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Biochemical and Pharmacological Properties of Biogenic Amines

Dincer Erdag, Oguz Merhan and Baris Yildiz

Abstract

Biogenic amines are low molecular weight organic nitrogen compounds. They are formed by the decarboxylation of amino acids or by amination and transamination of aldehydes and ketones during normal metabolic processes in living cells and therefore are ubiquitous in animals, plants, microorganisms, and humans. In food and beverages, they are formed by the enzymes of raw materials or are generated by microbial decarboxylation of amino acids. The structure of a biogenic amine can be aromatic and heterocyclic amines (histamine, tryptamine, tyramine, phenylethylamine, and serotonin); aliphatic di-, tri-, and polyamines (putrescine, cadaverine, spermine, spermidine, and agmatine); and aliphatic volatile amines (ethylamine, methylamine, isopentylamine, and ethanolamine). Many of them possess a strong pharmacologic effect, and others are important as precursors of hormones and components of coenzymes. The biogenic amine intoxication leads to toxicological risks and health hazards that trigger psychoactive, vasoactive, and hypertensive effects resulting from consumption of high amounts of biogenic amines in foods. The toxicological effects of biogenic amines increase when the mono- and diaminoxidase enzymes are deficient or drugs that inhibit these enzymes (pain reliever, stress, and depression drugs) are used. In this chapter, biosynthesis of biogenic amines, their toxic effects as well as their physiological functions, and their effect on health will be described.

Keywords: biochemistry, biogenic amines, health, pharmacology, toxicity

1. Introduction

Biogenic amines found in animals, plants, microorganisms, and humans are formed by the decarboxylation of amino acids or amination and transamination of aldehydes and ketones during the standard metabolic processes.

Biogenic amines, having several critical biological roles in the body, have essential physiological functions such as the regulation of growth and blood pressure and control of the nerve conduction. Besides, they are required in the immunologic system of intestines and in maintaining the activity of the standard metabolic functions, and when taking the nourishment in high concentrations, they cause disorders in nervous, respiratory, and cardiovascular systems and allergic reactions as well. In this chapter, biosynthesis of biogenic amines, their toxic effects as well as their physiological functions, and their effect on health will be presented.

2. Biogenic amines

2.1 Decarboxylation of amino acids

CO_2 and biogenic amine occur as a result of the enzymatic reaction catalyzed by pyridoxal phosphate to decarboxylate the amino acid (**Figure 1**) [1]. Biogenic amines are biologically active molecules, as they are formed by decarboxylation of amino acids or amination and transamination of aldehydes and ketones during standard metabolic processes [2]. Biogenic amines take charge of the proliferation and differentiation of cells and their metabolism by entering into the structure of hormones, cobalamin (vitamin and aminoacetone), and coenzyme A in the body [3]. They have importance regarding the environment by causing water pollution, as their formations pertain to the amino acid and microorganisms [3, 4]. Biogenic amines may cause intoxications when taken in high amounts [5].

2.2 Classification of the biogenic amines

Biogenic amines are organic nitrogen compounds having a low molecular weight [5, 6]. Their chemical structure can be classified as (i) aromatic and heterocyclic (histamine, tryptamine, tyramine, phenylethylamine, and serotonin); (ii) aliphatic di-, tri-, and polyamines (putrescine, cadaverine, spermine, spermidine, and agmatine); and (iii) aliphatic volatile amines (ethylamine, methylamine, isopentylamine, and ethanolamine) (**Figure 2**) [7, 8]. Besides, their amine group classifications include (i) monoamine (phenylethylamine, tyramine, methylamine, ethylamine, isopentylamine, and ethanolamine), (ii) diamine (histamine, tryptamine, serotonin, putrescine, and cadaverine), and (iii) polyamine (spermine, spermidine, and agmatine) [7–9].

2.3 Biosynthesis and functions

Biogenic amines generally occur as a result of free amino acid decarboxylations with the microbial enzymes. Amino acid decarboxylation happens by removal of the α -carboxyl group [10]. Their occurrences are as below: histamine from histidine amino acid, tyramine from tyrosine amino acid, tryptamine and serotonin from tryptophan amino acid, phenylethylamine from phenylalanine amino acid, putrescine from ornithine amino acid, cadaverine from lysine amino acid, and agmatine from arginine amino acid (**Figure 3**) [11–13].

Biogenic amines play an essential role in cell membrane stabilization, immune functions, and prevention of chronic diseases, as they participate in the nucleic acid and protein synthesis [14]. Besides, they are compounds created as the growth regulation (spermine, spermidine, and cadaverine), neural transmission (serotonin), and inflammation mediators (histamine and tyramine) [6, 15].

Histamine, a standard component of the body, consists of histidine amino acid as a result of histidine decarboxylase activity depending on pyridoxal phosphate

Figure 1.
Decarboxylation of amino acids.

(**Figure 3**) [16]. Histamine distribution and concentration found in the tissues of all vertebrates are very unsteady [17, 18]. Histamine takes charge of some functions related to balancing the body temperature and regulating the stomach volume, stomach pH, and cerebral activities [19] as it participates in the essential functions such as neurotransmission and vascular permeability [20, 21]. However, it also plays a role in starting the allergic reactions [22, 23].

Tryptamine consists of tryptophan amino acid as a result of the aromatic L-amino acid decarboxylase activity (**Figure 3**) [24, 25]. Tryptamine is a mono-amine alkaloid found in plants, fungi, and animals [26]. Tryptamine, found in trace amounts in mammalian brains, increases blood pressure [10, 27] as well as plays a role as a neurotransmitter or neuromodulator [26].

The amino acid of phenylalanine synthesizes phenylethylamine through the aromatic L-amino acid decarboxylase in humans, some fungi, and bacteria as well as several plants and animal species (**Figure 3**) [28–30]. It functions as a neurotransmitter in the human central nervous system [31, 32].

Classified Chemical Structures		
Aromatic and Heterocyclic Amines	Histamine
	Tryptamine
	Phenylethylamine
	Tyramine
	Serotonin
Aliphatic Di-, Tri- and Polyamines	Putrescine
	Cadaverine
	Spermidine
	Spermine
	Agmatine
Volatile Aliphatic Amines	Methylamine
	Ethylamine
	Isopentylamine
	Ethanolamine

Figure 2.
Classification of biogenic amines according to their chemical structures.

Figure 3.
Formation mechanism of biogenic amines.

Tyramine, consisting of tyrosine amino acid as a result of tyrosine decarboxylase activity, is generally found in low amounts (**Figure 3**) [33–36]. Tyramine leads to several physiological reactions such as blood pressure increase, vasoconstriction [37], tyramine active noradrenalin secretion, etc., as the sympathetic nervous system controls several functions of the body [38, 39]. Tyramine, stored in the neurons, causes the increase in the tear, salivation and respiratory as well as mydriasis [39].

Tryptophan synthesizes serotonin as a result of tryptophan hydroxylase and aromatic L-amino acid decarboxylase enzyme activities (**Figure 3**) [11, 40]. Serotonin, one of the crucial neurotransmitters of the central nervous system, plays a role in plenty of critical physiological mechanisms such as sleep, mood disorders, appetite regulation, sexual behavior, cerebral blood flow regulation, and blood-brain barrier permeability [41, 42].

Putrescine consists of ornithine amino acid as a result of ornithine decarboxylase activity. Besides, it may be synthesized by arginine through the agmatine and carbamoylputrescine (**Figure 3**) [12, 39, 43, 44]. Putrescine, produced by bacteria and fungi, contributes to the cell growth, cell division, and tumorigenesis [45, 46] as it is the preliminary substance of spermidine and spermine [12, 47].

Cadaverine, synthesized by lysine as a result of lysine decarboxylase enzyme activity, takes charge of the diamine and polyamine formations (**Figure 3**) [45, 48, 49].

Spermidine synthase catalyzes spermidine formation from putrescine (**Figure 3**) [50, 51]. Spermidine is a precursor of other polyamines such as spermine and structural isomer thermospermine [45, 52]. Spermidine, regulating several crucial biological processes ($\text{Na}^+ \text{-K}^+$ ATPase), protects the membrane potential and controls the intracellular pH and volume [53]. Besides, spermidine, a polyamine found in the cellular

metabolism, has a role in the neuronal nitric oxide synthase inhibitions and intestinal tissue developments [54].

Spermine, whose precursor amino acid is ornithine, is formed from spermidine through the spermine synthase enzyme (**Figure 3**) [51]. Spermine is present in several organisms and tissues, as it is a polyamine that is found in all eukaryotic cells and has a role in the cellular metabolism [52, 55]. It plays a role in the intestinal tissue developments and stabilizes the helical structure in viruses [52, 56, 57].

Agmatine is a biogenic amine formed by arginine decarboxylase enzyme activity of arginine amino acid (**Figure 3**) [12, 44, 58]. Agmatine participates in the polyamine metabolism over the putrescine hydrolyzed by the agmatine enzyme and has several functions such as nitric oxide synthesis regulation, polyamine metabolism, and matrix metalloproteinase and enzyme activity leading to H₂O₂ production [59, 60].

The detoxification system, splitting the biogenic amines in the human body, consists of monoamine oxidase (MAO), diamine oxidase (DAO), polyamine oxidase (PAO), and histamine-N-methyl transferase (HNMT) [17, 61, 62].

3. Effect of biogenic amines on health

Biogenic amines have several important biological roles in the body and constitute the first step of protein, hormone, and nucleic acid synthesis [61, 63]. The polyamines such as putrescine, spermine, and spermidine are the unique components of living cells. Besides, the polyamines were stated to require maintaining the intestinal immunologic systems and healthy metabolic function activities [52, 64–67]. The biogenic amines cause respiratory disorders, headache, tachycardia, hypo- or hypertension, and allergic reactions when taken in high concentrations together with nutrients [68].

Biogenic amines are vasoactive components, and taking them in high amounts leads to change in blood pressure in humans and animals. The amines bear essential psychoactive or vasoactive effects, as they have the biological activities such as histamine, tryptamine, tyramine, and phenylethylamine [33]. Histamine is a biologically active amine and quickly scatters to the tissues through blood circulation and leads to several reactions. However, in the case where aminoxidase enzyme inhibitors are present in the environment, the biogenic amine prevents detoxification, and health problems (erythema, edema, rash, headache, burning, etc.) show up [17, 68]. Histamine also has essential metabolic functions such as a role in the nervous system functions and blood pressure control. It mainly takes effect by binding to the cardiovascular system (vasodilatation and hypotension) and cell membrane receptors in several secretory glands (such as gastric acid secretion) [22, 23]. In addition to them, it may lead to some neurotransmission disorders and causes headache, flushing, gastrointestinal disorders, and edema by giving rise to blood vessel dilatations [61, 69]. Histamine intoxicates when orally taken in amounts of 8 mg and above [3]. Individuals generally have lower intestinal oxidase enzyme activities according to the healthy persons, as they hold the gastrointestinal problems such as gastritis, stomach and colonic ulcers [6, 69].

Intestinal mucosal injuries may decrease the enzyme functions by detoxifying the biogenic amines [17, 63]. The DAO activity disruption causes histamine intolerance and also allergic reactions as a result of the drug utilization, as it is caused by genetic and gastrointestinal diseases or DAO inhibition [17, 70]. It was found to increase the histamine toxicity by preventing the histamine oxidation of putrescine, cadaverine, and agmatine in humans [71].

Biogenic amines lead to hypertension, as they have vasoconstriction effects such as tyramine, phenylethylamine, and tryptamine [37, 68, 72]. Consuming tyramine-rich nutriment was found to react with the tyramine MAO inhibitor drugs and cause hypertensive crisis and also migraine in some patients [73]. Tyramine is revealed to inhibit MAO, tryptamine DAO, phenylethylamine DAO, and HNMT enzymes [74, 75].

In the case of deficiency of putrescine, found in the high concentration in brains, is stated to develop the depression and also useful in the depression physiopathology [3, 76].

The pharmacological effects of putrescine, cadaverine, spermine, and spermidine are at lower levels according to histamine, tyramine, and phenylethylamine [77]. Putrescine, causing hypotension, bradycardia, and lockjaw, creates carcinogenic heterocyclic compounds including nitrosamine, nitrosopyrrolidine, and nitrosopiperidine as some biogenic amines such as cadaverine, spermine, and spermidine react with the nitrite [5, 10, 39, 78].

Polyamines are known to lead to low-dose colon cancer by affecting the cell developments and differentiation [79, 80]. In addition to them, putrescine, cadaverine, spermine, and spermidine were also found to induce apoptosis and inhibit cell proliferation. The high-dose putrescine was found to induce apoptosis and prevent the spread [81, 82]. This putrescine effect pertains to increasing the nitric oxide synthesis, inhibiting the redox reactions and binding directly to the carcinogenic agents [82].

Eating disorders such as anorexia nervosa and bulimia nervosa disrupt the function of brain serotonin [83]. Albumin deficiency shows up due to inadequate nutrition, and tryptophan transition from the blood-brain barrier increases, as it could not connect to the albumin. As a consequence, an increase occurs in the brain serotonin concentration [84, 85]. The drugs (MAO inhibitors) are used, as they change the serotonin levels in the depression, generalized anxiety disorder, and social phobia treatments [86]. The MAO inhibitors, used in treating these diseases, increase the brain concentrations by preventing the neurotransmitter (serotonin) disruptions [73, 86].

Agmatine shows a nephroprotective effect by increasing the glomerular filtration rate, and it also has a hypoglycemic impact as a result of several molecular mechanisms taking place in the blood glucose regulation [56, 87]. Besides, the agmatine level of schizophrenia patients was shown to be higher compared to that of healthy humans [88].

4. Conclusion

The present information related to biogenic amines having different physiological functions and similar chemical structures and metabolic pathways was updated, undesirable effects were considered more comprehensively for human and animal health, and information was submitted about the essential diseases caused by biogenic amines.

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References

- [1] Cellini B, Montioli R, Oppici E, Astegno A, Voltattorni CB. The chaperone role of the pyridoxal 5'-phosphate and its implications for rare diseases involving B6-dependent enzymes. *Clinical Biochemistry*. 2014;**47**:158-165. DOI: 10.1016/j.clinbiochem.2013.11.021
- [2] Liu X, Yang LX, Lu YT. Determination of biogenic amines by 3-(2-furoyl)quinoline-2-carboxaldehyde and capillary electrophoresis with laser-induced fluorescence detection. *Journal of Chromatography A*. 2003;**998**:213-219. DOI: 10.1016/S0021-9673(03)00637-X
- [3] Doğan A, Otlu S, Büyük F, Aksu P, Tazegül E, Erdağ D. Effects of cysteamine, putrescine and cystemine-putrescine combination on some bacterium. *Kafkas Üniversitesi Veteriner Fakültesi Dergisi*. 2012;**18**:1015-1019. DOI: 10.9775/kvfd.2012.6928
- [4] Tiqua SM. Metabolic diversity of the heterotrophic microorganisms and potential link to pollution of the Rouge River. *Environmental Pollution*. 2010;**158**:1435-1443. DOI: 10.1016/j.envpol.2009.12.035
- [5] Biji KB, Ravishankar CN, Venkateswarlu R, Mohan CO, Gopal TKS. Biogenic amines in seafood: A review. *Journal of Food Science and Technology*. 2016;**53**:2210-2218. DOI: 10.1007/s13197-016-2224-x
- [6] Jairath G, Singh PK, Dabur RS, Rani M, Chaudhari M. Biogenic amines in meat and meat products and its public health significance: A review. *Journal of Food Science and Technology*. 2015;**52**:6835-6846. DOI: 10.1007/s13197-015-1860-x
- [7] Mafra I, Herbert P, Santos L, Barros P, Alves A. Evaluation of biogenic amines in some Portuguese quality wines by HPLC fluorescence detection of OPA derivatives. *American Journal of Enology and Viticulture*. 1999;**50**:128-132
- [8] Düz M, Fidan AF. Biogenic amines and effects. *Kocatepe Veterinary Journal*. 2016;**9**:114-121. DOI: 10.5578/kvj.23113
- [9] Spano G, Russo P, Lonvaud-Funel A, Lucas P, Alexandre H, Grandvalet C, et al. Biogenic amines in fermented foods. *European Journal of Clinical Nutrition*. 2010;**64**:95-100
- [10] Shalaby AR. Significance of biogenic amines to food safety and human health. *Food Research International*. 1996;**29**:675-690. DOI: 10.1016/S0963-9969(96)00066-X
- [11] Hofto LR, Lee CE, Cafiero M. The importance of aromatic-type interactions in serotonin synthesis: Protein-ligand interactions in tryptophan hydroxylase and aromatic amino acid decarboxylase. *Journal of Computational Chemistry*. 2009;**30**:1111-1115. DOI: 10.1002/jcc.21139
- [12] Landete JM, Arena ME, Pardo I, Manca de Nadra MC, Ferrer S. The role of two families of bacterial enzymes in putrescine synthesis from agmatine via agmatine deiminase. *International Microbiology*. 2010;**13**:169-177. DOI: 10.2436/20.1501.01.123
- [13] Pessione E, Cirrincione S. Bioactive molecules released in food by lactic acid bacteria: Encrypted peptides and biogenic amines. *Frontiers in Microbiology*. 2016;**7**:1-19. DOI: 10.3389/fmicb.2016.00876
- [14] Bjelakovic G, Stojanovic I, Stoimenov TJ, Pavlovic D, Kocic G,

Bjelakovic GB, et al. Polyamines, folic acid supplementation and cancerogenesis. Pteridines. 2017;**28**:115-131. DOI: 10.1515/pterid-2017-0012

[15] Soleas GJ, Carey M, Goldberg DM. Method development and cultivar-related differences of nine biogenic amines in Ontario wines. Food Chemistry. 1999;**64**:49-58. DOI: 10.1016/S0308-8146(98)00092-2

[16] Moya-Garcia AA, Pino-Angeles A, Gil-Redondo R, Morreale A, Sanchez-Jimenez F. Structural features of mammalian histidine decarboxylase reveal the basis for specific inhibition. British Journal of Pharmacology. 2009;**157**:4-13. DOI: 10.1111/j.1476-5381.2009.00219.x

[17] Maintz L, Novak N. Histamine and histamine intolerance. The American Journal of Clinical Nutrition. 2007;**85**:1185-1196. DOI: 10.1093/ajcn/85.5.1185

[18] Criado PR, Jardim Criado RF, Maruta CW, Machado Filho CA. Histamine, histamine receptors and antihistamines: New concepts. Anais Brasileiros de Dermatologia. 2010;**85**:195-210

[19] Jeong CD, Mamud LL, Kim SH, Choi YJ, Soriano AP, Cho KK, et al. Effect of soybean meal and soluble starch on biogenic amine production and microbial diversity using in vitro rumen fermentation. Asian-Australasian Journal of Animal Sciences. 2015;**28**:50-57. DOI: 10.5713/ajas.14.0555

[20] Shahid M, Tripathi T, Sobia F, Moin S, Siddiqui M, Khan RA. Histamine, histamine receptors, and their role in immunomodulation: An updated systematic review. The Open Immunology Journal. 2009;**2**:9-41. DOI: 10.2174/1874226200902010009

[21] Qin L, Zhao D, Xu J, Ren X, Terwilliger EF, Parangi S, et al. The vascular permeabilizing factors histamine and serotonin induce angiogenesis through TR3/Nur77 and subsequently truncate it through thrombospondin-1. Blood. 2013;**121**:2154-2164. DOI: 10.1182/blood-2012-07-443903

[22] Triggiani M, Patella V, Staiano RI, Granata F, Marone G. Allergy and the cardiovascular system. Clinical and Experimental Immunology. 2008;**153**:7-11. DOI: 10.1111/j.1365-2249.2008.03714.x

[23] Nakamura Y, Ishimaru K, Shibata S, Nakao A. Regulation of plasma histamine levels by the mast cell clock and its modulation by stress. Scientific Reports. 2017;**7**:1-12. DOI: 10.1038/srep39934

[24] Yuwen L, Zhang FL, Chen QH, Lin SJ, Zhao YL, Li ZY. The role of aromatic L-amino acid decarboxylase in bacillamide C biosynthesis by *Bacillus atrophaeus* C89. Scientific Reports. 2013;**3**:1-10. DOI: 10.1038/srep01753

[25] Torrens-Spence MP, Liu P, Ding H, Harich K, Gillaspay G, Li J. Biochemical evaluation of the decarboxylation and decarboxylation-deamination activities of plant aromatic amino acid decarboxylases. The Journal of Biological Chemistry. 2013;**288**:2376-2387. DOI: 10.1074/jbc.M112.401752

[26] Tittarelli R, Mannocchi G, Pantano F, Romolo FS. Recreational use, analysis and toxicity of tryptamines. Current Neuropharmacology. 2015;**13**:26-46. DOI: 10.2174/1570159X13666141210222409

[27] Önal A. A review: Current analytical methods for the determination of biogenic amines in foods. Food Chemistry. 2007;**103**:1475-1486. DOI: 10.1016/j.foodchem.2006.08.028

- [28] Berry MD. Mammalian central nervous system trace amines. Pharmacologic amphetamines, physiologic neuromodulators. *Journal of Neurochemistry*. 2004;**90**:257-271. DOI: 10.1111/j.1471-4159.2004.02501.x
- [29] Tieman D, Taylor M, Schauer N, Fernie AR, Hanson AD, Klee HJ. Tomato aromatic amino acid decarboxylases participate in synthesis of the flavor volatiles 2-phenylethanol and 2-phenylacetaldehyde. *Proceedings of the National Academy of Sciences of the United States of America*. 2006;**103**:8287-8292. DOI: 10.1073/pnas.0602469103
- [30] Parthasarathy A, Cross PJ, Dobson RCJ, Adams LE, Savka MA, Hudson AO. A three-ring circus: Metabolism of the three proteogenic aromatic amino acids and their role in the health of plants and animals. *Frontiers in Molecular Biosciences*. 2018;**5**:1-30. DOI: 10.3389/fmolb.2018.00029
- [31] Irsfeld M, Spadafore M, Prüß BM. β -Phenylethylamine, a small molecule with a large impact. *Webmedcentral*. 2013;**4**:1-15
- [32] Kaur N, Kumari B. Phenylethylamine: Health benefits—A review. *World Journal of Pharmacy and Pharmaceutical Sciences*. 2016;**5**:743-750. DOI: 10.20959/wjpps20164-6429
- [33] Connil N, Le Breton Y, Dousset X, Auffray Y, Rince A, Prevost H. Identification of the *Enterococcus faecalis* tyrosine decarboxylase operon involved in tyramine production. *Applied and Environmental Microbiology*. 2002;**68**:3537-3544. DOI: 10.1128/AEM.68.7.3537-3544.2002
- [34] Bargossi E, Tabanelli G, Montanari C, Lanciotti R, Gatto V, Gardini F, et al. Tyrosine decarboxylase activity of enterococci grown in media with different nutritional potential: Tyramine and 2-phenylethylamine accumulation and *tyrDC* gene expression. *Frontiers in Microbiology*. 2015;**6**:1-10. DOI: 10.3389/fmicb.2015.00259
- [35] Zhu H, Xu G, Zhang K, Kong X, Han R, Zhou J, et al. Crystal structure of tyrosine decarboxylase and identification of key residues involved in conformational swing and substrate binding. *Scientific Reports*. 2016;**6**:1-10. DOI: 10.1038/srep27779
- [36] Gonzalez-Jimenez M, Arenas-Valganon J, Garcia-Santos MP, Calle E, Casado J. Mutagenic products are promoted in the nitrosation of tyramine. *Food Chemistry*. 2017;**216**:60-65. DOI: 10.1016/j.foodchem.2016.08.006
- [37] Anwar MA, Ford WR, Broadley KJ, Herbert AA. Vasoconstrictor and vasodilator responses to tryptamine of rat-isolated perfused mesentery: Comparison with tyramine and b-phenylethylamine. *British Journal of Pharmacology*. 2012;**165**:2191-2202. DOI: 10.1111/j.1476-5381.2011.01706.x
- [38] Jacob G, Gamboa A, Diedrich A, Shibao C, Robertson D, Biaggioni I. Tyramine-induced vasodilation mediated by dopamine contamination: A paradox resolved. *Hypertension*. 2005;**46**:355-359. DOI: 10.1161/01.HYP.0000172353.62657.8b
- [39] Benkerroum N. Biogenic amines in dairy products: Origin, incidence, and control means. *Comprehensive Reviews in Food Science and Food Safety*. 2016;**15**:801-826. DOI: 10.1111/1541-4337.12212
- [40] Cote F, Thevenot E, Fligny C, Fromes Y, Darmon M, Ripoché MA, et al. Disruption of the nonneuronal *tph1* gene demonstrates the importance of peripheral serotonin in cardiac function. *Proceedings of the National Academy of Sciences of the United States of America*. 2003;**100**:13525-13530. DOI: 10.1073/pnas.2233056100

- [41] Perez-Garcia G, Meneses A. Memory formation, amnesia, improved memory and reversed amnesia: 5-HT role. Behavioural Brain Research. 2008;**195**:17-29. DOI: 10.1016/j.bbr.2007.11.027
- [42] Zhang X, Yan H, Luo Y, Huang Z, Rao Y. Thermoregulation-independent regulation of sleep by serotonin revealed in mice defective in serotonin synthesis. Molecular Pharmacology Fast Forward. 2018;**93**:657-664. DOI: 10.1124/mol.117.111229
- [43] Nakada Y, Itoh Y. Identification of the putrescine biosynthetic genes in *Pseudomonas aeruginosa* and characterization of agmatine deiminase and N-carbamoylputrescine amidohydrolase of the arginine decarboxylase pathway. Microbiology. 2003;**149**:707-714. DOI: 10.1099/mic.0.26009-0
- [44] Hao YJ, Kitashiba H, Honda C, Nada K, Moriguchi T. Expression of arginine decarboxylase and ornithine decarboxylase genes in apple cells and stressed shoots. Journal of Experimental Botany. 2005;**56**:1105-1115. DOI: 10.1093/jxb/eri102
- [45] Pegg AE, Casero RA. Current status of the polyamine research field. Methods in Molecular Biology. 2011;**720**:3-35. DOI: 10.1007/978-1-61779-034-8_1
- [46] Valdes Santiago L, Ruiz Herrera J. Stress and polyamine metabolism in fungi. Frontiers in Chemistry. 2013;**1**:1-10. DOI: 10.3389/fchem.2013.00042
- [47] Ioannidis NE, Sfichi L, Kotzabasis K. Putrescine stimulates chemiosmotic ATP synthesis. Biochimica et Biophysica Acta. 2006;**1757**:821-828. DOI: 10.1016/j.bbabi.2006.05.034
- [48] Jeong S, Yeon YJ, Choi EG, Byun S, Cho DH, Kim Il K, et al. Alkaliphilic lysine decarboxylases for effective synthesis of cadaverine from L-lysine. Korean Journal of Chemical Engineering. 2016;**33**:1530-1533. DOI: 10.1007/s11814-016-0079-5
- [49] Sagong HY, Kim KJ. Lysine decarboxylase with an enhanced affinity for pyridoxal 5-phosphate by disulfide bond-mediated spatial reconstitution. PLoS One. 2017;**12**:e0170163. DOI: 10.1371/journal.pone.0170163
- [50] Wu H, Min J, Ikeguchi Y, Zeng H, Dong A, Loppnau P, et al. Structure and mechanism of spermidine synthases. Biochemistry. 2007;**46**:8331-8339. DOI: 10.1021/bi602498k
- [51] Sanchez-Jimenez F, Ruiz-Perez MV, Urdiales JL, Medina MA. Pharmacological potential of biogenic amine-polyamine interactions beyond neurotransmission. British Journal of Pharmacology. 2013;**170**:4-16. DOI: 10.1111/bph.12109
- [52] Takahashi T, Kakehi JI. Polyamines: Ubiquitous polycations with unique roles in growth and stress responses. Annals of Botany. 2010;**105**:1-6. DOI: 10.1093/aob/mcp259
- [53] Carvalho FB, Mello CF, Marisco PC, Tonello R, Girardi BA, Ferreira J, et al. Spermidine decreases Na⁺, K⁺-ATPase activity through NMDA receptor and protein kinase G activation in the hippocampus of rats. European Journal of Pharmacology. 2012;**684**:79-86. DOI: 10.1016/j.ejphar.2012.03.046
- [54] Hu J, Mahmoud MI, El-Fakahany EE. Polyamines inhibit nitric oxide synthase in rat cerebellum. Neuroscience Letters. 1994;**175**:41-45
- [55] Paschalidis KA, Roubelakis-Angelakis KA. Spatial and temporal distribution of polyamine levels and polyamine anabolism in different organs/tissues of the tobacco plant. Correlations with age, cell division/expansion, and differentiation. Plant Physiology.

2005;**138**:142-152. DOI: 10.1104/pp.104.055483

[56] Medina MA, Urdiales JL, Rodriguez-Caso C, Ramirez FJ, Sanchez-Jimenez F. Biogenic amines and polyamines: Similar biochemistry for different physiological missions and biomedical applications. *Critical Reviews in Biochemistry and Molecular Biology*. 2003;**38**:23-59. DOI: 10.1080/713609209

[57] Welsh PA, Kuhn SS, Prakashgowda C, McCloskey D, Feith D. Spermine synthase overexpression in vivo does not increase susceptibility to DMBA/TPA skin carcinogenesis or Min-Apc intestinal tumorigenesis. *Cancer Biology & Therapy*. 2012;**13**:358-368. DOI: 10.4161/cbt.19241

[58] Morris SM. Arginine: Beyond protein. *The American Journal of Clinical Nutrition*. 2006;**83**:508-512. DOI: 10.1093/ajcn/83.2.508S

[59] Demady DR, Jianmongkol S, Vuletich JL, Bender AT, Osawa Y. Agmatine enhances the NADPH oxidase activity of neuronal NO synthase and leads to oxidative inactivation of the enzyme. *Molecular Pharmacology*. 2001;**59**:24-29

[60] Pegg AE. Mammalian polyamine metabolism and function. *International Union of Biochemistry and Molecular Biology Life*. 2009;**61**:880-894. DOI: 10.1002/iub.230

[61] Santos MHS. Biogenic amines: Their importance in foods. *International Journal of Food Microbiology*. 1996;**29**:213-231

[62] Schwelberger HG, Feurle J, Houen G. Mapping of the binding sites of human histamine N-methyltransferase (HNMT) monoclonal antibodies. *Inflammation Research*. 2017;**66**:1021-1029. DOI: 10.1007/s00011-017-1086-7

[63] Karovicova J, Kohajdova Z. Biogenic amines in food. *Chemical Papers*. 2005;**59**:70-79

[64] Yatin M. Polyamines in living organisms. *Journal of Cell and Molecular Biology*. 2002;**1**:57-67

[65] Soda K. The mechanisms by which polyamines accelerate tumor spread. *Journal of Experimental & Clinical Cancer Research*. 2011;**30**:1-9. DOI: 10.1186/1756-9966-30-95

[66] Mandal S, Mandal A, Johansson HE, Orjalo AV, Park MH. Depletion of cellular polyamines, spermidine and spermine, causes a total arrest in translation and growth in mammalian cells. *Proceedings of The National Academy of Sciences of The United States of America*. 2013;**110**:2169-2174. DOI: 10.1073/pnas.1219002110

[67] Pegg AE. Functions of polyamines in mammals. *The Journal of Biological Chemistry*. 2016;**291**:14904-14912. DOI: 10.1074/jbc.R116.731661

[68] Ladero V, Calles M, Fernandez M, Alvarez MA. Toxicological effects of dietary biogenic amines. *Current Nutrition and Food Science*. 2010;**6**:145-156. DOI: 10.2174/157340110791233256

[69] Stadnik J, Dolatowski ZJ. Biogenic amines in meat and fermented meat products. *Acta Scientiarum Polonorum Technologia Alimentaria*. 2010;**9**:251-263

[70] Kovacova-Hanusikova E, Buday T, Gavliakova S, Plevkova J. Histamine, histamine intoxication and intolerance. *Allergologia et Immunopathologia*. 2015;**43**:498-506. DOI: 10.1016/j.aller.2015.05.001

[71] Gardini F, Özogul Y, Suzzi G, Tabanelli G, Özogul F. Technological factors affecting biogenic amine content in foods: A review. *Frontiers*

in Microbiology. 2016;7:1-18. DOI: 10.3389/fmicb.2016.01218

InTech; 2017. p. 197-214. DOI: 10.5772/intechopen.68494

[72] Anwar MA, Ford WR, Herbert AA, Broadley KJ. Signal transduction and modulating pathways in tryptamine-evoked vasopressor responses of the rat isolated perfused mesenteric bed. *Vascular Pharmacology*. 2013;58:140-149. DOI: 10.1016/j.vph.2012.10.007

[79] Milovica V, Turchanowa L, Khomutov AR, Khomutov RM, Caspary WF, Stein J. Hydroxylamine containing inhibitors of polyamine biosynthesis and impairment of colon cancer cell growth. *Biochemical Pharmacology*. 2001;61:199-206

[73] Fisar Z. Drugs related to monoamine oxidase activity. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*. 2016;69:112-124. DOI: 10.1016/j.pnpbp.2016.02.012

[80] Linsalata M, Notarnicola M, Tutino V, Bifulco M, Santoro A, Laezza C, et al. Effects of anandamide on polyamine levels and cell growth in human colon cancer cells. *Anticancer Research*. 2010;30:2583-2589

[74] Ordonez AI, Ibanez FC, Torre P, Barcina Y. Formation of biogenic amines in Idiazabal ewe's-milk cheese: Effect of ripening, pasteurization, and starter. *Journal of Food Protection*. 1997;60:1371-1375

[81] Takao K, Rickhag M, Hegardt C, Oredsson S, Persson L. Induction of apoptotic cell death by putrescine. *The International Journal of Biochemistry & Cell Biology*. 2006;38:621-628. DOI: 10.1016/j.biocel.2005.10.020

[75] San Mauro Martin I, Brachero S, Garicano Vilar E. Histamine intolerance and dietary management: A complete review. *Allergologia et Immunopathologia*. 2016;44:475-483. DOI: 10.1016/j.aller.2016.04.015

[82] Doğan A, Aksu Kılıç P, Erdağ D, Doğan ANC, Özcan K, Doğan E. The protective effects of cysteamine, putrescine, and the combination of cysteamine and putrescine on fibrosarcoma induced in mice with 3-methylcholanthrene. *Turkish Journal of Veterinary and Animal Sciences*. 2016;40:575-582. DOI: 10.3906/vet-1510-49

[76] Zomkowski ADE, Santos ARS, Rodrigues ALS. Putrescine produces antidepressant-like effects in the forced swimming test and in the tail suspension test in mice. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*. 2006;30:1419-1425. DOI: 10.1016/j.pnpbp.2006.05.016

[83] Kaye W. Neurobiology of anorexia and bulimia nervosa. *Physiology & Behavior*. 2008;94:121-135. DOI: 10.1016/j.physbeh.2007.11.037

[77] Halasz A, Barath A, Simon-Sarkadi L, Holzapfel W. Biogenic amines and their production by microorganisms in food. *Trends in Food Science & Technology*. 1994;5:42-49. DOI: 10.1016/0924-2244(94)90070-1

[84] Richard DM, Dawes MA, Mathias CW, Acheson A, Hill-Kapturczak N, Dougherty DM. L-Tryptophan: Basic metabolic functions, behavioral research and therapeutic indications. *International Journal of Tryptophan Research*. 2009;2:45-60

[78] Atakisi E, Merhan O. Nitric oxide synthase and nitric oxide involvement in different toxicities. In: Saravi SSS, editor. *Nitric Oxide Synthase Simple Enzyme-Complex Roles*. 1st ed. Croatia:

[85] Jenkins TA, Nguyen JCD, Polglaze KE, Bertrand PP. Influence of tryptophan and serotonin on mood and

cognition with a possible role of the gut-brain axis. *Nutrients*. 2016;**8**:1-15. DOI: 10.3390/nu8010056

[86] Riederer P, Laux G. MAO-inhibitors in Parkinson's disease. *Experimental Neurobiology*. 2011;**20**:1-17. DOI: 10.5607/en.2011.20.1.1

[87] Satriano J. Arginine pathways and the inflammatory response: Interregulation of nitric oxide and polyamines: Review article. *Amino Acids*. 2004;**26**:321-329. DOI: 10.1007/s00726-004-0078-4

[88] Liu P, Jing Y, Collie ND, Dean B, Bilkey DK, Zhang H. Altered brain arginine metabolism in schizophrenia. *Translational Psychiatry*. 2016;**6**:1-9. DOI: 10.1038/tp.2016.144