

Nutritional Supplementary Role of Non-Standard Amino Acids and Amino Acid Derivatives

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ABSTRACT: Out of the several biological amino acids, 22 are considered protein building blocks. However, there are some non-standard amino acids and amino acid derivatives with health benefits and nutritional roles. There is a need for studies into the mechanisms by which these amino acids contribute to human health and nutrition. Lanthionine is a non-standard amino acid consisting of a trace of cysteine and a dehydrated serine. Its biosynthesis is a two-step metabolic pathway that is catalyzed in cystathionine beta-synthase and cystathionine gamma lyases. It is a non-protein amino acid produced as a side product of a trans-sulfuration reaction. Hydroxyproline is made with the assistance of the enzyme prolyl hydroxylase by hydroxylation of amino acid proline. Collagen stabilization is due to hydroxyproline which is a necessary form of protein collagen component. Dimethylglycine (DMG) is a derivative of glycine that plays a vital role in the body's overall metabolism. It helps the body to adapt to any stressful environment out of the comfort zone. Production of DMG in the body leads to the fast recovery of muscle and improve endurance in athletes. It is beneficial in dietary supplements and used in foods and beverages. Gamma-aminobutyric acid (GABA) is a vital amino acid and has several health benefits. GABA is involved in many physiological functions and has a role in signal transduction. Glutathione is made of three amino acids glycine, glutamic acid and cysteine. Glutathione has various functions such as antioxidant defense, nutrient metabolism, DNA and protein synthesis and has a significant role in ageing. Dopamine is that the initial endocrine synthesized from dihydroxyphenylalanine. This review aims to describe the health benefits of these non-standard amino acids and amino-acid derivatives and is an informative resource for physicians and researchers.

Keywords: Amino acids, DMG, Dopamine, GABA, Lanthionine.

INTRODUCTION

A. GABA (*Gama-amino-butyric acid*)

Gama-amino-butyric acid (GABA) is a non-protein amino acid found naturally in plants, animals, fungi and bacteria. It was first found in potato tuber, and after one year of that, it was identified in the brains of mammals. Data from the past few decades shows that GABA is more abundant in plants than animals, and the amount of GABA ranges in milligram/gram (Ramos-Ruiz *et al.*, 2018). In animals, GABA levels in the brain and central nervous system are abnormally high compared to other body parts and range in $\mu\text{g/g}$. Fungus is a large kingdom with 1.5 million species, and mushrooms are considered as higher fungi. Mushrooms are generally used as food and have a different level of GABA in other species (Bouché *et al.*, 2003; Dhakal *et al.*, 2012). Structurally it is a four-carbon compound with an amino group at fourth carbon. The mechanism of GABA metabolism is a three-enzyme pathway and known as GABA shunt. An irreversible enzyme

synthesizes it called glutamate decarboxylase (a cytosolic enzyme) and involves cytosolic acidification. Gamma-aminobutyric acid is the primary inhibitory neurotransmitter in the central nervous system. GABA is a brain relaxer, and that makes us feel good. A low GABA level can result in insomnia, mood disorders, and many more health-related issues (Ueno, 2000; Seifikalhor *et al.*, 2019). The source of GABA is sweet potato, broccoli, spinach, rice etc. The amount and dosage of GABA, which is essentially required in the body, depends on the person's age, gender, and body condition.

Synthesis of Gama-amino- butyric acid. GABA is primarily synthesized through the GABA shunt. Glucose is metabolized to form glutamates in the Krebs cycle by -ketoglutarate and transaminated by -oxoglutarate transaminase (GABA-T). Glutamate is also decarboxylated into GABA by glutamate decarboxylase (GAD).

The immediate and irreversible α -decarboxylation of glutamate-by-glutamate decarboxylase is the first phase in this shunt. GAD decarboxylation is demonstrated in vivo by the conversion of glutamate to CO_2 and unlabeled GABA. The operation of GAD in vitro has been studied. Many plant species and tissues have crude

extracts. Pyridoxal 5 α -phosphate-dependent, unique for L-glutamate Sulfhydryl groups, is inhibited by reagents that react with them and contain a calmodulin-binding domain sharp, acidic pH of 5.8. GAD genes have been found in Petunia, tomato (Shelp *et al.*, 1999).

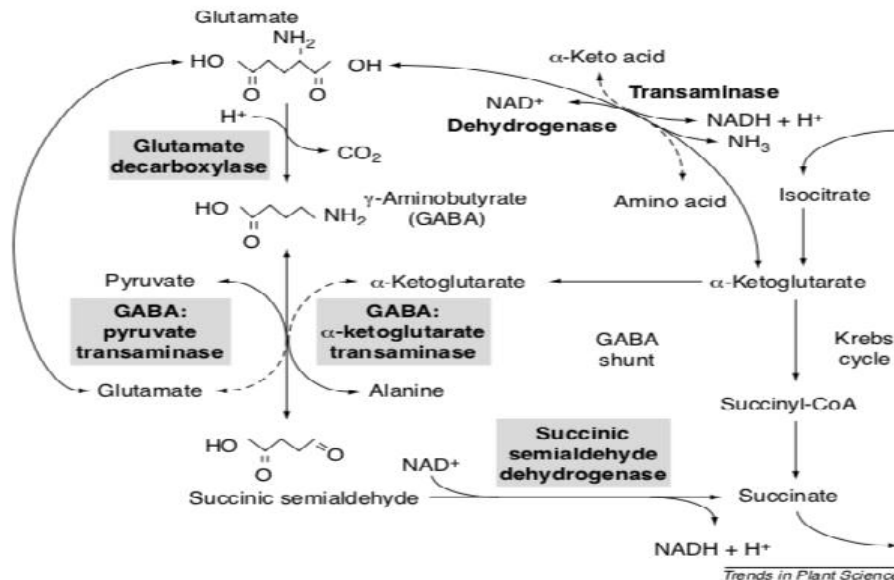


Fig. 1. Showing the biochemical pathway for GABA synthesis (Shelp *et al.*, 1999).

GABA's second enzyme, the GABA Shunt, is engaged in the GABA-T (transaminase) process by using either pyruvate or α -ketoglutarate as amino acceptors to catalyze reversible GABA transaminase reaction to succinic semialdehyde. Succinic semialdehyde dehydrogenase catalyzes the last step of the GABA shunt, irreversibly, which is oxidizing succinic semialdehyde to succinate (Shelp *et al.*, 1999).

Health benefits of GABA. Overall, GABA has several health benefits, and new techniques are being developed for the enhancement of GABA in foodstuffs. GABA plays a vital role in hypotensive effect and relaxation because when the level of GABA falls too low, it becomes difficult for our body to relax after release stress induces neurotransmitter. Two studies were conducted to prove the administration of GABA which the first study was on brain waves study. After 60 minutes of intake GABA has shown a significant increase in alpha wave and decrease in a beta wave which gives a feeling of calm and relaxation and shows its effect within 1 hour of administration. The enhanced level of GABA has shown inhibitory action on metastasis of cancer cells. One study showed the inhibitory activity of GABA on mammary cancer growth. GABA supplements result into reduction of body fat and triglyceride levels however it increases lean muscle mass. To measure the immunity condition of humans in an easy way is to check the immunoglobulin (IgA) in

saliva. The lower level of IgA indicates a high level of anxiety. In one clinical trial, GABA administration showed enhancement in immunity in a stressed condition. The levels of IgA were measured in the saliva of volunteers (Ramos-Ruiz *et al.*, 2018).

Table 1: GABA concentration in different food items (Oh *et al.*, (2003).

Food items	Concentration per g dry weight (DW)
Brown rice sprouts	389 nmole per g DW
Barley	190 nmole per g DW
Chestnut	188 nmole per g DW
Corn	199 nmole per g DW
Spinach	141 nmole per g DW

B. Glutathione

Glutathione is a tripeptide made up of three amino acids (glycine, glutamic acid and cysteine) that play a crucial role in many physiological processes, including reduction of oxidative stress, improving mitochondrial detoxification, and regulating immune system function. Glutathione is an essential antioxidant present in bacteria, fungi, plant and animals. Glutathione act as a biomarker and important drug target in many chronic, age-related diseases. Less glutathione can be responsible for various diseases such as cystic fibrous, pulmonary disease, immune disease, etc. Glutathione is present in two stages inside the cell reduced and oxidized. The ratio of GSH to GSSH represent the cell

redox status, and generally, the average cell at rest have a ratio of (GSH/GSSH) >100 (Minich and Brown, 2019). There are three methods from which the synthesis of glutathione take place. These methods are:

- One carbon metabolism
- Trans sulfuration pathway
- Glutamyl cycle

In the synthesis of GSH first, the formation of a peptide bond takes place in glutamate and cysteine, catalyzed by γ -glutamyl cysteine synthetase (GshA), followed by the formation of a peptide bond between Glu-Cys and glycine, which is catalyzed by glutathione synthetase. Sulfur is an important compound for glutathione synthesis, so taking sulfur-rich foods such as fish, beef and broccoli etc., help reduce oxidative stress. There are many ways by which glutathione level can be maintained, like regular exercise, avoid drinking alcohol and enough sleep (Lu, 2013).

Synthesis of Glutathione (GSH). Two ATP-consuming enzymes do GSH production: glutamate-cysteine ligase and GSH synthetase, producing GSH in a series of reactions. From glutamate and cysteine, GCL produces the dipeptide GluCys. Enzyme GSH synthetase catalyzes the conversion of GluCys to GSH by combining it with glycine. GCL affects the rate of reaction and acts as the rate-limiting enzyme for GSH production. It is tightly controlled with the help of GSH feedback inhibition. GCL is a heterodimeric protein made up of two subunits: a catalytic subunit (GCLc) and a modulatory subunit (GCLm). The GCLc, synthesis the GluCys, while GCLm, the modulatory subunit, modifies the GCLc activity by reducing the Km value for the substrates ATP (Schmidt and Dringen, 2012).

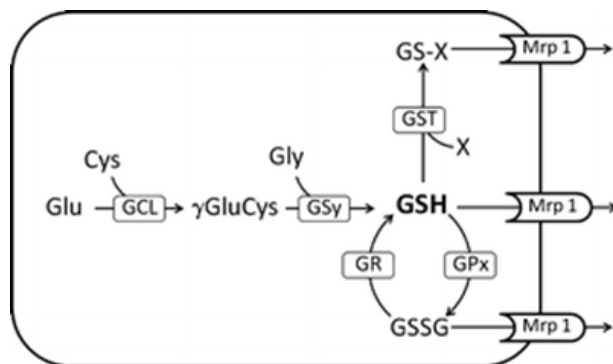


Fig. 2. Showing the biochemical pathway for synthesis of glutathione (Schmidt and Dringen, 2012).

GSH is synthesized from three amino acids: glutamate, cysteine, and glycine, by reactions of two different enzymes: glutamate-cysteine ligase (GCL) and GSH synthetase (GSy). GSH is oxidized by GSSG (glutathione disulphide) and regenerated by GSSG Glutathione Reductase (GR) during peroxide disposal. In reactions catalyzed by glutathione-S-transferases, GSH can also react with xenobiotics and endogenous compounds (X) (GST). Multi-drug-resistance proteins

such as Mrp1 can export the conjugates GSH, GSSG and GS-X from cells (Schmidt and Dringen, 2012).

Health benefits of glutathione.

1. Singlet oxygen, hydroxyl radicals, and superoxide radicals are also chemically neutralized directly.
2. Several antioxidant enzymes require glutathione as a co-factor.
3. Glutathione helps in vitamin C and E regeneration.
4. Neutralization of free radicals generated by chemical toxin metabolism in the liver.
5. Cellular proliferation and apoptosis are regulated.
6. Glutathione is essential for mitochondrial function and mitochondrial DNA maintenance (Minich and Brown, 2019).

Table 2: Dosage of glutathione of different food items (Minchiand Brown, 2019).

Food Items and Nutrients	Recommended Dosage
Brassica vegetables	250g/day
Glycine	100mg/day
Vitamin C	500-2000 mg/day
Green tea	4 cups /day
Salmon	150g twice a week

C. Lanthionine

Lanthionine (HOOC(NH₂)-CH₂-S-CH₂-CH(NH₂)-COOH) is a non-proteinogenic amino acid with a molecular formula. It generally consists of a trace of cysteine and a dehydrated serine. Lanthionine contains no lanthanum ingredient, notwithstanding its name. An amino acid containing sulfur was found, and thus the name was given lanthionine, where wool means "Lana" in Latin and "theion" means sulfur in Greek. It is a two-step metabolic pathway that is catalyzed in cystathionine beta-synthase and cystathionine gamma lyases. It is a non-protein amino acid produced as a side product of transsulfuration. Initially, lanthionine was used as a reliable H₂S supply predictor for the life system. The amino acid in circulation in uremia has been shown to suppress transsulfuration enzymes in cells, potentially leading to uremia-like hyperhomocysteinemia. The sources from which we take lanthionine are the treatment of sodium carbonate wool used to remove lanthionine. The alkylation of cysteine with beta chloroalanine was first synthesized. In nature, lanthionine is observed. The fur, lactalbumin and feathers are insulated. It is often present in the gene encoded cell walls of bacteria and peptide antibiotics, such as nisin, subtilin, epidermin, and gene-encoded. A range from sulfur oxidation of cystine to serine beta lactone and hetero-conjugate addition of cysteine to dehydroalanine has been reported for many lanthionine syntheses. The only mechanism for lanthionine used in the complete lantibiotic synthesis is the sulfur extrusion procedure (Hensley *et al.*, 2010).

Biosynthesis of Lanthionine. Lanthionine biosynthesis is the condensation in L-lanthionine consists of two cysteine molecules, while the condensation in two homocysteine molecules forms L-homolanthionine. Although CBS and CSE are sequentially working in the transsulfuration process, under physiological conditions, either the CBS or the CSE may independently catalyze lanthionine or homolanthionine biosynthesis. Cysteine, however, is a prevalent substrate compared to homocysteine for H₂S biosynthesis (render of lanthionine), although, under certain conditions, its contribution will increase. The high diversity of CBS (cystathionine beta-synthase) and CSE (cystathionine gamma-lyase) in sulfur metabolism is underlined in this feature. Carbon monoxide (CO)-heme oxygenase 1 has been identified as inherent in CBS (also in CBS mutants or deletions) in stress conditions (which could be associated with homocystinuria), thus providing the requirements for a relative decrease in total transsulfuration and increased CSE H₂S biosynthesis. On the contrary, we have obtained evidence that, while the circulation of H₂S is significantly reduced in patients with hemodialysis, lanthionine is a retention product (Denoël *et al.*, 2018). Lanthionine may also be formulated as a side product caused by a disulphide desulfurization deterioration in alkaline conditions despite its flexibility in peptide functional and structural studies. Firstly, the hydrolytic disulfide was explained, but later the -removal mechanism overshadowed this phenomenon. The degradation of cystine disulfide circulation through -removal leads to dehydroalanine and cysteine derivatives formation. The nuclear supplement of the thiolate replacing cysteine by the Michael addition mechanism to the olefin dehydroalanine side-chain generates lanthionine movement. In order to produce ornithinoalanine, lysinoalanine, and the corresponding histidine and tryptophan adduct, dehydroalanine could also take into account nucleophilic attacks from other amino acids as well as cysteine side chain thiolates (Hensley *et al.*, 2010).

Benefits of lanthionine. 1. The uremic lanthionine toxin characteristics have been further evaluated in a zebrafish animal model, showing lanthionine to establish significant cardiovascular larval development changes along with a behavioural intervention, which is partially reversible after the treatment with glutathione. 2. Lanthionine occurs in the mammalian brain at significant levels, where it is converted into a cyclical thioether, lanthionine ketimine. Lanthionine ketimine act as neuroprotective, neurogenic as well as anti-inflammatory effects. It is a natural metabolite of amino acid of sulfur produced by alternate transsulfuration reactions and transamination properties from where they associate with CRMP2 (collapsin reaction media protein). LKE, an artificial imitative engineered for cell penetrators, has also shown neuroprotective characteristics and is readily bioavailable.

3. In addition, LK attach to mammalian lanthionine synthetase, the protein 1, LanCL1 associated with the significant physiological processes and its homolog LanCL2, helps in signal transduction and sensitization.

4. Not only depolarization of membrane but also inhibiting peptidoglycans, they destroy bacteria through the forming of pores. These polycyclic peptides are modified after translation to form amino acids, lanthionine or methylanthionine thioether after translation.

5. Lanthionine can inhibit the generation of sulfide in hydrogen in hepatoma cells by inhibiting CBS, thereby creating a biochemical mechanism for altering sulfur metabolism in these topics, such as high homocysteine and low hydrogen sulphides (Hensley *et al.*, 2010).

D. Hydroxyproline

Hydroxyproline (Hyp) is produced with the assistance of the enzyme prolyl hydroxylase by hydroxylation of amino acid proline. This reaction takes place in the lumen of the ER. It provides strength to collagen proteins in the bones, tendons, cartilage and skin. Proline cannot be transformed to hydroxyproline for vitamin C deficiency because collagen does not have adequate strength to protect the integrity of the skin, resulting in gum and skin bleeding and other scurvy symptoms. Hydroxyproline is a derivative of non-essential amino acid that can be produced from the amino acid proline in your body, so you don't need to get it from food to be safe. Collagen stabilization is due to hydroxyproline which is a necessary form of protein collagen component. Xaa-hyp-gly sequence alteration helps the collagen stability of the triple helix by the prolyl hydroxy and primary chain group carboxylate hydrogen-bond networks. The sources from which we obtain the hydroxyproline are: the types of beef, bone meal, poultry meal, and salmon protein available are proline and hydroxyproline. These animals have an excellent source of proline and hydroxyproline for animals after weaning and post-hatching poultry (Srivastava *et al.*, 2016).

Biosynthesis of hydroxyproline. Primarily because of its high collagen content, Trans-Hyp is produced industrially by acid hydrolysis of mammalian collagen. It leads to multiple environmental problems and creates considerable problems in downstream processing. Many pathways have identified hydroxyproline biosynthesis. 4-hydroxyproline is catalyzed in animal tissue by prolyl 4-hydroxylase, and this is a substratum for peptidyl proline rather than a free proline. The enzyme can be converted into hydroxyproline by 4-hydroxy-2-oxoglutaric acid. Hydroxyproline was found to shape certain bacteria and fungi directly by fermentation.

The proline four hydroxylases (P4Hs), which can catalyze L-proline hydroxylation in 4 positions in the presence of 2-oxoglutarate, oxygen, and iron ferrous, were known from several microbial strains. The optimal

pH range of the P4Hs is between 6.0 and 7.5, and the temperature range is between 30 and 40°C. Metal ions, including Zn²⁺ and Cu²⁺, are inhibiting their action. The effects of co-substrates on P4H hydroxylation of L-proline were investigated, and noted that 2-oxoglutarate was necessary for proline hydroxylation since 2-oxoglutarate substitutions with 2-oxopentanoate, 2-oxoadipate, pyruvate, or 2-oxomalonate resulted in no observable L-Proline hydroxylation. While 2-oxoglutarate as a donor of oxygen is needed to hydroxy L-proline in vitro to 4-hydroxy-L-Proline, the development of 4-hydroxy-L-proline using recombinant strains requires no addition of extra 2-oxoglutarate in vivo. 2-oxoglutarate is a primary metabolic intermediate in the *Escherichia coli* tricarboxylic acid cycle that can result directly in glucose and proline hydroxyproline production. The potential metabolic pathways of 2-oxoglutarate were studied. They concluded that the proline dehydrogenase activity of L-proline and isocitric dehydrogenase of glucose could be supplied with 2, oxoglutarate. Adding the L-proline to a reduced glucose-containing medium had a favorable effect on the operation and development of the proline 4-hydroxylase. However, since the biosynthesis of proline in wild type *E. coli* is tightly regulated to deficient levels, intracellular proline supply is still reduced. Thus, a simultaneous consideration is needed of the precursor and co-factor in hydroxyproline microbial processing (Srivastava *et al.*, 2016).

Health benefits of hydroxyproline. 1. **Clinical significance:** Hydroxyproline absence induces scurvy because ascorbic acid is necessary for proline hydroxylation. The most evident first symptoms of gingival and hair complications related to the lack of ascorbic acid in humans resulted from a deficiency in the hydroxylation of proline collagen residues with diminished collagen stability. It is the central portion of the collagen protein, which constitutes approximately 14-15 per cent of collagen associate with mammalian. For collagen stabilization, hydroxyproline and proline play a significant role in the sharp twisting of the collagen helix.

2. **In the skin:** Collagen produces the amino acid hydroxyproline, having just three amino acids, which has been shown to cause in vitro skin cells to create more hyaluronic acid and which also helps to enhance the content of water in the skin.

3. Dietary supplements of 0.07, 0.14, 0.28 per cent hydroxyproline to a diet focused on plant protein improved salmon weight gains. Proline should be treated as a functional amino acid for humans, birds, marine organisms because of its regulatory functions in cellular biochemistry. More study is required to develop successful proline and hydroxyproline dietary supplementation strategies that support animal and human health, growth, and development.

4. Hydroxyproline was once thought to be of little nutritional importance and is now known as a substrate

for the synthesis of glycine, pyruvate, and glucose, particularly for newborns ruminants. It also scavenges oxidants and controls the redox state of the cell. Besides, hydroxyproline may substantially affect the diet of birds unable to synthesize glycine from other amino acids properly.

5. Hydroxyproline is a non-essential amino acid that is neutral as well as heterocyclic. Hydroxyproline is mainly used as a bone turnover and liver fibrosis diagnostic marker. Hydroxyproline is being investigated therapeutically as an experimental drug but is approved in France as a thin, superficial boundary combination topical gel product called Cicactive (Srivastava *et al.*, 2016; Wu *et al.*, 2019).

Table 3: Advantages of Dietary supplementation with 4-Hydroxyproline in women (Wu, 2020).

Age	Duration	Effects
35-55	8 weeks	Enhanced skin elasty
40-59	8 weeks	Decreasing the fragmentation of the dermal collagen network
35-55	8 weeks	Improvement in facial skin condition, wrinkles and roughness.
45-55	12 months	Prevent osteoporosis
50 above	24 weeks	Mitigating osteoporosis in postmenopausal women

E. Dimethylglycine (DMG)

Dimethylglycine (DMG) could be a non-essential amino acid glycine spinoff with the molecular formula (CH₃)₂NCH₂COOH. It is one of the essential amino acids and present in beans. It is synthesized from trimethylglycine. One of its methyl group separates away and lead to the formation of DMG. It's conjointly a side product of choline when it is metabolized. Dimethylglycine was first considered sustenance vitamin B16, but in contrast to fundamental B vitamins, less DMG in the daily routine doesn't result in any problematic effects. DMG is advised to be used by athletes to enhance their performances, immunostimulant, and to treat autism, epilepsy, and mitochondrial unwellness. There is no proof that DMG is as effective as earlier than treating mitochondrial unwellness. Studies on DMG research have demonstrated very little or no distinction between dimethylglycine treatment and placebo in syndrome spectrum disorders. Dimethylglycine has been reported to act as an agonist of the glycine places of the NMDA receptor (Kendall and Lawson, 2000).

Sites of Glycine of the NMDA receptor. Glycine is commercially on the market because of the morpheme organic compound and because of the complex salt. The alkylation of glycine could also prepare DMG through the Eschweiler-Clarke reaction. During the reaction, glycine reacts with aqueous formaldehyde in

formic acid, each solvent and chemical agent. Acid has been supplemental thenceforth to convey the complex salt. The unreacted organic compound could be formed by neutralizing the acidic salt, which has been performed with Ag compound $\text{NH}_2\text{CH}_2\text{COOH} + 2\text{CH}_2\text{O} + 2\text{HCOOH} \rightarrow (\text{CH}_3)_2\text{NCH}_2\text{COOH} + 2\text{CO}_2 +$ a pair of binary compounds. This non-protein organic compound is found naturally in animal and plant cells. Within the body, DMG is found solely in terribly tiny amounts and for less than seconds at a time. It is made in cells as an associate intermediate within the metabolism of B vitamin to glycine. It has been rumoured that dimethylglycine will enhance natural process at the cellular level, scale back fatigue and enhance physical stamina (Lee *et al.*, 2017).

Synthesis of DMG. It may be shaped when trimethyl glycine losses 1 of its methyl group. It is conjointly a side product when choline is metabolized.

(a) Prepare chloroacetic acid solution: Mono Chloro ethanoic acid is added to water beneath the ambient temperature, making chloroacetic acid.

(b) The chloroacetic acid is added to aqueous dimethylamine aqueous, and the gram molecule ratio of mono chloro ethanoic acid and dimethylamine are 1:2.5. The reaction is carried out at 20-70 °C for 2-5 hours.

(c) Take away excess dimethylamine when having reacted; unreacted dimethylamine is removed.

N,N-dimethylglycine enhances the coupling reaction of aryl bromides with substituted oxazolidinones happened at 120 °C in DMF, lead to the formation of the corresponding N-arylation merchandise with maximum yields (Kendall and Lawson, 2000).

F. Dihydroxyphenylalanine

DOPA is regenerated to dihydroxy Phenethylamine (dopamine) through the action of aromatic L-amino acid enzyme (AAAD), a catalyst present in most tissues in comparatively large concentrations. L- DOPA, conjointly legendary as levodopa and 1-3,4-dihydroxyphenylalanine, is an amino acid created and used as an essential intermediate in the neurobiology of humans, some animals and plants. L- dihydroxyphenylalanine is the precursor to neurotransmitter monoamine neurotransmitter, vasoconstrictive (Nor-adrenaline), and catecholamine (Adrenaline), that square measure put together called catecholamines (Patel and Burger, 1966).

Synthesis of Dihydroxyphenylalanine. Dopamine is that the initial endocrine synthesized from dihydroxyphenylalanine; in turn, vasoconstrictive and catecholamine square measure derived from an additional metabolic modification of monoamine neurotransmitter. The accelerator monoamine neurotransmitter hydroxylase needs copper as a compound, and the dihydroxyphenylalanine enzyme requires PLP. The speed limiting step in endocrine

synthesis through the predominant metabolic pathway is the hydroxylation of L-tyrosine to Bendopa.

L-3,4-Dihydroxyphenylalanine (DOPA) is an associate degree uncommon organic compound found in mussel adhesive proteins (MAPs) believed to lend adhesive characteristics to those proteins. Most previous efforts to incorporate amino acid into hydrogels have utilized aerobic cross-linking, which is hypothesized to cut back the adhesive properties of amino acid and needs reagents that square measure harmful to biological tissues. The impact of amino acid-containing monomers on gelation time, gel conversion, and the constant physical property of the photocured hydrogels was investigated. Despite an inhibitory effect of amino acids on photopolymerization, the amino acid was successfully incorporated into hydrogels with elastic moduli appropriate for many medical applications. Incorporating amino acids into hydrogels by photopolymerization could cause new adhesive hydrogels for medical applications (Patel and Burger, 1966).

Health benefits of Dihydroxyphenylalanine.

1. L-dopa crosses the protecting barrier, whereas monoamine neurotransmitter itself cannot. Thus, Bendopa is employed to extend monoamine neurotransmitter concentrations within the treatment of brain disease and dopamine-responsive dystonia. Once Bendopa enters the central system nervous, it regenerates into monoamine neurotransmitter by the accelerator aromatic l-amino acid enzyme, conjointly called dihydroxyphenylalanine enzyme.

2. Nbrija (previously called CVT-301) is an associate in Nursing inhaled powder formulation of dihydroxyphenylalanine indicated for the intermittent treatment of off episodes in patients with encephalopathy presently taking carbidopa/levodopa. It had been approved by the U.S Food and Drug Administration (Hardebo and Owman, 1980).

Table 4: Concentration of Dihydroxyphenylalanine in different food items (Castellar *et al.*, 2012).

Food items	Concentration in them
Fermented beans	8.56%
<i>Betalain opuntia</i>	17-32 %
Velvet beans	5.63%
<i>Vicia faba</i>	12%

CONCLUSION

Lanthionine and hydroxyproline have many health benefits hydroxyproline; the clinical significance of this is that the lack of ascorbic acid in humans due to a deficiency in the hydroxylation of proline collagen residues with diminished collagen stability. Lanthionine ketimine act as neuroprotective, neuritogenic, and has anti-inflammatory effects and many more. However, the biosynthesis of both lanthionine and hydroxyproline is complex. DMG is a derivative of glycine and plays a vital role in the overall metabolism of the body. It helps

the body to adapt to any stressful environment out of the comfort zone. Production of DMG in the body leads to the fast recovery of muscle and improve endurance in athletes. It is beneficial in dietary supplements and used in foods and beverages.

Moreover, GABA is the primary inhibitory neurotransmitter and present in many food supplements such as shellfish, tomato and many more. The metabolic and regulatory flexibility of GSH is exceptional. GSH / GSSG is the leading redox pair, instrumental in protecting antioxidants, synthesizing nutrients, and controlling pathways necessary to homeostasis in the body. The lack of glutathione leads to oxidative stress and may play a significant role in the ageing and pathogenesis of many diseases.

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Conflict of Interest. The authors declare no conflict of interest.

REFERENCE

Bouché, N., Lacombe, B., and Fromm, H. (2003). GABA signalling: a conserved and ubiquitous mechanism. *Trends in Cell Biology*, **13**: 607-610.

Castellar, M. R., Solano, F., and Obón, J. M. (2012). Betacyanin and other antioxidants production during growth of *Opuntia stricta* (Haw.) fruits. *Plant Foods for Human Nutrition*, **67**: 337-343.

Denoël, T., Lemaire, C., and Luxen, A. (2018). Progress in lantionine and protected lantionine synthesis. *Chemistry—A European Journal*, **24**: 15421-15441.

Dhakal, R., Bajpai, V.K., and Baek, K.H. (2012). Production of GABA (-aminobutyric acid) by microorganisms: a review. *Brazilian Journal of Microbiology*, **43**: 1230-1241.

Hardebo, J.E., and Owman, C. (1980). Barrier mechanisms for neurotransmitter monoamines and their precursors at the blood-brain interface. *Annals of Neurology: Official Journal of the American Neurological Association and the Child Neurology Society*, **8**: 1-11.

Hensley, K., Venkova, K., and Christov, A. (2010). Emerging biological importance of central nervous system lantionines. *Molecules*, **15**: 5581-5594.

Kendall, R.V., and Lawson, J.W. (2000). Recent Findings on N, N-Dimethylglycine (DMG): A Nutrient for the

New Millennium. *Townsend letter for Doctors and Patients*, 75-85.

Lee, M.Y., Lin, Y.R., Tu, Y.S., Tseng, Y.J., Chan, M.H., and Chen, H.H. (2017). Effects of sarcosine and N, N-dimethylglycine on NMDA receptor-mediated excitatory field potentials. *Journal of Biomedical Science*, **24**: 1-11.

Lu, S.C. (2013). Glutathione synthesis. *Biochimica et Biophysica Acta (BBA)-General Subjects*, **1830**: 3143-3153.

Minich, D. M., and Brown, B. I. (2019). A review of dietary (phyto) nutrients for glutathione support. *Nutrients*, **11**: 2073.

Patel, A.R., and Burger, A. (1966). 3, 4-Dihydroxyphenylalanine and related compounds. *Fortschritte der Arzneimittelforschung/Progress in Drug Research/Progrès des recherches pharmaceutiques*, **9**: 223-298.

Ramos-Ruiz, R., Poirot, E., and Flores-Mosquera, M. (2018). GABA, a non-protein amino acid ubiquitous in food matrices. *Cogent Food and Agriculture*, **4**: 1534323.

Schmidt, M. M., and Dringen, R. (2012). Glutathione (GSH) synthesis and metabolism. (Eds Choi IY., Gruetter R.) *Neural metabolism in vivo*. Springer, Boston, MA, p. 1029-1050.

Seifikalhor, M., Aliniaiefard, S., Hassani, B., Niknam, V., and Lastochkina, O. (2019). Diverse role of -aminobutyric acid in dynamic plant cell responses. *Plant Cell Reports*, **38**: 847-867.

Shelp, B.J., Bown, A.W., and McLean, M.D. (1999). Metabolism and functions of gamma-aminobutyric acid. *Trends in Plant Science*, **4**: 446-452.

Srivastava, A. K., Khare, P., Nagar, H. K., Raghuvanshi, N., and Srivastava, R. (2016). Hydroxyproline: A Potential Biochemical Marker and Its Role in the Pathogenesis of Different Diseases. *Current Protein and Peptide Science*, **17**: 596-602.

Ueno, H. (2000). Enzymatic and structural aspects on glutamate decarboxylase. *Journal of Molecular Catalysis B: Enzymatic*, **10**: 67-79.

Oh, S.H., Moon, Y.J., & Oh, C.H. (2003). -Aminobutyric acid (GABA) content of selected uncooked foods. *Preventive Nutrition and Food Science*, **8**(1), 75-78.

Wu, G. (2020). Important roles of dietary taurine, creatine, carnosine, anserine and 4-hydroxyproline in human nutrition and health. *Amino acids*, **52**(3), 329-360.

Wu, Z., Hou, Y., Dai, Z., Hu, C. A. A., and Wu, G. (2019). Metabolism, nutrition, and redox signaling of hydroxyproline. *Antioxidants & Redox Signaling*, **30**: 674-682.

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