

## Special Article - Amino Acid

Amino Acids: Molecules of *Life*Bojarska J<sup>1\*</sup>, Kaczmarek K<sup>2</sup>, Zabrocki J<sup>2</sup> and Wolf WM<sup>1</sup><sup>1</sup>Institute of General and Ecological Chemistry, Lodz University of Technology, Poland<sup>2</sup>Institute of Organic Chemistry, Lodz University of Technology, Poland**\*Corresponding author:** Joanna Bojarska, Institute of General and Ecological Chemistry, Faculty of Chemistry, Lodz University of Technology, Żeromski St. 116, 90-924 Łódź, Poland**Received:** October 03, 2019; **Accepted:** October 24, 2019; **Published:** October 31, 2019**Abstract**

Amino acids, the simplest biomolecules, carry the prime information. They link together, into a very specific sequences, and create polypeptide chains folding to proteins. Thousands of proteins (each with unique features) are organized in cells. Bio-complexes are stabilized *via* noncovalent interactions. Hence, amino acids are linked to nearly all biological processes and are the key to understanding them. In other words, *life* is based on molecular information processing, while amino acids are molecules of *life*. It is impressive that common repertoire of *life* melody consists only twenty amino acids. Each one contains the single-letter amino acids code, that resembles notes on a musical staff. In brief, some of amino acids can be produced by organisms, while others should be provided by the diet. From a nutritional perspective, an important feature of a protein is its proper amino acids composition in order to maintain balance in biologically functions. There is no doubt that the great relevance of so important biomolecules in the nutrition is difficult to underestimate. The recent years have witnessed growing interest in this topic. In view of the foregoing, this mini review is a *prelude* to special issue "Amino Acid", representing a fascinating subjects of nutritive aspects of these basic biological units, to help us unlock the secrets of *life* music played via amino acids orchestra.

**Keywords:** Amino acids; Proteins; Nutrition; Health**Abbreviations**

AA: Amino Acid; EAA: Essential AA; NEAA: Nonessential AA; BCAAs: Branched Chain Amino Acids; CAAs: Coded Amino Acids

**Discussion**

Scientific history of biomolecules is age-old [1-3]. Nonetheless, Amino Acids (AAs) are one of the first organic molecules to appear on Earth, at the origin of *life* [4]. AAs play various crucial roles. They not only form palette of chemical versatility of proteins, but also are *inter alia* the most important bio-regulators, source of energy, precursor compounds, chemical messengers in communication between cells, including neurotransmitters [4]. AAs take part in gene expression [5] regulation of insulin secretion from pancreatic  $\beta$ -cells [6] formation of hormones (insulin, growth hormone, glucagon, adrenaline, nor-adrenaline, thyroxin), enzyme or tissue protein, synthesis of melanin [7].

Interestingly, in nature over 500 AAs were discovered. However, there are only twenty proteinogenic AAs forming universal DNA genetic code, known also as CAAs alphabet. It possess, *via* the chemical nature of their side-chains, nearly all of the required chemical functionalities. This mysterious CAAs code was created probably during early evolution but is still considered. Causes of its genesis remain elusive. The evolution of this code is called the "universal enigma" of biology [8]. If other repertoire is possible? Scientists shed new lights on this point, especially in the context of the search of extraterrestrial *life* [9-12]. Notably, only the *L* forms of AAs are involved in this code, what is still a puzzle as well [13]. Encoded AAs are generally divided into nutritionally EAAs (indispensable) and NEAAs (dispensable). EAAs (lysine, tryptophan, phenylalanine, methionine, threonine, histidine, valine, leucine, isoleucine) can't be

produced by body but must be supplied by the diet to sustain *life*. NEAAs (alanine, asparagine, aspartic acid, glutamic acid, serine) are made by the body from other precursors [14-16]. Besides, conditionally NEAAs (functional or semi-essential) such as arginine, cysteine, glutamine, glycine, proline, tyrosine, which are synthesized in the body but their production can be insufficient, should be mentioned as well. They are mostly dietarily required only during certain circumstances (stress and illness e.g. phenylketonuria) [17]. Strictly speaking, every protein contains multiple units of the CAAs. If just one of the necessary AAs is unavailable, protein synthesis is not continued. Furthermore, unusual genetically-encoded AAs, selenocysteine and pyrrolysine, which are not used by all organisms, are writing about. Selenocysteine is known as unique the 21<sup>st</sup> encode AA [18-21]. It is essential for human health and survival. It is only AA containing an important dietary micronutrient (selenium) as a major component. It is the only AA encoded by a UGA codon and the only one synthesized on its tRNA in all *life* domains [22]. Pyrrolysine, named sometimes as 22<sup>nd</sup> AA, was discovered at the active site of enzyme of methyl-transferase from a methane producing archeon [23]. It is used in the protein biosynthesis in methanogenic archaea and bacteria [24]. In certain cases, there is considerable extra support provided by these two uncommon AAs carrying additional message [11,21,24-27]. In addition, it is worth noting that other AAs exist in cells, which are not encoded (ornithine, diaminopimelic acid, homocysteine or citrulline), but are produced in the synthesis of CAAs [12].

All common AAs were discovered before 1935. The first AA, asparagine, was isolated from asparagus in 1806 in France [28]. In general, according to *The American Heritage Dictionary of the English Language* [29] names of AAs come from Greek. In particular, glycine, the simplest AA, derives from gelatin and has name derived from its

sweet taste (*gr. gly* - sweet). Arginine was isolated as crystals similar to shiny silver (*gr. argiros*). Glutamic acid and glutamine names come from the wheat protein, gluten. A curiosity is that Prof. Ikeda in 1908 discovered that AAs hold the secret to delicious taste. More specifically, the taste of kombu dashi comes from glutamate. This new taste *umami* became the fifth basic taste after sweet, salty, sour and bitter [30,31]. Histidine was isolated from tissues (histology, the study of tissues), while lysine from tissues undergoing lysis. On the other hand, alanine name is caused by the mistake impression that it contained an aldehyde group (Al-a-nine). Tyrosine was isolated from cheese (*gr. tupi*), serine from ser(ic)ine, a protein that adheres to silk, while cysteine from urinary stones (and urinary bladder, or cyst). Methionine name is composed of Me(methyl)-Thio(sulfur)-N-ine. Phenylalanine is indeed a phenyl group (benzene ring) and alanine. Proline is named after the P(yr)ROL(ring)-ine. Threonine was named after its resemblance to the sugar (threose), valine after VAL(eric acid)-ine, while tryptophan after the enzymes that were used instead of hot hydrochloric acid to break down the parent proteins: TRYP(sin) and pep(T)ic enzymes-ophane (suffix - cellophane) [32].

The relevance of the AAs in nutrition was firstly reported at the beginning of XX century [33]. Recently, this subject has attracted an increasing interest due to bio-functional strength of AAs and progress of nutritional sciences. It is well known that poor diet leads to morbidity and mortality. Therefore, there needs to be a focus on a high-quality diet [34]. AAs, subcomponents in nutritional support, are also named “the most versatile nutrients”. It is caused by their very different side chains enabling much more various chemical modifications and reactions than is the case with other nutrients [35]. Optimal dietary supplementation with AAs, if is used properly and wisely, improves our health [36] mood or prolongs the *life*. Generally, EAAs are present in vegetables, fruits, eggs, rise, dairy and cereal products, nuts, almonds or linseed. EAAs play a variety of biological functions. Methionine (contain sulphur) is need in cell metabolism and detoxification, tissue growth and the absorption of zinc and selenium. It intervenes the biosynthesis of glutathione to counteract oxidative stress, decreases DNA damage or carcinogenic processes [37]. Threonine is constituent of collagen and elastin. It has relevance in immune function, fat metabolism and sleep regulation [38]. Histidine is important in histamine production and maintaining the myelin sheath (a protective barrier surrounding nerve cells). It is a neurotransmitter in immune response, digestion (prevent obesity), sleep-wake cycles, metabolites affecting renal function [39]. Valine is involved in stimulation of muscle growth, regeneration and energy production. Leucine helps in wound healing, regulate blood sugar levels and produces growth hormones. Isoleucine play role in immune system, hemoglobin production, energy regulation, muscle metabolism and muscle tissue [40]. Last three AAs are known as BCAAs (have a chain branching off to one side of its molecular structure), which are vital for muscle repair. Lately, new functions of BCAAs were discovered. This is especially the case for metabolic regulators also in lipid and glucose metabolism, influence on milk quality and embryo growth, enhancing intestinal development or biomarkers for early detection of chronic diseases like diabetes and insulin resistance [41]. Interestingly, “cocktail” of BCAAs was even named “elixir of *life*” [42]. Aromatic AAs (tryptophan, tyrosine, phenylalanine) are crucial in diet for normal mind function. They are

the precursors of biosynthesis of the neurotransmitters (serotonin, dopamine or norepinephrine) [43]. Also, keep in mind that AAs, e.g. lysine, playing a major roles in hormone and enzyme, collagen and elastin formation, immune system and calcium absorption, are implemented in antibiotics (especially co-crystal forms). Advantages resulting from application of AAs in formulation for new drug substances were proved [44]. And more importantly, nonessential AAs become essential in cancer therapy. The dietary manipulation of AAs metabolism is a potentially effective strategy for inhibiting tumor growth [45].

In conclusion, novel results concerning functions and applications of AAs are being continuously reported. Their significance for nutritional science and nutrition practice is crucial for improving health standards. This issue deserves further studies and cannot be neglected.

## References

- Vickery HB, Schmidt CLA. The history of the discovery of the amino acids. *Chem Rev.* 1931; 9: 169-318.
- Vickery HB. The history of the discovery of the amino acids II. A review of amino acids described since 1931 as components of native proteins. *Advances in Protein Chemistry.* 1972; 26: 81-171.
- Zelith I. Hubert Bradford Vickery 1893-1978. A biographical memoir. NAS Washington. 1985.
- Gutiérrez-Preciado A, Romero H, Peimbert M. An Evolutionary Perspective on Amino Acids. *Nature Education.* 2010; 3: 29.
- Scot R, Leonard S. New functions for amino acids: effect on gene transcription and translation. *Am J Clin Nutr.* 2006; 83: 500-507.
- Lorraine B, Katrin B. Amino Acid Metabolism,  $\beta$ -Cell Function, and Diabetes. *Diabetes.* 2006; 55: 39-47.
- Eiji K, Noriatsu K, Yoshiyuki U, Tooru S. Extracellular Branched-Chain Amino Acids, Especially Valine, Regulate Maturation and Function of Monocyte-Derived Dendritic Cells. *J Immunol.* 2007; 79: 7137-7146.
- Koonin EV, Novozhilov AS. Origin and evolution of the genetic code: The universal enigma. *IUBMB Life.* 2009; 61: 99-111.
- Lu Y, Freeland S. On the evolution of the standard amino-acid alphabet. *Genome Biology.* 2006; 7: 102.
- Kitadai N, Maruyama S. Origins of building blocks of life: A review. *Geoscience Frontiers.* 2018; 9: 1117-1153.
- Bywater RP. Why twenty amino acid residue types suffice(d) to support all living systems? *PLOS one.* 2018.
- Ilardo M, Bose R, Meringer M, Rasulev B, Grefenstette N, Stephenson J, et al. Adaptive properties of the genetically encoded amino acid alphabet are inherited from its subsets. *Scientific Reports.* 2019; 9: 12468.
- Innouve M. Mystery of the genetic code. *Cell Dev Biol.* 2018.
- Abderhalden E. Experiment on the feeding with completely degraded nutrition substances. *Z Physiol Chem.* 1912; 77: 22-58.
- Reeds PJ. Dispensable and indispensable amino acids for humans. *J Nutr.* 2000; 130: 1835S-1840S.
- Borman A, Wood TR, Black HC, Anderson EG, Oestekling M, Womack M, et al. The role of arginine in growth with some observations on the effects of argininic acid. *J Biol Chem.* 1946; 166: 585-594.
- van Spronsen FJ, van Rijn M, Bekhof J, Koch R, Smit PG. Phenylketonuria: Tyrosine supplementation in phenylalanine-restricted diets. *Am J Clin Nutr.* 2001; 7: 153-157.
- Turanov AA, Xu XM, Carlson BA, Yoo MH, Gladyshev VN, Hatfield DL. Biosynthesis of selenocysteine, the 21<sup>st</sup> amino acid in the genetic code, and

- a novel pathway for cysteine biosynthesis. *American Society for Nutrition*. 2011; 2: 122-128.
19. Bock A, Forchhammer K, Heider J, Leinfelder W, Sawers G, Veprek B, et al. Selenocysteine: the 21<sup>st</sup> amino acid. *Molecular Microbiology*. 1991; 5: 515-520.
20. Hatfield D. A forgotten debate: is selenocysteine the 21<sup>st</sup> amino acid? *J of the National Cancer Institute*. 2004; 96: 504-505.
21. Stadtman T. Selenium biochemistry. *Science*. 1974; 183: 915-922.
22. Schmidt RL, Simonovic M. Synthesis and decoding of selenocysteine and human health. *Croat Med J*. 2012; 53: 535-550.
23. Srinivasan G, James CM, Krzycki JA. Pyrrolysine encoded by UAG in archaea: charging of a UAG-decoding specialized tRNA. *Science*. 2002; 5572: 1459-1462.
24. Rother M, Krzycki JA. Selenocysteine, pyrrolysine, and the unique energy metabolism of methanogenic archaea. *Archaea*. 2010; 453642.
25. Polycarpo C, Ambrogely A, Be´rube´ A, Winbush SM, McCloskey JA, Crain PF, et al. An aminoacyl-tRNA synthetase that specifically activates pyrrolysine. *Proc Nat Acad Sci USA*. 2004; 101: 12450-12454.
26. Yuan J, Palioura S, Salazar JC, Su D, O'Donoghue P, Hohn MJ, et al. RNA-dependent conversion of phosphoserine forms selenocysteine in eukaryotes and archaea. *Proc Nat Acad Sci USA*. 2006; 103: 18923-18927.
27. Xu XM, Carlson BA, Mix H, Zhang Y, Saira K, Glass RS, et al. Biosynthesis of Selenocysteine on Its tRNA in Eukaryotes. 2007; 5: e4.
28. Vauquelin LN, Robiquet PJ. La decouverte d'un nouveau principe vegetal dans le suc des asperges. *Annales de Chimie*. 1806; 57: 88-93.
29. Morris W. *The American Heritage Dictionary of the English Language*. 1970.
30. Ikeda K. "On a new seasoning," *Journal of the Tokyo Chemical Society*. 1908; 30: 820-836.
31. Kurihara K. Umami the fifth basic taste: history of studies on receptor mechanisms and role as a food flavor. *Biomed Res Int*. 2015.
32. Saffran M. Amino acid names and parlor games: from trivial names to a one-letter code, amino acid names have strained students' memories. Is a more rational nomenclature possible? *Biochemical education*. 1998; 26: 116-118.
33. Rose WC. The role of the amino acids in human nutrition. *Proceedings of the American Philosophical Society*. 1947; 91: 112-116.
34. Bonnet J. Food revolution. *American J of Lifestzle Medicine*. 2017; 11: 387-396.
35. Brosnan JT, Rooyackers O. Amino acids: the most versatile nutrients. *Current Opinion in Clinical Nutrition and Metabolic Care*. 2013; 16: 56.
36. Wu G. Functional amino acids in nutrition and health. *Amino Acids*. 2013; 45: 407-411.
37. Martinez Y, Li X, Liu G, Bin P, Yan W, Mas D, et al. The role of methionine on metabolism, oxidative stress and diseases. *Amino Acids*. 2017; 49: 2091-2098.
38. Yoonhee K, Chunghun L. Sleep-promoting effects of threonine link AA metabolism in Drosophila neuron to GABAergic control of sleep drive. *eLife*. 2019; 8: e40593.
39. Kessler AT, Purich DL. *Biochemistrz, histidine*. 2019.
40. Ren W, Li Z, Zin Z, Blachier F. Structure, metabolism and functions of AAs: an overview. *Nutritional & Physiological Functions of Aas*. 2013; 91-108.
41. Zhang S, Zeng X, Ren M, Mao X, Qiao S. Novel metabolic and physiological functions of BCAAs: a review. *J of Animal Science & Biotechnology*. 2017; 8-10.
42. D'Antona G, Ragni M, Cardile A, Tedesco L, Dossena M, Bruttini F, et al. Branched-ChainAminoAcidSupplementationPromotes Survival and Supports Cardiac and Skeletal Muscle Mitochondrial Biogenesis in Middle-Aged Mice. *Cell Metabolism*. 2010; 12: 362-372.
43. Fernstrom JD. Dietary amino acids and brain function. *J of the Academy of Nutrition and Dietetics*. 1994; 94: 71-77.
44. Tilborg A, Norberg B, Wouters J. Pharmaceutical salts and cocrystals involving AAs: a brief structural overview of the state-of-art. *Eur J of Medicinal Chemists*. 2014; 16: 411-426.
45. Choi BH, Coloff JL. The diverse functions of non-essential amino acids in cancer. *Cancers*. 2019; 11: 675-692.