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Histamine Formation and Its Control in Cheese: A Review

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Abstract : Histamine is one of the biogenic amine formed in the biological systems. Histamine is formed in fishes such as tuna and in the ripened cheeses. Fresh milk contains histamine in a low amount (<0.3) while cheeses may have the amount as high as 2500 ppm. Histamine content of the cheeses is affected by many factors. Ingestion of 70-1000 mg of histamine in a single meal is necessary to elicit any symptoms of toxicity. Histamine poisoning shows symptoms of rash, urticario, edema, and localized inflammation affect the cutareous system; nausea, vomiting, diarrhea, and abdominal cramps in gastrointestinal track. Hypotension, headache, palpitations, tingling, flushing and burning sensations in the mouth are the other symptoms. Different biogenic amines are predominant in different kind of cheeses. HPLC, gas-liquid chromatography and TLC are used to determine bigenic amines. Many enzymatic methods including enzymelinked immunosorbent assay (ELISA) have been developed to detect histamine in blood and tissues.

Key words:- Histamine, cheese, food poisoning

Introduction

Histamine is one of the amines formed by the microorganisms possessing histidine decarboxylase enzyme (Arnold and Brown, 1978). The other amines are tyramine, putrescine, cadaverine, tryptamine and 2-phenylethylamine etc., and they may form in different kinds of foods (Santos, 1996). Biogenic amines are formed by removing the alpha-carboxyl group from the free amino acids and named by their originating amino acids, as histamine from histidine, tyramine from tyrosine, trypamine from tryptophane. They are organic and basic nitrogenous compounds with low molecular weight (Bodmer *et al.*, 1999). Histamine, tyramine, phenylethylamine and tryptamine are aromatic biogenic amines found in cheese. Putrescine and cadaverine are aliphatic amines (Van Boekel and Arentsen-Stasse, 1987). Biogenic amines may occure in various foods. Histamine contents of some foods were reported in a abroad range as 0.2-15.5 mg/L in American red wine, 2.6-20 mg/L European beer, not determined in cognac, <55.0 mg/100g in dry sausage, 0.7-20 mg/100g in sauerkraut, up to 274 mg/100g in soy sausage, 7.8-64 mg/100g in fish paste (Stratton *et al.*, 1991). Histamine content in milk and milk products can vary in different amounts, as well. In milk biogenic amines occur naturally. The content can be <0.3 ppm in fresh milk, 0.3-0.7 ppm in pasteurised milk, 0.8 ppm in UHT milk, 7.0 ppm in sour cream, and 13 ppm in yoghurt. However, cheeses may have the highest amounts among dairy products up to 2500 ppm. On the other hand, there are many kinds of cheeses produced in the world, and histamine content of the cheeses may be affected by many factors, namely the content of free amino acid, bacterial contamination, pH, salt concentration, storage temperature, water activity and ripening time. Biogenic amines result from the proteolysis of casein by various enzymes. Thus, each kind of cheese has its own characteristic amine profile as a result of different conditions. Many bacteria and some of yeasts may show histidine decarboxylase activity to form histamine. Among bacteria, Bacillus, Clostridium, Enterobacter, Escherichia, Lactobacillus, Pediococcus, Proteus, Pseudomonas, and Salmonella have decarboxylase activity (Pinho et al., 2001; Bodmer *et al.*, 1999). Since the most frequent foodborne intoxications and intolerances involves histamine, it is aimed to focus on histamine formation, poisoning, control methods, detection and regulation in cheeses in this work.

Histamine Poisoning: Some microorganisms produce toxins and cause foodborne diseases, and histamine poisoning result from the ingestion of the foods containing high levels of histamine (levels exceeding g/kg) (Casella *et al.*, 2001). In terms of histamine poisoning, some families of fishes such as Scombridae and Scomberesocidae come in the first order. Therefore, the term "s combroid fish poisoning" has been used to describe fish type of food poisoning (Taylor, 1986). After fish, cheese is the next most commonly implicated food associated with histamine poisoning. Histamine stimulates heart, both sensory and motor neurous, cause extravascular smooth muscle to contract or relax, and control gastric acid secretion. Thus, histamine poisoning shows symptoms in wide spectrum. Rash, urticario, eodema, and localized inflammation affect the cutaneous system. Nausea, vomiting, diarrhea, and abdominal cramps happen in gastrointestinal track. Furthermore, hypotension, headache, palpitations, tingling, flushing and burning sensations in the mouth happen. The most common symptoms are rash, diarrhea, flushing and headache (Stratton *et al.*, 1991). On the other side, some

agents such as certain drugs are accepted as contributing factors of histamine poisoning. Certain antihistamines and antimalarials can inhibit histamine-metabolizing enzymes (Bodmer *et al.*, 1999). Low amount of histamine is not a potential risk. However, if histamine intake is in a large amount, or the patients use mono amino inhibitor drugs, or amines catabolism is inhibited, then various symptoms may result. In case of insufficient and inhibition of diamine oxidase-activity or monoamine oxidases, due to secondary effects of medicines or alcohol, low levels of amines cannot be metabolised efficiently, and then they easily lead toxic effect. Furthermore, the levels of biogenic amines in cheese could be useful as indicators of freshness and hygienic quality of raw materials and manufacturing conditions of cheeses (Pinho *et al.*, 2001).

Histamine Contents of Various Cheeses : Histamine contents of some cheeses vary widely, and almost the content depends on variety. It means that the amount of histamine may range starting from not-detectable level to considerable high levels (Table 1). Some factors affect the content in cheeses. Ripening process or contamination of histamine forming bacteria increase the accumulation. If the cheeses are contaminated by Lb. buchneri (some subsp.), the formation of histamine and tyramine increase. Cheeses produced with starter bacteria result low levels of histamine (Bakýrcý, 2000). Different biogenic amines are predominant in different kind of cheeses. Putrescine, cadaverine and tyramine were predominant biogenic amines in Beyaz cheeses manufactured with and without starter culture. Tyramine was reported as predominant biogenic amine in Feta and Domiati cheeses. The content of histamine is correlated with the number of lactobacilli, tyramine and phenylethylamine with number of enterococci, putrescine and cadaverine with the number of enterobacteria (Durlu-Özkaya et al., 1999). Cadaverine, tyramine, histamine and putrescine were at levels up to 111.00, 21.25, 19.65 and 17.37 mg/100g, respectively (Vale and Gloria, 1998). In Turkey, the predominant amines were putrescine, cadaverine, histamine, tyramine and spermidine in Fresh Ka°ar, Milaliç, Otlu (Herby), and Örgü cheeses. Phenylethylamine cadaverine, tyramine and spermidine were predominant in Urfa cheese, putrescine cadaverine, histamine and tyramine in Civil cheese, and putrescine, and tyramine in Beyaz cheese which is commonly consumed in Turkey. On the other hand, some bacteria growing on the surface of Munster cheeses degrade histamine. During a 4-week ripening period, strains of B. linens reduced histamine and tyramine contents in course of deamination by 55 to 70 % (Leuschner and Hammes, 1997).

Table 1. Histamine Contents of Some Local and Foreign Cheeses (mg/kg)

Turkish cheses	Histamine content	References	Foreign Cheeses	Histamine content	References
Beyaz	29.2-2180	Durlu-Özkaya and Tunail, 2000	Cheddar (Mild)	1-108	Antila *et al.*, 1984
Kaþar (Fresh)	0.0-61.3	Durlu-Özkaya and Tunail, 2000	Cottage	ND	Antila *et al.*, 1984
Kaþar	390-2180	Nizamlioðlu, 1990	Roquefort and Bluet	t-409	Antila *et al.*, 1984
Tulum	180-510	Nizamlioðlu, 1990	Swiss	ND-2500	Antila *et al.*, 1984
Cicil	912.3-996.5	Durlu-Özkaya,, 2002	Edam (Fresh)	4.0	Antila *et al.*, 1984
Otlu	0.0-52.5	Durlu-Özkaya,, 2002	Edam (Ripened)	1.70	Antila *et al.*, 1984 T:trace,

ND: Not determined.

Formation of Histamine in Cheese : Cheeses contain high amount of proteins, and these proteins are hydrolized into peptides and free amino acids by enzymes of the starter bacteria. The formation starts from degaradation of proteins to free histidine amino acid. Then, this amino acid is decarboxilated by the microorganisms possessing the enzyme histidine decarboxilase, and histamine is formed (Gü ven and Hayaloðlu, 2002). Joosten and Standhouders (1987) found that the starter cultures (L. lactis ssp. lactis, L. lactis ssp. cremoris, Leuconostoc cremoris, L. lactis ssp. lactis biovar. diacetylactis) cannot form decarboxylases in cheese, at least not enough for significant amine formation. In addition, they suggested that biogenic amines are not produced in Gouda and Maasdam cheeses made from pasteurised milk with sufficient hygienic care. Joosten (1988) studied the factors influencing the amounts of biogenic amines in cheese and found that histamine formation was accelerated if the cheese stored at high temperatures (18 oC or 21 oC) while more histamine was also found in cheese with higher pH or a lower salt content than normal Gouda. Formation of histamine by contamination of Lactobacilu buchneri (st2A) was found to be greatly inhibited by 5.5% NaCl (Summer *et al.*, 1990).

Control of Histamine Formation : Proper storage temperature is the most effective method to prevent histamine formation in cheese. Milk quality is also important factor to prevent histamine accumulation. Histamine accumulates especially in cheese during ripening due to presence of lactic acid bacteria coming from milk. Usage of raw milk or the milk not fully pasteurised in cheese may result high levels of
histamine formation (Stratton *et al.*, 1991). In fact, the formation of free amino acids and biogenic amines are directly influenced by bacterial activity, pH and salt concentration. Water activity, storage temperature and ripening time influence indirectly (Vale and Gloria, 1997).

Methods to Detect Histamine : High performance liquid chromatography (HPLC), gas-liquid chromatography and thin-layer chromatography are used to determine biogenic amines. Chang (1985) described a method for determining some biologically active amines including histamine in cheeses by HPLC. Investigated amines and amino acids were separated after optimising a mobile phase and counter ion HPLC system using a reverse-phase column. The HPLC method was found useful for screening to detect cheese samples containing toxic amounts of histamine. Voight and Eitenmiller (1974) used TLC and described the use of 7-chloro-4-nitrobenzofurazan (NBD-Cl) for the quantitation of amines, and compared with other commonly used detection reagents. The extract obtained from cheese was spotted directly on TLC plates, chromatographed, and NBD-Cl derivatives formed. The fluorescent amine spots were scraped from TLC plates and eluted from silica gel with 5.0 ml of ethyl acetate. Fluorescent measurements were done with primary filter (365 nm) and a secondary filter (465 nm). Chambers and Staruszkiewicz (1978) determined histamine content of cheese by an official AOAC fluorometric method, which is the method for determining histamine in tuna. Application of the method to cheese had no special difficulties. Rapid methods were reviewed by Stratton et al., (1991). Many enzymatic methods including enzyme-linked immunosorbent assay (ELISA) have been developed to detect histamine in blood and tissues. Enzymatic methods utilize histamine Nmethyltransferase and radioactive S-adenosylmethionine. However, these methods and ELISA technique have not been applied to foods.

Histamine Regulation : Taylor et al., (1978) reported that ingestion of 70-1000 mg of histamine in a single meal is necessary to elicit any symptoms of toxicity depending on age and health of person. An exceeding level of histamine of 10 mg/100g is connected with product quality (Jay, 1992). In Turkish Food Codex, 200 mg kg-1 of histamine is accepted as a defect indicator for fishes, and 10 mg kg-1 for wines. No limitation is indicated for cheeses. In German Fish Order it is allowed upper level histamine for Mackerel and Herring fishes by 200 mg/kg. In USA, the limit of the hazard action level is established for tuna as 50mg histamine/100g. It is 10 mg/100 g for defect action level of histamine in tuna. However, more attention is necessary for regulation of histamine in foods (Stratton *et al.*, 1991).

Suggestions

It can be suggested that 1) consumer should be informed that which food contains what levels of histamine, 2) food producers should label their product in terms of histamine content, 3) physicians and dieticians should have enough information on histamine contents of foods, 4) records are needed for the suspect patients coming to hospitals, and 5) regulations has to be determined for all foods in all countries (Bodmer *et al.*, 1999).

References

Antila, P., V. Antila, J. Mathila and H. Hakkarainen, 1984. Biogenic amines in cheese. 1. determination of biogenic amines in Finnish cheese using HPLC. Milchwissenschaft, 39: 81- 85.

Arnold, S. H. and W. D. Brown, 1978. Histamine toxicity from fish products. Adv. Food Res.34: 13-154.

Bakirci, I., 2000. Peynirlerde biyogen amin olu°umu ve etkili faktörler. Süt Mikrobiyolojisi ve Katki Maddeleri (Sempozyum Kitabi).Tekirdag., 328-336.

Bodmer, S., C. Imark and M. Kneubü hl, 1999. Biogenic amines in foods: Histamine and food processing. Inflamm. Res. 48: 296-300.

Casella, I. G., M. Gatta and E. Desimoni, 2001. Determination of histamine by high-pH anionexchange chromatography with electrochemical detection. Food Chem. 73: 367-372.

Chambers, T. L. and W. F. Staruszkiewicz, 1978. Fluorometric detemination of histamine in cheese. J. Assoc. Off. Anal. Chem., 61:1092-1097.

Chang, S. F., 1985. Analysis of cheese for histamine, tyramine, tryptamine, Histidine, tyrosine, and tryptophane. J. Dairy Sci. 68: 2840-2846.

Durlu-Özkaya, F. and N. Tunail, 2000. Salamura Beyaz peynirlerde biyogen amin riski. Süt Mikrobiyolojisi ve Katki Maddeleri (Sempozyum Kitabi). Tekirdað., 146-153.

Durlu-Özkaya, F., 2002. Çesitli peynirlerimizin biyojen amin kompozisyonu. Türkye 7. Gida
Kongresi T. K., 2002 Mayis 22-24:465-472.

Durlu-Özkaya, F., I. Alichainidis, E. Litopoulou-Tzanetaki and N. Tunail, N. 1999. Determination of biogenic amine content of Beyaz cheese and biogenic amine production ability of some lactic acid bacteria. Milchwissenschaft 54: 680-681.

Gü ven, M. and A. Hayaloðlu, 2002. Peynir olgunlasmasi sirasinda biyojenik aminlerin olusumu ve etkili faktörler. Gida Teknolojisi 6: 65-71.

Jay, M. J., 1992. Modern food microbiology. New York. Published by Van Nostrand Reinhold.

Joosten H. M. L. J., 1988. Conditions allowing the Formation of Biogenic Amines in Cheese. 3. factors Influencing the Amongs Formed. Neth. Milk Dairy J., 41: 329-357.

Joosten H. M. L. J. and J. Stadhouders, 1987. Conditions allowing the Formation of Biogenic Amines in Cheese: 1. Decarboxylative Properties of Starter Bacteria. Neth Milk Dairy J. 41:247-258.

Leuschner, R. G. K. and W. Hammes, 1998. Degradation of Histamine and Tyramine by Brevibacterium linens during surface ripening on Munster cheese. J. Food Production, 61: 874-878.

Nizamlioglu, M., 1990. Kasar ve tulum peynirlerinde histamin ve tiramin düzey leri (Doktora Tezi). Selçuk Üniv . Saglik Bil. Enst. Konya.

Pinho, O., I. M. P. L. V. O. Ferreira, E. Mendes, B. M. Oliveira and M. Ferreira, 2001. Effect of temp. on evoluation of free amino acid and biogenic amine contents during storage of Azeitao cheese. Food Chem. 75:287-291.

Santos, M. H. S. 1986., Biogenic amines, their importance in foods. Int. J. Food Microbiology 29: 213-231.

Stratton, J. E., R. W. Hutkins and S. L. Taylor, 1991. Biogenic amines in cheese and other fermented foods: A review. J. Food Protection 54: 460-470.

Summer, S. S., F. Roche and S. L. Taylor, 1990. Factors controlling histamine production in Swiss cheese inoculated with Lb. buchneri. J. Dairy Sci. 73: 3050-3058.

Taylor, S. L., M. Leatherwood and E. R. Cieber, 1978. Histamine in sauerkraut. J. Food Sci. 43: 1030-1032.

Taylor, S. L., 1986. Histamine food poisoning: toxicology and clinical aspects. Crit. Rev. Toxicol 17: 91-128.

Vale, S., and M. B. A. Gloria, 1997. Determination of biogenic amines in cheese. J. AOAC Int. 60: 651-657.

Vale, S., and M. B. A. Gloria, 1998. Biogenic amines in Brazilian cheeses. Food Chem. 63: 343-348.

Van Boekel, M. A. J. S. and A. P. Arentsen-Stasse, 1987. Determ. of aromatic biogenic amines and their precursors in cheese by high-performance liquid chromatography. Jour. of Chromatography 389: 267-272.

Voigt, M. N., R. R. Eitenmiller, P. H. Koehler, M. K. Hamdy, 1974. Tyramine, histamine and tryptamine content of cheese. J Milk Food Technol., 37:377-381.