Tetracycline and Sulfonamide Antibiotics in Soils: Presence, Fate and Environmental Risks

Manuel Conde-Cid 1, Avelino Núñez-Delgado 2, María José Fernández-Sanjurjo 2, Esperanza Álvarez-Rodríguez 2, David Fernández-Calviño 1,⁎ and Manuel Arias-Estévez 1

1 Soil Science and Agricultural Chemistry, Faculty Sciences, University Vigo, 32004 Ourense, Spain; manconde@uvigo.es (M.C.-C.); mastevez@uvigo.es (M.A.-E.)
2 Department Soil Science and Agricultural Chemistry, Engineering Polytechnic School, University Santiago de Compostela, 27002 Lugo, Spain; avelino.nunez@usc.es (A.N.-D.); mf.sanjurjo@usc.es (M.J.F.-S.); esperanza.alvarez@usc.es (E.A.-R.)

⁎ Correspondence: davidfc@uvigo.es

Received: 30 October 2020; Accepted: 13 November 2020; Published: 17 November 2020

Abstract: Veterinary antibiotics are widely used worldwide to treat and prevent infectious diseases, as well as (in countries where allowed) to promote growth and improve feeding efficiency of food-producing animals in livestock activities. Among the different antibiotic classes, tetracyclines and sulfonamides are two of the most used for veterinary proposals. Due to the fact that these compounds are poorly absorbed in the gut of animals, a significant proportion (up to ~90%) of them are excreted unchanged, thus reaching the environment mainly through the application of manures and slurries as fertilizers in agricultural fields. Once in the soil, antibiotics are subjected to a series of physicochemical and biological processes, which depend both on the antibiotic nature and soil characteristics. Adsorption/desorption to soil particles and degradation are the main processes that will affect the persistence, bioavailability, and environmental fate of these pollutants, thus determining their potential impacts and risks on human and ecological health. Taking all this into account, a literature review was conducted in order to shed light on the current knowledge about the occurrence of tetracycline and sulfonamide antibiotics in manures/slurries and agricultural soils, as well as on their fate in the environment. For that, the adsorption/desorption and the degradation (both abiotic and biotic) processes of these pollutants in soils were deeply discussed. Finally, the potential risks of deleterious effects on human and ecological health associated with the presence of these antibiotic residues were assessed. This review contributes to a deeper understanding of the lifecycle of tetracycline and sulfonamide antibiotics in the environment, thus facilitating decision-making for the application of preventive and mitigation measures to reduce its negative impacts and risks to public health.

Keywords: adsorption; crops; degradation; desorption; food chain; microorganisms; transport; veterinary antibiotics; water bodies

1. Introduction

Antibiotics are substances that have various kinds of effects on microorganisms, in some cases causing their death (bactericides) and in other cases inhibiting their growth or metabolic activity (bacteriostatic). Originally, the term antibiotic referred to any agent with biological activity against living organisms. However, nowadays, the term antibiotic refers only to substances with antibacterial, antifungal or antiparasitic activity. There are other terms widely used to refer to these compounds, such as antimicrobials or chemotherapeutics; however, these terms are more general and include other types of drugs as well. Specifically, the term antimicrobial also includes those compounds that are
effective against viruses, in addition to acting against bacteria, fungi, or protozoa. Regarding the term chemotherapeutic, it includes those compounds that are used for the treatment of diseases by destroying cells, particularly microorganisms and cancer cells [1,2].

Today, many different antibiotics are widely used all over the world, mainly to treat and prevent infections in humans, plants and animals, but sometimes also as food additives (at subtherapeutic doses) to promote growth and improve feeding efficiency of animals, in activities related to food production. Although the development and use of antibiotics have strongly contributed to a reduction in mortality and morbidity rates, their massive utilization in recent years, especially in veterinary medicine, has caused residues of these compounds to be present in a ubiquitous form in the environment, which can imply important risks for public health [2]. An important risk that constitutes an issue of global concern is the development and spread of antibiotic resistance [3]. In this sense, around 700,000 deaths are caused annually by resistant pathogens, and it is estimated that this figure could increase up to 10 million deaths per year by 2050 [4].

There are different ways to classify these compounds, although the categorization by chemical structure can be seen as the most appropriate from the environmental point of view, since their behavior and fate in the environment largely depends on their physical and chemical properties. Furthermore, antibiotics with a similar structure tend to have a similar pattern of efficacy, toxicity, and eventual side effects [1,5]. Table 1 shows a classification of the main groups of antibiotics based on their structure, also including information on their mode of action, examples of representative compounds of each class, and their main use. It should be noted that many of the antibiotics are commonly used in medicine, both human and animal and, in some cases, also in plants to improve crop production.

### Table 1. Main classes of antibiotics, with their mode of action, examples of compounds, and their main use [5,6].

| Antibiotic Class       | Mode of Action                                      | Examples                        | Main Use                     |
|------------------------|-----------------------------------------------------|---------------------------------|-----------------------------|
| Aminoglycosides        | Inhibition of protein synthesis (Inhibits translation) | Amikacin, Apramycin, Gentamycin, Neomycin, Streptomycin | Veterinary, Veterinary, Human, Veterinary, Plants |
| β-Lactams              | Inhibition of cell wall synthesis                   | Amoxicillin, Cloxacillin, Cefuroxime, Oxacillin | Veterinary, Veterinary, Human, Veterinary |
| Glycopeptides          | Acting on the wall or membrane cell, inhibits peptidoglycan synthesis | Bleomycin, Polymyxins, Teicoplanin, Vancomycin | Human, Human, Veterinary, Human, Veterinary |
| Lincosamides           | Inhibition of protein synthesis by reversibly binding to the 50S ribosomal subunit | Clindamycin, Lincomycin | Humans, Veterinary |
| Macrolides             | Inhibition of protein synthesis by reversibly binding to the 50S ribosomal subunit | Azithromycin, Clarithromycin, Erythromycin, Roxithromycin, Tylosin | Human, Human, Veterinary, Human, Veterinary |
| Quinolones and Fluoroquinolones | Inhibition of DNA replication and transcription | Ciprofloxacin, Enrofloxacin, Flumequine, Ofloxacin | Human, Veterinary, Human, Human |
try of antibiotics into the environment takes place largely through the application of animal manures and slurries on agricultural soils, we will focus on two classes of antibiotics widely used in veterinary medicine: tetracyclines (TCs) and sulfonamides (SAs).

Tetracyclines have been chosen because they are the veterinary antibiotics most widely used in the world, representing 43.4% of total sales in the period 2015–2017 [7]. In the European Union, the use of tetracyclines in veterinary medicine represents 30.4% of the total consumption in this sector [8]. As regards sulfonamides, they have been chosen due to their very high mobility in soils and, therefore, their high potential risk to cause damage from an environmental point of view, although their use is clearly lesser than that of tetracyclines, representing 5.9% of the world consumption in veterinary medicine in 2017 [7], and reaching 9.25% in the European Union [8]. Furthermore, it should be also noted that both tetracyclines and sulfonamides are categorized as highly important antimicrobials for human medicine by the World Health Organization [9].

1.1. Chemical Characteristics of Tetracycline Antibiotics

Table 2 shows the main physicochemical properties of the three tetracycline compounds most typically used in veterinary medicine (tetracycline—TC, oxytetracycline—OTC, and chlortetracycline—CTC). These three antibiotics have high water solubility (231–630 mg L\(^{-1}\)), as well as low octanol-water partition coefficients (\(\text{Log} \, K_{\text{OW}}\) that varies between \(-1.30\) and \(-0.62\)), which indicates that they are hydrophilic compounds.

| Antibiotic Class | Mode of Action | Examples | Main Use       |
|------------------|---------------|----------|----------------|
| Sulfonamides     | Inhibition of the folic acid synthesis | Sulfachloropyridazine | Human, Veterinary |
|                  |               | Sulfadiazine | Veterinary     |
|                  |               | Sulfamethazine | Veterinary     |
|                  |               | Sulfamethoxazole | Veterinary     |
|                  |               | Sulfapyridine | Human          |
| Tetracyclines    | Inhibition of protein synthesis | Chlortetracycline | Veterinary |
|                  |               | Doxycycline | Human, Veterinary |
|                  |               | Oxytetracycline | Human, Veterinary, Plants |
|                  |               | Tetracycline | Human, Veterinary |

Table 1. Cont.

| Antibiotic Class | Mode of Action | Examples | Main Use |
|------------------|---------------|----------|----------|
| Sulfonamides     |               |          |          |
| Tetracyclines    |               |          |          |
| Main characteristics of three different tetracycline antibiotics.

| Common Name | Chemical Structure | Chemical Formula | Molecular Weight (g mol\(^{-1}\)) | \(\text{Log} \, K_{\text{OW}}\) \[^{10}\] | \(\text{pK}_a\) \[^{11}\] | Water Solubility (mg L\(^{-1}\)) \[^{10}\] |
|-------------|--------------------|-----------------|----------------------------------|---------------------------------|----------------|-------------------------------|
| Tetracycline | ![Tetracycline](image) | C\(_{22}\)H\(_{24}\)N\(_5\)O\(_8\) | 444.4 | \(-1.30\) | 3.3–7.8–9.6 | 231 |
| Oxytetracycline | ![Oxytetracycline](image) | C\(_{22}\)H\(_{24}\)N\(_5\)O\(_9\) | 460.4 | \(-0.90\) | 3.2–7.5–8.9 | 313 |
| Chlortetracycline | ![Chlortetracycline](image) | C\(_{22}\)H\(_{23}\)ClN\(_2\)O\(_8\) | 478.9 | \(-0.62\) | 3.3–7.6–9.3 | 630 |

The molecules of these antibiotics from the group of tetracyclines are amphoteric, with three different acid dissociation constants (\(\text{pK}_a\)), which allows that they can exist as cation, zwitterion and/or anion, depending on the pH of the medium. Specifically, the molecule of tetracycline (TC) has three different acidic functional groups, which are tricarbonyl methane (\(\text{pK}_a \approx 3.3\)), phenolic diketone...
(pKₐ ~ 7.8), and the dimethylammonium cation (pKₐ ~ 9.6). Furthermore, the three antibiotics of the group considered in this work present similar pKₐ values, which suggests that TC, OTC, and CTC have a similar pH-dependent speciation (Figure 1). Finally, it should be noted that TCs form complexes with chelating agents such as multivalent metal ions (like Mg²⁺, Ca²⁺, Fe²⁺, Zn²⁺, Al³⁺ and Fe³⁺) and β-diketones [12,13].

![Graph showing the percentage of each species of tetracycline (TC), oxytetracycline (OTC), and chlortetracycline (CTC) as a function of pH.](image)

**Figure 1.** Percentage of each species of tetracycline (TC), oxytetracycline (OTC), and chlortetracycline (CTC) as a function of pH.

### 1.2. Characteristics of Sulfonamide Antibiotics

Table 3 shows the main physicochemical properties of three sulfonamides widely used in veterinary medicine (sulfadiazine—SDZ, sulfamethazine—SMT, and sulfachloropyrydazine—SCP). Sulfonamides are relatively insoluble in water and have a clearly higher value than tetracyclines for the octanol-water partition coefficient (Log KₐOW, Table 3), indicating that these compounds can be considered as hydrophobic.

| Common Name      | Chemical Structure | Chemical Formula | Molecular Weight (g mol⁻¹) | Log KₐOW [10] | pKₐ [11]     | Water Solubility (mg L⁻¹) [10] |
|------------------|--------------------|------------------|-----------------------------|--------------|--------------|-------------------------------|
| Sulfadiazine     | ![Structure](image) | C₁₀H₁₀N₄O₂S      | 250.3                       | -0.09        | 2.10-6.28    | 77                            |
| Sulfachloropyridazine | ![Structure](image) | C₁₀H₈ClN₄O₂S   | 284.7                       | 0.31         | 1.87-5.45    | 35                            |
| Sulfamethazine   | ![Structure](image) | C₁₂H₁₄N₂O₂S      | 278.3                       | 0.89         | 2.07-7.49    | 1500                          |

In a similar way to that described above for TCs, sulfonamides are also amphoteric molecules, with two pKₐ values (Table 3), which causes that depending on the pH of the medium, they can be in cationic, neutral, and/or anionic form (Figure 2). In this sense, its amine nitrogen (N⁺) is protonated at pH ~ 2-2.5, while its amide nitrogen (N⁻) is deprotonated at pH > 5.5. For this reason, most sulfonamides are positively charged under acidic conditions between pH 2-2.5, are neutrally charged between pH 5.5-6, and are negatively charged under alkaline conditions. Finally, these compounds have a lower tendency to chelation compared to TCs [5].
Figure 2. Percentage of each species of sulfadiazine (SDZ), sulfamethazine (SMT), and sulfachlorpyridazine (SCP) as a function of pH.

2. Presence of TCs and SAs in Manures and Slurries

The antibiotics used in veterinary medicine can reach the soil mainly through spreading of manures and slurries used as fertilizers, which is affected by the excretion rates in animals, since the passage through their different digestive systems will determine the degree of degradation of these antibiotics. Table 4 shows excretion rates of various tetracyclines and sulfonamides, which can be considered quite high, ranging between 20–75% for tetracyclines and between 25–87% for sulfonamides.

Antibiotics are frequently detected in unchanged form in manure and slurries from animal farms. The concentrations detected vary depending on the animal species, the nature of the antibiotic, the geographical sampling area, and the type of livestock farm, ranging from a few µg kg$^{-1}$ to hundreds of mg kg$^{-1}$. The highest amounts of antibiotic residues are detected in the fertilizers of farms that work on an industrial scale, compared to family farms [2,4]. In addition, both detection frequencies and antibiotic concentrations are usually higher in pig manures, followed by poultry and cattle [14]. This is mainly because antibiotics are given in higher doses and more frequently to pigs, followed by poultry and cattle [15].

Regarding the main antibiotics detected in fertilizers, Ghirardini et al. [16] conducted a review on the presence of micro-pollutants (including antibiotic residues) in different raw manure and treated fertilizers, based on the results reported in 104 articles published between 1980 and 2019. These investigations were carried out in 20 countries (mainly in the United States, China, Canada, Spain, and Germany). Among all the samples analyzed, 37% referred to cattle manure, 34% to pig manure, 27% to poultry manure and 1% to sheep/goat and horse manure. Focusing on tetracyclines and sulfonamides, the antibiotics most frequently detected in cattle manure were sulfamethazine, followed by chlortetracycline, oxytetracycline, and tetracycline, while in raw manure from poultry they were sulfadiazine, chlortetracycline, and oxytetracycline; finally, in the raw pig manure, they were sulfadiazine, oxytetracycline, chlortetracycline, tetracycline, and sulfamethazine. Similarly, Wohde et al. [17] analyzed the results of 27 different publications since 2000, considering a total of 1568 manure samples from North America (Canada), Europe (Austria, Czech Republic, Denmark, Germany, Italy, and Switzerland), and Asia (China and Japan) and found that sulfamethazine was the active ingredient with the highest percentage of positive results (38.2%), followed by tetracycline (36.7%) and chlortetracycline (29.1%).

It is relevant that tetracycline compounds are generally detected at much higher concentrations than sulfonamides. In this sense, concentrations of up to 764 mg kg$^{-1}$ for chlortetracycline [18], 211 mg kg$^{-1}$ for oxytetracycline, and 300 mg kg$^{-1}$ for tetracycline have been quantified in pig manure [19]. Furthermore, Ghirardini et al. [16] reported mean values of 61.4, 11.2, and 4.1 mg kg$^{-1}$ for chlortetracycline, oxytetracycline, and tetracycline, respectively, in pig manures, and of 10.9 and 3.5 mg kg$^{-1}$ for oxytetracycline and chlortetracycline, respectively, in poultry manure.
However, sulfonamides are generally detected at lower concentrations, and data for high concentrations are only provided for sulfadiazine (91 mg kg\(^{-1}\)) and sulfamethazine (20 mg kg\(^{-1}\)) [20].

As indicated by authors like Spielmeyer [21], both the storage or the utilization of different processes (such as composting or aerobic digestion) to treat manures and/or slurries, could lead to the partial elimination of antibiotic residues, thus reducing the discharge of these compounds into the soil. The effectiveness of these treatments in the elimination of antibiotic residues depends on different parameters and conditions. For example, in the case of manure storage, the antibiotic removal efficiency depends on the time of storage and the nature of the antibiotics. In practice, that time usually varies from 0 to 50 months (average of 9 months) for slurry and between 0 and 48 months (average of 6 months) for solid manure [22]. Regarding antibiotics, TCs tend to be more persistent in fertilizers compared to SAs [23]. Regarding the effectiveness of antibiotic removal during composting, it also depends on different parameters, such as temperature, moisture content, type of substrate used, the coexistence of other contaminants, initial concentrations of antibiotics, the duration of composting, the mixture subjected to composting, and the physicochemical properties of the antibiotics, among others [21,24].

In general, composting is capable of reducing the levels of certain antibiotics in fertilizers, showing a very high elimination of both TCs and SAs, with a removal rate of 70 to 99% [24]. However, despite these high scores, mineralization generally contributes less than 1%, while sorption is considered the main route of removal. Therefore, in cases where compost residues, digestates, or manures are used for soil fertilization, the antibiotics contained in these products could be desorbed and thus incorporated once again into the soil.

Finally, it should be noted that, although some pretreatment techniques could reduce the concentration of antibiotics in manure, in most cases, excreted animal waste enters the farmland unprocessed, as there is no general regulation on the need for pretreatment of manure and slurry before its application to the soil [25]. Furthermore, no limits or quality standards have been established for the concentration of antibiotic residues in manure and plant products [14]. As a consequence, most of the antibiotics used in animal production are released into the environment by applying fertilizers to crop soils as a complement to commercial fertilizers [25].

**Table 4.** Excretion rate (%) as uncharged form of different tetracycline and sulfonamide antibiotics.

| Compound                  | Animal Type | Administration Way | Excretion Ratio (%) | References |
|---------------------------|-------------|--------------------|---------------------|------------|
| Chlortetracycline         | cattle      | Oral (feed)        | 75                  | [26]       |
| Tetracycline              | swine       | Oral (feed)        | 42–72               | [27]       |
| Oxytetracycline           | cattle      | Injection          | 20                  | [28]       |
| Sulfadiazine              | swine       | Oral (gelatin capsules) | 44              | [29]       |
| Sulfamerazine             | swine       | Oral (feed)        | 41–44               | [30]       |
| Sulfachloropyridazine     | swine       | Oral (feed)        | 57–66               | [30]       |
| Sulfadimoxine             | swine       | Oral (feed)        | 36–39               | [30]       |
| Sulfaquinoxaline          | swine       | Oral (feed)        | 83–87               | [30]       |
| Sulfamethazine            | swine       | Injection          | 25                  | [31]       |

In summary, veterinary antibiotics, including tetracyclines and sulfonamides, are poorly absorbed in the gut of the animals, so that a significant proportion of them (up to ~90%) is excreted unchanged through feces and urine. As a consequence, these contaminants are frequently detected in both manures and slurries. Besides, tetracycline compounds are generally detected at much higher concentrations than sulfonamides. The application of different treatment techniques to these wastes, such as composting or aerobic digestion, could significantly reduce their antibiotic content, thus reducing the entry of these pollutants into the soil. However, due to the absence of regulation, in most cases, excreted animal waste enters the farmland unprocessed.
3. Presence of TCs and SAs in Soils

Repeated application of animal manure and sludge on agricultural soils and continuous irrigation with antibiotic-contaminated wastewater result in the introduction of remarkable amounts of antibiotic residues into the terrestrial environment [32,33]. In this sense, different investigations have verified the transfer of antibiotics from fertilizers to agricultural soils. For example, De-Liguoro et al. [34] detected oxytetracycline concentrations of up to 7 µg kg\(^{-1}\) in agricultural soil after the application of cattle manure at a rate of 96 Mg ha\(^{-1}\), while Hamscher et al. [35] reported tetracycline and chlortetracycline concentrations of up to 198.7 and 7.3 µg kg\(^{-1}\), respectively, in fields amended with pig slurry. Furthermore, if the application of contaminated manure to the soil exceeds the dissipation rate of antibiotics, an accumulation of these compounds is expected [36]. In this regard, due to the extensive application of manure as an organic fertilizer on agricultural land, antibiotic residues are frequently detected in crop soils around the world, in concentrations ranging from a few micrograms to several milligrams per kilogram [16,37], as shown in Table 5.

| Country | TC (µg kg\(^{-1}\)) | OTC | CTC (µg kg\(^{-1}\)) | DC (µg kg\(^{-1}\)) | SDZ (µg kg\(^{-1}\)) | SMT (µg kg\(^{-1}\)) | SCP (µg kg\(^{-1}\)) | SMX (µg kg\(^{-1}\)) | Reference |
|---------|----------------------|-----|-------------------|-----------------|-----------------|----------------|----------------|----------------|----------------|
| China   | 22.0                 | 423.0 | 120.0             | 0.6             | 1.7             | 1.2          | [38] |
| China   | 105.0                | 2683.0 | 1079.0            | 2.5             | 0.9             | [39] |
| China   | 189.8                | 613.2  | 2668.9            | [40] |
| China   | 153                  | 571.4  | 10,967.0          | 495.0           | 3.2             | 177.9        | 52.9           | 58.1           | [41] |
| China   | 74.4                 | 79.7   | 104.6             | 85.5            | 74.0            | 54.5         | [42] |
| China   | 60.4                 | 415    | 222.0             | 0.7             | 2.58            | 9.3          | [43] |
| China   | 25.7                 | 31.9   | 161.5             | 184.8           | [44] |
| China   | 976.2                | 1398.5 | 1590.2            | 870.5           | 760.1           | 11.5         | [45] |
| China   | 197.0                | 530.0  | 105.0             | 0.9             | 0.6             | [46] |
| Denmark |                     |       | 15.5              |                 |                 |              | [47] |
| Germany | 443.0                | 27.0   | 93.0              | 4.5             | [48] |
| Korea   | 177.6                | 0.7    | 0.9               | 1.1             | 1.1             | [49] |
| Korea   | 2.9                  | 3.8    | 0.9               | 28.4            | 5.4             | [50] |
| Malaysia| 64.3                 | 105.4  | 34.4              | 45.7            | [51] |
| Spain   | 4.3                  | 20.4   | 2.6               |                 | [53] |
| Spain   | 100                  | 200    | 200               |                 | [54] |
| UK      | 305.0                | 0.8    |                   |                 | [55] |

| Country | TC | OTC | CTC | DC | SDZ | SMT | SCP | SMX |
|---------|----|-----|-----|----|-----|-----|-----|-----|
| China   | 22.0 | 423.0 | 120.0 | 0.6 | 1.7 | 1.2 |
| China   | 105.0 | 2683.0 | 1079.0 | 2.5 | 0.9 | |
| China   | 189.8 | 613.2 | 2668.9 | |
| China   | 153 | 571.4 | 10,967.0 | 495.0 | 3.2 | 177.9 | 52.9 | 58.1 |
| China   | 74.4 | 79.7 | 104.6 | 85.5 | 74.0 | 54.5 |
| China   | 60.4 | 415 | 222.0 | 0.7 | 2.58 | 9.3 |
| China   | 25.7 | 31.9 | 161.5 | 184.8 |
| China   | 976.2 | 1398.5 | 1590.2 | 870.5 | 760.1 | 11.5 |
| China   | 197.0 | 530.0 | 105.0 | 0.9 | 0.6 |
| Denmark | | | 15.5 | |
| Germany | 443.0 | 27.0 | 93.0 | 4.5 |
| Korea   | 177.6 | 0.7 | 0.9 | 1.1 | 1.1 |
| Korea   | 2.9 | 3.8 | 0.9 | 28.4 | 5.4 |
| Malaysia| | | 365.0 | |
| Spain   | 64.3 | 105.4 | 34.4 | 45.7 |
| Spain   | 4.3 | 20.4 | 2.6 |
| Spain   | 100 | |
| UK      | 305.0 | 0.8 | | |

TC: tetracycline; OTC: oxytetracycline; CTC: chlortetracycline; SDZ: sulfadiazine; SMT: sulfamethazine; SCP: sulfachloropyridazine; SMX: sulfamethoxazole.

Regarding the characteristics of the soil and its relations with the presence of antibiotics, contradictory results have been found. On the one hand, Ho et al. [51] obtained significant correlations between pH, total organic carbon content and metal content of the soils and the concentration of antibiotics, which indicates that these soil characteristics play an important role in the fate of antibiotics in the environment. Likewise, Li et al. [42] searched for statistical relations between the levels of TCs and SAs and soil characteristics and found that the concentrations of tetracyclines and sulfonamides were significantly and positively correlated with the organic matter content of the soils, with r values of 0.93 and 0.86, respectively. Contrary, on the other hand, Ok et al. [50] and Sun et al. [46] did not find significant correlations between the content of antibiotics and the chemical properties of the soils. In this sense, Sun et al. [46] indicated that other factors, such as human activity, could have a greater influence on antibiotic residues than soil characteristics.

In conclusion, due to the continuous application of manure and sludge as organic fertilizers in crop fields, residues of tetracyclines and sulfonamides are frequently detected in agricultural soils at concentrations of up to several milligrams per kilogram. Besides, different soil characteristics, such as
organic matter, pH, or metal content, could be closely related to the presence of these pollutants in soils, determining their persistence or dissipation.

4. Dynamics and Fate of Antibiotics in Soils

Once in the soil, antibiotics, like any organic chemical compound, are subjected to a series of physical, chemical, and biological processes taking place in the soil-water system, which depend on the physicochemical properties of the antibiotics, the characteristics of the soil, and weather conditions [3]. All these processes are interrelated and can be categorized into transfer or transport processes and transformation or degradation processes. Retention/transfer processes, such as adsorption/desorption, leaching, runoff, uptake by plants, diffusion, and volatilization, involve movement of the antibiotic from one phase to another in the soil, or within the same phase. Further, transformation processes, such as hydrolysis, photodegradation, biodegradation, oxidation and reduction, involve a structural change of the compound. Among these different processes, adsorption/desorption and degradation are the most relevant in terms of determining the persistence of antibiotics in soils, as well as their transfer from the soil to other environmental compartments, such as water bodies or crops [13,56,57].

4.1. Adsorption/Desorption

For soils and their components under natural conditions, adsorption can be defined as the passage of a solute from an aqueous phase to the surface of a solid phase, without producing changes in the composition of the latter, while desorption is the reverse process [58]. As indicated above, adsorption–desorption is one of the main processes that will determine the persistence and fate of antibiotics in the environment [57]. In this sense, adsorption–desorption determines the retention/mobility of antibiotics in the soil and, consequently, their potential transport to groundwater (leaching), surface water (runoff), and crops (plant uptake) [13,37]. In addition, adsorption can also affect the bioavailability of antibiotics towards soil microorganisms, thus conditioning biodegradation [13]. However, it should be noted that an increase in adsorption does not directly mean a proportional reduction in degradation. Finally, adsorption reduces the antimicrobial potency of antibiotics, while desorption produces a reactivation of that antimicrobial potency. In this regard, it should be also considered that adsorption does not necessarily result in a complete elimination of antimicrobial activity [59].

During the adsorption process, it is assumed that an equilibrium is established between the antibiotic that remains in solution and that adsorbed onto the surfaces of the different soil constituents. This balance can be expressed as:

\[ C_{aq} \leftrightarrow C_s \]

where \( C_s \) is the concentration of antibiotic adsorbed to the solid phase, and \( C_{aq} \) is the concentration of antibiotic present in the solution at equilibrium (not adsorbed).

The relation between \( C_s \) and \( C_{aq} \) in equilibrium is often expressed by the soil–water partition coefficient (\( K_d \), in units L kg\(^{-1}\)):

\[ K_d = \frac{C_s}{C_{aq}} \]

The soil–water partition coefficient (\( K_d \)) is often used to describe the adsorption potential of pollutants and the degree to which they will be transported from the soil to subsurface and groundwater.

Table 6 shows the \( K_d \) values obtained for different antibiotics in different agricultural soils. It is shown that \( K_d \) values reported in the literature are highly variable. In this sense, tetracycline antibiotics present the highest \( K_d \) scores, ranging from 417 to 312,447 L kg\(^{-1}\), which indicates that they are characterized by a high adsorption potential. On the contrary, sulfonamides show weak adsorption to soils, with \( K_d \) values ranging between 0.1 and 70.1 L kg\(^{-1}\) (Table 6).
Table 6. Partition coefficient ($K_d$) for different tetracycline and sulfonamide antibiotics in various soils.

| Compound | pH/OC/eCEC/Clay | $K_d$ (L kg$^{-1}$) | Reference |
|----------|------------------|--------------------|-----------|
| **Tetracyclines** | | | |
| TC | 5.5–6.2/1.1–3.9/13.7–19.9/26–49 | 450–15,278 | [60] |
| TC | 3.8–7.5/0.5–2.9/11.3–26.5/nd | 3102–312,447 | [61] |
| OTC | 5.6–6.3/1.1–1.6/6.7–35.3/5.2–16.9 | 417–1026 | [62] |
| OTC | 3.8–7.5/0.5–2.9/11.3–26.5/nd | 1229–269,097 | [61] |
| OTC | 4.0–7.1/0.8–4.4/16.9–20.2/32–78 | 650–2191 | [63] |
| OTC | 4.7–7.8/0.2–4.3/2.5–40.9/0.4–36.1 | 550–15,849 | [64] |
| OTC | 3.4–7.4/2.2–12.2/1.6–39.3/0.2–52 | 950–2191 | [65] |
| CTC | 3.8–7.5/0.5–2.9/11.3–26.5/nd | 5706–164,973 | [61] |
| CTC | 7.4/0.2/18.7/47.3 | 298 | [66] |
| **Sulfonamides** | | | |
| SDZ | 3.7–6.8/0.67–21.34/0.7–13.8/6.0–68.4 | 0.8–14.3 | [67] |
| SDZ | 4.4–6.7/0.5–2.9/7.4–14.8/16–43 | 0.1–24.3 | [68] |
| SMT | 4.7–7.8/0.2–4.1/3.2–5.4/0.4–36.1 | 1.1–26.3 | [64] |
| SMT | 5.1–6.9/1.1–8.2/7.6–35.6/2–37 | 1.0–5.1 | [69] |
| SMT | 3.7–6.8/0.67–21.34/0.7–13.8/6.0–68.4 | 1.0–32.0 | [67] |
| SMT | 7.4/2.0/18.7/47.3 | 8.2 | [66] |
| SCP | 3.7–6.8/0.67–21.34/0.7–13.8/6.0–68.4 | 0.7–70.1 | [67] |
| SCP | 5.1–6.9/1.1–8.2/7.6–35.6/2–37 | 19–10.6 | [69] |
| SCP | 4.1–5.0/0.9–1.9/1.9–6.6/6–55 | 1.0–4.5 | [70] |
| SCP | 3.4–7.4/2.2–12.2/1.6–39.3/0.2–52 | 0.4–35.0 | [65] |
| SMP | 4.1–7.3/0.3–10.9/3.0–27.7/9–29 | 0.9–26.0 | [71] |
| SMX | 3.7–6.8/0.67–21.34/0.7–13.8/6.0–68.4 | 0.7–28.5 | [67] |
| STZ | 5.1–6.9/1.1–8.2/7.6–35.6/2–37 | 1.1–3.1 | [69] |
| STZ | 3.7–6.8/0.67–21.34/0.7–13.8/6.0–68.4 | 1.0–67.1 | [67] |
| SPY | 7.5/1.6/nd/nd | 1.0 | [72] |

TC: tetracycline; OTC: oxytetracycline; CTC: chlortetracycline; SDZ: sulfadiazine; SMT: sulfamethazine; SCP: sulfachloropyridazine; SMP: sulfamethoxypyridazine; SMX: sulfamethoxazole; STZ: sulfathiazole; SPY: sulfapyridine; OC: organic carbon (%); eCEC: effective cation exchange capacity (cmol kg$^{-1}$); Clay: clay content (%).

$K_d$ values must be interpreted with care, as this parameter is often calculated using a single concentration, while, in most cases, the $K_d$ parameter depends on the concentration and does not exhibit linearity [73]. To avoid this limitation, $K_d$ must be determined by conducting adsorption experiments in which multiple concentrations of contaminants are used to construct adsorption curves, plotting $C_s$ versus $C_{aq}$ [73,74].

Depending on the nature of the adsorbate and the adsorbent (in this case antibiotic and soil, respectively), adsorption curves with different shapes can be observed, and they can be classified into four main categories: type C, type L, type H and type S [75]. The most common of these curves are type C (Linear) and type L. Type C curves are indicative of a constant distribution of the compound between the soil and the solution, which means that the adsorption of the compound is independent of its initial concentration. Therefore, the partition coefficient ($K_d$) is adequate to describe this type of adsorption curves, since, in this case, the value of this parameter is constant for the different concentrations tested. In L-type curves, the relation between the concentration of the compound in solution and the concentration adsorbed decreases as the concentration of the solute increases, giving rise to a concave curve. Therefore, these types of curves (L) suggest a progressive saturation of the available adsorption sites, taking place as the solute concentration increases.

These types of curves are usually modeled using two equations: Freundlich’s equation (Equation (1)) and Langmuir’s equation (Equation (2)).

$$C_s = K_d C_{aq}^{n}$$

(1)
where $C_s$ and $C_{aq}$ are the concentrations of the compound in the soil and in the aqueous phase at equilibrium, respectively; $K_F$ is the Freundlich affinity coefficient, and $n$ (dimensionless) is the Freundlich’s linearity index.

$$C_s = \frac{C_{smax} K_L C_{aq}}{1 + K_L C_{aq}}$$

(2)

where $C_s$ and $C_{aq}$ are the concentrations of the compound in the soil and in the aqueous phase at equilibrium, respectively; $C_{smax}$ is the Langmuir’s maximum adsorption capacity; and $K_L$ is a Langmuir constant relative to the energy of adsorption.

The adsorption curves for tetracycline antibiotics are usually type L or type H (which is a case of type L, obtained when the affinity of the adsorbate for the adsorbent is very high), and they are well modeled by means of the Freundlich equation. In fact, this is described for TC [61,76–80], as well as for OTC [61,63,77,79,81–83], and for CTC [61,77,79,83]. However, the Langmuir model satisfactorily described the adsorption curves just in some occasions [80,83], or it is even stated that the Langmuir model is not adequate to describe all the adsorption curves for TCs in soils [77,82].

The adsorption curves described for sulfonamides are C type, which is indicative of a constant distribution of antibiotics between the soil and the solution, suggesting that the adsorption of sulfonamides is independent of their concentration. Due to the linear nature of the curves, they are satisfactorily described by the $K_d$ parameter, and also by the Freundlich’s $K_F$ parameter, as indicated by numerous authors for SDZ [84,85], for SMT [86–88], and for SCP [65,70,87,89].

Table 7 shows values of the Freundlich’s affinity coefficient related to adsorption ($K_F$) and of the Langmuir parameter $C_{smax}$ which represents the maximum adsorption. As can be seen, $K_F$ and $C_{smax}$ values are much higher for tetracyclines than for sulfonamides, which indicates a lower retention and greater mobility in the soils for the latter.

Table 7. Values for the Freundlich’s affinity coefficient ($K_F$) and maximum adsorption capacity of Langmuir ($C_{smax}$) for tetracycline and sulfonamide antibiotics.

| Compound | pH/Organic Carbon (%) | $K_F$ (L kg$^{-n} n$ mg$^{-1}$) | $C_{smax}$ (mg kg$^{-1}$) | Reference |
|----------|-----------------------|---------------------------------|---------------------------|-----------|
| **Tetracyclines** | | | | |
| TC        | 4.1–7.1/1.1–10.9      | 731–7130                        | 3904–13,243               | [80]      |
| TC        | 3.9–8.2/1.0–8.8       | 240–1601                        | 412–2144                  | [77]      |
| TC        | 7.7–8.6/0.9–3.4       | 778–2375                        | 6810                      | [76]      |
| TC        | 8.3–0.5              | 180                             | 327–2874                  | [79]      |
| OTC       | 3.9–8.2/1.0–8.8       | 105–1362                        | 1330–6050                 | [78]      |
| OTC       | 5.3–8.3/0.3–5.9       | 53–928                          | 3656–13,354               | [83]      |
| CTC       | 3.9–8.2/1.0–8.8       | 323–1988                        | 418–1197                  | [77]      |
| CTC       | 8.3–0.5              | 302                             | 3210                      | [79]      |
| CTC       | 4.1–7.1/1.1–10.9      | 912–9465                        | 5039–14,541               | [83]      |
| **Sulfonamides** | | | | |
| SDZ       | 4.1–7.1/1.1–10.9      | 1.9–11.0                        |                            | [80]      |
| SDZ       | 4.0–5.0/1.3–3.4       | 0.45–2.6                        |                            | [91]      |
| SDZ       | 5.1–7.3/1.0–4.3       | 3.0–9.6                         |                            | [92]      |
| SMT       | 4.1–7.1/1.1–10.9      | 2.9–15.0                        |                            | [93]      |
| SMT       | 5.1–6.9/1.1–8.2       | 0.83–5.98                       |                            | [69]      |
| SMT       | 4.0–5.0/1.3–3.4       | 0.9–3.7                         |                            | [91]      |
| SMT       | 5.1–7.3/1.0–4.3       | 4.6–6.6                         |                            | [92]      |
| SCP       | 4.1–7.1/1.1–10.9      | 0.5–23.2                        |                            | [93]      |
| SCP       | 5.1–6.9/1.1–8.2       | 3.27–14.49                      |                            | [69]      |
| SCP       | 4.0–5.0/1.3–3.4       | 1.9–5.6                         |                            | [91]      |
| SMX       | 5.1–6.9/1.1–8.2       | 2.37–6.75                       |                            | [69]      |
| SMX       | 5.3–8.7/0.1–3.2       | 0.1–4.8                         |                            | [94]      |
| SMX       | 5.8–8.6/0.2–1.4       | 0.1–3.1                         |                            | [95]      |
| SMX       | 5.1–7.3/1.0–4.3       | 2.8–12.1                        |                            | [92]      |
| SFX       | 5.6–6.7/1.2–8.7       | 0.2–2.6                         | 7.4–12.4                  | [96]      |

TC: tetracycline; OTC: oxytetracycline; CTC: chlortetracycline; DC: doxycycline; SDZ: sulfadiazine; SMT: sulfamethazine; SCP: sulfachloropyridazine; SMX: sulfamethoxazole; SFX: sulfisoxazole.
Within tetracyclines, in general, CTC has a higher affinity for soils than TC and OTC. In this sense, different authors who studied adsorption of TCs in soils and sediments obtained the adsorption sequence CTC > TC > OTC [79,97–99]. Therefore, because all three TCs present similar structure, pKₐ and solubility, their different adsorption behavior would be due to differences in their molecular characteristics [99]. In this regard, Avisar et al. [100] indicated that the steric hindrance between the hydroxyl group at the C5 position and the protonated dimethylamino group causes that OTC adsorption is lower than that of TC and CTC. However, neither TC nor CTC have the hydroxyl group, but the CTC adsorption is greater than that of TC. Therefore, steric hindrance cannot be used to explain the higher adsorption of CTC with respect to TC. To obtain a possible explanation, it can be taken into account that Li et al. [79] indicated that the CTC molecule has a significantly higher mean molecular polarity (dipole moment) than that of TC and OTC, while TC and OTC have a similar mean molecular polarity. This higher molecular polarity of CTC would justify its higher affinity for soils [79]. Therefore, the differences in the adsorption behavior among TC, OTC, and CTC would be determined both by their different degrees of steric hindrance and by their differences regarding molecular polarity [79,99].

Another relevant aspect is the desorption of TCs, which is always described as very low (Table 8), showing great irreversibility taking into account the adsorption/desorption processes, judging by the hysteresis indexes (HI), which are generally higher than 1 (Table 8). In this sense, Conde-Cid et al. [80] obtained desorption percentages always lower than 9.0% in the case of TC, <9.9% in the case of OTC, and <5.7% in the case of CTC (Table 8). Values lower than 3% for DC were also reported for agricultural soils of NW Spain [101]. Similar results were also obtained by Fernández-Calviño et al. [102], who found desorption percentages of 9%, 18%, and 14% for TC, OTC, and CTC, respectively, for their soils. Similarly, Pils and Laird [103] studied the adsorption and desorption process of TC and CTC in clay minerals and in humic substances, obtaining desorption percentages lower than 1% in all cases.

Regarding sulfonamides, and depending on the values obtained for both K_{d(ads)} and K_{F(ads)} affinity sequences found were as follows: SDZ < SMT < SCP [104]; SDZ < sulfamethoxazole < SMT < SCP < sulfathiazole [67], for soils in Brazil; and SDZ < SMT < sulfadimethoxin < SCP < sulfaquinoxaline [91], also for acidic soils in Brazil; while Thiele-Bruhn et al. [105] reported the sequence sulfanilamide < SDZ < sulfadimethoxine < SMT < sulfapyridine for soils in Germany with pH values close to neutrality.

This different affinity of each of the SAs for soils suggests that the R substituent at the base of the sulfonamide structure plays an important role in the adsorption process of these compounds. In this sense, it should be noted that SAs are amphoteric molecules, presenting two different values for the acid dissociation constant (pKₐ), so that, depending on the pH of the medium, they can be found in cationic, neutral, and/or anionic form. However, Leal et al. [67] and Conde-Cid et al. [93] did not find a relation between the adsorption of different SAs to soils and the values of the acid dissociation constants (pKₐ). Another characteristic of sulfonamide molecules that also depends on the R substituent at the base of the sulfonamide structure is hydrophobicity. In this sense, the value of the octanol–water partition coefficient (K_{OW}) must be taken into account, and it follows the sequence: SDZ (log K_{OW} = −0.14) < SMT (log K_{OW} = 0.27) < SCP (log K_{OW} = 0.69) [106], suggesting that the adsorption of sulfonamides can be highly influenced by hydrophobicity and that the adsorption is greater as higher is the hydrophobicity of the molecule (higher value of log K_{OW}), in accordance with that indicated by Srinivasan et al. [69] and by Rath et al. [91].

Furthermore, in the same way as in the case of adsorption, desorption curves of sulfonamides are also close to linearity, which is why they are satisfactorily described by both the Linear and the Freundlich models. Table 8 shows values of the desorption parameters K_{d(ads)} and K_{F(ads)}, of desorption percentages, and of hysteresis indices (HI) for different sulfonamides. Data provided by Conde-Cid et al. [90,93] indicate that K_{d(ads)} ranged between 1.6 and 29.3 L kg⁻¹ (average 6.5) for SDZ, between 3.2 and 133.9 L kg⁻¹ (average 13.5) for SMT, and between 5.3 and 65.4 L kg⁻¹ (average 10.9) for SCP, while the K_{F(ads)} values ranged between 0.1 and 36.8 L⁻¹ µmol⁻¹⁻n kg⁻¹ (average 6.4) for SDZ, between 4.3 and
117.6 L\textsuperscript{n} µmol\textsuperscript{1−n} kg\textsuperscript{−1} (average of 15.7) for SMT, and between 5.2 and 73.7 L\textsuperscript{n} µmol\textsuperscript{1−n} kg\textsuperscript{−1} (average of 12.1) for SCP (Table 8). These values are very similar to those obtained by other authors, both for the desorption of SDZ [68,84,107,108], of SMT [109], and of SCP [70]. Furthermore, the scores reported by Conde-Cid et al. [90,93] for the desorption parameters ($K_{d(\text{des})}$ and $K_{F(\text{des})}$) are considerably higher than those obtained for the adsorption parameters ($K_{d(\text{ads})}$ and $K_{F(\text{ads})}$), indicating the presence of positive hysteresis, confirmed by the HI parameter, with values higher than 1 in many cases (Table 8), which means that part of the adsorbed antibiotic was retained in the soil after a desorption cycle [110], in accordance with what was observed by other authors who also studied the adsorption and desorption process of SAs in soils [68,70,108,111].

### Table 8. Values for desorption parameters corresponding to various tetracycline and sulfonamide antibiotics in different soils. $K_{d(\text{des})}$ (L kg\textsuperscript{−1}): coefficient of distribution for desorption; $K_{F(\text{des})}$ (L\textsuperscript{n} mg\textsuperscript{1−n} kg\textsuperscript{−1}): Freundlich’s affinity coefficient for desorption. %\textsubscript{des}: desorption percentage. HI: Hysteresis index.

| Compound | pH/Organic Carbon (%) | $K_{d(\text{des})}$ | $K_{F(\text{des})}$ | %\textsubscript{des} | HI | Reference |
|----------|-----------------------|---------------------|---------------------|-------------------|----|-----------|
| **Tetracyclines** | | | | | | |
| TC | 4.1–7.1/1.1–10.9 | 0.0–8.9 | | | | [80] |
| TC | 4.4–5/2.7–22.7 | 8.0–9.0 | | | | [102] |
| TC | 4.7/2.8 | 0.5 | | | | [112] |
| TC | 5.5–6.2/0.6–2.2 | 1820–13,183 | 0.9–1.4 | | | [113] |
| TC | 6.2/2.2 | 1963 | 1.0 | | | [78] |
| OTC | 4.1–7/1.1–10.9 | 948–13,695 | 0–9.9 | | | [83] |
| OTC | 4.4–4.5/2.7–22.7 | 12.0–18.0 | | | | [102] |
| OTC | 3.2–7.5/0.04–8.9 | 520–10,983 | 3.0–20.0 | | | [114] |
| OTC | 5.4/1.2–1.5 | 1169–3572 | | | | [115] |
| CTC | 4.1–7.1/1.1–10.9 | 1800–33,431 | 0.0–5.7 | | | [83] |
| CTC | 4.4–4.5/2.7–22.7 | 7.0–14.0 | | | | [102] |
| DC | 4.1–7/0.3–10.9 | 3.2–6.4 | 0.7–2.2 | 0.9–2.4 | 0.9–2.4 | [92] |
| DC | 6.9/2.1 | 1079 | 2.6 | | | [116] |
| **Sulfonamides** | | | | | | |
| SDZ | 4.1–7/1.1–10.9 | 1.6–29.3 | 7.0–59.0 | 0.2–2.1 | | [90] |
| SDZ | 4.4–6.7/0.5–2.9 | 1.2–90.4 | 3.2–32.5 | 0.8–1.1 | | [68] |
| SDZ | 4.3–6.5/1.0–1.1 | 0.5–2.4 | 0.9–2.2 | 10.8–38.9 | | [107] |
| SDZ | 4.1–5.0/0.9–1.9 | 0.2–5.0 | | | | [108] |
| SDZ | 6.1–7.6/0.5–1.9 | 4.6–11.6 | 30.3–52.1 | | | [84] |
| SDZ | 4.1–5.0/0.9–1.9 | 0.5–5.0 | | | | [91] |
| SDZ | 5.1–7.3/1.0–4.3 | 0.0–14.9 | | | | [92] |
| SMT | 4.1–7/1.1–10.9 | 3.2–133.9 | 3.0–37.0 | | | [93] |
| SMT | 4.1–5.0/0.9–1.9 | 3.9–12.9 | 1.2–1.4 | | | [111] |
| SMT | 5.2–7/1.2–3.0 | 46.0–85.0 | | | | [117] |
| SMT | 5.1–7.3/1.0–4.3 | 3.2–6.4 | | | | [92] |
| SCP | 4.1–7/1.1–10.9 | 5.3–65.4 | 4.0–33.0 | | | [93] |
| SCP | 4.1–5.0/0.9–1.9 | 1.7–29.0 | 1.0–16.3 | | | [70] |
| SCP | 4.1–5.0/0.9–1.9 | 18.0–37.0 | 1.4–1.7 | | | [91] |
| SDM | 4.1–5.0/0.9–1.9 | 0.9–7.8 | 0.9–1.1 | | | [111] |
| SDM | 4.1–5.0/0.9–1.9 | 0.8–7.8 | 0.9–1.1 | | | [91] |
| SQX | 4.1–5.0/0.9–1.9 | 6.8–27.0 | 1.0–1.1 | | | [111] |
| SMX | 6.1–7.6/0.5–1.9 | 5.4–6.5 | 43.7–48.3 | | | [84] |
| SMX | 5.1–7.3/1.0–4.3 | 7.7–35.9 | | | | [92] |

TC: tetracycline; OTC: oxytetracycline; CTC: chlortetracycline; DC: doxycycline; SDZ: sulfadiazine; SMT: sulfamethazine; SCP: sulfachlorpyridazine; SDM: sulfadimethoxine; SQX: sulfaquinoxaline; SMX: sulfamethoxazole.

These percentages of desorption are always greater than those indicated for tetracyclines. For instance, Conde-Cid et al. [90,93] reported percentages between 7 and 59% (average of 29%) for SDZ, between 3 and 37% (average 23%) for SMT, and between 4 and 33% (average 21%) for SCP.
4.1.1. Influence of Edaphic Variables and Adsorption/Desorption Mechanisms

Tetracycline Antibiotics

The process of adsorption and desorption of TCs to soils depends on multiple edaphic variables, mainly the organic matter content, the multivalent cation content, the clay content and the pH. Data provided by Conde-Cid et al. [80,83] indicate that the soil organic matter content is the property that has the greatest influence on the adsorption and desorption process of TCs, meaning that the soils with a higher content of this constituent are those that presented higher adsorption and lower desorption. In this sense, Conde-Cid et al. [80,83] found that the organic carbon content of the soils explained 38, 28, and 50% of the variance of the \( K_{F_{\text{ads}}} \) parameter for TC, OTC, and CTC, respectively. In addition, organic carbon explained 11% of the variance of the percentage of desorption for TC, as well as 29 and 52% of the variance of \( K_{F_{\text{des}}} \) for OTC and CTC, respectively. Similar results were also obtained by other authors [65,82,118–122], who also indicated that soil organic matter plays a positive role in the adsorption of TCs.

In this regard, it should be noted that the molecules of TC, OTC, and CTC can interact with soil organic matter through different mechanisms: (I) by cation exchange between the positively charged quaternary ammonium functional group of TCs and the \( H^+ \) of the carboxylate groups present on humic surfaces [103]. However, this reaction will not occur significantly at the pH values most frequently found in the environment (4–7), where the predominant form of TC molecules is zwitterionic (+ 0 −, see Figure 1), causing that the positive charges of the quaternary ammonium functional group are neutralized by the anionic functional group of the TCs molecules themselves [123]. (II) They can interact through hydrogen bonds between the multiple polar groups present in the molecules of TCs and the acid groups present on the surfaces of humic acids [103]. This mechanism is pH-dependent, since an increase in the pH value causes an increase in negative charges in the TC molecules and in humic acids, thus generating an increase in coulombic repulsions and, therefore, a decrease in adsorption. Furthermore, an increase in pH could also cause a decrease in the number of protonated sites present on the surfaces of soil organic matter available for hydrogen bonding [123]. (III) They can interact through interactions of the anionic and zwitterionic species of TCs with multivalent cations, giving rise to the formation of ternary complexes (organic matter-multivalent cation-TC molecule), which will be discussed later.

The presence of clay in soils also favors the retention of TCs, as pointed out by Sassman and Lee [61], who studied the adsorption of TC, OTC, and CTC in 8 different soils and observed a higher adsorption in acid soils and soils with high clay content. This influence of clay was also observed by Jones et al. [114] for OTC and by Teixidó et al. [77] for CTC and DC and has been confirmed by Conde-Cid et al. [80,83] in two recent studies with 63 acid soils. In a similar way to that described for organic matter, TCs molecules can interact with soil clays through three different mechanisms: (I) through cation exchange interactions between the surfaces of the clays and the protonated amino group in the molecules of TCs; (II) by surface complexation between the multivalent cations present in clays and the zwitterionic and anionic species of TCs; and (III) through interactions with Al ions exposed at the edges of the clays [124].

Another characteristic of soils that favors the adsorption of TCs is the content of exchangeable multivalent cations. In fact, in studies by Conde-Cid et al. [80,83], the soils with a higher content of exchangeable Al were those with the highest adsorption and lowest desorption of the three TCs discussed above. In this sense, it is well known that TCs molecules can form complexes with different cations, such as \( Ca^{2+}, Mg^{2+}, Fe^{2+}, Zn^{2+}, Fe^{3+}, \) and \( Al^{3+} \) [13]. Therefore, these multivalent cations can act as cationic bridges between the zwitterionic and/or anionic molecules of the antibiotics and the negatively charged surfaces of humic acids and clays, forming ternary complexes of the kinds: humic acid-multivalent cation-antibiotic molecule, or clay-multivalent cation-antibiotic molecule.

In addition, it is also well known that the adsorption of antibiotics is strongly influenced by the pH of the soil [59]. The adsorption of TCs decreases as the pH increases [61,76,77,80,83]. Specifically,
Sassman and Lee [61] studied the effect of pH on the adsorption of TC on a sediment and found that the value of the distribution coefficient \( K_d \) decreased from 1800 to 900 L kg\(^{-1}\) when increasing the pH from 3.5 to 5.5. As explained previously, TCs are amphoteric molecules (Table 1, Figure 1) with three acid dissociation constants (pK\(_a\)), and, therefore, depending on the pH of the medium, the TCs molecules can be in cationic, zwitterionic, and/or anionic form.

In this sense, at very acidic pH values, the cationic species are predominant, while as the pH increases, the proportion of cationic species decreases and the proportion of zwitterionic species increases, up to a pH of approximately 5.5, when the zwitterionic species begin to decrease and the anionic species increase. Therefore, the adsorption of TCs is higher at acidic pH values, where the dominant species are cationic and zwitterionic and where the surfaces of soil organic components, as well as clays, have predominantly negative charges. However, in neutral and alkaline conditions a repulsion will occur between the negative charges of the soil and the anionic species of the TCs.

It should be noted that the adsorption and desorption mechanisms may be affected by similar variables, since significant correlations have been described between the adsorption parameter \( K_{d(ads)} \) and the percentage of desorption, indicating that the soils that present a higher adsorption of TCs are those with less desorption [80,83]. Furthermore, a potential relation between the percentage of desorption and the Freundlich affinity coefficient for adsorption \( K_{F(ads)} \) was also pointed out, indicating that from a certain value of \( K_{F(ads)} \) (=5000 L\(^n\) mol\(^{-1-n}\) kg\(^{-1}\)), desorption remains low and constant, suggesting that the release process could be controlled by the degree of affinity of the antibiotic in the previous adsorption process [80,83].

**Sulfonamide Antibiotics**

The properties of the soils with the greatest influence on the adsorption and desorption process of SAs are the organic matter content (specifically organic carbon -OC- and N contents), texture (specifically sand and clay proportions), and variables related to the exchange complex, such as eCEC, M\(_{e}\), A\(_{e}\), N\(_{e}\), and K\(_{e}\). This has been highlighted by different authors [67,70,84,90,93,94,108,125,126]. For example, Leal et al. [67] studied the adsorption of 5 sulfonamides (including SDZ, SMT, and SCP) in 13 acid soils of Brazil and found that the parameter \( K_{d(ads)} \) was positively and significantly correlated with eCEC, and with OC and clay contents, while it was negatively correlated with the sand content of the soils, in the same way as that reported by Conde-Cid et al. [90,93].

Similarly, Vieira et al. [70] found for their soils that the \( K_{f(ads)} \) parameter was positively correlated with the OC and clay contents, as well as with eCEC and negatively correlated with the sand content. Finally, Doretto and Rath [108] studied soils in which the \( K_{f(ads)} \) parameter for SDZ was positively and significantly correlated with the OC and clay contents, and significantly and negatively correlated with the sand content. This tendency for sulfonamides to be preferentially retained in fine-textured soils was also previously highlighted by Thiele-Bruhn et al. [105].

By means of multiple regression procedures, different equations have been obtained that denote that the organic matter content is the variable with the highest influence on the processes of adsorption and desorption of SAs. In this sense, Conde-Cid et al. [90,93] reported that the OC content explained 82, 80, and 79% of the variance of \( K_{d(ads)} \) for SDZ, SMT, and SCP, respectively, as well as 63, 77, and 77% of the variance of \( K_{d(ads)} \) for SDZ, SMT, and SCP, respectively. Similar studies focused on SMT adsorption in soils of different characteristics, with pH between 5.4 and 8.2, and OC content between 0.1 and 3.8% [86], also indicate that the OC content was the edaphic variable explaining a higher percentage of the variance of \( K_{d(ads)} \), proposing the following model: \( K_{d(ads)} = 0.81 * \text{OC} + 0.38 \) (R\(^2\) = 0.92). Similarly, Chu et al. [117] also proposed for SMT the model \( K_{d(ads)} = 0.706 + 0.0316 * \text{OC} - 0.160 * \text{pH} - 4.42 * \text{SMTC} \) (R\(^2\) = 0.78), with SMTC being the initial concentration of SMT. In addition, they indicated that the OC content was the most important variable for the correct prediction of \( K_{d(ads)} \) by means of the model.

Finally, Laak et al. [65] studied the adsorption of SCP in 11 soils in Netherlands, and found that the OC content explained 29% of the variance of \( K_{d(ads)} \). Therefore, as a result of the previous studies, it is clear that the OC content is the main characteristic of the soil that determines the adsorption of
sulfonamides, so that the soils with a higher content of this constituent are those that present a greater adsorption and less desorption.

The linear nature of the adsorption curves obtained and the strong influence of the soil organic matter content and the degree of hydrophobicity of the molecules on the adsorption process indicate that at pH values lower than the $pK_{a2}$ of sulfonamides (therefore at acidic pH), where the non-ionized forms of the molecules are predominant, hydrophobic partitioning is the main mechanism that governs the adsorption of sulfonamides, with organic matter acting as a non-polar phase, in accordance with what was previously indicated by other authors [69,86,91,127]. However, in neutral and alkaline soils, at pH values higher than the $pK_{a2}$ of these molecules, where SAs are mainly in anionic form, this adsorption related to hydrophobic partitioning can be counteracted by an electrostatic repulsion between the anionic forms of sulfonamides and the negatively charged soil surfaces, thus leading to less adsorption [86]. However, at the same time, in alkaline soils, other adsorption mechanisms can also take place, such as those due to cationic bridges, where different polyvalent cations can act as a bridge between the anionic molecules of sulfonamides and the negative charges of clays of non-crystalline compounds, and of organic compounds present in soils [86].

Furthermore, in highly acidic soils, where sulfonamides are predominantly in cationic form, these antibiotics can also be adsorbed to deprotonated carboxylic groups of the organic matter through electrostatic interactions [73]. In addition, Hu et al. [84] indicated that sulfonamides can be adsorbed to soils through hydrogen bonds and $\pi-\pi$ interactions, although these mechanisms do not seem to be of high relevance.

4.2. Degradation

Degradation is a process that involves transformation and often plays an important role in the dissipation and general elimination of antibiotic residues in the environment. The degradation of antibiotics can occur through both abiotic processes (hydrolysis, photodegradation, oxidation, and reduction) and biotic processes (biodegradation). Among the different degradation mechanisms, hydrolysis, photodegradation, and biodegradation are considered the most important pathways for antibiotics in soils. The magnitude of each of these processes depends largely on the physical, chemical, and microbiological properties of the soil (pH, organic carbon content, nutritional status, presence of specific degrading bacteria, soil type, etc.), on environmental factors (temperature, rain, humidity, and intensity of solar radiation), and on properties of the antibiotics (solubility, stability, hydrophobicity, etc.) [12,13,22]. Thus, depending on these various aspects, the degradation rates indicated in the literature for different antibiotics are very different, with half-lives ranging from a few days to several months [22].

4.2.1. Hydrolysis

Hydrolysis is generally considered one of the most important processes that determine the abiotic degradation of antibiotics, constituting a significant pathway for the degradation of some of them in the environment [13,128]. This degradation mechanism largely depends on the properties of the antibiotic compound and on different environmental factors, especially temperature and pH [6,12,128,129].

Tetracyclines are susceptible to hydrolysis, but to a lesser degree than other antibiotics, such as $\beta$-lactams [130,131]. Tetracycline compounds are quite stable at acidic pH values, while they are unstable under neutral and alkaline conditions [13]. Furthermore, an increase in temperature also accelerates the hydrolysis of the tetracyclines. In this sense, Xuan et al. [132] investigated the hydrolysis of oxytetracycline in aqueous solutions and found that an increase in temperature from 4 to 60 °C led to a decrease in the half-life value from 120 to 0.15 days.

On the other hand, sulfonamides are resistant to hydrolysis, being relatively stable in the dark [1,13,128].
4.2.2. Photodegradation

Photodegradation is often considered another important abiotic degradation process [2,13], resulting in the decomposition of the antibiotic as a consequence of solar radiation. Therefore, antibiotics could undergo direct photodegradation through direct absorption of photons if there is an overlap between the absorption spectra of the antibiotic and the irradiation spectrum. Consequently, antibiotics can only undergo direct photodegradation if they absorb light at $\lambda > 290$ nm [133]. In this sense, the most widely used veterinary antibiotics, such as tetracyclines, sulfonamides, fluoroquinolones, macrolides, and $\beta$-lactams, are susceptible to photodegradation [134–138]. In addition, the extent of this process depends largely on the molecular composition of the antibiotic, as well as on different environmental factors, such as pH, water hardness (in the case of a liquid medium), type of matrix, temperature, location, season, and latitude [1,136,139].

Although photodegradation can play an important role in the attenuation of antibiotics in surface waters, in the terrestrial environment, it is likely to occur just in the upper layer of the soil surface. Therefore, the persistence of photodegradable antibiotics in soils will be affected and depend on agricultural practices, such as the timing and depth of plowing [22]. Furthermore, it is also well known that adsorption on soil particles, as well as penetration into soil pores, protect antibiotics from photodegradation [59]. In this sense, Thiele-Bruhn and Peters [140] investigated the photodegradation of nine antibiotics (oxytetracycline, chlortetracycline, sulfanilamide, sulfadimidine, sulfadiazine, sulfadimethoxine, sulfapyridine, fenbendazole, and $p$-aminobenzoic acid) in the soil surface and observed that the total concentration of photodegradable antibiotics was generally lower on the soil surface compared to that achieved in water.

Tables 9 and 10 show data on the degradation kinetic constant ($k$) and on the half-life ($t_{1/2}$), for antibiotics of the class of sulfonamides and tetracyclines, respectively.

The half-lives obtained for TC are highly variable, oscillating, under simulated light, in the range 4–866 min (Table 9). For OTC, it ranged between 10–102 min, and for CTC, it ranged between 11–134 min (Table 9). The degree of acidity of the medium has a great influence on this degradation, decreasing the half-lives as the pH increases [141–146]. This increase in the rate of photolysis with the increase in pH is due to different causes:

(a) TCs are amphoteric molecules, with three acid dissociation constants ($pK_a$), therefore, depending on the pH of the medium, they can be found in cationic, zwitterionic, and/or anionic form. For example, at pH 4.0, 17% of TC species are in the cationic form, while at pH 7.2 the cationic TC species only represent 0.01%, with percentage distribution being very similar for OTC and CTC. At the same time, increasing the pH from 4.0 to 7.2 causes a progressive decrease in the zwitterionic forms and a significant increase in the negatively charged forms. Furthermore, different researchers indicated that the degree of absorption of light radiation of the anionic species of TCs overlaps more with the spectrum of simulated sunlight, compared to the neutral and cationic species [142–144]. Therefore, an increase in pH is expected to favor direct photolysis of CTs.

(b) An increase in pH gives rise to an increase in the concentration of OH$^-$ ions, which react with the hydroxyl radicals (HO·) generated by the presence of the TCs molecules in the solution, producing highly reactive oxygen species (O$^-$), according to the following equation proposed by Liu et al. [147]:

$$\text{HO}^- + \text{OH}^- \rightarrow \text{O}^- + \text{H}_2\text{O}$$

Therefore, the increase in pH favors the formation of O$^-$. Taking into account that negatively charged TCs (which have a high electrical density in the ring structure) tend to attract reactive species such as HO· or O -, the increase in pH may thus finally facilitate photolysis [143].
(c) During the photolysis of TCs, H$_2$O$_2$ is also formed, which can also lead to the formation of HO-radicals as a consequence of the photolysis of the peroxide bond (-O-O-) [141]:

$$\text{H}_2\text{O}_2 + h\nu \rightarrow 2\text{HO}^-$$

This generation of H$_2$O$_2$ during photolysis increases with increasing pH, also justifying the higher rate of degradation at higher pH values.

Another factor that can affect photolysis is the presence of inorganic substances, which can act as photosensitizers, making TCs more sensitive to light. In this sense, Jiao et al. [144] observed that the presence of nitrates increased TC photolysis, while Werner et al. [145] indicated that TC can also form complexes with Ca and Mg, thus accelerating photolysis. In fact, Leal et al. [148] and Xuan et al. [132] reported that the presence of these cations had a significant influence on the degradation process for OTC.

Sulfonamides show generally higher half-lives than TCs, but their values are also highly variable, ranging between 14 and 5064 min (Table 10). Small differences in the results obtained by different authors can be attributed to diversity in aspects of the methodology used in each of the studies, such as the intensity of the light, the type of light source, the initial concentration of antibiotic, or the temperature [135,149,150].

In general, the sequences of photolytic degradation are SCP > SDZ ≈ SMT [135,151], indicating that SCP degrades more rapidly, with a half-life of 7 h, followed by SDZ and SMT, with half-lives of 10.1 and 11.5 h, respectively [148]. This higher degradation of SCP is mainly due to the presence of Cl atoms in its molecule, leading to the formation of eventual $p$-$\pi$ conjugations between the pairs of electrons present in Cl and the $\pi$ electrons present in the diazine ring, thus increasing the photolytic reactivity of the SCP molecule [152].

The effect of pH on the photolysis of sulfonamides has been studied by different authors [151–156]. In this sense, Periša et al. [155] studied the photolysis of SDZ and SMT at pH 4 and 8 and observed that the kinetic constant ($k$) increased with increasing pH, going from 0.0871 h$^{-1}$ to 0.3650 h$^{-1}$ for SDZ and from 0.0300 h$^{-1}$ to 0.1710 h$^{-1}$ for SMT. The effect of pH can be different depending on the sulfonamide in question. Specifically, the degradation of SDZ and SMT increased considerably with increasing pH, while for SCP, the observed half-lives did not change with increasing pH [141]. This effect of pH in the photolysis of SAs is due to different causes.

(a) On the one hand, as in the case of TCs, SAs are amphoteric molecules, presenting two acid dissociation constants (pKa), therefore, depending on the pH of the medium, one or other species of these compounds (cationic, neutral, and/or anionic) will dominate. In this sense, Boreen et al. [157] pointed out that the different species of SAs have different reactivity to light, indicating that the quantum yield (moles of a compound that are transformed per mole of photons that are absorbed by the compound) is 17, 3, and 8 times higher for the anionic species of SMT, SDZ, and SCP, respectively, than for the neutral species. Baeza and Knappe [158] also indicate that photolysis is higher for anionic species in relation to the neutral molecules. In this sense, at pH 4, 98%, 99%, and 96% of the species of SDZ, SMT, and SCP, respectively, are in neutral form. However, as the pH increases, the proportion of neutral species decreases, at the same time as the proportion of anionic species increases. Thus, at pH 7.2, the anionic species represent 89%, 34%, and 98% for SDZ, SMT, and SCP, respectively, thus justifying an increase in direct photolysis with increasing pH.

(b) On the other hand, an increase in pH also leads to an increase in indirect photolysis, favoring the oxidation of these antibiotics due to the generation of highly reactive free radicals [159]. This is due to the increase in the concentration of OH$^-$ ions available to react with hydroxyl radicals (OH$^-$), which are generated by the presence of SAs molecules in the solution, thus increasing the generation of reactive species O$^-$ [147].
Different elements and compounds can act as photosensitizers, promoting the photolysis of SAs [160–163]. However, other studies have shown that different compounds, such as NaCl, NaNO₃, Na₂HPO₄, and ZnCl₂, do not exert influence on the photodegradation process of sulfonamides, contrary to the effect due to the presence of humic acids [151], which do act as photosensitizers [162,164].

Table 9. Velocity constant (k) and half-life (t₁/₂) values obtained by different authors for photodegradation of tetracycline antibiotics in aqueous media.

| Compound | pH | Light Source | Light Intensity (W m⁻²) | k (min⁻¹) | t₁/₂ (min) | Reference |
|----------|----|--------------|-------------------------|-----------|------------|-----------|
| TC 4     | 4  | Xenon lamp   | 550                     | 0.0030    | 229        | [146]     |
| TC 5.5   | 5.5| Xenon lamp   | 550                     | 0.0060    | 126        | [146]     |
| TC 7.2   | 7.2| Xenon lamp   | 550                     | 0.0500    | 14         | [146]     |
| TC 4     | 4  | Mercury lamp | 500                     | 0.0020    | 347        | [144]     |
| TC 6     | 6  | Mercury lamp | 500                     | 0.0025    | 277        | [144]     |
| TC 7     | 7  | Mercury lamp | 500                     | 0.0253    | 27         | [144]     |
| TC 4     | 4  | Mercury lamp | 500                     | 0.1801    | 4          | [144]     |
| TC 6     | 6  | Xenon lamp   | 500                     | 0.0008    | 866        | [139]     |
| TC 7     | 7  | Xenon lamp   | 500                     | 0.0022    | 315        | [139]     |
| TC 8     | 8  | Xenon lamp   | 500                     | 0.0012    | 165        | [139]     |
| TC 10    | 10 | Xenon lamp   | 500                     | 0.0249    | 28         | [139]     |
| OTC 4    | 4  | Xenon lamp   | 550                     | 0.0070    | 101        | [146]     |
| OTC 5.5  | 5.5| Xenon lamp   | 550                     | 0.0170    | 42         | [146]     |
| OTC 7.2  | 7.2| Xenon lamp   | 550                     | 0.0390    | 18         | [146]     |
| OTC 4    | 4  | Mercury lamp | 500                     | 0.0068    | 102        | [143]     |
| OTC 6    | 6  | Mercury lamp | 500                     | 0.0089    | 78         | [143]     |
| OTC 7    | 7  | Mercury lamp | 500                     | 0.0186    | 37         | [143]     |
| OTC 9    | 9  | Mercury lamp | 500                     | 0.0692    | 10         | [143]     |
| CTC 4    | 4  | Xenon lamp   | 550                     | 0.0050    | 134        | [146]     |
| CTC 5.5  | 5.5| Xenon lamp   | 550                     | 0.0070    | 104        | [146]     |
| CTC 7.2  | 7.2| Xenon lamp   | 550                     | 0.0630    | 11         | [146]     |
| CTC 7.3  | 7.3| Xenon lamp   | 150                     | 0.0081    | 86         | [165]     |

TC: tetracycline; OTC: oxytetracycline; CTC: chlortetracycline.

Table 10. Velocity constant (k) and half-life (t₁/₂) values obtained by different authors for photodegradation of sulfonamide antibiotics in aqueous media.

| Compound | pH | Light Source | Light Intensity (W m⁻²) | k (min⁻¹) | t₁/₂ (min) | Reference |
|----------|----|--------------|-------------------------|-----------|------------|-----------|
| SDZ 4    | 4  | Xenon lamp   | 550                     | 0.0002    | 4230       | [151]     |
| SDZ 5.5  | 5.5| Xenon lamp   | 550                     | 0.0006    | 1146       | [151]     |
| SDZ 7.2  | 7.2| Xenon lamp   | 550                     | 0.0009    | 792        | [151]     |
| SDZ 5.5  | 5.5| Xenon lamp   | 550                     | 0.0009    | 792        | [151]     |
| SDZ 8    | 8  | Xenon lamp   | 500                     | 0.0006    | 1124       | [161]     |
| SDZ 7.9  | 7.9| Xenon lamp   | 500                     | 0.0015    | 462        | [161]     |
| SDZ 8.1  | 8.1| Xenon lamp   | 500                     | 0.0022    | 320        | [161]     |
| SDZ 8.3  | 8.3| Xenon lamp   | 500                     | 0.0037    | 189        | [161]     |
| SDZ 7    | 7  | Xenon lamp   | 500                     | 0.0043    | 1920       | [161]     |
| SDZ 6.7  | 6.7| Xenon lamp   | 500                     | 0.0043    | 161        | [166]     |
| SDZ 4    | 4  | Xenon lamp   | 500                     | 0.0015    | 476        | [155]     |
| SDZ 8    | 8  | Xenon lamp   | 500                     | 0.0061    | 114        | [155]     |
| SMT 4    | 4  | Xenon lamp   | 550                     | 0.0001    | 5064       | [151]     |
| SMT 5.5  | 5.5| Xenon lamp   | 550                     | 0.0004    | 1950       | [151]     |
| SMT 7.2  | 7.2| Xenon lamp   | 550                     | 0.0012    | 564        | [151]     |
| SMT 5.5  | 5.5| Xenon lamp   | 250                     | 0.0004    | 690        | [135]     |
| SMT 6.7  | 6.7| Xenon lamp   | 500                     | 0.0044    | 159        | [166]     |
| SMT 4    | 4  | Xenon lamp   | 500                     | 0.0005    | 1386       | [155]     |
| SMT 8    | 8  | Xenon lamp   | 500                     | 0.0029    | 243        | [155]     |
Table 10. Cont.

| Compound | pH | Light Source | Light Intensity (W m\(^{-2}\)) | \(k\) (min\(^{-1}\)) | \(t_{1/2}\) (min) | Reference |
|----------|----|--------------|----------------------------------|----------------------|-----------------|-----------|
| SCP      | 4  | Xenon lamp   | 550                              | 0.0095               | 72              | [151]     |
| SCP      | 5.5| Xenon lamp   | 550                              | 0.0043               | 162             | [151]     |
| SCP      | 7.2| Xenon lamp   | 550                              | 0.0050               | 138             | [151]     |
| SCP      | 5.5| Xenon lamp   | 250                              |                      | 420             | [135]     |
| SMX      | 6.7| Xenon lamp   | 500                              | 0.0031               | 227             | [166]     |
| SMX      | 5.5| Xenon lamp   | 750                              | 0.0508               | 14              | [136]     |
| STZ      | 5.5| Xenon lamp   | 250                              |                      | 183             | [135]     |
| STZ      | 6.7| Xenon lamp   | 500                              | 0.0093               | 75              | [166]     |
| SDM      | 5.5| Xenon lamp   | 250                              |                      | 738             | [135]     |
| SMR      | 5.5| Xenon lamp   | 250                              |                      | 672             | [135]     |
| SMP      | 6.7| Xenon lamp   | 500                              | 0.0085               | 82              | [166]     |
| SND      | 6.7| Xenon lamp   | 500                              | 0.0258               | 27              | [166]     |
| SGD      | 6.7| Xenon lamp   | 500                              | 0.0050               | 127             | [166]     |

SDZ: sulfadiazine; SMT: sulfamethazine; SCP: sulfachloropyridazine; SMX: sulfamethoxazole; STZ: sulfathiazole; SDM: sulfadimethoxine; SMR: sulfamerazine; SMP: sulfamethoxypyridazine; SND: sulfanilamide; SGD: sulfaguanidine.

4.2.3. Biodegradation

Biodegradation of antibiotics in soils will take place mainly through the action of native soil microbial populations, including bacteria, algae, or fungi [13,33]. Many antibiotics can be susceptible to enzymatic transformation reactions, such as oxidative decarboxylation and hydroxylation [59], but a significant number of studies indicate that the most relevant veterinary antibiotics are resistant to biodegradation [1]. In this sense, Alexy et al. [167] explored the biodegradability of 18 antibiotics, including \(\beta\)-lactams, tetracyclines, macrolides, sulfonamides, quinolones, lincosamides, and aminoglycosides, among others, and concluded that none of the antibiotics were readily biodegradable.

Additionally, Kim et al. [168] indicated that no evidence of biodegradation of tetracycline was observed during a biodegradability test. Furthermore, Ingerslev and Sørensen [169], after investigating 12 sulfonamides, concluded that these substances are not readily biodegradable. On the contrary, other investigations have shown the biodegradability of certain antibiotics and that, in addition, the degree of biodegradation depends largely on the physicochemical properties of the antibiotics, such as solubility, structure, soil adsorption capacity, capacity of fixation to the pores of the soil matrix, and on the nature of soil properties [12]. In this sense, Maki et al. [170] investigated the biodegradation of five antibiotics (ampicillin, doxycycline, josamycin, oxytetracycline, and thiamphenicol) and found that doxycycline and oxytetracycline were biodegraded in percentages of 68% and 54%, respectively, in 21 days. The causes of these contradictory results on the biodegradability of antibiotics may be the differences in the microbial activity of the matrix, the inoculum used in the case of laboratory experiments, and the methods used to assess degradation [171]. Furthermore, the duration of the experiment may be another important reason for these opposite results. In this sense, Adamek et al. [172] stated that, in some cases, the biodegradation of antibiotics was preceded by a period necessary for the adaptation of microorganisms to these compounds.

Regarding the environmental factors that affect the biodegradation process of antibiotics, it is worth highlighting the temperature. In this sense, it is well known that lower temperatures reduce the degradation rate of antibiotics [173].

Further, it should be noted that the biodegradation products can present a similar toxicity or even be more toxic to the organisms present in the environment than the original compound, as has been shown for several metabolites of fluoroquinolones [59] and tetracyclines [174]. Moreover, the decrease in the concentration of certain antibiotics of different classes is not always reflected in a decrease in toxicity on the microbial flora [59].

According to the data in the literature, biodegradation could be of less importance in the dissipation of antibiotics in the short term; however, the biodegradation of antibiotics will determine the long-term
processes of these compounds in soils. Furthermore, the application of manure and slurry, which have a high microbial content, can increase the microbial degradation of antibiotics in soils [13,36].

As noted above, Ingerslev and Sørensen [169] concluded that sulfonamides are not readily biodegradable, and similarly, Biošić et al. [162] studied the biotic and abiotic degradation of SDZ and SMT, also confirming that these compounds are resistant to biodegradation. However, other authors did observe biodegradation for sulfonamides [172,175]. These contradictions may be related to differences in experimental conditions, such as the duration of the experiment. It should be noted that Adamek et al. [172] indicated that in certain cases the biodegradation of sulfonamides did not start in a relevant way until a previous period had elapsed, which on such occasions was necessary for the adaptation of microorganisms to these antibiotics.

In summary, tetracyclines have a very high affinity for soil components, showing adsorption percentages close to 100% and desorption percentages less than 10% in most cases. On the contrary, sulfonamides show low adsorption and high desorption, being considered the most mobile antibiotics in the soil. This lower interaction of sulfonamides with soils is mainly due to the fact that sulfonamide molecules only have aniline and amide groups, while tetracycline molecules have multiple functional groups, whose combined action results in a high affinity for the different soil components through multiple adsorption mechanisms, such as cation exchange, surface complexation, cationic bridging and hydrogen bonds, among others, which are of little importance in the case of sulfonamides.

The adsorption and desorption process of tetracyclines depends on multiple edaphic variables. In this sense, the organic matter content, the multivalent cations content, and the clay content favor the retention of these compounds, while an increase in pH leads to a decrease in adsorption. Regarding sulfonamides, its retention is mainly controlled by the organic matter content, since the main mechanism of adsorption of these compounds is hydrophobic partitioning, with soil organic matter acting as the non-polar phase.

Regarding degradation, sulfonamides are resistant to hydrolysis, while tetracyclines are quite stable at acidic pH values, but they are unstable under neutral and alkaline conditions. Furthermore, tetracyclines are more susceptible to photodegradation than sulfonamides. In addition, the photodegradation rate of both antibiotic classes is highly pH-dependent, being favored in alkaline conditions. Finally, both tetracyclines and sulfonamides are not easily degraded by soil microorganisms, so biodegradation could be of less importance in the dissipation of these pollutants in the short term; however, this degradation mechanism could determine the long-term persistence of these compounds in soils.

5. Environmental Risks Associated to the Presence of Tetracycline and Sulfonamide Antibiotics

The presence of antibiotics in soils generates three fundamental types of environmental risks that will be considered in this section: transport of antibiotics to waterbodies causing their contamination, negative influence on soil microorganisms, and introduction of these antibiotics in the food chain through crops.

5.1. Transport of Antibiotics and Presence in Waterbodies

The processes of adsorption/desorption affecting to antibiotics in soils condition their transport to the various kinds of waterbodies. The presence of antibiotics in these waters can generate public health and ecological problems, making their transport and accumulation very important aspects to take into account from both points of view. In this sense, tetracycline compounds have a higher affinity for soil particles, tending to be more stable and accumulate in the edaphic compartment, compared to sulfonamides, that are more mobile and therefore more susceptible to leached into groundwater or be transported with subsurface or surface runoff [13,176].

Due to their high retention onto soils, transport studies using column experiments are not considered adequate for tetracyclines, since the conditions to be used would be very unrealistic both in terms of concentrations of tetracyclines used and in relation to the dimensions of the
columns, which would need to be very small. This is the reason why most column experiments refer to sulfonamides.

The mobility of sulfonamides studied in transport experiments with columns decreases as the organic matter content of the soils increases, as has been reported by Vithanage et al. [177]. These authors found that the mass of SMT retained increased as a function of the OC content of the soils, varying from 0.16 mg for a soil with 0.4% OC, to 0.19 mg for a soil with 2.9% OC. Similar results were obtained by Srinivasan and Sarmah [88] and by Conde-Cid et al. [104], who confirmed that soils with a lower organic matter content gave rise to curves that were narrow and high in shape, indicating little retention, while soils richer in organic matter gave rise to more elongated and flat curves, characteristics of a higher retention. The descriptive parameters of the breakthrough curves confirm these observations. In this sense, values higher than 1 are generally obtained for the retardation factors ($R$), confirming that the sulfonamides suffer delay with respect to an inert tracer (Br$^-$). Furthermore, the value of the $R$ parameter increases as the organic carbon content of soils increases. This same trend was also observed for the mean time of elution of the solute ($\tau$) [104].

Comparing different sulfonamides, starting with SDZ, in the case of a soil with a low organic matter content (1.1% OC), the maximum relative concentration ($C/C_0$) at the outlet of the column was 0.9, indicating low retention, since $C/C_0 = 1$ means that retention is zero. However, for a soil with a high organic matter content (10.9% OC), the breakthrough curve is clearly flatter, with a maximum value for $C/C_0$ less than 0.2, which indicates a high retention [104]. Regarding SMT, this antibiotic suffers higher retention than SDZ, and this even in soils with low organic matter content (1.1% OC), where the maximum for $C/C_0$ is less than 0.5, while in soils rich in organic matter (10.9% OC) breakthrough curves are practically flat [104]. Finally, the retention observed for SCP is even higher than for SMT, with a maximum value for $C/C_0$ less than 0.5 for soils poor in organic matter, while SCP is practically not detected at the outlet of the column in the case of soils richer in organic matter [104].

Results obtained by Park and Huwe [178], who studied the transport of different sulfonamides (sulfamethoxazole, sulfadimethoxine and SMT) in agricultural acid soils with OC contents between 2.2 and 4.0%, were similar. These authors also found variations in the form of the curves for each of the soils, as well as in the delay in the exit of the maximum relative concentration ($C/C_0$) for the different sulfonamides. Moreover, Srinivasan and Sarmah [88] investigated the transport of sulfamethoxazole, SMT and SCP in two acid soils with different organic matter contents (2.1 and 4.0% OC), obtaining that the outflow of the three SAs was affected by a greater delay with respect to the inert tracer in the soil with a higher organic matter content. Finally, Kurwadkar et al. [179] investigated the transport of seven SAs in different agricultural soils, at different pH values, obtaining that under acidic conditions, the SAs were practically immobile in soils with high OC and eCEC contents, while they were relatively mobile in the other soils, in a similar way to what was obtained by Conde-Cid et al. [104]. Furthermore, Kurwadkar et al. [179] also observed a higher retention for SCP than for SMT.

Table 11 shows data on the presence of tetracyclines and sulfonamides in surface and groundwater. Both types of antibiotics are usually detected in water, despite their different behavior in terms of mobility in soils. The presence of tetracyclines in water (antibiotics characterized by restricted mobility in soils) would be related to their higher use with respect to sulfonamides. Furthermore, as shown in Table 11, the concentrations, both for SAs and TCs, vary strongly among the different samples. This may be mainly related to the different rates of use of each of the antibiotics in each of the sampled areas, with the agricultural and livestock activities of the different areas, as well as with their climatic conditions.
Table 11. Maximum concentrations (ng L\(^{-1}\)) of tetracycline and sulfonamide antibiotics detected in samples of surface- and groundwater.

| Country | TC | OTC | CTC | DC | SDZ | SMT | SCP | SMX | Reference |
|---------|----|-----|-----|----|-----|-----|-----|-----|-----------|
| Surface water |     |     |     |     |     |     |     |     |           |
| China    | 114 | 85  | 17  | 47 | 41  | 623 | 54  | 55  | [180]     |
| China    | 1451| 2797| 876 | 500| 172 | 715 | 560 | 133 | [181]     |
| China    | 100 | 63  | 48  | 33 | 25  | 28  | 133 | 58  | [182]     |
| China    | 190 | 221 | 1037| 326| 776 | 58  |     |     | [184]     |
| China    | 16  |     |     |    | 16  | 940 |     |     | [185]     |
| China    | 101 | 55  | 5   | 2  |     |     |     |     | [186]     |
| China    | 2   | 23  | 4   | 6  | 72  | 89  | 57  |     | [187]     |
| Ghana    | 30  | 26  | 44  | 68 |     |     |     |     | 2861      |
| Luxembourg | 8  | 7   |     |    |     |     |     |     | [189]     |
| Spain    |     |     |     |    |     |     |     |     | [180]     |
| Spain    | 87  | 27  | 18  | 21 | 23  | 55  |     |     | [191]     |
| Spain    |     |     |     |    | 56  | 64  | 2   |     | [192]     |
| UK       | 4490|     |     |    | 4130|     |     |     | [193]     |
| USA      | 20  | 10  | 40  | 20 |     |     |     |     | 80        |
| USA      | 110 | 340 | 690 | 220| 1900| 220 |     |     | [194]     |
| Groundwater |     |     |     |    |     |     |     |     |           |
| China    | 23  | 19  | 31  | 20 | 2   | 40  |     |     | [183]     |
| China    | 48  | 39  | 76  | 39 | 49  | 117 | 250 |     | [196]     |
| Netherlands | 2  | 13  |     |    | 18  |     |     |     | [197]     |
| Spain    | 7   | 107 |     |    | 312 |     |     |     | [198]     |
| USA      |     |     |     |    | 220 |     |     |     | [195]     |

TC: tetracycline; OTC: oxytetracycline; CTC: chlortetracycline; DC: doxycycline; SDZ: sulfadiazine; SMT: sulfamethazine; SCP: sulfachloropyridazine; SMX: sulfamethoxazole.

Tetracycline and sulfonamide resistance genes are also frequently detected in water bodies [199]. For example, Ling et al. [200] identified two sulfonamide resistance genes (sulI and sulII) and seven tetracycline resistance genes (tetA, tetC, tetG, tetX, tetO, tetQ, and tetM) in twenty surface water samples from the Beijiang River (China), whereas Luo et al. [201] identified sulI and sulII at relatively high concentrations in 38 water samples from the Haihe River. Moreover, Harnisz et al. [202] detected two tetracycline resistant genes, tetB and tetM, in a surface water sample from the Łyna River (Poland), and they were related to the presence of doxycycline.

Antibiotic residues can also have ecotoxic effects in different aquatic organisms. In this sense, Kovalakova et al. [203] conducted an in-depth review focused on the toxicity of eight representative antibiotics (sulfamethoxazole, trimethoprim, erythromycin, tetracycline, oxytetracycline, ciprofloxacin, ofloxacin, and amoxicillin) in the aquatic environment, and indicated that cyanobacteria are the most sensitive aquatic organisms to these antibiotics, followed by green algae. In this sense, there are many works where different toxic effects of antibiotics on cyanobacteria and algae are shown [1,3,203]. Pomati et al. [204] studied the effects of antibiotics on the growth of the cyanobacterium *Synechocystis* sp., obtaining that tetracycline (at a level of 10 µg L\(^{-1}\)) caused an average reduction of 20% in cell density, while Gao et al. [205] indicated that tetracycline and oxytetracycline can inhibit the growth of the green algae *Selenastrum capricornutum*. Furthermore, Brain et al. [206] indicated that sulfathiazole could cause growth retardation of the macroalgae *Lemma gibba*. In addition, with respect to crustaceans and fish, Nunes et al. [207] observed that tetracycline can produce histological alterations in *Gambusia holbrooki* fish, such as enlarged sinusoids and hepatocellular vacuolization. Furthermore, Kim et al. [208] observed that tetracycline exposure can induce general responses on reproduction and somatic growth of *Daphnia magna*.
5.2. Influence on Soil Organisms

Veterinary antibiotics are pharmaceutical compounds explicitly designed to affect microorganisms, killing them (bactericidal effect) and/or inhibiting their growth (bacteriostatic effect) \[6,59\]. Therefore, the presence of these compounds in soils can cause potential alterations in the structure and abundance of the soil microbial community \[209\]. The main reason for this is that antibiotics, even those having broad-spectrum, often have a selective effect on several microorganisms, which can be as broad as a group of bacteria or fungi, or as narrow as a single genus or species. As a consequence, these selective effects can cause alterations in the relative abundance of microbial species, thus also affecting the interactions between the different species \[14\]. In this sense, several studies have shown that the presence of antibiotic residues in soils causes a reduction in microbial biodiversity and influences the enzymatic activities of bacterial communities, thus affecting important ecological functions, such as methanogenesis, reduction of sulfates, nitrogen transformation, biomass production, degradation of organic matter, and nutrient cycling, among others, leading to the loss of functional stability \[6,13\].

For example, Wei et al. \[210\] investigated the effects of residual tetracycline on the enzymatic activities of the soil and found that the presence of the antibiotic significantly altered the structure of the microbial communities. Specifically, it inhibited the microbial activities of the soil in terms of effects on enzymatic activities such as urease, acid phosphatase, and dehydrogenase. Similarly, Yao et al. \[211\] observed that oxytetracycline significantly decreased urease, sucrose, phosphatase, and hydroperoxidase activities, while Liu et al. \[212\] found that chlorotetracycline, tetracycline, tylosin, sulfamethoxazole, sulfamethoprim, and trimethoprim inhibited soil phosphatase activity. Furthermore, several studies showed that the presence of tetracycline and sulfonamide residues affected nitrification and denitrification processes, inhibiting them \[213–218\], as well as caused the inhibition of the iron reduction process \[214,217\].

It should be noted that the effects of antibiotics on the soil microbial population depend fundamentally on their bioavailability, which is strongly influenced by adsorption and degradation processes. In this sense, it has already been shown that greater adsorption and degradation implies a reduction in antibiotic potency \[13,14,59\].

It is of high relevance that there is an extensive bibliography on the increase in genes resistant to both tetracyclines \[219–224\] and sulfonamides \[225–232\], in bacteria from soils amended with livestock residues, a phenomenon of great concern to public health throughout the world, due to the possible transfer of resistance from microorganisms from the soil to human pathogens \[233\].

With regards to tetracyclines, studies on this subject can be approached from two points of view. The first one consists in using DNA fingerprints (such as the presence of resistant genes), and the second one is the determination of resistance from a functional point of view, that is, by quantifying the extent to which the bacterial communities present in the soil become tolerant to antibiotics. This second approach (denoted as PICT: Pollution Induced Community Tolerance) has been much less studied so far. Along this line, Song et al. \[234\] did not observe increases in the tolerance of bacterial communities to TC in a soil with pH 7.2 and 1.2% organic carbon content, after being contaminated with 100 mg kg$^{-1}$ of TC. Less studied is the effect of the accumulation of tetracyclines on the ecological functions of microorganisms, as well as their modulation by the different characteristics of the soils.

In general, basal respiration is little affected, or is even stimulated by tetracyclines, as described by Thiele-Bruhn and Beck \[235\] for OTC in two soils having pH 6.6 and 7.1, and organic carbon content between 0.8 and 1.6%, and similarly reported by Ma et al. \[236\] for TC in a soil with pH 6.3 and organic matter content of 1.3%. Thiele-Bruhn \[237\] studied the effect of several antibiotics, including CTC, OTC, and TC on the microbial reduction of Fe$^{3+}$, observing that this process was conditioned by the concentration of tetracyclines but modulated by the characteristics of the soil, especially its organic matter content and pH. Moreover, this author observed that the toxicity of the different antibiotics was variable depending on the compound considered, following the sequence: CTC > OTC > TC. Wei et al. \[210\] studied the effect of TC on the structure of microbial communities and on various
enzymatic activities, showing that the presence of TC alters the composition of microbial communities and inhibits the enzymatic activities urease (URE), phosphatase (PHOS), and dehydrogenase (DHA). However, other authors found divergent results in relation to the effects of tetracyclines on enzymatic activities. Thus, Chen et al. [238] found depressive effects of OTC on the activity of DHA and PHOS, while URE was not affected. Unger et al. [239] found depressive effects of OTC on DHA but found no negative effects on the hydrolysis of FDA.

However, Thiele-Bruhn and Beck [235] did not find negative effects of OTC on DHA. Rousk et al. [240,241] studied the effect of various antibiotics (including OTC) on the growth of bacterial communities, on fungal growth, and on basal respiration, showing that the effect of OTC on basal soil respiration is very low, with a tendency to increase as the concentration of OTC increases. It was also observed that there is a significant decrease in the growth of soil bacterial communities as the dose of OTC is increased, accompanied by a proportional increase in fungal growth. Recently, Santás-Miguel et al. [242,243] studied the toxicity effects of TC, OTC, and CTC on the growth of bacterial communities in 22 soils with pH between 4.1 and 7.4, and organic carbon content between 1.1 and 10.9%, confirming that the characteristics of the soils play an important role in modulating the toxicity of tetracyclines on the growth of bacterial communities, depending mainly on the content of soil organic matter, dissolved organic matter, pH and the cation exchange capacity. Furthermore, it was observed that the toxicity of this group of antibiotics can be considered semi-persistent, since after 40 days of incubation the inhibitory effect on the growth of bacterial communities remained at fairly high levels.

These studies also showed that the toxicity of the different tetracyclines on the growth of soil bacterial communities follows a similar sequence to that previously found by Thiele-Bruhn [237]: CTC >> OTC ≥ TC. Finally, the results also indicate that the concentrations of tetracyclines that are usually quantified in soils are far from being able to cause great inhibitions of the growth of bacterial communities in soils but are close to those necessary for causing that negative effects start appearing [242,243].

In relation to the group of sulfonamides, as with tetracyclines, most of the existing studies focus on the presence of resistance genes, as commented previously. However, functional tolerance to sulfonamides has been poorly studied. In this sense, Brandt et al. [244] showed that the tolerance of the soil bacterial communities to sulfadiazine increased when contaminating a soil of pH 6.6 with this antibiotic using concentrations equal to or greater than 1 mg kg\(^{-1}\), with the higher tolerance increases associated to higher doses of sulfadiazine. In relation to the effect of the accumulation of sulfonamides in soils on the ecological functions of microorganisms and their relation with the characteristics of the soil, there are fewer studies, as was the case with tetracyclines.

In general, the presence of sulfonamides in soils causes little inhibition of basal respiration (or even increases it), as observed in different soils with a pH range of 4.3 to 7.1 and organic carbon content between 0.8 and 2%, specifically for sulfadiazine [217,245], sulfamonomethoxine [236], sulfamethoxazole [212,246], sulfamethazine [247], and sulfapyridine [235]. No significant effects were detected on substrate induced respiration (SIR) in two soils, with pH 4.8–6.3 and organic matter content of 3.6%, contaminated by sulfadiazine [248]. However, in this study, a depressive effect of sulfadiazine was observed on N mineralization and nitrification, while ammonification increased [248]. In contrast, Awad et al. [247] found increases in nitrification in a soil with pH 6.0 and 2.36% organic matter. The microbial reduction of Fe decreased both in the presence of sulfamethoxazole [246] and in the presence of sulfapyridine [235]. In relation to the effect of sulfonamides on the enzymatic activities of soils, the results are highly variable, depending on the type of soil, type of sulfonamide, or enzymatic activity considered.

Gutiérrez et al. [249] studied the effect of a combination of sulfamethoxine, sulfamethoxazole, and sulfamethazine on the enzymatic activities of dehydrogenase (DHA) and urease (URE), obtaining small inhibitions or stimulations of DHA and increases in ERU. Xu et al. [217] studied the effect of sulfadiazine on the hydrolysis of FDA and on DHA, observing negative effects of this antibiotic
on both activities. In addition, Hammesfahr et al. [248] reported depressive effects of sulfadiazine on ERU but not on β-glucosidase (β-GLU). Sulfamethoxazole caused decreases in phosphatase (PHOS) activity [212], while Srinivasan and Sarmah [250] found no negative effects of this antibiotic on DHA. Sulfamethazine can cause inhibitions on both PHOS [212] and DHA and URE [109] activities. Thiele-Bruhn and Beck [235] found no negative effects of sulpyridine on DHA. Finally, it should be noted that the effect of sulfonamides on the growth of soil bacterial communities was much less studied, highlighting the work of Brandt et al. [244], which indicated that sulfadiazine can inhibit the growth of bacterial communities in the soil.

Regarding the toxic effects of antibiotics on the meso and macrofauna of the soil, these are much less pronounced than those described for microorganisms. However, different negative impacts of antibiotics on soil fauna have been reported in the literature. In this sense, Havelkova et al. [251] investigated the ecotoxicity of the antibiotics penicillin G, vancomycin, and tetracycline for springtails and earthworms and found that all three antibiotics could inhibit the reproduction of both animals, but at relatively high doses, whereas no significant effect was found on the mortality. Similarly, Litskas et al. [252] found that doxycycline had negative effects on the total number of juvenile earthworms at the concentration level of 30 mg kg⁻¹.

5.3. Entry of Antibiotics in the Food Chain Through Crops

As previously mentioned, antibiotics can be transported from the soil to waterbodies, in addition to being absorbed by crops, thus being able to enter the food chain through the ingestion of water and vegetables. Once in the human body, antibiotic residues can interact with the human microbiota and cause major alterations in the composition of the gut microbial community. In this sense, the imbalance of the microbiota in the intestine can result in the spread of harmful bacteria and opportunistic pathogens, which can cause pseudomembranous colitis, colorectal cancer, and various intestinal diseases. Furthermore, another important concern for humans is that intestinal bacteria acquire resistance to antibiotics, with the risk of dramatic effects on health and life [253].

The presence of antibiotics in different food crops has been less studied compared to their presence in water. Table 12 shows data regarding tetracyclines and sulfonamides in different crops. For example, Conde-Cid et al. [54] detected antibiotics in 12 of the 27 crop samples analyzed (>44%). The maximum concentrations detected were 0.3 mg kg⁻¹ for TC, 0.2 mg kg⁻¹ for OTC, 0.1 mg kg⁻¹ for CTC and DC, 0.5 mg kg⁻¹ for SDZ, 0.2 mg kg⁻¹ for SCP, and 0.6 mg kg⁻¹ for SMT (Table 12). Conde-Cid et al. [54] also reported that SAs were detected more frequently than TCs in plant tissues, which may be due to the lower molecular weight of SAs compared to TCs, thus facilitating plant uptake [254]. Furthermore, Conde-Cid et al. [54] also indicated that the concentrations of TCs and SAs detected in the crops were higher than those observed in the soils, suggesting that a bioaccumulation process takes place in the plant tissues.

Table 12. Maximum concentration values (μg kg⁻¹) detected for different tetracycline and sulfonamide antibiotics in various crops.

| Crop   | Country | TC    | OTC   | CTC   | DC    | SDZ   | SMT   | SCP   | SMX   | Reference |
|--------|---------|-------|-------|-------|-------|-------|-------|-------|-------|-----------|
| Cabbage| China   | 10.1  |       |       |       | 1.2   |       |       |       | [255]     |
| Cabbage| China   | 5.9   |       |       |       |       |       |       |       | [256]     |
| Cabbage| USA     |       | 11.4  |       |       |       |       |       |       | [254]     |
| Carrot | Pakistan| 0.8   |       | 0.8   |       |       |       |       |       | [257]     |
| Celery | China   | 3.1   | nd    | 12.6  |       | 0.1   | nd    |       |       | [39]      |
| Coriander| China | 5.6   | 330.0 | 532.0 |       | 0.3   | nd    |       |       | [39]      |
| Corn   | Spain   | 300.0 | 330.0 | 532.0 | 100.0 | 0.0   | 600.0 | 200.0 |       | [54]      |
| Corn   | China   | 6.6   |       |       | 100.0 | 0.0   |       | 0.0   |       | [255]     |
| Corn   | USA     | 3652.0| 3335.0| 372.0 | 423.0 | 3.0   | nd    | nd    |       | [258]     |
| Corn   | USA     | 3.8   |       |       |       |       |       |       |       | [259]     |
| Grass  | Spain   | 100.0 | 100.0 | 100.0 | nd    | 100.0 | 100.0 | 200.0 |       | [54]      |
Table 12. Cont.

| Crop     | Country | TC  | OTC | CTC | DC  | SDZ | SMT | SCP | SMX | Reference |
|----------|---------|-----|-----|-----|-----|-----|-----|-----|-----|-----------|
| Lettuce  | USA     | 1.0 |     |     |     |     |     |     |     | [259]     |
| Lettuce  | Spain   |     |     |     |     |     |     |     |     | [260]     |
| Onion    | USA     | 14.4|     |     |     |     |     |     |     | [254]     |
| Peanut   | China   | 20.1| 22.7| 21.8| 19.2| 5.3 | 3.6 |     |     | [261]     |
| Radish   | China   | 9.2 |     |     |     |     |     |     |     | [255]     |
| Radish   | USA     | 1.4 | 57.0| 18.0|     | 0.5 | 2.7 |     |     | [39]      |
| Radish   | USA     | 3.0 |     |     |     |     |     |     |     | [259]     |
| Rape     | China   | 1.8 | 187.0| 3.3|     |     | nd  | 0.2 |     | [39]      |
| Rice     | China   | 8.5 |     |     |     |     | nd  |     |     | [255]     |
| Spinach  | China   | 6.3 |     |     |     |     |     | 1.7 |     | [255]     |
| Spinach  | Pakistan| 0.8 |     |     |     |     | 0.8 |     |     | [257]     |
| Spinach  | USA     | 3.0 |     |     |     |     |     |     |     | [259]     |
| Spinach  | USA     |     |     |     |     | 5.0 |     |     |     | [259]     |
| Spinach  | Spain   |     |     |     |     | 1.7 |     |     |     | [260]     |
| Tomato   | Israel  |     |     |     |     |     |     |     | 2.0 | [262]     |
| Wheat    | Spain   | nd  | nd  | nd  | nd  | nd  | 100.0| 100.0|     | [54]      |
| Wheat    | Germany | 404.0| 487.0|     |     |     |     |     |     | [263]     |
| Wheat    | Pakistan| 0.5 | 0.6 |     |     |     |     |     |     | [257]     |
| Wheat    | USA     |     |     |     |     |     |     |     | 0.5 | [264]     |

TC: tetracycline; OTC: oxytetracycline; CTC: chlortetracycline; DC: doxycycline; SDZ: sulfadiazine; SMT: sulfamethazine; SCP: sulfachloropyridazine; SMX: sulfamethoxazole.

Antibiotic residues in the environment can also show toxicity to plants (phytotoxicity), including negative impacts on plant germination, growth, and development. In addition, toxicity is affected by the nature of the antibiotic, the properties of the soil, and the crop species [2,37,265]. For example, Liu et al. [212] investigated the effects of six antibiotics (chlortetracycline, tetracycline, tylosin, sulfamethoxazole, sulfamethazine, and trimethoprim) on the germination of seeds of three different plant species (sweet oats, rice, and cucumber), obtaining that sweet oats were the most common plant sensitive to all six antibiotics and that tetracyclines and sulfonamides were more toxic than tylosin and trimethoprim with respect to seed germination. Furthermore, Opris et al. [266] observed that doxycycline, tetracycline, ciprofloxacin, and amoxicillin negatively affected the photosynthesis rate and the chlorophyll content in wheat (*Triticum aestivum*). Similarly, Liu et al. [267] indicated that oxytetracycline, sulfamethazine, and ciprofloxacin had a toxic effect on the activity of the roots and the chlorophyll content of the leaves of *Phragmites australis*, a typical wetland plant.

In addition, it should be noted that horizontal transfer of antibiotic resistance genes between bacteria of different species occurs frequently and easily for different environmental compartments, including crops, which evidences the entry of antibiotic resistant genes into the food chain and, consequently, potentially allows its transfer to humans, which may contribute to the threat of incurable infections, posing a significant risk to public health [14,23].

Taking into account the potential risks derived from the presence of antibiotic residues in the environment, it is vitally important to establish preventive measures to reduce their entry into the various environmental compartments. In this sense, different effective measures can be established: (1) Ban the use of antibiotics as growth promoters in livestock. In this regard, although the European Commission has banned the use of antibiotics as growth promoters in animal feed since 2006 [268], this is still a very common practice in many parts of the world [13]; (2) limit and control the use of antibiotics to specific situations. As regard veterinary, antibiotics should only be used to treat animal diseases and always under veterinary supervision and prescription. In addition, regulations around the dosage and the treatment duration should be established [37]; (3) Promote among veterinarians and farmers a prudent use of antibiotics. In this sense, farmers can adopt different measures to maintain good hygiene and health of the animals, thus reducing the need for antibiotics [37]; (4) promote the application of effective pretreatment techniques to reduce antibiotics concentrations/amounts in
manures and slurries prior to the application of these materials to agricultural fields. This could be achieved by setting limits for the concentration of antibiotics in these wastes.

In summary, the presence of tetracyclines and sulfonamides in the environment presents three important environmental risks: pollution of waterbodies, ecotoxicity effects on soil organisms, and entry into the food chain. In this sense, sulfonamides present high mobility, especially in soils poor in organic matter, where they show a significant risk of transport to waterbodies. As a consequence, these compounds are frequently detected in both surface and groundwater. Regarding tetracyclines, although they are much less mobile in the soil, residues of these compounds are also frequently detected in waterbodies, which is possibly due to their greater use with respect to sulfonamides. The presence of these compounds in the aquatic environment can cause significant toxic effects on different organisms, especially on cyanobacteria and green algae, as well as favor the development and spread of antibiotic resistance genes. Similarly, the presence of antibiotic residues in the terrestrial environment can lead to a reduction in the soil microbial biodiversity, as well as causing a negative impact on the enzymatic activities of bacterial communities, thus affecting important ecological functions. Finally, antibiotic residues can enter the food chain through drinking water or crops, thus causing significant risks to human health.

**Author Contributions:** Conceptualization, D.F.-C. and M.A.-E.; investigation, M.C.-C.; resources, E.Á.-R. and M.A.-E.; writing—original draft preparation, M.C.-C., D.F.-C. and M.A.-E.; writing—review and editing, A.N.-D. and D.F.-C.; visualization, M.J.F.-S. and D.F.-C.; supervision, A.N.-D., M.J.F.-S. and D.F.-C.; project administration, E.Á.-R. and M.A.-E.; funding acquisition, E.Á.-R. and M.A.-E. All authors have read and agreed to the published version of the manuscript.

**Funding:** This study has been funded by the Spanish Ministry of Economy and Competitiveness through the projects CGL2015-67333-C2-1-R and -2-R (FEDER Funds) and by Xunta de Galicia via CITACA Strategic Partnership (ED431E 2018/07) and BVI research group (ED431IC 2017/62-GRC). D. Fernández-Calviño holds a Ramón y Cajal contract (RYC-2016-20411) financed by the Spanish Ministry of Economy Industry and Competitiveness. M. Conde-Cid holds a pre-doctoral contract (FPU15/0280, Spanish Government).

**Conflicts of Interest:** The authors declare no conflict of interest.

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