



DEPARTMENT OF HEALTH & HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION


Public Health Service

Memorandum

Date . FEB 25 2000 1504 '00 FEB 23 P2:10
From Senior Regulatory Scientist, Regulatory Branch, Division of Programs & Enforcement Policy
(DPEP), Office of Special Nutritionals, HFS-456
Subject 75-day Premarket Notification for New Dietary Ingredient
To Dockets Management Branch, HFA-305

New Dietary Ingredient: Proia cocos wolf.
Cuscuta epithimum
Rehmannia glutinosa Libosch.
Radix astragali
Cornus officinalis
Lygodium japonicum Sw.
Ground tortoise shell
Ground antelope horn
Firm: Mr. Gongjun Ji
Date Received by FDA: February 22, 2000
90-day Date: May 21, 2000

In accordance with the requirements of section 413(a)(2) of the Federal Food, Drug, and Cosmetic Act, the attached 75-day premarket notification for the aforementioned new dietary ingredient should be placed on public display in docket number 95S-0316 after May 21, 2000.


Robert J. Moore, Ph.D.

95S-0316

RPT 64



FEB 24 2000

Mr. Gongjun Ji
415 West 115th Street, #42
New York, New York 10025

Dear Mr. Ji:

This is in response to your letter to the Food and Drug Administration (FDA) dated February 11, 2000, making a submission for a new dietary ingredient pursuant to 21 U.S.C. 350b(a)(2) (section 413 of the Federal Food, Drug, and Cosmetic Act (the Act)) and 21 CFR 190.6. Your letter notified FDA of your intent to market a product containing substances that you assert are new dietary ingredients: *Proia cocos* wolf., *Cuscuta epithymum*, *Rehmannia glutinosa* Libosch., Radix Astragali, *Cornus officinalis*, *Lygodium japonicnm* Sw., ground tortoise shell, and ground antelope horn.

Under 21 U.S.C. 350b(a), the manufacturer or distributor of a dietary supplement that contains a new dietary ingredient that has not been present in the food supply as an article used for food in a form in which the food has not been chemically altered must submit to FDA, at least 75 days before the dietary ingredient is introduced or delivered for introduction into interstate commerce, information that is the basis on which the manufacturer or distributor has concluded that a dietary supplement containing such new dietary ingredient will reasonably be expected to be safe. FDA reviews this information to determine whether it provides an adequate basis for such a conclusion. Under section 350b(a)(2), there must be a history of use or other evidence of safety establishing that the new dietary ingredient, when used under the conditions recommended or suggested in the labeling of the dietary supplement, will reasonably be expected to be safe. If this requirement is not met, the dietary supplement is deemed to be adulterated under 21 U.S.C. 342(f)(1)(B) because there is inadequate information to provide reasonable assurance that the new dietary ingredient does not present a significant or unreasonable risk of illness or injury.

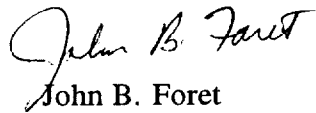
Your submission contained information that you believe establishes that the new dietary ingredients named above, when used under the conditions recommended or suggested in the labeling of the dietary supplement, will reasonably be expected to be safe. The information in your submission does not meet the requirements of 21 CFR 190.6 because it does not include reprints or photostatic copies of references to published information offered in support of the notification (see 21 CFR 190.6(b)(4)). The submission also does not describe the conditions of use recommended or suggested in the labeling of the dietary supplement, or the ordinary conditions of use of the supplement (see 21 CFR 101.90(b)(3)(ii)).

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If you market your product without submitting an amended notification that meets the requirements of 21 CFR 190.6, or less than 75 days after submitting such a notification, your product is considered adulterated under 21 U.S.C. 342(f)(1)(B) as a dietary supplement that contains a new dietary ingredient for which there is inadequate information to provide reasonable assurance that such ingredient does not present a significant or unreasonable risk of illness or injury. Introduction of such a product into interstate commerce is prohibited under 21 U.S.C. 331(a) and (v).

Please contact us if you have any questions concerning this matter.

Sincerely,

A handwritten signature in cursive script that reads "John B. Foret".

John B. Foret

Director

Division of Compliance and Enforcement

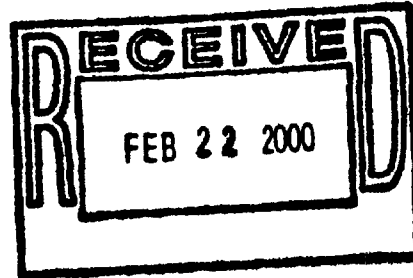
Office of Nutritional Products, Labeling,

and Dietary Supplements

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February 11, 2000

Robert J. Moore, Ph.D.
Senior Regulatory Scientist
Office of Special Nutritionals
Department of Health & Human Services
Food and Drug Administration
Washington, DC 20204



Dear Dr. Moore:

Thank you very much for your letter dated January 11, 2000 responding my inquire about marketing a dietary supplement product in the United States. I contacted Mr. Michael McGuffin, President of American Herbal Products Association, and he informed me that the new edition of "Herbs of Commerce", which I trust to be a reliable source for herbal products marketed in the U.S., will be available in the next two months. I would like to proceed with my application as soon as possible and I collected references for the eight ingredients. Those references include many books written by medical professionals and articles published by medical researchers. They are published in the United States, Europe, China and Japan. They described and discussed extensive human use of the herbal ingredients and I believe the references can substantiate my claim that the herbs are reasonably safety. Many of the references also discussed therapeutic use of the herbals. However, I do not claim any medical use of those ingredients and only would like to use the research results as proof that they are reasonably safe for human consumption. Please let me know if those references are sufficient to satisfy the safety requirement established by the FDA guidelines.

Furthermore, I received a letter from Department of Interior, Fish and Wildlife Service. There is no objection for the animal extracts included in the dietary supplement from that office. Instead the Service informed me the procedure to import the extracts in the future.

Please let me know if you need any further information.

Sincerely,

Gongjun Ji

This dietary supplement product "Metelline" constitutes the following eight herbs:

1. Proia cocos wolf. (pochymacocos Frios., India Bread) 18.75% (0.94g)
2. Cuscuta Epithymum (Dodder seed) 18.75% (0.94g)
3. Radix Rehmanniae (Rehmannia Glutinosa Libosch.) (Chinese Foxglove Root) 18.75% (0.94g)
4. Radix Astragali (Milkvetch Root) 9.375% (0.47g)
5. Cornus officinalis (Fructus Corni, asiatic cornelian, cherry fruit) 9.375% (0.47g)
6. Lygodium japonicnm Sw. (Spora Lygodii) 9.375% (0.47g)
7. Grounded form of tortoiseshell 9.375% (0.47g)
8. Grounded form of antelope's horn 6.25% (0.3g)

Manufacturing process: ingredients No 1 to 6 are plant's root, seed or spora. They are dried and grounded into powders. Ingredients No 7 & 8 are animals' extracts, they are dried and grounded into powders. The powders are mixed according the weight percent and the mixture is packed in capsules.

Claim: Metelline is beneficial to persons who have kidney problems. It provides minerals and vitamins.

1. Poria cocos wolf. (Pochymacocos Fries, India Bread)**DESCRIPTION:**

The dried sclerotium of the fungus *Poria cocos* (Schw.)Wolf (Polyporaceae).

REFERENCES:

1. McGuffin, M., Hobbs, C., Upton, R., and Goldberg, A. (1997). *American Herbal Products Association's Botanical Safety Handbook*, pp.124. Boca Raton, Fla.: CRC Press
2. Reid, D. (1995) *A Handbook of Chinese Healing Herbs*, pp.188-190. Boston : Shambhala
3. Evans, W.C. (1996) *Trease and Evans' pharmacognosy*, pp.508. London: WB Saunders
4. Zhu, You-Ping (1998) *Chinese Materia Medica*, pp.311-313. The Netherlands: Harwood Academic Publishers
5. Huang, Kee Chang. (1999) *The Pharmacology of Chinese Herbs*, 2nd Ed. pp. 156-157. Boca Raton: CRC Press
6. Fan, W. (1996) *A manual of Chinese herbal medicine: principles and practice of easy reference*, pp.220. Boston : Shambhala
7. *Recent Advances in the Pharmacology of Kampo (Japanese herbal Medicines: Poceedings of the Satellite Meeting on Kampo (Japanese Herbal) Medicines of the 10th International Congress of Pharmacology, Auckland, New Zealand, August 19-21, 1987*, pp.150-154, 155-162. Amsterdam : Excerpta Medica ; New York, NY: Elsevier Science Pub. Co.
8. Zhou, R.H. (1993) *Resources Science of Chinese Medicinal Materials*, pp. 163-168. Beijing: China Medical & Pharmaceutical Sciences Press
9. Yin, J., Guo, L.G. (1993) *Modern Research and Clinical Applications of Chinese Materia Medica (1)*, pp. 489-492. Beijing: Academic Publisher
10. Kaminaga, T., Yasukawa, K., Takido, M., Tai, T, Nunoura, Y. (1996) Inhibitory effect of *Poria cocos* on 12-O-tetradecanoylphorbol-13-acetate-induced ear oedema and tumour promotion in mouse skin. *Phytotherapy Research*, **10**, 581-584
11. Wang, Y.S. (1983) *Pharmacology and Applications of Chinese Materia Medica*, pp. 767-770. Beijing: People' Health Publisher

2. *Cuscuta Epithimum*, Semen *Cuscutae* (Dodder Seed)

DESCRIPTION:

The dried ripe seed of *Cuscuta chinensis* Lam. (Convolvulaceae). The plant is collected in the autumn when the fruit is ripe and dried in the sun. The seed is then removed from the fruit.

REFERENCES:

1. McGuffin, M., Hobbs, C., Upton, R., and Goldberg, A. (1997). *American Herbal Products Association's Botanical Safety Handbook*, pp.39. Boca Raton, Fla.: CRC Press
2. Reid, D. (1995) *A Handbook of Chinese Healing Herbs*, pp.103-104. Boston : Shambhala
3. Huang, Kee Chang. (1999) *The Pharmacology of Chinese Herbs*, 2nd Ed. pp. 311. Boca Raton: CRC Press
4. Zhu, You-Ping (1998) *Chinese Materia Medica*, pp.619-621. The Netherlands: Harwood Academic Publishers
5. Fan, W. (1996) *A manual of Chinese herbal medicine: principles and practice of easy reference*, pp.192. Boston : Shambhala
6. Yin, J., (1995) *Modern Research and Clinical Applications of Chinese Materia Medica (2)*, pp. 330-332. Beijing: Chinese Medical Classics Press
7. Yahara, S., Domoto, H., Sugimura, C., Nohara, T., Niiho, Y., Nakajima, Y., et al. (1994) An alkaloid and two lignans from *Cuscuta chinensis*. *Phytochemistry*, **37**, 1755-1757
8. Miyahara, K., Du, X.M., Watanabe, M., Sugimura, C., Yahara, S., Nohara, T. (1996) Resin glycosides. XXIII. Two novel acylated triaccharides related to resin glycoside from the seeds of *Cuscuta chinensis*. *Chemical and Pharmaceutical Bulletin*, **44**, 481-485
9. Nisa, M. Akbar, S., Tariq, M., Hussain, Z. (1986) Effect of *Cuscuta chinensis* water extract on 7, 12-dimethylbenz(a)anthracene-induced skin papillomas and carcinomas in mice. *Journal of Ethnopharmacology*, **18**, 21-31

3. Radix Rehmanniae (Rehmannia Glutinosa Libosch.) (Chinese Foxglove Root)

DESCRIPTION:

The dried root tuber of Rehmannia glutinosa Libosch. (Scrophulariaceae). The herb is collected in autumn, removed from crowns and fibrous roots and then baked to nearly dry.

REFERENCES:

1. McGuffin, M., Hobbs, C., Upton, R., and Goldberg, A. (1997). *American Herbal Products Association's Botanical Safety Handbook*, pp.95. Boca Raton, Fla.: CRC Press
2. Foster, S. and Yue, C. (1992) *Herbal Emissaries*, pp. 127-134. Rochester, Vt.: Healing Arts Press
3. Zhu, You-Ping (1998) *Chinese Materia Medica*, pp.157-161. The Netherlands: Harwood Academic Publishers
4. Evans, W.C. (1996) *Trease and Evans' pharmacognosy*, pp.509. London: WB Saunders
5. Reid, D. (1995) *A Handbook of Chinese Healing Herbs*, pp.170-171. Boston : Shambhala
6. Fan, W. (1996) *A manual of Chinese herbal medicine: principles and practice of easy reference*, pp.223. Boston : Shambhala
7. Huang, Kee Chang. (1999) *The Pharmacology of Chinese Herbs*, 2nd Ed. pp. 375-376. Boca Raton: CRC Press
8. *Recent Advances in the Pharmacology of Kampo (Japanese herbal Medicines): Pceedings of the Satellite Meeting on Kampo (Japanese Herbal) Medicines of the 10th International Congress of Pharmacology, Auckland, New Zealand, August 19-21, 1987*, pp. 291-319, 336-344. Amsterdam : Excerpta Medica ; New York, NY: Elsevier Science Pub. Co
9. Kitagawa, I., Nishimura, T., Furubayashi, A. Yosioka, I. (1971) Constituents of rhizome of *Rehmannia glutinosa* f. *hueichingensis*. *Yakugaoku Zasshi*, **91**, 593-596
10. Oshio, H. Inouye, H. (1981) Iridoid glycosides of *Rehmannia gluconosa*. *Phytochemistry*, **21**, 133-138.
11. Kitagawa, I., Fukuda, Y., Taniyama, T., Yoshikawa, M. (1986) Absolute stereostructures of rehmaglutins A, B, and D, three new iridoid isolated from Chinese rehmanniae radix. *Chemical and Pharmaceutical Bulletin*, **34**, 1399-1402

12. Nishimura, H., Sasaki, H., Morota, T., Chin, M., Mitsuhashi, H. (1989) Six iridoid glycosides from *Rehmannia glutinosa*. *Phytochemistry*, **28**, 2705-2709
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14. Yoshikawa, M., Fukud, Y. Taniyama, T., Kitagawa, I. (1986) Absolute stereostructures of rehmaglucin C and glutinoside, a new iridoid glucoside from Chinese rehmanniae radix. *Chemical and Pharmaceutical Bulletin*, **34**, 1403-1406
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16. Bubi, M. Asano, T. Shiomoto, H., Matsuda, H. (1994) Studies in Rehmanniae Radix. I. Effect of 50% ethanolic extract from steamed and dried Rehmanniae Radix on hemorheology in arthritic and thrombotic rats. *Biological and Pharmaceutical Bulletin*, **17**, 1282-1286
17. Wu. B.J. (1983) *Pharmacology of Chinese Herbal Medicines*, pp.222. Beijing: People's Health Publisher

4. Radix Astragali (Milkvetch Root)

DESCRIPTION:

The dried root of *Astragalus membranaceus* (Fisch.) Bge. Var. *mongholicus* (Bge.) Hsiao or *Astragalus membranaceus* (Fisch.) Bge. (Leguminosae). The root is collected in the spring and autumn, removed from fibrous roots and rootstock, and dried in the sun.

REFERENCES:

1. McGuffin, M., Hobbs, C., Upton, R., and Goldberg, A. (1997). *American Herbal Products Association's Botanical Safety Handbook*, pp.17. Boca Raton, Fla.: CRC Press
2. Reid, D. (1995) *A Handbook of Chinese Healing Herbs*, pp.63-65. Boston : Shambhala
3. Huang, Kee Chang. (1999) *The Pharmacology of Chinese Herbs*, 2nd Ed. pp. 386-387. Boca Raton: CRC Press
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Astragalus membranaceus Bunge. 3. Astragalosides III, V and VI.
Chemical and Pharmaceutical Bulletin, **31**, 709-715

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14. Zhou, R.H. (1993) *Resources Science of Chinese Medicinal Materials*, pp. 311-317. Beijing: China Medical & Pharmaceutical Sciences Press
15. Zhou, Q.J. (1980) Chinese medicinal herbs in the treatment of viral hepatitis. In *Advances in Chinese Medicinal Materials Research*, pp.215-219. Singapore: World Scientific

5. *Cornus officinalis* (Fructus Corni) (Asiatic Cornelian Cherry Fruit)

DESCRIPTION:

The dried ripe sarcocarp of *Cornus officinalis* Sieb. Et Zucc. (Cornaceae). The fruit is collected in late autumn and early winter. It is then removed from the kernel and dried.

REFERENCES:

1. McGuffin, M., Hobbs, C., Upton, R., and Goldberg, A. (1997). *American Herbal Products Association's Botanical Safety Handbook*, pp.37. Boca Raton, Fla.: CRC Press
2. Zhu, You-Ping (1998) *Chinese Materia Medica*, pp.668-670. The Netherlands: Harwood Academic Publishers
3. Reid, D. (1995) *A Handbook of Chinese Healing Herbs*, pp.104-105. Boston : Shambhala
4. Fan, W. (1996) *A manual of Chinese herbal medicine: principles and practice of easy reference*, pp.190-191. Boston : Shambhala
5. Yin, J., Guo, L.G. (1993) *Modern Research and Clinical Applications of Chinese Materia Medica* (1). Pp.96-99. Beijing: Academic Publisher
6. Zhou, R.H. (1993) *Resource Science of Chinese Medicinal Materials*, pp. 364-370. Beijing: China Medical & Pharmaceutical Sciences Press
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8. Hatano, T., Yasuhara, T., Okuda, T. (1989) Tannins of cornaceous plants. II. Cornusiins D, E and F, new dimeric and trimeric hydrolyzable tannis from *Cornus officinalis*. *Chemical and Pharmaceutical Bulletin*, 1989, 37, 2665-2669
9. Hatano, T., Yasuhara, T., Abe, R. Okuda, T. (1990) A galloylated monoterpene glucoside and a dimeric hydrolysable tannin from *Cornus officinalis*. *Phytochemistry*, 29, 2975-2978

6. Spora Lygodii (Lygodium Japonicnm)

DESCRIPTION:

The dried seeds of *Lygodium Japonicnm*

REFERENCES:

1. Fan, W. (1996) *A manual of Chinese herbal medicine: principles and practice of easy reference*, pp.207. Boston : Shambhala

7. Grounded Tortoise-shell

8.Saifa Tatarica

DESCRIPTION: Grounded Antelope Horn

REFERENCES:

1. Huang, Kee Chang. (1999) *The Pharmacology of Chinese Herbs*, 2nd Ed. pp. 376-377. Boca Raton: CRC Press
2. Fan, W. (1996) *A manual of Chinese herbal medicine: principles and practice of easy reference*, pp.225. Boston : Shambhala