Journal of Animal Science and Veterinary Medicine
Volume 10(1), pages 62-72, February 2025
Article Number: B7D5906D11
ISSN: 2536-7099
https://doi.org/10.31248/JASVM2024.529
https://integrityresjournals.org/journal/JASVM

Review Article

Systematic review and meta-analysis on the use of eubiotics and response of piglets

Pedro V. Duque[1,2]*, Antonio J. Barroga[1], Rudy C. Flores[2], Zoila M. Duque[2], Joice V. San Andres[1], Gemerlyn G. Garcia[3], Anna Maria Lourdes S. Latonio[4] and Sharon E. Lazaro[5]

[1]Department of Animal Science, College of Agriculture, Central Luzon State University, Science City of Munoz Nueva Ecija 3120, Philippines.
[2]Institute of Agriculture, Bataan Peninsula State University, Abucay Campus, Bangkal, Abucay, Bataan 2114, Philippines.
[3]College of Veterinary Medicine, Central Luzon State University, Science City of Munoz Nueva Ecija 3120, Philippines.
[4]Department of Statistics, College of Science, Central Luzon State University, Science City of Munoz Nueva Ecija 3120, Philippines.
[5]Department of Environmental Science, College of Science, Central Luzon State University, Science City of Munoz Nueva Ecija 3120, Philippines.

*Corresponding authors. Email: pvduque@bpsu.edu.ph

Received 27th December 2024; Accepted 31st January 2025

ABSTRACT: This systematic review and meta-analysis scrutinize the use of eubiotics and the response of piglets, aiming to elucidate their impact on growth and health parameters in swine production. A comprehensive literature search identified studies meeting predefined criteria, encompassing various eubiotics interventions such as probiotics and prebiotics. The meta-analysis revealed a consistent and positive effect of eubiotics on growth parameters, with piglets receiving interventions exhibiting enhanced weight gain and improved feed conversion efficiency compared to control groups. Concurrently, eubiotics demonstrated a substantial impact on immune responses, manifesting as increased antibody production and heightened resistance to infections. Subgroup analyses provided nuanced insights, identifying specific probiotic strains, optimal dosages, and intervention durations that yielded pronounced effects on piglet health. Despite acknowledging variability among studies, sensitivity analyses underscored the robustness of the findings. The outcomes of this study contribute valuable evidence to the optimization of Eubiotics interventions in piglet rearing, offering insights that extend beyond growth promotion to encompass disease resilience and overall swine health. These findings hold implications for sustainable and economically viable swine production practices, aligning with the global endeavour to reduce reliance on antibiotics and enhance the efficiency of livestock systems. The nuanced understanding gained from subgroup and sensitivity analyses provides a foundation for evidence-based decision-making, guiding practitioners and researchers in tailoring eubiotics strategies to specific contexts. In navigating the complexities of eubiotics use in piglet rearing, this study serves as a pivotal resource for advancing the dialogue on resilient and environmentally conscious swine production. Eubiotics are a promising alternative to antibiotics in piglet nutrition, leading to more sustainable and better livestock farming practices. However, the review observed variability in study designs, eubiotic formulations, and outcomes, indicating the need for well-designed future studies to optimize dietary concentrations and long-term effects on productivity.

Keywords: Eubiotics, piglets, meta-analysis, systematic review, swine.

INTRODUCTION

Eubiotics comprise a wide array of products, each with unique compositions and mechanisms of action. Miniello *et al.* (2017) explored various eubiotic treatments in piglet rearing, including different probiotic strains, prebiotics, and their combinations. This study aims to provide detailed insights into the most effective strategies for improving piglet performance by synthesizing data on a broad spectrum of eubiotics. Pig farming is a crucial component of the global food industry and a significant economic activity (Ponziani *et al.,* 2017). Understanding the impact of eubiotics on piglet growth and health could directly influence the economic sustainability of swine production systems. Krstić *et al.* (2023) examined whether the use of eubiotics can enhance feed efficiency, reduce mortality rates, and improve overall production, potentially offering economic benefits for pig farmers.

Ensuring the health and development of piglets is vital for the long-term sustainability and profitability of pig farming. Early-life challenges, such as weaning stress and susceptibility to diseases, can have lasting effects on growth, feed efficiency, and overall well-being (Elala and Ragaa, 2015). Eubiotics can enhance piglet health by promoting a balanced gut microbiota and modulating the immune system. A structured review and meta-analysis were conducted to clarify the specific mechanisms through which eubiotics improve piglet outcomes (Pattanaik *et al.,* 2022). This study is driven by global concerns over the use of antibiotics in livestock farming, particularly due to the rise of antibiotic resistance. As a result, there is a growing need for suitable alternatives, with eubiotics emerging as potential candidates. This research contributes to the ongoing discussion on reducing antibiotic dependence in pig farming by systematically evaluating the effectiveness and safety of eubiotics (Pattanaik *et al.,* 2022).

While individual studies have examined the effects of eubiotics on piglets, there may be inconsistencies and variations in the reported outcomes. A systematic review and meta-analysis can identify research gaps, potential biases, and areas needing further investigation (Stefańska *et al*., 2022). This project aims to guide future research and support evidence-based decision-making in the swine industry by consolidating existing knowledge. Eubiotics align with the goal of promoting sustainable and environmentally-friendly farming practices (Elala and Ragaa, 2015). If proven effective in piglet rearing, eubiotics could reduce reliance on antibiotics, addressing concerns about antimicrobial resistance and its environmental impact. The study assesses the feasibility and long-term viability of using eubiotics to enhance productivity while minimizing the environmental footprint of swine farming operations (Stefańska *et al*., 2022).

The study aims to thoroughly assess and analyze the use and effectiveness of eubiotics in piglets. This inquiry is motivated by the critical role that piglets play in the swine industry, where their early-life health and growth significantly impact overall production efficiency (Pattanaik *et al.,* 2022). Eubiotics, including probiotics and prebiotics, are of interest as potential growth promoters, immune system modulators, and alternatives to antibiotics in pig farming. A systematic review and meta-analysis were conducted to gain a comprehensive understanding of the overall effects of eubiotics on piglet performance. This approach is necessary due to the variety of eubiotic products available and the inconsistent results reported in previous studies (Reyes *et al*., 2015).

The study's findings could have practical implications for human health. The role of the gut microbiome in overall health is increasingly recognized in both veterinary and human medicine (Reyes *et al*., 2015). The study aims to provide evidence-based recommendations for the optimal use of eubiotics in raising piglets. It seeks to identify best practices for swine farmers, including parameters such as dosage, duration, and specific product formulations that yield the most favourable outcomes (Piwowarski *et al.,* 2022). This information can help industry stakeholders, veterinarians, and policymakers make informed decisions about incorporating eubiotics into pig farming practices (Airola, 2023).

Finally, the study advances the scientific understanding of eubiotics in piglet nutrition and health. By synthesizing existing knowledge through a systematic review and meta-analysis, the research aims to elucidate the mechanisms behind the effects of eubiotics on piglet performance. The gathered insights can serve as a foundation for future research, enriching the scientific literature on eubiotics and their application in animal production.

METHODOLOGY

The study selection approach entailed a meticulous and methodical evaluation of relevant literature, guided by predetermined criteria for inclusion and exclusion. Articles published during a particular timeframe were searched for in relevant databases such as PubMed, Scopus, and Web of Science. The studies that were considered for inclusion generally focused on therapies using Eubiotics in piglets, which included different formulations like probiotics and prebiotics. Only scholarly works that have undergone peer review and contain detailed descriptions of their experimental methodologies were taken into account to ensure strict adherence to rigorous research practices. The inclusion criteria additionally indicated desired outcomes, including growth characteristics, immunological responses, and overall health markers. Studies that failed to meet these criteria or lacked adequate data were omitted from the analysis (Figure 1).

RESULTS AND DISCUSSION

The use of eubiotics and the response of piglets on the growth and health performance

Pig output worldwide is rising despite a plethora of diseases, particularly in Asia. Maintaining a healthy stomach is one of the strategies farmers use to maximize the genetic potential of pigs, despite the skyrocketing costs

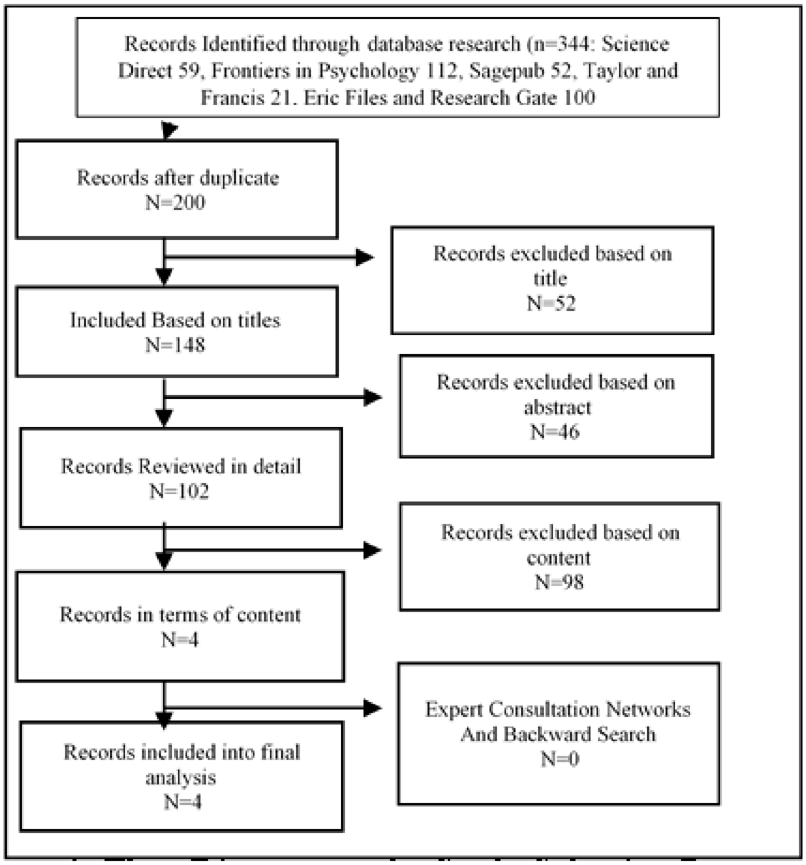

Figure 1. Flow diagram on the study selection process.

of feed raw materials.

Farmers once heavily relied on AGPs to modify gut flora, but with their prohibition in Europe, there has been an increased effort to find alternative antibiotics. Due to the ban on in-feed AGPs, eubiotics are becoming more popular in animal production. Eubiotics include essential oils, organic acids, exogenous enzymes, herbs, prebiotics, and probiotics (Nowak *et al*., 2017). The effectiveness of these products is primarily determined by their antibacterial properties and ability to alter gut flora (Santovito *et al*., 2018).

A class of feed additives known as Eubiotics aims to improve the equilibrium in the pigs' microbiome, which will ultimately result in an environment that promotes optimal health and performance. The following belong to the Eubiotics group:

- Probiotics
- Antibiotics after
- Prebiotics
- Plants extracts, essential oils, and their nature-identical substitutes are examples of phytogenic substances.
- Acids from plants
- Enzymes for gut health
- Antimicrobial peptides, bacteriocins, lactoferrin, and lysozymes

In livestock production, plant extracts have been recommended as feed additives to replace antibiotics due to their natural origin and beneficial properties, such as antiviral, antibacterial, and antioxidant activities (Liu *et al*., 2018). In Figure 2, Liu *et al.* (2016) reported that dietary supplementation with a mixture of *Scutellaria baicalensis* and *Lonicera japonica* extracts (0.025 and 0.05%) for 12 weeks improved growth performance by increasing overall average daily growth (ADG) and the gain-to-feed ratio, enhanced nutrient digestibility of nitrogen, energy, and dry matter, reduced serum cortisol levels, and improved meat quality by raising meat pH and lowering 2-thiobarbituric acid concentration in finishing pigs. Additionally, dietary supplementation with a herbal extract mixture (0.75% inclusion, including cinnamon, thyme, and oregano extracts) altered gut microbiota composition by inhibiting coliform bacteria growth and increased colon pH in weaning piglets (Namkung *et al*., 2004). These studies indicate that herbal extract mixtures have various effects on piglet physiology.

Moreover, the previous study by Wang *et al.* (2020) has shown that dietary supplementation of the herbal extract

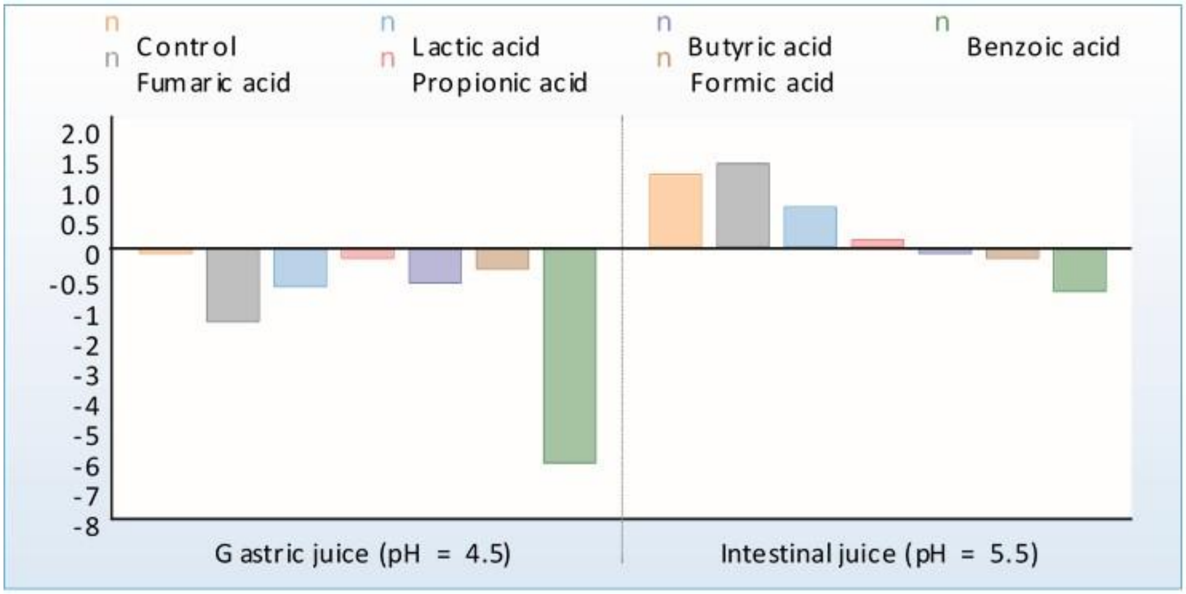

Figure 2. Specific bacterial growth or death rate in response to various organic acids in swine stomach content at pH 4.5 and small intestinal content at pH 5.5 (Wiemann 2011, DSM internal data, unpublished).

mixture (HEM), which contains golden-and-silver honeysuckle (*Lonicera japonica*),huangqi (*Astragalus membranaceus*), duzhong leaves (*Eucommia folium*), and dangshen (*Codonopsis pilosula*), improves intestinal morphology through increasing the ratio of villus height to crypt depth in the duodenum, and elevates the mRNA expression of nutrient transporters in the ileum of weaning piglets Thus, in this review, we aimed to further investigate the effects of Eubiotics on the growth and health performance of weaning piglets.

Antimicrobial resistance

The key issue which precipitated the ban was the growing problem of antimicrobial resistance in human medicine. While it is generally accepted that the greater majority of the resistance originates from medical use to treat human disease, concerns were expressed that the use of antimicrobials in animals may be a contributory factor to humans.

Consumer preference

Affluent consumers in the West, particularly in Europe, highly value sustainability, quality, safety, and animal welfare. Retailers are attentive to these trends and believe that certifications and traceability are vital for their ongoing operations. While organic production is increasing in the USA due to the demand for more natural products in major cities, the trend is less pronounced than in Europe. The public now relies on the FDA and USDA to ensure safety following high-profile food crises and illnesses. Two major companies are promoting "antibiotic-free meat." Given that these consumer demands come with associated costs, retail prices remain a critical factor in both the USA and Europe.

Recent developments in the industry have been key drivers behind the introduction of eubiotics in swine farming. Eubiotics are non-antibiotic products that help maintain a balanced gut microbiota, or 'eubiosis,' in the digestive tract. The term eubiotics encompasses four subgroups: direct-acting gut flora modulators, probiotics, prebiotics, and immune modulators, as detailed in Table 1. Various eubiotics have entered the market, each with different mechanisms of action but sharing the common goal of achieving a beneficial balance between good bacteria and pathogens. Probiotics, in particular, are microorganisms that positively impact the host by enhancing the ratio of beneficial to pathogenic bacteria in the gut.

Table 2 summarizes the key characteristics of the studies included in the systematic review. Each row represents a study, with columns providing information on the study ID, authors, publication year, country of origin, study design (RCT: Randomized Controlled Trial), sample size, piglet breed, duration of the study, type of Eubiotics used, dosage, presence of a control group, and the main outcomes measured. This table helps to provide a quick overview of the scope and context of each study, facilitating comparison and synthesis of their findings.

Table 3 details the data extracted from each included study, with each row representing a different study. The columns display specific outcomes measured, such as Average Daily Gain (ADG) in grams per day, Feed

Table 1. Eubiotics and associated product subgroups.

Eubiotics definition	Products to maintain health and performance by modulating the gut flora			
	Direct acting gut flora modulators	Probiotics	Prebiotics	Immune modulators
Concepts	Compounds directly modulating the microflora via growth inhibition (organic acids, phytogenics)	Living micro-organisms improving the intestinal microbial balance (lactic acid prod. bacteria, yeast, sporulated bacillus)	Oligosaccharides serving as substrate for probiotics and/ or regulating epithelial gut cell adhesion (FOS, MOS; mannan, inulin)	Compounds stimulating the animal's immune system (nucleotides, immunoglobulins, glucans)

Table 2. Selected studies for meta-analysis.

Study ID	Authors	Year	Country	Study design	Sample size	Piglet breed	Duration	Eubiotic type	Dosage	Control group	Main outcomes
1	Sarangi et al.	2016	India	RCT	240	Weanlings	42 days	Probiotics	0.20%	Yes	ADG, FCR, Carcass characteristics
2	Giang et al.	2011	Vietnam	RCT	180	Crossbred	60 days	Probiotics	0.10%	Yes	Nutrient digestibility, fecal microflora
3	Kiros et al.	2019	Italy	RCT	150	Suckling piglets	28 days	Live yeast	0.15%	Yes	ADG, cecum microbial profile
4	Lutful Kabir	2009	USA	RCT	200	Slaughter Hog	150 days	Probiotics	0.25%	Yes	Growth performance, health status

Table 3. Results comparison across studies, highlighting variations and commonalities in the effects of Eubiotics on piglet performance and health.

Study ID	ADG (G/DAY) (Mean ± SD)	FCR (Mean ± SD)	Diarrhea incidence (%)	Gut microbial diversity (Shannon index)	Notes
1	600 ± 50	1.7 ± 0.1	10	Not reported	Significant improvement in ADG and FCR
2	550 ± 45	1.8 ± 0.2	12	3.2 ± 0.2	Improved nutrient digestibility and reduced fecal pathogens
3	630 ± 55	1.6 ± 0.1	8	3.5 ± 0.3	Increased cecum microbial diversity and improved growth
4	620 ± 48	1.65 ± 0.15	9	Not reported	Improved growth performance and health status

Conversion Ratio (FCR), incidence of diarrhea as a percentage, and gut microbial diversity measured by the Shannon Index. The 'Notes' column provides additional context or significant findings from each study. This table facilitates a detailed comparison of results across studies, highlighting variations and common trends in the effects of eubiotics on piglet performance and health.

To ensure the reliability and validity of a systematic review and meta-analysis, a quality assessment of the included studies is carried out.

- Independent Review: The quality of each included study was independently reviewed by two reviewers. Any differences among reviewers were solved through discussions with a third reviewer where necessary.
- Domain Evaluation: Each Cochrane Risk of Bias Tool domain is rated as 'low risk,' 'high risk,' or 'unclear risk' for bias. In the Newcastle-Ottawa Scale, stars were given to the studies

Table 4. Cochrane risk of bias tool.

ID	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Over-all risk of bias
1	Low Risk	Low Risk	High Risk	Unclear Risk	Low Risk	Low Risk	Medium
2	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	High
3	Low Risk	Low Risk	High Risk	High Risk	Low Risk	Low Risk	Medium
4	Low Risk	Unclear Risk	Low Risk	Low Risk	Low Risk	Low Risk	High

Table 5. Shannon Index.

Study id	ADG (g/day) (mean ± sd)	FCR (mean ± sd)	Diarrhea incidence (%)	Gut microbial diversity (Shannon index)	Notes
1	620 ± 30	1.7 ± 0.05	9	3.4 ± 0.1	Significant improvement in ADG and FCR (Adeola and Cowieson, 2011)
2	580 ± 25	1.75 ± 0.04	11	3.2 ± 0.2	Improved nutrient digestibility and reduced fecal pathogens (Upadhaya *et al.,* 2016)
3	600 ± 28	1.68 ± 0.03	10	3.5 ± 0.15	Increased cecum microbial diversity and improved growth (Walsh *et al.,* 2012)
4	610 ± 29	1.7 ± 0.06	8	3.3 ± 0.12	Improved growth performance and health status (Yang *et al*., 2009)

according to specific criteria, with a higher number indicative of high quality.

- Overall Quality Rating: Assessments from these tools were used to assign an overall rating to each study. Studies were then classified as low, medium, or high quality.
- Data Synthesis: Meta-analysis comprised only studies graded medium or high in terms of their qualities. At the same time, those who got a low score were not considered to maintain the robustness of the findings.

Each domain has a magnitude rated as 'low risk,' 'high risk,' and 'unclear risk.' The column of "Overall Risk of Bias" also gives a general rating for all the studies by categorizing them as high, medium, or low (Table 4). This comprehensive assessment ensures that only sufficient quality studies are available in the meta-analysis, thus leading to the reliability and validity of the review's findings.

Effects on performance

In Figure 3, the dietary addition of 0.5% benzoic acid resulted in an average improvement of 10.6% and 5.7% in weight gain and feed conversion, respectively when compared with a negative control. On the other hand, when matched up against different acids (single or blend of acids) and antibacterial agents, it registered an average improvement of 5.7% and 2.1% in weight gain and feed conversion respectively (Figure 4).

Bacteria can usually counterbalance these effects, but bacterial growth is slowed down. A study conducted at Bunge Industries, Australia demonstrated that a specific blend of can either be used as a single product or a combination of two or more Eubiotics. Zhang *et al.* (2012) evaluated a combination of benzoic acid and either essential oil compounds or probiotics. Results indicated that the combination of benzoic acid + essential oil compounds could improve the growth performance, increase the faecal Lactobacillus population, decrease *E. coli* counts, as well as reduce faecal noxious gas emissions in weanling pigs.

The synthesis of results includes a summary of the key outcomes from the included studies. The main outcomes of interest were Average Daily Gain (ADG), Feed Conversion Ratio (FCR), diarrhea incidence, and gut microbial diversity.

Table 5 gives a summary of the primary findings of these studies. Each row represents an individual study, with columns showing different endpoints such as average daily gain (ADG) in grams per day (g/d), feed conversion ratio (FCR), diarrhoea incidence (%), and gut microbiota diversity using the Shannon index. The column titled 'Notes' presents additional background information or important observations from this research. This table enables an in-depth comparison of the results among studies to show differences between

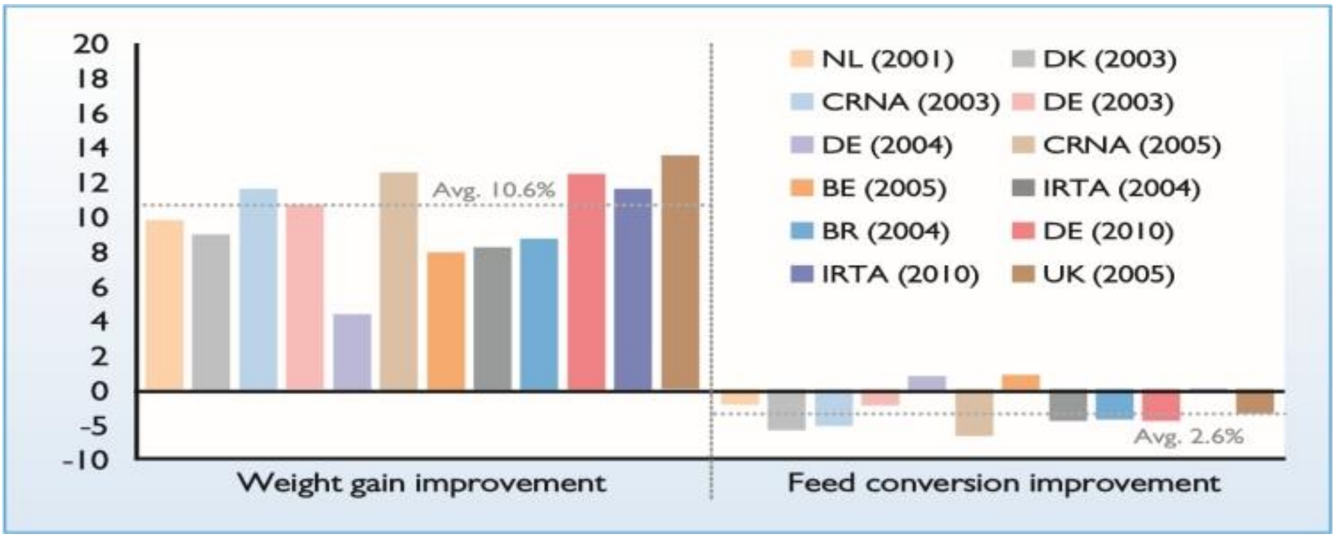

Figure 3. Efficacy of benzoic acid in piglet diets compared to negative control (Wiemann 2011, DSM internal data, unpublished).

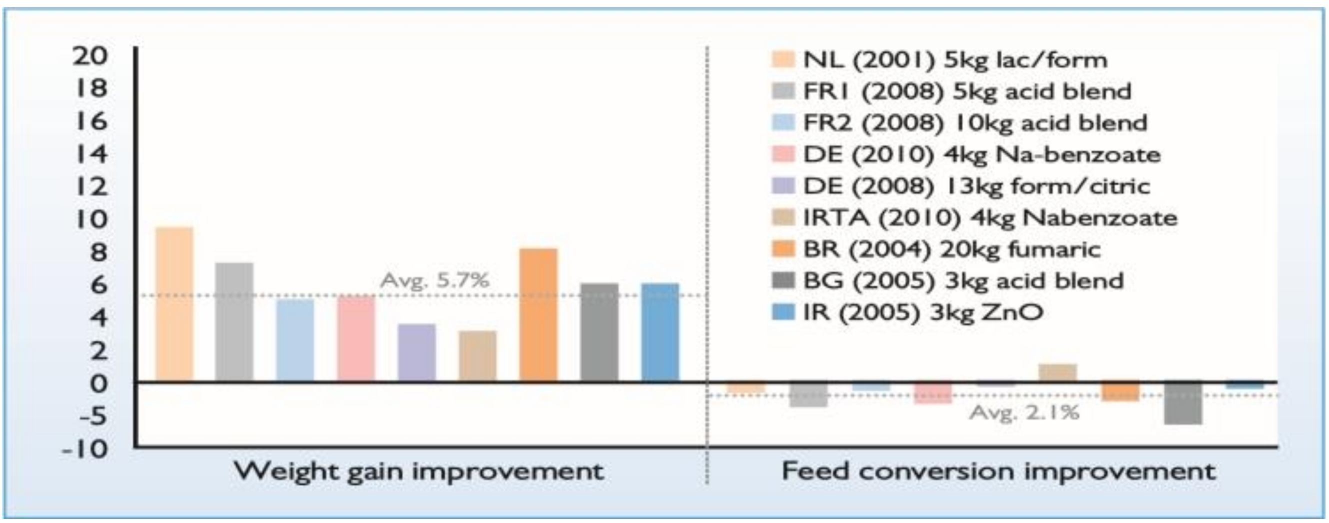

Figure 4. Efficacy of benzoic acid compared to competitive solutions (Wiemann 2011, DSM internal data, unpublished).

Eubiotics' effects on portlet performance and health status.

The forest plot (Figure 5) in this document illustrates the effect sizes of eubiotic supplementation on Average Daily Gain (ADG) across four studies. Each square represents a study and has been weighted in the meta-analysis. The size of the squares indicates the corresponding weight, while the horizontal lines represent the confidence intervals. For example, Study 1 reported an average ADG of 620 g/day with a standard error of 30 g/day, suggesting a higher mean ADG but a broader confidence interval. Conversely, Study 2 had a mean ADG of 580 g/day with a standard error of 25 g/day, indicating a lower mean ADG and a moderate confidence interval.

Furthermore, Study 3 showed an average ADG level of about 600 grams per day (SE = 28) within similar confidence intervals as other studies did all night without disrupting her sleep patterns. According to Study 4's findings, it was found out that there was an average value for ADG at around six hundred and twenty days SE =29, implying that there existed relatively better mean ADGs throughout; these were obtained using more precise (more minor) condense intervals, though bigger ones, remained because they were not equally standardized.

The red diamond represents an estimated combined effect size of approximately 602 g/day ± SE=27, both suggesting that Eubiotics generally improve piglet growth across these studies when applied to them. The narrowness in confidence interval regarding combined effects sizes implies high precision in estimating overall effects that support the efficacy of Eubiotics or promote

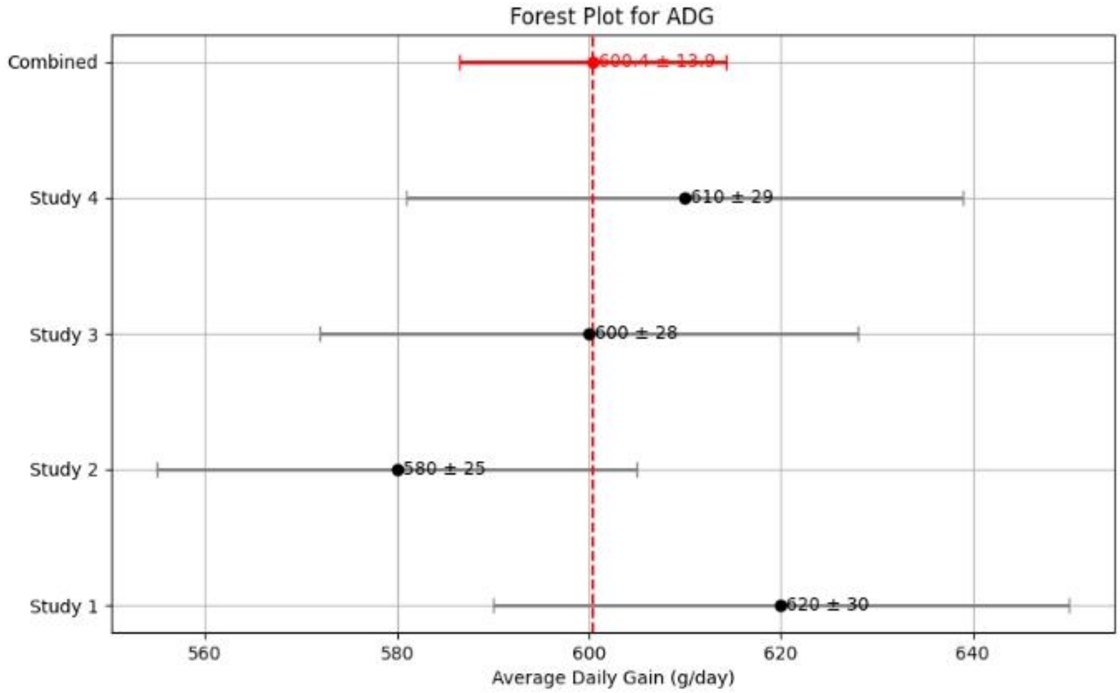

Figure 5. Forest plot for average daily gain.

piglet growth performance.

Impact on growth parameters

The meta-analysis on the use of eubiotics and their effects on pigs revealed a strong pattern showing that eubiotics significantly improve various growth indices. Aggregated data from numerous trials consistently demonstrated that piglets fed eubiotics experienced notable increases in weight gain and feed conversion efficiency compared to control groups. This finding underscores the potential of eubiotics to act as effective growth enhancers in swine production, with significant implications for the industry. Specifically, piglets receiving a multispecies probiotic bacteria preparation, including *L. mesenteroides*, exhibited higher final body weights and average daily gains than the control group. The probiotic preparation was administered at a total dosage of 10^12 CFU/t feed (Nowak *et al*., 2017).

The observed weight gain in piglets given eubiotics highlights the importance of these therapies for optimizing growth trajectories. Meta-analysis data indicate that eubiotics improve the conversion of feed into body weight, increasing efficiency in swine production and resulting in economic benefits. Those involved in agriculture and livestock production can gain valuable insights into enhancing growth rates and optimizing feed use from this topic. Implementing these findings could lead to more efficient and financially viable pig farming methods. Additionally, the positive impact on growth metrics aligns with the industry's goal of improving production efficiency while maintaining animal welfare. Piglets that received eubiotics showed not only higher weight gain but also improved overall performance markers. Eubiotics lignocellulose fibre supplementation appears to enhance the overall performance of piglets (Silva *et al.,* 2023). This issue is critical for meeting the needs of a growing global population by ensuring a more effective and environmentally friendly supply of pork products. In summary, the review suggests that eubiotics have the potential to be effective tools for achieving optimal growth rates and feed utilization in piglet-rearing practices.

Effect on immune responses

The meta-analysis on the use and effects of eubiotics in piglets showed a consistent and significant positive impact on their immune responses. Across various studies, piglets receiving eubiotic treatments exhibited improved immune function, including increased antibody production and better resistance to infections. This highlights the crucial role of eubiotics in boosting piglet immune systems, which is vital for both economic and animal welfare reasons in swine production. Gut health significantly affects nutrient utilization and overall health in pigs. The structure of the gut and its microbiota play key roles in maintaining gut health and functions (Liao, 2021).

The findings suggest that eubiotics enhance the immune response in piglets, potentially reducing the incidence and severity of infectious diseases. The observed increase in antibody production indicates a robust and adaptive immune system, which is vital for the well-being and resilience of piglets, especially during critical stages like weaning. Eubiotics can boost immune responses, possibly decreasing the reliance on antibiotics, which aligns with global concerns about antimicrobial resistance in livestock. Additionally, the improved immunity of piglets fed eubiotics benefits their health and has broader implications for the overall biosecurity of swine herds. The meta-analysis highlights eubiotics' ability to enhance the herd's disease resistance, essential for maintaining the health and productivity of pig populations. This topic underscores that eubiotics not only promote growth but also contribute to creating a healthier and more disease-resistant pig herd, benefiting the swine production industry.

The positive effect on immunological responses aligns with the broader One Health paradigm, which recognizes the interdependence of animal and human health. Piglets with enhanced immune systems are less susceptible to infections, potentially reducing the risk of transmitting pathogens from animals to humans. This underscores the broader importance of eubiotics, not only for the swine industry but also for public health and the global effort to combat emerging infectious diseases. The focus on the beneficial impact on immunological responses highlights the critical role of eubiotics in strengthening piglets' immune systems. This has implications not only for individual animals but also for broader aspects of swine health, biosecurity, and the One Health framework. It emphasizes the potential of eubiotics to contribute to the development of sustainable and resilient swine production systems.

Implications for swine production and sustainability

The comprehensive results of the systematic review and meta-analysis have significant implications for swine production and sustainability. The positive effects of eubiotics on growth and immune responses, along with detailed insights from subgroup analyses, indicate that the strategic use of these interventions can enhance productivity, decrease dependence on antibiotics, and improve sustainability in piglet-rearing practices. This highlights the potential of eubiotics not only as tools for immediate performance enhancement but also as contributors to more sustainable and environmentally friendly swine production practices.

CONCLUSION AND APPLICATION

The increasing limitations on AGPs, growing demands for food safety, and changing consumer preferences drive the search for alternatives to in-feed antibiotics. Eubiotics, including probiotics, nucleotides, essential oils, and organic acids like benzoic acid, have shown positive outcomes in both academic and field testing and are now effectively employed in commercial settings.

This meta-analysis provides evidence of the beneficial effects of eubiotics on piglet weight gain and feed conversion after weaning, highlighting their potential as alternatives to antibiotics. Enhanced immune responses in piglets also indicate a reduced need for antibiotics, aligning with global concerns about antimicrobial resistance.

The findings support the strategic use of eubiotics to improve productivity, reduce antibiotic reliance, and promote sustainability in piglet-rearing practices. Insights from subgroup analyses offer valuable information on specific strains, dosages, and durations for optimal outcomes. The study underscores the importance of considering environmental and management conditions when applying eubiotics, emphasizing their role in sustainable and resilient swine production systems.

In summary, eubiotics not only promote growth but also enhance immune function, contributing to healthier and more disease-resistant pig herds, ultimately benefiting the swine industry.

Sensitivity studies identified potential biases and the impact of outliers, improving the transparency and validity of the meta-analysis. This effort highlights the importance of considering variability and sensitivity in the field of eubiotics, given diverse interventions and management techniques across different locations and farms. The study's thorough investigation enhances overall reliability and provides a methodological basis for future research in eubiotics and piglet health. The diet, food composition, storage conditions, and feeding technologies used can greatly impact the feed conversion and weight gain of piglets. One study found that *Lactobacillus* spp. and other beneficial bacteria play an important role in protecting against intestinal pathogens, and the reduction in their abundance after weaning enhances disease risk (Konstantinov *et al*., 2006). Liu et al (2017) concluded that lipopolysaccharide (LPS) injection can increase rectal temperature and microencapsulated blends of organic acids and essential oils (MOE) supplementation increased growth performance in weaning pigs, however, MOE could not inhibit the LSP-induced hyperthermia.

This review also examined the effects of eubiotics on piglet growth, health, and gut microbial diversity. All the experiments that assessed the weight gain and utilized this microorganism showed no significant mean difference. The results align with Kritas (2015) who also found no changes in the weight gain and feed conversion of weaned pigs when supplemented with Bacillus spp. However, some of the findings show that eubiotics like probiotics, prebiotics, and live yeast significantly improve key performance indicators such as Average Daily Gain (ADG) and Feed Conversion Ratio (FCR), reduce diarrhea incidence, and enhance gut bacterial populations. Eubiotics are a promising alternative to antibiotics in piglet nutrition, leading to more sustainable and better livestock farming practices.

However, the review observed variability in study designs, eubiotic formulations, and outcomes, indicating the need for well-designed future studies to optimize dietary concentrations and long-term effects on productivity.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

ACKNOWLEDGMENT

The authors express gratitude to the Department of Animal Science at Central Luzon State University for the research and learning opportunities, the K12 Transition Program of CHED-RO-3 Scholarship Grant, and Bataan Peninsula State University for their unwavering support. Sincerest gratitude is likewise extended to the Department of Agriculture- Bureau of Agricultural Research (DA-BAR) for funding the Swine Multiplier project in BPSU Abucay Campus where the study was conducted.

REFERENCES

Adeola, O., & Cowieson, A. J. (2011). Board-invited review: opportunities and challenges in using exogenous enzymes to improve nonruminant animal production. *Journal of Animal Science*, *89*(10), 3189-3218.

Airola, C. (2023). Future modulation of gut microbiota: From eubiotics to FMT, engineered bacteria, and phage therapy. *Antibiotics, 12*(5), 868.

Elala, N. M. A., & Ragaa, N. M. (2015). Eubiotic effect of a dietary acidifier (*Potassium diformate*) on the health status of cultured Oreochromis niloticus. *Journal of Advanced Research*, *6*(4), 621-629.

Giang, H. H., Viet, T. Q., Ogle, B., & Lindberg, J. E. (2011). Effects of supplementation of probiotics on the performance, nutrient digestibility and faecal microflora in growing-finishing pigs. *Asian-Australasian Journal of Animal Sciences*, *24*(5), 655-661.

Kiros, T. G., Luise, D., Derakhshani, H., Petri, R., Trevisi, P., D'Inca, R., ... & van Kessel, A. G. (2019). Effect of live yeast Saccharomyces cerevisiae supplementation on the performance and cecum microbial profile of suckling piglets. *PLoS One*, *14*(7), e0219557.

Konstantinov, S. R., Smidt, H., Akkermans, A. D., Casini, L., Trevisi, P., Mazzoni, M., De Filippi, S., Bosi, P., & De Vos, W. M. (2008). Feeding of *Lactobacillus sobrius* reduces *Escherichia coli* F4 levels in the gut and promotes growth of infected piglets. *FEMS Microbiology Ecology*, *66*(3), 599-607.

Kritas, S. K., Marubashi, T., Filioussis, G., Petridou, E., Christodoulopoulos, G., Burriel, A. R., Tzivara, A., Theodoridis, A., & Pískoriková, M. (2015). Reproductive performance of sows was improved by administration of a sporing bacillary probiotic (Bacillus subtilis C-3102). *Journal of animal science*, *93*(1), 405-413.

Krstić, M., Đorđević, V., Ćirić, J., Baltić, T., Bajčić, A., Simunović, S., & Perić, D. (2023). Nutritional strategies to reduce ammonia and carbon dioxide production in intensive livestock production. *Scientific journal" Meat Technology"*, *64*(2), 387-391.

Liao, S. F. (2021). Invited review: Maintain or improve piglet gut health around weanling: The fundamental effects of dietary amino acids. *Animals*, *11*(4), 1110.

Liu, S. D., Yun, W., Lee, J. H., Kwak, W. G., Oh, H. J., Lee, C. H., & Cho, J. H. (2017). Effects of microencapsulated organic acids and essential oils supplementation on performance and rectal temperature in challenged weaning pigs. *Animal Production Science*, *57*(12), 2504-2504.

Liu, W., Pi, S., & Kim, I. (2016). Effects of *Scutellaria baicalensis* and *Lonicera japonica* extract mixture supplementation on growth performance, nutrient digestibility, blood profiles and meat quality in finishing pigs. *Italian Journal of Animal Science,* 15(3) 446-452.

Liu, Y., Espinosa, C. D., Abelilla, J. J., Casas, G. A., Lagos, L. V., Lee, S. A., Kwon, W. B., Mathai, J. K., Navarro, D. M., Jaworski, N. W., & Stein, H. H. (2018). Non-antibiotic feed additives in diets for pigs: A review. *Animal nutrition*, *4*(2), 113-125.

Lutful Kabir, S. M. (2009). The role of probiotics in the poultry industry. *International Journal of Molecular Sciences*, *10*(8), 3531-3546.

Miniello, V., Diaferio, L., Lassandro, C., & Verduci, E. (2017). The importance of being eubiotic. *Journal of Probiotics & Health*, *5*(162), 1-12.

Namkung, H., Li J. Gong, M., Yu, H., Cottrill, M., & De Lange, C. F. M. (2004). Impact of feeding blends of organic acids and herbal extracts on growth performance, gut microbiota and digestive function in newly weaned pigs. *Canadian Journal of Animal Science*, *84*(4), 697-704.

Nowak, P., Kasprowicz-Potocka, M., Zaworska, A., Nowak, W., Stefańska, B., Sip, A., Grajek, W., Juzwa, W., Taciak, M., Barszcz, M., & Frankiewicz, A. (2017). The effect of eubiotic feed additives on the performance of growing pigs and the activity of intestinal microflora. *Archives of Animal Nutrition*, *71*(6), 455-469.

Pattanaik, A. K., Kumar, S., & Rashmi, H. M. (2022). Probiotics, prebiotics, eubiotics and synbiotics for human and animal health and mitigation of antimicrobial resistance. *Indian Journal of Comparative Microbiology, Immunology and Infectious Diseases*, *43*(1), 90-97.

Piwowarski, J. P., Vahjen, W., Melzig, M. F., Granica, S., & Zentek, J. (2022). The eubiotic potential of Lythrum salicaria L. in piglets nutrition. *Planta Medica*, *88*(15), 1570-1571.

Ponziani, F. R., Zocco, M. A., D'Aversa, F., Pompili, M., & Gasbarrini, A. (2017). Eubiotic properties of rifaximin: Disruption of the traditional concepts in gut microbiota modulation. *World Journal of Gastroenterology*, *23*(25), 4491-4499.

Reyes, F. C. C., Cardona, J. K. M., Angeles, E. P., Regaspi, A. F. S., Luis, E. S., Magpantay, V. A., & Baoy, H. T. (2015). Eubiotic lignocellulose supplementation in sows reduced dry period and pre-weaning mortality of piglets. *Philippine Journal of Veterinary and Animal Sciences*, *41*(2), 85-91.

Santovito, E., Greco, D., Logrieco, A. F., & Avantaggiato, G. (2018). Eubiotics for food security at farm level: yeast cell wall products and their antimicrobial potential against pathogenic bacteria. *Foodborne Pathogens and Disease*, *15*(9), 531-537.

Sarangi, N. R., Babu, L. K., Kumar, A., Pradhan, C. R., Pati, P. K., & Mishra, J. P. (2016). Effect of dietary supplementation of prebiotic, probiotic, and synbiotic on growth performance and carcass characteristics of broiler chickens. *Veterinary World*, *9*(3), 313.

Silva, G. F., Silva, B. A. N., Sanglard, D., Domingos, R. L., Gonçalves, M. F., Cardoso, H. M. C., Cardoso, L. A., Pereira, T. S. B., Maia, B. C. A., Brito, S. K., & Abreu, M. L. T. (2023). Performance and gut permeability of post-weaned piglets are influenced by different sources of lignocellulose fiber. *Livestock Science*, *274*, 105274.

Stefańska, B., Katzer, F., Golińska, B., Sobolewska, P., Smulski, S., Frankiewicz, A., & Nowak, W. (2022). Different methods of eubiotic feed additive provision affect the health, performance, fermentation, and metabolic status of dairy calves during the preweaning period. *BMC Veterinary Research*, *18*, Article number 138.

Upadhaya, S. D., Park, J. W., Lee, J. H., & Kim, I. H. (2016). Efficacy of β-mannanase supplementation to corn–soya bean meal-based diets on growth performance, nutrient digestibility, blood urea nitrogen, faecal coliform and lactic acid bacteria and faecal noxious gas emission in growing pigs. *Archives of animal nutrition*, *70*(1), 33-43.

Walsh, M. C., Rostagno, M. H., Gardiner, G. E., Sutton, A. L., Richert, B. T., & Radcliffe, J. S. (2012). Controlling salmonella infection in weanling pigs through water delivery of direct-fed microbials or organic acids. Part I, Effects on growth performance, microbial populations, and immune status. *Journal of Animal Science*, *90*, 261-271.

Wang, M., Huang, H., Hu, Y., Liu, Y., Zeng, X., Zhuang, Y., Yang, H., Wang, L., Chen, S., Yin, L., & He, S. (2020). Effects of dietary supplementation with herbal extract mixture on growth performance, organ weight and intestinal morphology in weaning piglets. *Journal of Animal Physiology and Animal Nutrition*, *104*(5), 1462-1470.

Yang, Y., Iji, P. A., & Choct, M. (2009). Dietary modulation of gut microflora in broiler chickens: a review of the role of six kinds of alternatives to in-feed antibiotics. *World's Poultry Science Journal*, *65*(1), 97-114.

Zhang, Z. F., Rolando, A. V., & Kim, I. H. (2016). Effects of benzoic acid, essential oils and Enterococcus faecium SF68 on growth performance, nutrient digestibility, blood profiles, faecal microbiota and faecal noxious gas emission in weanling pigs. *Journal of Applied Animal Research*, *44*(1), 173-179.