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Review Article

Probiotics, prebiotics and bacteriocins as alternatives to antibiotics in the livestock industry- a Philippine perspective

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ABSTRACT

The widespread misuse and overuse of antibiotics in the animal industry have significantly accelerated the emergence of antimicrobial resistance (AMR), creating multidrug-resistant (MDR) strains that pose a serious threat to both animal and human health. This escalating problem risks reversing decades of medical progress, potentially returning healthcare to a pre-antibiotic era. In response, many countries have implemented policies restricting antibiotic use in livestock production; however, in developing nations such as the Philippines, enforcement remains weak due to limited resources, inadequate training of personnel, and the lack of effective, affordable alternatives to antibiotics. Addressing this issue requires not only stronger regulatory frameworks but also an aggressive information campaign that highlights the dangers of AMR and promotes sustainable solutions. Probiotics, which have been shown to improve animal health and productivity, represent a viable option, particularly when combined with prebiotics that can enhance their effectiveness. Nevertheless, challenges persist, as probiotic efficacy is highly strain-specific, and the market is increasingly saturated with products of unvalidated quality, often mislabeled due to weak oversight and the proliferation of e-commerce platforms. To maintain consumer confidence, probiotic strains must meet rigorous safety, functionality, and technological utilitystandards, with health benefits scientifically verified before approval. Advances in modern molecular biotechnology, particularly genome editing tools such as CRISPR-Cas9, offer powerful strategies to enhance probiotic strains by eliminating virulence genes and incorporating beneficial traits, including bacteriocin production. These genetically improved strains, when paired with prebiotics, could provide more consistent results, enhance livestock growth and productivity, and serve as effective, science-based alternatives to antibiotics. By fostering innovation, implementing stricter regulation, and promoting validated probiotic-prebiotic combinations, the livestock industry can reduce reliance on antibiotics while mitigating the global threat of MDR pathogens.

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INTRODUCTION

The accidental discovery of antibiotics in the early 20th century revolutionized healthcare and significantly increased human life expectancy by reducing mortality from infectious diseases. However, the excessive use of antibiotics, especially in the livestock industry, has led to serious negative implications that could affect human health for future generations. The growing human population exerts constant pressure on the demand for an increased food supply from both plant and animal sources. This demand has driven livestock and fishery farmers to adopt innovative practices, such as using sub-therapeutic dose of antibiotics as growth promoters to increase productivity and efficiency while reducing production costs (Helm et al., 2019; Hou et al., 2022). Over two-thirds (70%) of the total global antibiotic supply is used in the livestock and fishery industries, with more than 75% of these antibiotics used for prophylaxis and growth promotion rather than disease treatment (WHO, 2019). While the use of antibiotics beyond therapeutic purposes has indeed improved farm productivity, it has also inadvertently created a looming disaster that could revert our healthcare system to the pre-antibiotic era. Excessive antibiotic use in livestock provides consistent opportunities for the microbial flora in these animals to interact with antibiotic molecules or their fragments, triggering mutations that lead to the development of antibiotic-resistance genes, which then spread to different microbial ecosystems (Yang et al., 2021). The spread of antibiotic-resistant strains and their genetic determinants into human microbial flora occurs via the food chain by consuming antibiotic residue-contaminated food products (Figure 1). Meat and other livestock products from animals heavily treated with antibiotics have been shown to contain active antibiotic fragments. Several field studies have documented high antibiotic contamination rates in poultry and turkey meat and raw milk samples through chronic low-dose exposure (Khalifa et al., 2024; Jaber et al., 2025). Fruits and vegetables fertilized with manure and wastewater from livestock farms also contain antibiotic residues and resistance genes (ARGs). Several studies show that manure application increases the prevalence of ARGs in soils and can lead to their detection on roots as well as on leafy and root vegetables at harvest (Zalewska et al., 2021; Marti et al., 2013). Metagenomic analyses have demonstrated that these manure-derived resistomes overlap with plant microbiomes and facilitate ARG transfer onto plant surfaces and internal tissues (Wang et al., 2022; Marti et al., 2013). Furthermore, the use of reclaimed farm wastewater increases the diversity and abundance of ARGs detected on fresh produce and promotes the co-occurrence of mobile genetic elements that enable horizontal gene transfer (Gekenidis et al., 2021).

The excessive use of antibiotics in livestock and fisheries has accelerated the development of antibiotic resistance in the microbial ecosystem, leading to the emergence of multidrug-resistant (MDR) strains. MDR pathogens could render common antibiotics ineffective, triggering an antibiotic apocalypse. According to the World Health Organization (WHO), no major new types of antibiotics have been discovered in the last four decades. It is estimated that MDR infection-related deaths could reach up to 10 million annually by 2050 if antimicrobial resistance is not addressed (O'neill, 2016). The World Bank estimates that MDR could cause severe economic burdens, potentially reaching up to 1 trillion US dollars annually by 2030 (Tang et al., 2017).

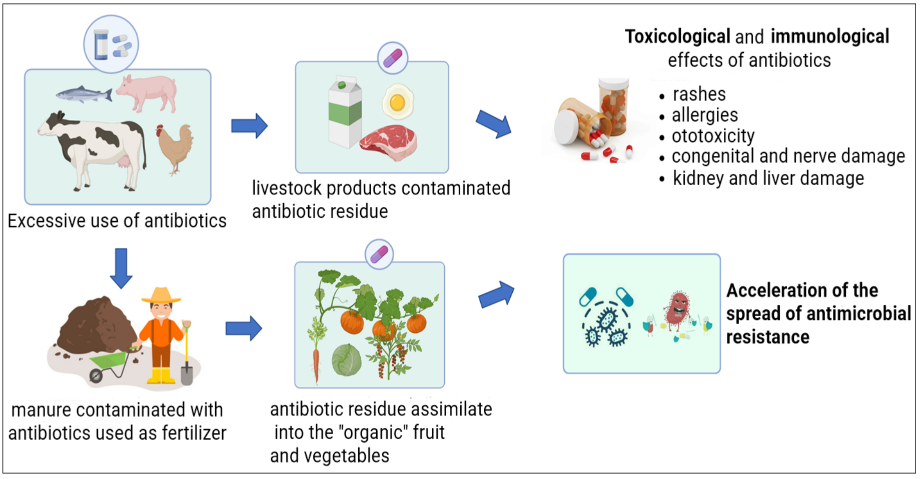

Figure 1. Route of antibiotic contamination into our food systems and its consequences to human health and the spread of antibiotic resistance in microbial ecosystems. Constant exposure to antibiotics, especially to infants, has been shown to cause several toxicological and immunological effects, including rashes, allergies, organ damage, and even learning disabilities (Aversa et al., 2020; Bacanlı, 2024) The figure was generated using Biorender (www.biorender.com).

To mitigate this impending catastrophe, many countries have implemented regulatory policies on the judicious use of antibiotics in livestock and fisheries (Table 1). As early as 2009, the Philippine Government developed guidelines to control antibiotic residues in food through the Administrative Order No. 24, Series of 2009, which outlined the implementing guidelines on the use of antibiotics in the veterinary setting, hoping to address drug residue contamination in food. It aims to protect public health by establishing rules for the rational use, control, and monitoring of veterinary drugs in food-producing animals to ensure that the foods produced do not exceed maximum residue limits for these substances. The AO focuses on activities related to manufacturing, importation, exportation, distribution, and regulation of veterinary drugs within the country. However, as in other resource-limited countries, the implementation of these policies has been challenging and largely ineffective due to several factors. Many livestock farms in the Philippines are small, backyard operations, particularly in rural areas. Philippine Government agencies implementing these policies face a lack of resources and trained personnel. Additionally, there is a lack of awareness about the gravity of antibiotic resistance and its connection to antibiotic overuse. Another critical issue is the lack of strict enforcement of veterinary prescription issuance, allowing farmers easy access to antimicrobials through local agro-vet outlets. A recent study by the United Nations Food and Agriculture Organization (FAO), in collaboration with the Philippines Bureau of Animal Industry (BAI), highlighted the almost nonexistent veterinary oversight in backyard farms (Barroga et al., 2020). The study's most concerning finding was the frequent use of clinically important antibiotics for human medicine at almost all stages of livestock production, which accelerates the development of MDR strains associated with human infections. The use of veterinary analogues of human antibiotics poses similar dangers; for instance, the resistance development of gentamicin was traced to the rampant use of its aminoglycoside analogue apramycin in veterinary settings (Jensen et al., 2006; Choi et al., 2011).

Table 1. Regulations on the use of antibiotics in the animal industry in different countries.

Country	Year	Regulatory Details
Australia	2017	Antibiotics used in human medicine are not licensed as growth promoters. But, five antibiotics (olaquindox, avilamycin, bambermycin, monensin, and salinomycin) are used as growth promoters in poultry, pigs, cattle, and sheep
Canada	2020	Growth promotion claims on medically important antimicrobials (MIAs) (Category I, II, and III antimicrobials) will no longer be permitted.
China	2020	All antibiotic growth promoters except herbal medicine have been banned
European Union	2022	Banned the importation of meat and dairy produced using antibiotic growth promoters.
Sweden	1986	First country to ban the use of antibiotics as growth promoters
USA	2017	Medically important antimicrobials are banned. However, bacitracin and carbadox, which are classified as medically important by the World Health Organization, are still used as growth promoters in pigs
Philippines	2009	Administrative Order No. 24, Series of 2009 – Implementing Guidelines on the National Veterinary Drug Residues Control Program in Foods.

* adopted with modifications from Rahman et al., 2022.

With the unavoidable need for strict regulation of antibiotic use in the animal industry to slow down the global crisis of antimicrobial resistance and avert a total antibiotic apocalypse, effective alternatives are urgently needed to replace antibiotics as growth promoters in livestock.

This paper discusses the potential and viability of probiotics, prebiotics, and bacteriocins, used singly or combined, as alternatives to antibiotics in improving the livestock industry.

Probiotics, Prebiotics and Bacteriocins as Alternatives to Antibiotics

The concept of enhancing animal health and performance by improving gut health is well-established. The gut health of animals is significantly influenced by the composition of bacterial flora in the intestinal tract. These microorganisms play a vital role in stimulating the host's immunity, nutrient absorption, maintaining gut peristalsis and mucosal integrity, and bioconverting toxic compounds to non-toxic residues, thereby contributing to overall animal health. These crucial functions are impaired when the gut bacterial population and composition become unbalanced, a condition known as dysbiosis. The principles of probiotics and prebiotics are based on promoting commensal bacterial strains in the intestinal microbiota—whether indigenous or introduced—to prevent dysbiosis.

Probiotics are defined as live microorganisms that, when administered in adequate amounts, confer health benefits to the host (FAO & WHO, 2001). Prebiotics, conversely, refer to non-digestible food ingredients that selectively stimulate the growth and proliferation of beneficial microorganisms in the gut, leading to health benefits for the host (Gibson et al., 2017). Common microorganisms used as probiotics include Gram-positive bacteria from the genera *Bacillus*, *Enterococcus, Lactobacillus, Pediococcus, Streptococcus*, and *Bifidobacteria*. Some yeast strains from the genus *Saccharomyces* are also used as probiotics. However, not all members of these microbial genera can be used as probiotics. For instance, there is a common misconception that all lactic acid bacteria are probiotics, stemming from the GRAS (Generally Recognized as Safe) designation of these microorganisms by the US FDA and their long history of association with food fermentation. However, some members of this group may pose health-related concerns. For example, some *Enterococcus* species are known to be opportunistic pathogens and can carry transmissible virulence genes and antibiotic resistance genetic elements (Franz et al., 2011; Hanchi et al., 2018).

The WHO, FAO, and European Food Safety Authority (EFSA) have outlined criteria for selecting strains that must be met before they can be used as probiotics. These criteria include ensuring the candidate strain's safety, functionality, and technological utility (Figure 2).

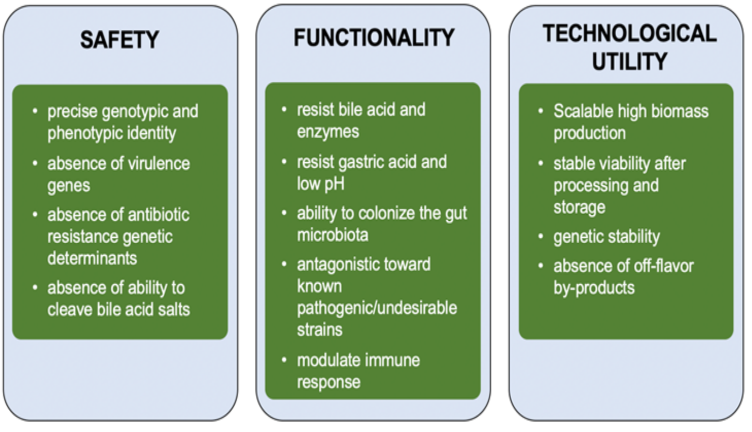

Figure 2. Selection criteria of candidate probiotic strains.

The effectiveness of a probiotic strain largely depends on its ability to colonize and dominate its ecological niche. The production of antimicrobial compounds, such as bacteriocins, significantly enhances this effectiveness. Bacteriocins are food-grade antimicrobial peptides with potent bioactivity, even against multi-drug-resistant strains, making their production a highly desirable trait for probiotic strains. The simplicity of the biosynthetic machinery for bacteriocins presents significant potential, as they can be easily introduced into other probiotic strains via plasmids or genome editing tools like CRISPR-Cas9 technology (Hidalgo-Cantabrana et al., 2019; Song et al., 2017). This approach can elevate the effectiveness of probiotics and can be further optimized through bioengineering.

Several studies have explored introducing point mutations in the bacteriocin structural gene, yielding phenotypes with enhanced potency. For example, the mutant phenotypes of enterocin NKR-5-3B derived from the previously established heterologous expression system (Figure 3) of this bacteriocin produced the V32C, V32A, and V32G bacteriocin derivatives from the respective mutants that demonstrated bioactivity enhancements of 233%, 217%, and 183% relative to the native form of the bacteriocin, respectively (Figure 3C; Perez et al., 2021). The bioengineering of nisin A, at the flexible region referred to as the "hinge", with small chiral amino acids, such as Ala, Leu, and Ile, produced bacteriocin derivatives with a two-fold enhancement in bioactivity against the pathogenic strains *Staphylococcus aureus* RF122 and *Streptococcus agalactiae* ATCC 13813 (Healy et al., 2013). Moreover, the introduction of mutations at the serine residue at the 29th position of nisin A resulted in bacteriocin derivatives with enhanced potency such as the Ser29Gly and Ser29Ala that displayed a two-fold potency against methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (VRE) relative to its native bacteriocin form (Field et al., 2012). The Lys12Ala mutation of nisin A also showed significant increase in its specific bioactivity towards the pathogenic strains MRSA ST528 and VRE EC533 (Molloy et al., 2013). Site-specific substitution mutagenesis of the well-studied lantibiotic nukacin ISK-1 also showed several bacteriocin derivatives with enhanced bioactivity. Notably, the D13E nukacin mutant derivative phenotype showed strong bioactivity enhancement of more than a two-fold increase against the indicator strain (Islam et al., 2009). These types of bioactivity-enhancing mutations can be seamlessly introduced to probiotic strains through modern genome editing tools such as CRISPR-Cas9 technology that can improve their effectiveness in targeted colonization of the hosts' guts.

For prebiotics, the health benefits associated with microbiota modulation must be demonstrated. Prebiotics are non-digestible components that reach the lower intestinal tract and selectively stimulate the growth and activity of beneficial strains such as *Bifidobacteria* and *Lactobacillus* spp. There is a misconception that all dietary fibers are prebiotics, stemming from the fact that all prebiotics are dietary fibers. The beneficial health effects of prebiotics must be validated before a substance can be truly considered as a prebiotic.

Selection Criteria and Requirements for Probiotics and Prebiotics

As mentioned above, several criteria must be met for a strain to be classified as a probiotic in terms of its safety, functionality, and technological utility. The safety of probiotic strains for human and animal health must be confirmed before use. Regulatory agencies such as the US FDA and the EFSA have established guidelines that many countries have adopted. In the US, inclusion on the GRAS list is the primary indicator of a strain's safety. In the EU, the Qualified Presumption of Safety (QPS) outlines additional criteria for the safety assessment of bacterial supplements, including a history of safe use and the absence of acquired antibiotic resistance risks (FDA, 2018; EFSA, 2020). For instance, some strains of the genus *Enterococcus* are associated with opportunistic pathogenicity, virulence, and the potential to carry antimicrobial resistance genes. Several members of this genus have been found to exhibit various virulence factors, including gelatinase, adhesion to collagen, aggregation substance, endocarditis antigen, and β-hemolytic substances (Henning et al., 2015). However, many *Enterococcus* species have proven safety and efficacy as probiotic strains, highlighting the importance of properly screening and characterizing candidate strains rather than relying solely on taxonomic identity for probiotic classification.

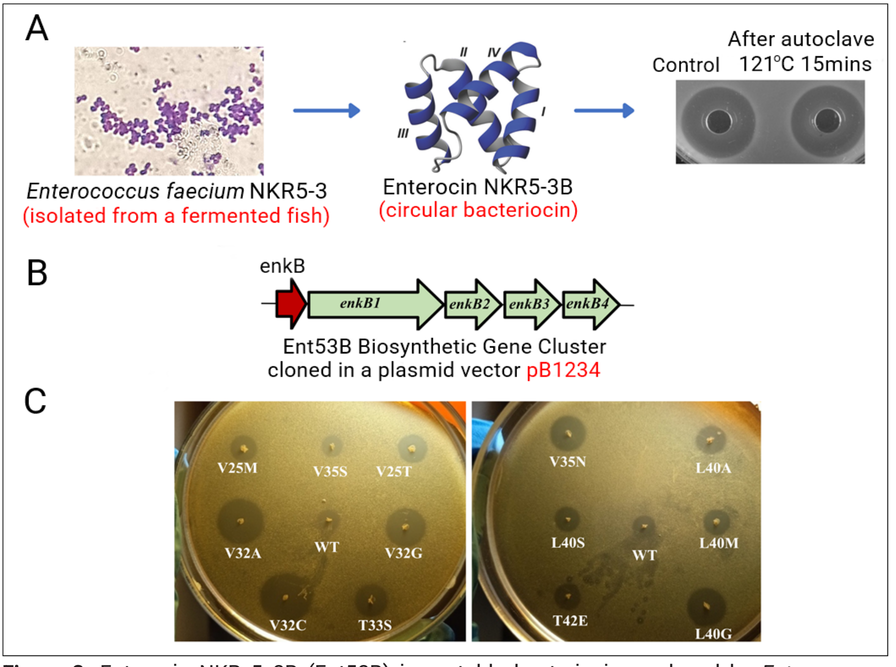

Figure 3. Enterocin NKR-5-3B (Ent53B) is a stable bacteriocin produced by *Enterococcus faecium* NKR-5-3 (A). The heterologous expression system of Ent53B was established by cloning its biosynthetic gene cluster, composed of five genes under a constitutive promoter in a plasmid termed pB1234 (B). Phenotypes with enhanced bioactivity were obtained when point mutations were introduced into the bacteriocin structural gene through the pB1234 plasmid (C). Amino acid substitutions are indicated using the single letter amino acid code, while the number indicates the amino acid position. WT means wild type, producing the native form of the Ent53B. (panel C adapted from Perez et al., 2021).

Another crucial aspect that needs confirmation is the strain's ability to confer health benefits to the host. The primary principle of a probiotic strain's health benefits is its ability to proliferate in the lower intestinal tract. To reach that area, the strain must survive and resist the harsh gastric acid and bile salts in the upper digestive tract. In some cases, microencapsulation can provide additional protection to ensure cell viability (Anadon et al., 2016).

Probiotics function through the concept of competitive exclusion. If a sufficient population of beneficial bacteria is present, the capacity of harmful bacterial species to overwhelm the host is reduced (Anadon et al., 2016). Thus, a key trait of a probiotic strain is its ability to colonize the gut microbiota. Essential traits for gut colonization include adherence to epithelial cells or the intestinal and/or the production of metabolites that inhibit or kill pathogenic bacteria (e.g., bacteriocins). Once the probiotic strain colonizes the gut microbiota, the modulation of immunological activity, such as increased cytokine and antibody production, needs to be confirmed (Haghighi et al., 2006).

For prebiotics, the candidate compound must meet several criteria demonstrated in both in vitro and in vivo studies: (1) non-digestibility in the upper GI tract; (2) fermentability by beneficial gut microbiota; and (3) selective stimulation of the growth and activity of intestinal bacteria (Anadon et al., 2016). Prebiotics must resist low pH gastric acid, enzymatic digestion, and intestinal absorption in the upper GI tract. Once these compounds reach the lower GI tract, they must be small enough to be assimilated into the microbial intracellular space to serve as an energy source through fermentation. These compounds include inulin and various oligosaccharides, which can promote the growth and metabolic activity of beneficial gut flora such as *Bifidobacteria* and *Lactobacillus*. Prebiotics serve as substrates that enhance the colonization and metabolic functions of commensal bacteria, leading to improved gut barrier integrity, modulation of immune responses, and production of beneficial metabolites such as short-chain fatty acids (SCFAs) (Gibson et al., 2017).

Similarity of the Mechanism of Action of Probiotics and Antibiotics as Growth Promoters

The strict enforcement of policies and regulations against the injudicious use of antibiotics in animal production, aimed at slowing the impending crisis of antibiotic resistance, has amplified the urgent need for alternatives. These alternatives are necessary not only for the prevention and treatment of diseases but also for the growth promotion of farm animals. Understanding the mechanism of growth promotion by antibiotics is vital to assess the utility of available alternatives. It is undeniable that administering sub-therapeutic doses of antibiotics to farm animals has significantly improved productivity, although the exact mechanism is not clearly understood. Nonetheless, four possible mechanisms that explain the improved animal growth and performance have been theorized: (1) inhibition of sub-clinical infections; (2) reduction of growth-depressing metabolites; (3) increased nutrient availability via reduced competition; and (4) improved nutrient uptake due to changes in intestinal epithelium composition (Niewold, 2007).

Similarly, the principles by which probiotics confer health benefits to the host are strikingly similar to the mechanisms of antibiotic-induced enhancement of animal performance. The concept of improving animal health and performance by enhancing gut health is not new. The science of probiotics and prebiotics is well-established for enhancing animal health and growth performance. The enhancement of overall health through probiotic administration is comparable to the prevention of clinical infections seen with antibiotic use. Another effect of probiotics, similar to growth-promoter antibiotics, is the improvement of nutrient digestion and absorption through alterations in intestinal composition (Kumar et al., 2025). The improvement in digestive capacity through the production and regulation of metabolites is also a similar effect of probiotics (Liao & Nyachoti, 2017). Owing to these similarities in mechanisms promoting improved health, the use of probiotics for enhancing animal productivity is a viable alternative to antibiotics.

Strengths and Weakness

The beneficial effects of probiotic administration are well-understood and accepted concepts. Numerous studies on the use of probiotics in animal feed have reported a wide variety of benefits for animal health and overall growth performance. Several studies have demonstrated that administering probiotics, either singly or in combination, improves average daily feed intake, average daily gain, and feed conversion ratio in pigs and poultry (Kumar et al., 2025; Liao & Nyachoti, 2017; Angelin & Kavitha, 2020). Probiotic administration has also been shown to reduce diarrhea and significantly improve feed digestion through the production of enzymes and the promotion of digestive enzyme secretion in the gut of broilers (Sinurat et al., 2020). However, it should be noted that the efficacy of probiotics is highly dependent on the strain used and usually takes longer to manifest its effects compared to antibiotics. This is perhaps the most notable weakness of probiotics (Table 2). This also highlights the threat of the blanket use of the term probiotics without confirming the in vivo and in vitro biological activities of the strains used. With the advent of e-commerce, where transactions are faster and more efficient, the proliferation of dubious products labeled as probiotics is apparent. If left unaddressed, this could trigger a loss of confidence in probiotics and cast doubt on the efficacy of genuine and proven probiotic products. Nevertheless, the Philippines, as a tropical country is known for its biodiversity. Its diverse microbial ecosystem can offer novel strains with exceptional biological activities that can be utilized in the livestock industry as probiotics.

Another established concept that can further improve the efficacy of probiotics and prebiotics is the combinational approach known as synbiotics. The SWOT analysis of probiotics, prebiotics, and combinatorial concepts is shown in detail in Table 2. Studies have shown that synbiotics enhance livestock performance, through synergistic mechanisms, significantly better than probiotics or prebiotics alone. The prebiotic substrate, when co-administered with probiotics, has been shown to improve the survival and colonization of the probiotic strains and thus enhance livestock performance. Studies in poultry and pigs show that synbiotics can increase body weight gain, improve feed conversion, and bolster survivability while reshaping the microbiota toward beneficial gut flora in broilers (Prentza et al., 2023) and in weaned piglets (Wang et al., 2019). Furthermore, as mentioned earlier, integrating the capacity of a probiotic strain to produce *in situ* food-grade antimicrobial peptide bacteriocins can also elevate the strain's colonizing capacity, thus improving its probiotic ability. Studies on bacteriocin-producing *Enterococcus faecium* strains used as probiotics have been shown to improve feed conversion ratio in broilers (He et al., 2021; Ben Lagha et al., 2017). Since bacteriocins can be degraded in the digestive tract, using live bacteriocin-producing probiotics to deliver peptides *in situ* is generally the most effective strategy for sustained gut activity and growth promotion in livestock. (Ben Lagha et al., 2017; Hernández-González et al., 2021; He et al., 2021).

Table 2. SWOT analysis of probiotics, prebiotics and bacteriocins

	Probiotics	Prebiotics	Probiotics + Prebiotics	Probiotics + Prebiotics + Bacteriocin
Strengths	• scientifically proven concept • established efficacy • established market	• proven to promote beneficial natural flora • inhibit the proliferation of pathogenic strains	• increased efficacy thru symbiotics • established market	• further strengthen efficacy • food-grade • targets even existing MDR pathogens
Weakness	• takes time for the efficacy to manifest • dependent on the probiotic strain used • Improper handling and storage may impact efficacy	• production cost • takes time for the efficacy to manifest • dependent of the type of prebiotic used	• production cost • takes time for the efficacy to manifest • Improper handling and storage may impact efficacy	• stability of the strain • production cost
Opportunities	• diverse microflora as source of probiotics (tropical country) • strain improvement using genome editing	• abundant supplies of raw materials • recombinant enzyme technology can lower production cost	• more combination of type and ratios can be explored	• easy introduction of bacteriocin producing capacity to other probiotic strains • bioengineering of bacteriocins
Threats	• abuse of the term probiotic • some strains have virulence and AMR genetic determinants	• prebiotics cannot prevent infection	• the same threats as pro/prebiotics	• anti-GMO advocates (when using bioengineered strains/bacteriocins)

Future Perspectives, Recommendations and Outlook

The demand for food is expected to continue to increase as the human population continues to grow. While the use of antibiotics as growth promoters for livestock animals is proven to improve animal productivity, its association with the rise of antimicrobial resistance could force authorities to more strictly implement policies in order to prevent a total antibiotic apocalypse. Hence, alternative strategies for the improvement of animal productivity are important. Probiotics, prebiotics and bacteriocins offer tremendous potential as alternatives to antibiotics in improving animal productivity. However, careful consideration must be given in using these concepts as their efficacy is highly dependent on the strain (for probiotics) and type of compound (for prebiotics). Regulatory agencies must be strengthened to prevent the blanket use of these terms for products that have not demonstrated their safety and efficacy.

To discourage the overuse of antibiotics in livestock production, the Philippine government needs to be aggressive in promoting awareness of the danger of antibiotic abuse. It also needs to empower agencies tasked with enforcing policies by providing training and equipment to monitor antibiotic contamination in meat and other livestock products. It is equally important that the Philippine government ensures that farmers have access to effective and affordable alternatives, such as probiotics, prebiotics, and bacteriocins, to reduce farmers' reliance on excessive antibiotics in their livestock.

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Availability of Data and Materials

Data and materials are available from the corresponding author upon request.

Ethical Considerations

Not applicable

Competing Interest

The authors declare no conflict of interest.

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