



JAN 9 1997

Mr. Fu Sheng Jin  
Chinese Herb Center, Inc.  
2025 I Street NW, Suite 507  
Washington, DC 20006

Dear Mr. Jin:

This is in response to your letter of November 5, 1996 to Dr. Elizabeth Yetley at the Food and Drug Administration (FDA). Your letter is in reference to a dietary supplement product, "Hawthorn Capsules."

Your letter requested a "certificate of free sale" that you interpret to mean "permission to import to the United States of America." A "certificate of free sale" is not required for a product to be imported into the United States. Certificates of free sale are issued for products produced in the United States that are to be exported for sale in other countries. Dietary supplements (except for their ingredients that are not dietary ingredients or that are color additives) do not require premarket review or approval from FDA before they can be imported for sale in the United States.

Your letter also appears to be intended to constitute the notification required by section 413(a)(2) of the Federal Food, Drug, and Cosmetic Act (the act). A notification under section 413(a)(2) of the act is only required if you intend to market a "new dietary ingredient." A "new dietary ingredient" is defined in section 413(c) of the act as a "dietary ingredient that was not marketed in the United States before October 15, 1994 and does not include any dietary ingredient which was marketed in the United States before October 15, 1994." Your letter indicates that this product was marketed in the United States before October 15, 1994. If this is true, a notification under section 413(a)(2) of the act is not required for this product.

Your letter further appears to be the notification required by section 403(r)(6) of the act notifying the agency that you intend to make a statement of nutritional support for Hawthorn Capsules. The label for your product, "Hawthorn (Shan Zha) Cholest-Down" shows that you are making the following statement for this product.

"May help to decrease Cholesterol and Triglyceride."

This claim does not come within the coverage of section 403(r)(6) of the act. We would point out the section 403(r)(6) of the act makes clear that a statement included in labeling under the authority of that section may not claim to diagnose, mitigate, treat, cure, or

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**Page 2 - Mr. Fu Sheng Jin**

prevent a specific disease or class of diseases. The statement that you are making for this product suggests that it is intended to prevent, treat, or mitigate heart disease, in that it claims that it "may help to decrease cholesterol and triglycerides."

A product that claims to "help decrease cholesterol and triglycerides," but is not used in the context of dietary management, is a drug within the meaning of section 201(g)(1)(B) of the act, and is subject to regulation under the drug provisions of the act. If you intend to make a claim of this nature, you should contact FDA's Center for Drug Evaluation and Research (CDER), Office of Compliance, HFD-310, 7520 Standish Place, Rockville, Maryland 20855.

Please contact us if we may be of further assistance.

Sincerely yours,

James Tanner, Ph.D.  
Acting Director,  
Division of Programs and  
Enforcement Policy  
Office of Special Nutritionals  
Center for Food Safety  
and Applied Nutrition

**Copies:**

FDA, Center for Drug Evaluation and Research, Office of Compliance, HFD-300  
FDA, Baltimore District Office, Office of Compliance, HFR-MA200  
FDA, Office of the Associate Commissioner for Regulatory Affairs, Office of  
Enforcement, HFC-200

RECEIVED BY THE  
OFFICE OF SPECIAL  
NUTRITIONALS, HFS-450

'96 NOV 12 P2:32

Nov, 5, 1996  
Mr. Fu Sheng Jin  
Chinese Herb Center, Inc.  
2025 I Street NW Suite 507  
Washington DC 20006  
Tel: (202)775-1108

Dr. Elizabeth Yetley  
Office of Special Nutrition  
HFS-450  
200 C Street, S. W.  
Washington, D. C. 20204

Dear Dr. Elizabeth Yetley:

According to "Dietary Supplement Health and Education Act of 1994" Public Law 103-417, Now I write a petitioner about hawthorn capsule (dietary supplement) to notice of structure/ function class for 30 days post-market. Also I want to get "certificate of free sale" permission to import to the United States of America. Although it has been delivered to the United State of America before October 15, 1994, we need to revise the "hawthorn capsules" labeling again.

Hawthorn Capsules  
Manufactured by Sanming Pharmaceutical factory, Fujing, China  
Distributed by Chinese Herb Center, Inc.

I included following data for hawthorn capsule for you check it, If you have any questions, Please tell me or write a letter to above address.

Sincerely Yours

Manager Mr. Fu Sheng Jin

Fu Sheng Jin

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## A petitioner to FDA about Hawthorn capsule

### A. Identity; Composition; Physical, Chemical and Organoleptic Characteristics

1. Name of Dietary supplement
  - a. Chemical name: Crataegus Pinnatifida Bge
  - b. Common name: Hawthorn Berry extract powder
  - c. CAS registry number: not available
  
2. Chemical identity:
  - a. Structure formula: not available
  - b. Molecular weight: not available
  - c. Molecular formula: not available
  
3. Organoleptic properties:
  - a. Appearance: powder
  - b. Color: brown
  - c. Taste: not sour
  
4. Physical and Chemical properties:
  - a. pH: ND
  - b. Melting point: ND
  - c. Water content: 1.3%
  - d. Solubility: soluble in alcohol and in water.
  - e. Specifications:

Hawthorn extract is manufactured by Sanming Pharmaceutical factory. They sent 30 samples of hawthorn extract powder (the batch number 940105) for analysis, and they received the certification from the Department of Environmental Health, Fujian, China. The average data measured per capsule are listed below.

(1) Content:

(a) Nutrition facts:

Serving size-1 capsule (contains 125 mg); Server per capsule

Amount per serving

Calories 0.6                      Calories from fat 0.2

		DRYS	% Daily value*
Total Fat	25.0mg	65g	0.04%
Cholesterol	0.00		
Sodium	1.0ng	24mg	0.04%
Total carbohydrate	90.0mg	300g	0.03%
Protein	1.7mg	50g	0.003%
Soft fiber	4.5mg	25g	0.02%
Vitamin A 3.0mg		Vitamin C -	
Biotin		Riboflavin -	
Niacin 6.5ug		Vitamin B6 -	
Vitamin E 0.5mg		Zinc 1.6ug	
Calcium 6.8ug		Iron 8.0ug	

\* Percent daily values are based on a 2,000 caloric

(b) Average amount of nutrition facts in one of 30 samples of the Hawthorn extract powder.

Reduce sugar	0.42%	Total sugar	2.8%	Carbohydrate	72.0%
Protein	1.4%	Fat	20.0%		
Fiber	3.6%	Cholesterol	0.00	others	3.0%

(c) Average metals contain in one of 30 sample of the Hawthorn extract powder

Sodium	0.01 mg/g	Calcium	0.06mg/g	Iron	0.07mg/g
Phosphorus	0.5mg/g	Magnesium	0.01mg/g	Zinc	0.01mg/g
Copper	0.02mg/g	Iodine	2.00ug/g	Potassium	0.75mg/g

(d) Average vitamin contain in one of 30 samples of the Hawthorn extract powder

Carotene	0.3mg/100g	Vitamin C	11.7mg/100g	Vitamin B1	0.1mg/100g
Niacin	54.0ug/g	Vitamin A	24.0 mg/g	Vitamin D	0.4mg/g
Vitamin E	4.0mg/g				

(e) Average amount of impurities, toxins and pesticides in one of 30 sample of the Hawthorn extract powder

Heavy metal	Lead (Pb)	1.1ug/g
	Arsenic (As)	0.018 mg/kg
	Cadmium (Cd)	0.0003mg/g
	Mercury (Hg)	268ug/g
Others	Nitrite	278ppg
	Nitrate	20.0ppg

(f) Other toxins

Aflatoxin B1 < 5ppb

Mycotoxin: Not to be found in the 30 samples of hawthorn extract powder.

(g) No contaminated pesticides such as 666 and DDT in 30 sample of the hawthorn extract powder.

The amount of impurities and toxins and pesticides measured are lower than that specified in the FDA standard

(2) Components:

The hawthorn extract powder contains crataegolic acid and some flavore, triterpene acid, and unsaturated fat acid such as oleanolic acid, and linoleic acid.

Method of measurement used in above tests:

1. Total Carbohydrate is measured by Ferriecyanide reduction method, method 939.03.
2. Protein is measured by Kjeldahl method, method 955.04D.
3. Total fat is measure by ether extraction method, method 960.39.
4. Other metals in hawthorn extract powder (plant) are measured by following methods:
  - Sodium, Phosphorus, Calcium (method 980.03)
  - Iron (method 975.03)
  - Magnesium (method 975.03)
  - Zinc (method 975.03)
  - Potassium (method 985.35)
  - Copper (method 975.03),
5. Cadmium, Lead, and Mercury are measured by atomic absorption spectrophotometric method.
6. Iodine is measured by bromide oxidation method.
7. Arsenic is measured by Silver salt methods.
8. Vitamin A, Vitamin E, Vitamin D, Vitamin B6, Vitamin B2, Vitamin B12, Niacin, Pantothenic acid, and Folic acid are measured by high pressure liquid chromatographic method.
9. Carotene is measured by Spectrophotometric method. (method 941.15)
10. Vitamin C is measured by 2,6-dichloroindophenol Titrimetric method. (method 967.21)
11. Nitrite is measured by naphthalene hydrochloric acid diamino ethylene method.
12. Nitrate is measured by cadmium-platinum reduction method.
13. Aflatoxin B1 is measured by thin layer chromatographic method.
14. 666, DDT, and organic phosphorus are measured by gas chromatographic method.

All data have been certified by the Department of Public Health, Fujian Medical University.  
All nutritional indexes of method numbers have been referenced from "the methods of analysis for nutrition labeling,"  
1993 by AOAC INTERNATIONAL.

**B. Intended use; projected average daily intake of hawthorn; proposed labeling**

**1. Amount of hawthorn extract proposed for use in the United States**

Projected marketing figures for hawthorn have not been determined at this time.

**2. Intended usage**

Hawthorn extract capsule is intended for use as a dietary supplement to help lower serum cholesterol and triglyceride.

**3. Calculation of expected intake and daily consumption of hawthorn extract powder:**

From information given by Sanming Pharmaceutical factory, the capsule is to be taken three times a day, one capsule each time. Each capsule weights 120 mg, and this projects a daily consumption of 360mg and yearly consumption of 131.0 g for an adult.

**4. Labeling**

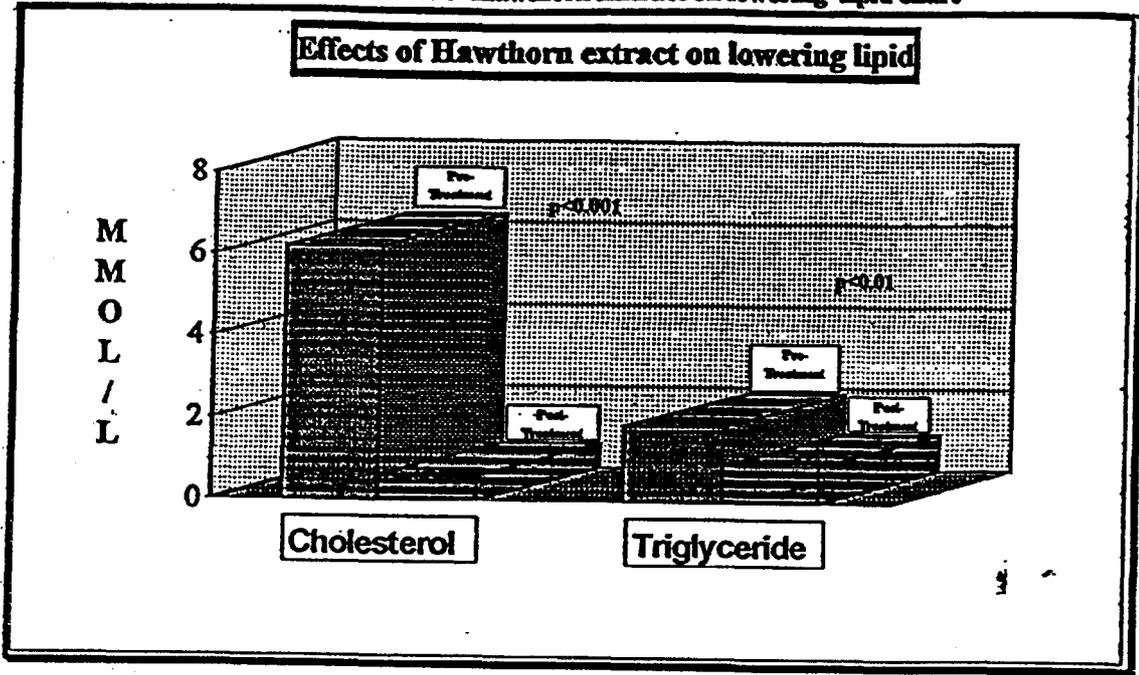
<p><b>Recommended use</b> Take 1 capsules after meal 3 times a day.</p> <p><b>INGREDIENTS:</b> Each capsule contains 120 mg hawthorn extract powder. Store at a cool &amp; dry location</p> <p>No artificial color, flavors or preservatives are added. No additives, fillers, or irradiated Herbs are used.</p> <p>Patent No. 871079801 Batch No: MFG date:</p>  <p>6 905817 4201390</p>	<p><b>100% Natural Chinese Herbs</b></p> <p><b>Hawthorn (Shan Zha) Cholest-Down</b> May help to decrease Cholesterol and Triglyceride* 100 Caps (120 mg each)</p> <p>Manufactured by Sanming Pharmaceutical factory, Fujian, China Distributed by Chinese Herb Products, Inc. 2025 Eye Street, NW Suite 507, Washington, DC 20006</p> <p>Like all natural generated products, appearance may vary from batch to batch. **This statement has not been evaluated by the Food and Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.**</p>
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**C. The Method and result of intended Effect**

32 patients presents hyperlipemia with average serum cholesterol greater than 6.2mmol/L and triglyceride greater than 1.84 mmol/L. Two measurements were taking during an one month trial period. Results are listed below:

32 patients with hyperlipemia before and after administrating hawthorn				
Item	Total Serum Cholesterol n=32		Serum Triglyceride n=32	
	Before	After	Before	After
P value	p<0.001		p<0.01	
X+/- S	6.2+/-0.5	0.597+/-1.0	1.84+/-0.4	1.91+/- 1.4

Chart #1 Effect of Hawthorn Extract on lowering lipid chart \*



Intended effect was established by above test results performed by the manufacturer. For the control group, there is no significant difference in blood cholesterol and triglyceride before and after the treatment. \*Above data has not been evaluated by the Food and Drug Administration now.

## E. Safety investigations (toxicological studies)

### 1. Overall toxicity:

As early as the 16th century, the most famous Chinese pharmacist, Shi Zhen Li, used hawthorn berry to treat patients for "food stagnancy and blood stasis," ailment caused by excessive dietary fat. This treatment has been kept till today and its efficacy is further improved by modern scientific studies. (See chart #1 and reference). Hawthorn berry (*Crataegus pinnatifida*) is a wild, fruit-bearing tree growing in China, England and North America. Its berry with a sour and sweet tastes is considered to be both a fruit and a herb. Eating raw hawthorn berries has an obvious disadvantage, the most notable is its acidity which causes stomach up-set. Now Sanming hawthorn extract is manufactured with an unique process that preserves and concentrates the richest crataegolic acid of fresh hawthorn berry. Already there are over millions people in the world taking Sanming hawthorn extract every day. Also Sanming hawthorn extract is delivered to many parts of the world, such as Europe, Africa, America, Canada and Australia, etc., and people's responses to this product have been extraordinary due to its effectiveness and safety. Also it has been delivered to the United States of America before October 15, 1994. Therefore it is considered as GRAS.

According to reports based on research experiments using 5% alcohol extracts derived from two hundred selected varieties of commonly used medicinal herbs, when said extracts were forced to male white mice using the Linchofield and Wilcoxon method in order to determine the LD 50 of each herb, the conclusive results showed that the average LD50 was 2,000-5,000 milligrams, with the exception of raw *Radix Aconniti Kusenezoffii* and *Semen Strychni*. Thus, for most commonly used medicinal herbs and formulas, the safe dosage was found to be relatively high: for a person weighting 50 kilograms, LD 50 was approximately 250 grams; when take in normal dosage, most medicinal herbs have almost no toxicity (see reference 5). The recommended usage for hawthorn extract is 360 mg per day; this dosage does not present any safety concerns.

### 2. Acute toxicity test for Hawthorn Extract Capsule

Animal species: Little white mice, Kun ming species of average weight 18-20g, is supplied by Fujian Epidemic Prevention Station. (license No. 94001, Certification by Min Medical animal Center, Fujian, China). The acute toxicity test has been done by the New Drug Pharmacological Study Center of Fujian Sanitation School, Animal room license is No. 94005.

The acute toxicity experiment proved that one time ingestion of Hawthorn extract can not induce LD50 in mice. In the second part of experiment, 20 white mice are divided two groups: 10 male and 10 female. They made with 20% Hawthorn extract solution (the maximum possible concentration). The amount of ingestion is calculated from 20% of 0.5ml/10g body weight every four hour for three times a day. For example, Mice body weight is 20g, each mice received 0.6g hawthorn one day. After observing for 7 days, no toxicity reaction and deaths occurred at this maximum dosage level. Above test shows that maximum daily dosage of 30g/kg of body weight/day in mice can be sustained for an extended period. The dosages used in the toxicity studies are equivalent to 4167 times of clinic dosage (0.36g/day) in human.

### 3. Long Term Toxicity Test for Hawthorn Extract

Animal species: big white mice (SD strain) used in the test are supplied by Sino-Britain Joint venture Shanghai SIPPR/BK lid. Animal are 7 weeks old, male mice weight 82±7g, female mice weight 84±7g All mice are divided into three groups: negative, high dose, low dose, and males and females are distributed equally in each group. Administrating method, dosage, and volume ingested for 60 days are listed in following table.

Group	Number	Dose (g/Kg/D)	Volume (ML/100g/BW)	Equivalent clinic dose
1. Negative	n=20	0.00	2.0ml water	0.00
2. High Dosage	n=20	3.50	17.5% of 2.0ml	386
3. Low Dosage	n=20	1.75	8.75% of 2.0ml	243

We fed mice according to above table every afternoon for 60 days. There were no toxic reactions and abnormality occurred in hematology (such as RBC count, reticular cells count, WBC count, Hb, platelet count and blood clot time); There were no abnormal blood biochemical index (such as serum in AST, ALT, ALP, BUN, urea, total protein, Glucose, Total cholesterol); and there were no pathological damage occurred in the body organs by pathologist,

including heart, liver, spleen, lung, adrenal gland, stomach, small intestine, large intestine, pancreas, thymus gland, lymph node, etc. The high dosage group (big white mice) taken hawthorn powder is 486 times high than the clinic dosage. The results of this study combined with the result of acute toxicity study proved the short term and long term safety of hawthorn extract. All experiments are performed by the New Drug Pharmacological Study Center of Fujian sanitation School. Their license number is 94005.

4. Impurities, byproducts(limits):

Heavy metal	Lead (Pb)	1.1mg/g
	Arsenic (As)	0.018mg/kg
	Cadmium (Cd)	0.0003mg/g
	Mercury (Hg)	26.8mg/g
	Nitrite	273ppg
	Nitrate	20.0ppg
Other toxins	Aflatoxin B1	5ppg
	Mycotoxin	not to be found

No contaminated pesticides such as 666 and DDT in 30 sample of hawthorn extract powder.

5. Microbiological examination of hawthorn extract powder:

Sanming Pharmaceutical factory sent 30 samples of hawthorn extract powder to New Drug Pharmacological Study Center of Fujian sanitation School for analysis and examination. They received following average results in one of 30 samples of hawthorn extract powder.

Total aerobic count (cfu/g)	<10
Escherichia Coli (clony/100 g)	<30
Microbial pathogens	Not to be found in the culture.
Lactics	Not growing in the culture.
Yeast count	<10
Moulds	Not growing in the culture.

\* Microbial Pathogens include bacillus cereus, Clostridium perfringens, Pseudomonas aeruginosa, Shigella, Staphylococcus aureus, and KF Streptococcus.

Reference:

1. James F. Balch, MD et al: "Prescription for nutritional healing" pp 54. Avery publishing group Inc. 1990
2. Jethro Kloss: "Back to Eden" pp 155-156. Back family books publishing Co. 1988
3. Lavon J. Dunne: "Nutrition Almanac" pp 233-234 Nutrition Search Inc. 1990
4. JD Chen et al Hawthorn (Shann Zha) drink and its lowering effect on blood lipid levels in human and rats. 1995
5. Dr. William Chang: "Reference guide of commonly used herbal formulas".1989.

## **F. Proposed tolerances**

**No tolerances are required to insure the safety of hawthorn because of its non-toxic nature.**

## **G. Environmental Assessment**

**1. Date: November 5, 1996**

**2. Name of Petitioner: Chinese herb Center, Inc.**

**3. Address of Petitioner:  
2025 Eye Street, NW Suite 507  
Washington DC 20006  
Tel: (202)775-1108**

### **4. Introduction of hawthorn berry extract into Environment**

The hawthorn powder extract capsule is manufactured in China for importation into the United States. It is consumed in small quantities in households across the country, under no circumstances this capsule will cause any environmental pollution when discarded by consumer. The capsule is packaged in transparent gelatin capsule, and there are no direct or indirect additives or irradiated herbs used in hawthorn extract powder. The amount of hawthorn extract consumed or discarded in any one area will generate no toxicity and will have no impact on the local waste treatment system.

The hawthorn extract powder capsule is manufactured in China. The manufacture states that their manufacturing process does not result in the emission of any pollutants of concern, and the process does no harm to the environment. The manufacturing process is carried out in conformance with all Chinese laws covering environmental safety, and patent number for this product granted by the Chinese government is 87107890.1.

## Consumer information leaflet

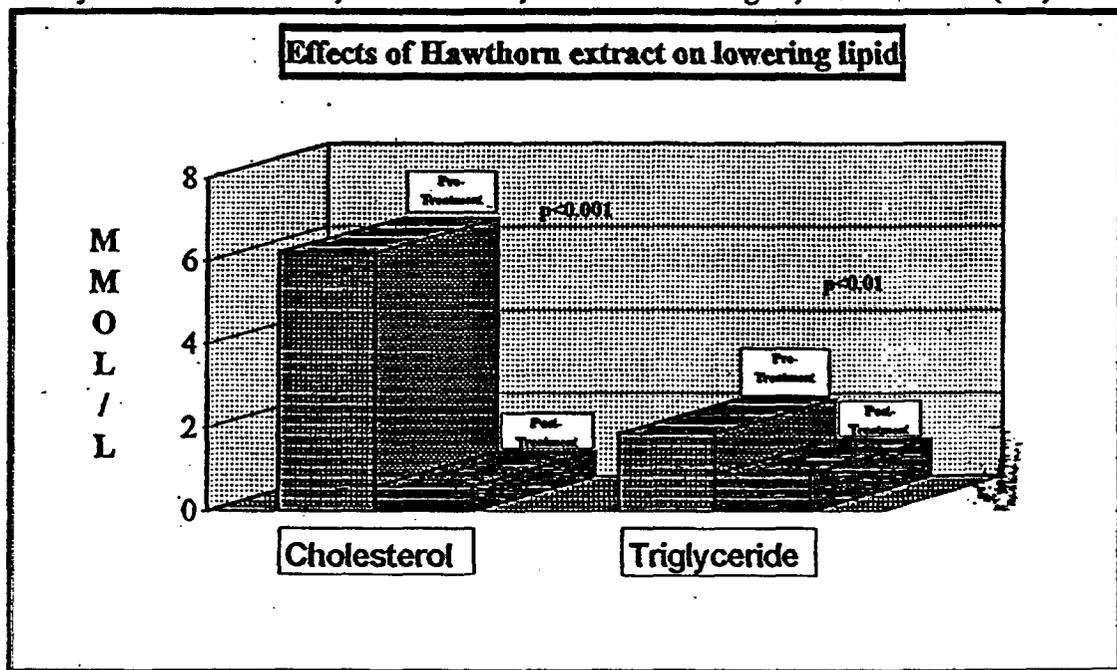
Sanming hawthorn berry extract capsule is an all natural dietary supplement for decreasing cholesterol and triglyceride. With this is highly concentrated hawthorn capsule, you can enjoy all the benefits of whole hawthorn berry without sour taste.

### Hawthorn berry history

As early as the 16th century, the most famous Chinese pharmacist, Shi Zhen Li, used hawthorn berry to treat patients for "food stagnancy and blood stasis", ailment caused by excessive dietary fat. This treatment has been kept till today and its efficacy is further improved by modern scientific studies. (See chart and reference). Hawthorn berry (*Crataegus pinnatifida*) is a wild, fruit-bearing tree growing in China, England and North America. Its berry with a sour and sweet tastes is considered to be both a fruit and a herb. Eating raw hawthorn berries has an obvious disadvantage, the most notable is its acidity which causes stomach up-set in some people. Now Sanming hawthorn extract is manufactured with an unique process that preserves and concentrates the richest crataegin of the fresh hawthorn berry. Already there are over millions people in the world taking Sanming hawthorn extract every day. Also Sanming hawthorn extract is delivered to many parts of the world, such as Europe, Africa, America, Canada and Australia, etc., and people's response to this product have been extraordinary due to its effectiveness and safety.

### Serving suggestion

Take 1 capsule three times daily with a glass of fresh water after meal. After you have taken this product for four or six weeks, you should check serum cholesterol and triglycerides. If your serum cholesterol and triglyceride decrease as illustrated,\*you may reduce to 2 capsules a day. If you develop excessive irritation, please do not take the product before you consult with your physician or professional herbalist.\*This statement has not been evaluated by the Food and Drug Administration and this product is not intended to diagnose, treat, cure, or prevent any disease. This product has been notified to FDA. Every bottle is sealed by Sanming pharmaceutical factory for safety. Store at room temperature. Keep this dietary supplements out of the children. This product is manufactured by Sanming Pharmaceutical Factory, Fujian, China. Fax: (598) 831-3131 and Distributed by Chinese Herb Center, Inc. 2025 I St., NW #507 Washington, DC 20006 Tel: (202) 775-1108.



### Reference:

1. Jamwes F. Balch, MD et al: "Prescription for nutritional healing" pp 54. Avery publishing group Inc. 1990
2. Jethro Kloss: "Back to Eden" pp 155-156. Back family books publishing Co. 1988
3. Lavon J. Dunne: "Nutrition Almanac" pp 233-234 Nutrition Search Inc. 1990
4. J D Chen et al Hawthorn (Shann Zha) drink and its lowering effect on blood lipid levels in human and rats. 1995

# **PERSHING PRODUCTS**

17 Jan. 1997

**James Tanner, Ph.D.  
Acting Director,  
Division of Programs and Enforcement Policy  
Department of Health & Human Services (HFS-456  
Food and Drug Administration  
200 C Street SW  
Washington DC 20204**

Dear Dr. Tanner:

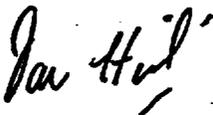
Thank you for your letter of January 9, 1997 concerning our statement regarding LDL-Lite. The product will actually be marketed with a booklet of recommended dietary management. We would therefore ask that if this fact is highlighted more prominently, along with the removal of the heart symbol, would the labeling then be acceptable according to the relevant section of the act.

We propose the change to the following:

"In conjunction with proper dietary management, you may reduce your cholesterol up to 15% in 4 weeks."

Please be advised that we are going to change the name of the company - actually do away with Pershing Products and revert to operating under the name of BioSphere technology, which is the parent company.

Yours sincerely,



**Ian Hicks  
President**