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Review Article

Sources, biosynthesis, and analytical methods of foodborne biogenic amines

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ABSTRACT

An excessive number of biogenic amines can lead to food poisoning. Ensuring proper food safety evaluation is essential to control this risk. Research has been conducted on the synthesis of biogenic amines, extraction methods, detection techniques, and pharmacological effects. However, there is a lack of comprehensive evaluations that encompass all these elements. Notable gaps remain in the toxic effects of various BAs, and their interactions with food have not been thoroughly investigated. This review aims to provide an assessment of the sources, synthesis pathways, extraction techniques, and detection developments of biogenic amines, as well as their toxicological consequences in foods. Focus is devoted to the relationship between the synthesis pathways of biogenic amines and their occurrence levels in food matrices, as well as the relationship between extraction and detection methods and their impact on safety evaluation. The results of this compilation indicate that the evaluation of biogenic amine occurrence and their toxic effects in food have notably improved food safety evaluation. Based on these findings, it is recommended that the understanding of biogenic amines in food be enhanced and that the urgent necessity for ongoing innovation and methodological improvement be highlighted. This work is significant as it assesses the relationship between biogenic amines and safety evaluation, thereby supporting compliance with food safety regulations and reducing health hazards associated with biogenic amine exposure.

1. Introduction

Biogenic amines (BAs) are nitrogen-containing organic compounds that can be found in protein-rich foods, such as seafood, meat, and fermented products. The most common BAs in food are histamine (HIS), tyramine (TYR), putrescine (PUT), cadaverine (CAD), and spermidine (SPD), which are predominantly generated by microbial decarboxylation of amino acids. While BAs have essential functions in neurotransmission and metabolism, excessive buildup in food can pose significant health hazards such as food poisoning, hypertension, and possible carcinogenic consequences. The growing concern about food safety emphasizes the need for monitoring BA levels to prevent foodborne illnesses and guarantee compliance with international safety standards [1].

Microbial activity, storage conditions, and processing procedures all influence the formation of BA in food. Studies on mackerel demonstrate that HIS levels can exceed the safety threshold of 100 mg·kg^{-1} within two days after refrigeration, causing health concerns to consumers [1]. Poor handling and storage can accelerate the accumulation of BA, especially in perishable items like seafood. Traditional BA extraction methods employ strong acids, such as trichloroacetic acid (TCA) and perchloric acid (PCA). However, recent advancements have led to more efficient and environmentally friendly procedures. Liquid-liquid microextraction (LLME), ultrasound-assisted extraction (UAE), and microwave-assisted extraction (MAE) all increase recovery rates while reducing chemical waste.

Despite advances in BA research, variations in extraction efficiency and testing methods pose hurdles to standardizing food safety measures. While individual BAs have been thoroughly studied, the cumulative harmful effects of many BAs in food are still poorly understood. Their interactions with other food components can influence toxicity, metabolism, and absorption, thereby complicating the assessment of risk. Furthermore, differences in BA concentrations owing to food processing and storage make regulation challenging.

Although substantial research has been conducted on BA synthesis, extraction methods, and pharmacological effects, there is a lack of comprehensive evaluations that encompass all these elements. Most investigations focus on specific food categories or detection techniques, overlooking the broader connections between BA sources, synthesis, extraction, and detection. Despite these efforts, a critical gap remains in which the integration of the entire BA life cycle, from synthesis mechanisms to toxicological impacts, into a unified framework for food safety

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evaluation. This is necessary to address the regulatory and analytical challenges simultaneously.

Therefore, this review provides an assessment of the sources, synthesis pathways, extraction techniques, and detection developments of biogenic amines, as well as their toxicological consequences in foods. Particular attention is devoted to the relationship between the synthesis pathways of biogenic amines and their occurrence levels in food matrices, as well as the relationship between extraction and detection methods and their impact on safety evaluation.

2. Synthesis pathways of BAs

The nitrogenous organic molecules known as BAs are produced when the building blocks of proteins, amino acids, undergo microbial decarboxylation [2]. Apart from decarboxylation, certain bacterial enzymes can aid in the amination or transamination of aldehydes and ketones, which can also result in the formation of BAs [3]. Their occurrence in food depends on more than just the pathway, but the occurrence and concentration of a specific BA in food are mainly influenced by (i) the amino acid composition of the raw material, (ii) the microbial ecology shaped by processing or fermentation, and (iii) environmental factors that promote the expression of decarboxylase genes [4]. The mere presence of decarboxylase genes does not necessarily result in high biogenic amine levels, as their expression is influenced by factors such as pH, salt concentration, temperature, and the bacterial growth phase [5]. The favorable conditions of BAs are low pH, anaerobic/microaerophilic, and rich in free amino acids [6]. In seafood and meat, high levels of biogenic amines often signal microbial spoilage [1]. In contrast, in fermented foods, moderate levels may be considered as a background due to the presence of traditional microbiota [7]. Table 1 lists the specific bacterial enzymes that facilitate these processes. Protein-rich foods that contain a variety of amino acids, including histidine, tyrosine, lysine, ornithine, and arginine, can contain low and high concentrations of BAs, including HIS, TYR, PUT, CAD, and SPD [8]. If taken in excess, these BAs may have pharmacological effects on consumers, causing harm to internal bodily systems [9]. The synthesis of HIS, TYR, PUT, CAD, and SPD is shown in Fig. 1. Based on their chemical structures, BAs can be divided into three primary groups: aliphatic polyamines, aliphatic diamines, and aromatic amines [10].

2.1. *Aromatic amines: Histamine and tyramine*

Aromatic amines are chemical molecules defined by a nitrogen atom directly attached to an aromatic ring, akin to the structures of HIS and TYR. HIS and TYR originate from histidine and tyrosine via decarboxylation, primarily by lactic acid bacteria (LAB), Enterococci, and Staphylococcus [11–13]. HIS tends to accumulate in protein-rich seafood like mackerel and tuna, where histidine levels are naturally high and storage often provides the low pH and anaerobic conditions that favor decarboxylase activity [1,6]. TYR, in contrast, is more prominent in fermented plant and dairy products where tyrosine is abundant and LAB dominate [14,15]. The contrast illustrates how precursor abundance and microbial ecology determine whether HIS or TYR is the dominant BA. From a safety standpoint, HIS is tightly regulated by a 50 ppm threshold [16], while TYR levels serve as spoilage markers in fermented products [17]. Detection methods, such as HPLC or LC-MS/MS, are critical, but their sensitivity also determines whether borderline concentrations are classified as safe or potentially harmful. For example, HIS is produced at refrigeration temperature, as low as 5 °C [1] may escape routine detection unless sensitive methods are applied, complicating risk evaluation.

2.1.1. *Histamine synthesis and presence in food*

HIS is predominantly formed in food via the decarboxylation of the amino acid histidine, a process catalyzed by histidine decarboxylase produced by certain bacteria. Microorganisms produce this enzyme during the preparation or storage of food [12]. A high bacterial load of *Lactobacillus, Pediococcus, and Leuconostoc* species facilitates the synthesis of HIS as a metabolic byproduct during the breakdown of protein-rich foods and beverages. HIS can also be synthesized via the amination and transamination of ketones and aldehydes. The duration of storage and temperature substantially influence HIS synthesis, as certain bacteria can produce BAs even at temperatures as low as 5 °C [1]. Fish, especially those belonging to the *Scombridae* family (e.g., mackerel, tuna, sardines), frequently exhibit heightened HIS levels, especially in their muscle, due to inadequate storage and handling, resulting in bacterial proliferation. This synthesis is especially significant in fermented aquatic goods, as beneficial bacteria enhance rapid HIS accumulation during fermentation [12]. Adequate storage and management of fish are crucial to mitigate the formation of excessive HIS. The United States Food and Drug Administration (US FDA) has established a maximum threshold of 50 parts per billion (ppb) for HIS in fish products to miti-

Table 1
Bacteria and enzymes play a role in the production of biogenic amines in food products.

BAs	Bacteria	Enzyme	Food Products	Implications	Ref.
HIS	**1.** *Lactobacillus* sp. **2.** *Pediococcus* sp. **3.** *Leuconostoc* sp.	Histidine decarboxylase	Mackerel Tuna Sardines	**1.** High levels linked to Scombroid poisoning. **2.** Strict regulatory limits (50 ppm, US FDA). **3.** Act as an indicator of spoilage in seafood.	[1,12]
TYR	**1.** *Enterococci* sp. **2.** *Staphylococcus xylosus*	Tyrosine decarboxylase	Fermented product Canned seafood Fruits Vegetables	**1.** Act as a spoilage marker. **2.** Excessive levels may cause headaches and gastrointestinal disturbances. **3.** Storage temperature strongly influences accumulation	[11,13,15,17,18]
PUT	**1.** *Enterobacteriaceae* sp. **2.** Lactic acid bacteria	Ornithine decarboxylase	Fish Meat Chocolate Cheese	**1.** Act as an indicator of microbial contamination. **2.** Enhances the toxicity of his and TYR by inhibiting detoxification enzymes.	[20,21]
CAD	**1.** *Enterobacteriaceae* sp. **2.** Lactic acid bacteria	Lysine decarboxylase	Cheese Fish Meat Dairy products	**1.** Associated with spoilage and unpleasant odor. **2.** Have synergistic toxicity with HIS and TYR. **3.** Act as a marker of poor hygiene or prolonged storage.	[7,12,13,22,23]
SPD	**1.** *Enterococcus faecalis*	SPD synthase	Sourdough Cheese Fermented product	**1.** Not strictly toxic, as it is associated with cell growth and longevity. **2.** Their levels reflect fermentation balance, and an excessive amount indicates poor raw materials.	[7,8,24]

BAs: Biogenic amines, HIS: Histamine, TYR: Tyramine, PUT: Putrescine, CAD: Cadaverine, SPD: Spermidine, SPD synthase: Spermidine synthase.