http://foodbulletin.net

FOOD BULLETIN

e-ISSN: 2979-9848

https://prensip.gen.tr

REVIEW ARTICLE

Biogenic Amines in Seafood

Yilmaz Ucar[1] • Fatih Ozogul[2]

[1]Çukurova University, Aladağ Vocational School, Department of Forestry, Adana/Türkiye
[2]Çukurova University, Faculty of Fisheries, Department of Seafood Processing Technology, Adana/Türkiye

ARTICLE INFO

Article History
Received: 23.05.2024
Accepted: 23.06.2024
First Published: 23.06.2024

Keywords
Biogenic amine
Food safety
Health risk
Prevention and control methods
Seafood

ABSTRACT

Biogenic amines (BAs) are organic compounds naturally formed in foods through the microbial decarboxylation of amino acids. These compounds are particularly significant in seafood due to the high susceptibility of these products to microbial contamination and improper storage conditions. Biogenic amines, including histamine, tyramine, putrescine, and cadaverine, are often indicators of food freshness and spoilage. Their presence at high levels can pose serious health risks to consumers, making the study of their formation, types, and control methods crucial for food safety. This comprehensive review examines the mechanisms underlying the formation of biogenic amines in seafood. The primary sources of these compounds are bacteria from the families Enterobacteriaceae, Lactobacillaceae, and Pseudomonadaceae. Factors such as temperature, pH, and oxygen availability significantly influence bacterial activity and, consequently, biogenic amine production. Histamine is highlighted as one of the most toxic biogenic amines, capable of causing histamine poisoning, which presents symptoms such as flushing, headaches, nausea, and vomiting. Control and prevention strategies for biogenic amine formation are critically discussed, including the maintenance of the cold chain, hygienic processing techniques, salting, fermentation, and the use of starter cultures. Additionally, innovative microbial inactivation methods such as high hydrostatic pressure and UV radiation are explored for their efficacy in reducing biogenic amine levels. The review also addresses current regulations and standards set by international health authorities, particularly focusing on histamine levels in fish and fish products. These regulations ensure regular monitoring and compliance to protect consumer health. Future research directions are proposed, emphasizing the need for developing new detection methods for rapid and sensitive identification of biogenic amines, improving bacterial inactivation techniques, and advancing genetic and molecular biology studies to better understand the production mechanisms of these compounds. Furthermore, raising consumer awareness about the health impacts of biogenic amines through educational programs is highlighted as a critical area for public health promotion. In conclusion, the review underscores the importance of biogenic amines in seafood quality and safety. Effective control and prevention measures, combined with ongoing research and regulatory compliance, are essential to minimize health risks associated with these compounds. Ensuring proper handling, storage, and processing conditions, along with increasing consumer awareness, will contribute significantly to managing and mitigating the risks posed by biogenic amines in seafood.

Please cite this paper as follows:

Ucar, Y., & Ozogul, F. (2024). Biogenic amines in seafood. *Food Bulletin*, 3(1), 9-15. https://doi.org/10.61326/foodb.v3i1.258

1. Introduction

In recent years, food safety and quality have become critical issues in public health, driven by increased consumer awareness and the globalization of food markets. Seafood, a significant component of human diet worldwide, is particularly prone to quality and safety concerns due to its perishable nature and susceptibility to microbial contamination. Among the various chemical hazards associated with seafood, biogenic amines (BAs) stand out due to their potential to cause adverse health effects and their role as food spoilage indicators.

Biogenic amines are low molecular weight organic bases formed by the decarboxylation of amino acids through the enzymatic action of microorganisms. This process can occur

Correspondence
E-mail address: yucar@cu.edu.tr

during food processing, storage, and fermentation. In seafood, biogenic amines are primarily formed due to bacterial activity, which is influenced by various factors such as temperature, pH, and oxygen availability. The most commonly found biogenic amines in seafood include histamine, tyramine, putrescine, and cadaverine. These compounds are of particular concern because they can reach toxic levels if seafood is not properly handled and stored.

Histamine, often associated with scombroid fish poisoning, is one of the most toxic biogenic amines. It is formed predominantly in fish of the Scombridae family, such as tuna and mackerel. Consumption of histamine-contaminated seafood can lead to histamine poisoning, characterized by symptoms such as flushing, headaches, nausea, vomiting, and in severe cases, cardiovascular disturbances. Tyramine, another significant biogenic amine, can cause hypertensive crises in susceptible individuals, particularly those on monoamine oxidase inhibitors (MAOIs). While putrescine and cadaverine are not directly toxic, they can potentiate the effects of histamine and are often used as indicators of microbial spoilage.

The formation of biogenic amines in seafood is a complex process influenced by several factors. Bacterial contamination is the primary source, with specific bacteria such as those from Enterobacteriaceae, Lactobacillaceae, and Pseudomonadaceae families playing key roles. Environmental factors such as temperature, pH, salt concentration, and the presence of oxygen also significantly affect the formation and accumulation of biogenic amines. For instance, improper refrigeration can accelerate bacterial growth and enzymatic activity, leading to higher levels of biogenic amines.

Given the health risks associated with biogenic amines, their control and prevention in seafood is of paramount importance. Effective management strategies include maintaining the cold chain from capture to consumption, employing hygienic processing techniques, and utilizing preservation methods such as salting and fermentation. Additionally, the use of starter cultures that inhibit or reduce biogenic amine formation has shown promise. Recent advancements in microbial inactivation techniques, such as high hydrostatic pressure and UV radiation, offer additional tools for controlling these compounds.

Regulatory frameworks have been established by international health authorities to limit the levels of biogenic amines in seafood, particularly histamine. These regulations mandate regular monitoring and compliance to ensure consumer safety. Despite these measures, incidents of biogenic amine poisoning still occur, underscoring the need for continuous research and improvement in detection methods, prevention strategies, and public awareness.

Future research should focus on developing rapid and sensitive detection methods for biogenic amines, improving the efficacy of bacterial inactivation techniques, and gaining a deeper understanding of the genetic and molecular mechanisms underlying biogenic amine production. Moreover, consumer education programs are essential to raise awareness about the risks associated with biogenic amines and promote safe handling and storage practices.

Biogenic amines represent a significant challenge in ensuring the safety and quality of seafood. Understanding their formation, health effects, and control measures is critical for mitigating their risks. This comprehensive review aims to provide an in-depth analysis of biogenic amines in seafood, highlighting the latest research, regulatory standards, and future directions for enhancing food safety.

2. Formation and Sources of Biogenic Amines

Biogenic amines (BAs) are formed primarily through the microbial decarboxylation of amino acids in seafood. This process is catalyzed by specific enzymes known as decarboxylases, produced by certain bacteria. The formation of biogenic amines in seafood is influenced by several intrinsic and extrinsic factors, including the type of microorganism present, temperature, pH, salt concentration, and oxygen availability. Understanding these factors is crucial for developing effective strategies to control BA levels in seafood.

2.1. Microorganisms Responsible for Biogenic Amine Formation

The primary microorganisms involved in BA production in seafood belong to several bacterial families. Key species include:

i. ***Enterobacteriaceae***: This family includes genera such as *Enterobacter*, *Klebsiella*, and *Escherichia*, which produce significant amounts of histamine, putrescine, and cadaverine. Recent studies, such as those by Rivas et al. (2023), have highlighted the prevalence of these bacteria in improperly stored seafood and their role in histamine formation.

ii. ***Lactobacillaceae***: Lactic acid bacteria (LAB) from this family, particularly *Lactobacillus* and *Pediococcus* species, are commonly associated with fermented seafood products. While LAB are often beneficial in food fermentation, certain strains can decarboxylate amino acids, leading to the production of tyramine and other BAs (Garai et al., 2007).

iii. ***Pseudomonadaceae***: Members of this family, especially *Pseudomonas* spp., are psychrotrophic bacteria that can grow at low temperatures, making them significant contributors to BA formation in refrigerated seafood. Research by Arulkumar et al. (2023) has demonstrated the ability of *Pseudomonas* spp. to produce putrescine and cadaverine even under cold storage conditions.

2.2. Factors Influencing Biogenic Amine Formation

Several factors affect the growth of BA-producing bacteria and the subsequent formation of BAs in seafood:

i. **Temperature**: Temperature is a critical factor influencing the bacterial growth rate and enzymatic activity. Higher temperatures generally accelerate the production of BAs. Studies by Biji et al. (2020) have shown that histamine formation in fish increases significantly at temperatures above 15°C. Proper refrigeration (below 4°C) is essential to slow bacterial activity and BA formation.

ii. **pH Levels**: The pH of the seafood environment can significantly impact bacterial metabolism. Most BA-producing bacteria thrive in neutral to slightly alkaline conditions (pH 6-8). Research by Ekici and Omer (2020) indicates that adjusting the pH of seafood products can be an effective strategy to inhibit BA production.

iii. **Salt Concentration**: Salt concentration can either inhibit or promote the growth of certain bacteria. High salt concentrations are typically used in fermented seafood products to control spoilage microorganisms. However, some halotolerant bacteria can still produce BAs under these conditions. A study by Gardini et al. (2016) found that specific LAB strains could produce tyramine even at high salt concentrations in salted fish products.

iv. **Oxygen Availability**: The presence or absence of oxygen affects the metabolic pathways of bacteria. While some BA-producing bacteria are facultative anaerobes and can thrive in both aerobic and anaerobic conditions, others are obligate aerobes or anaerobes. Anaerobic conditions can promote the production of certain BAs, such as cadaverine, as shown in the research by Eerola et al. (1993).

2.3. Recent Advances in Understanding BA Formation

Recent advances in molecular biology and genomics have provided deeper insights into the mechanisms of BA formation. High-throughput sequencing and metagenomic analyses have identified specific genes responsible for BA production. For instance, the histidine decarboxylase gene (hdcA) in *Morganella morganii* has been extensively studied for its role in histamine production (Oktariani et al., 2022).

Additionally, advances in microbial ecology have shed light on the complex interactions between different bacterial species in seafood matrices. For example, competition and cooperation between bacterial strains can influence the overall BA levels in seafood products. Studies by Kuley et al., (2017) have shown that certain non-BA-producing bacteria can inhibit the growth of BA producers through competitive exclusion or the production of inhibitory substances.

2.4. Mitigation Strategies

Understanding the factors influencing BA formation has led to the development of various mitigation strategies. These include:

i. **Cold Chain Management:** Maintaining a continuous cold chain from harvest to consumption is crucial. Implementing rapid cooling methods and using ice or refrigerated storage can significantly reduce BA formation (Naila et al., 2010).

ii. **Hygienic Handling and Processing:** Ensuring hygienic conditions during seafood processing and handling minimizes contamination with BA-producing bacteria. Good manufacturing practices (GMP) and hazard analysis and critical control points (HACCP) systems are essential tools in this regard (Abuhlega & Ali, 2022).

iii. **Use of Additives:** Certain food additives, such as organic acids (e.g., lactic acid, acetic acid), can inhibit the growth of BA-producing bacteria. These additives can be used in marinades or during processing to control BA levels (Shim et al., 2022).

iv. **Starter Cultures:** Utilizing starter cultures that do not produce BAs or can outcompete BA producers is an effective strategy in fermented seafood products. Recent studies have identified specific LAB strains that are effective in reducing BA formation during fermentation (Hernández-Jover et al., 1997).

3. Types and Quantities of Biogenic Amines

Biogenic amines (BAs) found in seafood are primarily histamine, tyramine, putrescine, and cadaverine. These compounds are formed by the microbial decarboxylation of specific amino acids. The type and quantity of biogenic amines present in seafood can vary widely based on factors such as the species of fish, the conditions of storage and handling, and the microbial flora present. Understanding the different types of biogenic amines and their concentrations in various seafood products is crucial for assessing potential health risks and implementing effective control measures.

3.1. Histamine

Histamine is the most well-known and toxic biogenic amine associated with seafood, particularly in fish from the Scombridae family (e.g., tuna, mackerel). It is formed from the decarboxylation of histidine by histidine decarboxylase enzymes produced by certain bacteria, such as *Morganella morganii*, *Klebsiella pneumoniae*, and *Hafnia alvei*.

Recent studies have highlighted the variability in histamine levels across different fish species and processing conditions. According to a study by Hungerford (2010), histamine levels in improperly stored tuna can exceed 500 mg/kg, far above the acceptable limit of 50 mg/kg set by the European Union.

Moreover, histamine production is highly temperature-dependent, with rapid increases observed at temperatures above 15°C (Colombo et al., 2018).

3.2. Tyramine

Tyramine is produced from the decarboxylation of tyrosine by the action of tyrosine decarboxylase. It is commonly found in fermented foods but can also occur in fresh and processed seafood. Bacteria such as *Lactobacillus spp.* and *Enterococcus spp.* are known producers of tyramine.

The health impact of tyramine is significant, particularly for individuals taking monoamine oxidase inhibitors (MAOIs), as it can cause hypertensive crises. According to Naila et al. (2010), tyramine levels in some fermented fish products can reach up to 200 mg/kg, posing a potential health risk if consumed in large quantities.

3.3. Putrescine and Cadaverine

Putrescine and cadaverine are formed from the decarboxylation of ornithine and lysine, respectively. These amines are commonly associated with spoilage and are not directly toxic but can potentiate the effects of histamine by inhibiting the enzymes responsible for histamine detoxification.

Recent research by Shim et al. (2022) has shown that putrescine and cadaverine levels can serve as reliable indicators of spoilage in seafood. In a study of various fish species, putrescine levels were found to range from 10 to 300 mg/kg, while cadaverine levels ranged from 20 to 500 mg/kg, depending on the storage conditions and duration.

3.4. Other Biogenic Amines

Other biogenic amines, such as serotonin, spermidine, and spermine, are also present in seafood, albeit in lower concentrations. Serotonin, while primarily known for its role in neurotransmission, can also be found in certain fish species. Spermidine and spermine are involved in cellular growth and function but can contribute to the overall biogenic amine load in seafood.

4. Quantitative Analysis and Acceptable Limits

Quantitative analysis of biogenic amines in seafood is typically performed using chromatographic techniques such as high-performance liquid chromatography (HPLC) and gas chromatography-mass spectrometry (GC-MS). These methods allow for precise measurement of biogenic amine concentrations and are essential for monitoring compliance with regulatory standards.

The acceptable limits for biogenic amines in seafood vary by region and regulatory body. For instance, the European Union has set a maximum allowable histamine level of 50 mg/kg for fresh fish and fish products (Commission Regulation (EU) No 2073/2005). The US Food and Drug Administration (FDA) has established a defect action level of 50 mg/kg for histamine in fish (Florida Sea Grant, 2011).

5. Recent Studies on Biogenic Amine Levels in Seafood

Recent studies have provided valuable insights into the levels of biogenic amines in various seafood products. For example, a study by Kuley et al. (2017) reported that histamine levels in improperly stored mackerel reached 400 mg/kg within 24 hours at 25°C. Another study by Mah et al. (2002) found that tyramine levels in salted anchovies could exceed 150 mg/kg, highlighting the need for careful monitoring and control.

In addition to these findings, research by Doeun et al. (2017) has demonstrated the effectiveness of certain preservation methods in reducing biogenic amine levels. For instance, the use of organic acids and vacuum packaging significantly decreased histamine and putrescine levels in refrigerated fish.

6. Health Effects of Biogenic Amines

Biogenic amines (BAs) in seafood can pose significant health risks to consumers. The severity of these health effects depends on the type and concentration of the biogenic amines, as well as individual susceptibility. Understanding the health implications of different biogenic amines is essential for public health and for developing effective control measures.

6.1. Histamine

Histamine is the most well-known biogenic amine associated with foodborne illness, particularly scombroid poisoning. Histamine poisoning occurs when individuals consume fish with high levels of histamine, typically resulting from improper storage. The symptoms of histamine poisoning can occur within minutes to hours after consumption and include:

- Flushing
- Headache
- Nausea
- Vomiting
- Abdominal cramps
- Diarrhea
- Palpitations
- Hypotension or hypertension

In severe cases, histamine poisoning can lead to respiratory distress and cardiac complications. According to Petrovic et al. (2022), histamine levels above 50 mg/kg in seafood are considered hazardous, and levels exceeding 500 mg/kg are associated with severe toxic reactions.

Recent epidemiological studies, such as those by Hungerford (2010), indicate that histamine poisoning is more common in warmer climates where inadequate refrigeration of fish is more prevalent. The study highlights the need for improved monitoring and handling practices to reduce the incidence of histamine poisoning.

6.2. Tyramine

Tyramine, while less commonly associated with seafood, can cause adverse health effects, particularly in individuals taking monoamine oxidase inhibitors (MAOIs). Tyramine ingestion can lead to hypertensive crises, characterized by:

- Severe headache
- Hypertension
- Palpitations
- Sweating
- Nausea
- Vomiting

Hypertensive crises occur because tyramine can induce the release of norepinephrine from nerve endings, leading to vasoconstriction and increased blood pressure. Naila et al. (2010) emphasize that even moderate levels of tyramine (above 6 mg per meal) can trigger hypertensive reactions in sensitive individuals.

6.3. Putrescine and Cadaverine

Putrescine and cadaverine, while not directly toxic, can enhance the toxicity of histamine by inhibiting histamine-N-methyltransferase and diamine oxidase, the enzymes responsible for histamine detoxification. This synergistic effect can exacerbate the symptoms of histamine poisoning.

Recent studies by Shim et al. (2022) have shown that the presence of putrescine and cadaverine in seafood can increase the severity of histamine poisoning symptoms. In their research, fish samples with high levels of putrescine and cadaverine showed significantly higher histamine toxicity compared to samples with histamine alone.

6.4. Other Biogenic Amines

Other biogenic amines, such as spermidine and spermine, are involved in cellular metabolism and growth. While generally less toxic, high levels of these amines can contribute to overall toxicity and spoilage. For instance, spermidine and spermine can decompose into putrescine and cadaverine under certain conditions, potentially increasing the biogenic amine load in seafood (Doeun et al., 2017).

6.5. Chronic Health Effects

Long-term exposure to low levels of biogenic amines has been less extensively studied, but there is growing concern about their potential cumulative effects. Chronic ingestion of biogenic amines could potentially lead to:

- Gastrointestinal disturbances
- Headaches
- Allergic reactions
- Increased risk of chronic inflammatory conditions

Khora (2016) suggest that continuous exposure to low levels of biogenic amines, particularly in populations with high seafood consumption, could contribute to subtle but significant health impacts over time. Their review calls for more research into the chronic effects of biogenic amine exposure and the mechanisms underlying these effects.

6.6. Preventive Measures and Recommendations

To mitigate the health risks associated with biogenic amines, several preventive measures are recommended:

i. **Proper Storage and Handling**: Maintaining the cold chain from harvest to consumption is crucial. Rapid cooling and proper refrigeration (below 4°C) can significantly reduce biogenic amine formation.

ii. **Hygienic Practices**: Implementing good manufacturing practices (GMP) and hazard analysis and critical control points (HACCP) systems can minimize contamination with biogenic amine-producing bacteria.

iii. **Consumer Education**: Educating consumers about the risks associated with biogenic amines and proper handling of seafood can help reduce the incidence of biogenic amine poisoning.

iv. **Regulatory Compliance**: Adhering to regulatory standards for biogenic amine levels in seafood is essential. Regular monitoring and testing can ensure compliance and protect consumer health.

v. **Research and Innovation**: Continued research into new preservation methods, such as modified atmosphere packaging and the use of bioprotective cultures, can provide additional tools for controlling biogenic amine levels.

7. Control and Prevention of Biogenic Amines

Controlling and preventing the formation of biogenic amines in seafood is crucial for food safety and quality control. Various methods have been developed for this purpose:

i. **Maintaining the Cold Chain**: Keeping seafood at low temperatures slows down the proliferation of biogenic amine-producing bacteria and minimizes amine formation.

ii. **Hygienic Processing Techniques**: Ensuring hygienic conditions during production reduces contamination and prevents biogenic amine formation.

iii. **Salting and Fermentation**: These methods can control microbial activity and reduce biogenic amine production.

iv. **Use of Starter Cultures**: Employing starter cultures that inhibit or reduce the formation of biogenic amines helps maintain acceptable amine levels.

v. **Microbial Inactivation Techniques**: Techniques such as high hydrostatic pressure, UV radiation, and irradiation can be used to inactivate biogenic amine-producing microorganisms.

7.1. Mechanisms of Biogenic Amine Formation

Recent research has elucidated the intricate pathways involved in biogenic amine formation during food processing and storage (ten Brink et al., 1990). Microbial decarboxylases, particularly those produced by certain species of bacteria, play a crucial role in amino acid metabolism and biogenic amine production. Understanding these mechanisms is essential for developing targeted interventions to inhibit biogenic amine formation.

7.2. Innovative Detection Methods

Advancements in analytical techniques have facilitated the development of rapid and sensitive methods for detecting biogenic amines in food samples (Stratton et al., 1991). Chromatographic techniques, such as high-performance liquid chromatography (HPLC) and gas chromatography-mass spectrometry (GC-MS), coupled with mass spectrometry detection, offer enhanced sensitivity and specificity for biogenic amine analysis. Additionally, emerging technologies, such as biosensors and spectroscopic methods, show promise for on-site monitoring of biogenic amines in realtime.

7.3. Preventive Strategies

Effective control and prevention of biogenic amines require a multifaceted approach that addresses various stages of food production, processing, and distribution. Recent studies have explored the use of natural antimicrobial agents, including plant-derived compounds and bacteriocins, to inhibit the growth of biogenic amine-producing microorganisms (Ko et al., 2015). Additionally, innovative packaging technologies, such as active and intelligent packaging systems, can help extend the shelf life of foods and prevent biogenic amine formation.

8. Regulatory Considerations and Future Directions

Regulatory agencies worldwide have established guidelines and maximum limits for biogenic amines in food products to ensure consumer safety (EFSA, 2011). Future research directions may focus on the development of risk assessment models to predict biogenic amine formation in specific food matrices and the exploration of synergistic effects between antimicrobial agents and other food additives. Furthermore, interdisciplinary collaborations between food scientists, microbiologists, chemists, and regulatory authorities are essential to address the complex challenges associated with biogenic amine control and prevention.

8.1. Regulations and Standards

International health authorities have established acceptable levels for biogenic amines and implemented regulations for their control. For example, the European Union has issued directives to limit histamine levels in fish and fish products. These regulations mandate regular monitoring of biogenic amine levels and ensuring they remain within legal limits.

8.2. Future Research Areas

Research on the formation and control of biogenic amines in seafood continues to evolve. Future research areas include:

i. **Development of New Detection Methods**: Creating new analytical methods for the rapid and sensitive detection of biogenic amines.

ii. **Improvement of Bacterial Inactivation Techniques**: Investigating new techniques for more effective inactivation of biogenic amine-producing microorganisms.

iii. **Genetic and Molecular Biology Studies**: Understanding the genetic structures and enzymes involved in the production of biogenic amines by bacteria.

iv. **Increasing Consumer Awareness**: Developing educational programs to raise consumer awareness about the health effects of biogenic amines.

9. Conclusion

Biogenic amines are critical compounds in terms of quality and safety in seafood. Controlling the formation of these amines and ensuring they remain within legal limits is vital for food safety. Ensuring hygiene and appropriate temperature conditions in food processing and storage processes is essential to minimize the formation of biogenic amines. Additionally, further research on the health effects of biogenic amines and increasing consumer awareness will contribute to managing the risks associated with these compounds.

Conflict of Interest

The authors declare no conflict of interest.

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