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Original article

# ALTERNATIVE METHODS OF DISEASE PREVENTION AND TREATMENT IN AQUACULTURE

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***Abstract***

**Background.** In recent years, the use of antibiotics in aquaculture has raised increasing concern due to the development of microorganism resistance to antibacterial drugs and the negative impact on the ecosystem. Therefore, search for alternative methods for treating and preventing fish diseases has become an urgent task. Promising alternatives for the prevention and treatment of aquaculture species include the use of probiotics, prebiotics, synbiotics, postbiotics, phytobiotics, bacteriophages, and quorum sensing (QS) inhibition mechanisms. The state of the microflora of aquatic organisms is crucial for enhancing the organism's resistance to infectious diseases. Thus, using agents that can positively influence the microbiota, exert antimicrobial effects, and modulate the immune system is essential for the effective development of the aquaculture industry. This article discusses some of the main fish diseases, the likelihood of which increases with the intensification of aquaculture. Bacteria of the genus *Aeromonas* are often the cause of diseases and financial losses in the industry. The work provides an overview of alternative methods for preventing and treating fish diseases that can reduce the use of antibacterial drugs, including the application of vaccines, probiotics, prebiotics, and bacteriocins.

**Purpose.** To investigate alternative methods of treatment and prevention of fish diseases.

**Materials and methods.** In the study, a method of collecting, analyzing, and systematizing of published scientific sources was used. The collection of literary information was carried out using reference databases such as Science Direct, Research Gate, Google Scholar, National Library of Medicine, Wiley Online Library, and others. To search for suitable scientific publications, keywords such as «aquaculture», «diseases», «bacterial fish diseases», «probiotics», «prebiotics», «synbiotics», «bacteriocins», «phytobiotics», and «quorum sensing» were used individually or in various combinations. The search period was limited to scientific works published between 2014 and 2024.

**Results.** As alternative methods, vaccination, quorum sensing inhibition, bacteriophages, as well as probiotics, prebiotics, phytobiotics, and others can be used. The state of the fish microbiome has an important impact on the likelihood of developing of infectious processes. For example, it has been reported that fish with a healthy microbiome more effectively controlled and suppressed the colonization and dissemination of bacteria of the genus *Aeromonas* than fish with a disrupted microbiota. Currently, probiotic microorganisms are most commonly used as agents that can influence the microflora and correct the microbial balance [36]. Probiotics are most commonly represented with bacteria, including species from cultures *Bacillus* sp., *Lactococcus* sp., *Micrococcus* sp., *Carnobacterium* sp., *Enterococcus* sp., *Lactobacillus* sp., *Streptococcus* and *Weissella* sp. Some strains of yeast and algae may be used too. Probiotics are most commonly represented with a group of lactic acid bacteria, as among all microorganisms with registered probiotic properties, they are considered to have a higher safety profile. They can produce antimicrobial substances and positively influence the immune system of the macroorganism. Probiotics used in aquaculture must undergo a special assessment to determine their potential for application, taking into account the specifics of the industry. The main spectrum of action of probiotic microorganisms in the intestines of aquatic organisms lies in their anti-adhesive effect against pathogenic strains, the production of antimicrobial substances (including bacteriocins and defensins), competition with pathogenic flora, enhancement of the host's resistance properties, alteration of the intestinal pH level, and activation of the immune system.

**Conclusion.** Thus, despite the intensification of aquaculture and the increased likelihood of infectious diseases in aquaculture species, the worsening issue of antibiotic resistance and the irrational use of antibacterial drugs necessitate the development and implementation of alternative methods for controlling fish diseases.

**Keywords:** aquaculture; diseases; bacterial diseases of fish; probiotics; prebiotics; bacteriocins

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Научная статья

# АЛЬТЕРНАТИВНЫЕ МЕТОДЫ ПРОФИЛАКТИКИ И ЛЕЧЕНИЯ ЗАБОЛЕВАНИЙ В АКВАКУЛЬТУРЕ

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***Аннотация***

**Обоснование.** В последние годы использование антибиотиков в аквакультуре вызывает все большее беспокойство из-за развития устойчивости микроорганизмов к антибактериальным препаратам и негативного воздействия на экосистему. Поэтому исследование альтернативных методов лечения и профилактики рыбных заболеваний стало актуальной задачей. Перспективными альтернативами для профилактики и лечения видов аквакультуры являются использование пробиотиков, пребиотиков, синбиотиков, постбиотиков, фитобиотиков, бактериофагов и механизмов ингибирования кворум-сенсинга (QS). Состояние микрофлоры водных организмов имеет решающее значение для повышения устойчивости организма к инфекционным заболеваниям. Таким образом, использование агентов, которые могут положительно влиять на микробиоту, оказывать антимикробное действие и модулировать иммунную систему, является важным для эффективного развития аквакультуры. В данной статье рассматриваются некоторые основные заболевания рыб, вероятность которых увеличивается с интенсификацией аквакультуры. Бактерии рода *Aeromonas* часто являются причиной заболеваний и финансовых потерь в отрасли. Работа предоставляет обзор альтернативных методов профилактики и лечения рыбных заболеваний, которые могут снизить использование антибактериальных препаратов, включая применение вакцин, пробиотиков, пребиотиков и бактериоцинов.

**Цель.** Исследовать альтернативные методы лечения и профилактики рыбных заболеваний.

**Материалы и методы.** В исследовании использовался метод сбора, анализа и систематизации опубликованных научных источников. Сбор литературной информации осуществлялся с использованием реферативных баз данных Science direct, Research Gate, Google academy, National Library of Medicine, ScienceDirect, онлайн-библиотека Wiley и др. Для поиска подходящих научных публикаций использовали ключевые слова «аквакультура», «заболевания», «бактериальные заболевания рыб», «пробиотики», «пребиотики», «синбиотики», «бактериоцины», «фитобиотики», «чувство кворума» по отдельности или в различных комбинациях. Период поиска ограничивался научными работами, опубликованными в период 2014-2024 гг.

**Результаты.** В качестве альтернативных средств можно использовать вакцинацию, подавление чувства кворума, бактериофаги, а также пробиотики, пребиотики, фитобиотиков и др. Состояние микробиома рыбы имеет важное значение на вероятность развитие инфекционного процесса. Так, например, сообщается, что у рыб со здоровым микробиомом более эффективно контролировалась и подавлялась колонизация и диссеминация бактерий рода *Aeromonas*, чем у рыб с нарушением микробиоты. На данный момент в качестве средств, которые могут влиять на микрофлору и корректировать микробный баланс, чаще всего применяются пробиотические микроорганизмы. В качестве пробиотиков чаще всего используют бактерии, включая бактерии рода *Bacillus* sp., *Lactococcus* sp., *Micrococcus* sp., *Carnobacterium* sp., *Enterococcus* sp., *Lactobacillus* sp., *Streptococcus* и *Weissella* sp., также могут использоваться некоторые штаммы дрожжей, водорослей. Чаще всего в качестве пробиотиков используется группа молочнокислых бактерий, так как среди всех микроорганизмов с зарегистрированными пробиотическими свойствами, считается, что у них более высокий профиль безопасности, они могут продуцировать антимикробные вещества и положительно влиять на иммунную систему макроорганизма. Пробиотики, применяемые в аквакультуре, должны проходить специальную оценку для определения их потенциала применения с учетом специфики отрасли. Основной спектр действия пробиотических микроорганизмов в кишечнике гидробионтов заключается в антиадгезивном эффекте в отношение патогенных штаммов, продукции антимикробных веществ (в том числе бактериоцинов и дефензинов), конкурирование с патогенной флорой, повышение резистентных свойств макроорганизма, изменение уровня pH кишечника и активация иммунной системы.

**Заключение.** Несмотря на интенсификацию аквакультуры и повышение вероятности развития инфекционных заболеваний у товарных объектов аквакультуры, усугубление проблемы антибиотикорезистентности и нерационального применения антибактериальных лекарственных средств диктуют необходимость разработки и внедрения альтернативных методов контроля развития болезней рыб.

**Ключевые слова:** аквакультура; болезни; бактериальные болезни рыб; пробиотики; пребиотики; бактериоцины

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**Introduction**

In recent years, aquaculture in the Russian Federation and around the world has shown significant growth in production volumes. Raising fish in artificial conditions allows to supply population with accessible animal protein. By 2017, more than 112 million tons of aquaculture products were produced, of which 80 million tons – fish and shellfish, and 32 million tons – seaweeds. The number of cultivated species increased from 300 species of plants and animals in 1997 to 425 species in 2017 [1].

The production intensification inevitably leads to an increase in cases of fish diseases. To solve this problem, farmers often use antibiotics. Irrational use of antibacterial therapy results in the selection and preservation of resistant strains of pathogenic bacteria. According to available information, up to 700,000 people die each year from infections caused by resistant bacteria, and by 2050, this number may rise up to 10,000,000 deaths per year [2]. This problem requires the development of new strategies to ensure biological safety in agriculture and other areas.

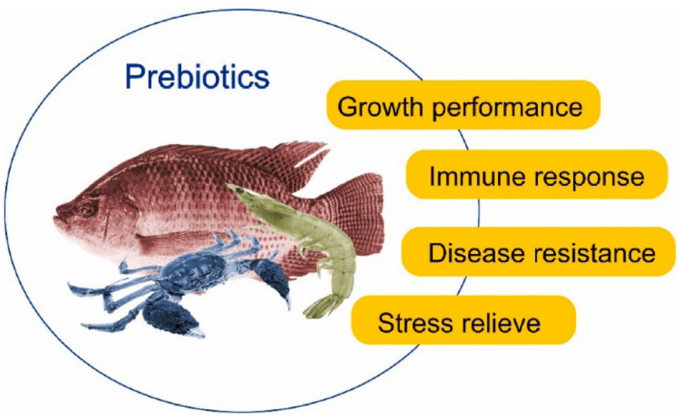


**Fig. 1.** Probiotic effect in aquaculture
*Source:* https://doi.org/10.1111/are.15846 [10]

In aquaculture, diseases of various etiologies are registered: bacterial [3], viral [4], parasitic [5], fungal [6]. The diversity of pathogens requires the selection of effective methods of prevention and treatment.

The use of probiotics [7; 8], prebiotics [9; 10], synbiotics [11; 12], postbiotics [13], phytobiotics [14], bacteriophages [15] and quorum sensing (QS) mechanisms is promising as alternative means of prevention and treatment of aquaculture objects [16].

In addition to inhibiting pathogens, many of the mentioned agents are a promising mechanism for enhancing the efficiency of aquaculture. For example, the introduction of prebiotics into fish diets has been observed to increase growth rates, improve feed efficiency, and reduce feed conversion ratios [17] (Fig. 1).

The present study analyzes and summarizes the main fish diseases in aquaculture, as well as promising methods for their prevention and treatment.

**Materials and methods**

In the study, a method of collecting, analyzing, and systematizing of published scientific sources was used. The collection of literary information was carried out using reference databases such as Science Direct, Research Gate, Google Scholar, National Library of Medicine, Wiley Online Library, and others. To search for suitable scientific publications, keywords such as «aquaculture», «diseases», «bacterial fish diseases», «probiotics», «prebiotics», «synbiotics», «bacteriocins», «phytobiotics», and «quorum sensing» were used individually or in various combinations. The search period was limited to scientific works published between 2014 and 2024.

**Results and discussion**

*1.1 Fish bacterial diseases in aquaculture*

In aquaculture, the most popular species are those from the sturgeon family (*Acipenseridae*), carp family (*Cyprinidae*), salmon family (*Salmonidae*), and catfish family (*Siluridae*). Among these cultivated species, bacterial pathogens are widespread, causing significant economic losses [18]. In aquaculture, both gram-positive and gram-negative bacteria can cause fish diseases. The genus *Aeromonas* is most often responsible for diseases and, hence, financial losses in the industry [19]. The estimation of the losses in China, caused by *Aeromonas* and some other bacteria, showed that the damage is equal to 120 million dollars for the period 1990-1992 [20]. In 2010, an outbreak of Motile Aeromonas septicemia (MAS) at fish farms in Alabama (United States) caused 3 million dollars damage [21].

Aeromonads are gram-negative motile rods that are typical representatives of the microbiota in water bodies [22]. The analysis of the 16S rRNA sequence allowed the classification of these bacteria into the family *Aeromonadaceae*, class *Gammaproteobacteria*, order *Aeromonadales*. [23]. Among the 31 species of the genus *Aeromonas* [24], a typical representative is *Aeromonas hydrophila*. This species is a freshwater facultative anaerobe with a chemoorganotrophic type of nutrition, characterized by a positive reaction in tests for catalase, oxidase, and indole. [25]. *A. hydrophila* causes septicemia, hemorrhagic septicemia, and ulcerative disease in fish. Clinical (external) manifestations of the disease include hemorrhages, ulcers on the body surface, and accumulation of free fluid in the abdominal cavity [20] (Fig. 2).

In some regions, other species of the *Aeromonas* genus may dominate. For example, studies in southern China have shown that *A. veronii* is the dominant etiological agent of MAS in this region [26].

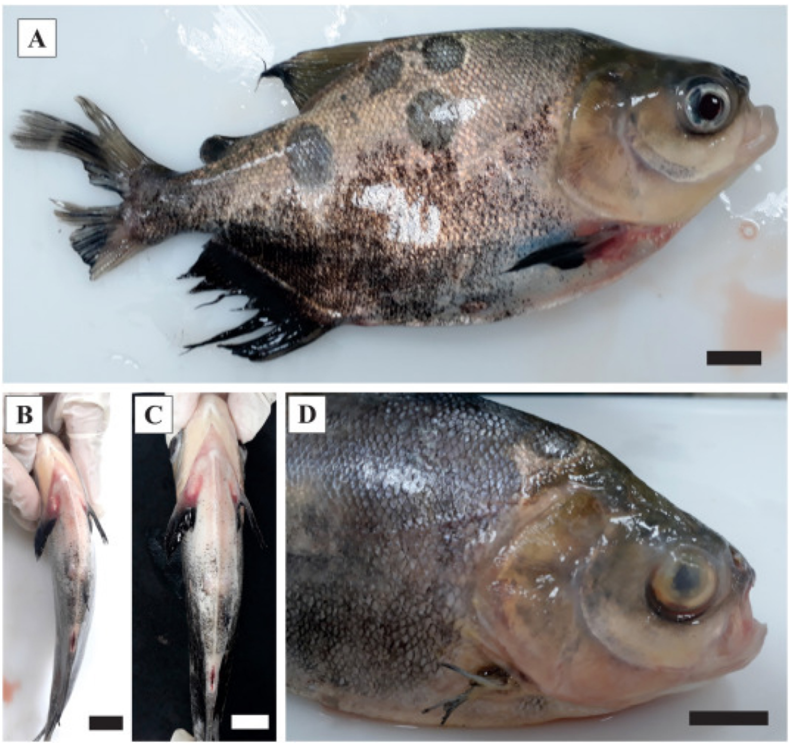


**Fig. 2.** External signs of *Motile Aeromonas* septicemia in *Colossoma macropomum*: A – lesions on the skin at the base of the fin, B, C – hemorrhages on the ventral side of the body, D – eye opacity
*Source:* https://doi.org/10.1016/j.aquaculture.2020.736068 [31]

Other gram-negative bacteria, causing diseases in aquaculture, include representatives of the genus *Pseudomona*s, which comprises more than 200 species [27]. Despite the fact that these bacteria are described as opportunistic pathogens, some studies report cases of 100% mortality in trout, bream, and other species [28]. The virulence of *Pseudomonas aeruginosa* is coordinated by the quorum sensing (QS), which increases the risks of pseudomonas outbreaks in aquaculture. This strain is recognized as one of the 10 most dangerous bacteria in the world for humans and animals [29]. In addition, due to the irrational use of pharmaceuticals, *P. aeruginosa* has developed resistance to most antibiotics and is therefore included in the ESKAPE list as a dangerous pathogen [30].

*1.2 Methods of disease treatment and prevention in aquaculture*

For a long time, there has been irrational use of nonspecialized antibacterial therapy in aquaculture. In most cases, antibiotics were used for prophylactic purposes. The lack of control has led to the formation of communities of bacteria resistant to antimicrobial agents (AMRB) [32]. Moreover, there is a threat of the emergence of superbacteria, partly due to the possibility of horizontal gene transfer among bacteria [33; 34]. To prevent further development of resistance in bacteria in aquaculture, it is necessary to impose a ban on the use of antibiotics as growth promoters and for disease prevention. Additionally, guidelines should be developed to reduce the frequency of antibiotic use in favor of alternative treatment methods [35].

There are already examples in the world practice. Some countries have introduced alternative methods aimed at preventing and treating bacterial diseases in fish farming technology. In Norway, which has been a leader in salmon farming for a long period of time, the use of vaccines has proven their efficiency [32].

As alternative methods, vaccination, quorum sensing inhibition, bacteriophages, as well as probiotics, prebiotics, phytobiotics, and others can be used (Fig. 3) [36].

The state of the fish microbiome has an important impact on the likelihood of developing of infectious processes [37, 38]. For example, it has been reported that fish with a healthy microbiome more effectively controlled and suppressed the colonization and dissemination of bacteria of the genus *Aeromonas* than fish with a disrupted microbiota [39]. Currently, probiotic microorganisms are most commonly used as agents that can influence the microflora and correct the microbial balance [36]. Probiotics are most commonly represented with bacteria, including species from cultures *Bacillus* sp., *Lactococcus* sp., *Micrococcus* sp., *Carnobacterium* sp., *Enterococcus* sp., *Lactobacillus* sp., *Streptococcus* and *Weissella* sp. Some strains of yeast and algae may be used too [40].

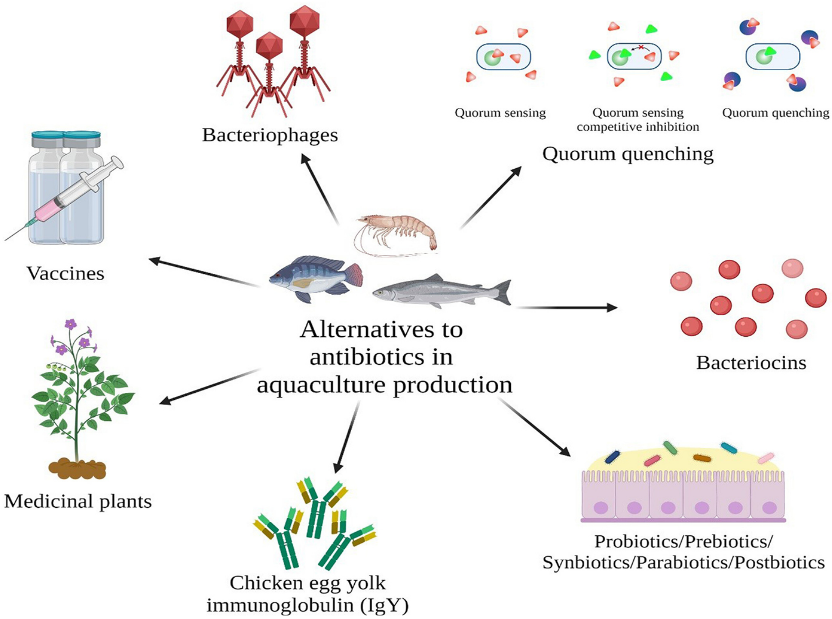


**Fig. 3.** Alternative methods of fish disease prevention and treatment in aquaculture
*Source:* https://doi.org/10.1111/raq.12786 [36]

Probiotics are most commonly represented with a group of lactic acid bacteria, as among all microorganisms with registered probiotic properties, they are considered to have a higher safety profile. They can produce antimicrobial substances and positively influence the immune system of the macroorganism [41]. Probiotics used in aquaculture must undergo a special assessment to determine their potential for application, taking into account the specifics of the industry [42]. The main spectrum of action of probiotic microorganisms in the intestines of aquatic organisms lies in their anti-adhesive effect against pathogenic strains, the production of antimicrobial substances (including bacteriocins and defensins), competition with pathogenic flora, enhancement of the host's resistance properties, alteration of the intestinal pH level, and activation of the immune system [36]. The mechanisms of action of probiotics and bacteriocins are graphically presented in Fig. 4.

Both prebiotics and probiotics can be used separately or together, with prebiotics serving as a nutritional substrate for the host's own microbiota. This enhances the competitive action of the host's microbiome by suppressing and modulating the concentration of pathogenic and opportunistic microorganisms

[43]. Synbiotics are a combination of probiotics and prebiotics, which include indigestible fiber, further stimulating the activity of commensal microorganisms in the gut and enhancing both systemic and local immunity in fish, thereby reducing the likelihood of developing infectious diseases [44].

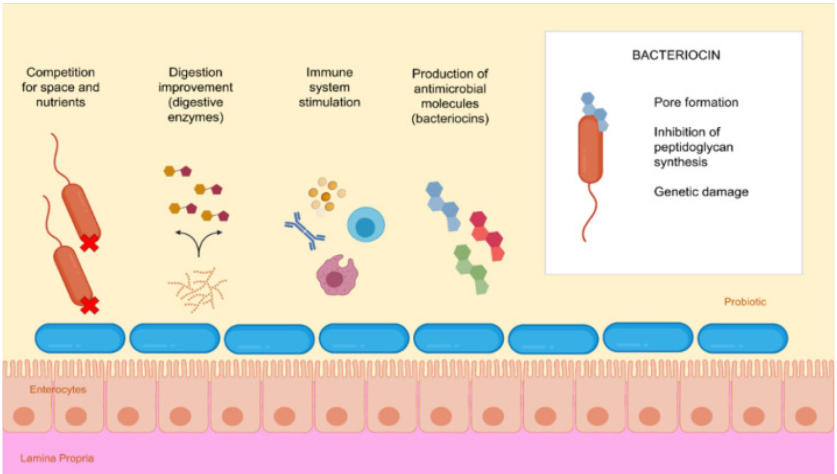


**Fig. 4.** Probiotics and bacteriocins mode of action
*Source:* https://doi.org/10.3390/microorganisms10091705 [42]

In recent years, bacteriocins have played a significant role in controlling fish health. Bacteriocins are low-molecular-weight bactericidal peptides synthesized by ribosomes. Their advantages include having less negative impact on the macroorganism while maintaining antagonistic effects against pathogenic microorganisms and stimulating the growth of beneficial microflora [36]. The action mechanism of bacteriocins is diverse and can depend on the characteristics of the molecules. Primarily, the mechanism of action is associated with damaging the bacterial cell wall by forming pores and disrupting the function of peptidoglycan transporters. They can also affect microorganisms through their genetic material and protein synthesis at the ribosomal level. However, the spectrum of action of bacteriocins depends on the presence of receptors in the microorganism for their absorption, which is why they can be classified as agents with a narrow spectrum of activity [42]. Bacteriocins, isolated from lactic acid bacteria, are used in the food industry, such as pediocin PA-1 produced by *Pediococcus acidilactici*, which exerts antimicrobial activity against *Listeria monocytogenes* in meat and dairy products [45].

**Conclusion**

Thus, despite the intensification of aquaculture and the increased likelihood of infectious diseases in aquaculture species, the worsening issue of antibiotic resistance and the irrational use of antibacterial drugs necessitate the development and implementation of alternative methods for controlling fish diseases.

**Conflict of interest information.** The authors declare that they have no conflict of interest.

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