

5-HTP

- Date:** December 17, 2007
- Proper name(s):** L-5-Hydroxytryptophan (O'Neil et al. 2001)
- Common name(s):** L-5-Hydroxytryptophan, L-5-HTP (O'Neil et al. 2001)
- Source material(s):** Isolated from Griffonia (*Griffonia simplicifolia* (Vahl ex DC) Baill. (Fabaceae)) seed (Lemaire and Adosraku 2002; Fellows and Bell 1970)
- Route(s) of administration:** Oral
- Dosage form(s):** Only allowable pharmaceutical dosage forms: tablets and capsules. This monograph is not intended to include food-like dosage forms such as bars, chewing gums or beverages.
- Use(s) or Purpose(s):** Statement(s) to the effect of:
- ▶ Helps to promote healthy mood balance (Pöldinger et al. 1991; Zmilacher et al. 1988; Nakajima et al. 1978).
 - ▶ Helps to relieve symptoms of fibromyalgia (Nicolodi and Sicuteri 1996; Sarzi Puttini and Caruso 1992; Caruso et al. 1990).
 - ▶ Helps to reduce the severity and duration of migraine headaches when taken as a prophylactic (Titus et al. 1986; Bono et al. 1984; Sicuteri 1973).
 - ▶ To be used with a program of reduced intake of dietary calories and increased physical activity (if possible) to help in weight management by reducing carbohydrate cravings (Cangiano et al. 1998; Cangiano et al. 1992; Ceci et al. 1989).
 - ▶ Used as a sleep aid (Soulaïrac and Lambinet 1977; Wyatt et al. 1971).

Dose(s):

Healthy mood balance: 50 (Nakajima et al. 1978) - 100 mg (Pöldinger et al. 1991), 3 times per day

Relief of symptoms of fibromyalgia:
100 mg, 3 - 4 times per day (Nicolodi and Sicuteri 1996; Caruso et al. 1990)

Migraine prophylaxis: 100 - 200 mg, 2 - 3 times per day (Titus et al. 1986; Sicuteri 1973)

Weight management: 250 - 300 mg, 3 times per day (Cangiano et al. 1998; Cangiano et al. 1992; Ceci et al. 1989)

Sleep aid: 100 - 200 mg per day (Soullairac and Lambinet 1988; Soullairac and Lambinet 1977; Wyatt et al. 1971)

Note for all uses: Tablets and capsules must be formulated to contain 100 mg or less of L-5-HTP.

Directions for use:

All uses (excluding sleep aid):

Statement(s) to the effect of:

To minimize the risk of gastrointestinal side effects, start dosing at 50 - 100 mg, 2 - 3 times per day and slowly increase to effective dose over 2 week period (Birdsall 1998).

Sleep aid: Take 30 - 45 minutes before bedtime (Pizzorno and Murray 2006).

All uses (excluding weight management):

Take with food (Pöldinger et al. 1991).

Weight management: Take 30 minutes prior to a meal (Cangiano et al. 1998; Cangiano et al. 1992; Ceci et al. 1989).

Duration of use:

Healthy mood balance:

- ▶ Use for a minimum of 1 week to see beneficial effects (Nakajima et al. 1978).
- ▶ Consult a health care practitioner for use beyond one year (Nicolodi and Sicuteri 1996).

Relief of symptoms of fibromyalgia:

- ▶ Use for a minimum of 2 weeks to see beneficial effects (Caruso et al. 1990).
- ▶ Consult a health care practitioner for use beyond one year (Nicolodi and Sicuteri 1996).

Migraine prophylaxis:

Use for a minimum of 2 - 3 weeks to see beneficial effects (Sicuteri 1973).

Products providing 200 - 400 mg per day:

Consult a health care practitioner for use beyond one year (Nicolodi and Sicuteri 1996).

Products providing > 400 mg per day:

Consult a health care practitioner for use beyond 6 months (Titus et al. 1986).

Weight management:

Consult a health care practitioner for use beyond 12 weeks (Cangiano et al. 1992).

Sleep aid:

No statement required.

Risk information:

Statement(s) to the effect of:

Caution(s) and warning(s):

Sleep aid:

Consult a health care practitioner if sleeplessness persists continuously for more than 3 weeks (chronic insomnia) (Berardi et al. 2002; Dipiro et al. 2002).

All uses:

- ▶ Consult a health care practitioner if symptoms persist or worsen.
- ▶ Consult a health care practitioner prior to use if you are pregnant or breastfeeding.
- ▶ Consult a health care practitioner prior to use if you are taking carbidopa or drugs/supplements with serotonergic activity. These may include, but are not limited to, L-tryptophan, S-adenosylmethionine (SAMe), St. John's wort, antidepressants, pain killers, over the counter cough and cold medication containing dextromethorphan, anti-nausea medication and anti-migraine medication (Mayo Clinic Staff 2007; Turner et al 2006).
- ▶ Discontinue use and consult a health care practitioner if you show signs of weakness, oral ulcers, or abdominal pain accompanied by severe muscle pain (Das et al. 2004) or if you experience skin changes (Lampert et al. 1992; Sternberg et al. 1980).

Contraindication(s): Do not use if you have scleroderma (Lampert et al. 1992; Sternberg et al. 1980).

Known adverse reaction(s):

- ▶ Some people may experience drowsiness. Exercise caution if operating heavy machinery, driving a motor vehicle or involved in activities requiring mental alertness (Caruso et al. 1990; Zmilacher et al. 1988; Takahashi et al. 1976).
- ▶ Some people may experience diarrhea, nausea, vomiting and abdominal pain (Turner et al. 2006; Byerley et al. 1987).

Non-medicinal ingredients: Must be chosen from the current NHPD *List of Acceptable Non-medicinal Ingredients* and must meet the limitations outlined in the list.

Specifications: Must comply with the minimum specifications outlined in the current NHPD *Compendium of Monographs*.

References cited:

Barlet P, Pailard P. [Etude clinique du 5-hydroxytryptophane dans les états dépressifs du troisième âge]. *Cahiers Médicaux Lyonnais* 1973;50:1985-1901 (in French).

Berardi RR, DeSimone EM, Newton GD, Oszko MA, Popovich NG, Rollings CJ, Shimp LA, Tietze KJ, editors. *Handbook of Nonprescription Drugs: An Interactive Approach to Self-Care*, 13th edition. Washington (DC): American Pharmaceutical Association; 2002.

Birdsall TC. 5-Hydroxytryptophan: a clinically-effective serotonin precursor. *Alternative Medicine Review* 1998;3(4):271-280.

Bono G, Micieli G, Sances G, Calvani M, Nappi G. L-5HTP treatment in primary headaches: an attempt at clinical identification of responsive patients. *Cephalalgia* 1984;4(3):159-165.

Byerley WF, Judd LL, Reimherr FW, Grosser BI. 5-Hydroxytryptophan: a review of its antidepressant efficacy and adverse effects. *Journal of Clinical Psychopharmacology* 1987;7(3):127-137.

Cangiano C, Ceci F, Cascino A, Del Ben M, Laviano A, Muscaritoli M, Antonucci F, Rossi-Fanelli F. Eating behavior and adherence to dietary prescriptions in obese adult subjects treated with 5-hydroxytryptophan. *American Journal of Clinical Nutrition* 1992;56(5):863-867.

Cangiano C, Laviano A, Del Ben M, Preziosa I, Angelico F, Cascino A, Rossi-Fanelli F. Effects of oral 5-hydroxy-tryptophan on energy intake and macronutrient selection in non-insulin dependent diabetic patients. *International Journal of Obesity and Related Metabolic Disorders* 1998;22(7):648-654.

Caruso I, Sarzi Puttini P, Cazzola M, Azzolini V. Double-blind study of 5-hydroxytryptophan versus placebo in the treatment of primary fibromyalgia syndrome. *Journal of International Medical Research* 1990;18(3):201-209.

Ceci F, Cangiano C, Cairella M, Cascino A, Del Ben M, Muscaritoli M, Sibilia L, Rossi Fanelli F. The effects of oral 5-hydroxytryptophan administration on feeding behavior in obese adult female subjects. *Journal of Neural Transmission* 1989;76(2):109-117.

Das YT, Bagchi M, Bagchi D, Preuss HG. Safety of 5-hydroxy-L-tryptophan. *Toxicology Letters* 2004;150(1):111-122.

Dipiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM. *Pharmacotherapy: a pathophysiologic approach*, 5th edition. New York (NY): The McGraw-Hill Companies, Inc.; 2002.

Fellows LE, Bell EA. 5-hydroxy-L-tryptophan, 5-hydroxytryptamine and L-tryptophan-5-hydroxylase in *Griffonia simplicifolia*. *Phytochemistry* 1970;9(11):2389-2396.

Lampert A, Joly P, Thomine E, Ortoli JC, Lauret P. [Scleroderma-like syndrome with bullous morphea during treatment with 5-hydroxytryptophan, carbidopa and flunitrazepam]. *Annales de Dermatologie et de Vénérologie* 1992;119(3):209-211 (in French).

Lemaire PA, Adosraku RK. An HPLC method for the direct assay of the serotonin precursor, 5-hydroxytryptophan, in seeds of *Griffonia simplicifolia*. *Phytochemical Analysis* 2002;13(6):333-337.

Mayo Clinic Staff. Serotonin Syndrome. Rochester (MN): Mayo Foundation for Medical Education and Research; 2007. [Accessed 2007-08-07]. Available from: <http://www.mayoclinic.com/print/serotoninsyndrome/DS00860/DSECTION=all&METHOD=print>.

Nakajima T, Kudo Y, Kaneko Z. Clinical evaluation of 5-hydroxy-L-tryptophan as an antidepressant drug. *Folia Psychiatrica et Neurologica Japonica* 1978;32(2):223-230.

Nicolodi M, Sicuteri F. Fibromyalgia and migraine, two faces of the same mechanism. Serotonin as the common clue for pathogenesis and therapy. *Advances in Experimental Medicine and Biology* 1996;398:373-379.

O'Neil MJ, Smith A, Heckelman PE, Budavari S, editors. *The Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals*, 13th edition. Whitehouse Station (NJ): Merck & Co., Inc; 2001.

Pizzorno JE, Murray MT, editors. Textbook of Natural Medicine, Volume 1, 3rd edition. St. Louis (MO): Churchill Livingstone Elsevier; 2006.

Pöldinger W, Calanchini B, Schwarz W. A functional-dimensional approach to depression: serotonin deficiency as a target syndrome in a comparison of 5-hydroxytryptophan and fluvoxamine. *Psychopathology* 1991;24(2):53-81.

Sarzi Puttini P, Caruso I. Primary fibromyalgia syndrome and 5-hydroxy-L-tryptophan: a 90-day open study. *Journal of International Medical Research* 1992;20(2):182-189.

Sicuteri F. The ingestion of serotonin precursors (L-5-hydroxytryptophan and L-tryptophan) improves migraine headache. *Headache* 1973;13(1):19-22.

Soulairac A, Lambinet H. [Clinical studies of the effect of the serotonin precursor, L-5-hydroxytryptophan, on sleep disorders]. *Schweizerische Rundschau für Medizin Praxis* 1988;77(34a):19-23 (in French).

Soulairac A, Lambinet H. [Effect of 5-hydroxytryptophan, a serotonin precursor, on sleep disorders]. *Annales Médico-Psychologiques* 1977;1(5):792-798 (in French).

Sternberg EM, Van Woert MH, Young SN, Magnussen I, Baker H, Gauthier S, Osterland CK. Development of a scleroderma-like illness during therapy with L-5-hydroxytryptophan and carbidopa. *New England Journal of Medicine* 1980;303(14):782-787.

Takahashi S, Takahashi R, Masumura I, Miike A. Measurement of 5-hydroxyindole compounds during L-5-HTP treatment in depressed patients. *Folia Psychiatrica et Neurologica Japonica* 1976;30(4):463-473.

Titus F, Dávalos A, Alom J, Codina A. 5-Hydroxytryptophan versus methysergide in the prophylaxis of migraine. Randomized clinical trial. *European Neurology* 1986;25(5):327-329.

Turner EH, Loftis JM, Blackwell AD. Serotonin a la carte: supplementation with the serotonin precursor 5-hydroxytryptophan. *Pharmacology & Therapeutics* 2006;109(3):325-338.

Wyatt RJ, Zarccone V, Engelman K, Dement WC, Snyder F, Sjoerdsma A. Effects of 5-hydroxytryptophan on the sleep of normal human subjects. *Electroencephalography and Clinical Neurophysiology* 1971;30(6):505-509.

Zmilacher K, Battagay R, Gastpar M. L-5-hydroxytryptophan alone and in combination with a peripheral decarboxylase inhibitor in the treatment of depression. *Neuropsychobiology* 1988;20(1):28-35.

References reviewed:

Agazzi A, De Ponti F, De Giorgio R, Candura SM, Anselmi L, Cervio E, Di Nucci A, Tonini M. Review of the implications of dietary tryptophan intake in patients with irritable bowel syndrome and psychiatric disorders. *Digestive and Liver Disease* 2003;35(8):590-595.

Amer A, Breu J, McDermott J, Wurtman RJ, Maher TJ. 5-Hydroxy-L-tryptophan suppresses food intake in food-deprived and stressed rats. *Pharmacology, Biochemistry, and Behavior* 2004;77(1):137-143.

Auffranc JC, Berbis P, Fabre JF, Garnier JP, Privat Y. [Sclerodermiform and poikilodermal syndrome observed during treatment with carbidopa and 5-hydroxytryptophan]. *Annales de Dermatologie et de Venereologie* 1985;112(9):691-692 (in French).

Battistella PA, Bordin A, Cernetti R, Broetto S, Corra S, Piva E, Plebani M. Beta-endorphin in plasma and monocytes in juvenile headache. *Headache* 1996;36(2):91-94.

Beers MH, Berkow R, editors. *The Merck Manual of Diagnosis and Therapy*, 17th edition. Whitehouse Station (NJ): Merck & Co., Inc; 1999.

Bhushan B, Seth SD, Saxena S, Gupta YK, Karmarkar MG. An adverse reaction to L-5-hydroxytryptophan. *The American Journal of Psychiatry* 1991;148(2):268-269.

Boiardi A, Crenna P, Merati B, Negri S, Tansini E, Bussone G. 5-OH-tryptophane in migraine: clinical and neurophysiological considerations. *Journal of Neurology* 1981;225(1):41-46.

Boiardi A, Picotti GB, Di Giulio AM, Bussone G, Galva MD, La Mantia L, Mantegazza P. Platelet met-enkephalin immunoreactivity and 5-hydroxytryptamine concentrations in migraine patients: effects of 5-hydroxytryptophan, amitriptyline and chlorimipramine treatment. *Cephalalgia* 1984;4(2):81-84.

Bono G, Criscuoli M, Martignoni E, Salmon S, Nappi G. Serotonin precursors in migraine prophylaxis. *Advances in Neurology* 1982;33:357-363.

Buckingham J, editor. *Dictionary of Natural Products*, Version 16:1. Boca Raton (FL): Chapman & Hall/CRC; 2007.

Bussone G, Boiardi A, Cerrati A, Girotti F, Merati B, Rivolta G. Monoamine oxidase activities in patients with migraine or with cluster headache during the acute phases and after treatment with L-5-hydroxytryptophan. *Rivista Di Patologia Nervosa E Mentale* 1979;100(5):269-274.

Cangiano C, Ceci F, Cairella M, Cascino A, Del Ben M, Laviano A, Muscaritoli M, Rossi-Fanelli F. Effects of 5-hydroxytryptophan on eating behavior and adherence to dietary prescriptions in obese adult subjects. *Advances in Experimental Medicine and Biology* 1991;294:591-593.

De Benedittis G, Massei R. Serotonin precursors in chronic primary headache. A double-blind cross-over study with L-5-hydroxytryptophan vs. placebo. *Journal of Neurosurgical Sciences* 1985;29(3):239-248.

De Giorgis G, Miletto R, Iannuccelli M, Camuffo M, Scerni S. Headache in association with sleep disorders in children: a psychodiagnostic evaluation and controlled clinical study--L-5-HTP versus placebo. *Drugs Under Experimental and Clinical Research* 1987;13(7):425-433.

Ek A, Witkop B. The synthesis of labile hydroxytryptophan metabolites. *Journal of the American Chemical Society* 1954;76(22):5579-5588.

EMA 2007: European Medicines Agency. London (UK): European Medicines Agency; 2007. [Accessed 2007-07-31]. Available from: <http://www.emea.europa.eu>.

Farinelli S, Mariani A, Grimaldi A, Mariani M, Iannessi A, De Rosa F. [Eosinophilia-myalgia syndrome associated with 5-OH-tryptophan. Description of a case]. *Recenti Progressi in Medicina* 1991;82(7-8):381-384 (in Italian).

FDA 2007: Food and Drug Administration. MedWatch Online Voluntary Reporting Form (3500). Rockville (MD): Food and Drug Administration; 2007. [Accessed 2007-07-31]. Available from: <https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm>.

FDA 2001: Food and Drug Administration. Information Paper on L-Tryptophan and 5-Hydroxy-L-Tryptophan. Rockville (MD): Food and Drug Administration, Center for Food Safety and Applied Nutrition, Office of Nutritional Products, Labeling, and Dietary Supplements; 2001. [Accessed 2007-08-02]. Available from: <http://www.cfsan.fda.gov/~dms/ds-trypl.html>.

FDA 1998: Food and Drug Administration. FDA Talk Paper: Impurities Confirmed in Dietary Supplement 5-Hydroxy-L-Tryptophan. Rockville (MD): Food and Drug Administration, US Department of Health and Human Services; 1998. [Accessed 2007-08-02]. Available from: <http://www.cfsan.fda.gov/~lrd/tp5hpt.html>.

FDA 1992: Food and Drug Administration. "Dear Colleague" Letter Regarding the Research on Eosinophilia-Myalgia Syndrome and Current Regulatory Status of L-Tryptophan. Rockville (MD): Food and Drug Administration, Office of Health Affairs; 1992. [Accessed 2007-08-02]. Available from: <http://www.cfsan.fda.gov/~dms/ds-ltr3.html>.

Frangatos G, Chubb FL. A new synthesis of 5-hydroxytryptophan. *Canadian Journal of Chemistry* 1959;37:1374-1376.

Fugh-Berman A, Cott JM. Dietary supplements and natural products as psychotherapeutic agents. *Psychosomatic Medicine* 1999;61(5):712-728.

Garcia C. [Mianserin agranulocytosis followed by oxitriptan eosinophilia]. *Der Nervenarzt* 1992;63(5):303-307 (in German).

Genazzani AR, Sandrini G, Facchinetti F, Rizzo V, Alfonsi E, Sances G, Calvani M, Nappi G. Effects of L-5HTP with and without carbidopa on plasma beta-endorphin and pain perception. Possible implications in migraine prophylaxis. *Cephalalgia* 1986;6(4):241-245.

Gijsman HJ, Van Gerven JM, De Kam ML, Schoemaker RC, Pieters MS, Weemaes M, De Rijk R, Van Der Post J, Cohen AF. Placebo-controlled comparison of three dose-regimens of 5-hydroxytryptophan challenge test in healthy volunteers. *Journal of Clinical Psychopharmacology* 2002;22(2):183-189.

Goodnick PJ, Sandoval R. Psychotropic treatment of chronic fatigue syndrome and related disorders. *Journal of Clinical Psychiatry* 1993;54(1):13-20.

Guilleminault C, Cathala JP, Castaigne P. Effects of 5-hydroxytryptophan on sleep of a patient with a brain-stem lesion. *Electroencephalography and Clinical Neurophysiology* 1973;34(2):177-184.

Gwaltney-Brant SM, Albretsen JC, Khan SA. 5-Hydroxytryptophan toxicosis in dogs: 21 cases (1989-1999). *Journal of the American Veterinary Medical Association* 2000;216(12):1937-1940.

Halford JC, Harrold JA, Lawton CL, Blundell JE. Serotonin (5-HT) drugs: effects on appetite expression and use for the treatment of obesity. *Current Drug Targets* 2005;6(2):201-213.

HC 2007: Health Canada. MedEffect Canada: Adverse Reaction Reporting. Ottawa (ON): Health Canada; 2007. [Accessed 2007-07-20]. Available from: http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index_e.html.

Imeri L, Mancina M, Bianchi S, Opp MR. 5-Hydroxytryptophan, but not L-tryptophan, alters sleep and brain temperature in rats. *Neuroscience* 2000;95(2):445-452.

Jacobsen FM, Sack DA, Wehr TA, Rogers S, Rosenthal NE. Neuroendocrine response to 5-hydroxytryptophan in seasonal affective disorder. *Archives of General Psychiatry* 1987;44(12):1086-1091.

Jellin JM. *Natural Medicines Comprehensive Database*. Stockton (CA): Therapeutic Research Faculty; 1995-2007. [Accessed 2007-09-17]. Available from: [http://www.naturaldatabase.com/\(S\(0hg55rvubxan4r55ymylyij5\)\)/Logon.aspx?li=0&st=2&cs=&s=ND](http://www.naturaldatabase.com/(S(0hg55rvubxan4r55ymylyij5))/Logon.aspx?li=0&st=2&cs=&s=ND).

Juhl JH. Fibromyalgia and the serotonin pathway. *Alternative Medicine Review* 1998;3(5):367-375.

Kahn RS, Westenberg HG. L-5-hydroxytryptophan in the treatment of anxiety disorders. *Journal of Affective Disorders* 1985;8(2):197-200.

Kahn RS, Westenberg HG, Verhoeven WM, Gispen-de Wied CC, Kamerbeek WD. Effect of a serotonin precursor and uptake inhibitor in anxiety disorders; a double-blind comparison of 5-hydroxytryptophan, clomipramine and placebo. *International Clinical Psychopharmacology* 1987;2(1):33-45.

Klarskov K, Johnson KL, Benson LM, Gleich GJ, Naylor S. Eosinophilia-myalgia syndrome case-associated contaminants in commercially available 5-hydroxytryptophan. *Advances in Experimental Medicine and Biology* 1999;467:461-468.

Maron E, Toru I, Vasar V, Shlik J. The effect of 5-hydroxytryptophan on cholecystokinin-4-induced panic attacks in healthy volunteers. *Journal of Psychopharmacology* 2004;18(2):194-199.

Martin TG. Serotonin syndrome. *Annals of Emergency Medicine* 1996;28(5):520-526.

Martinelli I, Mainini E, Mazzi C. [Effect of 5-hydroxytryptophan on the secretion of PRL, GH, TSH and cortisol in obesity]. *Minerva Endocrinologia* 1992;17(3):121-126 (in Italian).

Meyers S. Use of neurotransmitter precursors for treatment of depression. *Alternative Medicine Review* 2000;5(1):64-71.

MHRA 2007: Medicines and Healthcare Products Regulatory Agency: An Executive Agency of the Department of Health. Lambeth (London): Medicines and Healthcare Products Regulatory Agency; 2007. [Accessed 2007-07-31]. Available from: http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=5.

Michelson D, Page SW, Casey R, Truchsess MW, Love LA, Milstien S, Wilson C, Massaquoi SG, Crofford LJ, Hallett M, Gold PW, Sternberg EM. An eosinophilia-myalgia syndrome related disorder associated with exposure to L-5-hydroxytryptophan. *The Journal of Rheumatology* 1994;21(12):2261-2265.

Morris AJ, Armstrong MD. Preparation of 5-hydroxy-L-and D-tryptophan. *Journal of Organic Chemistry* 1957;22:306-308.

NIH 2007: National Institutes of Health. ChemIDplus Lite. Bethesda (MD): Specialized Information Services, National Library of Medicine, National Institutes of Health, US Department of Health & Human Services. 5-Hydroxytryptophan; RN: 56-69-9. [Accessed 2007-08-09]. Available from: <http://chem.sis.nlm.nih.gov/chemidplus/ProxyServlet?objectHandle=DBMaint&actionHandle=default&nextPage=jsp/chemidlite/ResultScreen.jsp&TXTSUPERLISTID=000056699>.

PDR Health 2007: Drug Information, Nutritional Supplements. 5-Hydroxytryptophan (5-HTP). Montvale (NJ): Thomson PDR; 2007. [Accessed 2007-09-19]. Available from: http://www.pdrhealth.com/drug_info/nmdrugprofiles/nutsupdrugs/5hy_0011.shtml.

Petre-Quadens O, De Lee C. 5-Hydroxytryptophan and sleep in Down's syndrome. *Journal of Neurological Sciences* 1975;26(3):443-453.

Pijl H, Koppeschaar HP, Cohen AF, Iestra JA, Schoemaker HC, Frolich M, Onkenhout W, Meinders AE. Evidence for brain serotonin-mediated control of carbohydrate consumption in normal weight and obese humans. *International Journal of Obesity and Related Metabolic Disorders* 1993;17(9):513-520.

Renson J, Goodwin F, Weissbach H, Udenfriend S. Conversion of tryptophan to 5-hydroxytryptophan by phenylalanine hydroxylase. *Biochemical and Biophysical Research Communications* 1961;6(1):20-23.

Ribeiro CA. L-5-Hydroxytryptophan in the prophylaxis of chronic tension-type headache: a double-blind, randomized, placebo-controlled study. For the Portuguese Head Society. *Headache* 2000;40(6):451-456.

Santucci M, Cortelli P, Rossi PG, Baruzzi A, Sacquegna T. L-5-hydroxytryptophan versus placebo in childhood migraine prophylaxis: a double-blind crossover study. *Cephalalgia* 1986;6(3):155-157.

Schruers K, Van Diest R, Overbeek T, Griez E. Acute L-5-hydroxytryptophan administration inhibits carbon dioxide-induced panic in panic disorder patients. *Psychiatry Research* 2002;113(3):237-243.

Shaw K, Turner J, DelMar C. Tryptophan and 5-hydroxytryptophan for depression. Oxfordshire (UK): The Cochrane Database of Systematic Reviews; 2002, Issue 1. Art. No.: CD003198. DOI: 10.1002/14651858.CD003198.

Sigma-Aldrich 2007: Sigma-Aldrich Corporation. H9772 5-Hydroxy-L-tryptophan Solid. St.Louis (MO): Sigma-Aldrich Co.; 2007. [Accessed 2007-07-30]. Available from: <http://www.sigmaaldrich.com/catalog/search/ProductDetail/SIGMA/H9772>.

Singhal AB, Caviness VS, Begleiter AF, Mark EJ, Rordorf G, Koroshetz WJ. Cerebral vasoconstriction and stroke after use of serotonergic drugs. *Neurology* 2002;58(1):130-133.

Takahashi S, Kondo H, Kato N. Effect of L-5-hydroxytryptophan on brain monoamine metabolism and evaluation of its clinical effect in depressed patients. *Journal of Psychiatry Research* 1975;12(3):177-187.

TGA 2007: Therapeutic Goods Administration. TGA Adverse Drug Reactions Unit. Symonston (AU): Commonwealth Department of Health and Ageing, Therapeutic Goods Administration. [Accessed 2007-07-31] Available from: <http://www.tga.gov.au/adr/index.htm>.

The Arthritis Society 2006. Scleroderma. Toronto (ON): The Arthritis Society; 2006. [Accessed 2007-08-07]. Available from: <http://www.arthritis.ca/types%20of%20arthritis/scleroderma/default.asp?s=1>.

Thorne Research, Inc. 5-Hydroxytryptophan. *Alternative Medicine Review* 1998;3(3):224-226.

Van Praag HM. In search of the mode of action of antidepressants. 5-HTP/tyrosine mixtures in depressions. *Neuropharmacology* 1983;22(3):433-440.

Van Praag HM. Management of depression with serotonin precursors. *Biological Psychiatry* 1981;16(3):291-310.

Van Praag HM. Central monoamine metabolism in depressions. I. Serotonin and related compounds. *Comprehensive Psychiatry* 1980;21(1):30-43.

Van Praag HM, De Haan S. Chemoprophylaxis of depressions. An attempt to compare lithium with 5-hydroxytryptophan. *Acta Psychiatrica Scandinavica Supplementum* 1981;290:191-201.

Van Praag HM, Korf J, Dols LC, Schut T. A pilot study of the predictive value of the probenecid test in application of 5-hydroxytryptophan as antidepressant. *Psychopharmacologia* 1972;25(1):14-21.

Van Vliet IM, Slaap BR, Westenberg HG, Den Boer JA. Behavioral, neuroendocrine and biochemical effects of different doses of 5-HTP in panic disorder. *European Neuropsychopharmacology* 1996;6(2):103-110.

Webb M, Kirker JG. Severe post-traumatic insomnia treated with L-5-hydroxytryptophan. *Lancet* 1981;1(8234):1365-1366.

Westenberg HG, Gerritsen TW, Meijer BA, Van Praag HM. Kinetics of l-5-hydroxytryptophan in healthy subjects. *Psychiatry Research* 1982;7(3):373-385.

WHO 2007: World Health Organization. Uppsala Monitoring Centre. Geneva (CHE): World Health Organization; 2007. [Accessed 2007-08-08]. Available from: <http://www.who-umc.org/DynPage.aspx>.

Yamada J, Sugimoto Y, Ujikawa M. Involvement of leptin in hypophagia induced by the serotonin precursor 5-hydroxytryptophan (5-HTP) in mice. *Biological and Pharmaceutical Bulletin* 2006;29(3):557-559.

Zarcone VP, Berger PA, Brodie KH, Sack R, Barchas JD. The indoleamine hypothesis of depression: an overview and pilot study. *Diseases of the Nervous System* 1977;38(8):646-653.