

# Bioactive Metabolites from Marine Algae as Next-Generation Immunotherapeutics for *Sus scrofa*: A Narrative Review of Mechanistic Insights and Applications in Precision Livestock Farming

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## Abstract

Rising antibiotic resistance and growing demand for sustainable livestock practices have driven increasing interest in marine algae as a source of natural immunomodulatory compounds that enhance disease resistance in pigs (*Sus scrofa*). This narrative review examined marine algae compounds including sulfated polysaccharides, polyphenols, carotenoids, bioactive peptides, and omega-3 polyunsaturated fatty acids, as potential therapeutic agents for precision livestock farming through their immunomodulatory effects. We conducted a comprehensive literature review across three databases, which included PubMed, Semantic Scholar, and Google Scholar, using Boolean-combined keyword combinations related to marine algae bioactives, *Sus scrofa* immunotherapy, and precision livestock farming (PLF). The review found that these metabolites interact with pattern-recognition receptors (PRRs), including Toll-like receptors (TLRs), on porcine immune cells, activating the nuclear factor kappa-light-chain-enhancer of activated B cells/mitogen-activated protein kinase (NF- $\kappa$ B/MAPK) signalling axis and modulating both pro- and anti-inflammatory cytokine production. There is varying quality of evidence for fucoidan-rich polysaccharides and  $\beta$ -glucans reducing intestinal inflammation, improving gut barrier integrity, and enhancing humoral immune response to a PRRSV vaccine in pigs. PLF can provide for targeted delivery of these bioactives through the use of AI-driven sensor networks and automatic feeding systems that are tailored to specific animal health status and production phase. There are several challenges, such as batch-to-batch variability in

algal composition and lack of standardisation in dosing across developmental stages. Multi-site randomised controlled trials, standardisation of extraction and testing methods, and interdisciplinary collaboration are recommended for future research to convert these bioactive compounds into evidence-based immunotherapeutics for sustainable production of swine.

## Keywords

Marine Algae Bioactives, Immunomodulatory Mechanisms, *Sus scrofa* Immunotherapy, Precision Livestock Farming

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## 1. Background

Rising antibiotic resistance and growing demand for sustainable livestock practices have driven increasing interest in marine algae as a renewable source of bioactive compounds with reported immunomodulatory, anti-inflammatory, antioxidant, and antimicrobial activities that may enhance disease resistance in pigs (*Sus scrofa*) [1]. Marine algae produce a large variety of structurally distinct biologically active molecules, such as sulfated polysaccharides, polyphenols, carotenoids, bioactive peptides, and omega-3 polyunsaturated fatty acids ( $\omega$ -3 PUFAs) [1]. Their biological activity is closely linked to their structure, how they interact with host immune receptors, and how they affect downstream signalling. Significant pathways involved are the nuclear factor kappa-light-chain-enhancer of activated B cells (NF- $\kappa$ B), mitogen-activated protein kinase (MAPK), and nuclear factor erythroid 2-related factor 2 (Nrf2), which control cytokine production and oxidative stress reactions [1].

One of the most therapeutically relevant metabolites of these marine algae is sulfated polysaccharides, which include fucoidans and carrageenans. Their effects are seen in enhancing innate immunity, inhibiting viral replication, and reducing inflammation in a variety of mammalian model systems [1] [2]. The properties make them attractive to be used as feed additives or immunonutritional supplements in commercial pig production.

The porcine system of *Sus scrofa* is highly complex, involving complex networks of cytokines, innate immune sensors, and adaptive lymphocytes [3]. It is crucial to balance pro-inflammatory and regulatory signals. Such as, interleukin-12 (IL-12) and Interferon-gamma (IFN- $\gamma$ ) as an example of pro-inflammatory signalling, and interleukin-4 (IL-4) and interleukin-10 (IL-10) are examples of regulatory signalling, to ensure optimal vaccine efficacy, disease protection, and avoid immunopathological sequelae [4].

The utilization of marine algae-based bioactives in PLF could be a novel approach to provide specific immunotherapeutic support to pigs, optimize animal well-being, and decrease the reliance on antibiotics. Current PLF systems include real-time monitoring, a network of sensors and integration of genetic information to enable individual animal health management and accurate medical interven-

tions [5] [6]. PLF could potentially allow algal bioactive feeds to be customised on a per-animal basis based on animal health condition, microbiota composition and environmental parameters, which would result in a more specific dietary immune-nutrition strategy based on *Sus scrofa* immunometabolism than blanket antibiotic feeding.

This review 1) provides an overview of the most important classes of bioactives that have been identified in marine algae, including microalgae and macroalgae and have potential relevance for swine, 2) examines the proposed immunological mechanisms and the level of supporting evidence, and 3) explores the potential of PLF to achieve targeted, stage-specific delivery.

## 2. Methods

A comprehensive literature review was performed using electronic databases including PubMed, Semantic scholar and Google Scholar. We used various keyword combinations such as “marine algae”, “*Sus scrofa*”, “bioactive metabolites”, “immunomodulation”, “immunotherapy” and “precision livestock farming” to find studies that were published in English between 2000 and 2025. Boolean operators (AND/OR) were used to adjust the search strategy. Only original experimental studies, systematic reviews, and mechanistic or cross-species studies on the effects of compounds derived from marine algae on mammalian immunity, specifically in *Sus scrofa*, were included. Conference abstracts and grey literature were not included in the primary evidence base. When commercial product data are referenced, the reference and the evidence sources are identified and non-peer-reviewed or industry-sponsored data are separated from independently replicated data.

## 3. Bioactive Compounds in Marine Algae

Marine algae produce diverse bioactive compounds which have potential uses in medicine and nutrition. Among the most frequently studied classes are polysaccharides and polyphenols [1] [7]. Sulfated polysaccharides show significant immunomodulatory and antiviral effects, with their biological activity determined by the sulfate groups and molecular weight differences [7]. In particular, fucoidans and carrageenans have been shown to regulate the expression of genes that are essential to innate immune responses, and to possess therapeutic potential in neuroinflammatory diseases; the mechanisms of their action seem to involve regulation of key transcription factors and downstream regulation of cytokine production [8].

Another important class of compounds is phlorotannins, a group of polyphenols only found in brown algae. Species like *Fucus vesiculosus*, *Ascophyllum nodosum* and *Ecklonia cava* contain very high levels of phlorotannins with strong antioxidant properties, which include reactive oxygen species (ROS) scavenging and chelating of redox-active metal ions, as well as anti-inflammatory effects, by inhibiting the production of pro-inflammatory cytokines, especially tumour necrosis fac-

tor- $\alpha$  (TNF- $\alpha$ ) and interleukin-6 (IL-6) [8]-[10]. Phlorotannins, particularly, because of their dual anti-oxidant and anti-inflammatory properties, are important for the management of immune pathologies caused by oxidative stress [11].

Carotenoids are another group of bioactives of interest. In microalgae, carotenoids, including astaxanthin, fucoxanthin and  $\beta$ -carotene, are synthesized along with other protective molecules like fatty acids and sulfated polysaccharides in response to abiotic stress in species like *Chlorella zofingensis*, *Haematococcus pluvialis*, and *Spirulina platensis* [12]. They act as antioxidants in the organism that produces them and have significant immunomodulatory activity in mammalian cells [12].

Bioactive peptides (usually small peptides between 3 and 20 amino acids) extracted from algae like *Chlorella vulgaris* and *Spirulina* spp. have been shown to have immunoregulatory, antimicrobial, and anti-inflammatory effects by modulating cytokines and directly binding to microbial and host cell membranes [13] [14]. Lastly,  $\omega$ -3 PUFAs from microalgae, including eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA) and  $\alpha$ -linolenic acid (ALA), are known to exert anti-inflammatory, cardioprotective and neuro-modulatory properties by modulating eicosanoid biosynthesis and membrane fluidity [15] [16]. **Table 1** is a tabulated description of these large groups of compounds, their sources in algae and principal modes of action.

Important is the gastrointestinal fate, as most of these compounds are used as complex algal preparations as opposed to pure compounds. These sulfated polysaccharides like fucoidan, carrageenan, laminarin, and ulvan are polysaccharides of high molecular weight, which are not expected to be completely digested by host enzymes, and therefore, some of their activity may take place locally in the gastrointestinal tract; however, microbial transformation can generate lower molecular weight fragments or metabolites that have different biological properties [17]. Phlorotannins are also poorly absorbed in the small intestine, with large molecules being metabolized by colonic bacteria into smaller molecules that can then be absorbed [18]. Carotenoids like fucoxanthin must be incorporated into lipid-containing micelles in the intestine to be absorbed and taken up into the blood and can be metabolized to fucoxanthinol and amarouciaxanthin A prior to systemic distribution [19]. Bioactive peptides are susceptible to gastric and intestinal proteolysis, which means that the amount of exposure by intact peptides is probably lower than the ingested amount of peptides, but smaller peptides or amino acids may be absorbed [20]. EPA and DHA, however, and the other fatty acids derived from algae, are broken down and taken up like normal lipids, and can then be used to build circulating lipids and cell membranes. Therefore, using cell-based mechanisms to infer systemic effects in pigs cannot be assumed without knowledge of the bioactive compound exposure, whether it be luminal or microbiota-mediated, and porcine studies of digestion, metabolism and tissue exposure are important gaps.

**Table 1.** Marine algae bioactive compounds, examples, mechanism of actions and their properties.

| Bioactive compounds      | Examples                                    | Algae source                                                                     | Biological activities                                                      | Mechanisms of action                                                          | References   |
|--------------------------|---------------------------------------------|----------------------------------------------------------------------------------|----------------------------------------------------------------------------|-------------------------------------------------------------------------------|--------------|
| Sulfated polysaccharides | Fucoidans, Carrageenans, Laminaran          | <i>Fucus vesiculosus</i> ,<br><i>Chondrus crispus</i> ,<br><i>Laminaria</i> spp. | Anti-inflammatory, antiviral, immunostimulatory                            | NF- $\kappa$ B pathway inhibition; Modulation of fene expression              | [1] [8] [21] |
| Polyphenols              | Phlorotannins                               | <i>Ecklonia cava</i> ,<br><i>Ascophyllum</i><br><i>Nodosum</i>                   | Antioxidant; anti-inflammatory; neuroprotective; analgesics; anti-allergic | TNF- $\alpha$ /IL-6 inhibition; scavenge free radicals and chelate metal ions | [8]-[10]     |
| Carotenoids              | Astaxanthin, Fucoxanthin, $\beta$ -carotene | <i>Haematococcus pluvialis</i> , <i>Spirulina platensis</i>                      | Cytoprotective; antioxidant; immunoenhancing; anti-inflammatory            | ROS scavenging; Membrane stabilization                                        | [11] [12]    |
| Bioactive peptides       | Oligopeptides (3 - 20 amino acids),         | <i>Chlorella vulgaris</i> ,<br><i>Spirulina</i> spp.                             | Immunomodulatory; antimicrobial; anti-inflammatory                         | Cytokine modulation; Cell membrane interaction                                | [13] [14]    |
| Omega-3 PUFAs            | EPA, DHA, ALA,                              | <i>Cryptocodinium cohnii</i> , <i>Schizochytrium</i> spp.                        | Anti-inflammatory; Cardioprotective; Neuromodulatory                       | Eicosanoid synthesis, Membrane; fluidity                                      | [15] [16]    |

The extraction techniques determine the resulting yields and purity of these bioactive compounds. The conventional method of solvent extraction is now being replaced by modern technologies such as enzyme-assisted extraction, microwave-assisted extraction, ultrasound-assisted extraction, supercritical fluid extraction and pressurized liquid extraction [7] [21]. These modern extraction methods achieve better results because they require shorter processing times, improved yields and maintain the stability of heat-sensitive materials [21].

In marine algae, the chemical composition is quite varied from species to species. The total polysaccharide content and uronic acids of three typical species (*Chlorophyta Ulva lactuca*, *Phaeophyta Sargassum crassifolia*, and *Rhodophyta Digenea simplex*) have been reported as 57 - 185 mg/g dry weight and 29 - 45 mg/g, respectively. Sulfate moieties and amino acids have been reported as 95 - 181 mg/g and 7 - 17 mg/g, respectively [22]. Sulfated polysaccharides are important structural and functional components of algal cell walls that have been characterised by Fourier-transform infrared spectroscopy (FTIR) and nuclear magnetic resonance (NMR) spectroscopy, which have revealed antioxidant properties [23] [24].

Below are conceptual figures of therapeutic activity spectra of marine algal bioactives useful for *Sus scrofa* as an emerging immunotherapy. These figures are used as qualitative interpretative summaries and all proportions and relationships shown are based upon qualitative interpretation of the literature and are not statistically or quantitatively based on primary data. **Figure 1** shows the different broadness of bioactivity of the major classes of compounds found in marine algae from targeted domain-specific effects, e.g., omega-3 PUFAs [15] [16] and glyceroglycolipids [25] to broad, multi-domain activity, e.g., sulfated polysaccharides [1] [7] [8] [21], phlorotannins [8]-[11] [26], carotenoids [12] [23] and bioactive

peptides [13] [14] [27].

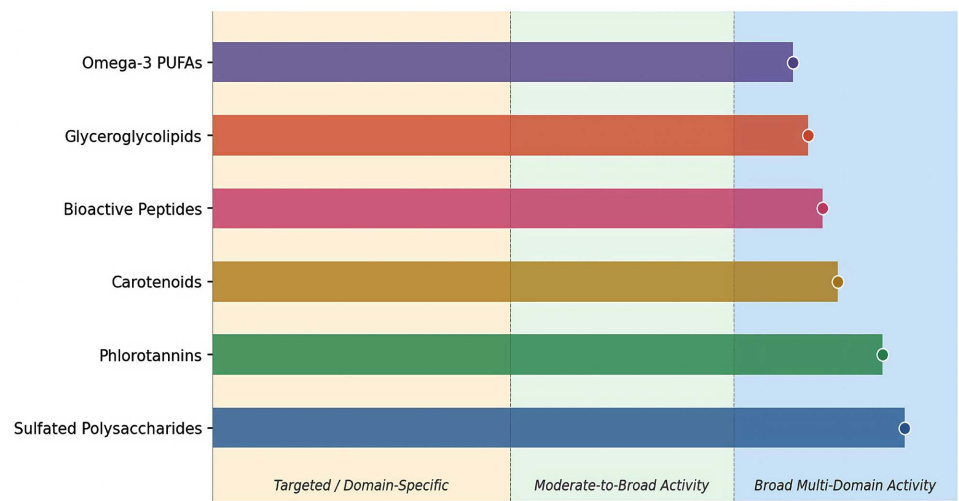


**Figure 1.** Illustrative conceptual summary; not a data-derived or evidence-weighted representation [1] [7]-[16] [26]-[30].

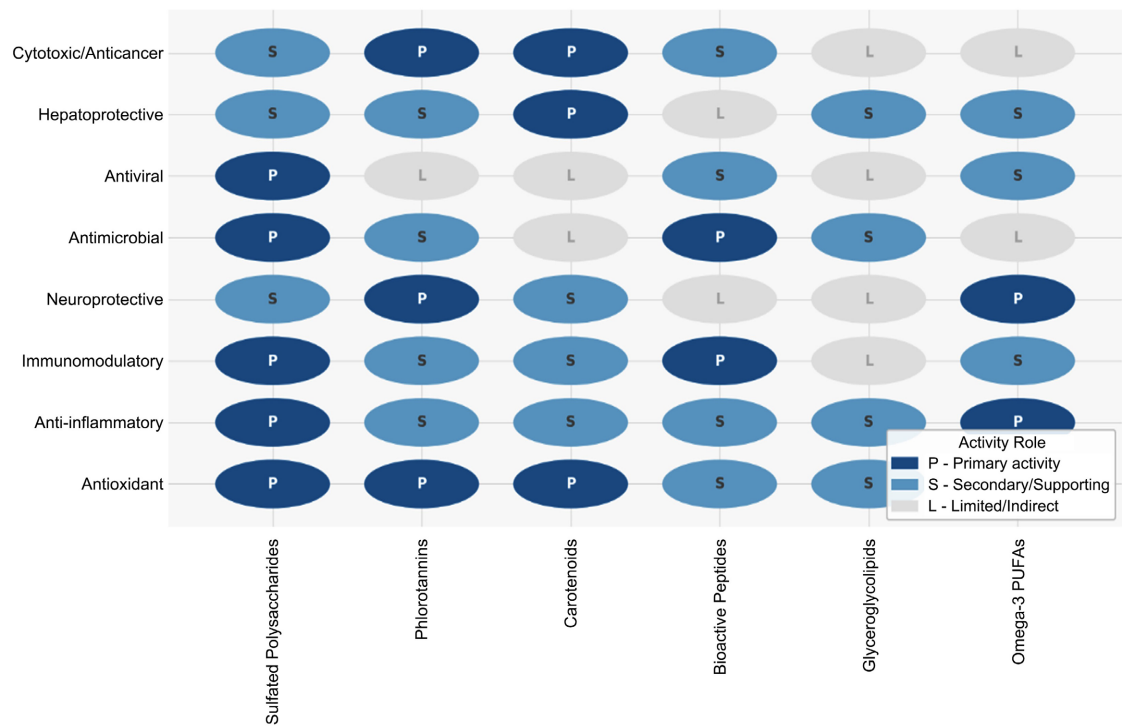


**Figure 2.** Illustrative conceptual representation; contribution levels are qualitative and not quantitatively derived from the literature [1] [7]-[16] [26]-[35].

A compound class-by-therapeutic domain activity matrix is shown in **Figure 2**, which was derived from the compound-specific evidence listed above [1] [7]-[16] [26]-[35]. The activity map demonstrates how each compound class contributes to therapeutic domains. It shows different types of contributions, which include primary, secondary and limited/indirect contributions. The marine algae com-

pounds demonstrate their ability to provide complementary biological activity through their various bioactive properties.

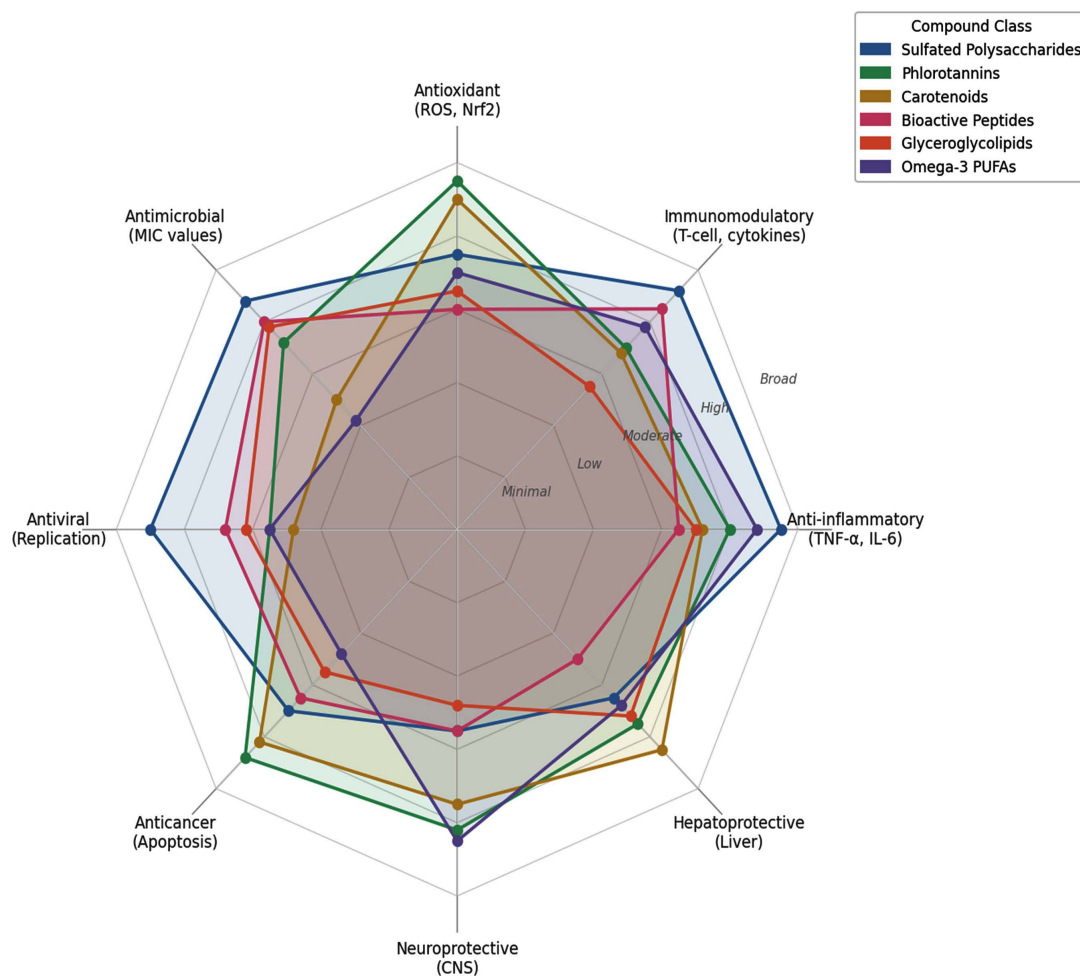


**Figure 3.** Illustrative conceptual summary; profiles reflect qualitative interpretation of the literature and are not statistically derived [7]-[14] [26] [27] [29] [30] [34] [35].

The mechanisms underlying each therapeutic domain are shown in specific molecular and physiological processes in the **Figure 3** above: the antioxidant activity through reactive oxygen species (ROS) scavenging and activation of the Nrf2 pathway by phlorotannins and carotenoids [8]-[12] [26] [30]; the antimicrobial activity through minimum inhibitory concentration (MIC) of bioactive peptides [13] [14]; the antiviral activity through inhibition of viral replication by sulfated polysaccharides [7] [8] [34] [35]; the anticancer/cytotoxic activity through induction of apoptosis by sulfated polysaccharides, carotenoids and bioactive peptides [26] [27] [29]; the hepatoprotective activity through sulfated polysaccharides and carotenoids [26] [29]; the neuroprotective activity in the central nervous system (CNS) through phlorotannins [30]; the anti-inflammatory activity through suppression of tumour necrosis factor-alpha (TNF- $\alpha$ ) and interleukin-6 (IL-6) by phlorotannins and  $\omega$ -3 PUFAs [8]-[10] [15] [16].

## 4. Immunomodulatory Mechanism of Bioactive Metabolites from Marine Algae

### Cross-Species Mechanistic Evidence (Extrapolated to *Sus scrofa*)

The main immunomodulatory compounds found in marine algae are sulfated polysaccharides (fucoidan, carrageenan, laminarin), phenolic compounds, flavonoids, bioactive peptides,  $\omega$ -3 PUFAs, and carotenoids, including fucoxanthin and astaxanthin [1] [31]. Both the polysaccharide- and peptide-rich fractions activate innate immune sensors and stimulate macrophage response to infection, while  $\omega$ -3 PUFAs and carotenoids provide antioxidant and anti-inflammatory support, which will affect the development of adaptive immunity [1] [31].

On a mechanistic level, polysaccharides and peptide-rich extracts are known to activate PRRs, such as TLRs, on antigen-presenting cells (APCs) that leads to activation of the NF- $\kappa$ B/MAPK signalling axis and thus modulation of the pro- and anti-inflammatory cytokine profiles [1] [32]. In several studies, marine algal extracts have been shown to upregulate activation markers (CD40, CD86 and MHC-II) on dendritic cells and macrophages in a dose-dependent manner, and to stimulate *in vivo* recruitment of neutrophils, monocytes and natural killer cells, resulting in an overall immunostimulatory effect in healthy individuals [33]. The uniformity of NF- $\kappa$ B/MAPK activation across these studies, even in models of pigs' macrophages and dendritic cells, is the most consistent mechanism discovery in the literature.

In all of these studies, there is a consistent trend of activation of innate immune pathways, but the magnitude of effect and specificity is quite variable depending on the source of compound, dose, and host species. Most of the cross-species mechanistic evidence comes from cell-based assays or rodent models, and should be treated with caution when extrapolating to *Sus scrofa*, because of reported differences in the *Sus scrofa* repertoire of innate immune receptors and cytokines, and the difference in their cytokine biology. Findings from *in vitro* or *in vivo* studies, or mechanistic studies, from non-porcine models are noted throughout this review and should not be confused with findings from porcine *in vitro* or *in vivo* studies.

## 5. Application in *Sus scrofa* Health

Bioactive metabolites of marine algae are emerging as promising feed-level immunotherapeutics for *Sus scrofa* that can enhance natural and acquired immune responses, reduce unnecessary inflammatory responses, and improve vaccine efficiencies in commercial production systems [36]. The most researched compounds relevant to swine applications are sulfated polysaccharides,  $\beta$ -glucans, and algal peptide-rich extracts, which can be added to the diet without significant changes in farming practices [34] [36].

### 5.1. Evidence from Porcine *in Vitro* Models

Mechanistically precise evidence, but under conditions which may not fully cap-

ture the whole-animal physiology, comes from controlled *in vitro* studies with primary porcine cells. Sulfated polysaccharides have been shown in short-term *in vitro* experiments to be dose-dependent stimulators of pro-inflammatory and antiviral mediators such as IL-6, IL-8, and interferon-beta (IFN- $\beta$ ) in porcine alveolar macrophages and to inhibit PRRSV replication [34] [35]. These results suggest that algal bioactives can act directly as antiviral agents and also as immunological adjuvants at the porcine mucosal surface of the respiratory tract. These *in vitro* data are informative in terms of mechanisms, and it provides good and preliminary support for use as an antiviral agent, but the evidence of significant antiviral protection and herd-level immunity under commercial field conditions needs to be validated in well-controlled *in vivo* studies, and caution should be exercised at this stage.

In pigs, commercial algal product formulations containing green alga (MSP®IMMUNITY) or red alga (MSP®BARRIER) have been shown to increase innate and adaptive immune protection and help to maintain the integrity of the gut barrier [35]. Although these observations are relevant to practice, replications by independent sources through peer review are also necessary to come to strong conclusions, and all sources of data and levels of industry involvement should be reported and weighed in interpreting these findings.

## 5.2. Evidence from Porcine *in Vivo* Trials

The most directly translatable evidence for commercial swine applications is from controlled *in vivo* studies in pigs, which, coupled with the NF- $\kappa$ B/MAPK mechanistic work from cell models of porcine, represent the highest level of evidence reviewed. In nursery pigs, dietary supplementation with fucoidan-rich polysaccharides at around 0.2% of the diet has been linked to a significant reduction in levels of intestinal tumour necrosis factor (TNF)  $\alpha$ , while responses for interleukin 6 (IL-6) are less consistent between studies, so full detailing of study design and stage of the animals is recommended to enhance general interpretability between trials [35]. Previous studies in weaned pigs that have been challenged with pathogenic *Escherichia coli* (*E. coli*) have shown that supplementation with algae-derived  $\beta$ -glucan has a strong anti-inflammatory effect, increases the barrier function of the intestine, and maintains normal immune homeostasis without suppressing the protective immune responses [35] [37]. These *in vivo* data are the most relevant to commercial use of weaner diets and should be reproduced at other farm locations and production situations.

Also, oral seaweed extract supplementation has been tested in commercial pig farms for its ability to stimulate humoral immune response after modified-live PRRSV vaccination, and good results have been reported [34]. These field-level data expand *in vitro* results into a whole-animal immune context and are the first to show that algal bioactives can enhance vaccine-induced immunity in commercial production. The effects need to be replicated across individual farms and supplementation timing and dose range defined in relation to vaccination.

### 5.3. Evidence Extrapolated from Cross-Species Studies and Inherent Limitations

Cross-species supplementary evidence expands the picture of mechanisms, and comes with important caveats about its interpretation that have to be stated explicitly. Studies in rodent and other mammalian models suggest that microalgae, being a source of essential minerals and micronutrients, may be able to enhance bone mineralisation, growth performance, and antibody production at inclusion levels as low as 2% - 5% [38]. Sulfated polysaccharides, polyphenols, and terpenoids have been shown to modulate NF- $\kappa$ B, MAPK, and downstream cytokine networks in a significant number of studies across multiple species at the pathway level [1]. Although these conserved pathways offer a mechanistic rationale for predicting similar outcomes in *Sus scrofa*, direct extrapolation from non-porcine models should be avoided, due to the differences in immune receptor repertoire and cytokine biology known to exist between these species.

Existing cross-species and porcine results are also limited in their applicability due to variation in the chemical composition of the seaweeds used and the lack of validated optimal dosing protocols and standardised trial designs throughout the production process [39]. Well-controlled multi-farm trials are needed in the future to assess algal immunomodulators in integrated vaccination schedules and antibiotic usage strategies tailored to *Sus scrofa* production.

## 6. Precision Livestock Farming Integration

The integration of PLF with *Sus scrofa* production has the potential to revolutionize marine-algal bioactive metabolites from a static feed additive to a dynamic immunotherapeutic agent delivered in response to real-time health status, not universally across a population [40]. Modern PLF systems use sensors, cameras and AI algorithms to monitor individual pig movement, feed intake behaviour and vocalisation patterns to detect early immune activation, stress or subclinical disease [40] [41]. In principle, these detection capabilities could allow the targeted delivery of algal-derived immunomodulators like sulfated polysaccharides,  $\beta$ -glucans and  $\omega$ -3-rich microalgal preparations through automated feeding and dosing systems calibrated to the health status and production stage of specific pigs or groups of pigs (neonates, weaners and gestating sows) [42].

PLF platforms have already proved to be more precise than human observers in the detection of sick or stressed pigs [41], and commercial swine operations are beginning to implement functional feed ingredients in smart-feeding systems where feeding algorithms adapt the dietary inclusion level of algae-rich meals or algal functional ingredients (e.g.,  $\omega$ -3 DHA from microalgae, algal  $\beta$ -glucans) depending on individual health trajectories and production phases [42]. Yet, it is important to bear in mind that closed-loop PLF systems that can provide truly immune-targeted feed are still conceptual; their implementation will require validated immunological biomarkers, interoperable dosing infrastructure that links sensor data to feed-mill outputs, and proven economic feasibility under commer-

cial conditions.

The early life to post-weaning stage is a particularly high-priority window for immune-nutritional intervention in *Sus scrofa*. This developmental stage is characterized by rapid maturation of the immune system but increased susceptibility to enteric disease and respiratory infections [42]. The evidence reviewed suggests that supplementation with seaweed and microalgae may be beneficial for improving gut function and immunoglobulin transfer during colostrum intake and may potentiate PRRSV vaccine-induced humoral immunity [34]. A PLF system capable of recognising early behavioural markers of immune challenge in weaner groups, such as decreased feed intake, increased lying times and alterations in vocalisation patterns, may initiate algal-based immune support at the most opportune moment for it to be successful. Completing this validation loop between PLF-detected signals and outcomes of algal supplementation is a key translational priority for future research.

## 7. Challenges and Future Directions

A major challenge to the development of marine algal bioactives as licensed immunotherapeutic agents for *Sus scrofa* is the lack of standardized production and quality assurance frameworks for raw algal biomass and purified fractions (sulfated polysaccharides,  $\beta$ -glucans and algal peptides). Variability in the chemical composition between batches due to differences between species, growth conditions and the method of harvesting and extraction can lead to inconsistent effects on the immune system. If the quality of the composition is not well-controlled, there is a risk of unwanted reactions that cause inflammation or hypersensitivity. Moreover, the possible accumulation of heavy metals, biotoxins and anti-nutritional factors in the biomass of algae presents real safety concerns that require the implementation of strong quality-control systems and safety standards of regulatory quality before such products are routinely incorporated into commercial swine diets. Future research programmes should focus on the development of harmonised testing and extraction protocols, standardised immune and gut-health outcome endpoints and coordinated partnerships between academic institutions, industry and regulatory authorities towards evidence-based guidelines for the use of bioactive marine algal metabolites in *Sus scrofa* production systems.

This is further complicated by the dose and context dependency of the immunomodulatory effects of algal metabolites in *Sus scrofa*. Low to moderate levels of dietary inclusion appear to promote immune function and gut health, with high doses potentially eliciting undesirable physiological responses or metabolic disruption. Dosing requirements are likely to vary markedly between life stages (sow, piglet, weaner and growing-finishing pigs) and production systems (conventional, organic and antibiotic-reduced), but the current literature provides little quantitative guidance on dose-response relationships in swine. Future mechanistic studies will be required to determine safe and effective dosing ranges for the primary algal immunomodulatory fractions and to characterise potential interactions with

co-administered vaccines, antibiotics and other feed additives.

Moreover, the delivery of targeted algal-based immunotherapy to *Sus scrofa* through the PLF system needs to solve both technical and economic problems that prevent its successful application. The current PLF systems succeed in capturing comprehensive behavioural and physiological information, but they lack immunotherapeutic connections to immune-targeted feed delivery systems and algal response algorithms, while their components from different sensor manufacturers and feed mills and farm management software systems remain unconnected. Future research development for *Sus scrofa* should focus on closed-loop systems which use “algae-PLF” modules to determine the optimal algal-immunomodulator levels through validated health indicators and cost-benefit assessments which show better treatment outcomes and improved animal welfare and production results without using antibiotics.

## 8. Conclusions

The studies reviewed offer compelling evidence for the substantial potential of marine algae bioactive metabolites as an emerging novel agent for the immunotherapeutic treatment of *Sus scrofa*. The evidence presented in the porcine *in vitro* mechanistic studies, controlled *in vivo* trials, and cross-species data can be ranked according to confidence, each of which lies on top of the previous one:

### Well supported evidence:

- The NF- $\kappa$ B/MAPK signalling activation is inhibited through sulfated polysaccharides, which show their effects in multiple studies that use porcine macrophage and dendritic cell models as test systems. The intestinal TNF- $\alpha$  is decreased by fucoidan-rich dietary preparations at an inclusion level of about 0.2% *in vivo*, which can be used as a reference level for dose-ranging.
- In controlled *in vivo* studies in pigs, algal  $\beta$ -glucan supplementation has been shown to enhance the integrity of the gut barrier and to attenuate inflammation provoked by *E. coli*. The results are most directly relevant to commercial weaner diets and should be replicated at multiple sites.

### Promising but requires stronger evidence:

- Technically, the idea of PLF-based adaptive algal dosing is well-founded, with current sensor-AI options available in commercial swine farms. However, closed-loop PLF systems for delivery to specific immune targets have not yet been demonstrated, and the critical validation loop between PLF-detected behavioural signals and immunological response outcomes is not complete.
- Most of the immunostimulatory evidence for carotenoids and polyphenols is from models other than porcine or *in vitro*. The bioavailability, metabolism and dose-response information for the species *Sus scrofa* is not complete enough to make strong recommendations for doses.

### Research gaps to address:

- Research needs to conduct multi-site randomized controlled trials to determine the minimum effective dose and maximum safe dose of fucoidan,  $\beta$ -glu-

can and  $\omega$ -3 fractions, which need to be tested on neonates, weaners, gestating sows and growing-finishing pigs through standardized immune endpoints which include serum cytokine profiles and vaccine-specific antibody titres and gut permeability markers.

- Regulatory-grade testing needs to assess heavy metals, which include arsenic, cadmium and lead, as well as biotoxins and anti-nutritional factors across all commercially relevant algal species and their harvest batches before any large-scale feed application. The existing lack of safety information now stands as the main obstacle that prevents regulatory bodies from granting their approval.
- The inter-laboratory standardization of sulfate content, molecular weight distribution, and polyphenol concentration tests needs standardization because it enables researchers to compare their results through various research studies. The absence of established reference materials makes it impossible to conduct accurate dose assessments between different studies.

The PLF testing for immune endpoints needs prospective research to determine whether PLF-detected behavioural signals (reduced feed intake, prolonged recumbency, altered vocalizations) can predict immune activation events in *Sus scrofa* and whether algal inclusion adjustments will result in measurable long-term immunological advantages. The validation loop needs completion because it represents the essential transition from scientific concept to practical clinical application.

## Author Contributions

Godwin Femi Ekundayo: conceptualization, methodology, investigation, data curation, formal analysis, visualization, writing—original draft, writing—review & editing. Daniel Oluwaleke Biaoku: conceptualization, methodology, supervision, validation, resources, writing—review & editing.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

## References

- [1] Matin, M., Koszarska, M., Atanasov, A.G., Król-Szmajda, K., Jóźwik, A., Stelmasiak, A., *et al.* (2024) Bioactive Potential of Algae and Algae-Derived Compounds: Focus on Anti-Inflammatory, Antimicrobial, and Antioxidant Effects. *Molecules*, **29**, Article 4695. <https://doi.org/10.3390/molecules29194695>
- [2] Cadar, E., Popescu, A., Dragan, A., Pesterau, A., Pascale, C., Anuta, V., *et al.* (2025) Bioactive Compounds of Marine Algae and Their Potential Health and Nutraceutical Applications: A Review. *Marine Drugs*, **23**, Article 152. <https://doi.org/10.3390/md23040152>
- [3] Zhao, Q., Wang, J., Ma, F., Chen, Q., Liu, H., Yang, J., *et al.* (2025) The Comprehensive Transcriptomic Atlas of Porcine Immune Tissues and the Peripheral Blood Mononuclear Cell (PBMC) Immune Dynamics Reveal Core Immune Genes. *Journal of Animal Science and Biotechnology*, **16**, Article No. 69. <https://doi.org/10.1186/s40104-025-01184-y>

- [4] Rodríguez, F., Rosales, R.S., Ramírez, A.S. and Poveda, J.B. (2023) Vaccination Up-regulates Th1 Cytokines in the Lung of Pigs Experimentally Infected with Mycoplasma Hyopneumoniae. *Animals*, **13**, Article 520. <https://doi.org/10.3390/ani13030520>
- [5] Nsabiyeze, A., Zhang, M., Li, J., Zhao, Q. and Zhang, X. (2025) Precision Livestock Farming for Climate-Resilient Livestock Management: A Review of Real-Time Monitoring and Decision Support Systems. *Journal of Cleaner Production*, **524**, Article 146454. <https://doi.org/10.1016/j.jclepro.2025.146454>
- [6] Jiang, B., Tang, W., Cui, L. and Deng, X. (2023) Precision Livestock Farming Research: A Global Scientometric Review. *Animals*, **13**, Article 2096. <https://doi.org/10.3390/ani13132096>
- [7] Kumar, A., Soratur, A., Kumar, S. and Venmathi Maran, B.A. (2025) A Review of Marine Algae as a Sustainable Source of Antiviral and Anticancer Compounds. *Macromol*, **5**, Article 11. <https://doi.org/10.3390/macromol5010011>
- [8] Belda-Antolí, M., Ros Bernal, F.A. and Vicente-Mampel, J. (2025) From Sea to Relief: The Therapeutic Potential of Marine Algal Antioxidants in Pain Alleviation. *Marine Drugs*, **23**, Article 270. <https://doi.org/10.3390/md23070270>
- [9] Jimenez-Lopez, C., Pereira, A.G., Lourenço-Lopes, C., Garcia-Oliveira, P., Cassani, L., Fraga-Corral, M., *et al.* (2021) Main Bioactive Phenolic Compounds in Marine Algae and Their Mechanisms of Action Supporting Potential Health Benefits. *Food Chemistry*, **341**, Article 128262. <https://doi.org/10.1016/j.foodchem.2020.128262>
- [10] Phang, S.J., Teh, H.X., Looi, M.L., Arumugam, B., Fauzi, M.B. and Kuppusamy, U.R. (2023) Phlorotannins from Brown Algae: A Review on Their Antioxidant Mechanisms and Applications in Oxidative Stress-Mediated Diseases. *Journal of Applied Phycology*, **35**, 867-892. <https://doi.org/10.1007/s10811-023-02913-4>
- [11] de Almeida, P.D.O., Bozorgzadeh, S.A., Martins, I.J.F. and Golbashirzadeh, M. (2025) Marine Algae-Derived Nanoparticles (MADNs): Green Synthesis, Characterization, and Therapeutic Applications. *Discover Applied Sciences*, **7**, Article No. 461. <https://doi.org/10.1007/s42452-025-06915-4>
- [12] Eze, C.N., Onyejiaka, C.K., Ihim, S.A., Ayoka, T.O., Aduba, C.C., Ndukwe, J.K., *et al.* (2023) Bioactive Compounds by Microalgae and Potentials for the Management of Some Human Disease Conditions. *AIMS Microbiology*, **9**, 55-74. <https://doi.org/10.3934/microbiol.2023004>
- [13] O'Connor, J., Garcia-Vaquero, M., Meaney, S. and Tiwari, B.K. (2022) Bioactive Peptides from Algae: Traditional and Novel Generation Strategies, Structure-Function Relationships, and Bioinformatics as Predictive Tools for Bioactivity. *Marine Drugs*, **20**, Article 317. <https://doi.org/10.3390/md20050317>
- [14] Cunha, S.A. and Pintado, M.E. (2021) Bioactive Peptides Derived from Marine Sources: Biological and Functional Properties. *Trends in Food Science & Technology*, **119**, 348-370. <https://doi.org/10.1016/j.tifs.2021.08.017>
- [15] Didrihsone, E., Dubencovs, K., Grube, M., Shvirksts, K., Suleiko, A., Suleiko, A., *et al.* (2022) Cryptocodinium Cohnii Growth and Omega Fatty Acid Production in Media Supplemented with Extract from Recycled Biomass. *Marine Drugs*, **20**, Article 68. <https://doi.org/10.3390/md20010068>
- [16] Literáková, P., Zavřel, T., Búzová, D., Kaštánek, P. and Červený, J. (2024) Marine Microalgae Schizochytrium Demonstrates Strong Production of Essential Fatty Acids in Various Cultivation Conditions, Advancing Dietary Self-Sufficiency. *Frontiers in Nutrition*, **11**, Article ID: 1290701. <https://doi.org/10.3389/fnut.2024.1290701>
- [17] Gotteland, M., Riveros, K., Gasaly, N., Carcamo, C., Magne, F., Liabeuf, G., *et al.*

- (2020) The Pros and Cons of Using Algal Polysaccharides as Prebiotics. *Frontiers in Nutrition*, **7**, Article ID: 163. <https://doi.org/10.3389/fnut.2020.00163>
- [18] Reis, S.F., Catarino, M.D., Braga, S.S., Coimbra, M.A., Silva, A.M.S. and Cardoso, S.M. (2026) Improving in Vitro Gastrointestinal Stability of Phlorotannins from Food Grade *Fucus vesiculosus* Extracts Using Cyclodextrins. *Journal of Food Science*, **91**, e70830. <https://doi.org/10.1111/1750-3841.70830>
- [19] Guo, B., Oliviero, T., Fogliano, V., Ma, Y., Chen, F. and Capuano, E. (2019) Gastrointestinal Bioaccessibility and Colonic Fermentation of Fucoxanthin from the Extract of the Microalga *Nitzschia laevis*. *Journal of Agricultural and Food Chemistry*, **68**, 1844-1850. <https://doi.org/10.1021/acs.jafc.9b02496>
- [20] Amigo, L. and Hernández-Ledesma, B. (2020) Current Evidence on the Bioavailability of Food Bioactive Peptides. *Molecules*, **25**, Article 4479. <https://doi.org/10.3390/molecules25194479>
- [21] Ebadi, A.G. (2025) Harnessing Bioactive Metabolites from Marine Algae: A Biotechnological Approach for Drug Discovery and Therapeutic Development. *Biomedical Journal of Scientific & Technical Research*, **61**, 53984-53988. <https://doi.org/10.26717/bjstr.2025.61.009652>
- [22] Al-Amoudi, O.A., Mutawie, H.H., Patel, A.V. and Blunden, G. (2009) Chemical Composition and Antioxidant Activities of Jeddah Corniche Algae, Saudi Arabia. *Saudi Journal of Biological Sciences*, **16**, 23-29. <https://doi.org/10.1016/j.sjbs.2009.07.004>
- [23] Rodríguez Sánchez, R.A., Matulewicz, M.C. and Ciancia, M. (2022) NMR Spectroscopy for Structural Elucidation of Sulfated Polysaccharides from Red Seaweeds. *International Journal of Biological Macromolecules*, **199**, 386-400. <https://doi.org/10.1016/j.ijbiomac.2021.12.080>
- [24] Soto-Vásquez, M.R., Alvarado-García, P.A.A., Youssef, F.S., Ashour, M.L., Bogari, H.A. and Elhady, S.S. (2022) FTIR Characterization of Sulfated Polysaccharides Obtained from *Macrocystis Integrifolia* Algae and Verification of Their Antiangiogenic and Immunomodulatory Potency *in Vitro* and *in Vivo*. *Marine Drugs*, **21**, Article 36. <https://doi.org/10.3390/md21010036>
- [25] Bailey, E., Wojcik, J., Rahn, M., Roos, F., Spooren, A. and Koshibu, K. (2025) Comparative Bioavailability of DHA and EPA from Microalgal and Fish Oil in Adults. *International Journal of Molecular Sciences*, **26**, Article 9343. <https://doi.org/10.3390/ijms26199343>
- [26] Mohibbullah, M., Haque, M.N., Sohag, A.A.M., Hossain, M.T., Zahan, M.S., Uddin, M.J., *et al.* (2022) A Systematic Review on Marine Algae-Derived Fucoxanthin: An Update of Pharmacological Insights. *Marine Drugs*, **20**, Article 279. <https://doi.org/10.3390/md20050279>
- [27] Yimam, M.A., Andreini, M., Carnevale, S. and Muscaritoli, M. (2024) The Role of Algae, Fungi, and Insect-Derived Proteins and Bioactive Peptides in Preventive and Clinical Nutrition. *Frontiers in Nutrition*, **11**, Article ID: 1461621. <https://doi.org/10.3389/fnut.2024.1461621>
- [28] Guo, S. and Wang, Z. (2022) Glyceroglycolipids in Marine Algae: A Review of Their Pharmacological Activity. *Frontiers in Pharmacology*, **13**, Article ID: 1008797. <https://doi.org/10.3389/fphar.2022.1008797>
- [29] Ngo, D. and Kim, S. (2013) Sulfated Polysaccharides as Bioactive Agents from Marine Algae. *International Journal of Biological Macromolecules*, **62**, 70-75. <https://doi.org/10.1016/j.ijbiomac.2013.08.036>
- [30] Barbosa, M., Valentão, P. and Andrade, P.B. (2020) Polyphenols from Brown Sea-

- weeds (Ochrophyta, Phaeophyceae): Phlorotannins in the Pursuit of Natural Alternatives to Tackle Neurodegeneration. *Marine Drugs*, **18**, Article 654. <https://doi.org/10.3390/md18120654>
- [31] Pradhan, B., Nayak, R., Patra, S., Jit, B.P., Ragusa, A. and Jena, M. (2020) Bioactive Metabolites from Marine Algae as Potent Pharmacophores against Oxidative Stress-Associated Human Diseases: A Comprehensive Review. *Molecules*, **26**, Article 37. <https://doi.org/10.3390/molecules26010037>
- [32] O'Doherty, J.V., Venardou, B., Rattigan, R. and Sweeney, T. (2021) Feeding Marine Polysaccharides to Alleviate the Negative Effects Associated with Weaning in Pigs. *Animals*, **11**, Article 2644. <https://doi.org/10.3390/ani11092644>
- [33] Ho, T.L., Lee, J., Ahn, S.Y., Lee, D., Song, W., Kang, I., *et al.* (2023) Immunostimulatory Effects of Marine Algae Extracts on in Vitro Antigen-Presenting Cell Activation and in Vivo Immune Cell Recruitment. *Food Science & Nutrition*, **11**, 6560-6570. <https://doi.org/10.1002/fsn3.3605>
- [34] Hervet, C., Bussy, F., Morvan, A., da Rocha Pinto, F., Belloc, C., Bourry, O., *et al.* (2025) Algae Extract Supplementation Boosts Humoral Immunity Induced by Attenuated PRRSV-1 Vaccination. *BMC Veterinary Research*, **21**, Article No. 653. <https://doi.org/10.1186/s12917-025-05085-0>
- [35] Cheng, Y., Garavito-Duarte, Y.R., Suarez, M.G., Rodríguez, M.A. and Kim, S.W. (2026) Effects of Dietary Marine Sulfated Polysaccharides Derived from Macroalgae on Intestinal Health of Nursery Pigs. *Animal Science Journal*, **97**, e70158. <https://doi.org/10.1111/asj.70158>
- [36] González-Meza, G.M., Elizondo-Luevano, J.H., Cuellar-Bermudez, S.P., Sosa-Hernández, J.E., Iqbal, H.M.N., Melchor-Martínez, E.M., *et al.* (2023) New Perspective for Macroalgae-Based Animal Feeding in the Context of Challenging Sustainable Food Production. *Plants*, **12**, Article 3609. <https://doi.org/10.3390/plants12203609>
- [37] Kim, K., Ehrlich, A., Perng, V., Chase, J.A., Raybould, H., Li, X., *et al.* (2019) Algae-derived B-Glucan Enhanced Gut Health and Immune Responses of Weaned Pigs Experimentally Infected with a Pathogenic *E. coli*. *Animal Feed Science and Technology*, **248**, 114-125. <https://doi.org/10.1016/j.anifeedsci.2018.12.004>
- [38] Prates, J.A.M. (2025) The Role of Microalgae in Providing Essential Minerals for Sustainable Swine Nutrition. *Frontiers in Animal Science*, **6**, Article 1526433. <https://doi.org/10.3389/fanim.2025.1526433>
- [39] Corino, C., Di Giancamillo, A., Modina, S.C. and Rossi, R. (2021) Prebiotic Effects of Seaweed Polysaccharides in Pigs. *Animals*, **11**, Article 1573. <https://doi.org/10.3390/ani11061573>
- [40] Benjamin, M. and Yik, S. (2019) Precision Livestock Farming in Swine Welfare: A Review for Swine Practitioners. *Animals*, **9**, Article 133. <https://doi.org/10.3390/ani9040133>
- [41] Tzanidakis, C., Simitzis, P., Arvanitis, K. and Panagakakis, P. (2021) An Overview of the Current Trends in Precision Pig Farming Technologies. *Livestock Science*, **249**, Article 104530. <https://doi.org/10.1016/j.livsci.2021.104530>
- [42] Bortoluzzi, E.M., Goering, M.J., Ochoa, S.J., Holliday, A.J., Mumm, J.M., Nelson, C.E., *et al.* (2023) Evaluation of Precision Livestock Technology and Human Scoring of Nursery Pigs in a Controlled Immune Challenge Experiment. *Animals*, **13**, Article 246. <https://doi.org/10.3390/ani13020246>