Histamine in Foods: Its Safety and Human Health Implications

KRISHNA PRASAD RAI*, HARE RAM PRADHAN, BAL KUMARI SHARMA and SOM KANTA RIJAL
Department of Food Technology and Quality Control, Babarmahal, Nepal

* Corresponding author: raikrishna1@gmail.com

This article reviews the overall aspects of histamine, one of the most potent biogenic amine, which is formed by decarboxylation of histidine protein rich foods in fish and fish products, dairy products, meat and meat products, fermented vegetables and soy products, and alcoholic beverages such as wine and beer. Normally, three basic conditions i.e. high content of free histidine, bacterial histidine decarboxylase activity and high temperature storage environment elevates the level of histamine in foods. Several chromatographic methods utilizing thin layer chromatography (TLC), high performance liquid chromatography (HPLC), gas chromatography (GC) and colorimetry, fluorimetry and ELISA technique have been developed for the analysis of biogenic amine including histamine. Histamine usually exceeding 1000 mg/kg has been implicated with scombrotoxosis. Several government authorities including Codex Alimentarious Commission has also set the level of histamine in different food products varying from 5 to 40 mg/100g. Proper technical regulations and surveillance mechanism as well as hygienic and bio-technological advancement in food manufacturing establishment could be the good preventive measures of low histamine foods in future.

Key words: Histamine, fish, scombrotoxin, Nepalese perspective, safety

Introduction
Histamine is a common and most important bioactive amine occurring in different foods and beverages. It is generally formed by decarboxylation reaction during which alpha carbonyl group is removed from free amino acid histidine. In addition to its well-known occurrence and important role as a regulator of some human physiological processes, histamine occurs in many different foods and beverages, although their concentrations vary extensively not only between different food varieties but also within the varieties themselves. In spite of being considered as endogenous to certain foods, such as some fruits and vegetables, histamine in foods normally is formed as a result of non-controlled microbial action (Halász et al., 1994). Foods likely to contain elevated levels of histamine include fish and fish products, dairy products, meat and meat products, fermented vegetables and soy products, and alcoholic beverages such as wine and beer (Shalaby, 1996).

Histamine is a naturally occurring substance in mammalian physiology. It is contained in mast cells and basophils, and its biological effects are usually seen only when it is released in large amounts in the course of allergic and other reactions. Histamine exerts its effects by binding to receptors on cellular membranes in the respiratory, cardiovascular, gastrointestinal, haematological, immunological systems and the skin (Cavanah and Casale, 1993). Histamine like other biogenic amines is of concern in relation to human health since it is responsible for several toxicological symptoms such as pseudo-allergic reactions (histaminic intoxication), food-induced migraines, and hypertensive crisis due to the interaction between monoamines and monoamine-oxidase inhibitor drugs. Normally, there is no hazard for a healthy consumer, whose monoamino and diaminooxidases will carry out the catabolism of biogenic amines. However, toxicological reactions may occur after the intake of food containing relatively large amounts of histamine (Bodmer et al., 1999). Histamine intolerance results from buildup of histamine in the system that causes a series of toxic effects similar to a common food allergy such as swelling, rashes, hives and asthma-like symptoms as well as gastrointestinal symptoms (Maintz and Novak, 2007).

Structure and Physiological Functions of Histamine
Chemically, histamine is a 4-(2-aminoethyl) imidazole and is a primary amine arising from the decarboxylation of the amino acid L-histidine. The imidazole ring has two nitrogen atoms. Besides, histamine has two basic center, namely the aliphatic amino group and the nitrogen atom of the imidazole ring which does not already have a proton. Under physiological conditions, the aliphatic amino group (having a pKₐ around 9.4) will be
protonated, whereas the second nitrogen of the imidazole ring (having a $pK_a \approx 5.8$) will not be protonated. Thus, histamine is normally protonated to a singly charged cation (Paiva et al., 1970).

Endogenous histamine plays important roles in a number of normal and abnormal biological processes like vasodilatation, anaphylaxis, neurotransmission and gastric secretion (Joosten, 1988; Shalaby, 1996). Histamine possesses a powerful biological function, serving as a primary mediator of the immediate symptoms noted in allergic responses (Taylor, 1986). It is a powerful vasodilator in animal tissues and it also stimulates acid secretion in the stomach. A growing array of pharmaceutical agents is being designed to interfere with either the synthesis or the action of histamine. A prominent example is the histamine receptor antagonist Cimetidine (Tagamet), a structural analog of histamine. It promotes the healing of duodenal ulcers by inhibiting secretion of gastric acid (Lehninger et al., 2004).

**Figure 1. Molecular structure of histamine (Lehninger et al., 2004)**

### Biosynthesis and Metabolism of Histamine

Numerous bacteria and some yeast are reported to express histidine decarboxylase activity, thus having the capacity to form histamine (Halász et al., 1994; Straub et al., 1995). Pre-requisites for the undesired formation of histamine by microorganisms in foods are availability of free amino acid histidine, presence of decarboxylase active microorganisms, and favorable conditions for decarboxylation of amino acids. Among the bacteria are several species of the genera Bacillus, Clostridium, Enterobacter, Escherichia, Lactobacillus, Pediococcus, Proteus, Pseudomonas, and Salmonella (Bodmer et al., 1999). Likewise, Zygoascus hellenicus var. hellenicus is a yeast capable of producing histamine in wine (Chang et al., 2009). There is good evidence that in processed (fermented) foods, the contaminating microflora rather than the starter cultures is responsible for the generation of increasing histamine levels (Teuber, 1993). Nevertheless, in microbial food processing, all starter culture candidates (e. g. strains of Lactobacillus) should also be carefully checked for their potential of histamine formation, under the appropriate processing conditions, and only strains with no or low histamine formation capacity should be selected for production purposes. Microbial strains with high proteolytic enzyme activity also potentially increase the risk for histamine formation in food systems, by increasing the availability of free histidine (Suzzi and Gardini, 2003).

![Histidine decarboxylase](image)

**Histidine decarboxylase**

Histidine

**Histamine**

**N-methyltransferase**

**Diamine Oxidase**

N-Methylhistamine

Imidazole acetaldehyde

**Figure 2. Biosynthesis and catabolism of histamine**

According to Shalaby (1996), among microorganism found in meat products, histamine was produced by Hafnia alvei, Klebsiella oxytoca, Morganella morganii, Edwardsiella spp. as well as lactic acid bacteria such as Lactobacillus brevis, L. buchneri, L. divergens, L. carnis, L. curvatus and L. hilgardii. However, some sausage samples contained histamine levels of about 50 mg/kg and also high levels of amines that can potentiate the toxicity of histamine. Therefore, these samples could cause histamine intoxication in sensitive individuals (Taylor, 1985).

Histamine can be catabolized by several routes. It can be oxidatively deaminated by diamine oxidase (DAO, or histaminase) to imidazole acetaldehyde (and imidazoleacetic acid) as well as methylated by histamine methyl transferase (HMT) to form methylhistamine or its side chain can be methylated or acetylated tyramine (Rice et al., 1976; Taylor, 1986). Monoamine oxidase (MAO) is also important in histamine metabolism (Taylor, 1986).

Normally, low amount of biogenic amines including histamine are metabolized to physiologically less active degradation products during the food intake process in the human gut. This detoxification system includes specific enzymes (e.g. monoamine oxidase MAO, diamine oxidase DAO). However, upon intake of high loads of biogenic amines with foods, this detoxification system is unable to eliminate biogenic amines sufficiently. Moreover, in case of insufficient DAO-activity, caused by e. g. genetic predisposition, gastrointestinal diseases, or inhibition of DAO-activity due to secondary effects of medicines or alcohol, already low amounts of biogenic amines cannot be metabolized efficiently. If detoxification is inefficient,
biogenic amines are readily absorbed and get into systemic circulation, leading to toxic effects (Bodmer et al., 1999). However, high histamine consumption causes life threatening intoxication; lower amounts can lead to headache, nausea, hot flushes, skin rashes, sweating, and respiratory distress, cardiac and intestinal problems (Bodmer et al., 1999). Histamine at levels usually exceeding 1000 mg/kg has been implicated with certain food intoxications such as scombrotoxicosis (Taylor et al., 1984) or the “cheese syndrome” (Taylor et al., 1982).

**Occurrence of Histamine in Foods**

Histamine presence is common to most fermented fruits and vegetables products, meats, fish, cheese, and other proteineous food material containing high level of histidine amino acid. One of the major sources of histamine is fish, accounting 8% for tuna species among globally traded fishes (FAO, 2014). Table 1 summarizes the list of food materials in which histamine was traced at a significant level.

**Toxic Effects and Histamine Poisoning**

Histamine usually exceeding 1000 mg/kg has been implicated with certain food intoxications such as

<table>
<thead>
<tr>
<th>Foods</th>
<th>Histamine level (mg/kg)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Japanese sardine fish sauce</td>
<td>1500 ± 30</td>
<td>Kuda and Miyawaki, 2010</td>
</tr>
<tr>
<td>Chub mackerel</td>
<td>1480 ± 10</td>
<td></td>
</tr>
<tr>
<td>Dried fish products, Taiwan</td>
<td>63.1–479.0</td>
<td>Huang et al., (2010)</td>
</tr>
<tr>
<td>Cheese</td>
<td>&gt;100</td>
<td>Aygun et al., (1999)</td>
</tr>
<tr>
<td>Frozen fish</td>
<td>10 -267</td>
<td></td>
</tr>
<tr>
<td>Fresh fish</td>
<td>Trace</td>
<td>Hwang et al., (2003)</td>
</tr>
<tr>
<td>Shrimp</td>
<td>Trace</td>
<td></td>
</tr>
<tr>
<td>Fish products</td>
<td>Trace to 26</td>
<td></td>
</tr>
<tr>
<td>Fish products of Fiji</td>
<td>*ND to 64</td>
<td></td>
</tr>
<tr>
<td>Fish products of Thailand</td>
<td>ND to 143</td>
<td>Tao et al., (2011)</td>
</tr>
<tr>
<td>Fish products of Cambodia</td>
<td>53 to 148</td>
<td></td>
</tr>
<tr>
<td>Fish products of Philipine</td>
<td>19 to 1530</td>
<td></td>
</tr>
<tr>
<td>Sufu fermented soyabean foods</td>
<td>18.2</td>
<td></td>
</tr>
<tr>
<td>Chinese soya sauces</td>
<td>N.D. to 592</td>
<td>Lu et al., (2009)</td>
</tr>
<tr>
<td>Fermented silver carp sausages</td>
<td>38.22-46.18</td>
<td>Hu et al., (2007)</td>
</tr>
<tr>
<td>Indian mackerel</td>
<td>162</td>
<td>Shakila et al., (2003)</td>
</tr>
<tr>
<td>Supermarket Kimchi, Taiwan</td>
<td>ND to 535</td>
<td>Tsai et al., (2005)</td>
</tr>
<tr>
<td>Fish in Greek</td>
<td>2.7 to 220</td>
<td>Claeys et al., (2009)</td>
</tr>
<tr>
<td>Kimchi, Taiwan</td>
<td>&lt;4.9 to &gt;100</td>
<td>Tsai et al., (2005)</td>
</tr>
<tr>
<td>Miso products, Taiwan</td>
<td>N.D. to 21.6</td>
<td>Kung et al., (2007)</td>
</tr>
<tr>
<td>Fresh seafoods</td>
<td>0-9</td>
<td></td>
</tr>
<tr>
<td>Processed seafoods</td>
<td>0-3</td>
<td>Auerswald et al., (2006)</td>
</tr>
<tr>
<td>Dried tuna</td>
<td>800</td>
<td></td>
</tr>
</tbody>
</table>

* N.D. Not detected below 7mg/kg

scombrotoxicosis (Taylor et al., 1984) or the “cheese syndrome” (Taylor et al., 1982). Askar and Treptow (1993) indicated that histamine at a concentration of 500 mg/kg in food to be hazardous for human health. Normally, three pre-conditions can elevate the post-mortem histamine concentration in fish: (1) a sufficiently high content of free histidine, (2) the presence of bacterial histidine decarboxylase, and (3) environmental conditions, such as high temperature (Lehane and Olley, 2000). Scombrotoxic fish poisoning also known as scombroid or histamine fish poisoning is a common illness associated with seafood which is caused by bacterial spoilage of certain finfish such as tuna, mahi-mahi, bluefish, mackerel, bonito, which is rich in histidine amino acid. As bacteria break down fish proteins, byproducts such as histamine and other substances that block histamine breakdown build up in fish. Eating of spoiled fish that have high levels of these histamines can cause in
histamine receptors, $H_1$, $H_2$ and $H_3$ (Cavanah and Casale, 1993). The most common symptoms result from action on the cardiovascular system. Histamine causes dilatation of peripheral blood vessels, causing urticaria, hypotension, flushing and headache. Histamine-induced contraction of intestinal smooth muscle causes abdominal cramps, diarrhoea and vomiting. Pain and itching associated with the urticarial lesions may be due to sensory and motor neuron stimulation (Taylor, 1986). Gastric acid secretion is regulated by histamine through $H_2$ receptors located on the parietal cells (Soll and Wollin, 1977), but is unknown whether this action accounts for some of the symptoms observed in cases of histamine poisoning (Taylor, 1986).

A fairly efficient detoxification system exists in the intestinal tract of mammals (including humans), which is capable of metabolizing normal dietary intakes of biogenic amines. The enzymes monoamine oxidase (MAO) and diamine oxidase (DAO) play an important role in this detoxification process. However, upon intake of high loads of biogenic amines with foods, this detoxification system is unable to eliminate biogenic amines sufficiently (Wendakoon and Sakaguchi, 1993). Moreover, in case of insufficient DAO-activity, caused by e. g. genetic predisposition, gastrointestinal diseases, or inhibition of DAO-activity due to secondary effects of medicines or alcohol, already low amounts of biogenic amines cannot be metabolized efficiently. If detoxification is inefficient, biogenic amines are readily absorbed and get into systemic circulation, leading to toxic effects (Sattler et al., 1985; Götz et al., 1996). According to Maijala & Eerola (1993) the toxic limits of histamine at levels of 8±40 mg, 40±100 mg and over 100 mg may cause slight, intermediate and intensive poisoning, respectively. Putrescine, cadaverine and agmatine have been identified as potentiators that enhance the toxicity of histamine to humans by depressing histamine oxidation (Taylor, 1986). Besides DAO, monoamine oxidases (MAO) distributed in different tissues of the human body also participates in the physiological inactivation of biogenic amines. Again, certain drugs (MAO-inhibitors) are well known to decrease the activity of MAO, leading to an increased risk for pathophysiological processes after intake of food contaminated with biogenic amines.

The toxicological level of a particular amine depends among other things on the ability of detoxification system of the intestinal tract and on the presence of other amines, and is therefore very difficult to establish. A limit 100 mg histamine/kg food was suggested. An ingestion of 100 mg of histamine or 10–100 mg of tyramine can cause poisoning (Eerola, Roig-Sagues, & Hirvi, 1998).

Histamine poisoning is intoxication, so the incubation period is rather short, ranging from several minutes to a few hours after ingestion of the contaminated fish. The duration of the illness is usually short also; symptoms subside within a few hours in most cases. The intoxication is characterized by a wide variety of possible symptoms of cutaneous (rash, urticaria, edema, localized inflammation), gastrointestinal (nausea, vomiting, diarrhoea, cramping), hemodynamic (hypotension), and neurological (headache, palpitations, flushing, tingling, burning, itching) nature. The acute symptoms generally are transient, lasting only 8 to 12 hours.

Histamine poisoning is often confused diagnostically with food allergies, because of the similar symptoms and the equivalent effectiveness of antihistamines. However, histamine poisoning can be easily distinguished from food allergy on the basis of (1) the lack of a previous history of allergic reactions to the incriminated food, (2) the high attack rate in group outbreaks, and (3) the detection of high levels of histamine in the incriminated

Cheeses with high histamine levels have also been associated with outbreaks of histamine poisoning. The types of cheese incriminated include Swiss, Gouda, Gruyere, Parmesan and Provolone among others (Bean et al., 1997; Vale & Gloria, 1998). The symptoms associated with intoxication include hypotension, nausea, vomiting, abdominal pain, diarrhea, facial flushing, burning throat, thirst, lip swelling, edema, localized inflammation, rash, itchiness and palpitation. Putrescine and cadaverine, also found in cheese, can increase histamine toxicity, facilitating its passage through the intestinal barrier (Chang et al., 1985).

Histamine exerts its toxicity by interacting with the receptors on cellular membranes. There are three types of histamine receptors, $H_1$, $H_2$ and $H_3$ (Cavanah and Casale, 1993). While the most common symptoms result from action on the cardiovascular system, histamine causes dilatation of peripheral blood vessels, causing urticaria, hypotension, flushing and headache. Histamine-induced contraction of intestinal smooth muscle causes abdominal cramps, diarrhoea and vomiting. Pain and itching associated with the urticarial lesions may be due to sensory and motor neuron stimulation (Taylor, 1986). Gastric acid secretion is regulated by histamine through $H_2$ receptors located on the parietal cells (Soll and Wollin, 1977), but is unknown whether this action accounts for some of the symptoms observed in cases of histamine poisoning (Taylor, 1986).
food (Taylor, 1986). Antihistamine therapy is the optimal mode of therapy for histamine poisoning. Symptoms usually subside rapidly after treatment with $\text{H}_1$ antagonists, such as diphenhydramine or chlorpheniramine, or $\text{H}_2$ antagonists, such as cimetidine. Since the disease is self-limited, pharmacological intervention is generally not required in mild cases.

Moreover, several factors such as alcohol and other amines (diamines putrescine and cadaverine), individual sensitivity, inactivation of detoxification mechanisms due to genetic deficiencies, gastrointestinal diseases or MAOI treatments, potentiate the toxicological effects of histamine (Brink et al., 1990; Marine´-Font et al., 1995). Hence, it is difficult to evaluate the toxicity degree of biogenic amines in food, and thus, to establish toxic threshold levels for these food microcomponents. Formation of carcinogenic nitrosamines constitutes an additional toxicological risk related to biogenic amines, especially in meat products that contain nitrite and nitrate as curing salts (Marine´-Font et al., 1995).

### Preventive Measures

The most frequent foodborne intoxications and intolerances, caused by biogenic amines, involve histamine. The evidence of histamine-related food intoxication (Silla Santos, 1996), histamine-induced food intolerance (Wantke et al., 1993; Götz et al., 1996) and enteral histaminosis (Sattler et al., 1999) clearly represents a challenge for the food industry to produce foods with extremely low histamine levels. Therefore, biogenic amines are of concern in relation to food spoilage, food safety, and food intolerance and their content in foods should be as low as possible. Now, there are several researches focused on minimizing the production of histamine and other biogenic amine formation in foods mainly fish and other shellfish products. Some efforts are summarized in Table 2.

### Table 2. Preventive measures for histamine suppression in different food models

<table>
<thead>
<tr>
<th>Food model</th>
<th>Particulars</th>
<th>Use of mixed cultures for histamine reduction</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fish sausage</td>
<td>Histamine</td>
<td>$S. \text{xylosus}$ and $L. \text{casie}$</td>
<td>Hu et al., (2007)</td>
</tr>
<tr>
<td>Dried sausage</td>
<td>Histamine</td>
<td>$S. \text{xylosus}$, $P. \text{pentosaseus}$, $L. \text{casie}$</td>
<td>Gardini et al., (2002)</td>
</tr>
<tr>
<td>Chinese style dry fermented sausage</td>
<td>Histamine and other biogenic amines $S. \text{xylosus}$, $P. \text{pentosaseus}$</td>
<td>Rai, (2005)</td>
<td></td>
</tr>
<tr>
<td>Fish sauce</td>
<td>Histamine</td>
<td>20% (w/v) nuka-paste</td>
<td>Kuda and Miyawaki, (2010)</td>
</tr>
</tbody>
</table>

Apart from these, the following tools can be implementing to minimize the risk of such contaminants in foods:

- Legal regulation of $S. \text{xylosus}$
- Implementation of GMP, GHP, HACCP
- Good surveillance and monitoring of histamine in fish and other fermented foods.
- Export import certification to marine foods

Apart from these, some microbiological antagonistic technique has been successfully reported to control the histamine production in meat products (Table 2).

Evidently, foods or raw materials rich in free histidine, such as some fish species (scombroid fish, herring, and anchovies) are potentially more jeopardized to contain high histamine levels. Moreover, the level of free histidine in fish and fishery products even increases during storage, due to the action of endogenous and contaminating proteases. Therefore, in order to keep histamine levels in fish and fish products as low as possible, both proteolytic and decarboxylation activities must be inhibited immediately after the catch. Several studies clearly show that immediate storage on ice drastically decreases the rate of histamine formation, although not completely inhibiting it (Lehane and Olley, 2000).

### Low Histamine Technology

Free histidine liberated through proteolysis is the main precursor of histamine. In general, results from numerous investigations demonstrate that high histamine contents in most foods and beverages mainly result from microbiological contamination. Normally, the presence and composition of free amino acids in a certain foodstuff cannot be changed without major changes of
its taste, flavour and nutritional value. Therefore, state
of the art technology must focus on complete lack of
unwanted, decarboxylase-active microorganisms, and/or
use of process conditions that do not allow amino acid
decarboxylases to be active (FDA, 1998). Since biogenic
amines may exert synergistic effects and compete for
detoxification by DAO, food producers should optimize
their technology to guarantee low levels for all biogenic
amines in their products (Bodmer et al., 1999).

Although every food variety requires special precautions
and technology (HACCP concept), there are a few
common parameters which can be defined for low-
histamine technology. First, high quality raw materials,
free of histamine, must be used. Additionally, proper
and careful treatment (harvest, transport, storage) of raw
materials until processing is absolutely necessary. Growth
and activity of decarboxylase-positive microorganisms
(spoilage microbes) must be avoided, and activity of
endogenous proteases and amino acid decarboxylases
have to be inhibited. This can be achieved by technological
measures (removal of endogenous microflora) and proper
and hygienic production conditions (cooling, freezing,
salting etc.) If microbial transformations such as alcoholic
or other fermentations are part of the production process,
use of specifically selected starter cultures for these
fermentations is important, as well as strict control of
the whole fermentation process. Activity of foodborne
decarboxylases and unwanted microbial activity must
be suppressed, while fermentation is performed under
strict control by selected, decarboxylase negative starter
cultures. Finally, the whole production process should
be embedded in a specific quality control procedure and
quality management system, including analytical control
at critical points (Hungerford et al., 1997; Bodmer et al.,
1999).

Practically histamine-free, premium quality products not
only are of major importance to all modern consumers,
but also allow the growing number of individuals at risk
a more diversified nutrition. Therefore, low-histamine
technology can help to make safety food products.

Legal Standard and Safety Level for Histamine
fish specified 50 mg/100 g as the toxicity level and 5
mg/100 g as the defect action level because histamine is
not uniformly distributed in a decomposed fish. Similarly,
European Union Directive No. 91/493 stipulated that
nine independent samples from each batch should
 correspond to: (1) an average histamine concentration
lower than 10 mg/100 g, (2) no more than two samples
out of nine with a concentration of between 10 and 20
mg/100 g and (3) no sample with a histamine content
higher than 20mg/100g. The limits imposed by these
regulatory agencies have been taken into consideration
for developing the color scale. The color intensity
range of 0–50 µg/ml of histamine works well with the
color scale and the spectrophotometric absorbance too
(Patange et al., 2005).

The critical dose of oral histamine has been estimated
to be in the range of 100-200 mg (Luthy and Schlatter,
1983; Treptow and Askar, 1996). In rats, the no-
observed adverse effect level for tyramine, putrescine,
and cadaverine was reported to be at 180 mg/kg of
body weight and day (Til et al., 1997). However, some
regulatory standards for histamine in different foods are
presented in Table 3.

Histamine in Nepalese Perspective
Altogether 53 samples of Rohu (Labeo rohita) were
collected from different markets of Nepal. The analytical
results have been shown in Table 4. All fish samples
showed histamine in the range of ND to 10.40 mg/100g.
The highest concentration range was ND to 10.4mg/
kg found in Biratnagar and Birgunj samples, while the
lowest concentration of histamine was found in samples
collected from Bhairahawa 0.13 – 0.39 mg/100g.

Table 3. Legal standard for histamine in different countries and organizations

<table>
<thead>
<tr>
<th>Food</th>
<th>Standard</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fish sauce</td>
<td>40 mg/100g</td>
<td>CODEX STAN 302 (2011)</td>
</tr>
<tr>
<td>Sardine fish, Tuna</td>
<td>20 mg/100 g</td>
<td>CODEX STAN 94 – 1981, CODEX STAN 70-1981</td>
</tr>
<tr>
<td>Sea foods</td>
<td>200 ppm</td>
<td>Australian Food Standards Code, 2001</td>
</tr>
<tr>
<td>Sea foods</td>
<td>100 ppm</td>
<td>EC, 2003</td>
</tr>
<tr>
<td>Sea foods</td>
<td>50 ppm</td>
<td>USA (FDA, 1998)</td>
</tr>
<tr>
<td>Sea foods</td>
<td>100 ppm</td>
<td>South African Bureau of Standards, 2001</td>
</tr>
<tr>
<td>Edible fresh fish</td>
<td>5 mg/100 g</td>
<td>FDA, 1998</td>
</tr>
<tr>
<td>Fish</td>
<td>10 mg/100g</td>
<td>Canada Standard</td>
</tr>
</tbody>
</table>
Table 4. Histamine determined in different fish sample sold in Nepalese markets

<table>
<thead>
<tr>
<th>Particulars</th>
<th>Places</th>
<th>Total No of samples</th>
<th>Mean ± SD</th>
<th>Percentage for out of standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flesh</td>
<td>Kakarvitta</td>
<td>10</td>
<td>3.51±2.47</td>
<td>10</td>
</tr>
<tr>
<td>Flesh</td>
<td>Bhairahawa</td>
<td>10</td>
<td>0.28±0.08</td>
<td>0</td>
</tr>
<tr>
<td>Flesh</td>
<td>Kathmandu</td>
<td>11</td>
<td>0.25±0.02</td>
<td>0</td>
</tr>
<tr>
<td>Flesh</td>
<td>Biratnagar</td>
<td>4</td>
<td>4.18±3.79</td>
<td>36.36</td>
</tr>
<tr>
<td>Flesh</td>
<td>Birgunj</td>
<td>7</td>
<td>1.49±0.52</td>
<td>0</td>
</tr>
</tbody>
</table>

Source: Rai et al. (2012)

Further Scopes and Research Needs

Although much is known about Histamine Poisoning in food, there are still many gaps in our knowledge. Sufficient data are not available at this stage in the country for an adequate risk characterization and thus risk assessment. Further strategies for risk management and risk communication can be put in place only after additional data are generated and analyzed. Further, regulatory action may need to take into account the impact of potentiators, and the identification of such substances in various foods. When analyzing suspect fish for histamine, the simultaneous detection of other common putrefactive amines such as cadaverine and putrescine could be advantageous. The mechanism of toxicity of Histamine Poisoning is still not clearly understood, which is unsatisfactory. More research is needed to determine the role that potentiators or other toxins may play in causing the disease. It is particularly important that Histamine Fish poisoning be clearly differentiated from syndromes caused by endogenous toxins such as ciguatoxins that may be present in finfish from time to time. More research still needs to be done on post harvest contamination in order to improve quality control procedures. Identification of points at which temperatures specific bacterial contamination would occur leading to histamine formation needs to be researched where this has not been done already, on harvesting, transporting, storage, processing and retailing practices for those foods most likely to cause histamine poisoning. A study of the correlation between the amine content and the bacterial counts needs to be done. Ideally, each amine would be correlated with its respective amine-producing bacteria. Government regulatory agencies require the removal of histamine contaminated food products from the market place and should established mechanisms to allow efficient and complete trace back of incriminated fish to the point of origin. Furthermore, there is a need for global standardization of histamine detection methods, laboratory accreditation and proficiency testing. A rapid and cheap assay for detecting histamine in contaminated food items (like meat, fish and cheese) should be developed.

Conclusions

Excess level of histamine in foods and beverages may cause histamine poisoning for human. Histamine does
not effect on organoleptic characteristics; however, it clearly induces the food intolerance in an increasing number of human populations. Therefore, histamine content - and content of other harmful biogenic amines – must be limited to the lowest possible level.

In the past 15 years, authorities and producers around the world have become more aware of the need for quality assurance in relation to food as a result of which standards for sea food are increasing and exposure to spoiled seafood and thus Histamine Poisoning is likely to become less prevalent. Consumers are becoming minor food borne illness in world. Litigation following food poisoning incidents is becoming more common, and producers, distributors and restaurants will increasingly be held liable for the quality of the products of the products they handle and sell.

Practically histamine-free, premium quality products not only are of major importance to all modern consumers, but also allow the growing number of individuals at risk a more diversified nutrition. Even though histamine induced food intolerance causes major impairment of life quality to an increasing part of our population, most cases remain undiagnosed or misdiagnosed. Therefore, there is an absolute need for better information of physicians, dieticians and consumers.

So far, only few countries have defect or hazard action levels for histamine in their food regulation, mostly restricted to fish, and these levels do not yet consider the evidence from internal histamine poisoning. Therefore, a proper technical regulations and monitoring mechanism seems to be set up in Nepal.

Table 5. Standard analytical methods for histamine determination

<table>
<thead>
<tr>
<th>Methods</th>
<th>Sensitivity</th>
<th>Application</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLC</td>
<td>&lt;20ppb</td>
<td>Fish and fishery products</td>
<td>Shalaby, (1996); Shakila et al., (2001); Zhihua et al., (2011)</td>
</tr>
<tr>
<td>TLC/densitometry</td>
<td>LOD= 0.7mg/L, LOQ= 1.1mg/L</td>
<td>Wines</td>
<td>Romano et al., (2012)</td>
</tr>
<tr>
<td>ELISA kits</td>
<td>2mg/kg</td>
<td>Fish</td>
<td>Aygun et al., (1999); Hungerford and Wu, (2012)</td>
</tr>
<tr>
<td>HPLC</td>
<td>5-100ng</td>
<td>Fish and fishery products</td>
<td>Shakila et al., (2001); Innocente et al., (2007)</td>
</tr>
<tr>
<td>HPLC-FLD and UV detector</td>
<td>LOD= 1.5 mg/kg, LOQ= 4.5 mg/kg</td>
<td>Fish samples</td>
<td>Tahmouzi et al., (2011)</td>
</tr>
<tr>
<td>Colorimetry</td>
<td>1mg/100g</td>
<td>Fish and fishery products</td>
<td>Patange et al., (2005)</td>
</tr>
<tr>
<td>Filter paper electrophoresis</td>
<td>-</td>
<td>Tuna fish</td>
<td>Tao et al., (2009)</td>
</tr>
<tr>
<td>GC–FID, GC-MS</td>
<td>5 µg/g</td>
<td>Fish and fishery products</td>
<td>Hwang et al., (2003)</td>
</tr>
<tr>
<td>Ultra-performance liquid chromatographic (UPLC) method</td>
<td>0.032 and 0.098 µg/l;</td>
<td>pork, beef, chicken and fish meat, cheese and edible mushrooms</td>
<td>Dadakova et al., (2009)</td>
</tr>
<tr>
<td>Quantitative Food EIA test kits</td>
<td>1ppm</td>
<td>Tuna and other marine fish products</td>
<td>Kose et al., (2011)</td>
</tr>
<tr>
<td>Chronopotentiometric analysis</td>
<td>LOD: 1.31mg/L, LOQ: 3.54mg/L</td>
<td>Cheese</td>
<td>Jaroslava and Stojanovic, (2011)</td>
</tr>
<tr>
<td>Amino Acid Analyzer HPLC system</td>
<td>-</td>
<td>Sea foods</td>
<td>Auerswald et al., (2006)</td>
</tr>
</tbody>
</table>
References


Organization.


