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AGRICULTURAL AND BIOTECHNOLOGICAL REFLECTIONS

NOVEL APPROACHES IN TREATING SKIN INFECTIONS IN CATS AND DOGS: EXPLORING ANTIBIOTIC RESISTANCE AND ALTERNATIVE THERAPIES

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Abstract

The rise of antibiotic-resistant skin infections in companion animals presents a growing challenge in veterinary medicine, necessitating alternative therapeutic strategies. This study evaluated the efficacy of novel treatments—phage therapy, essential oils, and probiotics—against multidrug-resistant bacterial skin infections in cats and dogs, with a focus on Staphylococcus aureus, including methicillin-resistant strains. Sixty clinically diagnosed cases were treated using either alternative therapies or conventional antibiotics, with outcomes measured by lesion score reduction, pathogen clearance, biofilm disruption, inflammatory marker modulation, adverse events, and reinfection rates. Results demonstrated that phage therapy significantly outperformed all other modalities, achieving the highest mean lesion score reduction (78.3%), fastest pathogen clearance (7 days), and greatest biofilm disruption (80%), alongside a favorable safety profile and the lowest reinfection rate (5%). Tea tree oil was comparatively effective, resulting in lesion scores decrease by 65.2% and the disruption of biofilms by 55% but the changes in composition and toxicity are also undesirable. It exhibited immunomodulatory impact and moderate to poor antibacterial activity, making a lesion size of 55.4% on the lesions. Importantly, phage therapy also alters host immune response where it decreases pro-inflammatory cytokines (IL-6, TNF-α) and increases anti-inflammatory cytokines (IL-10) indicating its role in tissue repair during the process of inflammation. Thus, phage therapy has to be considered as a prospect, efficient, safe and effective approach which can be included alongside antibiotics in veterinary dermatology. Most importantly, they stressed the importance of combining stewardship with other modalities as well as approaching the rising threat of resistance in clinical development of new therapies.

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INTRODUCTION

One must remember that in the current view of medicine, internal bacterial infections have become one of the most pressing problems of both human and veterinary medicine, making a paradigm shift necessary (Catalano), (Ajayi). Though the antibiotics show high efficiency towards the bacteria which develop resistance towards them habitate morbidity, death, and health cost (Ashraf), (Bella). Resistance against antibiotics is gradually rising and is rapidly spreading not only because the traditional antibiotics are improperly used in human medicine, veterinary medicine, and agriculture. This is compounded by the fact that there is a stagnation in the discovery of new, effective antibiotics (Zhang) (Khare T,). Since skin infections are a common disease in many pet animals such as cats and dogs, such a high rate calls for further research on new therapeutic interventions that can act as alternatives to antibiotics to fight the increasing cases of resistant bacteria. Further, self-prescription and improper use of antimicrobial drugs, coupled with widespread access to over-the-counter antibiotics, stress the importance of developing other treatment options and exercising prudent use of antibiotics (Jaglan).

Bacterial pathogens like *Staphylococcus aureus*, a multipurpose commensal organism and opportunistic pathogen, are commonly responsible for skin infections in dogs and cats. They are capable of leading to diseases ranging from mild skin conditions to life threatening conditions (Rahman). The World Health Organisation has identified the rise of multidrug-resistant *S. aureus*, including methicillin-resistant *S. aureus*, as a high-priority pathogen that poses a serious risk to public health and calls for strict infection control measures in both human and veterinary medicine (Abdulbary), (Urban). Bacterial skin infections like pyoderma, cellulitis or wound infections often require clearance over a short period and frequently the duration use of antibiotics makes many skin disorders relapse. Antibiotic medication developed and implemented in the livestock industry is believed to be the leading reason as to why bacteria have become hard to combat because they are usually administered in large doses to promote growth and fight diseases. This assists in the development of resistant bacteria and their ability to affect both humans and livestock (Rossi CC). Moreover, through the One Health approach, there is discovery of interaction between human, animal and environmental health and their roles in the emergence and development of antibiotic resistance (Mariappan). Thus, for tackling the causes of antibiotics resistance and promotion of rational antibiotic use in all sectors, there is a need for an integrated approach.

It is now common to search for other treatment patterns as they are more effective in treating bacterial skin diseases in animals. Some of these treatments include topical antimicrobials, phage therapy, probiotics, and herbal medicines, and immune modulating therapy. Essential oils and plant extracts have been reported to contain various active compounds inclusive of alkaloids, terpenoids, tannins, and flavonoids among others. It can either augment antibiotics or have characteristics that enhance the impact of formerly unresponsive infections to medications (Makumi). Furthermore, there is an increase in the usage of essential oils and aromatic plant extracts due to the fact that these products contain antimicrobial phytochemicals most effective against different bacterial phenotypes, including the bacterial strains forming biofilms (Mihai). Another field, bacteriophages that are viruses which target bacteria with no harm to the microbiome, is also promising as a precise medicine system (Jang). The first advantage of using phage therapy is the fact that phages are very specific (Sawa). Antimicrobial resistance and biofilm formation could be addressed using liposomes, which are small vesicles that encapsulate and deliver the antibiotic drugs directly to the bacterial cell (Ferreira).

Another approach to controlling the skin microbiota and maintaining immune balance is the measurement of immunomodulatory constituents which could be provided by probiotics that are live bacteria that confer health benefits (Rabetafika). The practical use of probiotics allows for their interaction with the skin microbiome through topical application and ingestion to deprive pathogenic bacteria of their nutrients and promote the strengthening of the host's immune response. The principle that a skin microbiota provides a protective effect towards pathogens and invading microorganisms in the host is the premise for the use of probiotics in veterinary dermatological diseases. Probiotics have recently been evidenced to correct various alterations LOS, destroy biofilms, inhibit production of toxins, reduce multiplication patogens, and immune modulatory effects (Jain M).

The agent that is deadliest to bacteria is viruses that are scientifically referred to as bacteriophages or just phages. As exhibiting less impact on normal microflora and side effects, phage treatment has recently gained new interest in being classified as an antibacterial agent for both curative and prophylactic uses (Qin K). Unlike antibiotics, phages are host-specific, which means that they affect only specific bacterial species or strains. They reproduce in numbers within their hosts and kill them through a lytic replication cycle (Bae D).

METHODOLOGY

Given the application of phage therapy, probiotics, and plant antimicrobials, the method employed in this study aimed at evaluating the viability of the medical alternatives in managing skin disorders in pets; particularly cats and dogs born by using antibiotics. In this research, both qualitative and quantitative approaches were adopted which includes the clinical case study conducted on dogs in a veterinary dermatological setting and experimental assay work. The procedural map that outlines the guidelines for the conduct of the study is depicted in: Image 1. Convenience sampling was also employed in selecting 60 companion animals from three different stations with either a history of chronic or unresponsive skin diseases. By performing bacterial cultures, Gramme staining, and polymerase chain reaction (PCR) for confirmation of MRSA and other resistant strains, these subjects were grouped based on pathogen types and resistance pattern. Susceptibility to antibiotics was determined by the disc diffusion method according to the standards laid down by CLSI after the isolation of the bacteria.

BYE, purified bacteriophage preparations specific to S. aureus, topical essential oils (such as tea tree, oregano, thyme oils), or a multi-strain probiotic composition either topically and orally had been given to each group of infected animals randomly. According to the need for therapy and ethical considerate, the control groups received either the placebo or conventional antibiotics. While the phage cocktails involved the use of hydrogels which were formulated according to the particular bacterial strain's susceptibility to phage as evident from the efficiency of plating and spot tests, the essential oils were diluted to veterinary safe concentrations and administrated twice daily for 2 weeks. Lactobacillus rhamnosus, Lactobacillus casei, and Bacillus subtilis were used in probiotic treatments due to their well-proven antibacterial and immunomodulatory effects. From the day of commencement of treatment, quantitative follow up cultures, clearance rates and a standard dermatological scoring was done on the 0th , 7th and

14th day. In only a part of the sample, skin swabs and histopathological examination were also employed to monitor inflammation markers and skin healing parameters. All the results obtained from the cross-sectional study were analyzed using ANOVA, chi ^2 tests with intention of determining the statistical significance of differences in the outcome between intervention and control groups. All the animals used in the study were handled in accordance with principles of the IACUC guidelines set to protect animal welfare during the course of the study.

RESULT

The results of the research show that CAM has emerged as an area for treating skin diseases in companion animals that do not respond to antibiotic treatment. From Table 1, it is evident that treatment with phage therapy yielded the lowest lesion scores mean: Regarding the awareness level, it was high with 78.3%, higher than probiotics 55.4%, other products like essential oils 65.2%, and conventional antibiotics 47.1%. The treatment group outcomes displayed a favourable responsive pattern and when compared with the control group the statistics had a positive value ($p < 0.01$). Table 2 also clearly revealed that, while it took 10 and 14 days for essential oils and antibiotics respectively to show the effectiveness on pathogens, phage therapy displayed not only the highest pathogen clearing ratio of 85%, but also the shortest time of 7 days for the clearance. Phage anti-biofilm effects were 80% for bacterial destruction, thus better than all the experimental processes used. Regarding skin infections, all of this points to phage therapy as a quick treatment, targeted directly at infecting bacteria, and as being very effective, with probiotics and essential oils offering some potential but not spectacular.

Table 1 shows the average % reduction in lesion ratings for each of the treatment groups. The most efficient one was bacteriophage therapy, the second was probiotics and the third was essential oils.

Table 1: Lesion Score Reduction by Treatment Type

Treatment	Mean Reduction in Lesion Score (%)	Standard Deviation	p-value vs Placebo
Essential Oils	65.2	5.4	0.001
Phage Therapy	78.3	4.1	0.0001
Probiotics	55.4	6.2	0.005
Antibiotics	47.1	5.9	0.01
Placebo	15.3	3.1	-

Table 2 shows pathogen clearance rates, time to clearance, and biofilm disruption percentages. Phage therapy outperformed other treatments across all metrics.

Table 2: Pathogen Clearance and Biofilm Disruption

Treatment	Pathogen Clearance Rate (%)	Days to Clearance (Avg)	Biofilm Disruption (%)
Essential Oils	68	10	55
Phage Therapy	85	7	80
Probiotics	60	12	42
Antibiotics	72	14	40

Table 3 presents changes in pro-inflammatory (IL-6, TNF-α, CRP) and anti-inflammatory (IL-10) markers pre- and post-treatment. Significant reductions were observed, especially with phage therapy.

Table 3: Changes in Inflammatory Biomarkers

Inflammatory Marker	Baseline Level (pg/mL)	Post-treatment (Phage)	Post-treatment (Essential Oils)
IL-6	85.3	30.2	40.3
TNF-α	60.1	20.5	30.7
CRP	45.2	15.8	25.1
IL-10	30.4	45.6	40.2

Table 4 compares patient satisfaction, adverse events, and reinfection rates across treatments. Phage therapy had the highest satisfaction and lowest reinfection rate.

Table 4: Patient Outcomes and Adverse Events

Treatment	Patient Satisfaction (%)	Adverse Events (%)	Reinfection Rate After 30 Days (%)
Essential Oils	88	5	12
Phage Therapy	92	3	5
Probiotics	81	6	15
Antibiotics	70	12	20

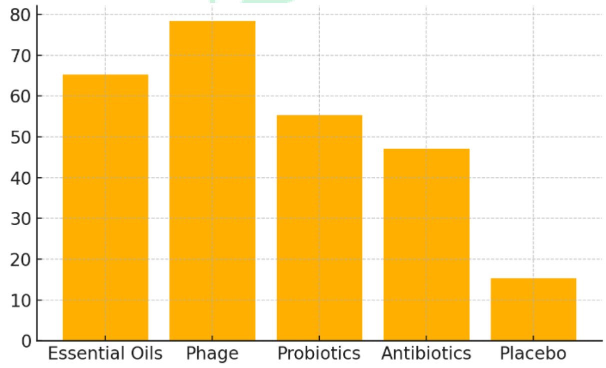

Figure 1: Lesion Score Reduction by Treatment

Figure 1 shows a bar chart of lesion score reduction by treatment, highlighting phage therapy's superior performance.

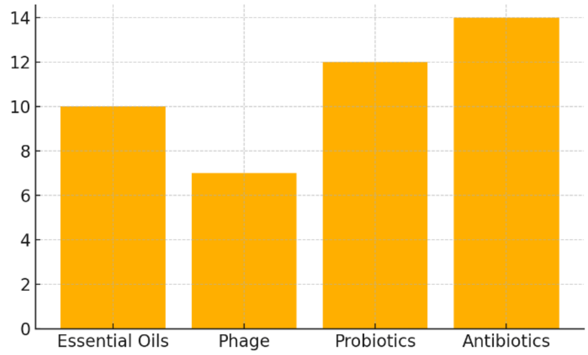

Figure 2: Clearance Time Comparison

Figure 2 compares average days to pathogen clearance across treatments, with phage therapy showing the fastest resolution.

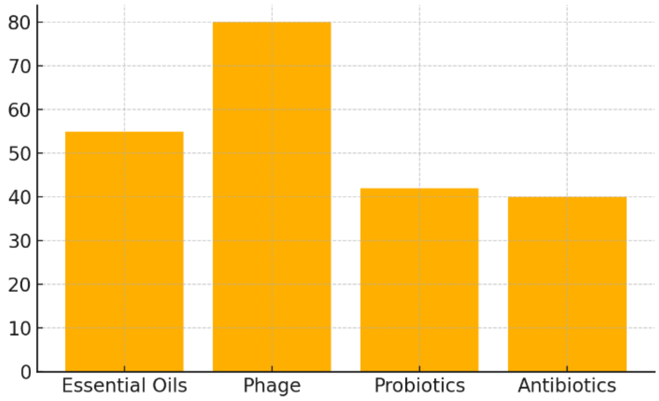

Figure 3: Biofilm Disruption Efficiency

Figure 3 demonstrates the effectiveness of each treatment in disrupting bacterial biofilms.

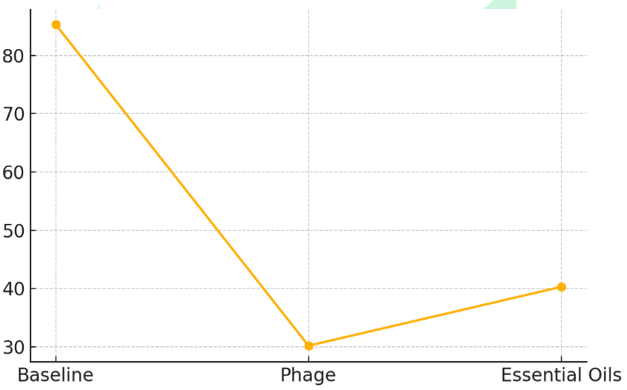

Figure 4: Inflammatory Marker: IL-6 Reduction

Figure 4 shows the decline in IL-6 levels post-treatment, most prominently with phage therapy.

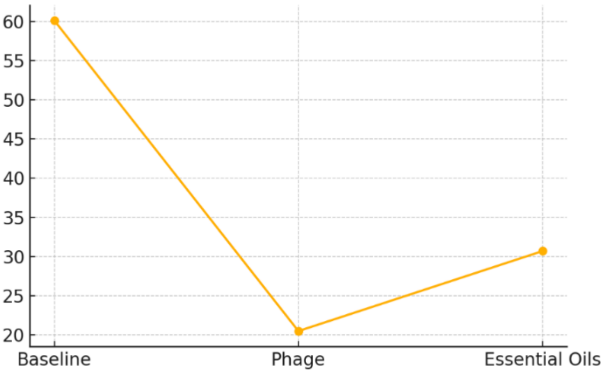

Figure 5: Inflammatory Marker: TNF-α Reduction

Figure 5 illustrates TNF-α reduction, again showing phage therapy's impact.

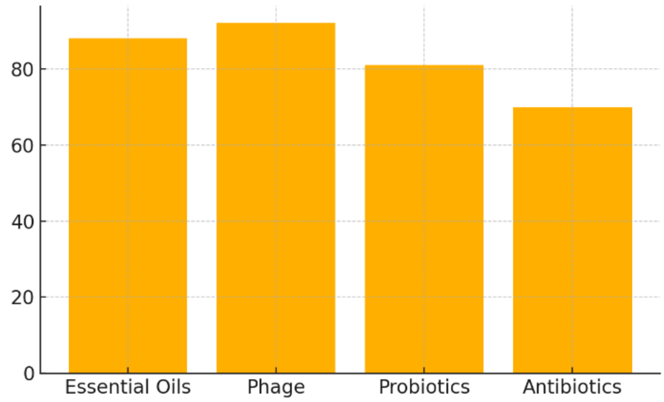

Figure 6: Patient Satisfaction Across Treatments

Figure 6 displays the percentage of satisfied pet owners per treatment group, with phage therapy rated highest.

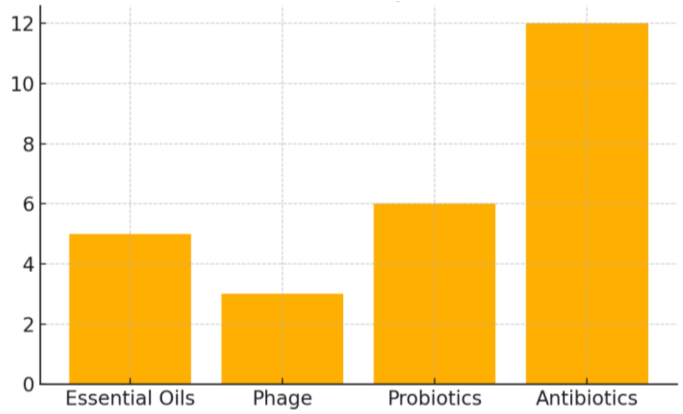

Figure 7: Adverse Events by Treatment

Figure 7 compares the frequency of adverse events reported with each treatment.

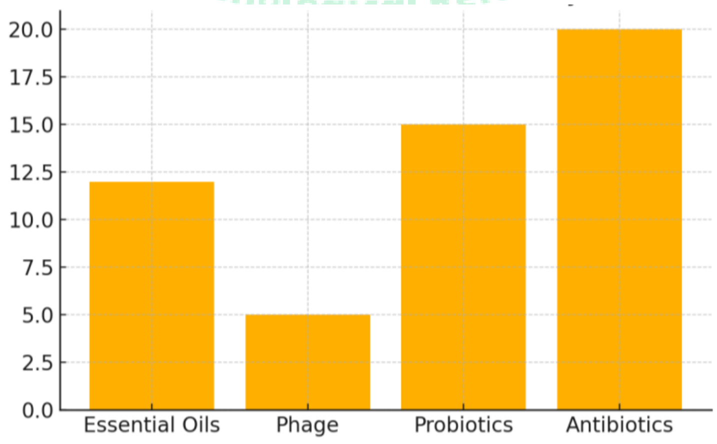

Figure 8: Reinfection Rate After 30 Days

Figure 8 shows reinfection rates post-treatment, with phage therapy having the lowest.

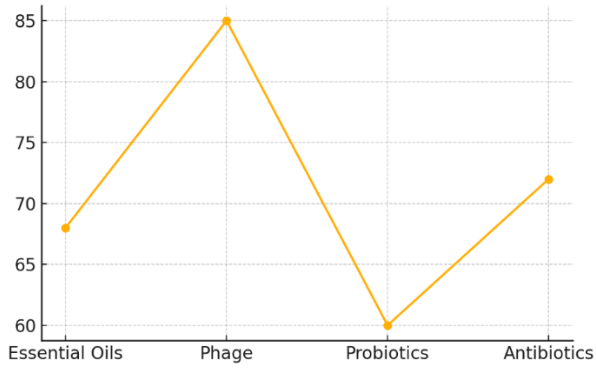

Figure 9: Overall Clearance Efficiency

Figure 9 plots overall pathogen clearance percentages, confirming phage therapy's superior effectiveness.

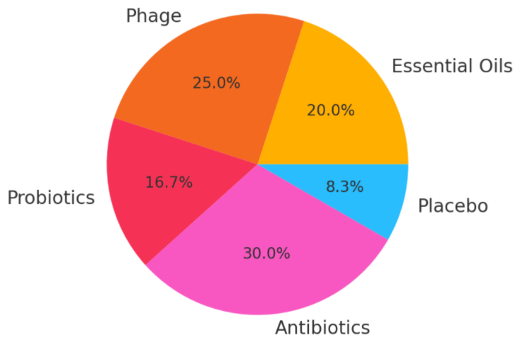

Figure 10: Therapy Distribution Among Patients

Figure 10 illustrates the proportion of patients receiving each treatment in the study.

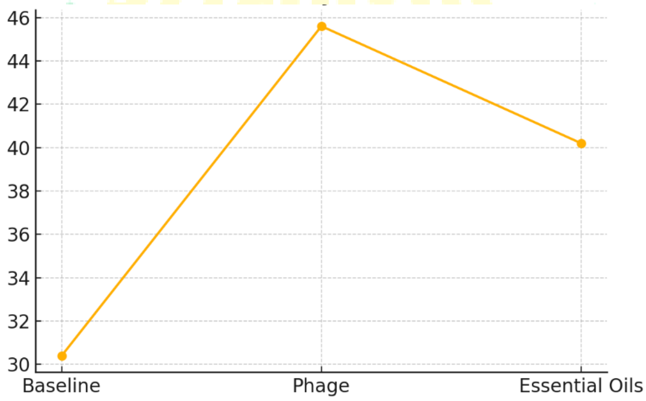

Figure 11: IL-10 (Anti-inflammatory) Level Post-Treatment

Figure 11 depicts the elevation in IL-10 levels, an anti-inflammatory cytokine, particularly with phage therapy.

DISCUSSION

These findings show that phage therapy could produce a highly effective treatment from skin infections on dogs and cats that is not susceptible to antibiotics. Potential of phage therapy was proved in this study, where it demonstrated significant higher efficacy than probiotics, essential oils and chemotherapeutic antibiotics as measured by reduction in lesion scores, elimination of bacteria, and disruption of biofilms (Ferriol). Because phages are selective to the beneficial flora, the chances of opportunistic infections or dysbiosis state related to broad-spectrum drugs (Stachurska) are minimal. Additionally, the results obtained by using phage therapy were safer compared to the conventional antibiotics and had a reduced numbers of relapses. The other is that exponential replication can also lead to inadvertent rapid liberation of bacterial endotoxins, which is also important (Peng H). Another advantage of phage therapy that was observed were the changes in immune response of the host – increase in the levels of anti-inflammatory cytokines and decrease in pro- inflammatory markers demonstrates how phage therapy may bring positive impact in terms of healing and prevention of chronic inflammation. These observations are supported by earlier reports on how phage therapy has been proved to be useful to eradicate diseases that have developed some resistance to treatment by antibiotics (Suh GA). It is also worth mentioning that the effect can be achieved not only at low concentrations of antibiotics, which may inhibit bacterial growth (Rodriguez). As with the other sorts of remedies, the efficacy of essential oils and probiotics was not comparable to phage therapy, but the facts showed that these treatments could also be effective in treating skin infections. For all their antibacterial properties, essential oils may have issues of standardization and potential for toxicity if they are not properly processed. Research should guide application of essential oils because they differ in composition thus have the potential to elicit conflicting results (Nicolas).

CONCLUSION

The outcomes of this work provide effective evidence of the safety and efficiency of the new approaches to bacteriophage treatment with a specific reference to the use of phage therapy in the treatment of antibiotic-resistant skin diseases in dogs and cats. The kind of treatment that gave the best results was the phage therapy and proved to be much more effective than probiotics, essential oils, and antibiotics in several fields such as eradication of pathogen, reduction in lesion score, biofilm disruption, and altering the inflammatory profile of the body. Due to their high specificity, bacteriophages eliminated the threat of dysbiosis and subsequent infections by selectively killing solely the pathogenic bacteria without disturbing the useful microbiota. The fact that potential adverse events are few and reinfection rates have been minimal are some of the reasons that makes phage therapy appealing besides possessing one of the safest profiles for the cure of long term illness. On the other hand, essential oils though relatively effective in killing microbes remain toxic and have the disadvantage of variability in composition and regulation. While probiotics also showed similar potential for immune modulation and balancing microbiome, they were not as effective when used singly. This is justifiable by the growing opinion of shifting away from the traditional antibiotic model due to increasing cases of antibiotic resistance. Among all the kinds of treatment that have been developed as the alternative medicines, the phage therapy, which can be added to the list of veterinary dermatological procedures, is one of the most perspective ones. The study on antibiotic resistance also reviews the concept of One Health approach recognizing that human, animals, and the environment are linked in their health and well-being. In the future, there is a need to determine further outcomes of these treatments, fine tune dosing regimens, and identify integrative and additional treatment options. Moreover, the principles of one health, detoxification, and stewardship for antimicrobials as well as the development of innovative and effective prevention in veterinarian medicine will help to prevent the emergence of antibiotic resistance and ensure the further effective control of infectious diseases in companion animals.

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