Journal of Biochemistry and Cell Biology

Review Article Open Access

Biochemistry and Microbial Activity of Tryptophan and Nicotine

Kashaf K*

Department of Molecular Biology, Saudi Arabia

Abstract

L-tryptophan is the only protein amino acid (AA) with an indole ring; through biotransformation in live creatures, it either helps to retain this chemical group in cells and tissues or breaks it down by producing a variety of bioactive chemicals in both scenarios. Studies on the biology of Trp emphasise the pleiotropic impact of its tiny derivatives on homeostasis mechanisms. In addition to protein turnover, the production of the neurotransmitter and hormone serotonin (5-HT), the pineal gland hormone melatonin (MLT), and the trace amine tryptamine is covered by the pathways of Trp indole derivatives in humans. Instead, the "kynurenine shunt," which results in cell-response adapters such L-kynurenine, kynurenic, and quinolinic acids, or the coenzyme nicotinamide adenine dinucleotide (NAD+), is defined by the breakdown of the Trp indole ring. One of the most promising approaches to cleaning up polluted surroundings with powerful, very effective bacteria is bioremediation. The very poisonous heterocyclic molecule nicotine and other tobacco alkaloids can be broken down by microbes using particular enzymes and metabolic pathways. These nicotinophilic bacteria use nicotine as their only supply of carbon, nitrogen, and energy following the metabolic conversion. The demethylation pathway in fungi, the pyridine pathway in Gram-positive bacteria, the pyrrolidine pathway, and variants of the pyridine and pyrrolidine pathways in Gram-negative bacteria are just a few of the identified nicotine breakdown pathways. In this review, we covered the biotechnological uses of nicotine intermediate metabolites as well as the enzymes and microorganisms that break down nicotine.

Keywords: Nicotine; Bioremediation; Pleiotropic

Introduction

L-Tryptophan (L-Trp) is one of the 20 L-amino acids (AAs) that are integrated into proteins during the process of mRNA translation. It is a large neutral amino acid (LNAA) that is found in living things. The letter W is typically used to denote all Trp residues in protein and peptide sequences. The AA L-Trp, discovered by the English chemist F. Hopkins in 1901, is one of the 9 essential AAs for humans that cannot be generated endogenously and must be given by food, as shown by experiments on diet manipulation [1]. In addition to being a step in the synthesis and turnover of proteins and peptides, Trp has been the focus of decades of scientific study in the field of human biology due to its transformation into a number of minute bioactive molecules with pleiotropic properties after absorption. Since these systems and organs-the gut-liver apparatus, the neuroendocrine, immunological, and CNS systems—are in charge of preserving the chemical, cellular, and behavioural homeostasis, it follows that changes in L-Trp-deriving chemicals can be linked to a wide range of metabolic disorders and syndromes [2]. These systems' capacity to interact with and distinguish between stressors and stimuli, exogenous and endogenous antigens, nutrients, and xenobiotics throughout development can be particularly hampered by an unbalanced metabolism of this AA [3].

The ancient neurotransmitter serotonin is one of the Trp-derived substances produced by the human body. This biogenic amine is known to regulate the main adaptive reactions and responses to environmental changes in the human CNS, such as mood-anxiety, cognition, nociception, impulsivity, aggression, libido, feeding behaviour, and body temperature. In addition to its function as a neurotransmitter, 5-HT also influences the activity of peripheral areas, particularly the gastrointestinal, immunological, and inflammatory responses, the development of blood stem cells, and hemodynamic function [4]. In fact, altered 5-HT transmission has been linked to disorders of mood and cognition, autism, anorexia or bulimia nervosa, obesity, and other illnesses with peripheral symptoms such fibromyalgia, chronic fatigue syndrome, and irritable bowel syndrome. The circadian regulators N-acetyl-5-HT (NAS) and melatonin (MLT), which are largely made in the pineal gland but are also made in the periphery where the two indoleamines act as scavenger substances, are precursors of 5-HT as well [5]. In animals and people, the indole ring breakdown via the so-called "kynurenine shunt," which results in a multitude of chemicals implicated in inflammation, immunological response, excitatory neurotransmission, and many other functions, is another major metabolic pathway of Trp. Given that only a very small portion of endogenous/dietary L-Trp gets converted into 5-HT, it is possible that changes in the control of this AA's metabolism in tissues, as well as its bioavailability, are crucial for preserving a healthy balance among all of its various pathways and destinations. Furthermore, 5-HT functions as a precursor for the circadian regulators N-acetyl-5-HT (NAS) and melatonin (MLT), which are largely made in the pineal gland but can also be found in the peripheral nervous system where they serve as scavenger substances. In vertebrates, including humans, the indole ring breakdown of Trp via the so-called "kynurenine shunt" results in a multitude of chemicals that are involved in inflammation, immunological response, excitatory neurotransmission, and many other processes [6]. The bioavailability of this AA and/or modifications in the regulation of its metabolism in tissues may be crucial for maintaining a healthy balance between all of its numerous pathways and destiny since only a very small quantity of endogenous/dietary L-Trp gets transformed into 5-HT. In Brazil, China, Cuba, India, and the United States, tobacco (Nicotiana, Solanaceae family) is mostly grown. According to reports, tobacco is produced at a rate of 6.7 million tonnes annually [7]. The top four tobacco-producing countries are China (39.6%), India (8.3%), Brazil

***Corresponding author:** Kashaf K, Department of Molecular Biology, Saudi Arabia, E-mail: Kmol@shaf.gmail.com

Received: 02-Sep-2022, Manuscript No: jbcb-22-74768, **Editor assigned:** 07-Sep-2022, PreQC No: jbcb-22-74768 (PQ), **Reviewed:** 21-Sep-2022, QC No: jbcb-22-74768, **Revised:** 23-Sep-2022, Manuscript No: jbcb-22-74768 (R), **Published:** 30-Sep-2022, DOI: 10.4172/jbcb.1000165

Citation: Kashaf K (2022) Biochemistry and Microbial Activity of Tryptophan and Nicotine. J Biochem Cell Biol, 5: 165.

(7.0%), and the USA (4.6%). Following China and the United States in terms of global tobacco consumption is India (275 million users). Every year, 3,00,274 tonnes of nicotine waste are expected to be produced by the tobacco industry. The majority of the alkaloid content of commercial tobacco, Nicotiana tabacum, is typically made up of nicotine. Tobacco goods like cigarettes, cigars, chewing tobacco, and snuff were all made using all or part of the tobacco leaf as the raw material. It was estimated that smoking contributed to 4.9 million deaths in the year 2000 [8]. It is anticipated that there would be more than 9 million fatalities annually by the year 2020. The industry produced solid and liquid tobacco wastes with high levels of nicotine due to the rising use of tobacco products. The tobacco companies create waste that contains 18 g of nicotine on average per kg of dry weight [9]. These non-recyclable powdered tobacco wastes have been labelled as toxic release inventory (TRI) compounds by the Environmental Protection Agency (EPA). According to European Union Regulations (EUR), something is considered "toxic and harmful" when the amount of nicotine surpasses 0.05%(w/w)[10].

Chemical Structure of Living Organism [11]

The chemical structure of the 20 L-AAs' -R groups has been chosen by Earth's molecular evolution as the one best suited for the production of proteins. L-Trp is the sole AA in proteins derived from indole, a bicyclic ring formed by a benzene and a pyrrole group, connected to the -carbon by a -CH2-group. Trp has one of the highest levels of hydrophobic properties among all protein AAs thanks to the indole ring's presence in its chemical structure. One of these AAs, L-Trp, has been "retained" as a component of proteins in living creatures, likely because it has the simplest structure of all potential indole AAs. Although other AAs could potentially be made starting from indole, only L-Trp has done so. Through the action of the enzyme chorismate mutase, prephenate is produced from chorismate, which then enters a 3-branch pathway to produce Tyr and Phe. Anthranilate synthase recognises chorismate and transfers an amino group from the AA glutamine to it, producing anthranilate and pyruvate; anthranilate is then converted into Trp via 5 additional enzymatic steps. The biosynthesis of Trp in bacteria shares genes and chemical reactions with plants or fungi. However, this metabolic pathway is followed by various regulatory mechanisms in bacteria, plants, and fungi. The Trp operon, one of the most well-studied models of prokaryotic gene expression regulation, regulates the production of Trp in bacteria. Depending on the intracellular concentrations of this AA, the Trp operon is either activated or repressed.

Tryptophan Residues in Proteins and Peptides

In particular, the Trp indole ring in -R residues affords proteins and peptides unique features that promote protein-protein, protein-peptide, or protein-biomolecule structural hydrophobic interactions. The presence of Trp residues in polypeptides, as previously described, merits a special note. Through Van der Waals forces, the Trp indole ring can stabilise structures, domains, and contacts, and the indole-N exhibits a predisposition to behave as a hydrogen bond donor, indicating that this AA is also involved in protein binding and recognition. Trp -R groups must be present in specific domains for the protein to be stable when assembled with the phospholipid bilayer, such as the transmembrane domains of membrane-bound proteins. In terms of cell physiology, hydrophobic interactions between proteins and peptides or between these and other physiologically active molecules are crucial.

Tryptophan Requirement and Content in Food

The importance of Trp for life is one of the main conclusions drawn from the preceding paragraphs. In fact, the biosynthetic pathway for Trp is energy-intensive and necessitates the expression of a number of enzymes and substrates, either for the Trp operon in bacteria or for the shikimate and chorismate pathways in plants. This likely explains why L-Trp is a rare AA in the alimentary chain and why its presence in animal cells and tissues needs to be carefully controlled. Leucine, the most prevalent AA, is present in proteins at a frequency of 9%, compared to 5% for other AAs and 1-2% for Trp residues. The model of Trp uptake that controls its passage through the blood-brain barrier is one that has received a lot of attention (BBB). In reality, it has been discovered that insulin and other big neutral AAs, such as valine (Val), leucine (Leu), isoleucine (Ileu), Tyr, and Phe, play a key part in this. Under the influence of insulin, LNAAs actually compete with one another for the same transporter system across the BBB. This explains why a meal high in protein raises plasma levels of Trp but not its absorption into the brain. Thus, meals high in carbohydrates are rather advantageous for trp absorption to the CNS [12]. Increased 5-HT production occurs in raphe nuclei following a meal high in carbohydrates. The effects of carbohydrates on insulin secretion and AA clearance from plasma have been thoroughly explored in mammals.

Nicotine

Nicotine is a dangerous substance that contributes to lung cancer from tobacco use and peripheral artery disease. Nicotine is the main ingredient in tobacco cigarette smoke, even though there are more than 4000 other chemicals present. Nicotine causes serious vascular problems and has an approximate 2-hour blood half-life time. Nicotine has been linked to gene mutation, cancer, and deformity. Tobacco lung cancer is brought on by a variety of harmful intermediate metabolites of nicotine, including N′-nitrosonornicotine, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone, cotinine, and N-nitrosamine. Nicotine's neurotoxin-developmental effects can naturally influence a number of cellular functions, including the production of oxidative radicals, apoptosis, and cell hyperplasia, as well as the enhancement of gene expression for the release of hormones and the control of enzymatic activity.

Microbial degradation of Nicotine [13]

Nicotine in tobacco can be broken down physically and chemically. These techniques frequently need solvent extraction operations, are costly, and take a lot of time. One of the promising ways to use microbes to clean up polluted surroundings is bioremediation. A process known as biomethanation was used to remove 60% of the nicotine, 75.6% of the chemical oxygen demand, and 80% of the biological oxygen demand from the tobacco wastes. Aerobic composting is an efficient way to eliminate 80% of nicotine and 50% of the volume and mass of tobacco solid wastes. Numerous bacteria and fungi that break down nicotine are used in the biological technique. Due to their high effectiveness and low cost, these eco-friendly biological technologies are widely utilised in the treatment of wastewater. According to reports, microbes that break down nicotine can rapidly adapt to a contaminated environment.

Biochemical Pathway of Nicotine Biodegradation

A. nicotinovorans and A. oxidans have both been found to biodegrade nicotine. These Gram-positive bacteria used a pyridine route. We were able to identify and describe the nicotine intermediary metabolites of the pyridine pathway. The way that the various strains of each species break down nicotine differently. According to previous studies, plasmids as well as bacterial chromosomes contain the encoding genes that mediate nicotine breakdown. In A. nicotinovorans, nicotine breakdown is mediated by plasmid-borne genes (160 Kb). Similar to this, P. convexa's chromosomes have nicotine-degrading genes on

their periphery [14]. The nicotine's pyridine ring was targeted during breakdown by bacteria like Arthrobacter sp. (Gram-positive), which followed the pyridine pathway. After attacking the pyrrolidine ring, the Gram-negative bacterium Pseudomonas sp. followed the pyrrolidine route.

Applications of Nicotine

The employment of microorganisms to catalyse the conversion of one metabolite into another is known as biotransformation or biocatalysis. Enzymes, cellular extracts, or entire microbial cells all participated in the catalysis of these compounds. The synthesis of bulk chemicals for the industry's usage in creating pharmaceutical, food, and agrochemical compounds uses the promising technology of biotransformation. The biocatalytic generation of functionalized pyridines from renewable sources uses nicotine as a starting ingredient. To turn harmful nicotine into useful molecules like HSP and DHP, the simplest and friendliest methods of biotransformation approach were employed. The development of anticancer, antimalarial, and analgesic drugs as well as the therapy of Parkinson's disease, hypertension, and central nervous system problems all makes use of nicotine's biotransformation intermediates [15].

Discussion

Through a multitude of molecular effectors, L-tryptophan biochemistry is at the centre of the converging nutritional, neuroendocrine, and immunological pathways. As mentioned in the preceding paragraphs, each of these pathways is likely responsible for important, complex, and severe diseases and syndromes. The understanding of Trp metabolism and its implications for clinical research and medical genetics has been enhanced thanks to developments in applied biochemistry and molecular biology technology. New perspectives are actually starting to take shape; in particular, it becomes more and more obvious that illnesses with ambiguous aetiological pathophysiology require multidisciplinary and multifactorial approaches. This would make it possible to categorise patients with the same condition into groups that have similar but separate symptoms or treatment-related reactions connected with certain biochemical patterns. For instance, further evidence would be provided by the discovery of biochemical clusters within neuropsychiatric disorders or other complicated diseases. In order to create the insecticide imidacloprid, which is used to treat Parkinson's disease, 2,5- or 3,5-disubstituted pyridines are catabolized from 6HLN and HSP. SIB-1508Y is one of these biologically active metabolites. 2,5-DHP, a significant nicotine intermediate metabolite, can serve as the starting point for the chemical production of aminolevulinic acid, a universal precursor. This precursor is used to make cancer-fighting medications, herbicides, plant growth regulators, and porphyrins like heme and chlorophyll.

Conclusion

Tryptophan, an essential amino acid (AA), differs chemically from all other protein AAs in that it is associated to stress/environmental adaptive response. Tryptophan derivatives are preserved in all living creatures. Multiple factors that can be involved in a variety of complex diseases and syndromes in humans can up- and downregulate the molecular effectors of their indole-conserving or indole-disrupting destinies. The application of high-dimensional biology techniques is supposed to give more insights about the regulation of Trp content in cells, its availability for human nutrition, and its role in the pathogenesis of disease. Molecular biology techniques and genetics are investigating Trp pathways' constituent parts. Efficacy, monitoring, and personalization of pharmaceutical therapies as well as the creation of novel therapeutic approaches are some further viewpoints in Trp research. One of the biggest issues facing the globe today is environmental degradation. Nicotine was generated in large quantities by the tobacco businesses. When nicotine is directly ingested into soil, it damages the environment and affects human health. Significant bacteria break down nicotine, a hazardous substance. All of the metabolic processes and genes involved in nicotine breakdown have been covered in this essay. During the breakdown of nicotine, these bacteria produce a number of intermediary metabolic chemicals with medicinal use. One of the effective methods for transforming harmful molecules into useful ones is bioremediation. These bacteria that break down nicotine can be employed to bioremediate nicotine-contaminated areas. These intermediate nicotine metabolites could be produced on a large scale for application in the pharmaceutical industry.

Acknowledgement

The author would like to acknowledge his Department of Molecular Biology, Genome institute of Stem cell and Developmental, Saudi Arabia for their support during this work.

Conflicts of Interest

The author has no known conflicts of interested associated with this paper.

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