Characterization of Veterinary Medications for Dairy Farms in Tupã, Brazil: Profile and Analysis

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Caracterização de medicamentos veterinários em fazendas leiteiras de Tupã, Brasil: Perfil e análise

RESUMO

Objetivo – Este estudo teve como objetivo caracterizar o perfil do uso de medicamentos veterinários em treze fazendas leiteiras em Tupã, São Paulo.

Metodologia - Questionários estruturados foram aplicados aos produtores de leite da região de Tupã - SP, investigando os tipos de medicamentos utilizados, frequência de aplicação e possíveis desvios de dosagem.

Originalidade/relevância - O uso de medicamentos veterinários em bovinos leiteiros é uma prática comum para prevenção e tratamento de doenças. Contudo, seu uso inadequado pode causar sérios problemas à saúde pública, como a presença de resíduos no leite e o aumento da resistência microbiana.

Resultados - Os medicamentos mais frequentes foram citados a oxitetraciclina (61,5%), nitrato de prata e sulfadiazina (61,5%), ivermectina (46,2%) e ocitocina (46,2%). A maioria dos produtores utilizou medicamentos terapêuticos de forma esporádica, porém 62,5% dos que empregam oxitetraciclina relataram uso repetido ao longo do ano. Apesar da aplicação profilática de vermífugos ser comum, apenas um produtor mencionou uso excessivo de ivermectina. Esses achados reforçam a necessidade de maior controle e orientação no uso de medicamentos veterinários para assegurar a saúde do rebanho, evitar resíduos químicos no leite e prevenir o surgimento de resistência microbiana.

Contribuições sociais e ambientais - O estudo reforça a importância de boas práticas na administração de medicamentos para assegurar a sustentabilidade da produção leiteira e a segurança alimentar.

PALAVRAS-CHAVE: Medicamentos veterinários. Produção de leite. Resistência microbiana.

Characterization of Veterinary Medications for Dairy Farms in Tupã, Brazil: Profile and Analysis

ABSTRACT

Objective – This study aimed to characterize the profile of veterinary drug usage on thirteen dairy farms in Tupã, São Paulo.

Methodology - Structured questionnaires were applied to milk producers in the region of Tupã - SP, investigating the types of drugs used, frequency of application and possible dosage deviations.

Originality/relevance - The use of veterinary drugs in dairy cattle is a common practice for disease prevention and treatment. However, their inappropriate use can cause serious public health problems, such as the presence of residues in milk and increased microbial resistance.

Results - The most frequently cited drugs were oxytetracycline (61.5%), silver nitrate and sulfadiazine (61.5%), ivermectin (46.2%) and oxytocin (46.2%). Most producers used therapeutic drugs sporadically, but 62.5% of those using oxytetracycline reported a repeated use throughout the year. Although prophylactic use of dewormers is common, only one producer reported excessive use of ivermectin. These findings reinforce the need for greater control and guidance in the use of veterinary drugs to ensure herd health, avoid chemical residues in milk, and prevent the emergence of microbial resistance.

Social and environmental contributions - The study reinforces the importance of good practices in drug administration to ensure the sustainability of dairy production and food safety.

KEYWORDS: Veterinary drugs. Milk production. Microbial resistance.

Caracterización de medicamentos veterinarios en granjas lecheras de Tupã, Brasil: Perfil y análisis

RESUMEN

Objetivo – Este estudio tuvo como objetivo caracterizar el perfil de uso de medicamentos veterinarios en trece tambos de Tupã, São Paulo.

Metodología - Se aplicaron cuestionarios estructurados a productores de leche de la región de Tupã - SP, investigando los tipos de medicamentos utilizados, frecuencia de aplicación y posibles desviaciones de dosis. **Originalidad/Relevancia** - El uso de medicamentos veterinarios en el ganado lechero es una práctica común para la prevención y el tratamiento de enfermedades. Sin embargo, su uso inadecuado puede provocar graves problemas de salud pública, como la presencia de residuos en la leche y el aumento de la resistencia microbiana.

Resultados - Los medicamentos más frecuentes fueron oxitetraciclina (61,5%), nitrato de plata y sulfadiazina (61,5%), ivermectina (46,2%) y oxitocina (46,2%). La mayoría de los productores utilizaron medicamentos terapéuticos esporádicamente, pero el 62,5% de los que utilizaron oxitetraciclina informaron su uso repetido a lo largo del año. Aunque es común la aplicación profiláctica de desparasitantes, sólo un productor mencionó el uso excesivo de ivermectina. Estos hallazgos refuerzan la necesidad de un mayor control y orientación en el uso de medicamentos veterinarios para garantizar la salud del rebaño, evitar residuos químicos en la leche y prevenir la aparición de resistencia microbiana.

Contribuciones sociales y ambientales - El estudio refuerza la importancia de las buenas prácticas en la administración de medicamentos para garantizar la sostenibilidad de la producción láctea y la seguridad alimentaria.

PALABRAS CLAVE: Medicamentos veterinarios. Producción de leche. Resistencia microbiana.

RESUMO GRÁFICO
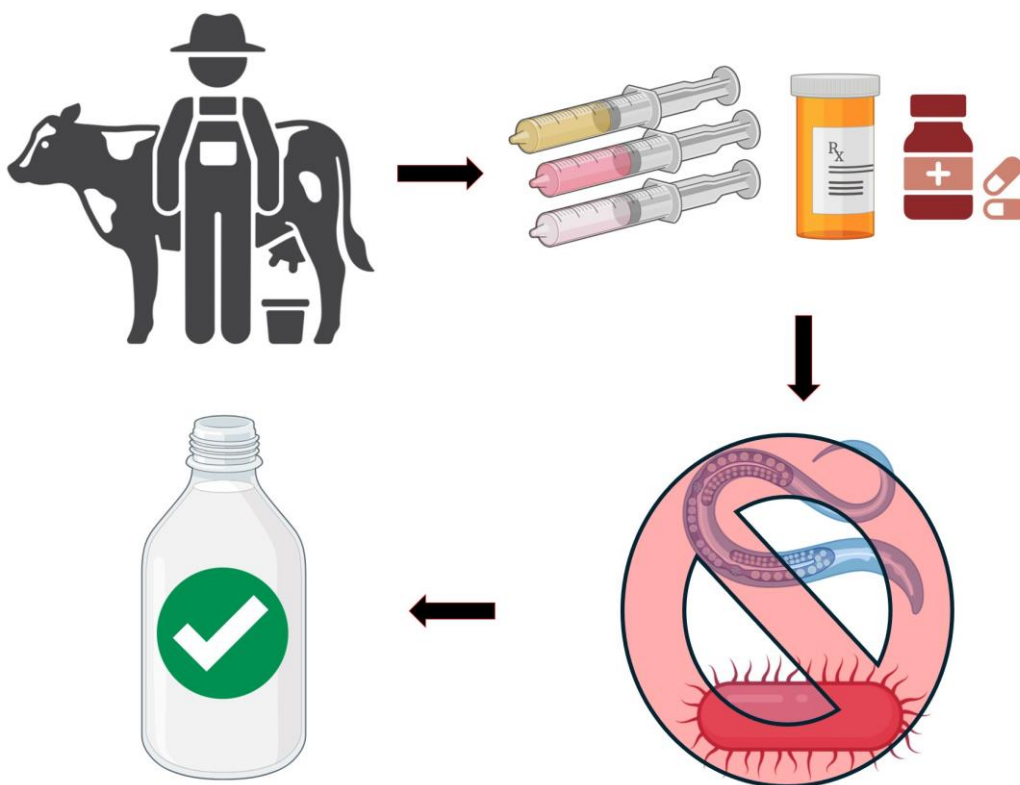
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INTRODUCTION

Brazil produced approximately 24.5 million tons of cow's milk, ranking as the sixth-largest milk producer in the world, behind the European Union, the United States, India, China, and Russia (Statista, 2023). Milk production is also one of the main sectors of the Brazilian food industry, representing 16% of net sales, surpassed only by the meat and derivatives sector (26.6%) and the cereals, teas, and coffee sector (16.9%) (ABIA, 2023). In this context, efforts have been focused on reducing animal diseases, improving dairy cattle growth, and enhancing productivity, with an emphasis on food safety.

Among many strategies adopted by dairy producers to control pathogens and increase productivity, the use of veterinary medications, such as antimicrobial and antiparasitic agents, has been widely employed (Gomes; Henriques, 2016). These substances are used both therapeutically and prophylactically, aiming to prevent and treat infections and diseases (Demirlek et al., 2021). However, the overuse of these drugs can lead to serious consequences, such as toxicity, side effects, and the emergence of antimicrobial resistance, either through intrinsic or acquired mechanisms (Rodrigues; Henriques, 2019; Käppeli et al., 2019).

Antimicrobial resistance has been a growing concern, as the emergence of resistant strains of pathogens and cross-resistance can compromise the effectiveness of traditional treatments (Farrell et al., 2021). Additionally, the presence of drug residues in milk intended for human consumption poses a risk to consumers, potentially causing adverse reactions and contributing to the selection of bacteria resistant to conventional antimicrobials (Oliver et al., 2020). The improper use of veterinary medications also leads to economic losses for dairy industries that rely on microbiological processes, as well as environmental problems (Sar et al., 2022; Sharma et al., 2018).

Therefore, the present study aims to characterize and evaluate the use of veterinary medications in dairy farms in the region of Tupã, São Paulo. The data analysis contributes to a better understanding of management practices and their impact on the dairy production chain, providing important insights for improving food safety.

METHODOLOGY

This study was conducted in three stages: (1) field research in selected dairy farms, (2) descriptive analysis of the collected data, and (3) analysis of the drug labels of the most used medications.

First, the field research began with a survey of dairy farmers in the municipality of Tupã, which was carried out in collaboration with the Kamby Extension Program (PROEC) at the Faculty of Science and Engineering, Tupã Campus, which maintains a register of producers across the region. Consequently, the producers located in the city of Tupã were contacted by phone to receive a brief introduction to the research.

The selection of farms followed specific criteria, such as: (i) geographical location within the municipality of Tupã, to ensure a representative sample of the local dairy production, and (ii) the willingness and availability of producers to participate in the study. These criteria were adopted to provide a broad view of the veterinary medication usage practices in the

region, encompassing different management and production profiles. Thirteen producers were selected to participate in the study.

During the technical visits, a structured questionnaire was administered to each producer. The questionnaire was designed to gather detailed information about the use of veterinary medications and their administration to the herd. The questions covered the following topics: (i) category of the medication—antibiotic, anti-inflammatory, antiparasitic, or others; (ii) commercial name or active ingredient; (iii) quantity or dosage administered; (iv) frequency of administration; and (v) management practices in which the medication was applied.

In the second stage, the data collected through the questionnaires were performed and they were analyzed using the software Excel and GraphPad Prism® 7.0. The descriptive analysis included categorizing the most frequently used medications, analyzing the frequency of use, and cross-referencing information on administered dosages and frequency of use by medication category.

In the third stage, to document the commercial data and compare it with the data obtained from the questionnaires, an analysis of the drug labels of the medications most commonly mentioned by the producers was conducted. The drug labels were consulted to verify the indications and recommended dosages for each substance. This analysis was then compared with the producers' responses to identify any discrepancies, such as the inappropriate use or use outside the recommended indications. The parameters evaluated included: (i) the primary therapeutic indication, (ii) the recommended dosage per kilogram of body weight or per treatment, (iii) the withdrawal time for milk after drug administration, and (iv) known contraindications and adverse effects.

This methodological approach was chosen to ensure the precision and relevance of the data collected. The in-person farm visits allowed for detailed responses to be obtained directly from the producers, as well as for observing on-site management conditions. The use of a structured questionnaire ensured that standardized information was collected from all participants, allowing for an efficient comparative analysis. The analysis of the drug labels verified the appropriateness of medication use according to official recommendations, providing a clear understanding of veterinary drug practices and their impact on animal health and food safety.

RESULTS

The producers in the Tupã region were interviewed about the use of veterinary medications on their dairy farms, and the data collected allowed for the construction of a detailed profile of the substances used, grouped by therapeutic class (Figure 1).

Figure 1 - Profile of veterinary drug application in a sample of small producers in the Tupã region. The first row illustrates, in blue bars, the total number of producers using each medication: larger bars represent a higher number of producers, while smaller bars indicate fewer producers. Highlighted in yellow are the veterinary drugs most used by producers in the region
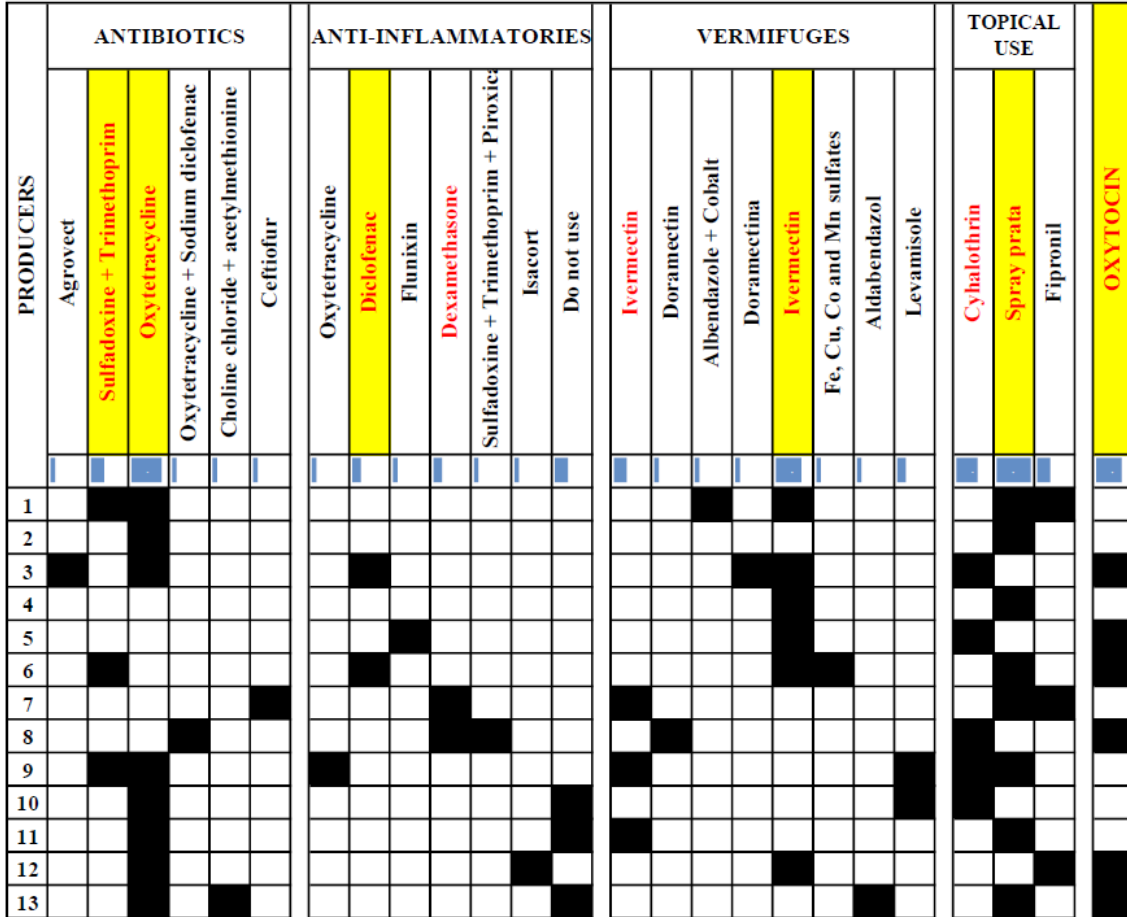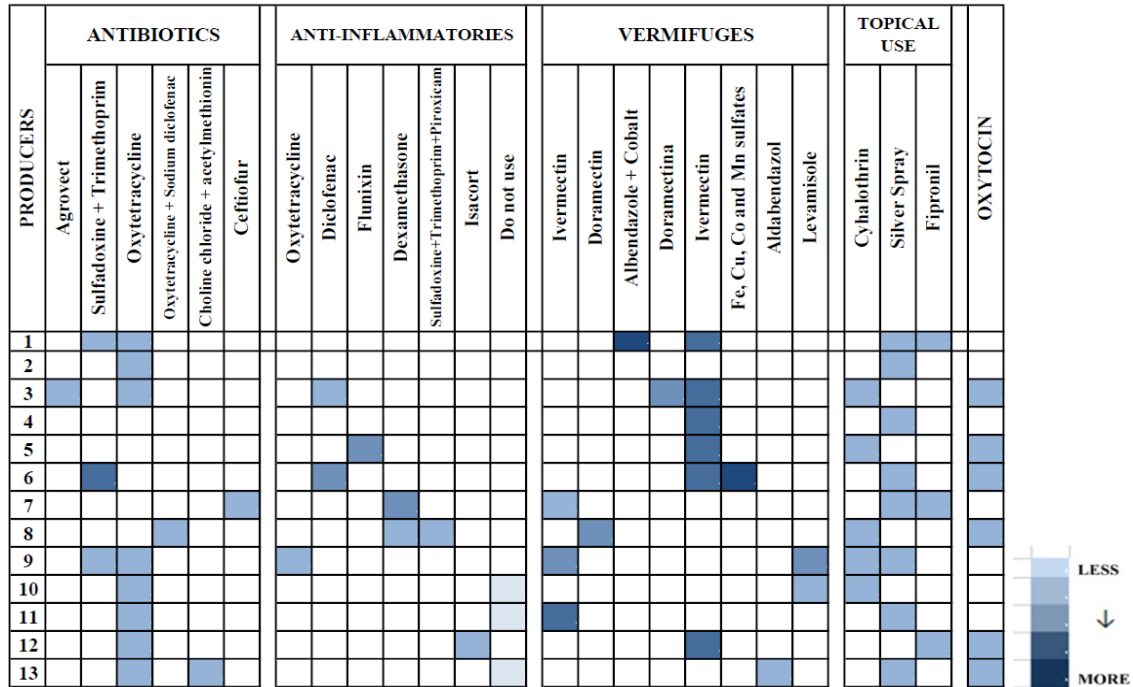

Source: Author (2024).

Antimicrobials were the most widely used class of medications among the producers. Among them, oxytetracycline and sulfadoxine with trimethoprim stood out as the most reported, with 84.6% of producers confirming their use. For anti-inflammatory drugs, diclofenac and dexamethasone were the most frequent, reported by 30% of respondents. Regarding antiparasitics, ivermectin was cited by 46.15% of the producers, while topical agents such as silver nitrate with sulfadiazine were mentioned by 61.5% of the participants.

Oxytocin was used by 46.15% of the producers, primarily to assist with calf delivery, placenta expulsion, and milk ejection during milking. Notably, many producers who use antimicrobials such as oxytetracycline or sulfadoxine with trimethoprim also reported the concomitant use of ivermectin and oxytocin, suggesting a preference for these medications as part of the overall herd care regimen.

For most of the substances, their use was described as mild, generally administered with therapeutic intent, such as treating infections, wounds, or diseases in animals. However, antiparasitic agents like ivermectin showed higher usage frequency, being applied three to four times per year, mainly for prophylactic purposes (Figure 2).

Figure 2 - Annual frequency of veterinary drug application reported by producers in the Tupã region. The frequencies are proportional to the intensity of the blue color: lighter shades represent lower drug usage, while darker shades indicate higher usage

PRODUCERS	ANTIBIOTICS						ANTI-INFLAMMATORIES							VERMIFUGES							TOPICAL USE			OXYTOCIN
	Agrovect	Sulfadoxine + Trimethoprim	Oxytetracycline	Oxytetracycline + Sodium diclofenac	Choline chloride + acetylmethionin	Ceftiofur	Oxytetracycline	Diclofenac	Flunixin	Dexamethasone	Sulfadoxine+Trimethoprim+Piroxicam	Isacort	Do not use	Ivermectin	Doramectin	Albendazole + Cobalt	Dorametina	Ivermectin	Fe, Cu, Co and Mn sulfates	Aldabendazol	Levamisole	Cyhalothrin	Silver Spray	Fipronil	OXYTOCIN
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Source: Author (2024).

These results demonstrate a common pattern of therapeutic use, where medications are employed in response to specific clinical conditions. However, the prophylactic use of antiparasitic drugs suggests concern with preventing parasitic infections, which may reflect the environmental and sanitary conditions of the analyzed properties. The high frequency of ivermectin use as an antiparasitic and oxytetracycline as an antimicrobial highlights the need for technical guidance, given the importance of adhering to dosage recommendations and withdrawal periods to prevent drug residues in milk intended for human consumption.

DISCUSSIONS

The use of oxytetracycline was reported by more than 60% of the respondents, reflecting the preference for this antimicrobial in Tupã region. Oxytetracycline is employed due to its broad spectrum of action, making it effective in treating a variety of conditions, such as endometritis, pneumonia, pododermatitis, and mastitis (Ghallab et al., 2023; Dorey et al., 2017). However, the use of this substance in dairy cows, although approved by the Food and Drug Administration (Dorey et al., 2017), must be approached with caution due to the presence of residues in milk during treatment and for 120 hours afterward, as indicated on the label.

Given the negative effects of improper veterinary medication use, strict control of its administration is imperative. The practice of administering doses higher than recommended, as observed in 62.5% of the producers who used oxytetracycline in doses exceeding 45 mL per adult bovine, presents a critical issue (Figure 3). Overdosing antimicrobials not only

compromises animal health but also contributes to the emergence of resistant bacterial strains, a growing challenge for global public health. Holman et al. (2019) demonstrated that prolonged use of this drug alters the fecal and nasopharyngeal microbiota of cattle, delaying microbiota recovery and increasing susceptibility to other pathogens. This finding, along with the overdoses reported by producers, reinforces the idea that antimicrobial use can accelerate the emergence of resistant bacteria, an issue well-documented in other studies (Farrell et al., 2021).

Figure 3 - Quantity (mL) of antibiotics administered to adult bovines by producers in Tupã region
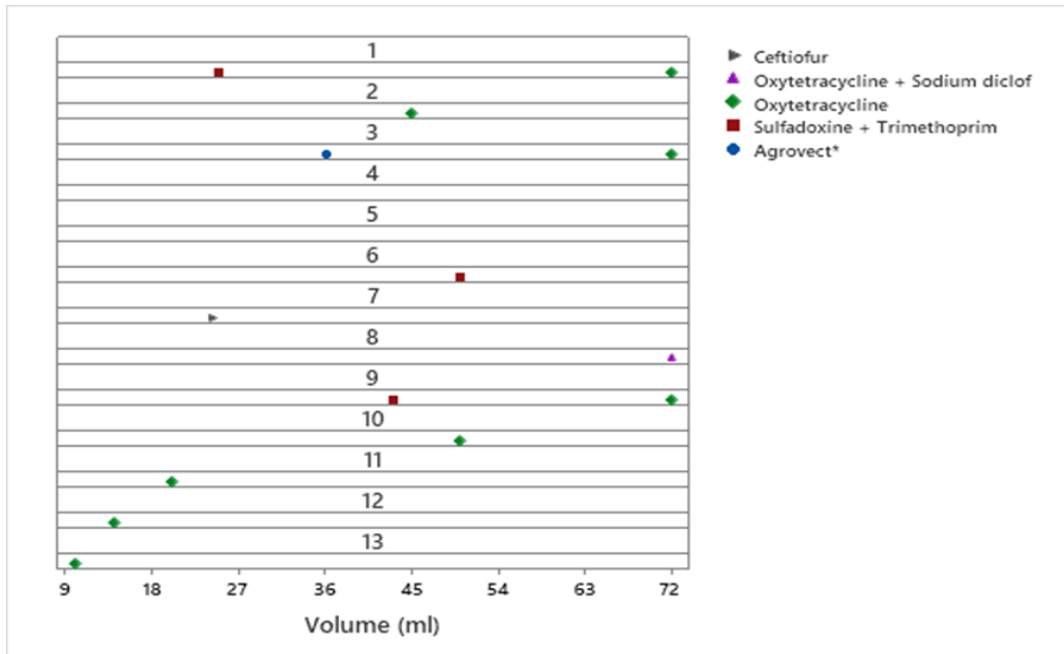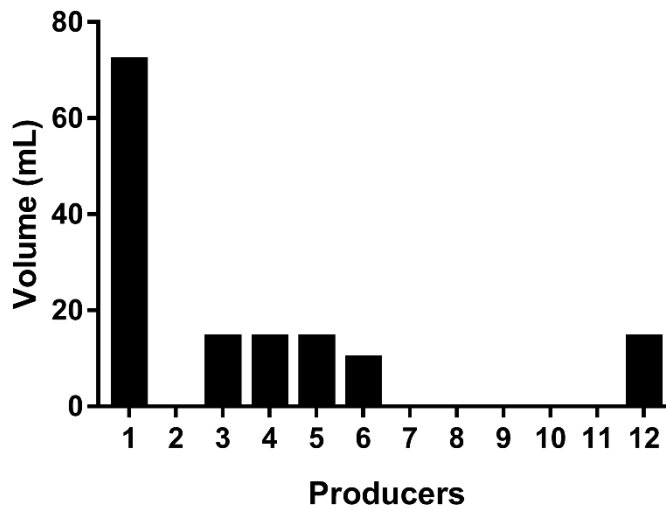

Source: Author (2024).

In contrast, the underdosing of antibiotics, also observed in a minority of cases, raises another concern. When antibiotics are administered at subtherapeutic doses, as reported in this study for oxytetracycline, the risk of bacterial resistance increases. Jun et al. (2019) demonstrated that sublethal concentrations of tetracycline, in combination with copper, induced bacterial defense responses, increasing resistance to other antimicrobials. This situation is particularly concerning in a context where controlling antimicrobial resistance is already a growing challenge.

Another aspect is the prophylactic use of antiparasitic medicines, particularly ivermectin, which was used at inappropriate doses by many producers (Figure 4). Although effective in parasite control, the underdosing of ivermectin observed may reduce treatment efficacy and allow the survival of resistant parasites, as highlighted by Laing et al. (2022) in their study on ivermectin-resistant parasites in livestock. The continuous use of subtherapeutic doses, in addition to being economically detrimental, can create parasitic infestation cycles, leading to significant productivity losses. This is particularly relevant in tropical regions where parasitic infestations are more frequent due to climatic conditions (Nicolas et al., 2021).

Figure 4 - Quantity (mL) of Ivermectin administered to adult bovines by producers in Tupã region

Source: Author (2024).

Furthermore, the economic implications of these inadequate medication administration practices are extensive. Excessive or inappropriate use of medications results not only in unnecessary costs but also in productivity losses, whether due to poorly controlled diseases or the need to discard milk contaminated with residues. Comparatively, farms in European regions that follow strict medication protocols optimize productivity, reduce treatment costs, and minimize drug residues in milk. In contrast, in Latin America, the lack of regulatory oversight and technical guidance remains a limiting factor (Sharma et al., 2018).

CONCLUSIONS

This study investigated the use of veterinary medications in dairy farms in the Tupã region, São Paulo, identifying frequent practices of improper administration, particularly concerning oxytetracycline and ivermectin. The results showed that many producers used doses higher or lower than recommended, which can pose serious risks to public health and food safety, as well as contribute to the emergence of microbial resistance in herds.

Given these findings, it is recommended that public policies be implemented to provide technical training for producers in the Tupã region. Rural extension programs and practical courses can be implemented, focusing on the correct use of medications, as well as the calculation of dosages and adherence to drug withdrawal periods.

Finally, this study highlights the importance of future research on the impact of microbial resistance in dairy farming, as well as on the economic effects of improper management practices. Conducting studies that track the evolution of antimicrobial resistance and the effectiveness of training programs will be crucial in guiding more effective and sustainable management strategies, ensuring herd health, consumer safety, and the competitiveness of the Brazilian dairy sector.

BIBLIOGRAPHICAL REFERENCES

ABIA – Associação Brasileira das Indústrias de Alimentação. **Relatório Anual 2023**. Disponível em: https://www.abia.org.br/vsn/temp/z2023417RelatorioAnual2023interativoFINAL.pdf. Acesso em: 8 out. 2024.

BRENTNALL, C. et al. Pharmacodynamics of oxytetracycline administered alone and in combination with carprofen in calves. **Veterinary Record**, v. 171, p. 273–277, 2012. DOI: 10.1136/vr.100935. Disponível em: https://pubmed.ncbi.nlm.nih.gov/22843613/. Acesso em: 09 out 2024.

DEMIRLEK, T. et al. Efficacy of inactivated *Parapoxvirus ovis* paraimmune activator as a prophylaxis against mastitis and therapy for subclinical mastitis in dairy cattle. **Veterinary Research Forum**, v. 12, n. 4, p. 421-427, 2021. DOI: 10.30466/vrf.2019.110810.2628. Disponível em: https://pub-med.ncbi.nlm.nih.gov/35529817/. Acesso em: 09 out 2024.

DOREY, L. et al. Pharmacokinetic/pharmacodynamic integration and modelling of oxytetracycline for the porcine pneumonia pathogens *Actinobacillus pleuropneumoniae* and *Pasteurella multocida*. **Journal of Veterinary Pharmacology and Therapeutics**, v. 40, p. 505–516, 2017. DOI: 10.1111/jvp.12385. Disponível em: https://pubmed.ncbi.nlm.nih.gov/28090673/. Acesso em: 09 out 2024.

FARRELL, S. et al. Understanding farmers' and veterinarians' behavior in relation to antimicrobial use and resistance in dairy cattle: A systematic review. **Journal of Dairy Science**, v. 104, n. 4, p. 4584-4603, 2021. DOI: 10.3168/jds.2020-19614. Disponível em: https://pubmed.ncbi.nlm.nih.gov/33612225/. Acesso em: 19 out 2024.

GHALLAB, R.S. et al. Efficiency of conventional and nanoparticle oxytetracycline in treatment of clinical endometritis in postpartum dairy cows. **Tropical Animal Health and Production**, v. 55, n. 2, p. 118, 2023. DOI: 10.1007/s11250-023-03536-0. Disponível em: https://link.springer.com/article/10.1007/s11250-023-03536-0. Acesso em: 14 nov 2024.

GOMES, F.; HENRIQUES, M. Control of Bovine Mastitis: Old and Recent Therapeutic Approaches. **Current Microbiology**, v. 72, n. 4, p. 377–382, 2016. DOI: 10.1007/s00284-015-0958-8. Disponível em: https://pubmed.ncbi.nlm.nih.gov/26687332/. Acesso em: 13 nov 2024.

GRAPHPAD SOFTWARE. GraphPad Prism®, versão 7.0; San Diego, Estados Unidos, 2017.

HOLMAN, D.B. et al. Antibiotic treatment in feedlot cattle: A longitudinal study of the effect of oxytetracycline and tulathromycin on the fecal and nasopharyngeal microbiota. **Microbiome**, v. 7, n. 1, p. 86, 2019. DOI: 10.1186/s40168-019-0696-4. Disponível em: https://pubmed.ncbi.nlm.nih.gov/31167657/. Acesso em: 13 nov 2024.

JUN, H. et al. Effects of sub-lethal concentrations of copper ammonium acetate, pyrethrins and atrazine on the response of *Escherichia coli* to antibiotics. **F1000Research**, v. 8, p. 32, 2019. DOI: 10.12688/f1000research.17652.1. Disponível em: https://f1000research.com/articles/8-32. Acesso em: 08 out 2024.

KÄPPELI, N. et al. *Staphylococcus aureus* related to bovine mastitis in Switzerland: Clonal diversity, virulence gene profiles, and antimicrobial resistance of isolates collected throughout 2017. **Journal of Dairy Science**, v. 102, n. 4, p. 3274–3281, 2019. DOI: 10.3168/jds.2018-15317. Disponível em: https://pub-med.ncbi.nlm.nih.gov/30799111/. Acesso em: 14 out 2024.

LAING, R. et al. Transcriptomic analyses implicate neuronal plasticity and chloride homeostasis in ivermectin resistance and response to treatment in a parasitic nematode. **PLoS Pathogens**, v. 18, n. 6, p.

e1010545, 2022. DOI: 10.1371/journal.ppat.1010545. Disponível em: https://journals.plos.org/plos-pathogens/article?id=10.1371/journal.ppat.1010545. Acesso em: 13 nov 2024.

NICOLAS, P. et al. Potential metabolic resistance mechanisms to ivermectin in *Anopheles gambiae*: A synergist bioassay study. **Parasites & Vectors**, v. 14, n. 1, p. 172, 2021. DOI: 10.1186/s13071-021-04675-9. Disponível em: https://parasitesandvectors.biomedcentral.com/articles/10.1186/s13071-021-04675-9. Acesso em: 14 out 2024.

OLIVER, J.P. et al. Invited review: Fate of antibiotic residues, antibiotic-resistant bacteria, and antibiotic resistance genes in US dairy manure management systems. **Journal of Dairy Science**, v. 103, n. 2, p. 1051-1071, 2020. DOI: 10.3168/jds.2019-16778. Disponível em: https://pub-med.ncbi.nlm.nih.gov/31837779/. Acesso em: 14 nov 2024.

RODRIGUES, C.; HENRIQUES, M. *Candida* sp. Infections in Patients with Diabetes Mellitus. **Journal of Clinical Medicine**, v. 8, n. 1, p. 76, 2019. DOI: 10.3390/jcm8010076. Disponível em: https://www.mdpi.com/2077-0383/8/1/76. Acesso em: 14 nov 2024.

SAR, T. et al. Potential utilization of dairy industries by-products and wastes through microbial processes: A critical review. **Science of the Total Environment**, v. 810, p. 152253, 2022. DOI: 10.1016/j.scitotenv.2021.152253. Disponível em: https://www.sciencedirect.com/science/article/pii/S0048969721073290. Acesso em: 13 nov 2024.

SHARMA, C. et al. Antimicrobial Resistance: Its Surveillance, Impact, and Alternative Management Strategies in Dairy Animals. **Frontiers in Veterinary Science**, v. 4, p. 237, 2018. DOI: 10.3389/fvets.2017.00237. Disponível em: https://www.frontiersin.org/journals/veterinary-science/articles/10.3389/fvets.2017.00237/full. Acesso em: 13 nov 2024.

STATISTA. **Major producers of cow milk worldwide in 2023, by country**. Disponível em: https://www.statista.com/statistics/268191/cow-milk-production-worldwide-top-producers/. Acesso em: 8 out. 2024.