Antimicrobial Resistance in Agricultural Soils

Subjects: Soil Science

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Excessive use of antibiotics in the healthcare sector and livestock farming has amplified antimicrobial resistance (AMR) as a major environmental threat in recent years. Abiotic stresses, including soil salinity and water pollutants, can affect AMR in soils, which in turn reduces the yield and quality of agricultural products.

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1. Introduction

Soil microbial communities have manifold benefits for plants, including nutrient supply, synthesis of phytohormones, antagonistic activity against phytopathogens, and generation of signal molecules involved in microbe–plant interactions [1]. Although microbial communities are indicators of overall soil health, their resistance to adverse conditions for survival and competition is a considerable concern [2] owing to their potential to create ecosystem imbalances and disease emergence [3]. Hence, many studies have been carried out on microbial ecology in the environment [4], and most investigations concentrate on bioactive antimicrobial compounds in fertilizers, soil, and water resources [5]. Antibiotics, as one of the most common antimicrobials and a valuable scientific discovery in the twentieth century, caused a massive shift in pharmaceutical and veterinary sciences [6]. Molecules with antibiotic properties existed prior to humans producing manufactured antibiotics. However, widespread production of these compounds, along with synthetic derivatives of natural antibiotics, began in the twentieth century [7]. Soil actinobacteria and myxobacteria are the most significant fundamental reservoirs of active metabolites. More than 60% of natural antimicrobial compounds belong to actinobacteria and fungi [8].

Antibiotics are applied to protect human health, inhibit animal disease emergence, and increase the production rate in dairy farms. However, their environmental consequences have recently been reconsidered as a significant concern [9][10][11][12] due to the low absorption of antibiotics in the guts of animals. Approximately 10–90% of these complexes are discharged through urine and feces in a stable form [12][13][14] that creates new sorts of antimicrobial resistance, such as antibiotic-resistant bacteria (ARB) and antibiotic-resistant genes (ARGs) [15][16]. Antimicrobial resistance (AMR) happens when microbes do not perish from intended drugs, thereby making them challenging or inconceivable to control [17]. The indiscriminate use of antibiotics accelerates AMR, leading to higher medical costs and mortality [18]. More than 700,000 people worldwide die each year from AMR, which is predicted to reach 10 million deaths by 2050 and reduce gross domestic product by 8.3% [19]. In this regard, the US Centers for Disease Control and Prevention (CDC) [20] reported that antibiotic-resistant diseases affect approximately 8.2 million

Americans every year. Accordingly, one of the top ten worldwide healthcare issues is AMR [21]. **Figure 1** summarizes the significant factors involved in the evolution of AMR.

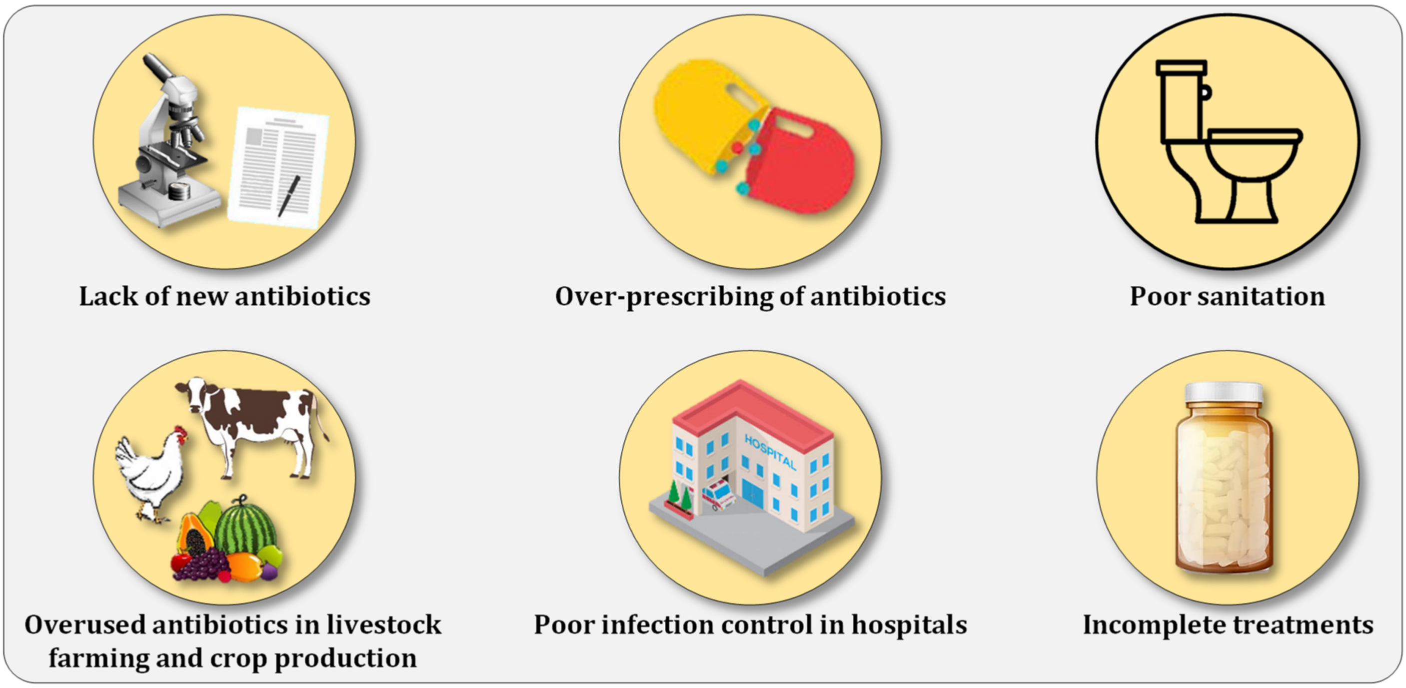

Figure 1. The most consequential causes of AMR, adapted from the World Health Organization (WHO) [22].

AMR, as a developing hidden ecological problem in farming soils, has been converted into a significant environmental and health threat worldwide [23][24][25]. Moreover, the lack of awareness of microbial responses lessens soil biodiversity protection in agricultural ecosystems [26]. Increasing evidence points to the crucial role of environmental factors in the transmission process of ARGs [27][28]. Hence, it is essential to cope with AMR in humans and animals via understanding ARG enrichment mechanisms and resistance gene stamina in plants and soil [24]. Due to enhanced selective pressure, the evolution of resistant bacteria has been accelerated in recent years [29], and abiotic stress agents may amplify bacterial resistance to a wide variety of antibiotics [27]. Though abiotic stresses such as salinity, heavy metal accumulation, application of untreated sewage, hydrocarbon pollutants, and irrational use of fertilizers and pesticides are the most critical production challenges in sustainable agriculture, there are few comprehensive studies concerning associations between abiotic stresses and the consequences of antibiotic residues in soils.

2. Combating Antibiotic Resistance Prevalence

Presumably, the most helpful and cost-effective solution to diminish the development of AMR is to optimize the use of antibiotics [30]. Flawless monitoring of antibiotic application in hospitals is a promising approach to declining human-resistant pathogens [31]. Antibiotic management policies must be executed effectively, despite the fact that antibiotics are essential in safeguarding animal health and financial benefits [32]. The antibiotic control policy between the 1990s and 2000s transformed the pig meat industry in Denmark. Notwithstanding the adverse economic consequence of decreasing antibiotics in the pork industry, a considerable decline in the abundance of vancomycin-resistant *enterococci* was detected in pigs' guts [33]. Furthermore, the Dutch mandatory policy to reduce antibiotic usage in the livestock sector in 2008 reduced beta-lactams, aminoglycosides, fluoroquinolones, and tetracycline consumption by roughly 50% by 2013 [34]. In the United States, the Food and Drug Administration (FDA) strategy decreased sales of primary veterinary antibiotics by approximately 43% between 2015 and 2017, whereas meat production remained unaffected [35]. Although governments must execute the policies of the Food and Agriculture Organization (FAO) and WHO to prevent the occurrence of AMR in agricultural soils [36], reducing antibiotic consumption may not be attainable in existing circumstances due to economic losses for growers [37]. Implementing precision agriculture approaches as an alternative to intensive farming is presumably an ideal method to decrease AMR. Since evidence demonstrates that intensive agriculture has a substantial share in antibiotic usage [38], for instance, approximately 3558–4279 tons of antimicrobials were applied in the livestock sector in Africa from 2015 to 2019; consequently, a high level of AMR was detected in farming soils [39]. Hence, precision agriculture enables administrators to maintain the health of the environment and agricultural sustainability by controlling fertilizer consumption as AMR causes and sustaining crop yield, leading to higher financial profitability and ensuring food security [40][41][42].

Controlling the sources of antibiotic remnants through treating urban wastewater and organic manure is another practical method to ameliorate the unfavorable impacts of antibiotics on agricultural ecosystems [43]. Since antibiotics are resistant to degradation due to their hydrophobic and lipophilic properties [44], traditional wastewater treatment processes cannot completely eliminate ARGs [45]. Therefore, it is necessary to employ additional techniques to improve the expulsion of ARGs. Recently, to enhance wastewater treatment efficiency, clay minerals having high adsorption traits, easy availability, and low cost have been regarded as alternatives to activated carbon in removing metal ions [46][47][48]. Mustapha et al. [49] pointed to kaolin as an effective adsorbent for removing chloride, sulfate, Cr, Cd, and Zn. In addition, Yang et al. [50] reported that kaolin increased the removal efficiency of naproxen and diclofenac from water. Clays can split heavy metals from water, although their adsorption efficiency depends on the metal concentration, pH, ion type, surface area, and adsorbent dose [51]. Hence, more research into the commercial use of clay is required. Salts can be applied for the biological treatment of wastewater comprising antibiotics [52] by inhibiting the growth of bacteria containing ARGs. Hence, using salts such as sodium chloride can be a viable method to reduce ARGs in wastewater systems [53]. Heating beef for 30 min reduces antibiotic residues by 10.8% [54], and Zhang et al. [55] also documented that oxidation of heat-activated persulfate residues of erythromycin could restrict the spread of MGEs; hence, heating is a potentially efficient method to diminish ARGs in sewage sludge. Thermophilic anaerobic digestion of urban sewage sludge in an analysis by Xu et al. [56] led to a 29.59% decline in *Proteobacteria* and 17.65% in *Chloroflexi,* as well as more effective elimination of tetracycline-, macrolide-, and fluoroquinolone-resistant genes. Thermal hydrolysis treatment of wastewater sludge also lessened ARGs and MGEs, tetracyclines, macrolides, and lincosamides by 94% [57]. In a study by Liao et al. [58], hyperthermophilic composting removed ARGs and MGEs by 89% and 49% more than traditional composting methods, respectively.

The composting operation helps with a decrease in pathogenic bacteria activities and ARGs, enriching the soil's beneficial microbiome and nutrients. The diversity of potential pathogenic bacteria declined from 37.18% to 3.43%, and probiotic species were enhanced from 5.77% to 7.12% during the composting process [59]. Gou et al. [60] indicated that levels of AMR in compost-treated soils were reduced, and compost remarkably lowered the relative diversity and abundance of ARGs and MGEs in cattle dung. Analysis of livestock manure containing 16 sorts of antibiotics showed that the composting process significantly reduced extractable antibiotics [61]. An experiment conducted by Keenum et al. [62] revealed that the composting operation reduces the risk of AMR spreading; however, it cannot prevent whole ARGs from penetrating the soil. Sardar et al. [63] considered conventional composting an inefficient technique to control AMR owing to a considerable increase in the abundance of *sul1* and *sul2* genes after 30 days of the initial composting phase. Additionally, Gao et al. [64] demonstrated that composting poses a prominent risk to human health by emitting bioaerosol pollutants containing ARGs into the atmosphere. At the same time, composting was an appropriate mechanism for removing polycyclic aromatic hydrocarbons such as chrysene and indenopyrene from soil [65]. Moreover, bioremediation, which employs microbial-base catabolic processes to environmental pollutants' degradation [66][67], can be adopted as an efficient method to ameliorate the health of hydrocarbon-contaminated soils [68]. In an examination by Ghazali et al. [69], a consortium of *Bacillus* and *Pseudomonas* species effectively decomposed medium-chain alkanes in diesel-contaminated soil. Gargouri et al. [70] revealed that the bacterial consortium effectively eliminated long-chain alkanes in contaminated soil after 30 days. It also reduced total petroleum hydrocarbon (TPH) from 63.4 to 2.5 mg g^{-1}. In an experiment by Guarino et al. [71], soil bioremediation with a bacterial consortium decreased TPHs by 86%.

Numerous bacteria can remove soil pollutants and antibiotic residues from ecosystems by bioremediation. Sulfate-Reducing Bacteria (SRB) are a diverse group of prokaryotes that can grow in various environmental conditions [72][73] and are a cost-effective, eco-friendly, and helpful method for the bioremediation processes of pollutants from wastewater and contaminated soils [74]. In a study by Jong and Parry [75], SRBs increased the removal of sulfate and heavy metals such as Cu, Zn, and Ni by elevating the pH of water from 4.5 to 7. Zhao et al. [76] found that SRB strains such as *Desulfobacteraceae* and *Desulfovibrionaceae* had a considerable impact on Cd immobilization in sediments. SRBs can also be used to purify soils contaminated with benzene, toluene, and xylene [77]. It has been reported that SRBs can effectively remove the antibiotic ciprofloxacin from wastewater [78][79]. In a study by Zhang et al. [80], it was demonstrated that approximately 35% of the total removal of ciprofloxacin from wastewater was related to SRB. Jia et al. [81] also reported that *Desulfobacter* decomposed nearly 28% of the 5000 μg L^{-1} ciprofloxacin concentration. In a study by Zhang et al. [82], *Arthrobacter nicotianae* OTC-16 was detected as an oxytetracycline biodegradation instrument. Maki et al. [83] demonstrated that microbes might be involved in the degradation of ampicillin, doxycycline, and oxytetracycline residues in marine fish farm sediments. In research by Hirth et al. [84], *Microbacterium* sp. increased the elimination of sulfamethazine residues in soil by 44% after 46 days. In addition, Mojiri et al. [85] reported that marine diatoms were able to decompose 39.8% of sulfamethoxazole and 42.5% of ofloxacin in an aqueous environment. While bioremediation of antibiotic residues is a promising and cost-effective method, more knowledge is required regarding the mechanisms of microbial degradation of antibiotics and the potential undesirable hazards of microbes in ecosystems [86]. Furthermore, the biodegradation of antibiotics in soils is highly conditional on microbiomes, pH, temperature, and different interactions among antibiotics [87].

The microbial electrolysis cell system (MECs), as an emerging contamination control technology, can diminish the release of ARGs [88]. Through analyzing the effects of microbial electrolysis cells on the decomposition of erythromycin in wastewater, Hua et al. [89] demonstrated that electrolysis is an effective technique to enhance the decomposition efficiency of antibiotics. Microbial electrolysis by Zhang and Li [90] in a sewage sludge treatment plant with a voltage range of 0 to 1.5 V removed most of the targeted ARGs. The results obtained by Zhang and Li [91] indicated that the removal efficiency of antibiotics at a voltage of 0.6 to 1 V was higher than at other voltages. In addition to microbial metabolism and electrochemical redox reactions, bioelectrochemical systems are promising alternatives for decomposing antibiotic residues [92]. Moreover, controlling the discharge of antibiotics into the environment should be characterized according to their adverse impacts [93].

The use of natural antibiotics is one of the most effective ways to reduce AMR. Investigations to discover natural alternatives to synthetic antibiotics have advanced in recent years, and antioxidants such as polyphenols, vitamins, and carotenoids have garnered considerable attention due to their antibacterial and anti-inflammatory activities [94][95]. Herbal antibiotics, which are derived from plants such as garlic and aloe vera, have fewer side effects than conventional antibiotics [96]. Some plant-derived compounds, such as quinine and artemisinin, have actively combated infectious diseases [97]. Fit et al. [98] examined the impact of plant extracts on pathogenic strains of *S. aureus* isolated from animal waste. They demonstrated that savory and fir had antibacterial activity. Awan et al. [99] reported that chloroform extract of cumin and turmeric had significant antibacterial activity against *Serratia marcescens* and *P. aeruginosa*. Saquib et al. [100] documented that combining the antibiotic metronidazole with the ethanolic extract of the Miswak plant had a synergistic influence against *Aggregatibacter actinomycetemcomitans*. Nweze and Eze [101] also reported that the ethanolic extract of lamiaceae leaves mixed with ampicillin had a synergistic effect against *E. coli* and *Candida albicans*. At the same time, it is recommended that more clinical trials be conducted on the effectiveness of plant-derived antibiotics to combat AMR [102][103]. In addition to herbal antibiotics, animals also contain peptides with antimicrobial functions [104]. Antimicrobial peptides (AMPs) are cationic and amphipathic peptides that are important in the natural defense of organisms and can be isolated from all kingdoms [105][106]. AMPs, such as defensins and cathelicidins, can eliminate bacteria by creating pores in the phospholipid membrane and disrupting its integrity, thereby diminishing AMR development [107][108][109]. Hence, the identification and optimization of AMPs have attracted ample attention, and more than 2493 AMPs have been documented in 2014 [110][111]. Despite the fact that AMPs appear to be a promising alternative for combating AMR due to their ability to damage pathogenic bacteria’s membranes, it is critical to investigate their structural changes and potential side effects on animal and human physiology [112][113]. AMR is gradually progressing into an unmanageable condition [114], and there are no geographical boundaries to stop its expansion as an international challenge [115]. Accordingly, global collaboration is needed to battle the imminent AMR crisis [116].

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