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Impact evaluation of using antibiotics in animal husbandry practices-Review

Andreea Matache,
Florin Nenciu,
Nicoleta Alexandra Vanghele,
Gabriel Nae

Testing Department
The National Institute of Research - Development for Machines and Installations designed to Agriculture and Food Industry - INMA Bucharest,
Bucharest; Romania
andmatache@yahoo.com

Abstract. *The use of antibiotics in the animal husbandry technologies is a practice known for decades, being usually included in the feed as a growth promoter and to prevent several diseases. However, the uncontrolled, excessive and unregulated use of antibiotics has shown multiple negative effects on animal growth, but also on human health and the ecosystem. Unmetabolized antibiotics contaminate the environment by releasing wastes into the soil, leading to the spread of antimicrobial resistance towards the human food chain. It is therefore important to analyze animal waste management practices in order to find other treatment solutions and to lower the negative impact of residues generated from animal husbandry on public health and the ecosystem. Health organizations have emphasized the need for improved regulatory controls for antibiotics and clear guidelines for farmers and veterinary professionals, in order to use antibiotics responsibly. The current paper evaluates the potential risks of using antibiotics in animal husbandry and identifies strategies for reducing unwanted hazards.*

Keywords — antimicrobial resistance, long-term impact, detection methods, organic agriculture

I. Introduction

Antimicrobial resistance has become an intensely discussed topic at the global level, the reason being the negative effects on public health caused by the uncontrolled use of antibiotics in agriculture and in the prevention of bacterial infections for animals and humans. Through the administration for various clinical and non-clinical purposes of antimicrobial agents, the selective pressure exerted on various pathogens has had a continuous increase. As a result, bacteria have developed different defenses against the antimicrobial environments [1, 2].

Pharmaceuticals used in animal treatment are frequently released into various environments. There is a continuous debate and disagreement over the role that agricultural medication plays in the emergence of clinical antibiotic resistance. The effect of antibiotic use in both clinical and agricultural contexts has been related to the prevalence and a significant increase in the prevalence of bacteria and genes that are resistant to drugs [3].

When consuming resistant infectious agents, humans and other organisms may contact very aggressive forms of the diseases. Contaminants in meat production and other foods may cause gastrointestinal illnesses like salmonellosis and campylobacteriosis. Using various microbial risk assessment models, can be calculated a safe approach for the antibiotic use in food-producing systems. Human exposure to resistant agricultural organisms may lead to further transmission within the human community.

It is highly challenging to track and measure the horizontal gene transfer of resistance pathogens from animals to humans, and it is still unknown with certainty whether animals are the primary source of the genes causing clinical resistance.

Antibiotics are drugs that contain a series of chemicals obtained naturally from living organisms or synthetic compounds produced in modern laboratories. Since the 1940s, antibiotics have undergone a fast and constant evolution. They have been utilized to prevent the growth of germs and are now regarded as the most significant class of pharmaceuticals for the treatment of different infections [4, 5]. Antibiotics are classified according to their effects, either bacteriostatic or bactericidal, but also according to the degree of effectiveness, with narrow or broad spectrum [6].

Antibiotics are typically administered to humans to avoid and cure diseases, but they additionally have applications in agriculture to increase agricultural output, enhance food quality, and enhance animal breeding [7,8]. Approximately 80% of the animals raised today, for food production, have been administered drugs for a long period of their lives [9].

Despite the multiple economic and social benefits, the negative impact on the environment of antibacterial agents through partial metabolism and the release of waste into the soil becomes a significant concern [10]. Due to the increase in antibacterial resistance as a result of the excessive use of antibiotics, it is vital to develop alternative methods for the safety of human health and the ecosystem [11].

The main cause of concern for human health are the residues from antibiotics in animal-derived foods and in the residues left in the feces.

It is well known that administering antibiotics inevitably results in the development of resistance, consequently using antimicrobials in animals stimulates the development of drug resistance for consumers [12]. Antibiotics used frequently in veterinary care, followed by slaughter for consumption, as well as widespread use in human medicine, can promote the evolution of resistant bacteria in both people and animals.

In addition, humans and animals may contract several germs from each other through touch, inhalation of contaminated aerosols, contaminated food, contaminated water, and other means [13,14]. Consistent consumption of foods containing antimicrobial residues can lead to various disorders such as severe or chronic allergic reactions, direct toxicity, reproductive disorders, mutagenicity, hepatotoxicity [15].

The Acceptable Daily Intake (ADI) is an assessment of the antibiotic residue that can be ingested daily, during life, without risk to human health and is based on the safety factor (often 100) and the No Observed Effect Level (NOEL). Sensitivity to chemical substances can be higher for humans than in animals, even 10 times more. It is also particularly important to establish the withdrawal period for the administration of antimicrobials to animals, so that food products of animal origin are considered safe [16, 17].

The use of antibiotics exacerbates the damaging effects of anthropogenic activity on the environment, which result in desertification and soil depletion [18-20].

II. Materials and Methods

The research started from the problem of antibiotic residues from animal farms. At this moment, the worldwide legislation regarding the bans on the use of antibiotics is very varied, which allows an efficient comparative analysis of the results identified in the specialized literature.

During the research, 70 scientific articles were analyzed, which dealt with detection methodologies, the accepted daily dose regarding antibiotic residues, impact studies and natural alternatives used to combat pathogenic microorganisms, of which 39 articles were included in the Bibliography.

The data were collected systematically, summarizing and tabulating the concentration levels identified in scientific works, highlighting the impact on agricultural practices and offering some ecological alternatives.

The effects of forbidding the use of antibiotics in agriculture

The E.U. had banned all preventive use of pharmaceuticals for animals while the USA, have introduced several antibiotic restrictions. The European Union's prohibition on farm for antibiotic use produced a sizable natural experiment where researchers could study the results of such an interdiction. It is unclear whether there is going to be a decrease in the prevalence of resistant organisms in the ecosystem even after antibiotic selection factors have been eliminated or diminished as a result of a prohibition. While it's plausible that not enough time has passed for patterns to be seen, it's also likely that resistant pathogen strains could continue to exist in the ecosystem, if there is no selective pressure from antibiotics. These other adaptations are kept alongside a resistance determinant that gets transmitted with them.

Synthetic versus natural agrochemicals and the impact in crop protection

Synthetic agrochemicals have an unfavorable reputation across the globe when compared to plant management products with natural origins. Biocontrol refers to all organic methods for protecting plants, including macroorganisms and biocontrol agents, which are now regulated as pesticides in Europe. Due to their specialization, biorationals are growing and showing potential, though this is not always the case. The natural compounds are microorganisms, semiochemicals, and natural compounds (of mineral, plant, microbial, and animal origin) that are used in plant defense.

Antibiotic detection methodologies in animal husbandry

For a careful monitoring of the use of antibiotics, their detection methods are also important. Two different methods for determining antimicrobial residues are presented in the specialized literature: confirmation methods and screening methods.

Confirmation methods are based on liquid chromatography (LC) that is associated to mass spectrometry evaluations (MS), which is one of the most used methods with a percentage of 38%. It continues with LC-UV and enzyme-linked immunosorbent assay (ELISA), this method having a percentage of use of 18%. The application of other screening tests (12%) and biosensors (8%) have a considerable increase.

Traditional evaluation methods used for finding antimicrobial pathogens are divided into analytical methods that are generally superior in selectivity and specificity, immunological tests, enzyme tests and microbial inhibition tests. The detection of drug residues can also be achieved with the help of microbial sensors with whole cells made using recombinant DNA technologies [7, 21].

III. Results

Since animals, soil, and plants are closely related, it implies that more than one ecosystem is susceptible to the propagation of antibiotics and antibiotic-resistant microorganisms. A network of antibiotic resistance genes (ARGs) is formed as a result of the movement of antibiotics along all of these pathways (Figure 1).

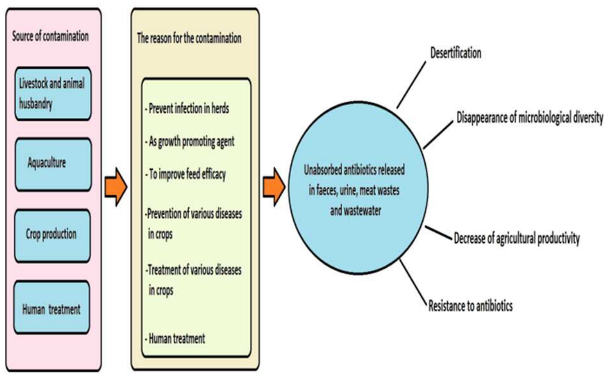

Fig.1. Possible sources of antibiotic pollution that negatively affects the ecosystem.

The use of antibiotic drugs in human and veterinary medicine is intensively analyzed, however the application in horticulture and plant development is a less explored field and needs continuous research [21].

Optimizing subsequent evaluations that address health risks for humans and the environment due to the presence of antibiotics in agroecosystems requires advances in analytical precision, sample monitoring for environmental matrices, and quantification method development. These factors are all crucial for understanding how antibiotics will behave in the environment [22].

The impact on increasing productivity following the use of antibiotics has been demonstrated. Antibiotics are often used in agricultural practices, animal husbandry and fish farming. In agricultural management practices, antibacterial agents are commonly employed to avoid and treat various crop diseases. On the other hand, in animal husbandry antibiotics are often administered as growth promoters and in the prevention or the cure of several infections [23, 24].

The accumulation of antibiotics in agriculture is becoming a serious and increasingly debated problem. Even if the field was not sufficiently investigated, in order to discover the influence of the accumulation of antibiotics in plants and soil. The conclusion was that symbiotic fungi control to a certain extent the development of lettuce and the accumulation of antibiotics in its shoots [25, 26].

The median yearly intake of antibiotics in the livestock industry has been calculated at 45 mg/kg for cattle, 148 mg/kg for poultry, and 172 mg/kg for swine globally [27].

Risks to human health and the environment from antibiotic usage in animal diets

Because of their detrimental impacts on the ecosystem, antibiotic use and release in the natural environment, including groundwater, soil, and surface waters, has gained interest recently [28].

Table 1. Representative levels of specific antibiotics in animal waste, fertilizers made from manure, and composted soils across China and several other countries from previous investigations.

Antibiotic Residue	Animal	Residues ($mg\ kg^{-1}$)	References
TC – tetracycline	Chicken swine/ cattle	0,110/ 0,602 / 0,074	[28, 29]
OTC – oxytetracycline	Chicken swine/ cattle	0,715/ 1,100/ 0,532	[28, 30]
CTC - chlortetracycline	chicken, swine, cattle	0,022/ 1,040 / 0,030	[28, 31, 32]
DOC – doxycycline	chicken, swine, cattle	0,104 / 0,637 / 0,074	[28, 33]
SCX - sulfachinoxalin	chicken, swine, cattle	0,020/ 0,011/ 0,011	[28, 29]
SDZ - sulfadiazine	chicken, swine, cattle	0,028/ 0,119/ 0,012	[28, 32, 33]
NFC - norfloxacin	chicken, swine, cattle	0,114/ 0,040/ 0,062	[28,34]
OFC - ofloxacin	chicken, swine, cattle	0,232/ 0,038 / 0,064	[28, 33]
CFC ciprofloxacin	chicken, swine, cattle	0,148/ 0,033/ 0,104	[28, 35]
EFC - enrofloxacin	chicken, swine, cattle	0,102/ 0,038/ 0,056	[28, 36]

Using natural extracts to replace the large-scale utilisation of antibiotics on farms

Knowing the risks of overuse of antibiotics in agricultural practices, alternative methods of antimicrobials are being researched.

Together with the quest for novel antibiotics recipes, the application of organic alternatives aims to reduce mortality, optimize the intestinal microbiota and preserve the health of the consumer. In the specialized literature, various plant extracts have been evaluated as initiators for animal breeding [37, 38].

Such an alternative is presented by [39], namely *Agrimonia procera* which proved to have antimicrobial effects in piglets treated with lipopolysaccharides (LPS). Consequently, *Agrimonia procera (AP*) can be considered a natural alternative to antibiotics and deserves continued research for its input in animal husbandry.

Another study analyzed fermented garlic extract to replace antibacterials in animal husbandry. The results showed that fermented garlic reduced the number of *E. coli* in growing pigs [40].

Discussions

In year 2010, almost 63,151 tons of antibiotics were given in animal husbandry at the global level, and this administration is expected to increase by 67% until 2030. On the other hand, it is estimated that by 2050, antimicrobial resistance in the agricultural environment will generate an increase in expenses of US$100 trillion and a rise in the death incidence from 700,000 to 10 million per year [41].

In 2018, 29,774.09 tons of antibiotics were used for animal husbandry practices in China (which is the leading user of antibiotics), and 53.20% of this consumption was administered to enhance animal husbandry [42].

Antimicrobial resistance is a hot topic globally. To protect against the importation of resistant pathogens through trade and travel, a close collaboration between the interested parties is needed: research, industry, health authorities and political factors [43-46].

Conclusions

We currently know very little about how resistant pathogens are effectively transferred from animals to humans (and vice versa). There is no doubt that the barriers between species have been crossed repeatedly in both ways, with strains that are suitable for animals giving rise to lines that are suitable for humans. It's uncertain how much co-selection of resistance factors will influence clinical resistance even after the use of antibiotics will be completely prohibited worldwide. The biggest benefit of limiting antibiotic use might not be to reverse resistance, but rather to stop further rises in frequency and the potential to limit the relevant genes to be horizontally transmitted into additional organisms.

Avoiding synthetic agrochemicals is a prevalent position against these compounds. Microorganisms, semi-chemicals, and natural compounds are starting to replace aggressive synthetic compounds as plant protection products, especially in organic agriculture. These natural compounds are used to safeguard crops from bio-aggressors in addition or replacing chemical pesticides. However, a substance status as a natural substance does not guarantee that it is very effective neither that is not as bad as the substance it replaced (in the context of plant protection). It is very important that future studies consider the level of efficiency of biological extractions used to replace synthetic chemical compounds through field validations.

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