Chapter 27: Scombrotoxin (Histamine) Formation

Updated:

Potential Food Safety Hazard

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Scombrotoxin formation as a result of time/temperature abuse of certain species of fish can cause consumer illness. The illness is most closely linked to the development of histamine in these fish. In most cases histamine levels in illness-causing fish have been above 200 ppm, often above 500 ppm. There are indications that decomposition can result in the production of other toxins (e.g. biogenic amines, such as putrescine and cadaverine) that have the potential to cause illness, even in the absence of histamine formation. Such illnesses have been reported in a number of fish species. FDA has also received a number of consumer complaints concerning illnesses that are associated with the consumption of decomposed shrimp (FDA, 2001a; FDA, 2001b).

Scombroid poisonings have primarily been associated with the consumption of tuna, mahi mahi, and bluefish. However, Table #3-1 lists a number of species that are also capable of developing elevated levels of histamine when temperature abused (FDA, 2001a).

Scombrotoxin formation

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Certain bacteria produce the enzyme histidine decarboxylase during growth. This enzyme reacts with free histidine, a naturally occurring chemical that is present in larger quantities in some fish than in others. The result is the formation of histamine.

Histamine-forming bacteria are capable of growing and producing histamine over a wide temperature range. Growth is more rapid, however, at high-abuse temperatures (e.g. 70°F [21.1°C]) than at moderate-abuse temperatures (e.g. 45°F [7.2°C]). Growth is particularly rapid at temperatures near 90°F (32.2°C). Histamine is more commonly the result of high temperature spoilage than of long term, relatively low temperature spoilage. Nonetheless, there are a number of opportunities for histamine to form under more moderate abuse temperature conditions.

Once the enzyme histidine decarboxylase has been formed, it can continue to produce histamine in the fish even if the bacteria are not active. The enzyme can be active at or near refrigeration temperatures. The enzyme is likely to remain stable while in the frozen state and may be reactivated very rapidly after thawing.

Freezing may inactivate the enzyme-forming bacteria. Both the enzyme and the bacteria can be inactivated by cooking. However, once histamine is formed, it cannot be eliminated by heat (including retorting) or freezing. After cooking, recontamination of the fish with the enzyme-forming bacteria is necessary for additional histamine to form. For these reasons, histamine development is more likely in raw, unfrozen fish.

The kinds of bacteria that are associated with histamine development are commonly present in the salt water environment. They naturally exist on the gills and in the gut of live, salt water fish, with no harm to the fish. Upon death, the defense mechanisms of the fish no longer inhibit bacterial growth, and histamine-forming bacteria start to grow and produce histamine. Evisceration and removal of the gills in a sanitary manner may reduce, but not eliminate, the number of histamine-forming bacteria. However, when done under insanitary conditions, these steps may accelerate the process of histamine development in the edible portions of the fish by spreading the bacteria to the flesh of the fish.

With some harvesting practices, such as long lining, death can occur before the fish is removed from the water. Under the worst conditions histamine formation can already be underway before the fish is landed on the vessel. This condition can be aggravated when the fish is allowed to remain on the line for a period of time after death, a situation that in certain tuna species may cause its internal temperature to increase to a more favorable growth range for the enzyme-forming bacteria.

The potential for histamine formation is increased when the flesh of the fish is directly exposed to the enzyme-forming bacteria. This occurs when the fish are processed (e.g. butchering or filleting).

At least some of the histamine-forming bacteria are halotolerant (salt-tolerant) or halophilic (salt-loving). This causes some salted and smoked fish products produced from scombrotoxin-forming species to continue to be suspect for histamine development. Further, a number of the histamine-forming bacteria are facultative anaerobes that can grow in reduced oxygen environments (FDA, 2001a).

Control Measures

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Rapid chilling of fish immediately after death is the most important element in any strategy for preventing the formation of scombrotoxin, especially for fish that are exposed to warmer waters or air, and for large tuna that generate heat in the tissues of the fish following death. It is recommended that:

- Generally, fish should be placed in ice or in refrigerated seawater or brine at 40°F (4.4°C) or less within 12 hours of death, or placed in refrigerated seawater or brine at 50°F (10°C) or less within 9 hours of death;

- Fish exposed to air or water temperatures above 83°F (28.3°C), or large tuna (i.e., above 20 lbs.) that are eviscerated before on-board chilling, should be placed in ice (including packing the belly cavity of large tuna with ice) or in refrigerated seawater or brine at 40°F (4.4°C) or less within 6 hours of death;
- Large tuna (i.e., above 20 lbs.) that are not eviscerated before on-board chilling should be chilled to an internal temperature of 50°F (10°C) or less within 6 hours of death.

This will prevent the rapid formation of the enzyme histidine decarboxylase. Once this enzyme is formed, control of the hazard is unlikely.

Further chilling towards the freezing point is also desirable to safe-guard against longer-term, low-temperature development of histamine. Additionally, the shelf-life of the fish is significantly compromised when product temperature is not rapidly dropped to near freezing.

The time required to lower the internal temperature of fish after capture will be dependent upon a number of factors, including:

- The harvest method;
    - Delays in removing fish from a long line may significantly limit the amount of time left for chilling and may allow some fish to heat up after death;
    - The quantity of fish landed in a purse seine or on a long line may exceed a vessel's ability to rapidly chill the product;
- The size of the fish;
- The chilling method;
    - Ice alone takes longer to chill fish than does an ice slurry or recirculated refrigerated sea water or brine, a consequence of reduced contact area and heat transfer;
    - The quantity of ice or ice slurry and the capacity of refrigerated sea water or brine systems must be suitable for the quantity of catch.

Once chilled, the fish should be maintained as close as possible to the freezing point (or held frozen) until it is consumed. Exposure to ambient temperature should be minimized. The allowable exposure time is dependent primarily upon the speed with which the fish were chilled on-board the harvest vessel and whether the fish has been previously frozen (e.g. on-board the harvest vessel).

Unfrozen scombrotoxin-forming fish has a safe shelf-life (days before elevated levels of histamine are formed) that is dependent upon the harvest methods, the on-board handling, and the time/temperature exposures throughout processing, transit, and storage. This safe shelf-life can be as little as 5 to 7 days for product stored at 40°F (4.4°C).

Any exposure time above 40°F (4.4°C) significantly reduces the expected safe shelf-life. For this reason, fish that have not been previously frozen should not be exposed to temperatures above 40°F (4.4C) for more than 4 hours, cumulatively, if any portion of that time is at temperatures above 70°F (21°C); or the fish should not be exposed to ambient temperatures above 40°F (4.4°C) for more than 8 hours, cumulatively, as long as no portion of that time is at temperatures

above 70°F (21°C) after chilling on board the harvest vessel. The safety of these limits is dependent upon proper handling at sea.

Fish that have been previously frozen can safely withstand considerably more exposure to elevated temperatures during post-harvest handling. Such fish should not be exposed to temperatures above 40°F (4.4C) for more than 12 hours, cumulatively, if any portion of that time is at temperatures above 70°F (21°C); or the fish should not be exposed to ambient temperatures above 40°F (4.4°C) for more than 24 hours, cumulatively, as long as no portion of that time is at temperatures above 70°F (21°C), after chilling on board the harvest vessel. The safety of these limits is again dependent upon proper handling at sea.

Extended frozen storage (e.g. 24 weeks) or cooking minimizes the risk of additional histamine development by inactivating the enzyme-forming bacteria and, in the case of cooking, the enzyme itself. As previously mentioned, recontamination with enzyme-forming bacteria and significant temperature abuse is necessary for histamine formation under these conditions. Such recontamination may not be likely if the fish is processed under a conscientious sanitation program.

Sensory evaluation is generally used to screen fish for spoilage odors that develop when the fish is exposed to time/temperature abuse. It is an effective means of detecting fish that have been subjected to a variety of abusive conditions.

However, odors of decomposition that are typical of relatively low temperature spoilage may not be present if the fish has undergone high temperature spoilage. This condition makes sensory examination alone an ineffective control for scombrotoxin.

Chemical testing is an effective means of detecting the presence of histamine in fish flesh. However, the validity of such testing is dependent upon the design of the sampling plan. The amount of sampling required to accommodate such variability is necessarily quite large. For this reason, chemical testing alone will not normally provide adequate assurance that the hazard has been controlled. Because histamine is generally not uniformly distributed in a decomposed fish, a guidance level of 50 ppm has been set. If 50 ppm is found in one section, there is the possibility that other sections may exceed 500 ppm.

Observations for the presence of honeycombing in precooked tuna loins intended for canning is also a valuable means of screening for fish that have been exposed to the kinds of temperature abuse that can lead to histamine development. Any fish that demonstrate the trait should be destroyed (FDA, 2001a).

FDA Guidelines

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1a. For receipt by primary (first) processor (Harvest Vessel Control Option):

All lots received are accompanied by harvest vessel records that show:

- Generally, the fish were:
    - Placed in ice, or in refrigerated seawater or brine at 40°F (4.4°C) or less, within 12 hours of death;

      OR

    - Placed in refrigerated seawater or brine at 50°F (10°C) or less within 9 hours of death and chilling continued to bring the internal temperature of the fish to 40°F (4.4°C) or less;

  OR

- Fish exposed to air or water temperatures above 83°F (28.3°C),), or large tuna (i.e., above 20 lbs.) that are eviscerated before on-board chilling, should be placed in ice (including packing the belly cavity of large tuna with ice) or in refrigerated seawater or brine at 40°F (4.4°C) or less within 6 hours of death;

  OR

- Large tuna (i.e., above 20 lbs.) that are not eviscerated before on-board chilling: The internal temperature of the fish was brought to 50°F (10°C) or less within 6 hours of death and chilling continued to bring the internal temperature of the fish to 40°F (4.4°C) or less;

  OR

- Other critical limits for on-board handling (e.g. maximum refrigerated brine or seawater temperature, maximum fish size, maximum fish to brine/seawater/ice ratio, maximum ambient temperature exposure time before chilling) necessary to achieve a cooling rate that will prevent development of histamine in the specific species, as established through a scientific study;

  AND

- For fish held refrigerated (not frozen) on-board the vessel: The fish were stored at or below 40°F (4.4°C) thereafter;

AND

- Sensory examination of a representative sample of fish shows no more than 2.5% decomposition (persistent and readily perceptible) in the sample. For example, no more than 3 fish in a sample of 118 fish may show signs of decomposition;

AND

- For fish held iced or refrigerated (not frozen) on-board the vessel and delivered 24 or more hours after death: The internal temperature should be 40°F (4.4°C) or below;

  OR

- For fish held iced or refrigerated (not frozen) on-board the vessel and delivered from 12 to less than 24 hours after death: The internal temperature should be 50°F (10°C) or below;

  OR

- For fish held iced or refrigerated (not frozen) on-board the vessel and delivered in less than 12 hours after death: The internal temperature should demonstrate that appropriate chilling methods were used onboard the harvest vessel. Chilling of the fish must begin on the harvest vessel regardless of the time from death to delivery, unless the environmental conditions (e.g. air and water temperatures) are consistently below 40°F (4.4°C) from the time of death to delivery (FDA, 2001a).

1b. For receipt by primary (first) processor Histamine Testing Option):

Analysis of a representative sample of fish shows less than 50 ppm histamine in all fish in the sample;

AND

- Sensory examination of a representative sample of fish shows no more than 2.5% decomposition (persistent and readily perceptible) in the sample. For example, no more than 3 fish in a sample of 118 fish may show signs of decomposition;

AND

- For fish held iced or refrigerated (not frozen) on-board the vessel and delivered 24 or more hours after death: The internal temperature should be 40°F (4.4°C) or below;

  OR

- For fish held iced or refrigerated (not frozen) on-board the vessel and delivered from 12 to less than 24 hours after death: The internal temperature should be 50°F (10°C) or below;

  OR

- For fish held iced or refrigerated (not frozen) on-board the vessel and delivered in less than 12 hours after death: The internal temperature should demonstrate that appropriate chilling methods were used onboard the harvest vessel. Chilling of the fish must begin on the harvest vessel regardless of the time from death to delivery, unless the environmental

conditions (e.g. air and water temperatures) are consistently below 40°F (4.4°C) from the time of death to delivery (FDA, 2001a).

2. For receipt by secondary processor (including warehouse):

- For fish delivered refrigerated (not frozen): All lots received are accompanied by transportation records that show that the fish were held at or below 40°F (4.4°C) throughout transit;

  OR

- For fish held under ice or chemical cooling media: There is an adequate quantity of ice or other cooling media at the time of delivery to completely surround the product (FDA, 2001a).

3. For processing steps:

During processing and refrigerated (not frozen) storage that occurs before cooking (e.g. canned tuna "precook"): For fish that have not been previously frozen:

- The fish are not exposed to ambient temperatures above 40°F (4.4°C) for more than 4 hours, cumulatively, if any portion of that time is at temperatures above 70°F (21°C);

  OR

- The fish are not exposed to ambient temperatures above 40°F (4.4°C) for more than 8 hours, cumulatively, as long as no portion of that time is at temperatures above 70°F (21°C);

  (Note: Only one of the above two limits may be selected. They may not be added for a total exposure of 12 hours.)

  OR

- For fish that have been previously frozen: The fish are not exposed to ambient temperatures above 40°F (4.4°C) for more than 12 hours, cumulatively, if any portion of that time is at temperatures above 70°F (21°C);

  OR

- The fish are not exposed to ambient temperatures above 40°F (4.4°C) for more than 24 hours, cumulatively, as long as no portion of that time is at temperatures above 70°F (21°C).

  (Note: Only one of the above two limits may be selected. They may not be added for a total exposure of 12 hours.) (FDA, 2001a)

FDA guidelines for histamine in tuna, mahi mahi, and related fish.

Analytical Procedures

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- Histamine by capillary electrophoresis (Mopper and Sciacchitano, 1993)
- Histamine in canned fish: High performance liquid chromatography method (Yen and Hsieh, 1991).
- Histamine in canned tuna: Fluorometric method (Lerke and Bell, 1976).
- Histamine in fish products: Thin layer chromatographic method (Schutz et al., 1976).
- Histamine in fish: Enzyme-based screening test (Lerke et al., 1983).
- Histamine in fish: Fluorometric method (Taylor et al., 1978).
- Histamine in fish: Oxygen-sensor-based method (Ohashi et al., 1994).
- Histamine in seafood: Automated kinetics-enhanced flow-injection method (Hungerford et al., 2001)
- Histamine in seafood: Biological method (AOAC, 1995a).
- Histamine in seafood: Chemical method (AOAC, 1995b).
- Histamine in seafood: Flow-injection method (Hungerford et al., 1990).
- Histamine in seafood: Fluorometric method (AOAC, 1995c).
- Histamine in tuna: Copper chelation method (Bateman et al., 1994).
- Histamine in unprocessed and canned fish: Guinea pig ileum method (Geiger, 1944).

Scombroid Poisoning Mechanism

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- Inhibitors of histaminase enzymes (Hungerford and Arefyev, 1992)

Commercial Test Products

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Commercial test products for histamine.

Test	Analytical Technique	Approx. Total Test Time	Supplier
ALERT® for Histamine [Sensitivity: 2.5 ppm]	ELISA	35 min	Neogen Corporation Web: www.neogen.com
EIA for Histamine in Fish Extract, K1-HTM [Sensitivity: 2.5 ppm, quantitative 1-50 ppm]	Enzyme immunoassay	90 min	Immuno-Diagnostic Reagents Web: www.idr-usa.com/

EIA for Histamine Fishmeal and Bonemeal, K2-HTM [Sensitivity: 5 ppm, qualitative]	Enzyme immunoassay	35 min	Immuno-Diagnostic Reagents Web: www.idr-usa.com/
EIA for Histamine in Raw and Canned fish, K3-HTM [Sensitivity: 5 ppm, qualitative]	Enzyme immunoassay	35 min	Immuno-Diagnostic Reagents Web: www.idr-usa.com/
HISQUICK™ Histamine (BA-20-3000 - 48 Columns) [Sensitivity: 20 ppm, quantitative]	Color test	12 min.	Rocky Mountain Diagnostics, Inc. Web: www.rmdiagnostics.com/
Histamine EIA Food (BA-10-3100 - 96 Wells) [Sensitivity: 0.5 ppb, quantitative]	Enzyme immunoassay	2 h	Rocky Mountain Diagnostics, Inc. Web: www.rmdiagnostics.com/
Histamarine Test Kit[1] [Sensitivity: 0.5 ppm, quantitative from 1 to 500 ppm]	Enzyme immunoassay	1 h	Immunotech (Beckman Coulter) Web: http://www.immunotech.cz/
HistaMeter [Sensitivity: 0-50 ppm, qualitative]	Enzyme immunoassay	1 h	Biomedix E-mail: cb4biomedx@aol.com
HistaQuant [Sensitivity: 0-500 ppm, quantitative]	Enzyme immunoassay	1-1/2 h	Biomedix E-mail: cb4biomedx@aol.com
HistaSure Dipstick Assay [5ppm Pass/Fail]	Fluorescence Labeled Optical-Read Immuno Dipstick Assay (F.L.O.R.I.D.A.)	5 min	Rocky Mountain Diagnostics Web: www.rmdiagnostics.com
RIDASCREEN® Histamin R1602	ELISA	2-5/6h	R-Biopharm, Inc. Web: www.r-biopharm.com/main.php?

[Sensitivity: 2.5 ppm; quantitative]			
RidaQuick Histamin (R1603-96 Wells) [Sensitivity 20 ppm; quantitative]	ELISA	12 min	R-Biopharm, Inc. Web: www.r-biopharm.com/main.php?
Transia Tube *Histamine*	ELISA	1 h	Diffchamb AB Web: www.bestlab.com.au/diffchamb.htm
Veratox® for Histamine [Sensitivity: < 2.5 ppm, quantitative from 0 to 50 ppm]	ELISA	35 min	Neogen Corporation Web: www.neogen.com

[1]AOAC Approved

References

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