Research Article

Migraine and Biogenic Amines

Nevin Sanlier[1]* and Melike Bektesoglu[2]

[1]Ankara Medipol University, Faculty of Health Sciences, Department of Nutrition and Dietetics, Ankara, Turkey; [2]Ankara Medipol University, Institute of Health Sciences, Department of Nutrition and Dietetics, Ankara, Turkey

Corresponding author:
Nevin Sanlier, PhD,
Ankara Medipol University, Faculty of Health Sciences, Department of Nutrition and Dietetics,
Ankara, Turkey,
Tel: +90532 585 59 44;
E-mail: nevintekgul@gmail.com;
nevin.sanlier@ankaramedipol.edu.tr

Abstract

Objective: Migraine emerges as one of the major causes of headache in today's world. It is a disease that is often characterized by a moderate or severe one-sided headache, nausea, or vomiting as well as sensitivity to light, and sound. According to the World Health Organization (WHO), it is among the first 20 diseases that reduce individuals' working capacity. Various factors may affect the formation of migraines, such as hormonal changes, stress, hunger, fatigue, sleeping disorders, and weather conditions. The mechanisms by which these factors trigger migraine in a patient have been popular research topics recently. **Materials & Methods:** It is generally acknowledged that the central nervous system is greatly affected by these factors. The possible potential mechanisms of migraine impact on human health, MEDLINE, Embase, the Cochrane Central, www.ClinicalTrials.gov, PubMed, Science Direct, Google Scholar, and selected websites including) and databases were examined. **Results:** Various theories have been proposed regarding the formation of migraine. Among these major theories are vascular theory, neurological theory, neurovascular theory, and biochemical theory. Scientific research usually focuses on these four leading theories. Although some migraine patients may suffer from headache attacks that occur without a reason, most migraine attacks are usually caused by internal or external factors. It was reported that while a single triggering factor might cause migraine attacks in some patients, others might suffer from migraine attacks occurring because of several triggering factors. The relationship between migraine and nutrition is a complex issue. Some substances in nutritional elements may affect nerve tracts and thus cause headaches by creating a vasoconstrictor or vasodilator effect. Various chemicals in different nutritional elements were held responsible for migraine attacks. Because tyramine, phenylethylamine, and histamine are considered to play a role in headache triggering mechanisms, biogenic amines, and nutritional elements such as cheese, chocolate, and red wine containing these chemicals can be considered as important triggering factors too. **Conclusions:** The present study analyzes the impact of biogenic amines such as histamine, tyramine, and phenylethylamine on migraine attacks.

Keywords: Migraine and Biogenic Amines

Introduction

Migraine is one of the most common reasons for headaches nowadays. [1] Derived from the Greek word 'hemicrania', the words have been used in its French pronunciation 'migraine' since the 18th century. [2] The disease is generally characterized by a moderate or severe one-sided headache, nausea or vomiting, sensitivity to light, and sound. [3] While migraine prevalence in men is 6 to 9%, the same percentage is 15% to 25% for women around the globe.

[4] According to WHO data, 18% of women in the world suffer from migraine attacks. [5] It has been also reported that migraine is twice as prevalent in women as men and thus women experience more severe migraine headaches compared to men. [6] WHO data also indicate that migraine is the 19th disease that reduces individuals' working capacity around the world, and it is ranked in the 12th place for women. [7] The reason for the difference between sexes in terms of migraine prevalence has not been exactly revealed yet. It is argued that women suffer from migraines more than men due to their hormonal differences. [8] The International Headache Society (IHS), which publishes international criteria for the classification of migraines, listed several standard criteria for migraine diagnosis and treatment in ICHD-II. [9] In this document, migraine was divided into six major categories. The first migraine subtype among the most common migraine types in the world is 'simple migraine' or 'migraine without aura', while the second subtype is 'typical migraine' or 'migraine with aura. [10] Aura can be defined as a mix of neurological symptoms occurring in certain parts of the head before during or, rarely, following a migraine attack [9] . Its symptoms usually develop within five minutes, and last less than 60 minutes. While patients may sometimes suffer from headache for 60 minutes following the occurrence of aura, it may also be delayed for a few hours or may not occur at all. [11,12] In addition migraines can be divided into two categories, that is episodic, and chronic, depending on headache frequency. While, in episodic migraine, patients suffer from headaches for less than an average of 15 days each month in the last three months,

How to Cite this Article: Sanlier N, et al. Migraine and Biogenic Amines . Ann Med Health Sci Res. 2021;11:1362-1371.

chronic migraine occurs for more than an average of 15 days or at least for eight days each month in the last three months. [13] Various factors may affect the formation of migraines. The leading factors are hormonal changes, stress, hunger, fatigue, sleeping disorders and weather conditions. The impact of these factors on migraine triggering mechanisms has been a popular research topic in recent years. It is generally argued that these factors create an effect on patients' central nervous systems. [14] One of the foremost theories about the formation of migraine as a disease is vascular theory, which still maintains its validity today. [15,16] According to vascular theory, migraine is experienced because of electrochemical disorder, which occurs due to intracranial vasoconstriction followed by vasodilation. As a result of these electrochemical disorders, various substances secreted by nerves cause inflammation. [17] The second most popular theory is neurological theory, argues that migraine attacks occur due to the overstimulation of different neurons, which is caused by various changes in the neurotransmission system. [18] Neurovascular theory is the third most popular theory and argues that migraine is caused by the release of inflammatory neuropeptides from the trigeminal system, which indicates neurovascular events. [19] Besides, it has also been argued that due to changes in the hypophysis, its pressure on the trigeminal nerve may also lead to migraine attacks. [15] Another popular theory is the biochemical theory, which argues that migraine attacks occur because of decreasing blood serotonin levels. [20-22] In parallel with this theory, thrombocytic theory was also proposed, as serotonin is stored in thrombocytes. [22] According to thrombocytic theory, migraine attacks are caused by thrombocyte dysfunction. [22,23]

Materials and Methods

A literature search was carried out through MEDLINE, Embase, the Cochrane Central, www.ClinicalTrials.gov, PubMed, Science Direct, Google Scholar, and selected websites including) and the World Health Organization (WHO).

Migraine commonly effects all over the world were included in the study. The reference articles were obtained from databases using key words such as "migraine attack, biogenic amines, nutrient" to collect existing information. The sub-references of the selected articles *via* the keywords were researched and these articles were examined as well. In studies on a migraine, primarily clinical human studies, laterally animal studies have been analyzed. The research, meta-analyses, and reviews have been the basis for the current work.

Triggering factors

Headache attacks may emerge without a particular reason in some migraine patients with migraine. However, most migraine attacks are often caused by internal factors such as hormonal changes or external factors such as weather conditions and some odors. Triggering factors do not affect all patients at a similar level. While a single triggering factor may lead to headaches in some patients, a mix of various factors may cause headaches in other patients. It was reported that these triggering factors were effective by 90% in migraine without aura and by 60% in migraine with aura. [24] Migraine may also be caused by dietary factors such as stress, menstruation, hormonal changes and skipping meals, sleep patterns (insomnia or hypersomnia), environmental factors, fatigue, weather conditions (humidity, pressure, wind, etc.), alcohol (particularly beer and wine), various odors (perfumes or other strong chemicals), brightness, smoke, high altitude, coughing, and some other nutritional elements. It was reported in various studies that a single triggering factor might lead to migraine attacks in some patients, while a mix of various factors might be responsible for these attacks in other patients. [25-27] Additionally, it is also known that sodium nitrite, which is used in instant foods for food coloring, botulism prevention, may cause headaches in some individuals, which may be related to nitric oxide release and resulting validation. In this respect, individuals who are sensitive to these foods are recommended to keep away from nutritional elements containing sodium nitrite, sodium nitrate, potassium nitrate, or potassium. [28] There is a complex relationship between migraine and nutrition. Foods may affect nerve tracts and thus cause headaches by creating a vasoconstrictor or vasodilator effect due to some substances that they contain. [10,29] In daily nutrition, although skipping meals and hunger are considered as critical triggering factors, other nutritional elements such as caffeine, dairy products, alcoholic beverages (alcohol consumption is a particular triggering factor in younger individuals), fermented products, chocolate, foods containing tyramine, and nitrite, citrus fruits, monosodium glutamate, aspartame, food coloring, and additives usually causing of migraine attacks. [30] Additionally, some chemicals in various foods also lead to migraine attacks. For instance, because tyramine, phenylethylamine and histamine are considered to play a certain role in headache triggering mechanisms, biogenic amines and foods containing these chemicals such as cheese, chocolate and red wine are also widely accepted among important triggering factors. [31-33]

Biogenic amines

Biogenic amine is organic based, biologically active, and nitrogenous compounds with low molecular weights. They are formed by decarboxylation of amino acids or animation and transanimation of ketones and aldehydes, all of which emerge because of metabolic activities in plants, animals, and microorganisms. [34] They are called biogenic amines because they are formed by the metabolic activities of living organisms. [35] An amine of an amino acid emerges because of the decomposition of carboxy groups. [32] Due to the structure of amino acids, biogenic amines consist of histamine from histidine, tyramine from tyrosine, tryptamine from tryptophane and cadaverine from tysine. Some amines (histamine, serotonin, and tyramine) affect many biological incidents in animals and humans. While some biogenic amines such as spermine, spermidine and putrescine contribute to physiological processes such as flowering, fruit development and cell division, they are also used as quality indicators in various foods. [36] Biogenic amines can be divided into two groups based on their effects: vasoactive (affecting vascular system) and psychoactive (affecting the nervous system). [37] These play various metabolic roles in the human body and take part in the synthesis of nitrogen-based compounds in the human body, being important sources of nitrogen. [38] It is widely known that biogenic amines play some roles in the regulation of several physiological functions in animals and humans. However, excessive intake of

biogenic amines may cause human body to overrun its natural amine detoxification capacity and thus it tends to result in some toxic effects in the body [32,39,40] Protein-rich foods and fermented products are included in risk groups in terms of the formation of biogenic amines. [41] Protein-rich foods such as meat and fish products, egg, cheese, soy products, fermented vegetables, alcoholic beverages, citrus fruits, nuts, and chocolate can be given as major examples of nutritional elements containing biogenic amines. [42] Some foods containing biogenic amines such as histamine, tyramine, phenylethylamine, putrescine, cadaverine ve spermidine play an important role in human metabolism. Among these biogenic amines, histamine, tyramine and phenylethylamine are particularly correlated with migraine and headache attacks. [43]

Histamine and migraines

Discovered by Dale and Laidlaw in 1910, histamine is an amine emerging because of histidine decarboxylation. [32] It is metabolized by N-methyl transferase enzyme and synthesized and stored in mast cells and basophils. [44-47] It is also the amine with the highest number of biological activities. [48] It stimulates gastric secretion, smooth muscle contraction, vasodilation, permeability, and many other processes and plays a certain role in both immunological and physiological multiple mechanisms. [44-46] Histamine displays its effects on biological activities through the cardio-vascular system and connecting cell membrane receptors in various secretory glands. [48]

The relationship between histamine and headaches has been studied for more than a few centuries. Numerous studies have been so far carried out to analyze the headache induction ability of histamine and the impact of antihistamines on the treatment of headaches. [32,45] The theory about the relationship between migraine and histamine is accredited to Horton. This theory argues that histamine levels increase during a headache attack, resulting in a higher histamine level in the post-headache period. It can be thus stated that migraine is related to the degranulation of mast cells. [49]

When the link between headaches and histamine in migraine patients is analyzed, it can be observed that brain vessels are exposed to vasodilation because of histamine, which eventually results in a headache attack. [50,51] Wantke et al. applied a diet that does not contain any histamines to 28 migraine patients for 4 weeks and found that headache attacks in 19 patients were reduced by 50% or more following the diet. In addition, the number of headache attacks and analgesic drug intake declined significantly due to the diet. [48] Histamine has been analyzed in detail along with cytokines, chemokines and vasoactive peptides to gain insight into the underlying cellular mechanisms that cause migraine attacks and help them persist. The correlation between migraine, which forms mast cell degranulation and neurogenic inflammation is widely accepted. [52] Under normal circumstances, histamine can be easily digested owing to amine oxidase and conjugation activities. Following the digestive process, the detoxification system functions to metabolize histamine formed by intestinal bacteria. This process is carried out by some enzymes such as diamine oxidase, monoamine oxidase and N-methyl transferase, which transform histamine into non-toxic substances. This mechanism is sufficient for a normal diet. However, the system is disturbed by a high level of histamine consumption or the use of monoamine oxidase inhibitors, resulting in various toxic effects. [35,53]

Histamine is one of the major toxic amines found in protein-rich foods such as cheese, meat and fish products. [54] It can also be found in various fish products such as anchovy, mackerel, and tuna fish (dark meat fish) and/or oily fish. [55] In addition it is also reported that histamine levels are high in fermented products compared to other types of products. For instance, it may reach 40 mg/liter in cabbage pickle juice. [56] The consumption of foods with a high histamine level may lead to the emergence of some symptoms. [54] Maximum histamine level in nutritional elements is specified as 10-100 mg/100g, whereas the same level for wines is 2-10 mg/L. [57,58] Maximum histamine level in wines is defined as follows in the following countries: Germany (2 mg/L), Belgium (2 mg/L), France (3.5 mg/L), Australia (10 mg/L) and Switzerland (10 mg). [59]

Tyramine and migraine

Tyramine is formed by bacterial activities of tyrosine amino acid and is also called tyramine monoamine due to its chemical properties. [39,57,58] Tyramine, which is also known as trace amine in the central nervous system, causes hypertension and diet-induced migraine. [57,58,60] In the human body, biogenic amines are transformed into less active substances through decomposition in a detoxification system. Histamine-N-methyl transferase enzymes called Diamine Oxidase (DAO) and Monoamine Oxidase (MAO) function in this system. [35] Tyramine decomposition is performed by some catabolic reactions, as it is often metabolized in the gastrointestinal mucosa and liver. [37,61] It is found in lower concentrations in the human body compared to histamine. [62] The foremost effects of tyramine are norepinephrine release in sympathetic nervous cells and agonist effects on adrenergic receptors, which trigger headaches. [63] Because enzyme activities are prevented in patients treated with MAO inhibitor drugs, the toxic effects of tyramine are remarkably high. The most common symptoms of tyramine toxicity are tachycardia, hypertensive crisis, hypertension, headaches, and migraine. Also, heart and respiratory failure, edema in the lungs, neural disorders and intracranial hemorrhages are other symptoms that are likely to result in death. Tyramine is one of the most common types of biogenic amines in fermented meat products and is found in cheese types such as cheddar and parmesan, ice cream, smoked products, tune fish stored at different ambient temperatures, soy sauce, broad bean, yeast, tomato, onion, circus fruits, canned food, fig, coffee, cabbage pickle, excessively ripe fruits as well as some types of beer and wine. [64-68] The link between tyramine and headaches was first discovered when patients treated with MOA inhibitor drugs suffered from headaches and hypertensive crisis after they consumed cheese with a high tyramine content. [69] Similarly, another study found a correlation between the consumption of food with high tyramine content and acute migraine and severe headaches. [63] When foods that trigger migraine attacks were analyzed, it was found that patients reported migraine or headache attacks by 0% to 19% following cheese consumption. [70] Another study also recommended a maximum level of 900 mg/kg for tyramine, histamine, putrescine and cadaverine

content in cheese. [71] Although a usual meal contains 40 mg tyramine, under normal physiological conditions, nearly 400 mg tyramine can be consumed by an individual without any visible hypertensive reactions. 8 mg of tyramine may increase blood pressure levels when MAO inhibitors are irreversibly destroyed. [72] When tyramine is consumed without any other nutritional elements, 10 to 80 mg of tyramine may cause swellings on the human body, while amounts higher than 100 mg may result in headaches and migraines. [58,73,74] EFSA set the standards for tyramine consumption, which does not cause any negative health effects on the human body per meal per person. According to these standards, healthy individuals who do not use MAO inhibitor drugs can consume up to 600 mg per meal. On the other hand, patients using third generation and conventional MAO inhibitor drugs can consume 50 mg and 6 mg tyramine, respectively. [75] In general, tyramine toxicity levels for alcoholic beverages are reported as 25 to 40 mg/L. [76]

Phenylethylamine and migraine

While phenylethylamine and other vasoactive amines affect vascular systems directly or indirectly, psychoactive amines such as histamine, putrescine, and cadaverine affect neurotransmitters in the central nervous system. [77] The chemical structure of phenylethylamine indicates that it is an aromatic biogenic amine, theobromine, caffeine, methylxanthines, and catechin phenolic compound. Similar to tyramine, these chemicals affect the norepinephrine release in sympathetic nervous cells and brain blood flow, which eventually causes headache. [64] Biogenic amines do not pose a threat to human health unless consumed in high concentrations. Nevertheless, it may lead to some disorders in genetically flawed individuals with a limited catabolism mechanism. [32] Phenylethylamine can inhibit both diamine oxidase and histamine methyltransferase, demonstrating that the tyrosine decarboxylase enzyme, which affects tyramine, displays a low decarboxylase activity on phenylalanine, too. It is stated that even a low amount of phenylethylamine may cause headaches in patients who do not take any drugs for treatment. [78]

Phenylethylamine reduces monoamine oxidase B activity in migraine patients and causes the release of vasoactive amines such as serotonin and catecholamine. When the amount of these amines increases in the body in parallel with a monoamine oxidase B deficiency, it may lead to migraine attacks. [71] It is reported that an average amount of 30 mg/kg phenylethylamine may result in headaches. [79,80]

Among many food products, cacao and chocolate abound in phenylethylamine. The amounts of phenylethylamine in chocolate made from lightly, moderately, and finely roasted cacao is reported as less than 2.9 mg/100 g, 10 mg/100 g and 12 mg/100 g, respectively. [81] A high amount of phenylethylamine may lead to various symptoms such as headaches, increased blood pressure and skin redness. [43,82,83] Although chocolate is considered as a triggering factor for migraine patients, the role of phenylethylamine has not been fully understood yet. It was argued that caffeine in chocolate products was likely to trigger migraine attacks. [28] However, a study on female patients suffering from chronic headaches reported that chocolate was not a triggering factor for migraine or other types of headache. [84] On the other hand, another study indicated that chocolate was a triggering factor in 20% of the patients suffering from headaches. [43] A theory argues that chocolate, which is considered to trigger migraine attacks, is one of the most easily accessible desserts to please patients' appetite during the prodromal period of a migraine attack. Therefore, chocolate is assumed to be a triggering factor in attacks due to its coincidence with the occurrence of migraine attacks. [85] (Another assumption is that chemical triggering factors such as caffeine and phenylethylamine in chocolate cause norepinephrine release and change cerebral blood flow, thus leading to headache attacks in patients. [31,33]

Serotonin and migraine

Tryptophan, which is an essential aromatic amino acid, is decarboxylated to 5-hydroxytryptophan by tryptophane hydroxylase enzyme to transform it into 5-hydroxytryptamine or serotonin. [86-89] Serotonin is an aromatic and heterocyclic amine. [90] It is synthesized in the central nervous system and intestines and, as a neurotransmitter, plays a vital role in the regulation of many different physiological functions such as sleeping, thirst, hunger, mood and sexual intercourse. [89,91]

Serotonin can be found in various food products such as strawberries, grape, tomato, orange, pineapple, banana, avocado, olive oil and walnut. [92-94] Noradrenalin, octopamine, dopamine, histamine, serotonin and phenylethylamine are found in banana and banana products. Biogenic amines such as serotonin, histamine and phenylethylamine function as preservative substances (for pest control and mold prevention) in bananas. [88] Serotonin is the most common biogenic amine in unripe fruits with an amount of 49.2%, followed by spermidine with 29.5% and putrescine with 21.3%. [95] Serotonin, tyramine, histamine, noradrenaline, and tryptamine are found in higher amounts in cheese compared to amino acids due to the fermentative- activities of bacteria. [58] In a study on cheese products in Brazil, Vale et al. reported the amount of histamine in cheese as 19.65 mg/100 mg, the amount of phenylethylamine, spermidine, serotonin, agmatine and tryptamine as <4.10 mg/100 g, cadaverine as 111 mg/100 g, tyramine as 21.25 mg/100 g and putrescine as 17.37 mg/100 g. [96] Another study found putrescine, cadaverine, tryptamine, β-phenylethylamine, serotonin and tyramine in ground Turkish coffee samples and putrescine, cadaverine, tryptamine, β-phenylethylamine, serotonin and tyramine in brewed Turkish coffee samples. It was also demonstrated that both ground and brewed coffee samples had the highest amounts of serotonin. [97]

Similar to other biogenic amines such as histamine and tyramine, serotonin is also of vital importance for the proper functioning of the nervous system and blood pressure control. [98-100] A certain amount of serotonin is stored in thrombocytes in the body, and serotonin release causes vasodilation in cerebral vessels, which is considered to trigger the formation of migraine attacks along with thrombocyte dysfunction. [22,101] The connection between migraine and serotonin was first raised during the 1950s. [102] In the following years, the relationship between serotonin levels in plasma and migraine attacks was revealed and called the "serotonin hypothesis". [103,104] It is known that thrombocyte aggregation in migraine patients is easier as a response to vasoactive amines. Amines

such as serotonin and tyramine trigger this aggregation activity. Serotonin levels in plasma may slightly increase during the early stages of migraine attacks, as serotonin release in thrombocytes require aggregation. Thrombocytes in migraine patients contain monoamine oxidase enzyme in lower concentrations between migraine attack intervals. Aggregation is considered to increase during the prodromal phase of migraine, while it decreases during the headache phase. [105,106]

In a study on tryptophane, which is a precursor to serotonin, two different groups consisting of migraine patients and healthy individuals were given an amino acid mixture containing tryptophane and a tryptophane-poor amino acid mixture, respectively, to reduce short term serotonin synthesis. It was found eight hours later that migraine patients who were given a tryptophane-poor amino acid mixture suffered more from sickness, headaches, and brightness- and light-induced headaches compared to healthy individuals. It was also argued that cerebral serotonin synthesis was reduced due to a lack of tryptophan, which contributed to migraine symptoms. In another study on tryptophane, similarly, some measurements were performed seven hours later after the patients consumed a tryptophane-poor amino acid mixture. It was observed again that migraine attacks and vestibulocochlear disorders increased due to a lack of tryptophane and reducing serotonin synthesis. [107] Fat rich foods cause an increase in the number of plasma thrombocytes and a decrease in plasma serotonin levels, thus resulting in headache attacks. [108] It was also reported that fish species such as morina and somon containing a high level of omega-3 fatty acids prevented migraine attacks. Besides, thanks to the regulatory effect of Omega 3 fatty acids on nervous cells, they are considered to create a resistance mechanism against migraine attacks. [33] As for the relationship between serotonin, estrogen, and migraine, estrogen increases serotonin levels and reduces serotonin reuptake and elimination, which increases a patient's pain tolerance. [109] Although serotonin intake does not pose a risk in lower amounts, it is known to lead to some toxic effects and a reaction called Serotonin Syndrome (a rare but fatal condition) in individuals with genetic disorders as well as due to the simultaneous use of Monoamine Oxidase Inhibitor (MAOI) and other drugs causing serotonin syndrome. [58]

Tryptamine and migraine

Biogenic amines are given a name based on an amino acid which is the reason for their formation. Tryptamine is formed by tryptophane. [36] It is a chemically aromatic and heterocyclic amine included in the group of diamines. [110] Different amines such as tryptamine, tyramine and histamine are found in high amounts in cheese due to fermentative functions. [48] In a study on legumes, Shalaby used beans, chickpeas, and lupin to measure their tryptamine levels and found that they contained 30.2 mg/kg, 24.3 mg/kg and 11.7 mg/kg, respectively. [111] Tryptamine, tyramine, cadaverine, putrescine and histamine are found in fermented products. [112] A study reported that tarhana soup, a traditional Turkish soup, contained putrescine, cadaverine, spermidine, spermine, tyramine, histamine and agmatine in varying amounts, while it did not contain any methylamine, β-phenylethylamine and tryptamine. [113] In a similar study, cadaverine, putrescine, tyramine and β-phenylethylamine were not found in durable yoghurt types, while only tryptamine was found in yoghurt samples. [114] Tryptamine is a quality indicator in tomato and tomato products. [115] It was also stated that spermine, spermidine, tyramine and tryptamine increased biological activities of histamine and created a synergistic effect. [79] Histamine, tryptamine, β-phenylethylamine and tyramine are biologically active amines, and they create vasoactive or psychoactive effects on the human body. Psychoactive amines play a role in neural transmitters and affect the nervous system, while vasoactive amines usually affect the vascular system. [35] A tryptamine amount of 10 to 25 mg/kg was reported to cause severe headaches. [36,80]

Cadaverine, putrescine and migraine

Cadaverine and putrescine are formed by bacterial activities of ornithine amino acids. [116] Putrescine is abundant in various foods such as fruits, cheese and non-green vegetables. [117] The amounts of tyramine, putrescine, histamine and cadaverine in dried fermented sausages in Greece were calculated as 197.7 mg/kg, 96.5 mg/kg, 7.0 mg/kg and 3.6 mg/kg, respectively. In Italy, on the other hand, the amounts of agmatine and spermine in salami samples were measured as 8.3 mg. [118] Another study on sausage samples in Poland demonstrated that total amounts of dominant biogenic amines such as tyramine, putrescine and 2-phenylethylamine were measured as 17.1 mg/kg. [119]

Fruit and fruit juices are particularly rich in putrescines. [35,120] Diamines such as putrescine and cadaverine do not directly affect human health. [121,122] Higher diamine concentrations increase the absorption of biogenic amines in intestines and reduce amine catabolism.[123] Also, diamines such as putrescine and cadaverine often increase the toxic effects of histamine and thus contribute to symptoms such as headache and food poisoning. [124] Putrescine and cadaverine (putrefactive amine) increase the toxic effects of tyramine and phenylethylamine. Enzymes that metabolize these biogenic amines interact with different enzymes such as diamine oxidase, monoamine oxidase and histamine methyltransferase to display their effects. [125] They inhibit enzymes (MAO and DAO) in the detoxification system and increase the toxic effects of histamine and other amines such as headache and respiratory distress. [126] It is known that biogenic amines in beer contribute to headache attacks in migraine patients. However, their effects vary from one patient to another. Izquierdo-Pulido et al. reported that agmatine and putrescine were found in all beer types. [127] 2000 ppm of cadaverine, tyramine and putrescine did not display any negative effects on migraine patients. Therefore, acute toxicity levels for tyramine and cadaverine were specified as more than 2000 ppm. [112,128]

Polyamines and migraine

Amines such as spermine and spermidine, which are also known as polyamines, play important roles in the human body. [129] Polyamines contribute to various mechanisms in the human body such as cell tissue regeneration, organ development, immune system and neurotransmitters in the nervous system. [129,130] Polyamines are responsible for RNA, DNA and protein synthesis in the human body. In addition to being produced endogenously, they can be also consumed exogenously in a diet. [81]

Polyamines such as spermidine and spermine are biological amines that are formed naturally in foods. However, their formations are not correlated with bacteriosis. [68] Spermine and spermidine are among the most common amine groups in nutritional elements. [131] Zhai et al. found eight biogenic amines in 13 different fish species among 49 fish species in South China (histamine, tryptamine, putrescine, phenylethylamine, cadaverine, spermine and spermidine). [132] Spermidine, histamine, putrescine and cadaverine are important quality indicators for fish and fish products. [133] In Czech Republic, 112 raw samples obtained from freshwater fish, saltwater fish and other sea creatures used in restaurants were found to contain high amounts of biogenic amines. [134] The most common biogenic amines in fresh fruit and vegetables and fermented products are spermine, spermidine, putrescine and tyramine. [83]

Although various biogenic amines in different structures are needed for the proper functioning of the human body and health, the consumption of foods containing a high amount of biogenic amine may result in some toxic effects. [135] For instance, spermine and spermidine increase the toxic effects of tyramine, histamine and phenylethylamine. Enzymes that metabolize these biogenic amines also interact with different enzymes such as diamine oxidase, monoamine oxidase and histamine methyltransferase, which cause various problems in the human body such as headache, respiratory distress and food poisoning. [124,125] (values for oral toxicity values in spermine and spermidine were calculated as 600 ppm. [128]

Nitrosamine and migraine

Nitrosamines are usually formed by reactions of secondary and tertiary amines with nitrite under certain conditions. [136] The existences of secondary and tertiary amines such as Dimethylamine (DA) and Trimethylamine (TMA) are effective in the formation of nitrosamine. Putrescine and cadaverine are transformed into secondary amines such as pyrrolidine and piperidine thanks to the heat. Pyrrolidine and piperidine can form cancerogenic nitrosamines through their reactions with nitrite, which may occur in an acidic, neutral, and basic environment. Nitrite is necessary for the formation of nitrosamine reaction. [136,137] Nitrosamines are cancerogenic amines. [138]. Nitrate degradation in saliva or intestinal bacterial can trigger nitrite formation. [57] Nitrate intake occurs through the consumption of processed foods such as beet, lettuce, celery, spinach, cauliflower, and potato. [31,139] Processed meat products (salami, fermented sausage, and sausage) create nitrites, nitrates and cancerogenic nitrosamines (E250, E251). Individuals who consume sausage and other dried meat and fish products may suffer from head attacks within several minutes. Metmyoglobin is formed by nitric oxygen release, reducing blood oxygen-carrying capacity. As a result, vasodilatory effects contribute to skin redness, headaches, and neck aches. [137] Fukui et al. reported that sausage and salami were triggering factors for migraine patients by 6% and 4.5%, respectively. [139]

Conclusion

Migraine is a polygenic disease that affects an individual's life negatively. Different theories have been so far proposed regarding migraine attacks. However, more studies are needed to reveal various migraine triggering factors in different patients. It is widely known that most of these factors is usually food-related factors that contain chemicals with biogenic amines. Until today, in different hypotheses, biogenic amines such as histamine, tyramine, phenylethylamine, and serotonin were held responsible for migraine attacks. Other amines too affect these amines and play a role in migraine attacks. Therefore, more studies must be carried out to explore the relationship between migraine and biogenic amines.

Conflict of Interests

The authors declare that they have no conflict of interest.

References

1. Siniatchkin M, Averkina N, Gerber WD. Relationship between precipitating agents and neurophysiological abnormalities in migraine. Cephalalgia. 2006;26:457-465
2. Silberstein Stephen D, Lipton Richard B, Goadsby Peter J. Headache in clinical practice. 1998;5:387- 396.
3. Sachdev A, Marmura M. Metabolic syndrome and migraine. Front Neurol. 2012;3:161.
4. Seferoğlu M, Karli N, Zarifoğlu M, Şen Ç, Albas M, Özkaya G, et al. Factors for progression and chronification of episodic migraine: one-year face-to-face follow-up study. J Neurol Sci. 2012;29.
5. World Health Organization. Mental Health: New Understanding, WHO: New HopeGeneva, 2004.
6. Lipton RB, Stewart WF, Diamond S, Diamond ML, Reed M. Prevelance and burden of migraine in the United States. Data from the American Migraine Study II. J Headache Pain. 2001;41:646-657.
7. World Health Organization. Mental Health: New Understanding, WHO: New Hope Geneva, 2001.
8. Peatfield R. Campbell JK. Başağrısı Çev.:Kahramanoğlu M. Koçak U., AND Yayıncılık. 2002;1. Baskı, İstanbul.
9. Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders. 2nd edition. Cephalalgia. . 2004;24 Suppl 1:8-160.
10. Bigal ME, Lipton RB. Migraine at all ages. Curr Pain Headache Rep. 2006.
11. Rockett FC, Oliveira VR, Castro K, Chaves ML, Perla AS, Perry ID. Dietary aspects of migraine trigger factors. Nutr Rev. 2012;70:337-356.
12. Olesen J, Bes A, Kunkel R, Lance JW, Nappi G, Pfaffenrath V, et al. The international classification of headache disorders. (beta version). Cephalalgia. 2013;33:629-808.
13. Fava A, Pirritano D, Consoli D, Plastino M, Casalinuovo F, Cristofaro S, et al. Chronic migraine in women is associated with insulin resistance: A cross-Sectional study. Eur J Neurol. 2014;21:267-272.
14. Ferrari MD. Migraine. Lancet 1998;351:1043-1051.

15. Raskin NH, Green MW. Migraine and other headaches. In: Rowland LP (Editor). Merritt's textbook of neurology. 2005; 11. Baskı. Philadelphia. Lippincott Williams & Wilkins. 981-989.

16. Ropper AH, Brown RH. Headache and other craniofacial pains. In: Foltin J, Nogueira I, Edmonson KG, Sheinis LA (Editors). Adams and Victor's principles of neurology. 8th ed, USA. Mc Graw Hill Inc. 2005;144-165.

17. Kıvrak Y, Özen Ş, Yücel Y. Anxiety and hopelessness levels in patients with migraine and tension headache. Dicle Med J. 2009;36:173-177.

18. Galletti F, Cupini LM, Corbelli I, Calabresi P, Sarchielli P. Pathophysiological basis of migraine prophylaxis. Prog Neurobiol. 2009;89:176-192.

19. Grossman W, Schmidrams H. An extract of petasites hybridus is effective in the prophylaxis of migraine. Altern Med Rev. 2001;6:303-310.

20. Arulmozhi DK, Veeranjaneyulu A, Bodhankar SL. Migraine. Current concepts and emerging therapies. Vascul Pharmacol. 2005;43:176 -187.

21. Nagata E, Shibata M, Hamada J, Shimizu T, Katoh Y, Gotoh K, et al. Plasma 5-Hydroxytryptamine (5- HT) in migraine during an attack free period. Headache. 2006;46:592-596.

22. Izzati-Zade KF. The Role of Serotonin in the pathogenesis and clinical presentations of migraine attacks. Neurosci Behav Physiol. 2008;38:501-505.

23. Matsunaga M, Murakami H, Yamakawa K, Isowa T, Kasugai K, Yoneda M, et al. Genetic variations in the serotonin transporter gene linked polymorphic region influence attraction for a favorite person and the associated interactions between the central nervous and immune systems. Neurosci Lett. 2010;14:211-215.

24. Siva A. Başağrısı Epidemiyolojisi. İ.Ü. Cerrahpaşa Tıp Fakültesi Sürekli Tıp Eğitimi Etkinlikleri. Baş, Boyun, Bel Ağrıları Sempozyum Dizisi. 2002;30:9-14.

25. Reid GJ, PJ McGrath. Psychological treatments for migraine. Biomed Pharmacother. 1996;50:58-63.

26. Yıldırım F, Kerem Gunel M, Akbayrak T. Investigation of the relationship between perceived pain intensity and stress symptoms, tendency to stress, and coping styles in migraineur women. The Pain Clinic. 2005;17:89-93.

27. Kelman L. The triggers or precipitants of the acute migraine attack. Cephalalgia. 2007;27:394-402.

28. Sun-Edelsteın C, Mauskop A. Foods and supplements in the management of migraine headaches. Clin J Pain. 2009; 25:446-452.

29. Bigal ME, Kurth T, Santanello N, Buse D, Golden W, Robbins M, et al. Migraine and cardiovascular disease. Neurology. 2010;74:628-635.

30. Blau JN, Diamond S. Dietary factors in migraine precipitation. The physician's view. Headache. 1985; 25:184-187.

31. http://www.americannutritionassociation.org/newsletter/role-diet-migraine-headaches 18.04.2020.

32. Yerlikaya P, Gökoğlu N. Gıdalarda biyojen aminler ve önemi. Gıda Mühendisliği Dergisi. 2002;6:24-30.

33. Arora H, Kaur R. The role of diet in migraine headaches. Delhi Psychiatry Journal. 2008;11:69-72.

34. Latorre-Moratalla ML, Bover-Cid S, Veciana-Nogues MT, Vidal-Carou MC. Control of biogenic amines in fermented sausages, role of starter cultures. Front Food Microbiol. 2012;3:1-9.

35. Shalaby AR. Significance of Biogenic Amines to Food Safety and Human Health. Food Res Int. 1996;29:675-690.

36. Karahan AG. Gıdalarda biyojen aminler. Orlab On-Line Mik Derg. 2003;1:21-32.

37. McCabe-Sellers BJ, Staggs CG, Bogle ML. Tyramine in foods and monoamine oxidase inhibitor drugs. A crossroad where medicine, nutrition, pharmacy, and food industry converge. J Food Compos Anal. 2006;19, 58-65.

38. Estevez M, Ventanas S, Cava R. Protein Oxidation in Frankfurters with Increasing Levels of Added Rosemary Essential Oil. Effect on Color and Texture Deterioration. Food Chem Tox. 2005;7:427-432.

39. Özoğul F, Küley E, Özoğul Y. Balık ve balık ürünlerinde oluşan biyojenik aminler. Ege Ürünleri Su Ürünleri Dergisi. 2004;21:375-381.

40. Karovičová J, Kohajdová Z. Biogenic amines in food. Chemical Papers. 2005;59:70-79.

41. Vatansever L. Et ve et ürünlerinde biyojenik aminler. Kafkas Univ. Vet. Fak. Derg. 2004;10:203-208.

42. Turgut Z. ''Starter Kültür Kullanılarak Üretilen Hıyar Turşularında Biyojen Amin Oluşumu Üzerine Araştırma''. Yüksek Lisans Tezi. Ankara Üniversitesi Fen Bilimleri Enstitüsü Gıda Mühendisliği Anabilim Dalı. 2006.

43. Wöber C, Holzhammer J, Zeitlhofer J, Wessely P, Wöber-Bingöl Ç. Trigger factors of migraine and tension-type headache. Experience and knowledge of the patients. J Headache Pain. 2006;7:188-195.

44. Simons FER, Simons KJ. Histamine and H1-antihistamines. celebrating a century of progress. J allergy Clin Immunol. 2011;128:1139-1150.

45. Alstadhaug KB Histamine in migraine and brain. Headache J Head Face Pain. 2014;54:246-259.

46. Panula P, Chazot PL, Cowart M, Gutzmer R, Leurs R, Liu WLS, et al. International union of basic and clinical pharmacology. XCVIII. Histamine receptors. Pharmacol Rev. 2015;67:601-655.

47. Lonvaud-Funel, A. Biogenic amines in wines: role of lactic acid bacteria. FEMS Microbiology Letters. 2001;199:9-13.

48. Joosten HMLJ. The biogenic amine contents of Dutch cheese and their toxicological significance. Neth. Milk Dairy. 1988;41:25-42.

49. Sacks O. Migren. 1. Baskı. İstanbul. İletişim yayınları. 2002.
50. Yuan H, Silberstein SD. Histamine and migraine. Headache J Head Face Pain. 2017.
51. Wantke F, Götz M, Jarisch R. Histamine-free diet. treatment of choice for histamine-induced food intolerance and supporting treatment for chronical headaches. Clin Exp Allergy. 1993;23:982-985.
52. Ramachandran R. Neurogenic inflammation and its role in migraine. Semin Immunopathol. 2018;40:301-314.
53. Hornero-Mendez D, Garrido-Fernandez A. Rapid high-performance liquid chromatography analysis of biogenic amines in fermented vegetable brines. J Food Prot. 1997;60:414-419.
54. Şahin Ercan S, Bozkurt H, Soysal Ç. Significance of Biogenic Amines in Foods and Their Reduction Methods. J Food Sci Eng. 2013;3.
55. Köse S. Su ürünlerinden kaynaklanan histamin zehirlenmesi ve önemi. Doğu Anadolu Bölgesi II. Su Ürünleri Sempozyumu. 1999;14-16.
56. Temiz A, Acar J. Bitkisel gıdalardaki doğal toksik bileşikler. Gıda. 1984;29-39.
57. Kohlstad I. Food and Nutrients in Disease Management. by Taylor & Francis Group, LLC, Sun-Edelstein C., Mauskop A. Food Triggers and Nutrient Therapies. 2009;429-444.
58. Alper N, Temiz A. Besinlerdeki Biyojen Aminler ve Önemi. Türk Hijyen ve Deneysel Biyoloji Dergisi. 2001;58:71-80.
59. Restuccia D, Loizzo MR, Spizzirri UG. Accumulation of biogenic amines in wine. Role of alcoholic and malolactic fermentation. Fermentatio. 2018;4:6.
60. Özdestan Ö, Üren A. Gıda ve Yem Bilimi - Teknolojisi Dergisi. 2012;12:32-40.
61. Glória MBA. Bioactive amines, H. Hui and L.L.Nollet, (Eds.). Handbook of Food Science. Technology and Engineering. Taylor & Francis. New York. 2005;1:13-32.
62. Bakirci İ. Peynirlerde Biyojen Amin Oluşumu ve Etkili Faktörler. Süt Mikrobiyolojisi ve Katkı Maddeleri. VI. Süt ve Süt Ürünleri Sempozyumu Tebliğler Kitabı. 2000;328-336.
63. Martin VT, Behbehani MM. Toward a rational understanding of migraine trigger factors. 2001;85:911-941.
64. Dora B, Yılmaz N, Apaydın-Doğan E, Özdemir-Karahasan C, Türkay M. Intergender differences in triggering factors among different subtypes of migraine and tension-type headache. J Neurol Sci. [Turkish]. 2010;27:386-394.
65. Aran D, Tomlınson S, Holt A, Mousseau DD, Baker GB. Trace amines and their relevance to psychiatry and neurology: a brief overview. J Clin Psychopharmacol. 2011;21:73-79.
66. www.migraine.org.uk. Migraine and food. 25.03.2020.
67. http://www.headaches.org/education/Headache_Topic_Sheets/Low_Tyramine_Diet_for_Migraine. Erişim tarihi:13:03:2020
68. Veciana-Nogues MT, Marine-Font MC. Vidal-Carou. Biogenic amines as hygenic quality indicators of tunas. Relationships with microbial counts, ATP-related compounds, volatile amines, and organoleptic changes. J Agric Food Chem. 1997;45:2036-2041.
69. Blackwell B. Hypertensive crisis due to monamine-oxidase inhibitors. Lancet.1963 ; 2:849.
70. Wöber-Bingol Ç, Wöber C. Triggers of migraine and tension-type headache. Handbook of Clinical Neurology. 2011;97:161-172.
71. Flick GJ, Granata LA. Biogenic Amines in Foods. In. Dąbrowski, WM and Sikorski, ZE. (eds.). Toxins in Food. CRC Press. USA. 2004;121-154.
72. Stahl SM, Felker A. Monoamine oxidase inhibitors. A modern guide to an unrequited class of antidepressants. CNS Spectrums. 2008;13:855-871.
73. Erginkaya, Z., Var, I. Et ve et ürünlerinde biyojenik aminler. Gıda. 1989 ;14 (3): 171-174.
74. Kalac P, Spicka J, Krizek M, Steidlova S, Pelikanova T. Concentrations of seven biogenic amines in sauerkraut. Food Chem.1999;67:275-280.
75. EFSA. Scientific Opinion on risk based control of biogenic amine formation in fermentedfoods. 2011.
76. Schumacher RL, Gardin JPP, Colimo AGSC, Bettoni JC, Messerschmidt I. Compostos nitrogenados do vinho. Fatores envolvidos na formação de aminoácidos e aminas biogênica. Evidência. 2012;12:137-154.
77. Cardozo M, Souza SP, Lima KD, Lima AL. Degradation of biogenetic amines by gamma radiation process and identification by GC/MS. Interna- tional Nuclear Atlantic Conference. Brazil. 2011; 24-28.
78. Yıldız F, Yetişemeyen A. Peynirlerde Biyojen Amin Riski. Tekirdağ Ziraat Fakültesi Dergisi. 2005;2:127-134.
79. Kurt S. Sucuğun bazı özellikleri ve biyojen amin oluşumu üzerinde fermentasyon süresi, nitrit seviyesi ve ısıl işlem sıcaklığı etkisi. Yüzüncü Yıl Üniversitesi Fen Bilimleri Enstitüsü Gıda Mühendisliği Anabilim Dalı Doktora Tezi. 2006;99.
80. Komprda T, Neznalova J, Standara S, Bover- Cid S. Effect of starter culture and storage temperature on the content of biogenic amines in dry fermented sausage polican. Meat Sci. 2001;59:267- 276.
81. Halasz A, Barath A, Simon-Sarkadi L, Holzapfel W. Biogenic amines and their production by microorganisms in food. Trends in Food Sci and Tech. 1994;5:42-49.
82. Pereira Monteiro JM, Dahlof CG. Single use of substances. In: Olesen J, Tfelt-Hansen P, Welch KMA, eds. The Headaches. 2nd ed. Philadelphia: Lippincott, Williams & Wilkins. 1999;861-869.
83. Papageorgiou M, Lambropoulou D, Morrison C, Kłodzińska

E, Namieśnik J, Płotka-Wasylka J. Literature update of analytical methods for biogenic amines determination in food and beverages. TRAC-Trend Anal Chem. 2017;98:128-142.

84. Marcus DA, Scharff L, Turk D, Gourley LM. A double-blind provocative study chocolate as a trigger of headache. Cephalalgia. 1997;17:855-862.

85. Erdine S. Ağrı. Nobel Tıp Kitabevleri. 1.Basım. İstanbul. 2000.

86. Sainio EL, Pulkki K, Young SN. L-Tryptophan: Biochemical, nutritional and pharmacological aspects. J Amino acids. 1996;10:21-47.

87. Onat T, Emerk K, Sözmen EY. [Human Bio- chemistry]. 2006; 2. Baskı. Ankara. Palme yayıncılık.

88. Glória MBA. Bioactive amines, H. Hui and L.L.Nollet, (Eds.). Handbook of Food Science. Technology and Engineering. Taylor & Francis. New York. 2005;1:13-32.

89. Rodriguez M, Carneiro C, Feijó M, Júnior C, Mano S. Bioactive amines. Aspects of quality and safety in food. Food Sci Nutr. 2014;5:138-146.

90. Azim Ö. Gıdalarda Yüksek Basınç Sıvı Kromatografisi (HPLC) ile Biyojen Amin Analizleri. Yüksek Lisans Tezi. Ege Üniversitesi Fen Bilimleri Enstitüsü. 2002;89.

91. Kalač P. Health effects and occurrence of dietary polyamines: A review for the period 2005-mid 2013. Food Chem. 2014;161:27-39.

92. Badria FA. Melatonin, serotonin and tryptamine in some egyptian food and medicinal plants. J of Med Food. 2002;5:153-157.

93. Cirilo MPG, Coelho AFS, Araujo CM, Gonçalves FRB, Nogueira FD, Gloria MBA. Profile and levels of bioactive amines in green and roasted coffee. Food Chemi. 2003;82:397-402.

94. Vieira SM, Theodoro KH, Gloria MBA. Profile and levels of bioactive amines in orange juice and orange soft drink. Food Chem. 2007;100:895-903.

95. Adão RC, Gloria MBA. Bioactive amines and carbohydrate changes during ripening of "Prata" Banana (Musa Acuminata x Musa balbisiana). Food Chemistry. 2005;90:705-711.

96. Vale S, Gloria MBA. Biogenic amines in Brazilian cheeses. Food Chem. 1998;63:343-348.

97. Özdestan Ö. Evaluation of bioactive amine and mineral levels in Turkish coffee. Food Res Int. 2014;61:167-175.

98. Askar A, Treptow H. Biogene Amine in Lebensmittein Vorkommen, Bedeutung und Bestimmung, Eugen Ulmer GmbH and Co. Stuggart, Germany. 1986.

99. Maijala R, Eerola S. Contaminant lactic acid bacteria of dry sausages produce histamine and tyramine. Meat Science. 1993;35:387-395.

100. Ten Brink B, Damink C, Joosten HMLJ, Huis In't Veld JHJ. Occurence and formation of biologically active amines in foods. Int J Food Microbiol. 1990;11:73-84.

101. Ayalp S, Şahin Ş, Benli Aksungar F, Karşıdağ S. Aurasız Migrende Trombosit Serotonin Düzeylerinin Değerlendirilmesi. Ağrı. 2012;24:117-122.

102. Ostfeld AM, Wolff HG. Studies on headache: arterenol (norepinephrine) and vasculer headache of the migraine type. Arch Neurol Phychiat. 1955;74:131.

103. Lance JW. Headache. Ann Neurol. 1981;10:1-10.

104. Lance JW, Lambert GA, Goadsby PJ, Duckworth JW. Brainstem influences on the cephalic circulation. Experimental data from cat and monkey of relevance to the mechanism of migraine. Headache.1983;23:258-265.

105. Erel C. Baş Ağrıları. İstanbul. Osmanlı Matbaası. 1987.

106. Weiller C, May A, Limmroth V, Jüptner M, Kaube H, Schayck RV, et al. Brain stem activation in spontaneous human migraine attacks. Nat Med Jul. 1995;1:658-660.

107. Drummond PD. Effect of tryptophan depletion on symptoms of motion sickness in migraineurs. Neurology. 2005;65:620-622.

108. Millichap JG, Yee MM. The diet factor in pediatric and adolescent migraine. Pediatr Neurol. 2003;28:9-15.

109. Maizels M, Blumenfeld A, Burchette R. A combination of riboflavin, magnesium, and feverfew for migraine prophylaxis, a randomized trial. Headache. 2004;44:885-890.

110. Peña-Gallego A, Hernández-Orte P, Cacho J, Ferreira V. High-performance liquid chromatography analysis of amines in must and wine, a review. Food Rev Int. 2012;28:71-96.

111. Shalaby AR. Changes in biogenic amines in mature and germinating legume seeds and their behavior during cooking. Nahrung. 2000;44:23-27.

112. Şanlıbaba P, Uymaz B. Biogenic amine formation in fermented foods. Cheese and Wine. Eur Int J Sci Technol. 2015;4:82- 92.

113. Keşkekoğlu H. Tarhana Üretimi ve Depolanması Süresince Biyojen Amin Oluşumunun Araştırılması. Ege Üniversitesi Fen Bilimleri Enstitüsü Yüksek Lisans Tezi. Bornova. İZMİR. 2009.

114. Sömer VF. Dayanıklı yoğurtların mikrobiyolojik, fizikokimyasal özelliklerinin ve biyojen amin içeriklerinin belirlenmesi. Mehmet Akif Esoy Üniversitesi Fen Bilimleri Enstitüsü. Biyoloji Anabilim Dalı Yüksek Lisans Tezi. Burdur. 2013.

115. Chiacchierini E, Restuccia D, Vinci G. Evaluation of two different extraction methods for chromatographic determination of bioactive amines intomato products. Talanta. 2006;69:548-555.

116. Fernández-Salguero J, Mackie IM. Technical note. Preliminary survey of the content of histamine and other higher amines in some samples of spanish canned fish. Int J Food Sci Technol.1987;22:409-412.

117. Bardocz S, Duguid TJ, Brown DS, Grant G, Pusztai A, White A, et al. The importance of dietary polyamines in cell regeneration and growth. Br J Nutr. 1995;73:819-828.

118. Palermo C, Muscarella M, Nardiello D, Iammarino M, Centonze D. A multiresidual method based on ion-exchange chromatography with conductivity detection for the determination of biogenic amines in food and beverages. Anal Bioanal Chem. 2013;405:1015-1023.

119. Wu H, Li G, Liu S ,Ji Z, Zhang Q, Hu N, et al. Simultaneous determination of seven biogenic amines in foodstuff samples using one-step fluorescence labeling and dispersive liquid–liquid microextraction followed by hplc- fld and method optimization using response surface methodology. Food Anal. Methods. 2015;8:685-695.

120. Maxa E, Brandes W. Biogenic Amine in Fruchtsaften. Mitteilungen Klosterneuburg. 1993;43:101-106.

121. Eerola S, Sagues AXR, Lilleberg L, Aalto H. Biogenic amines in dry sausages during shelf-life storage. Zeitung Lebensmittel For Untersuchung und Forschung A. 1997;205:351-355.

122. Hernandez-Jover T, Izquierdo-Pulido M, Veciana-Nogues MT, Marine-Font A, Vidal-Carou MC. Biogenic amines and polyamine contents in meat and meat products. J Agric Food Chem. 1997;45:2098-2102.

123. Bardocz S. Polyamines in food and their consequences for food quality and human health. Trends Food Sci Technol. 1995;6:341-346.

124. Bjeldanes, LF, Schutz DE, Morris MM. On the aetiology of scombroid poisoning: cadaverine potentiation of histamine toxicity in the guinea-pig. Food Chem Toxicol. 1978;16:157-159.

125. Landete JM, Ferrer S, Pardo I. Biogenic amine production by lactic acid bacteria, acetic acid bacteria and yeast isolated from wine. Food Control. 2007;18:1569-1574.

126. Stratton JE, Hutkins RW, Taylors SL. Biogenic amines in cheese and other fermented foods. A Review. J Food Prot. 1991;54:460-470.

127. Izquierdo-Pulido M, Hernandez-Jover T, Marine-Font A, Vidal-Carou MC. Biogenic amines in European beers. J Agric Food Chem. 1996;44:3159-3163.

128. Til HP, Falke HE, Prinsen MK, Willems MI. Acute and subacute toxicity of tyramine, spermidine, spermine, putrescine and cadaverine in rats. Food Chem. Toxicol. 1997;35:337-348.

129. Özdemir S, Kocabaşoğlu N. Serotonin sendromuna güncel bir yaklaşım. Klinik Psikofarmakoloji Bülteni. 2007; 17:217-225.

130. Mekki I, Caminc F, Perinid M, Smetia S, Hajjia H, Mahouachie M, et al. Differentiating the geographical origin of Tunisian indigenous lamb using stable isotope ratio and fatty acid content. J Food Com Anal. 2016;53:40-48.

131. Naila A, Flint S, Fletcher G, Bremer P, Meerdink G. Control of biogenic amines in food: existing and emerging approaches. J Food Scien Eng. 2010;75:139-150.

132. Zhai H, Yang X, Li L, Xia G, Cen J, Huang H, et al. Biogenic amines in commercial fish and fish products sold in southern China. Food Control. 2012;25:303-308.

133. Cinquina AL, Cali A, Longoa F, De Santis L, Severoni A, Abballe F. Determination of biogenic amines in fish tissues by ion-exchange chromatography with conductivity detection. J Chromatogr A. 2004;1032:73-77.

134. Buňka F, Budinský P, Zimáková B, Merhaut M, Flasarová R, Pachlová V, et al. Biogenic amines occurrence in fish meat sampled from restaurants in region of Czech Republic. Food Control. 2013;31: 49-52.

135. Büyükuslu N, Eröz SH. Poliaminler ve Kanser. Kanserli Hastaların Beslenmesinde Poliaminlerin Rolleri. MÜ Sağ Bil Enst Dergi. 2015;5:123-128.

136. Şahin Ercan S, Bozkurt H, Soysal Ç. Significance of biogenic amines in foods and their reduction methods. J Food Sci Eng. 2013;3.

137. Bulushi I, Poole S, Deeth HC, Dykes GA. Biogenic amines in fish. roles in intoxication, spoilage, and nitrosamine formation--a review. Crit Rev Food Sci Nut. 2009;49369-49377.

138. Kim MK, Mah JH, Hwang HJ. Biogenic amine formation and bacterial contribution in fish, squid and shellfish. Food Chem. 2009;116:87-95.

139. Fukui PT, Gonçalves TR, Strabelli CG, Lucchino NM, Matos FC, Santos JP, et al. Trigger factors in migraine patients. Arq Neuropsiquiatr. 2008; 66:3A:494-499.