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REVIEW ARTICLE **OPEN ACCESS**

Fate and Effect of Antimicrobials in Agriculture

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ABSTRACT
The potential sources of antimicrobials inputs in the environment are municipal waste-water discharge, municipal biosolids, pharmaceutical production and agriculture-related activities. However, the heavy use of antibiotics in the livestock industry and the dramatic shift in recent years toward more highly concentrated animal feed operations, thus a increase in the volume of animal wastes has drawn attention to the role of animal waste-borne antimicrobials and antibiotic-resistant bacteria on ecosystem and h//uman health. Most antibiotics have a high affinity for soil and sediment, thus residual soil concentrations are usually much higher than noted in water but still often below concentrations of concern. Measurable concentrations of many of these antimicrobials have been detected in soil, and ground and surface waters receiving runoff from fields fertilized with animal manure and downstream from farm animal operations. Research directed toward evaluating the facilitated transport processes with regards to antimicrobial inputs from manure-amended fields is in its infancy.
Keywords: *Antimicrobials, Crop production, Livestock, Degradation, Persistence, Sorption.*

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INTRODUCTION

There are several potential sources of antimicrobial inputs into agriculture, including municipal waste-water discharge, municipal biosolids, pharmaceutical production, and agriculture-related activities. Most antibiotics have a high affinity for soil and sediment, thus residual soil concentrations are usually much higher than noted in water but still often below concentrations of concern. These antibiotics reach agriculture fields via manure application or use of crop protection chemicals or plant growth enhancers. Though, they help in increasing crop production most of them remain in soil for longer periods and negatively affect crop and soil. Hence, pretreatment of the manure and other wastes before its application to agriculture is important.

An antimicrobial is an agent that kills micro organisms or stop their growth. It includes Antibacterials, Antifungals, Antivirals, Antiparasitics and Antimicrobial pesticides *etc*.

SOURCE OF ANTIMICROBIALS IN AGRICULTURE

Agriculture and other anthropogenic activities may act as point and nonpoint sources for both steroid hormones and antimicrobials in soils, water and sediment systems [31].

Major sources of antimicrobials are listed here-

1. Animal production: antimicrobials used in animal production for treatment of disease (therapeutic use), prevention of disease (prophylaxis) and for growth promotion.

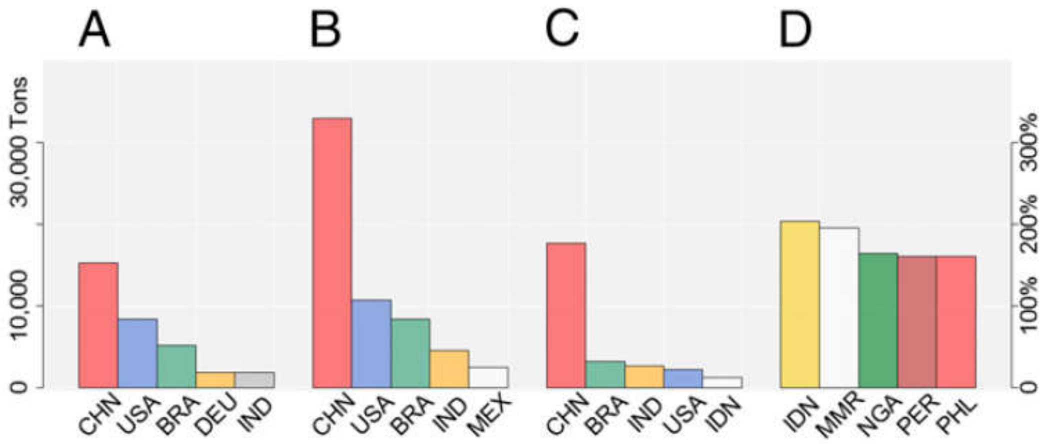

Fig. 1. (A) Largest five consumers of antimicrobials in livestock in 2010. (B) Largest five consumers of antimicrobials in livestock in 2030 (projected). (C) Largest Increase in antimicrobial consumption between 2010 and 2030. (D) Largest relative increase in antimicrobial consumption between 2010 and 2030. CHN, China; USA, United States; BRA, Brazil; DEU, Germany; IND, India; MEX, Mexico; IDN, Indonesia; MMR, Myanmar; NGA, Nigeria; PER, Peru; PHL, Philippines. Source: Global trends in antimicrobial use in food animals, [27].

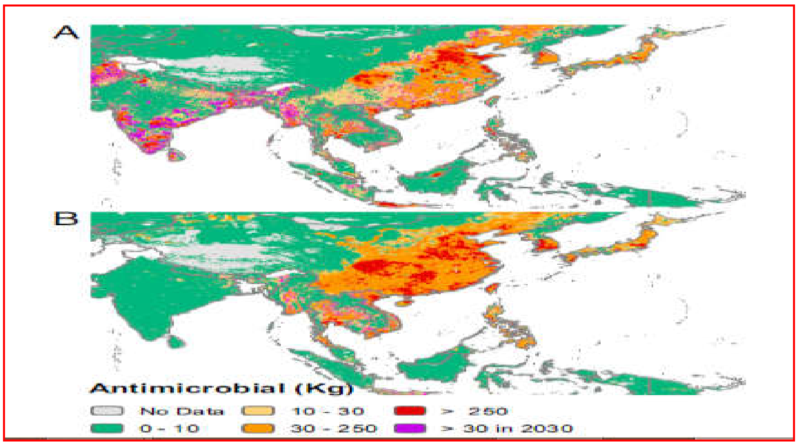

Fig 2. Antimicrobial consumption in Chickens (A) and Pigs (B) in 2010.
Source: Global trends in antimicrobial use in food animals,[27].

About 60–80 % of commercial livestock are administered antimicrobials as therapeutic, prophylactic, and growth-promoting agents during their productive life span [29],

In swine production, the most commonly used antimicrobials are chlortetracycline, xytetracycline, bacitracin, tylosin, sulfathiazole, sulfamethazine, penicillin, carbadox, and lincomycin [28]. In the poultry industry, monensin, roxarsone, bacitracin, amprolium, salinomycin, lasalocid, zoalene, and erythromycin are among the most frequently used antimicrobials. Major antimicrobials used in cattle production include chlortetracycline, oxytetracycline, tylosin, sulfamethazine, monensin, and lasalocid [29].

Because many antimicrobials are poorly absorbed in the digestive tract of animals, these compounds are often present in livestock wastes in significant concentrations. Tetracyclines, sulfonamides, β-lactams, macrolides and ionophores are examples of antimicrobial classes that are frequently detected in manure wastes [15].

Most veterinary antibiotics fed to animals are poorly absorbed in the animal gut and consequently do not accumulate in the animal [26]. Therefore, a substantial amount of antibiotics given to animals is excreted with the urine and feces within a few days of medication.

2. Aquaculture: Estimates of antimicrobials used annually in the aquaculture industry in the United States vary from 93 to 196 thousand kg, which include primarily oxytetracycline, sulfamerazine, sulfadimethoxine, ormetoprim, and formalin [3]. Although the quantity of antimicrobials used in aquaculture is small compared to other areas of animal husbandry, a direct comparison cannot be made because of the very different environments. In addition, food not eaten by fish and drugs excreted with feces settle at the bottom of net pens. When the sediments from these ponds are applied to agriculture fields, these antimicrobials enter the soil.

3. Plant production:

a. Against pests and diseases- Antibiotics have been in use since the 1950s to control certain bacterial diseases of fruits, vegetable, and ornamental plants. Only two antibiotics, streptomycin and oxytetracycline, are registered by the United States Environment Protection Agency for use in plant agriculture [20]. Fire blight is the most important bacterial disease of apple, pear and related ornamental plants. Streptomycin has been an effective antibiotic against fire blight because it is bactericidal and kills the pathogen on the flower surface. Oxytetracycline also inhibits the growth of the pathogen [25].

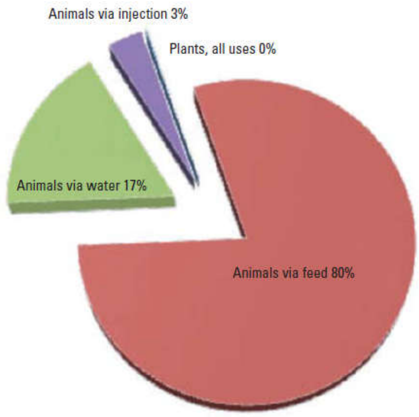

Fig 3. Distribution of antibiotic use in plant and animal agriculture in the United States in 2009. Source: data were obtained from the United States Department of Agriculture National Statistical Service (www.nass.usda.gov) [30] for antibiotic use on plants, and the Government Accountability Office, 2011.

Table 1. Some Common Antibiotics used for Plant Protection

Antibacterial	Antibiotic C6, Cellocidin, Chloramphenicol, Citrinin, Erythromycin, Gramicidin, Kanamycin, Novobiocin, Penicillin, Phtobacteriomycin, Polymycin, Polymyxin, Rhizopin, Streptomycin, Agrimycin, Phytostrep, Tetracycline and Vancomycin.
Antifungal	Antibiotic P3, Antibiotic P9, Antimycin,Antimvcin, Aureofungin, Blasticidin, Bulboformin, Candicidin, CRRI-antibiotic, Cycloheximide, Foliomvcin, Nystatin, Oligomvcin, Griseofulvin, Phytoactin, Polyoxin, Tetrin, Trichothecin, Benturicidin and Venturomycin.
Antimycoplasmal	Tetracycline, Erythromycin, and Methacycline
Antiviral	Actinomycin D, Antibiotic 205-2B, Blasticidin, Cycloheximide(actidione), Daunomycin DPB, Mithramycin, Mitomycin C, Pentaene G8 and Tubercidin.

Source: Arun, [1]

b. For plant growth and development- In addition to being used as cure against plant diseases, antibiotics may also be used as agents to stop preharvest fruit drop or as abscission agents to collect fruits in citrus crops. Smalla and Tiedje [22] estimated that the amount of antibiotics used for crops is relatively low in comparison to the quantities used in livestock, with estimates ranging from 0.2 to 0.4 percent of total agricultural antibiotic consumption. Antibiotics commonly found in pig, cattle, and turkey manures included tetracyclines, tylosin, sulfamethazine, amprolium, monensin, virginiamycin, penicillin and nicarbazine [15].

Fate of antimicrobials in agriculture soil

a. Persistence of antibiotics in soil- The concentration of antibiotics in soils can be elevated by repeated application of either fresh livestock manure or manure-based compost [10]. The inactivation of antibiotics in soil may be the result of one or more of three distinct processes:

(a) Intrinsic chemical instability of the antibiotic molecule (b) adsorption on soil clay minerals and organic matter and (c) microbiological degradation.

b. Sorption by soils- When manure containing antimicrobials is applied to field, a fraction of the added antimicrobials gets sorbed to soil constituents. Sorption mechanisms involved in soil include cation exchange, cation bridging at clay surfaces, surface complexation, hydrogen bonding and hydrophobic bonding. Organic soil contaminants are primarily neutral and hydrophobic, antimicrobials are moderately polar-to-polar and often posses functional groups (*e.g.*, –NO2, –NH2, –OH, –CN, –OH, –COOH) that contribute to moderately high aqueous solubility, while simultaneously promoting sorption to charged soil surfaces. pH-dependent species *i.e.*, cation, anion, zwitterions interact with the sorptive components of soil components like aluminosilicate clays, organic matter, oxides, and oxyhydroxides through cation exchange, cation bridging, complexation, and H-bonding. According to Sassman and Lee [18], binding of antimicrobials by cation exchange was an important sorption mechanism for compounds possessing a positive charge. Cation bridging with divalent and trivalent cations present in soils also an important sorption mechanism for zwitterionic antimicrobials possessing negatively charged functional groups as reported by Gu and Karthikeyan [7] in work on ciprofloxacin sorption to Al- and Fe-hydrous oxides.

The extent of antibiotic adsorption to soils depends on the antibiotic species present and soil properties including pH, organic matter content, and the concentration and type of divalent cations present [21]. Stephen and lee [24] found tetracyclines were highly sorbed, especially in acidic and high clay soils. The sorption behaviour of veterinary medicines may be influenced by changes in the pH of soil interstitial water brought about by levels of ammonia in manure and slurry applied to soils [5].

c. Degradation in soil- veterinary antibiotics released to soils through livestock manure, were degraded primarily by abiotic process rather than biotic processes, such antibiotics were not readily biodegradable as evidenced by Bao *et al*. [2]. Antimicrobials are typically large compounds with multiple functional groups, transformation of the parent may involve the change of a single functional group, which may or may not cause adverse effects on the ecosystem [17].

d. Transport of antimicrobials as faciliated by dissolved organic matter - Hesketh *et al*. [11] found that the mobility of pesticide and polynuclear aromatic hydrocarbons will be increased in the presence of dissolved organic matter (DOM). Antimicrobials may bind to Dissolved organic matter by cation exchange. It depends on the properties of the contaminant (*e.g*., polarity and charge) and the DOM (*e.g*., composition and acidity). The DOM act as a carrier and facilitate transport through soil profile. The presence of a large amount of dissolved organic matter (DOM) was also found to decrease the sorption of OTC to clay, suggesting that DOM may increase OTC mobility [14]. It was previously found by Haberhauer *et al*., [9] that the presence of humic acid increased the mobility of the pesticide MCPA whereas fulvic acids retarded movement.

e. Runoff and leaching from Soils- Antimicrobials transport within soils and to groundwater and surface water can occur by both leaching and runoff. Kay *et al*. [12] investigated the fate of veterinary antibiotics in clay soils following slurry application to agricultural land through column studies. They found that application of pig slurry had no significant effect on mobility of antibiotics in soil and caused a significant increase in soil water pH in the top 10 cm of the soil. Soil tillage prior to slurry application reduced the leaching of antibiotics viz. oxytetracycline, sulphachloropyridazine and tylosin found in slurry.

EFFECT OF ANTIMICROBIALS IN AGRICULTURE

a. Effect on plants- only a few studies have been conducted to investigate antibiotic uptake by plants. Previous studies have shown that plants take up less than 2 % of the pharmaceuticals applied to soil [7]. Chlortetracycline was translocated to the aboveground tissue of green onions, cabbage and corn from a CTC-treated soil [16]. Studies of the toxicity of sulfadimethoxine to plants found that a sulfadimethoxine concentration of 300 mg L^{-1} in agar and soil-based laboratory systems significantly reduced root, stalk and leaf growths in millet, pea, corn and barley [19]. For ionisable organic compounds, their neutral form generally favours root uptake, whereas ionisation can reduce their bioaccumulation in plants [21]. Significant reductions on biomass and elongation at the 100 mg/kg concentration of sulfachlorpyridazine were observed at 7 and 21 d of exposure was observed by Boleas *et al*., [4]. Carmen *et al*. [6] conducted an experiment on uptake of oxytetracycline, sulfamethoxazole and ketoconazole from fertilised soils by plants and found that grass and watercress took up sulfamethoxazole and ketoconazole. Whereas, oxytetracycline because of its strong bonding with metal cations through its multiple O- and N- functional groups influencing sorption on soil components, was not detected in any of the samples analysed.

b. Effect on agriculture soil- Kreuzig *et al*. [13] reported and attributed hindered infiltration of water into the soil due to surface sealing by manure and particle-bound transport. The effect of land application methods on the fate of antimicrobials in top soil is compound specific. Broadcast application led to higher tylosin concentrations in the top soil, whereas incorporation resulted in higher chlortetracycline concentrations [23]. A significant portion of the chlortetracyline could be photodegraded after being broadcasted on soil surface whereas mixing manure into soil would limit photodegradation.

CONCLUSION

The heavy use of antibiotics in the livestock industry and the dramatic shift in recent years toward more highly concentrated production units have brought attention to the role of animal waste-borne antimicrobials and antibiotic-resistant bacteria on ecosystem and human health. Currently, there is no cost-effective way to pretreat most animal wastes except for poultry litter for which composting and treatment is less cost prohibitive. However, further research is needed to optimize and assess composting strategies with regards to antimicrobial dissipation, but composting is unlikely to reduce the presence of manure-borne antibiotic-resistance bacteria. Small changes in how manure is stored or treated (*e.g.*, aeration) prior to land application may serve to reduce antibiotic concentrations.

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