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Microbial production of histamine and the imperatives of processed food consumption

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Abstract

Food processing and storage increase the value chain of food items, both for commercial purposes and for future use by peasant producers. The roles of lactic acid bacteria (LAB) and yeasts in the processing of dairy, brewed, bakery and traditionally fermented foods cannot be over-emphasized. These organisms improve the nutritional contents and organoleptic properties of these foods. However, certain undesired products, especially from protein-rich foods, notably, biogenic amines often characterize the process. This is usually a physiologic response by the organisms to the food environments such as pH, and is often influenced by temperature, time and salt concentration. Histamine production during such a process often results in the accumulation of exogenous histamine in the foods, thereby constituting health hazards to the consumers. Histamine food poisoning affects virtually every system of the body due to the widespread physiological roles of histamine in the body, presenting a wide range of symptoms that make diagnosis difficult. More regulated scientific approaches should be adopted by food processors and handlers especially in the developing countries where technologies may not be available.

Keywords: Histamine, Histamine intolerance, Histamine producers, Processed foods.

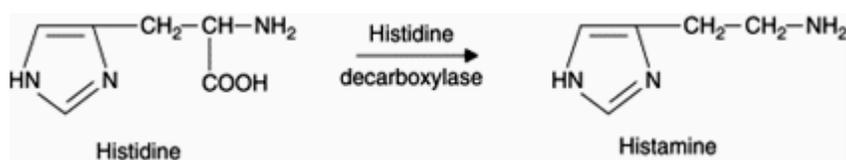
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INTRODUCTION

Consumption of freshly harvested foods is gradually becoming an old practice consequent upon increased daily activities, reduced farming activities and the invention of modern technology for food processing and storage. Foods are processed and preserved for future use and for commercial purposes. Microbial activities play major roles in processing of foods such as dairy, bakery, brewed and traditionally-fermented foods. The roles of yeasts and lactic acid bacteria (LAB) in the fermentation processes cannot be overemphasized. While the introduction of these organisms in the food is to get desired products, certain undesired microbial products are also formed. Biogenic amines are the most important of such products especially during lactic acid fermentation.

Histamine is the most biologically important biogenic amine owing to its role in body physiological and pathological processes. It can be endogenous or exogenous. Endogenous histamine is manufactured and stored in white blood cells: basophils and mast cells, liver, heart, skin, stomach etc from where it is released during allergic reactions and inflammatory responses during type 1 hypersensitivity reactions, or during



They are found in wide varieties of fermented foods such as yoghurt, sauerkraut, processed smoked meats and non-fermented foods such as avocados, dried fruits, shell fish, etc (Bover-Cid *et al*, 2014). While fruits are considered low histamine foods, fermented foods as well as fish and meat may contain high amount of histamine, resulting from microbial decarboxylation of histidine in the foods through decarboxylase enzymes (Comas-Baste *et al*, 2019). Exogenous histamine is also produced in the gut when histamine-producing bacteria outgrow the degrading ones or when there are reduced activities of Diamine Oxidase or its co-factors (Music, 2013). Food allergy occurs when food is

consumed and the body mounts immunological response against the food or its components. The food components are recognized as antigens by the body's cellular immunity. It can also result from chemical contaminants of the foods or microbial products during processing and storage. Allergic reactions following food consumption have been largely attributed to environmental factors such as chemical food additives for taste, flavor and antioxidants, herbicides and pesticides as well as genetic dispositions (Bartuzi, 2009) with little recourse to the role of histamine in such conditions. This article therefore seeks to bring to fore the role of histamine in food allergies including those of brewed drinks, fermented foods as well as spoiled foods.

infections to mediate inflammatory responses. (Kenedy *et al.*, 2012). It plays a wide range of roles in virtually every system of the body due to its effects on numerous cell types, which are dependent on its interaction with the receptor subtypes: H1, H2, H3 and H4 receptors (Singh and Jadhav, 2013; Thurmond, 2015; Seifert *et al*, 2013; Tiligada, 2012). Thus, it exerts a wide range of IgE-mediated allergic conditions such as asthma, rhinitis, food allergy, drug allergy, and allergic atopic eczema/dermatitis syndrome, pruritis, itching, vertigo and all IgE-mediated allergic conditions caused by histamine release (Panja *et al*, 2013). It also plays important roles in other immune responses, neurotransmissions and disease pathogenesis (Benly, 2015; Mirjam and Donald, 2012; Shahid *et al.*, 2009; Carlos *et al.*, 2009; Polazzi and Monti, 2010; Nuutinen and Panula, 2010; Passani *et al.*, 2014; Benly, 2015; Kenedy *et al.*, 2012; Steven *et al.*, 2008). Histamine was first discovered in 1910 but its role as a mediator of allergic reaction was first described in 1932 (Smolinska *et al.*, 2013).

Exogenous histamines on the other hand are histamines synthesized and stored outside the body cells. It is a product of decarboxylation of the amino-acid- histidine. A histamine-producing bacterium must be capable of decarboxylating histidine ie removing carbonic acid terminal of the amino acid and living only the amine terminal.

Table 1: Overview of different histamine sources

Histamine Type	Site of Production	References
Endogenous sources	White blood cells: (basophils and mast cells), liver, heart, skin, stomach etc.	Kennedy <i>et al.</i> , 2012
Exogenous sources	Fermented Foods: yoghurt, sauerkraut, oil-Bean Seed etc. Processed Foods: smoked fish, meats. Non-fermented Foods: avocados, dried fruits, shellfish, etc. Body System: gastrointestinal tract	Bover-Cid <i>et al.</i> , 2014, Comas-Baste <i>et al.</i> , 2019, Music, 2013.

Histamine Production during Food Spoilage

Food safety has remained a major problem among handlers due to microbial spoilage. The spoilage organisms that colonize a particular food depend largely on the type of food. Foods, especially those rich in dietary protein, have been found to be a suitable medium for most spoilage bacteria. The spoilage follows the degradation of the amino acid components of the proteins. Cases of food poisoning with scombroid fish such as tuna, skipjack, bonito and mackerel as well as some non-scombroid fishes such as sardines, herrings, pilchards, marling and mahi-mahi have been reported over the years due to the microbial decarboxylation of the abundant histidine in their gills, skin and muscles (Cheny *et al.*, 2010; Yoshinga and Frank, 1982). Evaluation of harvesting and post-harvesting procedure of longtail tuna fish using histamine level and histamine producer counts as parameters showed that the mean total and psychrophilic counts were 4.81 ± 0.26 and 4.66 ± 0.25 log₁₀ CFU/g, respectively. The examined samples of 20.0, 15.0 and 65.0% contained < 20, 20 to 50 and >50 ppm amount of histamine, respectively. Diverse bacterial isolates were identified as histamine-forming bacteria with *Clostridium perfringens* having the highest abundance in samples (24.4%) followed by *Proteus* spp. (23.0%), *Klebsiella* spp. (13.9%), and *Enterobacter* spp. (11.1%). (Valiollah *et al.*, 2012). Above studies also detected diverse

species of bacteria at different parts of the fish some of which were sufficiently shown to be histamine producers. These include *Lactobacillus* spp (eg *L. plantarum*), *Leuconostoc* spp (eg *L. mesenteroides*), *Streptococcus* spp, *Enterococcus durans*, *Vagococcus*, *Carnobacteria* spp. (eg *C. divergens*, and *C. maltaromaticum*), *Lactococcus* spp. (eg *L. lactis* and *L. raffinolactis*), *Aerococcus*-like bacteria, *Pediococcus*, *Vagococcus*, and *Weissella Carnobacterium*, *Vibrio* spp. (eg *V. fischeri*, *V. harveyi*, *V. pelagius*, and *V. splendidus*) etc. During food spoilage, certain spoilage flora synthesizes biogenic amine such as histamine and tyramine from their corresponding amino acids (Naila *et al.*, 2010). This has often been used as a quality index for such products. Analysis of pork and beef meats showed significant levels of biogenic amines (including histamine) with the levels increasing as spoilage progresses (Ruiz-Capillas and Jimenez-Colmenero, 2004; Komitopoulou 2017; Chung-Saint *et al.*, 2016).

Histamine Production during Lactic Acid Fermentation

Lactic acid bacteria (LAB) have been used in a wide range of fermentation-based food production such as in dairy products, fermented African condiments and brewed drinks. The global production and consumption of dairy and brewed products have been on the increase in recent times. According to Speedy (2003), milk

production will rise from 233 million metric tons in the year 2000 to 300 million metric tons in the year 2020 as a result of increased production of livestock as predicted by Food and Agricultural Organization (FAO). This projection is a consequence of increased demand on animal products (Speedy, 2003). According to a report by Sohravandi *et al.* (2011), the world per capita consumption of beer in 2004 was 72.9 L (annually) on average, while in some countries this figure was higher than 130 L. This has been on the increase as brewing technology is being developed.

Food processing using LAB is aimed at preserving and /or improving the nutritional contents and organoleptic properties of the foods. However, during the fermentation process, histamine and other biogenic amines are produced. The production of biogenic amines (which are alkaline substances) has been found to be a physiological response to the acidic medium following formation of lactic acid (Gale, 1946; Eitenmiller *et al.*, 1978). The optimum pH range for histamine production in most LAB-fermented foods is 4.8 - 6.0 (Shruti *et al.*, 2010). A number of lactic acid bacteria which are either starter probiotic or contaminant strains employed in food fermentation and brewing have been identified as histamine producers. These include: *Lactobacillus delbrukii*, *Pediococcus acidilactici*, *Lactobacillus brevis*, *Lactobacillus lindneri*, *Tetragenococcus muriatricus* *Bacillus licheniformis*, *B. coagulans* (Maijala and Eerola, 1993; Moon *et al.*, 2013; Priyadarshani and Rakshit, 2011; Sakamoto and Konings, 2003; Hammod *et al.*, 1999; Shilling *et al.*, 2015; Kobayashi *et al.*, 2016).

Conditions Affecting Histamine Production in Foods

The activities of microorganisms in any environment are influenced by a number of factors ranging from biological, chemical or physical factors. These include: nutrient availability, pH, temperature, salinity, pressure, growth phase, oxygen availability, strains of the organisms involved and presence of competing microbes. Some of these conditions are deliberately varied during processing and storage of food. Different foods and drinks have different methods of processing and storage. Each method has its peculiar physical or chemical conditions needed. However, microorganisms, including histamine producers, growing on/in the

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food item respond to these conditions, altering their activities and yielding a particular product. Histamine production has been found to be favoured by a number of factors. These factors could affect the organisms' ability to survive in the prevailing environment or their ability to utilize available substrates. These microbial responses are usually mediated by their genes but influenced by environmental conditions. Thus, during sequencing and analysis of genes of *Streptococcus thermophilus* used in the fermentation of dairy food products, low-temperature (4°C) incubation of milk inoculated with a histamine-producing strain showed lower levels of histamine than milk kept at 42°C. This reduction was attributed to a reduction in the activity of the *hdcA* enzyme itself rather than a reduction in gene expression or the presence of a lower cell number (Calles-Enriquez *et al.*, 2012). In fresh and canned tuna fish, McCarthy *et al.* (2002) reported that at ambient temperature (18°C), the level of histamine produced was higher after a certain period of time and decreased as the fish samples were stored at lower temperatures (4°C and 0°C). Optimum temperature for the growth of an organism ensures increased biomass in the growth medium and this often corresponds with their products in most cases. There may be variations. In a cell free extract of *S. thermophilus* strain, the histidine decarboxylase had its maximum activity at 50°C but decreased at higher temperature (60°C), while it maintained a detectable activity at 5°C. On the contrary, cells of the same strain produced more histamine at 40°C and decreased to a negligible at 25 and 20°C within the incubation period considered (Gardini *et al.*, 2001; Calles-Enriquez *et al.*, 2012; Marcobal *et al.*, 2012). The following are few important factors that greatly influence histamine production.

pH

The pH of the medium influences the production of histamine during fermentation. Lactic acid bacteria which have been much demonstrated to be histamine producers break down carbohydrate and other food sources to produce acidic environments which have been reported to ensure optimal activities of amino acid decarboxylases (Silla-Santos, 1996). Also, the stomach environment is naturally kept acidic through the secretion of gastric acid. The intestinal microbial flora capable of degrading histidine leverage on this low pH for their activities. Evaluation of biogenic amine levels in

traditionally fermented soybean paste in Korea revealed that a pH of 4.8-6.0 was the optimum range for their production (Shruti *et al.*, 2010). It has been stated that the production of biogenic amines in an acid environment is a physiological mechanism to counteract the acid environment, hence the correlation between the acidity and amine levels (Gale, 1946; Eitenmiller *et al.*, 1978). The amine production is a sole function of the decarboxylating bacteria not necessarily determined by the growth condition (Yoshinaga and Frank, 1982). The addition of glucono-d-lactone to acidify dry sausages decreased enterococci and Enterobacteriaceae counts without affecting the growth of lactic acid bacteria, resulting in lower histamine and tyramine concentrations (Maijala and Eerola 1993; Maijala, 1994). Thus, modulation of chemo-physical parameters to exclude the growth of biogenic amine producers is an essential step to reduce the production of histamine during fermentation (Suzzi *et al.*, 2003).

Salinity

The salt concentration of a growth medium is selective for microbial growth. Except for the halophilic microbes, the high salt environment causes cell death. The rate of amine production by *L. bulgaricus* (now *L. delbrueckii* subsp. *bulgaricus*) strain was considerably reduced when salt concentration in the medium increased from 0% to 6% (Chander *et al.*, 1989), while NaCl concentration ranging from 3.5% to 5.5% could inhibit histamine production (Henry-Chin and Koehler 1986). This can be linked to reduced cell yields obtained in the presence of high salt concentrations and to a distortion of the function of the membrane located microbial decarboxylase enzymes (Sumner *et al.*, 1990). A similar NaCl effect characterized cell yield and biogenic amine yields in *E. faecalis* EF37 (Gardini *et al.*, 2001). Cold brining innovative has been found to be useful in fish preservation. In an experiment carried out in Korea to determine the optimum condition for cold-brining of fresh whole herring and fillets, different concentration of brine (12, 14, 16 and 18%) and temperatures of 2, -1, -2, -4, -8 and -24°C for 25 and 18 days were used as parameters. The result showed that 14% brine at a temperature of -8°C was optimum (Won, 2008). Lactic acid bacteria are tolerant of moderate salt concentrations but not high concentration. Besas and Dizon, (2012) reported that histamine formation was detected at salt concentration of 10% which corresponds with

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total plate count of 10⁷ CFU/g lactic acid bacteria. The histamine level decreased at a salt concentration of above 17% as the LAB count decreased.

Temperature and Length of Storage

Different microorganisms have different temperatures for optimum activities. Some organisms may be thermophilic, mesophilic or psychrophilic. Newly harvested raw food may be contaminated with histamine producers but no histamine may be detected at the initial period. The histamine level produced has been found to be dependent on the temperature and duration of storage suitable to the colonizing organisms. Reports have shown that different natural and processed foods contain certain levels of histamine at varying temperatures and durations. Lactic acid bacteria can normally grow in the temperature range of 10-30 °C. Beyond this range their metabolism is reduced or stopped. The optimal temperature is 20-25 °C for *Oenococcus* and 25-30 °C (Kelly *et al.*, 1989) for *Lactobacillus*. A growth of LAB can be stopped at 35 °C. The effects of temperature and storage duration on histamine level in the Skipjack tuna have been investigated. The results indicated that histamine production was a function of both temperature and time. Fish samples were stored at temperatures of 30, 40 and 50°F and the mean histamine levels were found to be 2.01, 7.29 and 16.9mg/100g of tuna fish respectively. When the histamine levels were studied in relation to duration at different temperatures (30, 35, 40, 45, 50, 55 and 60°F) it was discovered that it took the shortest time of 52 days at 60°F to yield 500mg of histamine as against 104 days at 30°F to yield same quantity (Frank and Yoshinaga, 1987). The study did not however show any optimum temperature. Study undertaken to assess the shelf life and safety of yellowfin tuna at 0, 8 and 20°C revealed that after storage for 17 days at 0°C, histamine level was found to be lower than the Food and Drug Authority (FDA) safety level of 5 mg/100 g fish whereas fish stored at 8 and 20°C became unsafe for human consumption, reaching unacceptable histamine levels after 4 and 1 day, respectively (Guizani *et al.*, 2005). The production of histamine in foods especially fish does not only depend on active microbial activities. At temperatures of about 50°C, bacterial growth ceases, however, enzymic activity continues to produce more Biogenic Amines (Kosmerl 2013; Oyelakin and Adijivoni, 2017).

Table 2: Summary of conditions affecting histamine production in foods

Parameter	Effect on Histamine production	Mechanism of the Effect	Reference(s)
pH	Acidic pH favours histamine production	Amines are produced to counteract the harsh acidic environment.	Gale, 1946; Eitenmiller <i>et al.</i> , 1978, Silla-Santos, 1996
Salt Concentration	Decrease histamine production in non-halophiles; does not affect halophiles	High salt concentration causes cell death	Chander <i>et al.</i> , 1989, Gardini <i>et al.</i> , 2001, Besas and Dizon, 2012.
Temperature	Effects depend on optimum temperature; different bacteria have different optimum temperature	Higher cell yield at optimum temperature increase histamine yield	Kosmerl 2013; Oyelakin and Adijivoni, 2017; Kelly <i>et al.</i> , 1989
Time	The longer the duration the higher the amount of histamine yield if other factors are constant.		Frank and Yoshinaga, 1987

Histamine Intolerance

Histamine intolerance is the situation where there is excessive histamine in the body beyond the level the system can endure or decompose resulting in symptoms similar to allergy. Exogenous histamine is responsible for histamine intolerance. The term exogenous histamine is used to describe all the histamine that is not synthesized by the body cells. Exogenous sources of histamine range from natural plant sources such as fruits and garden crops to processed foods, meats and drinks as well as activities of intestinal microbial flora. Although exogenous histamine has been found in natural ripening fruits, berries, tomatoes, vegetables and spices (Sanchez-Perez, 2018), the main source has been found to be the activities of microbes either in the process of fermentation, spoilage or metabolic activities of gut microbial flora. The major cause of histamine intolerance is imbalance or disequilibrium between histamine production or consumption and its degradation. The human body tolerates a certain level of histamine. This threshold varies from one individual to the other. Under normal condition, the body checks this imbalance using two histamine degradative enzymes: Diamine

Oxidase (DAO) and Histamine-N-Methyltransferase (HNMT). Whereas HNMT breaks down the intracellular histamine, DAO keeps in check the extracellular histamine level.

Symptoms of Histamine Intolerance

There is a wide array of clinical manifestations of excess histamine or histamine intolerance. The symptoms of histamine intolerance are so vast that it is often difficult to suspect. They resemble most of other symptoms associated with food intolerance, other body system disorders and IgG-mediated allergen. The non-specific symptoms associated with excess histamine may involve the central nervous system (CNS), gastrointestinal tract, cardiovascular system, respiratory tract, skin, and reproductive system. CNS symptoms may include headaches, insomnia, agitation, dizziness, anxiety, depression, and panic disorder. Gastrointestinal symptoms include pain, bloating, diarrhea, indigestion and gastro-oesophageal reflux. Cardiovascular symptoms include changes in blood pressure, palpitations, and other heart rhythm disorders. Respiratory and airway symptoms include cough, respiratory distress, asthma, sneezing, rhinorrhea, nasal obstruction and phlegm. Symptoms of the skin and mucosal

intolerance include hives, itching, redness, pruritis, urticaria and swelling of the skin or lips and tongue similar to an anaphylactic reaction. Reproductive symptoms including dysmenorrhea and headaches associated with the menstrual cycle may be experienced in women (Maintz and Novak, 2007; Wantke *et al*, 1993). All symptoms may not occur in any single individual and the severity of symptoms varies, but the pattern seems to be consistent for each person.

Pathogenesis of Histamine Intolerance

Histamine intolerance, as reported, is not IgG-mediated. Histamine has a lot of reported non immunological activities in the body. The mechanism of the symptom presentation is as varied as the effects of histamine in the body. The principal mechanism could be impaired production of DAO or other factors that inhibit the function of the enzyme, DAO responsible for extracellular degradation of histamine. When present in excess in the gut, histamine can exert undesirable effects through the mechanisms earlier discussed in the roles of histamine in the body.

Epidemiology of Histamine Intolerance

Exogenous histamine, as earlier highlighted, come from food, wine, intestinal microflora among others. The distribution of this disease condition is as wide spread as the distribution of these consumables and histamine producers in the gut. Histamine intolerance is, therefore, a world disease since the incriminated organisms can be isolated from a wide range of foods found across the world. However, the incident rate depends largely on the level of technological advancement in terms of processing and storage of the food items since histamine formation takes place during these stages. It is expected that the incidents arising from processing and storage problems would be more in the remote poor communities where the facilities may be lacking. Continuous consumption of protein foods especially those rich in histidine is also a predisposing factor.

Although no clear-cut difference has been made between histamine intolerance and other allergies such as food allergy, reports about food intolerance, wine intolerance and fish poisoning have been published at different places with no detailed epidemiological reports made with reference to histamine intolerance. This is not

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unconnected with the difficulty in the diagnosis of the disease given its diverse symptoms which are often confused with other allergic reactions. However, some demographic information can be extracted from the available reports most of which have been made as food intolerance/allergy, wine intolerance and fish poisoning. No discrepancy in terms of age has been reported. Symptoms can be seen in all age groups, though with varying degrees. Based on more accurate measures as reviewed, the prevalence of clinical food allergy in preschool children in developed countries is now as high as 10%. In large and rapidly emerging societies of Asia, such as China, where there are documented increases in food allergy, the prevalence of proven food allergy is now around 7% in preschoolers, comparable to the reported prevalence in European regions (Prescot *et al*, 2013). In a study to determine the prevalence of wine intolerance in Mainz, a city in the wine-cultivating area of Rhine-Hesse, the results showed that out of the 948 respondents 68 (7.2% of respondents) reported intolerance to wine and/or allergy-like symptoms after drinking wine. Self-reported wine intolerance was more prevalent in women than in men (8.9% vs. 5.2%, $p = 0.026$). Wine-intolerant persons also more commonly reported intolerance to beer and alcohol in general (Wigand *et al*, 2012). In U. S., a retrospective study indicated that about 10.8% of the population had presented symptoms which were managed using antihistamines. It was also estimated that about 38% of the population suffer these symptoms once in their lifetime (Gupta *et al*, 2019). A review that focused on the role and likely adverse effects of both added and natural 'food chemicals' including benzoate, sulphite, monosodium glutamate, vaso-active or biogenic amines and salicylate found that a diet low in vasoactive amines alleviated chronic headache in 73 % of patients while another study reported a significant improvement of 27/44 (61 %) in idiopathic urticaria, angiooedema and pruritus on a diet low in dietary amines, although foods containing additives or high in natural salicylate were also restricted (Wantke *et al.*, 1993; Skypala *et al.*, 2015). Review studies on the prevalence of scombroid fish poisoning revealed that the highest number of cases were in the USA, Japan and the UK. This may be a reflection of reporting systems rather than incidence. Between 1992 and 2009, England and Wales reported 71 outbreaks affecting 336 people. Outbreaks were more common in summer than in winter. In the USA, between 1968 and 1980, 103 outbreaks involving 827 people were reported and in Japan

over the same period, 42 outbreaks affecting 4,122 people were recorded. A retrospective study in USA revealed 75% prevalence among retreat participants (Feldman *et al.*, 2005).

Diagnoses

There is no standardized diagnostic approach to histamine intolerance due to the complex number of symptoms it presents, mimicking allergic reaction and sometimes other gastrointestinal disorders. However, provisional diagnoses have been carried out at one time or the other to rule out the possibility of an allergic reaction or to establish absence of DAO activities. Skin prick test is used together with history of the symptoms to establish slow histamine degradation. In this, formation of wheal of 3 mm diameter for 50 minutes is a positive test (Kofler *et al.*, 2011). Serum diamine oxidase (DAO) activity and histamine level in patients with the symptoms have also been used as subjective tools. Here, enzyme immunoassay was used to determine the DOA level while high performance liquid chromatography can be used for histamine assay (Music *et al.*, 2013).

Treatment

Administration of antihistamines has remained the best approach to managing all symptoms of histamine intolerance. Medical supplementation of DAO and HNMT can also be recommended. Other management strategies include withdrawal from histamine-releasing diets or drugs that inhibit the activities of the degrading enzymes.

Conclusion

Histamine food allergy has remained one of the most poorly diagnosed food poisoning across the world making clinicians to shift attention to other forms of food poisoning. The handling (harvesting), processing and storage of foods are serious factors. Certain physico-chemical conditions needed for processing and storage are themselves thriving conditions for the histamine producers. For instance, certain ambient temperatures at certain durations are needed for fermentation. These same conditions are also needed by the organisms. The fermentation process provides internal acidic environments in the foods and these also trigger histamine

production. It is therefore important that food additives should include some natural buffers for foods that are fermented by lactic acid bacteria to ensure pH balance throughout fermentation process since pH is the main activator of histamine production. Care should be taken at the post-processing (storage) stage during which microbial activities continues. These problems are seen most at the remote poor areas where processing are inappropriately employed. Technological facilities to regulate these conditions may be lacking and there will be uncontrolled microbial activities, hence the need to introduce appropriate technology in the processing of the local foods. Since consumption of processed and packaged food items are on the increase, regulatory agencies should intensify efforts towards screening for histamine in foods. Food preservation methods should also include prevention of post-processing histamine production. Development of appropriate diagnostic protocol as well as drawing the attention of medical practitioners towards this menace will be of help in the management of histamine intolerance.

Conflict of interest

The authors have no conflict of interest to declare.

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