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Review: A systematic review on the use and effects of postbiotics on the general health, gut health, and performance of sows and piglets



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ABSTRACT

Growing concerns over antibiotic resistance have led to restrictions on antimicrobial use in various regions, including the European Union, prompting the search for alternative strategies to promote gut health. Of these, postbiotics have emerged as a promising strategy due to their potential immunomodulatory, anti-inflammatory, and gut barrier-enhancing properties. Despite extensive research regarding human health, the application of postbiotics in swine nutrition remains unexplored, with limited and inconclusive findings. The definition of postbiotics has evolved, leading to inconsistencies in the literature regarding their classification and functional properties. This review aimed to clarify the concept, the definition, and classification, and evaluate the types and effects of postbiotic supplementation on the health and performance of pigs. A literature search was conducted using PubMed, Google Scholar, Web of Science, and Scopus, employing search terms mainly related to “postbiotic preparation” (i.e., cell wall fragments, exopolysaccharides, etc.) and “pig category” (gestating and lactating sows, suckling and post-weaning pigs). The search yielded 2 151 articles (published between 1982 and 2025), and 33 fulfilled the eligibility criteria (studies on swine and studies in which the postbiotic respected the latest definition of the International Scientific Association for Probiotics and Prebiotics). The findings indicate that postbiotics derived from *Saccharomyces cerevisiae* and *Lactobacillus* species are the most extensively investigated. Based on the explored studies, the mechanisms of action of the various postbiotics appear to be closely linked to their specific bioactive components and, consequently, to the originating microbial strains. Postbiotics derived from both *Saccharomyces cerevisiae* and *Lactobacillus* demonstrated beneficial effects on gut health pillars in both sows and piglets. Sows' supplementation enhanced immunoglobulin concentrations in blood (31%) and milk (58%) while reducing oxidative stress markers (malondialdehyde, 34%). In weaned pigs, postbiotic supplementation reduced pro-inflammatory cytokines (Tumour Necrosis Factor- α , Interleukin 1 β and Interleukin 6) along with improvements in gut morphology parameters and α -diversity. These effects collectively contribute to improved overall health and growth performance in the animals. In conclusion, postbiotic supplementation, whether administered to sows or directly to pigs, appears to support and enhance piglet health and growth, even under challenging conditions. The limited characterisation of the postbiotic formulation employed in the studies precluded definitive attribution of the observed mechanisms of action to specific bioactive constituents. Future research should focus on defining the optimal dosage and timing of supplementation to exploit the potential benefits of postbiotics fully.

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Implications

Antimicrobial resistance represents a growing concern for both human and animal health. In the context of pig farming, this issue underscores the urgent need for alternative strategies which could enhance the health of pigs and avoid antimicrobial use. Of these alternatives, nutritional approaches have gained increasing

attention. Notably, postbiotics represent a promising solution. Unlike live probiotics, postbiotics are more stable, have a longer shelf life, and crucially, do not carry the risk of transferring antibiotic resistance genes. Therefore, it is important to investigate their mechanism of action and possible application to swine.

Introduction

In modern pig farming, the use of up-to-date management strategies is the cornerstone of preventing the occurrence of illness

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and, consequently, avoiding the use of antibiotics. The increasing concern related to the spread of antibiotic resistance has led some parts of the world, namely Europe, to limit the use of antibiotics and prohibit the use of pharmacological doses of zinc oxide, encouraging breeders to look for other solutions regarding pig health. Of the different reasons for using antibiotics, gut-related disorders still represent one of the main motives. The introduction of the gut health concept offers a comprehensive overview of the complexity of the gastrointestinal tract and its crucial role in maintaining the organism's physiological homeostasis. Kogut and Arsenault (2016) defined gut health as “the absence/prevention/avoidance of disease so that the animal is able to perform its physiological functions in order to withstand exogenous and endogenous stressors”. Factors affecting gut health include nutrient digestion and absorption, host metabolism and energy production, the gut microbiome, mucosal development, barrier function, and mucosal immune responses. These elements have recently been described and grouped into four pillars for monogastric animals (Chalvon-Demersay et al., 2021).

Several nutritional and feeding strategies have been proposed to ensure good gut health in pigs in the different phases of their life. In particular, feed additives including acidifiers (Luise et al., 2020), phytobiotics (Pandey et al., 2023), probiotics (Liao and Nyachoti, 2017), and prebiotics (Kiernan et al., 2023) have been widely reviewed and proposed as solutions for both promoting and maintaining pig gut health. Currently, a new class of products, postbiotics, has been proposed. Postbiotics have received attention in recent years due to their potential health benefits in both humans and animals. They appear to have the potential of positively influencing gut health with benefits including immunomodulatory effects (Salva et al., 2021), anti-inflammatory properties (Xu et al., 2023b), and promotion of the gut barrier function (Christensen et al., 2022). Postbiotics have been extensively studied in the human field, while their application in animal husbandry is relatively recent. Therefore, there are few studies regarding the use of postbiotics in swine, and the literature available is scarce and inconclusive. This is also because the definition of a postbiotic has been revised over time, and its meaning today is different from that which had been given before. For example, short-chain fatty acids, enzymes and vitamins produced by bacteria were included in the definition in the past. However, as Vinderola et al. (2024) clarified, a product cannot be identified as postbiotic if the metabolites derive from an inactivated microorganism and lack components of the inactivated bacterial cell, even if its effect is beneficial to health. As a result, not all scientific articles referring to postbiotics can be considered reliable sources.

The objective of this review was to elucidate the potential applications of postbiotic preparations in swine nutrition and to evaluate their effects on the general health, performance, and gut health of pigs, using a systematic approach. Given the existing ambiguity surrounding the term 'postbiotic,' the initial section of this review is devoted to its clarification, examining the definition and classification of postbiotics. Subsequently, the review will systematically explore the literature available regarding the use of postbiotics and discuss their effects on the general health, gut health, and performance of weaned pigs as well as of gestating and lactating sows.

Origin, definition, and development of the postbiotic concept

Postbiotic products are becoming increasingly prominent in the fields of nutrition, functional food (Aguilar-Toalá et al., 2018), and dietary supplements. They offer important health advantages without the concerns associated with live microorganisms (Tsilingiri et al., 2012), such as stability, storage and viability issues. The concept of postbiotics emerged from concerns regarding the stability of viable microbial cell preparations during the

storage period (Vinderola et al., 2022). During the shelf life of probiotic preparations, some microbial cells may become damaged or die as a consequence of exposure to environmental factors, such as high temperatures, oxygen exposure and humidity, which are very common and affect the preparation of livestock feed (Jannah et al., 2022). As a result, it is challenging to evaluate the number of living cells at the end of shelf life. The final question is whether, at the end of the storage period, the dead cells would have an impact or effect on the host. This is where the concept of postbiotics comes in.

The term “postbiotic” is defined as “a preparation of inanimate microorganisms and/or their components that confers a health benefit on the host”. This definition was coined thanks to an agreement reached during a panel hosted by the International Scientific Association of Probiotics and Prebiotics in 2019. The panel brought together researchers from different fields and perspectives with the aim of finding a definition that could be applied in a scientific context. During the discussion, several terms which had already been used in the literature from when the concept of this product came out were discussed (Salminen et al., 2021); some of them were: “non-viable probiotics”, “ghost probiotics” (Taverniti and Guglielmetti, 2011), “paraprobiotics” (Akter et al., 2020), “inactivated probiotics” (Kang et al., 2021), “tyndallised probiotics” (Piqué et al., 2019), and “heat-killed bacteria” (Ou et al., 2011; Arimori et al., 2012).

The objective of this panel was to find a definition and meaning distinct from those previously proposed, intending to provide a clear delineation between these compounds and those of a similar nature, such as probiotics and prebiotics. In accordance with the established definition, a postbiotic is constituted of inanimate microorganisms which have lost the replication capacity but have not diminished their beneficial effects on the host. These substances have been demonstrated to support gut health, modulate the immune system, improve digestive function, and potentially exert antimicrobial and anti-inflammatory effects, all of which can have a positive impact on host health. Furthermore, additional microbial compounds (cell wall fragments, short-chain fatty acids, enzymes) produced by the microorganism before the inactivation contribute to the positive effects provided by a postbiotic. However, based on the recent definition, metabolites or end-products produced during the fermentation process, such as enzymes, short-chain fatty acids, bacteriocins, vitamins, and minerals, cannot be classified as postbiotics by themselves if they are administered alone without the inactivated microorganism. These metabolites already have a chemical name (Vinderola et al., 2024), and their effects have already been demonstrated; therefore, a postbiotic must contain non-viable microbial cells or cell components with or without their metabolites (Salminen et al., 2021).

Classification of postbiotic products

Given the complexity and variability of the cellular structures of the different microorganisms, which could be used to obtain a postbiotic, postbiotics are generally classified as bacterial lysates, cell wall fragments, exopolysaccharides, and cell-free supernatants.

Bacterial lysates

Bacterial lysates, being composed of cell debris and secreted substances, fit the definition of postbiotic well. A bacterial lysate is a preparation containing the contents of lysed bacterial cells, derived from the chemical or mechanical breakdown of bacterial cells, obtained by Gram-positive and Gram-negative degradation and lyophilisation. The process results in the disruption of the bacterial cell walls, allowing the release of the internal components,

including proteins, nucleic acids, lipids, enzymes, and other cellular materials, into the solution. These products have been the subject of extensive research, with a particular focus on their potential for modulating the immune system and their activity on the respiratory tract (Navarro et al., 2011). The presence of bacterial components can stimulate the immune response, resulting in the production of cytokines and other immune-modulating molecules. As previously reported in the literature, bacterial lysates of a mixture of Gram-positive and Gram-negative bacteria have been shown to stimulate the production of pro-inflammatory cytokines and to activate Toll-like receptor (TLR) 2 and TLR 4 in mice (Coviello et al., 2014). Despite the abundance of literature addressing the impact of bacterial lysates on the human respiratory tract, there is a lack of research investigating their application in other fields.

Cell wall fragments

The cell wall of gram-positive bacteria is a complex structure composed of peptidoglycan, teichoic acids, polysaccharides, and proteins, all of which can be beneficial to the host. The peptidoglycan is the main component of the bacterial cell wall; it is found on the outside of the bacterial cytoplasmic membrane, which has a structural and defensive function, helping the membrane to maintain its shape (Vollmer et al., 2008). Several studies regarding the effects of Lactobacilli have shown that their peptidoglycans have a beneficial effect on the immune system. Kolling et al. (2015) have shown, for the first time, that a non-viable *Lactobacillus rhamnosus* CRL1505 and its components can have a favourable effect on immunity.

Teichoic acids are the second main component of the microbial wall (Danladi et al., 2022); they help to functionalize the peptidoglycan matrix. Teichoic acids include both lipoteichoic acid, attached to the membrane via glycolipids, and wall teichoic acids, which are covalently attached to the peptidoglycan layer of the bacterial cell wall (Brown et al., 2013). There are some conflicting data regarding the beneficial effects of lipoteichoic acid. For example, it has been reported that the oral administration of lipoteichoic acid led to modifications in the mice microbiome composition, notably enhancing the relative abundance of *Akkermansia muciniphila*, a bacterium known for degrading mucin; lipoteichoic acid promoted an increase in goblet cell numbers and stimulated mucin secretion in these cells by activating TLR 2 (Wang et al., 2020). In addition, in porcine intestinal epithelial cells, the lipoteichoic acid derived from *Lactobacillus plantarum* was found to inhibit TLR 3-mediated inflammatory responses (Kim et al., 2017), and components of the heat-killed *Enterococcus faecium* strain, such as the cell wall and lipoteichoic acid, may stimulate the porcine intestine and activate immunoglobulin (Ig) A production by means of Peyer's patches (Sukegawa et al., 2014). On the other hand, Atanasova et al. (2011) have reported that lipoteichoic acid produced by *Staphylococcus aureus* had an enhancing effect on the respiratory disease in pigs caused by porcine coronavirus; however, the mechanism of action is still unknown. Lipoteichoic acids exhibit structural variations within the same bacterial species and differ significantly across different microbial species (Villéger et al., 2014). These structural differences account for the species-dependent effects of lipoteichoic acids (Lee et al., 2021). Wall teichoic acids play a role in supporting cell wall integrity and ion homeostasis and have been linked to the adhesion of bacteria to host tissues. In addition to the Lactobacilli, the wall components (β -1,3/1,6-glucans and mannan-oligosaccharides) of *Saccharomyces cerevisiae* provided an increasing production of antioxidants, alleviating oxidative stress in weaning piglets (Alagbe et al., 2022).

Since many bacteria present in the outermost part of the wall, special proteins, the International Scientific Association of Probiotics and Prebiotics Consensus Statement also included the exter-

nal part of the wall, where the adhesion sites are located, in the definition of postbiotic (Salminen et al., 2021). For instance, both Archaea and Bacteria present surface layer proteins (Sleytr, 1997; Sára and Sleytr, 2000). These proteins self-assemble into a crystalline array, forming a continuous, protective layer on the cell surface and playing a critical role in adhesion to various surfaces (Sleytr et al., 2014). The capacity of microbes to adhere to epithelial and subepithelial tissue represents a pivotal initial phase in the successful colonisation of the mammalian intestine and other tissue sites, and therefore stimulates the host response to pathogens. Roselli et al. (2016) demonstrated *in vitro* that the *Lactobacillus amylovorus* surface layer protein may reduce the damage caused by *Escherichia coli* Enterotoxigenic F4⁺ on the human intestinal barrier.

Exopolysaccharides

Exopolysaccharides are biopolymers mainly produced by lactic acid bacteria and secreted into the extracellular environment. They can be classified into two groups based on their monomeric composition: homopolysaccharides, which are composed of identical monosaccharides, and heteropolysaccharides, composed of different monosaccharides (Angelin and Kavitha, 2020). Exopolysaccharides are used in a variety of contexts, including the food industry, where they are utilised for their stabilising and gelling properties. Moreover, they are used in the production of pharmaceuticals and in the development of functional foods. Exopolysaccharides have been summarised to possess a range of biological activities in both humans and animals (Werning et al., 2022), including immunomodulatory, antioxidant, anti-inflammatory, antibacterial, antiviral, and gastrointestinal activities (Angelin and Kavitha, 2020). As a result, it has emerged as a potential candidate for several biomedical and pharmaceutical applications.

Cell-free supernatant

Cell-free supernatants derived from microbial cultures have garnered significant attention in recent years for their potential applications in promoting animal health and performance. The term "cell-free supernatant" refers to the liquid component of a culture medium containing active metabolites and end-products derived from bacterial fermentation. These include organic acids, bacteriocins, peptides, and fatty acids, which vary according to the bacterial species (Moradi et al., 2019). As reported by Mani-López et al. (2022), cell-free supernatants derived from lactic acid bacteria exhibit a range of activities, including antioxidant, antimicrobial, antitumour and anti-inflammatory properties. These antimicrobial substances assist in maintaining a healthy microbial equilibrium and serve to protect against infections within the gastrointestinal tract. The cell-free supernatants of *Lactobacillus* spp. and *Pediococcus* spp. have been demonstrated to inhibit the growth of pathogenic *E. coli* isolated from pigs (Kaewchomphunuch et al., 2022), while the culture supernatant of *Lactobacillus plantarum* has been shown to have beneficial effects on the intestinal morphology of piglets with an increase in jejunal villus height (Maidana et al., 2019). Furthermore, cell-free supernatant obtained from *L. plantarum* can have a beneficial effect on the microbiota of the colonic mucosa in broilers, with an increase in the abundance of beneficial bacteria (Firmicutes) and a decrease in the abundance of harmful bacteria (Proteobacteria) (Danladi et al., 2022).

In some cases, the cell-free supernatants have been classified as postbiotics in their own right (Thorakkattu et al., 2022; Ali et al., 2023; Yan et al., 2024). However, in accordance with the conventional definition, a postbiotic must contain a proportion of microbial cells. In this instance, a cell-free supernatant is a preparation free from cell components which contains metabolites (Liu et al., 2023a). Additional research is required to ascertain whether these

compounds themselves meet the criteria for classification as postbiotics.

Material and methods

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (Liberati et al., 2009).

Search strategy

A systematic literature review was conducted between June 2023 and January 2025. The online databases “PubMed”, “Google Scholar”, “Web of Science”, and “Scopus” were applied using a Boolean approach, combining the operators (AND, OR, NOT) with keywords related to the identification of postbiotics and the pig species and pig category. The specific keywords used for the search are listed in Table 1, and the complete research strings are reported as Supplementary Table S1.

This review was not registered in PROSPERO as registration was not undertaken before initiating the analysis.

Eligibility criteria

To minimise bias during the screening process, a preliminary meeting was held to clarify the review’s purpose and establish the inclusion and exclusion criteria from the outset. Two reviewers (B.P. and F.C.) selected the studies by examining the titles, abstracts, and full manuscripts stored in a shared Zotero folder (version 7.0.27), following the predefined criteria. The resulting list of studies was then reviewed and approved by the other authors (P. T. and D.L.).

The literature search, conducted using the various keywords listed in Table 1, retrieved a total of 2 151 articles. As the primary objective of this review was to collect as much information as possible on the effects of these products on the growth and health parameters of pigs, and since the number of studies in the bibliography addressing the administration of postbiotics to pigs was limited, the inclusion and exclusion criteria were not highly restrictive. The articles were included or excluded based on the criteria outlined below.

The inclusion criteria were as follows:

(a) studies in which the postbiotic was tested *in vivo* on pigs or *ex vivo* on intestinal tissues derived from pigs; (b) articles based on interventional studies conducted on pigs, whether challenged or not orally supplemented with postbiotics; (c) articles in which at least a control group, without any inclusion of postbiotic, and a postbiotic group were included; (d) article reporting at least one of the parameters related to health, growth performance and/or gut health parameters listed in Supplementary Table S2.

Additional exclusion criteria were the following:

(a) duplicate articles; (b) articles not in the English language; (c) Thesis, review articles, abstracts, and short communications, opinions, and non-peer-reviewed articles; (d) studies in which the

postbiotic was defined as a set of bacterial metabolites without considering the cellular components in the preparation; in this case, the postbiotic definition and composition did not corresponded with the latest definition of postbiotic; e) studies in which the postbiotic was supplemented in combination with other additives, as prebiotics or probiotics; f) articles not focusing on the use of postbiotics in *in vivo* or *ex vivo* pigs were excluded. After filtering, 33 articles were retained. A specific description of the flow chart, including the article identification, is reported in Fig. 1. The complete list of articles is reported in Supplementary Table S3.

Evaluation of potential bias and study quality assessment

During the screening process for articles, potential sources of bias were examined and documented. These sources, which include publication bias, selection bias, and reporting bias, were examined to ensure the transparency of the evidence base. Cochrane Risk of Bias Tool 2 (RoB 2) was used to analyse the quality of the studies and the potential biases, including selection bias (randomisation and allocation of subjects), performance bias (blinding of operators), detection bias (blinding of outcome assessment), attrition bias (completeness of data), reporting bias (selective outcome reporting), and conflicts of interest. Each study was evaluated and classified as presenting low, moderate, or high risk of bias in each section. A comprehensive review of the extant evidence reveals limitations concerning the inadequate documentation of the absence of reported blinding, a factor that has the potential to influence the outcomes of studies. A comprehensive evaluation of the inherent risk of bias for each study is presented in Fig. 2(a), along with a summary of the overall risk of bias across individual domains in Fig. 2(b).

Data extraction

From the final set of 33 studies, data regarding pig class: sows or piglets, postbiotic classification, derived microbial species, dose, and duration of the supplementation were retrieved. In addition, data regarding general health, growth performance, and gut health parameters, including epithelial barrier and digestion, immunomodulation, oxidative stress homeostasis, and microbiota balance, were extracted (Supplementary Table S2).

To evaluate the effects of postbiotic supplementation, the increase or decrease in the parameters measured was calculated as a percentage in the groups fed with the postbiotics in comparison with the control group. Increase and decrease in percentage were calculated only in the presence of statistically significant ($P < 0.05$) or trend of significance ($P < 0.10$) between the postbiotic groups and the control group. Within each study, the control group was defined as the experimental group without postbiotics and antibiotics/pharmacological level of zinc supplementation. For the challenge studies, the control group consisted of pigs infected with bacteria (e.g., *Salmonella*, *E. coli*, etc.) without the use of antibiotics/pharmacological levels of zinc. For the studies with more postbiotic groups (i.e. different doses and/or different

Table 1

List of keywords used for the systematic research on the growth and health of sows and pigs supplemented with postbiotics.

Postbiotic name	Bacterial component	Swine	Category
Postbiotic	Exopolysaccharide	Pig	Gestating
Heat-treated product	Teichoic acid	Piglet	Lactating
Tyndallized probiotic	Peptidoglycan	Sow	Suckling
Inactivated probiotic	Cell-free supernatant	Litter	Weaning
Fermentation product		Offspring	Post-weaning
Yeast-derived product			
Treated yeast			
Bacterial lysate			

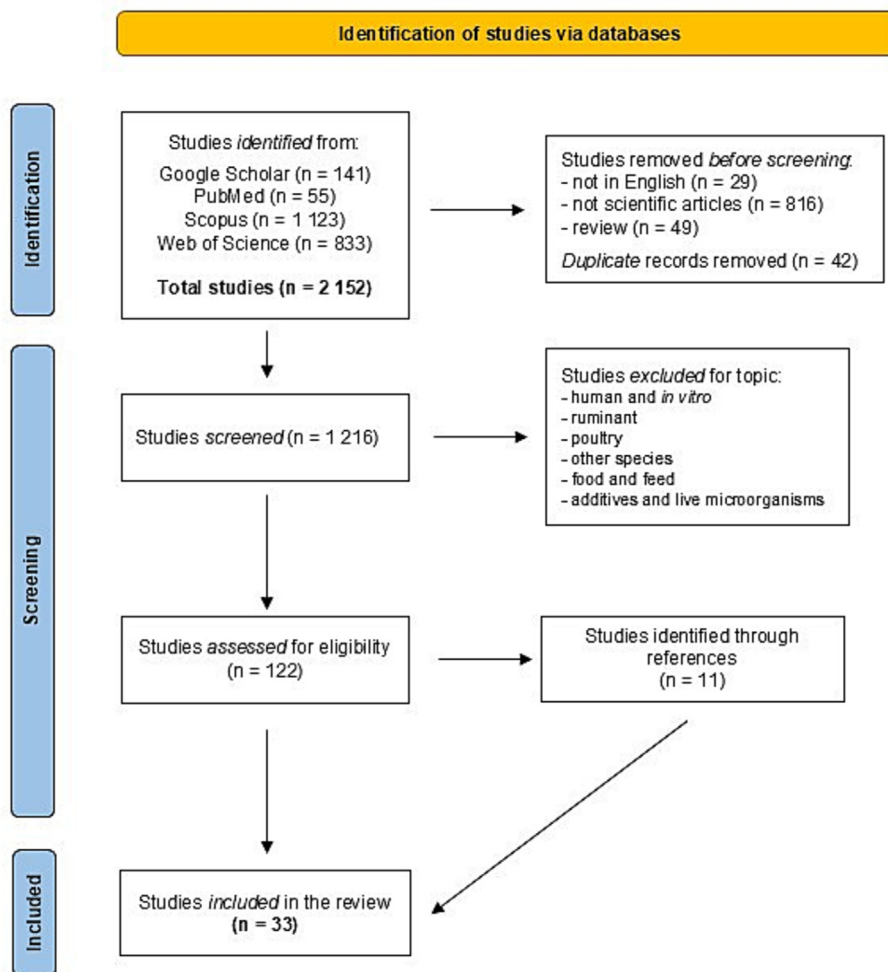


Fig. 1. Flow chart of the selection process of articles based on the postbiotic effects on pig gut health included in the systematic review.

strains), the comparison was achieved by calculating the average of the treatments against the control.

Results and discussion of the systematic search

Considering the origin of postbiotics, two macro categories of products were highlighted: postbiotics derived from yeast (18 studies) and postbiotics derived from bacteria (15 studies). Considering the class of pigs and their phases: 1 study concerned the administration of postbiotics to sows only during gestation, 9 studies concerned the administration of postbiotics to sows during gestation and lactation, 22 studies concerned the administration of postbiotics to lactating and post-weaning piglets, and there was 1 *ex vivo* study. Therefore, the presentation and discussion of the results will be divided into yeast-derived postbiotics and bacteria-derived postbiotics; within these macro categories, the results have been grouped according to the microbial species from which the postbiotic was produced, and its effect on sows and piglets. The results will be presented considering the effects on gut integrity, immune and oxidative status, microbiota balance and growth performance and health (mortality).

Yeast-derived postbiotics

The literature is particularly rich in studies involving the use of yeast as a postbiotic, especially postbiotics derived from different fermentation processes of *Saccharomyces cerevisiae* and, less fre-

quently, those from different *Pichia* species. The abundance of studies on postbiotics derived from yeast rather than bacteria could be attributed to the fact that, unlike bacteria, yeast used as a probiotic is unable to colonise the intestinal tract (Edwards-Ingram et al., 2007). Furthermore, some of the mechanisms of action behind their success as probiotics are often linked to cell wall stretching (Klis et al., 2002). Therefore, they are well-suited for use as postbiotics.

The results regarding the effects of postbiotics derived from *Saccharomyces cerevisiae* and *Pichia* on the gut health and performance of pigs are shown in Tables 2–5 for sows and piglets, respectively. Specifically, a total of 10 studies were identified regarding the postbiotics administered to sows, and 7 studies were identified regarding the yeast-based postbiotics administered directly to piglets during lactation and after weaning.

Saccharomyces cerevisiae

Since the ban of antibiotics as growth promoters in Europe (Reg. (CE) n. 1831/2003), the use of *Saccharomyces* yeast as a probiotic in livestock, particularly in swine, has increased (Ogbuewu et al., 2019). As described by Sampath et al. (2023), *S. cerevisiae* as a probiotic has multiple mechanisms of action in pigs, including the improvement of gut health and growth performance, immunomodulatory effects, and enhanced intestinal morphology (Trevisi et al., 2015; Luise et al., 2021). The mechanisms of action of the different components contained in the *Saccharomyces cerevisiae*-derived postbiotic are maintained due to its viable form,

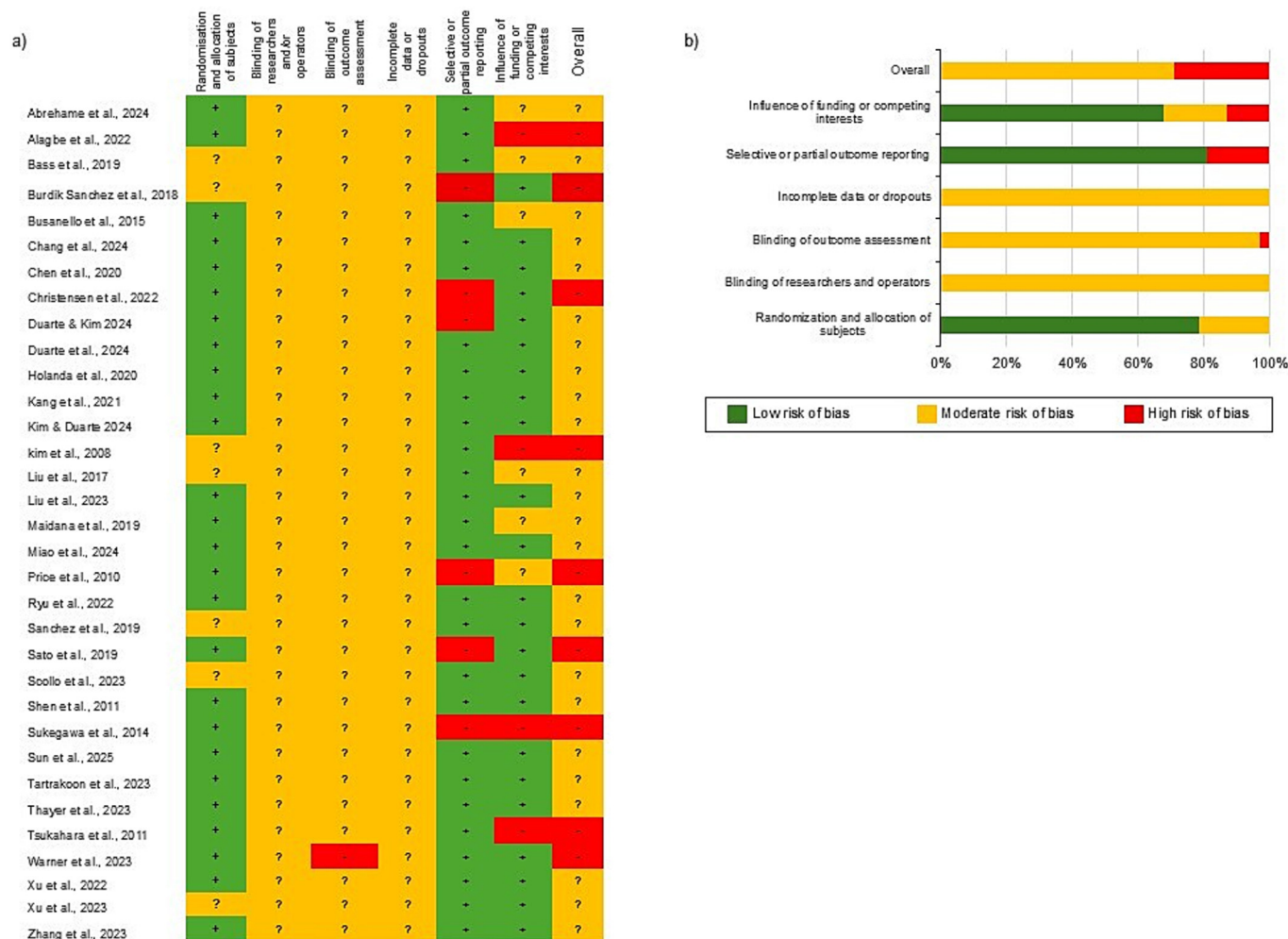


Fig. 2. (a) Risk of bias and overall quality assessment for the studies based on the postbiotic effects on pig gut health included in the review. (b) Summary of the risk of bias across individual domains.

thus resulting in its increased application in swine nutrition owing to its stability, ease of incorporation into feed, and potential of enhancing gut health, boosting immunity (Xu et al., 2023a), and improving overall animal performance (Kim and Duarte, 2024).

Sow

A total of 8 studies investigated the effects of postbiotic-derived *S. cerevisiae* on gestating and lactating sows (Tables 2 and 3). Parameters regarding its immunomodulatory effects were investigated on both colostrum and milk composition, as well as on the sow's blood. The effect of the *S. cerevisiae* fermentation product on immunity parameters in colostrum and milk composition is controversial. Shen et al. (2011) demonstrated that the supplementation of a *S. cerevisiae* fermentation product to the gestation and lactation diets of sows did not affect the colostrum and milk content of IgG. On the other hand, Xu et al. (2023a) reported no significant effects on colostrum immunoglobulin content but found increased IgA (+51%) and IgG (+65%) concentrations in milk at day 14 of lactation. Moreover, an immunomodulatory effect was observed on sows based on higher anti-inflammatory cytokine (Interleukin [IL]-10 and Transforming Growth Factor-β [+83%]) concentrations in the placenta. This enhancement in sow immunity was transferred to the piglets, which had higher concentrations of IgG and IgM in their blood. The immunostimulatory effect can be attributed to the presence of chitin and chitosan, two polysaccharides found in the cell wall of *S. cerevisiae* (Bulik

et al., 2003; Kliis et al., 2006). Due to its insoluble characteristics, chitosan, derived through the deacetylation of chitin, is hydrolysed by chemical or enzymatic treatments into chitosan oligosaccharide, becoming useful in different functional fields owing to its bio-compatible, mucoadhesive and non-toxic characteristics (Naveed et al., 2019). As described by Muanprasat and Chatsudthipong (2017), chitosan oligosaccharide has diverse biological properties, including anti-inflammatory, antioxidant and antibacterial effects. In fact, Duan et al. (2020) demonstrated that dietary supplementation of chitosan oligosaccharide in sows positively influenced colostrum IgM levels and increased the contents of IgG and IL-10 in piglet serum; the authors also noted a tendency for increased IgA, IgM, and lysozyme in the serum of piglets at weaning.

Several studies have demonstrated that the anti-inflammatory properties of chitosan oligosaccharides are mediated by means of various mechanisms, which include the suppression of the Mitogen-activated protein kinase and the Nuclear Factor Kappa-light-chain-enhancer of activated B cell (NF-κB) signalling pathways, as well as the activation of adenosine monophosphate-activated protein kinase (Muanprasat and Chatsudthipong, 2017; Naveed et al., 2019), inducing cascade reactions which ultimately downregulate the production of pro-inflammatory cytokines. Shen et al. (2011) also observed a decrease in neutrophil, white blood cell, and plasma urea nitrogen in sows (-30, -22, -12%, respectively). Interestingly, it is the reduction of plasma urea nitrogen (waste product created during the protein breakdown) in sows

Table 2
The effect of *Saccharomyces cerevisiae*-derived postbiotic supplementation on sows regarding their productive performance, immune status, oxidative stress, and microbiota balance.

Dose	Period	Gut health pillars					Reference
		Epithelial barrier and digestion	Immunomodulation	Oxidative stress homeostasis	Microbiota balance	Performance and health	
12 g/d + 15 g/d	12 g/d gestation + 15 g/d lactation	= ATTD of DM, ASH, CP, ether extract	↓ NEU (−30%), WBC (22%), PUN (−12%) = IgG (colostrum/milk)			= backfat thickness, BW, FI, wean to oestrus	Shen et al., 2011
3 g/kg	Late gestation to lactation			↑ T-AOC (serum) (+36%) ↓ MDA (colostrum, milk) (−38,-30%)		↑ n weaned pigs (+6%) = TB, BA,	Chen et al., 2020
2 g/kg	Late gestation to lactation	= VH, CD, V:C, goblet cells				↑ ADFI (+8%) = BA, n weaned pigs	Liu et al., 2023b
1.25–2 g/kg	Late gestation to lactation		↑ IgA (+51%), IgG (milk) (+65%), IgA (serum) (+31%), TGF-β (placenta) (+83%) = Igs (colostrum)	↓ GPX (Farrowing serum) (−18%), ↑ MDA (Lactation serum) (+44%)		↑ backfat deposition (gestation) (+142%) = TB, BA, SB, mummified	Xu et al., 2023a
50 mL/d	Gestation					↑ lactation efficiency (17%) = BA	Scollo et al., 2023
0.05–0.500 g/kg	Gestation and lactation					↑ BCS (farrowing) (+36%) ↓ wean to oestrus (−20%)	Kim and Duarte 2024
1.25–2.00 g/kg	Late gestation to lactation				↑ α-diversity, beneficial bacteria ¹ ↑ isobutyric acid (gestation) (+38%)		Chang et al., 2024

Abbreviations: ADFI = Average Daily Feed Intake; ASH = Ashes; ATTD = Apparent Total Tract Digestibility; BA = Born Alive; BCS = Body Condition Score; CD = Crypt Depth; FI = Feed Intake; GPX = Glutathione Peroxidase; Ig = Immunoglobulin; MDA = Malondialdehyde; NEU = Neutrophil; PUN = Plasma Urea Nitrogen; SB = Stillborn; T-AOC = Total Antioxidant Activity; TB = Total Born; TGF-β = Transforming Growth Factor Beta; VH = Villous Height; V:C = Villus To Crypt Ratio; WBC = White Blood Cell.

¹ = no numerical data available.

Table 3
The effect of *Saccharomyces cerevisiae*-derived postbiotic supplementation on sows and its effects regarding gut health indicators in piglets.

Dose	Period	Gut health pillars			Reference
		Immunomodulation	Oxidative stress homeostasis	Microbiota balance	
12 g/d + 15 g/d	12 g/d gestation + 15 g/d lactation				Kim et al., 2008
12 g/d + 15 g/d	12 g/d gestation + 15 g/d lactation	= IgG (plasma)		↑ LWV (+7%), ADG (+8%) = FI ↑ LWV (+11%), ADG (+12%)	Shen et al., 2011
3 g/kg 2 g/kg	Late gestation to lactation Late gestation to lactation		↑ MDA (thymus) (+101%) ↓ T-AOC (colon, ileum) (-13, 12%), GPX (liver, ileum) (-23, 45%)	↑ LWV (+9%), ADG (+6%) ↑ BW (+10%), ADG (+15%)	Chen et al., 2020 Liu et al., 2023b
1.25–2 g/kg	Late gestation to lactation	↑ IgM (serum) ¹ = IgG (serum)			Xu et al., 2023a
50 mL/d	Gestation			↓ mortality (-25%), diarrhoea ¹ ↓ mortality (-13%), antibiotic use in post-weaning (-41%) = LWV, faecal score	Scollo et al., 2023
0.05–0.500 g/kg	Gestation and lactation			↑ BW (+2%), ADG (+2%), G:F (+4%) ↓ ADFI (-48%), faecal score (-36%)	Kim and Duarte 2024
1.25–2 g/kg	Late gestation to lactation			↑ Bacteroidetes ¹ ↓ Butyric acid (-67%)	Chang et al., 2024

Abbreviations: ADFI = Average Daily Feed Intake; ADG = Average Daily Gain; FI = Feed Intake; G:F = Gain To Feed Ratio; GPX = Glutathione Peroxidase; Ig = Immunoglobulin; LWV = Litter Weaning Weight; MDA = Malondialdehyde; SCFAs = Short-Chain Fatty Acids; T-AOC = Total Antioxidant Activity.
¹ = no numerical data available.

during gestation; therefore, it can be deduced that the enhanced efficiency of protein utilisation during the final stages of gestation may be a contributing factor to the observed litter weight enhancement at weaning, probably due to an increase in milk production. According to Chen et al. (2020), in addition to supporting the immune system, *S. cerevisiae* postbiotics improved the antioxidant status of sows with a reduction in malondialdehyde levels in colostrum and milk (-34%), and an enhanced level of total antioxidant capacity in blood serum during gestation. Furthermore, the postbiotic enhanced the total antioxidant capacity in the sow placenta and decreased the glutathione peroxidase (GPX) concentration in sow serum during gestation (-18%) (Xu et al., 2023a). The antioxidant activity could be attributed to the antioxidant enzyme or vitamin content in the postbiotic preparation (Aguilar-Toalá et al., 2018) or to the exopolysaccharide capacity for inhibiting lipid peroxidation (Xu et al., 2011), thereby reducing the malondialdehyde concentration. Nonetheless, these findings appear to contradict Xu et al. (2023a), who reported elevated malondialdehyde levels in the serum of lactating sows. The study by Liu et al. (2023b) proceeded beyond the analysis of the oxidative status of sows, extending its scope to explore the potential effects of postbiotic administration on the oxidative status of piglets during the final stage of pregnancy. The authors found an enhanced level of malondialdehyde in the piglet thymus; the expression of antioxidant-related genes (*superoxide dismutase* and *GPX1*) in different tissues (thymus, spleen, jejunum, colon) was found to be downregulated to varying extents, and a reduction in total antioxidant capacity in the piglet colon was observed.

The effect of *S. cerevisiae* postbiotic was also investigated on the sow microbiota profile and short-chain fatty acids in two studies; in a recent study, Chang et al. (2024) showed that the *S. cerevisiae* postbiotic increased α -diversity in pregnant sow faeces, notably enhancing the abundance of Actinobacteria and *Limosilactobacillus*, a trend in reducing *Methanobrevibacter*, and promoted the growth of beneficial bacteria (Bacteroidetes) in piglet faeces. This postbiotic increased the content of isobutyric acid in gestating sows (+38%), while it reduced the content of butyric acid in piglet faeces, which was positively correlated with the increased abundance of *Bacteroides* (Chang et al., 2024). These effects could be attributed to the presence of β -glucans, which can act as prebiotic compounds, exerting a modulatory effect on commensal bacterial populations and promoting the enrichment of *Bacteroides*, thereby contributing to a beneficial effect on the gut microbiota (Fernandez-Julia et al., 2021). Conversely, Liu et al. (2023b) reported that the *S. cerevisiae* postbiotic reduced the abundance of *Lactobacillus* in the intestine of piglets from sows fed the postbiotic, while increasing the abundance of *Alloprevotella* and other genera related to gut health and growth performance.

The collective findings regarding the effects of postbiotic administration on immunity, oxidative status and intestinal health indicators have ultimately demonstrated an impact on growth performance in both sows and their offspring. Xu et al. (2023a) observed that the supplementation of the *Saccharomyces cerevisiae* postbiotic in the sow diet during both gestation and lactation periods increased backfat thickness at farrowing (+142%). Furthermore, Kim and Duarte (2024) demonstrated that the postbiotic had a beneficial impact on the growth performance of sows by ameliorating their body condition score (+36%), reducing the wean-to-oestrus period (-20%), and having a positive effect on their productive performance by enhancing the number of weaned pigs (Chen et al., 2020). It could be hypothesised that an increase in milk production by the sows occurred without affecting the nutrient composition of the colostrum and milk. In contrast, Shen et al. (2011) did not observe any differences in backfat thickness, BW or wean to oestrus period in sows with postbiotic supplementation. *S. cerevisiae*-derived postbiotic did not show any difference in sow

Table 4
The effect of *Saccharomyces cerevisiae*-derived postbiotic supplementation on lactating or post-weaning pigs regarding gut health indicators.

Dose	Period	Gut health pillars					Reference
		Epithelial barrier and digestion	Immunomodulation	Oxidative stress homeostasis	Microbiota balance	Performance	
20 g/kg	35 days	↑ CD (ileum) (+40%)			↑ Beneficial bacteria ¹		Price et al., 2010 (Salmonella challenge)
2 g/kg	36 days	↓ AID of DM (−9%), GE (−8%), nitrogen (−3%) = VH, VW, CD, V:C, Ki-67 ⁺	↓ AST (−23%), CPK (−54%), BUN/creatinine (−10%), TNF-α/IgA (−31%), ↑ glucose (+5%) = IL-1β, IL-10, TNF-α			↓ G:F (−3%) = BW, ADG	Holanda et al., 2020 (Mycotoxin challenge)
1–4 g/kg	43 days	↓ ATTD of ADF (−16%) ↑ ATTD of NDF (+8%), V:C (ileum) (+43%), ↓ PEPT1 (−22%), diarrhoea ¹ = OCLN, CLDN4, ZO-1	= IgA (ileum)	↑ CAT (+22%), GPX (+30%)	↓ <i>L. reuteri</i> (−41%) ↑ Butyrate (+33%)	= BW	Alagbe et al., 2022
5 + 2.5 g/kg	phase 1 (0–14d post-weaning) + phase 2 (15–42d post-weaning)	↑ ATTD of CP (+5%), DM (+3%), GE (+4%) ↓ CD (−12%) ↑ V:C (+22%) = B0AT1, EAAC1, PEPT1, SGLT1, ZO-1, OCLN	↑ IgA (jejunum) ¹ = IgA (plasma), IL-6, IL-10, TNF-α (jejunum)	= SOD	= SCFAs	↑ BW (+1%), ADG (+2%)	Christensen et al., 2022
0.175 g/kg	35 days	↑ VH (+12%), CD (+10%), Ki-67 ⁺ (+14%) ↓ faecal score (−45%) = CLDN-1, OCLN, ZO-1	↑ IFN-γ (+35%), mTOR (+38%) ↓ SGK1 (−8%), BAX1 (−19%), = IL-6, IL-8, TNF-α, IgA, IgG, NF-κB, TLR2, TLR4	= MDA, protein carbonyl			Duarte and Kim 2024
2 μg/kg	18 days		↑ TNF-α (+28%), IL-6 (+41%), ↓ NEU (−39%), = IFN-γ, red blood cells, haematocrit, haemoglobin, platelets, monocytes, eosinophils				Burdick Sanchez et al., 2018 (LPS challenge)
0.100–0.175 g/kg	119 days	↓ faecal score (−9%)				↑ BW (+3%), ADG (+4%), G:F (+2%)	Kim and Duarte 2024

Abbreviations: ADG = Average Daily Gain; AID = Apparent Ileal Digestibility; AST = Aspartate Aminotransferase; ATTD = Apparent Total Tract Digestibility; B0AT1 = System B(0) Neutral Amino Acid Transporter 1; BUN = Blood Urea Nitrogen; BAX1 = B-Cell Lymphoma 2-Associated X Protein 1; CAT = Catalase; CD = Crypt Depth; CLDN = Claudin; CPK = Creatine Phosphokinase; EAAC1 = Glutamate Transporter; GE = Gross Energy; GPX = Glutathione Peroxidase; G:F = Gain To Feed Ratio; Ig = Immunoglobulin; IL = Interleukin; IFN = Interferon; Ki-67+ = Cells Proliferation; mTOR = Mammalian Target Of Rapamycin; NEU = Neutrophils; NF-κB = Nuclear Factor Kappa-Light-Chain-Enhancer Of Activated B Cells; OCLN = Occludin; PEPT1 = Peptide Transporter 1; SCFAs = Short Chain Fatty Acids; SGLT1 = Sodium-Glucose Co-Transporter 1; SGK1 = Serum/Glucocorticoid Regulated Kinase 1; SOD = Superoxide Dismutase; TLR = Toll-like receptor; TNF = Tumour Necrosis Factor; VA = Villous Area; VH = Villous Height; VW = Villous Width; V:C = Villus To Crypt Ratio; ZO-1 = Zonula Occludens-1.

¹ = no numerical data available.

Table 5
The effect of the administration of *Pichia*-derived postbiotic on sows and post-weaning piglets.

Strain	Classification	Category	Dose	Period	Gut health pillars			Reference
					Epithelial barrier and digestion	Immunomodulation	Microbiota balance	
<i>Pichia guilliermondii</i>	Heat-inactivated product	Sow	1–2 g/kg 1.5 g/kg	Gestation and lactation	↓ NEU (+44%) = IgA, IgG, IgM (serum, colostrum, milk)		↑ mortality (+11%) = SB, mummified, BW, ADG, BW loss ↑ TB (+3%), BA (+3%), LW (+5%) ↓ treatment for scour (piglets) (–63%)	Bass et al., 2019 Thayer et al., 2023
<i>Pichia kudriavzevii</i>	Solid-state fermentation culture	Post-weaning pigs	5 g/kg	12 days (post-weaning)	↓ CD, diarrhoea ¹ ↑ VH, V:C ¹	↑ <i>L. reuteri</i> ¹	↑ ADG, F:G ¹	Zhang et al., 2023

Abbreviations: ADG = Average Daily Gain; BA = Born Alive; CD = Crypt Depth; F:G = Feed To Gain Ratio; Ig = Immunoglobulin; IL = Interleukin; LW = Litter Weight; NEU = Neutrophils; SB = Stillborn; TB = Total Born; VH = Villous Height; V:C = Villus To Crypt Ratio.
¹ = no numerical data available.

feed intake (Kim et al., 2008; Liu et al., 2023b; Scollo et al., 2023; Shen et al., 2011).

Scollo et al. (2023) observed that the administration of the *S. cerevisiae* postbiotic during gestation could enhance lactation efficiency by 17%, decreasing piglet mortality during lactation (–13%) and reducing the use of antibiotics after weaning (–41%), suggesting an improvement in the health status of piglets. The health benefit derived from the postbiotic could be associated with its ability to inhibit the adhesion of pathogens to the gut mucosa, as has been noted in humans (Mantziari et al., 2020), having the potential to reduce the necessity for antibiotics in piglets. *S. cerevisiae*-derived postbiotic administered to sows during gestation and/or lactation had a beneficial effect on the weaning weight of piglets (+7%) (Chen et al., 2020; Kim et al., 2008; Kim and Duarte, 2024; Liu et al., 2023b; Shen et al., 2011; Xu et al., 2023a) and on piglet performances from the weaning to the growing phase (BW, average daily gain [ADG], gain-to-feed [G:F] ratio) (Kim and Duarte, 2024). The observed increase in growth could be attributed to the protein content of the postbiotic preparation, which includes β-glucans, manooligosaccharides (Miguel et al., 2004), nucleotides, and surface layer protein (Shurson, 2018). Maternal supplementation of the postbiotic product enhanced other parameters regarding the growth performance of piglets, such as daily litter weight gain (Kim et al., 2008; Liu et al., 2023b) and the G:F ratio (Kim and Duarte, 2024), while also increasing the sow feed intake (+8%) (Liu et al., 2023b). The improved growth performance of the piglets was likely attributed to enhanced milk production, which was associated with the increased feed intake observed in the sows (Jiang et al., 2020). In some cases, *S. cerevisiae* postbiotic administration during gestation did not change the litter performance (Chen et al., 2020; Liu et al., 2023b; Scollo et al., 2023; Shen et al., 2017; Xu et al., 2023a), while in other cases, it reduced the incidence of diarrhoea and the mortality rate (–19%) during suckling (Scollo et al., 2023; Xu et al., 2023a).

The evidence suggests that supplementing gestating and lactating sows with *Saccharomyces cerevisiae*-derived postbiotics can exert multifaceted benefits, including immunomodulation (modulating immunoglobulins and cytokines), improved oxidative status (reducing GPX and malondialdehyde levels, and enhancing the total antioxidant capacity), favourable shifts in gut microbiota, and enhanced productive outcomes, although inconsistencies remain among studies. Due to the microbial cell structure, the β-glucans present in the *S. cerevisiae* cell wall seem to be primarily responsible for their mechanism of action, mediating the interactions with host receptors and the intestinal microbiota of the sow, exerting prebiotic effects. The main benefits, however, were observed indirectly in the litters, which exhibited an 8.25% increase in weaning weight, an 8.6% improvement in ADG, and a 19% reduction in mortality during lactation.

Suckling and weaning pigs

The administration of *S. cerevisiae* postbiotics to the suckling and weaning pigs' diets yielded a few promising results derived from a total of 7 studies, as reported in Table 4. In consideration of their potential mechanism of action, postbiotics have the capacity to function as antimicrobial compounds, thereby serving as a substitute for antibiotics. In this regard, *S. cerevisiae* postbiotics in piglets were predominantly tested in challenge models, with the objective of better clarifying their antimicrobial efficacy.

In a study conducted by Burdick Sanchez et al. (2018), weaned piglets were challenged with *E. coli* lipopolysaccharide, a cell wall component that stimulates innate immunity (Tan and Kagan, 2014). The authors explained that the administration of an *S. cerevisiae*-derived postbiotic could attenuate the acute phase response, thereby elevating the concentration of pro-inflammatory cytokines (Tumour Necrosis Factor-α [+28%], IL-6

[+41%]) in response to bacterial lipopolysaccharide. The stimulation of the immune system by lipopolysaccharides and other cell wall components (peptidoglycan) is achieved by means of a receptor-dependent process, which involves the host cell surface protein, CD14. This receptor is present on the surface of monocytes, macrophages, and polymorphonuclear leukocytes, and as a soluble protein in the blood, stimulating an immunological response (Tan and Kagan, 2014). *S. cerevisiae* postbiotic has been demonstrated to regulate the expression of pro-inflammatory cytokines (IL-6, IL-1 β , and NF- κ B) and enhance the levels of tight junction proteins in broilers (Chuang et al., 2021), thus showing the potential for fortifying the intestinal barrier function and reducing the occurrence of diarrhoea. However, Alagbe et al. (2022), Christensen et al. (2022) and Duarte and Kim (2024) did not observe any significant differences in the cytokine level of the jejunal mucosa of piglets when fed with the postbiotic product in an experimental study without the challenge test. The *S. cerevisiae* postbiotic had an immune activation in nursery pigs with an increasing IgA concentration in the jejunal tissue but not in the plasma (Christensen et al., 2022) or in the ileal mucosa (Alagbe et al., 2022). Furthermore, Duarte and Kim (2024) discovered an enhanced expression of Interferon- γ (+35%) and mechanistic Target Of Rapamycin (+38%) in the intestinal epithelium, and a reduced expression of Serum and Glucocorticoid-induced Protein Kinase 1 (*SGK1*) and B-cell Lymphoma 2-associated X protein 1 (*BAX1*) in the intestine.

In a mycotoxin challenge, Holanda et al. (2020) observed that when the *S. cerevisiae* postbiotic product (hydrolysed yeast cell wall) was added to the piglet diet, it led to a modification of the blood parameters by reducing aspartate aminotransferase (−23%), serum creatine phosphokinase (−54%), blood urea nitrogen/creatinine level, and enhancing glucose. The reduction in the blood urea nitrogen/creatinine ratio, concomitant with the increase in glucose, indicated that animals fed the postbiotic could exhibit enhanced efficiency in utilising protein and carbohydrate sources within their feed; in fact, the piglets maintained their growth performance. Several authors have illustrated the binding and absorbing capacity of the β -glucans contained in the cell wall of *S. cerevisiae* against mycotoxins (Yiannikouris et al., 2004; Jouany et al., 2005; Kogan and Kocher, 2007; El-Naggar and Thabit, 2014), thus reducing their bioavailability in the digestive tract, and maintaining or improving growth performance (Hahn et al., 2006; Weaver et al., 2023). Price et al. (2010) observed that the *S. cerevisiae* postbiotic was instrumental in helping to increase the BW in piglets challenged with *Salmonella*, probably by means of the improved immunity of the pigs due to the cell wall β -glucans which bind a receptor (Dectin-1) expressed on monocytes, macrophages and neutrophils, originating an inflammatory response (Brown et al., 2007), reducing the pro-inflammatory cytokine and enhancing the anti-inflammatory cytokine when the pigs were exposed to an immunological challenge (Li et al., 2005). The *S. cerevisiae* postbiotic also demonstrated a linear increase in catalase (+22%) and *GPX4* (+30%) expression with an increasing dose of postbiotic in the piglet diets, indicating a reduction in oxidative stress as reported by Alagbe et al. (2022). These outcomes are likely due to the antioxidant capacity of yeast β -glucans, which enhance the production of antioxidants by means of the activation of the Nuclear factor erythroid 2-related factor 2 (*NRF2*) signalling pathway, which regulates the expression of antioxidant proteins, thereby mitigating oxidative stress (He et al., 2022). However, on the other hand, the postbiotic supplementation did not show any differences in superoxide dismutase-1 (Christensen et al., 2022), malondialdehyde, and protein carbonyl in the study by Duarte and Kim (2024). Regarding the modulation of the microbiota, data from only two studies were available. Challenged pigs supplemented with *S. cerevisiae* postbiotic exhibited an increased abundance of *Bacteroides* and *Lactobacillus* in their faeces, promoting

the proliferation of beneficial bacteria in the gastrointestinal tract (Price et al., 2010), while according to Alagbe et al. (2022), the *S. cerevisiae* postbiotic reduced the abundance of *Lactobacillus reuteri* (−41%). These effects can be attributed to the β -glucans present in the postbiotic preparation, which serve as substrates for bacteria to produce short-chain fatty acids (Russo et al., 2012; Petit et al., 2022); however, data are too limited to conclude.

Regarding the epithelial barrier and the pillars of digestion, the *S. cerevisiae* postbiotic increased crypt depth (+41%) in *Salmonella*-challenged pigs (Price et al., 2010); without a challenged model, the postbiotic promoted the epithelial structures by reducing the crypt depths (−12%) and enhancing the villus height to crypt depth ratio (+32%) (Alagbe et al., 2022; Christensen et al., 2022), enhanced the levels of villus height, crypt depth and crypt cell proliferation (+14%) (Duarte and Kim, 2024), resulting in a greater absorptive and digestive capacity in pigs, even if the postbiotic supplementation did not alter the gene expression for nutrient transporters. The correlation between the villous growth and the mode of action of a heat-killed strain has been explained by Tsukahara et al. (2011), who showed the link between the stimulation of the immune system (IL-1 β and Tumour Necrosis Factor- α) and the villous extension already demonstrated by Maheshwari (2004). No differences in the tight junction proteins were observed in the above-mentioned studies. On the contrary, reduced apparent total tract digestibility of ACF (−16%) was demonstrated by Alagbe et al. (2022), and increased DM, gross energy, and CP were observed by Christensen et al. (2022). Holanda et al. (2020) demonstrated that pigs that underwent a mycotoxin challenge and were supplemented with a postbiotic exhibited a reduction in the apparent ileal digestibility of nutrients, thus implying a reduction in ADG and the G:F ratio (−3%) in the first week. This phenomenon can be attributed to the low digestibility of the β -D-glucans (Lam and Chi-Keung Cheung, 2013) present in the postbiotic preparation.

Finally, the physiological implication of *S. cerevisiae* postbiotic supplementation led to the improved growth of piglets (ADG) (Kim and Duarte, 2024; Christensen et al., 2022); an enhanced intestinal health was observed with a reduction in the faecal score (−27%) and diarrhoea (Alagbe et al., 2022, Kim and Duarte, 2024, Duarte and Kim, 2024).

The available evidence indicates that *Saccharomyces cerevisiae*-derived postbiotics can exert beneficial effects when directly supplemented to suckling or weaning pigs, particularly under pathogenic or mycotoxin challenge conditions. Their actions include modulation of inflammatory responses, enhancement of antioxidant defences, improvement of intestinal morphology, and partial stabilisation of gut microbiota by promoting beneficial bacteria such as Actinobacteria, reducing Spirochaetes abundance and diarrhoea incidence, and ultimately contributing to better digestive function due to the β -glucans' absorptive capacity of mycotoxins, thus reducing their bioavailability in the digestive tract. However, results across studies remain inconsistent, especially under non-challenge conditions. The variability observed in immune, oxidative, and microbial responses suggests that the efficacy of postbiotics is strongly context dependent.

Effect of *Pichia* postbiotic supplementation on sows and piglets

Species of the *Pichia* genus, particularly *Pichia guilliermondii* and *Pichia kudriavzevii*, have gained attention in animal nutrition and health due to their probiotic properties (Tran et al., 2024), enzyme production capabilities (Sharma et al., 2024), and potential as a feed additive. A total of 3 studies using postbiotics derived from *Pichia* were found; two of them were focused on sows and one on piglets (Table 5). According to the study by Bass et al. (2019), a whole-cell inactivated yeast product derived from *P. guilliermondii* was added to the sow diets (both in gestation and lacta-

tion); no differences were observed in the immunoglobulin profile of the sow serum, colostrum or milk, while an enhanced level of peripheral blood neutrophils (+44%) was reported.

However, the supplementation of *P. guilliermondii* postbiotic demonstrated a positive effect on the productive performance of the sows by increasing the number of piglets born alive, their birth weight, and weaned piglets/sow (Bass et al., 2019). Comparable outcomes were also obtained by Thayer et al. (2023) in which the postbiotic derived from *P. guilliermondii* increased the total number of piglets born (+3%), the number of piglets born alive (+3%), and heavier litter weights of the piglets born alive (+5%); moreover, the percentage of the litter treated for diarrhoea decreased (−63%) when the sow diets were supplemented with the postbiotic. Therefore, although the productive responses following postbiotic administration were positive, the data available are still too limited to clearly define the underlying mechanism of action.

Regarding piglets, the one study regarding the use of a *Pichia kudriavzevii* FZ12 postbiotic, supplemented in the piglet diets during the post-weaning phase, showed positive effects on ADG and intestinal health, including a reduction in diarrhoea incidence (Zhang et al., 2023). The positive outcomes observed regarding piglet growth and reduction in diarrhoea can be primarily attributed to the beneficial effects of the postbiotic on the intestinal parameters and on their immune status, due to the presence of mannan-oligosaccharide, β -glucan, d-mannose, and α -methyl-D-mannoside in the postbiotic preparation (Shanmugasundaram and Selvaraj, 2012). The *Pichia kudriavzevii*-derived postbiotic had a favourable effect in reducing the pro-inflammatory (IL-1 β , IL-6, IL-8) markers and in increasing the villus height in the jejunum (Zhang et al., 2023). It also increased the gut microbiota by enhancing *Lactobacillus*, *Ruminococcus*, *Prevotella*, and *Butyrivibrio* genera. In particular, the authors observed an increase in *Limosilactobacillus reuteri* and its biofilm formation in the intestinal microbiota of piglets associated with the presence of cytochrome c, acting as a scavenger of reactive oxygen species (Giannattasio et al., 2008), and glutathione S-transferase in the postbiotic product.

Overall, since only three studies are currently available concerning piglets and sows, additional research is required to confirm the positive effects of this postbiotic in piglets. Nevertheless, the *Pichia* genus used as a postbiotic has shown beneficial effects in both sows and pigs. It can be speculated that the yeast cell wall components, including mannan-oligosaccharides, β -glucans, D-mannose, and α -methyl-D-mannoside, are responsible for the mechanism of action, functioning both as prebiotics that stimulate the microbiota and as modulators that reduce pro-inflammatory cytokines.

Postbiotics derived from bacteria

Regarding bacterial-derived postbiotics, the literature predominantly focuses on various categories of postbiotics derived from different *Lactobacillus* species, with 11 studies examining their effects, while Enterococcus-derived postbiotics were investigated in only 3 studies of the review research.

Lactobacilli postbiotic supplementation in suckling and weaning pigs

Lactobacilli are widely used in animal husbandry, including in the rearing of pigs. The administration of these bacteria, which are commonly included as probiotics, has been demonstrated to promote a balanced gut microbiota (Huang et al., 2004) and improve digestion (Giang et al., 2011) and growth performance (Abe et al., 1995), thus reducing the incidence of gastrointestinal diseases in pigs (Huang et al., 2004). Notwithstanding the aforementioned outcomes attained through the utilisation of viable Lac-

tobacilli, there is some evidence about the administration of *Lactobacilli* in their postbiotic form in suckling and post-weaning piglets (Tables 6 and 7). To date, no studies have been identified in which *Lactobacilli* postbiotics have been assessed in sows.

One of the observations that emerged from the review was the ability of postbiotics derived from various *Lactobacillus* species to directly inhibit the growth and adhesion of certain pathogens, in particular *Escherichia coli*. According to the study by Wang et al. (2010), the exopolysaccharides derived from *Lactobacillus reuteri* inhibit the adhesion of *E. coli* K88 (F4) fimbriae on the intestinal epithelium of pigs, potentially through interaction with the β -D-galactose present on the cell surface receptors, which serve as binding targets for K88 fimbriae (Sellwood, 1980). Binding inhibition could be due to the presence of aggregating compounds, receptor analogues or competitive exclusion (Korakli and Vogel, 2006). Another hypothetical mechanism of action could be the presence of teichoic acid in the cell wall of *Lactobacilli*; lipoteichoic acids extracted from various *Lactobacillus* strains have been demonstrated to have an effect on the prevention of initial oral biofilm formation and the disruption of pre-established biofilms (Kim et al., 2019). Furthermore, in an *in vitro* study involving human epithelial cells, the pretreatment of host epithelial cells with surface layer protein, extracted from *Lactobacillus helveticus*, before infection with *E. coli* O157:H7, resulted in a reduction in pathogen adherence and attaching-effacing lesions in addition to the preservation of the barrier function of the monolayers (Johnson-Henry et al., 2007).

It is therefore possible that the preventive or antagonistic effect against pathogens is also mediated by a direct action of *Lactobacillus*-derived postbiotics on the structural integrity and architecture of the intestinal mucosa. In an *ex vivo* study using jejunal explants from weaning piglets, Maidana et al. (2019) observed that exposure to a culture supernatant from *L. plantarum* enhanced the intestinal morphology, characterised by increased villus height and decreased crypt depth. This beneficial effect could be attributed to the production of bioactive molecules during the culture process, promoting intestinal epithelial homeostasis by means of specific signalling pathways (Yan et al., 2007). Conversely, explants exposed to heat-inactivated *L. plantarum* demonstrated mild atrophy and bacterial adherence to the villi, resulting in a moderate toxic effect represented by villi atrophy, enterocyte flattening, and necrosis (Maidana et al., 2019). The administration of *Lactobacilli* has been shown to boost the immune system (Jang et al., 2013). As regards the blood parameters of piglets, Busanello et al. (2015) observed no differences in total serum protein, albumin, or glucose, but instead observed a reduction in the globulin level (−19%). Kang et al. (2021) also reported that the white blood cells and C-reactive protein remained unaffected, while Sanchez et al. (2019) reported a decrease in white blood cells, neutrophils, and lymphocytes. Specifically, regarding the immune parameters, the administration of postbiotics derived from *Lactobacillus* (*L. fermentum* and *L. delbrueckii*) enhanced the immunocompetence of weaned pigs in a challenge model (*E. coli* F18 +) by upregulating the expression of immune-stimulating molecules, including Interferon- γ and Peptidoglycan Recognition Protein 4. Concurrently, this treatment resulted in the downregulation of genes involved in pathogen recognition, including *TLR 4*, *Nucleotide-binding Oligomerisation Domain 1*, and *CD14*, which suggests a reduction in pathogen invasion (Duarte et al., 2024). In addition, exopolysaccharides from *Lactobacillus* have been shown to play a pivotal role in modulating the innate immune response by means of their interaction with pattern recognition receptors, including TLRs and C-type lectin receptors; these pattern recognition receptors are expressed on intestinal epithelial cells and immune cells within the lamina propria (Oerlemans et al., 2021). However, the correct mode of action and the activation pathway still need to

Table 6
The effect of different forms of postbiotic supplementation derived from various strains of *Lactobacillus* on gut health indicators in suckling or weaned pigs.

Strain	Classification	Dose	Period	Gut health pillars					Reference
				Epithelial barrier and digestion	Immunomodulation	Oxidative stress homeostasis	Microbiota balance	Performance	
<i>L. plantarum</i>	Heat-inactivated product	1 mL	35 days (suckling)		↓ globulin (−19%) = total serum protein, albumin, glucose		= Lactobacilli, Coliforms	↑ FI (+24%), ADG (+46%)	Busanello et al., 2015
		1.1 × 10 ⁸ – 2.0 × 10 ⁹ CFU/ml	4 h (post-weaning)	= VH, CD					Maidana et al., 2019 (<i>ex vivo</i>)
	CFS ²	0.02 g/kg + 0.004 g/kg	20 mg/kg from suckling + 4 mg/kg finisher phase 1	= VH, CD, VA, V:C	↑ IFN-β ¹ , platelet (+143%) = IL-12			↑ ADG (+9%), BW (+4%)	Tartrakoon et al., 2023
<i>L. reuteri</i>	Heat-inactivated product	1.1 × 10 ⁸ – 2.0 × 10 ⁹ CFU/ml	4 h (post-weaning)	↑ Villi atrophy, necrosis ¹ ↓ CD ¹ ↑ VH ¹					Maidana et al., 2019 (<i>ex vivo</i>)
		10 ⁸ CFU/mL	20 days (suckling)	↑ pBD2, pBD3, pBD114, pBD129, PPARγ, GPR41 ¹			↑ Butyrate (+34%), propionate (+22%)	↑ ADG (+15%) = BW	Liu et al., 2017
	CFS ²	0.5 g/kg	30 days (post-weaning)		↑ Coenzyme Q10 ¹ ↓ 3-hexanoyl-NBD cholesterol ¹	↓ MDA ¹ ↑ SOD ¹	↑ Firmicutes, propionate, butyrate ¹ ↓ Bacteroidetes ¹	↓ mortality ¹	Sun et al., 2025
		10–20 – 50 g/kg	24 h (post-weaning)		↓ endotoxin (serum) (−62%)			= F:G, FCR	Abreham et al., 2024

Abbreviations: ADG = Average Daily Gain; CD = Crypt Depth; FCR = Feed Conversion Ratio; F:G = Feed To Gain Ratio; FI = Feed Intake; GPR41 = Free fatty Acid Receptor 3 (GPR41 or FFAR3); IFN = Interferon; IL = Interleukin; MDA = Malondialdehyde; pBD = Porcine Beta Defensin; SOD = Superoxide Dismutase; PPARγ = Peroxisome Proliferator-Activated Receptor Gamma; VA = Villous Area; VH = Villous Height; V:C = Villus To Crypt Ratio.

¹ = no numerical data available.

² CFS = Cell Free Supernatant.

Table 7
The effect of different forms of probiotics derived from various strains of *Lactobacillus* supplementation on weaned pigs regarding gut health indicators.

Strain	Classification	Dose	Period	Gut health pillars				Reference	
				Epithelial barrier and digestion	Immunomodulation	Oxidative stress homeostasis	Microbiota balance		Performance and health
<i>L. rhamnosus</i>	Heat-inactivated product	1–4 g/kg	28 days (post-weaning)	↑ ATTD of GE (+3%), = ATTD of DM, CP	↓ TNF- α (–35%), TGF- β 1 (–23%), cortisol (–24%), = white blood cells, CRP			↑ BW (+10%), ADG (+26%), G:F (+26%) ↓ post-weaning diarrhoea* = ADFI	Kang et al., 2021
<i>L. fermentum</i> and <i>L. delbrueckii</i>		2 g/kg	28 days (post-weaning)	↓ Ki-67* (–25%) = VH, VW, CD, V: C	↓ IL-8 (–45%) = IgG, IgA, TNF- α , IL-6	= MDA, protein carbonyl ↓ MDA (–46%) = protein carbonyl	↑ Actinobacteria (+251%) ↓ Spirochaetes (–69%)	↑ BW (+14%), ADG (+30%), ADFI (+22%) = faecal score ↑ G:F (+12%), ADFI (+17%), ↓ faecal score (–10%), = BW, ADG	Xu et al., 2022 (<i>E. coli</i> challenge) Duarte et al., 2024 (<i>E. coli</i> challenge)
		2 g/kg	28 days (post-weaning)	= VH, VW, CD, V:C, Ki-67*	↑ IFN- γ , PGLYRP4 ↓ TLR4, NOD1, CD14 ¹ , TNF- α (–20%), = IL-8		↑ <i>P. stercora</i> (373%), <i>D. succinatiphilus</i> (+267%) = Firmicutes, Bacteroidetes, Proteobacteria, Actinobacteria		
<i>L. acidophilus</i>		0.6 g/kg	30 days (40 day post-weaning)				↑ α -diversity, Bacillus, Nitrospira, RB41, MND1 ¹ ↓ Methanospaera ¹ , = Lactobacillus = α -diversity	↑ BW (+8%), ADG (+14%), ADFI (+5%), ↓ F:G (–8%), diarrhoea rate (–55%) ↑ ADFI (+20%)	Miao et al., 2024
<i>L. salivarius</i>		2 g/kg	28 days (growing)					↓ BW (–10%), ADG (–37%), G:F (–47%) ↑ mortality (+10%), euthanised (+16%)	Ryu et al., 2022
<i>L. lactis</i>	Fermentation product	0.024 g/kg BW	42 days (post-weaning)					↓ antibiotic injection (–8%) = BW, ADG, ADFI, G:F ↓ ADG (–74%), G:F (–75%) = BW	Warner et al., 2023
<i>L. acidophilus</i>		1–2 μ g/kg	18 days (post-weaning)		↓ platelets (–7%), NEU (–16%), lymphocytes (–13%) ↑ monocytes (+12%), haematocrit (+3%)				Sanchez et al., 2019 (LPS challenge)

Abbreviations: ADFI = Average Daily Feed Intake; ADG = Average Daily Gain; ATTD = Apparent Total Tract Digestibility; CD = Crypt Depth; CD14 = Cluster Of Differentiation 14 (Pattern Recognition Receptor); CRP = C-Reactive Protein; F:G = Feed to Gain Ratio; GE = Gross Energy; G:F = Gain To Feed Ratio; IFN = Interferon; Ig = Immunoglobulin; IL = Interleukin; Ki-67* = Cells Proliferation; MDA = Malondialdehyde; NEU = Neutrophils; NOD = Nucleotide-Binding Oligomerization Domain-Containing Protein (Protein Receptor); PGLYRP = Peptidoglycan Recognition Protein; TGF = Transforming Growth Factor; TLR = Toll-like receptor; TNF = Tumour Necrosis Factor; VH = Villous Height; VW = Villous Width; V:C = Villous To Crypt Ratio.

¹ = no numerical data available.

be fully confirmed; in fact, according to the study of Xu et al. (2022), a *Lactobacillus*-derived postbiotic (*L. fermentum* and *L. delbrueckii*), tested in weaning piglets challenged with *E. coli* F18+, allowed reducing the IL-8 levels (−45%), indicating reduced inflammation; however, no differences were observed in IgG, IgA, IL-6 and Tumour Necrosis Factor- α .

In addition, the use of cell-free supernatant from various *Lactobacillus* strains (*Ligilactobacillus salivarius*, *Lactobacillus gasseri*, and *Limosilactobacillus reuteri*) demonstrated comparable outcomes to those observed in piglets receiving antibiotic treatment, as evidenced by reduced serum endotoxin levels (−62%) and increased anti-inflammatory cytokine IL-10, indicating improved resilience to the intestinal barrier damage induced by weaning (Abreham et al., 2024). This phenomenon could be attributed to the capacity of cell-free supernatant derived from lactic acid bacteria to stimulate IL-10 secretion by Peripheral Blood Mononuclear Cell-derived macrophages, either prior to or following a lipopolysaccharide challenge (De Marco et al., 2018). Non-viable *Lactobacillus rhamnosus* and its peptidoglycan have already been shown to have an immunostimulant effect in malnourished mice, enhancing the production of pro-inflammatory cytokines and IL-10 (Kolling et al., 2015).

Oxidative stress parameters were also analysed in the studies selected. Both Duarte et al. (2024) and Sun et al. (2025) observed reductions in malondialdehyde levels (−46%) following postbiotic supplementation, suggesting a potential role for postbiotics in mitigating oxidative damage. In addition, Sun et al. (2025) reported an increase in superoxide dismutase activity, additionally supporting the idea that these treatments could reduce oxidative stress during the post-weaning period. Interestingly, no significant effects were observed on protein carbonyl levels (Xu et al., 2022; Duarte et al., 2024), suggesting that the main benefits of postbiotic supplementation may lie in reducing oxidative damage rather than altering protein oxidation.

Regarding the microbiota and microbial-derived products, the literature is still scarce. *Lactobacillus reuteri* postbiotic upregulates the content of propionic and butyric acids in piglet faeces; those outcomes could be linked to the upregulation of Firmicutes and the downregulation of Bacteroidetes, thereby promoting an improvement in the structure of the intestinal microbiota (Sun et al., 2025). Moreover, inactivated *L. fermentum* and *L. delbrueckii* supplementation increased α -diversity and the abundance of beneficial taxa, such as *L. salivarius*, *Propionibacterium acnes*, *Phascolarctobacterium stercora* (+373%), and *Dialister succinatiphilus* (+267%), without major shifts in the dominant phyla (Duarte et al., 2024; Xu et al., 2022). In the same way, inactivated *Lactobacillus acidophilus* supplemented to growing pigs was able to influence the gut microbiota (α -diversity) (Miao et al., 2024), reduce the abundance of pathogenic bacteria as *Prevotella* and increase the Bacteroidetes (Ryu et al., 2022).

Several studies have investigated the effects of *Lactobacillus*-derived postbiotics on piglet performance and health, for the most part leading to beneficial outcomes with some variability depending on the strain, administration period, and measured outcomes. Kang et al. (2021) observed improved ADG (+26%) and G:F (+26%) in weaned piglets administered heat-killed *Lactobacillus rhamnosus* for four weeks post-weaning. Similarly, Busanello et al. (2015) reported that supplementing piglets with a combination of inactivated *Lactobacillus* spp. and *Lactobacillus plantarum* from birth to 35 days of age positively affected weight gain during the nursery phase (21–35 days) (+46%). Consistent outcomes were observed by Tartrakoon et al. (2023), who supplemented heat-killed *L. plantarum* from the suckling to the finishing phase. The supplementation increased weight gain in weaned pigs, improved ADG during both the weaning and the growing-finishing phases, and enhanced feed efficiency during the finishing phase. Similar

to the beneficial outcomes derived from *Lactobacillus plantarum*, a postbiotic derived from *Lactobacillus reuteri* enhanced the ADG and reduced the incidence of diarrhoea during the suckling period (4–24 days) (Liu et al., 2017). These potential benefits could be maintained during the growing period (\pm 30 kg) of piglets (Miao et al., 2024) integrated with heat-killed *Lactobacillus acidophilus*, having better growth performance (BW, ADG, feed to gain ratio) and reduced diarrhoea rate. While not observing significant improvements in growth performance in piglets fed a diet supplemented with *L. reuteri* postbiotic during the post-weaning period, Sun et al. (2025) reported a 6.37% reduction in mortality. This effect could be linked to reduced weaning stress, as evidenced by lower malondialdehyde levels and increased superoxide dismutase activity in the blood. A similar protective effect was observed by Sanchez et al. (2019), who investigated the effects of the postbiotic product from *Lactobacillus acidophilus* in weaned piglets challenged with lipopolysaccharides. Supplemented piglets showed increased BW and a reduced acute inflammatory response, indicating a protective immunomodulatory effect. Conversely, Duarte et al. (2024) found no significant improvement in the growth or general health of *E. coli*-challenged piglets receiving the postbiotic (*L. fermentum* and *L. delbrueckii*). However, Xu et al. (2022) provided mechanistic insight, showing that *Lactobacillus* can reduce the enterocyte proliferation in the crypt (−25%), suggesting a decreased need for crypt cell proliferation, which could indicate the prevention of epithelial damage, thus contributing to promoting growth performance, including BW (+14%), ADG (+30%), and average daily feed intake (+22%) in challenged piglets. Finally, Warner et al. (2023) observed no effect on the growth performance of weaned pigs supplemented with the *Lactococcus lactis* postbiotic administered via drinking water. However, the study reported a higher percentage of piglets requiring euthanasia during the first two post-weaning weeks, along with a reduction in the overall number of antibiotic injections per day (−8%).

In conclusion, *Lactobacillus*-derived postbiotics appear to positively influence pigs' health by enhancing gut integrity, modulating immune responses, and reducing oxidative stress. Their antimicrobial and anti-inflammatory properties contribute to improved resilience and, in some cases, better growth performance. Their effects are mainly attributed to the exopolysaccharides they produce, which interact with pattern recognition receptors and inhibit the adhesion of *E. coli* K88 F4 fimbriae to the intestinal epithelium. However, the variability among studies indicates that their efficacy depends on strain, dosage, and experimental conditions. Further research is needed to fully elucidate their mechanisms of action and optimise their use in swine nutrition.

Postbiotics from Enterococci

The use of Enterococci as postbiotics was found in three studies which dealt with post-weaning piglets. Sato et al. (2019) observed that a postbiotic derived from *Enterococcus faecium* administered in post-weaning diets improved piglet growth performance, achieving results comparable to the probiotic form. However, no differences were observed in α -diversity indices of gut microbiota, and there were no data regarding the effect on the epithelial barrier, digestion, or immunity. On the contrary, Sukegawa et al. (2014) did not observe improvements in weight gain but reported alterations in the microbial profile. Piglets treated with the postbiotic exhibited higher concentrations of *Lactobacillus* spp., *Enterococcus* spp., *Clostridium*, and Enterobacteriaceae. Similarly, treated piglets showed increased concentrations of secretory IgA, which may have been stimulated by specific components of the postbiotic preparation, such as cell wall fragments or lipoteichoic acids. The third study tested the effect of heat-killed and dried cell preparations from the *Enterococcus faecalis* postbiotic in early weaned piglets; according to the results, its supplementation alleviated the villus

atrophy induced by weaning, resulting in increased villus height (Tsukahara et al., 2011), thus improving intestinal health. However, no other data were reported.

These findings suggested that Enterococci-based postbiotics may have beneficial effects on intestinal health and growth performance, although more research is needed to fully understand their impact on the immune function and gut microbiota composition.

Conclusion

This systematic review summarises the potential mechanisms of action of postbiotic preparations in relation to their microbial origin. To the Authors' knowledge, only yeast-derived postbiotics, specifically from *Saccharomyces* and *Pichia*, have been tested in sows, limiting current findings to these two species. Postbiotics derived from *Lactobacillus* species have been more extensively studied in suckling and growing piglets, even under challenging environmental conditions involving pathogens or mycotoxins, thereby highlighting their potential role in recovery and resilience. As discussed throughout the review, the mechanisms of action appear closely linked to the structural components of the original microbial cell, which determine the functional properties of each postbiotic preparation. However, a major limitation identified across studies is the heterogeneity in both administered doses and the uncharacterised composition of the postbiotic hinders direct comparisons between trials. Future research should therefore aim to standardise postbiotic formulations and dosing protocols to allow for more reliable evaluation of their efficacy and mechanisms of action in pigs.

Supplementary material

Supplementary Material for this article (<https://doi.org/10.1016/j.animal.2025.101749>) can be found at the foot of the online page, in the Appendix section.

Ethics approval

Not applicable.

Data and model availability statement

None of the data were deposited in an official repository. All data and materials used in this study are available from the authors upon request.

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During the preparation of this work the author(s) did not use any AI and AI-assisted technologies.

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Declaration of interest

None.

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