

The
United
States
of
America



**The Director of the United States
Patent and Trademark Office**

Has received an application for a patent for a new and useful invention. The title and description of the invention are enclosed. The requirements of law have been complied with, and it has been determined that a patent on the invention shall be granted under the law.

Therefore, this

United States Patent

Grants to the person(s) having title to this patent the right to exclude others from making, using, offering for sale, or selling the invention throughout the United States of America or importing the invention into the United States of America for the term set forth below, subject to the payment of maintenance fees as provided by law.

If this application was filed prior to June 8, 1995, the term of this patent is the longer of seventeen years from the date of grant of this patent or twenty years from the earliest effective U.S. filing date of the application, subject to any statutory extension.

If this application was filed on or after June 8, 1995, the term of this patent is twenty years from the U.S. filing date, subject to any statutory extension. If the application contains a specific reference to an earlier filed application or applications under 35 U.S.C. 120, 121 or 365(c), the term of the patent is twenty years from the date on which the earliest application was filed, subject to any statutory extensions.

Nicholas P. Eodici

Acting Director of the United States Patent and Trademark Office

Cheri M. Fuson

Attest



US006294579B1

(12) **United States Patent**
Carnazzo(10) **Patent No.:** **US 6,294,579 B1**
(45) **Date of Patent:** **Sep. 25, 2001**(54) **METHOD FOR IMPROVING DELIVERY OF TYROSINE SUPPLEMENTATION**(76) Inventor: **Joseph W. Carnazzo**, P.O. Box 150, Boys Town, NE (US) 68010

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **09/415,808**(22) Filed: **Oct. 11, 1999**(51) **Int. Cl.**⁷ **A61K 31/155**(52) **U.S. Cl.** **514/567**(58) **Field of Search** 514/567(56) **References Cited**

U.S. PATENT DOCUMENTS

4,255,438	3/1981	Kane et al.	
4,390,523	6/1983	Huchette et al.	
4,435,424	3/1984	Wurtman	
4,542,123	9/1985	Wurtman	
5,096,812	3/1992	Wurtman	
5,206,220	* 4/1993	Hilton	514/19
5,290,562	* 3/1994	Meybeck et al.	424/450
5,767,159	6/1998	Hultman et al.	
5,866,537	2/1999	Bianchi	
5,925,378	7/1999	Carnazzo	

FOREIGN PATENT DOCUMENTS

0 449 787 A2	10/1991	(EP)
1357813	6/1979	(GB)

OTHER PUBLICATIONS

Anisman, H., et al. (1980). "Coping with stress, norepinephrine depletion and escape performance," *Brain Research* 191:583-588.

Davis, J. M. et al. (1997). "Possible mechanisms of central nervous system fatigue during exercise," *Med. Sci. Sports Exerc.* 29(1):45-57.

Groff, J. L., et al. (1996). *Advanced Nutrition and Human Metabolism* (2d ed.), West Publishing (p. 492 only).

Stone, E. A. (1971). "Hypothalamic norepinephrine after acute stress," *Brain Research* 35:260-263.

Banderet, L. E., et al. (1989). "Treatment with Tyrosine, a Neurotransmitter Precursor, Reduces Environmental Stress in Humans," *Brain Res. Bull.* 22:759-762.

The Merck Manual on Line 284. "Neurotransmission: Major Neurotransmitters, Major Receptors and Second Messenger Systems", 1996-1997 (Total of 13 p.).

Alonso, R., et al. (1982). "Elevation of Urinary Catecholamines and Their Metabolites Following Tyrosine Administration in Humans," *Biological Psychiatry* 17:781-790.

Owasoyo, J. O., et al. (1992). "Tyrosine and its Potential Use as a Countermeasure to Performance Decrement in Military Sustained Operations," *Aviation, Space, and Environmental Medicine*, pp.364-369.

Salter, C. A. (1989) "Dietary Tyrosine as an Aid to Stress Resistance Among Troops," *Military Medicine* 154:144-146.

Wurtman, R. J. et al. (1991). "Exercise, Plasma Composition, and Neurotransmission," *Advances in Nutrition and Top Sport Sci.* 32:94-109.

Applegate, L. (1998). "Beating the Brain Drain," *Runner's Worlds*, www.runnersworld.com/nutrition/nubrainfood.html (Total of 4 pp.).

Elwes, R. D. C., et al. "Treatment of Narcolepsy with L-Tyrosine: Double-Blind Placebo-Controlled Trial," *The Lancet*, pp. 1067-1069, Nov. 1989.

Lehnert, H., et al. (1993). "Amino Acid Control of Neurotransmitter Synthesis and Release: Physiological and Clinical Implications," *Psychother. Psychosom.* 60:18-32.

Lou, H. C. et al. (1987). "Increased Vigilance and Dopamine Synthesis by Large Doses of Tyrosine or Phenylalanine Restriction in Phenylketonuria," *Acta. Paediatr.Scand.* 76:560-565.

Maddrey, W. C., et al. (1976). "Effects of keto analogues of essential amino acids in portal-systemic encephalopathy," *Gastroenterology* 71:190-5 (abstract only) (Total 1 p.).

Druml, W., et al. (1989). "Phenylalanine and tyrosine metabolism in renal failure: dipeptides as tyrosine source," *Kidney Int. Suppl.* 27:S282-6 (abstract only) (Total 1 p.).

Fernandez-Lopez, J. A., et al. (1992). "Rat intestinal amino acid balances after the administration of an oral protein load," *Biochem. Int.* 26:297-308 (abstract only) (Total 1 p.).

Stehle, P. (1988). "Need-related availability of short-chain peptides—a prerequisite for their use in artificial feeding," *Infusionstherapie* 15:27-32 (abstract only) (Total 1 p.).

Martin-DuPan, R., et al. (1982). "Effect of Various Oral Glucose Doses on Plasma Neutral Amino Acid Levels," *Metabolism* 31:937-943.

Mauron, C., et al. (1982). "Co-Administering Tyrosine with Glucose Potentiates Its Effect on Brain Tyrosine Levels," *J. Neural Transmission* 55:317-321.

Reinstein, D. K., et al. (1985). "Dietary Tyrosine Suppresses the Rise in Plasma Corticosterone Following Acute Stress in Rats," *Life Sciences* 37:2157-2163.

(List continued on next page.)

Primary Examiner—Raymond Henley, III
(74) Attorney, Agent, or Firm—Rothwell, Figg, Ernst & Manbeck

(57) **ABSTRACT**

The base compound for practicing the present invention is L-tyrosine effervescent powder, granules or tablet. Soluble effervescent powders, granules and tablets are prepared by blending and/or compression and contain, in addition to active ingredients mixtures of acids (citric acid, tartaric acid) and sodium bicarbonate, which release carbon dioxide when dissolved in water. They are intended to be dissolved or dispersed in water before administration. Effervescent powders, granules and tablets should be stored in tightly closed containers or moisture-proof packs, labeled to indicate that they are not to be swallowed directly.

19 Claims, No Drawings