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REVIEWER'S REPORT

Manuscript No.: IJAR-55444

Title: Drug Repurposing: New Antimicrobial Applications of Non?Antibiotic Drugs in Veterinary Medicine

Recommendation:
Accept as it is .....
Accept after minor revision.....x.....
Accept after major revision .....
Do not accept (*Reasons below*) .....

Rating	Excel.	Good	Fair	Poor
Originality	x			
Techn. Quality	x			
Clarity		x		
Significance		x		

Reviewer Name: Dr. Mohammad Nadeem Khan

Detailed Reviewer's Report

1. Overall Assessment

This manuscript presents a comprehensive, well-structured, and timely systematic review addressing the emerging role of non-antibiotic drug repurposing as antimicrobial agents in veterinary medicine. The topic is highly relevant in the context of antimicrobial resistance (AMR) and aligns well with the One Health framework. The authors demonstrate strong command over the literature and provide a balanced synthesis of mechanistic, experimental, and translational evidence.

2. Novelty and Significance

- The manuscript offers novel integrative value by consolidating dispersed evidence on NSAIDs, antiparasitics, anticancer, psychotropic, and metal-based drugs as antimicrobial or antibiotic-sparing agents in veterinary contexts.
- Inclusion of clinically relevant case evidence (e.g., gallium maltolate in foal pneumonia) strengthens translational relevance.
- The review fills a clear gap in veterinary-focused repurposing literature, which is often overshadowed by human medicine studies.

3. Methodology

- The review follows PRISMA 2020 guidelines, with clear inclusion/exclusion criteria.
- Databases searched (PubMed, Web of Science, Scopus) and timeframe (2015–2025) are appropriate.
- Data extraction and thematic synthesis are logical and reproducible.

Suggestion:

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- Consider adding a PRISMA flow diagram (even as supplementary material) to visually enhance methodological transparency.

4. Content Quality and Scientific Accuracy

Strengths

- Mechanistic explanations are accurate and well-supported (membrane disruption, efflux pump inhibition, redox imbalance, iron mimicry).
- Balanced discussion of Gram-positive vs Gram-negative limitations.
- Appropriate emphasis on antibiotic synergy and adjuvant roles, rather than over-claiming monotherapy potential.
- Clear articulation of regulatory, residue, and food-safety challenges in veterinary deployment.

Minor Issues

- Some sections (e.g., psychotropic drugs) could benefit from clearer clinical prioritization (companion vs food animals).
- A concise summary table mapping drug class → target pathogen → mechanism → veterinary relevance would improve readability.

5. Organization and Clarity

- The manuscript is well organized, with logical flow from introduction to conclusions.
- Language is clear, academic, and appropriate for an international audience.
- Headings and subheadings are informative and consistent.

6. Ethical, Regulatory, and One Health Perspective

- The authors appropriately address:
  - Antibiotic stewardship
  - Zoonotic risk
  - Environmental and residue concerns
- The One Health framing is well integrated, not superficial.

This is a notable strength of the manuscript.

7. References

- References are current, relevant, and well-cited, with strong reliance on high-impact journals.
- DOI inclusion is appropriate.
- Citation style is consistent.

8. Specific Recommendations for Improvement

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1. Add a schematic or summary table highlighting key repurposed drug classes and mechanisms.
2. Include a PRISMA flow diagram (recommended).
3. Slightly condense overlapping mechanistic explanations across sections.
4. Clarify regulatory feasibility differences between food-producing vs companion animals in the Discussion.