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BIOGENIC AMINES IN FOODS: SURVEYING EFFECTIVE FACTORS AND MEASURING METHODS

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ABSTRACT

Biogenic amines (BAs) importance in food safety and nutrition is generally recognized. Many efforts have been made to control or reduce them to legally permitted levels. The results varied according to raw material, ingredients, starter culture types, and process. So different methods have been developed for biogenic amines detection are varied from advanced device methods such as chromatographic based methods to electrophoretic based and simplified sensor methods. This article aims to review the effects of these variables and provides an assessment of the types of BAs measurement methods and the advantages and disadvantages in accordance with the latest published articles.

Keywords: Biogenic amines, Foods, Measuring methods

INTRODUCTION

Biogenic amines (BAs) are nitrogenous compounds found in a wide range of foods, including fish products, meat products, dairy products, wine, beer, vegetables, fruits, nuts, and chocolate (**Santos, 1996**). They are formed by decarboxylation of amino acids or by amination and transamination of aldehydes and ketones (**Costa *et al.*, 2018**). They have different biological roles in human cells, such as synaptic transmission, blood pressure control, allergic response, and cellular growth control (**Russo *et al.*, 2010**). Interest in detecting and tracing BAs arises from their potential toxicity to human health, so they are considered food quality indicators. Intestine amine oxidases could detoxify small amounts of these compounds. However, ingestion of high quantities could inhibit or even disrupt amine oxidases activity (**Doeun *et al.*, 2017**). Different symptoms are associated with extra ingestion of BAs, including "nausea, respiratory distress, hot flush, sweating, heart palpitations, headache, bright red rash, oral burning, and hyper or hypotension" (**Ten Brink *et al.*, 1990a**). Microorganisms could be part of the contaminated flora introduced during processing or storage or intentionally added into fermented foods or beverages (**Sarkadi, 2019**). Some gram-negative bacteria such as *Acromonas hydrophila*, *Escherichia coli*, *Klebsiella* spp., *Hafnia alvei*, *Pseudomonas* sp., *Proteus morganii*, *Serratia* spp., and *Vibrio alginolyticus* are from contaminated bacteria with the capability to produce decarboxylase enzyme. Intentionally added microorganisms, especially in fermented foods, also have the ability of BAs production. This group includes a starter and probiotic cultures from the genera of *Lactobacillus*, *Leuconostoc*, *Lactococcus*, *Enterococcus*, and *Streptococcus* (**Costa *et al.*, 2018**). Some naturally present polyamines in foods such as putrescine, cadaverine, agmatine, spermine, and spermidine could react with nitrites and produce carcinogenic nitrosamines. In addition to toxicological effects, consumption of foods containing high levels of BAs may increase food spoilage, putrid odors, and off-flavors and disrupts sensorial characteristics (**Geornaras *et al.*, 1995; Naila et al., 2010**)). Present review surveys various effective factors on BAs formation based on food type including cheese and dairy products, meat and products, fish, vegetables and fruits, and beverages of BAs in foods including chemistry and classification, occurrence in different types of foods also measuring and determination methods.

CHEMISTRY AND CLASSIFICATION

The chemical structure of BAs could be classified into aliphatic (e.g., putrescine, cadaverine), aromatic (e.g., tyramine, phenylethylamine), heterocyclic (e.g., histamine, tryptamine) and volatile (e.g., methylamine, pyrrolidone). Also, according to the number of amines, BAs can be classified into monoamines (e.g., phenylethylamine and tyramine), diamines (e.g., cadaverine and putrescine), and polyamines (e.g., spermidine and spermine). However, in several kinds of literature, diamines have been classified in the polyamines group (**Mohammed *et al.*, 2016**). The most common monoamines, including histamine, tyramine, tryptamine, and diamines (or polyamines), including putrescine and cadaverine, are produced from histidine, tyrosine tryptophan, ornithine, and lysine, respectively. Polyamines, including spermidine and spermine, are formed from putrescine (**Önal, 2007**). Fig. 1 shows the classification and chemical structure of some common biogenic amines found in food.

BIOGENIC AMINES PRESENCE IN FOODS

Three prerequisites have been considered for BAs production in foods: 1) availability of free amino acids, 2) decarboxylase-positive microorganisms, 3) favorite conditions for bacterial growth also, decarboxylase synthesis, and decarboxylase activity. Generally, every food containing proteins and is subjected to suitable conditions for bacterial growth and enzymatic activity is prone to BAs formation (**Ten Brink *et al.*, 1990a**). Some of the processes, such as ripening, salting, fermentation, or marination, could increase the possibility of BAs formation (**Visciano *et al.*, 2012**). BAs formation is in high level in the fermented foods (e.g., cheese 5- 4500 mg/ kg^1, wine 5- 130 mg/ dm^3, beer 2.8-13 mg/ dm3, sauerkraut 110- 300 mg/ kg^1) and also in foods kept in undesirable conditions (**Karovičová and Kohajdová, 2005**). Undesirable conditions for BAs accumulation vary among different food types. For example, accumulation in dairy products depends on milk treatment, type of starter culture and enzymes, the duration and ripening temperature, the pH, the NaCl content, the oxygen presence, relative humidity, water activity, bacteria population, and synergistic effect between microorganisms (**Linares *et al.*, 2012).** In the following, we have surveyed BAs production according to the type of food. Adverse conditions that encourage BAs accumulation are discussed in detail for each product. Factors affecting the formation of biogenic amines in food are shown in Fig. 2.

Cheese and dairy products

Cheese is one of the most sensitive dairy products to BAs formation, as mentioned; it is the second food implicated in histamine poisoning after fish (**Valsamaki *et al.*, 2000**). Raw milk, full cream, and semi-skimmed milk have low levels of BAs, mainly polyamines (about 1 mg/ dm^3 for raw milk). In contrast, in the final produced cheese, some of the BAs, including tyramine, histamine, putrescine,

cadaverine, b-phenylethylamine, and tryptamine, have been identified (**Karovičová and Kohajdová, 2005; Santos, 1996; Spano *et al.*, 2010**). Among dairy products, yogurt was the product with no BAs detection; however, in another study, it was shown yogurt contains 13 mg/ kg of histamine (**Dabadé *et al.*, 2020**). Different studies have shown variations in BAs concentration even in the same type of food. Several factors are implicated in BAs content level in dairy products, including dairy type, period of ripening, milk treatment type (e.g., pasteurization, homogenization), pH, and NaCl concentration (**Gardini *et al.*, 2001; Ordonez *et al.*, 1997**). On the other hand, dairy production is not a sterile process, and nonstarter culture microorganisms have the opportunity to enter the product at any stage or even be indigenous to raw material (**Linares *et al.*, 2012).**

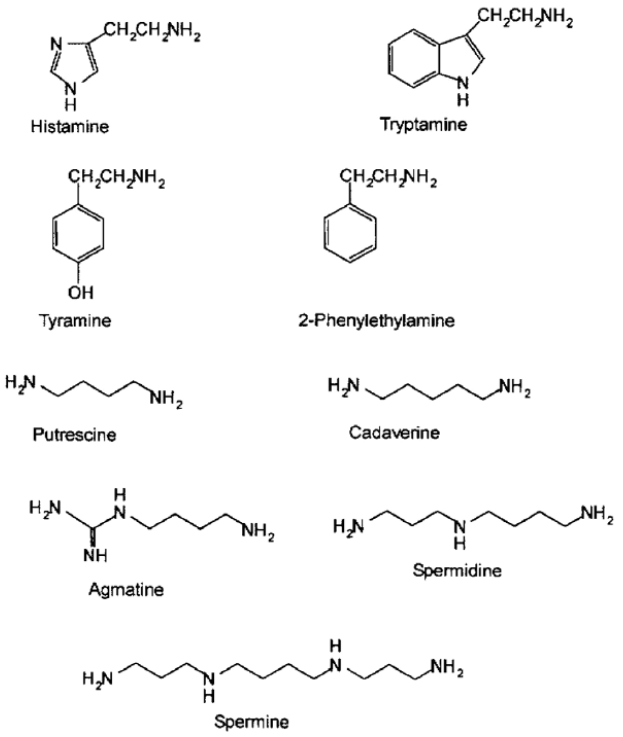

Figure 1 Chemical structure of biogenic amines (**Önal, 2007**)

The first histamine poisoning after cheese consumption was reported in Netherland in 1967 (**Taylor and World Health Organization, 1985**). Swiss cheese was involved in all of the outbreaks reported in the United States, with a level higher than 100 mg histamine/ 100 gr cheese **(Stratton *et al.*, 1991**). Some cheese-associated bacteria, including *Lactobacillus*, *Lactococcus*, *Streptococcus*, *Leuconostoc*, and *Enterococcus* are involved in BAs accumulation during cheese production (**Tittarelli *et al.*, 2019**). A study shows that microorganisms' growth and decarboxylase activity were determinative in BAs accumulation in cheese (**Gardini *et al.*, (2001**). Tyrosine and histamine decarboxylase activity was reported in some Gram-positive lactic acid bacteria (**Linares *et al.*, 2012**). An increase in decarboxylase gene expression is reported in the presence of amino acid precursors and low pH. Also, variation in tyrosine decarboxylase gene expression was observed between different species of the same strain (**Tittarelli *et al.*, 2019**). However, another study showed low pH, and high salt concentration inhibited BAs formation in Feta cheese. BAs concentration increased during ripening and reached 617 mg/ kg in matured cheese (**Valsamaki *et al.*, 2000**). Also, different sections of the same cheese may have different BAs content due to some reasons, including the difference in aw content, the difference in favorable growth conditions for aerobic or anaerobic bacteria, and the availability of O_2 requirements (**Komprda *et al.*, 2007**).

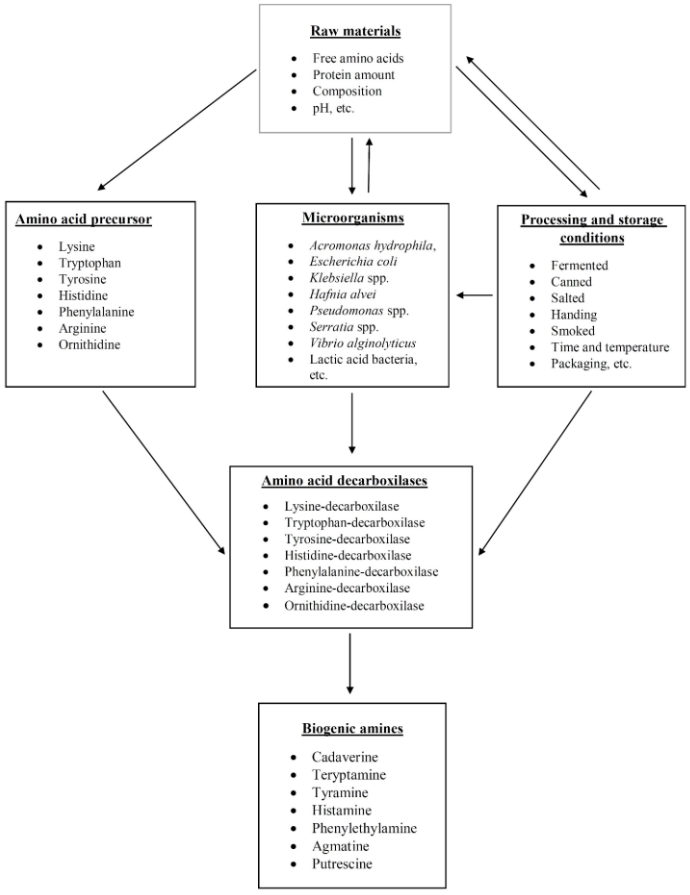

Figure 2 Factors affecting the formation of biogenic amines in food

Pasteurization destroys decarboxylase positive microorganisms and cofactors responsible for decarboxylation reaction activity, reducing BAs concentration in cheese **(Schirone *et al.*, 2013**). A reduction in tyramine concentration was observed in the investigation of high-pressure treatment on BAs production in blue-veined cheeses. In contrast, tryptamine, phenylethylamine, and putrescine concentration were higher in treated samples (**Calzada *et al.*, 2013**). Another study investigated the effect of milk type, mild thermal treatment, and high-pressure homogenization (HPH) on BAs concentration of produced cheese. Results showed that cheese obtained from ovine milk has higher BAs concentration than bovine milk cheese, independent of treatment type. HPH treatment reduced BAs content in both of the cheeses. Still, adversely thermalized samples showed higher BAs concentration than control samples, which is attributed to selecting the microbial population owning decarboxylation activity by applying mild heat treatment (**Lanciotti *et al.*, 2007**). The effect of raw or pasteurized milk, thermophilic or mesophilic starter, and also unheated or heated curd treatment was investigated on BAs formation in semi-hard Italian cheese. Results showed the lowest BAs concentration was obtained in the experimental group of pasteurized milk (due to the deadly effect on decarboxylating bacteria and mesophilic starter) and heated curd (**Gennaro *et al.*, 2003**).

The type of packaging material (nonvacuum and vacuum) on BAs concentration was investigated during Kashar cheese ripening. The storage period had a significant effect on BAs accumulation in both packagings. Obtained data didn't support the efficacy of vacuum packaging in reducing BAs (**Andiç *et al.*, 2011**). However, the capability of *lactobacillus casei* strains in reducing tyrosine and histamine accumulation in cheese was observed due to the inhibition of BAs producing strains, especially enterococci (**Herrero-Fresno *et al.*, 2012**). On the other hand, some of the starter cultures (e.g., *lactococcus lactis* subsp. *cremoris*) used in cheese production showed capability in BAs accumulation (**Flasarová *et al.*, 2016**). Tyramine, putrescine, and cadaverine were among the most reported BAs in cheese produced from ewe's milk (**Buňková *et al.*, 2013**). Table 1 summarizes the type of BAs found in different kinds of cheese along with milk type and other effective factors in BAs concentration

Table 1 Summary of some of the BAs found in different cheese types.

Cheese type	Predominant BAs	Concentration	Raw milk	Treatment	Microorganism	Ripening conditions	Reference
Traditionally smoked cheese	Putrescine Cadaverine Histamine Tyramine Spermidine	3.51- 19.07 mg/kg (Sum of the BAs)	Bovine, caprine or ovine milk	Raw or pasteurized	NP†	NP †	(Pluta-Kubica et al., 2020)
Model Dutch-type	Tyramine	328 mg/kg (Sum of the BAs and highest concentration between groups)	NP	NP	Non-starter strains of *Lactobacillus curvatus* and *Lactobacillus paracasei*	90 days at 10 ± 1 °C	(Pachlová et al., 2018)
Commercial cheeses	Histamine Tyramine Putrescine Cadaverine	150-313 mg/100g	NP	NP	NP	NP	(Mayer and Fiechter, 2018)
Traditional goat cheese	Tyramine Histamine	26.4- 175.1 mg/kg	Goat milk	Pasteurization	Mesophilic mixed starter culture	NP	(Poveda et al., 2016)
Blue-veined cheese	Tryptamine Phenylethylamine Putrescine	4.11- 120 mg/kg	Ovine milk	Pasteurization Homogenization	*Penicillium roqueforti*	90 days ripening followed by 270 day refrigerated storage	(Calzada et al., 2013)
Kashar cheese	Putrescine Tryptamine	174.26 mg/ kg	Cow milk	Non-vacuum and vacuum packaging	*Lactococcus lactis* ssp. *lactis* and *Lactococcus lactis* ssp. *cremoris*	180 days storage at 4˚C	(Andiç et al., 2011)
Ewe's cheese	Phenylethylamine Spermine Tryptamine	115.70- 819.12 mg/kg	Ewe milk	Pasteurization	*Lactococcus lactis* ssp. *lactis* and *Lactococcus lactis* ssp. *cremoris*	210 days ripening at 10 ˚C	(Renes et al., 2014)
Pecorino cheese	Histamine Tyramine	5861 mg/kg	Cow or sheep or a mix of cow and sheep	Raw or pasteurized	Autochthonous microbiota	Max ripening time was 10 months in the range of 10-16 ˚C	(Schirone et al., 2013)
Uncooked pressed model cheese	Cadaverine Putrescine	2.18 mmol/ l	Pasteurized milk inoculated with Gram-negative bacteria	Pasteurized milk	*Streptococcus salivarius* ssp. *thermophilus*	28 days ripening at 9 ˚C	(Delbès-Paus et al., 2012)
Cabrales-like mini-cheese model	Tyramine Histamine (Between checked BAs)	5.1 mM Histamine in the absence of BA-degrading strains of *Lactobacillus casei*	NP	Pasteurized milk	BA-producing strain (*E. durans* or *L. parabuchneri*) in combination with BA-degrading strains of *Lactobacillus casei* strains	120 days ripening at 15 ˚C	(Herrero-Fresno et al., 2012)
Dutch-type cheese	Tyramine Putrescine	1517.8 mg/l	Cow milk	Pasteurized milk	Strains of *Lactococcus lactis* subsp. *cremoris*	90 days ripening period at 10 ˚C	(Flasarová et al., 2016)
Pecorino and Caciotta cheeses	Cadaverine Tyramine	350 mg/kg (Tyramine concentration in cheese from thermized milk)	Bovine and ovine milk	Thermization and homogenization	Thermophilic lactic acid bacteria and milk starter culture	27 days and 21 days ripening at 16 ˚C for Caciotta and Pecorino cheeses, respectively	(Lanciotti et al., 2007)
Pecorino di Farindola cheese	Tyramine	209.- 2393.0 mg/kg (Sum of the BAs)	Ewe milk	Preheated milk at 37°C	NP	90 days ripening at 14-15°C	(Schirone et al., 2011)
Cheeses from small scale farms and fermented dairy products	Tyramine Putrescine Cadaverine (in cheeses produced from pasteurized ewe's milk)	37.2- 529.8 mg/kg (Total BAs in brined cheese)	Different types of ewe, goat, and cow cheese	Raw or pasteurized cheese	NP	NP	(Buňková et al., 2013)
Semi-hard Italian cheese (Toma)	Cadaverine Putrescine	1076 mg/kg (Total BAs in cheese produced by raw, heated curd, and thermophilic starter culture)	Bovine milk	Raw or pasteurized milk	Thermophilic or mesophilic starter cultures	30 days ripening at 10°C	(Gennaro et al., 2003)
Dutch-type hard cheese	Tyramine	419 mg/kg (Total BAs in cheese containing 45% fat ripened during 22 weeks)	NP	Pasteurized milk	Different commercial starter culture	180 days ripening	(Komprda et al., 2007)
Pecorino Abruzzese cheese	Tyramine	697 and 1086 mg/kg (Total BAs in raw milk without starter culture and pasteurized milk with starter culture, respectively)	Sheep milk	Raw or pasteurized milk	*Streptococcus thermophilus*, *Lactobacillus casei* and *Lb. delbruekii* subsp. *bulgaricus*	60 days ripening at 12- 13 °C	(Martuscelli et al., 2005)

Goat cheese	Putrescine Tryptamine Tyramine	94.59 mg/kg (Tyramine concentration)	Goat milk	Pasteurized milk	*Lactococcus lactis* subsp. *lactis* *Lactococcus lactis* subsp. *cremoris* *Lactococcus lactis* subsp. *lactis*	60 days ripening at 14 °C	(Novella-Rodríguez et al., 2002)
Azeitao cheese	Tyramine Histamine	1393 mg/kg (Total BAs)	NP	NP	NP	30 days ripening	(Pinho et al., 2001)
Manchego cheese	Cadaverine Putrescine	1881.7 mg/kg (Total BAs in ram milk cheese after 240 days ripening period)	Ewe milk	Raw or pasteurized milk	Autochthonous strains in the combination with *Lactobacillus paracasei* subsp. *paracasei*	240 days ripening at 12 °C	(Poveda et al., 2015)
Twenty Apulian and Sicilian cheese	Cadaverine Histamine Putrescine Tyramine	137.1 mg/kg (Median value)	Ewe, goat, or cow milk	Raw or pasteurized, or thermized milk	None or natural whey starter or thermophilic and mesophilic starter	2- 270 days	(Guarcello et al., 2015)
Blue cheese	Tyramine	2310.2 (Sum of BAs in non gamma irradiated cheese at 90 days)	NP	Raw milk	NP	90 days ripening at 5˚C	(Rabie et al., 2011a)

†No information was provided **Meat and meat products**

Raw meat is the natural source of free amino acids and, in the presence of decarboxylase positive microorganisms, could also be considered a natural source of BAs (**Ruiz-Capillas and Jiménez-Colmenero, 2005**). Spermine and spermidine are the only amines found in raw meat (**Stadnik and Dolatowski, 2010**). Polyamines enhance toxicity by inhibiting tyramine detoxifying enzymes rather than direct toxicity (**Algahtani *et al*., 2020**). Meat processing and storage conditions could influence the accumulation of BAs in meat and meat products. Type of processing (cooking, fermentation, boiling, and curing) has a considerable effect on BAs concentration. Fermented meat products tend to develop high amounts of BAs; however, sometimes, significant amounts have been found in fresh and cooked meat products (**Ruiz-Capillas and Jiménez-Colmenero, 2005**). Meat type affects the formation and accumulation of BAs. It was observed main differences between BAs types in various pork, beef, and poultry meat during storage (**Jastrzębska, 2012**). Adrenaline, spermidine, and spermin were reported as the highest value in fresh pork meat, whereas putrescine was highest in chicken breast (**Costa *et al*., 2018**). It seems white meat is more sensitive to BA formation than red meat due to shorter muscular fibres in white meat, such as chicken, that facilitate the activity of proteolytic enzymes and promotion of BAs precursors (**Vinci and Antonelli, 2002**).

Fish and meat quality have been measured by an indicator referred to as the biogenic amine index (BAI). This index has been proposed based on increases in putrescine, cadaverine, and histamine and decreases in spermine and spermidine during fish or meat storage.

BAI = (histamine + putrescine + cadaverine)/ (1 + spermidine + spermine)

BAI values below 1 are considered the best quality, whereas values above 10 reflect microbial spoilage conditions (**Sarkadi, 2019**). Another BAI value was proposed as the sum of cadaverine, putrescine, tyramine, and histamine, so that BAI< 5 mg/kg indicates fresh meat, between 5 and 20 mg/kg acceptable meat but with initial spoilage indication, and finally, BAI>50 mg/kg spoiled meat (**Jastrzębska, 2012**).

Different experiments are conducted to correlate BAs type with microbial population. In ground beef, putrescine was a good indicator of microbial growth, which between different examined models (linear, quadratic, and geometric), the quadratic model presented the best fit equation with the highest determination coefficient. So that 20 mg of putrescine/ kg of ground beef was equal to 10^5 total aerobic count/ gram of ground beef. Also, a high correlation was found between *Enterobacteriaceae* spp. counts. Cadaverine and putrescine are proposed as valuable indicators of direct count (**Halász *et al*., 1994**). Several studies investigated and found significant high correlation coefficients between BAs levels and different bacterial groups, including *Pseudomonadaceae*, *Enterobacteriaceae*, and *Lactobacilaceae* counts (**Fraqueza *et al*., 2012; Lázaro *et al*., 2015**). Decarboxylase-positive microorganisms in meat depend on conditions during rearing, slaughtering, and processing (**Lázaro *et al*., 2015**). It seems bacterial load could not always be employed as an indicator of BAs. Despite UV-C irradiation on the inactivation of the bacterial population, BAs content increased as a consequence of UV irradiation (**Lázaro *et al*., 2014**).

On the other hand, gamma irradiation degraded some BAs such as tyramine, putrescine, and spermine and enhanced the formation of spermidine, phenylethylamine, cadaverine, and tryptamine (**Wei *et al*., 2009**). Gamma irradiation showed superior activity in controlling *Bacillus cereus*, *Enterobacter cloacae*, and *Alcaligenes faecalis* than organic acids, but its activity in reducing BAs was such as organic acids (**Min *et al*., 2007**).

Meat packaging affects on type of microorganisms and also BAs accumulation. So that under air packaging, *Pseudomonas* and *Enterobacteriaceae* are dominant, while lactic acid bacteria are the main microflora under vacuum packaging. Cadaverine level was correlated with *Enterobacteriaceae* count while the psychrotrophic bacteria, *Pseudomonas* spp. and *Bacillus thermosphacta* were primarily associated with tyramine and, to a lesser extent, putrescine, cadaverine, and histamine contents (**Galgano *et al*., 2009**). In another study, the synergistic effect of complex starter culture containing *Staphylococcus xylosus* and *Lactobacillus plantarum* with vacuum packaging was observed in the inhibition of BAs accumulation in dry sausages (**Sun *et al*., 2019**).

pH has a significant effect on BAs accumulation in fermented sausage products. As pH decreases during fermentation by lactic acid bacteria, delaying the activity of decarboxylase positive bacteria and reducing total BAs content were observed (**Lorenzo *et al*., 2017**).

Type of meat affects BAs concentration in produced fermented sausages. Turkey sausages have the highest levels of total BAs (730 mg/kg) compared with beef and horse sausages (500 and 130 mg/kg, respectively). So, taking necessary precautions were advised during the consumption of turkey sausages (**Rabie *et al*., 2014**).

In addition, fermented meat products may have several different levels of BAs according to the microbial composition of the original meat and the type of starter culture. Also, the time and temperature of ripening and availability of free amino acids play critical roles in this phenomenon (**Ten Brink *et al*., 1990b**). The ability of gamma-aminobutyric acid-producing starter culture on BAs reduction was established during pork sausage fermentation with the highest reduction for β-phenylethylamine and lowest reduction for spermidine (**Kantachote *et al*., 2016**). Reduction of the bacterial population, improvement of sensory quality and physicochemical properties, and also reducing BAs content as a result of spice addition during sausage fermentation was reported in different studies (**Jia *et al*., 2020; Komprda *et al*., 2009; Sun *et al*., 2018**). BAs formation in sausages could be minimized by precise selection of spice mixes, starter cultures with negative decarboxylase activity and also up to possible thinner sausages (**Komprda *et al*., 2009**). Partial replacement of sodium nitrite with a probiotic starter culture reduced BAs threat by reducing tyramine content (**Zhu *et al*., 2020**). Also, the salt percentage in sausage formulation is effective on BAs concentration. The total content of BAs was variable between 345.40 to 796.68 mg/kg in low salt sausages, while it was between 88.86 and 332.13 mg/kg in regular sausages with 6% salt (**Laranjo *et al*., 2017**). Table 2 summarizes some treatments and their effects on BAs content in meat and fish products.

Fish and fish products

Several BAs have been found in fish. Among them, histamine, cadaverine, and putrescine are attracting lots of attention regarding fish safety and quality (**Ten Brink *et al*., 1990b**). Fish tissue is a good resource of free histidine, so histamine is the main BA found in fish and its products. This biogenic amine is responsible for scombroid or histamine poisoning. High histamine contents (higher than 500 ppm) are ingested due to fish consumption from *Scombridae* and *Scomberesocidae* families such as tuna, mackerel, bonito, and bluefish (**Ruiz-Capillas and Herrero, 2019**). This poisoning is not limited to these families, and non-scombroid fish such as sardine, pilchards, and anchovies have also been implicated in scombroid poisoning (**Hwang *et al*., 1995**). Microorganisms that live in the gut and fish gills are the main factors in histamine production that can grow and increase after fish death. High abused temperature (21.1 ˚C or higher) makes bacteria grow better than moderate abused temperatures. Refrigeration could be used as a histamine inhibition factor; however, after the histidine decarboxylase enzyme is formed, histamine production will be continued even at refrigerated temperatures. Cooking temperatures also cannot degrade formed histamine (**Visciano *et al*., 2012**). Generally, BAs contents in fishery products could be reached toxicity levels according to the freshness of raw material, storage, and processing conditions, especially time and temperature. In comparing BAs formation at 4 and 25˚C, histamine contents increased significantly up to 36.6-2123 mg/kg at 25˚C during 24 hours, while in the samples kept at 4˚C, contents increased slowly after 2-3 days (**Kim *et al*., 2009**). Various microorganisms such as *Morganella morganii*, *Klebsiella pneumoniae*, and *Hafnia alvei* are implicated in scombroid poisoning (**Koral *et al*., 2013**).

Single histamine at low concentrations doesn't cause poisoning, but toxicity could occur when other BAs are present at concentrations 5 times higher than histamine

(**Naila *et al*., 2010**). When focusing on one BA toxicity in a food, it is advised not to focus on its single toxicity, and other factors such as the amount of consumed food, other BAs concentration, and BAs content in other consumed foods should be considered. Simultaneous consumption of foods rich in BAs, such as wine, cheese, and sausage, could be threatening. Also, the consumption of medicine and alcohol should be considered (**Ten Brink *et al*., 1990b**). According to FDA maximum allowed level of histamine in fish is 50 mg/kg. Also, the tolerance level of Tyramine and total BAs in fish is recommended at 100 and 1000 mg/kg, respectively (**FDA, 1996**).

The effectiveness of several treatments has been examined on BAs production in fish and its products. For example, the application of lactic acid and *Carum compticum* essential oil on common carp significantly decreased histamine, cadaverine, and putrescine during storage at 4 ˚C; however, a significant higher reduction level was observed for lactic acid (**Noori *et al*., 2018**). The effectiveness of vacuum or non-vacuum packaging depends on storage temperature. Application of vacuum packaging decreased BAs content at 3 ˚C. However, its effect at 15 ˚C was negligible (**Křížek *et al*., 2004**). Low dose irradiation of vacuum-packed trout flesh reduced histamine, putrescine, and tyramine in dose-dependent manner. However, spermine and spermidine polyamines did not show significant changes with dose and time (**Křížek *et al*., 2012**). Four preservation methods, including pasteurization, salting, smoking, and treating with lactic acid bacteria, were evaluated for BAs formation and sensory properties of Carp roe (*Cyprinus carpio*). Results showed all four treatments fixed histamine and tyramine contents to less than 5 and 25 mg/ kg, respectively, during 55 days of storage at 2 ˚C. Pasteurization and smoking treatment yielded the lowest histamine, tyramine, putrescine, and cadaverine values, with the highest sensory scores at the end of 55 days (**Křížek *et al*., 2011**).

Salting is one of the methods used for fish preservation. This preservation mechanism includes aw reduction, inhibition of bacterial growth, and toxin formation. Various studies showed that this method alone could not inhibit BAs formation, and other preservation techniques such as refrigerated conditions should be applied. However, some psychrotrophic bacteria produce histamine at high levels, even at 2 ˚C (**Emborg *et al*., 2005; Koral *et al*., 2013**). Salted fish and fish sauces are fermented fish products typically prepared by indigenous microflora without adding starter culture (**Lee *et al*., 2016; Zaman *et al*., 2011**). Histamine or other BAs such as cadaverine, putrescine, and tyramine contents in brined fish could increase to a threatening toxicity level if the salt concentration were 25% or lower (**Koral *et al*., 2013**). The effectiveness of starter culture in reducing overall amines was established. However, this reduction was higher in the buffer system due to the complexity of the fish sauce than the buffer system and the competition of starter culture with indigenous bacterial flora (**Zaman *et al*., 2011**). In this way, various studies have shown the capability of starter culture bacteria such as *Bacillus polymyxa*, *Staphylococcus carnosus*, *Bacillus amyloliquefaciens* in BAs degradation (**Lee et al., 2016; Zaman *et al*., 2011**). The ability of a different variety of spices, including garlic, green onion, red pepper, clove, and cinnamon, on BAs reduction in salted and fermented anchovy products was examined. Garlic showed the highest inhibitory variation from 11.2 to 30.9% for putrescine and tyramine. The effect of other spices was less or negligible (**Mah *et al*., 2009**). Table 2 summarizes some treatments and their effects on BAs content in meat and fish products.

Table 2 Effect of different treatments on BAs content of fish and meat products

Product	Treatment	Consequence effect	Reference
Bighead carp (*Aristichthys nobilis*)	Different freezing treatments at -40◦C and -18◦C	Reduction of spermine and spermidine BAs	(Hong et al., 2013)
Wild white grouper (*Epinephelus aeneus*)	Keeping in ice and chill temperature (4 ◦C)	The gradual increase during storage days in both of the treatments	(Özogul et al., 2008)
Fermented Sardine	Cell-free extracts prepared using *Lactobacillus plantarum* or *Pediococcus acidolactici* alone or in combination with thyme and laurel extracts	The highest reduction in TMA formation by *Pd. acidolactici* in combination with thyme extract	(Kuley et al., 2018)
Vacuum packed fillets of carp (*Cyprinus carpio*)	Thyme and oregano essential oil or UV-C irradiation	Oregano oil was effective in the reduction of BAs. UV-C irradiation showed lower efficiency.	(Křížek et al., 2018)
Sardines (*Sardina pilchardus*)	Different packaging types (air, modified atmosphere pack, and vacuum pack)	BAs formation increased with increasing storage time. The highest contents were seen in samples stored in the air.	(Özogul and Özogul, 2006)
Silver carp sausage	Amine-negative *Lactobacillus plantarum* for fermentation	Reduction of putrescine and cadaverine contents by more than 70%. Tyramine contents didn't change.	(Zhang et al., 2013)
Trout fillets	Different treatments of lactic acid bacteria and brine solutions	Highest BAs were seen in treated samples with lactic acid bacteria and food-borne pathogens. Adding brine solutions partly inhibited BAs formation.	(Kuley et al., 2011)
Pike (*Esox lucius*)	Effect of vacuum packaging followed by 300 and 500 Mpa pressure and storing at 3.5 and 12 ◦C	Putrescine contents showed a good correlation with applied pressure. Cadaverine and tyramine contents increased with increasing temperature	(Křížek et al., 2014)
Rain-bow trout (*Oncorhynchus mykiss*)	Effect of vacuum packaging followed by 300 and 500 Mpa pressure and storing at 3.5 and 12 ◦C	Putrescine, cadaverine, and tyramine contents showed a good correlation with applied pressure. There were no detection levels of tryptamine, phenylethylamine, and histamine in pressure-treated samples stored at 3.5 ◦C.	(Matějková et al., 2013)
Mullet (*Mugil Cephalus*) and tuna (*Thunnus thynnus*)	180 days storage at 4 ◦C	BAs concentration increased with increasing storage days. Tyramine and histamine were the highest and lowest detected BAs.	(Restuccia et al., 2015a)
Bighead carp (*Aristichthys nobilis*)	Effect of *Shewanella putrefaciens*, *Aeromonas sobria*, *Acinetobacter bohemicus,* and *Pseudomonas helmanticensis* were investigated.	Putrscine was produced by *A. sobria*, *P. helmanticensis*, and *S. putrefaciens*- Cadaverine was produced by *S. putrefaciens*	(Liu et al., 2018b)
Red drum (*Sciaenops ocellatus*) fillet	Treatment with clove, cumin, and spearmint essential oils	Reducing histamine, putrescine and cadaverine	(Cai et al., 2015)
Black carp (*Mylopharyngodon piceus*) fillets	low salt and sugar dry-curing	Treatments containing 1.5% salt (T1) and 5% salt + 1.2% sugar (T2) showed lower putrescine and cadaverine values.	(Fan et al., 2014)
Tuna (*Thunnus albacares*)	Vacuum-packaging or modified atmosphere packaging on BAs formation by psychrotolerant bacteria at 2 ◦C and 10 ◦C	The strong effect of modified atmosphere packaging with 40% CO2/60% O2 on histamine formation by psychrotolerant bacteria was seen.	(Emborg et al., 2005)
Beef cuts	Vacuum packed beef kept under chilled conditions	Increasing histamine and spermidine and decreasing spermine contents were observed during 60 days of storage	(Marquezini et al., 2016)

Smoked turkey breast fillets	Effect of air, vacuum, skin, and two modified atmosphere packaging at 4◦C	Highest and lowest histamine, tyramine, and tryptamine values for air packed and skin packed samples, respectively	(Ntzimani et al., 2008)
Dry-cured pork loins	Inoculation with *Lactobacillus casei* (Probiotic strain)	Increase in cadaverine, putrescine, and tryptamine levels and decrease in spermine levels with storage time	(Stadnik and Dolatowski, 2012)
Fermented sausages	Two concentrations of sodium sulfite	Sausages containing sulfite had higher tyramine contents than the control group. Sulfite inhibited cadaverine production.	(Bover-Cid et al., 2001c)
Fermented sausages	Sugar addition effect	Tyramine, putrescine, and cadaverine were higher in sausages without sugar addition. Obtained results were variable between trials. Sugar elimination was not advised.	(Bover-Cid et al., 2001a)
Fermented sausages	Effect of *Lactobacillus curvatus* and *Staphylococcus xylosus* starter cultures	Lower putrescine, tyramine, and cadaverine were seen in sausages containing starter culture. Refrigeration was advised for inhibition of BAs accumulation.	(Bover-Cid et al., 2001b)
Dry fermented sausages	Effect of starter culture and storage temperature	The effect of 8 or 22 ◦C wasn't significant on BAs formation. Starter culture types didn't show any significant impact on total BAs at the end of ripening, but their impact was significant at the end of either refrigerated storage or room temperature.	(Komprda et al., 2001)
Dry-cured foal sausage	Commercial starter cultures	Sausages with inoculated *Pediococcus pentosaceus* and *Staphylococcus xylosus* combination showed the highest BAs levels	(Dominguez et al., 2016)
Egyptian fermented sausages	Gamma irradiation	Irradiation reduced total BAs content. Cadaverine was the principle BA in non-irradiated samples. However, tyramine overcame in irradiated samples.	(Rabie et al., 2011a)
Pepperoni sausage	Gamma irradiation and packaging air, vacuum, and CO2/N2 (25%/75%)	Putrescine, spermidine, spermine, and tyramine were reduced under irradiation. Irradiation was effective in reducing. The highest b-Phenylethylamine levels were observed in CO2/N2 packaging.	(Kim et al., 2005)
Sucuk	Starter cultures and nitrite levels	Starter culture produced sausages contained lower levels of putrescine, cadaverine, and tyramine. Except for spermine and spermidine, nitrite usage decreased putrescine, cadaverine and tyramine contents.	(Gençcelep et al., 2007)

Vegetables and Fruits

Putrescine from diamine and spermine and spermidine from polyamines are BAs involved in several physiological processes in plants, such as cell division, flowering, fruit development, response to stress, and senescence (**Karovičová and Kohajdová, 2005**). Other BAs can reach dangerous limits upon particular conditions, such as accumulating BAs in *Acacia berlandieri* because of their defensive role against insects and herbivores (**Moret *et al*., 2005**). Generally, the main differences between BAs have been found in animal and plant origins. Foods with plant origins have higher putrescine, spermine, and spermidine content, while the presence of histamine is negligible. Fresh products of plant origin have been considered safe with regard to BAs concentration. However, microbial fermentation could lead to BAs accumulation (**Sarkadi, 2019**). So fermented vegetable products like sauerkraut could accumulate higher BAs than fresh vegetables (**Moret *et al*., 2005**). Low levels of BAs in fruits and vegetables are considered endogenous to food, but in some vegetables, such as spinach, tomato, and eggplant, BAs, especially histamine, could be accumulated under microbial enzymatic activity during storage (**Comas-Basté *et al*., 2019**). It was advised that people with lower detoxification activity, such as patients who are consuming psychoactive drugs, should be taken necessary precautions during the consumption of BAs-rich foods, like peas, spinach, and tomato (**Kalač *et al*., 2002**).

Mushrooms could be threatening during storage at 25◦C due to the accumulation of BAs (**Kalač and Křížek, 1997**). Some treatments have been applied for BAs reduction in fresh or fermented fruits or vegetables. Sauerkraut could be prepared by indigenous micro flora or inoculation of particular starter cultures. Efficacy of *Lactobacillus casei* and *Lactobacillus curvatus* in BAs reduction during sauerkraut fermentation have been confirmed (**Rabie *et al*., 2011b**). The ability of *Lactobacillus plantarum* isolates for BAs formation was demonstrated in naturally fermented pickles. Results showed putrescine, cadaverine, and histamine were produced by all isolates, and 9% of isolates produced more than 1000 mg/L of total BAs (**Alan *et al*., 2018**). *Leuconostoc mesenteroides* produced lower BAs than *Lactobacillus plantarum* in both NaCl concentrations (0.5 and 1.5%). However, lower NaCl concentration caused lower BAs production in the presence of *L. plantarum* or *L. mesenteroides* as starter cultures (**Peñas *et al*., 2010**). In another study, *L. plantarum* significantly suppressed tyramine, putrescine, and cadaverine formation (**Kalač *et al*., 2000**). So, the effect of a particular bacterial strain as a starter culture on BAs formation depends on several factors such as vegetable type, ripening temperature and duration, additives type and level, and indigenous microflora. Based on these factors formation of one or more of the BAs may be increased or inhibited. So the higher efficacy of onion or caraway additives in BAs reduction was seen at 18 ◦C than 31 ◦C during sauerkraut fermentation (**Majcherczyk and Surówka, 2019**).

Furthermore, different fermented products such as Miso, soy sauce, Mejo, and Tofu are produced from soybeans (**Prester, 2016; Shukla *et al*., 2018**). It was shown that two bacterial strains of *Pediococcus acidilactici* and *Staphylococcus carnosus* could degrade all kinds of BAs and high levels of histamine and tyramine during soy paste fermentation, respectively, in addition to producing more desirable flavor products (**Zhao *et al*., 2020**). The inhibitory effect of garlic, clove, lotus leaves, and ginkgo leaves on BAs formation was studied during Mejo fermentation. Results showed adding plant extracts kept BAs levels within the safety limit proposed by regulatory authorities (**Shukla *et al*., 2018**).

Furthermore, variation in BAs levels between different wheat cultivars could be seen. Despite storage conditions and seasonal variations, wheat cultivars undergo other flour preparation separations (according to wheat parts, including starch, germ, and bran), so BAs can be concentrated in products according to applied conditions. Bran milling fraction showed the highest agmatine and spermidine levels among different cultivars; after that, whole and white wheat flour and semolina showed the highest BAs contents (**Karayigit *et al*., 2020**).

Beverages

Beer and wine are among the most popular fermented beverages that could be rich in BAs concentration. Exceeding BAs concentration from an upper limit could restrict wine export or import. Histamine content limits are varied between European countries, from 2 to 10 mg/L for Germany and Switzerland, respectively (**Russo *et al*., 2010**). In alcoholic beverages, toxicological effects could happen in the ranges of 8 to 20 mg/L for histamine, 25 to 40 mg/L for tyramine, and at 3 mg/L for phenylethylamine, because of synergistic effects that could happen between BAs and alcohol (**Silva *et al*., 2020; Stojanović and Kos, 2020**).

Three origins have been reported for BAs occurrence in wines. They can be present in the must, can be formed by yeasts during malolactic fermentation, or result from the action of bacteria involved in malolactic fermentation (**Karovičová and Kohajdová, 2005**). Generally, red wines, because of different fermentation processes, contain higher histamine concentrations than white wines. This phenomenon is related to the original material used for their production. Whole

grape with contaminant microorganisms is used for red wine, whereas grape juice without the skin is used for white wine production (**Sarkadi, 2019**). The presence of histamine and tyramine was reported in red wines at high concentrations (**Santos, 1996**). Production of low histamine wine is based on a controlled strategy using high-quality hygiene raw material, especial starter culture addition, and specific production technique (**Comas-Basté *et al*., 2019**). In addition to beverage type, storage duration, time of fermentation, raw material quality, producing region, and possible contamination during processing could affect BAs concentration in wines (**Stojanović and Kos, 2020**). Also, it was shown viticulture and grape variety could be effective in BAs content in wine. Careful selection and addition of commercial malolactic starter culture to the vinification process could decrease BAs formation (**Marques *et al*., 2008**). A major contribution to BAs production was seen by lactic acid bacteria. None of the yeast and acetic bacteria was involved in BAs formation in wine (**Landete *et al*., 2007**). It is possible to detect the presence of histidine decarboxylase, ornithine, or tyrosine decarboxylase strains by PCR or DNA probe during winemaking. If the fermentation process contains these microorganisms inoculate selected malolactic starters (**Lonvaud-Funel, 2001**). Wines are poor in protein content, so free amino acids are the main precursors of BAs production (**Stojanović and Kos, 2020**). Also, beers with characteristics of ethanol (0.5-10% w/w), bitter compounds (17-55 ppm), pH (3.8-4.7), low oxygen content (<0.1 ppm) and presence of carbohydrates such as glucose, maltose, and maltotriose, could be a source of BAs because of growth of contaminated bacteria during storage and processing. So the presence of histamine, tyramine, and cadaverine could be originated from decarboxylase positive microorganisms. In contrast, spermidine, 2-phenylethylamine, and spermine could be originated from raw materials, putrescine could be produced from both origins (**Poveda, 2019**). It seems raw material and brewery have the main role in BAs content in beer than brewing type (**Poveda, 2019**).

Tea, coffee, and cocoa are other popular drinks worldwide that are less prone to BAs production. In contrast to alcoholic beverages, less investigation has been made on BAs in these products. These commodities have complex processing, production, and trade, so in addition to the availability of free amino acids and the presence of decarboxylase enzymes that are linked to the presence of particular bacterial strains, also environmental conditions such as pH, temperature, oxygen, and humidity may be effective in this regard **(Restuccia *et al*., 2019)**. Putrescine was the most abundant BA detected in ground coffee, while all BAs decreased during roasting. Coffee brews showed very low levels of BAs than roasted ground coffee. Machines such as espresso and capsule, which use higher pressure and physical stress, produce products with higher BAs content than machines such as mocha which use lower pressure (**Restuccia *et al*., 2015b**).

Tyramine was the highest-level BA in fermented cereals produced from rice, millet, maize, or wheat. Total BAs level was between 25 and 69 mg/kg. However, precaution was advised during consumption of this beverage for patients taking monoamine oxidase drugs (**Yeğin and Üren, 2008**). The addition of three strains of Gluconobacter to produce a fermented strawberry beverage was successful in ensuring the consumption of free amino acids beverage with no detectable BAs (**Ordóñez *et al*., 2015**).

MEASURING OF BA$_S$ IN FOODS

Because of BAs roles as an indicator of food freshness and their toxicity and undesirable health effects, different analytical methods have been developed for their detection in the food matrix. Analytical methods used for BAs quantification have been extended from chromatographic methods, including high-performance liquid chromatography (HPLC), gas chromatography (GC), ion-exchange chromatography, and thin-layer chromatography (TLC) to methods are mainly based on using sensors and biosensors (Figure 3) (**Stojanović and Kos, 2020**). Because BAs are present in a complex matrix with low concentrations and structurally similar compounds, a suitable pretreatment method is required for BAs detection. The more complex material, such as cheese, needs frequent extraction and purification stages to enhance sample purity (**Zhang *et al*., 2019**). **Yu-Jia *et al.* (2019**) classified pretreatment methods into different categories, including dilute and shoot and protein precipitation, adsorption on poly(vinylpolypyrrolidone) (PVPP), solid-liquid extraction (SLE), Liquid-liquid extraction (LLE) and dispersive liquid-liquid microextraction, extraction using ultrasonic, solid-phase extraction (SPE), solid-phase microextraction (SPME) and finally matrix solid-phase dispersion (MSPD) (**Zhang *et al*., 2019**). The dilute and shoot method is mainly used for beers and wines. The challenge of this method includes balance creation between sample dilution, matrix effects, and method sensitivity. Adsorption on PVPP is described as a suitable method for removing impurities from wines. SLE is the best and most common method for purifying BAs from complex matrixes with the best accuracy and efficiency. LLE causes minor damage to analytes but displays lower extraction efficiency and higher purification stages. SPE, based on reverse-phase chromatography, was introduced due to its simultaneous enrich and purify ability. Easy blocking of SPE filler pores was eliminated by introducing SPME. MSDP is a sample preparation method with many advantages, such as no need for specific devices, single extraction on a solid adsorbent, and a greener method than others (**Zhang *et al*., 2019**).

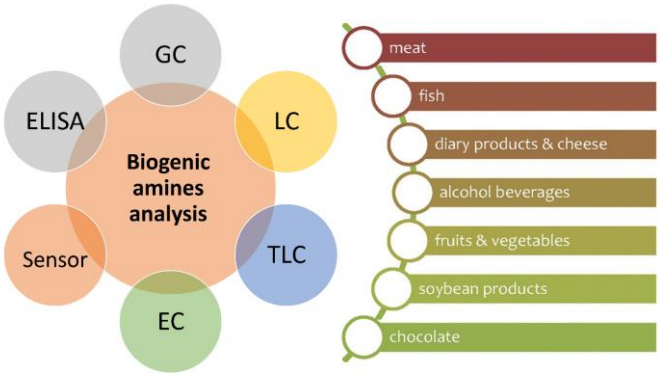

Figure 3 Analytical methods used for BAs quantification

Chromatographic based methods

HPLC is the most common method used for BAs detection in foods. The lack of chromophores and low volatility make the UV spectrophotometer an unsuitable detector for BAs. HPLC linked fluorescence detector and precolumn or postcolumn derivatization techniques are mostly used in literature (**Önal, 2007**). LC-MS/MS is a general detector with several advantages, including omitting derivatization, simultaneous screening, identifying and quantifying, and improved detection efficiency for different substrates (**Zhang *et al*., 2019**). However, the sensitivity of the fluorescence detector was more than UV/Vis in beverages matrixes, and LOD of LC-MS was not significantly different from those obtained by the fluorescence detector (Ordóñez et al., 2016). Freshness assessment is one of the main goals for BAs quantification. In this way, (**Gianotti *et al*.** (**2008**)) extended an improved method of LC-MS/MS called hydrophilic interaction liquid chromatography (HILIC)- PI APCI MS/MS. The main advantage of this system is the short sample pretreatment time because of better chromatographic separation. This result is obtained due to hydrophilic interactions between polar BAs and silica stationary phase and higher organic and lower aquatic mobile phase. This method used another mechanism of ionization (APCI instead of ESI) that allowed using of higher volatile buffer concentration (**Gianotti *et al*., 2008). Restuccia *et al*.** (**2011**) developed a new LC method coupled with evaporative light scattering detection (ELSD). ELS detectors are suitable for nonvolatile compounds with no absorbance above 200 nm. It enables these compounds' quantification without derivatization, so it removes drawbacks of this stage, including the requirement for optimization of parameters, incomplete derivatization reaction, long analysis time, and extra cost needed for reagents and devices (**Restuccia *et al*., 2011**).

BAs are very polar, so different derivatization techniques were used to reduce their polarity and provide chromophore substances suitable for UV or fluorescence detectors. The most common derivatization methods include amine derivatization with fluorogenic agents, benzoyl chloride, fluorescein isothiocyanate, and O-phthalaldehyde **(Restuccia *et al*., 2019**). **Hwang *et al*. (1997**) used benzoyl chloride derivatization at the optimized condition of 30 ˚C for 40 min to remove the effect of interfering peaks. **Jastrzebska *et al.* (2016**) used 1-fluoro-2-nitro-4-(trifluoromethyl) benzene (FNBT) as a new reagent for precolumn derivatization of BAs before detection by HPLC. Their results showed higher reactivity of FNBT with BAs derivatization so that reaction can happen at room temperature. A lower coefficient of variation (< 2.5%) and higher recovery value (100%) were obtained by the FNBT method. **Jia *et al*. (2013**) developed in situ derivatization method with benzoyl chloride, extracted with (dispersive liquid-liquid microextraction) DLLME based on solidification of floating organic droplets (DLLME-SFO) and detected by HPLC-UV. They assessed this method precise, accurate, and sensitive method for BAs detection in wine compared to fluorescence or mass spectrometer detection-based methods. Derivatization with dansyl chloride is more common due to the creation of more stable compounds that can be detected by UV or fluorescence detectors. In this way, **Angulo *et al.* (2019**) used several optimizations to achieve fast and repeatable dansylation with dansyl chloride, including high-speed stirring in a hot plate, increasing reaction volume, and providing constant temperature for reaction. Modifications made reaction time 88% lower than the usual oven method. One of the drawbacks of dansyl chloride is its non-specificity, causing it to react with substances such as alcohols or phenols. This reagent was applied for BAs determination in matrixes such as beer, orange juices, or wine (**Ordóñez *et al*., 2016**). Derivatization of BAs with 1-naphthylisothiocyanate has been described as a more efficient method than dansyl chloride because of instability of derivatives at temperatures above 65˚C, excess consumption of reagent, and the need to scavenge excess reagent with ammonia (**Jain *et al*., 2015**).

The kind of derivatization reagent depends on whether it is being reacted off-line or online. Derivatization reagents such as 9-fluorenylmethoxycarbonyl chloride and dansyl chloride were not suitable for BAs detection by batch injection using HPLC due to instability of derivatives, whereas dansyl chloride and benzoyl chloride was suitable when the batch injection was used (**Liu *et al*., 2018a**). One

fast method that omits the derivatization stage in BAs detection is ion mobility spectrometry (IMS). This technique "separates gas-phase ions based on differences in their mobilities through a gaseous atmosphere under the influence of a uniform electric field." Appearing overlapping peaks is one of the disadvantages of this system that could be overcome with gas-phase modifiers. **Parchami *et al*. (2017)** examined the introduction of 18-crown-6 in the carrier gas to increase the resolution of peaks.

Ultra-high-performance liquid chromatography (UHPLC), a kind of HPLC but with improved resolution and detection abilities, shorter analysis time, and lower solvent consumption, was introduced. Transferring from HPLC to UHPLC was obtained by adjusting the gradient program and flow rate (**Angulo *et al*., 2020; Ordóñez *et al*., 2016**). **Redruello *et al*. (2013)** used derivatization with diethyl ethoxymethylenemalonate (DEEMM) followed by UHPLC to simultaneously determine BAs in cheese. HPLC problems, including consumption of high amounts of organic solvents, have been compensated by GC-MS. On the other hand, deficiencies such as the existence of BAs in low concentrations and interfering agents such as polyphenols limit BAs determination by direct GC-MS determination. In this way, different extraction and derivatization methods that increase BAs volatility could be used to facilitate detection by GC. Suitable derivatization methods increase adsorption wavelength, so improve detection limit. Extraction like DLLME was used as an efficient method with a high enrichment factor for BAs detection by GC in complex matrices such as meat, beer, and homemade alcoholic drinks (**Almeida *et al*., 2012; Płotka-Wasylka *et al*., 2016; Wojnowski *et al*., 2019). Papageorgiou *et al*. (2018)** reported direct SPME GC-MS method for BAs quantification in wine for the first time. The method enabled simultaneous derivatization and extraction of BAs with advantages, including easy use, low solvent use, and higher rate. The higher prices of SPME fiber and destruction under immersion in wine could be considered limiting factors (**Papageorgiou *et al*., 2018**).

Cation exchange chromatography with integrated pulsed amperometric detection (IPAD) was introduced. Advantages of this method stated removing derivatization problems associated with the HPLC method, simple applicability, usability in broad matrices, isocratic elution, and lower detection limit (1.25 to 2.50 ng in different matrices) (**Draisci *et al*., 1998). Cinquina *et al*. (2004)** used ion-exchange chromatography with a conductivity detector for simultaneous detection of underivatized BAs detection in fish tissue. They evaluated this method as simple and complete because of the minimal use of reagents (alone with methane sulphonic acid) and the capability of instruments to be automated and so reduced operator errors. **Saccani *et al*. (2005)**) used cation exchange chromatography linked with suppressed conductivity and mass spectrometry detector for BAs detection in fresh and processed meat tissue. Methane sulfonic acid was used to extract BAs from meat tissue, and no additional derivatization or clean-up stages were used. Detection limits varied according to detector type. It was variable from 9 µg/L to 34 µg/L for agmatine and spermidine, respectively (MS detector), and from 23 µg/L to 155 µg/L for putrescine and spermidine, respectively (suppressed conductivity).

TLC is one of the simplest chromatographic methods that enables the quantification of many samples (compared with the single sample in the HPLC method) in a short time. Some drawbacks have been mentioned for TLC include lower sensitivity (higher than 500 mg/L for histamine) and the need for derivatives such as other chromatographic methods (**Latorre-Moratalla *et al*., 2009**). On the other hand, in comparison to HPLC, TLC-densitometry with little loss in linearity and repeatability was offered as a rapid and less expensive method (**Shakila *et al*., 2001). Romano *et al*. (2012)** developed amine dansylation and TLC/densitometry for BAs detection in wine. The method allowed the determination of histamine, tyramine, putrescine, and cadaverine in the range of 1 and 20 mg/L. Method equipment could be set in all parts of the wine facility instead of sophisticated HPLC equipment (**Romano *et al*., 2012**).

Electrophoretic based method

Capillary electrophoresis (CE) is more available than HPLC. Comparing HPLC and micellar electrokinetic capillary chromatography (MECC), several important differences were observed, including 1. Detection limit: HPLC showed lower detection limit (0.1 mg/100 g) than MECC (1 mg/100g). 2. Number of BAs: HPLC could detect nine BAs simultaneously, whereas MECC was disabled to detect tyramine and agmatine 3. Interference: benzoyl chloride peak was among other peaks in HPLC and may be interfered with amine identification, whereas it was observed at the end of the peak in MECC without interference effect. 4. Other MECC advantages: MECC method could be applied faster and more automated with a lower price and more resolution than HPLC (**Su *et al*., 2000). Simo´ *et al*. (2008)** evaluated the efficacy of CE linked to Ion-trap (CE-IT-MS) or time-of-flight mass spectrometry (CE-TOF-MS) on sensitivity, selectivity, and quantitation of BAs in wine. Both of the methods needed no previous treatment except dilution. In comparison, CE-TOF-MS showed better capability in detecting BAs in a single analysis and a lower detection limit (10 ng/mL) than CE-IT-MS. Compared to HPLC analysis done without previous derivatization using a fluorescence detector, one-fifth time was needed by CE-TOF-MS. Pre-capillary derivatization is one of the problems in CE or capillary electrochromatography (CEC) methods. This problem arises because the same separation buffer and reaction buffer are needed in derivatization, limiting the choice of the separation buffer. **Oguri *et al*. (2008)** designed a capillary electrochromatography (CEC) system to accomplish post-column derivatization of BAs. The system consisted of silica packed column, a T-junction connector, a fluorescence detector, and an energy supplier. The main part of the system, called the "T-junction connector", played several critical roles, including a reactor for derivatization equipped with a reagent-loading capillary tube, a connector with three capillary tubes, a capillary separation tubes, and a capillary tube for in-line fluorescence detection. Recently **Kvasnicka *et al*. (2019)** developed capillary zone electrophoresis (CZE) to determine histamine in foodstuff. The system's sensitivity was increased by the online combination of CZE and cITP using a capillary-coupled electrophoretic analyzer. This assembling presented both advantages of high loading capacity and high resolution due to the cITP and CZE. Other advantages described are no need for derivatization, lower cost, and sufficient sensitivity. Findings were confirmed by HPLC with a fluorescence detector.

Other methods

In addition to chromatographic and electrophoretic methods mentioned above, several methods such as enzyme-linked immunosorbent assay (ELISA) and biosensor could be used uncommonly in BAs determination. However, their use should not be underestimated. ELISA method is based on antigen-antibody reaction (**Zhang *et al*., 2019**). This method has been developed for routine detection of histamine in a large number of samples. In this way, monoclonal antibodies were prepared by stimulating the mice's immune system using histamine-protein conjugates (**Serrar *et al*., 1995**). Results showed ELISA could be used as a primary simultaneous screening method for many samples. Still, in the case of concentrations beyond legal limits, confirmation should be done by HPLC or CE techniques (**Muscarella *et al*., 2005**). The **Marcobal *et al*. (2005)** study suggested competitive direct ELISA as an alternative method for HPLC for histamine determination in wines (**Marcobal *et al*., 2005**).

Electrochemical biosensors use commercial or home purified enzymes such as diamine oxidase (DAO) or other amine oxidases that convert amines to related aldehydes, obtained from different sources (e.g., microorganisms, plants, and animal tissue) with various activity levels (**Carelli *et al*., 2007**). Oxygen consumption amount or H_2O_2 production amount has been used to quantify BAs. Hydrogen peroxide quantification could be done by amine oxidase coupling with peroxidase enzyme using amperometric biosensors (**Pérez *et al*., 2013**). Quantification of total BAs could be done using nonspecific enzymes, whereas for selective determination, selective and specific enzymes should be used (**Stojanović and Kos, 2020**).

The membrane containing immobilized MAO and an oxygen electrode has been used for meat freshness estimation. Putrescine oxidase (PO) in soluble form or immobilized on an electrode also have been developed. These sensors are disabled to distinguish putrescine from other amines. However, reports of establishing PO and MAO in coupled electrodes are developed to assess different spoilage stages in fish and meat (**Tombelli and Mascini, 1998**). Transducer type and enzyme immobilization method could play a critical role in electrochemical detection. In this way, carbon nanotubes (CNTs) have excellent electrochemical potency due to providing some advantages, including high current response, high surface to volume ratio, high chemical stability, and minimum surface fouling onto electrochemical devices. **Pérez *et al*. (2013)** developed a bienzymatic biosensor by DAO and horseradish peroxidase (HRP) co-immobilized in polysulfone (PS)/carbon nanotubes/ferrocene membrane by phase inversion technique. PS polymer possesses high chemical, biochemical and thermal stability and can also be used in extreme pH values. On the other hand, it is a nonconductive polymer, so its introduction into a conductive polymer such as CNTs is essential to developing an amperometric biosensor. Elements that were needed for amperometric detection, including enzymes, transducer, and redox mediator, have been employed in this study. The effect of interfering agents could be reduced by enzyme selectivity and sensitivity. **Henao-Escobar *et al*. (2016)** immobilized histamine dehydrogenase (HMD) and putrescine oxidase (PUO) enzymes on two working electrodes for simultaneous detection of histamine and putrescine by amperometric detection. Tetrathiafluvalene (TTF) was used as an electrochemical mediator to reduce working potential and decrease the effect of interfering agents.

Colorimetric sensors make another type of sensor with some advantages such as high selectivity and good environmental tolerance activity, ability to visual sensing, simple sampling, and easy miniaturization. Traditionally colorimetric sensors are based on weaker interactions such as van der Waals that reduce sensitivity between different analytes. To increase sensitivity, designing colorimetric sensors based on strong interactions such as electrostatic ion-ion and acid-base interactions is recommended. In addition to strong interactions, the utilization of specific functionalized devices with nanomaterials helps to improve sensitivity. The nanomaterials that have been used for amine detection include TiO2 nonporous films, single-walled carbon nanotube/metalloporphyrin composites, and organic nanoparticles (**Zhong *et al*., 2018**). In this way, **Zhong *et al*. (2018)** combined the two mentioned methods above. They designed a colorimetric sensor based on the acid-base reaction between BAs and nanocomposite material composed of gold nanoparticles, graphene oxide, silicone hydrogel, and pH-sensitive dyes. Due to the difference in alkalinity of BAs, pH-

sensitive dye shows different color changes according to BA type that could be distinguished from others. Recently **Siripongpreda *et al*. (2020)** developed poly lactic acid (PLA) film using calcium carbonate nanoparticles to increase porosity and provide better surface area for the colorimetric sensors. Bromocresol purple was immobilized on the porous PLA substrate as a pH indicator of putrescine and cadaverine released from pork samples. Also, they developed a dual-platform contained GO-coated filter paper attached to the nonporous side of the PLA substrate and LDI-MS for screening and quantification. The calorimetric sensor provided a simple, easy, cheap, and portable vehicle for BAs detection in smart packaging. In contrast, GO-coated for LDI-MS provided a specific and sensitive determination of putrescine and cadaverine.

CONCLUSION

The effect of different factors from indigenous such as pH or aw of material to exogenous such as process conditions on BAs concentration was surveyed in this article. Exogenous factors ranged from those involved during production, such as lactic acid bacteria or salt during cheese production, to the processing, such as homogenization, UV irradiation, or vacuum packaging. Decarboxylase positive microorganisms could facilitate BAs formation, whereas lactic acid bacteria effect was variable according to strain type or even ripening and storage conditions. Despite pasteurization's positive impact on BAs reduction in produced cheese, thermization leads to adverse impact. BAs content increased due to UV-C irradiation; however, gamma irradiation degraded some of the BAs in meat.

In some cases, the type of BA reflects contaminated microorganisms species. While the increase of salt content was effective in BAs controlling in sausages, it should be considered in a hurdle technology to inhibit BAs formation in fish. The effect of specific starter culture on BAs formation in pickles depends on the vegetable type, type of indigenous microflora, storage, and fermentation conditions. General results showed that refrigeration is a common method to control BAs formation. Still, the use of more novel emerging technologies such as radiation, vacuum packaging, and HPP and their combination with conventional methods (refrigeration, heat treatment, plant or synthetic additives, and suitable starter cultures) could be helpful in reducing BAs contamination to an acceptable level.

BAs' measuring and detection approaches should be selected according to selectivity, sensitivity, chemical solvents consumption, equipment availability, precision, analysis time, cost, and human resources. There are two highest disadvantages in BAs analysis in food, including 1) the complex matrix of food samples and 2) the low concentration of these compounds in food samples. Some of the food compounds have interfering effects with BAs detection, limiting the simultaneous detection of BAs in the food samples. Overcoming this problem could be done by pre clean-up procedure consisting of sample extraction with suitable extracting solvents.

Compared to chromatographic and electrophoretic methods, different sensors and biosensors supply more accessible analytical methods at a low price and short time. Still, their preliminary design and instability of enzymes could be limiting factors.

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