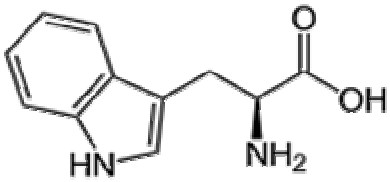
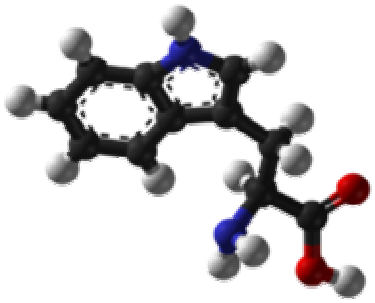
Tryptophan

From Wikipedia, the free encyclopedia

Tryptophan (IUPAC-IUBMB abbreviation: **Trp** or **W**; IUPAC abbreviation: L-Trp or D-Trp; sold for medical use as **Tryptan**)[2] is one of the 22 standard amino acids and an essential amino acid in the human diet, as demonstrated by its growth effects on rats. It is encoded in the standard genetic code as the codon *UGG*. Only the L-stereoisomer of tryptophan is used in structural or enzyme proteins, but the R -stereoisomer is occasionally found in naturally produced peptides (for example, the marine venom peptide contryphan).[3] The distinguishing structural characteristic of tryptophan is that it contains an indole functional group.

L-Tryptophan	
	
	
IUPAC name	
Tryptophan or (2S)-2-amino-3-(1H-indol-3-yl) propanoic acid	
Other names	
2-Amino-3-(1*H*-indol-3-yl)propanoic acid	
Identifiers	
CAS number	73-22-3 ✓
PubChem	6305
ChemSpider	6066 ✓
UNII	8DUH1N11BX ✓
DrugBank	DB00150
KEGG	D00020 ✓
ChEBI	CHEBI:27897 ✗
ChEMBL	CHEMBL54976 ✓
IUPHAR ligand	717
ATC code	N06AX02 (http://www.whocc.no/atc_ddd_index/?code=N06AX02)
Jmol-3D images	Image 1 (http://chemapps.stolaf.edu/jmol/jmol.php?model=c1ccc2c%28c1%29c%28c%5BnH%5D2%29C%5BC%40%40H%5D%28C%28%3DO%29O%29N)
SMILES	

Contents

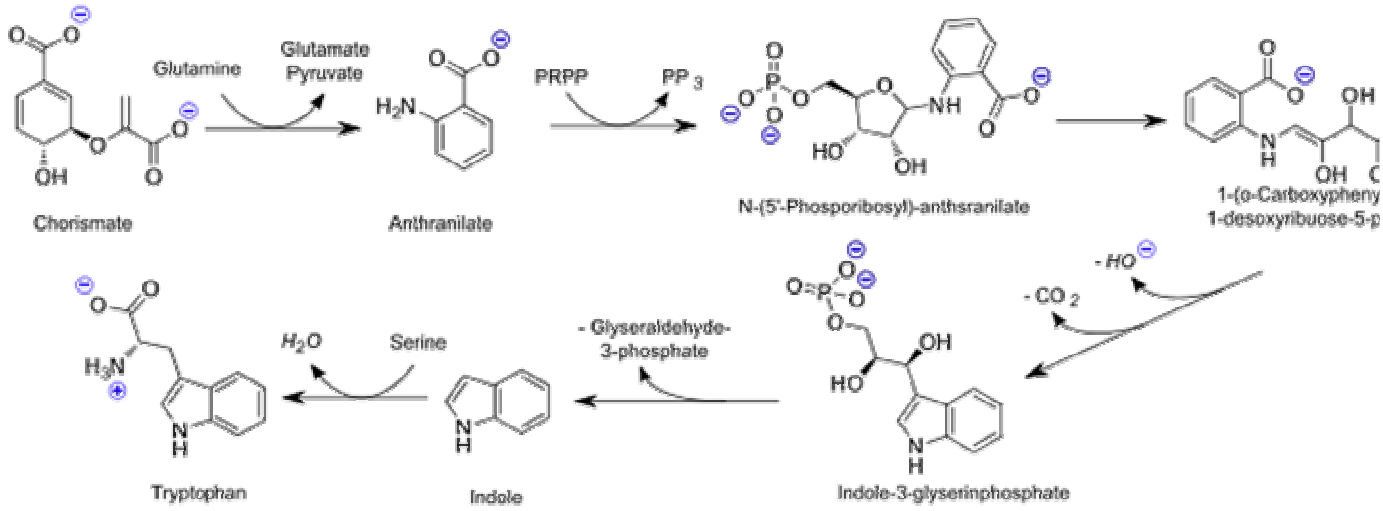
Isolation

The isolation of tryptophan was first reported by Frederick Hopkins in 1901[4] through hydrolysis of casein. From 600 grams of crude casein one obtains 4-8 grams of tryptophan.[5]

Biosynthesis and industrial production

Plants and microorganisms commonly synthesize tryptophan from shikimic acid or anthranilate.[6] The latter condenses with phosphoribosylpyrophosphate (PRPP), generating pyrophosphate as a by-product. After ring opening of the ribose moiety and following reductive decarboxylation, indole-3-glycerinephosphate is produced, which in turn is transformed into indole. In the last step, tryptophan synthase catalyzes the formation of tryptophan from indole and the amino acid serine.

InChI	
Properties	
Molecular formula	$C_{11}H_{12}N_2O_2$
Molar mass	204.23 g mol^{-1}
Solubility in water	Soluble: 0.23 g/L at 0 °C, 11.4 g/L at 25 °C, 17.1 g/L at 50 °C, 27.95 g/L at 75 °C
Solubility	Soluble in hot alcohol, alkali hydroxides; insoluble in chloroform.
Acidity (pK_a)	2.38 (carboxyl), 9.39 (amino)[1]
Supplementary data page	
Structure and properties	*n*, ε_r, etc.
Thermodynamic data	Phase behaviour Solid, liquid, gas
Spectral data	UV, IR, NMR, MS
Except where noted otherwise, data are given for materials in their standard state (at 25 °C (77 °F), 100 kPa)	
✘ (verify) (what is: ✓/✘?)	
Infobox references	

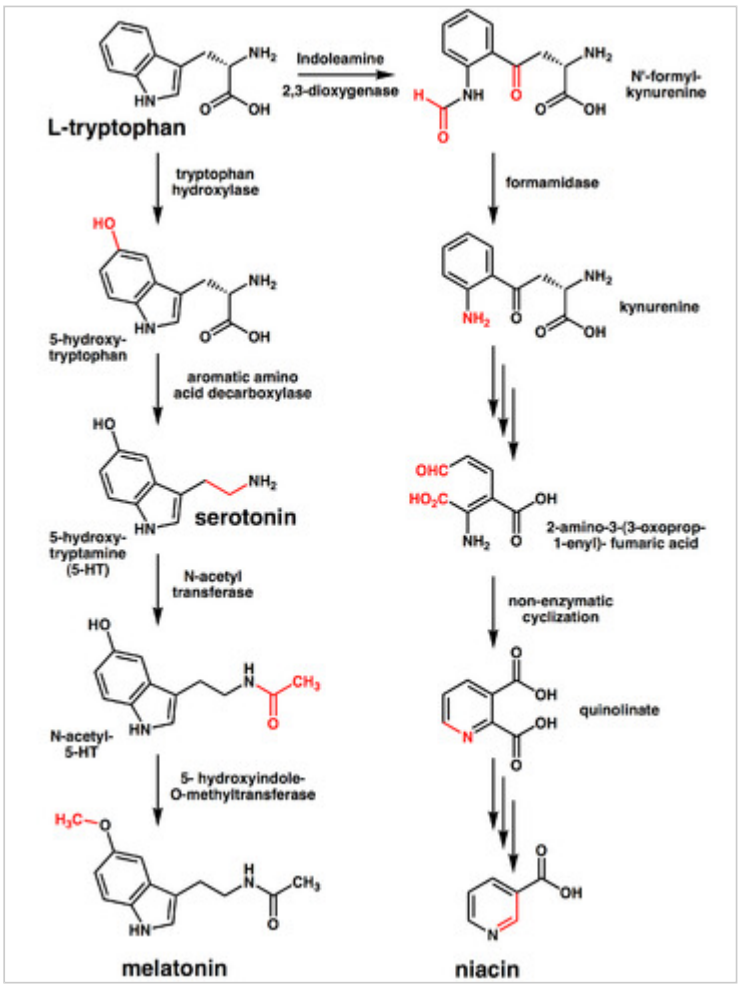


The industrial production of tryptophan is also biosynthetic and is based on the fermentation of serine and indole using either wild-type or genetically modified bacteria such as *B. amyloliquefaciens*, *B. subtilis*, *C. glutamicum* or *E. coli*. These strains carry either mutations that prevent the reuptake of aromatic amino acids or multiple/overexpressed trp operons. The conversion is catalyzed by the enzyme tryptophan synthase.[7][8][9]

Function

For many organisms (including humans), tryptophan is an essential amino acid. This means that it is essential for human life, cannot be synthesized by the organism, and therefore must be part of our diet. Amino acids, including tryptophan, act as building blocks in protein biosynthesis. In addition, tryptophan functions as a biochemical precursor for the following compounds (see also figure to the right):

- Serotonin (a neurotransmitter), synthesized via tryptophan hydroxylase.[10][11] Serotonin, in turn, can be converted to melatonin (a neurohormone), via N-acetyltransferase and 5-hydroxyindole-O-methyltransferase activities.[12]
- Niacin is synthesized from tryptophan via kynurenine and quinolinic acids as key biosynthetic intermediates.[13]
- Auxin (a phytohormone) when sieve tube elements undergo apoptosis tryptophan is converted to auxins.[14]



Metabolism of L-tryptophan into serotonin and melatonin (left) and niacin (right). Transformed functional groups after each chemical reaction are highlighted in red.

The disorder fructose malabsorption causes improper absorption of tryptophan in the intestine, reduced levels of tryptophan in the blood[15] and depression.[16] The authors did not find reduced tryptophan in lactose maldigestion. [17]

In bacteria that synthesize tryptophan, high cellular levels of this amino acid activate a repressor protein, which binds to the trp operon.[18] Binding of this repressor to the tryptophan operon prevents transcription of downstream DNA that codes for the enzymes involved in the biosynthesis of tryptophan. So high levels of tryptophan prevent tryptophan synthesis through a negative feedback loop and, when the cell's tryptophan levels are reduced, transcription from the trp operon resumes. The genetic organisation of the trp operon thus permits tightly regulated and rapid responses to changes in the cell's internal and external tryptophan levels.

Dietary sources

Tryptophan is a routine constituent of most protein-based foods or dietary proteins. It is particularly plentiful in chocolate, oats, dried dates, milk, yogurt, cottage cheese, red meat, eggs, fish, poultry, sesame, chickpeas, sunflower seeds, pumpkin seeds, spirulina, bananas, and peanuts.[19] Despite popular belief.[20][21][22] that turkey has a particularly high amount of tryptophan, the amount of tryptophan in turkey is typical of most poultry.[23] There is also a myth that plant protein lacks tryptophan; in fact, tryptophan is present in significant amounts in almost all forms of plant protein, and abundant in some.

Tryptophan (Trp) Content of Various Foods[23][24]

Food	Protein [g/100 g of food]	Tryptophan [g/100 g of food]	Tryptophan/Protein [%]
egg, white, dried	81.10	1.00	1.23
spirulina, dried	57.47	0.93	1.62
cod, atlantic, dried	62.82	0.70	1.11
soybeans, raw	36.49	0.59	1.62
cheese, Parmesan	37.90	0.56	1.47
sesame seed	17.00	0.37	2.17
cheese, cheddar	24.90	0.32	1.29
sunflower seed	17.20	0.30	1.74
pork, chop	19.27	0.25	1.27
turkey	21.89	0.24	1.11
chicken	20.85	0.24	1.14
beef	20.13	0.23	1.12
oats	16.89	0.23	1.39
salmon	19.84	0.22	1.12
lamb, chop	18.33	0.21	1.17
perch, Atlantic	18.62	0.21	1.12
chickpeas, raw	19.30	0.19	0.96
egg	12.58	0.17	1.33
wheat flour, white	10.33	0.13	1.23
baking chocolate, unsweetened	12.9	0.13	1.23
milk	3.22	0.08	2.34
Rice, white, medium -grain, cooked	2.38	0.028	1.18
Quinoa, uncooked	14.12	0.167	1.2
Quinoa, cooked	4.40	0.052	1.1
potatoes, russet	2.14	0.02	0.84
tamarind	2.80	0.018	0.64
banana	1.03	0.01	0.87

Use as a dietary supplement and drug

There is evidence that blood tryptophan levels are unlikely to be altered by changing the diet,[25] but tryptophan is available in health food stores as a dietary supplement.[26]

Clinical research has shown mixed results with respect to tryptophan's effectiveness as a sleep aid, especially in normal patients.[27][28][29] Tryptophan has shown some effectiveness for treatment of a variety of other conditions typically associated with low serotonin levels in the brain.[30] In particular, tryptophan has shown some promise as an antidepressant alone[31] and as an "augmenter" of antidepressant drugs.[31][32] However, the reliability of

these clinical trials has been questioned because of lack of formal controls and repeatability.[33][34][35] In addition, tryptophan itself may not be useful in the treatment of depression or other serotonin-dependent moods, but may be useful in understanding the chemical pathways that will give new research directions for pharmaceuticals.[36]

Metabolites

A metabolite of tryptophan, 5-hydroxytryptophan (5-HTP), has been suggested as a treatment for epilepsy[37] and depression, since 5-HTP readily crosses the blood–brain barrier and in addition is rapidly decarboxylated to serotonin (5-hydroxytryptamine or 5-HT).[38] Clinical trials, however, are regarded inconclusive and lacking.[39] Serotonin has a relatively short half-life since it is rapidly metabolized by monoamine oxidase.

Due to the conversion of 5-HTP into serotonin by the liver, there may be a significant risk of heart valve disease from serotonin's effect on the heart.[40][41]

It is marketed in Europe for depression and other indications under the brand names Cincofarm and Tript-OH. In the United States, 5-HTP does not require a prescription, as it is covered under the Dietary Supplement Act. Since the quality of dietary supplements is now regulated by the U.S. Food and Drug Administration, manufacturers are required to market products whose ingredients match the labeling, but are not required to establish efficacy of the product.[42]

The primary product of the liver enzyme tryptophan dioxygenase is kynurenine.[13][43]

In 1912 Felix Ehrlich demonstrated that yeast attacks the natural amino acids essentially by splitting off carbon dioxide and re-placing the amino group with hydroxyl. By this reaction, tryptophan gives rise to tryptophol.[44]

Tryptophan supplements and EMS

There was a large tryptophan-related outbreak of eosinophilia-myalgia syndrome (EMS) in 1989, which caused 1,500 cases of permanent disability and at least thirty-seven deaths. Some epidemiological studies[45][46][47] traced the outbreak to L-tryptophan supplied by a Japanese manufacturer, Showa Denko KK.[48] It was further hypothesized that one or more trace impurities produced during the manufacture of tryptophan may have been responsible for the EMS outbreak.[49][50] The fact that the Showa Denko facility used genetically engineered bacteria to produce L-tryptophan gave rise to speculation among anti-GMO activists[51] that genetic engineering itself was responsible for such impurities.[52]

Most tryptophan was banned from sale in the US in 1991, and other countries followed suit.[53] In February 2001, the FDA loosened the restrictions on marketing (though not on importation).[48]

The specific cause of the EMS outbreak remains unknown, but regulators' best estimate is that it was caused by one or impurities in certain batches produced by Showa Denko.[48][53]

Turkey meat and drowsiness

See also: Postprandial somnolence § Turkey and tryptophan

A common assertion is that heavy consumption of turkey meat results in drowsiness, due to high levels of tryptophan contained in turkey.[20][21][22] However, the amount of tryptophan in turkey is comparable to that contained in most other meats.[23][21] Furthermore, post-meal drowsiness may have more to do with what else is

consumed along with the turkey and, in particular, carbohydrates.[54] It has been demonstrated in both animal models[55] and humans[56][57][58] that ingestion of a meal rich in carbohydrates triggers release of insulin. Insulin in turn stimulates the uptake of large neutral branched-chain amino acids (BCAA), but not tryptophan (an aromatic amino acid) into muscle, increasing the ratio of tryptophan to BCAA in the blood stream. The resulting increased ratio of tryptophan to BCAA in the blood reduces competition at the large neutral amino acid transporter (which transports both BCAA and aromatic amino acids), resulting in the uptake of tryptophan across the blood–brain barrier into the cerebrospinal fluid (CSF).[59][60] Once in the CSF, tryptophan is converted into serotonin in the raphe nuclei by the normal enzymatic pathway.[55][57] The resultant serotonin is further metabolised into melatonin by the pineal gland.[12] Hence, this data suggests that "feast-induced drowsiness"— or postprandial somnolence — may be the result of a heavy meal rich in carbohydrates, which, via an indirect mechanism, increases the production of sleep-promoting melatonin in the brain.[55][56][57][58]

Fluorescence

Main article: Fluorescence spectroscopy § Tryptophan fluorescence

See also

- 5-HTP
- Attenuator (genetics)
- Dimethyltryptamine
- Serotonin
- Tryptamine
- Hopkins Cole reaction
- Acree-Rosenheim reaction

References

1. ^ Dawson RMC, et al. (1969). *Data for Biochemical Research*. Oxford: Clarendon Press. ISBN 0-19-855338-2.
2. ^ IUPAC-IUBMB Joint Commission on Biochemical Nomenclature. "Nomenclature and Symbolism for Amino Acids and Peptides" (http://www.chem.qmul.ac.uk/iupac/AminoAcid/). *Recommendations on Organic & Biochemical Nomenclature, Symbols & Terminology etc*. Retrieved 2007-05-17.
3. ^ Pallaghy PK, Melnikova AP, Jimenez EC, Olivera BM, Norton RS (1999). "Solution structure of contryphan-R, a naturally-occurring disulfide-bridged octapeptide containing D-tryptophan: comparison with protein loops". *Biochemistry* **38** (35): 11553–9. doi:10.1021/bi990685j (http://dx.doi.org/10.1021%2Fbi990685j). PMID 10471307 (https://www.ncbi.nlm.nih.gov/pubmed/10471307).
4. ^ Hopkienns FG, Cole SW (1901). "A contribution to the chemistry of proteids: Part I. A preliminary study of a hitherto undescribed product of tryptic digestion" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1540554). *J. Physiol. (Lond.)* **27** (4–5): 418–28. PMC 1540554 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1540554). PMID 16992614 (https://www.ncbi.nlm.nih.gov/pubmed/16992614).
5. ^ Cox GJ, King H (1943), "L-Tryptophane" (http://www.orgsyn.org/demo.aspx?prep=CV2P0612), *Org. Synth.*; *Coll. Vol.* **2**: 612–616

6. ^ Radwanski ER, Last RL (1995). "Tryptophan biosynthesis and metabolism: biochemical and molecular genetics" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC160888). *Plant Cell* **7** (7): 921–34. doi:10.1105/tpc.7.7.921 (http://dx.doi.org/10.1105%2Ftpc.7.7.921). PMC 160888 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC160888). PMID 7640526 (https://www.ncbi.nlm.nih.gov/pubmed/7640526).
7. ^ Ikeda M (2002). "Amino acid production processes". *Adv. Biochem. Eng. Biotechnol*. Advances in Biochemical Engineering/Biotechnology **79**: 1–35. doi:10.1007/3-540-45989-8_1 (http://dx.doi.org/10.1007%2F3-540-45989-8_1). ISBN 978-3-540-43383-5. PMID 12523387 (https://www.ncbi.nlm.nih.gov/pubmed/12523387).
8. ^ Becker J, Wittmann C (2012). "Bio-based production of chemicals, materials and fuels -Corynebacterium glutamicum as versatile cell factory". *Curr. Opin. Biotechnol.* **23** (4): 631–40. doi:10.1016/j.copbio.2011.11.012 (http://dx.doi.org/10.1016%2Fj.copbio.2011.11.012). PMID 22138494 (https://www.ncbi.nlm.nih.gov/pubmed/22138494).
9. ^ Conrado RJ, Varner JD, DeLisa MP (2008). "Engineering the spatial organization of metabolic enzymes: mimicking nature's synergy". *Curr. Opin. Biotechnol.* **19** (5): 492–9. doi:10.1016/j.copbio.2008.07.006 (http://dx.doi.org/10.1016%2Fj.copbio.2008.07.006). PMID 18725290 (https://www.ncbi.nlm.nih.gov/pubmed/18725290).
10. ^ Fernstrom JD (1983). "Role of precursor availability in control of monoamine biosynthesis in brain" (http://physrev.physiology.org/cgi/reprint/63/2/484). *Physiol. Rev.* **63** (2): 484–546. PMID 6132421 (https://www.ncbi.nlm.nih.gov/pubmed/6132421).
11. ^ Schaechter JD, Wurtman RJ (1990). "Serotonin release varies with brain tryptophan levels" (http://wurtmanlab.mit.edu/publications/pdf/790.pdf). *Brain Res.* **532** (1–2): 203–10. doi:10.1016/0006-8993(90)91761-5 (http://dx.doi.org/10.1016%2F0006-8993%2890%2991761-5). PMID 1704290 (https://www.ncbi.nlm.nih.gov/pubmed/1704290).
12. ^ *a b* Wurtman RJ, Anton-Tay F (1969). "The mammalian pineal as a neuroendocrine transducer" (http://wurtmanlab.mit.edu/publications/pdf/104.pdf). *Recent Prog. Horm. Res.* **25**: 493–522. doi:10.1016/b978-0-12-571125-8.50014-4 (http://dx.doi.org/10.1016%2Fb978-0-12-571125-8.50014-4). PMID 4391290 (https://www.ncbi.nlm.nih.gov/pubmed/4391290).
13. ^ *a b* Ikeda M, Tsuji H, Nakamura S, Ichiyama A, Nishizuka Y, Hayaishi O (1965). "Studies on the biosynthesis of nicotinamide adenine dinucleotide. II. A role of picolinic carboxylase in the biosynthesis of nicotinamide adenine dinucleotide from tryptophan in mammals" (http://www.jbc.org/cgi/reprint/240/3/1395). *J. Biol. Chem.* **240** (3): 1395–401. PMID 14284754 (https://www.ncbi.nlm.nih.gov/pubmed/14284754).
14. ^ Palme K, Nagy F (April 2008). "A new gene for auxin synthesis". *Cell* **133** (1): 31–2. doi:10.1016/j.cell.2008.03.014 (http://dx.doi.org/10.1016%2Fj.cell.2008.03.014). PMID 18394986 (https://www.ncbi.nlm.nih.gov/pubmed/18394986).
15. ^ Ledochowski M, Widner B, Murr C, Sperner-Unterweger B, Fuchs D (2001). "Fructose malabsorption is associated with decreased plasma tryptophan". *Scand. J. Gastroenterol.* **36** (4): 367–71. doi:10.1080/003655201300051135 (http://dx.doi.org/10.1080%2F003655201300051135). PMID 11336160 (https://www.ncbi.nlm.nih.gov/pubmed/11336160).
16. ^ Ledochowski M, Sperner-Unterweger B, Widner B, Fuchs D (1998). "Fructose malabsorption is associated with early signs of mental depression". *Eur. J. Med. Res.* **3** (6): 295–8. PMID 9620891 (https://www.ncbi.nlm.nih.gov/pubmed/9620891).

17. ^ Ledochowski M, Widner B, Murr C, Sperner-Unterweger B, Fuchs D (2001). "Fructose malabsorption is associated with decreased plasma tryptophan". *Scand. J. Gastroenterol.* **36** (4): 367–71. doi:10.1080/003655201300051135 (http://dx.doi.org/10.1080%2F003655201300051135). PMID 11336160 (https://www.ncbi.nlm.nih.gov/pubmed/11336160).
18. ^ Gollnick P, Babitzke P, Antson A, Yanofsky C (2005). "Complexity in regulation of tryptophan biosynthesis in Bacillus subtilis". *Annu. Rev. Genet.* **39**: 47–68. doi:10.1146/annurev.genet.39.073003.093745 (http://dx.doi.org/10.1146%2Fannurev.genet.39.073003.093745). PMID 16285852 (https://www.ncbi.nlm.nih.gov/pubmed/16285852).
19. ^ Tryptophan background (http://www.vitamins-supplements.org/amino-acids/tryptophan.php)
20. ^ *a b* Helmenstine AM. "Does Eating Turkey Make You Sleepy?" (http://chemistry.about.com/od/holidaysseasons/a/tiredturkey.htm). About.com. Retrieved 2013-11-13.
21. ^ *a b c* Ballantyne C (2007-11-21). "Does Turkey Make You Sleepy?" (http://www.scientificamerican.com/article.cfm?id=fact-or-fiction-does-turkey-make-you-sleepy). Scientific American. Retrieved 2013-06-06.
22. ^ *a b* McCue K. "Chemistry.org: Thanksgiving, Turkey, and Tryptophan" (http://web.archive.org/web/20070404111342/http://www.chemistry.org/portal/a/c/s/1/feature_ent.html?DOC=enthusiasts%5cent_tryptophan.html). Archived from the original (http://www.chemistry.org/portal/a/c/s/1/feature_ent.html?DOC=enthusiasts%5Cent_tryptophan.html) on 2007-04-04. Retrieved 2007-08-17.
23. ^ *a b c* Joanne Holden, Nutrient Data Laboratory, Agricultural Research Service. "USDA National Nutrient Database for Standard Reference, Release 22" (http://www.ars.usda.gov/ba/bhnrc/ndl). United States Department of Agriculture. Retrieved 2009-11-29.
24. ^ Rambali B, Andel I van, Schenk E, Wolterink G, Werken G van de, Stevenson H, Vleeming W (2002). "[The contribution of cocoa additive to cigarette smoking addiction]" (http://rivm.nl/bibliotheek/rapporten/650270002.pdf) (PDF). *RIVM* (report 650270002/2002).- The National Institute for Public Health and the Environment (Netherlands)
25. ^ Soh, Nerissa L. AU - Walter, Garry TI (2011). "Tryptophan and depression: can diet alone be the answer?". *Acta Neuropsychiatrica VL* **23** (1): 1601–5215;. doi:10.1111/j.1601-5215.2010.00508.x (http://dx.doi.org/10.1111%2Fj.1601-5215.2010.00508.x).
26. ^ Fernstrom JD (2012). "Effects and side effects associated with the non-nutritional use of tryptophan by humans". *J. Nutr.* **142** (12): 2236S–2244S. doi:10.3945/jn.111.157065 (http://dx.doi.org/10.3945%2Fjn.111.157065). PMID 23077193 (https://www.ncbi.nlm.nih.gov/pubmed/23077193).
27. ^ Hartmann E (1982). "Effects of L-tryptophan on sleepiness and on sleep". *Journal of Psychiatric Research* **17** (2): 107–13. doi:10.1016/0022-3956(82)90012-7 (http://dx.doi.org/10.1016%2F0022-3956%2882%2990012-7). PMID 6764927 (https://www.ncbi.nlm.nih.gov/pubmed/6764927).
28. ^ Schneider-Helmert D, Spinweber CL (1986). "Evaluation of L-tryptophan for treatment of insomnia: a review". *Psychopharmacology (Berl.)* **89** (1): 1–7. doi:10.1007/BF00175180 (http://dx.doi.org/10.1007%2FBF00175180). PMID 3090582 (https://www.ncbi.nlm.nih.gov/pubmed/3090582).
29. ^ Wyatt RJ, Engelman K, Kupfer DJ, Fram DH, Sjoerdsma A, Snyder F. (Oct 24, 1970). "Effects of L-tryptophan (a natural sedative) on human sleep". *Lancet* **2** (7678): 842–6. doi:10.1016/S0140-6736(70)92015-5 (http://dx.doi.org/10.1016%2FS0140-6736%2870%2992015-5). ISSN 0140-6736 (https://www.worldcat.org/issn/0140-6736). PMID 4097755 (https://www.ncbi.nlm.nih.gov/pubmed/4097755).
30. ^ "research summary of Dr. Richard Wurtman, MIT" (http://web.mit.edu/bcs/people/wurtman.shtml). Retrieved 2007-08-12.

31. ^ [a] [b] Thomson J, Rankin H, Ashcroft GW, Yates CM, McQueen JK, Cummings SW (1982). "The treatment of depression in general practice: a comparison of L-tryptophan, amitriptyline, and a combination of L-tryptophan and amitriptyline with placebo". *Psychological Medicine* **12** (4): 741–51. doi:10.1017/S0033291700049047 (http://dx.doi.org/10.1017%2FS0033291700049047). PMID 7156248 (https://www.ncbi.nlm.nih.gov/pubmed/7156248).
32. ^ Levitan RD, Shen JH, Jindal R, Driver HS, Kennedy SH, Shapiro CM (2000). "Preliminary randomized double-blind placebo-controlled trial of tryptophan combined with fluoxetine to treat major depressive disorder: antidepressant and hypnotic effects" (http://www.cma.ca/index.cfm/ci_id/12652/la_id/1.htm). *Journal of psychiatry & neuroscience : JPN* **25** (4): 337–46. PMC 1407729 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1407729). PMID 11022398 (https://www.ncbi.nlm.nih.gov/pubmed/11022398).
33. ^ Meyers S (2000). "Use of neurotransmitter precursors for treatment of depression" (http://www.thorne.com/altmedrev/.fulltext/5/1/64.pdf). *Alternative medicine review : a journal of clinical therapeutic* **5** (1): 64–71. PMID 10696120 (https://www.ncbi.nlm.nih.gov/pubmed/10696120).
34. ^ Shaw K, Turner J, Del Mar C (2002). "Tryptophan and 5-hydroxytryptophan for depression". In Shaw, Kelly A. *Cochrane database of systematic reviews (Online)* (1): CD003198. doi:10.1002/14651858.CD003198 (http://dx.doi.org/10.1002%2F14651858.CD003198). PMID 11869656 (https://www.ncbi.nlm.nih.gov/pubmed/11869656).
35. ^ Sarris J, Mischoulon D, Schweitzer I (2011). "Adjunctive nutraceuticals with standard pharmacotherapies in bipolar disorder: a systematic review of clinical trials". *Bipolar Disord* **13** (5–6): 454–65. doi:10.1111/j.1399-5618.2011.00945.x (http://dx.doi.org/10.1111%2Fj.1399-5618.2011.00945.x). PMID 22017215 (https://www.ncbi.nlm.nih.gov/pubmed/22017215).
36. ^ Waider J, Araragi N, Gutknecht L, Lesch KP (April 2011). "Tryptophan hydroxylase-2 (TPH2) in disorders of cognitive control and emotion regulation: a perspective". *Psychoneuroendocrinology* **36** (3): 393–405. doi:10.1016/j.psyneuen.2010.12.012 (http://dx.doi.org/10.1016%2Fj.psyneuen.2010.12.012). PMID 21257271 (https://www.ncbi.nlm.nih.gov/pubmed/21257271).
37. ^ Kostowski W, Bidzinski A, Hauptmann M, Malinowski JE, Jerlicz M, Dymecki J (1978). "Brain serotonin and epileptic seizures in mice: a pharmacological and biochemical study". *Pol J Pharmacol Pharm* **30** (1): 41–7. PMID 148040 (https://www.ncbi.nlm.nih.gov/pubmed/148040).
38. ^ Hardebo JE, Owman C (1980). "Barrier mechanisms for neurotransmitter monoamines and their precursors at the blood-brain interface". *Annals of Neurology* **8** (1): 1–31. doi:10.1002/ana.410080102 (http://dx.doi.org/10.1002%2Fana.410080102). PMID 6105837 (https://www.ncbi.nlm.nih.gov/pubmed/6105837).
39. ^ Turner EH, Loftis JM, Blackwell AD (2006). "Serotonin a la carte: supplementation with the serotonin precursor 5-hydroxytryptophan". *Pharmacol Ther* **109** (3): 325–38. doi:10.1016/j.pharmthera.2005.06.004 (http://dx.doi.org/10.1016%2Fj.pharmthera.2005.06.004). PMID 16023217 (https://www.ncbi.nlm.nih.gov/pubmed/16023217).
40. ^ Gustafsson BI, Tømmerås K, Nordrum I, Loennechen JP, Brunsvik A, Solligård E, Fossmark R, Bakke I, Syversen U, Waldum H (March 2005). "Long-term serotonin administration induces heart valve disease in rats". *Circulation* **111** (12): 1517–22. doi:10.1161/01.CIR.0000159356.42064.48 (http://dx.doi.org/10.1161%2F01.CIR.0000159356.42064.48). PMID 15781732 (https://www.ncbi.nlm.nih.gov/pubmed/15781732).

41. ^ Xu J, Jian B, Chu R, Lu Z, Li Q, Dunlop J, Rosenzweig-Lipson S, McGonigle P, Levy RJ, Liang B (December 2002). "Serotonin mechanisms in heart valve disease II: the 5-HT2 receptor and its signaling pathway in aortic valve interstitial cells" (http://www.journals.elsevierhealth.com/periodicals/ajpa/article/S0002-9440(10)64497-5/abstract). *Am. J. Pathol.* **161** (6): 2209–18. doi:10.1016/S0002-9440(10)64497-5 (http://dx.doi.org/10.1016%2FS0002-9440%2810%2964497-5). PMC 1850896 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1850896). PMID 12466135 (https://www.ncbi.nlm.nih.gov/pubmed/12466135).
42. ^ "Dietary Supplements: Background Information" (http://ods.od.nih.gov/factsheets/dietarysupplements/). Retrieved 2011-05-10.
43. ^ Opitz CA, Litzenburger UM, Sahm F, Ott M, Tritschler I, Trump S, Schumacher T, Jestaedt L, Schrenk D, Weller M, Jugold M, Guillemin GJ, Miller CL, Lutz C, Radlwimmer B, Lehmann I, von Deimling A, Wick W, Platten M (October 2011). "An endogenous tumour-promoting ligand of the human aryl hydrocarbon receptor". *NATURE* **478** (7368): 197–203. doi:10.1038/nature10491 (http://dx.doi.org/10.1038%2Fnature10491). PMID 21976023 (https://www.ncbi.nlm.nih.gov/pubmed/21976023).
44. ^ Jackson RW (1930). "A synthesis of tryptophol" (http://www.jbc.org/content/88/3/659.full.pdf). *Journal of Biological Chemistry* **88** (3): 659–662.
45. ^ Slutsker L, Hoesly FC, Miller L, Williams LP, Watson JC, Fleming DW (1990). "Eosinophilia-myalgia syndrome associated with exposure to tryptophan from a single manufacturer". *JAMA* **264** (2): 213–7. doi:10.1001/jama.264.2.213 (http://dx.doi.org/10.1001%2Fjama.264.2.213). PMID 2355442 (https://www.ncbi.nlm.nih.gov/pubmed/2355442).
46. ^ Back EE, Henning KJ, Kallenbach LR, Brix KA, Gunn RA, Melius JM (1993). "Risk factors for developing eosinophilia myalgia syndrome among L-tryptophan users in New York". *J. Rheumatol.* **20** (4): 666–72. PMID 8496862 (https://www.ncbi.nlm.nih.gov/pubmed/8496862).
47. ^ Kilbourne EM, Philen RM, Kamb ML, Falk H (1996). "Tryptophan produced by Showa Denko and epidemic eosinophilia-myalgia syndrome". *The Journal of rheumatology. Supplement* **46**: 81–8; discussion 89–91. PMID 8895184 (https://www.ncbi.nlm.nih.gov/pubmed/8895184).
48. ^ *a b c* "Information Paper on L-tryptophan and 5-hydroxy-L-tryptophan" (http://web.archive.org/web/20050225100757/http://www.cfsan.fda.gov/~dms/ds-tryp1.html). FU. S. Food and Drug Administration, Center for Food Safety and Applied Nutrition, Office of Nutritional Products, Labeling, and Dietary Supplements. 2001-02-01. Archived from the original (http://www.cfsan.fda.gov/~dms/ds-tryp1.html) on 2005-02-25. Retrieved 2012-02-08.
49. ^ Mayeno AN, Lin F, Foote CS, Loegering DA, Ames MM, Hedberg CW, Gleich GJ (1990). "Characterization of "peak E," a novel amino acid associated with eosinophilia-myalgia syndrome". *Science* **250** (4988): 1707–8. doi:10.1126/science.2270484 (http://dx.doi.org/10.1126%2Fscience.2270484). PMID 2270484 (https://www.ncbi.nlm.nih.gov/pubmed/2270484).
50. ^ Ito J, Hosaki Y, Torigoe Y, Sakimoto K (1992). "Identification of substances formed by decomposition of peak E substance in tryptophan". *Food Chem. Toxicol.* **30** (1): 71–81. doi:10.1016/0278-6915(92)90139-C (http://dx.doi.org/10.1016%2F0278-6915%2892%2990139-C). PMID 1544609 (https://www.ncbi.nlm.nih.gov/pubmed/1544609).
51. ^ Raphals P (2000). "Does medical mystery threaten biotech?". *Science* **250** (4981): 4981. doi:10.1126/science.2237411 (http://dx.doi.org/10.1126%2Fscience.2237411). PMID 2237411 (https://www.ncbi.nlm.nih.gov/pubmed/2237411).

52. ^ Mayeno AN, Gleich GJ (September 1994). "Eosinophilia-myalgia syndrome and tryptophan production: a cautionary tale". *Trends Biotechnol.* **12** (9): 346–52. doi:10.1016/0167-7799(94)90035-3 (http://dx.doi.org/10.1016%2F0167-7799%2894%2990035-3). PMID 7765187 (https://www.ncbi.nlm.nih.gov/pubmed/7765187).
53. ^ *a b* "COT statement on tryptophan and the eosinophilia-myalgia syndrome" (http://cot.food.gov.uk/pdfs/tryptophanamend200401.pdf). UK Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment. June 2004, updated December 2005.
54. ^ "Food & mood. (neuroscience professor Richard Wurtman) (Interview)" (http://www.highbeam.com/doc/1G1-12520128.html). *Nutrition Action Healthletter* (HighBeam Research). September 1992.
55. ^ *a b c* Fernstrom JD, Wurtman RJ (1971). "Brain serotonin content: increase following ingestion of carbohydrate diet". *Science* **174** (4013): 1023–5. doi:10.1126/science.174.4013.1023 (http://dx.doi.org/10.1126%2Fscience.174.4013.1023). PMID 5120086 (https://www.ncbi.nlm.nih.gov/pubmed/5120086).
56. ^ *a b* Lyons PM, Truswell AS (1988). "Serotonin precursor influenced by type of carbohydrate meal in healthy adults" (http://www.ajcn.org/cgi/reprint/47/3/433.pdf). *Am. J. Clin. Nutr.* **47** (3): 433–9. PMID 3279747 (https://www.ncbi.nlm.nih.gov/pubmed/3279747).
57. ^ *a b c* Wurtman RJ, Wurtman JJ, Regan MM, McDermott JM, Tsay RH, Breu JJ (2003). "Effects of normal meals rich in carbohydrates or proteins on plasma tryptophan and tyrosine ratios" (http://www.ajcn.org/cgi/content/abstract/77/1/128). *Am. J. Clin. Nutr.* **77** (1): 128–32. PMID 12499331 (https://www.ncbi.nlm.nih.gov/pubmed/12499331).
58. ^ *a b* Afaghi A, O'Connor H, Chow CM (2007). "High-glycemic-index carbohydrate meals shorten sleep onset" (http://www.ajcn.org/cgi/content/full/85/2/426). *Am. J. Clin. Nutr.* **85** (2): 426–30. PMID 17284739 (https://www.ncbi.nlm.nih.gov/pubmed/17284739).
59. ^ Pardridge WM, Oldendorf WH (1975). "Kinetic analysis of blood–brain barrier transport of amino acids". *Biochim. Biophys. Acta* **401** (1): 128–36. doi:10.1016/0005-2736(75)90347-8 (http://dx.doi.org/10.1016%2F0005-2736%2875%2990347-8). PMID 1148286 (https://www.ncbi.nlm.nih.gov/pubmed/1148286).
60. ^ Maher TJ, Glaeser BS, Wurtman RJ (1984). "Diurnal variations in plasma concentrations of basic and neutral amino acids and in red cell concentrations of aspartate and glutamate: effects of dietary protein intake". *Am. J. Clin. Nutr.* **39** (5): 722–9. PMID 6538743 (https://www.ncbi.nlm.nih.gov/pubmed/6538743).

External links

- Tryptophan MS Spectrum (http://gmd.mpimp-golm.mpg.de/Spectrums/d556367f-50ea-4d71-b1ff-879d09188b69.aspx)
- "KEGG PATHWAY: Tryptophan metabolism - Homo sapiens" (http://www.genome.jp/dbget-bin/www_bget?path:hsa00380). KEGG: Kyoto Encyclopedia of Genes and Genomes. 2006-08-23. Retrieved 2008-04-20.
- G.P. Moss. "Tryptophan Catabolism (early stages)" (http://www.chem.qmul.ac.uk/iubmb/enzyme/reaction/AminoAcid/TrpCat1.html). Nomenclature Committee of the International Union of Biochemistry and Molecular Biology (NC-IUBMB). Retrieved 2008-04-20.
- G.P. Moss. "Tryptophan Catabolism (later stages)" (http://www.chem.qmul.ac.uk/iubmb/enzyme/reaction/AminoAcid/TrpCat2.html). Nomenclature

Committee of the International Union of Biochemistry and Molecular Biology (NC-IUBMB). Retrieved 2008-04-20.

- B Mikkelson, DP Mikkelson (2007-11-22). "Turkey Causes Sleepiness" (http://www.snopes.com/food/ingredient/turkey.asp). *Urban Legends Reference Pages*. Snopes.com. Retrieved 2008-04-20.
- Wood RM, Rilling JK, Sanfey AG, Bhagwagar Z, Rogers RD (2006). "Effects of tryptophan depletion on the performance of an iterated Prisoner's Dilemma game in healthy adults". *Neuropsychopharmacology* **31** (5): 1075–84. doi:10.1038/sj.npp.1300932 (http://dx.doi.org/10.1038%2Fsj.npp.1300932). PMID 16407905 (https://www.ncbi.nlm.nih.gov/pubmed/16407905).
- Ron Sturtz (2009). "what is the difference between L-Tryptophan and 5-HTP?" (http://www.lidtke.com/difference-between-l-tryptophan-5-htp-article). *Neuropsychopharmacology*: 1.