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The Increase of Amines Content in the Intake of a Vegan Diet

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Abstract

Vegetarian and vegan consumers have increased in the last years. However, the food industry is facing problems responding to this growing market, since the food safety of several plant-based products is not well established. Fruits, vegetables and fermented products, such as nut and grains milks and cheeses, may be rich sources of biogenic amines; whereas, the levels of these compounds should be considered before the inclusion on a daily diet. Biogenic amines are a class of compounds with wide physiological activities as antioxidant properties, inductors of cell division and allergic processes, and sleep, sexual and behavioral disorders. In addition to the levels of biogenic amines, the levels of some of its precursors as tryptophan, 5-hydroxytryptophan and tryptamine will be presented. The foods eaten by vegans are consumed raw, cooked, fried, fermented and mainly through homemade processing methods, which have influence on the levels of bioactive compounds from the food matrix. Exposure to processing conditions such as handling, sanitary conditions, high temperatures, preparing methods (cooking in water or oil) influencing the levels of amines, will be discussed in this chapter to enrich the knowledge on food safety associated to vegan diets.

Keywords: antioxidants, biogenic amines, histamine, tyramine, food safety

1. Introduction

Human metabolism is influenced by dietary, lifestyle, environmental and genetic factors [1]. Analysis of plasma metabolites by groups showed significant differences between meat eaters, fish eaters, vegetarians, and especially vegans [2]. Randomized clinical studies have shown that plant-based diets are associated with reduced risk of mortality and morbidity from cardiovascular disease (CVD) [3]. The association of low CVD index and vegetarian dietary patterns are the result of the constant reduction of organisms' exposure to harmful substances contained in products of animal origin (for example: saturated fat, cholesterol, heme iron, N-glycolylneuramine acid, persistent organic pollutants, polycyclic aromatic hydrocarbons, heterocyclic amines and advanced glycation end products), in addition to the increased consumption of fibers and phytochemicals present in whole plant foods. Phytochemicals in plant-food include carotenoids (α - and β -carotene, lycopene, phenolic compounds, vitamin C, tocopherols, biogenic amines, among others [4], which can act synergistically by reducing inflammation and oxidative stress, providing protection against CVD [3, 5].

Biogenic amines are aliphatic organic bases of low molecular weight and have biological activity in microorganisms, plants and animals. Polyamines (putrescine, cadaverine, spermidine and spermine) and biogenic amines (serotonin, dopamine, histamine, tyramine, among others) are called bioactive amines (BAs) and are relevant for both shelf life and final product quality, as well as for human health [6]. Some polyamines play an important role in growth and can act as antioxidants [7–9], while other amines are neuroactive or vasoactive [6]. In addition, amines are also described as being indicators of plant-food safety and some countries already limit the amount of some BAs, mainly in fermented foods [10, 11].

Although many BAs, such as histamine, tyramine and putrescine are necessary for many functions in humans, consumption of foods containing large amounts of these amines can have toxicological effects. For example, excessive consumption of histamine can induce histaminic intoxication and is mainly related to heart disease (hypotension and palpitations) and headache [12]. Tyramine is also considered harmful to the body [13]. Even though some studies show the levels of amines in plant-based food [7–9, 14], the number of studies that establish legal limits in foodstuffs is still insufficient.

While histamine and tyramine can have adverse effects, the ingestion of foods rich in some amines, such as spermidine and spermine, has been linked to longevity, both in humans [15] and in plants [16]. Diamines such as putrescine and cadaverine have been described due to their occurrence in higher levels in contaminated foods or in senescent plant tissue. Besides these polyamines, monoamines such as serotonin and dopamine have important neurological and antioxidant functions in both animals and plants. These amines can be obtained by eating some foods plant-based (banana, cauliflower, grapes - *in natura* and byproducts) and/or animal (fish and meat). However, the synthesis and *turnover* of serotonin depends on the intake of the amino acid tryptophan for the formation of serotonin in the brain, since this neurotransmitter does not cross the blood–brain barrier [17]. In mammals, serotonin is a neurotransmitter that acts on the central nervous system, affecting appetite, sleep, anxiety and mood. In addition to being an important precursor to the formation of serotonin in the brain, tryptophan is also a precursor to melatonin, an indolamine, which has antioxidant action, besides acting in physiological processes related to the regulation of circadian rhythm, mood and sleep. This chapter provides an overview of the presence of amines in plant-based diets, the impacts of food handling and processing on these molecules, in addition to the mechanisms by which these compounds are absorbed and affect physiological functions in humans.

2. Fruit, vegetables and their bioactive amines against human diseases

Fruit and vegetables play an important role in human health, since they contain many essential nutrients and phytochemicals that are responsible for preventing or reducing the risk of various chronic diseases, including cardiovascular disease, diabetes, obesity, certain types of cancer, inflammation, heart attack, stroke and septic shock. Additionally, vegans, vegetarians and omnivores, consume fruits and vegetable by-products that contribute to significant levels of important health compounds, which have been extensively researched, in addition to being profitable raw materials and easily available to the food and pharmaceutical industries.

Cells are constantly exposed to oxidizing agents and a key point is the balance of the oxidative effect by antioxidant mechanisms. To reduce the risk of developing chronic diseases in humans and possibly delay the appearance of age-related problems,

nutritional recommendations are that young and old people eat at least seven portions a day of different fruits and vegetables. For a lowest risk of total cancer, studies showed that it is important to intake of 600 g/day (7.5 portions/day), however, for coronary heart disease, stroke, cardiovascular disease and all-cause mortality the lowest risk was observed at 800 g/day (10 portions/day) [18]. Many studies show a strong and positive correlation between the content of BAs and the antioxidant potential of fruits and vegetables [7, 8].

BAs are involved in several physiological processes and can act as antioxidants [7, 8] and some studies relate polyamines to ion channel regulation, DNA methylation, histone acetylation, protein biosynthesis, RNA translation, apoptosis and regulation of the immune response [19], in addition to being considered a secondary messenger, mediating some growth factors in plants [20]. Studies indicate that the BAs present in fruits and vegetables are strong antioxidant compounds with more effective free radical scavenging properties, compared to some natural antioxidants, for example, phenolic compounds [8, 21] or well-accepted synthetic compounds, such as α -tocopherol, octyl gallate and palmitoyl-ascorbic acid [22]. In fruits and vegetables, around 22 BAs have already been described, and the most detected BAs are tyramine, putrescine, cadaverine, histamine, spermine and spermidine [10], while few studies report the detection of serotonin and dopamine [7, 8].

In addition to the ingestion of BAs by food, the body synthesizes endogenous amines by producing intestinal bacteria [19, 23], which can promote excess of these amines, facilitating the increase of diseases, mainly involving high cell proliferation. Amines such as spermidine have been described as being related to increased longevity. Spermidine - the most absorbed polyamine from the human gut - is most consumed by women and is related to the increase of survivability in humans [15], due to the capacity to restore or induce efficient autophagy [24], among others factors. However, ingestion of high levels can promote cancer development when critical immunoregulatory circuits are afflicted [25]. Studies demonstrate the lesser cytotoxic effect of spermine using an *in vitro* human intestinal cell model, compared to spermidine [26]. The cytotoxic level of spermidine ranges from 5 mM (NOAEL) to 10 mM (LOAEL), while for spermine, the levels are lower (NOAEL - 2.40 mM and LOAEL - 3.23 mM) [26]. Autophagy plays an important role in the prevention of several diseases [27], who demonstrated that spermidine may decrease the level of lipids and necrotic core formation.

In plants, putrescine is formed from ornithine or arginine by the action of ornithine decarboxylase (ODC, EC 4.1.1.17) or arginine decarboxylase (ADC, EC 4.1.1.19). The addition of aminopropyl groups from S-adenosylmethionine (SAM) to putrescine is catalyzed by S-adenosylmethionine (SAM) decarboxylase (SAMDC, EC 4.1.1.50) forming spermidine, through spermidine synthase. A new aminopropyl group is added to spermidine, forming spermine by the action of spermine synthase. In contrast, the action of 1-aminocyclopropane-1-carboxylate (ACC) synthase leads to the formation of 1-aminocyclopropane-1-carboxylic acid (ACC), a precursor to ethylene [16]. Thus, ethylene and the polyamines spermidine and spermine use the same precursor, that is, SAM. Several studies have shown that higher levels of spermidine and spermine indicate juvenility, and the $\text{Put}/(\text{Spd} + \text{Spm}) > 1$ ratio would indicate the formation of ethylene, related to senescence. Evidently, the levels of these amines affect post-harvest life and the action of ethylene may be an indicator of a decrease in the content of spermidine and spermine. Thus, juvenile fruits and vegetables contain higher levels of spermidine and spermine and their consumption can lead to improved

health, in addition to the fact that diets with adequate levels of these polyamines can increase longevity.

3. Factors that affect the content of bioactive amines in foods

Fresh fruits and vegetables contain BAs as endogenous components and, due to uncontrolled microbial enzymatic activity, they can be accumulated during storage or even after some type of post-harvest processing [8, 28]. Amines are generally not destroyed during thermal processing, using high temperature, or during storage. Often there may be an increase in content due to the ease of extracting amines from food after cooking or in overripe fruits, due to cell wall degradation, making these molecules more available [7, 8]. These data point out the importance of detecting these compounds in different food matrices for a better understanding of the amino acid profile in fresh and processed products [8, 29].

The levels of spermidine and spermine in plant-food vary depending on the physiological stage, the cultivation method and the type of thermal processing. In bananas, during the fruit ripening process, there was an accumulation of putrescine, mainly in plantains. High levels of spermidine and spermine have been found in some genotypes of plantains (**Table 1**) [8]. Besides the differences between genotypes of the same species, the BAs contents are also modified by thermal processing in colored cauliflowers [7], which often provides increased palatability, digestibility and flavor [30] (**Table 1**). The lowest levels of spd and spm were found in cauliflower 'Grafitti', although all other genotypes analyzed ('Verdi de Maceratta', 'Cheddar' and 'Foratta') showed an increase with cooking (boiling, steaming or microwaving) (**Table 1**). This effect is due to the ease of extracting the compounds by softening the cell wall; however, this same beneficial effect may induce losses to cooking water due to the hygroscopicity of BAs and other anti-oxidant compounds, such as polyphenols. In colored green beans, boiling induced increased levels of BAs, and steaming maintained the lowest levels [30].

The processing temperature is an important measure to prevent or inhibit the formation of BAs in foods [31]. Heat treatment, such as cooking and pasteurization, can reduce the content of BAs in foods [31], recommending methods for reducing bioactive amines in mushrooms. For example, the pasteurized pickled and sterilized natural marinade of white button mushrooms showed substantially lower amounts of Spd compared to the unprocessed product (**Table 1**) [32]. The high temperature used in the processing contributes to the reduction of the microflora contained in the food, which is involved in the production of BAs [31], even though they are considered heat stable and are not destroyed by cooking, baking or even canning [33]. BAs are produced by mesophilic bacteria, especially at temperatures ranging from 20 to 37°C and, therefore, unprocessed and untreated mushrooms should preferably be stored under refrigeration conditions to avoid the accumulation amines, which can cause some type of toxicity to the human organism in excess [31]. Initial studies showed that intact fruit bodies of *Agaricus bisporas* stored for 48 h at 6°C did not exhibit the presence of Put and Cad, but when stored at room temperature (20°C) the levels of these amines increased significantly [34]. However, no amounts of Cad and Put were detected (only one of the three samples tested) after storage of mushrooms at room temperature [32]. These authors point out that the method of handling mushroom fruit bodies during harvest and after technological processing significantly influences the content of these amines during storage. Mechanical bruises caused by poor handling on soft mushroom tissues, during harvest and technological processing, can accelerate the activity of decarboxylating bacteria causing the synthesis and/or the accumulation of BAs [35].

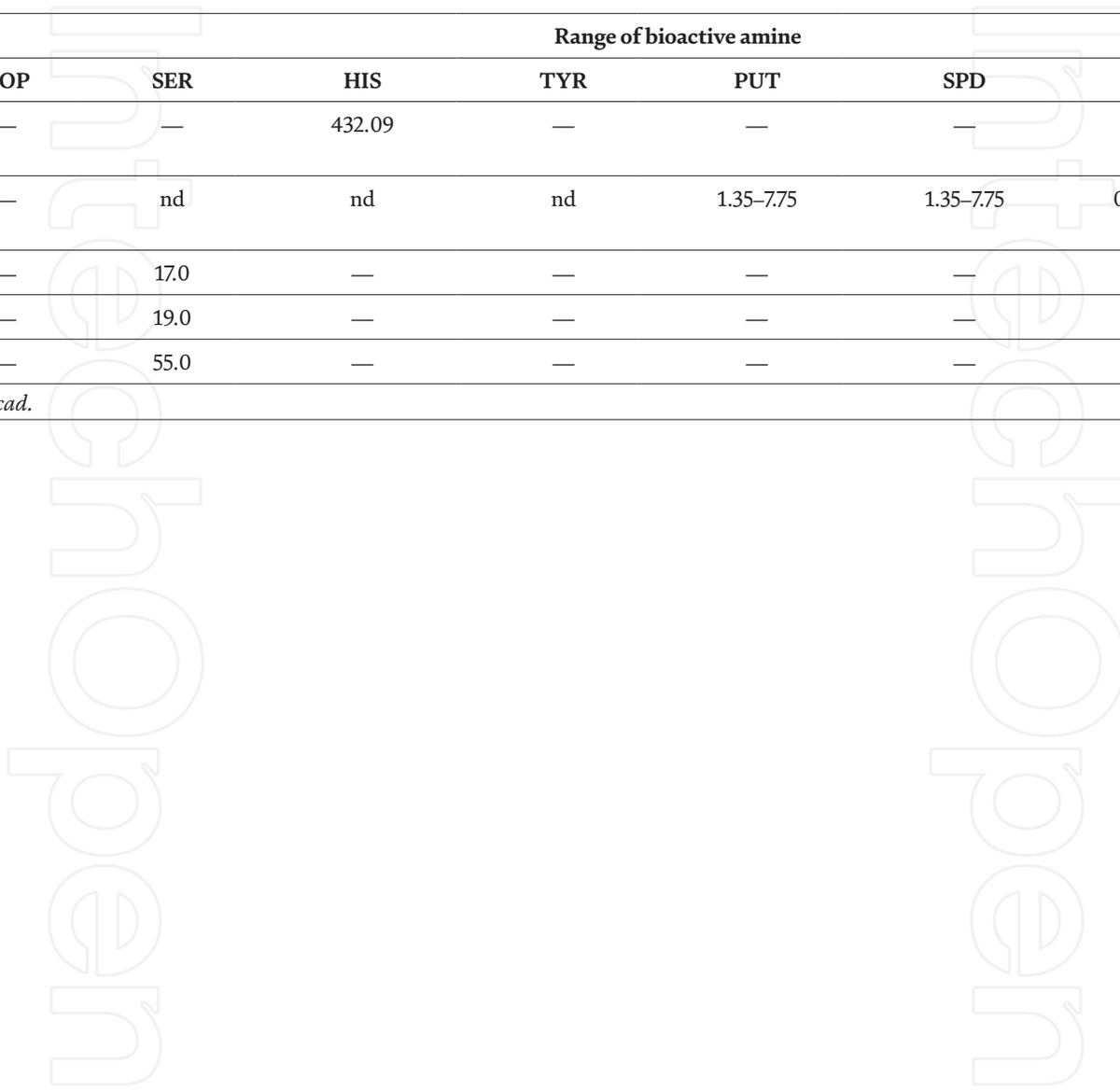
Food	Range of bioactive amine							Citation
	DOP	SER	HIS	TYR	PUT	SPD	SPM	
Fermented								
Mushrooms raw (mg/kg f.w.)	—	—	nd	nd	nd–53.4	1686–2714.	nd	[32]
Mushrooms pickled, pasteurized (mg/kg f.w.)	—	—	nd	nd	462.0–716.7	470.2–1129.3	nd	[32]
Mushrooms marinade, sterilized (mg/kg f.w.)	—	—	nd	nd	38.0–141.6	2475–264.9	nd–34.19	[32]
Mushrooms 48 h storage, 6°C (mg/kg d.w.)	—	—	—	—	nd	—	—	[34]
Mushrooms 48 h storage, 20°C (mg/kg d.w.)	—	—	—	—	368.0	—	—	[34]
Jurubeba pickled (vinegar), after 1 h (mg/kg f.w.)	—	—	8.5–75.3	33.9–105.7	255.7–582.3	95.7–323.2	4.9–6.8	[14]
Jurubeba pickled (vinegar) after 90 days (mg/kg f.w.)	—	—	0.1–59.6	1.6–59.8	208.3–537.1	0.4–93.1	0.2–21.4	[14]
Fermented fish product (fish sauce) (ppm)	—	—	45–1220	nd–42	2.0–243	nd–98	nd–121	[48]
Kimchi (green onion and mustard leaf) (mg/kg f.w.)	—	—	8.7–386.0	nd–181.1	nd–254.5	2.3–28.5	nd–58.6	[53]
Sauerkraut samples (mg/kg f.w.)	—	—	nd–229	nd–951	2.8–529	nd–47.0	—	[54]
Sauerkraut, after 12 months	—	—	nd	168–570	63.7–216	8.3–12.5	nd–8.6	[55]
Sauerkraut (mg/kg f.w.)	—	—	37.0	60.7	108.9	10.9	1.2	[56]
Fermented pickles (<i>L. plantarum</i> isolates) (mg/L f.w.)	—	—	nd–668	—	nd–994	—	—	[58]
Soft tofu (mg/kg f.w.)	—	—	nd–21.8	nd–7.2	15.9–42.5	nd–23.8	—	[60]
Firm tofu (mg/kg f.w.)	—	—	nd–65.3	nd–179.7	nd–306.2	nd–73.1	—	[60]

Food	Range of bioactive amine							Citation
	DOP	SER	HIS	TYR	PUT	SPD	SPM	
Household sauerkraut (mg/kg f.w.) Sterilized	—	—	nd–32.40	nd–384.0	4.0–260.0	nd–28.3	—	[54]
sauerkraut (mg/kg f.w.)	—	—	nd–26.4	26.3–345.0	18.4–359.00	nd–15.2	—	[54]
Fruits and vegetables								
Banana raw pulp (green, stg 2) (mg/100 g d.w.)	26.8–38.1	7.9–20.3	6.9–7.4	8.9–10.3	13.9–21.4	16.0–19.0	13.8–14.8	[8]
Banana raw pulp (ripe, stg 5) (mg/100 g d.w.)	26.7–34.4	7.5–13.7	6.8–8.6	9.1–9.6	17.4–27.1	15.8–17.5	13.5–14.2	[8]
Kiwi raw ($\mu\text{g}/100\text{ g f.w.}$)	—	952.0	—	—	—	—	—	[36]
Banana raw peel (mg/100 g d.w.)	32.7–305.5	8.2–74.3	11.8–118.3	9.2–14.0	16.5–25.0	15.0–23.6	15.1–31.0	[8]
Plantain raw pulp (mg/100 g d.w.)	27.7–33.7	8.9–15.5	6.8–7.2	9.2–10.0	14.7–63.6	15.7–18.6	13.5–14.4	[8]
Plantain raw peel (mg/100 g d.w.)	82.1–642.7	8.2–104.8	66.3–257.8	9.5–18.6	15.5–41.3	14.5–21.3	13.2–66.6	[8]
Banana and plantain cooked (mg/100 g d.w.)	28.0–59.5	10.3–15.1	7.4–7.8	9.2–9.6	32.4–67.1	18.0–23.9	13.8–14.5	[8]
Tomato raw ($\mu\text{g}/100\text{ g f.w.}$)	—	881.0–1244	—	—	—	—	—	[36]
Cauliflower raw ($\mu\text{g}/100\text{ g d.w.}$)	8.0–42.0	45–203.0	4.0–46.0	—	34–358.0	52.0–460.0	13.0–85.0	[7]
Cauliflower raw ($\mu\text{g}/100\text{ g f.w.}$)	—	23.0	—	—	—	—	—	[36]
Cauliflower cooked, 5 min ($\mu\text{g}/100\text{ g d.w.}$)	0.02–0.35	0.73–3.0	0.10–0.65	—	0.71–8.08	0.63–27.7	0.32–7.6	[7]
Cauliflower cooked, 10 min (pg/100 g d.w.)	0.02–0.28	0.70–4.3	0.12–0.71	—	0.78–12.0	1.20–37.4	0.55–8.2	[7]
Green beans (mg/100 g f.w.)	—	nd	nd	nd	1.48–7.78	1.27–7.36	0.20–2.01	[30]
Canned apples, 1 month after production (mg/kg f.w.)	—	—	165.86	—	—	—	—	[44]

Food	Range of bioactive amine							Citation
	DOP	SER	HIS	TYR	PUT	SPD	SPM	
Canned apples, 12 month after production (mg/kg f.w.)	—	—	432.09	—	—	—	—	[44]
Green beans cooked (mg/100 g f.w.)	—	nd	nd	nd	1.35–7.75	1.35–7.75	0.29–2.83	[30]
Broccoli raw (µg/100 g f.w.)	—	17.0	—	—	—	—	—	[36]
Spinach raw (µg/100 g f.w.)	—	19.0	—	—	—	—	—	[36]
Asparagus raw (µg/100 g f.w.)	—	55.0	—	—	—	—	—	[36]

fresh weight: f.w.; dry weight: d.w.; nd: not identified.

Table 1.
 Bioactive amine content in food.



4. Bioactive amines with neurotransmitter function present in food

As well as spermidine and spermine, other amines like monoamine serotonin, present in fruits and vegetables, have also been described for their antioxidant and anti-senescent actions in plant tissues, besides having beneficial (neurotransmitter) effects related to human health [36]. Considering the effects of serotonin in humans, diets enriched with plant-based food rich in serotonin may prevent certain diseases, such as the metabolic syndrome [36]. In humans, the ingestion of tryptophan and 5-hydroxytryptophan is essential for the formation of serotonin in the brain, since this neurotransmitter does not cross the blood – brain barrier, thus the synthesis and turnover of serotonin depends on the ingestion of these compounds through food [17]. The daily recommendation of tryptophan for adults is around 4 mg kg^{-1} body weight per day and 12 mg kg^{-1} body weight for children [17]. Thus, foods that contain higher levels of tryptophan and 5-hydroxytryptophan can help in the balance of serotonin and melatonin levels. Melatonin is produced from tryptophan and from serotonin and has also been identified in fruits and vegetables [7, 37].

Serotonin levels also vary depending on the ripening stage, as described in studies with wines grape [38] and bananas and plantains (**Table 1**) [8]. Reduced levels of amines, i.e., serotonin and dopamine in advanced stages of fruit ripening may be associated with an oxidative pathway activated during senescence, which can be considered markers of this development phase [7]. Serotonin levels can also be changed in function of the cooking (**Table 1**). An increase in the content of serotonin in banana pulps ('Pelipita') was also verified after cooking treatments in microwave with the peel (14.4%), in addition to boiling the fruit with the peel (3.8%) [8]. Cooking (i.e., boiling, steaming or microwave) induce an increase in serotonin levels in colored cauliflower, with emphasis on 'Cheddar' and 'Forata' cooked by microwave [7]. However, cooking time can be harmful (**Table 1**). Some studies on thermally processed foods indicate that prolonged exposure to high temperatures can result in substantial losses of amine compounds [39]. The frying process in *Musa* spp. fruit, for example, induced serotonin losses, and is not recommended when the objective is to ingest higher levels of this indolamine [8]. The significant decrease in serotonin has also been observed in other processes used in banana fruit (e.g., frozen fruit, ice cream and fruit nectar after pasteurization) [39].

Using fruits and vegetables with the peel for domestic processing can be a very interesting strategy to increase the intake of BAs. High amounts of catecholamines and indolamines have been identified in fruit (banana pulps) submitted to thermal processing with the peel (**Table 1**) [8]. Bananas boiled with the peel resulted in increases in serotonin content of up to 3% (cooking banana 'Pelipita') and 73% dopamine ('D'Angola'). This effect can be attributed to the migration of serotonin and dopamine from the peel to the pulp, as already verified with other bioactive compounds analyzed in fruits submitted to the cooking process [8, 40]. Fruit and vegetable peels are generally more exposed to sunlight than pulp and can protect themselves from oxidative stress caused by strong sunlight and high temperatures, producing large amounts of antioxidants.

Amines considered to be dangerous to health, mainly histamine and tyramine, do not occur only in products of animal origin or processed or fermented. People who present intolerances, such as monoamine oxidase (MAO) or diamine oxidase (DAO) deficiency, should avoid some fruits and vegetables due to the levels of these amines. Treatment with monoamine oxidase inhibitors can promote hypertension due to an increase tyramine and phenethylamine in susceptible individuals [41] Doses of 200 to 800 mg of tyramine increase the systolic blood pressure by 30 mmHg [42] and

this increase can cause heart failure or brain hemorrhage [43]. The knowledge of the content of the levels of these amines in foods, whether of plant or animal origin, is important to avoid damages to health. However, few studies classify foods in relation to the levels of these amines. Despite the damages, histamine plays an essential role in promoting growth and metabolic activity of the gut and is active in nervous system [44].

Alcoholic and non-alcoholic fermented drinks, as well as long-ripened cheese, meat, fish, and some fruits and vegetables should be avoided by people sensitive to histamine and/or tyramine. Preserving plant-food in canned form can affect histamine and tyramine levels, as well as shelf life. The storage time increases the histamine content in canned apple; i.e., after twelve months of production, the samples showed almost three times more histamine compared to those stored for 30 days [44]. However, other species do not have the same result. In canned jurubeba, there was a decrease in the content of histamine and tyramine during the storage time (90 days), mainly in fruits preserved in vinegar, compared to those preserved in soy oil [14]. To cause toxicity, histamine levels vary between 10 and 100 mg/100 g in food [19] and the effect can be enhanced when there are high contents of putrescine and cadaverine in the food [14]. In addition, the cooking method may increase histamine levels, as described in bananas ('Pelipita') cooked without the peel in microwave (**Table 1**) [8].

5. Fermented food and beverages and their bioactive amines against human

Amines can be found in fermented plant-based foods [45] and, in high concentrations, they can be undesired, due to causing an unpleasant aroma, in addition to physical problems such as headaches (**Table 1**). Thus, there is a growing interest in controlling the accumulation of biogenic amines using antimicrobial agents to inhibit the proliferation of amine-producing bacteria. An efficient way to control the accumulation and/or formation of undesirable amines would be to control the fermentation process and/or the introduction of spices, which can have significant potential as antimicrobial agents. The control of the fermentation process using initial cultures ensures quality control and product safety. For example, spontaneously fermented carrot juice, a novel food product, can benefit from the development of starter cultures to avoid high numbers of Enterobacteriaceae and/or high concentrations of BAs [46]. In general, *Lactobacillus plantarum* starter-culture strains are frequently used to control vegetable fermentation processes [46, 47].

Many vegetarians consume fish products. However, fish and fermented fish products (e.g., fish sauce) contain significant levels of aminoacids and BAs, some of which are undesirable, such as histamine, with levels greater than 500 ppm (**Table 1**) [48]. Besides histamine, undesirable amines such as putrescine, cadaverine and tyramine can occur in these products. Levels of 1257 and 1178 ppm of putrescine and tyramine, respectively, have been reported in fish sauce [49]. The addition of additives in the fermentation process, such as spices, can alter fermentation conditions, possibly leading to an increase or decrease in the quantities of some endogenous compounds, such as BAs in the final product [12].

In recent years, increased shelf life and food safety through the use of bioprotective microbial cultures, in particular lactic acid bacteria (LAB) and/or their antimicrobial compounds have gained great attention. One approach is based on the growing consumer demand for probiotic non-dairy products and beverages. *Lactobacillus plantarum* and *L. delbrueckii* were detected in fermented cabbage juice and can be interesting as probiotics for vegetarian and lactose intolerant consumers.

In addition, certain strains of fermented LAB, which often belong to species of the genus *Lactobacillus*, can have health-promoting effects, for example, through immunomodulation and inhibition of pathogens [46, 50]. The food product itself could be used as a new product for traditional (dairy-based) marketed probiotics, allowing the access to a new market niche, focusing on consumers who are lactose intolerant and who do not want to purchase probiotics from products of animal origin (i.e., milk) [45].

Food companies specializing in vegetable products are looking for preservation methods that guarantee functional, sensory and nutritional quality and, at the same time, microbiological safety of products. The vegetable fermentations are gaining popularity for their rich flavors and health benefits, but due to the lack of information about the microbiological process, there are concerns about food safety [46]. Despite the controversy and the negative effects of the presence of some BAs in fermented products, studies indicate that amines present in fermented plant-based foods can be used as pharmaceutical compounds to promote cardiovascular health and longevity [51]. Histamine is well known for its pro-inflammatory effects on allergy and anaphylaxis; however, several studies have demonstrated anti-inflammatory or immunoregulatory functions of histamine. For example, histamine derived from *Lactobacillus reuteri* can suppress the inflammatory action of TNF, a proinflammatory cytokine, leading to anti-inflammatory strategies for chronic immune-mediated diseases. Probiotic species can target specific signaling pathways and immune responses, that is, strains of these bacteria can represent future therapeutic agents that can serve to suppress chronic inflammation [52]. In addition, fermented plant-based foods can be an interesting source for the detection of new bacterial strains with great potential for various probiotic and industrial applications, thus the study of microbial ecosystems during the fermentation process is interesting [45].

In comparison to dairy-based food fermentations, fermentations that use plant materials as the main substrate are little explored, except for a few examples such as kimchi (fermented with *Chinese mustard*), sauerkraut (fermented with cabbage) and pickles and can be interesting to lactose intolerants, to people allergic to milk or to vegans [45]. In kimchi samples collected on the Korean market, histamine and tyramine content above safe levels were found (**Table 1**) [53]. Sauerkraut is one of the best known and most commercialized traditional vegetable foods in Europe. In a study working with 121 commercial and household samples of sauerkraut, low levels of amines such as tryptamine, spermidine and spermine were found, however, high values of putrescine and tyramine have been identified (**Table 1**) [54]. It is noteworthy that the amount of amines present in the sauerkraut depends on the market and/or on the method of preparation of the product, with variations between the works found in the literature. In sauerkraut spontaneously fermented for one year, low concentrations of spermine and spermidine have been reported, but with high concentrations of tyramine and putrescine, as the predominant amines (**Table 1**) [55]. In commercially distributed sauerkraut samples, high levels of tyramine and putrescine were also identified, but with also high concentrations of histamine [56]. The values obtained for the BAs in the sauerkraut in the different researches, place this product as of special care due to the negative effects on the consumer, taking into account that histamine and tyramine are considered toxic amines when found in high quantities.

Another important fermented vegetable product produced in the United States and Europe is pickles, which are produced by fermenting cucumber (*Cucumis sativus* L.) with lactic acid bacteria [57]. In naturally fermented pickles (pepper, cucumber, cabbage, beans, tomatoes, Armenian cucumber and mixed vegetables) by *L. plantarum* for domestic consumption, high levels of cadaverine, putrescine

and histamine were found, but not in a toxic limit [58]. However, these levels must be taken into account in people with a low level of tolerance to these amines.

Soy (*Glycine max* L.) and its derivative products are nutritional solutions for vegetarians, due to their high protein content and ease in preparing foods similar to meat and milk substitutes [59]. Tofu is one of the best known products made from soy and is an important source of minerals, proteins, among others. Firm tofu is produced by pressing and containing less water, thus they contain high levels of amines, when compared to soft tofu (**Table 1**) [60]. Tolerable levels of tyramine in foods are 100 mg/kg [61]. However, depending on the sensitivity to tyramine, some care must be taken regarding the ingested amount. Small doses of tyramine can often cause severe migraines with intracranial hemorrhaging in patients treated with classic monoamine oxidase inhibitor (MAOI). However, people who use reversible MAO-A inhibitor (RIMA) can tolerate doses between 50 and 150 mg of tyramine [41, 62].

6. Conclusions

Biogenic amines are known to occur in food, and the highest concentrations are reported especially in fermented products. Despite the association of a low disease index with vegan and vegetarian dietary patterns, these people consume some processed foods. Several processed food and by-products with high amounts of proteins and amino acids, including fermented products, can contain significant amounts of BAs, impacting the food quality and safety. The antioxidant and anti-inflammatory effects of polyamines can play an important role in preventing chronic health conditions, such as cardiovascular disease and diabetes. In contrast, cancer is associated with high levels of some polyamines, caused by a change in your homeostasis. Basic care must be taken when purchasing food, which must be handled and/or industrialized under ideal hygienic quality conditions to avoid the proliferation of undesirable bacteria and, consequently, the accumulation of BAs that cause damage to health; however, more research on practical measures to reduce the BA content is needed to ensure food safety.

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