



REVIEW ARTICLE

Soil-pharmaceutical residue interactions: Understanding sorption and desorption mechanisms for effective risk assessment and mitigation

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Abstract

Pharmaceutical residues are increasingly recognised as persistent environmental contaminants, with soils acting as both sinks and secondary sources following their entry through wastewater irrigation, biosolid application and improper disposal. Pharmacological properties and soil characteristics interact in shaping the environmental fate of these compounds and the mechanisms governing sorption and desorption largely determine their mobility, persistence and bioavailability in soil systems. Compound-specific characteristics such as ionisation state, hydrophobicity, molecular structure and functional groups, together with soil properties including pH, organic matter content, texture, mineralogy, cation exchange capacity, moisture, ionic strength and redox conditions, strongly influence pharmaceutical behaviour in soils. Partial and hysteretic release can prolong environmental persistence and expose soil microorganisms and plants to sustained low-dose contamination, even where substantial retention initially limits transport. Such exposure has been linked to shifts in microbial community structure, suppression of key soil enzymes, disrupted nutrient cycling and accumulation of antibiotic resistance genes, threatening soil fertility and health. Uptake and translocation of residues into edible crops further raise concerns for food safety and human health. Critically, current risk assessment frameworks remain limited because they inadequately account for chemical mixtures, transformation products and integrated soil-plant-microbial interactions, a gap compounded by the scarcity of long-term, field-scale data and studies addressing combined effects of co-occurring pollutants. This review synthesises recent evidence on soil-pharmaceutical interactions to address that gap and highlights the need for integrated mitigation strategies including soil amendments, microbial degradation, phytoremediation and improved wastewater treatment for the long-term management of pharmaceutically contaminated soils.

Keywords: antibiotic resistance genes; bioavailability; dietary exposure; emerging contaminants; phytoremediation; soil-plant-microbial interactions

Introduction

The global increase in pharmaceutical manufacture and use has established these substances as ubiquitous environmental contaminants, with usage rising more than 2.5 times in the last decade (1). Pharmaceutically active chemicals (PhACs) penetrate land and aquatic systems and form intricate "source-to-receptor" exposure routes that endanger non-target creatures. The PhACs are intended to have biological effects at trace concentrations (2). Sorption and desorption processes at the soil-water interface govern their mobility, permanence, bioavailability and potential leaching into groundwater in soil systems. These processes are controlled by soil qualities and environmental conditions; hence soil is an important medium for determining contaminant behaviour. A thorough understanding of these relationships is

required for effective risk assessment and mitigation methods aimed at maintaining agricultural output and public health.

Pharmaceutical residues have been identified in agricultural soils at varying concentrations, indicating widespread environmental contamination from antibiotics, analgesics and hormones. Their permanence is frequently described as "pseudo-persistence," in which ongoing anthropogenic input compensates for deterioration, resulting in long-term exposure of soil organisms. These residues have a substantial impact on soil health because they modify microbial community structure, reduce biodiversity and inhibit key enzymatic processes involved in nutrient cycling, lowering soil fertility. Certain chemicals, such as nimesulide are direct toxic to soil fauna, posing ecological problems at the base of the terrestrial food chain (Fig. 1) (3).

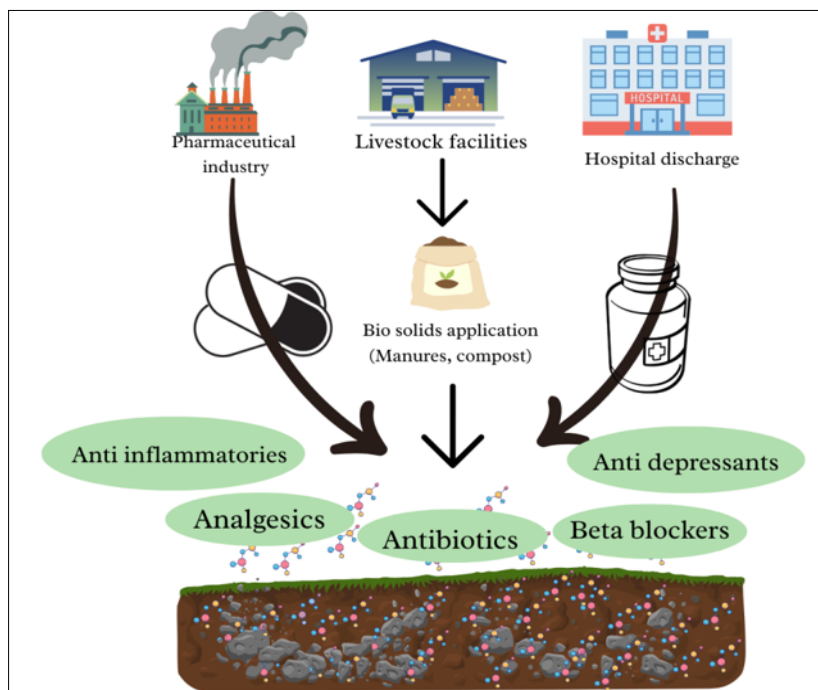


Fig. 1. Sources of pharmaceuticals in the soil.

Soils also serve as reservoirs for antibiotic resistance genes (ARGs), as prolonged exposure to sublethal antibiotic doses increases resistance development and horizontal gene transfer between environmental and pathogenic bacteria (4). This contributes to a growing worldwide health concern and may reduce the efficacy of clinical treatments. Furthermore, pharmaceutical residues can bioaccumulate crops, entering edible tissues and posing risks to people, including endocrine disruption and long-term toxicity. Industrial effluents, wastewater irrigation and biosolid applications are significant sources of contamination, especially in areas with limited treatment facilities.

In water-scarce areas, wastewater irrigation is a major route for pharmaceuticals into soils, with long-term practices increasing residues such as carbamazepine and sulfamethoxazole (5). Improper disposal of unwanted or expired medications increases contamination by allowing residues to migrate from municipal garbage into soil and leachate systems. Emerging mechanisms, such as atmospheric deposition and microplastic interactions, aid in the transport and bioavailability of medicines in soils. These combined sources and channels demonstrate the complexities of pharmaceutical contamination in soil systems, emphasising the necessity for integrated management and long-term mitigation

solutions. This review aims to synthesise current knowledge on sorption-desorption mechanisms governing pharmaceutical residues in soil, evaluate the soil and drug properties controlling their fate and assess implications for plant uptake and ecosystem health to guide future risk assessment.

Materials and Methods

The analytical process was organised into four main stages, as illustrated in Fig. 2. The first stage involved a systematic literature search, screening and selection of relevant studies. Study selection was carried out in three sequential steps: titles were first screened for relevance, followed by abstract screening of the remaining records and only studies passing both stages were retrieved and read in full to confirm eligibility for inclusion. The second stage focused on thematic classification and conceptual structuring, emphasising physicochemical interactions, mobility and persistence of pharmaceutical residues. The third stage included critical evaluation and comparative analysis to understand plant uptake pathways, soil health impacts and environmental risk perspectives. The fourth stage synthesised the analysed information to provide an integrated understanding of pharmaceutical behaviour in soils and to highlight sustainable remediation and management strategies.

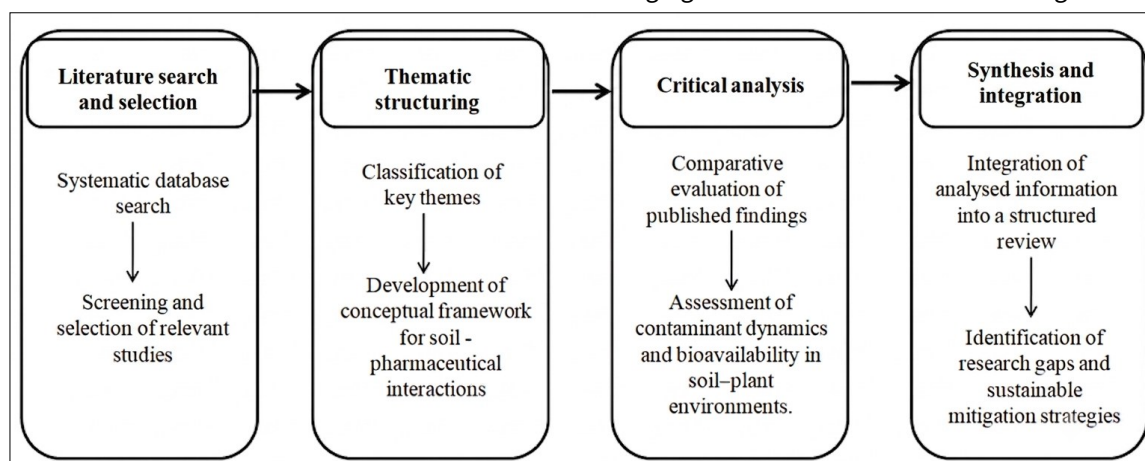


Fig. 2. Methodology followed for literature review.

Bibliometric evaluation of global research trends and emerging focus areas in pharmaceutical-contaminated soils

A comprehensive database-driven literature search was conducted using sources such as Scopus, incorporating keywords related to contamination sources, environmental fate, soil interactions and remediation approaches. The search covered the period from 2017 to 2025. The search strategy combined the following keyword groups using Boolean operators: ("pharmaceutical*" OR "drug residue*" OR "pharmaceutical residue*") AND ("soil" OR "soil pollution" OR "sorption" OR "desorption") AND ("contamination" OR "environmental fate" OR "soil interaction*" OR "remediation"). The search was restricted to documents published in English and document type was limited to original research articles and review articles. The selected studies were systematically reviewed, cross-referenced and synthesised to develop a coherent and critical framework for soil-pharmaceutical interactions.

Bibliometric analysis was performed using datasets retrieved from the Scopus database, with network visualisation carried out using VOS viewer (version 1.6.20) software (Fig. 3). Co-occurrence analysis of author keywords identified dominant research themes and interconnections. Out of 683 retrieved documents, 186 relevant studies were selected for detailed evaluation. From 1152 identified keywords, 157 met the minimum occurrence threshold of three, resulting in a refined and strongly connected keyword network.

Pharmaceutical residues in the soil

Pharmaceutical residues are increasingly acknowledged as widespread environmental contaminants, with active pharmaceutical ingredients (APIs) found in over 1000 survey locations across 258 rivers in 104 countries (6). Field investigations in metropolitan areas such as Sekondi-Takoradi in Ghana found pharmaceutical concentrations as high as 18.4 mg/L in hospital effluents and landfill leachates, indicating that these are major point sources of environmental entry. These residues reach the ecosystem

via a variety of routes, including the discharge of treated and untreated wastewater, the land application of biosolids or animal manure and the leaching of illegally disposed pharmaceuticals from landfills (7).

The occurrence of these residues is no longer confined to localised hotspots but has emerged as a pervasive global environmental concern, reflecting the widespread and continuous input of pharmaceuticals into soil systems. Monitoring of deep hydrological cycles has demonstrated that these residues, including hormones and pharmaceuticals, enter groundwater systems used for human consumption (8). Companion animals are an overlooked but major source of contamination because they release parasiticides and antimicrobials directly onto urban hard surfaces, which are then washed into soil and water systems. Spatial bioaccumulation investigations in river systems have verified the presence of target residues in all examined sediments and primary producers, demonstrating their widespread environmental persistence.

Classification and chemical nature of pharmaceuticals in soils

The chemical speciation of pharmaceuticals in terrestrial environments is a significant predictor of their behaviour and is determined by the surrounding soil pH, which determines whether a substance is neutral, anionic, cationic or zwitterionic. Basic medicines with a positive charge in Mediterranean calcareous soils, such as flecainide and venlafaxine, have high stability due to electrostatic attraction to negatively charged soil organic matter (8). Furthermore, certain antibiotics, such as sulfamethoxazole, can interact with trace metals by forming surface ternary complexes, affecting their solubility and availability. These residues' partitioning behaviour is highly impacted by their hydrophobicity, which is frequently evaluated using the pH-adjusted octanol-water partition coefficient, $\log D_{ow}$. According to research, medicines with a $\log D_{ow}$ value less than 2 are largely dissolved in soil pore water rather than sorbing to bulk soil. This dissolved fraction is the most bioavailable component for transit through the soil profile and uptake by plant root systems Table 1 (9).

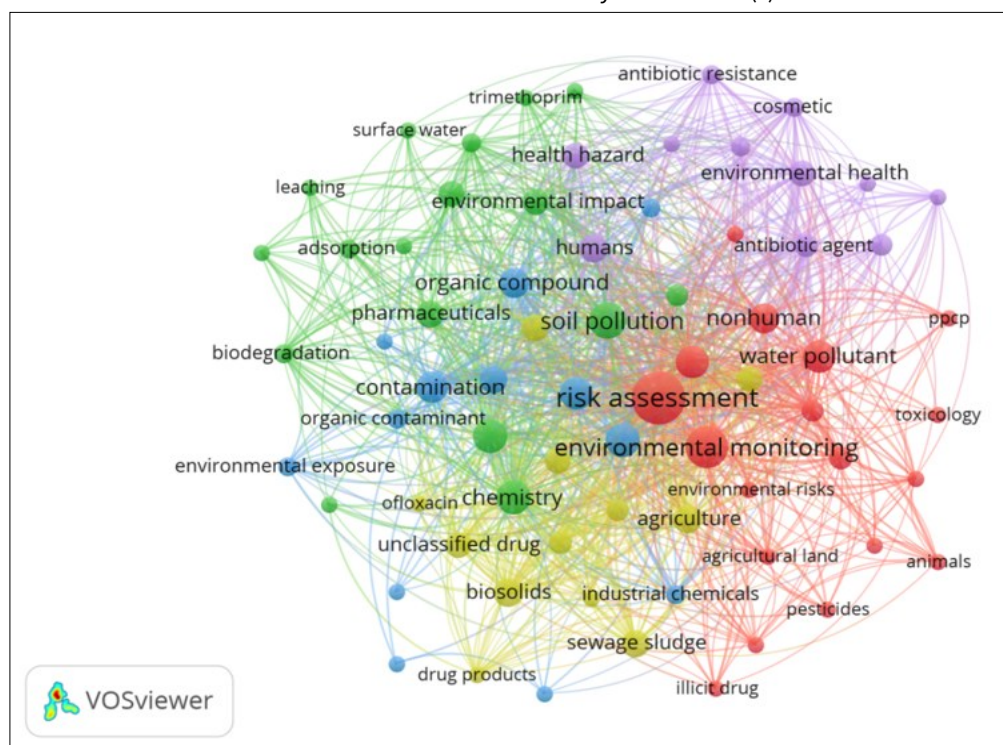


Fig. 3. Network visualisation on recent researches on pharmaceuticals.

Table 1. Physicochemical properties of selected pharmaceutical compounds

Pharmaceutical compound	Abbreviation	Chemical formula	Classification	pK _a Value	Log K _{ow}	Log D _{ow}	Reference
Carbamazepine	CBZ	C ₁₅ H ₁₂ N ₂ O	Antiepileptic	13.9	2.45	2.45	(9)
Ibuprofen	IBU	C ₁₃ H ₁₈ O ₂	NSAID/ Anti-inflammatory	4.85	3.84	0.85	(10)
Sulfamethoxazole	SMX	C ₁₀ H ₁₁ N ₃ O ₃ S	Antibiotic	1.97 6.16	0.89	-0.11	(11)
Atenolol	ATL	C ₁₄ H ₂₂ N ₂ O ₃	β-blocker	9.60	0.16	0.16	(12)
Acetaminophen	ACE	C ₈ H ₉ NO ₂	Analgesic	9.38	0.46	0.44	(13)
Ciprofloxacin	CIP	C ₁₇ H ₁₈ FN ₃ O ₃	Antibiotic	6.09	0.28	Zwitterion	(14)
Oxytetracycline	OTC	C ₂₂ H ₂₄ N ₂ O ₉	Antibiotic	3.23, 7.3	-0.90	-1.76	(15)
Metformin	MTF	C ₄ H ₁₁ N ₅	Anti-diabetic	12.4	-1.36	-1.36	(2)
Propranolol	PRN	C ₁₆ H ₂₁ NO ₂	β-blocker	9.50	3.50	0.19	(16)
Sulfadiazine	SDZ	C ₁₀ H ₁₀ N ₄ O ₂ S	Antibiotic	2.00, 6.44	-0.09	-0.09	(17)
Tramadol	TRA	C ₁₆ H ₂₅ NO ₂	Opioid analgesic	9.41	2.45	1.12	(18)

pK_a: acid dissociation constant; log K_{ow}: octanol-water partitioning coefficient; log D_{ow}: (pH dependent) octanol-water partition coefficient.

Molecular structure also influences chemical interactions in soil; reactive moieties like triazine rings and amino groups can greatly increase a compound's sorption affinity by allowing hydrogen bonds to form with polar soil functional groups. Furthermore, physicochemical factors influence membrane permeability, with molecular weight (MW) being one of several determinants; molecules exceeding 500 Da typically show reduced permeability (19). Large molecules, such as the antibiotic tylosin, show minimal plant uptake despite their ambient prevalence due to molecular size restrictions. The history of land management also influences the chemical composition of these leftovers in the soil. Long-term irrigation with treated wastewater creates a background level of pseudo-persistent residues, such as carbamazepine, which persists beyond natural attenuation processes. This accumulation can result in the soil acting as a reservoir, gradually releasing residues back into the interstitial water over time (8).

Persistence, mobility and transformation

Environmental persistence varies dramatically across drug classes, with research conducted in temperate climates finding that fluoroquinolone antibiotics have dissipation half-lives varying from 750–2500 days. In contrast, common non-steroidal anti-inflammatory medicines such as ibuprofen degrade substantially faster, with half-lives often measured under 300 days in comparable field circumstances (20). The permanence of these residues in soil may pose a long-term risk of buildup following repeated fertiliser applications. The mobility and fate of these compounds are frequently dictated by their transformation into metabolites with differing environmental mobilities than their parent medicine such as the conversion of atenolol to atenololic acid. According to research, these transformation products can be more permanent in agricultural soils than the original medications, creating distinct risk assessment issues. Furthermore, polar residues such as carbamazepine have low sorption and high persistence, making them especially susceptible to leaching through the soil profile into groundwater systems (8).

Transformation kinetics in soil are determined by the intricate interaction between soil parameters and the unique composition of the microbial population. Studies have shown that the dissipation of various organic micropollutants is very sensitive to parameters such as soil organic matter concentration and temperature, which influence biological breakdown. These biodegradation mechanisms are critical in assessing the environmental sustainability of pharmaceutical formulations (12). One key consequence of these residues' mobility and modification is

their introduction into the human food chain via plant absorption. Randomised controlled investigations have proven this trophic transfer by detecting residues and metabolites in the urine of human volunteers who ate vegetables grown in soils watered with reclaimed wastewater. Long-term studies have also shown that these residues can accumulate in edible sections of crops, such as fruits and leaves, depending on plant physiology and soil distribution (21).

Soil-pharmaceutical interactions

The presence of anthropogenic residues and environmental stressors has a significant impact on soil-pharmaceutical interactions, with carbamazepine translocation from roots to edible plant parts demonstrated to be extremely efficient across diverse crop species (5). Plant physiological responses are further influenced by certain therapeutic classes, such as antiretroviral compounds, which may induce toxicity at elevated exposure levels while remaining mobile within plant vascular systems (22). Regional land-use patterns, particularly the use of animal manure and poultry litter as organic fertilisers, have been associated to direct soil pollution and antibiotic infiltration into shallow groundwater systems. According to studies of intensive livestock operations, swine farming activities promote the growth of antibiotic resistance genes in the underlying groundwater more than non-impacted regions (4). Groundwater replenishment with reclaimed water produces diverse risk profiles for fluoroquinolone antibiotics, necessitating soil-specific risk assessments to forecast bioaccumulation (14, 21). Long-term irrigation with impacted surface waters shows that pharmaceutical residues survive through the water-soil interface, despite natural attenuation.

Role of soil physicochemical properties

The acidity of the soil solution is an important driver of pharmacological behaviour, especially because it influences the molecular speciation of ionisable residues (17). According to experimental studies on basic compounds, increasing alkalinity can improve electrostatic attraction by increasing the negative charge density of soil colloids (9). The presence of co-contaminants such as trace metals modulates residue sequestration, allowing the formation of surface ternary complexes (8). High electrical conductivity in soil solution indicates the presence of multivalent minerals, which may compete for binding sites or facilitate complexation with drug molecules in their ionic states (7). Sequestration of veterinary antibiotics such as doxycycline is strongly and positively associated with both cation-exchange capacity and clay content, indicating that mineral-driven pathways such as cation exchange are the primary removal mechanisms (23).

For neutral pharmaceutical species, the sorption process is primarily driven by hydrophobic partitioning into the soil's organic domain via van der Waals forces and electron donor-acceptor interactions (9). The fraction remaining in soil pore water, which serves as the major reservoir for root uptake, determines residue dispersion within the soil-water-plant system. Food crops' selective accumulation is regulated by how strongly residues are maintained within the distinct organic fractions of various soil types, ranging from Haplic Luvisols to Dystric Cambisols (12). Soil organic matter quality specifically the C/N and O/C ratios of peat, acts as a primary predictor of polar sulfonamide's sorptive potential (17).

Influence of pharmaceutical structure and functional groups

The speciation of ionisable pharmaceutical residues is a key structural factor in determining how they interact with the soil matrix. Modelling attempts for sulfonamide and tetracycline antibiotics show that the energy of these interactions is substantially influenced by structural dissociation constants that vary with environmental circumstances. Organomineral associations are influenced by the age and quality of organic amendments, which supply the precise functional reactive sites required for residue immobilisation.

Molecular descriptors such as molar volume and hydrophilic parameters are reliable predictors of active pharmaceutical ingredient sorption across different sediments (9). The presence of structural motifs, such as the piperazine rings present in fluoroquinolones, promotes localised electrostatic attraction and thus sequestration on soil-like surfaces (24). Large-scale whole-river investigations show that structural characteristics such as aromaticity considerably influence the spatial deposition of residues in riverine sediments and aquatic biota (25).

Structural determinants of pharmaceutical uptake into plants

Molecular size limits transpiration-driven uptake into agricultural crops, as bulky residues have limited permeability through the root cortex and endodermis (12). Lipophilicity and the ionisation character of organic molecules acts as main filters for residue translocation into edible plant tissues, as demonstrated by cereal crop research. Certain drug classes, such as antiviral drugs, exhibit distinct structural characteristics that affect their passage through the soil-water-plant interface, increasing the risk of food chain contamination (22).

Sorption mechanisms

Pharmaceutical residues and the soil matrix interact in a complex way that is controlled by sorption mechanisms (Fig. 4) that establish environmental persistence and bioavailability. The sorption coefficients for various elements may vary significantly, based on the examination of these interactions, making general predictive models ineffective unless they include specific molecular and soil attributes (9). In these processes, soil organic matter plays a transformative role by providing hydrophobic domains and reactive functional groups (carboxyl, phenolic, hydroxyl) that drive sorption via hydrophobic partitioning, hydrogen bonding and cation bridging. These interactions collectively govern the retention and mobility of pharmaceuticals in soil.

The physical structure of the soil affects its retention as well; pore-filling with colloidal organic matter improves sequestration by creating nanopores that limit diffusion, while surface coating with molecular organic matter may reduce the sorption of dissociated compounds (15). The sorptive capacity for antibiotics like sulfadiazine is significantly higher in specialised settings like peat soils than in typical mineral soils. This capacity is mainly controlled by the ambient pH and the stoichiometric characteristics of the organic fraction (17). According to chemical studies of sulfonamides, their retention is a spontaneous process controlled by the interaction of π - π interactions, hydrogen bonds and electrostatic forces (11). Through processes like multilayer bonding or complexation with cationic metals and organo-clays, pharmacological classes can demonstrate cooperative sorption behaviour when they coexist (26). Sorption affinity for certain antibiotics, including doxycycline, is directly correlated with the agricultural soil's clay ratio and cation exchange capacity (23). Additional complexity is introduced by dissolved organic matter (DOM) from sludge amendments, which may facilitate leaching by forming stable complexes. The solid-water partitioning coefficient (K_d) and a compound's half-life are the two major characteristics governing long-term soil accumulation, according to modelling these transport pathways (27). These soil-dependent interactions ultimately determine residue uptake by terrestrial species, with accumulation parameters varying dramatically between soil types. The selective accumulation of these compounds in plants is highly dependent on molecular speciation, with neutral molecules rapidly translocating to leaves and ionic species predominantly limited to root tissues (Table 2) (12).

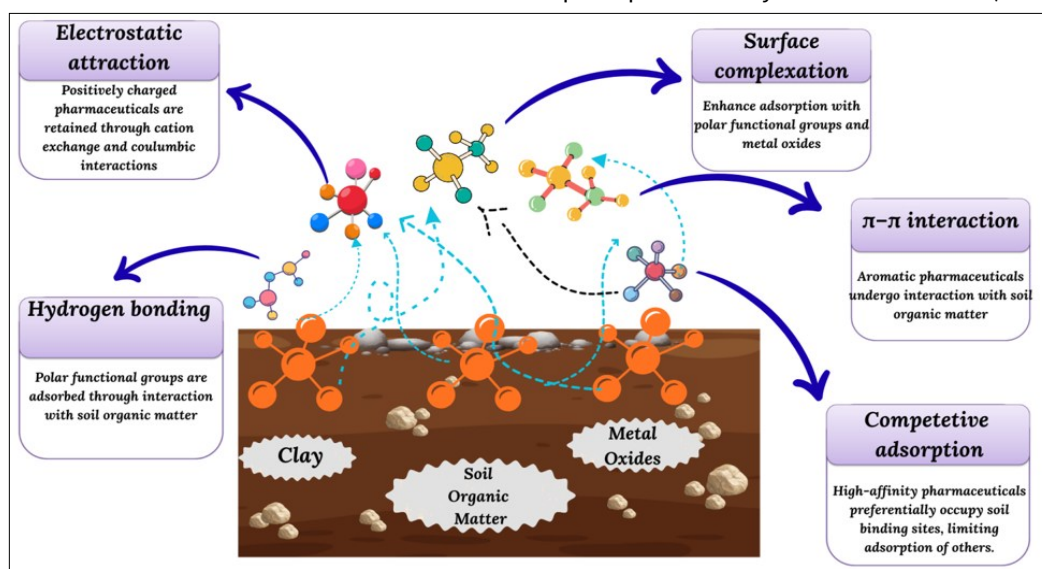


Fig. 4. Sorption mechanisms of pharmaceuticals in soil.

Table 2. Sorption behaviour of major pharmaceutical classes in soils

Pharmaceutical class	Sorption mechanism	Key factors influencing	References
Fluoroquinolones	Cation exchange Cation bridging surface complexation with metal oxides	Soil pH (sorption decreases as pH increases) Clay content Presence of Al/Fe/Mn oxides.	(28)
Sulfonamides	Hydrophobic partitioning (neutral form) H-bonding Electrostatic interaction	Soil pH (negative correlation; high mobility at alkaline pH) Organic carbon (OC) content	(17)
NSAIDs	Hydrophobic interaction (non-ionised) Electrostatic repulsion (anionic).	Soil organic matter (SOM) quality Soil pH	(26)
Antiepileptics	Hydrophobic partitioning Van der Waals forces	Soil organic carbon content Soil texture	(29)
Beta-blockers	Cation exchange Electrostatic attraction to negatively charged surfaces	Cation exchange capacity (CEC) Clay content	(9)
Tetracyclines	Cation bridging Surface complexation Cation exchange	Clay mineralogy Soil pH Divalent metals	(30)
Macrolides	Cation exchange Surface complexation Hydrophobic interactions	Soil pH (sorption increases as pH decreases) CEC	(9)

Adsorption processes

The adsorption of pharmaceutical residues in soil systems is principally determined by the compounds' molecular speciation and the pH of the soil solution. According to research conducted in Chinese agricultural soils, the sorption of common sulfonamides is strongly pH-dependent, with distribution coefficients considerably lowering as pH rises from 4 to 9 due to an increased fraction of anionic species (11). This shift reduces the number of neutral molecules that are more vulnerable to stable binding, resulting in a drop in overall sorption capacity when electrostatic interactions change. Predictive modeling research has revealed that for ionisable medicines, the degree of dissociation must be weighted individually to appropriately estimate affinity, as completely ionised bases exhibit a substantial association with pH-adjusted lipophilicity (9).

The physical properties of the soil matrix, specifically the cation exchange capacity and clay concentration, form the major structural framework for adsorption. In research on doxycycline retention in agricultural soils, sorption affinity was found to be highly positively linked with clay ratio and cation exchange capacity, resulting in rapid and irreversible sequestration within twelve hours (23). These inorganic fractions provide negatively charged sites that attract cationic and zwitterionic species, allowing for accumulation in the higher soil layers. According to pedotransfer rules defined across 13 soil types, base cation saturation is the best predictor for beta-blocker adsorption, as these weak bases are cationic at soil pH and bind via cation exchange, whereas clay concentration governs macrolide retention through hydrogen bonding and surface complexation with their bulky, multi-ring structures (18).

Surface complexation and cation bridging are two examples of molecular-level interactions that further differentiate residue accumulation within the soil profile. The sorptive capacity of specialised habitats, such as peat soils, is governed by the organic fraction's stoichiometric characteristics and the ambient pH, which regulates cationic species interaction via Lewis acid-base electron exchanges (17). These processes are the result of a variety of mechanisms, including hydrogen bonding and ion exchange,

which together determine the geochemical behaviour of antibiotics such as ciprofloxacin and norfloxacin (10). Furthermore, the presence of multivalent cations in soil solutions can aid in the retention of anionic medicines by forming stable ternary complexes at the mineral interface.

As the amount of organic matter decreases, electrostatic interactions become more important in the sorption process, potentially increasing the mobility of previously sequestered pollutants. This reduced sorption directly increases the bioavailable fraction of pharmaceuticals in soil solutions, making them more accessible for uptake by soil organisms and plant roots.

Partitioning mechanisms

Partitioning mechanisms primarily govern the distribution of neutral or nonpolar medicinal compounds into the hydrophobic regions of soil organic matter. According to principal component studies, for neutral substances such as carbamazepine, the octanol-water partition coefficient and total organic carbon are the key retention drivers (9). Unlike site-specific adsorption, this process is commonly seen as the solvation of the organic solute into a three-dimensional organic network, like the dispersion of water and an organic solvent. Predictive transport modelling in silty loam environments assumes linear and instantaneous adsorption, with the solid-water partitioning coefficient as the key parameter influencing accumulation patterns (27).

The chemical and qualitative heterogeneity of the soil organic matter matrix determines the strength of partitioning via various intermolecular interactions. Using Chinese silt loam soils, sulfonamide retention is a spontaneous process driven by hydrogen bonding and π - π electron donor-acceptor interactions (11). These interactions are sensitive to the ratio of aliphatic to aromatic chemicals in the soil, which varies when microbes metabolise energy-rich substances.

The physical organisation of colloidal particles in the soil causes a surface-pore integrated effect, which complicates partitioning dynamics. Surface coating with molecular organic

matter has been shown to boost sorption of non-dissociated medicines, whereas pore-filling with colloidal matter improves retention by providing nano- and micro-pores that limit mass transfer (15). This structural entrapment limits the diffusion of chemicals such as carbamazepine into the larger soil solution, acting as a natural filter that slows off-site migration. Intact peat soils have similar structural advantages, with strong sorptive capacities for active polar chemicals preserved by the presence of natural, non-mineralised organic fractions (17).

The presence of DOM in the aqueous phase serves as a competing third phase, facilitating or inhibiting partitioning to the solid soil phase. The DOM from recovered wastewater or organic waste additives might improve medications' apparent solubility, increasing their mobility and the danger of groundwater pollution (10). At the same time, the coexistence of many pharmacological classes in agricultural settings can result in cooperative partitioning behaviour. Evidence from mixture-compound systems indicates that the presence of additional residues considerably alters the retention of individual medications such as naproxen and ibuprofen via multilayer bonding effects or complexation with cationic metals from the soil (26).

Desorption mechanisms

The environmental release of pharmaceutical residues from the soil matrix into the aqueous phase is a multi-step process governed by several interacting mechanisms (Fig. 5). Technical assessments of Chinese agricultural soils show that the desorption of sulfonamides, specifically sulfadiazine and sulfamethoxazole, exhibits positive hysteresis, indicating that established chemical bonds between antibiotic molecules and soil particle surfaces are only partially

reversible (11). This observed resistance to release is primarily driven by a surface-pore integrated process in which colloidal organic matter occupies soil nano- and micro-pores to physically sequester residues and prevent their diffusion into the larger soil solution (15). Quantitative assessments of doxycycline in agricultural soils demonstrate that its adsorption is quick and practically irreversible, with recorded desorption percentages consistently less than 11 % across diverse soil textures. The presence of multicomponent combinations further modifies these release dynamics, as the coexistence of different nonsteroidal anti-inflammatory drug classes can result in a significant reduction in desorption compared to single-compound systems via the formation of stable ternary complexes or multilayer bonding (26).

According to research on peat soils, their high sorptive capacity for antibiotics such as sulfadiazine is regulated by the organic fraction's stoichiometric properties and ambient pH, allowing these specialised landscapes to function as effective retention areas. According to studies on terrestrial species, forecasting environmental uptake and potential secondary poisoning within the food chain requires a mix of soil factors and specific chemical qualities of a medication, such as its ionisation state. Observations of diclofenac in soils modified with organic wastes suggest that, while it is abundant, its desorption from soil appears to be limited, resulting in low mobility in organic-rich matrices. The solid-water partitioning coefficient and chemical half-life play key roles in pharmaceutical accumulation and off-site migration (27). Large-scale data analysis across many therapeutic classes shows that generic predictive models must include both molecular and soil descriptors to effectively estimate the distribution coefficients of ionisable substances Table 3 (9).

Table 3. Desorption behaviour of major pharmaceutical classes in soils

Pharmaceutical class	Speciation	Desorption mechanism	Key factors influencing	References
Fluoroquinolones	Zwitterionic	Highly irreversible; characterised by high binding energy and strong sequestration within the soil matrix	Soil pH (alkaline pH promotes release) Clay content CEC Metal oxide (Al/Fe/Mn) levels	(31)
Sulfonamides	Anionic at neutral/alkaline pH Neutral at acidic pH	Partially reversible; frequently exhibits significant hysteresis due to specific bonding of amino groups to soil carboxyl groups	Soil pH (negative correlation; high mobility at alkaline pH) Organic carbon content Ionic strength	(17)
NSAIDs	Primarily anionic at typical environmental pH	Ready reversibility for ibuprofen and naproxen via simple elution; diclofenac exhibits higher hysteresis due to ligand exchange	SOM content and quality (aromaticity) Soil pH (repulsion at higher pH) Presence of trivalent metal cations (Al^{3+} , Fe^{3+})	(32)
Antiepileptics	Neutral and non-ionisable	Significant hysteresis; release is limited by physical entrapment within the polyaromatic scaffold of organic matter	Soil organic carbon content, salinity Soil texture (highest retention in organic-rich topsoils) CEC	(29)
Beta-blockers	Cationic	Reversible ion exchange; release is primarily governed by displacement through competition with inorganic cations like Na^+ and Ca^{2+}	Base Cation Saturation (BCS) Clay content Ionic strength	(9)
Tetracyclines	Zwitterionic and amphoteric	Highly irreversible; strong fixation and formation of stable surface complexes with aluminum and iron hydrous oxides	Clay mineralogy (especially smectites) SOM content Presence of divalent metals Soil pH	(30)
Macrolides	Cationic (protonated in neutral/acidic solutions)	Low release; governed by strong electrostatic attraction to negatively charged soil surfaces and cation exchange	Soil pH (sorption stability increases as pH decreases) Clay fraction CEC	(13)

CEC: cation exchange capacity; SOM: soil organic matter; BCS: base cation saturation.

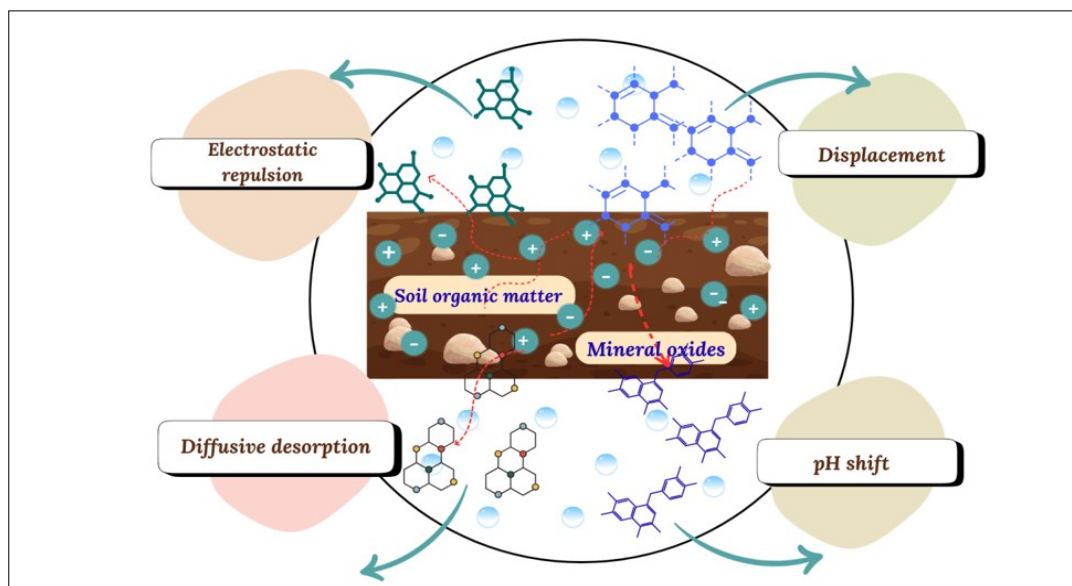


Fig. 5. Pharmaceutical desorption processes in soil.

Factors influencing release of pharmaceuticals back into soil solution

The release of medicines from soil solids into the aqueous phase is primarily governed by the speciation of molecules as determined by solution pH. According to research on the behaviour of doxycycline in agricultural soils, the molecule's ionic state fluctuates between anionic and zwitterionic forms, with greater pH increasing the anionic proportion and electrostatic repulsion from negatively charged soil surfaces (23). This speciation-dependent mechanism means that tetracyclines have a substantially larger desorption potential in alkaline settings than in acidic environments where neutral or cationic forms predominate. Measured distribution coefficients for various ionisable components demonstrate that when pH rises, the neutral fraction decreases, resulting in a significant reduction in stable surface binding and an increase in residue concentrations in the soil solution (32).

Temporal variations in soil organic matter quality are the key driver for the release of sequestered residues during the growing season. As energy-rich aliphatic chains are digested by soil bacteria, the soil's ability to retain neutral substances decreases, frequently resulting in an increase in desorption as electrostatic interactions take over the system. The durability of these residues is further controlled by fungal activity, which alters the soil organic carbon pool and enzyme landscape, influencing the long-term sequestration of persistent chemicals (33).

Dissolved organic matter acts as a mobile phase, facilitating or inhibiting medication release via competitive or carrier-mediated routes. The addition of mobile organic matter from pig manure amendments has been found to reduce the sorption of sulfonamides and beta-blockers by competing for limited hydrophobic locations on the soil surface. This interaction is determined by the polarity and size of the dissolved organic components, which can form stable, soluble complexes with medicinal molecules and "wash" them through the soil. Fertilisation regime differences also affect the availability of labile organic carbon, resulting in variable residue distribution within the soil profile (34). Pharmaceuticals exist in complex mixes rather than single substances, which dramatically alters release kinetics. Evaluations of nonsteroidal anti-inflammatory drug combinations in loam soils show that cooperative adsorption and multilayer bonding effects

can minimise desorption of individual components such as ibuprofen and naproxen (26). These interactions are regulated by the presence of cationic metals and organoclay complexes, which stabilise the adsorbed phase. The selective accumulation and potential release of these compounds into edible plant tissues is heavily reliant on the molecule's neutral speciation, with uncharged species such as carbamazepine translocating more efficiently to leaves and ionic species remaining largely sequestered in root tissues (12).

Role of soil moisture, ionic strength, redox conditions and temperature

Soil moisture influences the connectedness of the pore network and the pace of biochemical transformation of pharmaceutical residues. Higher water content in agricultural soils has been shown to accelerate doxycycline degradation, lowering its half-life by increasing the metabolic activity of soil microbes (23). Under conditions of low surface moisture, the soil matrix maintains a high surface acidity, which can activate abiotic transformation processes. When moisture levels are low, surface-catalysed hydrolysis mediated by clay minerals like montmorillonite becomes the major dissipation pathway for antibiotics like chloramphenicol, demonstrating how desiccation can paradoxically enhance some degradation events (35).

Ionic strength influences the interfacial potential of soil colloids and the strength of electrostatic interactions with ionisable medicines. Increased background electrolyte concentrations can limit pharmaceutical sorption by competing for accessible negative charge sites on soil and sediment surfaces (24). This behaviour is frequently nonlinear, as demonstrated in sulfonamide interactions in silt loam environments, where intermediate ionic strengths increase retention through cation bridging with divalent ions such as Ca^{2+} . When salinity levels reach extremes, competitive displacement by monovalent cations causes previously bound molecules to be released back into the soil solution (11).

Redox conditions act as a master switch that controls the metabolic pathways available to soil microbial populations for pharmaceutical degradation. The transition from aerobics to anaerobic environments substantially affects the dissipation rates of emerging pollutants, with various enzymatic mechanisms

governing transformation in oxygen-depleted horizons (36). In flooded or tropical soil systems, redox-induced alterations determine whether a component mineralises or remains as a parent residue. Antibiotic dissipation in these environments is primarily regulated by oxygen availability and microbial phylotypes, even when other variables such as salinity are constant (37).

Environmental temperature and thermodynamic cycles influence the energetics of surface binding and residue diffusion inside the soil matrix. Acidic medicines, such as ibuprofen, require higher ambient temperatures to break exothermic surface interactions and release into the aqueous phase. Temperature changes also affect the structure of soil organic matter and humic compounds, influencing the accessibility of interior pores for big molecules. These thermodynamic mechanisms are usually spontaneous and control the distribution of veterinary medications such as sulfamethazine between solid soil components and pore water (34).

Bioavailability and plant uptake pathways

Contaminants from wastewater treatment plants enter soil and water matrices directly, creating entry channels for pharmaceutical residues into the agro-food system. Through certain internal biodegradation mechanisms, the presence of antibiotics like sulfamethoxazole in aquatic media promotes uptake by edible plants like *Ipomoea aquatica* Forssk. (38). Both aerobic and anaerobic circumstances influence soil availability and the rates at which substances such as gemfibrozil and carbamazepine biodegrade range from rapid decay to total recalcitrance (36). In areas with extensive agriculture, groundwater distribution acts as a constant bioavailable supply for a range of personal care items including artificial sweeteners. The multi-compartmental transport of pharmaceuticals through local trophic levels is demonstrated by comprehensive distribution patterns in sediments and aquatic animals (39). The environmental load accessible for eventual bioaccumulation in area biota is defined by high concentrations of several antibiotic classes in urban canals. The importance of manure-based exposure routes is demonstrated by the discovery of up to 28 veterinary antibiotic residues in swine wastewater after systematic monitoring (40). Pharmaceutical residues are continuously released into nearby aquatic environments because of treatment techniques that fail to fully remove developing contaminants. The movement of pharmaceutical residues from contaminated soils into plants through root uptake, translocation and accumulation in edible tissues are illustrated in Fig. 6.

Mechanisms of pharmaceutical absorption by roots

Passive diffusion is widely regarded as a major mechanism governing pharmaceutical residue absorption into plant roots, primarily driven by the concentration gradient between soil pore water and the root surface (34), however, uptake also depends on compound-specific speciation, lipophilicity and molecular size, so passive diffusion alone doesn't fully explain absorption across all pharmaceutical classes. According to research on the transfer of these residues from wastewater treatment facilities to agro-food systems, the chemical mass arriving in the rhizosphere directly determines the initial ingress potential.

Binary mixture interactions and transpiration rates have a substantial impact on physiological accumulation, as the upward pull of water through the vascular system alters the kinetics of root-to-shoot passage. High concentrations of perfluoroalkyl compounds in farmland soils irrigated with recycled water provide a consistent source of root contact, defining long-term bioaccumulation profiles in area crops (41).

Small pharmacological residues with molecular weights less than 300 g/mol successfully transcend endodermal constraints in green vegetables and reach the vascular bundle (42). Field tests of tomato crops evaluate the passage of various microcontaminants into edible shoot tissues, indicating that residues like venlafaxine reach quantifiable amounts in aerial sections (43). The presence of pharmaceutical residues in eggplant, cucumber and wheat tissues demonstrates that chronic exposure to reclaimed water causes pollutants to accumulate in underground plant organs (44).

Plants activate protective mechanisms during such as the stimulation of glutathione S-transferases in cucumber to reduce the potential toxicity of chemicals like acetaminophen (13). Shortly after root entrance, the metabolic transformation of absorbed antibiotics in lettuce produces a variety of different metabolites for clarithromycin and sulfadiazine (45). Variations in growing media influence accumulation efficiency, with hydroponically grown crops frequently having higher translocation factors for perfluoroalkyl acids than those cultivated in traditional soil conditions. Interactive dynamics in heavy metal-enriched soil alter roots' ability to sequester residues such as triclosan and carbamazepine, complicating traditional risk assessments (46). Primary producers, such as seaweed, have fast absorption kinetics, allowing them to sequester antibiotic residues from the surrounding aquatic environment within a 24 hr window.

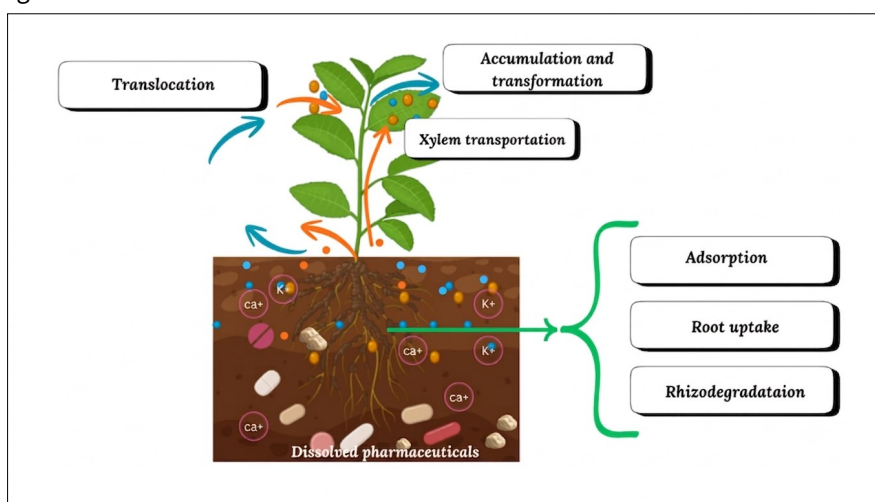


Fig. 6. Soil-plant transfer of pharmaceuticals.

Translocation and accumulation in plant tissues

Pharmaceutical residue translocation in agricultural crops is compound-specific and determines the final distribution of pollutants across plant organs. Vascular movement can be quantified using the root-to-leaf passage ratio, found to be 0.67 for diclofenac in chicory (47). Growing media also affects translocation efficiency: hydroponic crops show much greater translocation factors for perfluoroalkyl acids than soil-grown crops (48). Binary mixture interactions and changing transpiration rates further influence accumulation, suggesting co-contaminants can disrupt individual translocation kinetics. Translocation also varies by species, with carbamazepine levels higher in arugula and radish than in lettuce or spinach.

Internal plant metabolism quickly alters ingested residues after they enter the vascular system; eight unique clarithromycin metabolites have been detected in leaf tissues (45). A structurally analogous mechanism, involving xylem sap latex-like proteins, has been shown for hydrophobic pollutants like polychlorinated biphenyls (PCBs) in cucurbits and may extend to similar hydrophobic pharmaceuticals, though this remains unconfirmed (49).

Factors influencing plant uptake

Real agricultural scenarios including long-term irrigation over four decades show that pharmaceutical residues such as ibuprofen and sulfamethoxazole remain in eggplant and wheat tissues (44). Investigations in Jordanian farmlands show how regional wastewater reuse strategies influence the chemical load reaching the rhizosphere and the subsequent bioaccumulation patterns (41). Desorption from soil particles serves as the primary regulatory step for root contact and subsequent ingress. Bioavailable fractions are thus determined by the equilibrium between sorbed and dissolved phases.

Soil alteration with wood-derived biochar at 1.0 % concentrations considerably lowers the bioaccumulation of chemicals such as carbamazepine and lamotrigine in radish roots (50). Accumulation in leafy vegetables is also influenced by binary mixture interactions and changing transpiration rates, implying that co-contaminants can disrupt individual uptake kinetics. These environmental and chemical combination elements determine the overall mass reaching the plant's interior. Soil amendment methods can be used as a mitigation strategy to reduce crop residual loads.

Cucumber uptake of lamotrigine, for example, is increased in the presence of carbamazepine, although carbamazepine uptake is unaffected by lamotrigine coexistence (29). Observations in real agricultural systems demonstrate that soil features and regional irrigation regimes influence current residue burdens in local crops.

The ability of beetroot to acquire residues such as triclosan and carbamazepine is influenced by interactive dynamics in heavy metal-enriched soil. The choice of growing media also influences bioaccumulation efficiency; hydroponically grown chicory has much greater translocation factors for toxins than soil-based systems (48). The absence of soil sorption sites increases the bioavailable percentage for direct root absorption. Understanding these processes is critical for conducting reliable risk assessments in multicontaminant soil environments.

Impacts on soil ecosystem

Pharmaceutical residues accumulate in terrestrial ecosystems, altering the biological integrity and nutritional capability of

agricultural soils. Continuous contamination in manufacturing environments is frequently aggravated by handling and microorganisms on processing equipment. Soil microbes provide critical ecological services by degrading and transforming pharmaceutical residues within the soil matrix, converting stored xenobiotics into less persistent or non-toxic metabolites. In waste-impacted environments like landfill leachate, bacterial communities also host and disseminate antibiotic resistance genes. This links microbial community structure to both pollutant turnover and resistance gene spread in soil systems (51). The soil microbiome's overall structure and metabolic activity are still predominantly determined by stabilising mechanisms and the habitat's inherent physicochemical features.

Effect on soil health and fertility

The accumulation of imidazolium-based ionic liquid residues in terrestrial environments has been found to exert measurable toxicity on soil microorganisms, which serve as critical indicators of ecosystem health. In agro-ecosystems where manure is frequently applied, the presence of antibiotics can shift the microbial community structure and facilitate the spread of resistance genes, potentially undermining natural nutrient cycles. Efforts to mitigate these effects include the use of biochar-induced immobilisation to stabilise residues and reduce their detrimental impact on soil-plant signaling pathways (52). Co-contamination of pharmaceutical wastes with heavy metals or dyes further complicates soil detoxification processes by affecting the removal efficiency of resistance genes in wastewater treatment systems.

The interaction between pharmaceutical pollutants and arbuscular mycorrhizal fungi can significantly alter crop development and yield by disrupting the beneficial symbiosis required for optimal soil nutrient management. Research into the rhizosphere suggests that the availability of specific minerals like boron and silicon plays a role in determining the accumulation patterns and toxicological effects of contaminants in the soil-root interface (53).

Alteration of microbial community structure

Even though overall diversity looks unaltered, selective pressure from macrolide antibiotics such as erythromycin causes considerable changes in soil bacterial community composition (54). High selective pressure from numerous antibiotic pollutants increases the relative abundance of phyla like Acidobacteria and Bacteroidetes, which adapt to use these chemicals as primary metabolic substrates. The structural reaction to pharmaceutical residues is frequently antibiotic-specific, as seen by different tetracycline types causing differential alterations in phospholipid fatty acid (PLFA) patterns depending on the chemical molecule present (55). Under such pharmacological stress, indigenous denitrifying bacteria remain transcriptionally active, frequently serving as important carriers of multi-antibiotic resistance in the terrestrial microbiome.

Long-term agricultural exposure to pharmaceuticals via reclaimed water irrigation is linked to a significant drop in overall bacterial abundance, particularly in surface soil layers (56). The discharge of untreated industrial pharmaceutical effluents significantly alters the soil microbiological profile by providing high nutrient levels that promote the expansion of specific bacterial populations (57). Production activities near pharmaceutical companies show that, while microbial evenness may stay stable, the principal bacterial genera are dramatically altered by the localised environmental conditions associated with manufacture.

In complicated environments, such as landfill leachate-contaminated zones, most pharmaceutical and personal care items have a substantial positive link with microbial development because they provide extra energy sources for survival (58). The soil microbiome's makeup is significantly influenced by stabilising mechanisms, with certain genera such as soil isolates participating in wastewater biodegradation can create organic acids that significantly reduce soil pH over time. Synergistic degrading strains can be used to improve the mineralisation of residues that have become trapped in the soil matrix (51).

The overall distribution and richness of the bacterial community are frequently limited by the habitat's physicochemical features, such as soil pH functioning as a major physiological filter. Improper handling and the presence of pathogens on pharmaceutical manufacturing equipment might transfer external fungal diseases into the local soil. The use of industrial waste such as swine biogas slurry alters the soil microbiome by increasing the prevalence of bacterial pathogens and resistance genes. Aeration techniques are employed in contaminated soils to control microbial gas-water dynamics and reduce greenhouse gas emissions from the changed community (58).

Interference with nutrient cycling (nitrogen, phosphorus and carbon cycles)

Long-term irrigation with reclaimed water containing pharmaceuticals causes a large accumulation of chemicals such as sulfamethoxazole in the soil profile, which correlates negatively with overall bacterial abundance (56); because soil bacteria drive organic matter decomposition and nutrient mineralisation, this decline directly reduces the microbial capacity to cycle nitrogen (N), phosphorus (P) and carbon (C) through the soil system. Within the N cycle specifically, urease is a key enzyme responsible for hydrolysing urea into plant-available ammonium and its suppression under antibiotic contamination (55) therefore slows N mineralisation and limits N availability to plants, particularly in soils with minimal organic matter to buffer this effect. Bioactive pharmaceutical effluents can increase soil total organic C and P levels, suggesting short-term nutrient enrichment; however, the concurrent shift in microbial profile toward genera such as *Staphylococcus* and *Escherichia* (57) indicates that this added C and P may not be efficiently cycled, since these genera are not the primary drivers of

organic matter turnover or P solubilisation in healthy soils. Collectively, these disruptions to bacterial abundance, enzymatic activity and microbial community composition alter N, P and C cycling and broader ecosystem functioning, as summarised in Fig. 7.

Effects on soil enzyme activities

The release of untreated pharmaceutical effluents into agricultural environments causes severe dysregulation of key soil catalysts such as phosphatases, dehydrogenases and ureases. These enzymatic changes act as main bio-indicators of soil functional deterioration, linking industrial pollution to detectable decreases in soil fertility (57). Industrial production activities around manufacturing facilities encourage the adaptability of novel microbial species, a shift driven mostly by localised soil organic matter and metal content rather than drug concentration alone.

Soil enzymes react differently to synthetic residues, with urease showing higher inhibition rates than phosphomonoesterase or β -glucosidase when exposed to tetracycline (55). The accumulation of pharmaceutical residues in soil profiles, such as sulfamethoxazole, correlates negatively with overall bacterial abundance, limiting the biological system's potential for nutrient cycling (56). Microbial populations in acidic settings frequently exhibit limited diversity and richness, which coincides with much longer persistence of macrolide antibiotics such as erythromycin (54). Handling and the presence of infections on manufacturing processing equipment commonly worsen ongoing biological contamination in production settings. The stabilisation procedures and inherent habitat characteristics of a contaminated site have a significant impact on the overall metabolic functions and composition of the soil microbiome. The effects of pharmaceutical residues on soil enzyme activity and overall soil health are illustrated in Fig. 8.

Effects on crop growth and productivity

The introduction of pharmaceutical residues into agricultural systems has a significant impact on food crop morphology and metabolic efficiency. Experimental evidence from maize cultivation shows that ciprofloxacin absorption significantly reduces root elongation and initial germination rates (59). The addition of nonsteroidal anti-inflammatory medications, which cause toxicities inside thylakoid membranes, further inhibits photosynthetic ability

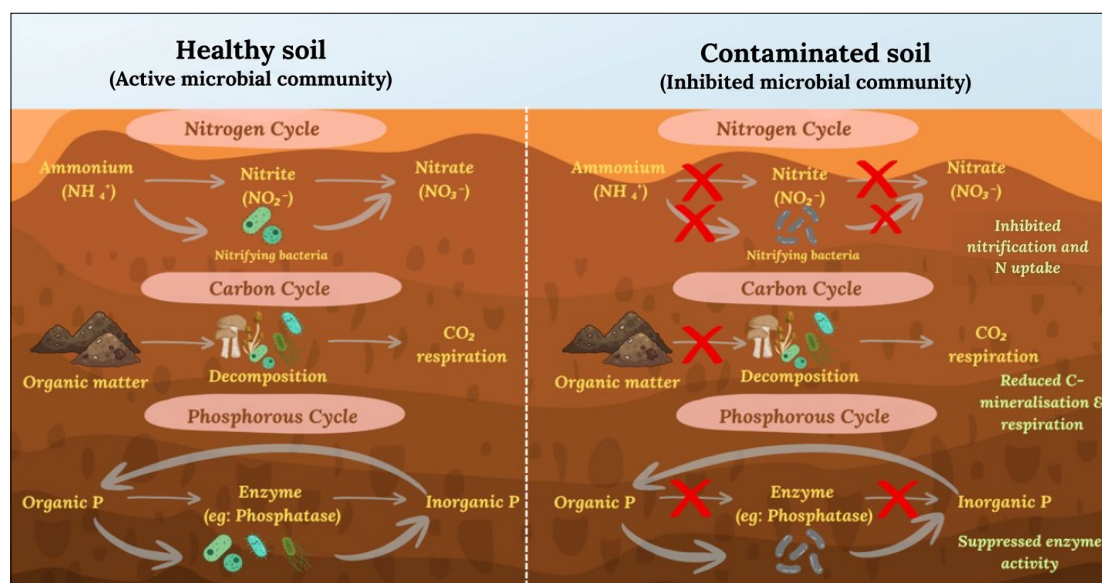


Fig. 7. Effects of pharmaceuticals on soil nutrient cycling.

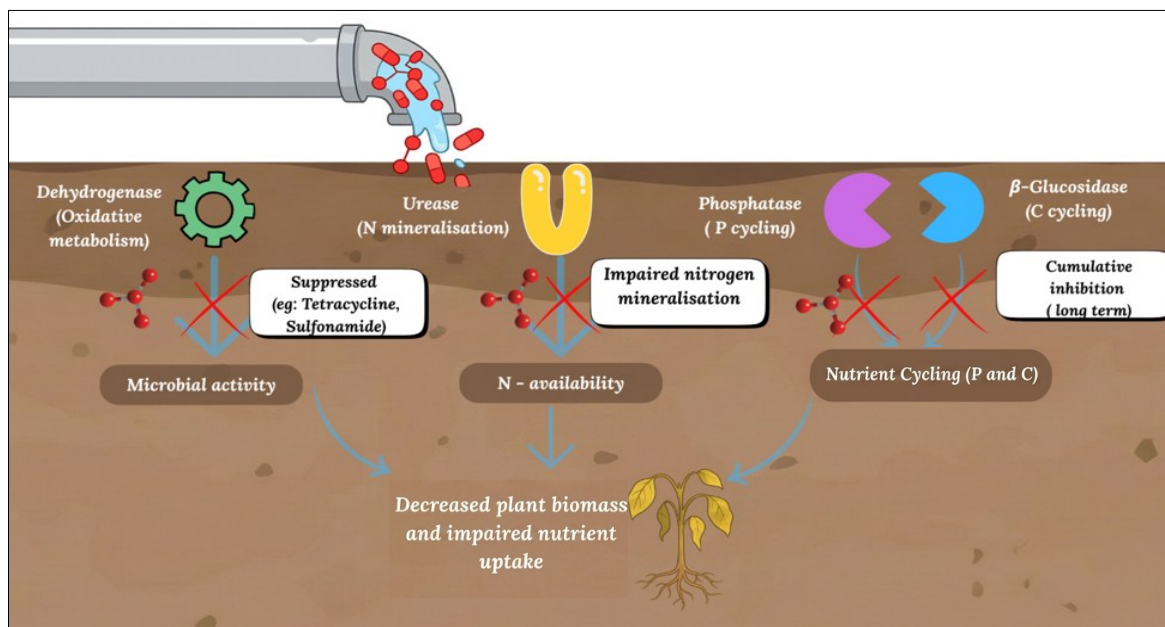


Fig. 8. Effects of pharmaceuticals on soil enzyme activity and soil health.

in primary producers. Chemical stress in legume species such as *Vicia faba* L. has been quantitatively related to a decrease in potential physiological capacity as determined by integrated biomarker response indices (60). Comprehensive ecological investigations reveal that these pharmacologically active chemicals are disseminated throughout aquatic species and sediments in major deltas, posing a considerable risk to trophic chain stability (39). These findings show the complicated connections between soil pharmaceutical residues and crop productivity, stressing the importance of sophisticated risk assessment in modern agriculture.

Physiological and morphological impacts on plants

Early phases of cereal crop development are severely hampered by the uptake of pharmacologically active substances. Exposure to some residues has been associated with a measurable decrease in root elongation and total biomass production in maize seedlings (59). According to research, the soil-plant-water continuum affects these interactions; in wastewater-irrigated soils, residue persistence causes reduced vegetative growth. The symbiotic interactions between plants and soil microorganisms can be upset by the presence of antibiotics in agricultural soil, which eventually weakens the root system's structural integrity (39).

In aquatic systems, pharmaceutical pollutants significantly impact the photosynthetic efficiency of primary producers. Amoxicillin exposure decreases growth rate and chlorophyll content in aquatic macrophytes, likely by disrupting chlorophyll biosynthesis, while veterinary antibiotic mixtures produce more complex, species-specific suppression of metabolic activity (61). Such reductions in pigment content and photosynthetic performance are frequently indicative of broader physiological stress in aquatic species.

In sensitive crop varieties, the introduction of pharmaceutical residues into the growing media sets off intricate biochemical defence mechanisms. These stresses cause intracellular radicals to be produced, which can hinder the early establishment phase's ability to absorb vital nutrients (52). It has been shown that fluoroquinolone buildup in the rhizosphere causes systemic toxicity, requiring the activation of specific scavenging systems to preserve cellular homeostasis (14). Persistent antibiotic residues in wastewater-

irrigated crops may also drive selection for antibiotic resistance genes within the plant-soil system, potentially impeding the normal microbial breakdown of environmental contaminants.

Certain pharmaceutical residues have the potential to be genotoxic, endangering the genetic stability of agricultural systems in addition to physiological changes. Reduced agricultural output is mostly caused by structural damage at the cellular level, which frequently involves root apical meristem deformation and restricted cell division (59). Chemical classes have different patterns of toxicity, with greater doses causing irreversible damage to cell membranes and mitochondrial structures. These results highlight how important it is to incorporate toxicological endpoints into existing risk assessment frameworks for soils affected by pharmaceuticals.

Potential risks to food safety and human health

One important route that pollutants can enter the human diet is through the absorption of pharmacologically active components from soil and irrigation water. Antibiotics are absorbed and translocated inside the plant matrix, enabling their direct passage into the food chain, according to research on the absorption processes of these drugs in plants. Exogenous caffeine and ibuprofen effectively translocate into rice grains, according to quantitative analysis of cereal crops. This suggests that human populations may annually absorb considerable amounts of these substances through a daily staple meal.

The extensive dissemination of these wastes across several trophic levels in agricultural settings increases ecological problems. Pharmaceutical residues in water and sediments are dispersed throughout aquatic creatures, offering a quantifiable health risk to the nearby human population through eating, according to extensive research conducted in major deltas (39). It has been demonstrated that antibiotics and other common agrochemicals interact to cause certain physiological changes in aquatic macrophytes, demonstrating how the complexity of chemical mixtures can confound existing risk mitigation techniques (59).

One of the main issues for long-term human health is the selection and spread of drug-resistant bacteria within the soil-plant system. The inactivation of antibiotic-resistant bacteria and the breakdown of resistance genes can be impacted by ongoing

exposure to pharmaceutical residues; this process is heavily reliant on the existence of secondary environmental contaminants. To effectively remove antibiotics and related resistance genes from manure-based fertilisers before they reach agricultural land, managing these risks requires evaluating the effectiveness of industrial composting and anaerobic digestion.

Exposure to pharmaceuticals causes biochemical changes that could lower the total nutritional value of foods that people eat. It has been demonstrated that soil-borne ionic residues significantly change the levels of lipid peroxidation and enzymatic antioxidants in wheat seedlings, indicating a disrupted metabolic state during the key establishment phase (62). Because any interference with the accumulation of vital nutrients and minerals in edible tissues directly jeopardizes global food security and public health, such toxicological effects are especially problematic for staple crops (63).

To guarantee a safe food supply, advanced risk assessment techniques are currently concentrated on measuring physiological harm at the cellular level. A reliable framework for evaluating the long-term biological effects on human health is provided using integrated biomarker response indices, which enable a standardised and accurate toxicity assessment of pollutants on sensitive crop types (60). The major pathways through which pharmaceutical residues are transferred from contaminated soils to humans via crops and environmental exposure are illustrated in Fig. 9, emphasising the potential implications for food safety and public health.

Remediation and mitigation strategies

To effectively reduce pharmaceutical residues in soil and water matrices, biological, physical and chemical techniques must all be combined. Advanced carbonaceous materials, such as magnetically functionalised biochars, offer large adsorption sites for the fast removal of antibiotics like tetracycline (63). Engineered mineral phases, such as thermally modified bentonite, have shown improved kinetics for sequestering fluoroquinolones compared to natural clay forms (64). Microbial biodegradation is a key reactive route, with specialised strains such as *Sphingobium* sp. WTD-1 successfully mineralising chloramphenicol residues (65). Bioaugmentation technologies that use fungal biomass in fluidised bed reactors considerably improve the removal rates of complicated pharmaceutical combinations from wastewater streams (66).

Microalgal species, such as *Chlorella sorokiniana*, have been found as effective agents for the biotransformation of analgesics and salicylic acid via metabolic reactions (67). Innovative sequestration systems, such as ordered mesoporous C-alginate beads, enable the steady recovery and regeneration of antibiotic-laden adsorbents (68). These nature-based and artificial solutions are crucial for restoring ecosystem health and preventing pharmaceutical metabolites from entering groundwater reservoirs Table 4.

Physical and chemical remediation

Magnetic functionalised biochar generated from rice trash removes tetracycline antibiotics with over 96 % effectiveness in

Table 4. Advanced remediation and mitigation strategies for pharmaceutical residues in soil systems

Technique or method used for remediating the soil	Treatment type	Target pharmaceuticals	Mechanism	Reference
Magnetic functionalised rice waste biochar	Physical	Tetracycline	High-capacity surface adsorption and sequestration	(63)
Thermally modified bentonite clay	Physical	Ciprofloxacin	Enhanced adsorption kinetics and surface complexation	(64)
Ce-doped ZnO heterogeneous photocatalysis	Chemical	Acetaminophen and Nizatidine	Reactive oxygen species-driven mineralisation under radiation	(69)
Microbial bioaugmentation sp. WTD-1)	Biological	Chloramphenicol	Complete mineralization via multiple metabolic pathways	(65)
Wetland plant rhizoremediation (<i>Canna</i>)	Biological	Sulfonamides	Rhizosphere interaction and selective plant uptake	(70)
Struvite-loaded zeolite amendment	Physical / Chemical	Tetracycline and ARGs	Physical immobilisation and reduction of microbial host abundance	(71)
Ordered mesoporous carbon-alginate beads	Physical	Chloramphenicol	Multi-stage adsorption and stable recovery/regeneration	(68)
Iron-activated bermudagrass biochar	Physical	Sulfamethoxazole	Iron-facilitated surface sequestration	(72)
Corn cob xylose residue-derived biochar	Physical	Sulfamethoxazole	Large specific surface area adsorption	(73)
Microbial bioaugmentation (<i>Pseudomonas moorei</i> KB4)	Biological	Diclofenac	Enzymatic cleavage and metabolic utilisation	(74)
Integrated waste-fungus-chaff-biochar (WFCB) with <i>H. huttiae</i>	Biological / Physical	Enrofloxacin and Oxytetracycline	Combined physical adsorption and enzymatic degradation	(75)
High-temperature pyrolysed biochar (> 500°C)	Physical	Ceftiofur and Florfenicol	Enhanced micropore sequestration	(76)
Microbial extract bioaugmentation strategy	Biological	Diclofenac	Accelerated biodegradation via acclimated microbial extracts	(77)
Fungal-pelleted fluidised bed	Biological	Complex Pharmaceutical	Fungal biomass-mediated elimination of	(66)

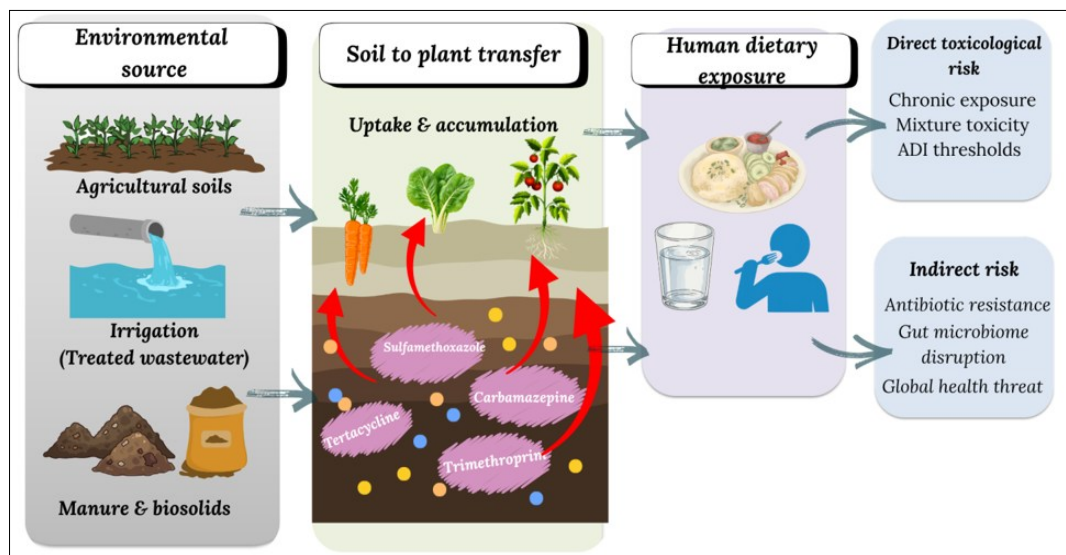


Fig. 9. Pathways of pharmaceutical exposure from soil to humans.

contaminated water systems (63). Iron-activated biochar generated from bermudagrass is an excellent platform for the sequestration of aqueous sulfamethoxazole at iron impregnation ratios (72). Large specific area biochars generated from corn cob xylose residue have been shown to remove sulfamethoxazole with high performance (73). The adsorption efficacy of veterinary antimicrobials such as ceftiofur and florfenicol rises dramatically when biochars are pyrolysed at temperatures above 500 °C (76). Rice straw biochar produced at 500 °C has a considerable impact on the soil bacterial population while permitting a 71 % breakdown rate for crude oil components (78). The effectiveness of biochar in mitigating soil acidity is strongly influenced by both the pyrolysis temperature and the feedstock composition (79). High-temperature date palm biochar has a 122-fold larger specific surface area than biochar produced at 300 °C, making it easier to sequester a variety of organic contaminants (80). Adding 2 % biochar improves rhizoremediation by *Lolium perenne*, displaying great efficacy in polycyclic aromatic hydrocarbon elimination (50). The use of sugarcane bagasse biochar in conjunction with *Bacillus* sp. improves the physiological and agronomical characteristics of maize in diesel-contaminated environments (81). These designed carbonaceous platforms act as a strong barrier to the vertical transport of medicines via soil profiles.

Thermally treated bentonite clay provides a specific surface for ciprofloxacin adsorption with much higher kinetics than native mineral forms (64). Innovative sodium-alginate montmorillonite composite beads provide an enhanced mechanism for tetracycline adsorption with capacities reaching 745 mg/g (16). Cation exchange interactions influence fluoroquinolone sorption in agricultural soils, which vary depending on the soil type's mineralogy.

The presence of root-derived organic acids has a considerable impact on the adsorption properties of pharmaceuticals in sandy topsoils by changing surface charge (82). The adsorption behaviour of fluoroquinolone antibiotics on soil organic matter pools is significantly influenced by land use-induced soil heterogeneity (83). Struvite-loaded zeolite amendments effectively reduce the abundance of host bacteria containing antibiotic resistance genes in contaminated soils (71). Natural clays, such as montmorillonite, cause tetracycline transformation under anoxic dark conditions (84). These mineral-based techniques are a natural, sustainable alternative for immobilising persistent medicines in terrestrial ecosystems.

For the recovery and subsequent regeneration of adsorbents loaded with chloramphenicol, ordered mesoporous carbon-alginate beads offer a stable platform (68). In a two-stage stirring adsorber analysis, magnetic chicken bone biochar eliminates 96 % of tetracycline (85). Under UV light, Ce-doped ZnO photocatalysts enable the reactive degradation of acetaminophen and nizatidine by reactive oxygen species (69). Compared to conventional pyrolysed forms, ball-milled biochar efficiently eliminates sulfapyridine due to improved microporosity and increased surface area (86). By making it easier to remove dangerous water contaminants, waste-derived nano biochar is a crucial step toward a circular bioeconomy.

Biological approaches

Within 60 hr, the bacterial strain *Sphingobium* sp. WTD-1 completely mineralises chloramphenicol via various metabolic routes (65). *Pseudomonas moorei* KB4 degrades paracetamol by releasing acetate and breaking down hydroquinone rings (74). The isolate *Bosea* sp. Ads-6 eliminates almost 90 % of amoxicillin residues by 4-hydroxybenzoate hydroxylation and the beta-keto adipate pathway (87). *Pseudomonas* strain PrS10 removes 96.37 % of paracetamol from pharmaceutical effluents during 7 days of remediation (88).

Microalgal-induced antibiotic co-metabolism is mediated by cytochrome P450 enzymes, which control the kinetics and transformation products of levofloxacin. Microbial reactions to pharmaceutical amendment in agricultural soils might be stimulated, inhibited, stressed, or dormant, depending on soil parameters and exposure period. When microalgal cultures are combined with certain plant consortia, sulfamethazine biodegradation increases considerably (89). Synergistic interactions between *Paenarthrobacter ureafaciens* and *Pseudomonas korensis* increase sulfamethoxazole breakdown at an ideal temperature of 30 °C (90). These bacteria pathways are the principal reactive mechanisms responsible for pharmaceutical environmental modification.

Wetland plant species such as *Canna indica* L. and *Iris pseudacorus* L. effectively disperse complex sulfonamide combinations in hydroponic systems (70). Submerged aquatic plants, such as *Vallisneria spiralis* (Lour.) H.Hara, help to remove sulfonamide medications while controlling physiological stress responses (91). *Myriophyllum aquaticum* (Vell.) Verdc. may remove

up to 99 % of tetracycline drugs from contaminated water in 7 days (92). Duckweed systems that use *Spirodela polyrhiza* (L.) Schleid. contribute to the breakdown of ofloxacin while demonstrating distinct phytotoxic reactions (61). Microalgal species like *Chlorella vulgaris* remove fluoroquinolones in a concentration-dependent manner while accumulating lipids (28). These nature-based solutions use selective plant uptake and rhizosphere biodegradation to rehabilitate contaminated habitats.

The addition of fungal biomass in pelleted bioreactors improves the removal of complicated combinations of medicinal chemicals from municipal wastewater (66). Bioaugmentation with microbial extracts promotes the biodegradation of developing pollutants such as diclofenac in various environmental mediums (77). Microalgae species have physiological defensive responses to remove seven frequently identified antibiotics (67). Waste-fungus-chaff-biochar coupled with *Herbaspirillum huttiense* degrades enrofloxacin and oxytetracycline while also immobilising heavy metals (75). *Chlorella sorokiniana* removes several antibiotics in a concentration-dependent manner using increased photosynthetic efficiency (93).

A metagenomic investigation of the soybean rhizosphere demonstrates that field-aged biochar alters nitrogen-cycle microbial populations, promoting plant growth (94). Integrated fixed-film activated sludge systems remove estrogens more effectively than typical mechanical facilities. These biological frameworks ensure that medications are completely mineralised and converted into ecologically friendly metabolites.

Wastewater treatment and regulatory measures to prevent soil contamination

Nanofiltration performance anticipated by experimental design optimisation enables successful treatment of antibiotic-containing wastewater. Integrated fixed film activated sludge reactors outperform typical treatment facilities in terms of removing estrogenic activity and tracing organic pollutants. Biofiltration using active granular activated carbon greatly lowers the health risks associated with medication concentrations in drinking water. Membranes designed with water-repellent PVDF-HNT create a strong barrier for extracting oxytetracycline from wastewater streams (95). Titanium dioxide (TiO₂)-based dual membrane photocatalysis reactors totally remove 18 medicinal chemicals within 1 hr of treatment (96). Ultra-high-performance liquid chromatography combined with high-resolution mass spectrometry enables the measurement of hundreds of hazardous chemicals in nutraceutical goods. Soybean peroxidase systems, when paired with hydrogen peroxide, provide a sulfamethoxazole detoxifying mechanism (97). These technological improvements are critical to ensuring that treated effluents meet severe environmental safety requirements.

Sludge contamination levels are in the following order: limed sludge > digested sludge > composted sludge > solid digestate, demonstrating that maturation reduces drug levels (10). Long-term agricultural recycling of pharmaceutical-laden sewage sludge on soil increases organic matter quality but may increase exchangeable salt concerns. Soil organic matter decomposition is a major contributor to medicinal retention in Mollisol soils throughout a simulated vegetation season (82). Understanding the dynamics of protected and non-protected C pools is critical for forecasting pharmacological

bioavailability across land uses. Soil organic C transformation and microbial dynamics are greatly affected by various organic additions. Biochar addition to seagrass environments increases photosynthetic rate while changing the bacterial community structure. The use of biochar-based materials as a restoration technique in petroleum-contaminated soil reduces hydrocarbon leaching. Sustainable soil management must include these results to maintain long-term terrestrial functionality and biodiversity.

Struvite-loaded zeolite amendments effectively reduce the abundance of host bacteria containing antibiotic resistance genes in microplastic-contaminated soils (70). Antibiotics dissipate in flooded tropical soils regardless of salinity, underscoring the importance of microbial-induced breakdown in a variety of climates (37). Soil parameters can be used to predict sorption and assess the mobility of micropollutants in agricultural soils, while multi-tracer approaches to groundwater recharge seasonality help identify the pathways through which urban wastewater contaminants migrate into aquifers (18). The interaction of DOM from pig manure with soil influences caffeine and atenolol absorption (98). The presence of mobile organic matter from manure considerably regulates veterinary antibiotic transport in farmland soils. The presence of biological filters such as *Daphnia magna* influences the adsorption of estradiol by natural clays. The partition of pharmaceutical residues in soil pore water is an important indicator for determining plant accumulation (34). Together, these regulation and treatment procedures are critical to ensuring clean water availability and public health.

Conclusion

The evidence reviewed here indicates that pharmaceutical fate in soil cannot be explained by any single property or mechanism in isolation; sorption and desorption behaviour emerges from the interaction of soil physicochemical conditions, pharmaceutical structural characteristics and site-specific environmental variables, making generalisable prediction difficult. A recurring limitation across the studies synthesised is their reliance on single-compound, single-soil laboratory conditions, which fail to capture the mixture effects, transformation-product behaviour and field-scale heterogeneity of real agricultural systems; reported effects also vary considerably between studies and this variability is rarely interrogated. Current risk-assessment approaches remain structurally limited as a result, since they are largely built on this same narrow evidence base. Advancing the field will require fewer single-variable laboratory studies and more long-term, multi-compound field research integrating soil-plant-microbe interactions to test whether laboratory-derived mechanisms hold under realistic conditions. Until such evidence exists, claims about pharmaceutical persistence, mobility, or remediation efficacy in soil should be treated as context-dependent rather than universal.

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Authors' contributions

RS conducted the literature survey, compiled the information and prepared the manuscript. PPC conceptualised and supervised the study. BK, KR and JP contributed to manuscript review and provided technical inputs. PS and AJJ assisted with literature collection, editing and proofreading. All authors have read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest: Authors do not have any conflicts of interest to declare.

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Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this manuscript, the authors used “QuillBot” for language editing, grammar correction and paraphrasing. The images in the manuscript was created by the author using “Canva”. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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