Current status of veterinary antibiotic uses and solutions for existing problems

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Abstract: Antibiotics have been used in many applications since their discovery and have brought many benefits. Veterinary antibiotics as a feed additive can promote the growth of livestock and poultry to improve economic efficiency, while applied in disease treatment and prevention. However, with the occurrence of misuse, many aspects of the problem have emerged. This paper summarizes the biological problems that arise from the misuse of veterinary antibiotics, environmental pollution, and proposes solutions.

1. Introduction

1.1. Brief history of antibiotic research

In 1929, Alexander Fleming, a British bacteriologist, found that Penicillium contaminated staphylococcal culture on the plate of the growth of Penicillium has the role of antagonism and lysis of staphylococcal colonies, and the substance that produces this effect is called penicillin, which is the discovery of the first antibiotic. In 1944, Waksman et al. extracted streptomycin from Streptomyces griseus. In 1947, Burkholder et al. discovered streptomycin in the culture of Streptomyces venezuelanus. In 1952, Mcguiret et al. discovered erythromycin. From then on, a boom in antibiotic research began and new manufacturing techniques were continuously developed for medical use [1] .

1.2. Current status of antibiotic application

Since their discovery, antibiotics have been widely used in animal husbandry and have brought a lot of convenience to people. The history of the application of antibiotics in animal husbandry can be traced back to as early as 20 actual United States and Europe, applied in feed additives and disease treatment. Antibiotics as feed additives can promote animal growth, improve feed utilization, improve production performance, improve breeding stock reproductive performance, reduce mortality and other issues. It is also widely used as a preventive and therapeutic drug for infectious diseases and other animal diseases [2].

However, with the abuse of anti-biotics also brings many problems, such as suppression of animal immune system, environmental pollution and other ecological problems. Meanwhile, with the development of globalization, each country has made different policies to respond to the use of antibiotics in livestock production.

In this paper, we summarize the problems arising from the use of antibiotics and propose corresponding solutions to provide reference for subsequent research.

2. Biohazards and Solutions

Although the use of antibiotics certainly has many good effects, it also has many negative aspects.

2.1. Biological hazards

2.1.1. Suppression of the immune system

Intestinal microecology is closely related to the function of the body's immune system and plays an important role in the formation of both the extraintestinal immune system and the body's autoimmune diseases. Although the addition of antibiotics in the feed can reduce the harm of exogenous antigens to the organism, it also changes the composition of microorganisms, affecting the immune response and weakening the resistance of the animal itself to antigens [3].

2.1.2. Increase of drug resistance

Experimentally, drug resistance is proven to be highly heritable. The long-term excessive use of antibiotics in livestock and poultry farming will increase the resistance of pathogenic microorganisms and spread between species or genera of bacteria and viruses through plasmids that can carry resistance genes, causing more bacteria and viruses to develop resistance and leading to the emergence of superbugs [4].

2.1.3. Harm to human health

The emergence of antibiotic resistance genes in livestock and poultry farming can affect human health in a variety of ways. Breeders engaged in farming are exposed to livestock manure for long periods of time, increasing the likelihood of carrying and contracting drug-resistant bacteria. The presence of antibiotic residues in animal-derived foods can also cause antibiotic resistance in humans, which can have an impact on the treatment of disease. Also, the long-term accumulation of antibiotics in the human body can lead to increased carcinogenicity and enhanced mutagenicity.

2.1.4. Hazardous to public health

Due to the early mixing of human and animal antibiotics, the possibility of animal bacteria and viruses carrying resistance genes homologous to humans increases, leading to an increased probability of zoonotic diseases and endangering public health and safety issues. At the same time, as more farmers do not have professional technical training, they blindly add antibiotics for a long time regardless of the existence of bacterial diseases, and also do not distinguish the growth of livestock and poultry only use a single antibiotic, resulting in the accumulation of livestock and poultry poisoning and the increased probability of drug resistance problems.

2.2. Solutions

In this regard, in recent years, people have explored a variety of alternative methods to veterinary antibiotics.

2.2.1. Micro-ecological preparations

Micro-ecological preparations made of probiotics or secondary metabolites of probiotics, with green, non-polluting, not easy to produce drug resistance and other characteristics. There are 34 kinds of microbial feed additives allowed in China, mainly including Lactobacillus, Bacillus and so on. It can effectively improve the composition of intestinal microorganisms, promote the value-added of beneficial bacteria, inhibit the colonization of harmful bacteria, and regulate the health of the body [5, 6].

2.2.2. Plant extracts

The application of plant extracts has also been a popular research direction in recent years. Plants are rich in metabolites, mainly including saponins, polysaccharides, alkaloids, volatile oils, polyphenols, flavonoids and many other types, and the raw materials are generally cheap and easy to obtain. Studies have shown that plant extracts can promote the absorption of nutrients and stimulate the growth of animals; improve the immunity of the body; reduce oxidative stress and improve antioxidant capacity. Plant extracts can also be developed into various delivery forms that can reduce animal stress, an emerging industry with broad market prospects [7, 8].

2.2.3. Enzyme preparations

Enzymes have roles in vivo and in vitro. In feed additives, enzymes are mainly divided into two categories: one is endogenous digestive enzymes, which can be secreted by the animal's digestive tract to supplement the lack of digestive enzymes in the body; the other is exogenous digestive enzymes, which cannot be produced by the animal itself and can better destroy plant cell walls and improve feed utilization. Improve feed utilization, while helping the organism to improve immunity [9].

2.2.4. Acid preparation

Organic acid has the effect of antibacterial and bactericidal, as feed additives can reduce the number of bacteria in the feed, and at the same time can adjust the pH value of the feed to facilitate the utilization of gastrointestinal flora, and can also provide a suitable living environment for the flora. Organic acid can also diffuse directly into the bacterial cells to inhibit their activities and play a protective role.

3. Environmental Hazards and Solutions

Nowadays, the extensive use of antibiotics in medical treatment, agriculture, animal husbandry, and the food industry lead to the continuous discharge of these pollutants into the natural environment in various ways, seriously affecting aquatic and terrestrial ecosystems. Specifically, antibiotics used to treat animal diseases or growth promoters can leach animal feces into the soil through surface runoff. At the same time, the untreated feces of various livestock and poultry animals will enter the ground in the form of fertilizer through compost, and the antibiotics carried by them will also pollute the soil, bringing a series of problems. Therefore, it is of great significance to study the harm of antibiotics to the environment and to degrade/remove antibiotics.

3.1. Environmental Hazards

Table 1 DNA damage of earthworm coelomocytes exposed to serial concentrations(mg·kg-1)of tetracycline, chlortetracycline or their mixtures of different duration [11]

Group	Dose (mg·kg-1 soil)	Olive Tail Moment (OTM) values 7-d	14-d	28-d
Tetracycline	Control	$0.73{\pm}0.69^{a}$	$0.81{\pm}0.69^{a}$	$0.95{\pm}0.99^{a}$
	3	$5.26{\pm}2.74^{b}$	$5.50{\pm}3.44^{b}$	$7.22{\pm}3.59^{b}$
	30	$7.84{\pm}3.76^{c}$	$8.72{\pm}3.62^{c}$	$8.37{\pm}4.79^{c}$
	100	$9.07{\pm}5.62^{cd}$	$9.07{\pm}5.08^{c}$	$9.38{\pm}3.47^{d}$
Chlortetracycline	Control	$0.73{\pm}0.69^{a}$	$0.81{\pm}0.69^{a}$	$0.95{\pm}0.99^{a}$
	3	$9.20{\pm}4.20^{c}$	$8.03{\pm}4.65^{c}$	$6.95{\pm}3.15^{c}$
	30	$11.26{\pm}4.11^{d}$	$9.95{\pm}5.84^{d}$	$8.54{\pm}3.90^{d}$
	100	$12.99{\pm}4.17^{e}$	11.76±5.56e	$11.51{\pm}4.75^{e}$
Mixture	Control	$0.73{\pm}0.69^{a}$	$0.81{\pm}0.69^{a}$	$0.95{\pm}0.99^{a}$
	3	$9.48{\pm}4.50^{c}$	$8.46{\pm}3.61^{c}$	$8.82{\pm}3.91^{b}$
	30	$10.44{\pm}4.84^{c}$	$9.45{\pm}4.72^{cd}$	$9.43{\pm}4.39^{bc}$
	100	$13.05{\pm}5.45^{d}$	$10.60{\pm}4.02^{de}$	$10.11{\pm}2.99^{c}$

The invention of antibiotics has dramatically reduced the treatments for animal diseases and many human infections. While providing convenience to people, it also harms the environment, resulting in soil species and plants being exposed to large amounts of antibiotic residues. The residual antibiotics affect the soil, the plants and the species that depend on it. For plants, although small amounts of antibiotics increase the activity of antioxidant enzymes in plants which will be helpful for them to withstand the disease better, today's high use of antibiotics results in a decrease in enzyme activity that affects germination. Although antibiotics affect plants, the effect depends on the type of antibiotics and plant species. According to the research, the two sulfonamides (sulfamethoxazole and sulfamethazine) and trimethoprim significantly affect plant growth in soil, and cucumber was the least tolerant of the antibiotic compounds compared with sweet oat and rice [10]. For the species that live in soil, antibiotics will cause a different degree of influence on species. The results (as shown in Table 1) of experiments conducted by Dong et al. show that tetracycline and chlortetracycline cause harm to the DNA of earthworms, and the mixture also affects the earthworm's DNA. However, the influence level depends on the length of the days. Overall, the mix has more damage to the earthworm's DNA at the low level. The DNA damage of earthworms will eventually affect the growth of species that are essential for the soil's ecosystem, thus leading to many chain reactions.

3.2. Treatment of antibiotics after entering soil environment

3.2.1. Adsorption of biochar

Biochar is made by burning wood, straw, or waste crops without oxygen. It is a low-cost adsorbent material because of its high nano porosity, large specific surface area, and wealthy oxygen-containing functional groups. When applied to soil, it can integrate soil carbon and improve soil properties. Biochar can significantly affect the adsorption/desorption and degradation of antibiotics in the soil through physical, chemical, and electrostatic interactions. However, because biochar will be affected by its properties and soil environment, the removal effect of antibiotics is not so significant. Therefore, domestic and foreign scholars have established various modification methods from different levels, such as acid treatment, surfactant modification, increasing the specific surface area, and improving the adsorption efficiency. Although biochar has good adsorption properties, most of the current experiments are aimed at the adsorption of a single substance. It is not clear how biochar can adsorb each pollutant in soil. Therefore, in the future, it is necessary to systematically evaluate the adsorption effect of biochar on antibiotics based on the actual soil environment and the characteristics of biochar.

3.2.2. Graphene-based nanocomposites for antibiotics adsorption

Graphene is a carbon nanomaterial with excellent adsorbability besides biochar. It promotes the adsorption of antibiotics mainly through π-π stacking, hydrogen bonding, and electrostatic interaction. Graphene's structure is made up of a single layer of carbon, allowing it to maximize the uptake of antibiotics on both sides. In addition, graphene also has the characteristics of low acquisition cost, high porosity, and large body surface area. But current 2D graphene tends to aggregate due to strong van der Waals forces between molecules, reducing the adsorption area. In order to maximize the performance of graphene, scientists developed a new structure of graphene, a 3D structure that prevents graphene from clumping together.

4. Government and personal plan to enact

4.1. The arise of the issue

Antibiotic resistance and bacterial mutation occur spontaneously as a result of genetic diversity and natural selection, which is the most fundamental force of biology. However, if we can reduce the misuse of antibiotics in animals, we can slow down this process. Antibiotics are becoming less efficient, making it increasingly difficult to cure common diseases such as blood poisoning and eating disorders. The number of bacteria in a person's body may be in the millions. There are likely to be few individuals in the group who carry an allele that makes them resistant to drugs like penicillin. These people will have a huge advantage in the selection process. They can continue to reproduce, while the rest cannot. Due to natural selection, their descendants, all of whom carry the trait that gives penicillin resistance, may soon establish a large population of penicillin-resistant bacteria. Since we use less antibiotics, bacteria that are resistant to them have no selection advantage, and resistant bacteria populations are much less likely to emerge. The antibiotics will then function when someone really needs to be treated with them.

4.2. Solutions

4.2.1. Possible methods for individuals to follow

As a global citizen, everyone has a responsibility to prevent the spread of antibiotic resistance. The following are four suggestions that might be adopted in an individual's everyday life. Firstly, prevent bacteria illnesses from occurring in the first place by frequently washing hands and administering vaccination in hospitals. Second, when exposed to large amounts of bacteria, such as while making food, people should adhere to the WHO's Five Keys to Safer Food (keep clean, separate raw and cooked, cook thoroughly, keep food at safe temperatures, use safe water and raw materials). Third, individuals should only use the dosage and variety of antibiotics recommended by a licensed doctor or health expert. Never use or distribute antibiotics from others or surplus.

4.2.2. Possible methods and project for governments to promote

To prevent and control the spread of antibiotic resistance, the government can monitor the agricultural sector and firms. Farms and companies that use antibiotics should follow the following methods. First, only give antibiotics to animals under veterinary supervision instead of using antibiotics just to promote growth. Vaccinate animals regularly to avoid diseases that require antibiotics and use alternatives to antibiotics when available. The agricultural sector should strengthen bio-security on farms and prevent diseases through improved hygiene and animal welfare. This includes the use of ethanol to disinfect the environment and strict control over the import and export of animals and plants. The government could give awards, certificates and other benefits, such as bonuses and subsidies, to companies that support slowing down animal resistance to antibiotics.

As mentioned above, the government could encourage companies to adopt methods to slow the rate of animal resistance to antibiotics. The practice of Food and Drug Administration(FDA) in 2012 is of high reference value. In 2012, FDA enacted the Food and Drug Administration Safety and Innovation Act (FDASIA) to promote the development of qualified infectious Disease products (QIDP). The designation of antimicrobial or antifungal products for the treatment of serious or life-threatening infectious diseases requires a determination of QIDP status within 60 days of receipt of the application, which has a 5-year exclusive market right and can be granted priority review and fast track certification[12].

On the other hand, central control could refer to the management of USAID in 2002 and enact new, targeted policies. In 2002, USAID formulated guidelines for the use of antibiotics in hospitals according to WHO international indicators for rational drug use. This includes: utilization rate, quantity, time, etc. This provides a theoretical basis for hospital managers to evaluate and improve the use of antibiotics in hospitals. In the same year, the FDA specified the dosage of antibiotic use in detail and issued medication specifications for special constituents such as allergic constitutions and adverse drug reactions.

In summary, this paper provides an overview of the problem from a biological perspective, environmental issues, and policy responses in the hope of drawing increased attention to the scientific use of veterinary antibiotics.

5. Future development trend

Based on the existing solutions, cross-disciplinary construction is carried out to synthesize professional knowledge and provide an integrated view of biological and environmental hazards and innovate more effective treatment methods. Directly or indirectly reduce the hazards of veterinary antibiotic use. The application of big data analysis to more accurately grasp the state of animal feeding, improve cage science, timely adjustment, and thus reduce the use of veterinary antibiotics.

The governments of all countries should increase the supervision of scientific breeding, grace and power, the illegal use of veterinary antibiotics should be made serious treatment. Farm staff should be trained in scientific breeding to increase professional knowledge and make farms operate scientifically. Strict penalties should be introduced along with corresponding support policies to actively help farms with scientific breeding willingness to carry out good operation.

With the development of globalization, agricultural products are traded more closely. Countries should promptly announce the incidence of infectious diseases and other issues to reduce economic losses. At the same time, it is recommended that each country will actively share the cure to help each other and reduce losses.

6. Conclusion

This paper summarizes the relevant improvement methods by analyzing the existing use of veterinary antibiotics. New additives that replace the use of veterinary antibiotics are developed from a biological perspective to reduce the use of veterinary antibiotics at the source. More attention should be paid to the subsequent disposal of veterinary antibiotics to reduce environmental pollution and the pressure on public health and safety. The government and other departments should strengthen the supervision and publicity, educate the professionals and public with scientific knowledge. Although veterinary antibiotics can certainly bring benefits in animal breeding, they need to be used rationally. It is believed that with the concept of sustainable green development, the use of veterinary antibiotics will become more regulated and the problems of animal breeding will be solved while other negative effects of veterinary antibiotics will be better handled.

References

[1] Hoel D., Williams D. N., Berkelman R. L. Antibiotics: Past, present, and future [J]. Postgraduate Medicine,2015:114-122.

[2] van den Bogaard A. E., Stobberingh E. E. Antibiotic usage in animals [J]. Drugs, 1999, 58(4): 589-607.

[3] Yang I, Zhang H Q., Zhao J. B., Gu J. J., Wang C. Effects of added antibiotics on animal intestinal health [J]. Swine Production, 2015, (3): 125-8.

[4] Capita R., Alonso-Calleja C. Antibiotic-resistant bacteria: a challenge for the food industry [J]. Critical reviews in food science nutrition, 2013, 53(1): 11-48.

[5] Huang W. Q., Zhang H. Research progress on the replacement of antibiotics with microecological formulations for feeding [J]. Chinese Journal of Microecology 2015, 27(04): 488-94.

[6] Zhou H., Wang W., Wang L., Li A. K. Research progress in the development and utilization of lactic acid bacteria preparations for feeding [J]. Journal of Animal Nutrition, 2019, 31(5): 10.

[7] Hashemi S. R., Davoodi H. Herbal plants and their derivatives as growth and health promoters in animal nutrition [J]. Veterinary Research Communications2011, 35(3): 169-80.

[8] Harish Chandra, Parul Bishnoi, Archana Yadav, Babita Patni, Abhay Prakash Mishra, Anant Ram Nautiyal. Antimicrobial Resistance and the Alternative Resources with Special Emphasis on Plant-Based Antimicrobials—A Review [J]. Plants, 2017, 6(2): 16.

[9] WJ. W. Study on alternative pathways of growth promoter antibiotics [J]. Animal Science and Animal Medicine, 2003, (09): 54-7.

[10] LIU, YING, GG, et al. Effects of six selected antibiotics on plant growth and soil microbial and enzymatic activities [J]. ENVIRON POLLUT, 2009, 2009,157(5)(-): 1636-42.

[11] L Dong, G Jie, X Xie, Q Zhou. DNA damage and biochemical toxicity of antibiotics in soil on the earthworm Eisenia fetida [J]. Chemosphere, 2012, 89(1): 44-51.

[12] Zhu L. B., Lin S. W., Liu Y. H. National governance strategies to address antibiotic resistance in the United States and implications for China [J]. China Pharmacoeconomics, 2018, 13(09): 117-21.