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Konishi

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(54) **BIOACTIVATING SUBSTANCE**

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(56) **References Cited**

U.S. PATENT DOCUMENTS

4,089,883	A	5/1978	Blount
4,863,518	A	9/1989	Blount
4,985,254	A	1/1991	Konishi et al.
4,985,354	A	1/1991	Toyomaki et al.
5,013,558	A	5/1991	Konishi
5,057,324	A	10/1991	Shibayama et al.
5,534,509	A	7/1996	Konishi et al.
5,560,935	A	10/1996	Konishi et al.
5,658,896	A	8/1997	Konishi et al.
5,807,951	A	9/1998	Konishi et al.
6,051,613	A	4/2000	Ohno et al.
6,165,515	A	* 12/2000	Matsuyama et al. 424/520

FOREIGN PATENT DOCUMENTS

EP	0 300 973	1/1989
EP	0 315 591	5/1989
EP	0341209 A2	11/1989
EP	0 348 353 A2	12/1989
EP	0 621 038 A1	10/1994
EP	0 645 142 A1	3/1995
EP	0 953 352 A1	11/1999
GB	697351	9/1953
JP	53-101515	9/1978
JP	57-77697	5/1982
JP	58-035117	3/1983
JP	63/025600	5/1988
JP	63/039572 B	8/1988
JP	03/043279	7/1991
JP	2594222	12/1996
WO	WO 93/08828	5/1993

OTHER PUBLICATIONS

Takeoka, Y. et al., "Influence of Neurotrophin on Thymic Microenvironmental Abnormalities of NZB Mice," *Int. J. Immunotherapy*, XI(2), pp. 49-56 (1995).
"Drugs in Japan, Ethical Drugs," Yakugyo Jiho Co., Ltd., 1994, p. 1434-1435.

Yokoi et al., "Effect of Degree of Polymerization of Silicic Acid on the Gastrointestinal Absorption of Silicate in Rats," *Chem. Pharm. Bull.*, vol. 27, No. 8, 1979, pp. 1733-1739. Derwent Publications Ltd., London, GB: AN 82-10241J, "Drug For Cultivated Fish," & JP A57183720 (Mitani J.), Nov. 12, 1982, abstract.

"Remedy For Burn," *Patent Abstracts of Japan*, vol. 7, No. 255 (C-189), Oct. 6, 1983, & JPA58121217 (Kagitani Takeo) Jul. 19, 1983, abstract.

"Drug for Food Poisoning," *Patent Abstracts of Japan*, vol. 11, No. 371 (C-462), Dec. 3, 1987 & JPA62145022 (Sofuto Shirika) Jun. 29, 1987, abstract.

"Adsorbent For Peroxylipid," *Patent Abstracts of Japan*, vol. 15, No. 474 (C-890), Dec. 3, 1991 & JPA3204803 (Shiscido Co., Ltd.) Sep. 6, 1991, abstract.

The Merck Index, 9th ed. 1976, No. 7456, 8443, 8233-8243 & 5514-5515.

Section CH, Week 9645, Derwent Publications Ltd., Class B04, AN 96-450925 XP002109698 & JP 08 225452 A, Sep. 3, 1996, abstract.

De Reuck J., et al., "A double-blind study of neurotrophin in patients with acute ischemic stroke," *ACTA Neurologica Scandinavica* vol. 89, No. 5, 1994, pp. 329-335, XP002109696.

Sprumont, et al., "Morphometrical Quantification of Brain Edema Related to Experimental Multiple Micro-Infarcts in Mice: Assessment of Neurotrophin Effect," *Meth Find Exp Clin Pharmacol* 1993, 15(3): 169-177, XP002109697.

Database BIOSIS, XP-002113089, Li S-Y, et al. Studies on the Protective Action of Silicon Compound of Equisetum Against Experimental Liver Injury in Rats and Mice & Zhongguo Yaolixue Yu Dulixue Zazhi. ISSN: 1000-3002, abstract.

* cited by examiner

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(57) **ABSTRACT**

A highly active bioactivating substance which exhibits suppressing action on histamine liberation and inhibition of hyaluronidase activity may be obtained by adding a silicate to an extracted substance from tissues activated by adding internal or external stressors to animals or animal tissues such as infecting with poxvirus. The highly active bioactivating substance may also be obtained by performing a special extraction to effect a high content of silicic acid in the extracted substance from the activated tissues. The bioactivating substance may be in the form of a powder and may have a silicon component content which is more than 20 μg , for example greater 22 μg , preferably greater than 25 μg , calculated as silicon per mg of dried substance. The powder may be obtained by admixing an extract from activated tissue, which extract contains at least one silicon component, with at least one additional silicon component to obtain a mixture, and drying the mixture to obtain a powder which exhibits positive color reactions to amino acid (by a ninhydrin reaction), saccharide (by an orcinol-iron (III) chloride-hydrochloric acid method), phosphorus (by a molybdenum blue method) and silicic acid (by a molybdenum blue method), and negative qualitative reactions to protein (by a trichloroacetic acid method) and phenol (by a ferric chloride method).

20 Claims, No Drawings