hysteresis was demonstrated by recorded values of HI that were higher than zero. The order of descend of the values was: DCF > NPX > KTF ~ IBF. In the individual system, the desorbed amounts for DCF, KTF, NPX, and IBF were 13%, 28%, 30%, and 43% respectively. In mixed compound system the amounts for DCF, KTF, NPX, and IBF were 8%, 16%, 25% and 33% respectively.

Adsorbed NAP and IBF were expected to quickly desorb from OM and mineral surfaces as they have low HI values. However, the presence of a strong  $\pi$ - $\pi$  interaction between the carboxyl groups of IBF, NPX, KTF and soil OM are responsible for a higher sorption-desorption hysteresis observed in this study [37].

Furthermore, pharmaceutical ionization was reported to influence the process of desorption. This was observed by *Martínez-Hernández et al.* where the main objective was the sorption and the desorption of CBZ, acetaminophen (ACP), NPX, ATN, SMX, and caffeine (CAF). Sediment acquired from unsaturated zone of the Manzanares-Jarama groundwater body, Spain, was used. A solution of reclaimed water was prepared by dissolving NH<sub>4</sub>Cl (0.07 g/l), MgSO<sub>4</sub> (0.1 g/l), CaCl<sub>2</sub> (0.01 g/l), K<sub>2</sub>HPO<sub>4</sub> (0.02 g/l), NaHCO<sub>3</sub> (0.25 g/l), peptone (0.01 g/l), and meat extract (0.01 g/l) in tap water. This synthesised reclaimed water was used to simulate desorption of the studied substances and 0.01 M CaCl<sub>2</sub> was used to mimic infiltration of rainwater. Competition for sorption sites between pharmaceuticals and inorganic ions and enhancement of acidic organic compound sorption via the reduction of repulsive electrostatic forces was expected. However, no such competition was observed during the experiment. Moreover, negligible sorption was recorded for ACP and CBZ, thus no desorption was observed. On the other hand, the cationic species of CAF and ATN were reversibly desorbed. The calculated data showed that 69.9% of ATN and 20.6% of CAF was desorbed [45].

The anionic compounds SMX and NPX had hysteretic sorption. In both cases, hysteresis was observed in sorption-desorption behaviour. Only 4.2% of SMX desorbed, which shows strong affinity for sediment. This is due its higher interaction with inorganic surfaces of the sediments. Furthermore, the bonds between non-hydrophobic compounds and natural OM

are weaker compared to the ligand exchange bonds. In contrast, in the case of NPX, the desorbed amount was 31.2%. NPX has an aromatic skeleton which can interact with aromatic moieties of OM via  $\pi$ - $\pi$  interaction. Since these interactions are non-covalent bonds, they are weaker than ligand exchange bonds. These interactions are responsible for the more pronounced hysteresis of SMX and can result in increased sorption irreversibility at higher concentrations. Overall, the probability of these pharmaceuticals entering the unsaturated zones of the sediment decreases in the following order: CBZ > ACP > NPX > ATN > SMX > CAF [45].

## 5.4 pH

The value of pH is an important parameter that can significantly affect the process of sorption by influencing the electrical charge of the sorbed compound and soil or clay aggregates. The progress of sorption of organic chemical pollutants, such as pharmaceuticals, can be determined by their  $pK_a$  value [42].

The aforementioned study conducted by *Zhang J. et al.* also focused on the influence of pH on sorption of NOR within pH range of 4, 7, and 10. The detailed description of the soils used in the study can be found in the previous *Chapter 5.2*. In total, six different types of soils were used in this study [42].

As the pH of the solution increased, the sorbed amount of NOR decreased in soils F and B, while it increased in soil R. The influence of different pH values on NOR distribution coefficient ( $K_D$ ) was also considered. The decrease in  $K_D$  values was observed in soils F and B with increase of pH [42].

Due to the change in pH, the process of sorption was attributed to the change in the dominant form of NOR. At the same time, the pH change caused the change in the surface charge on the clay minerals contained in the soil used. NOR has two binding groups (carboxyl and piperazil group) and  $pK_a$  value of 6.22 and 8.51. Therefore, it can be assumed that when the pH of the solution was less than 6.22, the positive form was the most prominent form of NOR. On the other hand, when the pH of the solution was above 8.51, the dominant form of NOR was negative. Within the pH values of 6.22 and 8.15, NOR is present in zwitterionic form [42].

The value of pH was balanced in the pH range of 3.4 and 7.5., with the maximum value of  $K_D$  reached at pH 6. Due to the gradual protonation of NOR at pH 6, the electrostatic attraction between NOR and the soil particles contributed significantly to the sorption process [42].

As mentioned in the previous Chapter *Sanghwa et al.* also focused on the influence of pH on the sorption of IBF. The sorption process was studied at the pH value of 4, 7 and 5.3. The pH value of the electrolyte was adjusted by 0.01 M solution of acetic buffer for pH 4 and by phosphate buffer, containing 6.74 g/l  $K_2HPO_4$  and 8.34 g/l  $KH_2PO_4$  for pH 7. Additionally, no adjustment of the solution pH was necessary for pH 5.3. This value is similar to the  $pK_a$  value of IBF (5.2).

Knowledge of the  $pK_a$  value allows the form of IBF at a given pH to be determined. Therefore, IBF was assumed to be present in neutral form at pH 4, anionic form at pH 7 and in form of anion or zwitterion at pH 5.3 [43].

The results of the study showed increased tendency of IBF to sorb onto sediment at pH 4 and due to the negative charge allocated on the surface of the sediment, showed no indication of sorption to the sediment at pH 7. Furthermore, values of  $K_D$  and  $K_F$  of IBF were determined, the values of  $K_D$  were higher than  $K_F$  values. This suggests that sorption occurred through hydrogen bonding of carboxyl groups of IBF and silanol groups of soil or sediment particles [43].

Another study by *Zhang et al.* investigated the influence of pH on the sorption of the antibiotics TRM, sulfapyridine (SPD), sulfameter (SME) and sulfadimethylehoxine (SDM).

The experiment was conducted at pH value 4, 5, 6, 7, 8, 9 and 10. The sorbate was an agricultural soil from Chongming, China. The soil was sampled from depths 0-20 cm, 20-80 cm and 80-100 cm [46].

The highest sorption was observed with TMP. Depending on the pH, the sorption tendency of individual pharmaceuticals was: TMP > SPD > SDM > SME.

At low pH, TMP was present in the form of cation and in neutral form at pH above 7. The strongest sorption of TMP was present in the pH range of 4 to 6. TMP showed no affinity to soil at pH higher than 6 [46].

On the other hand, SPD with the  $pK_a$  value of 8.4 showed the strongest sorption tendency in the pH range of 4 to 8. However, this tendency decreased continuously at pH higher than 8. The main reason for this is the presence of sulphonamides at high pH in an anion form, leading to electrostatic repulsion between these components and negatively charged minerals.

The study by *Yuxuan et al.* focused on the influence of pH on the sorption of tetracycline (TC). The experiment was conducted using pH solution 2, 3, 4, 5, 6, 7, 8, 9 and 10. The matrix was a soil sampled from various areas in China from soil surface at a depth of 0 to 20 cm. The pH of soil sampled in range from 5.16 to 8.15 [47].

In the pH range of 2 to 4, the sorption decreased in alkaline soils, and the opposite was observed in the pH range from 4 to 6. From the pH value of 6 and higher, the sorption in soils decreased again. The opposite course of the sorption process was observed in acidic soils. In the pH range from 2 to 7, the sorption of TC in acidic soils increased and the opposite course of sorption was observed from pH 7 to 10 [47].

The main reason for the observed changes in the sorption process at different pH was a result of different TC species. The species of TC was cationic at  $pH < 3.3$ , zwitterionic in the pH range from 3.3 to 7.7, and anionic at  $pH > 7.7$ .

The point of zero charge (p.z.c) of the sampled soils was also measured and taken into account. This unit is the value of pH at which the total surface particle charge is zero under given pressure, temperature, and composition of the aqueous solution. At  $pH_{PZC}$ , the surface of the sorbate has an equal amount of positive and negative charges [48].

The surface charge of the sorbent was positive at  $pH_{PZC}$  of the sorbent higher than the pH of the solution, otherwise it was negative. All the soil samples had  $pH_{PZC}$  values lower than 7.63, indicating that at pH higher than 7.63, the soil surface charges were negative. Similarly, at pH higher than 7.7, TC was present in the form of anion, resulting in electrostatic repulsion. This mechanism was observed in the pH range of 7 to 10. The opposite course of sorption was observed at pH lower than 7 [47].

For example, the soil with  $pH_{PZC}$  2.75 had negative surface charge due to the solution pH range (2 to 6). On the other hand, the other soils with  $pH_{PZC}$  in the pH range from 6.45 to 7.63 were positively charged at the same solution pH. Therefore, the observed changes in sorption of TC at different solution pH (2 to 6) may be affected by differences of TC species rather than surface charges of the soils [47].

Furthermore, the results showed that in the pH range of 2 to 4, the amount of cation TC forms decreased and the sorption capacity of TC to alkaline soils increased. Cation exchange between alkaline soils and the cationic form of TC was found to be the main sorption mechanism. Moreover, in the same pH range, the amount of TC in the form of zwitterions

and the sorption capacity of TC increased. In this case, the main sorption mechanism was the interaction of TC in zwitterionic form and sorption capacity [47].

The authors concluded that for acidic soils, the main sorption mechanisms could be hydrophobic interaction between soils and the neutral form of TC. On the other hand, for alkaline soils, the proposed sorption mechanism was cation exchange [47].

The study conducted by *Conde-Cid et al.* mentioned in *Chapter 5.2*, also considered influence of soil pH on the sorption of three sulphonamides SDZ, SMT, and SCP. All three antibiotics are amphoteric molecules with two  $pK_a$  values. They exist in a neutral form at an environmental pH (2.5 and 5-6). Therefore, at a pH between 2.5 and 6, these contaminants are present in a non-ionised form, while at a pH above 6, the anionic form is also relevant [44].

The soils used in the experiment differed in their pH values. While soils S1, S2, and S3 had an acidic pH (from 4.5 to 4.8) in water, soils S4, S5, and S6 had pH in water close to natural values (from 6.2 to 7.1). The pH in KCl was lower for all soils with values ranging from 4 to 6.4. This indicates the predominance of negative charge on the reactive surface of all soils [44].

In general, at neutral and alkaline pH, the electrostatic repulsion between the anionic form of sulphonamides and the negatively charged soil surface is expected. The pH effect became remarkable only in the case of SCP. This was due to its lower value of  $pK_{a2}$  compared to other sulphonamides. Therefore, SCP was present mostly in anionic form in the range of the pH values studied (4.5 to 7.1). In addition, SMT had the highest value of  $\log K_{ow}$  at pH 7 (0.14). Due to this high hydrophobicity, it has the highest affinity in neutral soils [44].

Based on the values of  $K_D$  and  $K_F$ , the affinity of sulphonamides for soils S1, S2, S3, and S6 was:  $SDZ \leq SMT \ll SCP$ . This was attributed to the hydrophobicity of sulphonamides. However, this was not observed in soil S5 where the affinity was  $SDZ \sim SCP < SMT$ . This was attributed to the influence of pH, as the hydrophobicity of sulphonamides varies depending on the pH of the medium [44].

## 5.5 Temperature

Temperature is one of the main factors that can influence the process of sorption. Therefore, valuable information can be obtained by studying its influence on the sorption of pharmaceutical compounds.

Sorption of pharmaceutical compounds is either an exothermic or an endothermic process. For endothermic sorption, an increase in temperature results in an increase of the sorption. Furthermore, an increase in temperature would decrease the viscosity of the solution and increase the diffusion rate of the molecules. This ensures easier incorporation of pharmaceuticals into the internal pores through the boundary layer of the sorbent. This effect was observed in the sorption of oxytetracycline, and tetracycline on magnetite, and tetracycline on palygorskite [36].

However, a decrease in sorption with increasing temperature was observed in the case of sulfamethazine, and pyraoxystrobin on HA and soil, and soil respectively. On the other hand, the sorption of spiramycin on palygorskite was not affected by the increase of temperature [36].

The study by *Maszkowska et al.* also contributed to the research of temperature and its influence on the sorption of pharmaceutical compounds. This study focused on the adsorption thermodynamics of three pharmaceuticals representing three different ionic species. Sulphonamides sulfisoxazole (SXX), sulfaguanidine (SGD) and beta-blocker propranolol (PRO) were studied [49].

The adsorption process of these polar compounds at temperatures 20 °C, 30 °C and 40 °C was investigated. Calculations revealed that sorption of PRO was exothermic, spontaneous and enthalpy driven. For SGD, the sorption process was endothermic, spontaneous and entropy-driven, while sorption of SXX was endothermic, spontaneous only above 30 °C and entropy-driven. This study suggests that the partitioning mechanism of these pharmaceuticals differs and that it mainly depends on their ionic form. For example, the sorption of PRO onto soil surface was a spontaneous process and would be unfavourable at higher temperatures. The calculated negative entropy indicated a more specific surface reaction due to the presence of positively charged functional groups in PRO. On the other hand, neutral SGD and anionic SXX did not sorb onto the surface as strongly and displayed endothermic sorption. In general, all pharmaceuticals showed physical sorption which is a fast and reversible process due to the low energy requirements [49].

Despite the presence of a strong positive charge, the calculated enthalpy change for PRO sorption was quite small. This suggests that weaker forces other than ion-exchange may have affected the sorption of PRO to a large extent. In the case of beta-blockers, ion-exchange attraction is considered to be the main sorption mechanism onto soil. Therefore, the presence of steric hindrance may cause reduction in this attraction [49].

## **6. Methods used for detection**

The most commonly used methods for the accurate detection of pharmaceuticals in complex matrices are chromatographic methods, such as gas chromatography (GC), high performance thin-layer chromatography (HPLTC), and high-performance liquid chromatography (HPLC).

In recent years, near-infrared spectroscopy, fluorimetry, and phosphorimetry have gained more attention in the quantitative analysis of drugs in pharmaceutical formations and biological fluids. Electrochemical techniques have also drawn attention in pharmaceutical research due to their sophisticated instrumentation. Methods such as voltammetry, polarography, potentiometry, and amperometry also have been used for analysis in recent studies [50].

More advanced detection and analysis is provided by hyphenated techniques. By coupling separate techniques, these techniques guarantee the formation of a more advanced analytical method. Techniques such as LC-MS (mass spectrometry)/HPLC-MS, GC-MS, LC-NMR (nuclear magnetic resonance), ICP (induced coupled plasma)-MS, CE (capillary electrophoresis)-MS are used for the determination of pharmaceuticals in complex biological and environmental samples [50].

Recently, more sensitive and specific analytical methods have been used. These methods include LC-MS/MS, GC-MS/MS in which chromatographic techniques are coupled with tandem mass spectrometry. In elemental analysis, GC-AES (atomic emission spectroscopy)

and GC-AAS (atomic absorption spectrometry) are emerging as valuable analytical techniques.

Even though LC-MS/MS provides a full-scan information procedure, other methods such as combination of HPLC with quadrupole time-of-flight is more commonly used for the determination and separation of NSAIDs. For higher process sensitivity and lower cost, hyphenated methods NMR, more precisely LC-NMR are developed.

## 6.1 Detection in soil

Due to the low concentrations of pharmaceuticals present in soil samples, advanced separation and detection techniques are required for sensitive and accurate detection and identification. Most techniques used for analysis in solid samples are those developed for analysis of aqueous samples. Such analysis is more challenging because of heterogeneity of the samples.

Current methods for separation and detection of pharmaceuticals in solid environmental samples rely on the application of chromatographic techniques (GC or LC) hyphenated to MS. Most pharmaceuticals are non-volatile, and some are highly polar compounds containing ionizable functional groups. Therefore, a derivatization step is included before GC analysis using derivatization agents. This step can reduce the accuracy of the method due to the loss of analytes, introduction of unwanted contaminants, or incomplete reaction. In addition, pharmaceuticals such as TCs are thermolabile, which requires the use of GC instead of LC [51].

### 6.1.1 Gas Chromatography

GC-MS is used for the analysis of environmental substances as a cost-effective technique suitable for routine analysis. The advantage of this technique compared to LC-MS is the lower susceptibility to matrix effect, especially in complex environmental matrices or wastewater.

The matrix effect can suppress or amplify the signal of the analyte during the ionisation process. This can occur due to the coagulation of matrix components that have similar ions as the target analyte.

Furthermore, full scan GC-MS can be used to identify non-target pharmaceuticals and their environmental transformation products. The application of tandem MS ensures higher selectivity of the method, while higher sensitivity can be achieved by a large volume injection. Moreover, cost-saving GC-MS is more commonly used since single quadrupole GC-MS is more frequently used than HPLC-MS/MS in routine environmental laboratories. However, most pharmaceuticals are polar, non-volatile, and thermolabile compounds that are unsuitable for GC analysis. Therefore, derivatization of hydroxyl and carboxyl groups is necessary prior to the analysis [51].

In study by *Kumírská et al.*, optimisation of GC-MS method was performed to ensure simultaneous determination of 20 different pharmaceuticals (8 NSAIDs, 5 oestrogenic hormones, 2 beta-blockers, and 3 antidepressants) in soil samples collected in northern Poland. The method used in this study was based on ultrasound-assisted extraction with



purification of the extracts using silica columns, and derivatisation by N, O-bis(trimethylsilyl)trifluoroacetamide (BSTFA) and 1% trimethylchlorosilane (TMCS) in pyridine prior to the analysis. Mass spectrometric analysis was performed using single ion monitoring (SIM) mode. The target compounds were identified based on their retention time and two characteristic m/z ions for each compound. Quantitative analysis was based on the peak area of the quantitative ions [52].

Twelve of the 20 compounds analysed were detected at least once in the sampled soils. Where concentration of seven drugs – salicylic acid, IBF, fluriprofen, diflunisal, DCF, diethylstilbestrol and estrone was below the method quantification limit (MQL), MQL was assessed as the lowest point of the calibration curves obtained with accuracy of 80 to 120% and < 10% relative standard deviation. The highest concentration detected was for naproxen (3 ng/g), clomipramine (5.6 ng/g), estrone (7.2 ng/g) and estriol (1.3 ng/g).

This method allowed the analysis of five different classes of pharmaceuticals in one analytical run. Furthermore, the extraction procedure used with purification of the extracts on a silica column ensured satisfactory recovery results for nine pharmaceuticals [52].

### 6.1.2 Liquid Chromatography

The determination of pharmaceuticals in solid environmental samples is performed by LC coupled with a sensitive and specific detection system. The multiresidue analysis usually refers to LC in combination with MS [51].

The separation of pharmaceutical compounds is mostly carried out using reverse-phase analytic column.

The use of UPHPLC has also been applied for the analysis of solid samples. Presence of particles with size of <2 µm packed in the column provides sensitivity two or three times higher than HPLC. The presence of these particles in the column ensures better resolution, increases peak capacity, and reduces run time. Consequently, the peaks are narrower, the separation is improved, and peaks do not overlap thus quality of the mass spectra is higher.

Mobile phase used is a crucial factor determining the correctness of the analysis. Typically, mixtures of acetonitrile-water or methanol-water at different pH values have been used as mobile phases for the LC separation under gradient elution. Volatile additives can be used to improve ionisation of the analytes and the sensitivity of MS detection. On the contrary, use of non-volatile additives should be avoided, especially when using electrospray ionisation (ESI).

ESI is an excellent ionisation technique used for both polar and non-polar compounds and for compounds with poor thermal stability. Therefore, it is the most commonly used ionisation technique. Despite the ability of LC-MS to determine pharmaceuticals in complex matrices, efficient separation of the analytes from interferences is still required. Single quadrupole MS methods produce low fragmentation, and pseudomolecular ions. Reported was the use of single quadrupole MS in the determination of NSAIDs, sulphonamides, macrolides and TCs.

LC-MS<sup>2</sup> is preferred for the analysis of complex matrices as it overcomes drawbacks of single quadrupole MS methods. This method enables one to distinguish between individual compounds that have same molecular mass by induced collision with inert gas. Although

LC-MS<sup>2</sup> is not always necessary, it can reduce matrix effects and thus ensure amplification of the analyte signal. Furthermore, MS<sup>2</sup> offers increased sensitivity and the selectivity in analysis of complex matrices.

The analysers used as LC detectors are quadrupole (Q), ion trap (IT), or time of flight (TOF) either alone or in various combinations. Triple tandem quadrupole (QqQ) is the most commonly used tandem MS capable of analysing parent pharmaceuticals and their metabolites. IT analysers are capable of multiple stages of fragmentation in time (MS<sup>n</sup>) and trapping product ions, resulting in high sensitivity and full scan mass spectra. The application of these analysers helps to infer the degradation pathways and identification of the unknown substances in the samples.

Most recently, the development of hybrid MS has been achieved by combining two MS principles into one instrument. Hybrid MS includes Q-TOF-MS, and Q-linear IT (Q-LIT). This way, more information about the sample can be obtained while the run time of the analysis is reduced. Furthermore, this instrumentation enables true positive analysis of target compounds in complex samples with higher confidence. However, the use of hybrid MS for the analysis of solid environmental samples is scarce [51].

So far, an analytical LC-MS/MS method capable of simultaneous determination of 44 pharmaceuticals in different soil samples has been developed. The method was optimised using 13 different types of soil from the Czech Republic and Central Europe.

The analysis was performed using a column with a particle size of 4 µm, as it offered better separation and peak shapes. Due to low recoveries for some pharmaceutical compounds, the application of the method was restricted to 44 out of 91 compounds evaluated. The best results were obtained using acetonitrile: water (1:1). Here the extraction efficiency for these compounds ranged from 55 to 135% in all soils [53].

The method was applied to determine pharmaceuticals in two contamination scenarios – soil continuously affected by the effluent from the WWTP, and soil annually enriched with WWTP sludge. The results showed that 24 out of 44 target compounds were above the limit of quantification. The measured concentrations ranged from 0.83 to 223 ng/g.

Overall, a sensitive LC-MS/MS method was developed for the determination of 44 pharmaceutical compounds in various soil samples [53].

## EXPERIMENTAL PART

### 7. Materials

#### 7.1 Laboratory Equipment and Machinery

- Analytical weights, SCALTEC SBC 31
- Weights, Denver Instrument S-4002
- Mili-Q water Deionisation system, PURELAB flex, ELGA
- Magnetic mixer, Thermo Fisher™ CIMAREC™ Poly 15
- UV-VIS spectrometer, Hitachi U-3900H
- pH meter, METTLER TOLEDO, SevenMulti
- Conductometer, METTLER TOLEDO, SevenEasy
- Syringe filters:
  - VWR® Syringe Filter, diameter 22 mm, 0,45 µm, LLC 100 Matsonford Rd
  - CHROMSERVIS® Filterpure Syringe Filters, diameter 13 mm, 0,22 µm
- Centrifuge, Hettich Rotina 420R
- General laboratory instruments

#### 7.2 LC-MS Method

- Liquid chromatograph Agilent 1 100 Series, Agilent
  - Gradient pump
  - Vacuum degasser
  - Automatic sampler
  - Thermostat space for columns
  - UV-VIS detector with diode array – deuterium and wolfram source of light, 1 024 photodiode, wavelength range 190 – 950 nm, programmable width of slit 1 – 16 nm
- Column KINETEX C18, size 150x3 mm, particle size 2,6 µm
- Mass spectrometer Agilent 6 320 Series, Ion Trap LC-MS
- Infusion pump kdS 9 100, kd Scientific
- Nitrogen generator, Peak Scientific

### 7.3 Chemicals Used

- Deionised water prepared by PURELAB Flex, ELGA
- Ibuprofen, Sigma Aldrich
  - Prepared Ibuprofen solutions 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 and stock solution 20 mg/l
- Britton-Robinson buffer with pH 3, 7 and 10 prepared from:
  - 99% Acetic acid, p.a. Penta
  - Sodium hydroxide, beads for analysis, mikroCHEM
  - 85% Phosphoric acid, p.a. Penta
  - Boric acid, Sigma Aldrich

### 7.4 Software for Data Analysis

- MS Excel, 2019

## 8. Soils

Three different types of soil were used as a matrix for the sorption and desorption experiments. The soils were sampled from Jablůnka, Hodonín and Brno, Czech Republic (49.3836° N, 17.9502° E; 48.8529° N, 17.1260° E; 49.1951° N, 16.6068° E). To differentiate between individual soils, they were branded soil A (Jablůnka), B (Hodonín), and C (Brno). These soils were primarily chosen due to their OM content. The characteristic properties of each soil were analysed. This included elemental composition, moisture content, and OM content. Data describing individual soil types can be found in *Table 3*. The analysis was carried out using EURO EA Elemental Analyzer (Euro Vector Instruments & Software) and Thermogravimetric Analyzer TGA Q50 (TA Instruments). As can be seen in the listed soils there is a significant difference in their OM content.

Table 3: Characteristic properties of soils used for sorption and desorption experiments

Parameters	Soil A	Soil B	Soil C
Area	Jablůnka, CZ <sup>6</sup>	Hodonín, CZ	Brno, CZ
Carbon (at. %)	10.93	19.28	10.96
Hydrogen (at. %)	68.73	61.28	70.98
Nitrogen (at. %)	0.91	1.10	0.72
Oxygen (at. %)	19.43	18.34	17.35
Hydrogen/Carbon	6.29	3.18	6.48
Carbon/Oxygen	0.56	1.05	0.63
Moisture (wt. %)	1.57	0.22	3.24
Organic fraction (hm. %)	5.75	1.17	6.86

## 9. Procedures

### 9.1 Influence of Organic Matter Content on Sorption and Desorption

The stock solution of IBF with a concentration of 20 mg/l was prepared by weighing 2 mg of IBF on an analytical balance. This stock solution was used to prepare solutions in 100 ml volumetric flasks with the following concentrations: 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10 mg/l. The detailed volumes used for the preparation are shown in *Table 4*.

Table 4: Volumes used for each IBF solution

<b>Volume of stock solution (ml)</b>	5	10	15	20	25	30	35	40	45	50
<b>Concentration (mg/l)</b>	1	2	3	4	5	6	7	8	9	10

IBF solutions in concentration range from 6 to 10 mg/l were used for interaction with soil type A, while solutions in concentration range from 1 to 10 mg/l were used for soil type B and C. This is due to soil A being previously used in an experiment conducted as a part of the bachelor thesis. Data from this experiment were also taken into account and will be presented together with all results acquired.

The whole experiment was carried out in two cycles – sorption and desorption. In the first cycle, each soil was crushed to ensure a small and homogenous particle size. Afterwards, 0.5 g of each soil was weighed and put into a 50 ml polypropylene centrifuge tube. Each tube was filled with 25 ml of a solution, in triplicate for each concentration. The same procedure was used for blank using 25 ml of deionized water. The soil suspensions were then mixed at 270 rpm at room temperature on magnetic mixer for precisely 48 hours.

After 48 hours, centrifugation was carried out at 5 000 rpm for 15 minutes. This ensured separation of the solid and aqueous phases. Acquired were 15 ml of filtered supernatants using syringe filters with pore size of 45 µm. The solid phase was moved to a Petri dish where it was left to dry.

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<sup>6</sup> CZ – Czech Republic

All dried soil samples were weighted and used for the second cycle of the experiment – desorption. The soil was put into the 50 ml polypropylene centrifuge tube and filled with 25 ml of deionised water. Followed was the same procedure as was used for the sorption cycle.

The filtered supernatants were used for the measurement of pH, conductivity, and absorbance. These parameters were also measured for all standard solutions prepared for this experiment. Sorption samples with a concentration of 5 mg/l and higher had to be diluted to ensure proper measurement with a UV-VIS spectrophotometer. More detailed data were acquired by LC-MS analysis. Before the measurement the samples were stored in a fridge at 4°C degrees. All samples had to be additionally filtered using syringe filters with a pore size 0.22 µm. Samples with IBF concentration 5 mg/l and higher had to be diluted. The dilution ratio used in UV-VIS analysis was 1:2 (v/v) and 1:1 (v/v) in LC-MS analysis.

## 9.2 Influence of pH on Sorption and Desorption

The whole experiment was carried out in two cycles – sorption and desorption. Three types of soil were used for this experiment. However, the experiment was executed using only one IBF concentration. After evaluation of the previous data acquired from the first experiment, chosen was concentration 10 mg/l. The interaction of this specific concentration offered better understanding of pH influence on IBF in different types of soil. The preparation of the soil was the same as in *Chapter 9.1*.

The influence of pH was observed using the Britton-Robinson buffer (BRB). This buffer is known as universal buffer capable of creating pH in range from 2 to 12. The pH used in this experiment was 3, 7, and 10. Prepared was 1 l of BRB by 1:1:1 (v/v/v) dilution of 0.04 M H<sub>3</sub>PO<sub>4</sub> (0.684 ml/0.25 l), 0.04 M CH<sub>3</sub>COOH (0.578 ml/0.25 l) and 0.04 M H<sub>3</sub>BO<sub>3</sub> (0.618 g/0.25 l). The pH was adjusted to required value using 0.2 M NaOH (0.8 g/0.1 l).

A stock solution was prepared by dissolving 10 mg of IBF in 1 l of BRB. The pH was adjusted with NaOH to achieve required pH values. Using the stock solution, prepared were calibration solutions with the concentrations 6, 7, 8, 9 and 10 mg/l.

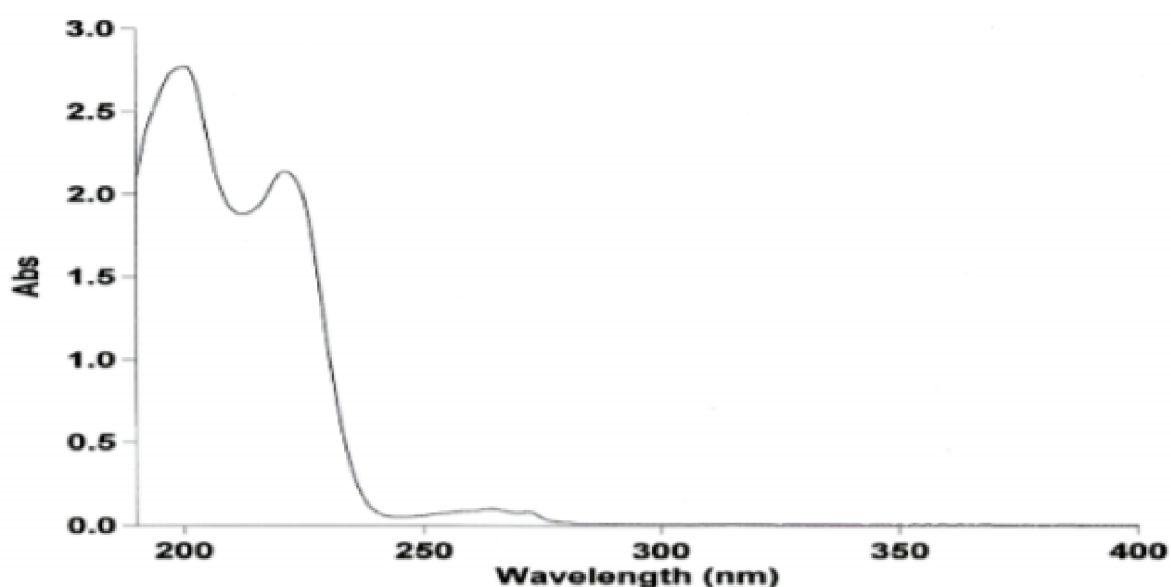
The 50 ml polypropylene centrifuge tubes with weighted soils (0.5 g) were filled with 25 ml of the stock solution with pH 3, 7, and 10. Due to time related issues, prepared were two test tubes with the specific pH values and one blank for each soil type. The blank solution was prepared as a buffer solution without IBF.

The samples were put onto magnetic mixer at 270 rpm at a room temperature for precisely 48 hours. The treatment of the samples was the same as in *Chapter 9.1*. Acquired were supernatants and soil samples that were left to dry at a room temperature. The conductivity, pH, and absorbance of all filtered samples was measured. The samples were stored in a fridge at 4°C degrees. Followed was the measurement of the samples by LC-MS analysis. Before the analysis, the treatment of each sample was the same as is described in *Chapter 9.1*.

The dried soil was weighted and sampled into 50 ml polypropylene centrifuge tubes, which were filled with 25 ml of buffer. The following steps were the same as in case of the sorption experiment. The treated samples were used to measure pH, conductivity, and absorbance. Afterwards, the samples were stored in a fridge at 4°C degrees. The final measurement was performed by LC-MS. No dilution was necessary for LC-MS and UV-VIS analysis.

### 9.2.1 UV-VIS Spectrometry

The analysis of all samples was carried out using Hitachi U-3900H spectrometer. This included samples from both experiments. A scan of absorbance spectra was performed by measuring absorbance in small volumes in the wavelength range from 200 nm to 600 nm. In the absorbance spectrum shown in *Figure 7*, IBF has two peaks at 218 nm and 264 nm [54]. Therefore, the measurement in the mentioned range ensured a better evaluation of the concentration contained in the samples. All samples and standard solutions were measured. The calculation of the final concentration was achieved by using absorbance at 218 nm. All the calculations were performed using MS Excel. The results were used to describe the course of sorption and desorption in the studied soils.



*Figure 7: UV-VIS spectrum of pure Ibuprofen solution [54]*

### 9.2.2 LC-MS Method

The LC-MS method was used for precise identification and detection of IBF in all samples. This was carried out on the chromatograph Agilent 1 100 Series, Agilent, with detection ensured by Agilent 6 320 Series, Ion Trap. The separation of the sample was performed on KINETEX C18 column (150 mm x 3 mm x 2.6  $\mu$ m). The conditions used for the analysis are listed in *Table 5* and *Table 6*.

Table 5: LC-MS analysis parameters

LC Conditions	
Injection	20 µl
Column temperature	40 °C
Mobile phase	MeOH and 0.001 M HCOOH
Rt <sup>7</sup> of Ibuprofen	11.6 min
MS Conditions	
Nebuliser pressure	30 psi
Nebuliser flow	10 l/min
Nebuliser temperature	350 °C
Scan	110-290 m/z, average
Mode	Negative
Target mass	205 m/z

Table 6: Mobile phase gradient

Time (min)	MeOH (%)
0	40
1	40
6	90
14.5	90
17	40

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<sup>7</sup> Rt – retention time



## 10. Results and Discussion

### 10.1 Influence of Different OM Content on Sorption and Desorption Process

The first experiment focused on the interaction of IBF at various concentrations with three different types of soil. The acquired results were evaluated in MS Excel. To have better understanding of the interaction between IBF and soil OM the results acquired from author's previous work were also taken into consideration [54]. This included the interaction of IBF in concentrations range from 1 to 5 mg/l with soil A.

#### 10.1.1 Sorption of IBF in Different Studied Soils, UV-VIS Data

The values of IBF concentration were calculated in each sample. The data obtained from UV-VIS spectrometry were used to describe the course of the sorption. The sorption and desorption differed in each soil.

The data acquired from UV-VIS spectrometry analysis showed a linear sorption of IBF in soil A. An increase of sorbed amount with rising concentration of the applied soil solution was observed. This can be seen in *Figure 8*. The difference between each concentration is not significant at first. However, this gradually changes at higher concentrations, where the sorbed amount increases from the concentration 7 mg/l onwards. The acquired data indicate that the sorption process of IBF in soil A was influenced by the increasing concentration of the soil solution.

An average of 66.89% of IBF was present in a stationary fraction and 33.11% was present in a mobile fraction. The highest amount of IBF present in the stationary fraction was at concentration 1 mg/l. This can be attributed to lower amount of IBF present in the solution applied onto the soil. The recorded values for IBF present in the stationary and the mobile fraction in soil A can be found in *Figure 9*.

The sorption process in soil B had different course. IBF showed low sorption affinity at low concentrations with increase at concentration 5 mg/l. Overall, a nonlinear course of sorption was observed in soil B, where the lowest sorbed amount was recorded at concentration 4 mg/l (20.23  $\mu\text{g/g}$ ) and the highest at concentration 9 mg/l (418.78  $\mu\text{g/g}$ ). The whole course of the sorption in soil B can be seen in *Figure 10*. Compared to soil A, the sorbed amount of IBF at each concentration was low, with two exceptions, at concentrations 7 and 9 mg/l, where the recorded sorbed amount was higher than in soil A. Furthermore, low amount was sorbed onto the soil B at 10 mg/l. This can be due to the saturation of the sorption sites that were available in the soil at this concentration.

The average calculated sorption efficiency of IBF in soil B was 52.98%. The calculated sorption efficiency in soil B can be seen in *Figure 11*.

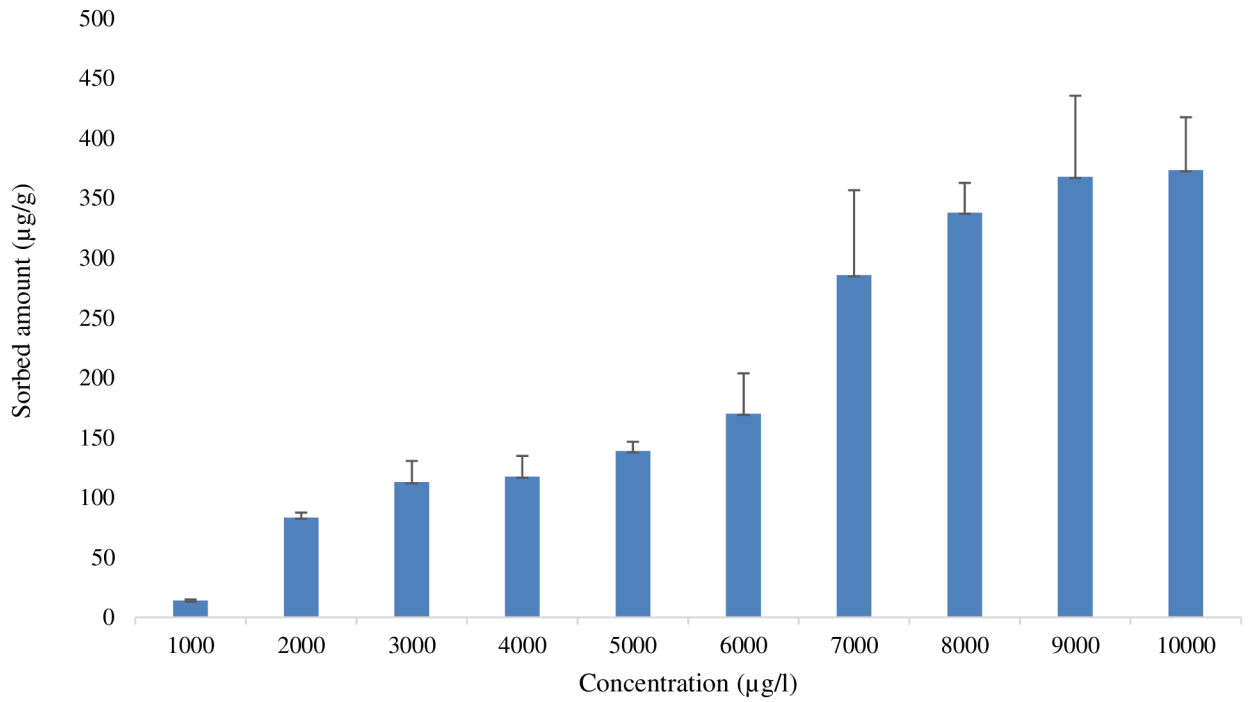


Figure 8: Sorption of IBF in soil type A, UV-VIS data [54]

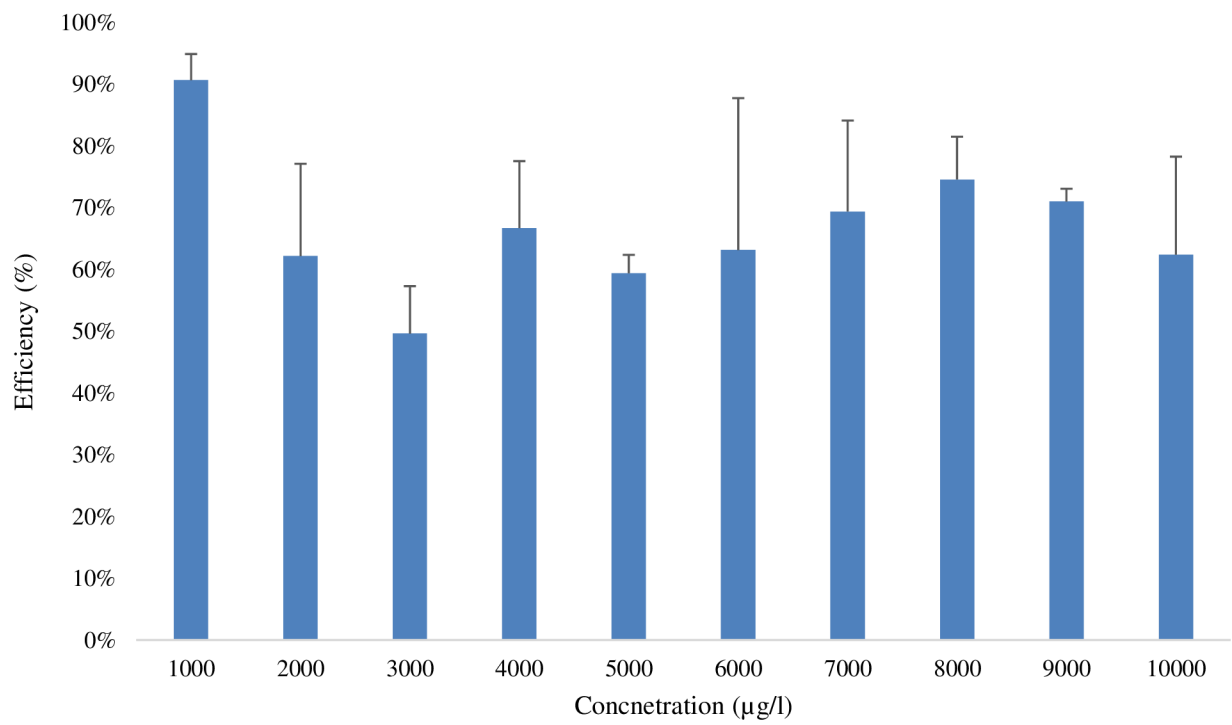


Figure 9: Sorption efficiency of IBF in soil A, UV-VIS data [54]

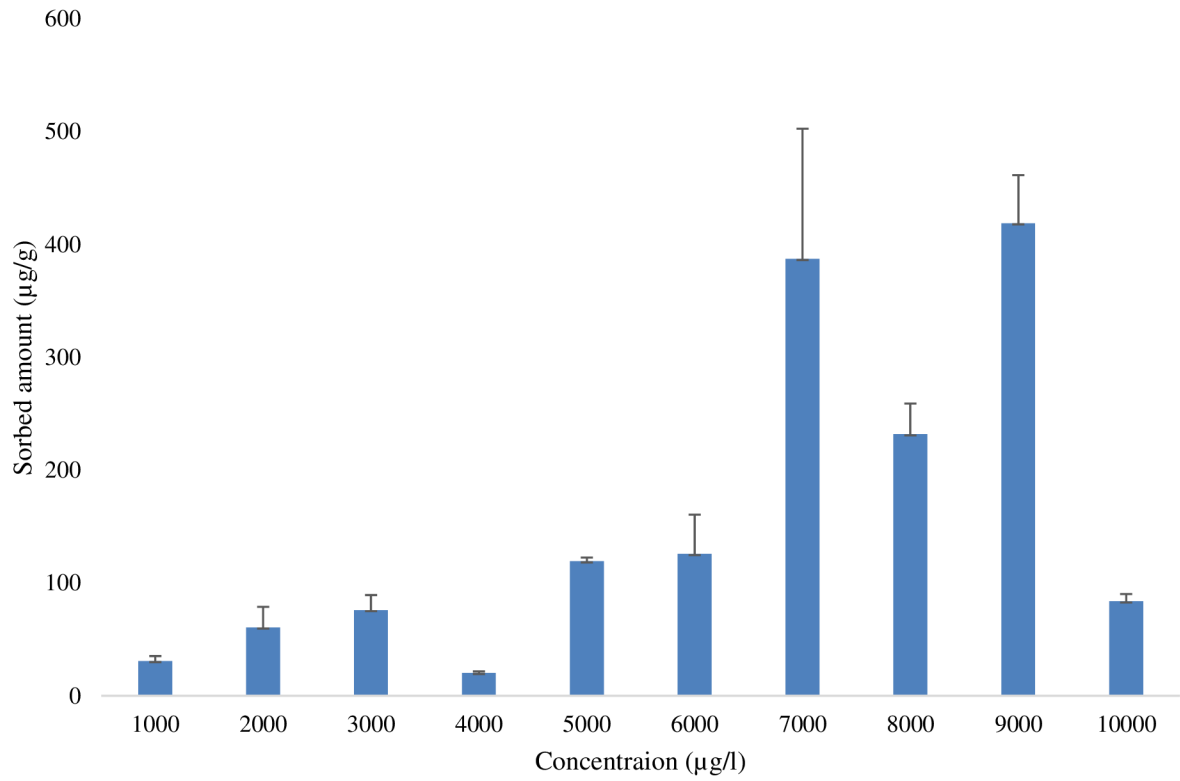


Figure 10: Sorption of IBF in soil B, UV-VIS data

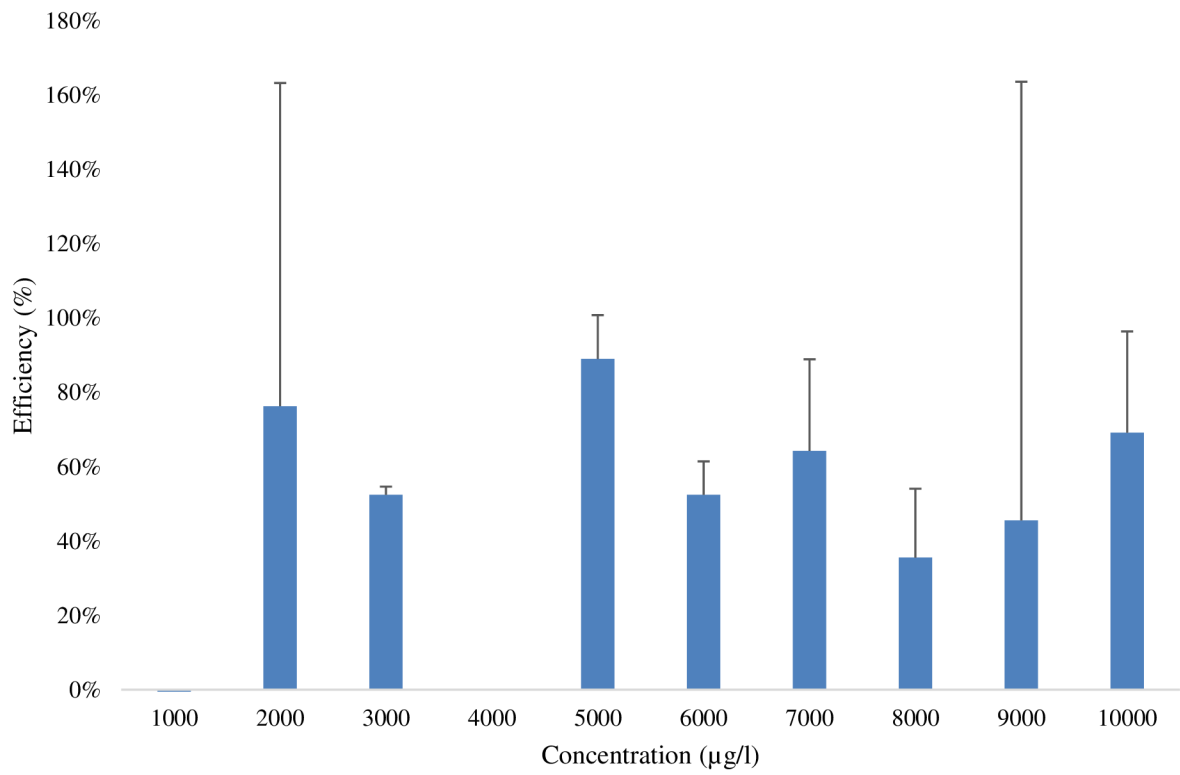
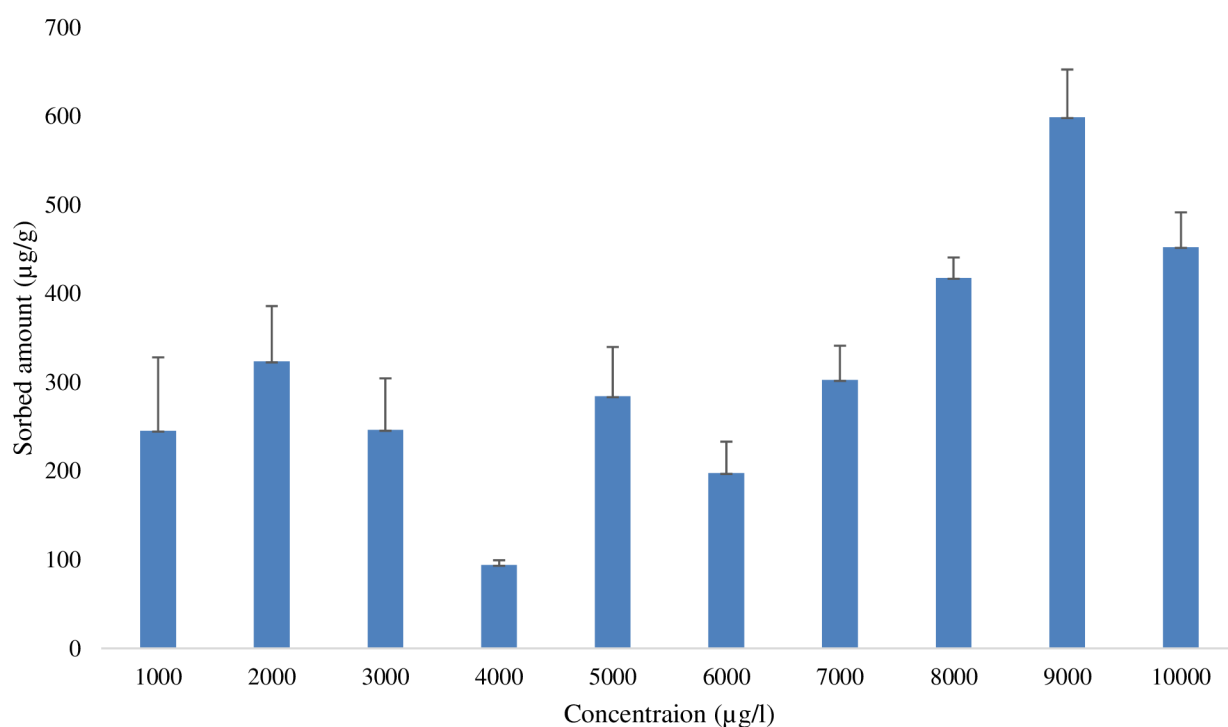


Figure 11: Sorption efficiency of IBF in soil B at each concentration, UV-VIS data

Compared to previous soils, the overall sorbed amount recorded for soil C was the highest of all soils. The course of the sorption was nonlinear, where the lowest sorbed amount was recorded at concentration 4 mg/l (94.103  $\mu\text{g/g}$ ), and the highest was recorded at concentration 9 mg/l (598.765  $\mu\text{g/g}$ ).

The average calculated sorption efficiency of IBF in soil C was 81.49%. The highest amount was calculated at concentration 9 mg/l, 91.93%. As can be seen in *Figure 12*, in concentration range from 1 mg/l to 9 mg/l, the calculated efficiency was very high.

Overall, recorded was strong sorption affinity of IBF at higher concentrations in all studied soils.



*Figure 12: Sorption course of IBF in soil C, UV-VIS data*

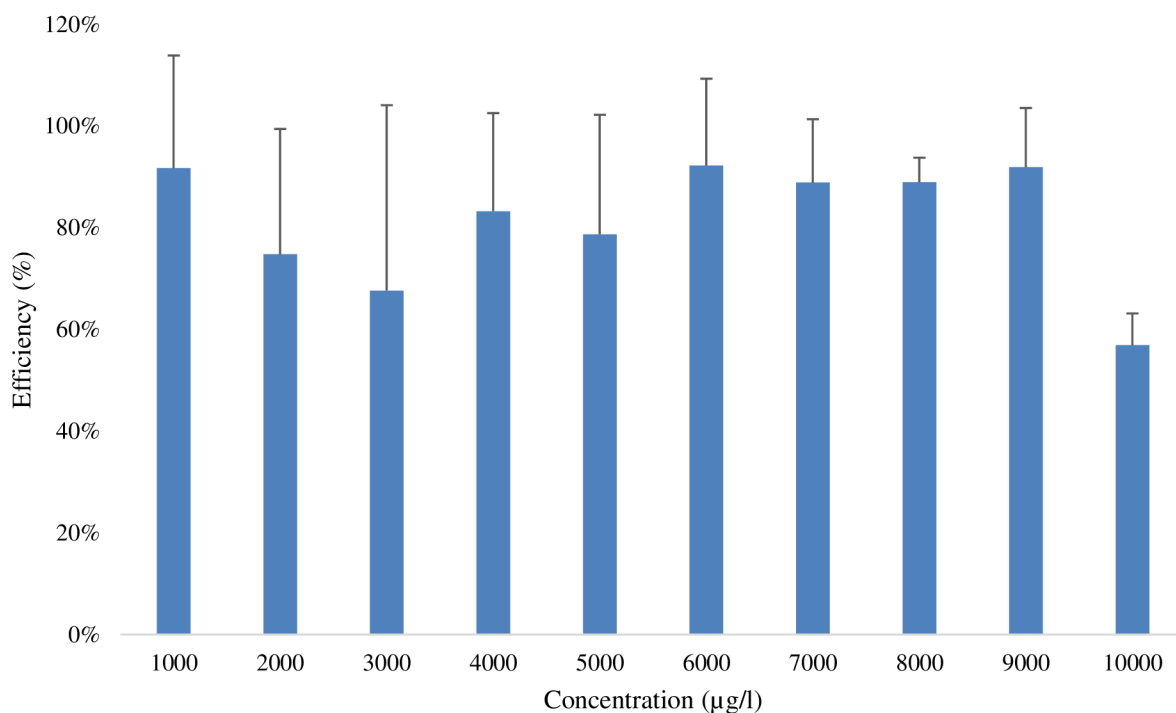


Figure 13: Efficiency of sorption of IBF in soil C, UV-VIS data

The comparison of the acquired data showed that there was a different sorption affinity of IBF in each soil, which decreased in the following order: C > A > B. The average of the calculated sorption efficiency of IBF in each soil decreased as follows: C (81.49%) > A (66.89%) > B (58.71%). This indicates that IBF had higher tendency of sorption in soil with high OM content i.e., soil C. Furthermore, the linear sorption of IBF was recorded only in soil A. A nonlinear course of sorption was observed in both soils C and B. Moreover, stronger sorption was observed at higher concentrations and weaker sorption at lower concentrations in soil A and C.

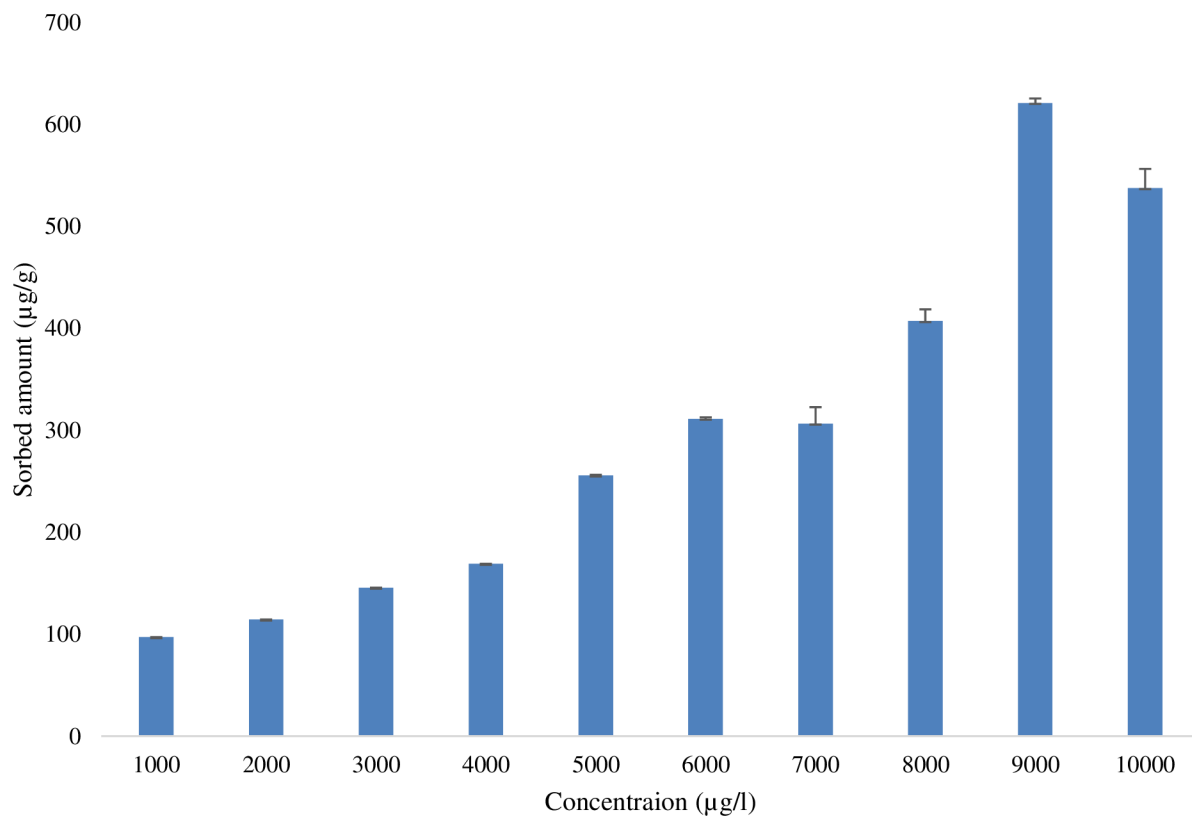
### 10.1.2 Sorption of Ibuprofen in Different Types of Soils, LC-MS Data

The analysis using LC-MS ensured understanding of the sorption process in different soils in greater detail. However, due to technical issues with the chromatograph, the data presented in this chapter are incomplete and contain only data describing the sorption in soil A and B.

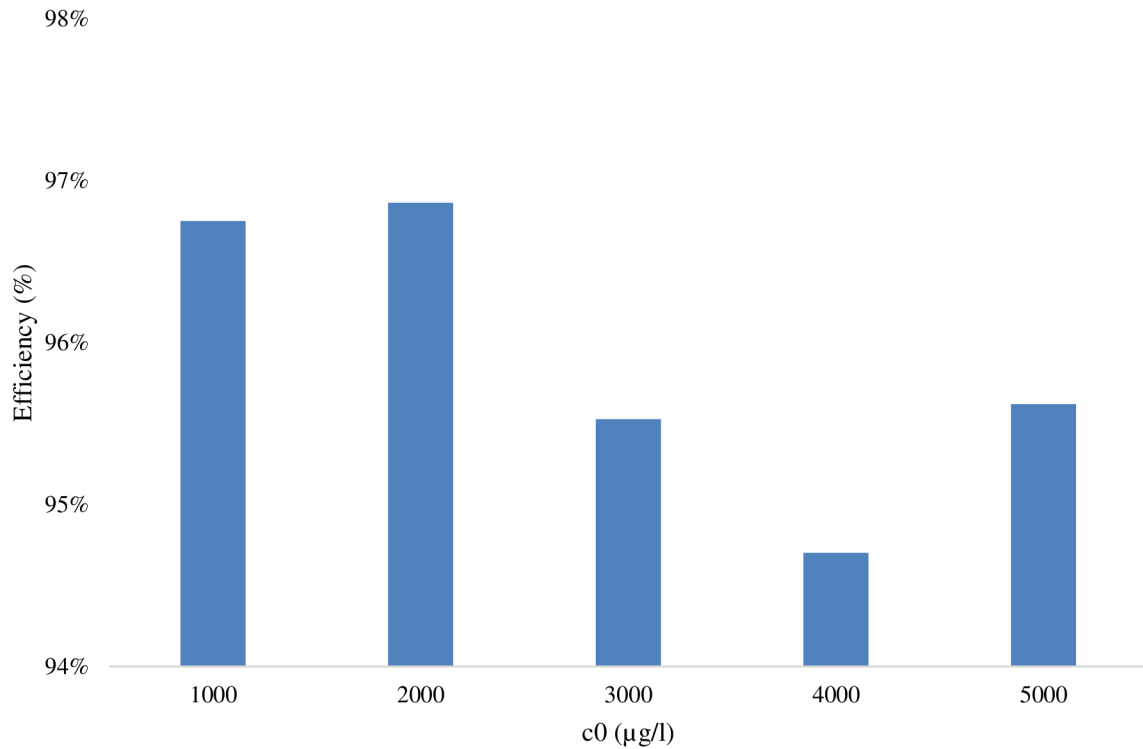
The sorbed amount of IBF increased with each concentration. The rise was linear up to concentration 9 mg/l. A decrease in the sorbed amount was recorded at concentration 10 mg/l. Therefore, the sorption of IBF in this soil was influenced by the increasing solution concentration up to concentration 9 mg/l. This can be a result of swelling and disordering of the soil at higher concentrations of solute, which in return increases the number of the sorption sites. The course of the sorption process in soil A can be seen in *Figure 14*.

The average sorption efficiency was calculated to be 95.89%. However, this average considers only sorption efficiency in concentration ranges from 1 to 5 mg/l. The calculation at higher concentrations could not have been carried out as the desorption data for

concentrations from 6 to 10 mg/l were not acquired. The samples were meant to be remeasured, as previous LC-MS results were not comprehensible. However, this could not have been carried out due to technical issues with the chromatograph. The course of the sorption efficiency of IBF in soil B can be seen in *Figure 15*. The highest efficiency was calculated to be at concentration 2 mg/l and the lowest at concentration 4 mg/l. However, due to insufficient data, we cannot conclude whether a strong sorption is favourable at high or low concentrations.



*Figure 14: Sorption course of IBF in soil A, LC-MS data[54]*



*Figure 15: Sorption efficiency of IBF in soil A, LC-MS data[54]*

Compared to soil A, a different course of sorption was recorded in soil B. A linear course of sorption was recorded at the lower concentrations, from 1 to 3 mg/l. This indicates that at lower concentrations, the sorbed amount was influenced by the increase in IBF concentration. However, a nonlinear sorption was observed in concentration range from 5 to 10 mg/l. Overall, compared to soil A, the sorbed amount of IBF in soil B was low. The course of sorption in soil B can be seen in *Figure 16*.

The average sorption efficiency was calculated to be 57.48% in soil B. The detail is depicted in *Figure 16*. Compared to soil A, the recorded sorption efficiency in soil B was significantly lower. This can be attributed to the lower OM content present in this soil.

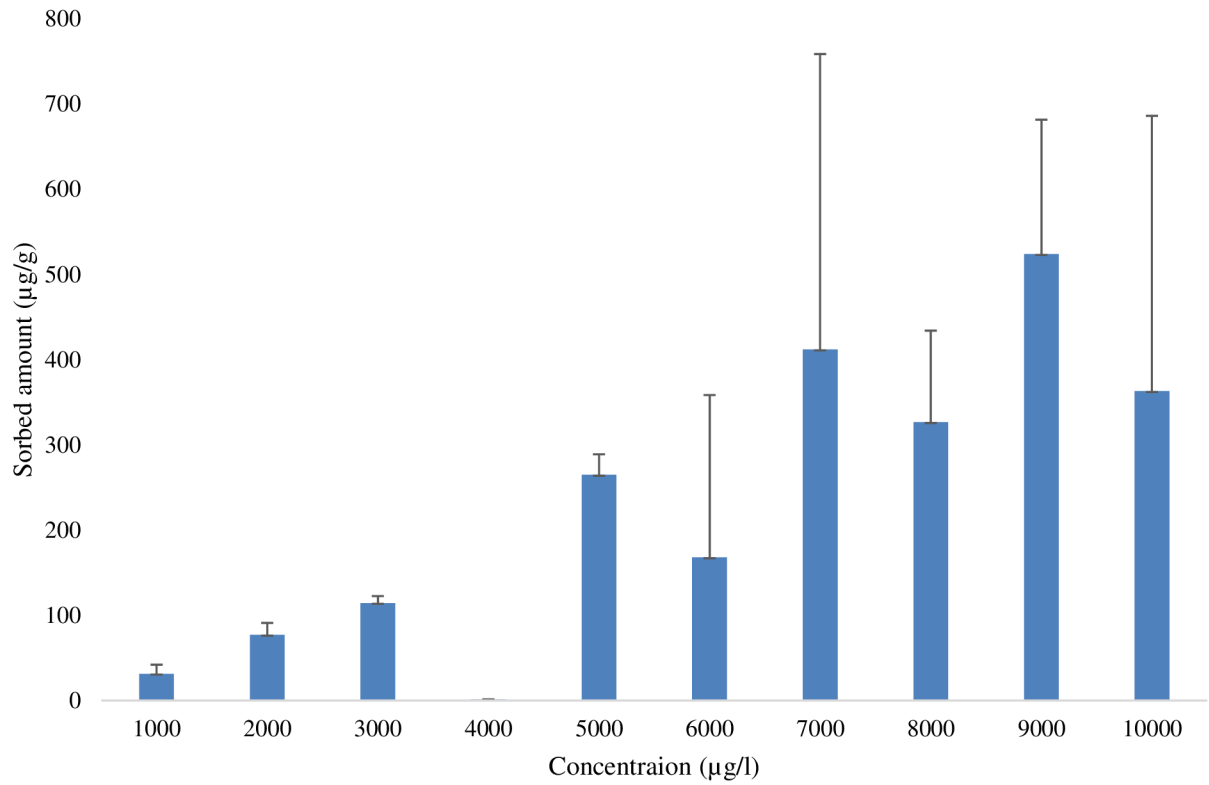


Figure 16: Sorption course of IBF in soil B, LC-MS data

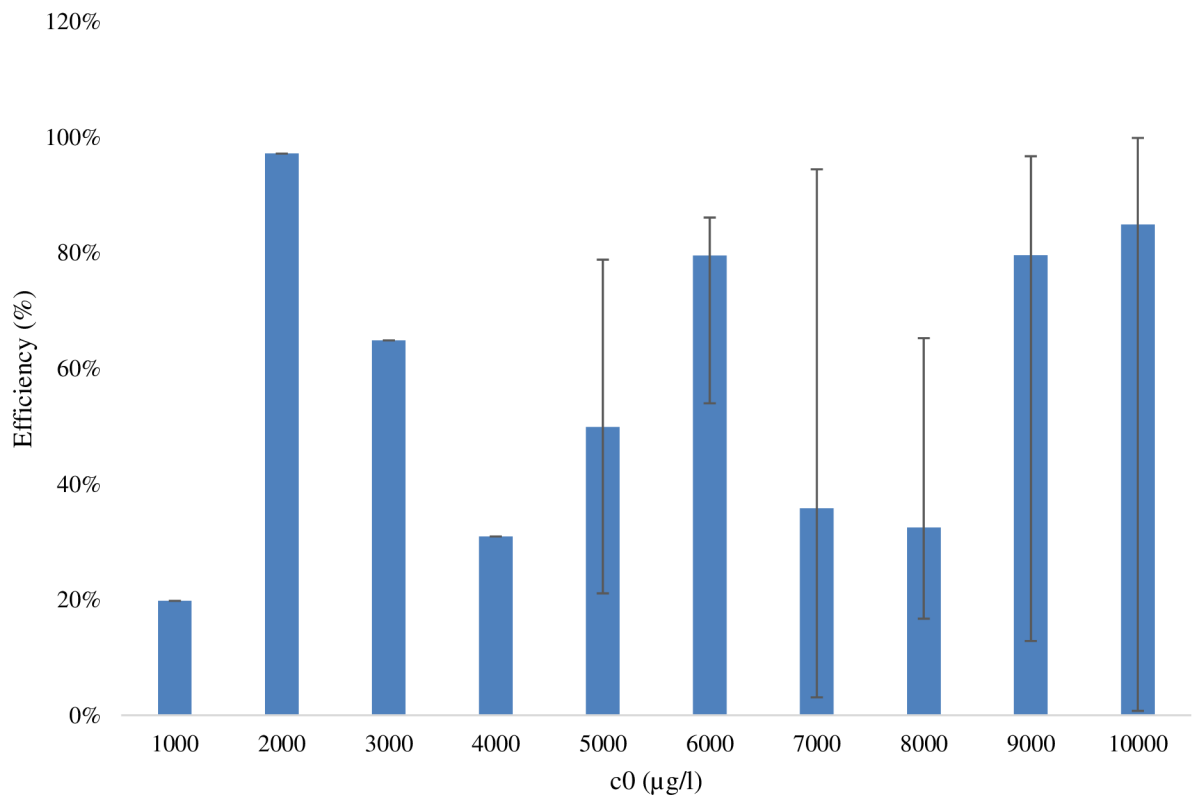


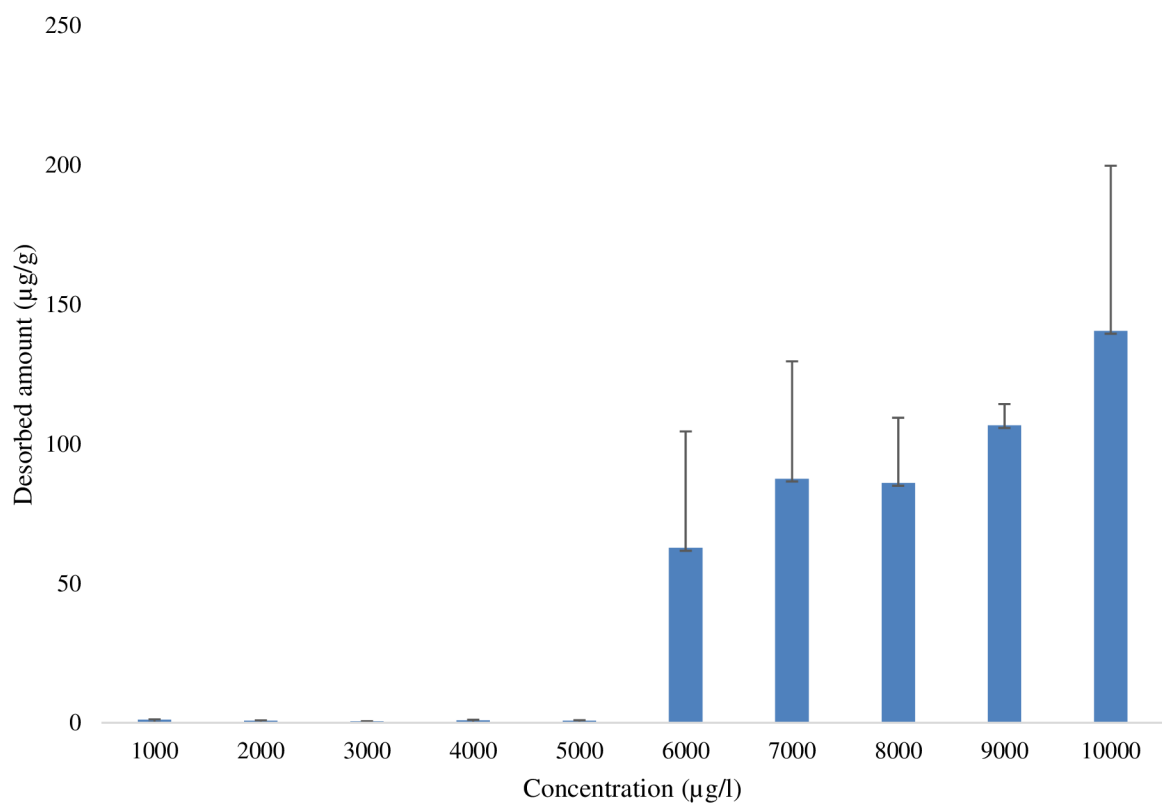
Figure 17: Sorption efficiency of IBF in soil B, LC-MS data



### 10.1.3 Desorption Process of IBF in Different Soils, UV-VIS Data

The data describing the desorption of IBF were analysed by UV-VIS spectrometry. For soil A, the obtained data show an insignificant desorption of IBF, especially at lower concentrations. On the other hand, a linear increase in the desorbed amount was observed at higher concentrations.

Compared to the recorded sorption data, the desorbed amount of IBF was low. As mentioned in *Chapter 10.1.1*, the calculated average sorption efficiency was 66.89%. The calculated average of desorption efficiency was 33.11%. This indicates that the retention of IBF in the soil is stronger at lower concentrations and lower amount of IBF is present in the mobile fraction. The recorded course of desorption and desorption efficiency in soil A can be seen in *Figure 18* and *Figure 19*.



*Figure 18: Desorption of IBF in Soil A, UV-VIS[54]*

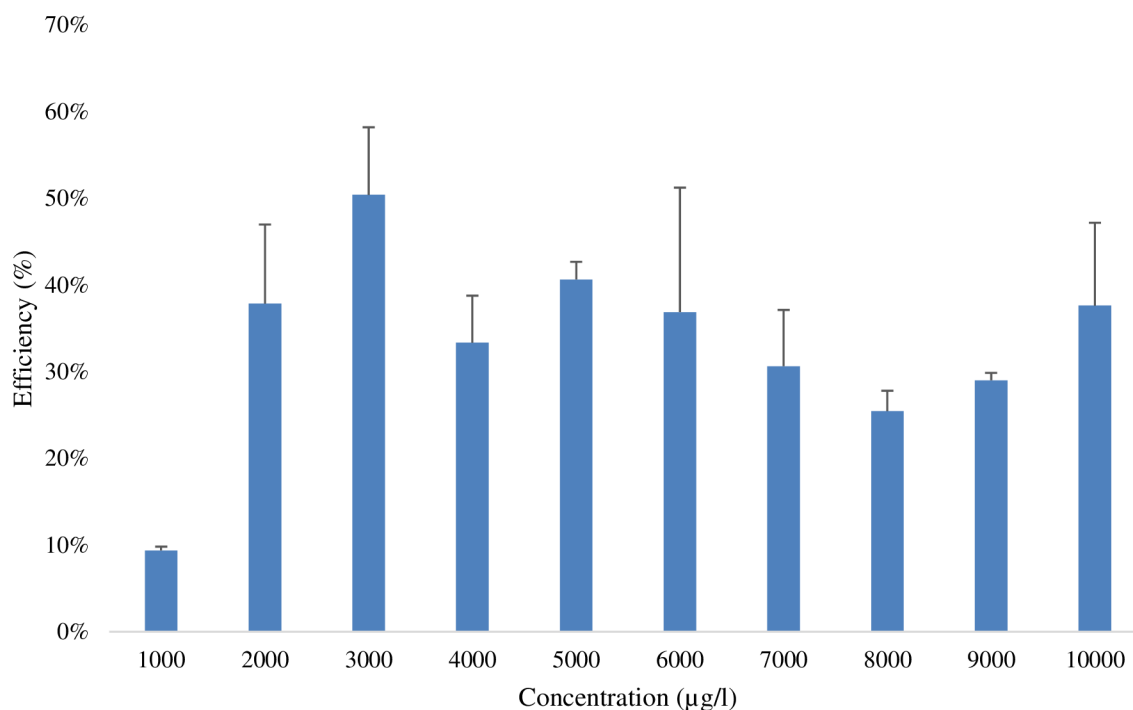


Figure 19: Desorption efficiency of IBF in soil A, UV-VIS data[54]

The course of desorption was different in soil B. Overall, compared to soil A, the amount of desorbed IBF was lower. This can be attributed to a low amount of initially sorbed IBF onto soil B. As can be seen in *Figure 20*, the amount of desorbed IBF slowly increases. However, noticeable is a low amount in the concentration range from 1 to 6 mg/l. The highest recorded amount is 32.090 µg/g at 6 mg/l. This is followed by an abrupt increase up to 9 mg/l followed by a significant decrease at 10 mg/l. Furthermore, compared to soil type A, the amount of desorbed IBF, in this case, is higher in the concentration range of 1 to 5 mg/l. On the other hand, lower amounts are recorded in the range between concentration 6 and 10 mg/l.

For soil B, calculated was that 47,02% of IBF were present in a mobile fraction and 52,98% in a stationary fraction. Compared to soil A, higher desorption efficiency was recorded in soil B. Moreover, higher tendency to desorb was observed, especially at higher concentrations.

The course of desorption in soil type C can be seen in *Figure 22*. The amount of desorbed IBF slowly rises with the rising concentration. A nonlinear desorption is observed in the concentration range between concentration 1 and 6 mg/l, followed by a linear increase at higher concentrations. A higher tendency of desorption was observed at higher concentrations. On average, the calculated desorption efficiency of IBF in soil C was 18.51%. This indicates that the high OM content present in soil C could have contributed to the strong retention of IBF. As compared to soil A and B, the average amount of IBF contained in the mobile fraction was the lowest.

In conclusion, the desorption efficiency in each soil decreased in the following order: B > A > C. This suggests that the presence of high OM content in soil C ensured retention of IBF in the soil.

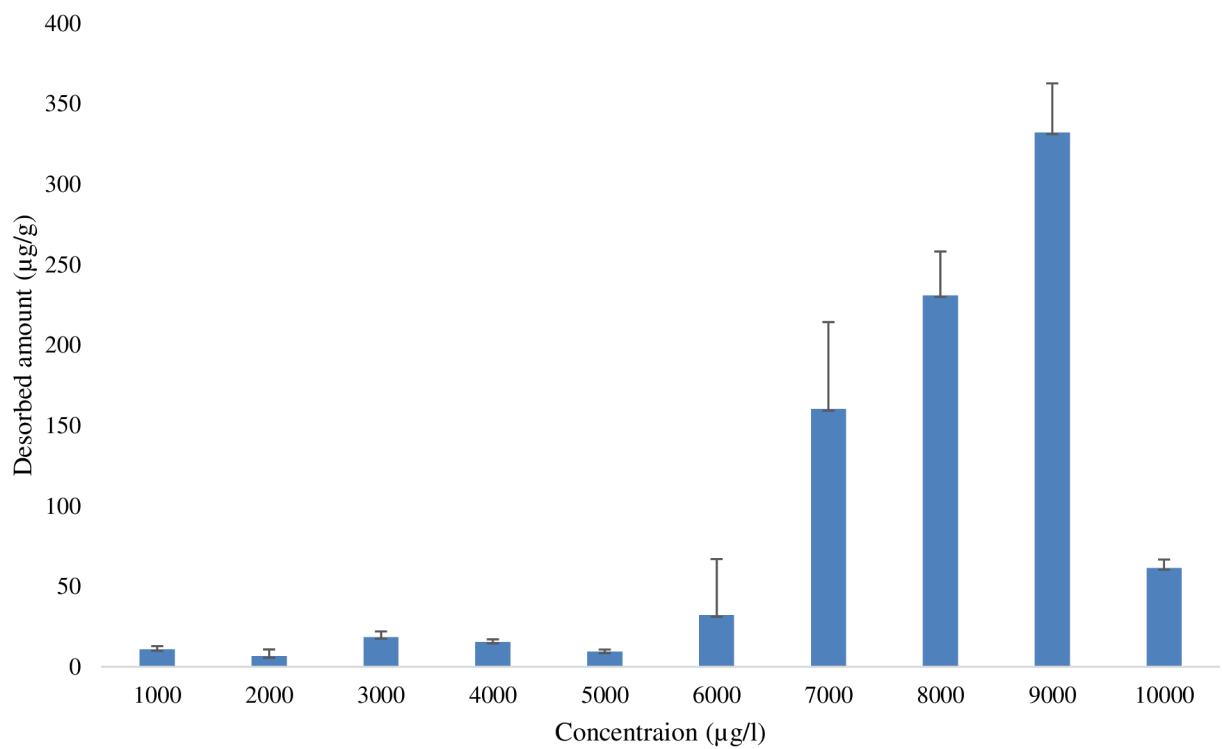


Figure 20: Desorption of IBF in soil B, UV-VIS data

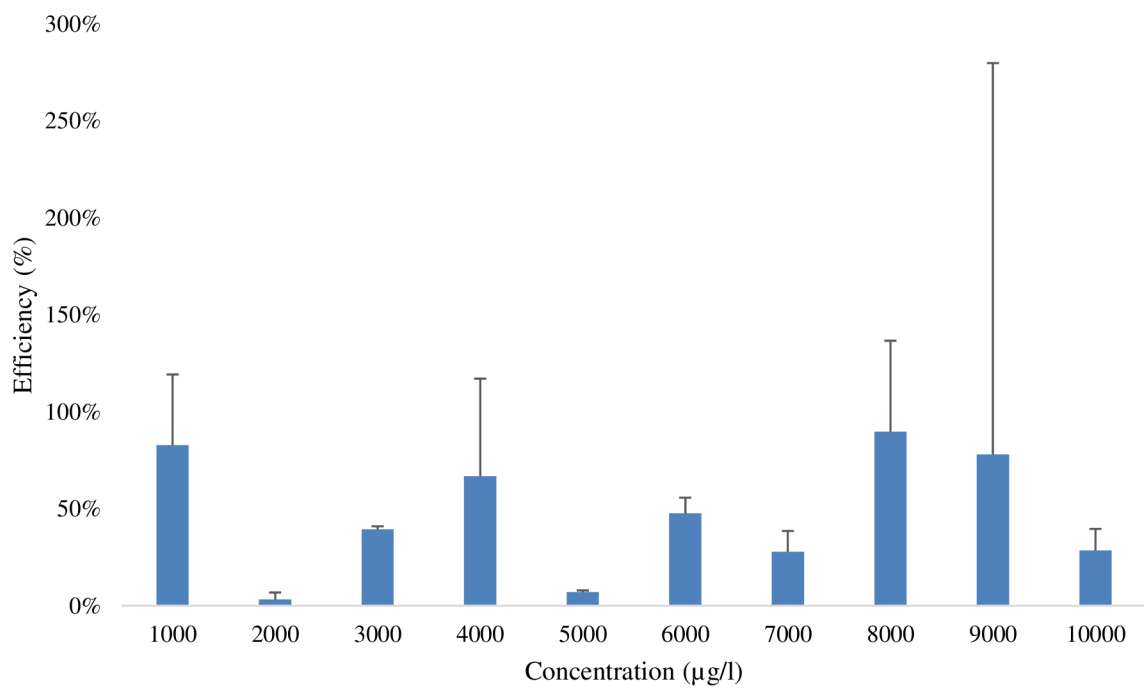


Figure 21: Desorption efficiency of IBF in soil B, UV-VIS data

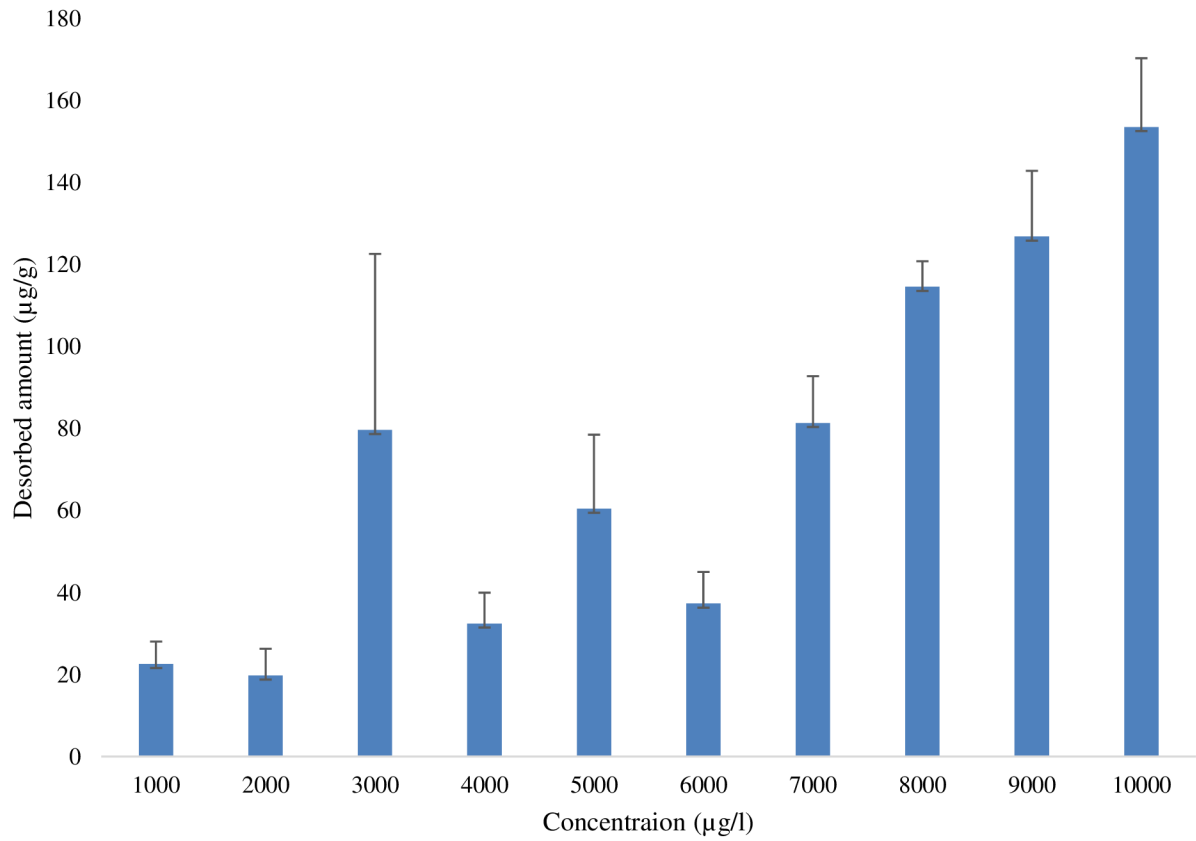


Figure 22: Desorption of IBF in soil C, UV-VIS data

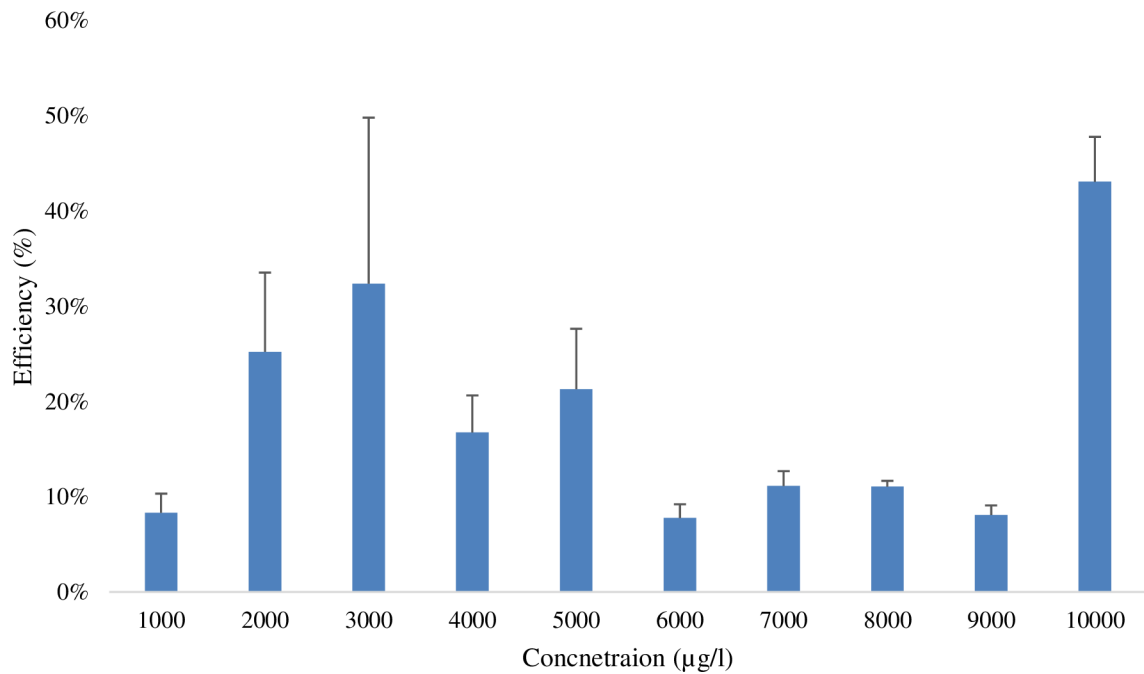


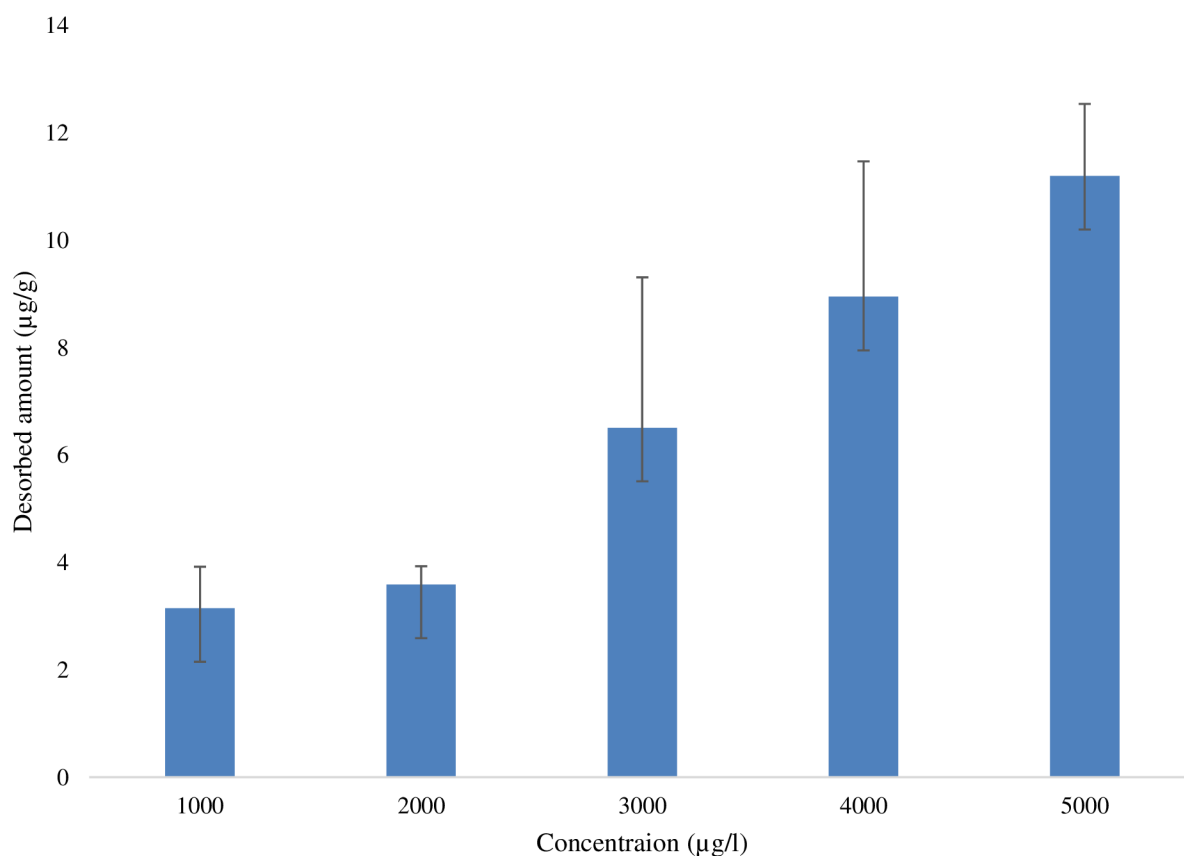
Figure 23: Desorption efficiency of IBF in soil C, UV-VIS data

#### 10.1.4 Desorption Process of IBF in Different Soils, LC-MS Data

Using LC-MS, the samples after desorption of IBF in three studied soils were measured. However, due to technical issues with the chromatograph, presented are only data for soil A and B. Furthermore, in the case of soil A, this includes concentrations in range from 1 to 5 mg/l.

The course of desorption in soil A can be seen in *Figure 24*. With rising concentrations, the tendency of IBF to desorb increased. However, due to insufficient data, it is not certain whether the same increase would have been observed in the concentration range from 6 to 10 mg/l.

The average desorption efficiency of IBF in soil A was calculated to be 4.11%. This can be seen in detail in *Figure 25*, with the highest value at concentration 4 mg/l. This indicates that in the concentration range from 1 to 5 mg/l the tendency of IBF to desorb in soil A was low.



*Figure 24: Desorption of IBF in soil A, LC-MS data[54]*

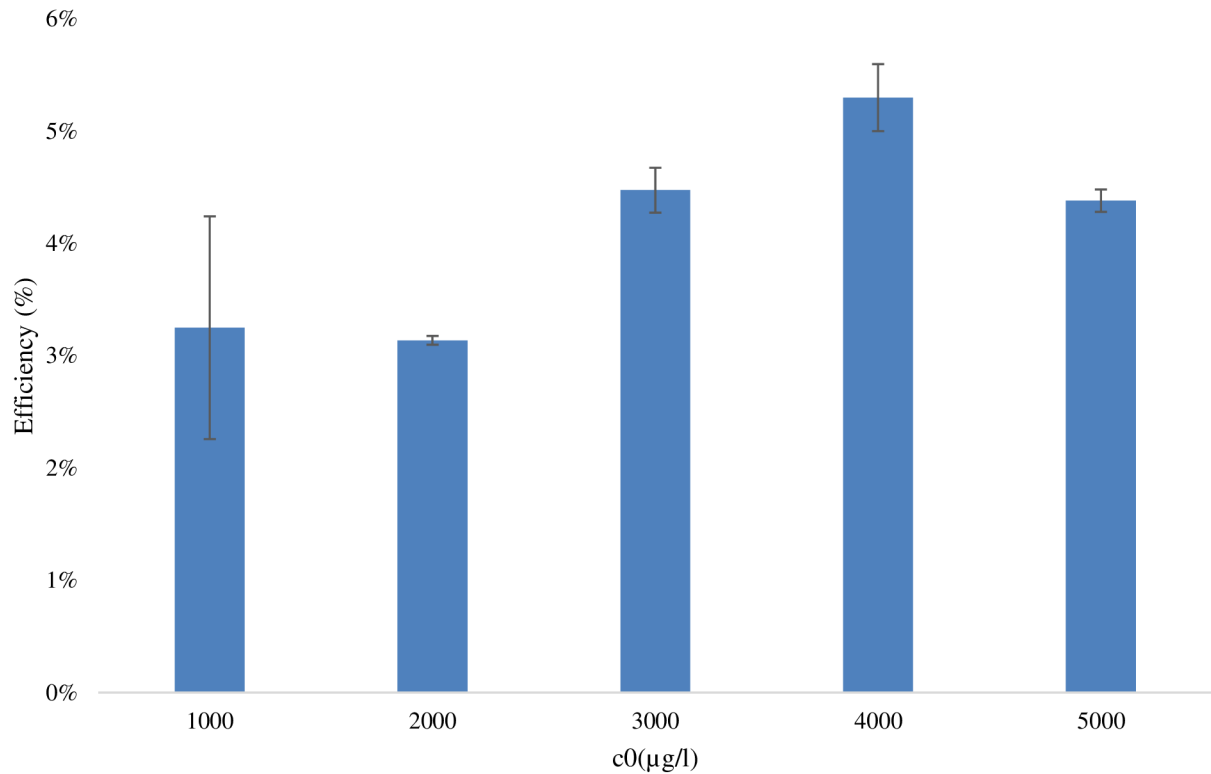


Figure 25: Desorption efficiency in soil A, LC-MS data[54]

Desorption of IBF in soil B was nonlinear in the concentration range from 1 to 10 mg/l. The course of desorption can be seen in *Figure 26*, where the highest value was recorded at concentration 7 mg/l and the lowest at concentrations 2 and 4 mg/l. Moreover, compared to soil A, the desorbed amount is higher at concentrations 1, 3, and 5 mg/l. However, the minute amount was recorded at 2 and 4 mg/l.

The average desorption efficiency, seen in *Figure 27*, was calculated to be 42.52%. In the concentration range from 1 to 5 mg/l the average efficiency equalled 47.48%. This is significantly higher than in soil A. This suggests that in soil B, IBF had a higher tendency of desorption. This can be accredited to the low OM content present in soil B.

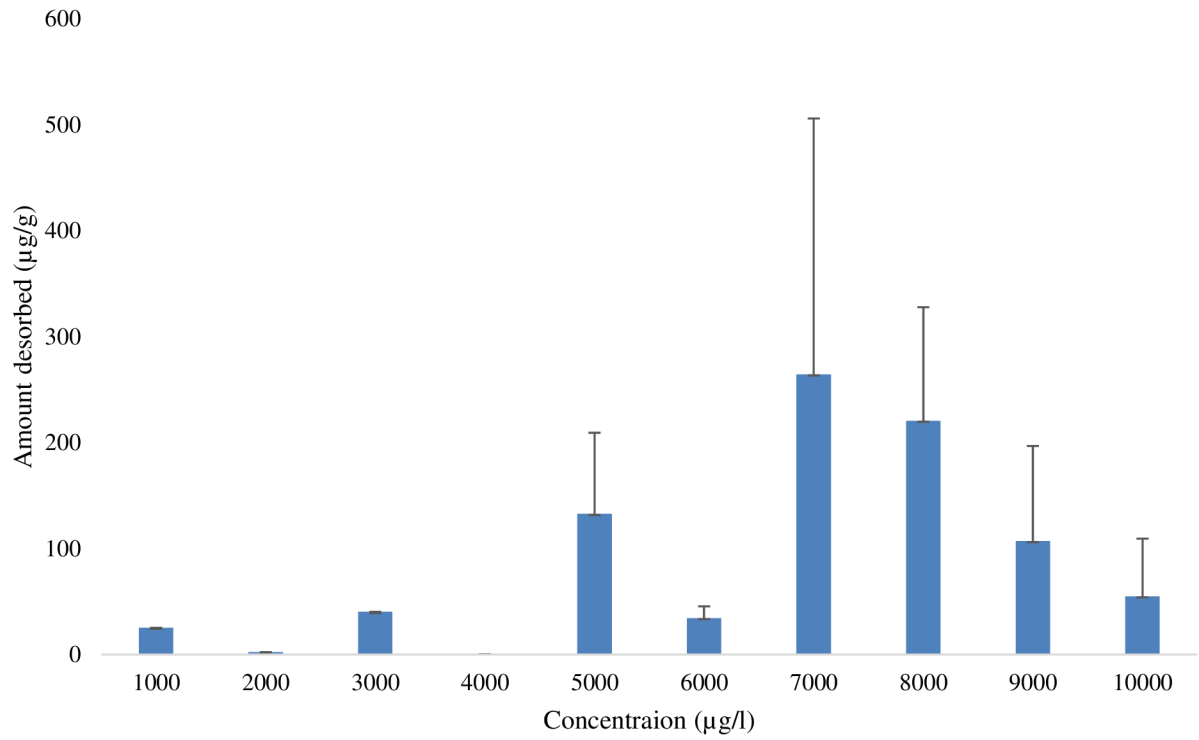


Figure 26: Desorption of IBF in soil B, LC-MS data

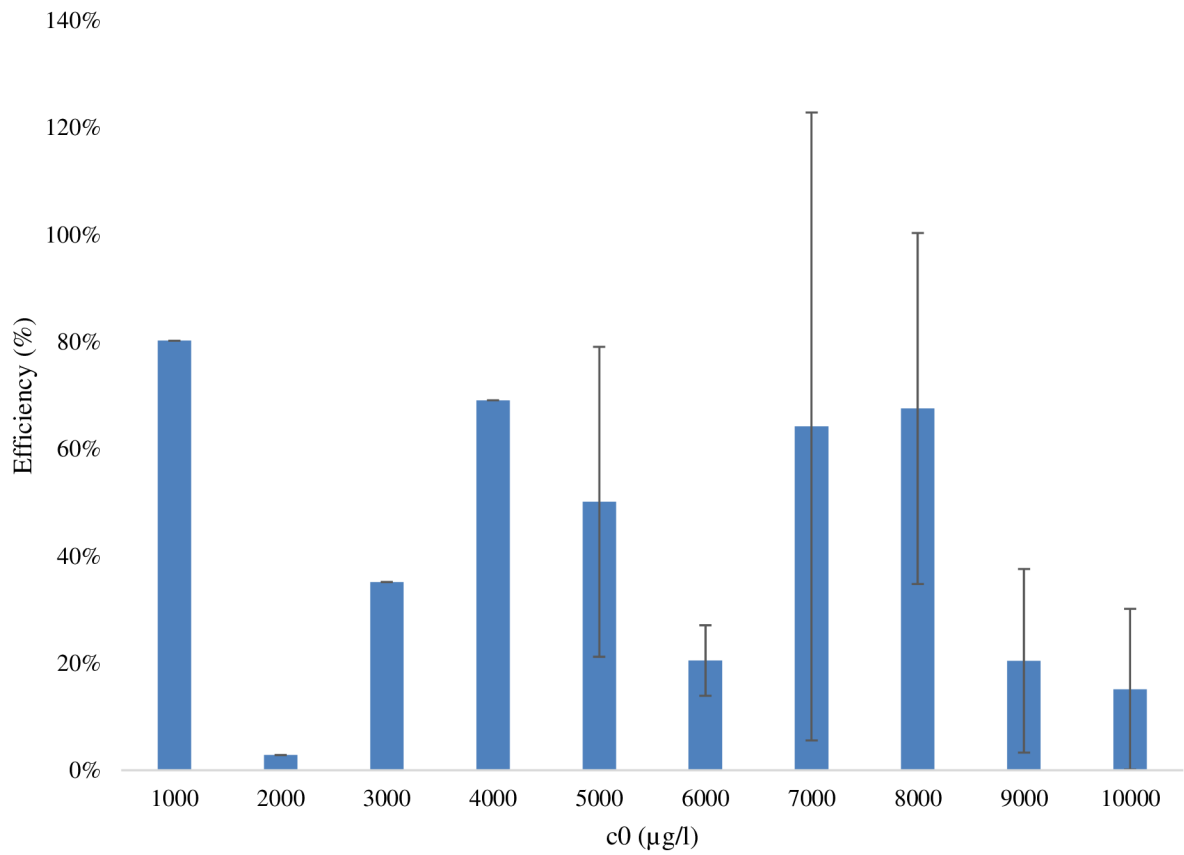


Figure 27: Desorption efficiency of IBF in soil B, LC-MS data

### 10.1.5 Recorded pH and Conductivity of Soil Solution in First Experiment

pH and conductivity values were acquired for each sample after sorption and desorption. This was also carried out for each IBF solution that was applied onto the soil before the experiment. The average values for pH and conductivity of IBF solutions were 6.27 and 11.57  $\mu\text{S}/\text{cm}$ . On average, the recorded pH of samples after the sorption in each soil decreased in the following order: C (8.07) > A (7.08) > B (4.48). A linear increase or decrease with rising IBF concentrations was not observed. Prepared solutions of IBF and soil solutions acquired after sorption from soil A and C had pH value higher than  $pK_a$  of IBF. On average, the increase or decrease of pH in soil solutions could have indicated whether stronger or weaker sorption was occurring. However, the change in the pH was not used as a marker of IBF sorption affinity in the studied soils. The recorded pH values for soil A, B and C can be seen in *Figure 28*, *Figure 32* and *Figure 36*, respectively.

The conductivity of soil solutions after the sorption, decreased as follows: C (165.23  $\mu\text{S}/\text{cm}$ ) > A (137.82  $\mu\text{S}/\text{cm}$ ) > B (12.07  $\mu\text{S}/\text{cm}$ ). As it was in the case of pH, no linear increase or decrease with increasing concentration was observed. The highest value was recorded for soil with the highest OM content and the lowest in soil with the lowest OM content. However, the increase or decrease in the recorded data in individual soil solution samples were not considered as indicators of high or low sorption affinity. The recorded data for soil A, B and C are depicted in *Figure 30*, *Figure 34* and *Figure 38*, respectively.

In the case of desorption experiment, used was ultra-pure water with pH and conductivity values of 7 and 1.7  $\mu\text{S}/\text{cm}$ . The average value of the recorded pH in the samples decreased as follows: C (7.68) > A (6.5) > B (5.28). The highest value was recorded in soil C, in which the retention of IBF was the highest. The acquired data for soil A, B and C can be found in *Figure 29*, *Figure 33* and *Figure 37*.

The recorded average conductivity of samples for each soil decreased in the following order: C (98.38  $\mu\text{S}/\text{cm}$ ) > A (69.96  $\mu\text{S}/\text{cm}$ ) > B (10.41  $\mu\text{S}/\text{cm}$ ). All the summarised data for soil A, B and can be found in *Figure 31*, *Figure 35* and *Figure 39*, respectively.



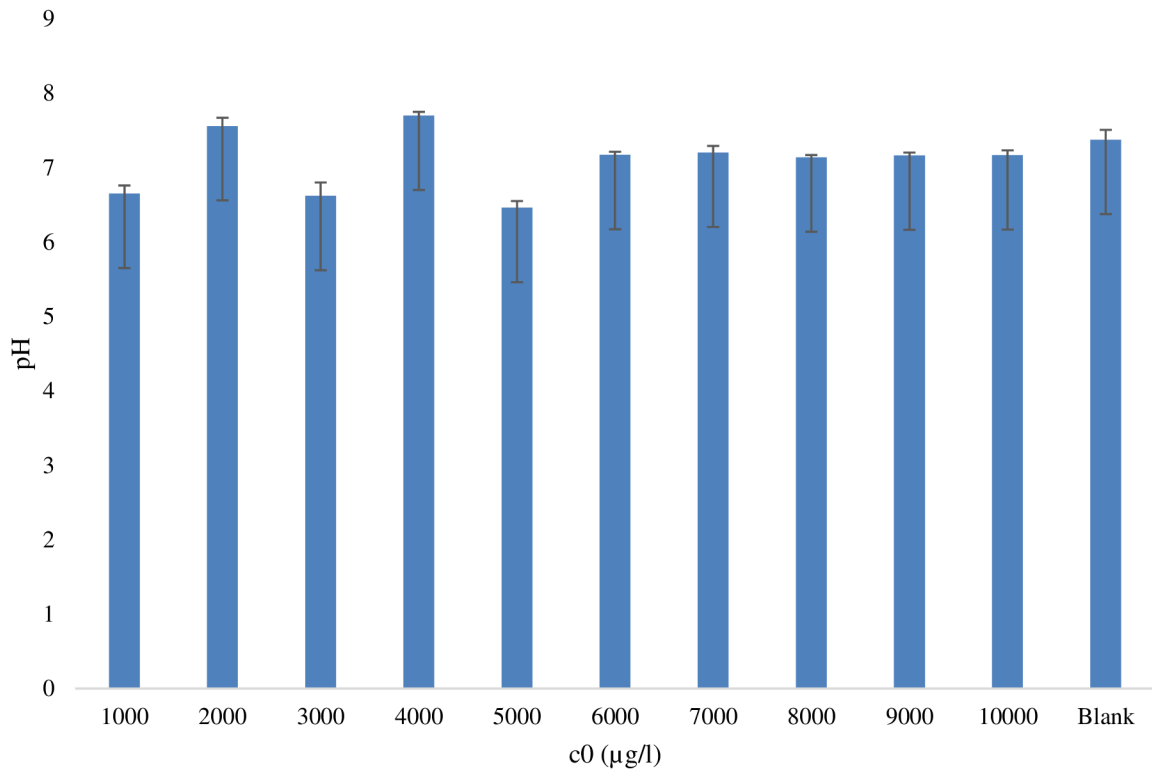


Figure 28: Recorded pH of samples after sorption, soil A

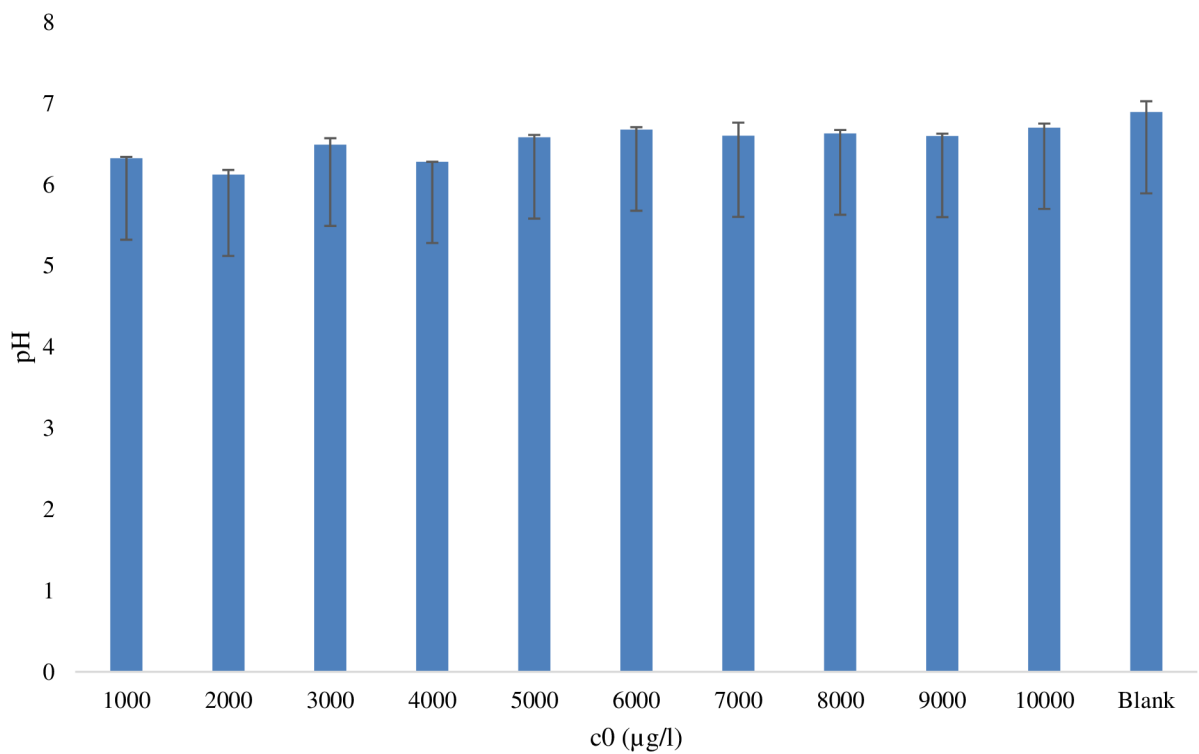


Figure 29: pH values recorded in samples after desorption, soil A

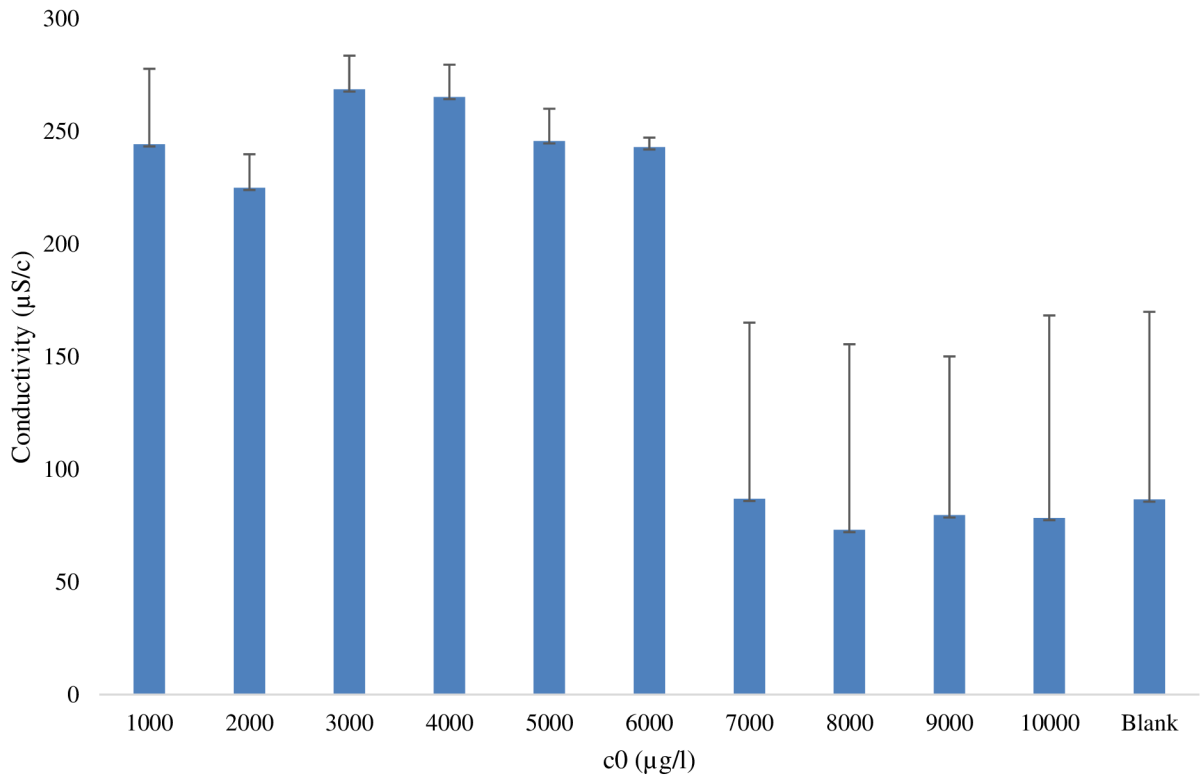


Figure 30: Conductivity recorded in samples after sorption, soil A

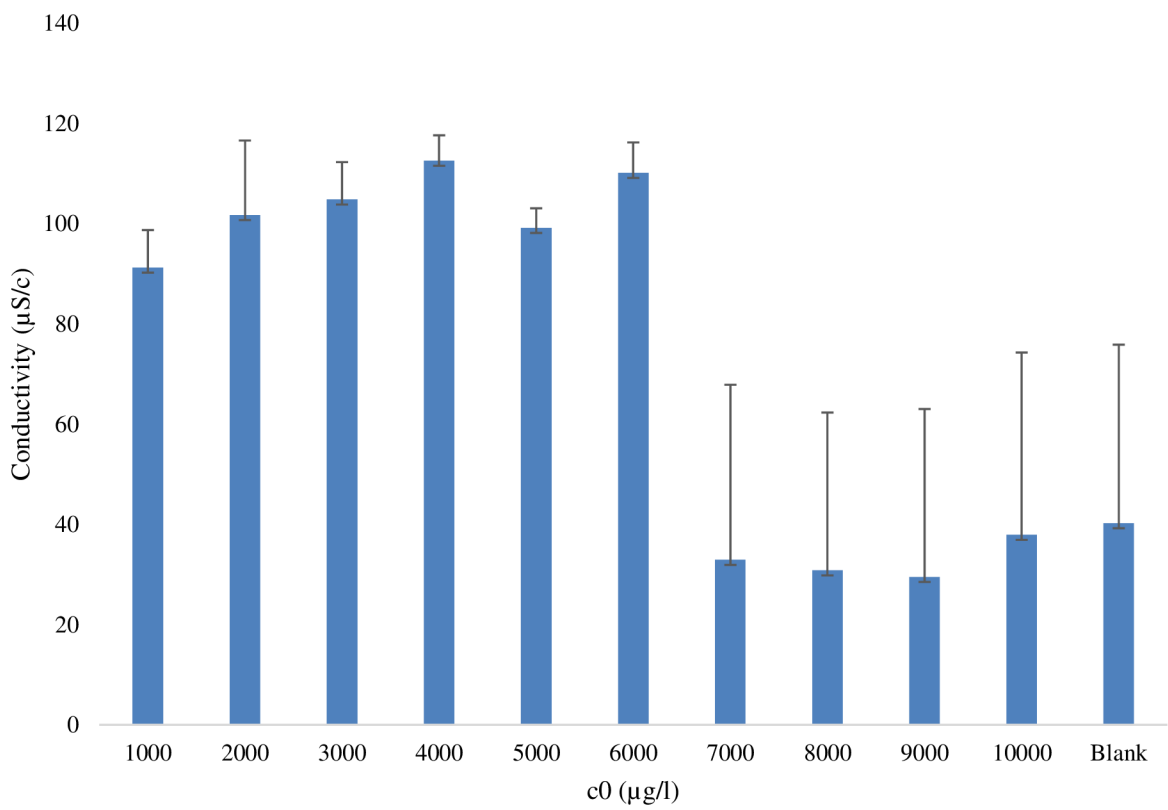


Figure 31: Conductivity recorded in samples after desorption, soil A

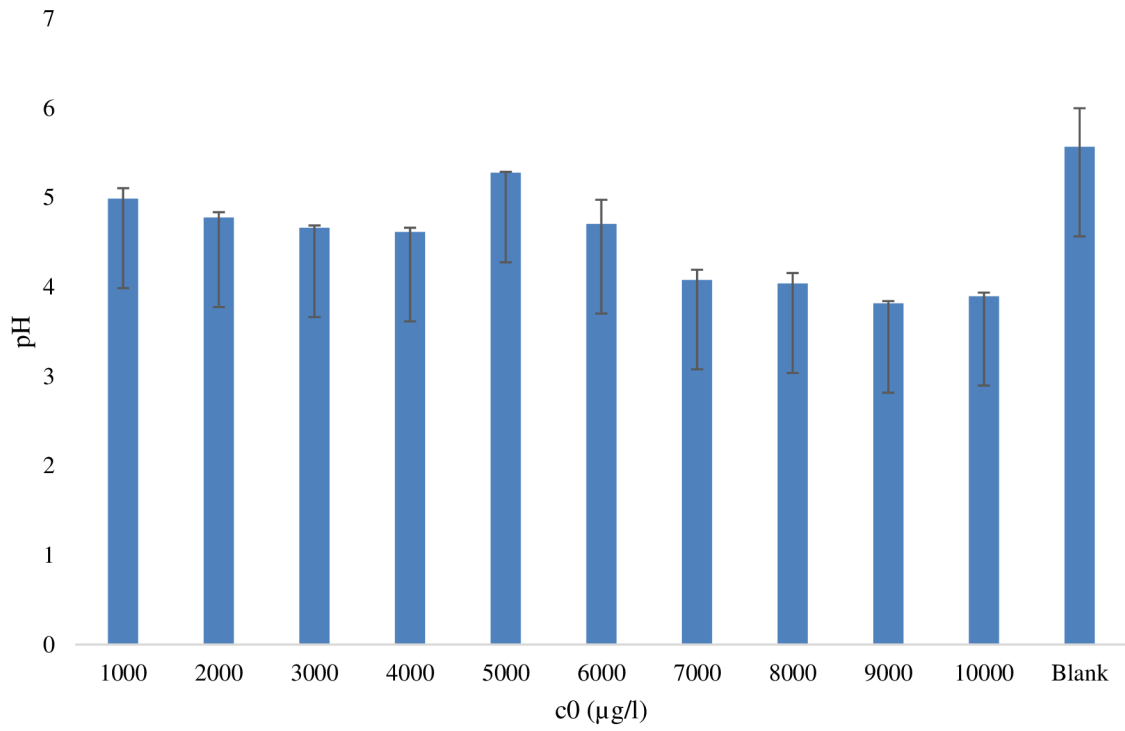


Figure 32: Recorded pH values in samples after sorption, soil B

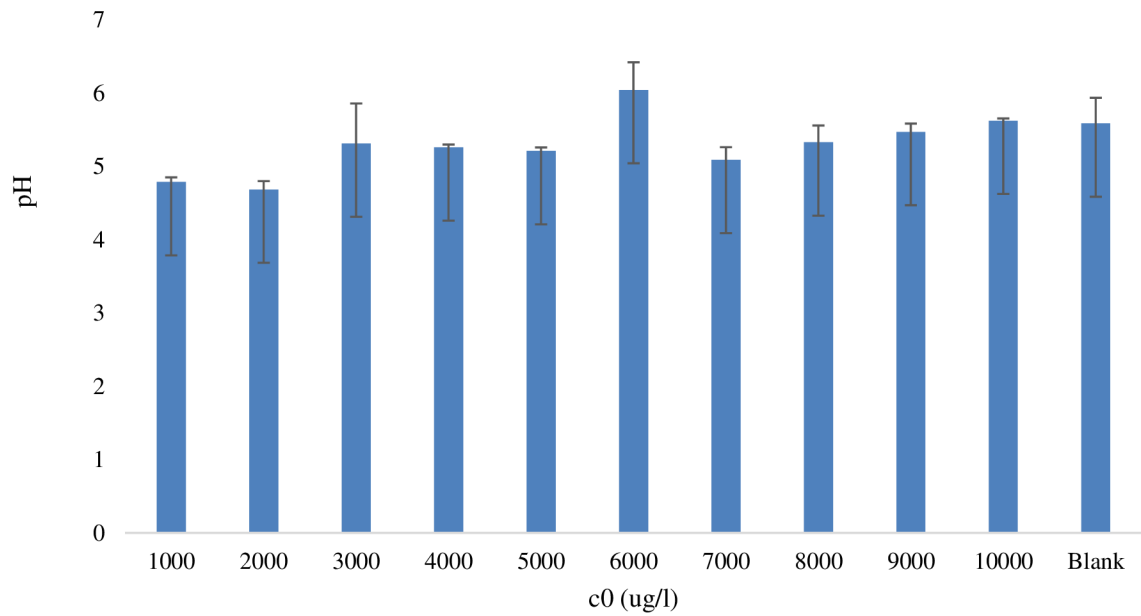


Figure 33: Recorded pH values of samples after desorption, soil B

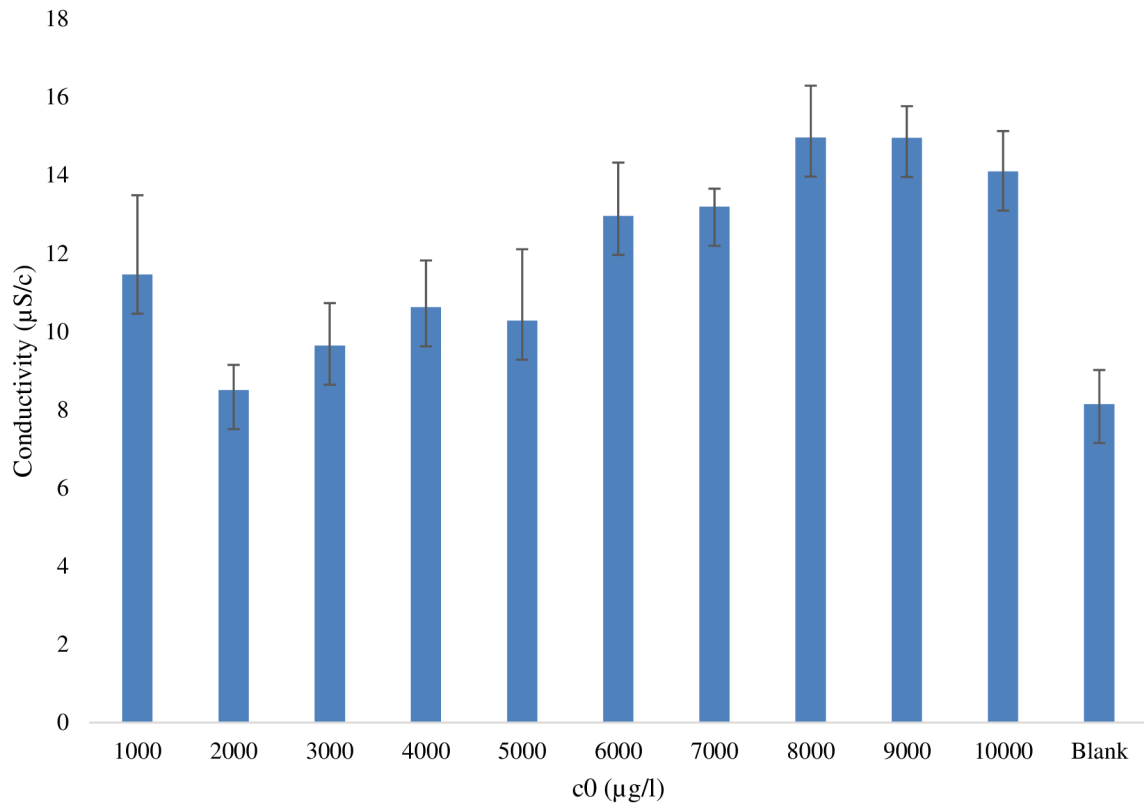


Figure 34: Conductivity recorded in samples acquired after sorption, soil B

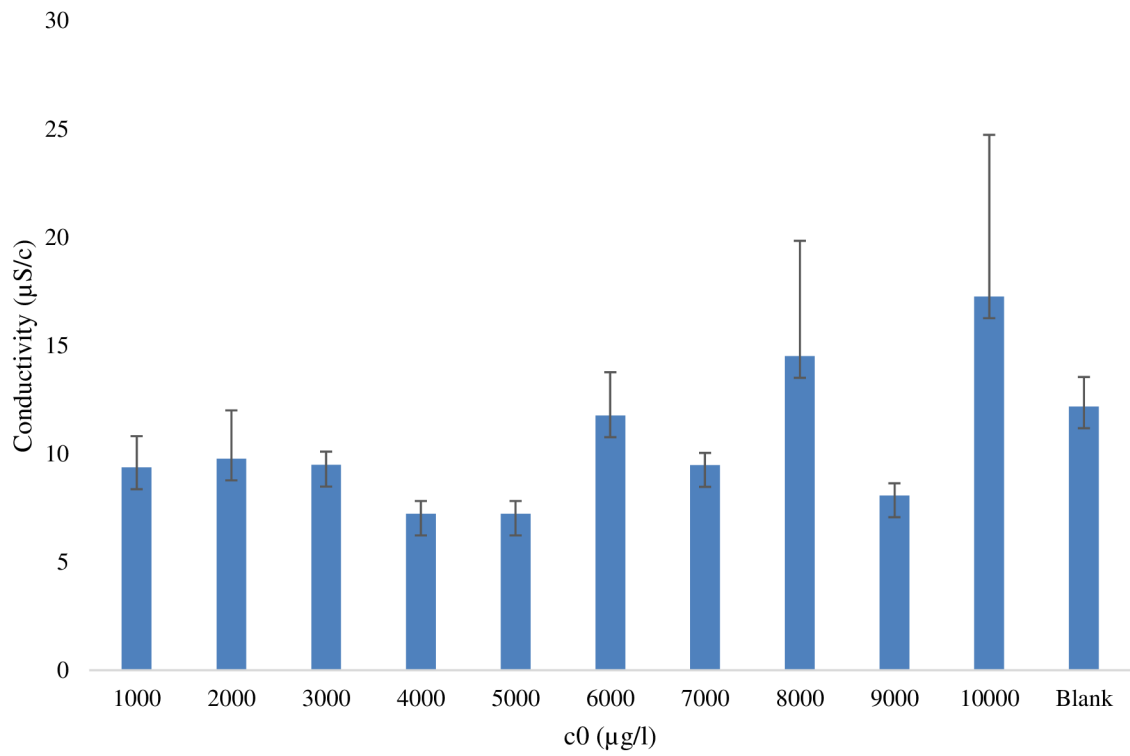


Figure 35: Conductivity recorded in samples after desorption, soil B

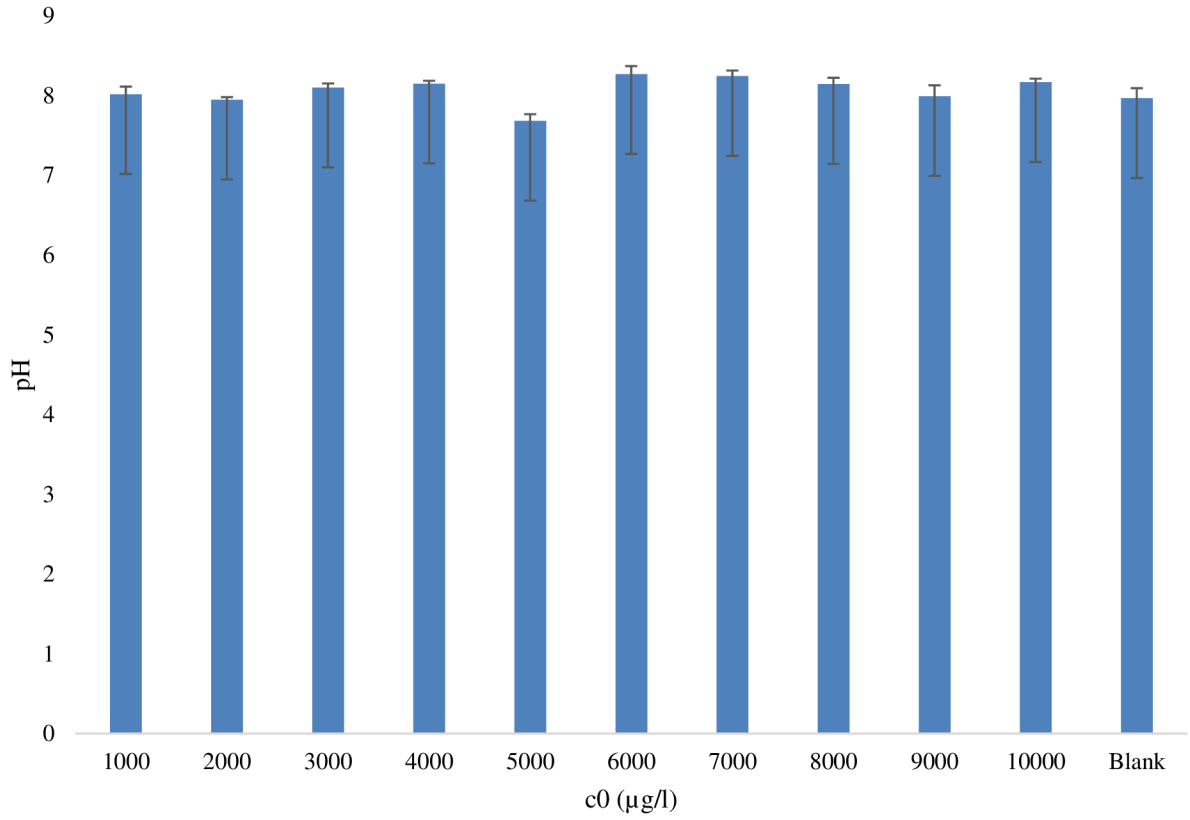


Figure 36: pH values of samples acquired after sorption, soil C

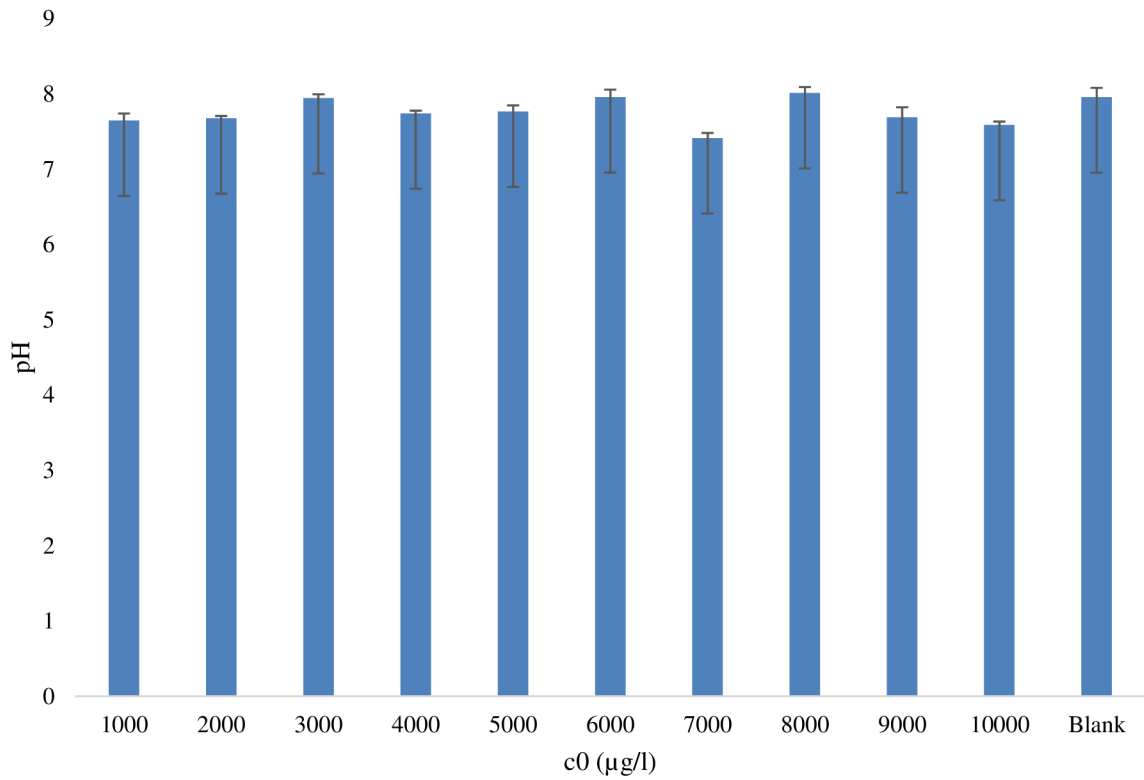


Figure 37: pH values of samples after desorption, soil C

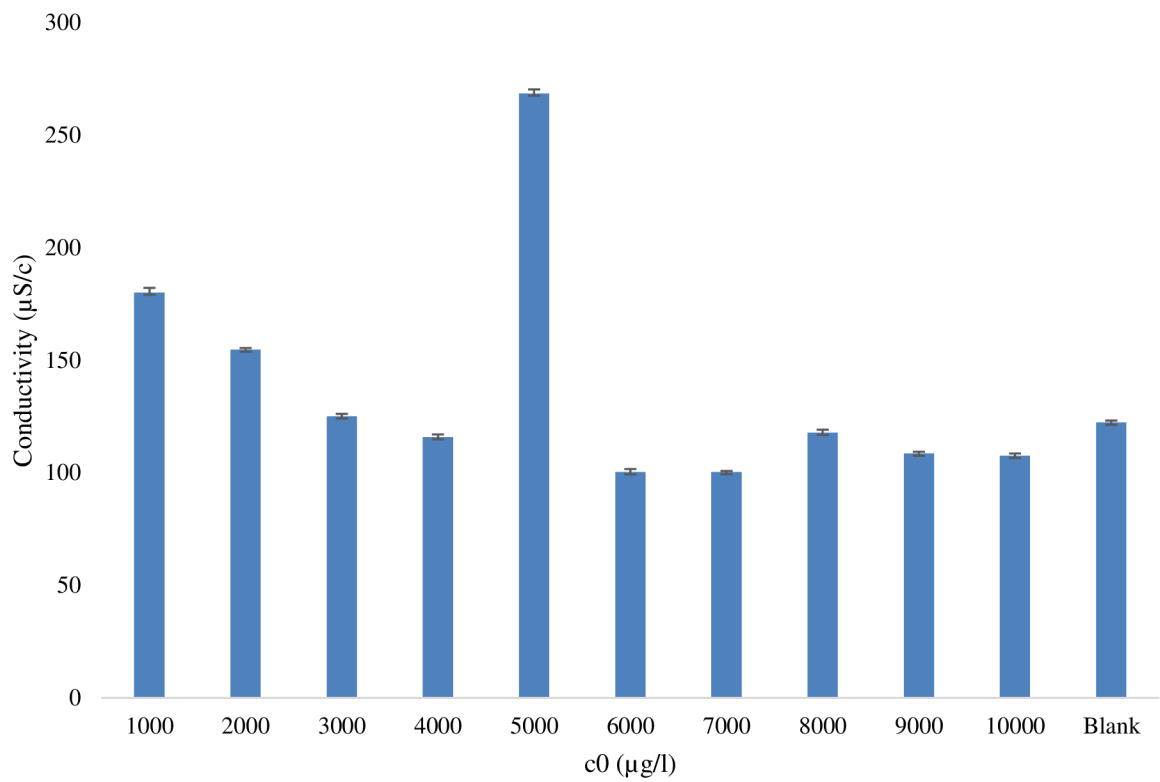


Figure 38: Conductivity values of samples after sorption, soil C

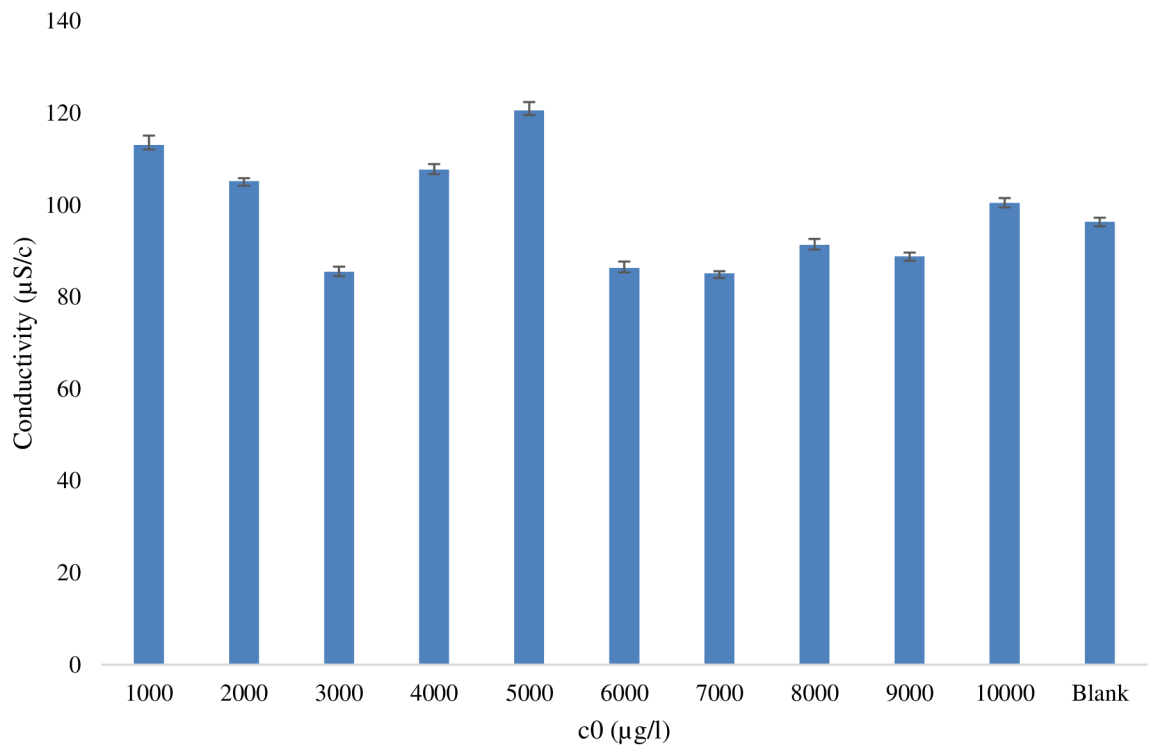


Figure 39: Conductivity of the samples acquired after desorption, soil C

## 10.2 Influence of pH on Sorption and Desorption of IBF

The goal of the second experiment was to study influence of different pH values on the sorption and the desorption of IBF in soil A, B and C. Concentration 10 mg/l was chosen to ensure better understanding of the change occurring in different soils at each pH. The experiment was conducted using Britton-Robinson buffer with pH 3, 7 and 10.

### 10.2.1 Sorption of IBF at Different pH, UV-VIS Data

The absorption spectra of all samples in the second experiment. The sorbed and the desorbed amount was calculated for each pH value and soil type. This was accomplished by using absorption value at 218 nm for all calculations in MS Excel. A different course of sorption was observed in each soil at different pH.

The sorbed amount of IBF increased with the decreasing pH of the IBF solution. The recorded amount for soil A was in the range from 191.217  $\mu\text{g/g}$  to 482.794  $\mu\text{g/g}$ , with the highest value recorded at pH 3. The course of the sorption can be seen in *Figure 40*.

As can be seen in *Figure 41*, a similar course of sorption was observed for IBF in soil B. The amount of sorbed IBF increased with the decrease of pH. The recorded amount at pH 3 was significantly smaller than in soil A. However, in the case of pH 10 and 7 the amount was higher.

A nonlinear sorption in soil C was recorded. The course of sorption can be found in *Figure 42*. The highest recorded value was at pH 3. Compared to previous soils, this was the highest recorded amount.

As was previously mentioned in *Chapter 2.1* IBF is an ionisable compound with  $pK_a$  value of 4.91 [9]. Therefore, at pH 3 IBF would be present in a form of a conjugated acid. Furthermore, soil surface is expected to have low net negative charge at low pH. This is attributed to partial ionization of soil OM and minerals at acidic pH. Therefore, expected would be minor effect of electrostatic repulsion between a neutral form of IBF and soil OM. The interaction between IBF and the soil surface would be promoted more by creation of hydrogen bonds [55].

At higher pH, IBF is expected to occur in a form of an anion. Additionally, as pH rises the negative charge of organic and mineral components of the soil would increase. According to *Šebesta et al.* this is due to point of zero charge of most soil components being lower than 5 [55]. Generally, this would result in a stronger electrostatic repulsion between the soil and the studied pharmaceutical compound.

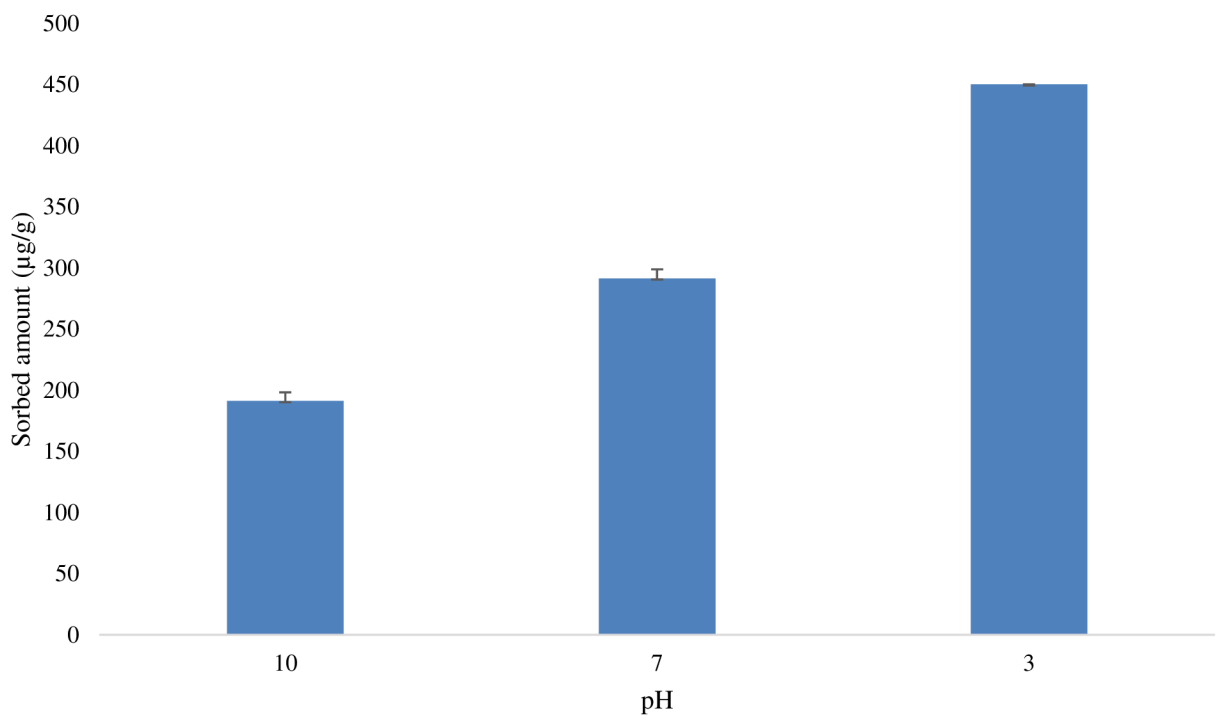


Figure 40: Sorption of 10 mg/l solution of IBF at different pH values in soil A

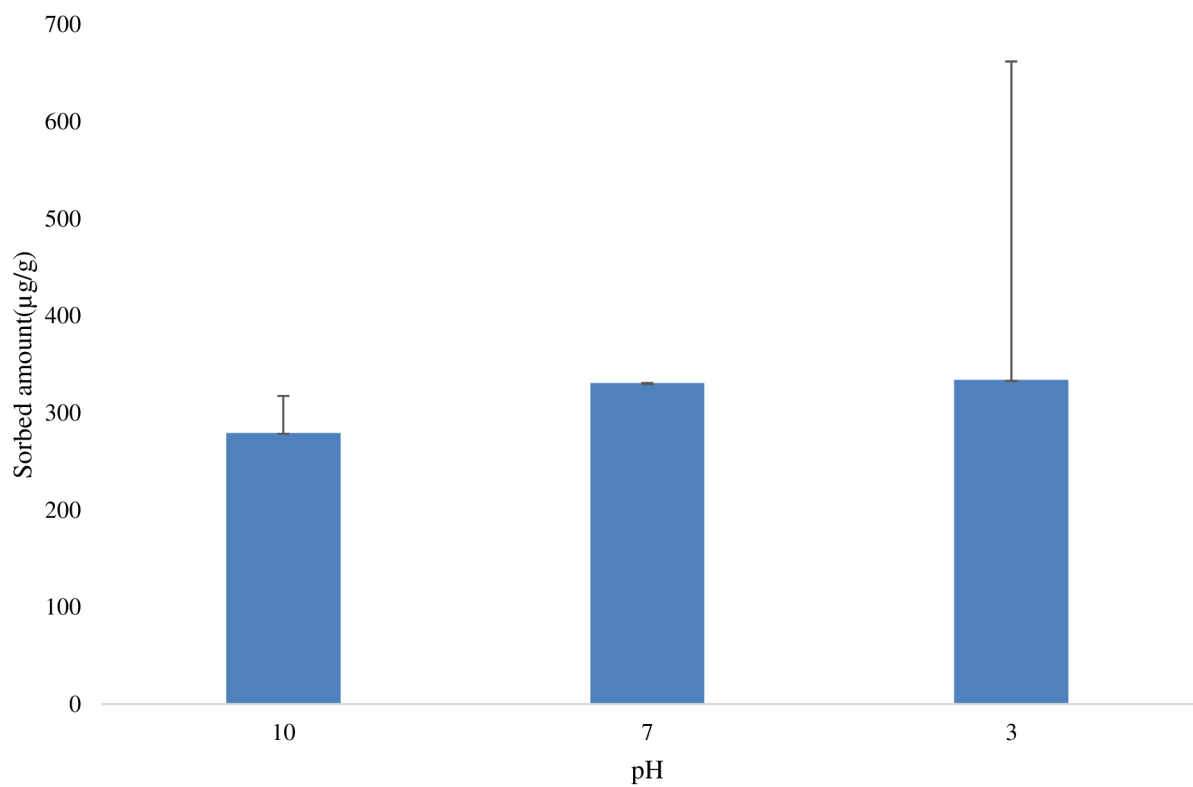
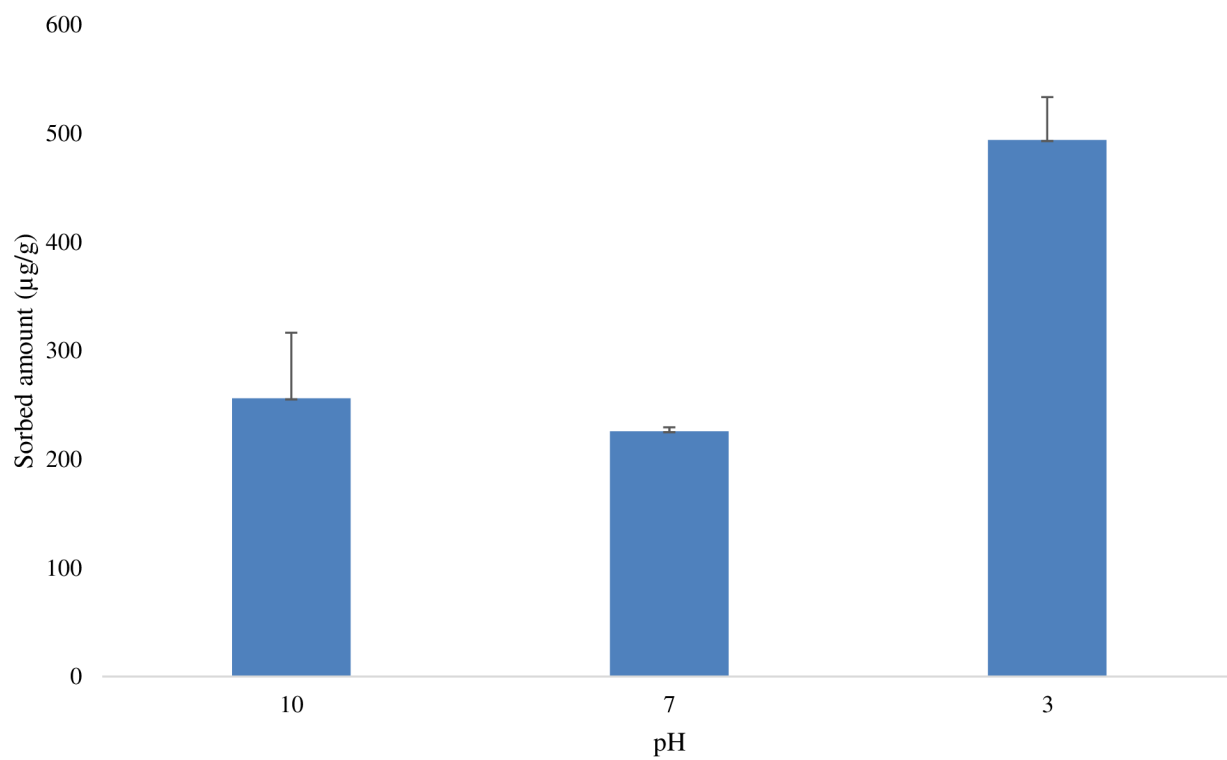


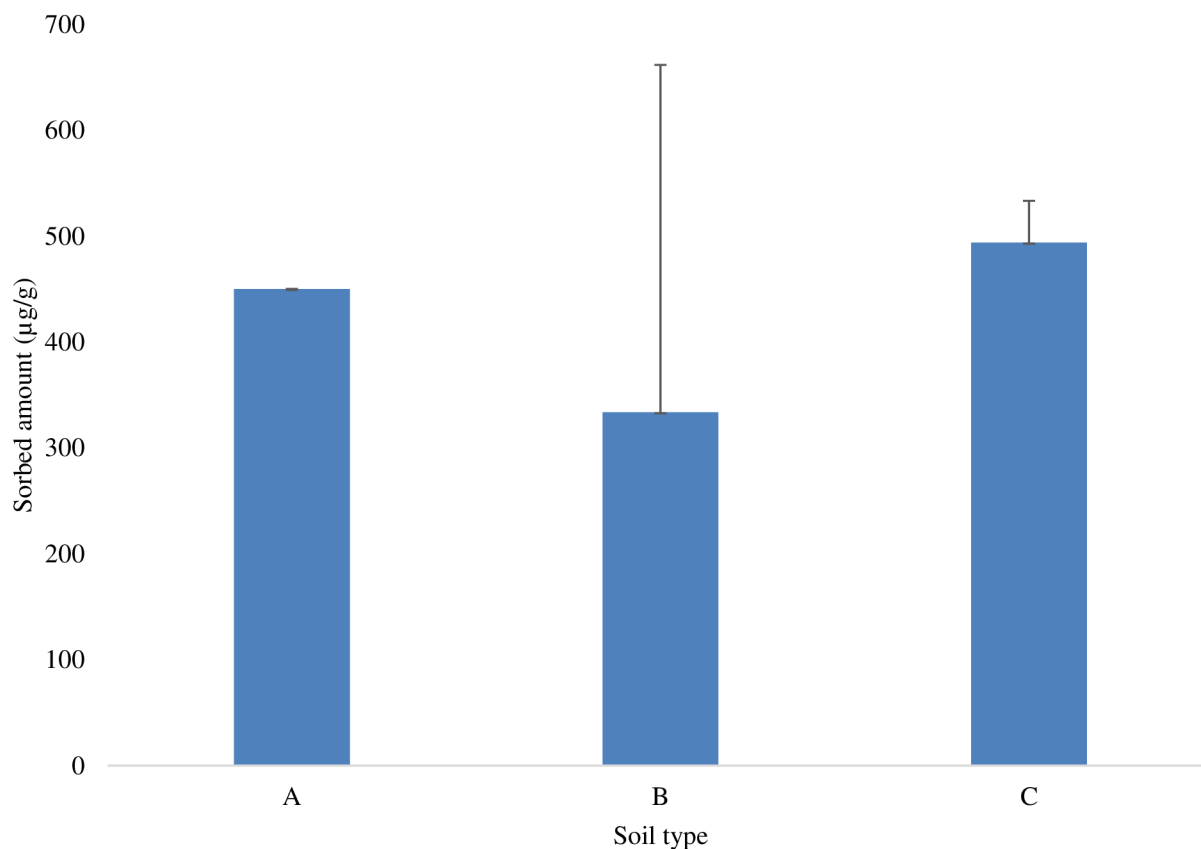
Figure 41: Sorption of 10 mg/l IBF solution at different pH values in soil type B



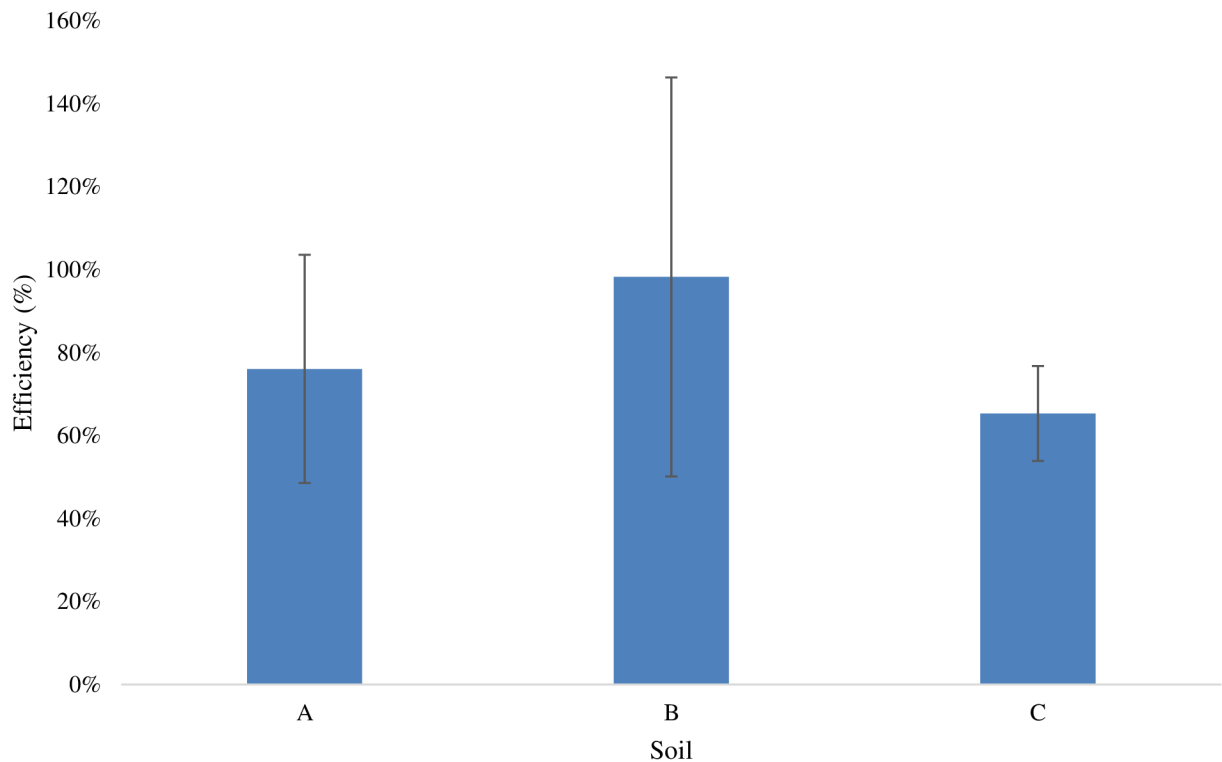


*Figure 42: Sorption of 10 mg/l IBF solution at different pH values in soil type C*

Overall, the sorbed amount at pH 3 in each soil decreased in the following order: C > A > B. The sorption efficiency decreased as follows: B > A > C. Each soil differed in its OM content, where soil C had the highest amount and the soil B the smallest. This indicates that the sorption of IBF was favoured in soil C which provided more sorption sites for the pharmaceutical compound. However, the retention of IBF was stronger in soil B. The course of sorption and the sorption efficiency at pH 3 are depicted in *Figure 43* and *Figure 44*, respectively.



*Figure 43: Comparison of sorption in studied soils at pH 3*



*Figure 44: Sorption efficiency of IBF in each soil at pH 3*

At pH 7 the sorbed amount and sorption efficiency of IBF decreased in the following order: B > A > C and C > A > B, respectively. This indicates that the higher amount of OM in soil interfered with sorption of negatively charged IBF. This could be possibly attributed to the negative charge of soil OM. Despite this observation, the retention of IBF was mainly favoured in this soil. This could be attributed to higher OM content, which contributed to its retention in soil C. The course of sorption together with sorption efficiency at pH 7 in each soil is provided in *Figure 45* and *Figure 46*, respectively.

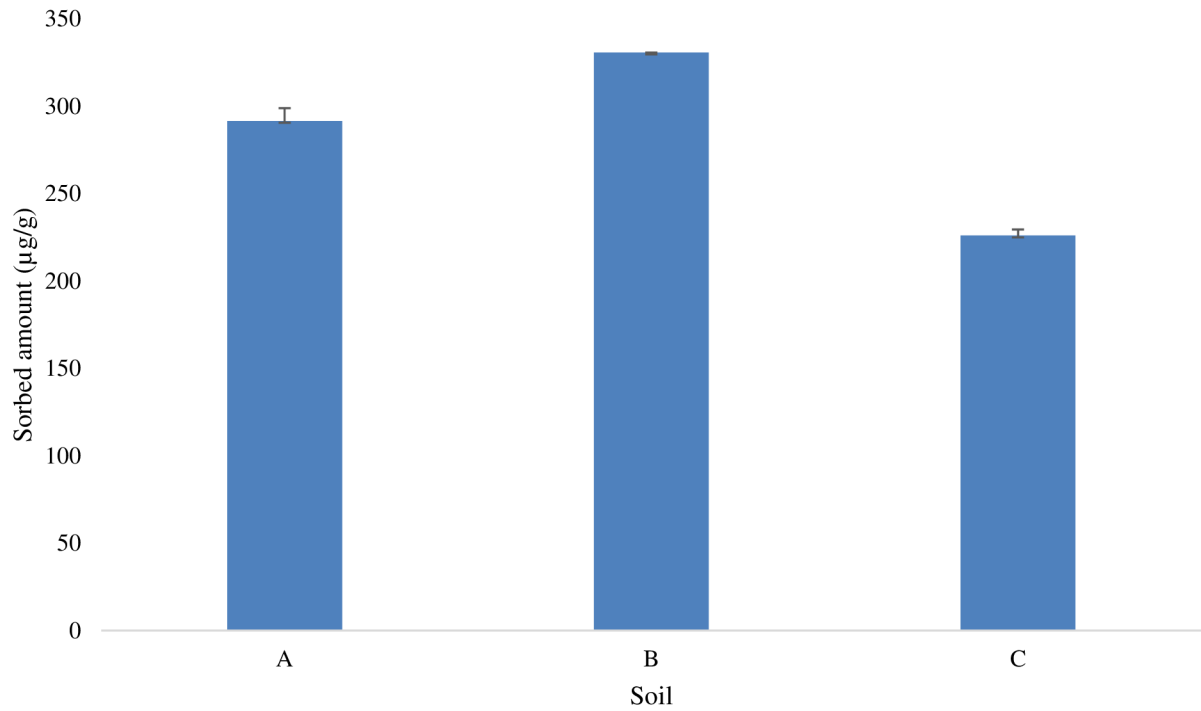


Figure 45: Comparison of sorption in each soil at pH 7

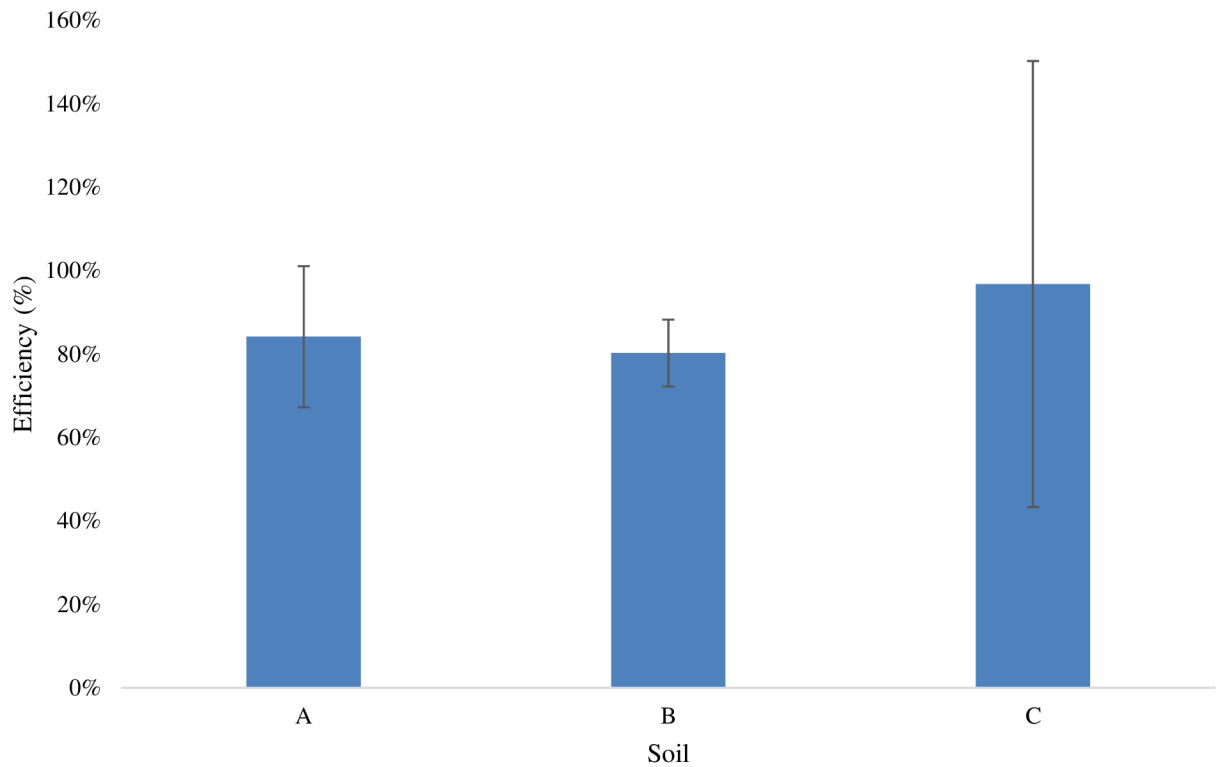


Figure 46: Sorption efficiency of IBF in each soil at pH 7

In the case of pH 10, the course of sorption and its efficiency both decreased in the following order: B > C > A. The course of sorption and the sorption efficiency can be seen in Figure 47 and Figure 48, respectively. No increase or decrease was observed with decrease

of OM content. Due to the presence of the anionic form of IBF, a similar course of sorption was expected, to that observed at pH 7. The highest amount as well as the highest sorption efficiency were recorded in the soil with the lowest OM content. However, due to the course of sorption observed, we can conclude that the difference in OM content did not have a significant influence on sorption of IBF at pH 10.

Overall, the highest sorbed amount in soils was recorded at pH 3. This indicates that the sorption of the neutral form was favoured in each soil, with the highest amount recorded in soil C. Furthermore, with the increasing pH the sorbed amount of IBF decreased. The sorption of the anionic IBF was not encouraged in the three studied soils, especially in soils A and C. Despite their high OM content, the sorption process was suppressed.

However, the highest sorption efficiency was recorded at pH 10. This indicates that the retention of IBF in the three soils was the most efficient at pH 10. This observation can be attributed to the presence of strong forces between the anionic form and the soil surface in the soil solution.

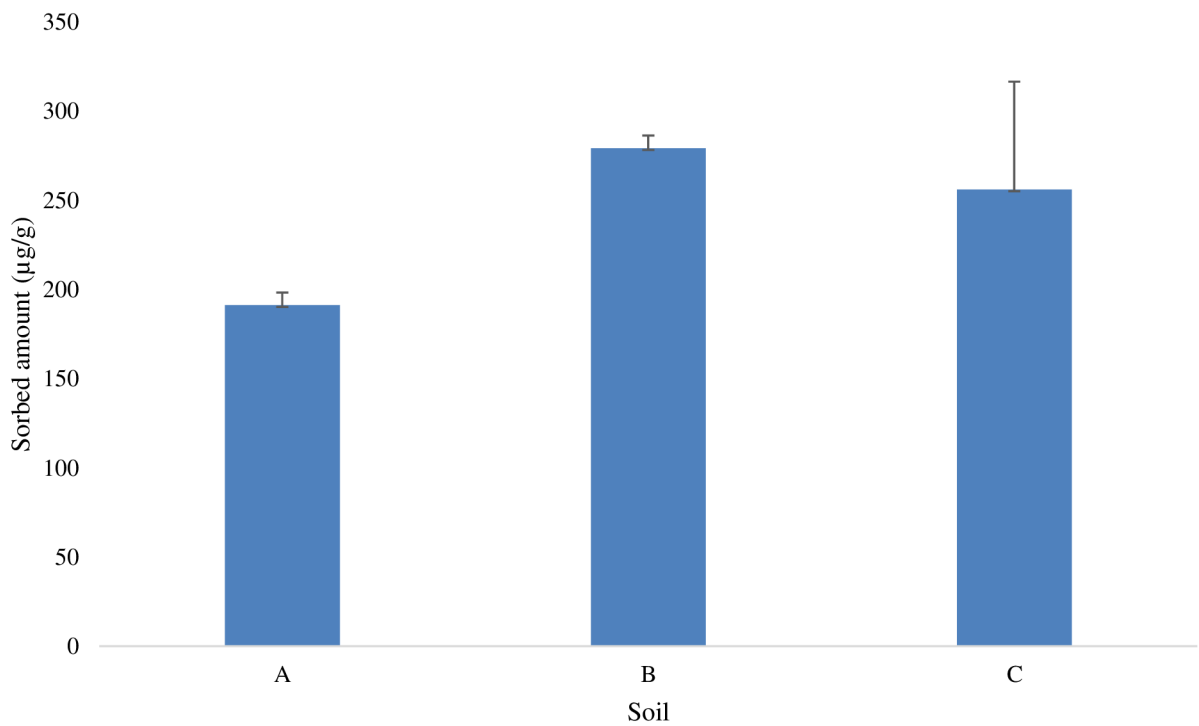


Figure 47: Comparison of sorption of IBF in different soils at pH 10

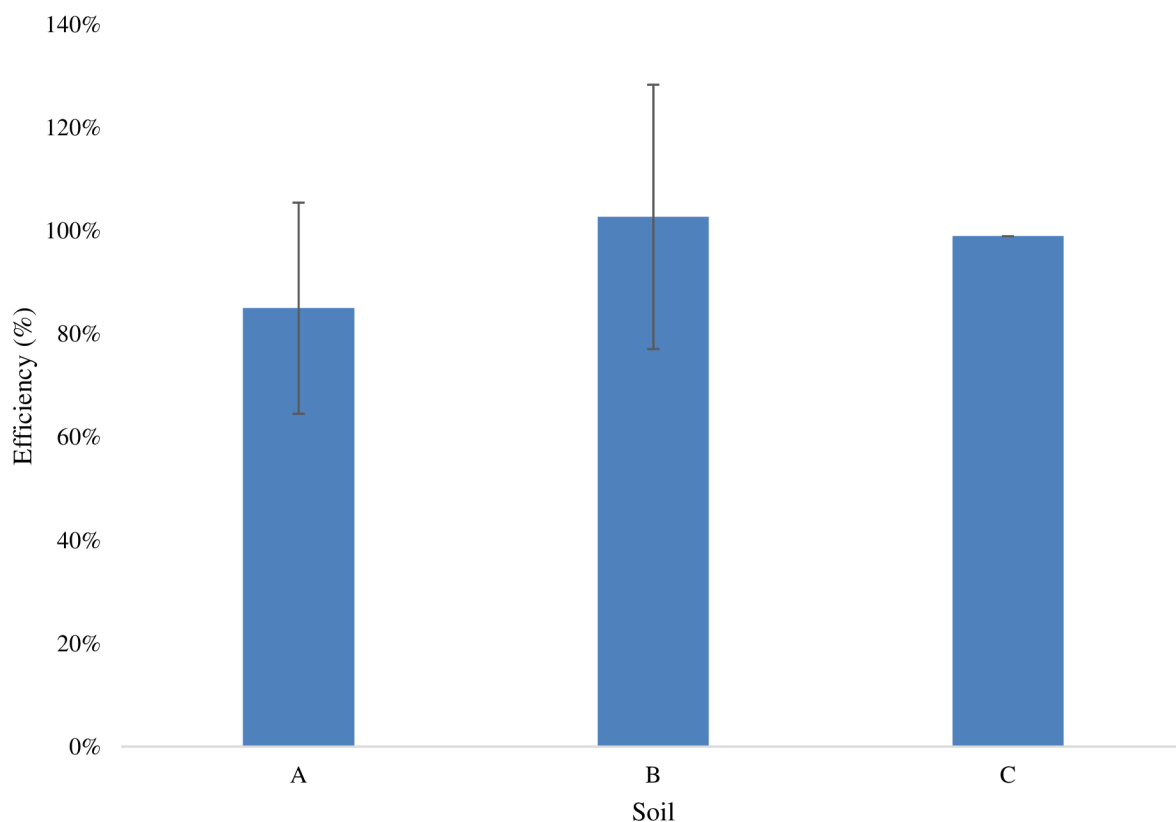


Figure 48: Sorption efficiency of IBF in studied soils at pH 10

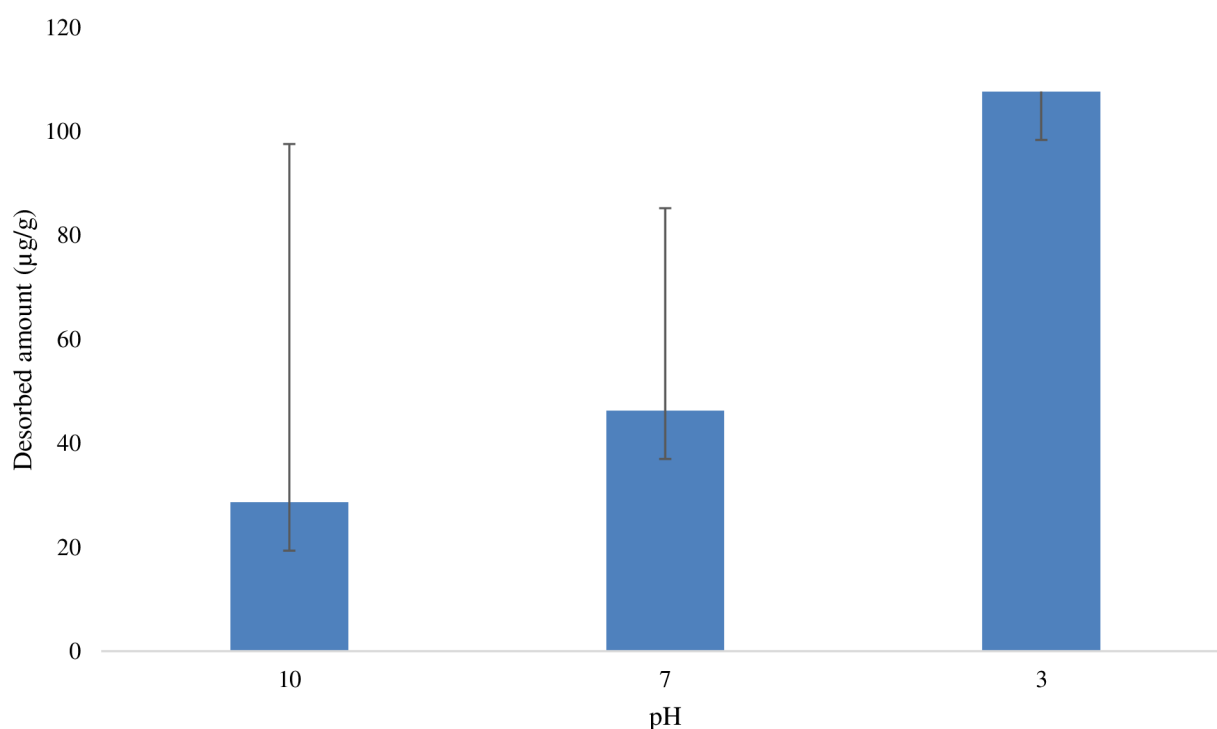
### 10.2.2 Desorption of IBF in Soils at Different pH, UV-VIS Data

The desorption in soil type A displayed a linear increase with decreasing pH, where the highest desorbed amount was recorded at pH 3. Furthermore, the desorbed amounts at high pH were not as high compared to the sorbed amount. The calculated desorption efficiency and the desorbed amount both decreased with increasing pH of the soil solution. The acquired data indicates that the retention of IBF was more favourable at higher pH values. This could be a result of stronger forces present between the negatively charged pharmaceutical compound and the soil surface. The course of the desorption can be seen in *Figure 49*.

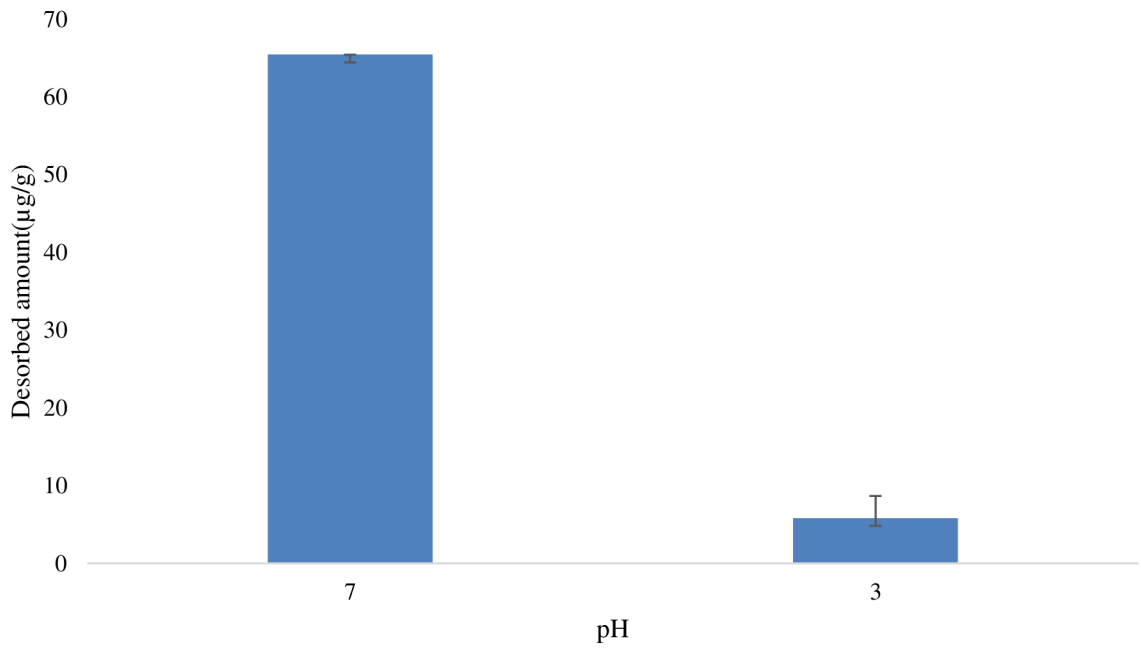
The desorbed amount at pH 10 for soil B could not have been calculated. Therefore, included are only values acquired for pH 3 and 7. The recorded desorbed amount at these values differed compared to soil A. The course of desorption can be seen in *Figure 50*. The desorbed amount and the desorption efficiency both decreased in the following order: pH 7 > pH 3. The amounts recorded at pH 7 were significantly higher compared to pH 3. This suggests that at pH 7 the desorption of IBF was the most efficient. However, the retention of IBF was stronger at pH 3.

The described observations indicate that lower OM content in soil B and the presence of IBF at the experimental pH in its specific state have a distinctive influence on the desorption process of IBF.

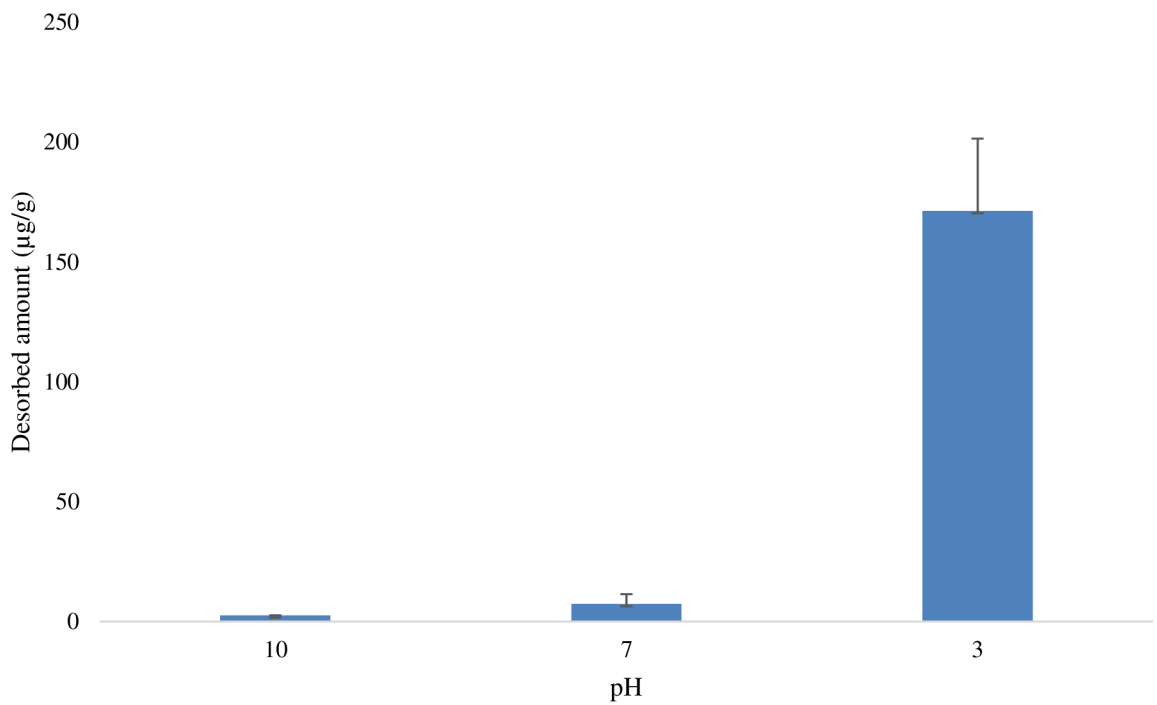
A linear desorption of IBF was observed in soil C, where the highest recorded amount was at pH 3. On the other hand, desorbed amounts at pH 10 and 7 were significantly lower. The recorded desorbed amounts and the desorption efficiency both decreased as follows: pH 3 > pH 7 > pH 10. The neutral form of IBF exhibited the least efficient desorption. Additionally, this indicates that the anionic form of IBF preferred to be sorbed onto soil C at high pH levels. The course of the desorption in soil C can be seen in *Figure 51*.



*Figure 49: Desorption of IBF at different pH in soil A*



*Figure 50: Desorption of IBF in soil B at different pH*

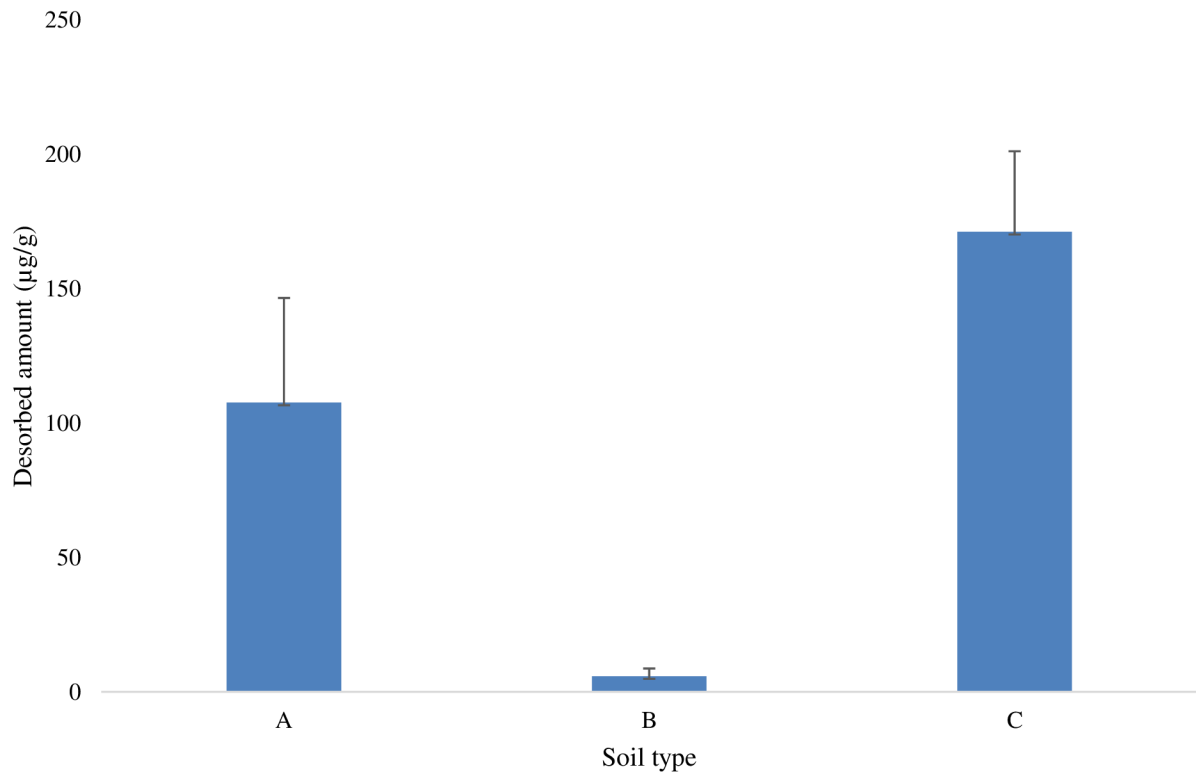


*Figure 51: Desorption of IBF in soil C at different pH*



The course of desorption observed at pH 3 decreased as follows: C > A > B. This can be seen in *Figure 52*. The same course was recorded for desorption efficiency.

Moreover, in soil B the desorbed amount was very low, where the calculated average efficiency of desorption was 1.74%. In the case of soils C and A, the calculated average of the desorption efficiency was 23.91% and 34.66%, respectively. This can be seen in *Figure 53*. Thus, desorption affinity increased with increasing OM content. This suggests that the neutral form of IBF had tendency to be strongly retained in soil that had lower OM content.



*Figure 52: Comparison of desorption in different soils at pH 3*

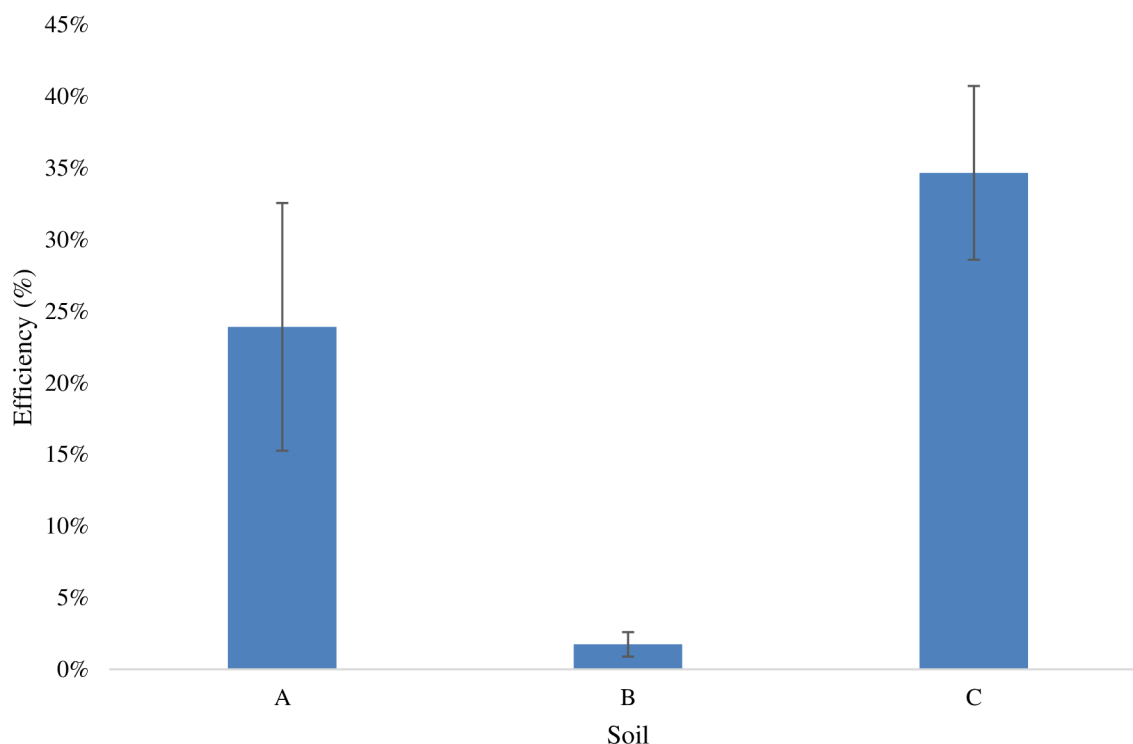


Figure 53: Desorption efficiency at pH 3 in studied soils

The course of desorption and the desorption efficiency at pH 7 can be seen in *Figure 54* and *Figure 55*, respectively. Observed was decrease of the desorbed amount and the desorption efficiency in the following order: B > A > C. This suggests that IBF had higher tendency to desorb in soil with the lowest OM content. This indicates that the presence of high OM content could have provided sorption sites for the anionic form of IBF, which ensured its retention. Furthermore, possible contributor could have been also the creation of the strong bonds between the anionic form of IBF and soil.

The course of desorption together with the desorption efficiency of IBF at pH 10 can be seen in *Figure 56* and *Figure 57*, respectively. The desorption of IBF and its efficiency decreased in the following order: C > A and A > C, respectively. However, due to unavailable data from soil B, it is not certain whether IBF had higher tendency of desorption in soil with higher or lower OM content at this specific pH.

Overall, the data collected so far indicates that neutral form of IBF had the highest tendency of desorption in soils with the high OM content. The lowest desorption tendency was recorded at pH 10.

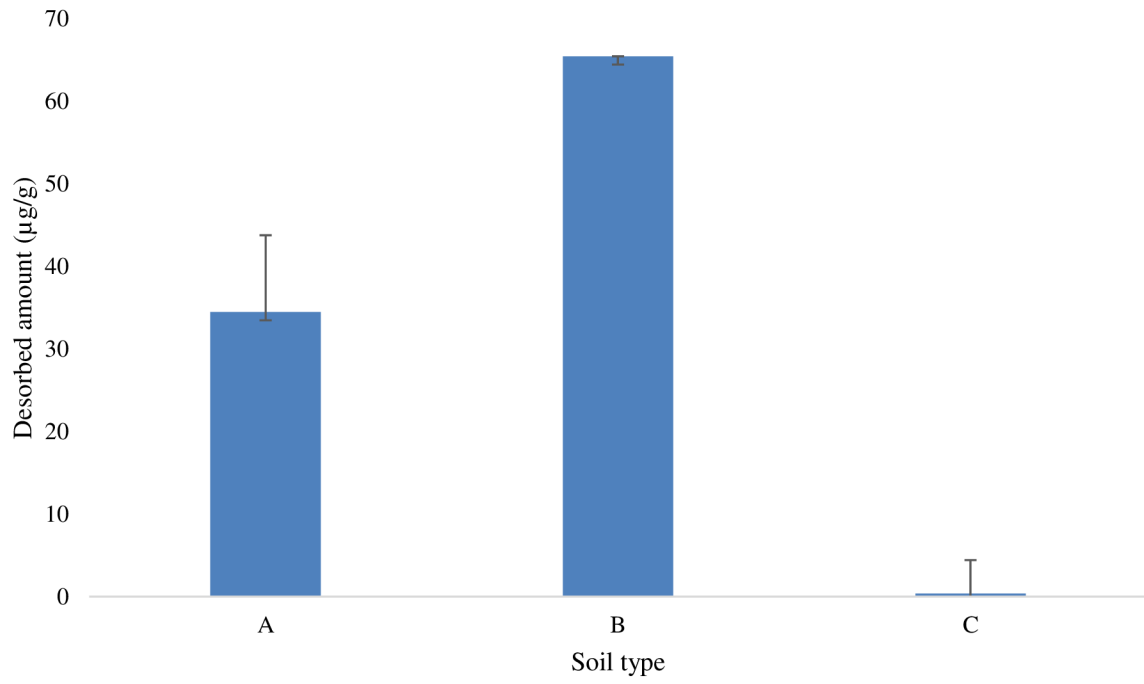


Figure 54: Comparison of desorption in different soils at pH 7

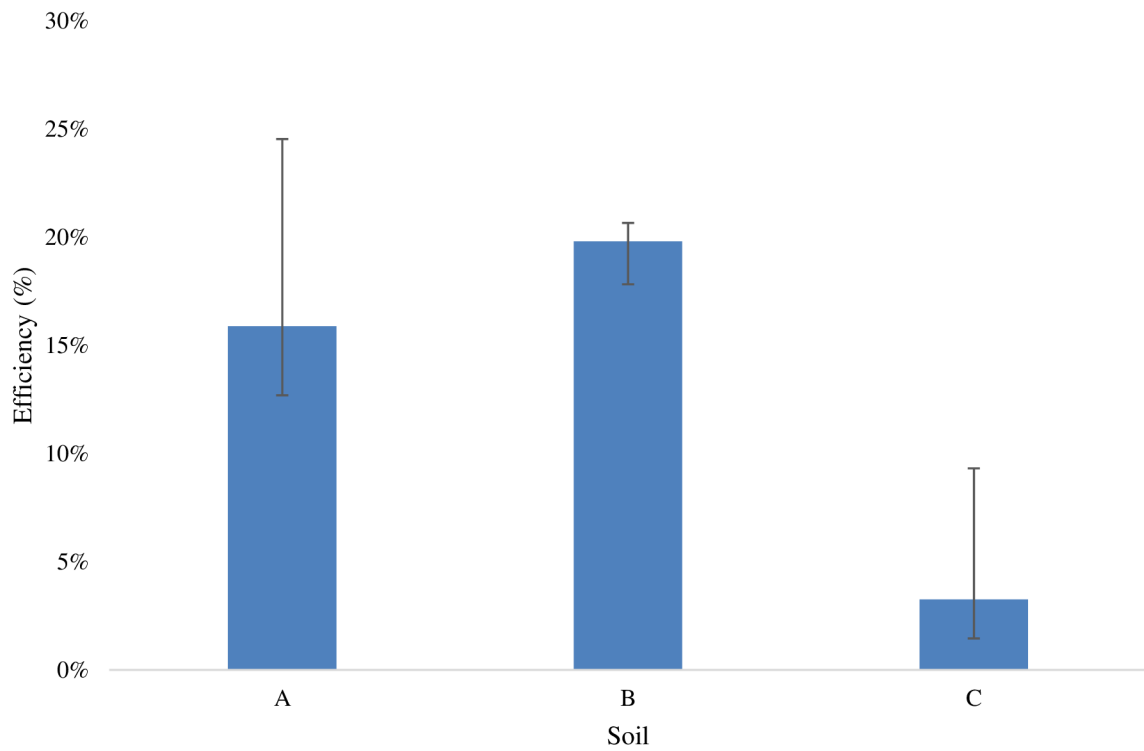


Figure 55: Desorption efficiency at pH 7 in studied soils

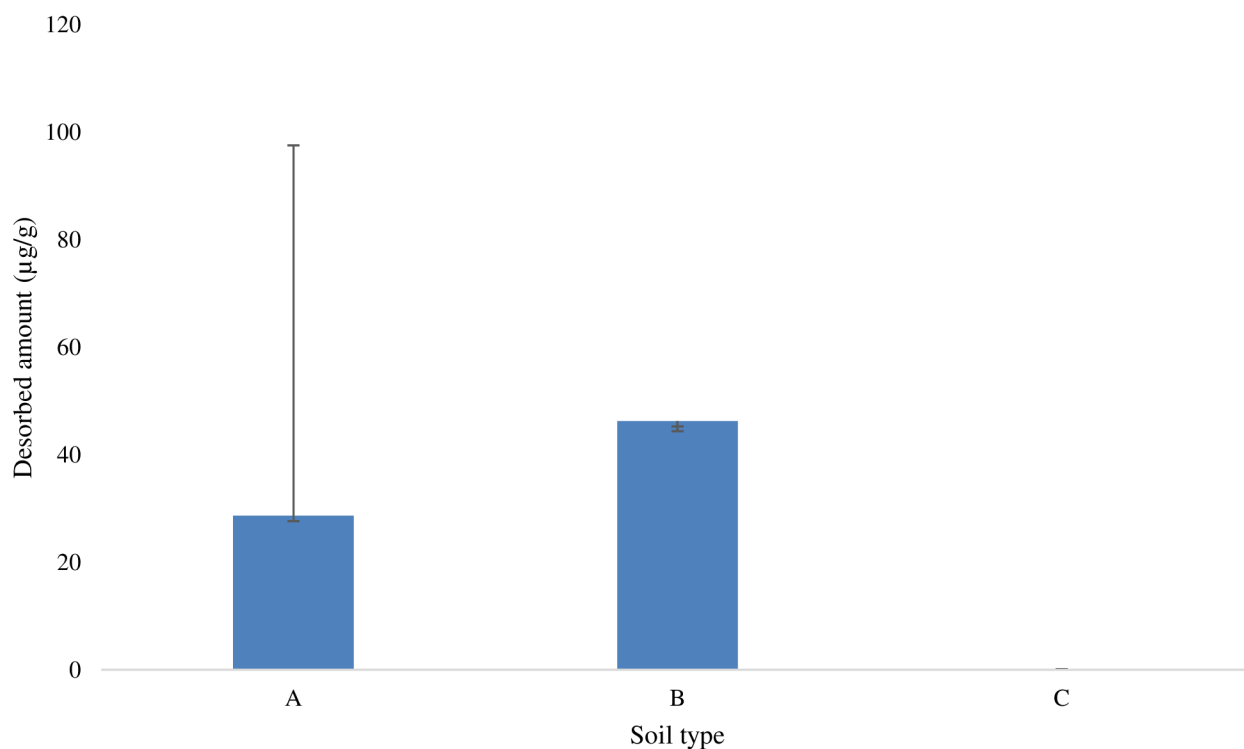


Figure 56: Comparison of desorption in different soils at pH 10

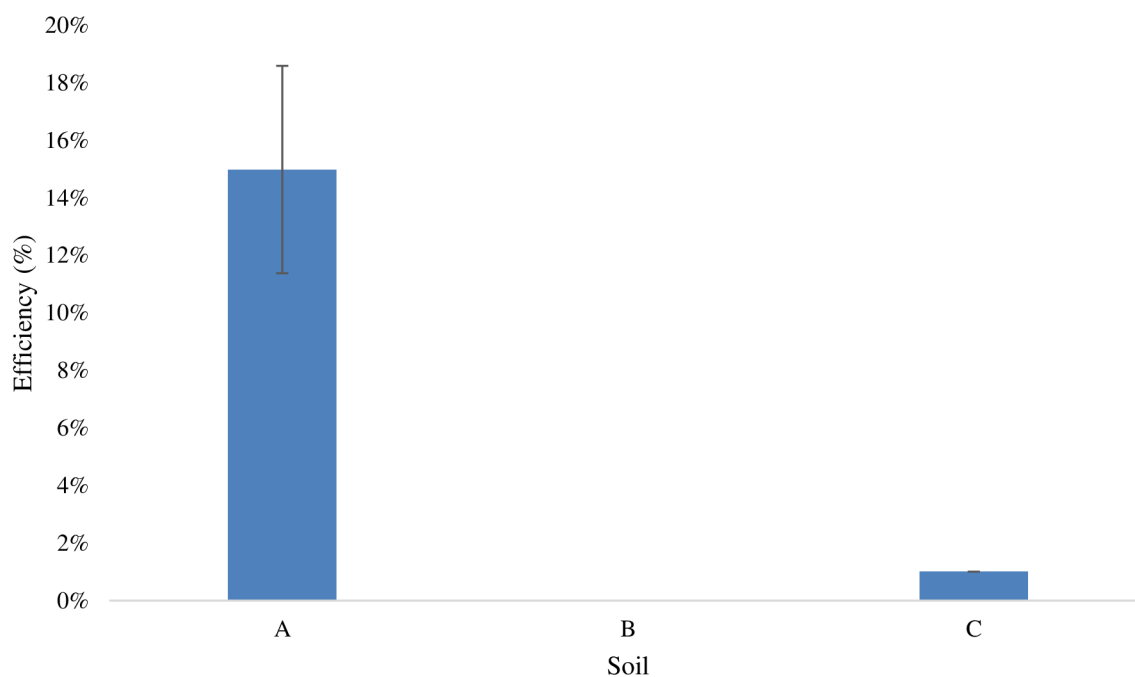


Figure 57: Desorption efficiency at pH 10 in studied soils

### 10.2.3 Influence of pH on Sorption and Desorption, LC-MS Data

Due to technical issues with the chromatograph, the measurement of samples acquired after sorption and desorption could not have been carried out. Therefore, all the information

regarding the influence of pH on the sorption and desorption of IBF in the studied soils were provided only from UV-VIS spectrometry.

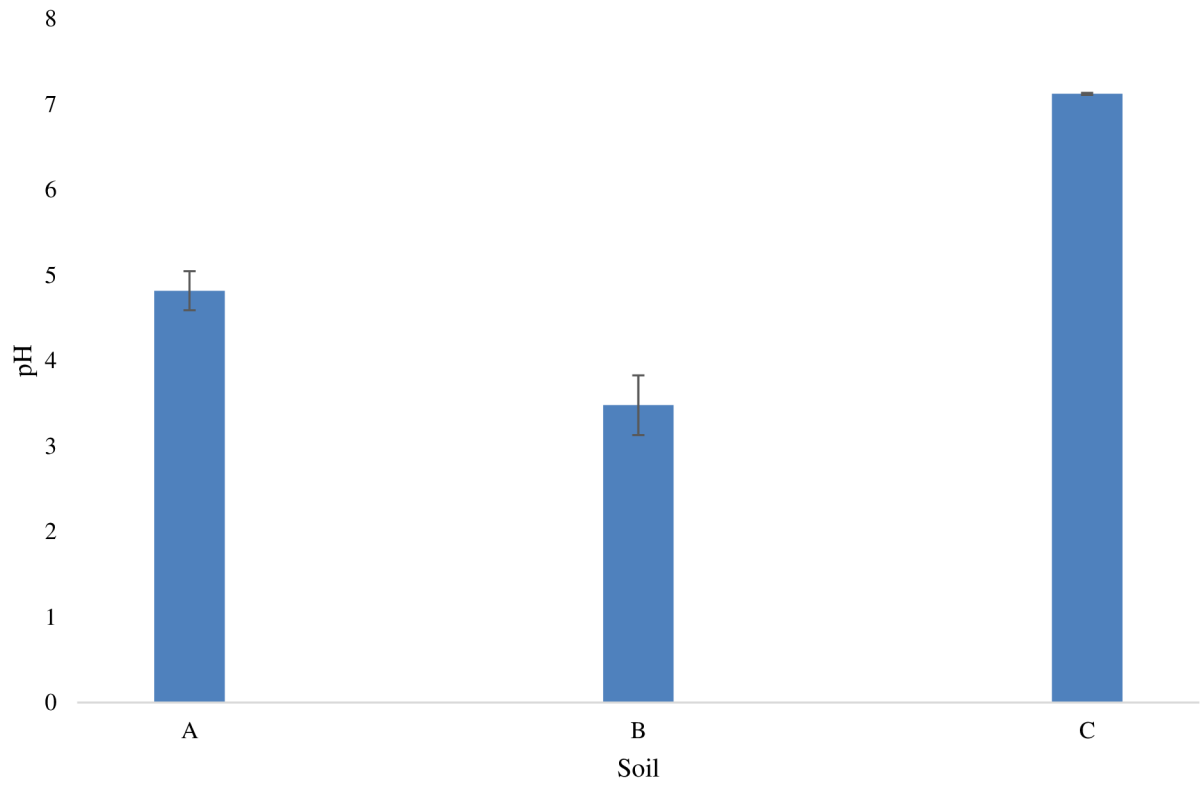
#### **10.2.4 Conductivity and pH of Soil Solution in the Second Experiment**

The conductivity and pH of the soil solutions at different pH were recorded. The initial pH of the applied solutions was pH 3 (3.012), pH 7 (7.012) and pH 10 (10.001).

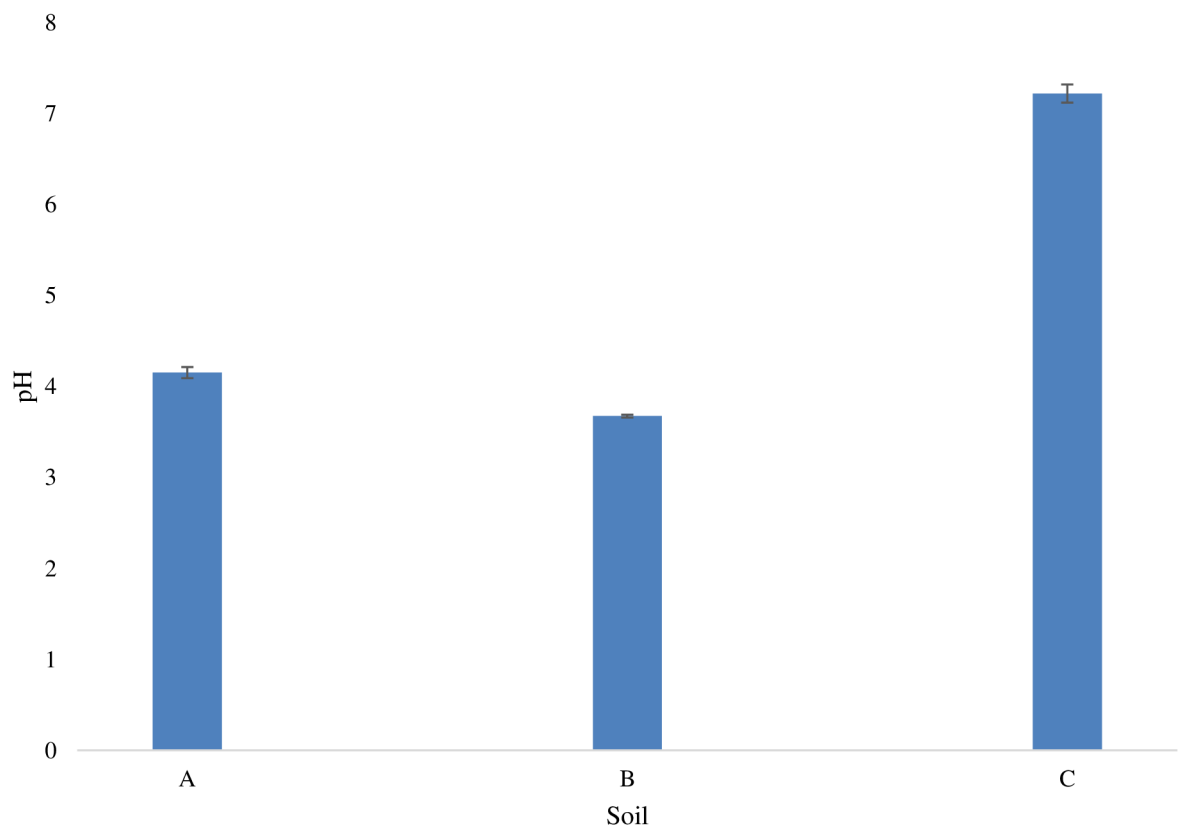
The recorded pH value of samples after the sorption at pH 10 and 7 did not deviate significantly from the initial pH. Detailed data at pH 10 and 7 can be seen in *Figure 62* and *Figure 60*, respectively. Furthermore, as can be seen in *Figure 58*, the recorded values at pH 3 in soils decreased as follows:  $C > A > B$ . The higher deviation in soils could be attributed to different composition of the used soil.

In the case of desorption, recorded pH values at pH 10 and 7 decreased in the following order:  $A > B > C$  and  $C > A > B$ , respectively. This can be seen in *Figure 63* and *Figure 61*, respectively. At pH 3 the acquired pH values decreased in the following order:  $C > A > B$ . The detail of the recorded data can be seen in *Figure 59*.

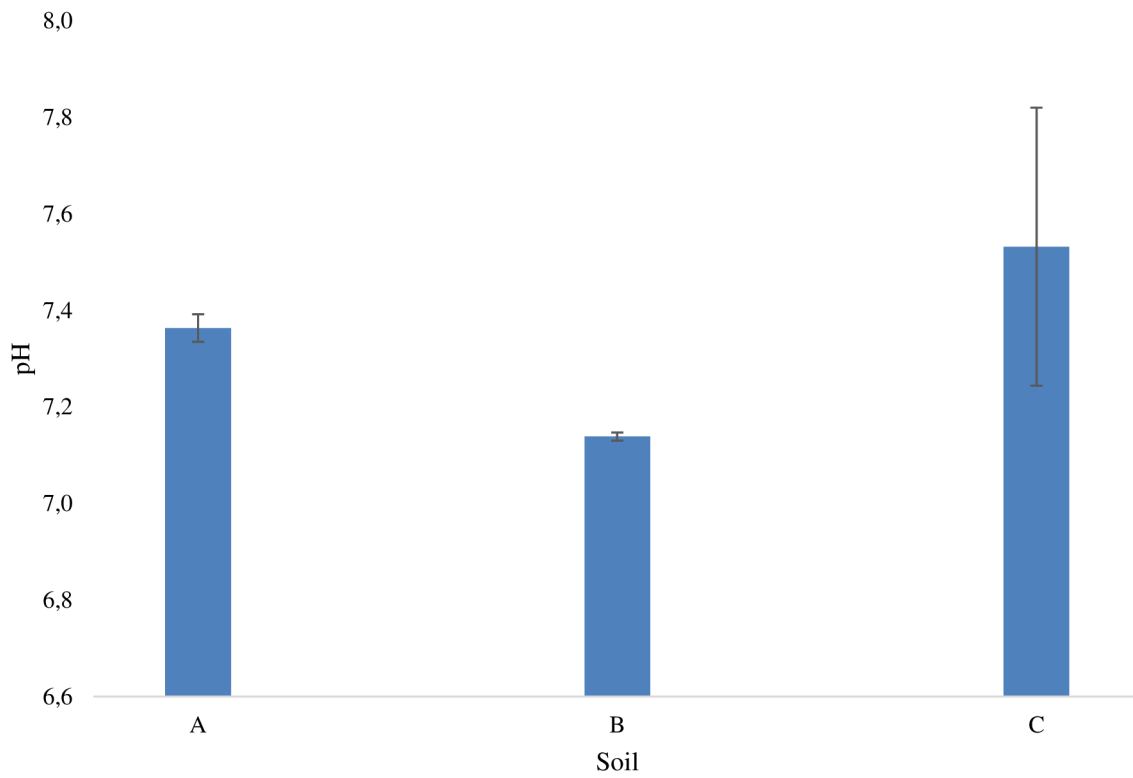
The recorded conductivity differed in each soil. At pH 3, the conductivity after the sorption and desorption decreased in the following order:  $B > C > A$  and  $C > B > A$ , respectively. The detailed data for the sorption and desorption can be found in *Figure 64* and *Figure 65*, respectively. At pH 7, the decrease of conductivity in samples after the sorption and desorption was as follows:  $C > A > B$  and  $C > A > B$ , respectively. This can be seen in *Figure 66* and *Figure 67*. In the case of pH 10, the decrease of conductivity after sorption and desorption was as follows:  $A > B > C$  and  $C > A > B$ , respectively. The recorded data for sorption and desorption at pH 10 can be found in *Figure 68* and *Figure 69*, respectively. The observed change could be attributed to different composition of each soil e.g., OM content.



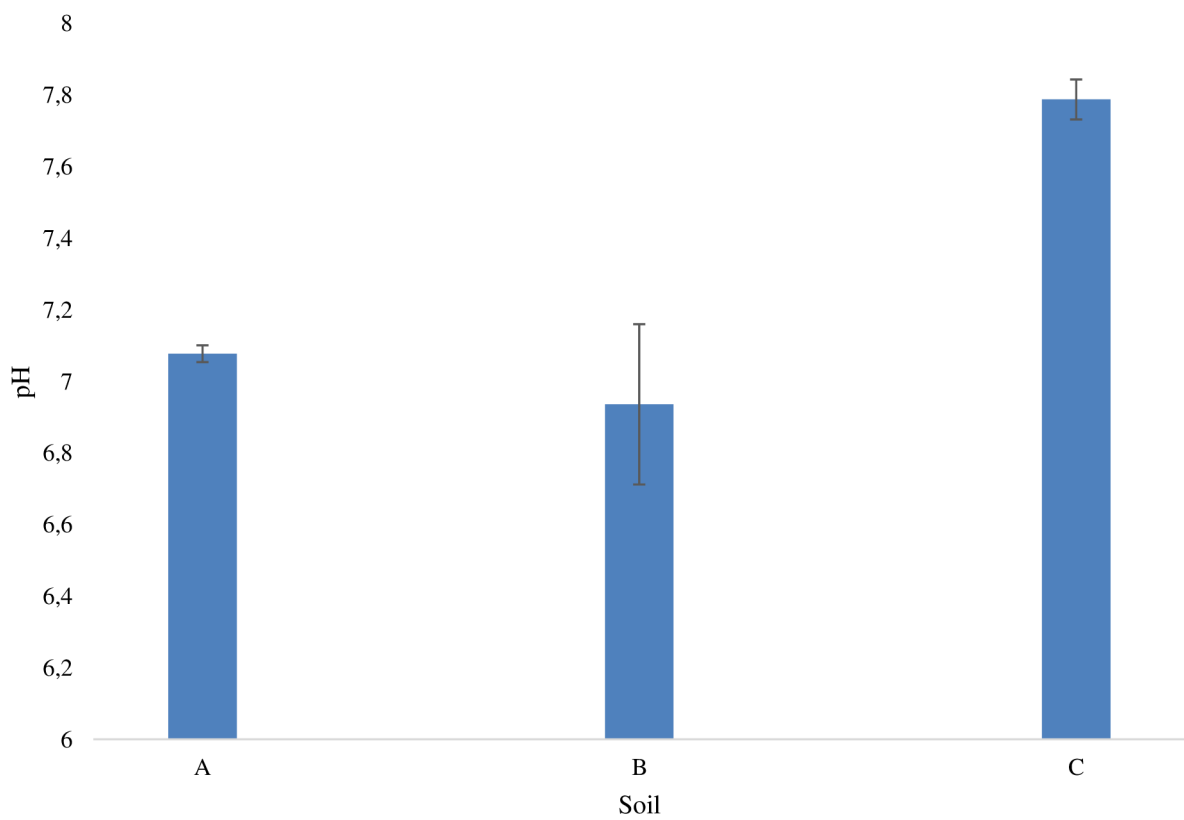
*Figure 58: pH values of samples after sorption in studied soils, pH 3*



*Figure 59: pH values of samples after desorption, pH 3*



*Figure 60: pH values of samples after sorption in different soils, pH 7*



*Figure 61: pH of samples acquired after desorption in different soils, pH 7*

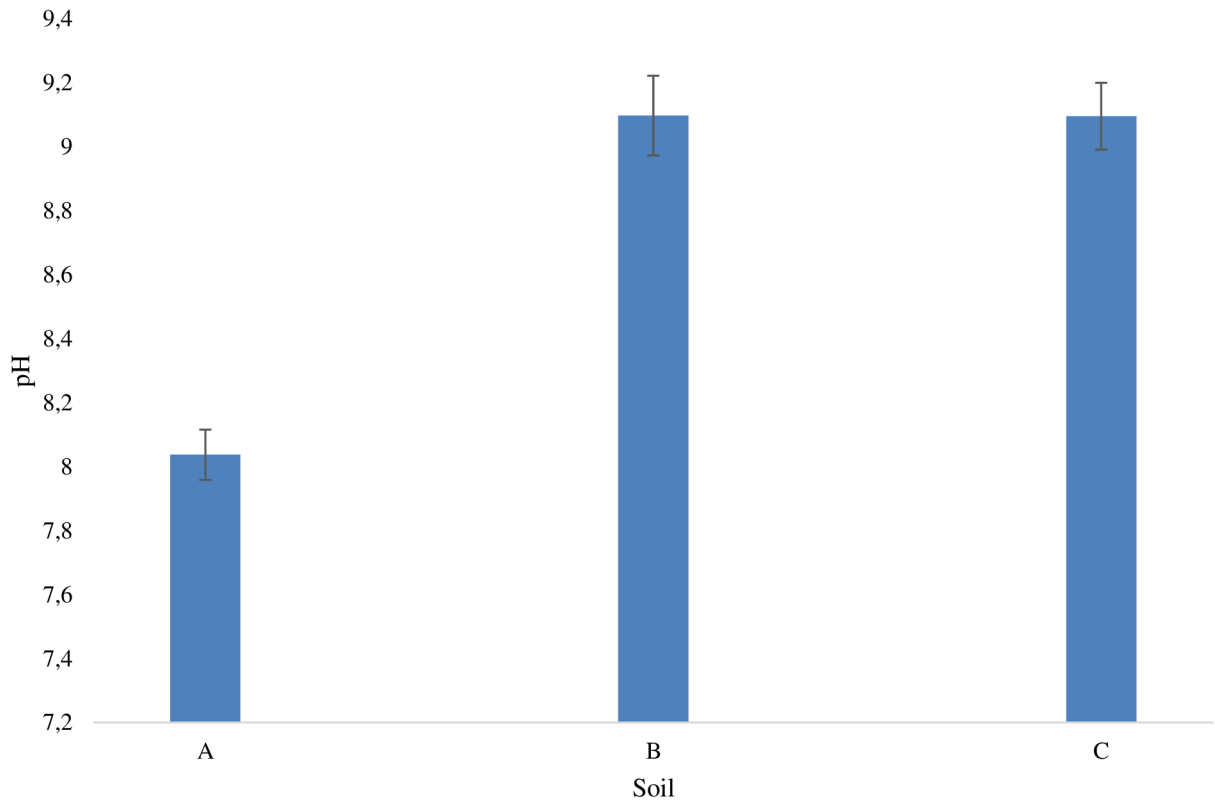


Figure 62: pH values of samples after sorption, pH 10

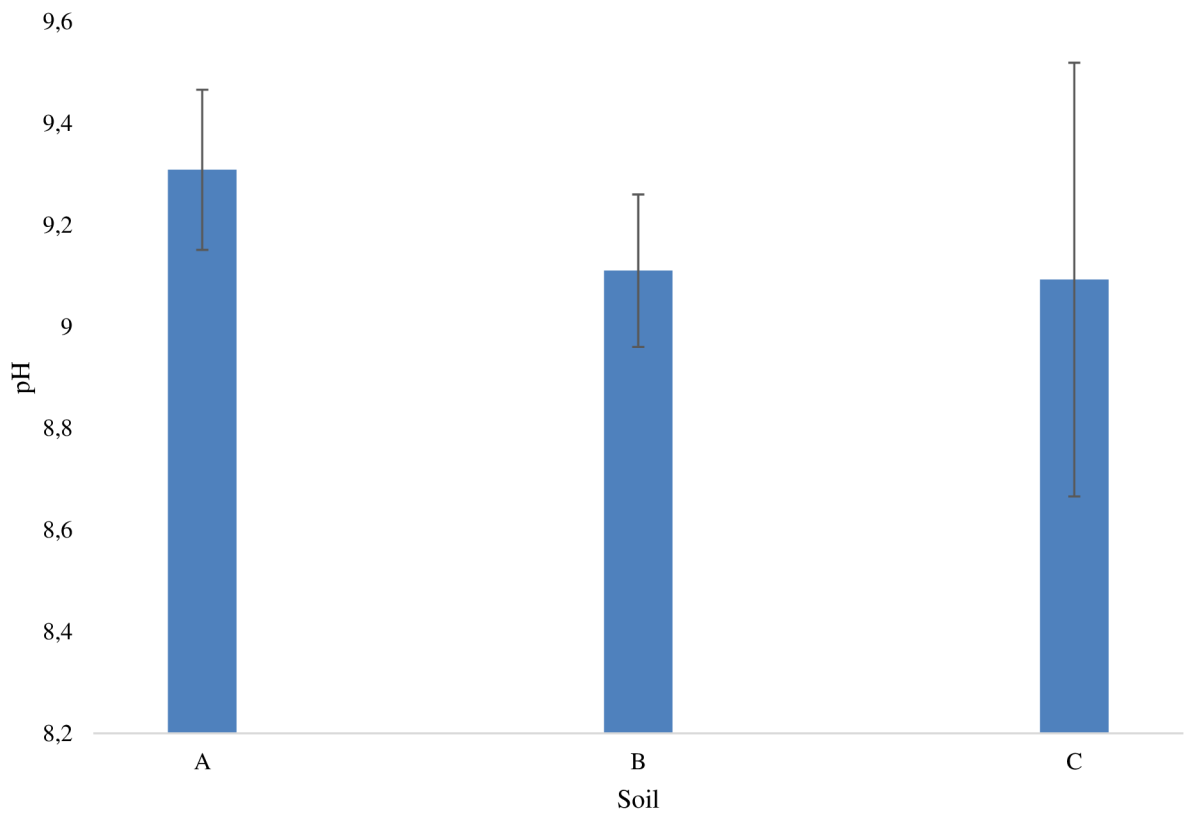
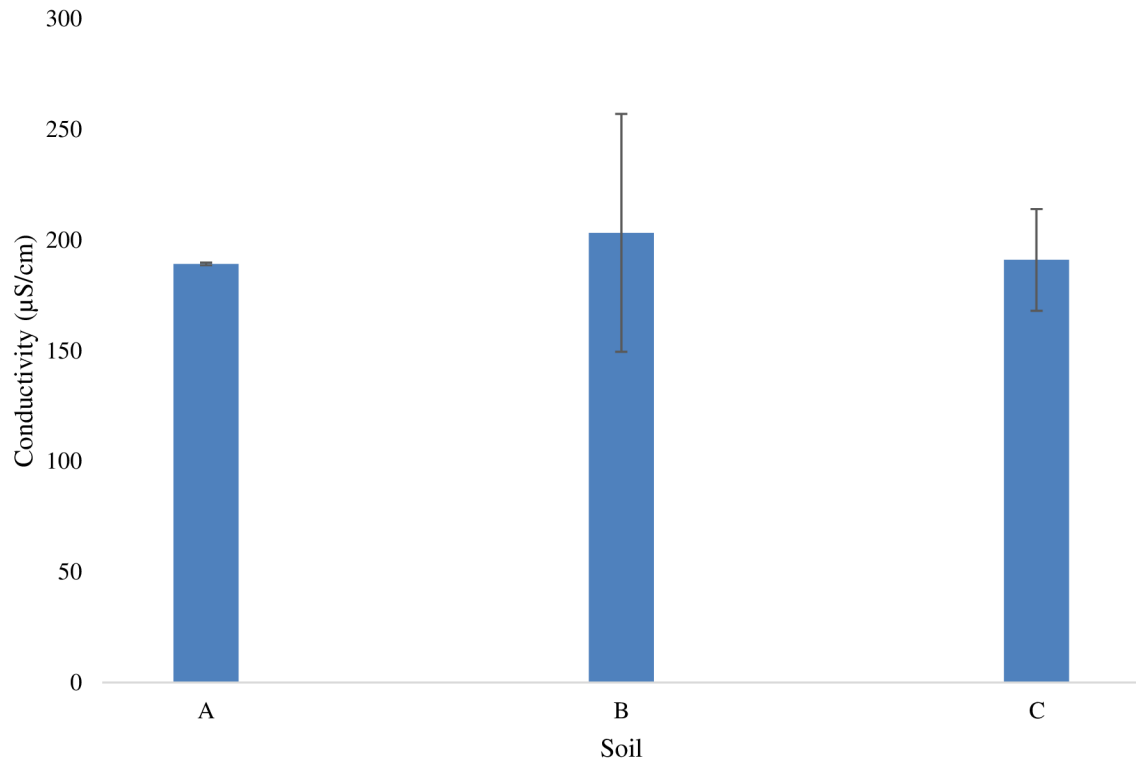
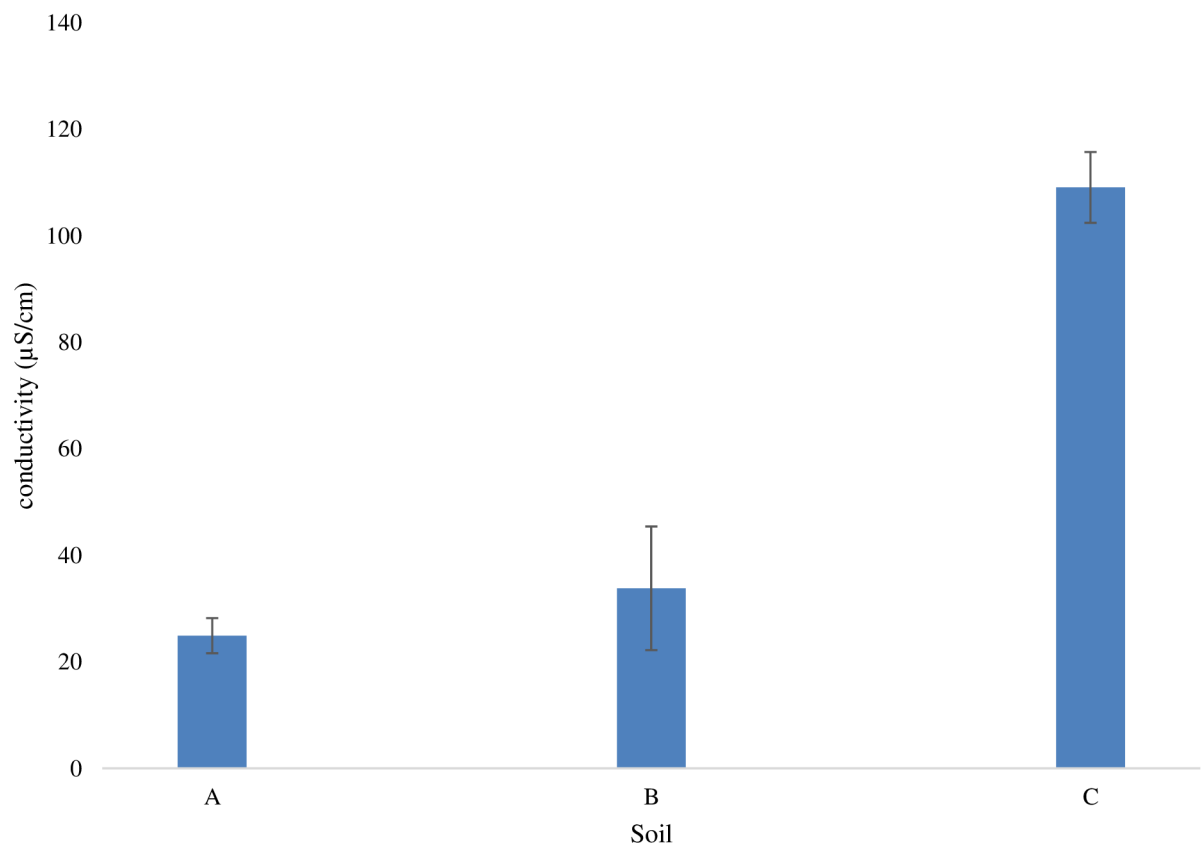


Figure 63: pH of samples acquired after desorption in different soils, pH 10





*Figure 64: Conductivity of samples after sorption, pH 3*



*Figure 65: Conductivity of samples after desorption, pH 3*

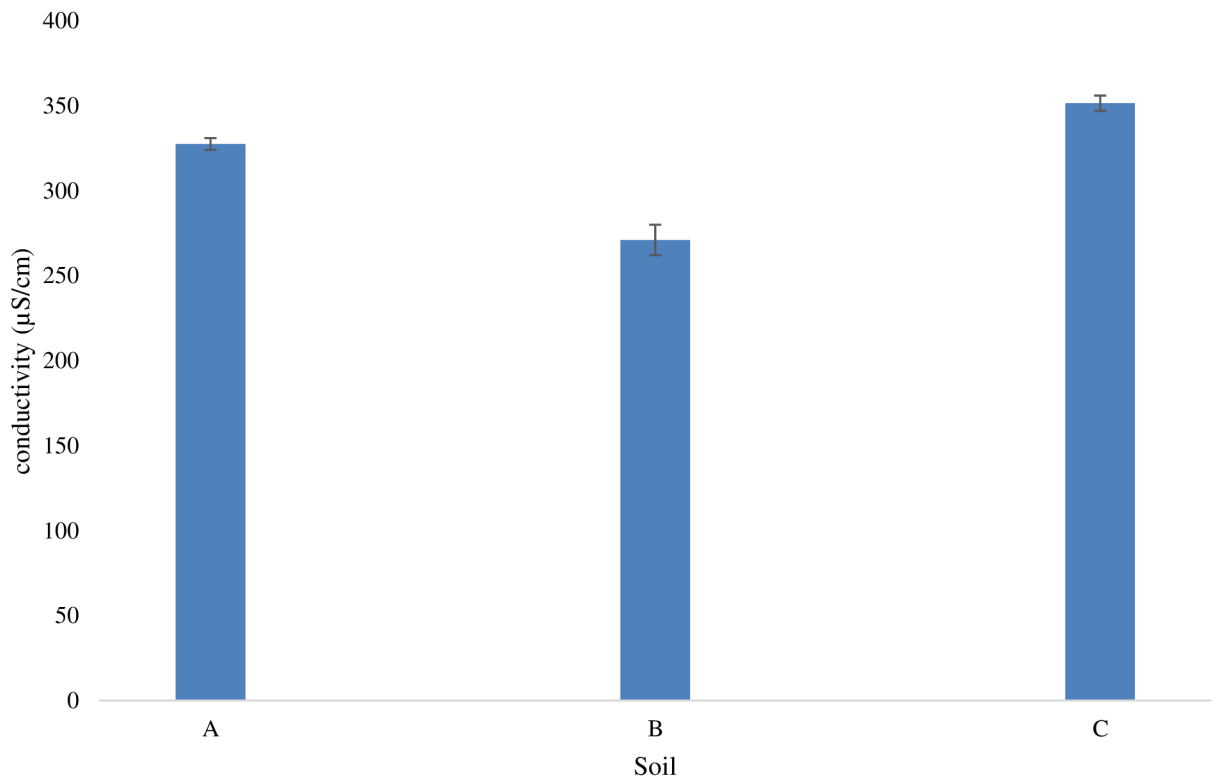


Figure 66: Conductivity of samples after sorption in different soils, pH 7

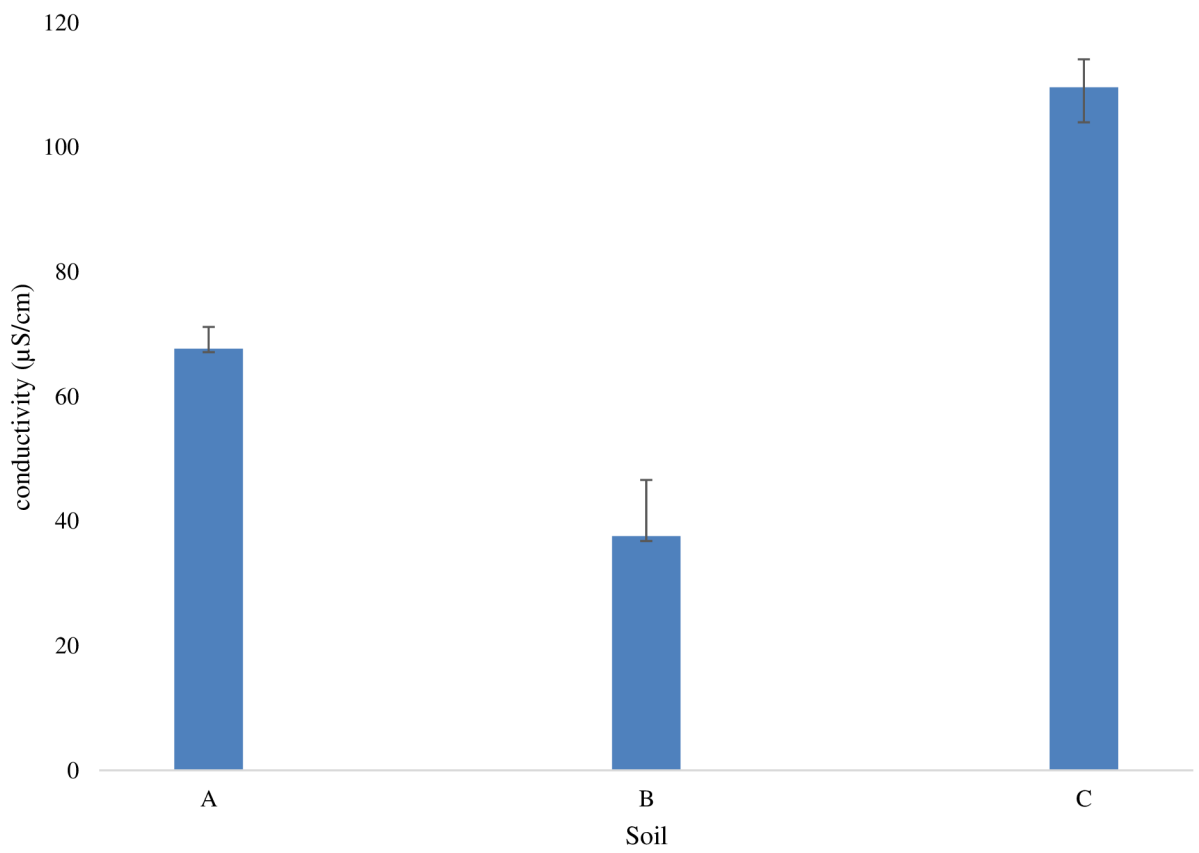
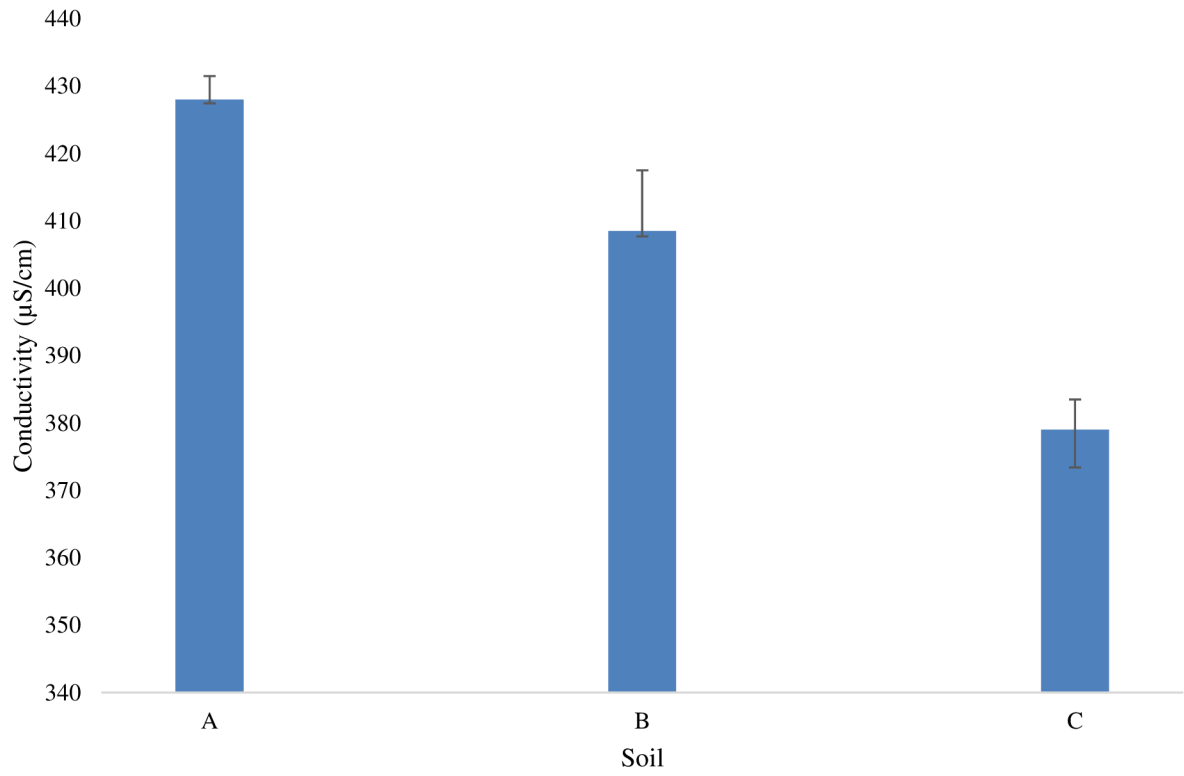
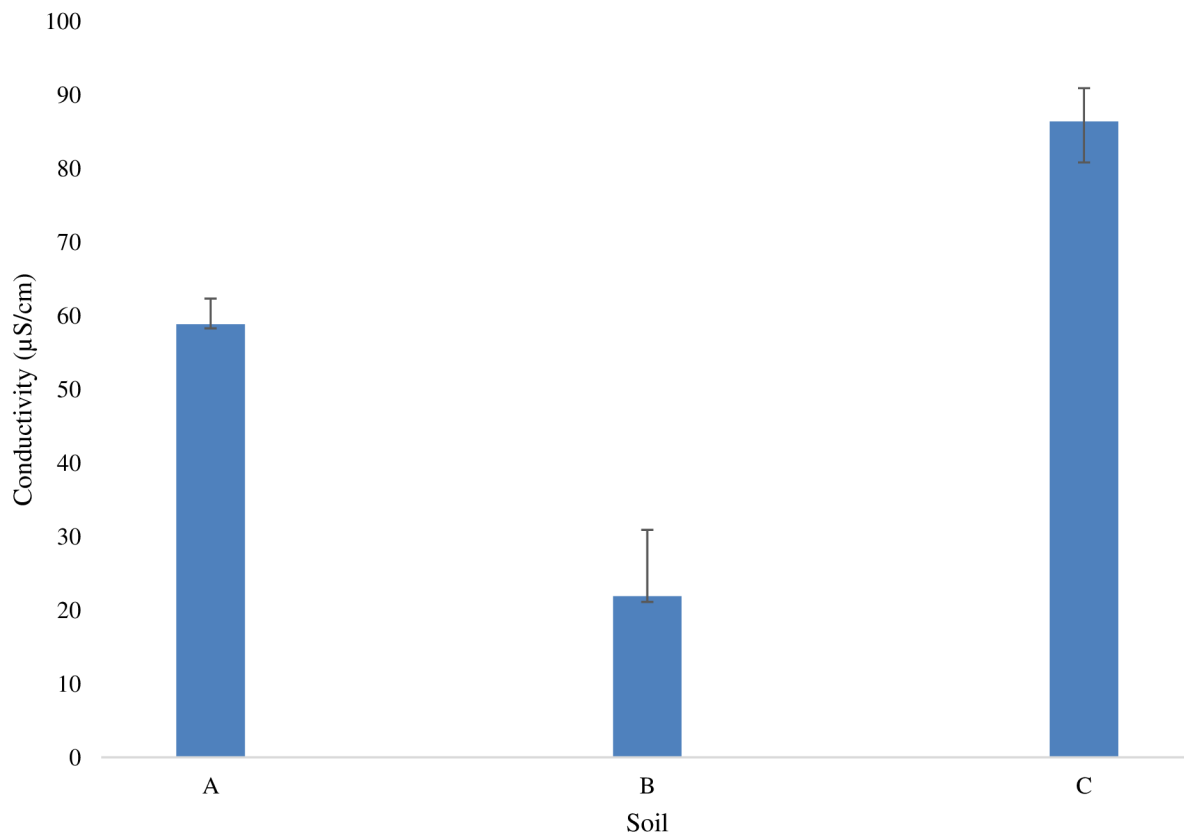


Figure 67: Conductivity values of samples after desorption in different soils, pH 7



*Figure 68: Conductivity in samples after sorption in different soils, pH 10*



*Figure 69: Conductivity of samples after desorption in different soils, pH 10*

## 11. Conclusion

This thesis focuses on the interaction of ibuprofen with different types of soil. Ibuprofen is a non-steroidal anti-inflammatory drug that is highly available and consumed in high amounts. This is subsequently closely connected with its occurrence in the environment. Continuous transport of this contaminant can have adverse effects on living organisms. Furthermore, the transport of ibuprofen and other pharmaceuticals is influenced by several factors i.e., soil organic matter content, pH. These factors were considered in the experimental part of this thesis.

The experiment was conducted using three soils from different regions in the Czech Republic – Hodonín, Jablůnka and Brno. Each soil differed mainly in its soil organic matter content. These soils were uncontaminated and were used as a matrix for the sorption and desorption experiments.

The experimental part consisted of two main experiments. The first focused on the influence of different organic matter content on the sorption and desorption of ibuprofen. In the second experiment, the goal was to study its sorption and desorption in three soils under different pH conditions. Each experiment was followed by a measurement of pH, conductivity, and absorbance. The detailed information regarding the sorption and desorption of ibuprofen was achieved using liquid chromatography with mass spectrometry detection.

However, due to technical issues with the chromatograph, the measurement of several samples from the first experiment and all samples from the second experiment was not possible.

The amount of ibuprofen sorbed onto soil increased with increasing OM content. Overall, the retention of ibuprofen was more favourable at higher concentrations in these soils. On the other hand, in the case of desorption, high efficiency was detected in soil B, where it was more profound at higher concentrations.

In the second experiment, the sorbed amount increased with the decreasing pH of the soil solution. A similar course was recorded for desorption in soils A and C. Opposite was observed in soil B. Therefore, the desorption efficiency was the highest at pH 3 in soils A and C. In contrast, the retention of ibuprofen increased with the increasing pH values with the highest value in soil B.

Overall, the high desorption efficiency of IBF at lower concentrations indicates that in the environment IBF could be more present in a mobile form. This can pose a higher risk for underground waters that could transport this contaminant further into the environment. Furthermore, the difference in pH can significantly influence the course of sorption. High desorption efficiency was observed in soils, which due to their high OM content ensured efficient sorption of IBF.

In conclusion, the sorption and desorption of IBF are influenced by numerous other factors besides OM content and pH which should be more explored. Moreover, IBF does not always leave the human body in its original form. It can be present in various metabolic forms that can have a more serious effect on the environment than IBF itself. Therefore, the course of their sorption and desorption together with possible factors influencing these processes should be studied more.

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## List of Used Abbreviations

API	active pharmaceutical ingredient
WWTP	wastewater treatment plant
OM	organic matter
NSAIDs	non-steroid anti-inflammatory drugs
IBF	ibuprofen
NPX	naproxen
DCF	diclofenac
KTF	ketoprofen
PRC	paracetamol
$K_{ow}$	octanol-water partitioning coefficient
$pK_a$	acidity dissociation constant
$\log D_{ow}$	logarithm of distribution ratio n-octanol/water
$M_w$	molecular weight
SOM	soil organic matter
S	source in the literature
ND	not detected
LOQ	limit of quantification
NOR	norfloxacin
SMZ	sulfamethazine
HA	humic acid
IS	ionic strength
TRM	trimethoprim
CLN	clindamycin
CLR	clarymycin
MET	metoprolol
ATN	atenolol
SMX	sulfamethoxazole
CBZ	carbamazepine
CEC	cation exchange charge
Soil B	black soil used by Zhang et al
Soil F	fluvo-aquatic soil used by Zhang et al
Soil R	red soil used by Zhang et al.
SDZ	sulfadiazine
SMT	sulfamethazine
SCP	sulfachlotpyridazine
S1, S2, S3	A Limie soils used by Conde-Cid et al.
S4, S5, S6	Sarria soils used by Conde-Cis et al.
SOC	soil organic carbon
HI	hysteresis index
ACP	acetaminopren
CAF	caffeine
SPD	sulfapyridine

SME	sulfameter
SDM	sulfadimethylehoxine
TC	tetracycline
p.z.c	point zero charge
SXX	sulfisoxazole
SGD	sulfaguanidine
PRO	propranolol
GC	gas chromatography
HPLTC	high-performance thin-layer chromatography
HPLC	high-performance liquid chromatography
LC-MS	liquid chromatography coupled with mass spectrometer
NMR	nuclear magnetic resonance
ICP	induced coupled plasma
CE	capillary electrophoresis
AEC	atomic emission spectrometry
AAS	atomic absorbance spectrometry
BSTFA	bis(trimethylsilyl)trifluoroacetamide
TMCS	trimethylchlorosilane
MLQ	method quantification limit
ESI	electrospray ionisation
Q	quadrupole
IT	ion trap
TOF	time of flight
QqQ	triple coupled quadrupole
Q-LIT	quadrupole coupled with linear ion trap
Soil A	soils from Jablunka, used in experimental part
Soil B	soils from Hodonín, used in experimental part
Soil C	soils from Brno, used in experimental part
BRB	Britton Robinson buffer
Rt	retention time
CZ	Czech Republic