

# Recent Advances in Research on the Effects of Chinese Herbal Extracts on the Immune Function of Aquatic Animals

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**Abstract:** Against the backdrop of intensive development in the aquaculture industry, the overuse of antibiotics has led to a series of problems, including drug residues and antibiotic resistance. Consequently, the development of green alternatives to antibiotics has become an urgent requirement for the industry. Due to their combined nutritional and medicinal value, as well as their low toxicity, high efficacy and environmental friendliness, Chinese herbal extracts have become a research focus for immune enhancers in aquaculture. This paper systematically reviews the immunomodulatory mechanisms of key active components in Chinese herbal extracts, including polysaccharides, flavonoids, polyphenols and alkaloids. It summarises research findings on the application of single-herb extracts (such as *Atractylodes macrocephala*, Isatis root and *Astragalus membranaceus*) and related compound extracts in aquaculture, and analyses core issues in current research, including poor controllability of component quality, insufficient elucidation of mechanisms of action, low bioavailability, unclear dose-response relationships, and outlines future research directions in four areas: deepening mechanistic studies, innovating formulation technologies, establishing standardisation systems, and conducting ecological safety assessments. This aims to provide theoretical support and practical guidance for the research, development, and industrial application of green immunostimulants for aquaculture.

**Keywords:** Chinese herbal extracts; aquatic animals; immune function; antioxidant; gut health

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## 1 Introduction

With the rapid development of aquaculture towards high-density and intensive farming, the frequent occurrence of diseases has become a core issue constraining the sustainable development of the industry. The traditional model of relying on antibiotics for disease prevention and control is facing increasingly stringent regulatory restrictions due to the resulting drug residues, the spread of antibiotic-resistant genes, and ecological risks. The Ministry of Agriculture and Rural Affairs continues to promote initiatives to reduce the use of feed additives and antibiotics in aquaculture, creating an urgent need to develop green and highly effective alternatives to antibiotics.

As natural plant resources, traditional Chinese medicinal herbs possess both nutritional and medicinal value. Their extracts have become a research focus in the aquaculture sector due to their low toxicity, high efficacy and environmental friendliness. In recent years, *Atractylodes macrocephala* extract (*Atractylodes* polysaccharides) has been officially approved as a new feed additive, marking a crucial step in the transition of Chinese herbal extracts from research to industrial application. Studies indicate that active components in Chinese herbal extracts, such as polysaccharides, flavonoids, polyphenols and alkaloids, can regulate the immune function of aquatic animals through multiple targets, thereby enhancing disease resistance and improving growth performance.

This paper aims to systematically review the research progress on the effects of Chinese herbal extracts on the immune function of aquatic animals, analyse their mechanisms of action and current applications, and explore existing issues and future directions, with a view to providing a theoretical basis for the development of green immunostimulants for aquaculture.

## 2 Major Active Components and Immunomodulatory Mechanisms

### 2.1 Major Active Components and Their Sources

Chinese herbal extracts can affect the immune system because they contain many different bioactive compounds. Polysaccharides have been studied the most. Examples include *Atractylodes* polysaccharides, *Astragalus* polysaccharides, and Ginseng polysaccharides. These polysaccharides act like prebiotics, shaping the gut microbiota and supporting stronger immune responses. Flavonoids are another common group. Quercetin and rutin show up in a lot of medicinal herbs, including honeysuckle and *Scutellaria baicalensis*. They can neutralize free radicals and slow down lipid peroxidation. Polyphenols like curcumin and resveratrol can affect how inflammatory factors are expressed. This happens through activation of Toll-like receptors and the NF- $\kappa$ B signalling pathway. Alkaloids such as matrine help protect against oxidative stress. They support intestinal barrier function as well.

### 2.2 Mechanisms of Immunomodulatory Action

Non-specific immune activation: Aquatic animals are lower vertebrates, so most of their immune defence comes from the non-specific immune system. Herbal extracts can switch on this system in a few different ways. In spotted tilapia, *Astragalus* polysaccharides significantly boost serum lysozyme (LZM) activity. They increase acid phosphatase (ACP) and alkaline phosphatase (AKP) too. White blood cells show higher phagocytic activity as well. *Atractylodes macrocephala* extract works differently. In the hepatopancreas, it switches on immune pathways like Toll-Dorsal and IMD-Relish, which boosts the non-specific immune capacity of *Macrobrachium rosenbergii*.

Keeping the antioxidant defence system working matters a lot in high-density aquaculture, since oxidative stress is a frequent strain on

aquatic animals. Herbal extracts can ease this kind of oxidative damage by adjusting how antioxidant enzymes function. Research reports that *Atractylodes macrocephala* polysaccharides raise superoxide dismutase (SOD) and catalase (CAT) activity. MDA levels drop as a result. *Astragalus membranaceus* polysaccharides can boost SOD and CAT activity. This helps the body clear out free radicals more effectively.

**Gut health and microbiota regulation:** In aquatic animals, the gut acts as the largest immune organ. Herbal extracts can help reshape the gut microbiota. They raise the amount of beneficial bacteria and keep pathogenic bacteria from multiplying. At the same time, they support gut barrier function through short-chain fatty acid metabolism. Isatis root extract has been linked to higher gut microbiota diversity and stronger digestive enzyme activity. It works through the gut-liver axis and helps promote nutrient absorption.

### 3 Research on the Application of Single-Herb Extracts

#### 3.1 *Atractylodes macrocephala* Extract

*Atractylodes macrocephala* extract (whose active component is *Atractylodes* polysaccharide) is the first Chinese herbal-derived feed additive to be approved. Systematic research by Researcher Liu Bo's team indicates that adding *Atractylodes macrocephala* extract to low-fishmeal diets can significantly improve the growth performance of *Macrobrachium rosenbergii* and reduce the feed conversion ratio. In terms of immune modulation, *Atractylodes macrocephala* polysaccharides activate the hepatopancreatic immune pathway and enhance non-specific immune capacity; challenge tests showed that the disease resistance of the experimental group was significantly improved. Gut microbiome analysis further confirmed that this additive can increase the abundance of beneficial bacteria such as *Lactobacillus* spp. and inhibit pathogenic bacteria such as *Aeromonas* spp. .

#### 3.2 Isatis Root Extract

A research team led by Researcher Zhao Jian at the Pearl River Fisheries Research Institute investigated the immune-enhancing effects of Isatis root extract using hybrid snakehead as the study subject. The results indicated that adding 1.5%–2.0% Isatis root extract to the feed promoted growth in juvenile fish, improved antioxidant capacity, and enhanced liver and intestinal health. More importantly, the survival rate of juvenile fish in the treatment group against the virus was significantly increased to 50%–60%. Mechanistic studies revealed that Isatis root extract improves gut microbiota composition and liver health by modulating the gut-liver axis .

#### 3.3 *Astragalus* Polysaccharides

Cheng An-da et al. conducted a clinical evaluation of the efficacy and safety of *Astragalus* polysaccharides in spotted tilapia, in accordance with the standards of the Clinical Trial Centre for New Aquatic Drugs under the Ministry of Agriculture and Rural Affairs. Phase II clinical trials demonstrated that *Astragalus* polysaccharides significantly increased serum SOD, CAT, LZM, ACP and AKP activity, as well as white blood cell phagocytic activity; Phase III clinical trials further confirmed that *Astragalus* polysaccharides not only enhance immunity and improve resistance to bacterial infections, but also promote growth, with an optimal dosage of 20 mg/kg body weight. Safety evaluations confirmed that this dosage is harmless to the target animals .

#### 3.4 Other Chinese herbal extracts

*Scrophularia baicalensis*: Research by the Institute of Hydrobiology, Chinese Academy of Sciences has found that *Scrophularia baicalensis* extract can alleviate food-borne enteritis in fish by increasing the abundance of probiotics (*Bifidobacterium*, *Faecalibacterium*), promoting intestinal epithelial proliferation, and inhibiting the inflammatory aggregation of intestinal mucosal immune cells. Network pharmacology analysis indicates that its primary active component, hexahydroxanthoxin F, binds to proteins associated with macrophage function, thereby exerting an anti-inflammatory effect .

**Ginseng polysaccharides and Litsea cubeba essential oil:** Research from Hunan Agricultural University indicates that appropriate doses of ginseng polysaccharides (200–800 mg/kg) and *Litsea cubeba* essential oil (100–200 mg/kg) can significantly enhance digestive enzyme activity in spotted tilapia. By regulating intestinal tight junction genes, cytokine balance and beneficial bacterial flora, they strengthen intestinal barrier function; the ginseng polysaccharide group demonstrated significantly enhanced resistance to *Yersinia rorvansi* .

### 4 Compound Extracts and Synergistic Effects of Formulations

Although single-herb extracts possess immunomodulatory functions, compound formulations often produce synergistic effects. Studies have shown that when Yupingfeng polysaccharides (a formulation comprising *Astragalus*, *Atractylodes macrocephala* and *Saposhnikovia divaricata*) are used in combination with *Bacillus coagulans*, they not only effectively improve the growth performance of *Macrobrachium rosenbergii* but also synergistically activate antioxidant enzyme activity, thereby enhancing immunomodulatory effects . This finding suggests that the combined application of Chinese herbal extracts and probiotics may represent an important direction for future research and development.

Concurrent studies on hybrid snakehead fish examined the effects of *Schisandra chinensis*, Isatis root, Forsythia, and their compound extracts. The results demonstrated that the compound group exhibited comprehensive advantages in terms of growth performance, antioxidant indicators, and disease resistance, reflecting the characteristics of multi-component synergistic action . A review by Liu et al. also noted that the combined application of multiple bioactive components often produces synergistic effects in promoting growth, immune modulation, and stress resistance .

### 5 Research Prospects and Challenges

#### 5.1 Current Major Challenges

Although significant progress has been made in research on the application of Chinese herbal extracts in aquaculture, numerous challenges remain. Firstly, the complexity of constituents and quality control: the active components of Chinese herbs are subject to significant variation due to factors such as origin, harvesting period and extraction methods, and there is a lack of uniform quality standards. Secondly, the mechanisms of action remain to be elucidated: most studies are limited to describing effects, with insufficient in-depth analysis of molecular mechanisms, particularly regarding the synergistic effects of multiple components. Thirdly, bioavailability issues: some active components (such as saponins) have high molecular weights and poor fat solubility, resulting in low absorption and metabolic efficiency in aquatic animals. Fourthly, the dose-response relationship remains unclear: there is a lack of systematic research into the optimal additive dosage for different species and growth stages.

## 5.2 Future Research Directions

**Advancing mechanistic research:** Utilising approaches such as network pharmacology and multi-omics technologies to systematically analyse the target sites and signalling pathways of Chinese herbal extracts. Research on *Scrophularia baicalensis* provides a good example; by combining transcriptomic analysis, network pharmacology predictions and molecular docking validation, the potential mechanism of action of Jianhuang F has been elucidated.

**Innovation in Formulation Technology:** Developing novel formulation processes, such as nano-encapsulation and fermentation technology, to enhance the bioavailability and stability of active ingredients.

**Standardisation System Development:** Establishing comprehensive quality control standards covering raw material sources, extraction processes, active ingredient testing and potency evaluation, thereby laying the foundation for industrial application.

**Ecological safety assessment:** Conducting long-term toxicity, environmental fate and ecological risk studies to ensure that the application of herbal extracts does not give rise to new environmental issues.

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