BIOCHEMICAL MED TRYPTOPHAN pdf

1: Biochemical and medical aspects of tryptophan metabolism.

L-Tryptophan is the unique protein amino acid (AA) bearing an indole ring: its biotransformation in living organisms contributes either to keeping this chemical group in cells and tissues or to breaking it, by generating in both cases a variety of bioactive molecules.

I have talked to thousands of clients who showed classic signs of depression. Yet many, mostly male denied any such problem. I can empathize with them: It was a few years after I buried my husband and my teenage son that I was watching a TV show on the subject of depression. All of the panelists remarked they cried every day. The "expert" psychiatrist assured them that was common to depression. It was as though the reservoir occasionally spilled over and automatically emptied the overflow. We adjust to life as well as we can, given the tools we have. My philosophy remained, "this too shall pass," as, over the next ten years, I grieved more losses: When I look back at these years I believe I would have retreated to a dark closet to live were it not for what I was learning about ortho-molecular medicine and how to restore the important brain chemicals that ongoing stress and sadness wipe out! Many studies confirm that childhood abuse physical, emotional, sexual creates lifelong depression. Ongoing losses and heavy stresses are also a set up for depression. Remember the description of the concentration camp survivors in "Its Not In Your Mind," and how they finally came out of their post-traumatic states with biochemical repair? Those "walking wounded" are not unlike many of us who have existed through long periods of unrelenting stress. Certainly therapy is a comforting release, but in these cases, talk alone is not enough to undo the damage. At Health Recovery Center we continually see clients whose presenting symptom is depression, despite their current use of one of the popular anti-depressant drugs. Often their doctors have tried them on more than one anti-depressant but oddly enough, have never assessed their patients for the many other underlying biochemical causes of depression before prescribing. In this section we will cover fifteen biochemical conditions known to create clinical depression. Prescription anti-depressants assume the problem is too little serotonin or norepinephrine or dopamine, but neurotransmitter depletion is just one problem on this list. Selective Serotonin Reuptake Inhibitors The New SSRI Drugs For Depression Three major drug companies, each with annual revenues exceeding 7 billion dollars, have exerted their powerful influence on psychiatry, government, media, and the public, to mass-market anti-depressant drugs. It appears that using SSRI drugs will, over time make serious biochemical changes in the brain receptors for serotonin and these changes may be permanent. The mechanism called down-regulation, causes receptors for serotonin to literally disappear from the brain. For example, if you continually take large amounts of cortisone, a synthetic adrenal hormone, your own production of natural adrenalin will stop and your adrenals will gradually atrophy. Likewise taking thyroid will shut down your own natural thyroid production. Thus it stands to reason when you flood your brain with inordinate amounts of serotonin, the same sensing mechanism will begin to shut down some of your serotonin receptors as happened in animal trials in an attempt to control the overload. We do know that organs like the thyroid and adrenals do not restore themselves. The drug companies refuse to carry out these easy and inexpensive tests on humans; they may fear a finding of irreversible receptor loss could be used in lawsuits. It is bewildering that the FDA has not required such studies. It may surprise you to know FDA trials were only four to six weeks and the grand total of Prozac-taking patients in those studies amounted to None of these participants included hospitalized psychiatric patients, none were suicidal, nor were children or elderly adults included. Although the study outcomes are never public domain, Dr. Breggin has obtained the actual results through the Freedom of Information Acts. Four compared Prozac to a placebo and, of these, three were used by the FDA as evidence of some beneficial effect one showed none at all. Of the remaining ten studies, eight showed an older anti-depressant to be more effective. The FDA selected only the five positive studies and discarded the other nine! I recommend them to you for the sake of your own mental health. As a professional who worked with drug addiction for the past twenty years, I marveled at his comment on EFFEXOR, a later developed anti-depressant drug, that blocks the reuptake of not just serotonin but norepinephrine as well. Effexor was described in Psychiatric News, Feb. Breggin notes that cocaine and amphetamines also block serotonin and

norepinephrine. But when the dangerous effects of amphetamines were understood, they were reclassified as controlled substances along with narcotics and cocaine! Dexamyl has not appeared in the Physicians Desk Reference since , but we now see the SSRIs being prescribed for almost identical purposes: This report underscores the surprisingly low benefits attained from drugs and therapy. Orthomolecular approaches have proven far more rewarding, as you are about to see. Some of our experiences in treating depression with these techniques were documented as part of my dissertation research and published in a peer review journal. The data was collected on Health Recovery Center clients in the last decade. It showed sixty-one percent were seriously depressed at entry. Of these, ninety-five percent were depression-free within six weeks. At the three-year follow-up, seventy-four percent stated they continue to follow the regimen that took them out of depression and that they still felt stable. Many confirm the connections between brain biochemistry and depression, and offer methods of repair, which have worked more reliably than drugs or talk therapy. Despite the millions of Prozac prescriptions, there is no single biochemical glitch i. In this section you will learn about 15 different biochemical sources of depression and how to overcome your particular chemical problems. This may mean taking even more nutrients. It may require further changes in your diet. Or you may need drug treatment to correct a medical condition that can precipitate depression. First, of course, you have to confirm that you are depressed. Then you can evaluate the severity of your case. As many as one out of five Americans suffer from depression, and one in seven of those with major depression, commit suicide. These are common red flags: External changes such as loss of a relationship, a job, or a loved one, may result in a self-limiting kind of depression. In the interim this psychological setback will respond well to therapy. Group or individual counseling offers give human empathy for the interim, and gradually new hopes replace the disappointments. You have been depressed for a long time despite changes in your life. Talk therapy has little or no effect; in fact, psychological probing questions like "Why do you hate your father? You cannot trace the onset of your depression to any event in your life. Your mood may swing between depression and elation over a period of months in a regular rhythm this suggests bipolar or manic-depressive disorder. Drinking alcohol worsens your depression the following day. And this is true even though they are raised in completely separate environments! Suicide, too, clusters in families. When Your Depression is Severe As important as identifying the cause of your depression is determining the depth of your feelings. If you have suicidal thoughts, please confide in your physician and a close friend or relative. The "high risk" person was seen to have such clinical features as: A depressive disorder The presence of anxiety and agitation Decreased feelings of physical well-being and multiple physical ailments Drug and alcohol abuse Taking prescribed medications like sleeping pills Presence of self-blame and guilt Loss of self-control fits of anger and loss of temper Lack of support system; no one to turn to and no one dependent on the patient. Today, the psychiatric profession has no trouble acknowledging the physical basis of depression. Here is an illustration of the consequences of not probing for the underlying physical causes of depression: Recently the daughter of a dear benefactor of our foundation called me in tears. After a week there was brief relief, then nothing. The dose was promptly doubled and the same response occurred. By yesterday her MD had raised the dosage to four daily. Slowly her depression has become severe; She now feels suicidal! I began to ask her a few questions and a probable basis for her depression began to emerge: Frequent yeast infections and sinus problems Cold hands and feet, chilly all the time Works full time in a hair salon around chemicals This translates as: All can be proven or disproved through lab tests. If true, the high level of Prozac she takes, only serves to toxify her liver and disrupt her serotonin receptor sites. Within two weeks lab test results will point us in the right direction. Carl Pfeiffer comments that in his clinical experience, he has found "the greatest factor in teen-age suicide is pyroluria, the stress-induced deficiency in B6 and zinc. The onset of this disorder is between 15 to 17 years. A second biological cause of teen suicide is the presence of too much histamine in the body. High histamine creates energetic, compulsive "doers" the self-starters that ordinarily make the world better. But it also causes many to go through life in continuous depression, and this group has the drive and the impulsiveness to carry out a suicide. As I describe both of these biochemical triggers for suicide, I strongly suspect, that my own teenager had many of these symptoms. It is twenty-five years too late for Robby, but not for your teen or yourself or family member who may be suicide prone. If symptoms cluster on your written screening tests, take the results

to your physician who can order the confirming lab work. The repair formulas in Depression Free, Naturally have been the acceptable methods of treatment at Health Recovery Center for over a decade. They usually do not include drugs. We have continued to use natural replacement chemicals with our clients because of the astonishing turnaround they produce. Manic-Depression Bi-Polar Disorder Another category of mood disorder is one that alternates a depressed mood with sudden shifts into a manic state. The identifying characteristic of these mood swing disorders is that they occur and reoccur in cycles, which may be predictable. Manic episodes can become exhausting yet there is no way to slow down without biochemical intervention.

2: Tryptophan Biochemistry: Structural, Nutritional, Metabolic, and Medical Aspects in Humans

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References What is it? L-tryptophan is an amino acid. Amino acids are protein building blocks. It must be acquired from food. People use L-tryptophan for some mental health disorders, to help quit smoking, for athletic performance, and for emotional symptoms in people with premenstrual dysphoric disorder PMDD , but there is no good scientific evidence to support many of these uses. There is also concern that using L-tryptophan might cause a condition called eosinophilia-myalgia syndrome EMS. How effective is it? Natural Medicines Comprehensive Database rates effectiveness based on scientific evidence according to the following scale: Premenstrual dysphoric disorder PMDD. Taking 6 grams of L-tryptophan per day seems to decrease mood swings, tension, and irritability in women with PMDD. To help people quit smoking. Taking L-tryptophan seems to help people quit smoking when used with conventional treatment. Insufficient evidence to rate effectiveness for Some research shows that taking L-tryptophan for 3 days before exercising can improve power during exercise. This improvement in power helps increase the distance an athlete can go in the same amount of time. Reasons for the conflicting results are not clear. It is possible that L-tryptophan improves some measures of athletic ability but not others. On the other hand, L-tryptophan might need to be taken for a few days before exercise in order to see any benefit. Attention deficit-hyperactivity disorder ADHD. Problems with mental function in the elderly. Taking a mixture of L-tryptophan and other ingredients can slightly improve mental function in older people. But the improvement is very small, so it might not be meaningful. Early research suggests that L-tryptophan might improve the effectiveness of common medications for depression. Healing ulcers caused by the bacteria Helicobacter pylori H pylori. Research shows that taking L-tryptophan in combination with the ulcer medication omeprazole improves ulcer healing rates compared to taking omeprazole alone. Taking L-tryptophan might decrease the amount of time it takes to fall asleep and improve mood in healthy people with sleep problems. Seasonal affective disorder SAD. Early research suggests L-tryptophan might be helpful in SAD. There is some evidence that taking L-tryptophan might decrease episodes in some people who periodically stop breathing during sleep sleep apnea. More evidence is needed to rate L-tryptophan for these uses. How does it work? L-tryptophan is naturally found in animal and plant proteins. It is important for the development and functioning of many organs in the body. After absorbing L-tryptophan from food, our bodies convert it to 5-HTP 5-hyrdoxytryptophan , and then to serotonin, melatonin, and vitamin B6 nicotinamide. Serotonin is a hormone that transmits signals between nerve cells. It also causes blood vessels to narrow. Changes in the level of serotonin in the brain can alter mood. Melatonin is important for sleep and vitamin B6 is essential for energy metabolism. Are there safety concerns? It has been linked to over reports of eosinophilia-myalgia syndrome EMS and 37 deaths. EMS is a neurological condition with symptoms that include fatigue; intense muscle pain; nerve pain; skin changes; baldness; rash; and pain and swelling affecting the joints, connective tissue, lungs, heart, and liver. Symptoms tend to improve over time, but some people may still experience symptoms up to 2 years after they develop EMS. Some people report that their symptoms have never gone away completely. In , L-tryptophan was recalled from the market due to these safety concerns. After the limitation of L-tryptophan products, the number of EMS cases dropped sharply. The exact cause of EMS in patients taking L-tryptophan is unknown, but some evidence suggests it may be due to contaminated L-tryptophan products. L-tryptophan can cause some side effects such as heartburn, stomach pain, belching and gas, nausea, vomiting, diarrhea, and loss of appetite. It can also cause headache, lightheadedness, drowsiness, dry mouth, visual blurring, muscle weakness, and sexual problems. Not enough is known about the safety of L-tryptophan during breast-feeding. Avoid using L-tryptophan during pregnancy and breast-feeding. A white blood cell disorder called eosinophilia: L-tryptophan might make this condition worse. L-tryptophan has been associated with the development of eosinophilia-myalgia syndrome EMS. Liver or kidney disease: L-tryptophan might make these conditions worse since it has been associated with the development of eosinophilia-myalgia syndrome

EMS. Are there interactions with medications? Major Do not take this combination. Sedative medications CNS depressants L-tryptophan might cause sleepiness and drowsiness. Medications that cause sleepiness are called sedatives. Taking L-tryptophan along with sedative medications might cause too much sleepiness. Some sedative medications include clonazepam Klonopin , lorazepam Ativan , phenobarbital Donnatal , zolpidem Ambien , and others. Moderate Be cautious with this combination. Dextromethorphan Robitussin DM, and others L-tryptophan can affect a brain chemical called serotonin. Dextromethorphan Robitussin DM, others can also affect serotonin. Taking L-tryptophan along with dextromethorphan Robitussin DM, others might cause there to be too much serotonin in the brain and serious side effects including heart problems, shivering and anxiety could occur. Do not take L-tryptophan if you are taking dextromethorphan Robitussin DM, others. Medications for depression Antidepressant drugs L-tryptophan increases a brain chemical called serotonin. Some medications for depression also increase the brain chemical serotonin. Taking L-tryptophan along with these medications for depression might increase serotonin too much and cause serious side effects including heart problems, shivering, and anxiety. Do not take L-tryptophan if you are taking medications for depression. Some of these medications for depression include fluoxetine Prozac , paroxetine Paxil , sertraline Zoloft , amitriptyline Elavil , clomipramine Anafranil , imipramine Tofranil , and others. This chemical is called serotonin. Some medications used for depression also increase serotonin. Taking L-tryptophan with these medications used for depression might cause there to be too much serotonin. This could cause serious side effects including heart problems, shivering, and anxiety. Some of these medications used for depression include phenelzine Nardil , tranylcypromine Parnate , and others. Meperidine Demerol L-tryptophan increases a chemical in the brain called serotonin. Meperidine Demerol can also increase serotonin in the brain. Taking L-tryptophan along with meperidine Demerol might cause too much serotonin in the brain and serious side effects including heart problems, shivering, and anxiety. Pentazocine Talwin L-tryptophan increases a brain chemical called serotonin. Pentazocine Talwin also increases serotonin. Taking L-tryptophan along with pentazocine Talwin might cause serious side effects including heart problems, shivering, and anxiety. Do not take L-tryptophan if you are taking pentazocine Talwin. Phenothiazines Taking L-tryptophan with phenothiazines can cause serious side effects including movement disorders. Some phenothiazines include chlorpromazine Thorazine , fluphenazine Prolixin , trifluoperazine Stelazine , thioridazine Mellaril , and others. Sedative medications Benzodiazepines Sedative medications can affect the nervous system. L-tryptophan can also affect the nervous system. Taking L-tryptophan along with sedative medications can cause serious side effects. Do not take L-tryptophan if you are taking sedative medications. Some of these sedative medications include clonazepam Klonopin , diazepam Valium , lorazepam Ativan , and others. Tramadol Ultram Tramadol Ultram can affect a chemical in the brain called serotonin. L-tryptophan can also affect serotonin. Taking L-tryptophan along with tramadol Ultram might cause too much serotonin in the brain and side effects including confusion, shivering, and stiff muscles could result. Are there interactions with herbs and supplements? Herbs and supplements that act like sedatives L-tryptophan can cause drowsiness and relaxation. Using it along with other herbs and supplements that also have sedative effects might cause too much drowsiness. Some of these herbs and supplements include 5-HTP, calamus, California poppy, catnip, hops, Jamaican dogwood, kava, St. Herbs and supplements that increase serotonin levels L-tryptophan seems to raise the level of serotonin, a hormone that transmits signals between nerve cells and affects mood. There is a concern that using it with other herbs and supplements that increase serotonin, might increase the effects and side effects of those herbs and supplements.

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3: L-Tryptophan: MedlinePlus Supplements

An essential component of the human diet, L-tryptophan is critical in a number of metabolic functions and has been widely used in numerous research and clinical trials. This review provides a brief overview of the role of L-tryptophan in protein synthesis and a number of other metabolic functions.

Biochemistry[edit] Indole is generated by reductive deamination from tryptophan via the intermediate molecule indolepyruvic acid. Tryptophanase catalyzes the deamination reaction, during which the amine -NH2 group of the tryptophan molecule is removed. Pyridoxal phosphate is required as a coenzyme. Performing a Test[edit] Indole test positive: Escherichia coli Like many biochemical tests on bacteria, results of an indole test are indicated by a change in color following a reaction with an added reagent. Pure bacterial culture must be grown in sterile tryptophan or peptone broth for 24â€”48 hours before performing the test. A positive result is shown by the presence of a red or red-violet color in the surface alcohol layer of the broth. A negative result appears yellow. A variable result can also occur, showing an orange color as a result. This is due to the presence of skatole , also known as methyl indole or methylated indole, another possible product of tryptophan degradation. The positive red color forms as a result of a series of reactions. The para-Dimethylaminobenzaldehyde reacts with indole present in the medium to form a red rosindole dye. The isoamyl alcohol forms a complex with rosindole dye, which causes it to precipitate. The remaining alcohol and the precipitate then rise to the surface of the medium. Indole-Positive Bacteria[edit] Bacteria that test positive for cleaving indole from tryptophan include: Aeromonas hydrophila , Aeromonas punctata, Bacillus alvei, Edwardsiella sp. Indole-Negative Bacteria[edit] Bacteria which give negative results for the indole test include: The other three tests include: Example of typical indole reactions Angen, O. International Journal of Systematic Bacteriology.

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4: Indole test - Wikipedia

Biochemical and medical aspects of the indoleamine 2,3-dioxygenase-initiated l-tryptophan metabolism l-Tryptophan (Trp) is the least abundant of the essential.

Received Sep 7; Accepted Dec 6. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. This article has been cited by other articles in PMC. Abstract L-Tryptophan is the unique protein amino acid AA bearing an indole ring: Investigations on the biology of Trp highlight the pleiotropic effects of its small derivatives on homeostasis processes. All Trp residues in protein and peptide sequences are conventionally indicated with the alphabetic letter W. Hopkins in , is also one of the 9 essential AAs for humans which cannot be endogenously synthesized and need to be supplied with aliments, as revealed through diet manipulation studies [1]. Hence, alterations of L-Trp-deriving compounds can be found associated with a variety of metabolic diseases and syndromes affecting those systems and organs responsible for maintaining the chemical, cellular, and behavioural homeostasis: In particular, an imbalanced metabolism of this AA can interfere with the ability of these systems to interact with as well as discriminate, during development, stressors and stimuli, exogenous and endogenous antigens, and nutrients and xenobiotics. Amongst Trp-derived compounds produced in the human body, there is the ancient neurotransmitter serotonin 5-hydroxy-tryptamine, 5-HT , a biogenic amine which is known to regulate, in the human CNS, the main adaptive reactions and responses to environmental changes, such as mood-anxiety, cognition, nociception, impulsivity, aggressiveness, libido, feeding behaviour, and body temperature [2 , 3]. Next to its role as a neurotransmitter, 5-HT also modulates the activity of peripheral districts, in particular the gut function, the immune and inflammatory responses, the differentiation process of blood stem cells, and the hemodynamic function [3]. Indeed, an altered 5-HT transmission has been found associated with mood-affective disorders [4], autism and cognitive deficit [5 , 6], anorexia or bulimia nervosa and obesity [6], and other syndromes presenting peripheral symptoms, such as fibromyalgia, chronic fatigue syndrome, and irritable bowel syndrome IBS [7]. Moreover, 5-HT is in turn the precursor of the circadian regulators N-acetylHT NAS and melatonin MLT , primarily produced in the pineal gland but also in periphery where the two indoleamines act as scavenger compounds [8]. We will then underpin those molecular players in Trp biochemistry which are considered or are possible vulnerability markers in the physiopathology of human complex diseases, trying to point out their regulation. At the same time, we will briefly introduce some Trp research targets actually under investigation for therapeutic strategies in human pathology as well as the utility of -Omics approaches. The presence of the indole ring in the chemical structure of Trp gives high hydrophobic features to this molecule among all protein AAs. In fact, Trp is the AA at the highest number of C atoms C11 and the presence of other C atoms or substituent groups would be unnecessary. The advantage to keep indole in life chemistry derives either from the possibility to exploit its C11 skeleton in metabolism or to utilize it as â€”R residue in proteins and peptides to promote and stabilize their structure. Also, Trp is metabolized to produce biologically active indole compounds which have great impact on life functions. In fact, beside being present in the chemical structure of the neurotransmitter 5-HT and, in turn, in the circadian molecules NAS and MLT in animals and humans Figure 1 c , the indole ring of Trp can be transformed into bioactive compounds also by plants: In particular, the plant hormone auxin has been found linked to a specific Trp metabolism pathway involved in plant photoperception and development [11 , 12]. Interestingly, indoleamines as 5-HT and MLT have been detected also in plants where their function is under investigation [13].

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5: Dissolving Biochemical Depression

Conference Title: Biochemical and medical aspects of tryptophan metabolism. Abstract: This volume contains the proceedings of the 3rd International Meeting of the International Study Groups for Tryptophan Research held in Kyoto, Japan 4 to 7 August

The recommended daily allowance for a 79 kg lb adult is to mg. Upon investigation, the source of the outbreak was traced to a single manufacturer, the Showa Denka Company of Japan, and the cause was determined to be a change in their processes of tryptophan synthesis. Following the identification of the source of the outbreak, the ban was lifted in The importance of tryptophan for a multitude of metabolic functions, and information on the research methodologies and uses, as well as therapeutic uses of tryptophan are discussed. Metabolic processes Protein synthesis The principal role of tryptophan in the human body is as a constituent of protein synthesis. Because tryptophan is found in the lowest concentrations among the amino acids, it is relatively less available and is thought to play a rate-limiting role during protein synthesis. Each of these metabolites has the potential to affect other neurotransmitters; specifically kynurenic acid is a glutamate receptor antagonist, while quinolinic acid is a glutamate receptor agonist. The immediate decarboxylation of tryptophan results in the synthesis of trace amounts of tryptamine i. These enzymes can be synthesized de novo from ingested tryptophan, or from ingestion of niacin i. However, this is a less efficient use of tryptophan since approximately 60 mg of tryptophan are necessary to generate a single milligram of niacin. Other metabolic functions Tryptophan also exerts effects on other neurotransmitters and CNS compounds. Dopamine, norepinephrine, and beta-endorphin have been shown to increase following oral dosing of tryptophan. While there are three primary functions of tryptophan i. Pharmacokinetics Tryptophan is the sole precursor of serotonin 35 and, once consumed, tryptophan is distributed throughout the human body in the circulatory system. This can be accomplished by changing plasma concentrations of tryptophan, or by changing concentrations of the CAAs, either of which affect tryptophan availability and, by extension, serotonin synthesis. To some extent, tryptophan availability to the brain can be enhanced by ingestion of carbohydrates and reduced by ingestion of proteins. Carbohydrate ingestion does not change the levels of circulating tryptophan, but it does decrease concentrations of CAAs through activation of insulin, 3 , 5 which increases the relative availability of tryptophan for transport into the brain. The ability of carbohydrate and protein meals to modify tryptophan availability may be dependent on the time of ingestion. In contrast, a subsequent study administered a standard breakfast at 8 AM and a test lunch administered 4 hours later. The breakfast in the latter study was comprised of kcal, whereas the starch and sucrose test meals were and kcal respectively and the protein meal was kcal. When taken together, the findings from these studies suggest that changes in tryptophan availability can be manipulated to some extent through dietary intake, although it is unlikely that ordinary changes in dietary tryptophan or the CAAs through protein or carbohydrate manipulations will produce changes substantial enough to have a noticeable impact on behavior in a healthy individual. Experimental manipulations of tryptophan are dependent on the two-step process required for serotonin synthesis in the brain. Second, 5-hydroxytryptophan is converted to serotonin by the aromatic amino acid decarboxylase enzyme. It is the activity of tryptophan hydroxylase that is dependent on the availability of brain tryptophan. The ability to change the rates of serotonin synthesis is the foundation of a large body of research examining the relationship of serotonin dysregulation to mood, behavior, and cognition. One experimental method that has been used for studying the effects of decreased serotonin synthesis is the use of parachlorophenylalanine PCPA. However, this method is limited by a relatively lengthy period of dietary restrictions e. This method typically involves the administration of an amino-acid beverage that contains approximately g of 15 amino acids see Table 2 , but lacks tryptophan. First, the intake of the large amount of amino acids stimulates protein synthesis in the liver; however, without a proportionate intake of tryptophan, the protein synthesis clearly reduces the concentration of existing plasma tryptophan. Tryptophan loading is accomplished by adding a disproportionately large amount of tryptophan to the amino-acid formulation. Mood and memory effects were specific to tryptophan depletion, which would seem to rule out general inhibition of

protein synthesis that would also likely impair mood and memory functions. Moreover, when compared to control conditions e. Amino acid compositions of 50 g and g L-tryptophan depletion and loading formulations.

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6: Tryptophan | C11H12N2O2 - PubChem

Tryptophan (symbol Trp or W) is an Î±-amino acid that is used in the biosynthesis of www.enganchecubano.comphan contains an Î±-amino group, an Î±-carboxylic acid group, and a side chain indole, making it a non-polar aromatic amino acid.

This is an open access article distributed under the Creative Commons Attribution License , which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. Abstract L-Tryptophan is the unique protein amino acid AA bearing an indole ring: Investigations on the biology of Trp highlight the pleiotropic effects of its small derivatives on homeostasis processes. All Trp residues in protein and peptide sequences are conventionally indicated with the alphabetic letter W. Hopkins in , is also one of the 9 essential AAs for humans which cannot be endogenously synthesized and need to be supplied with aliments, as revealed through diet manipulation studies [1]. Hence, alterations of L-Trp-deriving compounds can be found associated with a variety of metabolic diseases and syndromes affecting those systems and organs responsible for maintaining the chemical, cellular, and behavioural homeostasis: In particular, an imbalanced metabolism of this AA can interfere with the ability of these systems to interact with as well as discriminate, during development, stressors and stimuli, exogenous and endogenous antigens, and nutrients and xenobiotics. Amongst Trp-derived compounds produced in the human body, there is the ancient neurotransmitter serotonin 5-hydroxy-tryptamine, 5-HT , a biogenic amine which is known to regulate, in the human CNS, the main adaptive reactions and responses to environmental changes, such as mood-anxiety, cognition, nociception, impulsivity, aggressiveness, libido, feeding behaviour, and body temperature [2 , 3]. Next to its role as a neurotransmitter, 5-HT also modulates the activity of peripheral districts, in particular the gut function, the immune and inflammatory responses, the differentiation process of blood stem cells, and the hemodynamic function [3]. Indeed, an altered 5-HT transmission has been found associated with mood-affective disorders [4], autism and cognitive deficit [5 , 6], anorexia or bulimia nervosa and obesity [6], and other syndromes presenting peripheral symptoms, such as fibromyalgia, chronic fatigue syndrome, and irritable bowel syndrome IBS [7]. Moreover, 5-HT is in turn the precursor of the circadian regulators N-acetylHT NAS and melatonin MLT , primarily produced in the pineal gland but also in periphery where the two indoleamines act as scavenger compounds [8]. We will then underpin those molecular players in Trp biochemistry which are considered or are possible vulnerability markers in the physiopathology of human complex diseases, trying to point out their regulation. At the same time, we will briefly introduce some Trp research targets actually under investigation for therapeutic strategies in human pathology as well as the utility of -Omics approaches. The presence of the indole ring in the chemical structure of Trp gives high hydrophobic features to this molecule among all protein AAs. In fact, Trp is the AA at the highest number of C atoms C11 and the presence of other C atoms or substituent groups would be unnecessary. The advantage to keep indole in life chemistry derives either from the possibility to exploit its C11 skeleton in metabolism or to utilize it as â€”R residue in proteins and peptides to promote and stabilize their structure. Also, Trp is metabolized to produce biologically active indole compounds which have great impact on life functions. In fact, beside being present in the chemical structure of the neurotransmitter 5-HT and, in turn, in the circadian molecules NAS and MLT in animals and humans Figure 1 c , the indole ring of Trp can be transformed into bioactive compounds also by plants: In particular, the plant hormone auxin has been found linked to a specific Trp metabolism pathway involved in plant photoperception and development [11 , 12]. Interestingly, indoleamines as 5-HT and MLT have been detected also in plants where their function is under investigation [13]. Tryptophan and other indole-containing compounds. If Trp is essential for animals, bacteria or other eukaryotes as fungi and plants are instead able to synthesize it from chorismic also the precursor of Tyr and Phe and anthranilic Trp path only acids. In bacteria, fungi, and plants, the biosyntheses of Trp, Tyr, and Phe are linked together by the shikimate pathway: Prephenate derives from chorismate through the activity of the enzyme chorismate mutase; in turn, prephenate enters into a 3-branch path producing Tyr and Phe. The biosynthesis of Trp in bacteria shares common genes and chemical reactions

with plants or fungi: Bacteria and plants or fungi follow, however, different regulatory mechanisms of this metabolic path. In bacteria, chorismate produces Trp under the control of one of the most studied models of gene expression regulation in prokaryote organisms, the Trp operon, activated or repressed depending upon the intracellular concentrations of this AA: The regulation of Trp formation then diverges from the bacterial one because of the different gene organization in eukaryotes. Additionally, Trp formation in plants has been found tightly regulated by several transcriptional factors acting on gene expression of the enzymes of the shikimate pathway and AAA metabolism, as evidenced in the Brassicaceae Arabidopsis. Many of these transcriptional factors have been identified, each differentially stimulated by diverse stressors, as infections by pathogens, trauma, or light. In the common ancestor of animal and vegetable cells, the shikimate path was localized in the cytosol whereas in higher plants this metabolic shunt occurs inside plastids [15]. Thus, genes of Trp biosynthesis would have been lost in plastid-lacking animal eukaryote cells. These considerations lead to reasonably think that AAAs metabolism and production of their bioactive derivatives occupy a central position in the early stages of the evolution of living organisms and trophism lineages. It is not therefore surprising that AAAs represent foremost compounds for human nutrition and health. The importance of maintaining intact the indole ring in Trp derivatives is mirrored by natural therapeutic agents: Also, indole derivatives have been used in pharmacological research as the starting point for the synthesis of therapeutically relevant compounds. Tryptophan Residues in Proteins and Peptides The presence of Trp residues in polypeptides, as previously introduced, deserves a specific mention: The Trp indole ring is able to stabilize structures, domains, and interactions through Van der Waals forces while the indole-N shows propensity as a hydrogen bond donor evidencing a role of this AA also in protein binding and recognition. Hydrophobic interactions between proteins and peptides or between these and other biologically active molecules have great importance in cell physiology. Some reviews in the current literature show interesting investigations focusing on these structural aspects of Trp residues: Tryptophan Requirement and Content in Food A main consideration deriving from previous paragraphs is that Trp is precious for life: This probably explains why L-Trp is an AA scarcely represented in the alimentary chain [21 , 24 â€” 26] and its presence in animal cells and tissues must be tightly regulated. Together with cysteine Cys , Trp is the essential AA required in lesser amount in human diet [27 , 29]. The AA Trp is introduced along with all other AAs in the body with protein-rich foods, mainly of vegetal or animal origin. Aliments at higher Trp content include animal origin: Lower Trp amounts can be found in some varieties of cereals and maize. Thus, a normal, varied, and balanced diet, as in developed countries, can largely ensure the daily Trp requirement. A main nutritional impact of Trp for human diet is represented by chronic exposure to a diet low in niacin vitamin B3 and Trp, which produces pellagra, a metabolic dysfunction defined by severe alterations of the skin, gut, and brain activity [30]. In fact, niacin is classified as a vitamin, but this compound can be produced through the metabolic transformations of L-Trp into its precursor quinolinic acid; this explains why L-Trp exerts a protective action against the onset of pellagra symptoms in low-niacin diets. Thus, in economically disadvantaged countries, Trp content in foods, together with other essential AAs, can be of great importance. The analysis of the composition of nutrients, vitamins, essential elements, and AAs represents the basis for good health and children development in these countries. Besides, the amount of Trp in diet represents a challenge for human health and nutritional status worldwide, especially as concerns the regulation of its concentration in plasma as well as its uptake to tissues and brain. The role of the gut microbiome is also an interesting aspect that is emerging as a link between nutrition, gut absorption, Trp fates, and health. Tryptophan Absorption, Transport, and Uptake: AA uptake occurs in all tissues and cells according to the need for protein synthesis or degradation, with gut, liver, and muscle tissue primarily involved in its modulation. Once introduced with food, all AAs, including Trp, are absorbed by the gut, pass into the bloodstream, are transported to all main tissue districts, overall muscles, and liver, and are finally taken by cells to be part of the AA pool used for the synthesis and turn-over of proteins. Proteolysis and protein catabolism inside cells regenerate, in part, the intracellular reserve of AAs and Trp for subsequent protein synthesis and, in part, provoke their release in the bloodstream. Insulin, glucagon, and cortisol are the regulatory hormones of endogenous protein turn-over: Cortisol increases the AAs plasma levels efflux from

muscle , shifting the balance towards proteolysis [31]. At the same time, each AA can undergo its own regulation originating its own cell in- and out-flow, in relation to AA composition of both endogenous proteins and those derived from the diet; these last at more variable content [32]. Also, multiple factors as age, gender, or physical activity concur to affect plasma concentrations of AAs [32]. Differently from nonessential AAs, for which, in addition to diet, the rate of de novo synthesis is able to control the homeostatic balance of endogenous contents, essential AAs and Trp plasma concentrations are more directly related to their amount in diet. A foremost and intriguing aspect of human Trp biology is in fact defined by the observation that diet and the type of meal can change its plasma levels as well as its uptake by different cell types. After food digestion, for gut absorption this AAA shares its passage across enterocytes with other neutral AAs through two distinct carrier molecules: Tryptophan has also the lowest affinity for the apical carrier than other competitive NAAs, except lysine Lys , confirming that tissues require defined amounts of Trp and suggesting that gut absorption is a regulated step for the subsequent transport and biotransformation of this AAA. A widely studied model of Trp uptake mechanism is that regulating its transport across the blood-brain barrier BBB. For that, insulin and other large neutral AAs, valine Val , leucine Leu , isoleucine Ileu , Tyr, and Phe, have been found to play a chief role: This explains why a protein-rich meal increases Trp plasma levels but not its uptake to the brain. Trp uptake to CNS is thus rather favoured by carbohydrate-rich meals. After a carbohydrate meal, 5-HT biosynthesis in raphe nuclei is increased. This mechanism has been extensively studied in mammals: Val, Ileu, and Leu , transported from the bloodstream to muscles, thus increasing Trp availability for CNS uptake and, as described later, to 5-HT synthesis. The 5-HT release at the hypothalamic level activates specific 5-HT receptor subtypes devolved to inhibit appetite brain nuclei [34]. Thus, meal composition, palatable food, and poor protein foods all contribute to Trp uptake across the BBB in favor of 5-HT synthesis. Protein-rich foods in fact contain Trp, but at lower levels than other LNAAs, which, on the whole, rather provoke inhibition of Trp brain uptake. Thus, conclusively, proteins can enhance 5-HT synthesis but in relation to their low or high content in Trp [35 , 36]. Another important uptake regulatory aspect is represented by the fact that Trp is highly lipophilic and scarcely soluble in aqueous solutions at the physiological pH, so that its transport in blood requires plasma albumin binding: Trp is the only AA transported by albumin. Therefore, a finely regulated equilibrium between free and bound Trp levels exists in plasma, an argument of actual scientific interest and debate. Next to nutritional considerations, for a deeper understanding of Trp uptake, the transport proteins across tissues and the BBB are currently under investigation. The ratio between free and albumin-bound Trp has been also found to modulate Trp passage into the brain: This reveals that Trp uptake follows a tissue-dependent regulation based upon a molecular heterogeneity of Trp protein carriers in various tissues [41]. Research in metabotropic receptors has evidenced a surprising diversity of these proteins and their ligand specificity, also involving elements, nutrients, and metabolites [42]. It can be supposed that the extensive study of their localization, gene expression, and function within the body would provide useful information and clinical application. Metabolic Fates of Trp After its uptake into the various districts, tissues, and cells, Trp is introduced into protein metabolism and synthesis or can enter into various metabolic paths depending upon the tissue expression of specific enzyme activities. Figure 2 summarizes Trp transport in the bloodstream, its uptake to different tissues, and its main metabolic fates. In substance, beside protein turn-over, Trp metabolism can be divided into two main branches: We thus will follow herein this schema for describing the Trp metabolic paths which generate low-molecular weight derivatives. The limiting enzymatic reaction for 5-HT biosynthesis is Trp-hydroxylase, TPH, which is active in specialized tissues: The synthesis of 5-HT occurs in two enzymatic steps: O2 and tetrahydrobiopterin, TBH4 by TPH leading to 5-hydroxy-Trp; the second one is the decarboxylation of 5-hydroxy-Trp to 5-HT, a reaction catalyzed by the enzyme L-amino acid aromatic decarboxylase cofactor: This last enzyme is ubiquitous. Newly synthesized 5-HT can enter into storage vesicles to be released as a neurotransmitter in CNS or a modulator in periphery; after its release, excess 5-HT is internalized again through 5-HT reuptake 5-HT transporter, SERT , degraded to 5-hydroxy-acetaldehyde by monooxygenase activities MAO-A on mitochondrial outer membrane and then oxidized into 5-hydroxyindoleacetic acid 5-HIAA by aldehyde dehydrogenase cofactor: This last compound is excreted in

urine. Both isoforms are partially saturated in tissues, so that the rate of 5-HT production depends on Trp levels in the SNC and periphery. Another metabolic fate which maintains the indole ring is the formation, by Trp direct decarboxylation, of the trace amine tryptamine, a compound with a physiological meaning which has not been fully understood. Trace amines, present in mammalian tissues at very low, nanomolar, concentrations, can be divided into those deriving from Trp 5-HT-related and those deriving from phenylalanine and tyrosine catecholamine-related and are thought to regulate monoamine transmission [51]. TAARs have been widespread localized in mammalian brain, prevalently in the amygdale region; they are highly expressed in populations of nonmonoaminergic neurons colocalized with monoaminergic neurons [52], implying that trace amines can exert a GPCR-mediated regulation of monoamine neurotransmission. Interestingly, in humans, TAARs genes have been located in chromosome 6, within a DNA region linked to schizophrenia and bipolar disorder [53]; these receptors TAAR1 , which activate adenylate cyclase and cAMP via a protein, have been also found to exert a chief role in drug addictions.

7: Tryptophan: Biochemical and Health Implications - Herschel Sidransky - Google Books

Volume , number 1 FEBS LETTERS Biochemical and Medical Aspects of Tryptophan Metabolism September Developments in Biochemistry, volume

8: Tryptophan - Wikipedia

L-Tryptophan biochemistry lies in the heart of converging nutritional, neuroendocrine, and immune paths, through a variety of molecular effectors, each presumably contributing to relevant, complex, and severe diseases and syndromes, as reported in previous paragraphs.

9: L-Tryptophan: Basic Metabolic Functions, Behavioral Research and Therapeutic Indications

Tryptophan dioxygenase (also known as tryptophan oxygenase or tryptophan pyrrolase) has a short half-life in vivo (of the order of 2 h) and is subject to regulation by three mechanisms: stabilization by its heme cofactor, hormonal induction, and feedback inhibition and repression by high concentrations of NADP.

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