



Risks of Biogenic Amines Accumulations From Probiotics

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Abstract. Probiotics, defined as live bacteria that provide health benefits when taken in sufficient quantities, are commonly used in functional foods owing to their functions in pathogen suppression, immunological modulation, and gut barrier enhancement. Nevertheless, their ability to generate biogenic amines (BAs) during fermentation poses significant safety concerns. BAs like histamine, tyramine, putrescine, and cadaverine are produced primarily by microbial decarboxylation of amino acids and are found in fermented dairy, meat, vegetable, and beverage products. While BAs play an important role in physiological processes, excessive consumption has been related to negative consequences such as histamine intolerance, hypertensive crises, migraines, gastrointestinal discomfort, and possible carcinogenicity due to interactions with nitrites. BA formation is influenced by raw material quality, microbial strain diversity, and environmental factors like pH, temperature, and salt content. Some lactic acid bacteria and Enterococcus strains are remarkable high producers, while others show little or no activity, emphasizing the necessity of strain-specific evaluation. Mitigation strategies include carefully selecting non-BA-producing strains, following strict hygiene measures, optimising fermentation settings, and using starter cultures capable of decomposing BA. Emerging omics methods offer significant capabilities for tracking BA-related genes, proteins, and metabolites, making probiotic treatments safer. Besides, consumer awareness and regulatory control are critical, as toxicologically substantial BA levels may not result in sensory deterioration. Moreover, assuring the safety of probiotic foods necessitates a balanced risk-benefit analysis that includes technological controls, genetic screening, and rapid detection techniques. By solving these issues, the probiotic sector can maintain innovation while also protecting public health.

Keywords: Probiotics; Biogenic amines; Fermented foods; Food safety

1 Introduction

1.1 . Overview of Probiotics

Probiotics, meaning "for life," are defined as Live microbes which confer a health benefit to their host when administered in adequate amounts by the World Health Organisation (WHO) [1]. The most frequently employed probiotics are Lactobacillus, Bifidobacterium, Enterococcus, Lactococcus, and Streptococcus [2]. Probiotics are microorganisms that directly or indirectly affect human health. Fighting pathogens, stimulating the immune system, and protecting and improving the intestinal epithelial barrier are among the most fundamental effects of probiotics [3]. Probiotics prevent pathogens



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from adhering to intestinal epithelial cells and inhibit their growth by competing with them for nutrients. They also suppress pathogen growth by producing antimicrobial substances (defensins, bacteriocins, and/or hydrogen peroxide) and by lowering the pH of the organic acids they produce [4]. Probiotics can regulate the immune system by directly interacting with the intestines through the molecules they produce or by utilising their cell structure components [5]. Microbe-Associated Molecular Structures (MAMPs), such as peptidoglycan, lipopolysaccharide, teichoic acid, lipoteichoic acid, bacterial DNA, exopolysaccharide, and flagella, interact with receptors (pattern recognition receptors, PRRs) that recognise these structures in the immune system, activating the innate and adaptive immune systems [6, 7]. The epithelial barrier is damaged by toxins produced by pathogens and pro-inflammatory cytokines produced by the immune system against pathogens, increasing the permeability of epithelial cells. Thus, pathogens and unwanted metabolites cross the epithelial barrier and enter the bloodstream. Probiotics help ensure the stability of epithelial cells by activating various signalling pathways and triggering mechanisms such as preventing programmed cell death, producing defensins, strengthening the bonds between epithelial cells, and increasing mucus secretion [8].

1.2 What are Biogenic Amines?

Biogenic amines (BAs) are a class of structurally varied, basic nitrogen-containing compounds that are prevalent in numerous food products. These compounds are particularly common in items produced through fermentation, such as cheese, wine, and beer, in addition to being found in fish, meats, and other derived products [9]. BAs are called biogenic because they are formed as a result of the activity of living organisms. The cleavage of the carboxyl radical of amino acids forms amines. This process is called decarboxylation, and the enzyme responsible is called decarboxylase. The enzymes responsible for decarboxylation can be produced by both microorganisms and are present in animal and plant tissues [10]. Endogenously, biogenic amines are low-molecular-weight organic compounds produced by tissues. Exogenously, they are antinutritional factors resulting from the decarboxylase activity of fermenting microorganisms in processed foods [11]. Endogenous amines, which play essential roles as neurotransmitters in the body, include catecholamines (dopamine, epinephrine, and norepinephrine), indolamines (serotonin, melatonin, and 5-hydroxytryptamine), and histamines. The name of exogenous amines comes from the amino acid from which they originated [12, 9].



1.3 Importance of Studying Their Risks

Biogenic amines are considered fundamental precursors for the biosynthesis of essential macromolecules, including proteins, hormones, and nucleic acids. Certain polyamines, such as putrescine, spermidine, and spermine, are particularly critical for maintaining intestinal function and regulating healthy metabolic processes [11, 12]. While vital for biological activity, the excessive intake of these compounds from dietary sources can elicit a range of adverse systemic effects. These psychoactive and vasoactive substances, including histamine, tyramine, and tryptamine, are known to influence blood pressure and neurological function. For instance, histamine, a potent vasoactive amine, can induce vasodilation and subsequent hypotension, leading to symptoms such as headaches, flushing, and oedema. The ingestion of more than 8 mg of histamine is capable of causing acute intoxication [9, 12].

The body's ability to manage biogenic amine levels relies on the activity of detoxifying enzymes like diamine oxidase (DAO) and monoamine oxidase (MAO) [13,10, 14]. Impaired function of these enzymes, whether due to genetic predispositions, gastrointestinal pathologies, or pharmacological inhibition, can lead to amine intolerance and heightened toxicity. Furthermore, some amines, such as putrescine and cadaverine, can competitively inhibit the oxidation of histamine, thereby exacerbating its toxic effects [10]. Beyond histamine, other biogenic amines pose distinct health risks. The vasoconstrictive properties of tyramine, tryptamine, and phenylethylamine can contribute to hypertension. Notably, the consumption of tyramine-rich foods by individuals on MAO inhibitor therapy may precipitate a hypertensive crisis or trigger migraine attacks [9, 13]. In the central nervous system, biogenic amines are crucial for neurotransmission. A deficiency in cerebral putrescine has been implicated in the pathophysiology of depression. Similarly, imbalances in serotonin levels are linked to eating disorders, and MAO-inhibiting medications are widely utilized to modulate these levels for the treatment of depression and anxiety disorders [10]. Conversely, certain polyamines exhibit potential carcinogenic properties. Putrescine, cadaverine, and spermidine are capable of reacting with nitrites to generate carcinogenic compounds [10, 15]. In high concentrations, polyamines can also induce programmed cell death (apoptosis) and suppress cellular proliferation, with high-dose putrescine specifically linked to these effects through increased nitric oxide synthesis and direct binding to carcinogens [9, 15]. Agmatine is a biogenic amine with diverse pharmacological effects. It is noted for its nephroprotective benefits through an increase in glomerular filtration rate and its role in glucose



homeostasis. Interestingly, research indicates that agmatine levels are elevated in individuals with schizophrenia compared to healthy controls [10, 11].

2 Biogenic Amines: Formation and Types

Biogenic amines are formed from the breakdown of proteins primarily through enzymatic pathways such as the decarboxylation of amino acids, as well as the amination and transamination of other organic compounds [10, 16]. BAs are classified according to the number of amine groups they contain and their chemical structure. According to the first classification system, these compounds can be divided into monoamines (e.g., tyramine, dopamine, norepinephrine, histamine, and serotonin), diamines (e.g., putrescine and cadaverine), and polyamines (e.g., spermine and spermidine). Alternatively, they are classified according to their chemical structure as aliphatic (e.g., putrescine, cadaverine), aromatic (e.g., tyramine, phenylethylamine), and heterocyclic (e.g., histamine, serotonin) compounds [9, 11, 17, 18].

2.1 Mechanisms of Biogenic Amine Production

The formation of biogenic amines is a consequence of the microbial decarboxylation of amino acids, a process that is catalyzed by specific decarboxylase enzymes found in various bacterial strains [10, 11, 16]. The microorganisms responsible for this enzymatic activity include both Gram-negative and Gram-positive species, such as those from the *Enterobacteriaceae*, *Lactobacillaceae*, and *Staphylococcus* families [19]. The accumulation of these compounds is a multifaceted process determined by three primary groups of factors. Intrinsic factors: These relate to the raw material's composition, including its pH and the availability of free amino acids. Extrinsic factors: These encompass the conditions under which the food is processed and stored, such as temperature, storage duration, and the type of processing (e.g., cooking, fermentation). Microbiological factors: This involves the presence and activity of specific microbial strains that possess decarboxylase capabilities. Consequently, the establishment of proper sanitary conditions during food production and handling is critical, as it serves to control the growth and proliferation of these amine-producing microbial strains [11, 20].

The most critical process in the formation of biogenic amines is the secondary changes that result from the decarboxylation of amino acids. This process occurs due to either tissue- or microbe-derived decarboxylase enzymes. In foods, decarboxylation caused by microbial degradation is more common [18]. Specifically, in fermented foods, amine formation happens in three main ways. The amination of



aldehydes and ketones, the secondary conversion of certain amino acids through microbial decarboxylation, and the hydrolysis of nitrogen-containing components, such as nitrogenous compounds and their degradation products [10, 11, 20]. Common amino acids preceding BAs and the BAs they produce are histidine (histamine), tyrosine (tyramine), phenylalanine (phenylethylamine), tryptophan (tryptamine), ornithine and agmatine (putrescine), and lysine (cadaverin). Among these, the single-step decarboxylation of histidine, tyrosine, tryptophan, lysine, and phenylalanine can directly form the corresponding amine. Putrescine is a diamine that can be produced by decarboxylation of ornithine or deamination of agmatine. Spermine and spermidine are polyamines formed by the sequential addition of aminopropyl groups to putrescine [10, 11, 21].

2.2 Common Biogenic Amines in Probiotic Fermentation

Biogenic amines play a vital role in numerous biological processes, including cell membrane stability, immune system function, and the prevention of some chronic illnesses. They contribute to essential cellular activities like the synthesis of nucleic acids and proteins. Additionally, certain biogenic amines act as signaling molecules and mediators in the body. For example, some are involved in growth regulation (spermine, spermidine, and cadaverine), neural communication (serotonin), and inflammatory responses (histamine and tyramine) [10].

Histamine is a natural compound in the body, synthesised from the amino acid histidine with the help of the enzyme histidine decarboxylase and pyridoxal phosphate. The amount and location of histamine differ significantly among the tissues of all vertebrates. This compound has several essential functions. It acts as a neurotransmitter and regulates vascular permeability. It's also involved in controlling body temperature, stomach acid levels (pH), stomach volume, and brain activity. Additionally, it is a key player in triggering allergic reactions [22].

Tryptamine is a monoamine alkaloid formed when the enzyme aromatic L-amino acid decarboxylase acts on the amino acid tryptophan. This compound is found in trace amounts in the brains of mammals, where it can act as a neurotransmitter or neuromodulator and has been shown to increase blood pressure. Additionally, tryptamine is present in plants, fungi, and other animals [10].

In a similar fashion, tyramine is produced from the amino acid tyrosine via the enzyme tyrosine decarboxylase. While commonly found in fermented foods, it can also be present in fresh and processed seafood. Specific bacteria, such as *Lactobacillus* spp. and *Enterococcus* spp., are known to be tyramine



producers [10, 22]. Tyramine also has a strong antioxidant effect due to the amine and hydroxyl groups in its structure [23]. The health implications of tyramine are significant, especially for individuals on monoamine oxidase inhibitors (MAOIs), as its consumption can lead to hypertensive crises. In some fermented fish products, tyramine levels can reach as high as 200 mg/kg, posing a health risk if consumed in large amounts [22, 24]. Humans, as well as certain fungi, bacteria, and a variety of plant and animal species, can produce phenylethylamine from the aromatic amino acid phenylalanine. This synthesis is carried out by the enzyme aromatic L-amino acid decarboxylase [10]. In the human central nervous system, phenylethylamine acts as a neurotransmitter, helping to regulate blood pressure and remove norepinephrine. However, high levels of this compound can cause adverse health effects, with symptoms including hypertension, and cerebral hemorrhage [16, 25]. Consuming phenylethylamine in the presence of tyramine has been linked to several adverse health effects. This combination is known to trigger migraine attacks in susceptible individuals and can also lead to an increase in blood pressure [26].

The most common cellular polyamines, putrescine, spermidine, spermine, and cadaverine, play a role in bacterial cell growth and proliferation. These compounds possess a polycationic structure that allows them to easily attach to anions within the cell. In addition to their role in cell growth, polyamines are also vital for regulating nucleic acids, aiding in protein synthesis, and maintaining the stability of cell membranes [15].

Both putrescine and cadaverine are biogenic amines that signal food spoilage. Putrescine is derived from the decarboxylation of the amino acid ornithine, a reaction catalyzed by ornithine decarboxylase. It can also be synthesized from arginine via the agmatine and carbamoylputrescine pathways. Cadaverine, on the other hand, is formed from the decarboxylation of lysine [10].

These two amines are often found in decaying food, particularly seafood, and are considered reliable indicators of decomposition. While not directly toxic, they can potentiate the effects of histamine by blocking the enzymes that normally break it down. Shim et al. found that putrescine and cadaverine levels in various fish species varied significantly based on storage conditions and duration, with ranges of 10–300 mg/kg and 20–500 mg/kg, respectively. Beyond their role in spoilage, putrescine, which is produced by bacteria and fungi, also serves as a precursor for spermidine and spermine, and is involved in essential biological processes like cell growth, cell division, and tumorigenesis [22, 27].



Spermidine synthase is the enzyme responsible for synthesizing spermidine from putrescine. This compound is a vital precursor for other polyamines, including spermine and its structural variant, thermospermine. Spermidine plays a critical part in many key biological functions. It helps maintain membrane potential and regulates both intracellular pH and cell volume. Furthermore, as a polyamine involved in cellular metabolism, spermidine contributes to the inhibition of neuronal nitric oxide synthase and supports the development of intestinal tissues [10].

Spermine, a polyamine found in all eukaryotic cells, is formed from its precursor, spermidine, through the enzyme spermine synthase. Although its precursor amino acid is ornithine, it's not a direct conversion. Spermine is present in a wide range of organisms and tissues due to its vital role in cellular metabolism. It contributes to the development of intestinal tissues and helps stabilize the helical structure of viruses [28].

Agmatine is produced from the amino acid arginine through the action of the enzyme arginine decarboxylase. It plays a key role in polyamine metabolism, as it's converted to putrescine via the agmatine enzyme. This compound has several important functions. It helps regulate the synthesis of nitric oxide and is involved in the activity of matrix metalloproteinases and other enzymes that lead to the production of H_2O_2 [10, 28].

In humans, putrescine, cadaverine, and agmatine can hinder the breakdown of histamine, which in turn raises its toxicity levels. Furthermore, spermine, spermidine, and putrescine demonstrate antioxidant properties. These compounds are capable of preventing the oxidation of polyunsaturated fatty acids, with their effectiveness being directly proportional to their amine content [10, 29].

2.3 Factors Influencing Their Production

Several factors influence biogenic amine formation in fermented foods during processing, such as raw material quality, microbial cultures, and environmental conditions like pH, temperature, and fermentation time [26].

Since the level of biogenic amines (BAs) in food is influenced by sanitation and can fluctuate throughout its preparation and storage, measuring these compounds offers a reliable way to assess food quality. In their natural state, BAs are already present in raw ingredients such as grapes, fresh milk, and uncooked meats. For instance, using unsanitary meat for sausage production is known to severely inhibit the



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activity of the beneficial bacteria *Lactobacillus sakei* CTC494, a strain that lacks amino acid decarboxylase. Furthermore, significant quantities of spermidine, putrescine, and cadaverine have been shown to accumulate in the skins and seeds of grapes as part of the winemaking process [16, 30].

The quantity and variety of amines in food depend on the product's composition and the presence of microorganisms. Many bacteria from the Enterobacteriaceae family, along with species of *Pediococcus*, *Enterococcus*, and *Lactobacillus*, are known to contribute to biogenic amine (BA) formation. Several microbial groups have been found to have decarboxylase activity. Specifically, bacteria like *Lactobacilli*, *Pseudomonads*, *Enterobacteriaceae*, and *Enterococci* found in meat products are known to possess this ability. While most yeasts can produce significant amounts of cadaverine and putrescine, only a few—such as *Debaryomyces hansenii* and *Yarrowia lipolytica* isolated from cheese—can also produce histamine and tyramine [31]. For seafood, particular bacterial species have been confirmed as histamine producers. These include *Staphylococcus xylosum* from salted anchovies, *Morganella morganii*, *Hafnia alvei*, and *Klebsiella pneumoniae* from tuna, and *Aeromonas hydrophila* from mackerel. Furthermore, researchers like Pessione et al. have identified *Lactobacillus sp.* 30a and *Lactobacillus sp.* w53 from wine as producers of histamine, putrescine, and cadaverine [9, 21, 31]. In yoghurt, the formation of BAs, particularly tyramine and histamine, is primarily attributed to *Streptococcus thermophilus*. A number of studies have also shown that histamine-producing bacteria exist in fermented soybean products [31].

Amine formation in foods is a complex process influenced by a combination of factors, including temperature, pH, and salt content. Amine production accelerates under specific temperature conditions. Research indicates that the optimal temperature range for the activity of amine-forming microorganisms is 20-37°C. For instance, *Morganella morganii* in fish produces the most histamine at 25°C. Similarly, *Carnobacterium divergens* generates more tyramine in meat-fat mixtures at 25°C compared to 15°C. Studies have also shown that higher storage or processing temperatures lead to increased biogenic amine (BA) formation in various food products, including carp meat [29, 31, 32]. The pH level also plays a crucial role. The ideal pH for the decarboxylation activity responsible for amine formation is around 5.0. However, the relationship is not always straightforward; in wine production, for example, a higher pH can lead to increased biogenic amine accumulation. In fermented sausages, a slow or insufficient drop in pH during the initial stages of ripening has been linked to higher histamine levels. Additionally, some bacteria, like *Carnobacterium divergens*, produce more tyramine at a pH of 5.3 than at 4.9.



Conversely, high salt concentrations can inhibit this process. When salt content exceeds 5%, the formation of biogenic amines is significantly reduced [19, 29, 32].

3 Probiotic Strains and Biogenic Amine Production

3.1 Lactic Acid Bacteria and Fermented Foods

Several species of Lactic Acid Bacteria (LAB) are recognised as safe by food safety authorities around the world. They are considered beneficial bacteria that enhance food safety and quality and have been part of traditional diets for centuries. LAB create lactic acid during fermentation by breaking down sugars like lactose and fructose. Found naturally in plants, food, and animal digestive systems, these microorganisms are among the most researched [33]. They are central to food fermentation and have been used for millennia in a process called lacto-fermentation [34]. Although the term "lactic" comes from the Latin word for milk, this fermentation isn't limited to dairy; it also occurs in foods like pickles, sauerkraut, kimchi, and sourdough bread. The resulting lactic acid gives these foods their characteristic sour flavour and acts as a preservative. Many LAB species are considered safe by global food authorities and are valued for improving both food safety and quality [35].

LAB are highly adaptable microbes that can thrive with or without oxygen. However, their fermentation metabolism is only triggered when oxygen is limited [36]. These bacteria are fundamental to the fermentation of many foods, transforming everyday ingredients like milk, grains, vegetables, and meat into distinct, tangy products such as yoghurt, sourdough bread, kimchi, and cured sausages. LAB can occur naturally in foods under the right conditions, or specific "starter cultures" can be added to achieve a desired outcome [37].

LAB enhances food quality in several key ways. They act as a natural preservative by lowering the food's pH, which creates an acidic environment that prevents harmful bacteria from growing and extends shelf life. They are also responsible for the unique flavor and texture of fermented foods; for instance, they give sourdough its signature tang and yogurt its creamy consistency by producing exopolysaccharides. Furthermore, some LAB species improve food safety by creating antimicrobial compounds that inhibit the growth of dangerous pathogens [35, 36]. LAB also has applications in agriculture, medicine, cosmetics, and the production of eco-friendly plastics (Raman et al. 2022).



The lactic acid produced by LAB is a key component in a wide variety of foods. These include fermented dairy products like yoghurt, cheese, and kefir; vegetables and fruits such as cabbage, cucumber, and mangoes; and grains found in products like sourdough bread and miso paste. They are also essential in fermenting beverages like kombucha and boza, as well as cured meats and fish [36].

3.2 Variability Among Strains

Lactobacilli are considered significant BA producers in various fermented foods, including meat, cheese, and beverages. While their role is generally beneficial, some strains can accumulate high levels of BA, which can be a food safety concern [19].

In fermented sausages, *Lactobacillus curvatus* and *Lactobacillus sakei* are the predominant species. Most *L. curvatus* strains are known to be tyramine producers. Other species, such as *L. paracasei*, *L. brevis*, and *L. plantarum*, have also been identified as BA producers in meat [19, 39].

Lactobacilli are responsible for BA accumulation in many cheeses. Certain strains of *L. buchneri*, *L. parabuchneri*, and *L. helveticus* can produce high levels of histamine even under refrigerated conditions. *L. brevis* and *L. curvatus* strains in cheese are also known to produce tyramine [19, 40].

In wine and cider, *Lactobacillus* species such as *L. brevis*, *L. hilgardii*, and *L. rhamnosus* are responsible for the accumulation of BAs, particularly histamine and tyramine. Production is influenced by conditions such as pH and the presence of specific decarboxylase-positive strains [19].

Some LAB strains that cause spoilage in beer, such as *L. brevis*, *Lactobacillus lindneri*, and *Lactobacillus paracollinoides*, have been identified as sources of BAs. These bacteria can produce tyramine, ornithine, and histamine as a metabolic strategy for survival in acidic and nutrient-poor environments. *Lactobacillus rossiae* is one of the putrescine-producing bacteria in sourdough. This strain utilises a specific metabolic pathway to produce putrescine, which serves as a biochemical defence mechanism and helps it survive in acidic conditions [19, 41].

The ability to produce BAs is highly strain-dependent, even among the same species. It is often linked to the presence of specific genes such as *hdc* (for histamine) and *tdc* (for tyramine). Some strains can acquire the genes necessary for BA production through horizontal gene transfer [19].



The *Enterococcus* genus has a dual reputation in food science. While not formally designated as "Generally Regarded As Safe" (GRAS) or included on the Qualified Presumption of Safety (QPS) list, some species are widely used in traditional food fermentation, particularly in cheeses and dry sausages. They are valued for their ability to thrive in challenging conditions like high salt and low pH, and for their contribution to flavor through proteolytic and lipolytic activities. Certain strains even show promise as probiotics and can produce bacteriocins that inhibit harmful bacteria [19, 39].

However, their presence is also a significant concern due to their strong potential for producing biogenic amines (BAs), especially tyramine. This capability is not universal across the genus but is highly dependent on the specific strain. For example, species like *E. faecium*, *E. faecalis*, and *E. durans* are frequently identified as tyramine producers in cheese, meat, and wine. The production of BAs is not just a random occurrence; it's a biochemical defense mechanism that helps the bacteria survive in harsh, acidic environments by regulating their internal pH [18, 19].

Research shows that the presence of the gene clusters responsible for BA production, such as the *tdc* gene for tyramine, is common in many *Enterococcus* strains. However, simply having the gene does not guarantee BA production. The actual accumulation of these compounds depends on the gene's expression, which is influenced by environmental factors like pH, temperature, and salt concentration. For instance, some studies indicate that a lower pH and salt stress can actually upregulate the expression of the genes that lead to increased tyramine production. This variability underscores the importance of a case-by-case evaluation of each *Enterococcus* strain used in food production to ensure safety [19].

Bifidobacteria are a key group of bacteria, largely found in the human gut, that play a significant role in human health and nutrition. They are notable for their ability to synthesise crucial vitamins, including riboflavin, thiamine, vitamin B6, and vitamin K, along with other important bioactive compounds like folic acid, niacin, and pyridoxine. The presence of these bacteria in fermented milk products enhances their nutritional profile, making them rich sources of free amino acids and vitamins [42].

While some *Bifidobacterium* strains have the potential to produce BA, their ability to do so is generally more limited than that of other fermentative microorganisms such as LAB. These strains produce small amounts of cadaverine and tyramine [43].



3.3 Case Studies from Fermented Dairy, Vegetables, and Beverages

BA synthesis in fermented foods is an enzymatic process that primarily begins with the hydrolysis of proteins. This first step, carried out by microbial proteases, releases free amino acids, which then serve as precursors for the formation of BA. As previously mentioned, the most common and critical pathway for this conversion is amino acid decarboxylation, where microbial enzymes act on amino acid substrates. Less common pathways for BA production include amination and transamination of ketones and aldehydes [26, 44].

Besides histamine, which has been the most extensively researched, tyramine, phenylethylamine, tryptamine, putrescine, cadaverine, spermidine, and spermine are the BAs detected in fermented fish that pose a risk. Among these, histamine, putrescine, and cadaverine levels typically rise as fish begins to spoil, while spermine and spermidine concentrations simultaneously decrease [31]. Bacteria identified as BA producers in fermented fish include Enterobacteriaceae and Lactobacillus species. Methods such as ensuring the use of hygienic raw materials, optimising processing and storage conditions, and using effective starter cultures are used to prevent or reduce BA formation in fermented fish [16].

Dairy products, especially aged cheeses, are a significant source of BA. Among these, the cheese reaction, caused by tyramine produced in high concentrations in cheese, is a foodborne illness. Furthermore, cheese is second only to fermented fish in terms of histamine production. The synthesis of these compounds is attributed to various microorganisms [9, 19]. Many of the starter and adjunct cultures intentionally used in cheesemaking and the dairy industry are known to produce BA. These include lactic acid bacteria from various genera, such as *Lactobacillus*, *Pediococcus*, *Enterococcus*, *Leuconostoc*, *Lactococcus*, and *Streptococcus*. Some yeast species, such as *Debaryomyces hansenii*, *Yarrowia lipolytica*, *Pichia jadinii*, and *Geotrichum candidum*, also play a role in this process [45].

Polyamines play a fundamental role in plant physiology, where they are integral to a wide range of cellular processes. These compounds are essential for functions like cell division and differentiation, the biosynthesis of nucleic acids and proteins, and maintaining membrane stability. They also contribute to a plant's ability to cope with environmental stress and delay senescence [46].

The distribution of these compounds is not uniform across all produce. Fruits and their juices, for example, are particularly rich in putrescine, while green vegetables contain higher concentrations of spermidine. While other aromatic amines, such as tyramine, are less common than polyamines, they can



still accumulate to exceptionally high levels in certain vegetables, where they are believed to act as a defence mechanism against insects and herbivores [46, 47].

Fermentation has long been employed as a preservation technique for fruits and vegetables across various cultures. This traditional method is applied to a wide array of produce, from staple items like white and red cabbage (sauerkraut) to a more diverse range including broccoli, cauliflower, Brussels sprouts, peppers, carrots, beets, and tomatoes [26, 48]. The final concentration of biogenic amines (BAs) in these products is not uniform, as a confluence of variables determines it. The specific properties of the raw material, climatic conditions, and agricultural practices all play a role, as do the particular processing and storage parameters applied during fermentation [48, 49, 50].

4 Mitigation Strategies

Although biogenic amines play a role in human health, some can lead to negative health effects when present in high concentrations. These adverse reactions can also occur if the body's metabolic processes are impaired due to genetic factors, certain illnesses, or the use of medications that inhibit amine oxidase enzymes.

4.1 Selection of Non-BA-Producing Strains

Bacterial growth and fermentation processes can lead to the formation of amino acid derivatives known as biogenic amines (BAs), which can have various effects on human physiology and well-being [21]. When consumed in high concentrations, these compounds can pose a health risk, leading to symptoms like headaches, heart palpitations, and gastrointestinal distress [19]. The level of toxicity is influenced by the specific type of BA, individual sensitivity, and the co-consumption of substances like alcohol or monoamine oxidase inhibitors, which impair the body's ability to detoxify these compounds [19, 51].

Histamine and tyramine are considered the most dangerous BAs due to the severity of their symptoms. Histamine, often found in fish like tuna and sardines, can trigger "scombroid fish poisoning," an allergic-like reaction. Tyramine, commonly linked to the "cheese reaction," can cause migraines and other severe cardiovascular and respiratory issues. Other BAs, including putrescine and cadaverine, can also cause toxicity and enhance the effects of histamine and tyramine by interfering with the enzymes that break them down [19].



Despite these risks, there is no global legal standard for BAs in food, with the key exception of a specified maximum histamine level in certain fish products in the European Union [19, 52].

BA contamination can come from various sources, including spoilage bacteria like *Enterobacteriaceae*. However, LAB, a group of Gram-positive microorganisms central to food fermentation, are considered particularly efficient producers of tyramine and other BAs like histamine, putrescine, and cadaverine [25].

Given that BA production varies greatly between different bacterial strains, the development of safe probiotic products hinges on careful strain selection. This involves a comprehensive in vitro screening process where bacteria are tested for their ability to produce BAs under various food-like conditions. Crucially, genetic analysis using techniques like genome sequencing is employed to verify the absence of the genes—such as *tdc* (tyrosine decarboxylase), *hdc* (histidine decarboxylase), *odc* (ornithine decarboxylase) ve *ldc* (lysine decarboxylase)—that are responsible for BA synthesis. This rigorous approach allows for the creation of a detailed safety profile for each probiotic strain, ensuring they are both beneficial and safe for human consumption [53].

4.2 Technological Approaches in Fermentation Control

The BA profile and amount in fermented products vary depending on the microorganism population and environmental conditions. The most fundamental and first step in controlling biogenic amine formation is ensuring the initial quality of the raw material and the hygienic conditions of the production process. A large portion of BAs found in foods is produced by decarboxylase-positive microorganisms, either naturally occurring or introduced during the production process. The presence of contaminating bacteria capable of producing BAs, particularly *Enterobacteriaceae*, can cause rapid and uncontrolled amine accumulation from the beginning of fermentation. This severely limits the effectiveness of subsequent technological control methods. Even the use of commercial starter cultures may be insufficient to address this high level of contamination, increasing the risk of undesirable BA levels in the final product. Therefore, the most effective strategy for BA control begins at the source and necessitates the selection of high-quality raw materials and the implementation of strict hygiene standards [29].

The physical and chemical conditions of fermentation processes are the most critical parameters directly affecting BA formation. These parameters work synergistically to determine microorganism growth and decarboxylase enzyme activity. Temperature: While temperatures near optimal growth values can boost



cell metabolism and proliferation, which often increases the production of BAs due to a higher cell count, a large number of decarboxylating cells alone doesn't guarantee a high final amount of Bas [11, 29]. Studies using *E. faecalis* EF37 in a model system showed that increasing temperature from 16°C to 44°C corresponded to faster growth and more rapid and intense tyramine accumulation. The highest activity of a pure commercial tyrosine decarboxylase extracted from *E. faecalis* was found at a temperature between 30 and 37°C. In contrast, the optimum temperature of a tyrosine decarboxylase obtained from *L. brevis* was 50°C. However, it was rapidly inactivated at higher temperatures, and the enzyme's activity at the optimum temperature decreased rapidly during storage at 50°C for one hour [29, 54, 55].

There are limited reports on the relationship between temperature and other BAs (putrescine, cadaverine, and tryptamine). Generally, the accumulation of BAs, including cadaverine and putrescine, increased with temperature [29]. pH: Decarboxylation is a cellular response to acidic conditions; therefore, numerous studies have investigated the relationship between pH and BA accumulation. The effect of pH varies depending on whether the focus is on the activity of a pure enzyme or the decarboxylase activity of living cells. Regardless of the specific focus, low pH has been widely demonstrated to trigger the transcription of genes in many decarboxylase clusters, thereby increasing the ability of cells to withstand acidic stress [29].

The pH range in which amino acid decarboxylase enzymes exhibit optimal activity is between 5.0 and 6.5. Therefore, lowering the pH below this range during the production process, particularly to below 4.0, inhibits the growth and enzyme activity of BA-producing microorganisms, thereby suppressing amine formation [25].

Salt Concentration: Elevated salt levels typically lead to lower biogenic amine (BA) accumulation in food products, primarily by hindering the metabolic processes of decarboxylating microbes. Gram-negative bacteria are particularly susceptible to this effect, showing greater inhibition from increased salt concentrations compared to Gram-positive bacteria. This approach to controlling BAs, however, conflicts with the current health-conscious trend of reducing sodium chloride in food. Different bacterial species exhibit varied responses to salt concentration, resulting in inconsistent effects on biogenic amine (BA) production [29].



The influence of salt on histidine decarboxylase activity in *Streptococcus thermophilus* is not uniform across different contexts: it acts differently on whole, living cells than on a cell-free extract. While a 2.5% salt concentration virtually stopped histamine formation in the living cells, the enzyme's activity in the extract was unaffected up to 5% NaCl. Furthermore, even when the NaCl level reached 20–30%, the decarboxylase in the extract still maintained some function, though it started to decrease after 5% [29, 56].

Conversely, a *Tetragenococcus muriaticus* strain, isolated from fish sauce, exhibited maximum histamine generation later in its exponential growth phase, specifically when salt levels were between 5–7% NaCl. This strain is known for its ability to sustain histidine decarboxylase activity even in a 20% salt environment [29, 56]. Furthermore, during the fermentation of sauerkraut, the overall amine content was greater in products with 1.5% NaCl compared to those with 0.5% NaCl for both *Lactobacillus plantarum* and *Leuconostoc mesenteroides* [50]. These observations suggest a complex relationship where, despite salt's potential to slow down bacterial growth, rising NaCl levels can sometimes directly increase certain biogenic amines. This phenomenon is often attributed to the critical function of Na⁺ ions in the sodium/proton antiport system, a mechanism that helps cells cope with stress by actively pumping H⁺ ions out [29].

Several established methods exist for reducing biogenic amine (BA) accumulation in foods, ranging from processing techniques to ingredient additions [31].

Modified Atmosphere Packaging (MAP) utilises carbon dioxide to significantly extend a food's shelf life by suppressing the growth of bacteria that form histamine [57]. Additionally, incorporating preservatives and additives into food has been shown to effectively curb BA production [31]. Applying high hydrostatic pressure is an effective way to lower both the bacterial count and the resulting BA levels in both raw ingredients and finished food items [24].

Irradiation is another physical method used for BA reduction, with reports showing that gamma irradiation successfully lowers histamine, tyramine, cadaverine, and putrescine in fish, such as blue jack mackerel, dramatically reduces histamine in Bonito, and effectively controls BA formation in products like soybean paste [31, 59]. Smoking also proves beneficial; smoked samples consistently show lower levels of histamine, tyramine, cadaverine, putrescine, spermine, and spermidine compared to non-smoked samples. The smoking process inherently creates aseptic qualities in the product, thereby



inhibiting the growth of amine-decarboxylating bacteria and reducing BA concentration [31]. The choice of starter culture plays a critical role in controlling BA formation. While some strains produce BAs, others have "negative" decarboxylase activity or contain enzymes capable of oxidising and breaking down existing biogenic amines in the food. The strategic use of selected starter cultures has successfully prevented the buildup of BA in various fermented products, including sausage, wine, fish sauce, and cheese [29, 31, 60]. Another technique for lowering biogenic amines (BAs) in food involves using oxidising agents to break down the BAs. Several microorganisms are recognised for their ability to oxidise these compounds, including *Natrinema gari*, *Vergibacillus sp SK33*, *Micrococcus varians*, *Lactobacillus sakei*, *Lactobacillus curvatus*, *Staphylococcus xylosum*, and *Brevibacterium linum* [31].

4.3 Consumer Awareness and Labeling

Food safety remains a top concern for both consumers and global health organisations. The World Health Organisation (WHO) estimates that more than 200 diseases are foodborne, and that the majority of the worldwide population will experience a foodborne illness at some point. Because it is difficult to establish a definitive causal link between food contamination and related illness or death, the true incidence of these diseases is likely underestimated. Given that food contamination can occur at any stage of the global supply chain (from production and distribution to preparation and consumption), every stakeholder, from producer to consumer, bears the responsibility for ensuring the safety of the food supply [61, 62, 63].

BA control and monitoring are critical not only for toxicological and public health reasons, but also because they can serve as valuable indicators of food quality and acceptability. Managing food quality, encompassing safety, nutrition, availability, convenience, integrity, and freshness, is a fundamental component of ensuring food safety [62, 63].

BAs have been widely used as quality indices in various food matrices, including meat, fish, and wines, indicating freshness and/or spoilage levels and helping to control food and beverage processing processes [62]. Traditional BA-based indices, such as the one developed by Mietz and Karmas, have been used to assess fish decomposition. This index is based on the correlation between increasing putrescine, cadaverine, and histamine levels and decreasing spermidine and spermine levels during storage. Scores below 1 indicate good quality, scores between 1 and 10 indicate tolerable quality, and scores above 10 indicate product decomposition [62, 64]. However, this traditional index has proven



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less effective for products such as cheese, meat, and meat products because it does not account for tyramine, the predominant BA in these foods. To address this issue, an alternative Biogenic Amine Index (BAI) has been proposed for meat, defined as the sum of the concentrations of putrescine, cadaverine, histamine, and tyramine. $BAI < 5$ mg/kg indicates good quality, fresh meat; 5-20 mg/kg indicates acceptable quality meat showing the first signs of spoilage; 20-50 mg/kg indicates poor quality meat; and >50 mg/kg indicates spoiled meat [62]. The effectiveness of BAs as a quality index is highly product-dependent, influenced by factors such as the nature of the product (e.g., fresh, canned, fermented). BA indices have demonstrated higher reliability in fresh and heat-treated meat products than in fermented products. This inconsistency is attributed mainly to the significant variability in BA concentrations in fermented foods. Numerous processing variables, such as ripening, fermentation, yeast cultures, and additives, influence this variability. Consequently, developing a universally reliable BA index to predict product quality is a complex task [62, 63]. A significant concern is that foods containing toxicologically unacceptable levels of some BAs (e.g., histamine or tyramine) may appear organoleptically "normal." For example, in products like tuna and salmon, histamine levels that pose a health risk may not be detectable by consumers' senses before consumption. This critical disconnect between sensory perception and chemical safety highlights the need for rigorous external oversight of these compounds [62]. Consequently, a comprehensive understanding of the aetiology and control mechanisms of foodborne illness is essential for effective prevention [62, 63].

5 Future Perspectives

5.1 Advances in Omics Approaches

The study of biological systems has been revolutionised by "Omics" technologies, defined as methodologies for the large-scale investigation and quantification of data representing the complete composition and function of a biological system at a specific molecular level. For decades, four core omics disciplines, genomics, transcriptomics, proteomics, and metabolomics, have significantly advanced biological research [65, 66]. Genomics permits the decoding of the entire genetic complement of probiotic microorganisms. This capability is essential for identifying key genes that confer tolerance to the harsh conditions of the gastrointestinal tract, thereby improving their survival within the host. Furthermore, comparative genomics allows for the analysis of evolutionary relationships among strains, their connection to the gut microbiome, and the detection of gene acquisition or loss via horizontal gene transfer [65, 67]. Transcriptomics is widely employed to investigate host-microbe interactions,



specifically focusing on elucidating how probiotics modulate the host's immune responses through changes in gene expression patterns [65, 68]. Proteomics provides comprehensive identification of critical proteins involved in the interactions between probiotics and their environment, including the intestinal tract and nutrient sources within food. A unique strength of proteomics is its ability to identify post-translational modifications (e.g., methylation, phosphorylation, or glycosylation), which can profoundly alter protein function and are frequently missed by other analytical techniques [65]. Metabolomics centers on the analysis of bioactive compounds secreted by probiotic organisms that are directly responsible for conferring health benefits to the host [65, 67]. The synergistic integration of these four major omics platforms, genomics, transcriptomics, proteomics, and metabolomics, forms the basis of Pro-biomics. This combined approach facilitates a holistic and comprehensive analysis of probiotic organisms, fundamentally deepening our understanding of their function, mechanism of action, and potential therapeutic applications [65].

5.2 Risk-Benefit Assessment of Probiotics in Functional Foods

Functional foods are traditionally understood as natural or modified food products that contain biologically active compounds (known or unknown) and that provide a clinically confirmed health benefit when consumed in defined, effective, and non-toxic amounts [69, 70]. This benefit is particularly relevant to the prevention, management, or treatment of chronic diseases [71]. Common characteristics that distinguish functional foods from standard dietary components are their consumption methods and biological effects. One of their characteristics is their dietary integration. They are incorporated into the regular diet but can also be offered in concentrated forms such as capsules or other nutritional supplements. Their key distinction lies in their capacity to beneficially influence one or more targeted physiological functions beyond the simple provision of essential nutrients [70]. This beneficial effect is likely to be associated with an improvement in overall health and well-being, or a documented reduction in disease risk. Functional foods represent a category of dietary interventions that essentially aim to manage health through targeted biological effects proactively [70, 72].

5.3 Research Gaps and Emerging Solutions

The assessment of food quality, freshness, and hygienic status fundamentally relies on accurately quantifying Biogenic Amines (BAs). Although conventional separation techniques such as High-Performance Liquid Chromatography (HPLC), Gas Chromatography (GC), and Capillary Zone



Electrophoresis (CZE) are routinely employed for BA detection, they present significant practical drawbacks [73]. These methods are inherently costly, requiring access to centralised laboratories and expertise from highly trained personnel. Current analytical challenges include the necessity of optimising derivatisation reagent levels and, critically, minimising analytical time. Complex food matrices often necessitate extended chromatographic separations to effectively resolve BAs from interfering amino acids [74].

The complex matrix of food materials remains a major impediment to accurate BA quantification. While techniques like sample cleanup, preconcentration, and the use of internal standards can mitigate the "matrix effect" and allow for ultra-trace detection, these preparatory steps contribute to the overall time consumption. Crucially, standard laboratory-based analytical methods cannot be performed outside the laboratory, resulting in a significant time lag between sample collection, analysis, and result reporting. This delay is a severe disadvantage, as it precludes timely intervention in cases of food spoilage where initial amino acid degradation may already be detectable. Consequently, there is an urgent demand for alternative methodologies that deliver rapid, reliable, cost-effective, and user-friendly devices suitable for on-site, in-field use [75].

To address these shortcomings, the development of an automated, green pre-concentration method for BAs is projected to establish a new gold standard for the food industry. Such a development would represent a significant achievement in creating an ideal "green" analytical methodology for BA detection within complex food systems. Future regulations, particularly concerning fermented products, will undoubtedly require rapid and robust analytical techniques to ensure compliance and public safety [73].

6 Conclusion

The incorporation of probiotics into functional foods has shown significant health benefits, particularly in improving gut health, modifying immunological responses, and adding to general well-being. However, the ability of several probiotic and fermentative microorganism to create biogenic amines (BAs) poses a significant food safety risk. Histamine, tyramine, putrescine, and cadaverine, among others, are not only necessary for physiological functions but, when present in high concentrations, can cause adverse effects ranging from headaches and gastrointestinal distress to hypertensive crises, allergic-like reactions, and carcinogenic outcomes. The complexity of BA production, which is influenced by strain variability, environmental parameters like pH, temperature, and salt, and raw material quality, demonstrates the multifactorial nature of this risk.



Mitigation solutions must be proactive and multidisciplinary. The selection of non-BA-producing probiotic bacteria, confirmed by genetic screening for decarboxylase genes, is critical. Complementary technological solutions, such as strict hygiene, process optimization, and the use of BA-degrading starting cultures, can further reduce risks. Advances in omics technologies provide potential methods for identifying, monitoring, and regulating BA-related pathways, allowing for more precise risk-benefit assessments of probiotic applications. Additionally, advances in rapid, on-site BA detection tools will be critical in maintaining product safety and facilitating regulatory supervision.

Consequently, while probiotics remain valuable in functional foods, their safe application necessitates balancing known benefits with the potential risks of BA accumulation. A comprehensive, science-driven approach (covering microbiological, technological, analytical, and regulatory perspectives) will be required to ensure that probiotic-based foods remain safe, effective, and health-enhancing dietary components.

Table 1. Common Probiotic Strains Associated with Biogenic Amine Production and Their Occurrence in Various Fermented Foods

Probiotic Genus/Species	Biogenic Amine(s) Produced	Fermented Food Source	Key Reference(s)
<i>Lactobacillus curvatus</i>	Tyramine, Histamine	Fermented Sausages, Cheese	Holck et al. 2017; Barbieri et al. 2019
<i>Lactobacillus buchneri</i> , <i>L. parabuchneri</i> , <i>L. helveticus</i>	Histamine	Cheeses (aged)	Diaz et al. 2018; Barbieri et al. 2019
<i>Lactobacillus brevis</i>	Histamine, Tyramine	Wine, Cider, Cheese, Beer	Barbieri et al. 2019
<i>Lactobacillus rossiae</i>	Putrescine	Sourdough	Xu et al. 2020; Barbieri et al. 2019
<i>Enterococcus faecium</i> , <i>E. faecalis</i> , <i>E. durans</i>	Tyramine (High Producers)	Cheese, Dry Sausages, Wine	Natrella et al. 2024; Barbieri et al. 2019
<i>Streptococcus thermophilus</i>	Tyramine, Histamine	Yogurt	Doeun et al. 2017
<i>Bifidobacterium spp.</i>	Cadaverine, Tyramine (Low amounts)	Fermented Milk Products	Lorencová et al. 2012
<i>Enterobacteriaceae spp.</i> (Spoilage)	Histamine, Tyramine, Putrescine, Cadaverine	Fermented Fish, Meat	Ding et al. 2024; Barbieri et al. 2019



Table 2. Types of Biogenic Amines, Their Precursor Amino Acids, and Associated Health Effects

Biogenic Amine	Precursor Amino Acid	Classification	Associated Health Effects (Exogenous Intake)	Reference(s)
Histamine	Histidine	Heterocyclic Monoamine	Vasoactive effects: Vasodilation, hypotension, headaches, flushing, allergic-like reactions ("scombroid poisoning").	(Durak-Dados et al. 2020; Sudo 2019)
Tyramine	Tyrosine	Aromatic Monoamine	Vasoconstrictive effects: Can trigger hypertensive crisis and migraines, especially in individuals on MAOIs ("cheese reaction").	(Kettner et al. 2020; Durak-Dados et al. 2020)
Putrescine	Ornithine, Agmatine	Aliphatic Diamine	Inhibits DAO, potentiating Histamine toxicity. Precursor for Spermidine/Spermine. Potential carcinogen with nitrites.	(Erdag et al. 2019; Nair et al. 2025)
Cadaverine	Lysine	Aliphatic Diamine	Inhibits DAO, potentiating Histamine toxicity. Indicator of food spoilage. Potential carcinogen with nitrites.	(Erdag et al. 2019; Shim et al. 2022)
Phenylethylamine	Phenylalanine	Aromatic Monoamine	Vasoconstrictive: Hypertension, cerebral hemorrhage. Linked to triggering migraines in susceptible individuals.	(Ding et al. 2024; Visciano et al. 2020)

Abbreviations: DAO: Diamine Oxidase, MAOIs: MAO Inhibitors

Table 3. Health Risks Associated with Biogenic Amines: Intolerance, Toxicity, and Regulatory Guidance

Risk Component	Description/Mechanism	Toxicological Thresholds & Guidance	Reference(s)
Intolerance Mechanism	Impaired degradation of BAs, often due to low activity of detoxifying enzymes DAO or MAO, caused by genetic factors, GI pathologies, or pharmacological inhibition.	Individual tolerance varies significantly, complicating risk assessment. The body's ability to detoxify is a critical factor.	(Kettner et al. 2020; Erdag et al. 2019)
Acute Toxicity Thresholds	The ingestion of more than 8 mg of Histamine is capable of causing acute intoxication. Tyramine-rich foods pose a severe risk to individuals on MAO inhibitor therapy.	Histamine in Fish (EU): Specified maximum levels exist for certain fish products (e.g., tuna) but no single global legal standard for BAs in all foods.	(Durak-Dados et al. 2020; EFSA 2011; Barbieri et al. 2019)



Chronic/Long-term Risks	Certain polyamines (Putrescine, Cadaverine, Spermidine) can react with nitrites to generate carcinogenic compounds. High concentrations of polyamines can also suppress cellular proliferation and induce apoptosis.	Quality Indices (BAI): Used as a proxy for safety/freshness. Meat: BAI (Good Quality); (Spoiled).	(Nair et al. 2025; Ruiz-Capillas and Herrero 2019)
Drug Interactions	MAOIs: Medications used for depression/anxiety. Consumption of Tyramine-rich foods can precipitate a life-threatening Hypertensive Crisis due to blocked MAO activity.	Alcohol: Impairs the body's ability to detoxify BAs, potentially exacerbating symptoms.	(Kettner et al. 2020; Barbieri et al. 2019)

Abbreviations: BA; Biogenic Amine, DAO: Diamine Oxidase, MAO: Monoamine Oxidase, MAOIs: MAO Inhibitors, GI: Gastrointestinal

Table 4. Strategies for Mitigating Biogenic Amine Formation in Probiotic Foods

Strategy Type	Approach/Technique	Mechanism of Action	Reference(s)
Genetic/Strain Control	Non-BA-Producing Strain Selection	Rigorous in vitro screening and genetic analysis (checking for genes) to create a detailed safety profile before application.	(Fentie et al. 2024; Barbieri et al. 2019)
Technological Control (Raw Material)	Strict Hygiene & Quality Control	Selecting high-quality, uncontaminated raw materials; this is the fundamental step to control amine-producing microbial strains (e.g., <i>Enterobacteriaceae</i>).	(Gardini et al. 2016; Özogul et al. 2018)
Technological Control (Fermentation)	Optimization of Process Parameters	Rapidly lowering pH below (inhibits decarboxylase growth/activity). Controlling temperature to avoid the optimal range for amine production.	(Visciano et al. 2020; Gardini et al. 2016)
Technological Control (Post-Processing)	Physical/Chemical Methods	MAP (suppresses histamine formers). Irradiation (Gamma rays reduce BAs in fish/soybean paste). Smoking (creates aseptic qualities, inhibiting bacteria). Oxidizing Agents (break down existing BAs).	(Doemun et al. 2017; Özogul et al. 2006)
Biological Control	Use of Specific Starter Cultures	Strategic use of strains that either lack decarboxylase activity or contain enzymes capable of oxidizing and breaking down existing BAs in the food matrix (BA-degrading strains).	(Gardini et al. 2016; Doemun et al. 2017)
Future/Analytical Focus	Omics & On-Site Detection	Integrating Genomics/Metabolomics for holistic BA monitoring. Developing rapid, cost-effective, on-site analytical devices to overcome the time lag of traditional lab methods (HPLC/GC).	(Verma et al. 2025; Ahmad et al. 2019)

Abbreviations: BA; Biogenic Amine, MAP: Modified Atmosphere Packaging, HPLC: High-Performance Liquid Chromatography, GC: Gas Chromatography

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