

Review Article



Functional feed additives for enhancing immune response and disease resistance in shrimp aquaculture

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Abstract

The escalation of shrimp aquaculture has been linked to frequent occurrences of bacterial (*Vibrio* spp.) and viral (white spot syndrome virus and infectious myonecrosis virus) illnesses that limit productivity and have traditionally resulted in significant antibiotic application. Due to their dependence on inherent cellular and humoral immunity, dietary immunomodulation has become a critical non-antibiotic approach for health management in penaeid shrimp. This analysis consolidates existing research on four primary categories of functional feed additives probiotics/symbiotic, prebiotics, β -glucans and associated immunostimulants, and phytogenic/herbal extracts along with their recorded impacts on immune metrics, gastrointestinal health, and survival rates post-pathogen exposure in *Litopenaeus vannamei* and *Penaeus monodon*. The examined literature indicates that additive supplementation is regularly linked to increased hemocyte activity, heightened expression of antimicrobial-peptide and pattern-recognition-receptor genes, augmented antioxidant enzyme activity, and better survival rates post-challenge, with combined (symbiotic or multi-additive) approaches often surpassing single-ingredient diets. The evaluation delineates the mechanistic pathways connecting gut microbiota modulation to systemic immune augmentation, encapsulates notable dose–response results, and addresses significant obstacles in standardization, strain/extract specificity, and field-scale validation that need resolution for the translation of laboratory discoveries into dependable commercial applications.

Keywords: *Litopenaeus vannamei*, Probiotics, Prebiotics, β -glucan, Phytogenic, Disease resistance, Shrimp aquaculture

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Introduction

Shrimp farming constitutes one of the most lucrative sectors of worldwide aquatic food production, dominated by the Pacific white leg shrimp (*Litopenaeus vannamei*) and the black tiger shrimp (*Penaeus monodon*). The swift escalation of the industry has, meanwhile, been consistently interrupted by illness outbreaks, including white spot syndrome virus (WSSV), infectious myonecrosis virus (IMNV), and *Vibrio*-related ailments such as acute hepatopancreatic necrosis sickness. Historically, these epidemics prompted extensive prophylactic antibiotic usage, a practice that is now being curtailed due to apprehensions regarding antimicrobial resistance, drug residues, and environmental pollution (Abdel-Latif *et al.*, 2022; Bondad-Reantaso *et al.*, 2023).

Due to the absence of antibody-mediated adaptive immunity in crustaceans, the health management of shrimp farming relies predominantly on enhancing and promoting the innate immune system (Knipe *et al.*, 2021). This limitation has directed research efforts towards functional feed additives including probiotics and symbiotic, prebiotic oligosaccharides, β -glucans, various immunostimulants, and phytogenic or herbal extracts which can be integrated into commercial diets to improve immune function and lessen dependence on chemotherapeutics. This analysis consolidates recent experimental findings regarding these four additive categories, outlines their suggested mechanisms of action, and

examines the practical obstacles that persist before their advantages may be consistently realised at a commercial level.

The shrimp innate immune system: Rationale for dietary immunomodulation

Shrimp protect themselves from pathogens via cellular mechanisms hemolytic phagocytosis, nodulation, and encapsulation as well as humoral mechanisms that encompass the prophenoloxidase (proPO) activation cascade, antimicrobial peptides, lectins, and antioxidant enzymes like superoxide dismutase (SOD) and glutathione peroxidase (GPx) (Knipe *et al.*, 2021). The gut microbiota operates at the junction of these systems: recent studies on the innate immune deficiency (IMD) pathway indicate that the composition of gut microbes and the host's immune and metabolic equilibrium are closely interconnected in penaeid shrimp, whereby disturbances in the gut community can directly affect disease vulnerability (Supungul *et al.*, 2025). Due to the inability of shrimp to develop pathogen-specific immunological memory like vertebrates, farmers mostly rely on feeding approaches that consistently stimulate innate defenses instead of a singular vaccination event to enhance disease resistance (Citarasu, 2010).

Categories of functional feed additives

Probiotics and symbiotic

Probiotics are living microbes that, when provided in sufficient quantities, offer a

health advantage to the host. In shrimp aquaculture, they principally function by competitively excluding harmful bacteria, releasing antimicrobial metabolites and short-chain fatty acids, and directly enhancing hemolytic and mucosal immune responses (Knipe *et al.*, 2021). Due to the complementary advantages of probiotics and prebiotics, numerous recent formulations merge the two as symbiotic; an extensive review of shrimp vibriosis control strategies emphasises probiotics, post biotics, prebiotics, and symbiotic collectively as a unified non-antibiotic arsenal for managing *Vibrio* (Abdel-Latif *et al.*, 2022).

Prebiotics

Prebiotics are indigestible carbohydrates such as mannan oligosaccharide (MOS), fructo-oligosaccharide (FOS), inulin, and galacto-oligosaccharide (GOS) that specifically promote advantageous gut microbiota and can directly activate pattern-recognition mechanisms. Dietary inulin and MOS, administered individually and in conjunction at concentrations of 2.5–10 mg/g of feed, enhanced the expression of toll-like receptor (TLR1/2/3), signal transducer and activator of transcription (STAT), crustin, and anti-lipopolysaccharide factor genes in *L. vannamei*, with the combined treatment offering superior defense against WSSV and *Vibrio alginolyticus* compared to each prebiotic separately (Li *et al.*, 2018). MOS supplementation has been demonstrated to enhance gut structure and stress resilience in juvenile *L. vannamei*

(Zhang *et al.*, 2012), and when administered to larvae by enriched *Artemia*, it boosts digestive enzyme function, immunity, and resistance to *Vibrio harveyi* (Widanarni *et al.*, 2018). Comparable immune-boosting and growth-stimulating effects of dietary MOS against white spot disease have been documented in juvenile white leg shrimp (Prastiti *et al.*, 2018), whereas inulin-coated feed has demonstrated enhancements in growth, disease resilience, immune-gene expression, and gut microbial diversity in commercial farming settings (Allie *et al.*, 2025).

β -glucans and other immunostimulants

β -glucans sourced from yeast and fungal cell walls are acknowledged by shrimp pattern-recognition receptors, including lipopolysaccharide- and β -1,3-glucan-binding protein (LGBP), which initiates the activation of the proPO cascade and respiratory burst activity (Campa-Córdova *et al.*, 2002; Khanjani *et al.*, 2022). Supplementation with 1,000 mg/kg of β -1,3/1,6-glucan enhanced the survival rates of *L. vannamei* exposed to IMNV, demonstrating no signs of immunological fatigue during extended exposure (Neto and Nunes, 2015), while β -1,3-glucan supplementation has also been proven to positively influence intestinal microbiota and diminish inflammatory signaling in the same species (Shen *et al.*, 2023). Live yeast (*Debaryomyces hansenii*), a natural source of β -glucan, when combined with inulin, enhanced survival rates and upregulated the expression of lysozyme, SOD, and GPx genes in juvenile *P.*

vannamei exposed to *Vibrio parahaemolyticus* (Ceséña *et al.*, 2021), demonstrating the efficacy of integrating glucan sources with prebiotic substrates.

Phytogenics and herbal extracts

Phytogenic feed additives provide bioactive substances from plants, including polyphenols, alkaloids, and essential oils, which exhibit direct antibacterial and antioxidant properties along with immunomodulatory effects (Citarasu, 2010). Initial research indicated that antibacterial botanicals like *Solanum trilobatum*, *Andrographis paniculata*, and *Psoralea corylifolia* enhanced survival rates, growth, and diminished bacterial presence in *P. monodon* post-larvae (Citarasu *et al.*, 2003), while a combination of Indian medicinal herbs ameliorated haematological, biochemical, and immunological metrics in *P. monodon* confronted with WSSV (Citarasu *et al.*, 2006). A synergistic immunostimulant formulation derived from five medicinal flora (*Eclipta alba*, *Aegle marmelos*, *Tinospora cordifolia*, *Picrorhiza kurooa*, and *Cynodon dactylon*) decreased viral load and enhanced survival rates to roughly 74% post-viral exposure (Citarasu, 2010). Recent studies have expanded upon these discoveries: a blend of nine herbs, featuring *Aloe vera* and *Andrographis paniculata*, enhanced growth, survival, and immune protection in *P. monodon* (AftabUddin *et al.*, 2017); a commercial phytogenic supplement augmented growth performance and immune response in *L. vannamei* on reduced-

fishmeal diets (Kesselring *et al.*, 2021); and the inclusion of *Wedelia chinensis* extract in the diet elevated total hemocyte count and fortified the innate immunity of white leg shrimp against *V. parahaemolyticus* (Ngoc *et al.*, 2026).

Mechanistic synthesis

Table 1 encapsulates the many additive classifications, their suggested mechanisms, and the often-observed consequences. Despite each category operating via somewhat unique receptors and pathways, the examined evidence aligns on a common downstream process: alteration of the gut microbiota and mucosal interface, stimulation of hemocyte-mediated and humoral immune responses, and, ultimately, enhanced resilience to bacterial and viral threats (Fig. 1). The recognition of the intrinsic immune IMD pathway as a mediator connecting gut microbiome structure to metabolic and immune equilibrium in *P. monodon* offers a molecular foundation for understanding why modifications to the gut community via probiotics, prebiotics, or phytogenics can yield widespread immune advantages (Supungul *et al.*, 2025).

Evidence from experimental studies

Table 2 enumerates notable experimental investigations referenced in this review, categorised by additive type, shrimp species, and the pathogen or stressor employed to assess effectiveness. *Litopenaeus vannamei* serves as the primary experimental model, with *Vibrio* spp. WSSV and other

challenge agents are predominantly utilized, underscoring their significant economic relevance to the sector. A consistent trend observed in research indicates that combined treatments, like inulin with MOS (Li *et al.*, 2018) or yeast with inulin (Ces  a *et al.*, 2021),

generally surpass the efficacy of single-ingredient supplements, implying an additive or synergistic interaction of complimentary immunological mechanisms.

Table 1: Major categories of functional feed additives used in shrimp aquaculture, their principal mechanisms of action, and commonly reported effects.

Additive category	Representative examples	Primary mechanism(s) of action	Key reported effects
Probiotics / synbiotics	<i>Bacillus</i> spp., <i>Lactobacillus</i> spp., yeasts; combined with prebiotics as synbiotics	Competitive exclusion of pathogens, production of antimicrobial metabolites and short-chain fatty acids, priming of hemocyte and mucosal immunity	Improved gut microbiota balance, growth, and resistance to <i>Vibrio</i> spp.
Prebiotics	Mannan oligosaccharide (MOS), fructooligosaccharide (FOS), inulin, galacto-oligosaccharide (GOS)	Selective stimulation of beneficial gut bacteria; upregulation of pattern-recognition and antimicrobial-peptide genes	Better gut morphology, immune gene expression, and survival after viral/bacterial challenge
β -glucans & other immunostimulants	Yeast/fungal β -1,3/1,6-glucan, lipopolysaccharides, nucleotides	Binding to pattern-recognition receptors (e.g., LGBP), activation of the prophenoloxidase cascade, respiratory burst, and antioxidant enzymes	Elevated phagocytosis, phenoloxidase and SOD activity, improved survival against WSSV and IMNV
Phytogenics / herbal extracts	<i>Andrographis paniculata</i> , <i>Solanum trilobatum</i> , <i>Eclipta alba</i> , <i>Wedelia chinensis</i> , commercial botanical blends	Direct antimicrobial/antiviral activity, antioxidant scavenging, modulation of hemocyte count and immune-gene transcription	Reduced pathogen load, higher hemocyte counts, improved growth and survival under challenge

Note: LGBP, lipopolysaccharide- and β -1,3-glucan-binding protein; SOD, superoxide dismutase; WSSV, white spot syndrome virus; IMNV, infectious myonecrosis virus; spp., species (plural).

As depicted in Figure 2, the evidence gathered for this review is widely spread among prebiotics, β -glucans/immunostimulants, and phytogenic, whereas there exists a relatively smaller yet swiftly expanding collection of specific probiotic/symbiotic studies. This distribution aligns with recent systematic evaluations of antibiotic

substitutes in aquaculture, which similarly indicate a growing yet still disjointed body of evidence across additive categories (Bondad-Reantaso *et al.*, 2023).

Challenges, safety, and regulatory considerations

Notwithstanding the continual favorable outcomes, various obstacles hinder the

conversion of these studies into dependable commercial use. Efficacy is sometimes contingent upon the individual strain, extract, and dosage: a probiotic or herbal extract that is successful against a certain disease may provide minimal defense against a different one, and the ideal dosages determined in one study may not be applicable across other rearing systems or phases of shrimp development. Secondly, the market for commercial functional additives encompasses items with inconsistent quality assurance and inadequately defined active ingredients, which complicates comparisons among

research and agricultural operations (Bondad-Reantaso *et al.*, 2023). Thirdly, the majority of corroborative evidence derives from regulated laboratory challenge trials; a limited number of researches affirm these advantages amongst the variable water quality, stocking density, and multi-pathogen stress characteristic of commercial ponds. Ultimately, the regulatory structures overseeing the registration, labelling, and allowable assertions for feed additives vary significantly among shrimp-producing nations, resulting in ambiguity for feed producers aiming to expand evidence-based formulations.

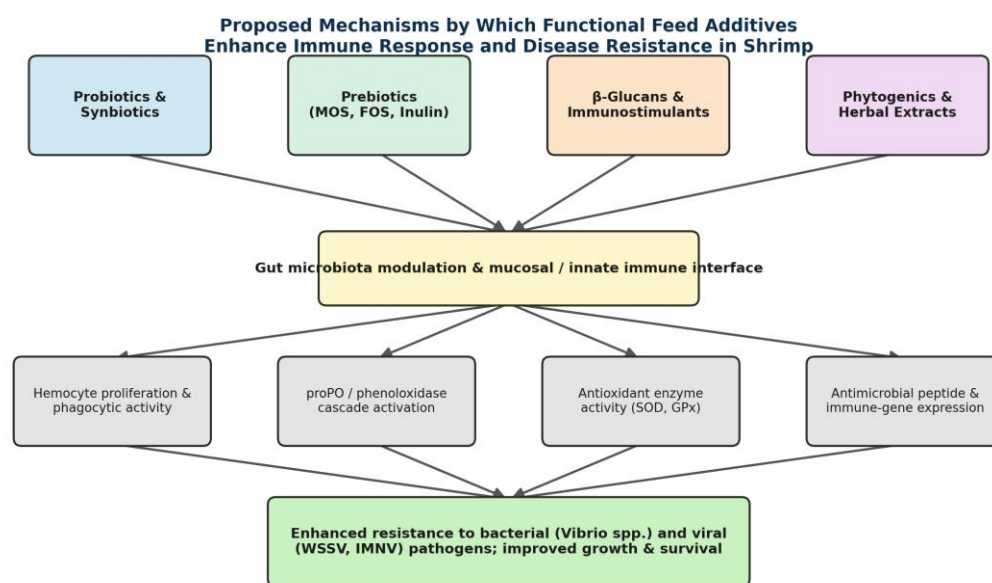


Figure 1: Proposed mechanistic pathway linking dietary functional feed additives to enhanced immune response and disease resistance in shrimp, via modulation of the gut microbiota and innate immune interface. FOS: fructooligosaccharide; GPx: glutathione peroxidase; IMNV: infectious myonecrosis virus; MOS: mannan oligosaccharide; proPO: prophenoloxidase; SOD: superoxide dismutase; WSSV: white spot syndrome virus.

Future perspectives

Numerous avenues seem auspicious for progressing in this domain. Multi-omics methodologies encompassing transcriptome, microbiome, and metabolomics analyses might elucidate

the specific molecular pathways activated by various additive categories and facilitate more precise formulation, drawing on current mechanistic research into the shrimp gut-immune axis (Supungul *et al.*, 2025). Further

investigation into symbiotic and multi-additive mixtures (such as prebiotic-yeast or glucan-phytogenic combinations) is justified due to the consistent finding that combined therapies exceed the efficacy of individual components (Li *et al.*, 2018; Ceséña *et al.*, 2021). Enhanced encapsulation and delivery methods may also aid in stabilizing delicate bioactive substances, including herbal

polyphenols, throughout feed preparation and exposure to water. Ultimately, extensive farm-scale experiments that integrate immunological and growth metrics with economic and ecological results will be crucial for transitioning functional feed additives from encouraging laboratory findings to routine elements of sustainable shrimp health management.

Table 2: Representative experimental studies evaluating functional feed additives on immune response and disease resistance in shrimp.

Additive	Shrimp species	Pathogen / stressor	Key reported outcome	Source
Inulin + MOS (2.5–10 mg/g)	<i>Litopenaeus vannamei</i>	WSSV; <i>Vibrio alginolyticus</i>	Combined supplementation raised expression of TLR1/2/3, STAT, crustin and anti-lipopolysaccharide factor genes more than either prebiotic alone	Li <i>et al.</i> , 2018
Mannan oligosaccharide	<i>L. vannamei</i> (juvenile)	Rearing stress	Improved growth performance, gut morphology and stress tolerance	Zhang <i>et al.</i> , 2012
MOS via <i>Artemia</i> (3–12 mg/L)	<i>L. vannamei</i> (larvae)	<i>Vibrio harveyi</i>	Higher digestive enzyme activity, immunity and resistance in larval stages	Widanarni <i>et al.</i> , 2018
Mannan oligosaccharide	<i>L. vannamei</i>	White spot disease	Enhanced immune response and growth performance	Prastiti <i>et al.</i> , 2018
Inulin-coated feed	<i>L. vannamei</i>	Field disease pressure	Improved growth, disease resistance, immune-gene expression and gut microbial diversity	Allie <i>et al.</i> , 2025
β -1,3/1,6-glucan (1000 mg/kg)	<i>L. vannamei</i>	Infectious myonecrosis virus (IMNV)	Enhanced survival with no signs of immunological fatigue over continuous exposure	Neto & Nunes, 2015
β -1,3-glucan	<i>L. vannamei</i>	Intestinal inflammation model	Modulated intestinal microbiota and reduced inflammatory response	Shen <i>et al.</i> , 2023
<i>Debaryomyces hansenii</i> yeast $\pm$ inulin	<i>Penaeus vannamei</i> (juvenile)	<i>Vibrio parahaemolyticus</i>	Increased survival and upregulated lysozyme, SOD and GPx gene expression	Ceséña <i>et al.</i> , 2021
Five-herb immunostimulant blend	<i>P. monodon</i>	Viral challenge	Reduced viral load; survival increased to about 74%	Citarasu, 2010
Nine-herb blend (<i>Aloe vera</i> <i>et al.</i>)	<i>P. monodon</i>	Bacterial challenge	Improved growth, survival and immunoprotection	AftabUddin <i>et al.</i> , 2017
Phytogenic feed additive (commercial)	<i>L. vannamei</i>	Low-fishmeal diet	Improved growth performance and immune response	Kesselring <i>et al.</i> , 2021
<i>Wedelia chinensis</i> extract	<i>Penaeus vannamei</i>	<i>Vibrio parahaemolyticus</i>	Increased total hemocyte count and strengthened innate immunity	Ngoc <i>et al.</i> , 2026

Note: GPx, glutathione peroxidase; IMNV, infectious myonecrosis virus; MOS, mannan oligosaccharide; SOD, superoxide dismutase; STAT, signal transducer and activator of transcription; TLR, toll-like receptor; WSSV, white spot syndrome virus.

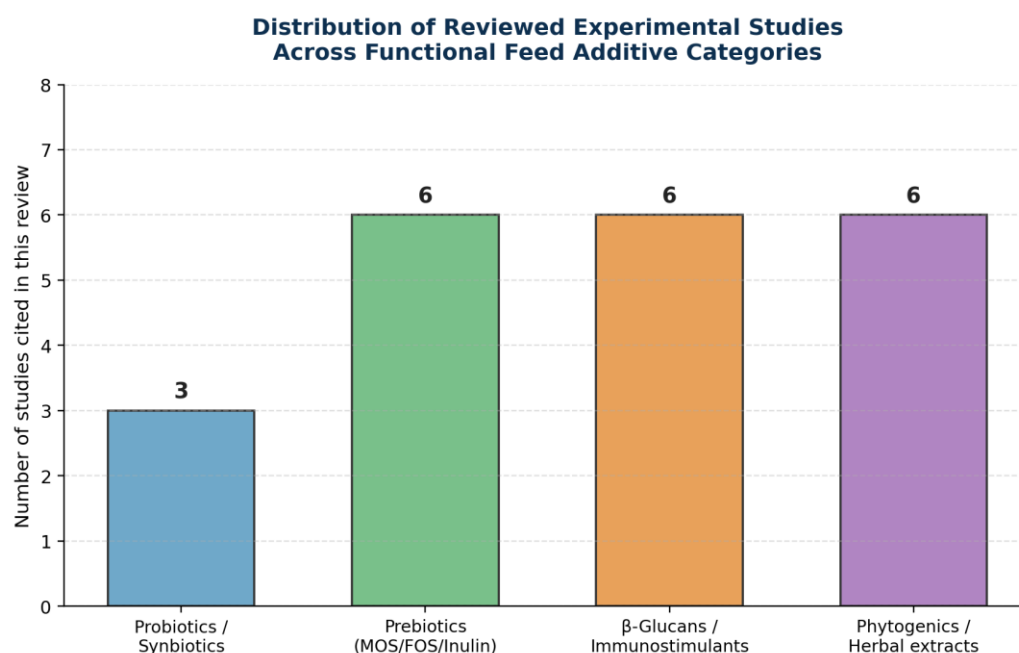


Figure 2: Distribution of the experimental studies cited in this review across the four major functional feed additive categories. FOS: fructooligosaccharide; MOS: mannan oligosaccharide.

Conclusions

Functional feed additives such as probiotics and symbiotic, prebiotics, β -glucans, and associated immunostimulants, along with phytochemical extracts, constitute a substantiated, non-antibiotic approach to augmenting immune response and disease resilience in aquaculture shrimp. In the trials examined, these additions uniformly enhanced both cellular and humoral immune responses as well as survival rates following challenges, particularly when utilized in conjunction. Achieving their complete potential at a commercial level necessitates enhanced product standardization, a more precise comprehension of strain- and dose-related effects, and broader validation in actual agricultural settings.

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Consent for publication

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