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Profiling of Antibiotic Residues in Soil and Vegetables Irrigated Using Pharmaceutical-Contaminated Water in the Delhi Stretch of the Yamuna River, India

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Abstract: The movement of emerging pollutants, particularly antibiotics, from surface water to crops through the process of plant uptake poses a significant public concern related to the agricultural utilization of untreated water and biosolids. It is essential to consider the potential risk of inadvertent human exposure and the accumulation of drug residues in fresh food crops, particularly in the case of various green vegetables. Nowadays, environmental research is mainly focusing on the bioaccumulation and threat posed by pharmaceutical residues, especially antibiotics and personal care products in the soil–plant ecosystem. In the present study, the concentration of pharmaceuticals in soil samples collected from agricultural fields irrigated with Yamuna water were evaluated using suitable extraction and sophisticated instrumentation techniques. Out of the five sampling locations, the highest concentration of ofloxacin was reported at Site-V (0.265 µg/mg) during the premonsoon period and the lowest concentration (0.014 µg/mg) during the postmonsoon at Site-II, in terms of the average concentration; this could be due to the combined effect of anthropogenic activities, surface water runoff, and the combined load of drains in the vicinity. For the quantification of the selected antibiotics in a green leafy vegetable (*Spinach oleracea*), the concentration of ofloxacin was found to be the highest at Okhla barrage Site-V (5.586 µg/mg) during the premonsoon period, with the lowest concentration observed at Site-I, from 1.382 µg/mg to 1.698 µg/mg, during the postmonsoon period. The higher concentration of ofloxacin in crops is because of its susceptibility to being absorbed at the soil's surface. Plant absorption of antibiotics is influenced primarily by the biological characteristics of the plant, encompassing factors like the lipid and carbohydrate composition of the plant roots. Additionally, the physiochemical properties of the drugs, including molecular size, Kow, and pKa, play a significant role in this process. The antibiotics showed greater variation in their concentration during the premonsoon than in the postmonsoon period, which may be because of precipitation, dilution, and the leaching effect of the soil. For all three of the drugs studied, the concentrations followed the order of ofloxacin > amoxicillin > erythromycin. Thus, the effective management of contaminated soils and vegetables must consider continuous monitoring and risk assessment of high-priority antibiotics to prevent negative effects on the natural environment and human health.

Keywords: drug residues; surface water; bioaccumulation; risk assessment; human health

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1. Introduction

Pharmaceuticals are a broad category of chemical compounds that include over-the-counter, prescription, and veterinary medications, as well as consumer items that are used for personal care, cosmetic, and health purposes [1]. Pharmaceutical active ingredients are often found in high concentrations in both water and land environments due to their persistent release from treated municipal wastewater, biosolids, and manure in which they are disposed [2]. The extensive use of treated wastewater and biosolids in agriculture presents various economic and environmental benefits; however, a novel challenge has arisen from the perceived risk to food safety from emerging contaminants, particularly antibiotics, which have been discovered in these resources almost everywhere [1]. The prevalence of antibiotics in soil has grown to be a serious issue over the past ten years, much like other contaminants [3]. Even after undergoing water treatment processes, treated sewage still contains varying levels of antibiotic residue, which can eventually find its way into sewage sludge or the resulting wastewater [4]. It is standard practice in many nations to use treated or untreated wastewater for irrigation; for example, Israel's agricultural industry used approximately fifty percent of the country's total water for irrigation in 2010 [4].

Antibiotics are most often found in treated wastewater and biosolids, with concentrations ranging from ng/l to low µg/l in treated wastewater and from µg/kg to low mg/kg (dry weight) in biosolids [5,6]. While certain studies suggest that manure-based fertilizers contain only minimal amounts of antibiotics [7], a significant portion of these antibiotics can be retained in the soil after application [8]. Manures used as organic fertilizers in agricultural sectors can drive the selection of soil microbes because of the presence of antibiotic residues and result in an increase in antibiotic resistance in soils, both in terms of antibiotic-resistant bacteria and genes [6]. Residues from diverse antibiotics present in the soil environment may hinder seed germination and impede the growth of crops. Additionally, these residues have the potential to be absorbed by crops, posing a potential risk to soil ecosystems [3]. Because of the possibility of unintended human exposure, the accumulation of drug residues in crops that are consumed raw, like many green vegetables, is important. Pharmaceuticals may reach plant tissues by root absorption after entering the soil via wastewater or biosolids [9]. Studies have shown that vegetables containing pharmaceuticals pose a threat to human health, as they will support the use of recovered water and improve humans' favorable impression of water reuse [10]. The eating of raw vegetables, especially leafy vegetables, may unintentionally expose humans to antibiotic consumption [4]. The unique chemical nature of antibiotics render them naturally biodegradable in the environment, allowing them to readily move through the food chain and, ultimately, accumulate within the human body [11].

There is an urgent need to study the issue of antibiotic contamination, which poses a significant threat to organic vegetable farms, contributing to food security crises. It is imperative to pinpoint pharmaceuticals with high priority, given their capacity to significantly impact the environment. The widespread presence of pharmaceutical remnants leads to potential threats aquatic ecosystems, influencing the water quality and lower organisms. In spite of being present in lesser concentrations, these substances may not manifest immediate effects but can accumulate over time, hence leading to chronic repercussions in living organisms in the foreseeable future [12,13]. Remarkably, there is a limited understanding of how antibiotics behave in soil and organic vegetable environments. Laboratory simulations have revealed the clear ecotoxic impacts of antibiotics on crops such as wheat, Chinese cabbage, and tomatoes. Research has delved into the persistence and sorption of antibiotics in soil, examining their potential impact on soil microorganisms. While field studies have provided closer insight into real-world conditions, there remains a notable lack of knowledge regarding the occurrence and source analysis of typical high-priority antibiotics in fields, particularly in organic vegetable bases [14]. In India, there is a lack of foundational data regarding the surveillance of wastewater discharge of antibiotics into agricultural lands. This absence of information leads to elevated levels of antibiotic contaminants, posing potential threats to health and adding to the buildup of antibiotic drugs in crops [15,16]. Thus, the foci of the current study are to (i) examine the dispersal of three high-priority antibiotics from the surface water of the Yamuna River to surrounding agricultural fields (soil and crops) and to (ii) evaluate the antibiotic uptake by green leafy vegetables.

2. Occurrence of Antibiotics in Soil and Vegetable

Globally, a significant quantity of animal waste is produced and reintegrated into the soil, either directly or through the utilization of fertilizers derived from manure. Even though most drugs are made to be biodegradable and water soluble, many compounds exhibit a high log K_{ow}, which means they have a strong affinity for soil and sludge [4]. The agricultural sector is the largest consumer of raw wastewater by volume, and this use is anticipated to rise in the ensuing decades. Agricultural irrigation using treated wastewater is a developing technique in semi-arid locations that provides a new terrestrial channel for environmental exposure to antibiotics [17]. Limited information is accessible regarding the concentrations of most antibiotics in fertilizers, although some research reports that only trace amounts of antibiotics are still present in manure-based fertilizers [7,18]; for example, the presence of 6.7 μg/kg and 5 μg/kg concentrations of anoxytetracycline at depths of 0 cm, 30 cm, and 60 cm were reported following the application of manure at a rate of 96 Mg/ha. In another study, tetracycline concentrations of 86 mg/kg, 199 mg/kg, and 172 mg/kg were recorded at depths of 0–10 cm, 10–20 cm, and 20–30 cm in soils that had been amended with liquid swine manure [19]. A significant portion of drugs in manure might remain in the soil after being administered [8], as shown in the studies conducted in different nations presented in Table 1. The fate and behavior of antibiotics in soil are influenced by a number of chemical, physical, and biological phenomena [17]. In many developing nations, the inadequate management of hospital wastewater leads to the accumulation of antibiotic residues in agricultural lands. Hospitals of all sizes lack proper facilities for wastewater treatment, resulting in the direct discharge of untreated wastewater into drains and streams. This untreated wastewater then finds its way into surface waters and canals, from where farmers utilize it for irrigation purposes without any prior treatment.

References [15,20,21]. Depending on the antibiotics' physicochemical characteristics and the recipient soils' characteristics, antibiotics are usually stored in the top soil layer, leached into groundwater, or discharged into surface water and then accumulated in edible crops [3,22,23]. Analyses carried out in actual, uncontrolled circumstances with changing soil properties containing manure and/or biosolids have shown antibiotic absorption in various agricultural processes. Similar to this, a number of researchers have verified that raw wastewater application results in antibiotic uptake in real-field or simulated real-field circumstances [22]. However, specialized research on the prevalence of antibiotics in agroecosystems according to various agricultural techniques, which are necessary for accurate estimates of the danger to human health, are scarce. The physicochemical characteristics (Table 2) of selected antibiotics, such as their chemical structure, size, shape, solubility, and hydrophobicity, as well as fundamental qualities such as soil type, soil texture, pH level, and other organic matter content, have an important effect on the actions and outcomes of such drugs in soil [24].

Additionally, antibiotics may continuously exert a selection pressure on soil microorganisms over an extended duration, favoring microbial genes for antibiotic resistance (ARGs). Antibiotic-resistant genes might spread to prospective pathogens through the technique of horizontal gene transfer, causing antibiotic resistance to persist in the environment and aggravating this public health issue [6,25,26].

Table 1. Literature survey of antibiotics absorption and accumulation by vegetables and crops.

Study Area	Plant Species	Antibiotics	Concentration (µg/Kg)	Reference
USA	Corn	*Sulfamethazine*	<1060	[27]
Minnesota, USA	Green onion, cabbage	*Chlortetracyclineand tylosin*	17–10,002	[27]
Minnesota, USA	Carrot, lettuce	*Enrofloxacin, florfenicol, levamisole, and trimethoprim*	2.8–170	[28]
USA	Wheat	*Chlortetracycline and sulfadiazine*	1.1, 0.5, 0.043	[29]
Minnesota, USA	Lettuce and potato	*Sulfamethazine*	100–1200	[30]
China	Alfalfa (*M. sativa* L.)	*Oxytetracycline*	300–900	[31]
Zhejiang, China	Radish, celery, leek, and pak choi cabbage	*Chlortetracycline*	277–364; 139	[32]
Guangdong, China	Chinese cabbage, green pepper, sweet potato, potato, ipomoea aquatica, white gourd, carrot, lettuce, and bitter melon	*Oxytetracycline and tetracycline*	41–174, 0–48	[33]
Guangdong, China	Chinese flowering cabbage, green pepper, sweet potato, white gourd, lettuce, bitter melon, and carrot	*Sulphapyridine sulfathiazole, sulfameter, sulfadiazine, sulfamethazine, and sulfonamides*	380–2240	[34]
Tianjin, China	Radish, coriander, rape, celery, and coriander	*Oxytetracycline, tetracycline, chlortetracycline, sulfamethazine, sulfadoxine, sulfachloropyridazine, sulfachloropyridazine, chloramphenicol, ofloxacin, pefloxacin, ciprofloxacin, and lincomycin*	0.1–532	[35]
USA	Soybean	*Carbamazepine, diphenhydramine, and fluoxetine*	216 ± 2.6, 16.9 ± 2.6	[36]
Norway	Barley, wheat oat, carrot potato, and tomato	*Metformin*	500–1500	[37]
China	Cucumber	*Ciprofloxacin, enrofloxacin, and naproxen*	2.4–651.6 0.1–166.9 0.4–288.3	[38]
Iran	Honey	*Oxytetracycline*	5.32–369.1	[39]
Spain	Tomato	*Sulfamethazine*	1.70	[40]
China	Radish	*Lincomycin*	0.50–3.50	[25]
USA	Cucumber	*Sulfamethoxazole*	490	[41]
China	Radish, rape, celery, and coriander	*Chlortetracycline*	0.1–532	[42]
USA	11 Common vegetables	*Chlortetracycline*	<10	[42]
China	Ginger	*Tetracycline*	28.1	[43]
Brazil	Soybean, bean, and corn tissues	*Enrofloxacin* *Ciprofloxacin*	1.68−26.17 8.23–51.05	[44]
Sri Lanka	Cabbage	*Naproxen*	38	[5]

The movement of emerging pollutants, particularly antibiotics, from "waste streams" to crops through plant absorption poses significant public concern regarding the agricultural utilization of untreated water and biosolids. As an example, the use of untreated irrigation introduces a substantial amount of drugs, such as carbamazepine (4.4 mg/kg), chloramphenicol (2.7 mg/kg), gemfibrozil (0.98 mg/kg), N, N-diethyl-meta-toluamide (DEET) (0.68 mg/kg), and caffeine (2.9 mg/kg), to the soil surface [45]. Human health concerns from these substances contaminating food may exist [1]. Although it is anticipated that the danger to humans via food exposure is minimal for each antibiotic component, their effects on hyposensitive groups may, thus, also differ [46].

Table 2. Physiochemical properties of selected antibiotics.

Pharmaceutical Classes	Representative Compound	Core Structure	Basic Properties	Half-Life ($t_{1/2}$)
β-Lactams	Amoxicillin	Consisting of a side chain linked to a thiazolidine ring and a β-lactam ring.	***MM***: *334.4–470.3 (g/mol)* ***WS***: *22–10,100 (mg/L)* *log* K_{OW}: *0.9–2.9* *pKa: 2.7* ***HC***: 2.5×10^{-19}–1.2×10^{-12}	*0.43–0.57 d*
Macrolides	Erythromycin	Consisting of one or more saccharides glycosidically linked to hydroxyl groups on a highly substituted monocyclic lactone. Typically, the lactone rings include 12, 14, or 16 members.	***MM***: *687.9–916.1 (g/mol)* ***WS***: *0.45–15 (mg/L)* *log* K_{OW}: *1.6–3.1* *pKa: 7.7–8.9* ***HC***: 7.8×10^{-36}–2.0×10^{-26}	*6.4–57.8 d*
Fluoroquinolones	Ofloxacin	Comprising two fused rings with a ketone group and a carboxylic acid.	***MM***: *229.5–417.6 (g/mol)* *WS: 3.2–17,790 (mg/L)* *log Kow:* -1.0*–1.6 pKa: 8.6* ***HC***: 5.2×10^{-17}–3.2×10^{-8}	*1153–3466 d*

Note(s): ***MM***: molecular mass; ***WS***: water solubility: ***HC***: Henry's law: half-life [12,13].

3. Persistence of Antibiotic in Soil

When a drug is administered to a human or animal, only a portion of it is taken up and processed by the body's tissues. The remaining drug has one of three fates: it can mineralize into carbon dioxide and water, have lipophilic properties that make it difficult to break down, or change into a more hydrophilic form that cannot be treated because it is persistent [47]. Antibiotics can exhibit varying persistence in the natural environment, ranging from days to several months. Once released from any source, they can become enduring environmental contaminants. Despite their relatively short half-lives, these compounds display a pseudo-persistent nature, persistently revealing their existence and participation in the environment [15,25,48–53]. The response of various plants and their organs/tissues varies depending on the concentration and duration of exposure to antibiotics [15,54]. Nowadays, environmental research is mainly focused on bioaccumulation and the threat posed by pharmaceutical, especially antibiotic residues and other personal care products in the soil–plant ecosystem [1,40]. Wastewater and manure are typically regarded as the two main sources of antibiotics in agricultural soil [35,55]. The antibiotics accumulated in soil via irrigation are absorbed by crops. Root absorption by plants grown in antibiotic-contaminated soil is likely to constitute a substantial route of exposure. The degradation of antibiotics in manure and the subsequent reduction in residual levels in manure-based fertilizers can be achieved through composting or anaerobic digestion processes [3,14]. When antibiotic concentrations in soil surpass 100 mg/kg, there is a significant concern regarding ecological risks [3]. Therefore, establishing a reference standard by testing antibiotic residues in manure and quantifying drug concentrations in soil before manure application is crucial. This approach ensures not only profitable agricultural production but also minimizes potential ecological risks.

Additionally, there is a need for the improved regulation of antibiotic use. Alongside this, efforts should be made to reduce infection rates by promoting better hygiene and improving the living conditions of animals. Research indicates that enhancing hygiene practices can reduce the dependence on antibiotics in animal agriculture [6]. The potential to decrease antibiotic usage has also been proposed through the advancement of veterinary vaccines [56].

3.1. Adsorption

The study of antibiotic adsorption on soils is crucial since this process is strongly related to antibiotic toxicity, degeneration, transfer, and bioaccumulation in soil. Even within the same antibiotic class, antibiotics have varying degrees of interactions with soil minerals [57]. Antibiotic adsorption is significantly affected by the various basic physicochemical characteristics of soil, including the soil constituents, soil pH, ionic environment, soil texture, and organic matter (OM). Furthermore, the amphiphilic and amphoteric characteristics of antibiotics, along with their steric configuration, play a crucial role in influencing their adsorption onto soil. It is crucial to emphasize that the physicochemical properties discussed are primarily influenced by the molecular structures of antibiotics [24]. The adsorption mechanisms of antibiotics are intricate, particularly in the case of fluoroquinolones and tetracyclines, which have Kd values that are notably higher compared to other pharmaceuticals. This implies that antibiotics like ciprofloxacin, norfloxacin, ofloxacin, and enrofloxacin have a tendency to concentrate in surface soil, displaying limited mobility. In contrast, the macrolide group of antibiotics easily adhere to soils characterized by a high mineral content, including iron (Fe), aluminum (Al), and manganese (Mn), leading to diminished migration tendencies. Consequently, distinct types of antibiotics exhibit varied distributions and behaviors in natural soil. Given that antibiotics are ionizable and polarizable organic chemicals, existing in both ionic and molecular forms and readily dissolving in water, their adsorption through soil and sediment becomes a complex process [58,59].

3.2. Degradation

Both living and nonliving mechanisms have sufficient potential to contribute to the breakdown or transformation of antibiotics in soil. The most important abiotic processes involve photochemical modifications, as well as chemically mediated activities including hydrolysis, oxidation, and reduction. The majority of the photodegradation occurs on the soil's surface, and humic substances serve as mediators of this process [60]. Additionally, the process of biodegradation is crucial in removing antibiotics from the environment [11,17]. The degradation of soil by microorganisms is largely driven by various factors, such as oxygen levels, pH, temperature, water content, microbial population, adaptation level, availability of chemical compounds, molecular structure of compounds, and cellular transport properties [61]. The degradation of antibiotics depends on the soil's organic content, as well as other soil properties. The presence of a significant content of organic matter in the soil can decrease the bioavailability of antibiotics, thus slowing down the rate at which they degrade [62]. The application of biosolids or animal dung improves the capacity of antibiotics to bind to soil and, usually, inhibits their degradation [63]. Physicochemical properties (such as the hydrophobicity and dissociation) of antibiotics, on the other hand, significantly influence the pathways through which these antibiotics degrade [59].

3.3. Leaching

Despite extensive research on the transfer of pesticides and inorganic chemicals in the environment, little is known about how antibiotics behave when they escape from soil. The ability of antibiotics to leak into the environment depends on a variety of physicochemical factors, including soil physiochemistry, the use of organic waste, and climatic circumstances. Sulphonamides' low soil partition coefficient make it more likely that they may migrate into groundwater [64]. As topsoil contains a greater concentration of organic matter compared to deeper layers, this enhances the adsorption of inhibitors and reduces the downward leaching of those substances. Placing animal feces there may lessen the soil's ability to drain antibiotics like tetracycline hydrochlorides. Most antibiotic residues are somewhat soluble in water and, therefore, able to ionize, but the soil pH also influences the percentage of organic molecules that are ionized. Factors, like solubility in water, dissociation constants, sorption–desorption processes, and partitioning coefficients, also affect how easily antibiotics leach. The release of antibiotics into the environment, also known as leachability, is influenced by both their ability to adsorb to soil particles and their persistence in the soil, but it is not solely dependent on their hydrophobic properties [59].

4. Antibiotic Uptake by Plants/Leafy Vegetable

Numerous authors have concentrated on analyzing the uptake of antibiotics by plants in connection to recycled animal waste manure. However, little is known about how antibiotics are absorbed by edible plants, and it is not well addressed why plants are able to absorb chemicals [65,66] Investigations on agricultural plants have revealed that many sulphanilamide's, tetracyclines, and quinolones are found in vegetables (such as radish, rape, celery, spinach, and coriander). An intriguing finding showed that the increasing use of organic manure in organic vegetable fields resulted in higher antibiotic concentrations than those in conventional agricultural fields [14]. The discovery that plants can absorb and store antibiotics not only in their roots but also in edible parts has raised concerns about the presence of these drugs in food crops [66]. According to [14], the finding that the increased application of organic manure increased the antibiotic concentrations in organic vegetable areas above those in conventional fields is intriguing. A study revealed that their concentrations levels were lower in soil than in manure [67]. The investigation's focus was on edible plants, including spinach, potatoes, carrots, and tobacco, according to which the potential for drug uptake into vegetables under typical agricultural situations is less than in greenhouse experiments, which showed substantial absorption into crops [68].

Antibiotics are taken up by plants from soil and its component soil solution through the root system [69]. Passive diffusion is used to move the antibiotics over the cell membrane. Diffusion is the most basic kind of passive transport, since it does not involve the cell using energy. Although active uptake has been seen to move some emerging pollutants that resemble hormones, it is not believed to be a crucial component in the absorption of emerging pollutants. After plants have absorbed antibiotics through roots, chemicals are migrated to the aerial areas of plant using the xylem of the vascular system. This xylem transports nutrients and water from the roots to the upper sections of the plant [70]. Numerous studies have been conducted in hydroponic environments to study the absorption mechanisms and to evaluate the potential for antibiotic bioaccumulation in plants. The bioconcentration factor (BCF), calculated as the ratio of the amount of antibiotics present in plant tissue to the amount added to the growth medium, is often used to determine the level of antibiotic absorption by plants [1]. The impacts of antibiotics on human health often emerge in two distinct ways: first, undesirable pharmacological responses (such as hypersensitivity reactions, delayed toxic effects from frequent exposure to antibiotics, or aberrant digestion); and, second, the possible prevalence of antibiotic resistance because of the application of selection pressure on microorganisms with clinical value [66,71–73].

Factors Affecting the Uptake of Antibiotics in Plants/Vegetables

There is a limited availability of data on the uptake of antibiotics and other pharmaceuticals in plants to the areal parts of the plant under field conditions. A small number of antibiotics and their transfer to the surrounding portions of the plant have been, nevertheless, reported in several investigations. Actual field-grown tomato leaves were watered with recycled water, in which 17 drugs were discovered with concentrations ranging from 0.04 to 32 ng/g [72]. Similar to this, one study found that peanut plants were exposed to antibiotics through the prolonged application of manure under actual agricultural conditions [73]. Findings also show that ciprofloxacin has the lowest translocation factor, followed by sulfamethoxazole, enrofloxacin, erythromycin, and chlortetracycline [74].

The pharmaceuticals' absorption and translocation from the planting medium to the roots and areal sections by the plants are influenced by several variables. The main factors affecting the plant's absorption of antibiotics include the biological traits of the plants, like lipids and carbohydrates; physiochemical qualities of the drugs, like molecular size, K_{ow}, and pKa; and the medium's environmental factors [6,75]. The absorption and movement of drug residues within plants are also influenced by their molecular weight, hydrophobicity (as represented by the partition coefficient between octanol and water), and ionic nature (positive, neutral, or negative charges) [75]. A plant can effectively collect antibiotics with a molecular weight of <1000 g/mol. Volatile substances and low-molecular-weight antibiotics are readily absorbed by the roots and shoots of plants. However, hydrophobic, nonvolatile chemicals with a larger molecular weight can only collect in roots [53]. Additionally, the log K_{ow} of drugs is a crucial quantitative metric that demonstrates the impact on its absorption by the plant; pharmaceuticals with a much higher log K_{ow} (>4) are thought to be extremely hydrophobic substances [59].

If a plant has shown a strong relationship with the soil or root tissues, these substances often do not translocate through the plant. Lower log K_{ow} (<1) drugs are thought to be extremely hydrophilic molecules with a low propensity to pass through the phospholipid membrane of the plant root. Pharmaceuticals with log K_{ow} values ranging from one to four demonstrate easy translocation within plant tissues [69]. Another factor that affects the intake of drugs is their ionic nature. The K_{ow} phenomenon may be used to explain neutral drugs, like coffee, carbamazepine, and estrone [76]. Antibiotic absorption and translocation by plants may be influenced, particularly in the case of ionic antibiotics, by the attraction or repulsion between ionized pharmaceuticals (either anionic or cationic) and the negatively charged cell membranes of the roots. Neutral and cationic pharmaceuticals are more likely to translocate to different plant parts, including the leaves, stems, or fruits. In contrast, anionic pharmaceuticals tend to concentrate in the roots [66]. Metoprolol and other positively charged pharmaceuticals have been identified in much higher concentrations in cucumber and tomato leaves than negatively charged ones. This is probably because negatively charged cell membranes are attracted to the positively charged metoprolol. Ibuprofen, ketoprofen, gemfibrozil, and sulfamethoxazole are preferentially collected in the roots because they undergo anionic dissociation in the cytosol upon entry and are repelled by the cell walls [9]. Because diclofenac and sulfamethoxazole have weak acidic properties, they accumulate in the roots in large concentrations and in little portions in the leaves. In contrast, as compared to weak acidic pharmaceuticals, trimethoprim, as a basic drug, exhibits greater accumulation in roots and high translocation to leaves [77]. Environmental factors, such as the quantity of drugs in soil, the pH of the surrounding medium, the temperature, and accessible organic carbon concentration in the soil, are important factors that impact the absorption of pharmaceutical concentrations in plants [74].

5. Materials and Methods

5.1. Description of Sampling Locations

The Yamuna River, originating from the Yamunotri Glacier, spans approximately 1376 km and drains an extensive area of about 366,220 km^2. The second-largest tributary of the Ganga River, it plays a crucial role in supporting irrigation, industrial activities, urbanization, and sustains diverse ecosystems. It also serves as an essential source of drinking water along its course. Notably, the Yamuna River flows alongside Delhi, India, for a distance of 22 km, with its entry into the city facilitated by the Wazirabad barrage. Subsequently, before merging with the Agra canal, it passes through the Okhla barrage (Figure 1). As per reports by the Central Pollution Control Board (CPCB), the Yamuna River's water quality remains good upstream of Delhi's Wazirabad area, starting from its origin. However, after entering the national capital of Delhi, a relatively short stretch, constituting less than 2% of the total length of the Yamuna River, from Wazirabad to Okhla, experiences severe pollution primarily due to sewage and industrial discharge. The selected drugs were chosen for the study's purpose due to their higher concentrations in the water samples [13,78]

A total of five soil samples from depths of 0–20 cm and V samples of leafy vegetable spinach were collected from open agricultural fields situated in five locations around the catchment area of the Yamuna River from November to December (premonsoon) to April to May (postmonsoon) 2022. Detailed information on the sampling sites, along with their geographical locations, is shown in Table 3. Each soil and vegetable sample was collected from the same field. The chosen farmland is located 5–10 km apart from each other. Most of the water used for the irrigation of the agricultural fields is drawn from the riverside. From Wazirabad to Okhla, five locations were selected, marked as I to V. One reference sampling site was also chosen, the homegrown vegetable market, Jamia Nagar, near Jamia Millia Islamia (Site-VI), to observe the variation in the concentrations of the selected drugs. All of the sampling was conducted in adherence with the established protocol [79].

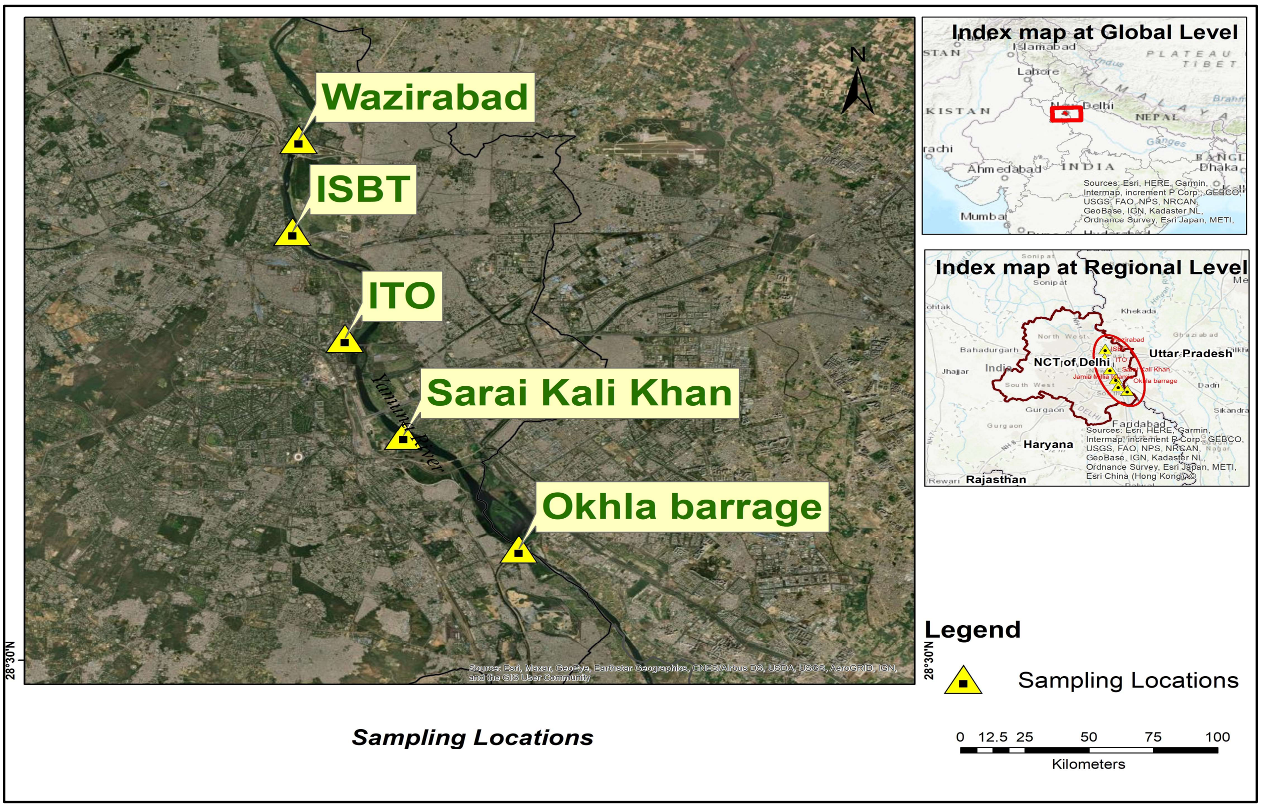

Figure 1. Sampling locations for the soil and vegetable samples around the catchment of the Yamuna River.

Table 3. Description of the soil and vegetable sampling locations.

Location	Location Area	Location Description	Latitude	Longitude
I	Wazirabad area	Initial Location	28.7116	77.235
II	ISBT	9.2 km (Wazirabad area)	28.67417	77.23235
III	ITO	14.9 km (Wazirabad area)	28.6308	77.2506
IV	Sarai Kali Khan	18.6 km (Wazirabad area)	28.5915	77.27115
V	Okhla barrage	21.5 km (Wazirabad area)	28.54538	77.31149
VI	Jamia Millia Islamia	Reference sampling location	28.5623	77.2804

5.2. Chemicals, Standards, and Reagents

For the present study, the antibiotic drugs chosen for analysis were sourced from Sigma-Aldrich chemicals in Bengaluru, India. A superior grade of each standard was utilized. All solvents employed in the liquid–liquid extraction (LLE) and UPLC-MS analysis met the quality standards for UPLC, except for the water. Milli-Q water was used to prepare the calibration standards and reagents. Filtration was performed using a sterilized syringe filter with a pore size of approximately 0.45 µm, as well as disposable syringes with a capacity of 3 mL, following the method described in [13,80]. Analytical-grade chloroform was utilized for extracting the antibiotics, and the distilled water required for the rotary evaporator was obtained from the laboratory's distillation plant.

5.3. Instrumental Analysis for Estimation of Antibiotics in Soil and Vegetables

The instrumental analysis for the quantification of the antibiotics in the soil and vegetables was carried out as per the standard protocol in [13]. It is a bit more difficult to extract antibiotics from soil/plant tissues, as the metabolites (primary and secondary), pigments, and other cellular components may interfere with pharmaceuticals during the evaluation of the samples.

For the analysis of the soil and vegetable samples, the optimal operating conditions included maintaining a specific flow rate of 0.35 mL/min. In the UPLC column, 10 µL of sample was injected. The temperature of the column was 40 °C. The quantification limit (LOQ) and the detection limit (LOD) were calculated by utilizing the standard deviation (S.D) of the response and the slope of the calibration curve [77,80–82] The LOD and LOQ values for ofloxacin, amoxicillin, and erythromycin were 1.5 ng/mL and 5 ng/mL, respectively. For ofloxacin, the value of the calibration curve obtained was y = 269.05x +1172.69, the value of the R^2 obtained was 0.992, and the values of the precursor ion (m/z) and product ion (m/z) obtained were 362.3 and 318.3. For amoxicillin, the value of the calibration curve obtained was y = 221.43x +227.59, the value of the R^2 obtained was 0.992, and the values of the precursor ion (m/z) and product ion (m/z) were 366.2 and 114. For erythromycin, the value of the calibration curve obtained was y = 644.30x +673.29, the value of the R^2 was 0.992, and the values of the precursor ion (m/z) and product ion (m/z) were 734.5 and 158.1, respectively.

5.4. Extraction and Analysis

For the analysis of the targeted drugs in the soil, the collection of the samples was conducted as per the optimized protocol in [83–85]. The water supply in those agricultural fields usually comes from the Yamuna River. So, there is the possibility that the surrounding agricultural crops may accumulate pharmaceuticals in their tissues. For the extraction of drugs from the soil and vegetable spinach (*Spinacia oleracea*), the soil samples and fresh-grown vegetable samples, whose edible parts were leaves collected from the field, were ground, spiked with mass-labeled by internal standards, allowed to sit overnight at room temperature, and subjected to liquid–liquid extraction (LLE) with 100% chloroform. The extracts were evaporated to dryness, reconstituted in a mixture of methanol, centrifuged, and then filtered through 0.2 µm filters before analysis. By using ultra performance liquid chromatography (UPLC) mass spectrometry (MS), the antibiotic concentrations in the soil and vegetable samples were quantified [84].

5.5. Statistical Evaluation

A two-way analysis of variance (ANOVA) was performed for the statistical data analysis, aiming to identify significant differences ($p < 0.05$) among the three antibiotics during the premonsoon and postmonsoon periods. Subsequently, box plots were generated for the specific antibiotic drugs. Seasonal variations in the concentrations of antibiotics were assessed using correlation coefficients, revealing notable higher drug concentrations in the premonsoon period compared to the postmonsoon period.

6. Results and Discussion

6.1. Soil

Samples of soil taken from agricultural fields irrigated with water from the Yamuna River underwent assessment using appropriate extraction methods and advanced instrumentation techniques. The results reveal differing antibiotic concentrations at various sampling points along the stretch from Wazirabad to Okhla, as shown in Figures 2–4. Out of the six sampling locations, the highest concentration of ofloxacin was reported at Site-V (0.265 µg/mg) during the premonsoon season and the lowest concentration (0.014 µg/mg) during the postmonsoon at Site-II, in terms of the average concentration, with no concentration observed at the reference site; this could be due to the combined effect of anthropogenic activities, surface water runoff, and combined load of drains in the vicinity. These observations are similar to the results in [86,87], according to which the fluoroquinolones had a detectable ratio of 100% in soil, and this could be because of having high sorption capacities of soil and low leaching potentials. The adsorption of fluoroquinolone antibiotics in the soil was notably impacted by the soil's cation exchange capacity, elevated organic matter content, and pH [87]. The concentration of amoxicillin exhibited considerable variation in the soil samples, with Site-V registering the highest concentration (0.265 µg/mg) in the premonsoon period, while Site-II recorded the lowest concentration (0.014 µg/mg) during the postmonsoon season. This variability is attributed to the direct introduction of antibiotics through practices such as sewage water irrigation, manure application, and sludge application.

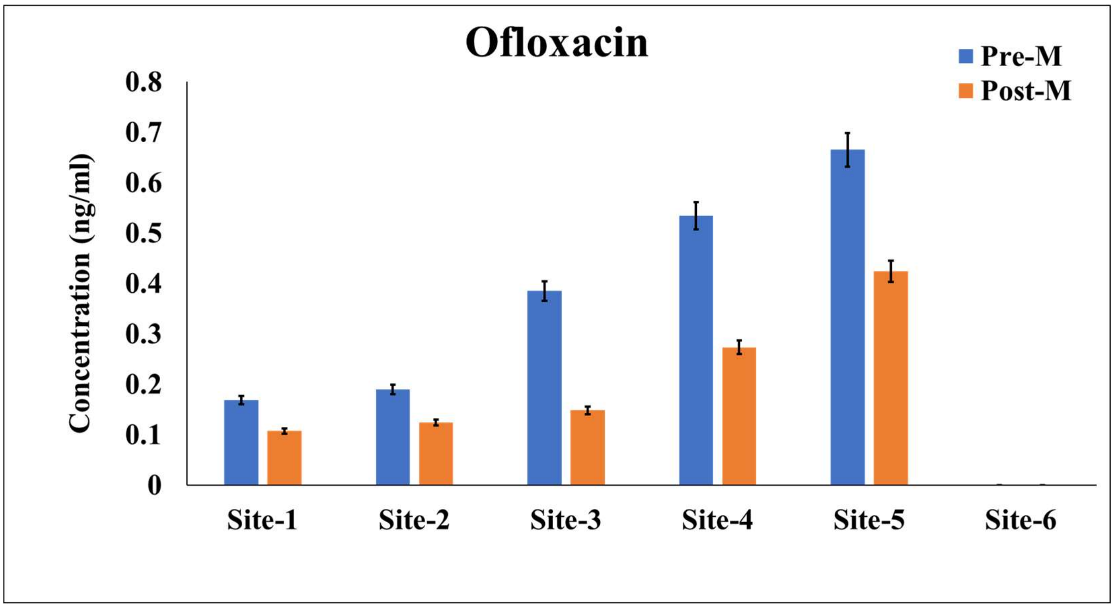

Figure 2. Concentrations of ofloxacin in the soil samples during the premonsoon (Pre-M) and postmonsoon (Post-M); sampling area directly irrigated by Yamuna River water.

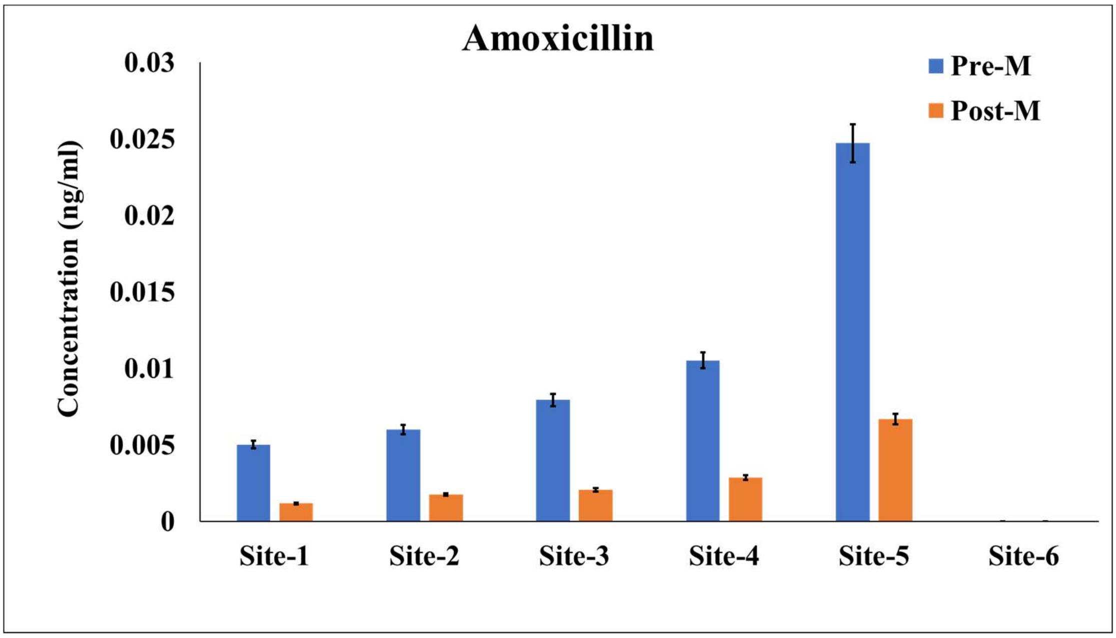

Figure 3. Concentrations of amoxicillin in the soil samples during the premonsoon (Pre-M) and the postmonsoon (Post-M); sampling area directly irrigated by Yamuna River water.

Agricultural operations have reportedly been linked to higher antibiotic concentrations in their soils [87]. Antibiotics may continue to be added to the soil and crops by irrigation with recovered wastewater, which would keep these contaminants present in the agroecosystem. For erythromycin, the highest concentration (0.0018 µg/mg) was observed at Site-V during the premonsoon period, and the lowest concentration was observed at Site-I (0.000101 µg/mg) during the postmonsoon period. This is most likely due to the region's more regular irrigation. The other sampling locations' antibiotic concentrations may have been impacted by transit distances and wastewater irrigation techniques [88]. The highest concentrations of ofloxacin, amoxicillin, and erythromycin measured at Site-V, Site-III, and Site-II within the Yamuna River catchment probably resulted from the more frequent irrigation containing direct untreated discharge of surface and wastewater into the river [87]. Moreover, temperature changes caused by seasonal fluctuations have an impact on antibiotic removal. Antibiotics degrade more readily at higher temperatures because of increased microbial activity. Reduced removal efficiencies may be caused by low microbial activity during the winter, as well as the desorption of drug molecules attached to substrates and possible conjugate cleavage [89]. Among all three studied antibiotics, the concentration of drugs in soil samples were in the following order: fluoroquinolones > β-lactams > macrolides [82,90]. The significance of a farming management system becomes evident in its pivotal role in regulating manure application to effectively manage residual antibiotic levels, thereby mitigating the risk of soil and crop contamination. Antibiotics can react with other compounds, like metal or alkaline earth cations, forming complexes or chelates. These interactions have the potential to reduce bacterial population, diversity, and metabolic capabilities in the soil, significantly impacting both the fate of antibiotics and soil fertility [87].

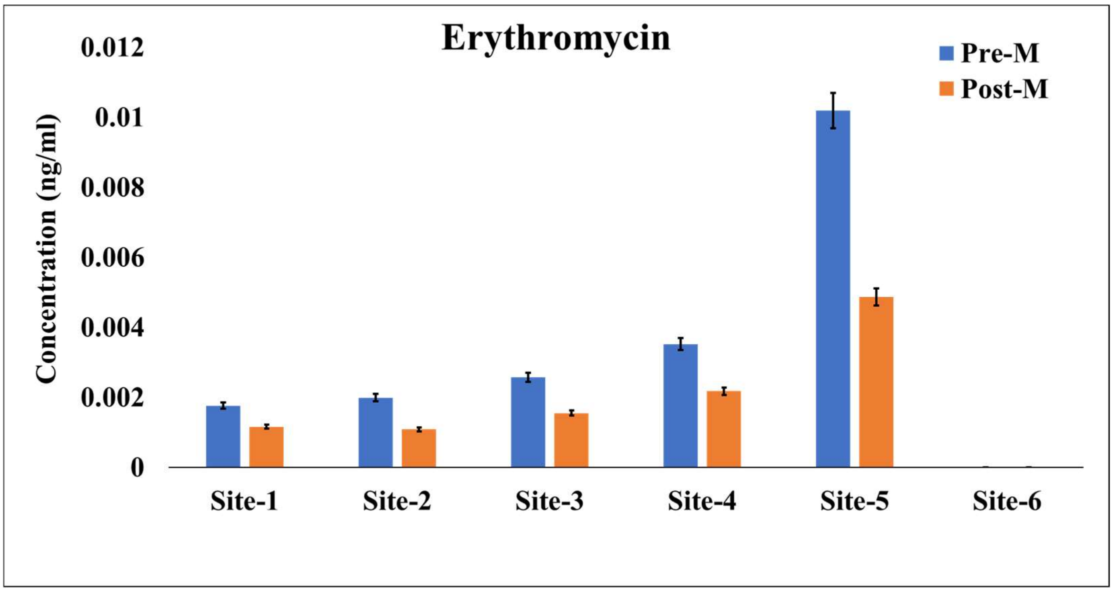

Figure 4. Concentrations of erythromycin in the soil samples during the premonsoon (Pre-M) and the postmonsoon (Post-M); sampling area directly irrigated by Yamuna River water.

6.2. Vegetables

For the quantification of studied antibiotics in green leafy vegetables, the investigation was carried out as per the standard protocol. Fewer compounds from consumed pharmaceuticals are found in fruits, whereas a larger number have been discovered in leaves [9,66,91,92]. Among the investigated drugs, as shown in Figures 5–7, the concentration of ofloxacin was found to be higher at Okhla Site-V (5.586 μg/mg) during the premonsoon period, with low concentrations observed at Site-I, from 1.382 μg/mg to 1.698 μg/mg, during the postmonsoon period. The frequency of the detection of ofloxacin is higher than other antibiotics [25,61]. Our results are also in line with similar studies [14,22], according to which ofloxacin was detected in crops grown in pharmaceutically irrigated plots with soils amended with manure. Higher concentrations of ofloxacin in crops are because of their susceptibility to being absorbed by the soil's surface. As a result, more remains in the soil for absorption by crops [93]. The data indicate that the Okhla barrage site experienced the lowest concentration of ofloxacin (0.0618 μg/mg) during the premonsoon season, surpassing the other sampling locations. Conversely, for amoxicillin, the highest concentration (0.374 µg/mg) was recorded at the Okhla barrage during the premonsoon period. In contrast, Site-1 exhibited the lowest amoxicillin concentration (0.021 µg/mg) during the postmonsoon season. Notably, Wazirabad Site-I consistently showed the lowest concentration in both seasons, suggesting minimal pharmaceutical residue in the water and reflecting the overall water quality as the river enters the city. Additionally, the reference site's samples displayed relatively lower amoxicillin concentrations compared to the samples from various locations within the Yamuna River catchment area.

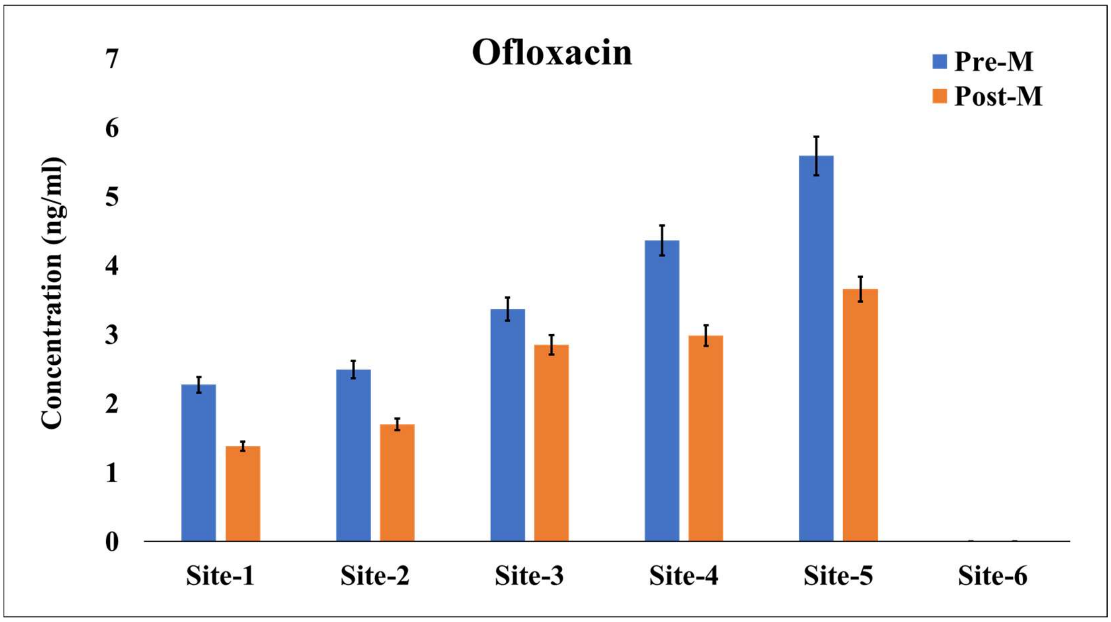

Figure 5. Concentrations of ofloxacin in the vegetable samples during the premonsoon (Pre-M) and the postmonsoon (Post-M); sampling area directly irrigated by Yamuna river water.

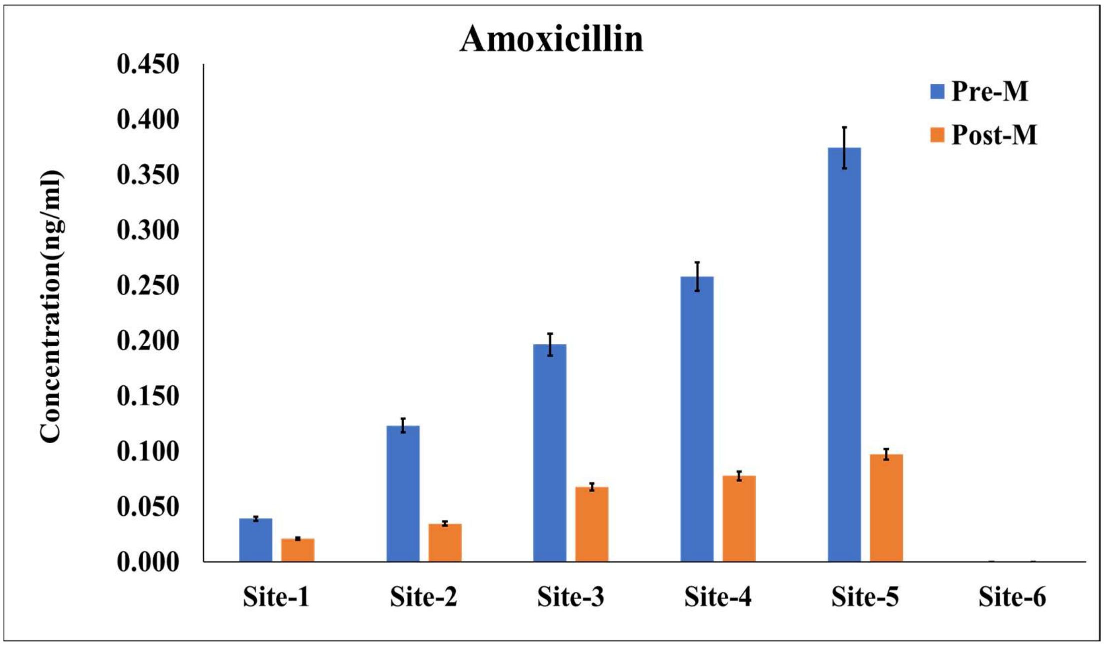

Figure 6. Concentrations of amoxicillin in the vegetable samples during the premonsoon (Pre-M) and the postmonsoon (Post-M); sampling area directly irrigated by Yamuna River water.

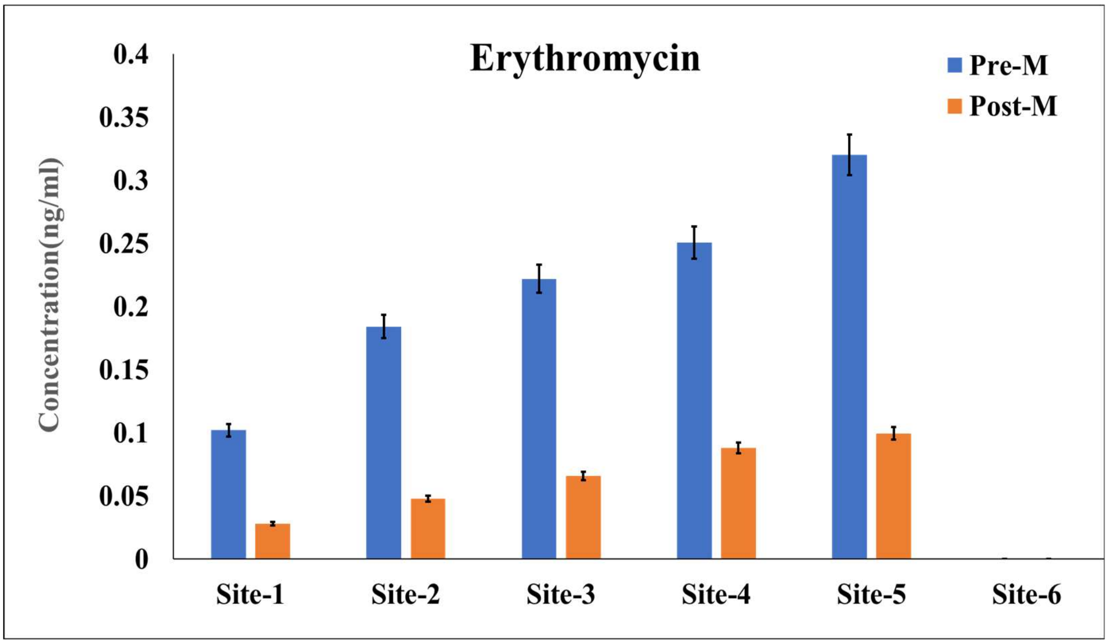

Figure 7. Concentrations of erythromycin in the vegetable samples during the premonsoon (Pre-M) and the postmonsoon (Post-M); sampling area directly irrigated by Yamuna River water.

The concentration of amoxicillin reported from the experiments was lower than those reported in [9,77] in lettuce and carrot. The concentrations of erythromycin were shown to be higher at Site-V (0.320 µg/mg) followed by Site-III (0.251 µg/mg) during the premonsoon and with a lower concentration detected at Site-I (0.028 µg/mg) during the postmonsoon period. The samples from the reference site showed no concentration of erythromycin in both seasons. The lower concentration of erythromycin could be due to its higher molecular weight, which makes it difficult to translocate into crops and absorb via cellular membranes [93]. Compounds with a high molecular weight, such as tylosin, are not easily absorbed by plants due to their size, making it difficult for them to be transported via the transpiration stream or actively taken up by the plant. This can account for the limited translocation ability of tylosin in plant tissues [73]. Also, the high transpiration in hydroponic systems may help plants to absorb erythromycin [10,78]. Additionally, it is noteworthy that green leafy vegetable had different levels of erythromycin accumulation, particularly under a hydroponic growing regime, which may be attributed to variations in the plant's lipid contents, growth rates, water usage efficiency, enzyme-mediated metabolisms, etc. [76,94,95] Thus, from the above results, it can be confirmed that the concentrations of the ofloxacin antibiotic were found to be significantly higher than amoxicillin and erythromycin in both the soil and plant samples due to its adsorption ability, indicating the irrigation water as the primary source contributing to antibiotics entering the agricultural environment. Antibiotics continue to endure in the terrestrial environment following their release from irrigation water [95,96].

Antibiotics uptake by plants is also due to dose–response effect, as observed in previous literature. For example, carrot and lettuce show similar results for antibiotics taken up from irrigated water [97]. Higher exposure to increased concentrations of antibiotic residues in soil leads to the higher accumulation of chlortetracycline (CTC) in crops like onions and cabbage, as seen in the observed dose–response. This implies that plants absorb greater concentrations of drugs if they are exposed to higher concentration levels in the soil [96]. According to the authors of [93], the utilization of water contaminated with antibiotics and the application of animal manure in agriculture lead to the increased absorption and accumulation of antibiotics in food crops. Consistent with this investigation, several studies have reported the presence of CIP in soil used for vegetable farming, ranging from 0.11 to 0.52 µg g^{-1} [43,52,97], and ciprofloxacin and ofloxacin in carrot (0.51–0.85 µg kg^{-1}) [98].

Higher antibiotic concentrations in soil can result in their significant accumulation in edible crops because of their distinct resistance, molecular structures, adsorption, and varying half-lives in soils [99]. The frequent use of manure or irrigation with wastewater over a prolonged period can lead to significant increases in antibiotic levels in the soil environment [62]. While applying manure can enhance soil fertility, it may also raise concerns regarding human health due to the buildup of antibiotics [64]. During the premonsoon period, the concentrations of antibiotics in both the soil and vegetable samples were elevated, reaching their peak at Site-V. The higher concentrations at Okhla barrage (Site–V) is due to the maximum pollution load received from the whole city at this location.

7. Conclusions and Future Directions

The escalating global environmental concern stems from the deterioration of soil quality linked to the increased use of pharmaceuticals. As these pharmaceuticals are toxic in nature, they pose a severe threat to soil, aquatic organisms, plants, and humans because there is no regulatory restriction on their usage. The results of this study show that the antibiotic residues are taken up by the soil and plants in remarkable concentrations as a result of the direct irrigation from Yamuna River. The soils that are under the influence of pharmaceutical wastes, sewage sludge, and wastewater with higher levels of antibiotics can contaminate the food chain and alter the soil microbiome, hence, affecting the processes involved in the circulation of essential minerals and nutrients. The concentration levels of antibiotics in this study showed seasonal variations with more significant variations during the premonsoon season compared to the postmonsoon season. This seasonal variation was due to factors such as precipitation, dilution, and soil leaching effects. The concentration of amoxicillin exhibited a pronounced variation in the soil samples, with the highest level recorded at Site-V (0.265 μg/mg) prior to the monsoon season, while the lowest concentration was detected at Site-II (0.014 μg/mg) after the monsoon season. The highest concentration of erythromycin (0.0018 μg/mg) was recorded at Site-V in the premonsoon period, while the lowest concentration was found at Site-I (0.000101 μg/mg) in the postmonsoon period. For the vegetables, the highest ofloxacin concentration was found at Okhla Site-V (5.586 μg/mg) during the premonsoon period, with the lowest concentration observed at Site-I (1.382 μg/mg−1.698 μg/mg) during the postmonsoon period. This variation is likely attributed to the more consistent irrigation practices in the region. The concentration levels of all of the three studied drugs follows the order of ofloxacin > amoxicillin > erythromycin. The highest concentration of pharmaceuticals was observed at the fifth sampling location (Site-V), which reflects the cumulative load originating from twenty-two main drains and inefficient wastewater treatment facilities. The findings of this study emphasize the need for a minimum tertiary treatment of the effluents from major drains and wastewater directly discharged from urban runoff according to the CPCB guidelines. The overabundance of antibiotics in water, which then spread to soil and plants through irrigation and fertilizers, is a major threat because of the growing concern regarding resistance genes due to antibiotics (ARGs) and bacteria (ARB) that have been discovered in crops and their potential to spread in humans. The findings suggest that antibiotics, when present at the reported concentrations in soil, can have detrimental effects on soil plants. This implies that caution should be taken, when directly applying manure and fertilizers (derived from manure) to the soil due to the risks of antibiotic residue contamination. The results of this study also show that residues of antibiotics in the tissues of edible crops are influenced by the concentrations of antibiotics in irrigation water. Additionally, there is an exacerbated risk associated with crops that are irrigated by antibiotic-polluted water. Antibiotics, even at lower concentrations, produce harmful effects due to their potential to bioaccumulate in the food chain. They cause harmful effects to both aquatic and terrestrial organism.

Thus, the effective management of contaminated soil must consider the continuous monitoring and risk assessment of human and veterinary antibiotics to prevent the adverse effects on the natural environment and human health. Antibiotic residues are predominantly employed to protect crops against harmful diseases. However, this process involves utilizing waste products, such as livestock manure, treated sewage water, sewage sludge, and pharmaceutical waste, in agricultural practices. In order to reduce the negative environmental effects of antibiotics, strict regulatory measures must be implemented to the set permissible limits or maximum residual limits. The results, thus, increase our understanding of the parameters controlling the accumulation of antibiotics and helps in the detection of human exposure to antibiotics. Subsequent research endeavors should prioritize investigating the impact of antibacterial pharmaceuticals on soil microorganisms and the alterations in the antibiotic resistome within the soil environment. This approach is essential for developing a more thorough comprehension of the practical ecological risks associated with soil amendments from animal manure and fertilizers, as well as their potential bioaccumulation in leafy vegetables.

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