DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date: November 26, 2002

From: Division of Standards and Labeling Regulations, Office of Nutritional Products, Labeling and Dietary Supplements, HFS-822

Subject: 75-Day Premarket Notification of New Dietary Ingredients

To: Dockets Management Branch, HFA-305

New Dietary Ingredient:	Golden Phoenix
Firm:	Hounghwa Global, Inc.
Date Received by FDA:	August 26, 2002
90-Day Date:	November 24, 2002

In accordance with the requirements of section 413(a) of the Federal Food, Drug, and Cosmetic Act, the attached 75-day premarket notification and related correspondence for the aforementioned new dietary ingredient should be placed on public display in docket number 95S-0316 as soon possible since it is past the 90-day date. Thank you for your assistance.

Catalina Ferre-Hockensmith

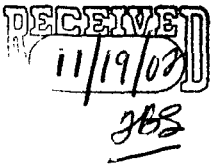
Catalina Ferre-Hockensmith

Attachments

95S-0316

RPT152

Hounghwa Global, Inc.
705 Canterbury Road
San Marino, CA 91108



November 14, 2002

Felicia Satchell
Director
Division of Standards
and Labeling Regulations
Office of Nutritional Products, Labeling
and Dietary Supplements
Center for Food Safety
and Applied Nutrition

RE: Docket No. 95S-0316

Dear Ms Satchell,

This is in response to your letter dated Nov 6, 2002. Regarding the historical information on *Trifolium pretense* L, we will provide more published data within the following week. We will also provide the copy of the studies as well as soon as possible.

My contact information is as follows:
Tel: 626 796 2988
Fax:626 395 9319
e-mail: hounghwa_global@yahoo.com

Thank you for your attention. If you have any questions or concerns, please free feel to contact me.

Sincerely,

Zhijian Zhang

DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Food and Drug Administration
College Park, MD 20740

NOV 6 2002

Mr. Zijian Zhang
President
Hounghwa Global, Inc.
705 Canterbury Road
San Marino, California 91108

Dear Mr. Zhang:

This is in response to your letter to the Food and Drug Administration (FDA) dated August 20, 2002, 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 Golden Phoenix, a product containing an extract from the herb *Trifolium pratense* L., a substance that you assert is a new dietary ingredient.

Under 21 U.S.C. 350b(a)(2), 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.

FDA has carefully considered the information in your submission, and the agency has significant concerns about the evidence on which you rely to support your conclusion that Golden Phoenix, a dietary supplement containing *Trifolium pratense* L., will reasonably be expected to be safe. You state in your submission that this substance has been used in traditional Chinese medicine for several centuries. However, your submission contains no information to support this statement nor that establishes that historical use, if any, is relevant

to reaching a conclusion that your product, when used under the conditions recommended or suggested in the notification, will reasonably be expected to be safe. Your submission also contains references to articles published in the scientific literature. However, you did not provide copies of any of these studies as required by 21 CFR 190.6(b)(4). Therefore, it is unknown whether these reference citations provide any support for the safety determination of Golden Phoenix.

For the reasons discussed above the information in your submission does not provide an adequate basis to conclude that Golden Phoenix, when used under the conditions recommended or suggested in your submission, will reasonably be expected to be safe. Therefore, your product may be 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).

Your submission will be kept confidential for 90 days from the date of receipt, and after November 24, 2002, your submission will be placed on public display at Dockets Management Branch (Docket No. 95S-0316). Commercial and confidential information in the notification will not be made available to the public.

We note that your notification does not include either a phone or facsimile (fax) number or an electronic mail address as a means to contact you. Although you are not required to provide us with this information, we would appreciate your sharing it with us, if it exists, as it provides a more rapid means for us to communicate with you. Please contact us if you have questions concerning this matter.

Sincerely yours,

Felicia B. Satchell

Felicia B. Satchell
Director
Division of Standards
and Labeling Regulations
Office of Nutritional Products, Labeling
and Dietary Supplements
Center for Food Safety
and Applied Nutrition

Hounghwa Global, Inc.
705 Canterbury Rd
San Marino, CA 91108

Date: August 20, 2002

Division of Standards and Labeling Regulations
Office of Nutritional Products, Labeling, and Dietary Supplements
Center for Food Safety and Applied Nutrition
Food and Drug Adminstration
5100 Paint Branch Parkway
College Park, MD 20740-3835

Re: Premarket notification

To Whom It May Concern:

Dear Sir/Madam,

Pursuant to Section 8 of the Dietary Supplement Health and Education Act of 1994, Hounghwa Global wishes to notify the Food and Drug Administration that it would market a new dietary supplement, Golden Phoenix, a product with ingredient: an extract from herb Trifolium Pratense L. Accordingly, enclosed please find (2) copies of this notification.

The dietary supplement which contains an extract of Trifolium Pratense L., at a level of 480 mg of Trifolium Pratense in a capsule which will be suggested to be taken three times day, 2 capsules in the morning, 2 capsules in the afternoon, and 4 capsules at bedtime.

Attached please find report of the safety and other information which establish that this dietary ingredient, when used under the conditions suggested in the labeling of the dietary supplement, is reasonably expected to be safe. These supporting documents include:

1) Background information on Golden Phoenix
2) Detailed information on Trifolium Pratense L.
3) Clinical trial data on Trifolium Pratense L.

Thanks for your attention. If you have any questions, please do not hesitate to contact us.

Sincerely Yours,

Zijian Zhang
President

RECEIVED 8/26/02

Background

Background

This Golden Phoenix brand product is made from Trifolium Pratense L. which contains phytoestrogen. Brief introductions to this background are as follows:

Development of studies on phytoestrogens

The use of plants and herbs by human being as medicine was several thousands years before, at that time, the ancient Egyptian and Greek women took plant and herb preparations after their labor and deliver. People began theoretically to research phytoestrogen only until the fiftieth, specially the effectiveness of phytoestrogens contented in food to human beings. The following phenomenon urges people to study these materials constantly:

1. Some forage grass (for example, white tip clover) can make sheep abortional and sterilities;
2. Why eastern people get less incidents of breast cancer, prostate cancer and coronary heart disease than western people, Is it because of eastern people partiality for vegetarian food or bean products?
3. Some non-steroid estrogenic materials examined from the urines of human beings and animals, these materials come from food;
4. With the development of the studies on estrogenic acceptors, it was found that the functions of these acceptors not only relative to the sexual function and child-bearing, but also to many kind of diseases of human beings.

The paper summarized the documentary published in recent years concerning the researches of pyhtoestrogens with brief introductions to their types of structures, relation of structure and effectiveness, methods of active examinations and application prospects for your references.

(1) Types of structures

Until now, 8 types of chemical structures were found for phytoestrogens.

(1.1) Isoflavonoids

The popularly found from isoflavonoids were genistein, daidzein, genistin, daidzin, biochanin A, equol and etc.

(1.2) Coumestans

The popularly found from coumestans was coumestrol.

(1.3) Lignans

The popularly found from lignans were enterolatone, enteroliol, matairesinol and etc.

(1.4) Chalcones

The popularly found was the derivatives of phloridzin.

(1.5) Stilbenes

Most of stilbenes estrogens are artificial ones and their derivatives[3], but recourses of resveratrol and etc. are from the plants.

(1.6) Triterpenoids

The most popularly found from triterpenoids were materials like ginseng saponin.

(1.7) Sterols

The most popularly found were β-sitosterol and diosgenin.

(1.8) Cyclic peptides

Recently, Mortia and his party divided a series of estrogenic active cyclic peptides from a kind of king traditional Chinese herb medicine ***Buliuhang*** Which cures women's ischogalactia and amenorrhoea, the earliest found were segetalin A and B.

Segetalin A: cyclo (Gly-Val-Pro-Val-Trp-Ala)

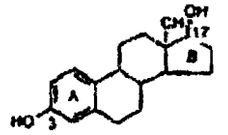
SWgetalin B: cyclo(Gly-Val-Ala-Trp-Ala)

(2) The relation of structure and effective of the estrogenic action

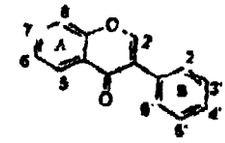
It was found from the researches long time ago, that the compound which had effectiveness of estrogens took effect through competitive joint with estrogenic acceptors and it was similar in structures for these compounds: planarity hydrophobic molecule, the positions of two hydroxyls at two ends and one phencycl existed. Better understanding reached with the development of profound researches in recent years.

There were two aryl cycles found for each of the phytoestrogens and 17βestradiol when compared with their structures and each cycle had a hydroxyl substitution. Though the connecting desmolases were not the same, but the suitable positions of hydroxyl substitutions that could produce the estrogenic activity were the same. Corresponding to 3- and 17- hydroxyls on 17βestradiol, the positions of hydroxyls of isoflavonoids were 4- and 7-, among them, B cycle substituted by 4- hydroxyl corresponding to A cycle of 17βestradiol, the hydroxyls on them together with the acceptors formed hydrogen chains directly influenced the infinity of jointing force with the acceptors. The hydroxyl positions of stilbenes and chalcones are 4- and 4-. Beside that, the distance between the two hydroxyls was 12A, this was also very important to the estrogenic activity.

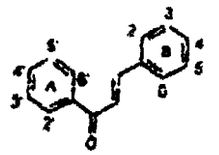
Data gained from a series of researches on compounds showed that some changes were possible for above mentioned structures but the estrogenic activity of the compounds still existed. For example, the positions of hydroxyl substitutions on A cycle of these phytoestrogens may be 5- or 6-, but hydroxyl positions on B cycle could not be changed, as hydroxyl on B cycle was directly jointed with the acceptors, so the specificity was comparatively high in the structure[2,5,6].



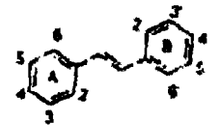
17βestradiol



Isoflavonoids



Chalcones



Stilbenes

Among the above eight compounds, the structure of cyclic peptides had no similarity with the former seven compounds, so there was no above mentioned specialty for this compound. The reason for its action of estrogen may not make effect through the joint with the acceptors, it may joint with other points of the acceptors. The further researches for their applied mechanism remain to study for better understanding.

(3) Test method of estrogenic activity

(3.1) Typical animal experiment

Estrogen can promote the growth of endometrium and increase the weight of the hystera and help vaginal cuticular cell dyskerated. According to this principle, the testee objects were given to those female mice or rats who were immaturate or their ovaries were cut to survey the weight increase of hysteras or ossifying conditions of vagina, at the same time, 17βestradiol were taken as fiduciary objects to evaluate the size of their activities.

Typical animal experiment was the earliest and most popular method to inspect the estrogens, the advantage for this method was that the effect from testee to the activities

could be directly measured, but the problem of this method was that the process of the experiment was trouble-taking and in high cost, easy influenced by other factors and the result was rough and difficult to scan in large scale.

(3.2) Culture of cells

The cells which were sensitive to estrogens were normally used to cultivate the cells, such as MCF-7,T47D cells from breast cancers of human beings, lshikawa-var I cells from endometrium adenocancer of human beings, primary cells from the uterus of rats, hypophyseal primary cells from rats and lymphocyte of the mice whose gene through infection, the Lec-9 cells. MCF-7 cells were most popularly used as they were most sensitive to foreign estrogens. When using MCF-7 to make experiment of proliferation of cells, the cells were put in human blood which were adsorpted with 10% charcoal-glucose and culture medium of acceptors of different densities, the number of proliferation of cells were measured after 6 days[7].

party proposed that Alkaline phosphatase catalytic activity in Lshikawar-varl cells may be used to evaluate the activity of estrogens, as to stimulate such catalytic action was the special feature of estrogens. This kind of method was used by party to have inspected a series of estrogenic activities of compounds, the evaluating data was EC_{50}. keukeleire and his party tested the compositions of estrogenic activities in hops by means of this method[10].

The most advantages of cell culture was high in sensitivity, if use the cells from human being, some indefinites would be avoided when apply the result from animal experiments to human beings.

(3.3) Estrogenic acceptor joint experiment

According to the theory of estrogenic action, estrogen will first joint with the estrogenic acceptors in plasmin, and then the produced estrogen with acceptors compounds will induce the idiotype protein combined to take effect, so the infinity of testee and estrogenic acceptors measured externally may use as an index to evaluate the size of the activity. But some scholars thought that the testee which can be jointed with estrogen acceptors may not sure to make effect of estrgens. Duax and Griffin thought that A cycle of estradiol relates to the jointing force and D cycle relates to whether it can make effect or not[5]. proposed that the evaluation of the estrogenic activity must include the overall process of the act of hormone and the demonstration of estrogenic control gene.[11]

(3.4) Combined use of the methods

Klots and his party in their articles said that three kind of external experiment methods were used to test the estrogenic activity of testee. The first method was yeast estrogenic scanning, by using the HER-ERE of the yeast interacting with the testee to evaluate the size of estrogenic activity with the increase of galactosidase activity, then to test the size of the jointing force of these compounds with estrogenic acceptors of human beings. At last, MCF-7 cells contenting two estrogenic reflected component plasmid were used to interact with testee with Luciferase activity as evaluation target[12].

The internal and external experiments were jointly made by Dhleby and his party to test the estrogenic activity. The two separate external body experiments were (1) the acceptor joint experiment, (2) to simultaneously transfer prsv plasmid contented estrogenic acceptor cDNA and ERE T81 CAT plasmid reflecting to estrogens to the cells of human beings, then to test the quantity of CAT protein produced from the cells which interacted with the testee. The internal body experiment was to test the weight of uterus of the mouse[13].

Jointly use of the methods and experiments not only advantageous to the test of estrogenic activities, but also help better understanding of the mechanism of adjustment function of compounds on molecule level to the estrogens, and also very important for the researchers to have their attentions to it.

(4) The apply prospects of phytoestrogens

(4.1) The action on the hormone dependence tumours

Hormone dependence tumours including breast cancer, prostate cancer, endometrium adenocancer and ovary cancer, the incidence of these diseases in Asian and East European countries are less than western countries; this is relative to the estrogens content in their food. Isoflavonoids content in bean products for Asian food is 25-45mg/day, but Isoflavonoids content in western food less than 5mg/day[14].

Research data from Adlerceutz showed that phytoestrogens have the functions to prevent breast cancer, prostate cancer and endometrium adenocancer, so less possibilities for vegetarians to get these diseases than others[15].
People paid special attention to the rich supply of among phytoestrogens. From Zava and Duwe researches, it was found that genistein had strong action on promoting estrogens and checked the tumour cells[16]; this showed that the genistein could be used as a new kind of anti-cancer medicine.

(4.2) The action on heart diseases

Heart diseases are a kind of disease relative to hormone. Comparing with the males, incidence rate of heart diseases of females before menopauses were less than males and at the same rate as males after menopauses, this could be explained by the more or less estrogens. The incidence rate of angiocardiopathy for Asian people less than that of western people, this was relative to the food which contented soybean protein that can change the fatty level in the blood[17]. It was considered, as comparing with the animal protein, soybean protein can change the density of cholesterone to prevent arteriosclerosis. From the researches of Anthony and his party, it was showed that soybean protein contented food were provided to the nearly grown up monkeys for a period of time, it was found that the density of LDL+VDL cholesterone dropped down 30-40% for both male and female monkeys, the HDLC of male monkeys were increased 15% and the whole density of cholesterone , as compared with that of HDLC in the blood, was obviously dropped down (20% for males and 50% for females)[18]. These helped to prevent and cure angiocardiopathy, especially coronary heart diseases.

(4.3) The action on osteoporosis

The secret of estrogens for females are not enough after menopause, such case last long, the risk for getting osteoporosis will increase with the time going on.

Anderson found that after the low ingredient of genistein used on ovary-cut rat, the ostea maintaining effect were equivalent to the conjugated equine estrogen[19]. Another evidence for using phytoestrogens to cure osteoporosis was that the structure of iprflavone similar as that of genistein were widely used to prevent osteohalsiteresis for females after menopauses[20].Dodge found that coumestrol could effectively slow down the reduction of osteo for the ovary-cut rats and recovered the level of osteo density equivalent to that of the rat whose ovary was not cut[21].

(4.4) The action on premenopause symptom

Some comparisons of food were made between different countries by Kigt and Eden in their articles, Malaysia covers 57%, China 18% and Singapore 14%, their food relative to the content of bean products[22]. Adlercreutz showed in his studies for the reason of why the number of cheek hectic fever of Japanese women less than that of Canadian women and phytoestrogens were found considerably high from the urine of Japanese women who take traditional low-fat food, especially genistein, daidzein and equol, the content in these compounds from the urine of Japanese women were higher than that of from America and Finland. He thought that the action of lsoflavonoids on those women who were in menopause with lower estradiol can explain the phenomenon[23].

(4.5) The action on Alzheimer's sclerosis

Found in recent researches, the estrogenic acceptors widely existed in the brain and the level of estrogens had close relation to Alzheimer's sclerosis. Estrogen treatment was used to the women after menopause, the incidence rate of Alzheimer's sclerosis were dropped down 40%. It was sure from these cases that phytoestrogens can prevent women's Alzheimer's sclerosis.

(5) Prospects for the studies on phytoestrogens

The contents of phytoestrogens in food are not small, so scientifically and reasonably pay attention to your food can help to prevent much kind of diseases. Food treatment can substitute some of recent medical treatment and it is more safe, cheap and less side effect than that of the medical treatment. To make phytoestrogens as food additive has been under the stage of researches in nowadays, it is estimated that such kind of products can enjoy big market share in the future.

Reference

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Trifolium Pratense L.

Development of Studies on Effective Ingredients of Trifolium Pratense

Trifolium pratense L. is a Leguminosae renascent pant, the alternate names are white tip clover, bur clover and etc. belonging to Trifolium L. Trifolium pratense is a kind of excellent feed and forage grass, and the overseas locally decoct their flowers to ease expectoration, cure cold and pulmonary tuberculosis (TB) and use for diuresis and diminishing inflammation, also they are used externally for diminishing abscess, burns and eye diseases. It is also reported[1] that the flowers, seeds, stalk and roots of the Trifolium pratense are made as plaster, electuary, and paste, decocted water and tea as well to drink to act on anti-tumour, gastric ulcer, gastric carcinoma, breast cancer and intestine cancer. The main effect reported in the documentation[2] was to ease spasm, relieve cough and asthma. The ointment made of the whole plant was to partially cure ulcer. Trifolium pratense and its preparations enjoy high market share now, people not only use it as food, the most important thing is that Trifolium pratense is one of the fewer plants which content 4 kind of Isoflavonoids (phytoestrogens), these ingredients act on prevention of breast cancer, prostate cancer, intestine cancer and improvement of osteoporosis and climacteric of women to a certain extends and more and more widely used in clinical practices and as a matter of fact, it makes trifolium pratense become a prospected nature healthy food for people. The usage, chemical ingredients and act of its pharmacological actions are summarized as follows:

(1) Featured Form of Botany

Trifolium pratense originally were produced in Europe, western Asian countries and now are popularly produced all over the world, they are the plant scattered in temperature zone. They play an important role in crop rotation, they are excellent feeds and green manure[3,4]. As their leaves are rich in protein, so they are took as traditional food and flavoring[5] in many countries. They are planted in southern and northern China and wild trifolium pratense also available in the country. Trifolium pratense is a renascent plant, the florescence 8-10 months[4].

(2) Chemical Ingredients

As trifolium pratense contents flavonoid materials, protein, amino acid, carbohydrate, vitamin and etc. Among them, so people paid special attention to the act of phytoestrogens and anti-cancer act of flavonoid materials contented in isoflavonoids.

2.1. Flavonoid materials: 16 kind of flavonoid materials found in the inspections, total content covers 2%[5] of the dry weight.

2.1.1. Isoflavonoid: trifolium pratense contents 4 kind of Isoflavonoids: biochanin A,

formonetin B, genistein and daidzein. They, as plant, exist in the form of glucoside, such as Indian sissoirin, ononin, genistin and daidzin. Trifolium pratense has most high content for biochanin A and B, covers approximately 0.1%--0.9% of the dry weight, other isoflavonoid and flavonoids about 0.08%[7]. Isoflavonoid ingredients like trifoside, calycosin, peclolinarigenin, pratensein and pseudobaptigenin and etc. are also contented in trifolium pratense, they are high in the part above land, less medium in the root and during the growing period, they are high in florescence and quickly drop down after blossom.

2.1.2. Flavonol: 3 kinds of Flavonol materials recently were found in trifolium pratense: quercetin, isoquercitrin and hyperoside. It was found from physical active experiments that quercetin and its derivatives have the function to antagonize the free radical and prevent the lipin peroxidized, directly check the cell growth and antagonize the carcinogenic factors, so it plays an important role in the cure and prevention of retrograde diseases like cancer, senile, angiocardiopathy and so on.

2.1.3 Flavonoids: Many kind of flavonoid ingredients are contented in the flowers of trifolium pratense, such as trifolin, isorhamnetin and pratol and etc.

2.2 Other ingredients

2.2.1. Coumarin and phenolic hydroxyl acid: Fresh trifolium pretense contents about 15.5ug/g dicoumarol mainly in leafs and fewer in dry ones, having anticoagulant action[2.7]. It also contents trace coumestrol, having action of female plants.

2.2.2 Volatile oil: The infloresence contents about 0.03% volatile oil, including more than 40 kinds of ingredients, such as gaultherolin, benzyl ethanol, 2-phenethylol, ortho-aminobenzoic ester, furfural and etc. The seed contents about 12% volatile oil.

2.2.3 Protein, sugar and vitamin: Calculated by dry weight, the mass fraction of protein is up to 23% at the last period of the growth, contenting different kind of necessary amino acid. The mass fraction of carbohydrate is 24.4%; there are cane sugar, glucose, xylose, amylum and etc. among them. There are carotenes, Vit D, and Vit E in the whole plant. The mass fraction of carotenes is at top when blossoming, the mass fractions of a- and β carotenes are separately 4.3% and 53.6% at the spring florescence, 3.2% and 45.9% at the summer florescence.

2.2.4 Others: The leaves also content lipidol ingredients like folic acid, 5-leucovorin, some sterol, glyceride, C_{23} -C_{31} alkyline, phosphatide and glucolipide[2].

3. Pharmacological action

3.1 Selective anti spasm, inflammation and disinfect actions: trifolium pretense can act externally to check the paramecium (0.2% alcohol infusion can stop the activity of paramecium within 30 minutes). Daidzein has the same action like opium poppy alkaline to remove the spasm of smooth muscle. Daidzin and daidzein can ease the headache and other symptoms of hypertension patients. So some foreign countries locally make them as antimalarial medicine, using them to ease expectoration, spasm, cure the pertussis and bronchitis. The pollen has antibacterial action to some of the gram-negative rods, so their disinfect actions are made use of to cure the skin diseases, like eczema, burns, ulcer and psoriasis.

3.2 Estrogenic action

Genistein, biochanin A, B and daidzein all have the estrogenic actions, it may be course of their structures similar to that of diethylstilbestrol and estradiol, but their activities are approximately 1/10 (ten thousand unit) that of diethylstilbestrol and 1/2~1/50 (ten thousand unit) that of estradiol (calculated by weight). Taking uterus weight of rat as a target, mixed the medicinal powder in the feed to raise the rats and compare the strength of their activities, the results showed that the daidzein had most active action, Genistein and biochanin A were similar, biochanin B was the worst. But some people had used the same method to do the experiment, they took 3 ingredients (quantities were 1,2,3 times of that used in above mentioned experiments), the ratio of re-tested strength of their activities were: Genistein - biochanin A -Daidzein = 1.5: 1.0: 0.4 and biochanin B was considered no effectiveness. Trifolium pretense is unique as a kind of phytoestrogen: they act almost everywhere in every cell in the human body and the estrogen from human body itself is not possible to act like that: they have dual adjust actions, when the level of estrogen of the human body gets high, they can check the secrete of estrogen, as they can joint with the estrogenic acceptors, so they can prevent the joint of self estrogen of human body. On the contrary, when the level of estrogen of human body goes down, they can provide extra estrogenic actions. As for this reason, Trifolium pretense is not only clinically used for cure of female premenstruum symptom when their internal levels of estrogens get high, but also used for cure of climacteric syndrome and menopause when the estrogens go down. Besides these, trifolium pretense can be used for cure of estrogenic diseases like fibroids, adenomyosis and osteoporosis [7-9].

3.3 Anticancer action

Trifolium pretense contents high concentration of Isoflavonoids and the like flavonoid materials. American State Cancer Center listed genistein in the tumour chemical prevention medicine clinical development plan in 1996; the main prevention diseases were

prostate cancer and breast cancer. The estrogen is high in the blood of breast cancer suffered patient; phytoestrogen has the resistance action to them and therefore to check the breast cancer. The recent researches from the Queen Elisabeth II Medicare Center in west Australia demonstrated that the women who eat much phytoestrogens get less rate of suffering from breast cancer. Trifolium pretense also gains cure achievement for colon cancer. Isoflavonoid materials were clearly shown from the experiments; they are of strong antioxidant, a strong removing agent for free radical and with effective resistance to cancers[7-11].

Trifolium pretenses have been made to different preparations and agents in foreign countries and more and more studies have been made on trifolium pretense in recent years. The healthy foods made from trifolium pretense are already getting into the world market. These plants are rich in resources and the development of their activities should be paid much attention to and from those to make them as nature healthy preparations and products to prevent women from suffering much kind of diseases and this should result in the achievement of excellent social and economic benefits.

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Clinical Trial

Clinical Data

Method:

Total 170 patients randomly divided into three groups: 70 in Golden Phoenix group, 50 in another corresponding group of estriol and 50 in the last group of placebo capsule.

In estriol group: 1-2mg a day for three weeks, then stopped for one week;

In Gold phoenix group: three time a day, 2 capsules each in the morning and afternoon, 4 capsules in the evening before bed for three weeks, then stopped for one week;

In control group: dosage the same as that of in Gold Phoenix group.

Table 1. General conditions of the patients

Item		Phoenix Gp. (n=70)	Estriol. Gp. (n=50)	Control Gp(n=50).
Age	Ranges (average)	37years -- 63years 47.5 years±5.1years	32years -- 62years 46.3years ± 4.8years	35years -- 62years 46.3years ± 4.8years
illness history	Ranges (average)	10months -- 5years 5.6years ±1.2years	10months -- 5.2years 5.7years ±1.3years	10months -- 5.2years 5.6years ±1.3years

Table 2. Marks comparison of therapeutic effect between the three groups before and after treatment

Item	Phoenix Gp.(n=70)		Estriol. Gp(n=50)		Control Gp(n=50).	
	Before T.	After T.	Before T.	After T.	Before T.	After T.
Sore waist & aching back	2.32±0.70 (38cases)	1.06 ± 0.68*	2.19 ± 0.54 (36cases)	2.01 ± 0.73	2.20 ±0.51 (35 cases)	2.18 ± 0.41
Sore waist & aching heel	2.33±0.59 (36cases)	1.06 ±0.73*	2.27 ± 0.65 (31 cases)	2.26 ± 0.64	2.24 ± 0.63 (32 cases)	2.21 ± 0.46
Abnormal menstruation	2.25 ±0.45 (42cases)	1.83 ±1.03	2.23 ± 0.73 (33 cases)	2.32 ± 0.63	2.21 ± 0.71 (31 cases)	2.20 ± 0.61
Breast atrophy	2.55 ±0.51 (32cases)	2 35± 0.59	2.57 ± 0.31 (34 cases)	2.50 ± 0 52	2.54 ± 0.49 (35 cases)	2.50 ± 0.51
Cold sexed	2.36 ±0.66 (40cases)	1.05±0.49*	2.19 ± 0.66 (36 cases)	1.88± 0.81	2.17 ± 0.65 (36 cases)	2.15 ± 0.62
Total marks	7.68±2.23 (70 cases)	4.75±1.82*	8.05 ± 1.54 (50 cases)	7.75 ± 2.24	8.06 ± 1.53 (50 cases)	8.02 ± 2.22

Comparison between before and after treatment $^{*}P < 0.05$

Conclusion

From above tables we can clearly see that the therapeutic effects of Gold Phoenix group have much superiority than other corresponding groups, especially in the cure of sore waist & aching back, sore waist & aching heel as well as cold sexed females.

Dosage:

2 capsules each in the morning and afternoon, 4 capsules in the evening before bed with warm water.

Summary

Summary

The Golden Phoenix is made from natural plant contains several kinds of phytoestrogens. The product not only has comprised the research achievements gained in recent years, but also the formulation (*Wu yun yan zong wan*) of traditional Chinese herb medicines for cure of sterility symptoms and cold sexed women for several hundred years in Chinese history. Phytoestrogens that contained in the natural plants and herbs are of the healthy function with strong affinity and long last safe performances. These materials are one kind of derivatives of Isoflavonoids of non-steroid molecules. In the plants and herbs, the main action of there materials are antioxidant: in the internal human body, these materials can not only act with relative to estrogens, but also can active the interaction of those cells with no relation to the estrogens to wholly improve the human health and thus to essentially prevent and cure the aging of the females and to reach the purposes of having women got healthy skin and radiate the vigor of their youth.

In short, the effect of this product is to delay the aging of the females.