Review article

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Seafood histamine intervention to alcohol intake: regulation, metabolism and control

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Abstract

Background and objective: Seafood have high nutritional value since they contain sufficient amounts of protein, lipid, micronutrients and long-chain polyunsaturated fatty acids, especially omega3 fatty acid. However, histamine, a chemically hazardous biogenic amine, is produced by decarboxylation of histidine in the products through bacterial metabolism. Moreover, exessive alcohol intake may induce histamine intolerance. This study overviews histamine regulation, metabolism, and the control measures form technical intervention to alcohol consumption preventing histamine formation and its adverse effects.

Results and conclusion: Spoilage microorganisms are present in the environment and in raw materials, which might contaminate fish during catching, transportation and processing stages and produce a high concentration of histamine. Several studies revealed that the histamine concentration of fish products exceeded the permitted limits because of improper sanitation practices and storage conditions. *Morganella morganii* was recognized as the strongest histamine forming bacteria. Histamine is hardly detectable in food products due to its odorless and colorless features. This compound is highly stable and cannot be eliminate or disintegrated by processes such as cooking, canning and freezing. The best practical approach in control of histamine is applying HACCP system by focusing on proper chilling from fishing to table, to prevent growth of histamine-producing bacteria. Importantly, excessive alcohol consumption exposes the consumers at risk of histamine intolerance by interfering in the metabolism and degradation of histamine conducted by the enzymes in the human body. Therefore, both technical measures and consumers' atitude in alcohol consumption favor better histamine tolerance in body.

Keywords: Alcohol intake, biogenic amines, histamine, histamine-producing bacteria, seafood

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1. Introduction

Thirty percent of world population suffer from malnutrition. Given that seventy percent of earth covered with water, seafood consumption plays a pivotal role in human diet from the point of food security and public health [1]. Fish and other seafood products have a high nutritional value since they contain sufficient amounts of protein, lipid, micronutrients and high levels of long-chain polyunsaturated fatty acids. There is a direct association between seafood ingestion and positive clinical effects in human such as decrease in risk of heart diseases, reduction of inflammatory diseases especially arthritis, autoimmune diseases and cancer [2]. Fish oil mostly contain omega-3 fatty acids such as eicosapentaenoic acid (EPA) and docosa-hexaenoic acid (DHA) [3]. Although, fish consumption is essential for a balanced diet and has always been recommended, high levels of proteins and free amino-acids in fish would elevate the spoilage [4]. However, histamine (that is a microbial-derived byproduct) is one of biogenic amines mainly found in seafoods and may induce allergenic symptomes in the consumers. Therefore, consumtion of these food products can result in the risks associated with histmine intake rather than their favorable nutrinal properties.

Despite developments in food industry and application of various preservation methods such as canning, as the most conventional method of processing seafood products, the risk of food poisoning has been a great concern for both consumers and food manufacturers [5]. Since pathogenic microorganisms reside ubiquitously in the environment and on raw materials, they might contaminate the fish during fishing, transportation and processing stages and threaten the consumer's health under uncontrolled proce-sses. Among many pathogens, toxin-producing bacteria such as non-proteolytic psychrotroph *Clostridium botulinum* and histamine-producing bacteria such as Photobacterium are of high concern [6]. The first one can be avoided by visual evaluations of swelled cans but the other cannot be checked visually and may pose higher adverse impact on individuals [4]. Histamine food poisoning is a food-borne disease, which is generated by marine microorganisms, or those able to grow in the potent food products. It can be suppressed by the activity of some enzymes in gastrointestinal tract but intake of some inhibitors such as alcohol may inhibit the activity of these enzymes in the lumen. Inclusion of safe seafood in food supply chain has been of main concerns [7,8]. Interestingly, preparation of healthy foods is also in accordance with halal status, which is defined as providing safety to people. In the present study, regulations, formation, toxicology, health impact, and preventive approaches of histamine are highlighted.

2. Biogenic amines

In chemical, the biogenic amines are organic, aliphatic, alicyclic, and heterocyclic nitrogen bases that are non-volatile with low molecular weight. They are generated via decarboxylation of amino acids by amino acid decarboxylases [9]. A number of food products, notably fish and fish products, cheese and fermented foods (meat, dairy products, vegetables, beer and wine) may contain high amounts of biogenic amines [10]. These amines were considered as indicators of food quality spoilage level in some products as they reduce the organoleptic score of food [11,12].

The most important biogenic amines found in food products are: histamine, tyramine, putre-scine, cadaverine and phenylethylamine that are produced by decarboxylation of histidine, tyro-sine, ornithine, lysine and phenylalanine, respec-tively. Putrescine could also originate from dea-mination of agmatine [13]. The formation mecha-nism of biogenic amines is illustrated in Figure 1. In food products, different gram negative bacteria species such as *Escherichia coli*, *Hafnia alvei*, *Klebsiella pneumoniae*, *Morganella morganii*, *Pseudomonas* species and *Serratia* are capable of producing biogenic amines. These bacteria are

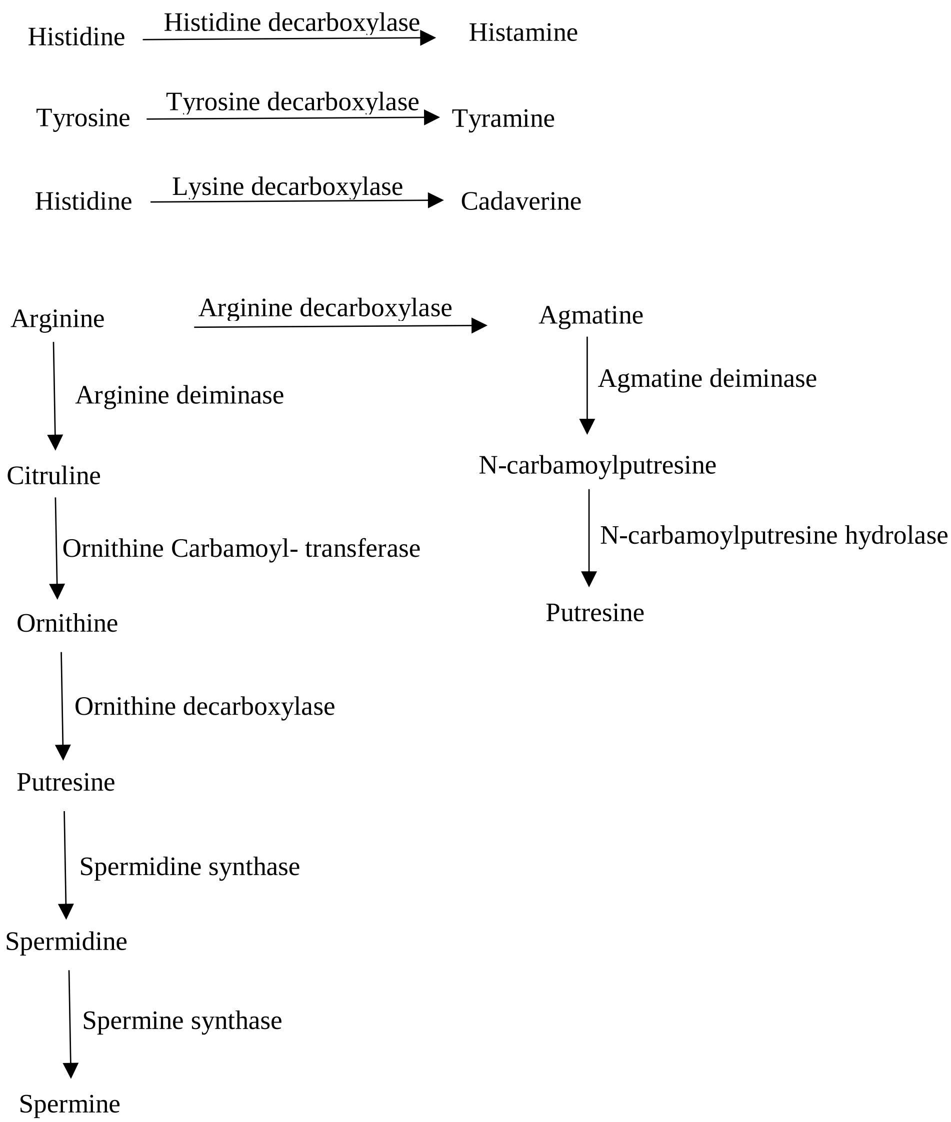

Figure 1- Formation pathway of some biogenic amines

generally responsible for food safety issues which necessitates their control by Good Manufacturing Practice (GMP) and effective sanitary actions [14]. Gram positive bacteria especially lactic acid bacteria (LAB) may also produce biogenic amines [15]. LAB are of fermented food micro-flora or a part of starter culture [13]. A study reported tyramine biosynthesis by *Enterococcus faecalis*, *E. faecium* and *E. durans* species [16]. Another study reported synthesis of putrescine by *Lactococcus lactis* in dairy products [17]. Under normal conditions, the absorbed biogenic amines from food are quickly detoxified by amine-oxidase enzymes of intestinal mucus cells and excreted to urine [18]. The enzymes are classified into Monoamine Oxidases (MAOs) and Diamine oxidases (DAOs). Histamine could also be detoxified by methyl or acetyl transferase [15, 19]. These enzymes protect digestive system from harmful biogenic amines [20]. If the function of aforementioned enzymes become compromised due to genetic disorders, gastro-intestinal diseases or enzyme inhibitors such as alcohol and antidepressants, biogenic amines might enter to blood and lead to toxic effects on different organs [12,21,22]. The most probable incidence of biogenic amines in foods is uncontrolled microbial activity that lead to high detoxification activity of body and ultimately may result in food-borne poisoning [23,24].

Contaminated food products mainly contain several types of biogenic amines. Thus, more investigations are required to study their synergistic effects. For example, presence of putrescine and cadaverine may increase histamine toxicity and reduce the threshold dose of histamine poisoning by five times [12,20,25].

2.1. Regulations on histamine in food products

The toxic effects of biogenic amines depend on factors including the type of biogenic amine, presence of inhibitor compounds, efficiency of detoxifying mechanisms and individual sensitivity. Therefore, accurate determination of toxicity threshold of biogenic amines is difficult. Generally, intake of biogenic amines more than 40 mg kg^{-1} per meal is considered potentially toxic. Currently, histamine is the only biogenic amine with maximum permitted level declared by regulatory organizations [20].

According to Codex Alimentarius, higher than 20 mg of histamine per 100 g of fish or fish products may lead to scombroid fish poisoning [26,27]. In November 15th 2005, European Commission (EC No 2073/2005) set a permissible limit for histamine in seafood products containing high levels of histidine (families of *Scombroidae*, *Clupeidae*, *Engraulidae* and *Scombresosidae* species). EC declared that the mean histamine amount in nine samples from a single batch must be below 100 mg kg^{-1}, for two samples of a batch between 100 to 200 mg kg^{-1} histamine and no sample must exceed 200 mg kg^{-1}. In case of processing with brine, histamine can be less than two times of the above limits [4,9,28]. FDA has declared a maximum permissible amount of 50 mg kg^{-1} for histamine in fresh and canned Scombridae fish to prevent poisoning [29], whereas in national standards of countries such as Iran, Indonesia, Brazil and South Africa the limit is 100 mg kg^{-1}. Also, Codex Alimentarius, Turkey and Australia have set 200 mg kg^{-1} as the legal maximum level [30-36]. Joint FAO/WHO Expert Committee on Food Additives (JECFA) has considered a dose of 50 mg histamine, as NOAEL. However, based on the collected data of Codex Alimentarius from various industries, applying the principles of Good hygiene practice (GHP) and Hazard analysis of critical control point (HACCP) will reduce histamine levels in fish to less than 15 mg kg^{-1} [37].

2.2. Histamine metabolism and adverse effects

Histamine ($C_5H_9N_3$), scientifically called (2-(4-imidazolyl) ethylamine was first discovered by Dale and Laidlaw in 1910 [38]. In 1932, histamine was identified as a mediator of anaphylactic reaction which indicated that it is of natural amines found in the body [39]. Histamine is naturally produced by mast cells, basophils, platelets, neurons and enterochromaffin cells and stored as histamine-heparin complexes in intracellular vesicles and released by stimulus. Histamine is a significant player in different biological reactions and contributes in vasodilation, allergy and gastric acid secretion [37,40].

Histamine affects the body by binding to four histamine receptors (H_1R, H_2R, H_3R, H_4R) in target cells [38]. It would be metabolized in two paths: 1. Oxidative deamination by MAO and DAO (previously known as histaminase) enzymes 2. Methylation of the ring by histamine-N-methyltransferase (HMT) [41].

MAO can be found in nerve terminals, liver and gastrointestinal tract. There are two types of MAO: Type A, first was found in liver and gastrointestinal tract and Type B, first discovered in nervous system [20]. HMT is capable of converting histamine into methyl-histamine, which itself can be converted into N-imidazole acetic acid by MAO and finally combined with ribose for its urinary excretion. In humans, DOA is often expressed in the intestines and restricts the entry of external histamine into the blood circulatory system. HMT can extensively be found in different organs such as liver, colons, small intestine, lungs and spleen and exclusively involved in histamine metabolism while DAO can also break down other biogenic enzymes such as putrescine and cadaverine [18,37].

Histamine intolerance occurs due to an imbalance of histamine intake and the capacity of histamine detoxifying of the body. DAO is the key enzyme in metabolizing digested histamine [38]. Histamine degradation depends on DAO activity and not-affected histamine may cause various symptoms similar to allergic reactions. Consumption of histidine and histamine-rich foods, alcohol (in particular, red wine that is rich in histamine) and drugs that release histamine or inhibit DAO function may cause diarrhea, headache, nasal congestion, asthma, low blood pressure, cardiac arrhythmia, itching and flushing [42,43]. In addition, histamine accumulation might occur in the presence of other biogenic amines as competitor in binding to DAO enzymes, allergens and bacteria and in the case of gastrointestinal bleeding. For example, the biogenic amines such as putrescine may occupy histamine binding sites in the active sites of detoxifying enzymes and lead to elevation of free histamine in blood. Moreover, in digestive disorders, due to change in enterocytes, DAO production decreases [38]. Although, some histamine intolerance are temporary and the symptoms will disappear after the causes are eliminated (for instance, by stopping the use of DAO-inhibiting drugs) [44].

2.3. Potent food sources, outbreaks and the most histamine-producing microorganisms

High levels of histamine mostly occur in products that undergo biological fermentation such as ripened cheese, sauerkraut, wine and processed food or in products that were subjected to microbial spoilage such as fish and fish products [19]. Fish, especially families of Scombridae (Tuna and Mackerel), Clupeidae (Sardine and Herring) and Engraulidae (anchovy), were commonly reported as the responsible cause of scombroid poisoning in various countries [6,45-47]. They have high amounts of free histidine in the muscle tissue and include species such as skipjack, yellowfin, big-eye, bluefish, albacore, Bonito and saury. Scombroid poisoning caused by yellowfin and mackerel were regularly reported worldwide due to their large-scale distribution and high consumption rates. Some non-Scombridae species such as mahi-mahi and bluefish were involved in scombroid poisoning as well in the United States of America (USA) [48,49]. According to Centers for Disease Control and Prevention (CDC), 16 cases of histamine poisoning were reported in the USA following to the ingestion of fish and its products in 2014 [6]. In August 2003, the largest outbreak of scombroid poisoning occurred in California, USA, in which fish consumption with high levels of histamine (2000-3800 mg kg^{-1}) was accounted as the cause. Similarly, an incidence of poisoning due to consumption of yellowfin containing high histamine amounts (4900 mg kg^{-1}) were reported in Senegal [32].

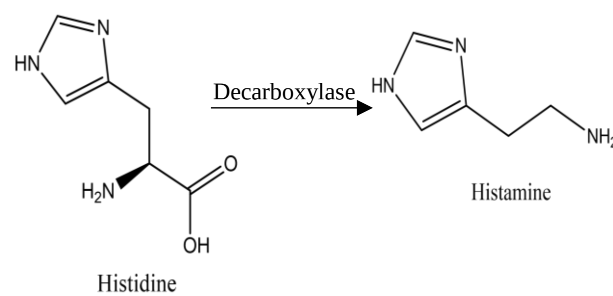

Figure 2- Mechanism of histamine formation from histidine

Scombroid poisoning outbreak has been frequently reported in Taiwan which mostly was associated with consuming tuna fillet, mackerel and marlin [49]. Histamine may reach toxic levels prior to fish spoilage or organoleptic alteration. After rigor mortis, histamine is generated from histidine through growth and metabolism of decarboxylase-forming bacteria. Not only such bacteria were found in fish and other seafood products but they were isolated from cheese, fermented sausage and wine as well [48]. Figure 2 illustrates chemical structure and conversion of histidine into histamine.

Though numerous fish species are capable of producing histamine, they have different production capacity. According to European Food Safety Authority (EFSA) reports, *Morganella morganii*, *Klebsiella pneumoniae*, *Hafnia alvei* (as the main histamine-producing bacterial species), *Morganella psychrotolerans*, *Photobacterium damselae* and *Photobacterium phosphoreum* were recognized as histamine-forming bacteria [19,37,49]. Also, intestinal bacteria such as *Proteus vulgaris*, *Proteus mirabilis*, *Enterobacter aerogenes*, *E. cloacae*, *Serratia fonticola*, *Serratia liquefaciens* and *Citrobacter freundii* are capable of producing histamine in fish as well [50].

In addition to intestinal bacteria, species such as *Clostridium, Vibrio alginolyticus*, *Acinetobacter lwoffii, Plesiomonas shigelloides*, *Pseudomonas putida*, *Pseudomonas fluorescens*, and *Aeromonas* were reported to produce histamine as well [49]. Furthermore, a recent study has reported the presence of histamine-producing bacteria related to *Proteus*, *Klebsiella*, *Rahnella* sp. and Acinetobacter in fillets of a marlin species but none of three main histamine-producing bacteria (i.e. *Morganella morganii***,** *Klebsiella pneumoniae* and *Hafnia alvei*) were found [51]. Some yeast species such as *Debaryomyces hansenii*, *Pichia jadinii*, and *Geotrichum candidum* are capable of producing biogenic amines [24,52,53].

Staphylococcus species were frequently reported as histamine-producing bacteria in salted fish. It has been reported that they comprise 50 percent of total histamine-producing microorganisms. It has been indicated that such bacteria including *Staphylococcus epidermidis* and *Staphylococcus capitis* isolated from salted Anchovy fish can produce more than 1000 and 400 mg kg^{-1} of histamine, respectively [49].

Morganella morganii, with the potential to produce histamine more than 1000 mg kg^{-1} in broth, is recognized as the most vigorous producer of histamine in fish and other seafood products [54], especially in spoiled fish that were stored at temperatures above 15ºC. Bacterial growth of *M. morganii* is directly associated with accumulation of high levels of histamine in mackerel stored at 25ºC highlighting its significant role in histamine production and scombroid poisoning [54].

In 2007, 347 students were poisoned due to consumption of fried fish in a Taiwanese high school. It was observed that histamine level (52.3 mg per 100 g) were higher than other biogenic amines in the samples. Considering the development of allergy-like symptoms in victims and notable histamine levels, it was speculated that use of low quality fish in school meal commenced the outbreak and therefore the incident classified as histamine poisoning. Additionally, *Acinetobacter baumannii* was identified as the poisoning agent [55].

Another episode of food poisoning occurred in southern Taiwan in 2014 due to consumption of fried Milkfish steaks. 37 people were poisoned because of eating fried steaks containing 86.6 to 235 mg per 100 g histamine. *Enterobacter aerogenes*, *Enterobacter cloacae*, *Morganella morganii*, *Serratia marcescens*, and *Hafnia alvei* were identified as the histamine producers [56].

3. Control measures of histamine

3.1. Technical considerations

Amongst all identified seafood hazards, histamine is the primary cause of seafood-borne diseases in the U.S [45,57]. In 1998, a low permitted level of 5 mg per 100 g was set by US FDA for seafood products to prevent foodborne diseases based on HACCP principles, called Seafood Hazard Analysis and Critical Control Point [57-59]. Histamine is hardly detectable in food products due to its odorless and colorless features. This compound is highly stable and cannot be eliminate or disintegrated by processes such as cooking, canning and freezing. Therefore, monitoring histamine in seafood industry is a critical matter [60].

Histamine formation may occur as a result of poor hygiene, incorrect storage temperature and time during processing and distribution of fish and fish products [22,57]. Immediate cooling of freshly caught tuna is an important action to prevent histamine production. Scombroid poisoning mostly happens because of lengthened intervals between fishing and cooling time (mainly more than 6 hours from the time of death) or failure in reducing storage temperature below 4.4ºC [27,61]. In 1998, a scombroid poisoning outbreak occurred in Pennsylvania. it was reported that prolonged retaining of fish in 25.8ºC in fishing vessels was the reason, though the fish were kept in the ice-pack hold prior to transportation to factory for processing [62].

The majority of histamine-producing bacteria are mesophilic. Thus, among other environmental determinants, temperature is the key factor for their growth and production of histamine [63].

In fish products, a hygienic procedure should be undertaken to prevent contamination of *M. morganii* during processing and distribution. The microorganism is capable of producing 25 mg per 100 g histamine in Salmon fish (non-scombroid species) which has levels of free histidine in their muscle tissue [48]. Smoked Salmon that kept in 5ºC has been reported to contain over 100 mg kg^{-1} of histamine [64].

Fish freezing can relatively reduce the bacterial growth, particularly gram-negative bacteria in which histamine formation can be reduced within three months by inhibition of histidine decarboxylase. Despite that, histamine can build-up in muscles due to inappropriate preparation prior and after storage under freezing condition. In this case, the enzymatic activity may initiates prior to freezing [19,28,57].

In canned fish, presence of histamine toxic levels indicates use of poor-quality fish or inappropriate preparation. During tuna fish thawing and processing period, high bacterial population can be found until canning process [48]. Indeed, high level of bacteria and histamine load in these products are directly related to inappropriate storage parameters such as temperature [65].

3.2. Beneficial microorganisms' intervention

Given the discovery of some bacterial enzymes similar to amine oxidases, which break down biogenic amines of food products, the initial studies were focused on bacteria isolated from foodstuffs and the possibility of using biogenic amine-decomposing microorganism (mainly belonged to probiotics) to reduce biogenic amines of food products. Recent tendency to use health-friendly live bacteria called probiotics in the commercial food products is increasing due to their beneficial effects on the immune system and generally on the human health [66].

Dapkevicius et al. mentioned that four species of *Lactobacillus casei* (*L. casei*) were able to break down histamine in fermented fish paste [67]. Some researchers found that two species of *L. casei* successfully reduced biogenic amines of vegetables. They linked this finding to antagonistic characteristics of *L. casei* against biogenic amine-producing bacteria [68]. Zaman et al. discovered that *Bacillus amyloliquefaciens* and *Streptococcus carnosus* can decline histamine accumulation in fermented fish sauce [69]. In another study concerned with investigating various probiotics in starter culture of Turkish fermented sausage, researchers were able to significantly reduce the content of biogenic amines during the storage period by *L. casei* and *L. acidophilus* in starter culture [70].

Capozzi et al. investigated decomposition of biogenic amines in wine by two species of *L. plantarum* (*L. plantarum* NDT 09 and *L. plantarum* NDT 16) that were able to degrade putresine and tyramine. They found that using such bacteria leads to decrement in biogenic amines [71]. Zhang et al. studied the reduction of biogenic amines in silver carp sausage by *L. plantarum* ZY-40. They found that this species significantly reduces the accumulation of putrescine and cadaverine by acidification of environment and hence preventing the growth of Pseudomonas and Enterobacteriaceae [72].

Xie et al. investigated on the reduction of biogenic amines in fermented sausages with the emphasis on starter culture. They used different starter cultures with different groups of bacteria: group L (*L. plantarum*), group X (*Staph. Xylosus*), group M (*L. plantarum* + *Staph. xylosus*) and group C (no starter culture). They observed that *Staph. xylosus* reduced biogenic amines of tyramine (21%), histamine (25%) and cadaverine (27%) compared to other groups [73]. Kongkiattikajorn studied the potential of starter culture (including cultures of *L. sakei* KM5474 and *L. plantarum* KM1450) in reducing biogenic amines of traditional Thai fish sausage. Compared to control samples, these micro-organisms showed inhibitory effects on histamine formation. Moreover, comparison of starter cultures revealed that *L. plantarum* KM1450 had the maximum inhibitory effect [74]. Turhan et al. investigated the effect of *L. rhamnosus* microencapsulation on Turkish sausage (sucuk) during six months storage. They found that samples without *L. rhamnosus* contained more biogenic amines and simultaneous application of *L. rhamnosus* and *L. plantarum* provides higher efficacy in reducing biogenic amines [75]. *L. casei* and *L. plantarum* sequestered from industrial fermented sausages in Argentina were capable of catalyzing tyramine and histamine degradation [76]. In a study, samples of various cheese products were investigated for the presence of lactic acid bacteria that are able to break down biogenic amines. The results have shown that 17 isolated species decomposed tyramine and histamine [77].

A number of wine lactic acid bacteria were evaluated for their potential degradation of biogenic amines. *In vitro* studies have been reported that *L. casei*, *L. hilgardii, Pediococcus parvulus, Oenococcus oeni*, *L. plantarum*, and *P. pentosaceus* demonstrated remarkable potential for degrading histamine, tyramine and putrescine [78].

3.3. Reducing alcohol/alcoholic beverages consumption

Recent research have not dealt with the relation between histamine intoxication and alcohol or alcoholic beverage intake in details, as a principal public health concern. However, histamine is abundantly found in fermented beverages, notably wine [79]. As mentioned before, a high intake of this monoamine may lead to severe adverse reactions and histamine-mediated symptoms in humans with a low capacity to catabolize extrinsic histamine, although below the toxicity thresholds [12,21]. In some cases, dietary exposure to histamine through the consumption of wine (red and white) was higher than the recommended maximum values [80]. Microbiota present in wines was mainly composed of *L. hilgardii, L. mali, Oenococcus oeni, Pediococcus parvulus, E. faecium*, Enterobacteria, and *Staph. epidermidis* [12,81-83]. It has been identified a great relevance of the alcoholic fermentation by yeasts and LAB as the fundamental cause of histamine formation in wine. Incorrect processing and preservation can elevate histamine levels, due to the bacterial activity [12,84]. During a biological deacidification, L-malic acid is transformed into L-lactic acid by LAB, leading to a higher pH, microbiological stability, and better wine taste. Spontaneously, LAB can start producing undesirable substances, such as histamine, which negatively affect wine quality and safety [83]. Nowadays, no legal or regulatory restrictions exists for histamine content in wine in most countries but some European countries recommend higher limits that range from 2 to 10 mg l^{-1} [83,85]. In general, alcohol intake occurs in two pathways: 1-direct consumption by drinkers, 2-indirect through consumption of alcohol-containing foods. Available studies highlighted the great relevance of brain histamine and alcohol addiction [86]. Given the recent reports, Histamine H_3 receptor (H_3R) in brain has an important role in the regulation of alcohol abuse-related behaviors. H_3R, mediating the neural effects of histamine, is highly expressed in the brain and regulates the release of histamine and a variety of neurotransmitters, such as dopamine, acetylcholine, and noradrenaline [87,88]. Histamine is naturally removed by histamine-N-methyl-transferase (HMT) by conversion to tele-methylhistamine, which is further metabolized to N-tele-methylimidazole-acetic acid by monoamine oxidase and aldehyde dehydrogenase (ALDH). About 30 to 40 percent of total histamine is oxidized by diamine oxidase (DAO) and aldehyde oxidase to imidazolacetic acid. Alcohol metabolite can interfere with histamine degradation by competition with N-tele-methyl-imidazole and imidazole acetaldehyde for these enzymes [89]. Several studies have demonstrated significantly higher levels of histamine in cortical grey matter of postmortem brain in alcoholics than in normal control brains. It may imply that histamine synthesis and/or metabolism are basically altered by alcohol or alcoholic beverage consumption [87,90]. Chronic alcohol consumption in neonatal rats suckling alcohol-feeding mother increased brain histamine. Alcohol selectively prevents the monoamine oxidase activity in the brain and platelet membranes and also diamine oxidase activity in rat tissues. This is a reason why alcohol ingestion can provoke food-induced histamine intolerance [89].

Alcohol remains a main reason of liver disease worldwide [91]. Findings have indicated that 60% of people in North America and Europe consume alcohole and about 50% of cirrhosis are associated with alcohol intake worldwide. Excessive intake of alcohol is of main ethiologies of global mortality [92]. It has been observed a 4-fold increase in histamine concentration significantly in the cortical regions of patients with hepatic encephalopathy. Changes in brain histamine and H_3R are found in patients with hepatic failure, which is encountered with sleep disturbances, abnormal circadian rhythm, and other neuropsychiatric disorders [87,90]. Alcohol is consumed by more than half of the population in Europe (59.9% of current drinkers), America (54.1%) and Western Pacific Region (53.8%) [93]. Worldwide, alcohol consumers drink approximately 32.8 grams of pure alcohol per day or 15.1 liters of pure alcohol annually [94]. In 2016 alcohol consumption in the EU countries in adults (aged 15 and above) was higher than 11.3 liters of pure alcohol per capita (women: 4.7 liters; men: 18.3 liters), 9.9 liters of which were consumed in the form of recorded alcohol and 1.4 liters in the form of unrecorded alcohol [93]. The consumption of homemade produced alcohol may be associated with an increased risk potentially dangerous impurities or contaminants such as histamine in these beverages [95-97]. According to the close rela-tion between alcoholism and histamine increase, it is suggested to change the lifestyle and decline alcoholic beverage consumption in the countries that have no restriction in consumption of alcohol containing foods.

4. Conclusion

Histamine food poisoning is the most prevalent hazard related to marine products. US Food and Drug Administration and Codex Alimentarius has announced that histamine with levels greater than 50 and 200 mg kg^{-1}, respectively, can lead to adverse health effects. The simplest and most practicable approach in control of histamine is applying HACCP system focusing on proper chilling from fishing to table in order to prevent the metabolism and growth of histamine-producing bacteria. In addition, some lactic acid bacteria especially *L. casei*, *L. plantarum*, *L. acidophilus*, *L. rhamnosus*, and *Streptococcus carnosus* can degrade biogenic amines. On the other hand, direct relevance of brain histamine and alcoholism was observed. Importantly, alcoholic beverage consumption may exacerbate the toxic effects of histamine due to suppression of natural detoxification system in the intestine. Therefore, having a balanced lifestyle towards no or reduced alcohol intake in favor of other bioactive compounds consumption are recommend by scientists.

5. Conflict of interest

Tuthors declare no conflict of interest.

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