Aquaculture is a rapidly growing economic area that represents an important alternative to satisfy future food demands. Nevertheless, one of the main threats to aquaculture is infectious outbreaks that generate significant productive losses. In response, large quantities of antimicrobials have been used and released into aquatic ecosystems, with the associated risk to human health and the environment, making it necessary to develop new products that are safe for humans and the environment. This chapter focuses on the use of marine microbial biosurfactants, a wide variety of compounds with remarkable physical and biological properties, as an alternative to antibiotic therapy in aquaculture.

**Keywords** biosurfactants; antimicrobials; fish pathogens

### 1. Introduction

The overexploitation of marine resources, combined with climate change, is reducing marine resources as a food source. In this scenario, aquaculture is a rapidly growing activity that offers an important alternative to satisfy future food demands. According to the Food and Agriculture Organization of the United Nations (FAO), food resources produced by aquaculture have increased 12 times in recent decades, at an average annual rate of 8.8 percent, with about 600 different species, and 190 countries involved in farming systems [1]. The main threats to this activity are infectious diseases that can cause total losses to farmers. In order to maintain growth rates, large quantities and varieties of antimicrobial agents have been used in aquaculture, including orally dispensed antibiotics in fish feed. The worldwide-approved antimicrobials agents for aquaculture include a variety of aminoglycosides, beta-lactams, macrolides, quinolones sulfonamides and tetracyclines that are also employed for prophylaxis and treatment of infections in humans. These drugs are applied under specific regulations established by the respective health agencies of each country. Despite regulation, it is widely recognized that the overuse or misuse of antibiotics for the treatments of zoonotic bacteria is a food safety problem with risk to human health [2]. In addition, the administration route for the treatment of fish implies the release of large quantities of antibiotics into the environment, resulting in the selection and spread of genetic determinants of resistance, which affects ecosystems around fish farming operations. In this context, the research and development of new and safer strategies for controlling bacterial diseases in aquaculture is required. Because of their biological and chemical diversity, marine environments are sources of alternative products for prophylaxis and treatment of microbial infectious diseases [3, 4]. Specifically, the great variety of marine molecules (produced by microorganisms) with surface-active properties known as biosurfactants (BS), offer the potential for developing innovations for the control of infectious diseases. BS produced by marine bacteria participate in biological interactions such as intra or inter species communication (quorum sensing) or competition (antimicrobials). They also have physical properties of industrial interest, such as micelle formation, with potential applications in the development of functional foods, active coatings (paints), vaccines, and nano structures for bioactive delivery systems.

### 2. Antibiotics in aquaculture

The infectious diseases caused by microorganisms are affecting aquaculture globally. They attack numerous species with high incidence, resulting in heavy productive losses. The outbreaks that have occurred in Africa, Asia, Europe and South America in the last decade have caused partial or total loss of production [2]. For example, Piscirickettsiosis is a severe condition caused by *Piscirickettsia salmonis*, which caused losses of US$100 million in only one year of production in the Chilean salmonid industry [5]. The economic and social impact associated with the main bacterial pathologies of reared confined fish affect marketable biomass, employment and related business activities. Unfortunately, the complex techniques of farming and the requirements of commercial production result in raising fish in high densities that favor stress and, consequently, the emergence and rapid spread of pathogens. In addition, climate...
change and the deterioration of the water quality used for cultivation promote infectious outbreaks [6]. In response, the aquaculture industry uses large amounts of antimicrobial agents to control microbial diseases. This practice is considered a risk for aquatic ecosystems, animal and human health, and a food safety problem (Figure 1).

2.1. Risk for aquatic microbial ecosystems

As mentioned before, the main strategy to prevent and control bacterial outbreaks in fish farms is the administration of antibiotic therapy on food. Unfortunately, this practice involves the release of antibiotics into aquatic ecosystems since large amounts of food are not eaten or completely metabolized [7], which has a major environmental impact. Microbial communities of major importance are affected by the presence and accumulation of these products in sediments and the water column [8], and microcosm studies show that communities of microorganisms responsible for converting ammonium to nitrate are highly susceptible to antibiotics such as oxytetracycline [9].

2.2. Risk for animal health

The constant outbreaks caused by different pathogens and the emergence of drug-resistant infectious diseases, combined with the complex tasks involved in administering antibiotics in aquaculture (incorporated in feed, immersion or injections) indicate that control measures based on antimicrobial agents are inappropriate [10,11]. Moreover, because the emergence of drug-resistant bacteria is considered a major issue in aquaculture, the World Health Organization, together with the FAO and the OIE, are attempting to reduce antibiotic use [2]. Given that antibiotic resistance has been found in most of the pathogenic species, dealing with these infectious diseases is highly complex [12, 13]. Major pathogens causing significant pathologies in aquaculture species that require antimicrobial therapy are listed in Table 1.

Table 1 Main pathogenic bacteria in aquaculture.

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Pathology</th>
<th>Virulence Factors</th>
<th>Main affected species</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Aeromonas salmonicida</em></td>
<td>Furunculosis</td>
<td>Adhesins, aerolysine*, serine protease*, haemolysin, lipase, glycerophospholipid, cholesterol acyl transferase*, biofilm formation *</td>
<td>Atlantic salmon, rainbow trout, zebrafish</td>
<td>[14,15]</td>
</tr>
<tr>
<td><em>Listonella anguillarum</em> (Prev. <em>Vibrio anguillarum</em>)</td>
<td>Vibriosis</td>
<td>Flagellum, siderophore anguibactin, haemolysin, cytotoxins, dermatotoxins, zinc metalloprotease</td>
<td>Pacific and Atlantic salmon, rainbow trout, turbot, seabass, striped bass, cod, European and Japan eel, and ayu</td>
<td>[14]</td>
</tr>
<tr>
<td><em>Photobacterium damselae subsp. piscicida</em></td>
<td>Photobacteriosis (Pasteurellosis)</td>
<td></td>
<td>Striped bass, Atlantic salmon, yellowtail, ayu, red seabream, seabass</td>
<td>[17,18]</td>
</tr>
</tbody>
</table>
Tenacibaculum maritimum  Flexibacteriosis  Adhesion, biotin, exotoxins, proteolytic compounds, high-affinity iron-uptake mechanisms.  Turbot, sole, gilthead seabream, seabass, red seabream, black seabream, flounder, salmonids  [19]

Pseudomonas anguilliseptica  Pseumonadiasis  Capsular (K) antigen, proteinases, lipases  Eel, ayu, black seabream, turbot, black spot seabream  [14]

Renibacterium salmoninarum  Bacterial kidney Disease  Cytolsyn, haemolysin.  Salmonids  [20]

Mycobacterium marinum  Mycobacteriosis  Erp protein, actin polymerization,  Pacific and Atlantic salmon, pejerrey, snakehead fish, turbot, tilapia, European tilapia, red drum.  [21]

Piscirickettsia salmonis  Piscirickettsiosis  Not specified  Pacific salmon, Atlantic salmon, rainbow trout, coho salmon.  [14]

* Virulence factors under quorum sensing regulation

Chile is the second largest producer of salmon in the world. It is also one of the major users of antibiotics for aquaculture [22]. Despite the latter, outbreaks of *P. salmonis* have caused major losses [5], which exemplifies that the use of antibiotics does not control outbreaks. A major factor affecting efficacy of antibiotic therapy is the oral administration route for these treatments. Infected fish suffer loss of appetite. For this reason, they do not ingest the adequate antibiotics doses, and the disease progresses from an asymptomatic condition to evident deterioration and death. During these stages, infected fish act as vectors in spreading bacterial pathogens. Because of the high-density conditions, and the inability to identify, separate and confine infected animals, disease progress rapidly. At the same time, rearing conditions on fish farms favor the evolution of bacterial pathogens to antibiotic resistance.

2.3. Risk for human health and food safe

The antibiotic presence in microbial communities exerts positive selection pressure favoring antibiotic resistant and/or hypermutator strains to acquire genetic determinants for resistance by mutation or horizontal gene flow [23-25]. Microorganisms positively selected by antibiotics become reservoirs for resistance and when are pathogens cause antibiotic resistant diseases in plants, animals and humans. While it is true that species barriers limit bacterial pathogens, the spread of antibiotic resistance appears to be a more promiscuous mechanism that finally favors microbial evolution. The most serious problem with the antibiotics used to treat infectious diseases in aquaculture is that they are the same as those employed in human medicine. In fact, according to the WHO, the antibiotics used in aquaculture (aminopenicillins, macrolides, quinolones, fluoroquinolones and tetracyclines) are critical in human medicine [26, 27]. Major antibiotics used in aquaculture are listed in Table 2.

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Mechanism of Action</th>
<th>Route</th>
<th>Dosage</th>
<th>Pathogens</th>
<th>Approved</th>
<th>Target species</th>
</tr>
</thead>
<tbody>
<tr>
<td>Florfenicol</td>
<td>Inhibition of protein synthesis</td>
<td>Oral</td>
<td>10 mg/kg of fish/10 days</td>
<td><em>A. salmonicida</em></td>
<td>USA*</td>
<td>Salmonids</td>
</tr>
<tr>
<td>Oxytetracycline dehydrate</td>
<td>Inhibition of protein synthesis</td>
<td>Oral</td>
<td>60-80 mg/kg of fish/10 days</td>
<td><em>A. salmonicida</em>, <em>A. hydrophila</em>, <em>A. sobria</em>, <em>Pseudomonas</em> spp., <em>Cytophaga psychrophilia</em>, <em>Chondrococcus columnaris</em>, <em>Yersinia ruckeri</em>, <em>Haemophilus piscium</em>.</td>
<td>USA*</td>
<td>Salmonids Lobster Catfish</td>
</tr>
<tr>
<td>Sulfadimethoxine/ormetoprim</td>
<td>Inhibition of DNA synthesis</td>
<td>Oral</td>
<td>50 mg/ kg of fish/day, up to 5 days</td>
<td><em>Edwardsiella ictaluri</em> <em>A. salmonicida</em></td>
<td>USA*</td>
<td>Salmonids Catfish</td>
</tr>
</tbody>
</table>
### Table: Antibiotics and Their Modes of Action

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Mode of Action</th>
<th>Route</th>
<th>Dosage</th>
<th>Organisms</th>
<th>Countries/Regions</th>
<th>Fish Species</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ampicillin, Amoxicillin</strong></td>
<td>Inhibition of cell-wall synthesis</td>
<td>Oral</td>
<td>50-80 mg/kg of fish/10 days</td>
<td><em>Vibrio spp.</em>, <em>Pasteurella piscicida, Mixobacterium spp.</em></td>
<td>Japan, United Kingdom**</td>
<td>Yellowtail</td>
</tr>
<tr>
<td><strong>Neomycin</strong></td>
<td>Inhibition of protein synthesis</td>
<td>Oral</td>
<td>50-80 mg/kg of fish/10 days</td>
<td>Not mentioned</td>
<td>Indonesia**</td>
<td>Shrimp</td>
</tr>
<tr>
<td><strong>Doxycycline</strong></td>
<td>Inhibition of protein synthesis</td>
<td>Immersion</td>
<td>20 mg/liter of water</td>
<td>Not mentioned</td>
<td>China**</td>
<td>Not mentioned</td>
</tr>
<tr>
<td><strong>Tetracycline</strong></td>
<td>Inhibition of protein synthesis</td>
<td>Oral</td>
<td>50-80 mg/kg of fish/10 days</td>
<td>Not mentioned</td>
<td>India**</td>
<td>Not mentioned</td>
</tr>
<tr>
<td><strong>Erythromycin</strong></td>
<td>Inhibition of protein synthesis</td>
<td>Oral</td>
<td>50 mg/kg of fish/10 days</td>
<td><em>Renibacterium salmoninarum, Streptococcus spp.</em></td>
<td>Japan**</td>
<td>Yellowtail</td>
</tr>
<tr>
<td><strong>Sulfamerazine, Sulfamethoxine, Sulfaguanidine</strong></td>
<td>Inhibition of DNA synthesis</td>
<td>Oral</td>
<td>200 mg/kg of fish/10 days</td>
<td><em>Yersinia ruckeri, A. salmonicida, Vibrio spp.</em></td>
<td>China**</td>
<td>Salmonids</td>
</tr>
<tr>
<td><strong>Oxolinic acid</strong></td>
<td>Inhibition of DNA synthesis</td>
<td>Oral</td>
<td>12 mg/kg of fish/10 days</td>
<td>Gram negative bacteria</td>
<td>Japan, United Kingdom**</td>
<td>(Yellowtail, Japan)</td>
</tr>
<tr>
<td><strong>Flumequine</strong></td>
<td>Inhibition of DNA synthesis</td>
<td>Injected</td>
<td>12 mg/kg of fish/10 days</td>
<td>Gram negative bacteria</td>
<td>Noway, Japan**</td>
<td>Yellowtail, Japan</td>
</tr>
<tr>
<td><strong>Sarafloxacin</strong></td>
<td>Inhibition of DNA synthesis</td>
<td>Oral</td>
<td>10 mg/kg of fish/5 days</td>
<td><em>Aeromonas spp., Vibrio spp.</em></td>
<td>Europe***</td>
<td>Salmonids</td>
</tr>
</tbody>
</table>

* Approved by the Food and Drug Administration [28].
** Approved by local regulatory agencies [29].
***Approved by the European Medicines Agency [30].

Epidemic aspects of antibiotic resistance have been extensively studied in humans, but clinical evidence connecting antimicrobial-resistant bacterial infections in persons to the extensive (mis)use of antibiotics in aquaculture remains under discussion. However, it is clear that the genetic determinants for resistance can be mobilized among different genera of bacteria by horizontal flows in the aquaculture ecosystem [31-35], the food chain [36,37] and in the human microbiome [38]. In this scenario, aquaculture ecosystems exposed to antibiotics act as reservoirs for antibiotic-resistant genes and strains that, by different routes, can affect human health, directly or indirectly (Fig. 1). Direct effects include the infection of humans by contact with aquatic antibiotic-resistant bacteria, while indirect effects include the mobilization of bacteria and/or genes with antibiotic resistances through drinking water or foods produced by aquaculture. Given the above, the World Health Organization declared that the use of antibiotics to control diseases in aquaculture represents a risk to human health [26]. Considering the increasing quantities of food produced by aquaculture; food processing (manipulation, storage and delivery) tasks and; eating habits, food consumption can be regarded as the most important route for the flow of antibiotic resistance to humans. For example, there is a risk in consuming food produced by aquaculture and contaminated with antibiotic-resistant bacteria if it is not cooked at an adequate temperature. Unfortunately, this is increasingly common given the wide range of aquacultural food products and the growing custom of consuming raw fish and shellfish. Thus, efforts should be made not only to reduce antibiotics in aquaculture, but also to control and diagnose genes and antibiotic-resistant microorganisms in food produced by aquaculture.

### 3. Marine bacterial biosurfactants

The highly heterogeneous physical-chemical and biotic conditions in oceans drove marine microbial evolution toward greater diversity, with a wide array of metabolic and physiological adaptations. Consequently, a great variety of molecules can be obtained from marine microorganisms. Many of these molecules, by their surface-active properties, perform their function outside the cell in order to interact with other molecules or other cells. These compounds have been termed biosurfactants and are amphiphilic molecules or cellular structures being their main characteristic the affinity for both organic and aqueous phases. The chemical structure of biosurfactants is composed by a variable hydrophilic moiety (ester or alcohol group of neutral lipids; carboxylate group of fatty acids or aminoacids; phosphate group of phospholipids; and the carbohydrates of glycolipids) and a more constant hydrophobic moiety (length-variable fatty acids) (Fig. 2).
In general, hydrophilic and hydrophobic moieties are synthesized and assembled through specific biosynthetic pathways that, depending on the microorganism and the biosurfactant, involve non-ribosomal peptide synthetases, glycosyl-transferases, amino-transferases, acyl-transferases and oxidoreductases, which produce a wide variety of surface-active glycolipids, lipopeptides, glycolipopeptides, phospholipids, acylated serine-lactones and hydroxy fatty acids (Fig. 2) [39]. As shown in Table 3, marine bacterial biosurfactants can be produced by different genus and species of microorganisms. They present diverse chemical structures and have wide range of applications, depending on their physical, chemical and biological properties. Hydrocarbon-degrading marine bacteria (HDMB) are an interesting source of BS, producing amphiphilic compounds in response to the presence of hydrophobic (aromatic or aliphatic) hydrocarbons, increasing the bioavailability of these substrates used as carbon and energy sources [40]. Nevertheless, the production of biosurfactants have been also studied and characterized in other non-HDMB (Table 3).

3.1. Physical-chemical properties

Biosurfactants are a diverse group of compounds with a common structural pattern; a hydrophilic group termed the hydrophilic head, attached to a hydrophobic group termed the hydrophobic tail, and can be found in monomers or forming micellar structures. These chemical structures allow biosurfactants to interact simultaneously with hydrophilic and hydrophobic phases. This phenomenon reduces interfacial and surface tension, in the case of two immiscible phases (solid-liquid or liquid-liquid) and in the case of a liquid phase and air, respectively. Micelles are physical structures formed by the aggregation of monomers, generating two separated environments between immiscible phases. At low concentrations, surfactants form a monolayer in the interface of two these phases. It is only when they reach an adequate concentration that they aggregate and form micellar structures (Fig. 2). This concentration value is termed a critical micellar concentration (CMC), and is the lowest concentration at which the monomers of surfactants aggregate to form micelles. When this phenomenon occurs between two liquid phases and one phase is dispersed into the other, it is called an emulsion. There are different kinds of emulsions, the most common being: oil-in-water (o/w), where the hydrophobic phase remains inside the structure surrounded by the aqueous phase; water-in-oil (w/o), where the hydrophilic phase is inside the micelle and the hydrophobic phase surrounds the structure (Fig. 2). In addition to their physical and chemical characteristics, the biological properties of biosurfactants make them of interest to the food and aquaculture industries.

3.2. Biological Properties

In marine ecosystems, amphiphilic surface-active compounds are involved in different biological processes, such as: microbial competition, when they exhibit antimicrobial properties; cell-to-cell communication, when they act as diffusible signals in quorum sensing; nutrition, when they favor the accession and assimilation of water-insoluble nutrients; and survival when they bind and sequester toxic compounds. Because of the variety of roles of bacterial biosurfactants in nature, they are an interesting alternative to conventional therapies in animal and human health. Given the great diversity of chemical, biological and physical properties of biosurfactants (Table 3), they represent an interesting source for a new generation of molecules to prevent and control bacterial infections by inhibiting virulence.
Bacterial virulence is a set of mechanisms that enables pathogenic cells, accessing, colonize and spread in a host. It is known that some virulence factors of bacterial fish pathogens, such as *Aeromonas salmonicida*, *Vibrio anguillarum* and *Yersinia ruckeri*, are regulated by quorum sensing (QS) cell-to-cell communication system. This mechanism is mediated through the secretion of small signals molecules that allows bacterial cells to act in coordination, increasing the effect on the host organism. Bacterial pathogenic phenotypes controlled by QS include: swarming, biofilm formation, sporulation and expression of virulence factors as lytic enzymes, adhesion molecules and toxin production [41, 42]. For example, in *A. salmonicida*, production of aerolysin, glycerophospholipid cholesterol acyltransferase and biofilm formation is under QS control [43]. Therefore inhibiting virulence mechanisms of fish pathogens, by inhibiting QS, has emerged as an alternative to antibiotic agents in aquaculture [44].

**Table 3** Marine bacterial biosurfactants and their biotechnological applications.

<table>
<thead>
<tr>
<th>Classification</th>
<th>Molecular structure</th>
<th>Name</th>
<th>Bacterial strain</th>
<th>Biotechnological properties</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Molecular weight</td>
<td>Lipopeptides</td>
<td>Lipopeptide</td>
<td>Bacillus circular*</td>
<td>Antimicrobial activity</td>
<td>[45-48]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Alcaligenes sp. S-X1-1</td>
<td>Demulsifier</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Proline lipid</td>
<td>Alcanivorax dieselolei B-5</td>
<td>Oil-recovery in extreme Environments</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tyrosine lipid</td>
<td>Alcanivorax hongdengensis A-11-3T</td>
<td>Alkane degradation</td>
<td></td>
</tr>
<tr>
<td>Fatty Acids</td>
<td>Hydroxy fatty acids</td>
<td>Cobetia sp. MM1IDA2H-1</td>
<td></td>
<td>Biofilm inhibition**</td>
<td>[49,50]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hydroxyl fatty acids and iso-fatty acids</td>
<td>Myroides sp. SM1</td>
<td>Nanostructures formation Inverse micelles formation Inhibition of virulence factors in fish pathogens**</td>
<td></td>
</tr>
<tr>
<td>Polypeptides</td>
<td>Polypeptide</td>
<td>Acinetobacter sp. A3</td>
<td></td>
<td>Bioremediation of crude oil</td>
<td>[51]</td>
</tr>
<tr>
<td>Glycolipids</td>
<td>Glucose lipid</td>
<td>Alcaligenes sp.</td>
<td></td>
<td>Antimicrobial activity</td>
<td>[52-54]</td>
</tr>
<tr>
<td></td>
<td>Glucose lipid'</td>
<td>Alcanivorax borkumensis</td>
<td></td>
<td>Oil degradation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Threalose lipid</td>
<td>Arthrobacter sp.</td>
<td></td>
<td>Oil recovery</td>
<td></td>
</tr>
<tr>
<td>Lipoproteins</td>
<td>Ornithine lipids</td>
<td>Myroides sp. SM1</td>
<td></td>
<td>Oil remediation</td>
<td>[55]</td>
</tr>
<tr>
<td>Lipopolysaccharides</td>
<td>BD4 Emulsan</td>
<td>Acinetobacter calcoaceticus BD4</td>
<td></td>
<td>Oil/water emulsion stabilization</td>
<td>[56]</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>A. calcoaceticus</em> RAG-1</td>
<td></td>
<td>Stabilization of oil/water emulsions</td>
<td></td>
</tr>
<tr>
<td>High molecular weight</td>
<td>Polysaccharide</td>
<td>Biodispersan</td>
<td>A. calcoaceticus A2</td>
<td>Limestone powder dispersion</td>
<td>[57,58]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Halomonas eurihalina*</td>
<td>Oil pollution bioremediation</td>
<td></td>
</tr>
<tr>
<td>Glycoproteins</td>
<td>HE39</td>
<td>Halomonas sp. TG39*</td>
<td></td>
<td>Bioremediation</td>
<td>[59]</td>
</tr>
<tr>
<td></td>
<td>HE67</td>
<td>Halomonas sp. TG67*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yansan</td>
<td>Yarrowia lipolytica IMUFRJ 50682*</td>
<td></td>
<td>Bioremediation Bioremediation / Formulation of perfluorocarbon-based emulsions</td>
<td>[60,61]</td>
</tr>
<tr>
<td>Polymeric BS</td>
<td>Polymeric BS</td>
<td>Pseudomonas nautica 617</td>
<td></td>
<td>Bioremediation</td>
<td></td>
</tr>
</tbody>
</table>

* Non hydrocarbon-degrading bacteria.
** Inhibition of the Quorum Sensing communication system.
3.3. Antimicrobial activity and quorum sensing inhibition

As presented in Table 3, biosurfactants of marine origin have diverse structures, properties and potential applications. Among them, lipopeptide of *Bacillus circulans* and the glucose-lipid of *Alcaligenes* sp. have been demonstrated to have antibacterial properties, but their mechanisms of action have not been specified. Other marine biosurfactants of interest for the prophylaxis and control of bacterial infections are those compounds with fatty acid structure. It has been reported that fatty acids from biological sources can inhibit the quorum sensing communication system in human pathogenic bacteria such as *Proteus mirabilis* and *Escherichia coli* [62,63]. In this context, hydroxyl fatty acids from *Cobetia* sp. MM1IDA2H-1 offer an alternative way to control infectious outbreaks in fish farming, due to their ability to disrupt the QS communication system of fish pathogenic bacteria such as *A. salmonicida* and *L. anguillarum* [49]. This fatty acid inhibit the expression of virulence factors such as enzyme synthesis and biofilm formation, by hijacking the signal molecules involved in QS. This mechanism does not involve interaction with cellular structures and, therefore, no resistance is developed. QS can be inhibited at different levels, for example, compounds that antagonize the receptor of the signaling molecules can also inhibit cell-to-cell communication and alter bacterial pathogenicity. Another mechanism that interrupts QS is inhibiting signaling molecule synthesis. Molecules with structural analogy to chemical substrates need to form acyl-homoserine lactones, which can be inhibited. In this context, the great variety of chemical structures of biosurfactants produced by marine bacteria offer an interesting source for compounds that inhibit quorum-sensing systems.

3.4. Immunomodulation

In addition to inhibiting growth, dissemination and virulence of pathogenic bacteria, to prevent infectious outbreaks it is important to consider it the efficiency of the fish immune system of fish to confront and control pathologies [64]. The main immunological response in fish is based on the innate immune system [65,66], which can be activated by several molecules, such as lipopolysaccharides, lipoproteins and glycoproteins of bacterial origin, as well as by enzymes produced by immune cells, such as cytokines, transferrin, lysozyme and interleukins [67,68]. The innate immune system of fish involves receptors responsible for activating immune and pro-inflammatory responses called toll-like receptors or TLRs [67,68]. It has been reported that biosurfactants can act as immunostimulating molecules [69,70], making marine bacteria an interesting source of compounds to strengthen fish immune system and, thus, reduce the quantity of antibiotics required to control infectious outbreaks.

4. Innovations based on marine microbial biosurfactants

Although synthetic surfactants are currently the most commonly used surface-active compounds, the main advantages of biosurfactants are their low toxicity, high biodegradability and high stability at extreme conditions, such as high temperatures and high levels of salinity and pH [71, 72]. In some cases, stability is higher than that of chemically based surfactants [73]. Biosurfactant molecules can form stable emulsions in solutions with high ionic force, which is especially relevant in aquacultural applications, since most fish farms are located in high salinity environments, making the stability of biosurfactants at high ionic strength essential. For example, biosurfactants from *Cobetia* sp. MM1IDA2H-1 [49] and emulsions formed from this compound present high stability at wide ranges of pH, temperature and strength force (3-20 % w/v of sodium chloride).

Synthetic surface-active compounds have been classically used in the food industry as food additives and emulsifying agents. Due to the emulsifying properties and high stability of emulsions the marine bacterial bioactive biosurfactants can be incorporated into food. For example, nowadays, the incorporation of antibiotics in the fish feed is accomplished during the extrusion of the feed. In this case due to the ability to form stable emulsions, biosurfactants with remarkable biological functions can be incorporated (after the extrusion process) during the food oiled. In this context, biosurfactants can be incorporated into polymeric food matrices by emulsifying the food components. Likewise, because of the ability to form micelles, biosurfactants can be used as a delivery system for a variety of bioactive molecules in order to improve the fish health (Fig. 2). This allows the incorporation of compounds into aqueous and organic phases during feed manufacture.

The main application of biosurfactants has been forming oil and water emulsions with applications in bioremediation and the food industry (Table 3). Nevertheless, water-in-oil micelles, also called reverse micelles, have applications in several fields. The core structure of reverse micelles is formed by an aqueous phase dispersed in an organic phase. Therefore, these structures have a major potential for the recovery, separation and purification of bioactive hydrophilic molecules [74-78]. Because of their chemical structure and amphiphilic nature, reverse micelles also have potential application for administering hydrophilic drugs since they can pass through biological membranes and release active molecules [79]. Reverse micelles can also reduce the degradation of oxygen sensitive molecules such as citral, with potential applications in food, beverage and perfume production [80]. A remarkable application of reverse micelles is their ability to host hydrophilic enzymes in the water core, and hydrophilic enzymes with hydrophobic substrates are of particular interest [81-83]. Water-in-oil emulsions can also act as a delivery system for inorganic antimicrobials like silver nanoparticles [84]. Although the majority of reverse micelle applications involve synthetic surfactants, marine
biosurfactants offer an interesting alternative. For instance, by the ability to form stable emulsions in different chemical conditions, is possible to use reverse micelle technology to manufacture bioactive polymer coatings for preventing biofilm formation on surfaces submerged in the aquaculture installations. Biofilm formation in farm facilities is a reservoir of potential microbial pathogens. Biofilm formation in the facilities of the farm is a reservoir of potential microbial pathogens. Therefore, paints containing heavy metals contaminants are used to prevent biofilm formation. Then, using paints without contaminants to prevent biofilms with active environmentally friendly innovations is a technological breakthrough.

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