Histamine Behavior during the Fermentation Process in the Manufacture of Fish Sauce†

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The behavior of histamine in fish sauce making was investigated using fresh and spoiled fish with or without histidine added during fermentation. The histamine content in the 2% histidine added fresh fish mixture did not change significantly even after a lapse of 4 months incubation. However, when histidine was added to spoiled fish, the histamine content rose to a high level but decreased continuously with incubation time. This decrease may suggest the presence of histamine-decomposing bacteria in the samples. Eight of the 10 commercial fish sauces analyzed contained histamine levels below the "decomposition level" of 50 mg/kg set by the FDA. The increase in histamine at the initial stage and the decrease in histidine might suggest that histidine was converted to histamine by a microorganism possessing the enzyme histidine decarboxylase.

Keywords: *Fish sauce; histamine behavior; histidine*

1. INTRODUCTION

Fish sauce is a clear brown liquid hydrolysate of salted fish obtained after about 1 year of salting which has a characteristic odor. In Southeast Asia, it is commonly used as a condiment, but in some areas and certain classes in the region, it is the main source of protein in the diet. It contains 20 g/L nitrogen, of which 16% is in the form of amino acids; thus it may be considered an important source of protein (LaFont, 1955). Our previous study has shown that addition of histidine accelerated the fermentation process in the manufacture of fish sauce (Sanceda et al., 1996). Fermented fish products which include fish sauce and fish paste contain high amounts of histamine (Fardiaz and Markakis, 1979); however, our preliminary work on histamine in commercial fish sauces (unpublished report) showed very low, if any, histamine in the product.

Biogenic amines have been found to occur during processing of foods which include fishery products and other fermented foods (Maga, 1978). Amino acid decarboxylation is the main mode of biosynthesis of these amines (Rice and Koehler, 1976). These compounds are generally vasoactive and can cause changes in blood pressure. Severe headache, hypertension, renal intoxication, or in, other severe cases, intracerebral hemorrhage and eventually death (Kuhn and Lovenberg, 1982; Antila, 1983) are the most common effects of these amines.

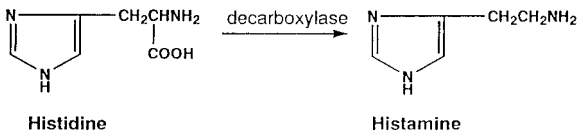

Figure 1. Conversion formula of histidine to histamine

Scombroid poisoning (histamine toxicosis) has occasionally broken out as a result of ingesting fish such as saury, tuna, mackerel, and bonito, which are characterized to contain high levels of free histidine in their tissues (Kawabata et al., 1956; Arnold and Brown, 1978; Kimata and Kawai, 1953). High levels of histamine in the incriminated fish are generally formed via microbial decarboxylation of histidine (Taylor and Sumner, 1986; Merson et al., 1974; Stratton et al., 1991). Okuzumi et al. (1994) characterized a histamine-producing bacterium isolated from marine fish. Also, nonscombroid fish belonging to the families *Pomatomidae* (bluefish), *Coryphenaenidae* (mahi mahi), *Carangidae* (jack mackerel, amberjacks, yellowtail), *Clupidae* (herring, sardines), and *Engraulidae* (anchovies) have occasionally been implicated (Taylor, 1986); however, only spoiled fish of these species can cause histamine poisoning. Fish containing hazardous histamine are not detected by sensory tests. Figure 1 shows the conversion formula of histidine to histamine. It has been reported that trimethylamine, trimethylamine oxide, agmatine, and choline (Hayashi, 1954), cadaverine (Arunlanshana et al., 1956), and putrescine (Parrot and Nioct, 1966) are food-borne potentiators of histamine toxicity.

Fujii et al. (1994) reported that outbreaks of scombroid fish poisoning are caused by ingestion of frozen−thawed fish and its products, even when the viable count of histamine-forming bacteria is low. The amount of histamine accumulated in the sample depended both on the bacterial production and decomposition of histamine (Fujii et al., 1994; Sato et al., 1994). Hayashi (1970) found that once accumulated, histamine content may

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decrease and/or disappear possibly due to bacterial decomposition of histamine.

This study aimed to investigate the behavior of histamine under varied fermentation conditions in the manufacture of fish sauce.

2. MATERIALS AND METHODS

2.1. Materials. Fish iwashi of the sardine family (*Sardinops melanostictus*), 13 cm in length, were used. Commercial fish sauces were obtained in bottles from their country of origin. Histidine of standard grade was obtained from Nacalai Tesque Inc., Tokyo, and 99% NaCl was purchased from a Japanese supermarket. Fungal amine oxidase, a Cu-containing enzyme for histamine assay, was generously provided by Kikkoman Corp., Chiba, Japan, at the request of Dr. Minoru Ohashi.

2.2. Methods. 2.2.1. "Spoilage" Experiment. Fish were cut 3−4 cm long, placed in a shallow and wide plastic container, and left at an ambient temperature for 1 day without addition of salt after which the fish showed slight deterioration and foul odor.

2.2.2. Sample Preparation. Uneviscerated fish were cut 3−4 cm long and were used for all the experiments. Three sets of experiments were carried out. (A) In the first experiment, histidine (in its original solid form) in the concentrations of 0.1, 0.2, 0.5, 1.0, and 2.0% salt used (salt:fish ratio was 1:3) was for each mixed concentration with salt first and added to fresh fish. The mixtures were placed in layers in glass beakers, covered loosely with Parafilm, and incubated at 30 °C for 4 months, and then the liquid was collected. (B) In the second experiment, the spoiled fish were used in the following experiments: (1) only salt (30%) was added. (2) A 2% histidine sample of the salt used (salt:fish ratio was 1:3), and salt was added. (3) Only histidine was added (same amount as in the B2 experiment) directly to spoiled fish. All the mixtures were prepared similar to the procedure in the first experiment but incubated at ambient temperature for 16 days. (C) In the third experiment, fresh fish were added with 30 (control), 20, 10, and 5% NaCl. The same procedure used in the above experiments was used except that incubation was carried out at ambient temperature for 49 days.

For histamine analysis, the pH of the samples collected was first neutralized by dropwise addition of 10 N KOH until pH 7.0 was achieved and then by dropwise addition of 1 N KOH to obtain a final pH 8.0.

2.2.3. Histamine Analysis. Histamine was assayed using an oxygen sensor (freshness meter KV-101 from Oriental Electric Co. Ltd., Niiza, Saitama, Japan) and employing a fungal amine oxidase (Ohashi et al., 1994). A 10 mL volume of the sample extracts containing Hm < 0.2 mM was placed into a 100 mL BOD bottle and aerated using a small air pump in a water bath for about 10 min at 37 °C. For foaming samples, a few drops of silicone antifoamer (Toshiba silicone No. 737) was added before aeration. The reaction cell, controlled at 37 °C (with cell volume of 1150 μL), was filled with about 1200 μL of aerated sample solution capped. The reading point of d_o [amount of DO (dissolved oxygen) for air-saturated water (mm)] was adjusted to 80 mm by a span controller, 15 μL of enzyme was injected into the cell through a capillary tube on the cap, and the output current of DO was recorded within 3−5 min.

2.2.4. Histidine Determination. Histidine content was determined by analyzing the amino acids content of the samples with an amino acid analyzer (Hitachi 835) using a Hitachi custom ion-exchange resin (Mitsubishi Chemical Industries Ltd., Tokyo). A 2 mL volume of each fish sauce sample was hydrolyzed with 2 mL of 6 N HCl in an air-free sealed tube at 110 °C for 24 h. The HCl was removed from the hydrolyzed sample on a rotary evaporator, brought to a known volume (10 mL) with 0.02 N HCl, filtered, and stored at −20 °C until analyzed.

2.2.5. Statistical Analysis. A test of significance was done using a Student *t* test (NEC, 1983).

Table 1. Histamine Contents (mg/mL) of Histidine-Added Fish Sauces[a]

added histidine (%)[b]	incubation period (months)	
	2	4
0	0.11 ± 0.03	0.12 ± 0.02
0.1	0.05 ± 0.02	0.07 ± 0.02
0.2	0.04 ± 0.02	0.05 ± 0.01
0.5	0.07 ± 0.01	0.08 ± 0.03
1.0	0.05 ± 0.03	0.05 ± 0.01
2.0	0.12 ± 0.04	0.15 ± 0.01

[a] Results are mean values of triplicate determination ± standard deviation. [b] Histidine was added to fresh fish before incubation.

3. RESULTS AND DISCUSSION

The formation behavior of histamine during fermentation in the manufacture of fish sauce was studied. In this study, the control had a 5.29 pH, those of the histidine added sauces ranged from 5.62 to 5.82, and commercial sauces had pH ranging from 5.29 to 5.74. The initial pH for the control was 5.60, and that for the histidine added mixture was 7.15. It was observed that the pH of the control and the histidine-added samples decreased after 4 months of fermentation. Table 1 shows the concentrations of histamine after fermentation in fish sauces with added concentrations of histidine. Results showed that, in both the 2 and 4 month fermented samples, the levels of histamine in the 0.1, 0.2, 0.5, and 1.0% histidine-added samples were slightly lower than the control but not significantly different. In the 2.0% histidine added sample, the histamine seemed to be numerically higher than the control but the difference was not significant. The values of histamine in both the control and the 2.0% added histidine samples were higher while those in the 0.1, 0.2, 0.5, and 1.0% added histamine (Table 1) were lower than the "decomposition level" of 50 mg/kg of scombrotoxigenic fish imposed by FDA (1995).

The sauces from histidine-added fresh fish were sensorially tested, and no symptoms of histamine poisoning, gastrointestinal (nausea, vomiting, diarrhea, abdominal cramps), cutaneous (rash, urticaria, edema), or neurological (flushing, itching, burning, tingling, headache) as described by Murray et al. (1982) and Merson et al. (1974) were observed. During the test, about a half teaspoon of the sauces was given to each of 10 panel members and they orally tasted the samples. The panelists were first observed for about 5 h, and extended until 24 h, for any symptoms of the above-mentioned poisoning signs, but none of these were noticed. It seemed that addition of histidine even in a relatively large amount did not result in the formation of histamine provided that the fish were in the fresh state. The very high concentration of salt used in the mixture during fermentation might inhibit the growth of microorganisms that could decarboxylate free histidine to form histamine. According to Chin and Koehler (1983), formation of histamine and tyramine in miso appeared to be inhibited by high salt concentration. Good hygiene prevents bacterial contamination that plays a role in the formation of histamine. In the study conducted on fish stored at 5 °C (Sato et al., 1994), histamine was accumulated, decreased, and disappeared as histamine-decomposing bacteria took over when the sample putrefied, but at 30 °C, histamine did not always decrease. This suggests that the capacity of histamine-decomposing bacteria might be inhibited.

Table 2. Histamine Contents of Commercial Fish Sauces

samples[b]	mean ± SE (mg/mL)[a]
Patis (Philippines)	
A	0.04 ± 0.01
B	0.02 ± 0.01
C	0.10 ± 0.02
D	0.07 ± 0.03
E	0.03 ± 0.01
Nampla (Thailand)	0.04 ± 0.02
Nampla (Japan)	0.04 ± 0.01
fish sauce (Korea)	0.14 ± 0.02
Shottsuru (Japan)	nd
anaerobically fermented (Japan)	nd

[a] Values are the average of two replicates. [b] All samples were obtained from their county of origin. nd: not detected.

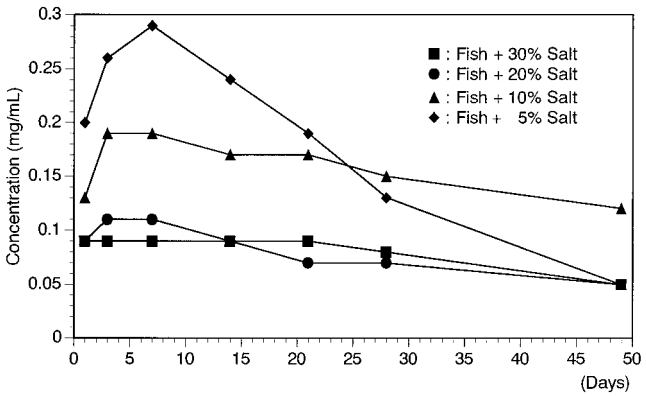

Figure 2. Histamine formation in fish sauce during fermentation with added concentrations of salt.

They further described the formation of histamine from histamine-metabolizing bacterial flora in fish sauce during fermentation (Sato et al., 1995). Fujii et al. (1994) reported that outbreaks of scombroid fish poisoning were caused by ingestion of frozen−thawed fish and its products, even when the viable count of histamine-forming bacteria was low. The L-histidine decarboxylation activity of halophilic histamine-forming bacteria was highest at the beginning of the stationary phase of the growth and gradually decreased as the stationary phase proceeded (Kurihara et al., 1993). This fact might explain the very low content of histamine in the commercial sauces analyzed in this study as shown in Table 2. Commercial sauces made in Japan showed that 2 of the 3 had no detectable level of histamine, but one was slightly high and similar to the one from Thailand, while those from the Philippines were very low. The Japanese food industries are extra careful when it comes to hygiene in foods and food products, which might also explain the inhibited growth of microorganisms in the samples during fish sauce production. The Korean sauce contained a little higher amount of histamine compared with other samples analyzed. The threshold toxic dose for histamine is not precisely known (Lahsen, 1991), but histamine levels above 200 mg/kg are considered an indication of the potential to cause scombroid poisoning (Bartholomew et al., 1987). The Food and Drug Administration (FDA, 1995) uses a hazard action level for histamine in fish of 500 mg/kg but has recently imposed a further "decomposition level" of 50 mg/kg for scombrotoxigenic fish.

Figure 2 shows the behavior pattern of histamine during fermentation in the supernatant of fresh fish with added 30, 20, 10, and 5% salt. Results indicate that histamine is hardly formed in the control sample (30%), but as the concentration of salt used decreased, the

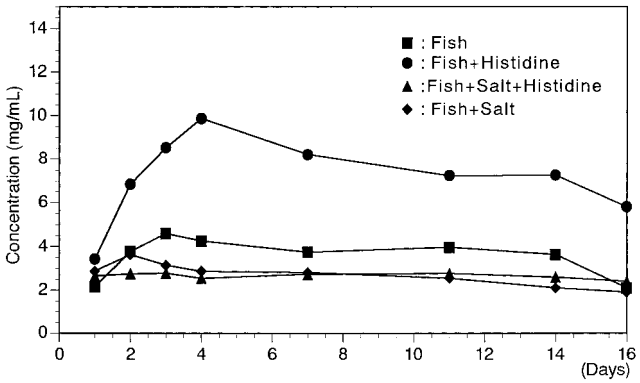

Figure 3. Histamine formation in fish sauce fermentation with spoiled fish added histidine, and salt. Fish were left to spoil for 1 day before use. A 2% histidine salt ratio was used. Salt was 99% NaCl.

histamine content increased. The fish body deteriorated faster in the lower salt concentrations (10% and 5%) than in the higher concentrations (30% and 20%). This indicates that salt inhibits both the proteolytic enzymes in the fish as well as growth of microorganisms. In all samples, the content of histamine decreased from around the seventh or eighth day of fermentation and continued to decrease as fermentation progressed.

Figure 3 shows the behavior pattern of histamine formation during fermentation of spoiled fish. In the spoiled fish, control no salt, histamine started to increase on the second day but gradually and continuously decreased from the third day and until the end of the experiment. In the absence of salt, fish with added histidine showed a sharp increase in histamine on the second day and continued to increase until it reached a peak on the fourth day and then started to descend following the same pattern in the control sample. In the added histidine and salted sample, the histamine was a little lower initially than in the histidine-added sample but without salt but never increased and showed a slight decrease in the content of histamine was observed. In the mixture of fish and salt without any histidine added, the change in the amount of histamine was similar to salt plus histidine and was not significant. The same decreasing tendency in histamine also observed in the only fish sample (control spoiled) and decomposed linearly with the progress of incubation time. Among the samples analyzed, histamine was detected in all the spoiled fish samples regardless of the addition of histidine; however, the histidine-added sample without salt showed the highest production of histamine. It appeared that histidine added to fresh fish had no significant effect on the formation of histamine, but when added to spoiled fish, it enhanced the histamine formation. Histamine is not present in the flesh of fish when it is caught: it occurs when histamine-producing bacteria decarboxylate histidine to histamine during the spoilage process (Klausen and Huss, 1987; Morrow et al., 1991). It was reported that histamine had been formed prior to smoking and that histamine-producing bacteria were eliminated during smoking (Fletcher et al., 1998).

In short, histamine concentration in the histidine added samples increased at the initial stage of fermentation but decreased linearly with the progress in incubation time. Though this experiment was carried out in a short time, the very low concentration of histamine in fish sauces fermented for a long time (as

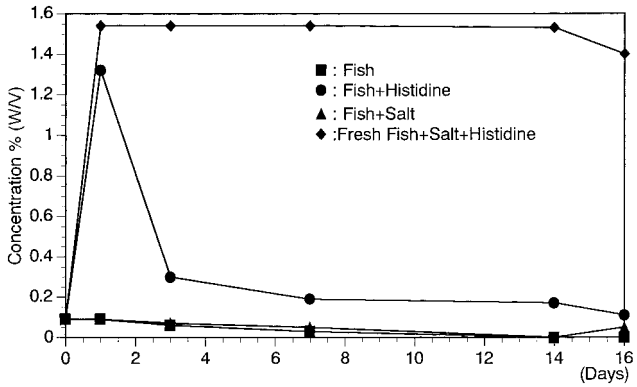

Figure 4. Histidine remaining during fermentation of fish sauce. Fish was left to spoil before use. A 2% histidine was used.

commercial fish sauces) might support the behavior of histamine during fermentation in this study. This is assuming that the fish used in the commercial fish sauces are in the fresh state.

Figure 4 shows the remaining soluble histidine in the fish mixture after 16 days of incubation. At this stage of incubation, histidine in fish has not been solubilized to its fullest; therefore, the amount of histidine seemed to be low in the control of spoiled fish. There was very little change in the amount of histidine in the fresh fish salt mixture added with histidine during the 16 days of incubation. It seemed that histidine could be added to fish without undergoing degradation or change provided that growth of bacteria was inhibited by salt, and in this study, the presence of salt in high concentrations and the condition of fish before incubation were important. This phenomenon might be explained in our previous study (Sanceda et al., 1996) where the amount of histidine that remained in the product was at a fairly high level even after the lapse of 4 months of incubation time. The fermentation condition in this experiment was a normal traditional one, except for the addition of 2% histidine to the salt in fish mixture before fermentation. However, in the histidine-added spoiled fish without salt, the histidine added was almost retained 1 day after addition but abruptly decreased on the third day and continuously decreased until hardly detected on day 16.

Although the relation between the decrease in histidine and the increase in histamine was not statistically determined, it could be that histidine was microbially decarboxylated to form histamine. The total amount of amines in a histidine-added spoiled fish mixtures increased with incubation time; however, in a histidine-added fresh fish mixture with salt, amines remained at a low level and remained constant throughout the incubation period (data not shown). This result seems to follow the pattern for the formation of histamine where salt inhibited the formation of histamine and addition of histidine to salted fresh fish did not increase the histamine in the mixture but, when added to spoiled fish with or without salt, histamine content rose to a high level and the increase was parallel to the incubation time.

4. SUMMARY

Addition of histidine to fresh fish did not increase the amount of histamine formed, contrary to that observed for spoiled fish; in both cases, histamine decreased as fermentation progressed. The amount of soluble histidine decreased with the progression of incubation time. The state of freshness of fish greatly influenced the formation of histamine during the fermentation process in the manufacture of fish sauce. The very high concentration of salt also inhibited the growth of microorganisms that could decarboxylate histidine to form histamine.

The very low concentration of histamine in commercial sauces analyzed in this paper could be due to the high salt concentration and might also be explained by the appearance, decrease, and disappearance of histamine during fermentation.

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