MAR 2023
ISSUE 03

In this issue:

News bulletin of AMBI West Bengal Chapter

The Biochemistry Chronicles

Non-Protein Amino Acids: beyond building block of proteins

Prof. Soma Gupta, Head, Department of Biochemistry, NRS Medical College

(This is transcript of the lecture given in 2nd National PG Update cum CME, AMBI)

In biochemistry, non-proteinogenic amino acids are those amino acids which are not encoded in the genome of organisms for the assembly of proteins. Almost 140 non-proteinogenic amino acids occur naturally in proteins and thousands more may occur in nature or be synthesized in the laboratory. Hence, one of the way to classify amino acids are proteinogenic and non-proteinogenic, the differentiating features of these two types are given in Table 1.

Table 1: Comparison of proteinogenic and non-proteinogenic amino acids

Proteinogenic	Non- Proteinogenic
These amino acids can be incorporated in protein during translation as they are genetically coded	These amino acids can not be incorporated in protein during translation as they have no genetic code
Ex: All 20 standard amino acids	Ex: Amino acids other than standard amino acids like citrulline, GABA etc
They are natural constituents of protein	They are not natural constituents but often derivatives of protein
Function: building block of protein	Function: NT, metabolic intermediates etc. Some are even hazardous to health

One thing must be noted that selenocysteine (21st) and pyrrolysine (22nd) amino acids, are also proteinogenic amino acids as both have genetic code, UGA and UAG respectively.

So far non proteinogenic amino acids are concerned, they are classified into a) Naturally obtained and b) synthetically produced amino acids.

Natural non-proteinogenic amino acids (NPAA) are found in human body in following conditions: a) as important metabolic intermediates, b) as metabolic end -product and c) produced by post-translational modifications.

NPAAS acting as important metabolic intermediates:

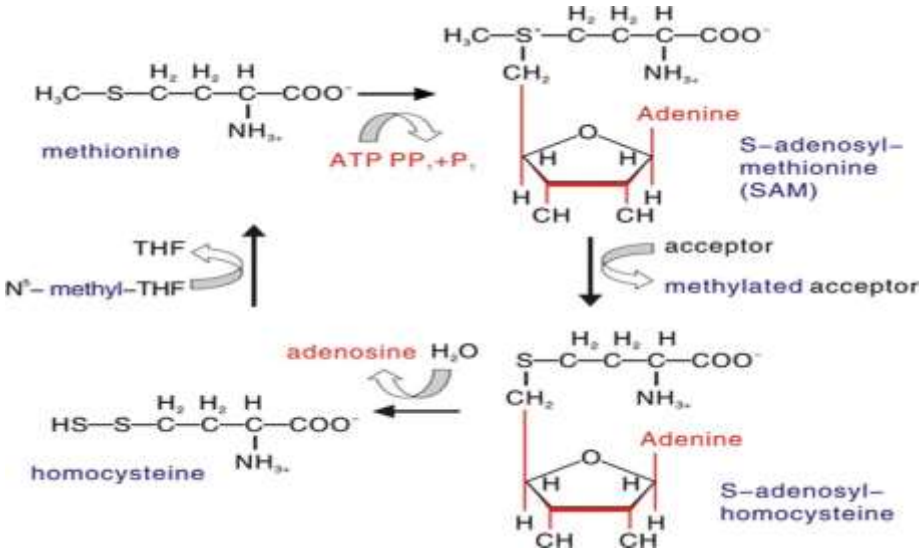
In urea cycle, there are 3 NPAAS, ornithine, citrulline and arginosuccinate. The clinical significance of these 3 NPAAs are given in Table 2:

Table 2: NPAA of urea cycle

Defective Enzyme	Product accumulated	Resultant disease
Ornithine Transcarbamoylase	Ammonia	Hyperammonemia II
Arginosuccinate Synthase	Citrullinemia	Citrulline
Arginase	Arginosuccinate	Arginosuccinicaciduria

Another important NPAA in this group is Homocysteine, Formation, and fate of which is given in Figure 1 and 2.

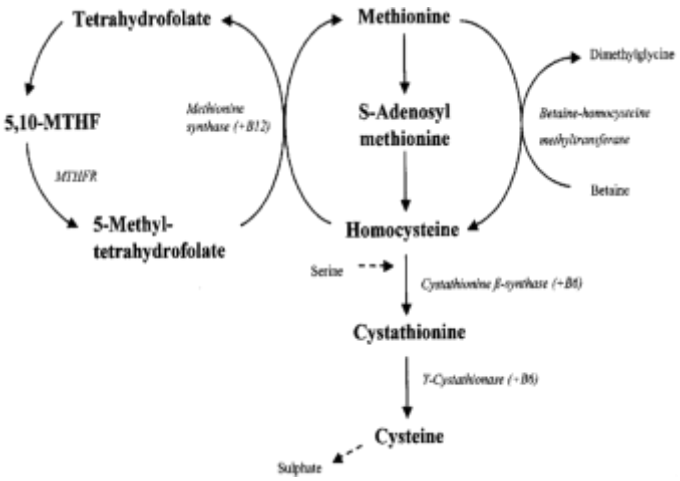
Figure 1: Formation of Homocysteine



A normal level of homocysteine in the blood is less than 15 micromoles per liter of blood. Higher levels of homocysteine are found in vitamin B6, B12 or folate deficiency. MTHFR gene mutations are also one of the potential causes of homocystinuria. High homocysteine levels are associated with several medical conditions like cardiovascular disease like atherosclerosis and heart attack. Higher levels of homocysteine can be divided into three main categories:

Mild: 15-30 mcmol/L, Moderate: 30-100 mcmol/L and Severe: greater than 100 mcmol/L

Figure 2: Fate of Homocysteine



L DOPA (Dihydroxy phenylalanine) formed from tyrosine is another NPAA, which acta as a neurotransmitter. Delta amino levulinate is formed in the 1st step of heme synthesis and is an important NPAA.

NPAAS acting as important metabolic end products:

Gamma amino butyric acid (GABA), an inhibitory neurotransmitter, formed by decarboxylation of Glutamic acid; thyroxine hormone (T3, T4) formed from Tyrosine, 3 amino isobutyric acid, a metabolic product from thymine and inducer of brown fat function are NPAA of this group. Beta alanine in human is produced from uracil, whereas it is produced from aspartate. Beta alanine is one of the components of coenzyme A.

NPAA produced by post-translational modifications:

Hydroxylation of proline and lysine produces hydroxyproline and hydroxylysine respectively, which give stability to structure of collagen and are examples of this group of NPAA. Gamma Carboxy glutamic acid also belongs to this group, which is formed from carboxylation of glutamic acid and is involved in activation of vitamin K dependent coagulation factors, namely Factors II, VII, IX, X. Glutamine is converted to pyroglutamic acid by Deamidation, which is a NPAA. This modification can change the protein structure, stability, and function.

In nature, NPAAs are not only found in human body but also in meteorites, sediments, rivers, lakes, other water bodies and plants. Plant is considered important as we take plants as food.

In plants NPAAs perform several functions, like, a) provide protection against stress b) Involved in cell Signaling, c) tale part in Nitrogen storage d) act asToxins against invertebrates and vertebrates. But their action in human is different, which are as follows:

NPAAs with cyclic, heterocyclic, or aromatic_skeletons possess greater significance as goitrogens, stress inducers and inhibitors of ion transport.

Homoarginine, beta N oxalyl diaminopropionic acid (beta ODAP) are obtained from seeds of a legume, lathyrus. If they are consumed by humans, they give rise to a serious complication known as lathyrism. Some other non-protein amino acids obtained from plant and contributing to serious health problems are,

a) L-thialysine: Toxic analogue of L-lysine. This compound is cytotoxic as it inhibits protein synthesis
b) Canavanine: It is structurally related to the L-arginine. Alfalfa seeds and sprouts contain L-canavanine. The L-canavanine in alfalfa has been linked to lupus-like symptoms in primates, including humans, and other auto-immune diseases.
c) Azetidine-2-carboxylic acid: homologue of proline. Misincorporation of Aze into human proteins can alter collagen, keratin, hemoglobin, and protein folding
d) Cyanotoxins are produced by blue-green microalgae classified according to their effect into hepatotoxins (microcystins, nodularins), neurotoxins (ß-N-methylamino-l-alanine) and dermatotoxins.

NPAA obtained from plants may be used as pharmacologic agents eg Cephalosporin C (Isolated from a fungus of the genus Acremonium**)**, Penicillamine etc.

Synthetically prepared NPAAs act by different mechanisms. Drug-like properties of peptide medicines, due to the smaller size and simpler structure compared to large proteins, can be changed fundamentally by introducing NPAAs in its sequence. While peptides composed of natural amino acids can be used as drug candidates, the majority have shown to be less stable in biological conditions. The impact of NPAA incorporation can be extremely beneficial in improving the stability, potency, permeability, and bioavailability of peptide-based therapies. Conversely, undesired effects such as toxicity or immunogenicity should also be considered.

Activity News

BIO-BOOST 2023, a brainstorming tutorial session on high yield topics of Biochemistry was organised by AMBI WB Chapter for students appearing in Final MD exam. The first session on BIO-BOOST took place in the year 2020 February with a huge success. But due to pandemic of SARS Cov 2, it could not be organised subsequently.

This year, with highly enthusiastic members of AMBI WB chapter, and with high demand from the students, it was organised as a 4 days program which was on 16th, 17th, 23rd and 24th March, 2023. The classes were taken in the Department of Biochemistry of IPGMER (under the leadership of Prof. Mousumi Mukhopadhyay) on 16th & 17th March and in Department of Biochemistry of NRSMCH (under leadership of Prof. Soma Gupta) and Medical College (under leadership of Prof. Debasis Basu) on 23rd and 24th March respectively.

Huge effort was provided by Dr. Sanghamitra Chakrabarty and Dr. Priyanka Datta to make the program a grand success.

Classes were taken by Prof Indranil Chakraborty ,Prof Soma Gupta , Prof. Debashish Basu, Prof. Mousumi Mukhopadhyay, Prof. Swati Bhattacharyya, Prof. Chandan Sarkar, Prof Anindya Dasgupta, Prof. Pinaki Sarkar, Prof. Debojyoti Bhattacharjee, Dr Debosmita Bandyopadhyay, Dr Indranil Dawn, Dr Sayantan Dasgupta, Dr Sharmistha Chatterjee, Dr Satwika Sinha, Dr Manali Sinha Ray, Dr Jayati Roy Choudhury, Dr Kasturi Mukherjee, Dr Sanghamitra Chakraborty, Dr Soumika Biswas, Dr Amrita Karmakar, Dr Arghya Ray Choudhuri, Dr Aritri Bir and Dr Priyanka Datta.

Illustrator

Dr Manali Sinha Ray, Associate Professor, Dept. of Biochemistry, CNMCH, Kolkata

Dr Abhra Ghosh, Associate Professor, Dept. of Biochemistry,, DMCH, Ludhiana