

Review of the potential of bioactive compounds in seaweed to reduce histamine formation in fish and fish products

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Abstract

The formation of histamine in food is influenced by temperature, and histamine growth can be inhibited by maintaining a cold

chain. However, simply relying on temperature control is insufficient, as certain bacteria can produce the enzyme histidine decarboxylase even at temperatures below 5°C. To address this issue, various methods, such as modified atmosphere packaging, high hydrostatic pressure, and irradiation, have been developed to control histamine in fishery products. However, these methods often require significant investments. Therefore, there is a need for a cost-effective solution to overcome this problem. This review explores a cost-effective solution through the utilization of bioactive compounds derived from underexplored seaweeds. Seaweed bioactive compounds, either in their pure form or as extracts, offer a promising alternative method to regulate histamine generation in fishery products due to their antibacterial activity, and this review provides comprehensive insights into the potential of different seaweed-derived bioactive compounds as inhibitors of histamine production, detailing their diverse applications in fishery products. It also explores the mechanism by which bioactive compounds prevent histamine formation by bacteria, focusing on the potential of seaweed bioactive compounds to inhibit bacterial histidine decarboxylase. Future trends in the inhibition of histidine decarboxylase are also discussed. The bioactive compounds considered, such as flavonoids, alkaloids, terpenes, and phenolic acids, exhibit their antibacterial effects through various mechanisms, including the inhibition of DNA and RNA synthesis, disruption of cytoplasmic and cell membranes, and inhibition of enzymes by reacting with sulfhydryl groups on proteins. In conclusion, the integration of underexplored seaweeds in fishery product preservation represents a promising and innovative approach for future food safety and sustainability.

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Introduction

Fishery products are a significant global source of animal protein (Golden *et al.*, 2021). These products come from both capture fisheries and aquaculture (Gephart *et al.*, 2021). Fish, being rich in animal protein and having a high water content and neutral pH, creates favorable conditions for microbial spoilage and biochemical processes (Ojagh *et al.*, 2010; Ramezani *et al.*, 2015). After the death of fish, enzymatic reactions, oxidation, and microbial activity occur, leading to changes in sensory and nutritional properties. These changes can reduce the shelf life of fish (Kostaki *et al.*, 2009; Karoui and Hassoun, 2017; Olatunde and Benjakul, 2018). Histamine is commonly acknowledged as a significant indicator of food spoilage (Xie *et al.*, 2017) and can serve as a measure of freshness or degree of spoilage (Alberto *et al.*, 2002; Hwang *et al.*, 2003). The gills and skin are the primary sources of histamine-producing bacteria (Phuvasate and Su, 2010; Costanza *et al.*, 2013;

Bjornsdottir-Butler *et al.*, 2015). Histamine is a biogenic amine produced when bacteria break down histidine in raw fish and fishery products. This breakdown occurs when the fish is not stored at the correct temperature and for the proper amount of time (Rawles *et al.*, 1996). The production of histamine is primarily observed in Gram-negative bacteria (Emborg *et al.*, 2006; Ibrahim *et al.*, 2017). Histamine synthesis is known to increase significantly at temperatures around 32.2°C (90°F) according to the (FDA, 2022). However, there are certain types of bacteria, such as *Photobacterium damsela* (Kanki *et al.*, 2007), *Raoultella planticola*, and *R. ornithinolytica* (Kim *et al.*, 2000), that are capable of synthesizing histamine even at a temperature as low as 4°C. This ability can lead to poisoning. Histamine is produced in fish and fish products via the process of decarboxylation of the amino acid histidine. This conversion is facilitated by the bacterial enzyme histidine decarboxylase (Maldonado and Maeyama, 2013; Altieri *et al.*, 2016;). The bacteria that can produce histamine include *Morganella morganii* (Emborg *et al.*, 2006; Ibrahim *et al.*, 2017; Wang *et al.*, 2020), *Photobacterium* spp. (Bjornsdottir-Butler *et al.*, 2018), *Proteus vulgaris*, *Enterobacter* spp. and *Klebsiella pneumoniae* (Rodtong *et al.*, 2005; Ferrario *et al.*, 2012; Gopi *et al.*, 2016), *Aeromonas* spp., *Clostridium* spp., *Pseudomonas putida* dan *Acinetobacter lwoffii* (Okuzumi *et al.*, 1994; López-Sabater *et al.*, 1996;). Consuming fish and fish products that have a high histamine content can lead to poisoning, resulting in symptoms such as skin rash, hives, nausea, vomiting, diarrhea, and flushing (Chen *et al.*, 2010; Silva *et al.*, 2011; Evangelista *et al.*, 2016; Elik *et al.*, 2019). Furthermore, these noxious substances are recognized for inducing hyperallergic responses prompted by inflammation; however, they never result in fatality among those who ingest histamine-infused fish (Reber *et al.*, 2017). For instance, between 1998 and 2008, there were 333 outbreaks of histamine poisoning in the United States that involved 1,383 people and resulted in 59 hospitalizations (Dewey-Mattia *et al.*, 2018). In the United States and the European Union, fish consumption-related histamine poisoning accounts for approximately 40% of all cases of food poisoning; incidences range from 2 to 5 cases per million people in New Zealand, France, and Denmark to 31 cases per million people in Hawaii (Marcus, 2024). A 2017 incident of histamine poisoning in Italy was linked to tuna steak consumption, while a 2019 outbreak was linked to frozen raw tuna (Annunziata *et al.*, 2022).

To address these issues, it is possible to inhibit the growth of microorganisms, namely bacteria that produce histamine. Blocking the histamine-forming bacteria may effectively limit the conversion of histidine into histamine by these bacteria. Elevated microbial decarboxylation activity leads to the production of larger levels of histamine, which can be harmful (Al Bulushi *et al.*, 2009; De Mey *et al.*, 2014). Once histamine is generated, it becomes challenging to eliminate it effectively, regardless of whether temperatures are high or low (Wendakoon and Morihiko, 1995). In general, the inhibition process can be achieved by introducing an inhibitor and bioactive chemicals derived from plants, particularly seaweed, either in the form of extracts or in their pure form. These plant-based substances can serve as a viable alternative for inhibiting certain processes. This review aims to present information regarding the utilization of different bioactive compounds as inhibitors of histamine synthesis and their diverse applications in fishery products. It also discusses the mechanism by which bioactive compounds prevent histamine formation by bacteria, highlighting the potential of seaweed bioactives in inhibiting bacterial histidine decarboxylase. Additionally, it explores future trends in the inhibition of the enzyme histidine decarboxylase.

Formation of histamine in fishery products

The production of histamine in fishery products is closely correlated with the quantity of its precursor, histidine, and the bacterial population in the product (Altieri *et al.*, 2016). Microorganisms present in fish tissue can decarboxylate histidine, leading to the synthesis of histamine in fishery products (Harmoko *et al.*, 2022). Several types of bacteria, such as *M. morganii*, *M. psychrotolerans*, *Photobacterium damsela*, *P. phosphorum*, *Raoultella planticola* and *Hafnia alvei*, have the ability to decarboxylate histidine into histamine (Tsai *et al.*, 2006; Gardini *et al.*, 2016; Ruiz-Capillas and Herrero, 2019; Visciano *et al.*, 2020). Among these bacteria, enteric bacteria including *Proteus vulgaris*, *Enterobacter* spp., *M. morganii*, and *K. pneumoniae* are capable of producing histamine from histidine (Rodtong *et al.*, 2005; Ferrario *et al.*, 2012; Gopi *et al.*, 2016;). Additionally, non-enteric bacteria such as *Aeromonas* spp., *Clostridium* spp., *Photobacterium* spp., *Pseudomonas putida*, and *Acinetobacter lwoffii*, also can produce histamine (Huang *et al.*, 2010; Kung *et al.*, 2015; Krell *et al.*, 2021; Oktariani *et al.*, 2022).

The production of histamine by histamine-forming bacteria is influenced by a number of factors, including temperature, pH, oxygen content, processing, packaging, and storage. For example, *M. morganii* when exposed to tuna (*Thunnus albacares*) for 24 hours at a temperature of 15-37°C and a pH of less than 7, can form histamine >5000 ppm (Kim *et al.*, 2000), *P. phosphoreum*, at 5-37°C and pH <4 in cod, for 48 hours, can form histamine of 1188 ppm (Bjornsdottir-Butler *et al.*, 2020) and *K. pneumoniae* at 37°C in tuna for 7 hours, can form histamine 442 ppm (Taylor *et al.*, 1979). Studies (Mercogliano and Santonicola, 2019; Visciano *et al.*, 2020) have shown that these factors play a role. Specifically, temperature and storage time are significant factors that impact the synthesis of histamine by histamine-forming bacteria in fishery products, as demonstrated by Nevado *et al.*, 2023). The excessive growth of disease-causing microbes, combined with the production of histamine, occurs when fishery goods are subjected to improper temperature conditions during storage after fish are caught or harvested, as well as during the marketing process. Fishery products are typically stored in the freezer to inhibit the growth of microorganisms and enzymatic activity, as temperatures over 4°C might facilitate these processes (Nevado *et al.*, 2023). This freezing method helps to slow down the breakdown of fishery products caused by the creation of biogenic amines (Koo and Lim, 2023).

According to (Tabanelli *et al.*, 2012), bacteria that make histamine multiply quickly when the temperature exceeds 21.1°C. Additionally, the synthesis of histamine increases at 32.2°C since the activity of histidine decarboxylase is most effective at 30°C. Nevertheless, bacteria that produce histamine are capable of thriving at both cold (psychrophilic) and moderate (mesophilic) temperatures, with a range of 5°C (Takahashi *et al.*, 2015) to 37°C in fishery products (Valiollah *et al.*, 2012). Storage duration has a notable impact on the chemical and biological makeup of fishery products. In particular, inappropriate storage time and thermal conditions can negatively affect the shelf life of these products and facilitate the proliferation of histamine-forming bacteria, leading to histamine production (Nevado *et al.*, 2023). Table 1 presents a comprehensive compilation of microorganisms that have the ability to produce histamine in fish and fishery products.

Certain bacteria, such as *M. morganii*, *P. damsela*, *P. phosphorum*, and *R. planticola*, are capable of producing histamine but are not active at cold temperatures. However, there are other histamine-producing bacteria, like *M. psychrotolerans*, that can still

produce histamine even when stored at low temperatures (Gardini *et al.*, 2016; Wang *et al.*, 2020). The optimal pH for histamine production in meals is within the mild acidic range of 4.0 to 5.0 (Diaz *et al.*, 2020). For instance, *K. pneumoniae*, a bacteria commonly found in tuna, has the ability to convert histidine into histamine at a high rate when the pH is 4.0. However, this activity decreases when the pH is raised to 6.0 (Baranowski *et al.*, 1985). It is worth noting that pH 4.0 is considered the optimal pH for the maximum production of biogenic amines, including histamine, in fermented fish. Additionally, the activity of microorganisms is significantly hindered at pH 3 due to changes in enzyme structure caused by extremely high or low pH levels (Meng *et al.*, 2022). The activity of histidine decarboxylase persists despite the inactivation of bacterial activity (Gardini *et al.*, 2016; Visciano *et al.*, 2020). Therefore, it is crucial to take this into account when managing histamine synthesis in fish and fishery products by regulating both the bacteria and the enzymes they create. Mast cells in living fish store and release histamine, a process mediated by histidine decarboxylase, an essential enzyme involved in histamine production triggered by lipopolysaccharides and cytokines (Reite, 1972; Crivellato and Ribatti, 2010; Inami *et al.*, 2021). Mast cells become triggered by directly interacting with particular microbial components or by host chemicals that are produced due to tissue damage (Gomez-Gonzalez *et al.*, 2014). When mast cells are activated, they release different substances that cause inflammation and activate other white blood cells (Marshall, 2004). These substances include preformed mediators like histamine, tryptase, chymase, and tumor necrosis factor- α , as well as newly synthesized mediators like leukotrienes, cytokines, chemokines, and growth factors (Galli *et al.*, 1991; Pater-huijsen *et al.*, 1997; Triggiani *et al.*, 1995). Furthermore, histamine is produced from scratch in different cells by activating histidine decarboxylase at sites of inflammation (Hirasawa, 2019). In these locations, histamine serves a cru-

cial function in initiating inflammation, which is the initial reaction of living organisms to infection or cellular injury (Beer and Rocklin, 1987; Crivellato & Ribatti, 2010). This discussion demonstrates that the production of histidine decarboxylase in mast cells can be regulated while the fish is alive. However, once the fish is dead, the enzyme's activity persists and converts histidine into histamine through decarboxylation (Gardini *et al.*, 2016; Visciano *et al.*, 2020). Therefore, it is crucial to promptly control this enzyme after catching or harvesting the fish.

Mitigating histamine formation in fishery products: exploring seaweed-derived bioactives and their antimicrobial mechanisms

Bioactive compounds have the ability to regulate the production of histamine in fishery products. The process by which bioactive compounds reduce the levels of biogenic amines, including histamine, is primarily linked to their antimicrobial properties (Tsafack and Tsopmo, 2022). Examples of bioactive compounds that exhibit this effect include flavonoids, alkaloids, terpenes, and phenolic acids (Houicher *et al.*, 2021). Figure 1 illustrates the antibacterial mechanism of bioactive substances.

Flavonoids are effective antimicrobials due to their ability to hinder energy metabolism, impede DNA and RNA synthesis, disrupt cytoplasmic membrane function, and alter membrane permeability. These are the primary mechanisms by which flavonoids exhibit antibacterial properties (Cushnie and Lamb, 2005; Xie *et al.*, 2015). Furthermore, it suppresses the release of histamine from mast cells that produce histamine and the process of tyrosine phosphorylation, which is linked to the suppression of histidine decarboxylase activity (Yamashita *et al.*, 2000; Rodríguez-Caso *et al.*,

Table 1. Presence of histamine-producing bacteria in fish and fishery products.

| No | Histamine forming bacteria | Fishery products | Results | Reference |
|----|--|---|--|--|
| 1 | <i>M. morgani</i> | Japanese Spanish Mackerel (<i>Scomberomorus niphonius</i>) | Bacteria that produce dangerous levels of histamine at 935 ppm | Hwang <i>et al.</i> , 2019 |
| 2 | <i>M. morgani</i> | Tuna albacores | Generated the most elevated histamine concentration, measuring 5.253 ppm | Kim <i>et al.</i> , 2000 |
| 3 | <i>R. planticola</i> and <i>R. ornithinolytica</i> | Tuna, bonito and sardines | The histamine production capacity ranged from 2810 to 5250 mg | Kim <i>et al.</i> , 2000 |
| 4 | <i>P. damsela</i> | Blue mackerel (<i>Scomber australasicus</i>) | Strong histamine producer (Average histamine level 4330 mg/L) | Chen <i>et al.</i> , 2012 |
| 5 | <i>Enterobacter aerogenus</i> | Dried milkfish (<i>Chanos chanos</i>) products | Productive histamine formers with values > 500 ppm | Hsu <i>et al.</i> , 2009 |
| 6 | <i>P. damsela</i> | <i>Mugil cephalus</i> | Histamine levels of 1053 $\mu\text{g/mL}$ at 30°C in 24 hours | Trevisani <i>et al.</i> , 2017 |
| 7 | <i>Hafnia alvei</i> | Dried milkfish (<i>Chanos chanos</i>) products | Weak histamine formers with a value of 152 ppm | Hsu <i>et al.</i> , 2009 |
| 8 | <i>Clostridium perfringens</i> | Tuna and Spanish mackerel | The histamine levels were measured at 6.345 ppm and 1.223 ppm | Kristin Bjornsdottir-Butler <i>et al.</i> , 2013 |
| 9 | <i>M. psychrotolerans</i> | Tuna (<i>Thunnus albacares</i>) of vacuum and modified atmosphere-packaging | Histamine levels >5000 mg/kg at 1.7°C on day 24 | Emborg <i>et al.</i> , 2005 |
| 10 | <i>P. kishitani</i> | Cod fish | Generate a concentration of 1545 ppm of histamine | Bjornsdottir-Butler <i>et al.</i> , 2020 |
| 11 | <i>P. phosphoreum</i> | <i>Iwashi Maruboshi</i> | Histamine levels of 1700mg/kg stored at 4°C and 12°C | Kanki <i>et al.</i> , 2004 |

2003; Melgarejo *et al.*, 2010). Flavonoids, specifically flavanols like quercetin and catechin, exhibit antibacterial properties by inhibiting the formation of adenosine triphosphate (Chinnam *et al.*, 2010; Silva *et al.*, 2016) and disrupting the cell membrane, as demonstrated (Ollila *et al.*, 2002; Zhou *et al.*, 2022).

Alkaloids can be classified based on their chemical structure. They are divided into two main groups: non-heterocyclic alkaloids, also known as protoalkaloids or biological amines, and heterocyclic alkaloids. Non-heterocyclic alkaloids include compounds like hordenine, N-methyltyramine, colchicine, and erythromycin. Heterocyclic alkaloids, on the other hand, are further categorized into subgroups such as pyrrole and pyrrolidine (which include hydrines) and quinoline (which includes qinine) (Evans, 2009). Alkaloids are capable of establishing hydrogen bonds with enzymes, receptors, and proteins due to the presence of nitrogen atoms that can take protons, as well as amine hydrogen atoms that can give protons (Othman *et al.*, 2019). Alkaloids can serve as antimicrobials by inhibiting cell division, binding to bacterial enzymes to impede respiration, disrupting cell membranes, and deactivating virulence genes.

Virstatin is an isoquinoline alkaloid that can inhibit the regulatory protein ToxT, thereby inhibiting the virulence factors (Yang *et al.*, 2011). Additionally, alkyl methyl quinolone alkaloids exhibit potent and specific antibacterial activity by inhibiting respiration (Tominaga *et al.*, 2002). Agelasine D, a diterpene alkaloid, inhibits bacterial enzymes (Arai *et al.*, 2014). Squalamine is a polyamine alkaloid that functions by disrupting the outer cell membrane and causing depolarization of the membrane of Gram-positive bacteria (Alhanout *et al.*, 2010). Alkaloids like berberine have been found to impede cell division (Boberek *et al.*, 2010), while ungeremine has the ability to hinder bacterial topoisomerase (Casu *et al.*, 2011).

Tannins are a group of polymeric phenolic compounds that can be categorized into two main groups, namely hydrolyzable tannins

and condensed tannins. Whereas condensed tannins derived from flavonoid monomers are more common in nature. The biological properties of tannins are closely related to their structural characteristics, particularly their oxidation patterns and polymerization, which affect their interactions with biological systems (Cano *et al.*, 2020; Štumpf *et al.*, 2023). Tannins exhibit significant antimicrobial activity, primarily through their ability to form complexes with proteins, which occurs *via* covalent and non-covalent interactions. This complexation can inhibit bacterial growth and protease activity by binding to the bacterial cell wall, thereby disrupting essential cellular functions (Biswas *et al.*, 2013). Additionally, tannins can bind to components of the bacterial cell wall, causing mechanical inhibition of growth (Dimech *et al.*, 2013; Neumann *et al.*, 2022). This binding not only disrupts the structural integrity of the bacterial cell wall but also affects the activity of extracellular and soluble proteins, which are crucial for the survival and proliferation of bacteria (Biswas *et al.*, 2013). The structural characteristics of tannins, such as molecular weight and flexibility, play an important role in their antimicrobial efficacy. Tannins with higher molecular weights tend to exhibit stronger antibacterial activity, as they can more effectively penetrate bacterial cell walls and disrupt cellular functions, thereby enhancing their antimicrobial effects (Olchowik-Grabarek *et al.*, 2020).

Phenolic acids, such as cinnamic acid and caffeic acid, are characterized by their phenolic rings with varying degrees of substitution and hydroxylation. The degree of hydroxylation in these compounds is closely related to their antimicrobial activity. In general, the more oxidized the structure of phenolic acids, the greater their inhibitory effect on microbial growth and enzyme activity (Oh and Jeon, 2015; Purnamasari *et al.*, 2021). The mechanism of phenolic acid inhibition primarily involves interaction with the sulfhydryl groups on proteins. By reacting with these groups, phenolic compounds can inhibit the activity of enzymes that are crucial for the survival and proliferation of microbes (Sánchez-

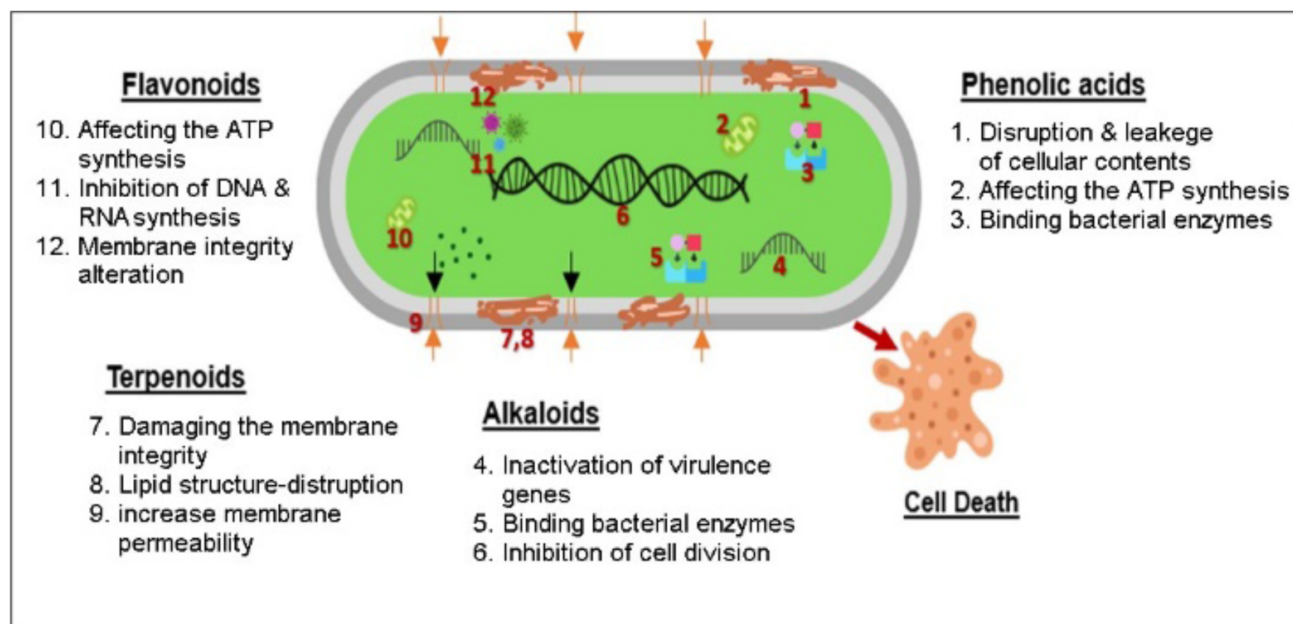


Figure 1. Antimicrobial mechanism of action of bioactive compounds. ATP, adenosine triphosphate.

Maldonado *et al.*, 2011). The structural characteristics of phenolic acids, including the presence of hydroxyl groups, play an important role in their antimicrobial properties. The presence of multiple hydroxyl groups is often correlated with increased antimicrobial activity, as these groups enhance the ability of phenolic acids to interact with and disrupt microbial membranes (Yamazaki and Kawano, 2010).

Application of bioactive compounds for histamine inhibition

Implementing a cold chain is an effective method for regulating histamine levels in food. The synthesis of this histamine is affected by temperature, and keeping temperatures low can inhibit microbial growth and reduce the activity of decarboxylating enzymes (Mah *et al.*, 2019; Sun *et al.*, 2016; Sun *et al.*, 2019). However, simply controlling temperature is not enough, as certain bacteria can produce histamine at temperatures below 5°C (Tsafack and Tsopmo, 2022). One such bacterium is *Photobacterium damsela*, a halophilic bacterium found widely in marine environments, which possesses the capability to produce histamine (Chen *et al.*, 2012; Trevisani *et al.*, 2017) It is a potent histamine producer, as demonstrated by studies conducted by (Bjornsdottir-butler *et al.*, 2010; Bjornsdottir *et al.*, 2009). It has the capability to generate over 500 mg/kg of histamine at a temperature of 4°C during a 24-hour period. Additionally, it can sustain 50% - 60% of its original effectiveness in dried tuna and sauri fish for a duration of up to 12 weeks at a temperature of -20°C (Kanki

et al., 2007). Various techniques, such as modified atmospheric packaging, high hydrostatic pressure, and irradiation, have been developed to manage biogenic amines (Naila *et al.*, 2010). A further method for regulating the production of histamine in fishery products involves the utilization of secondary metabolites in their pure form or as extracts (Tsafack and Tsopmo, 2022), as indicated in Table 2. The utilization of secondary metabolites, either in their pure form or as extracts, for the regulation of histamine in fresh fish meat, involves immersion in water at a specified concentration and duration (Houicher *et al.*, 2015; Ozogul *et al.*, 2011). In fishery products, this is achieved by incorporating extracts or pure compounds at designated concentrations and times (Cai *et al.*, 2015; Zhou *et al.*, 2016).

The concentration of secondary metabolites must be carefully evaluated, as it significantly influences the sensory attributes of the final product. For instance, the application of secondary metabolites like polyphenols at concentrations of 0.2%, 0.3%, 0.4%, and 0.5% demonstrates that all natural ingredients at these levels can effectively regulate histamine formation. However, treatments at 0.4% and 0.5% may induce sensory detriments, such as undesirable taste or discoloration of the product (Cai *et al.*, 2015). The application of unsuitable phenolic concentrations frequently results in heightened bitterness and astringency, potentially deterring consumers (Esteves *et al.*, 2020). Furthermore, secondary metabolites like tannins can influence the color stability of food products, as they have been demonstrated to interact with proteins and other phenolic compounds, thereby impacting sensory attributes (Al-Hijazeen *et al.*, 2016).

Various bioactive compounds have been identified as effective in controlling the formation of biogenic amines. These compounds

Table 2. The application of bioactive compounds for the controlling of histamine levels in fishery products.

| No | Fishery products | Treatment | Results | Reference |
|----|---|---|------------------|-------------------------------|
| 1 | Pacific Mackerel Fillets | Gallic acid 5% with storage for 12 days at 4°C | 63-84% reduction | Wu <i>et al.</i> , 2016 |
| 2 | Sardine (<i>Sardina pilchardus</i>) Fillets | Phenolic compounds in 1% ethanol extract at 21 days of storage at 3°C | 27-66% reduction | Houicher <i>et al.</i> , 2015 |
| 3 | Sardine (<i>Sardina pilchardus</i>) Fillets | Phenolic compounds in 1% ethanol extract at 20 days of storage at 3°C | 18-25% reduction | Ozogul <i>et al.</i> , 2011 |
| 4 | Shrimp paste | Polyphenols in 0.3% tea at 120 days 25°C storage | 54-68% reduction | Cai <i>et al.</i> , 2015 |
| 5 | Fish sauce | Garlic ethanol extract 2% at 15 days fermentation temperature 30°C | 18-37% reduction | Zhou <i>et al.</i> , 2016 |

Table 3. Antimicrobial properties of bioactive compounds in seaweed.

| No | Seaweed species | Bioactive compounds | Extraction method | Reference |
|----|---|-------------------------------------|--|-----------------------------------|
| 1 | <i>Caulerpa racemosa</i> | Phenolics and tannins | Maceration with methanol solvent produces the best antibacterial activity | Palaniyappan <i>et al.</i> , 2023 |
| 2 | <i>Caulerpa sertularioides</i> and <i>Caulerpa racemosa</i> | - | Maceration with methanol solvent with <i>Caulerpa sertularioides</i> has antibacterial activity on more bacterial strains. | Avila-Romero <i>et al.</i> , 2023 |
| 3 | <i>Padina tetrastrumatica</i> and <i>sargassum muticum</i> | Phenolics and flavonoids | Maceration with methanol, ethanol and acetone solvents with methanol extract gave the best antibacterial activity. | Afrin <i>et al.</i> , 2023 |
| 4 | <i>Caulerpa racemosa</i> | Polyphenols, flavonoids and tannins | Soxhlet with methanol, chloroform and hexane solvents. | Belkacemi <i>et al.</i> , 2020 |
| 5 | <i>Caulerpa racemose</i> and <i>Caulerpa lentillifera</i> | Phenolics and flavonoids | Maceration with chloroform, methanol and water. | Yap <i>et al.</i> , 2019 |
| 6 | <i>Sargassum latifolium</i> and <i>Cladhopora socialis</i> | Phenol | Maceration with methanol and acetone solvents. The best antibacterial activity on brown seaweed seeds is with methanol solvent while green seaweed with acetone. | Moubayed <i>et al.</i> , 2017 |

include polyphenols such as (Tsafack and Tsopmo, 2022), quercetin, 4-hexylresorcinol, and cinnamic acid as studied by (Qian *et al.*, 2018). Gallic acid, phloretin, and flavonoids have also been found to be effective in this regard (Wu *et al.*, 2016; Wang *et al.*, 2019). Catechins, specifically epicatechin, epigallocatechin, epicatechin gallate, and epigallocatechin gallate, have also demonstrated their ability to control biogenic amine formation (Lee *et al.*, 2018). The mechanism of action of these bioactive compounds is primarily attributed to their ability to inhibit microbial growth.

The inhibition of histamine by bioactive compounds is typically linked to their antimicrobial activity (Tsafack and Tsopmo, 2022). Consequently, numerous reviews have been conducted to explore the use of bioactive compounds in inhibiting histamine formation in fish and fishery products by targeting histamine-forming bacteria (Chen *et al.*, 2012; Trevisani *et al.*, 2017; Hwang *et al.*, 2019). However, the regulation of histamine by inhibiting the activity of histidine decarboxylase is not commonly practiced, particularly in relation to bioactive substances derived from seaweed. Therefore, utilizing seaweed bioactives as inhibitors of bacteria and histamine-forming enzymes poses a future challenge. This is due to the promising potential of bioactive chemicals found in seaweed that can be utilized to effectively block histamine in fish and fishery products.

Possible utilization of seaweed bioactive compounds as histamine inhibitors in fishery products

Seaweeds are a diverse set of photosynthetic communities that thrive in the marine environment and can be harnessed as a sustainable resource (Ragunath *et al.*, 2020). Furthermore, seaweed cultivation is relatively straightforward, with a brief production cycle and minimal production expenses (Adharini *et al.*, 2019; Lomartire

and Gonçalves, 2022). Seaweed is an excellent choice for substituting synthetic compounds with natural compounds because it is non-toxic, edible, and cost-effective (Lomartire and Gonçalves, 2022). Seaweed-derived bioactive compounds possess various biological activities, including antimicrobial properties. Alkaloids, flavonoids, phenols, and tannins are examples of bioactive compounds found in antibacterial seaweed (Marraskuranto *et al.*, 2021; Qurniasih *et al.*, 2022). Moreover, the bioactive compounds in seaweed possess the ability to suppress bacterial proliferation and enzymatic function. Extracts from brown algae have been demonstrated to markedly suppress the proliferation of *Morganella morganii*, a notable histamine-producing bacterium, thereby diminishing histamine buildup in fish muscle. This suppression correlates with the presence of phenolic compounds and polysaccharides in seaweed, which not only impede bacterial proliferation but also directly block the enzymatic activity of histidine decarboxylase (Kim *et al.*, 2014; Nitta *et al.*, 2016). The utilization of these seaweed bioactive antimicrobials is illustrated in Table 3.

Seaweed has abundant phenolic compounds that possess antibacterial properties, making them suitable for use as agents to combat microorganisms in fish and fishery products. Seaweed contains phenolic compounds that can hinder the growth of microorganisms (Reguant *et al.*, 2000; Alberto *et al.*, 2002). The effectiveness of these compounds depends on their composition and concentration. The inhibitory activity also varies depending on the solvent used and the type of seaweed (Manilal *et al.*, 2009). Some bioactive substances found in seaweed can dissolve in certain solvents but not in others. Methanol is the most suitable solvent for extracting antimicrobial compounds from brown seaweed, while acetone is the preferred solvent for green seaweed (Cox, 2010). Seaweed possesses a biological activity that acts as an antibacterial agent. This antibacterial property has the potential to be utilized as an inhibitor of histamine synthesis in fish and fishery products.

Currently, there is limited research on the use of bioactive seaweed to inhibit histidine decarboxylase activity. This presents a

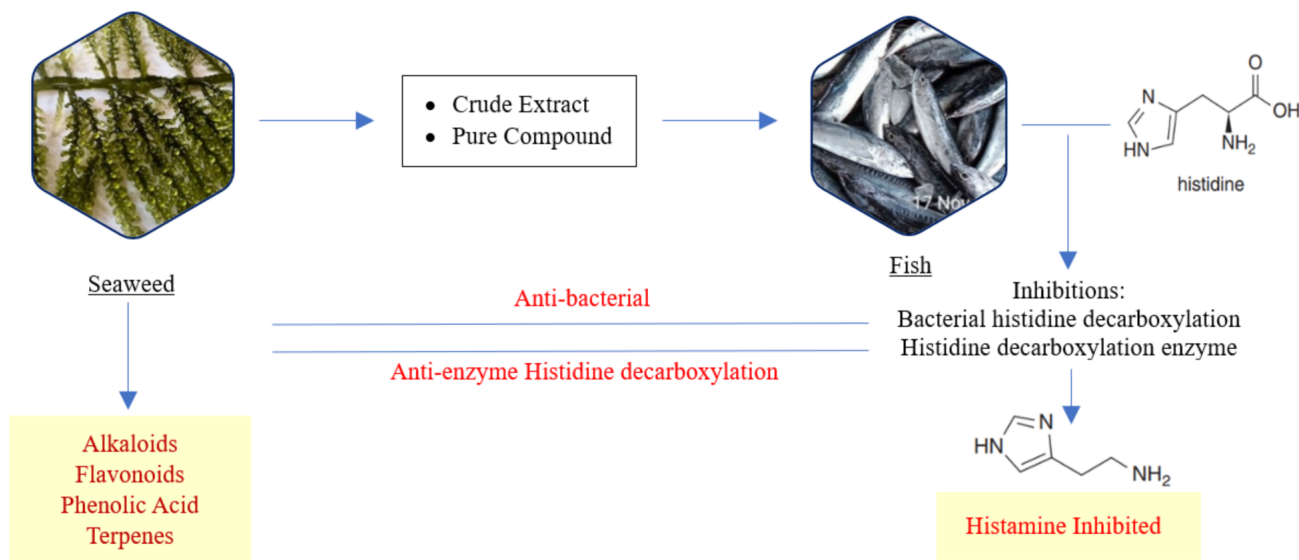


Figure 2. Antimicrobial mechanism of action of bioactive compounds.

future challenge. Bioactive seaweed, in the form of crude extracts or pure compounds, not only has antibacterial properties but also has the potential to be used as an inhibitor of histidine decarboxylase activity in fish and fishery products. Figure 2 illustrates the process of inhibiting histamine in fish and fishery goods during storage. This is achieved by utilizing bioactive chemicals derived from seaweed, which act as antibacterial agents and inhibit the activity of histidine decarboxylase, an enzyme responsible for histamine production in fish and fishery products.

Conclusions

The level of histamine in fishery products is determined by the quantity of histidine and bacteria in the product. Histidine in fish tissue is converted into histamine by bacteria that have the ability to produce histamine, resulting in the synthesis of histamine in fishery goods. Bioactive compounds can serve as an alternative method for controlling the formation of histamine in fishery products. The reduction of histamine by these compounds is linked to their antimicrobial properties. Examples of such bioactive compounds include flavonoids, alkaloids, terpenes, and phenolic acids. These compounds act as antibacterial agents by inhibiting the synthesis of DNA and RNA, disrupting the function of the cytoplasmic membrane, preventing the release of histamine from mast cells, and damaging cell membranes.

The ongoing development of utilizing bioactive chemicals derived from seaweed as antibacterials is a prevailing trend. There is currently limited use of histamine inhibition in fish and fishery products. Therefore, it is necessary to explore the future potential of inhibiting histamine using crude extracts or pure chemicals derived from seaweed. The mechanism of inhibition targets not only the bacterial histidine decarboxylase, but also the enzymatic activity of histidine decarboxylase. This enzyme remains active even when the bacteria are in a dormant or deceased state. Moreover, it is imperative to devise novel or contemporary extraction techniques to address the limitations of conventional extraction procedures like maceration. Ultrasonically aided extraction stands out among contemporary extraction techniques due to its cost-effectiveness, minimal reliance on organic solvents, ability to achieve high compound yields, and reduced extraction time. Therefore, it is imperative to further advance this method for seaweed extraction.

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