DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date: JAN 27 2004

2002 '04 FEB -3 A10:08

From: Division of Dietary Supplement Products, Office of Nutritional Products, Labeling and Dietary Supplements, HFS-810

Subject: 75-Day Pre-market Notification of New Dietary Ingredients

To: Dockets Management Branch, HFA-305

Subject of the Notification: *(Dong Chong Xia Cao)* Biodiatab

Firm: New Century Company

Date Received by FDA: May 6, 2003

90-Day Date: August 5, 2003

In accordance with the requirements of section 413(a) of the Federal Food, Drug, and Cosmetic Act, the attached 75-day pre-market notification and related correspondence for the aforementioned substance 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.

Tanya L. Jackson

Attachments

95S-0316

RPT193

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
College Park, Maryland 20740

JUL 21 2003

Mr. David Hsu, President
New Century Company
3392 Falcon Ridge Road
Diamond Bar, California 91765

Dear Mr. Hsu:

This is to inform you that the notification, dated April 28, 2003, that you submitted pursuant to 21 U.S.C. 350b(a)(2)(section 413(a)(2) of the Federal Food, Drug, and Cosmetic Act (the Act)) was filed by the Food and Drug Administration (FDA) on May 6, 2003. Your notification identified Momordica charantia L.(Balsam pear) extract and Cordyceps sinensis (Berk.) Sacc. (Dong Chong Xia Cao) extract as the substances that you intend to market as new dietary ingredients in the product Biodiatab.

Your notification states that the dietary supplement, Biodiatab, will be marketed in 1000 mg caplets. These caplets will contain:

80 mg	Bee propolis
320 mg	Balsam pear extract
80 mg	Chrome yeast
160 mg	Dong Chong Xia Cao extract
80 mg	Grape seed extract
80 mg	Ginger extract

According to the notification, the recommended intake is one caplet per day but the notification fails to note the maximum dosage and the duration of use of the Biodiatab product which is required by 21 C.F.R. 190.6(3)(ii).

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.

Federal regulations found at 21 CFR 190.6 specify the requirements for a pre-market notification on a new dietary ingredient. The notification you sent us concerning Balsam pear extract and Dong Chong Xia Cao extract does not comply with the requirements of 21 CFR 190.6(b)(2). It fails to provide information regarding history of use or other evidence of safety that would provide a basis for reasonable assurance of safety for the proposed new dietary ingredients in the Biodiatab product. In addition, the information that was submitted is inadequate because it is also unclear how the clinical information (pp.9-12) submitted relates qualitatively and quantitatively to the proposed dietary supplement. The product used in the clinical studies is identified as Bee Colloid while your product containing the new dietary ingredients is identified as Biodiatab.

For the reasons discussed above, the information in your submission does not provide an adequate basis to conclude that Balsam pear extract and Dong Chong Xia Cao in the Biodiatab product, when used under the conditions recommended or suggested in the labeling of your product, 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).

You also indicate in your submission that your product, Biodiatab, "... helps the sugar metabolism for the individual with diabetics [sic]. It also provides nutrition for individual [sic] with diabetics [sic] or elevated blood sugar level." Under 21 U.S.C. 321(g)(1)(B), a drug is defined as an article intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease. The information in your submission suggests that your product is intended to be used to treat medical conditions and is subject to regulation as a drug under 21 U.S.C. 321(g)(1)(B) and is not a dietary supplement. See 21 CFR 101.93(g). If you wish Biodiatab to be evaluated for its use in the treatment of these medical conditions, you should contact FDA's Center for Drug Evaluation and Research (CDER).

Your notification will be kept confidential for 90 days after the filing date of May 6, 2003. After the 90-day date, the notification will be placed on public display at FDA's Docket Management Branch in docket number 95S-0316. Prior to that date, you may wish to identify in writing specifically what information you believe is proprietary, trade secret or otherwise confidential for FDA's consideration.

If you have any questions concerning this matter, please contact Victoria Lutwak at (301) 436-2375.

Sincerely yours,

Susan J. Walker, M.D.
Acting Division Director
Division of Dietary Supplement Programs
Office of Nutritional Products, Labeling
and Dietary Supplements
Center for Food Safety
and Applied Nutrition

NEW CENTURY COMPANY

3392 Falcon Ridge Rd., Diamond Bar, CA 91765 U.S.A.
Tel: (909) 861-7575 Fax: (909) 396-8706

RECEIVED 5/6/03 HFS-811

Division of Standards and Labeling Regulations
Office of Nutritional Products, Labeling and Dietary Supplement
Center for Food Safety and Applied Nutrition
Washington D. C. 20204

April 28, 2003

RE: 75 DAYS PRE-MARKET NOTIFICATION LETTER FOR STATEMENT ON DIETARY SUPPLEMENT - BIODIATAB

To whom it may concern,

As the consultant for Bionutripharm Syatems, Inc. I am sending you our application for 75 days pre-market notification for "Biodiatab" (a dietary supplement product) per Section 413 (a)(2) of the Federal Food, Drug, Cosmetic Act.

I believe there are only two new dietary supplement ingredients in Biodiatab - Balsam Pear Extract (Bitter melon), and Dong Chong Xia Cao extract (they may not be new in your definition) for which I attached the literature to show their safety for human consumption. (The cover and essential information about the books on the referenced information are stapled together). However, I also included literature on most of the other ingredients used in Biodiatab. In addition, we also included the original and translated versions of the clinical study results, Chinese government certificates, processing details, etc. We feel we have done our best to assure you the food safety of Biodiatab for the intended use. **About the Structure / functional claim, if our listed claim on Mr. Wong's letter is not allowed, our second choice will be as follows:**

> This formula helps you to maintain a healthy carbohydrate metabolism and enhance your body's ability to digest sugar. This statement has not been evaluated by the FDA, this product is not intended to diagnose, treat, cure or prevent any disease.

Please inform me if there is any other requirements or amendment needed for the application.

Best Regards,

David Hsu

David Hsu, President

NEW CENTURY COMPANY

3392 Falcon Ridge Rd., Diamond Bar, CA 91765 U.S.A.
Tel: (909) 861-7575 Fax: (909) 396-8706

This is to confirm my translation on the following documents from Chinese for Bionutrapharm Inc. for its "Beijing Xipu Global Biology Insulin / Biodiatab" product :

DH / Systems DH

(1) Formulas, Technologies, and Diagrams
(2) Clinical Trial Report
(3) Chemical Analysis Report
(4) Treatment and Theory
(5) Virulence Report
(6) Certification

David Hsu 4/15/03
David Hsu date

DAVID H HSU
SUBSCRIBED AND SWORN TO BEFORE ME
THIS 15th DAY OF APRIL 2003 ~~19~~
AT Los Angeles County CALIFORNIA
Jenny Leung
NOTARY PUBLIC

JENNY LEUNG
COMM. # 1273340
NOTARY PUBLIC-CALIFORNIA
LOS ANGELES COUNTY
COMM. EXP. SEPT. 5, 2004

BIONUTRIPHARM SYSTEMS INC.
403 Fairview Ave., #B Arcadia, CA 91007 U.S.A.
Tel: (626) 446-3208, Fax: (626) 574-8158

Division of Standards and Labeling Regulations
Office of Nutritional Products, Labeling and Dietary Supplement
Center for Food Safety and Applied Nutrtition
Washington D. C. 20204

Dear FDA officers: April 18, 2003

This is to clarify some important points in the supporting documents for our filing for FDA pre-market notification of "Biodiatab" product as per Code of Federal Regulation, Volume 21, part 101.93 (Section 413 (a)(2) of the Federal Food, Drug, Cosmetic Act):

(1) Beijing Xipu Global Biological & Pharmaceutical Co., Ltd. is a joint venture company in China to BioNutripharm Syatems Inc., and Mr. Wang Wenbing is the corporate representative of Beijing Xipu Global Biological & Pharmaceutical Co., Ltd
(2) "Biodiatab" is the brand name in U. S. for "Beijing Xipu Global Biology Insulin", they are identical products in terms of the active ingredients.
(3) Bee Colloid is the same as bee propolis., Balsam Pear is just another name of Chinese bitter melon.
(4) We appoint Mr. David Hsu as our translator and FDA regulation representative in U. S. , for any future correspondence, please contact him, his address and contact no. are:

New Century Company
3392 Falcon Ridge Rd.
Diamond Bar, CA 91765
Tel: (909) 861-7575

William Wong, President
Bionutripharm Syatems Inc.

Wang Wenbing
Beijing Xipu Global Biological & Pharmaceutical Technology Co., Inc.

BIONUTRIPHARM SYSTEMS INC.
403 Fairview Ave., #B Arcadia, CA 91007 U.S.A.
Tel: (626) 446-3208, Fax: (626) 574-8158

Division of Standards and Labeling Regulations
Office of Nutritional Products, Labeling and Dietary Supplement
Center for Food Safety and Applied Nutrtition
Washington D. C. 20204

RE: 75 DAYS PRE-MARKET NOTIFICATION LETTER FOR STATEMENT ON DIETARY SUPPLEMENT

Dear FDA officers:

Per Code of Federal Regulation, Volume 21, part 101.93 (Section 413 (a)(2) of the Federal Food, Drug, Cosmetic Act), we are enclosing all the required documents for the filing of the pre-market notification on our new upcoming herbal product – "Biodiatab".

1. **Statement of Purpose**

   2. This is a letter to provide notification of a statement of nutritional support, including the ingredient statement, supplement fact, new dietary supplement ingredient usage history and safety data, the text for Structure / Function statement, translation of the following documents: finished product formulas; technologies, and diagrams; clinical trial report; chemical analysis report; stability experiment report; treatment and theory; virulence report; and certification granted by Chinese government,.

2. **Company Information**

   BIONUTRIPHARM SYSTEMS INC.
   403 Fairview Ave., #B Arcadia, CA 91007 U.S.A.
   Tel: (626) 446-3208, Fax: (626) 574-8158

3. **Co-packing manufacturer for "Biodiatab":**

   Life Cycle Herbal Products, Inc.
   2746 Durfee Ave., #K
   El Monte, CA 91732

4. **FDA Consultant information:**

   David Hsu
   New Century Company
   3392 Falcon Ridge Rd.
   Diamond Bar, CA 91765
   Tel: (909) 861-7575, Fax: (909) 396-8706

5. **Product identification:**

   The trade name of the product:

   BIODIATAB (in caplet form)

The common and usual name for the product:

NONE

The label will reads like this:

6. **Ingredient Statement:** Balsam pear extract, Dong Chong Xia Cao extract, Bee propolis extract, Chrome Yeast, Grape seed extract, Ginger extract, Microcrytalline cellulose, Maltodextrin, Steraic acid, and sodium starch glycolate.

7. **Supplement facts:**

Serving Size : 1 caplet per day
Amount per serving 1,000mg
Serving per container ; To be determined.

	Amount per serving	%Daily Value
Bee propolis	80mg	*
Balsam pear extract, Momordica charantia,	320mg	*
Chrome Yeast	80mg	*
Dong Chong Xia Cao, Cordyceps sinensis Extract	160mg	*
Grape seed extract	80mg	*
Ginger extract, Zingiber officinale	80mg	*

* NOT ESTABLISHED

8. **The text for Structure / Function statement:**

This formula helps the sugar metabolism for the individual with diabetics. It also provides nutrition for individual with diabetics or elevated blood sugar level.

9. **New dietary supplement ingredients in "Biodiatab":**

Common Name	Latin binomial name
Balsam pear / Bitter melon extract	Momordica charantia
Dong Chong Xia Cao extract	Cordyceps sinensis

10. Main active ingredients and % in "Biodiatab":

Common Name	Latin binomial name	Origin
Bee colloid / Bee propolis extract	n/a	China
Balsam pear extract / Bitter Melon	Cordyceps sinensis	China
Chrome Yeast	n/a	China
Dong Chong Xia Cao extract	Momordica charantia	China
Grape seed extract	n/a	China
Ginger extract	Zingiber officinale	China

11. **Percentage of main active ingredient in the finished product – 79.365%**

12. **Each caplet weight: 1,000mg.**

We appoint Mr. David Hsu as our translator and FDA regulation representative in U. S. , for any future correspondence, please contact him, his address and contact no. are:

New Century Company
3392 Falcon Ridge Rd.
Diamond Bar, CA 91765
Tel: (909) 861-7575

Attachment:

- Usage history and safety data of new dietary supplement ingredients
- Original and translated copies of the documents:

(1) Finished product formulas; technologies, and diagrams
(2) Clinical trial report
(3) Chemical analysis report
(4) Stability experiment report
(5) Treatment and theory
(6) Virulence report
(7) Certification granted by Chinese government

William Wong

William Wong, President
Bionutripharm Systems Inc.

Translated Copy

1

Application Documents 1

Formulas, Technologies and Diagrams

Beijing Xipu Global Biological & Pharmaceutical Technology Co., Ltd.

translated by: Daisy Ma 4/3/03

I. Prescriptions

Formula Name	Content (mg)	Percentage (%)	Place of Origin
Bee colloid extract	50	10	China
Balsam Pear extract	200	40	China
Chrome Yeast	50	10	China
Insect and Grass extract	100	20	China
Grape Seeds extract	50	10	China
Ginger extract	50	10	China
Total	500	100	China

II. Processing Methods

1 Production Technology

A Bee colloid extract

Bee colloid meal was extracted twice from alcohol circumfluence. Soaking paste will be got after recycling. The meal is kept for standby using.

B. Balsam Pear extract

Clean the Balsam Pear, chop into plasm, freezing twice under -20°C, filtrating then hyperfiltrating, drying filtrating under vacuum in low temperature, the powder is kept for standby using.

C. Chrome Yeast

Fermented from Beer Yeast

D Insect and Grass extract

Insect and grass meal powder was distilled twice with 70% degree alcohol circumfluence, soaking paste will be got after the alcohol liquid recycling, picking up after acidizing, drying the liquid and keep it for standby using.

E Grape seeds extract

Clean and chop the grapes into pieces, abstracting with organic solvent, drying for standby using after purifying

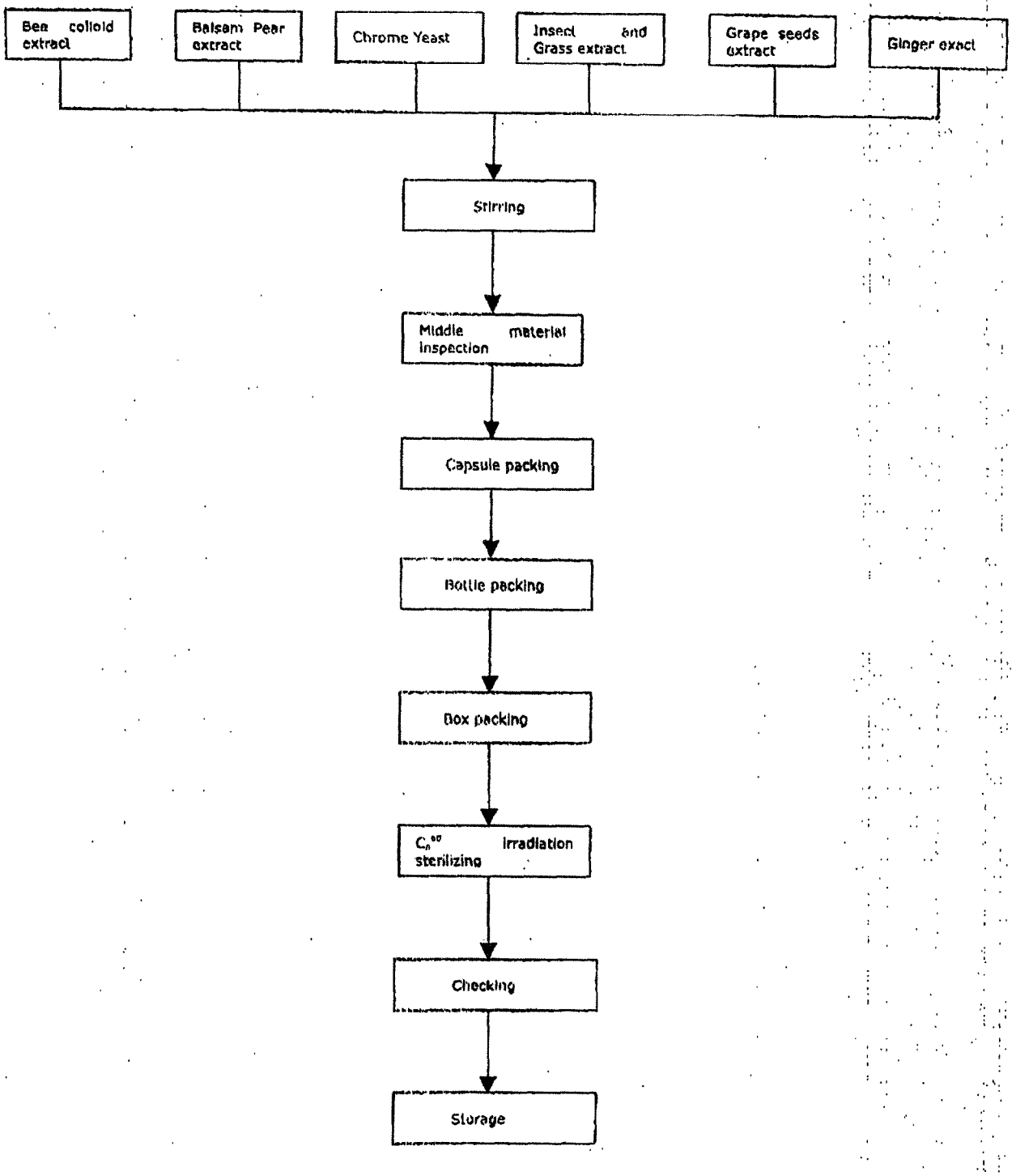
F Ginger extract

Pour water into the ginger meal and stir to even, add more water and filter; pouring salty water which occupies 10%-20% the total volume into the filtered water, not remove and filter again; dissolved into hot water, filter a third time while hot; adjust the water to PH=2 level; placing and filtering once more till to medium level; then dry it for standby using.

translated by Diana Hs 4/3/03

3

2 Technology procedure diagram



translated by: [illegible] 4/3/03

4

Application documents 2

Clinical Trial Report

Beijing Xipu Global Biological & Pharmaceutical Technology Co., Ltd.

translated by: David HS 4/3/03

Healthy Food Function Inspection Center, Applying Literal and Science Institution, Beijing United University

Inspection Report

Objective Name: Beijing Xipu Global Biology Insulin

Application Company: Beijing Xipu Global Biological & Pharmaceutical Technology Co., Ltd.

Production Company: Beijing Xipu Global Biological & Pharmaceutical Technology Co., Ltd.

Case Code: [2002] 0052 Sample Approve Number: 20020501

Inspection Item: Subsidiary Function on Reducing Blood Sugar

Sample Receiving Date: September, 2002 Report Date: November 2002

Inspection Foundation: Healthy Food Function Subject Appraisement Program and Inspection Methods

---

Results and conclusion

Injecting different dosage of Beijing Xipu Global Biology Insulin to mice with different level blood sugar, differences happen in the sugar resistance experiment after 4 weeks. Half an hour after taking glucose, sugar value drops at 25% ($P<0.001$), 15% ($P<0.01$) and 17% ($P<0.05$) with different dosage of low (0.17g/kg. bw), middle (0.33g/kg.bw) and high (1.00g/kg.bw) comparing with high sugar model group; 2 hours later, they change to 29% ($P<0.01$), 23% ($P<0.01$) and 22% ($P<0.05$) respectively. But no outstanding changes happen on weight of them. Before and after injection, the normal mice aren't remarkably vary with comparing group on blood sugar and weight ($P>0.05$).

Conclusion made on basis of Healthy Food Function Subject Appraisement Program and Inspection Methods: Beijing Xipu Global Biology Insulin performance to drop blood sugar.

The following is empty.

This report is only effective to the sample sending.

Technology Chief: _____

Date: Nov 7, 2002

translated by: David Hs 4/3/03

6

2. **Results:**

2.1 Effect on blood sugar of normal mice

Form 1 effect on blood sugar of normal mice (X±SD)

Group	Dosage (g/kg.bw)	Animals Quantity	Blood Sugar(mmol/L)			
			Before Injection	P Value	4 Weeks after Injection	P Value
Empty Compare Group	0	10	5.0±0.7	---	4.8±0.6	---
Injection Group	1.00	10	5.4±0.9	0.2274	4.8±1.6	0.9284

Above form 1 shows that, blood sugar values of injection group are not remarkably different from that of empty group after 4 weeks of injection ($P>0.05$).

2. **Results:**

2.1 Effect on blood sugar of normal mice

Form 1 effect on blood sugar of normal mice (X±SD)

Group	Dosage (g/kg.bw)	Animals Quantity	Blood Sugar(mmol/L)			
			Before Injection	P Value	4 Weeks after Injection	P Value
Empty Compare Group	0	10	5.0±0.7	—	4.8±0.6	—
Injection Group	1.00	10	5.4±0.9	0.2274	4.8±1.6	0.9284

Above form 1 shows that, blood sugar values of injection group are not remarkably different from that of empty group after 4 weeks of injection (P>0.05).

2.2 Effect on blood sugar of mice with high blood sugar caused by Four-Oxygen Pyridine.

Form 2 Effect on mice of high blood sugar caused by Four-Oxygen Pyridine (X±SD)

Group	Dosage (g/kg.bw)	Animals Quantity	Blood Sugar(mmol/L)			
			Before Injection	P Value	4 Weeks after Injection	P Value
High Blood Sugar Model Compare Group	0	10	18.8±3.0	—	31.8±6.4	—
Minimum Group	0.17	10	18.7±3.1	0.0.9886	25.3±10.4	0.1110
Middle Group	0.33	10	18.7±5.0	0.9831	26.6±11.6	0.2363
Maximum Group	1.00	10	18.1±4.6	0.7234	25.5±10.5	0.1248

Above form 2 shows that: there is no remarkable difference on blood sugar value between high blood sugar model injection group and high blood sugar model comparison group before injection; either after injection 4 weeks.

2.3 Effect on blood sugar resistance of mice with high blood sugar caused by Four-Oxygen Pyridine.

Form 3 Effect on mice of high blood sugar caused by Four-Oxygen Pyridine (X±SD)

Group	Dosage (g/kg.bw)	Animals Quantity	Blood Sugar(mmol/L)					
			0 hour	P Value	0.5 hour	P Value	2 hours	P value
High Blood Sugar Model Compare Group	0	10	31.8±5.4	—	50.0±3.3	—	34.6±4.9	—
Milimium Group	0.17	10	25.3±10.4	0.1110	37.7±6.4 ***	3.822×10	24.4±8.4 **	0.0036
Middle Group	0.33	10	26.6±11.6	0.2363	42.6±5.3 **	0.0014	26.8±7.0 **	0.0095
Maximum Group	1.00	10	25.5±10.5	0.1248	41.7±8.5*	0.0101	27.1±8.8*	0.0298

*: Obvious difference, comparing with high blood sugar model comparison group (P<0.05);

**: Remarkably difference, comparing with high blood sugar model comparison group (P<0.01);

***: Outstanding difference, comparing with high blood sugar model comparison group (P<0.001)

Above Form 3 shows that: Half an hour after taking glucose, sugar value drops at 25%(P<0.001), 15% (P<0.01) and 17% (P<0.05) with different dosage of low (0.17g/kg. bw), middle (0.33g/kg.bw) and high (1.00g/kg.bw) comparing with high sugar model group; 2 hours later, they change to 29% (P<0.01), 23% (P<0.01) and 22% (P<0.05) respectively.

translated by: David Hu 4/3/03

Beijing Municipal Center for Disease prevention and Control

West Garden Hospital of China Academy of Traditional Chinese Medicine

Certificate of Assay

Sample Code:	(2002) Food B2114
Inspection Code:	2002S0046
Objective Company:	Beijing Jishitang Herbal Medicine Healthy Institution; Liaocheng Luyuan Bee Colloid Science and Trade Co., Ltd
Production Unit:	Beijing Jishitang Herbal Medicine Healthy Institution
Production Date:	May 1st, 2002
Objective Product:	Jishicihang Brand Bee Colloid Sugar Capsule
Sample Quantity:	0.4g/pill*75pills/bottle*140bottles
Inspection Item:	Blood Sugar Function Human Taking Trial
Date of Sample Receipt:	Nov 23, 2002
Report Date:	Jan 24, 2003
Inspection Foundation:	Healthy Food Function Subject Appraisement Program and Inspection Methods

---

Results and conclusion:

Applying double self-comparison and intergroup comparison, 60 experiment people of high blood sugar are divided into trial taking group and comparison group. During the period, keep the dosage of old medicine unchanged, one group is specially given Jishicihang Brand Bee Colloid, and the other group is given consolation drug. One month later, it shows that Jishicihang Brand Bee Colloid performance to drop blood sugar at 1.11±1.51mmol/L before dinner, and 1.91±2.20mmol/L after dinner. 21 groups effective, occupies70.00% of total; while that is not obvious among the comparison group which just taking consolation drug, 9 groups effective, occupies 30.00% of total, there is remarkable variety between the two groups. All the clinical inspection indexes before or after the injection, such as hemoglobin, erythrocyte, leucocyte, serum albumen, albumen, millet straw transaminase, millet third transaminase, carbamide, flesh glycoside and so on are not beyond the normal range. It shows that Jishicihang Brand Bee Colloid doesn't have any bad effect to experiment people.

This inspection report is only responsible for the sample receiving.

Technology Chief:
Date:

translated by : Diana Hs 4/3/03

8

Jishicihang Brand Bee Colloid Capsule foretasting Report

1 Material and Methods:

1.1 Sample: Jishicihang Brand Bee Colloid Capsule and consolation drug, all provided by Beijing Jishitang Herbal Medicine Healthy Institution.

1.2 Experiment Objectives: 60 people of II type high blood sugar patient, age of 18-65, without heavy disease in heart, liver or kidney. Dividing into trial group and comparison group randomly. Comparing with each other within same group and the other group between the two groups.

1.2.1 Standard: choosing the patients of adult II type with steady situation after taking sugar-dropping drug, who is no need to replace drug and dosage, but taking normal dosage, whose blood sugar≥ 7.8mmol/L(140mg/dl) under limosis or ≥11.1mmol/L(200mg/dl) 2 hours after dinner; People with high blood sugar also can be as choice, whose blood sugar≥6.7mmol/L under limosis and ≥ 7.8mmol/L after dinner.

1.2.2 Adopted standard.

People with II type high blood sugar condition, which meeting the above requirement, can all be adopted for observation.

1.2.3 Excluding standard:

1.2.3.1 Aging below 18 or above 65, pregnant or women in period of breast-feeding.

1.2.3.2 Suffering from heavy disease in heart, liver or kidney, or other serious diseases, such as psychosis patients.

1.2.3.3 People unable to cooperate with

1.3 Taking Methods: 60 people with II type sugar diabetes were divided into 2 group, being given Jishicihang Brand Bee Colloid Capsule and consolation drug separately, 3 for morning and 2 for night, total 5 pills per day. The people are required to control their diet and eat according to labor pressure and health condition of their own.

1.4 Instruments and Reagent: F-820 type haemacytometer, MIDRON emiction analysis meter(Made in German), Olympus Full Automatic biology analysis machine AU600(Made in Japan). Zhong Sheng company offers all the reagent boxes.

2 Observation Index:

All the indexes are offered 1 time at the beginning and the end of the experiment respectively, extra inspection is carried out at the 15th day after experiment start.

2.1 Performance Observation:

2.1.1 Symptom Observation:

Inquiring the disease history, getting information of diet and activities, observing main clinic symptom, such as overeating, overdrinking, diuresis, tired and so on; count the score before and after the experiment according to the light and heavy degree of symptom (Serious-3 score, medium-2 score, light 1-score), and observing the improving condition (2 score of each symptom improvement-obvious effect, 1 score-effective).

2.1.2 Inspection on blood sugar under limosis and 2 hours after dinner

2.1.3 Emiction sugar and ketone inspection

2.1.4 Blood grease inspection (general cholesterin TC, glycerin TG)

translated by: Dai HS 4/3/03

2.2 Safety Observation

2.2.1 Blood and emiction routine inspection:

Red blood cell counting, blood red albumen, white blood cell counting, emiction sample test

2.2.2 Biology and chemistry index test

Blood serum white albumen Al.B, general albumen TB, heart, liver and kidney function(millet straw transaminase AST, millet third transaminase ALT, carbamide UREA, flesh glycoside Cre).

2.2.3 Abdomen B Ultrasonic, Heart Cardiogram, X-ray.

3 Function conclusion standard

3.1 Effective: Obvious improvement on basic symptom, blood sugar drop more than 10% under limosis or after meal.

3.2 Ineffective: No obvious improvement on basic symptom, blood sugar drop rate is below the above rate.

4 Result:

It is Jishichang Brand Bee Colloid Capsule group, which taking type I. It is comparison group, which taking type II.

4.1 General material:

Total 60 people, 13 men and 17 women in group taking Jishichang Brand Bee Colloid Capsule, whom aging from 34 to 65 with average age 51.03 and average disease history 4.83years; In comparison group: 18 men and 12 women, whom aging from 34 to 65 with average age of 52.74 and average disease history 3.47 years.

4.2 Comparison between two groups before observation

Form 1. Comparison before observation (x±SD)

Group	Quantity	Age	Gender		Medical History (Year)	Blood Sugar (mmol/L)	
			Man	Woman		Limosis	Hours after meal
Bee Colloid Capsule	30	55.23±6.76	11	19	5.8±3.77	9.49±2.79	13.38±4.55
Comparison group	30	53.17±4.26	11	19	5.8±4.26	9.26±2.72	12.25±3.44

Form 2. Blood sugar dropping medicine List

Group	Quantity	Sulfur urea	Double Carbamidine	Sulphur+Carbamidine	Never taking
Bee Colloid Capsule	30	7	7	4	3
Comparison group	30	6	6	3	4

Form 1 and 2 shows that, there is no remarkable difference between the two groups before trial, valid for comparing.

translated by : David He 4/3/03

4.3 Blood sugar dropping function

4.3.1 Blood sugar comparison under limosis and after meal:

Form 3. Blood sugar comparison under limosis(mmo1, X±SD)

Group	Pretrial	Past-trial	Value Difference
Bee Colloid Capsule	9.49±2.80	8.37±2.82	-1.11±1.51**
Comparison group	9.26±2.72	9.28±2.97	+0.02±1.42##

Self-comparison ** P<0.01 Intergroup comparison ## P<0.01

Form 4. Blood sugar comparison 2 hours after meal(mmo1, X±SD)

Group	Pretrial	Past-trial	Value Difference
Bee Colloid Capsule	13.38±4.55	11.47±3.42	-1.91±2.20**
Comparison group	12.25±3.44	12.02±3.42	+0.23±1.92##

Self-comparison ** P<0.01 Intergroup comparison ## P<0.01

One month later, blood sugar of the group taking Jishicihang Brand Bee Colloid Capsule drops average at 1.11mmol/L, and at 1.91mmol/L 2 hours after meal; while no obvious change happens for the other group.

4.3.2 Blood Sugar, emicgtion and emiction ketone comparison

Form 5 Limosis Blood Sugar, emiction sugar and ketone comparison (X±SD)

Item	Quantity	Before trial	During trial	Front Difference value	Post trial	Later Difference value
Blood Sugar	30	9.49±2.80	8.03±1.84	1.46±2.28*	8.37±2.82	1.11±1.51**
(mmol/L)	(30)	(9.26±2.72)	(9.18±2.79)	(-0.08±0.97)	(9.28±2.97)	(-0.02±1.42)
Emiction Sugar	30	0.53±1.22			0.37±0.84	-0.17±0.66
	(30)	(0.45±1.00)			(0.57±1.13)	(0.12±0.80)
Emiction Ketone	30	-			-	
	(30)	(-)			(-)	

( ) comparison group Self comparison ** P<0.01

4.4 Blood Sugar Function Comparison:

Form 8: Blood sugar value function statistics

Group		Effective	Invalid	Total effective rate(%)
Jishicihang Brand Bee Colloid Capsule	Quantity	21	9	21
	Function rate (%)	70.00	30.00	70.00
Comparison Group	Quantity	9	21	9
	Function rate (%)	30.00	70.00	30.00

Total effective rate difference is obvious after X-ray inspection. P<0.05

translated by : Diana HS 4/3/03

4.5 Symptom improvement state:

Form 9 Changes of clinical symptOm pre and post trial

Syptom	Obvious Effects		Effective		Ineffective		Improvement Percentage (%)	
	Comparison group	Trial taking group	Comparison group	Trial taking group	Comparison group	Trial taking group	Comparison group	Trial taking group
Overtaking	0	1	5	6	6	6	45.45	53.85
Overdrinking	0	1	6	6	9	4	40.00	63.64
Diuresis	0	1	6	7	10	6	37.50	57.14
Tiring	0	2	8	9	11	6	42.10	64.71

Jishicihang Brand Bee Colloid Capsule is better than the comparison group on all the main symptom improvement.

4.6 Statistics on clinical symptom

Form 10 Statistics on clinical symptom(x±SD)

Group	Quantity	Pre-trial	In-trial	Post-trial
Bee Colloid Capsule	30	7.07±5.43	5.37±4.15***	4.90±4.30***
Comparison	30	6.80±3.16	5.57±3.16***	4.27±3.20***

Self comparison *** P<0.001

Jishicihang Brand Bee Colloid Capsule and the comparison group perform to improve clinic symptom.

4.7 Blood grease state

Form 11. Blood grease comparison(x±SD)

Item	Bee Colloid Capsule (N=30)		Comparison (N=30)	
	Pro-trial	Post-trial	Pro-trial	Post-trial
TC (mmol/L)	4.99±0.94	4.94±0.85	4.95±1.05	4.64±0.99
TC (mmol/L)	2.09±1.58	1.89±1.44	1.83±1.39	1.87±1.54

Jishicihang Brand Bee Colloid Capsule and the comparison group perform no effect on blood grease.

translated by: David He 4/3/03

4.8 Blood safety index observation

Form 11 Blood safety index comparison (x±SD)

Item	Bee Colloid Capsule (N=30)		Comparison (N=30)	
	Pro-trial	Post-trial	Pro-trial	Post-trial
TP (g/L)	73.95±4.41	74.63±5.79	70.77±5.19	72.18±6.07
ALB (g/L)	43.70±2.44	43.95±4.12	42.36±4.22	42.78±4.08
ALT (u/L)	22.77±9.53	21.73±10.23	19.93±9.33	20.00±10.88
AST (u/L)	25.20±7.00	25.07±8.39	21.87±7.29	21.13±5.86
UREA (mmol/L)	5.41±1.29	6.00±1.30	5.35±1.31	5.39±1.50
Cre (udol/L)	93.57±12.43	94.92±12.02	88.29±13.06	92.49±13.68
HGB (g/L)	130.13±12.97	132.53±11.99	133.63±12.89	137.80±13.59
RBC ($\times 10^{12}$/L)	4.39±0.41	4.38±0.37	4.36±0.39	4.40±0.39
WBC ($\times 10^{9}$/L)	6.69±1.55	6.57±1.33	6.61±1.55	6.49±1.39

All the indexes of blood testing are in normal range.

4.9 X-ray, Cardiogram and B ultrasonic testing: normal

5 Summarization:

5.1 Jishicihang Brand Bee Colloid Capsule group performance well on blood sugar dropping, by 1.11±1.51mmol/L limosis and 1.91±2.20mmol/L after meal. 21 persons effective, occupy 70.00% of total; the comparison group slightly performance on blood sugar, 9 persons effective, occupy 30.00% of total, there is remarkable difference between the two groups, shows that Jishicihang Brand Bee Colloid Capsule can performance on subsidiary blood sugar dropping.

5.2 Jishicihang Brand Bee Colloid Capsule performs on main symptoms, such as overdiet, overdrinking, diuresis, tire and so on.

5.3 Jishicihang Brand Bee Colloid Capsule have no bad effects on human health, which can be seen from all the following indexes are in normal rang: hemoglobin, erythrocyte, leucocyte, serum, white protein, millet straw transaminase, flesh glycoside, carbamide and emiction.

5.4 Jishicihang Brand Bee Colloid Capsule have no any other bad effects during observation.

Beijing Disease Preventing & Controlling Center
Jan. 24, 2003

West Garden Hospital, Chinese Herbal Medicine Institution, China
Jan. 24, 2003

translated by : Dixed Hs 4/3/03

Application Document 3

13

Chemical Analysis Report

Beijing Xipu Global Biological & Pharmaceutical Technology Co., Ltd.

translated by: David HS 4/3/03

14

Beijing Disease Preventing & Controlling Center

Test Report

Sample Code: (2002) Food B2114 Page Total

Sample Name: Beijing Xipu Global Biology Insulin Test Code: (2002) Food B2114h1-3-1310
Company Name: Beijing Xipu Global Biology Pharmaceutical Technology Co., Ltd.
Production Factory: Beijing Xipu Global Biology Pharmaceutical Technology Co., Ltd.

Sample Place: /
Accepting Date: 2002. 07.31
Sample Form: Capsule
Storage condition: Normal Temperature
Name of Testing Department: Nutrition and Food Sanitation Institution

Testing Objective: Hygienic
Testing Date: 2002. 07.31
Sample Quantity: 8 bottle*3

Testing accordance: Arsenic (GB/T5009, 11-1996), mLead(GB/T5009,12-1996), Hg.(GB/T5009,17-1996), Ca.(GB/12390-90), Ge.(GB/T5009,15-1996), Water(GB5009.3-85), Dirt(GB5009.4-85), Yellow Ketone(GB/T5009.35-1996), Origin anthocyanin (GB/T5009.39-1996), Biding(Health Food Function Components Testing Methods), Pigment, Ethanol remains, Loosing time(Pharmaceutical Dictionary of Chinese People's Republic of China 2000 edition)

Testing Result:

	Arsenic	Lead	Hg	Water	Dirt	Ca	Ge	Ethanol remains
	(mg/kg)	(mg/kg)	(mg/kg)	(g/100g)	(g/100g)	(g/100g)	(mg/kg)	(ug/g)
(2002) B2114h1-1310	0.053	0.16	0.066	6.2	38.3	23.1	0.033	37.8
(2002) B2114h1-1310	0.056	0.15	0.068	6.3	40.1	23.7	0.040	43.7
(2002) B2114h1-1310	0.034	0.11	0.072	6.3	39.4	24.7	0.042	37.4

	Origin anthocyanin	Biding	Yellow Ketone (count on Luding)	Loosing time	Light Orchis	Lemon Yellow	
	(g/100g)	(mg/g)	(Mg/100g)	(min)	(g/kg)	(g/kg)	Permit No.
(2002) B2114h1-1310	8.5	1.0	26.8	11.0	0.0077	0.019	20020501
(2002) B2114h1-1310	8.3	1.1	24.6	10.0	0.0081	0.017	20020502
(2002) B2114h1-1310	8.9	1.0	25.8	13.0	0.0075	0.017	20020503

Following is empty

Testing Organization (Stamp)

This report only responsible for the sample sending

Sign Person: Wu Guohua

Date: Jan. 20, 2003

translated by : David Hu 4/3/03

Beijing Health Sanitation & Epidemic Prevention Station

15

Sanitation Testing Result Report

File No.: (2002) FOOD B2114f1-3
Sample receiving Date: Jul. 31, 2002
Testing Date: Jul. 31, 2002

Sample Name: Beijing Xipu Global Biology Insulin
Company Name: Beijing Xipu Global Biology Pharmaceutical Technology Co., Ltd.
Testing Objective: Hygienics
Production Factory: Beijing Xipu Global Biology Pharmaceutical Technology Co., Ltd.
Test Code: (2002) Food B2114f1-3-0939

Test Accordance: GB4789, 15-94
Sample Quantity: 150g*3lot
Sample Form: Capsule
Testing Item: Mildew Sourdough
Storage condition: Normal Temperature

Testing results:

Sample Code	(2002)food B2114	(2002)foodB2114	(2002)food B2114
Sample Name	Beijing Xipu Global Biology Insulin	Beijing Xipu Global Biology Insulin	Beijing Xipu Global Biology Insulin
Sample Lot Number	20020501	20020502	20020503
Sourdough	<5	<5	<5
Mildew	<5	<5	<5

Following is empty

Report date: Aug 12, 2002

Date of Terminal Verifying: Aug 12, 2002

Principal of test unit:

This report only responsible for the sample sending Page Total

translated by Dicid Hs 4/3/03

16

Beijing Health Sanitation & Epidemic Prevention Station

Sanitation Testing Result Report

File No.: (2002) FOOD B2114m1-3
Sample receiving date: Jul. 31, 2002
Testing Date: Jul. 31, 2002

Sample Name: Beijing Xipu Global Biology Insulin
Company Name: Beijing Xipu Global Biology Pharmaceutical Technology Co., Ltd.
Testing Objective: Hygienic
Production Factory: Beijing Xipu Global Biology Pharmaceutical Technology Co., Ltd.
Test Code: (2002) Food B2114m1-3-2158

Test Accordance: GB4789, 2-5, 10-11-94
Sample Quantity: 150g*3
Sample Form: Capsule
Testing Item: Colony Group, Coliform Group, Pathogen
Storage condition: Normal Temperature

Testing results:

Sample Code	(2002) B2114m2-2158	(2002) B2114m2-2158	(2002) B2114m2-2158
Sample Name	Beijing Xipu Global Biology Insulin	Beijing Xipu Global Biology Insulin	Beijing Xipu Global Biology Insulin
Sample Lot Number	20020501	20020502	20020503
Colony Group (cfu/g)	60	20	30
Coliform Group(MPN/100g)	<30	<30	<30
Golden Grape	No found	No found	No found
Salmonella	No found	No found	No found
Zhiheshi	No found	No found	No found
Haemolytic Streptococcus No found	No found	No found	No found

Following is empty

Reporting date: Aug. 9, 2002

Date of Terminal Verifying: Aug. 9, 2002
Principal of test unit:

This report only responsible for the sample sending Page 1 Total 1

translated by: Dzind Hs 4/3/03

17

Beijing Health Sanitation & Epidemic Prevention Station

Stability Experiment Report

Experiment Product: Beijing Xipu Global Biology Insulin.
Company Name: Beijing Xipu Global Biology Pharmaceutical Technology Co., Ltd.
Production Factory: Beijing Xipu Global Biology Pharmaceutical Technology Co., Ltd.
Testing Organization: Beijing Disease Prevention Controlling Center

Storage Condition: 37-40°C, humidity 75%
Testing Time: July, 2002-January, 2003(Humidity Experiment)
Result: List Below

Form 1. Beijing Xipu Global Biology Insulin Stability Experiment Report Results

Testing Item and time	Products Lot Number	20020501	20020502	20020503
Colony Total Quantity (cfu/g)	Before Heat Preservation	60	20	30
	Heat Preservation one month	<10	<10	10
	Heat Preservation two month	20	30	10
	Heat Preservation three month	20	20	30
Coliform Group (MPN/100g)	Before Heat Preservation	<30	<30	<30
	Heat Preservation one month	<30	<30	<30
	Heat Preservation two month	<30	<30	<30
	Heat Preservation three month	<30	<30	<30
Pathogen (Salmonella,Zhiheshi, Haemolytic Streptococcus)	Before Heat Preservation	No found	No found	No found
	Heat Preservation one month	No found	No found	No found
	Heat Preservation two month	No found	No found	No found
	Heat Preservation three month	No found	No found	No found
Sourdough (cfu/g)	Before Heat Preservation	<5	<5	<5
	Heat Preservation one month	<5	<5	<5
	Heat Preservation two month	<5	<5	<5
	Heat Preservation three month	<5	<5	<5
Mildew (cfu/g)	Before Heat Preservation	<5	<5	<5
	Heat Preservation one month	<5	<5	<5
	Heat Preservation two month	<5	<5	<5
	Heat Preservation three month	<5	<5	<5
Yellow Ketone (count in Luding) (mg/g)	Before Heat Preservation	26.8	24.6	25.8
	Heat Preservation one month	26.4	24.9	25.2
	Heat Preservation two month	26.1	25.1	25.7
	Heat Preservation three month	26.6	24.8	25.5

translated by: Dicid HS 4/3/03

Form 2. Beijing Xipu Global Biology Insulin Stability Experiment Report Results (followed in Form 1)

Testing Item and time	Products Lot Number	20020501	20020502	20020503
Arsenic (mg/kg)	Before Heat Preservation	0.053	0.056	0.034
	Heat Preservation one month	0.069	0.075	0.052
	Heat Preservation two month	0.092	0.089	0.082
	Heat Preservation three month	0.088	0.089	0.093
Lead (mg/kg)	Before Heat Preservation	0.16	0.15	0.11
	Heat Preservation one month	0.10	0.10	0.12
	Heat Preservation two month	0.17	0.10	0.14
	Heat Preservation three month	0.12	0.10	0.11
Hg (mg/kg)	Before Heat Preservation	0.066	0.068	0.072
	Heat Preservation one month	0.043	0.043	0.047
	Heat Preservation two month	0.053	0.048	0.062
	Heat Preservation three month	0.038	0.041	0.033
Water (g/100g)	Before Heat Preservation	6.2	6.3	6.3
	Heat Preservation one month	6.3	6.5	6.4
	Heat Preservation two month	6.5	6.4	6.7
	Heat Preservation three month	6.5	6.7	6.6
Dirt (g/100g)	Before Heat Preservation	38.3	40.1	39.4
	Heat Preservation one month	39.7	39.5	40.2
	Heat Preservation two month	40.0	40.7	39.9
	Heat Preservation three month	40.1	40.3	40.4
Ca (g/100g)	Before Heat Preservation	23.1	23.7	24.7
	Heat Preservation one month	23.6	24.7	25.7
	Heat Preservation two month	24.5	24.9	24.5
	Heat Preservation three month	25.4	25.1	25.5
Biding (mg/g)	Before Heat Preservation	1.0	1.1	1.0
	Heat Preservation one month	1.1	1.0	0.99
	Heat Preservation two month	1.1	1.2	1.1
	Heat Preservation three month	1.2	1.1	1.0
Origin Anthocyanin (g/100g)	Before Heat Preservation	8.5	8.3	8.9
	Heat Preservation one month	8.0	7.9	8.1
	Heat Preservation two month	8.1	8.4	8.2
	Heat Preservation three month	7.9	8.2	8.1

translated by David Hu 4/3/03

1P

Form 3 Beijing Xipu Global Biology Insulin Stability Experiment Report Results (followed in Form 2)

Testing Item and time	*Products Lot Number*	*20020501*	*20020502*	*20020503*
Ge (mg/kg)	Before Heat Preservation	0.033	0.040	0.042
	Heat Preservation one month	0.052	0.055	0.054
	Heat Preservation two month	0.061	0.021	0.036
	Heat Preservation three month	0.038	0.018	0.032

Conclusion: Jishicihang Brand Bee Colloid Capsule produced (Production Date: 20020501, 20020503, 20020503) by Liaocheng Green Source Bee Colloid Science and Trade Company, is Offered by Beijing Jishitang Chinese Herbal Medicine Health Institution together with Liaocheng Green Source Bee Colloid Science and Trade Company. 3 month-Period Humidity experiment is carried out under 37-40°c and humidity of 75%, all the indexes are steady after physics and chemistry testing.

Testing Chief:_____

Jan 21, 2002

translated by David Hs 4/3/03

20

Application Documents 4

Treatment & Theory

Beijing Xipu Global Biological & Pharmaceutical Technology Co., Ltd.

translated by Dr. Li HS 4/3/03

I. **Bee Colloid Capsule**

It contains rich yellow ketone, terpene, aminophenol, vitamine, Calcium, Magnesium, Kalium, Zinc and Chrome, which are all good for human health.

Bee colloid contained many kinds of useful substances, such as Vitamine B, Steapsin and Yellow Ketone. Vitamine B is origin material of making Insulin. Steapsin performs well renewing function of pancreas and viscera. Yellow Ketone and terpene can accelerate liver sugar compounding from outside grape sugar, hasten human using on grape sugar.

2 Chrome yeast (C_r^{3+})

C_r^{3+} is main substance improving grape sugar gene (GTF). If lack of C_r^{3+} , β cell will be damaged, Insulin excreting and transmission will be restrained and obstructed.

3 Balsam Pear

Modern research shows that Balsam Pear performance well on blood sugar dropping, dispelling heat and relieving tire.

4 Grape seeds extract (OPC)

It is the most effective oxidizer found from plants at present. It performs more oxygen resistance times over Vitamin C and E, thus it can get rid of liberty radicel enhance human's immunity.

5 Insect and Grass extract

Aminophenol, peptide and sugar can performance well on blood dropping and immunity enchancing.

6 Ginger exact

Reducing cold, reducing phlegm and relieving cough.

Bee Colloid Capsule combine functions of all above materials, thus make it scientific and perfect, processing very remarkable function on health caring.

translated by David Hu 4/3/03

Application Documents 5

22

Virulence Report

Beijing Xipu Global Biological & Pharmaceutical Technology Co., Ltd.

translated by: David Hsu 4/3/03

23

Capital Medical University Virulence Research Department

Testing Report

Sample Code: 2002041

Sample Name: Beijing Xipu Global Biological Insulin

Company Name: Beijing Xipu Global Biological & Pharmaceutical Technology Co., Ltd.

Sending Date: Nov 20, 2002

translated by: Dai HS 4/3/03

Capital Medical University

Virulence Testing Report Total 11 Page 1

Sample Code: 2002041 Sample Lot Code: 20020501
Experiment Product: Beijing Xipu Global Biology Insulin Sample Weight: 3.0kg
Company Name: Beijing Xipu Global Biology Pharmaceutical Technology Co., Ltd.

Production Factory: Beijing Xipu Global Biology Pharmaceutical Technology Co., Ltd.
Sample Arriving Date: Aug 29, 2002 Report Date: Nov 20, 2002
Testing objective: Safety Appraisement on Virulence

Testing Item:
1. Acute virulence experiment
2. Three-Phrase experiment
3. 30-day feeding experiments

Experiment Foundation: Food Safety Virulence Appraisement Program and Methods GB15193-94

Experiment Result and conclusion:

Acute virulence experiment: on LD50 Wistar adult mouse and 10g/kgBW baby mouse, the activity is usual, no unusual symptom found, it is substance of no poison.

Three-Phrase experiment: Ames experiment, micronucleus experiment on baby mouse m medulla PCE and sperm aberrance experiment, are all in negative quality.

30-day feeding experiment: Beijing Xipu Global Biology Insulin have no bad effects on body growing, blood system, liver, kidney, albumen, fattiness, sugar performance and main viscera organs.

(Testing method and results referring to the attachment)

This report is only responsible for sample receiving.

Technology Chief: _____

translated by Dai Hs 4/3/03

Acute Virulence Half Death Quantity (LD50) Experiment Report

Sample Code: 2002041 Sample Lot Code: 20020501
Experiment Product: Beijing Xipu Global Biology Insulin Sample Weight: 3.0kg
Company Name: Beijing Xipu Global Biology Pharmaceutical Technology Co., Ltd.
Production Factory: Beijing Xipu Global Biology Pharmaceutical Technology Co., Ltd.

Experiment Animal: Wistar adult mice, weight 180-200g, ICR baby mice, weight 18-22g, all offered by Experimental Animal Dept., Capital Medical University (Certificate No.:01-4059), are divided into 2 groups randomly, half in female and male.

Feeding environment: qualified room of SPF level (Certificate no.: 01-4059) room temperature 22±2°c, humidity 60%RH, vacuum package feeding stuff is provided by Beijing Jiujiangkou Company (Certificate no.:052).

Sample process: Picking up 50g of sample, pouring purified water to 100ml, consistency is 50%, 23.2%, 10.75% and 5% respectively.

Experimental Methods: Huoenshi Method. Sample is given by irrigating stomach. Stopping diet 16hours before experiment; observing a whole week, recording poisonous symptom and death.

Experimental Results:

Wistar Adult Mouse					ICR Baby Mous				
Dosage	Male mouse		Female mouse		Dosage	Male mouse		Female mouse	
	Total Q'ty	Death Q'ty	Total Q'ty	Death Q'ty		Total Q'ty	Death Q'ty	Total Q'ty	Death Q'ty
10.0g/kg	5	0	5	0	10.0g/kg	5	0	5	0
4.64g/kg	5	0	5	0	4.64g/kg	5	0	5	0
2.15g/kg	5	0	5	0	2.15g/kg	5	0	5	0
1.00g/kg	5	0	5	0	1.00g/kg	5	0	5	0

The mice behave as usual in experiment, being with normal hair color and light good, no any symptom is found, dosage-causing death is (LD50g/kg) 10g/kg.

Results: Experiment Product (Beijing Xipu Global Biology Insulin) belongs to real innocuous substance after being graded by acute poison.

Tested by: Chen Zhenliang Wu Tao

Checked by: Su Yilan

Technology Chief: Jiang Zhicheng

Capital Medical University Virulence Institution

September 10, 2002

translated by : Dai HS 4/3/03

Micronucleus Experiment Report

Sample Code: 2002041 Sample Lot Code: 20020501
Experiment Product: Beijing Xipu Global Biology Insulin Sample Weight: 2.0g/day
Company Name: Beijing Xipu Global Biology Pharmaceutical Technology Co., Ltd.
Production Factory: Beijing Xipu Global Biology Pharmaceutical Technology Co., Ltd.

Experiment Animal: ICR baby mice, weight 24-28g, all offered by Experimental Animal Dept., Capital Medical University (Certification No.: 01-4059), are divided into 2 groups randomly, half in female and male.

Feeding environment: qualified room of SPF level (Certificate no.: 01-4059) room temperature 22±2°c, humidity 60%RH, vacuum package feeding stuff is provided by Beijing Jiujiangkou Company(Certificate no.:052).

Sample process: Picking up 10g of sample, pouring purified water to 20ml, consistency is 50%, 25% and 12.5% respectively.

Dosage Arrange: Maximum 10g/kgBW, then 1/2(5.0g/kgBW) and 1/4(2.5g/kgBW); at the same time, masculine comparison group and negative comparison group is arranged, the consistency are 50%, 25% and 12.5% respectively.

Experimental Methods: Huoenshi Method. Sample is given by irrigating stomach. Stopping diet 16hours before experiment; observing a whole week, recording poisonous symptom and death.

Statistics Methods: Posong U Testing Methods.

Experimental Results:

Group	Animal Quantity	Observation	Micro Nucleus Contained	Value	Animal Quantity	Observation	Micro Nucleus Contain	value
	Male mouse	PCE value	PCE value	(‰)	Male mouse	PCE value	PCE value	(‰)
10.0g/kg	5	5×1000	5	1.00±0.71	5	5×1000	5	1.00±0.71
5.0g/kg	5	5×1000	4	0.80±0.45	5	5×1000	4	0.80±0.84
2.5g/kg	5	5×1000	3	0.60±0.55	5	5×1000	3	0.60±0.55
Cp35mg/g	5	5×1000	102	20.40±1.82	5	5×1000	102	20.60±2.51
Negative comparison group	5	5×1000	3	0.60±0.55	5	5×1000	3	0.60±0.55

No obvious difference (P>0.05) happens in experiment, obvious difference found between masculine group and negative group (P<0.01). It shows that within the range of dosage as this experiment, will not result micronucleus increasing.

Tested by: Shen Jiaqin Zhu Jinhua
Checked by: Su Yilan
Technology Chief: Jiang Zhicheng

Capital Medical University Virulence Institution

September 10, 2002

translated by : Dzin Hs 4/3/03

Sperm Experiment Report

Sample Code: 2002041 Sample Lot Code: 20020501
Experiment Product: Beijing Xipu Global Biology Insulin
Sample Weight: 2.0g/day (0.033g/kgW)
Company Name: Beijing Xipu Global Biology Pharmaceutical Technology Co., Ltd.
Production Factory: Beijing Xipu Global Biology Pharmaceutical Technology Co., Ltd.

Experiment Animal: Male ICR baby mice, weight 24-28g, all offered by Experimental Animal Dept., Capital Medical University (Certificate No.: 01-4059), are divided into 2 groups randomly, half in female and male.

Feeding environment: qualified room of SPF level (certificate no.: 01-4059) room temperature 22 ±2°c, humidity 60%RH, vacuum package feeding stuff is provided by Beijing Jiujiangkou Company(certificate no.:052).

Sample process: Picking up 20g of sample, pouring purified water to 40ml, consistency is 50%, 25% and 12.5% respectively.

Dosage Arrange: Maximum 10g/kgBW, then 1/2(5.0g/kgBW) and 1/4(2.5g/kgBW); at the same time, masculine comparison group and negative comparison group is arranged,

Experimental Methods: Killing sample after 35days continuous eating for 5 days, dying the testis and testing through microscope, 1000 of each mouse, record aberrance quantity and get the ratio.

Statistics Methods: Posong U Testing Methods.

Experimental Results:

Group	Animal Q'ty	Observation Sperm Q'ty	Aberrance Type						Aberrance Sperm Q'ty	Aberrance rate
			Unsteady	Banana	No hook	Fat head	Rolling tail	Double tail		
10.0g/kg	5	5×1000	49	7	0	0	0	0	56	1.12±0.19
5.0g/kg	5	5×1000	48	3	0	1	2	0	54	1.08±0.13
2.5g/kg	5	5×1000	50	5	0	2	0	0	57	1.14±0.18
Cp35mg/g	5	5×1000	321	72	62	65	69	0	589	11.7±0.56
Negative comparison group	5	5×1000	47	5	1	2	3	0	58	1.16±0.15

No obvious difference (P>0.05) happens in experiment, obvious difference found between masculine group and negative group (P<0.01). It shows that within the range of dosage as this experiment, will not result bad effects on procreation cell.

Tested by: Fengya Zhangjie
Checked by: Su Yilan
Technology Chief: Jiang Zhicheng

Capital Medical University Virulence Institution
Oct. 25, 2002

translated by: Daint He 4/3/03

Ames Experiment Report

Sample Code:	2002041 Sample Lot Code: 20020501
Experiment Product:	Beijing Xipu Global Biology Insulin
Sample Weight:	2.0g/day (0.033g/kgBW)
Company Name:	Beijing Xipu Global Biology Pharmaceutical Technology Co., Ltd.
Production Factory:	Beijing Xipu Global Biology Pharmaceutical Technology Co., Ltd.
Experiment Animal:	Male ICR baby mice with weight of 24-28g, are all offered by Experimental Animal Dept., Capital Medical University (Certification No.:01-4059), and divided into 2 groups randomly, half in female and male.
Operation Method:	Experiment is carried out in qualified room of SPF level (Certificate No.: 01-4059) with temperature of 22 ± 2°c and humidity of 60%RH. Vacuum package feedingstuff is provided by Beijing Jiujiangkou Company (Certificate no.:052).
Sample processing:	20g Sample is weighted, soaked in 40ml purified water with consistency of 50%, 25% and 12.5% respectively.
Masculine Comparison:	2-AF Amino Group 10ug/utensil, MMS 2ul/utensil, fluorene keone 0.2/utensil, 2AA 12ug/utensil
Experimental parameter:	(1) Protein content of Aroclo-1254 induced adult mice plasm is 33mg/ml; (2) S-9 is added at 20ul/utensil, according to AMES Test law revises in 1983. (3) Results of the experiment is average value of data of the three utensils.
Experimental Results:	Five consistency tests are carried out on samples, which are not suffered from bad effects under active metabolization of +S9 system and -S9 system.
Experimental Conclusion:	It shows that within the range of dosage as this experiment, will not result bad effects on procreation cell.

Tested by: Liu Yi Feng Ya

Checked by: Su Yilan

Technology Chief: Jiang Zhicheng

Capital Medical University Virulence Institution

September 20, 2002

translated by: [illegible] HS 4/3/03

Ames Test Results(Flat Plate Pre-soaking Method)

Experimental Product Mg/m	TA97a +S9	TA97a -s9	TA98 +S9	TA98 -s9	TA100 +S9	TA100 -s9	TA102 +S9	TA102 -s9
Beijing Xipu Global Biology Insulin				The first time				
1.00	90.00 ±29.46	67.00 ±22.63	32.33 ±6.03	18.67 ±4.73	131.33 ±8.14	137.00 ±9.85	293.00 ±18.36	184.67 ±37.07
0.50	138.33 ±39.88	127.33 ±2.52	30.67 ±4.61	26.67 ±3.79	128.67 ±6.43	132.33 ±10.69	312.00 ±8.54	246.00 ±12.49
0.25	130.67 ±16.07	136.00 ±13.75	31.67 ±6.03	30.67 ±3.06	141.00 ±7.94	139.67 ±13.43	298.33 ±11.50	254.33 ±4.73
0.1	137.33 ±8.08	150.33 ±24.13	36.67 ±3.51	31.00 ±4.00	139.50 ±12.02	191.00 ±4.36	313.67 ±20.21	253.67 ±15.50
0.05	132.33 ±20.55	129.33 ±4.51	33.33 ±4.62	28.67 ±2.52	136.67 ±16.26	137.33 ±7.51	298.00 ±19.31	258.67 ±14.01
0.01	134.33 ±3.51	133.00 ±8.19	30.67 ±3.06	30.33 ±3.06	137.67 ±8.02	135.33 ±6.03	300.67 ±14.22	263.33 ±7.09
His- (PBS+0.1MIDMSD)								
	139.67 ±7.51	138.00 ±6.56	33.67 ±4.73	29.67 ±3.51	132.67 ±9.29	129.67 ±9.07	281.33 ±13.2	260.33 ±8.50
0.50	130.00 ±9.64	127.33 ±8.33	29.67 ±2.52	28.33 ±3.06	142.33 ±14.01	137.33 ±8.50	312.67 ±10.26	268.67 ±13.43
0.25	139.33 ±9.07	136.67 ±10.69	33.67 ±2.52	33.33 ±5.03	128.67 ±3.51	133.33 ±8.74	307.33 ±14.22	254.33 ±10.41
0.1	131.67 ±7.37	133.33 ±3.51	32.33 ±4.16	32.67 ±5.69	139.67 ±13.2	134.00 ±12.00	298.33 ±19.86	264.67 ±10.97
0.05	142.67 ±13.50	128.67 ±4.51	34.33 ±3.21	29.67 ±3.21	145.67 ±14.57	135.33 ±8.02	301.33 ±10.69	255.00 ±18.52
0.01	135.00 ±14.53	131.33 ±4.04	30.33 ±3.79	31.33 ±3.06	140.67 ±8.33	136.67 ±9.45	292.33 ±9.45	248.33 ±13.05
His-(PBS+0.1MIDMSD)								
	127.67 ±5.69	133.00 ±6.24	31.33 ±5.69	31.67 ±5.03	134.33 ±9.29	132.33 ±10.97	313.00 ±14.18	250.67 ±17.9
Masculine comparison	(ug/m)							
2-AF 1C	1461±94.75		2688±771.53					
Ketone 0.2		2724±130.11		2182±93.34				
2-AF 10					1512±90.51			
MMS 2ul						1993±188.09		3412±265.87
2AA 12							1326±138.59	

translated by : Dai HS 4/3/03

30-day Feeding Experiment Report

Sample Code: 2002041 Sample Lot Code: 20020501

1.Product Name: Beijing Xipu Global Biology Insulin, which is made from bee colloid, biding, grape beed and pearl powder. 2.0g/day is recommended to group and 0.033g/kgBW to adult count on per 60kg.

2.Company Name: Beijing Xipu Global Biology Pharmaceutical Technology Co., Ltd.

3.Production Factory: Beijing Xipu Global Biology Pharmaceutical Technology Co., Ltd.

4.Experiment Animal: Male ICR baby mice, weight 24-28g, all offered by Experimental Animal Dept., Capital Medical University(Certification No.:01-4059), are divided into 2 groups randomly, half in female and male.

5.Dosage Arrange: Maximum 10g/kgBW, then 1/2(5.0g/kgBW) and 1/4(2.5g/kgBW); at the same time, masculine comparison group and negative comparison group is arranged,

6.Taking methods: Feedstuff is adopted and freely absorbed

7.Feedstuff formulation: 10% of the adult mice weight is taken as feedstuff absorbing dosage, feedstuff of different consistency is made according to dosage, that is 3.3%, 2.48 and 1.65%.

8.Observation indexes:

8.1 Observing activities of the animals, as well as hair color, absorption and drainage. The body will be dissected if it is dead.
8.2 Growth and food usage rate: Animals should be weighted daily before and after the experiment, as well as record information of feedstuff adding and balance thus food usage rate is made.
8.3 Blood index: Hb, RBC, PLT, WBC and assorting.
8.4 Biology and chemistry index: ALT, AST, TP, ALB, GLB, A/G, BUN, and CRE...
8.5 Viscus indexes: heart, liver, spleen, kidney, stomach, bowels, pancreas, spermary and ovary.
8.6 Pathology inspection: Inspecting with light microscope on theart, liver, spleen, kidney, stomach, bowels, pancreas, spermary and ovary.

9.Statistics Methods: Square Difference Method.

10.Experimental Results:

No obvious difference ($P>0.05$) happens in experiment, obvious difference found between masculine group and negative group($P<0.01$).

10.1.It shows that within the range of dosage as this experiment, will not result bad effects on procreation cell.

translated by : Diana Hu 4/3/03

List 1 Animal weight in every week (X±sd)

Group type	Animal Q'ty	Before Experiment	First week	Second week	Third week	Fourth Week
Beijing Xipu Global Biology Insulin				Male mouse		
3.30g/kg	10	65.80±2.90	109.70±11.60	159.70±9.19	207.10±8.95	255.50±11.19
2.48g/kg	10	65.70±2.98	112.40±11.41	160.20±11.63	209.80±8.80	258.20±7.18
1.65g/kg	10	66.00±2.75	110.30±8.93	158.80±8.24	206.10±1.75	252.40±6.54
Negative comparison	10	65.80±3.01	111.30±5.48	163.40±6.85	211.20±9.40	259.40±8.93
				Female mouse		
3.30g/kg	10	66.00±2.11	106.80±6.41	134.80±5.79	161.00±8.82	188.20±7.83
2.48g/kg	10	66.10±1.91	100.70±5.68	135.30±5.62	163.30±7.56	188.90±6.17
1.65g/kg	10	66.10±1.91	101.40±4.65	132.20±5.33	162.20±4.76	168.30±5.96
Negative comparison	10	66.20±1.99	101.80±6.86	132.40±[illegible].17	157.90±8.50	183.10±8.16

Form 1 shows that weight comparison with negative group, no obvious difference found(P>0.05).

10.2 Food using rate: referring to Form 2.

Form 2 Weigh increasing(g) and food using rate(X±SD)

Group	Male mouse			female mouse		
	Weight increasing	Total capacity	Food using rate	Weight increasing	Total capacity	Food using rate
Beijing Xipu Global Biology Insulin						
3.30g/kg	189.70±10.31	504.40±14.32	37.59±1.05	122.20±8.20	454.60±29.70	26.94±0.88
2.48g/kg	192.50±6.43	512.30±10.31	37.58±0.97	122.80±5.92	470.10±16.37	26.14±1.43
1.65g/kg	186.40±6.45	495.50±23.53	37.67±1.64	122.20±6.76	448.90±20.01	27.25±1.42
Negative comparison	193.60±8.82	501.95±14.76	38.57±1.06	116.90±6.64	445.00±18.42	26.27±0.94

Form 2 shows that no obvious difference found on weight increasing and food usage rate, comparison with negative group, (P>0.05).

translated by: [illegible] 4/3/03

10.3 Blood index: Referring to list 3

List 3 Animal blood index result (X±SD)

Group	Hb (g/L)	RBC ($X10^{17}$/L)	WBC ($X10^{9}$/L)	PLT ($X10^{9}$/L)	Lymph (%)	Neutral (%)	Others (%)
Beijing Xipu Global Biology Insulin				Male mouse			
3.30g/kg	143.40±16.05	5.94±0.62	15.05±2.50	378.60±118.11	81.70±1.16	14.20±1.23	4.10±0.74
2.48g/kg	145.10±14.46	6.02±0.87	15.77±3.45	320.40±341.80	80.90±1.45	15.20±0.38	3.90±0.74
1.65g/kg	146.00±13.91	6.88±0.48	17.01±4.55	351.90±164.03	81.30±1.70	15.00±1.15	3.70±0.82
Negative comparison	146.30±9.24	5.98±0.44	16.72±3.72	378.90±9.17	81.00±1.70	15.30±1.30	3.70±0.67
				Female mouse			
3.30g/kg	152.80±10.04	6.61±0.80	15.34±3.45	286.80±101.58	82.00±1.25	14.50±1.35	3.50±0.53
2.48g/kg	153.70±16.86	6.60±0.86	16.56±2.70	404.20±108.38	82.80±0.79	13.50±0.97	3.70±0.82
1.65g/kg	158.70±18.52	4.36±0.79	17.04±3.14	353.70±126.21	83.10±1.29	13.70±1.16	3.20±0.42
Negative comparison	148.00±7.97	0.43±0.42	15.86±3.79	418.70±137.48	81.80±1.69	15.00±1.41	3.20±0.42

Form 3 shows that weight comparison with negative group, no obvious difference found (P>0.05).

10.4 Biology chemical index: referring to Form 4 & 5.

Form 4 Biology chemical index results(X±SD)

Group	ALT u/L	AST U/L	TP g/L	ALB g/L	GLB g/L	A/C
Beijing Xipu Global Biology Insulin				Male mouse		
3.30g/kg	27.30±6.19	136.42±7.80	65.80±2.00	31.94±0.69	33.86±2.23	0.95±0.07
2.48g/kg	22.21±4.64	137.99±9.42	65.44±1.93	31.66±0.52	34.78±1.94	0.91±0.05
1.65g/kg	25.95±4.87	144.16±9.06	66.63±2.04	32.06±.76	34.57±1.89	0.93±0.05
Negative comparison	23.74±6.38	148.24±9.60	66.34±2.00	32.14±0.96	34.20±2.45	0.95±0.09S
				Female mouse		
3.30g/kg	21.57±6.39	135.55±8.80	66.88±2.58	32.24±0.96	34.54±2.86	0.94±0.09
2.48g/kg	18.56±4.28	140.48±12.18	67.80±2.48	32.05±0.71	35.75±2.21	0.90±0.06
1.65g/kg	23.44±5.21	142.79±9.19	67.01±2.31	31.84±0.73	35.17±2.17	0.91±0.06
Negative comparison	22.85±4.53	146.49±9.33	67.33±2.18	32.31±0.91	35.02±2.96	0.93±0.10

translated by: Dzing He 4/3/03

List 5 Animal blood index result (X±SD)

Group	CRE Umol/L	BUN Umol/L	GLU Umol/L	TC Umol/L	TC Umol/L
Beijing Xipu Global Biology Insulin				Male mouse	
3.30g/kg	44.30±9.85	5.14±0.58	4.59±0.21	1.53±0.17	0.72±0.14
2.48g/kg	45.78±14.69	5.19±0.60	4.47±0.30	1.57±0.10	0.75±0.17
1.65g/kg	44.30±13.92	5.19±0.57	4.47±0.14	1.58±0.14	0.70±0.13
Negative comparison	47.25±6.23	4.83±0.90	4.41±0.13	1.51±0.19	0.75±0.16
				Female mouse	
3.30g/kg	39.87±7.13	4.74±0.80	3.73±0.27	1.45±0.09	0.49±0.10
2.48g/kg	39.87±7.13	4.61±0.84	3.85±0.34	1.46±0.08	0.51±0.10
1.65g/kg	39.87±7.13	4.56±0.68	3.89±0.33	1.37±0.09	0.57±0.14
Negative comparison	47.25±13.57	4.80±0.69	4.10±0.43	1.51±0.10	0.53±0.14

Form 4 & 5 shows that weight comparison with negative group, no obvious difference found.

10.5 Viscera organ index: referring to Form 6

Form 6 Viscera organ index results (X±SD)

Group	Heart	Liver	Spleen	Pancreas	Kidney	Stomach	Spermary(ovary)
Beijing Xipu Global Biology Insulin					Male mouse		
3.30g/kg	0.31±0.01	2.83±0.10	0.23±0.02	0.17±0.02	0.72±0.02	0.51±0.02	0.91±0.05
2.48g/kg	0.31±0.01	2.86±0.14	0.23±0.01	0.16±0.01	0.72±0.02	0.53±0.03	0.89±0.03
1.65g/kg	0.31±0.01	2.86±0.09	0.23±0.02	0.17±0.02	0.72±0.02	0.51±0.05	0.89±0.06
Negative comparison	0.31±0.02	2.58±0.17	0.24±0.02	0.17±0.02	0.73±0.01	0.51±0.03	0.91±0.05
					Female mouse		
3.30g/kg	0.32±0.02	2.87±0.14	0.24±0.02	0.19±0.02	0.72±0.03	0.56±0.02	0.062±0.008
2.48g/kg	0.31±0.01	2.87±0.12	0.25±0.02	0.17±0.02	0.73±0.02	0.54±0.03	0.057±0.007
1.65g/kg	0.32±0.02	2.80±0.10	0.25±0.02	0.17±0.02	0.72±0.03	0.56±0.02	0.057±0.005
Negative comparison	0.33±0.01	2.91±0.29	0.26±0.02	0.18±0.02	0.74±0.03	0.58±0.02	0.061±0.006

translated by : Dzing Hb 4/3/03

Form 6 shows that weight comparison with negative group, no obvious difference found (P>0.05).

10.6 Disease principal organization observation

Liver and viscera organs in right color with sharp edge, no abnormality found, no obvious organs variation happen except that is slight bad on part of liver cell(Maximum dosage 5/20, middle dosage 2/10, minimum 2/10 and comparison 5/20).

10 Conclusion

In the dosage range as this experiment (1.65-3.30g/kgBW), no obvious effects found to animals growth, food usage rate, blood system, liver, kidney, procreation system and metabolizing of albumen, fattiness and sugar.

Tested by: Chen Zhenliang Feng Ya
Checked by: Su Yilan
Technology Chief: Jiang Zhicheng

Capital Medical University Virulence Institution
Nov 20, 2002

translated by: David Hu 4/3/03

Application Documents 6

Certification

Beijing Xipu Global Biological & Pharmaceutical Technology Co., Ltd.

translated by: [illegible] HS 4/3/03

36

NO.Y.05-1

Sanitation License

Duplication Chang Wei Shi Jian Zi 2002 No.2085

Corporation Name: Beijing Xipu Global Biological & Pharmaceutical Technology Co., Ltd.

Corporate Representative: Wang Wenbing

Address: NO. 9, Zhenxing Road, Science & Technology Park District, Changping Town, Beijing City

Certified Item: Authorization on Processing and Sale of Xipu Global Biology Insulin

License-issuing Authority: Sanitation Bureau, Changping District, Beijing City

Nov 15, 2002

Valid Period: From Nov 15, 2002 to Nov 14, 2004

translated by: David Hs 4/3/03

37

Beijing Standard Certificate of Products Registration

Registration No.: CP0450

Corporation Name: Beijing Xipu Global Biological & Pharmaceutical Technology Co., Ltd.

Registration Address: NO. 9, Zhenxing

Road, Science & Technology Park District, Changping Town, Beijing

Corporate Representative: Wang Wenbing

Authority Code: 80266437-8

Registration Valid Period: From Nov 19, 2002 to Nov 19, 2007

Registration Authority: Beijing Quality Technology Supervision Bureau

translated by: David HB 4/3/03

Original. Copy

申报资料 1

Application Document 1.

配方、工艺及简图

柏洛理糖

Biodiatab

北京玺圃环球生物医药技术有限公司

一：处方

成份名称	含量（mg）	百份含量（%）	产地
蜂胶提取物	50	10	中国
苦瓜提取物	200	40	中国
富铬酵母	50	10	中国
虫草提取物	100	20	中国
葡萄籽提取物	50	10	中国
生姜提取物	50	10	中国
合　　计	500	100	

二　加工方法

1　生产工艺

A　蜂胶提取物

蜂胶粗粉用酒精回流提取两次，酒精回收得浸膏，萃取后的干粉用。

B　苦瓜提取物

苦瓜洗净，粉碎匀浆，—20 度以下冻融两次，过滤后再超滤，滤液真空低温干燥，干粉备用。

C　富铬酵母

用啤酒酵母发酵而成。

D　虫草提取物

虫草粗粉用 70%酒精回流提取两次，酒精液回收得浸膏，酸化后萃取，萃取液干燥备用。

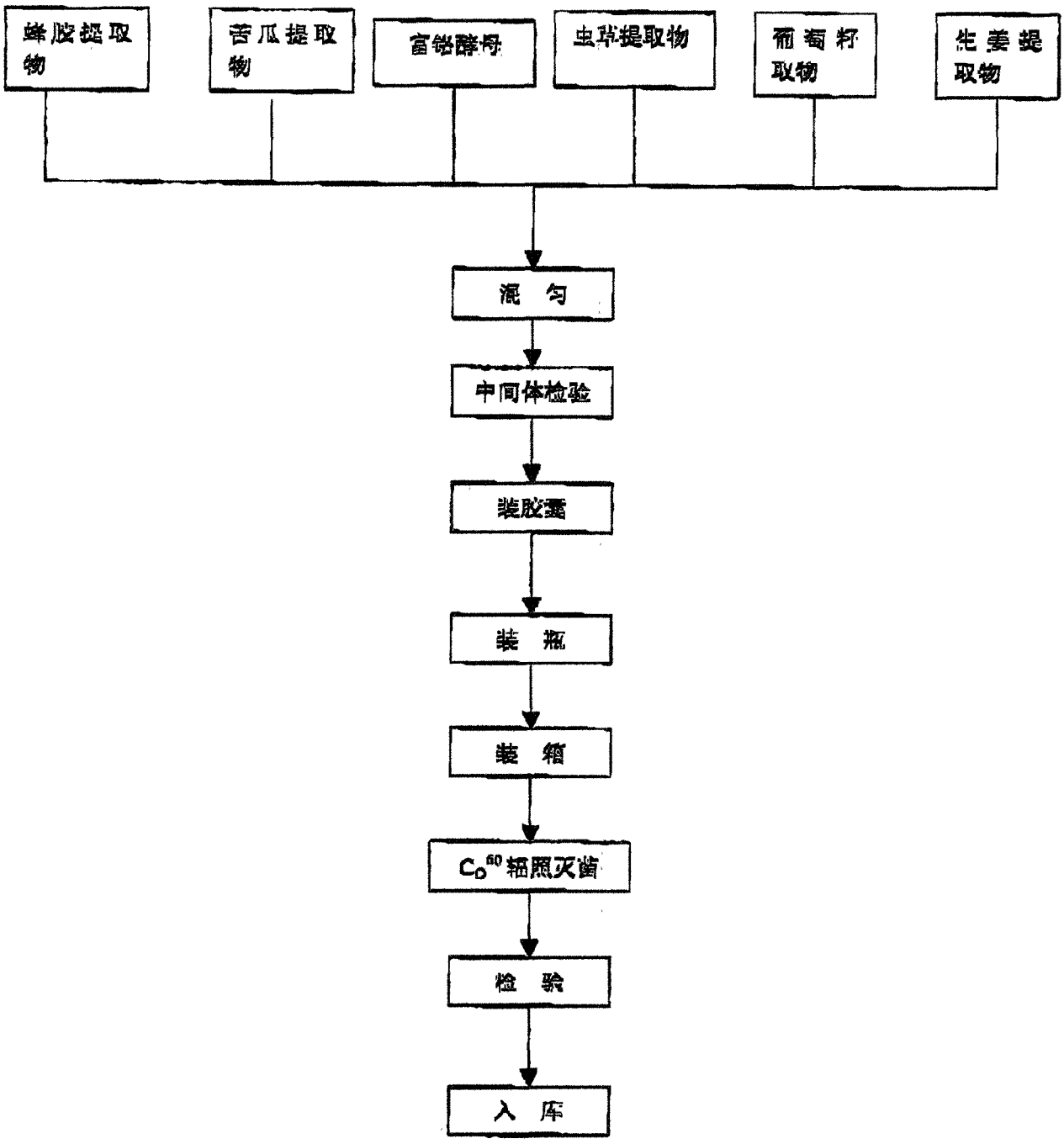
E　葡萄籽提取物

葡萄洗净粉碎，有机溶剂提取，萃取后干燥备用。

F　生姜提取物

生姜粗粉，适量加水搅拌均匀，浸后渗滤，渗滤液加总体积的 10%—20%盐水静置过滤，沉淀溶于热水，趁热过滤，滤液调至 PH=2，放置过滤，沉淀纯水洗至中性，干燥备用。

2 工艺流程图


蜂胶提取物
苦瓜提取物
富锌酵母
虫草提取物
葡萄籽取物
生姜提取物
混 匀
中间体检验
装胶囊
装 瓶
装 箱
Co^{60}辐照灭菌
检 验
入 库

申报资料 2

临床实验报告

北京玺圃环球生物医药技术有限公司

北京联合大学应用文理学院保健食品功能检测中心

(2001)量认(京)字(00270)号

检 验 报 告 单

检品名称：北京垦圃环球生物胰岛素　送检单位：北京垦圃环球生物医药技术有限公司

生产单位：北京垦圃环球生物医药技术有限公司

受理编号：[200210052　样品批号：20020501

检验项目：辅助降血糖作用

收样日期：2002 年 9 月　报告日期：2002 年 11 月

检验依据：《保健食品功能学评价程序和检验方法》

结果与判定

经口给予小鼠不同剂量的北京垦圃环球生物胰岛素四周后，高血糖模型小鼠在糖耐量实验中，灌胃葡萄糖后 0.5 小时，低（0.17g/kg.bw）、中（0.33g/kg.bw）、高（1.00g/kg.bw）剂量组的血糖值与高血糖模型组比较分别降低了 25%（P<0.001）、15%（P<0.01）和 17%（P<0.05）；灌胃葡萄糖后 2 小时，低、中、高剂量组的血糖值与高血糖模型组比较分别降低了 29%（P<0.01）、23%（P<0.01）和 22%（P<0.05）；各剂量组体重与高血糖模型对照组比较无显著差异（P>0.05）。给受试物前后，正常小鼠受试物组与空白对照组比较，空腹血糖及体重均无显著差异（P>0.05）。

根据《保健食品功能学评价程序和检测方法》判定：北京垦圃环球生物胰岛素具有辅助降血糖作用。

以下空白。

本检验报告仅对送检样品负责

技术负责人：金宇倩

日　　期：2002 年 11 月 7 日

2. 结果

2. 1 对正常小鼠血糖的影响

表 1 对正常小鼠血糖的影响 (X±SD)

组别	受试物剂量 (g/kg. bw)	动物数 (只)	血糖 (mmol/L)			
			给受试物前	P 值	给受试物四周后	P 值
空白对照组	0	10	5.0±0.7	—	4.8±0.6	—
受试物组	1.00	10	5.4±0.9	0.2274	4.8±1.6	0.9284

由表 1 可见，给予正常小鼠受试物四周后，受试物组的血糖值与空白对照组比较无显著差异 (P>0.05)。

2. 2 对四氧嘧啶所致高血糖模型小鼠血糖的影响

表 2 对四氧嘧啶所致高血糖模型小鼠血糖的影响 (X±SD)

组别	受试物剂量 (g/kg. bw)	动物数 (只)	血糖值 (mmol/L)			
			给受试物前	P 值	给受试物四周后	P 值
高血糖模型对照组	0	10	18.8±3.0	——	31.8±6.4	——
低剂量组	0.17	10	18.7±3.1	0.9886	25.3±10.4	0.1110
中剂量组	0.33	10	18.7±5.0	0.9831	26.6±11.6	0.2363
高剂量组	1.00	10	18.1±4.6	0.7234	25.5±10.5	0.1248

由表 2 可见，给受试物前，高血糖模型小鼠各剂量组血糖值与高血糖模型对照组比较均无显著差异 (P>0.05)。给予不同剂量的受试物四周后，各剂量组的血糖值与高血糖模型组比较均无显著差异 (P>0.05)。

2. 3 对四氧嘧啶所致高血糖模型小鼠糖耐量的影响

表 3 对四氧嘧啶所致高血糖模型小鼠糖耐量的影响 (X±SD)

组别	受试物剂量 (g/kg. bw)	动物数 (只)	血糖值 (mmol/L)					
			0 小时	P 值	0.5 小时	P 值	2 小时	P 值
高血糖模型对照组	0	10	31.8±6.4	——	50.0±8.3	——	34.6±4.9	——
低剂量组	0.17	10	25.3±10.4	0.1110	37.7±6.4 ***	3.822×10^{-7}	24.4±8.4 **	0.0036
中剂量组	0.33	10	26.6±11.6	0.2363	42.6±5.3 **	0.0014	26.8±7.0 **	0.0095
高剂量组	1.00	10	25.5±10.5	0.1248	41.7±8.5*	0.0101	27.1±8.8*	0.0298

*：与高血糖模型对照组比较有显著差异 (P<0.05)

**：与高血糖模型对照组比较有非常显著差异 (P<0.01)

***：与高血糖模型对照组比较有极显著差异 (P<0.001)

由表 3 可见，灌胃葡萄糖后 0.5 小时，低、中、高剂量组的血糖值与高血糖模型组比较分别降低了 25% (P<0.001)、15% (P<0.01) 和 17% (P<0.05)。灌胃葡萄糖后 2 小时，低、中、高剂量组的血糖值与高血糖模型组比较分别降低了 29% (P<0.01)、23% (P<0.01) 和 22% (P<0.05)。

北京市疾病预防控制中心
Beijing Municipal Center for Disease prevention and Control

中国中医研究院西苑医院
Xiyuan Hospital of China Academy of Traditional Chinese Medicine

检验报告
CERTIFICATE OF ASSAY

样品编号：(2002)食B2114
检测编号：2002S0046
送检单位：北京济世堂中医药保健研究所；聊城市绿源蜂胶科贸有限公司
生产单位：北京济世堂中医药保健研究所
生产日期：2002年5月1日
检品名称：济世慈航牌蜂胶糖泰胶囊
样品数量：0.4g/粒×75粒/瓶×140瓶
检测项目：降糖功效人体试食实验
收样日期：2002年11月23日
报告日期：2003年1月24日
检验依据：《保健食品功能学评价程序和检验方法》

结果与判定：

采用双盲自身及组间对照法，将60例高血糖试食者随机分为试食组和对照组，每组30例，观察期间原服用降糖药物品种和剂量不变，试食组加食济世慈航牌蜂胶糖泰胶囊，对照组加食安慰剂。一个月后，其结果表明济世慈航牌蜂胶糖泰胶囊有降低血糖的功效，空腹血糖下降1.11±1.51mmol/L，餐后血糖下降1.91±2.20mmol/L，有效21例，总有效率 70.00%；对照组空腹血糖、餐后血糖下降不明显，有效9例，总有效率30.00%，两组对比有显著差异。试食前后血红蛋白、红细胞、白细胞、血清总蛋白、白蛋白、谷草转氨酶、谷丙转氨酶、尿素、肌苷及尿常规等各项临床检验指标均在正常范围，说明济世慈航牌蜂胶糖泰胶囊对试食者身体健康无明显的不良影响。

本检验报告仅对送检样品负责

技术负责人：

日　　期：2003年1月24日

“济世慈航牌蜂胶糖泰胶囊”人体试食观察报告

1．材料与方法：

1．1．样品：济世慈航牌蜂胶糖泰胶囊，对照组为安慰剂。全部由北京济世堂中医药保健研究所提供。

1．2．受试对象：Ⅱ型糖尿病人或高血糖者60例，年龄在18-65岁，无严重心肝肾等并发症者，随机分为受试组和对照组。各组采用自身对照设计，两组间为组间对照设计。

1．2．1．诊断标准：选择经饮食控制或口服降糖药治疗后病情较稳定，不需要更换药物品种及剂量，仅服用维持量的成年Ⅱ型糖尿病病人，空腹血糖≥7.8mmol/L(140mg/dl)或餐后2h血糖≥11.1mmol/L(200mg/dl)；也可选择空腹血糖≥6.7 mmol/L及餐后2h血糖≥7.8 mmol/L的高血糖人群。

1．2．2．纳入者标准：

凡符合上述诊断标准的Ⅱ型糖尿病及高血糖者，均可进行试食观察。

1．2．3．排除者标准：

1．2．3．1．年龄在18岁以下或65岁以上者，妊娠或哺乳期妇女。

1．2．3．2．有严重心、肝、肾等并发症，或合并有其它严重原发性疾病，精神病患者。

1．2．3．3．不合作者，无法判断功效或资料不全者。

1．3．试食方法：60例Ⅱ型糖尿病及高血糖试食者，随机分为二组，原服用降糖药物品种及剂量不变，分别加食济世慈航牌蜂胶糖泰胶囊和安慰剂，每日5粒，早3粒，晚2粒。要求试食者长期坚持饮食控制，按不同劳动强度和体型进食。

1．4．仪器与试剂：F-820型血球计数仪，MIDIRON尿十项分析仪(德国产)，Olympus全自动生化分析仪型号AU600(日本产)，生化试剂盒全部由中生公司提供。

2．观察指标：

各项指标于试食实验开始及结束时各测试一次，试食第15天加测空腹血糖一次。

2．1．功效性观察：

2．1．1．症状观察：

详细询问病史，了解患者饮食情况，活动量，观察主要临床症状：多食、多饮、多尿、疲乏无力等。按症状轻重(重症3分、中度2分、轻症1分)在试食前后统计积分值，并就其主要症状改善(每一症状改善2分显效，改善1分为有效)，观测症状改善率。

2．1．2．空腹血糖及餐后2小时血糖检测。

2．1．3．尿糖尿酮体检测。

2．1．4．血脂(总胆固醇TC、甘油三脂TG)检测。

2．2．安全性观察：

2．2．1．血尿常规检查：

红细胞计数，血红蛋白，白细胞计数，尿十项测定。

2．2．2．生化指标测定：

血清白蛋白ALB，总蛋白TB，心肝肾功能(谷草转氨酶AST，谷丙转氨酶ALT，尿素UREA，肌苷Cre)。

2．2．3．腹部B超，心电图，X线胸部透视。

3．功效判定标准：

3．1．有效：基本症状明显改善，空腹血糖或餐后血糖较治疗前下降≥10%

3．2．无效：基本症状无明显改善，血糖下降未达到上述标准。

4．结果：观察结束双盲揭晓：服食Ⅰ号者为济世慈航牌蜂胶糖泰胶囊组，服食Ⅱ号者为安慰剂对照组。

4．1．一般资料：

共观察 60例，济世慈航牌蜂胶糖泰胶囊组男性 13例，女性 17例，年龄最小 34岁，年龄最大 65岁，平均51.03岁，平均病程 4.83年；对照组男性18例，女性 12例，年龄最小34岁，最大65岁，平均52.47岁，平均病程3.47年。

4．2．两组观察前一般情况比较：

表1．观察前一般情况比较(X±SD)

分组	例数(例)	年龄(岁)	性别 男	性别 女	病程(年)	血糖(mmol/L) 空腹	血糖(mmol/L) 餐后2小时
蜂胶糖泰胶囊	30	55.23±6.76	11	19	5.80±3.77	9.49±2.79	13.38±4.55
对照组	30	53.17±4.26	11	19	5.85±4.26	9.26±2.72	12.25±3.44

表2．试食者服用降糖药物情况

分组	例数	磺脲类	双胍类	磺脲+双胍类	未服用
蜂胶糖泰胶囊	30	7	7	[illegible]	[illegible]
对照组	30	6	6	4	4

表1、表2可见，两组试食前各项指标无明显差异，具有可比性。

4．3．降糖功效：

4．3．1．空腹及餐后血糖比较：

表3．两组试食前后空腹血糖比较(mmol/L，X±SD)

分 组	试食前	试食后	差值
蜂胶糖泰胶囊	9.49±2.80	8.37±2.82	-1.11±1.51**
对 照 组	9.26±2.72	9.28±2.97	+0.02±1.42##

自身对照 ** P < 0.01 组间对照 ## P < 0.01

表4．两组试食前后餐后2小时血糖比较(mmol/L，X±SD)

分 组	试食前	试食后	差值
蜂胶糖泰胶囊	13.38±4.55	11.47±3.42	-1.91±2.20**
对 照 组	12.25±3.44	12.02±3.42	0.23±1.92##

自身对照 ** P < 0.01 组间对照 ## P < 0.01

一个月后，济世慈航牌蜂胶糖泰胶囊组空腹血糖平均下降1.11mmol/L，餐后2小时血糖平均下降1.91mmol/L；对照组空腹血糖及餐后2小时血糖下降不明显。

4．3．2．空腹血糖、尿糖、尿酮体比较：

表5．试食前中后空腹血糖及尿糖尿酮体变化比较(X±SD)

项目	例数	试食前	试食中	前中差值	试食后	前后差值
血糖	30	9.49±2.80	8.03±1.84	1.46±2.28*	8.37±2.82	1.11±1.51**
(mmol/L)	(30)	(9.26±2.72)	(9.18±2.79)	(-0.08±0.97)	(9.28±2.97)	(-0.02±1.42)
尿糖	30	0.53±1.22			0.37±0.84	-0.17±0.66
	(30)	(0.45±1.00)			(0.57±1.13)	(0.12±0.80)
尿酮体	30	-			-	
	(30)	(-)			(-)	

( ) 对照组 自身对照 ** P< 0.01

4．4．降血糖功效比较：

表6．血糖值功效统计

分 组		有效	无效	总有效率(%)
蜂胶糖泰胶囊	例 数	21	9	21
	功效率(%)	70.00	30.00	70.00 #
对 照 组	例 数	9	21	9
	功效率(%)	30.00	70.00	30.00

经X^2检验，两组总有效率差别显著，P < 0.05

质量检测中心

4．5．症状改善状况：

表9. 试食前后临床症状的变化

症状	显效（例）		有效（例）		无效（例）		改善率%	
	对照组	试食组	对照组	试食组	对照组	试食组	对照组	试食组
多食	0	1	5	6	6	6	45.45	53.85
多饮	0	1	5	6	9	4	40.00	63.64
多尿	0	1	6	7	10	6	37.50	57.14
乏力	0	2	8	9	11	6	42.10	64.71

在各主要症状改善方面，济世慈航牌蜂胶糖泰胶囊均好于对照组。

4．6．临床症状积分统计：

表10. 临床症状积分统计（X±SD）

分 组	例数	试食前	试食中	试食后
蜂胶糖泰胶囊	30	7.07±5.43	5.37±4.15***	4.90±4.30***
对 照 组	30	6.80±3.75	5.57±3.16***	4.27±3.20***

自身对照 *** $P < 0.001$

济世慈航牌蜂胶糖泰胶囊和对照组均有改善临床症状的作用。

4．7．血脂变化情况：

表11. 试食前后血脂变化比较（X±SD）

项 目	蜂胶糖泰胶囊(n=30)		对照组(n=30)	
	试食前	试食后	试食前	试食后
TC(mmol/L)	4.99±0.94	4.94±0.85	4.59±1.05	4.64±0.99
TG(mmol/L)	2.09±1.58	1.89±1.44	1.83±1.39	1.87±1.54

济世慈航牌蜂胶糖泰胶囊组与对照组对血脂各项均无明显影响。

4．8．血液安全指标观察：

表11：试食前后血液安全指标变化比较(X±SD)

项 目	蜂胶糖泰胶囊(n=30)		对照组(n=30)	
	试食前	试食后	试食前	试食后
TP (g/L)	73.95±4.41	74.63±5.79	70.77±5.19	72.18±6.07
ALB(g/L)	43.70±2.44	43.95±4.12	42.36±4.22	42.78±4.08
ALT(u/L)	22.77±9.53	21.37±10.23	19.93±9.33	20.00±10.88
AST(u/L)	25.20±7.00	25.07±8.39	21.87±7.29	21.13±5.86
UREA(mmol/L)	5.41±1.29	6.00±1.30	5.35±1.31	5.39±1.50
Cre(umol/L)	93.57±12.43	94.92±12.02	88.29±13.06	92.49±13.68
HGB(g/L)	130.13±12.97	132.53±11.99	133.63±12.89	137.80±13.59
RBC($\times10^{12}$/L)	4.39±0.41	4.38±0.37	4.36±0.39	4.40±0.39
WBC($\times10^{9}$/L)	6.69±1.55	6.57±1.33	6.61±1.55	6.49±1.39

两组试食前后，血液检测各项指标均在正常范围。

4．9．胸透、心电图、B超检查： 受试者均在正常范围。

5．总结：

5．1．济世慈航牌蜂胶糖泰胶囊有较为明显的降低血糖的功效， 空腹血糖值下降1.11±1.51mmol/L，餐后血糖下降 1.91±2.20mmol/L，有效21例，总有效率 70.00%；对照组空腹血糖及餐后血糖下降不明显，有效9例，总有效率30.00%，两组比较有显著差异，说明济世慈航牌蜂胶糖泰胶囊辅助降血糖有一定的功效。

5．2．济世慈航牌蜂胶糖泰胶囊试食者对多食、多饮、多尿、疲乏无力等主要症状，有较好的改善作用。

5．3．试食济世慈航牌蜂胶糖泰胶囊后，血红蛋白、红细胞、白细胞、血清总蛋白、白蛋白、谷丙转氨酶、谷草转氨酶、 肌苷、尿素及尿常规各项等检查指标均在正常范围，说明本品对试食者身体健康无不良影响。

5．4．济世慈航牌蜂胶糖泰胶囊在试食过程中未观察到过敏及其它不良反应。

北京市疾病预防控制中心

2003年1月24日

中国科学研究院西苑医院

2003年1月24日

申报资料 3

化验分析报告

北京玺圃环球生物医药技术有限公司

北京市疾病预防控制中心

检测报告

样品受理编号 (2002)食 B2114 第 1 页 共 1 页

样品名称	北京玺圃环球生物胰岛素	检测编号	(2002)食 B2114h1-3-1310
送检单位	北京玺圃环球生物医药技术有限公司	生产单位	北京玺圃环球生物医药技术有限公司
采样地点	/	检测目的	卫生学
受理日期	2002.07.31	检测日期	2002.07.31
样品性状	胶囊	样品数量	8 瓶×3
保存条件	常温	检测室名称	营养与食品卫生所

检测项目(依据) 砷(GB/T5009.11—1996) 铅 (GB/T5009.12-1996) 汞(GB/T5009.17-1996) 钙 (GB12390-90) 镉 GB/T5009.15-1996 水分 GB5009.3-85 灰分(GB5009.4-85) 总黄酮、原花青素、吡啶甲酸铬(《保健食品功效成分检测方法》) 色素(GB/T5009.35-1996) 乙醇残留(GB5009.37-1996) 崩解时间(《中华人民共和国药典》2000 年版)

检测结果:

	砷 (mg/kg)	铅 (mg/kg)	汞 (mg/kg)	水分 (g/100g)	灰分 (g/100g)	钙 (g/100g)	镉 (mg/kg)	乙醇残留 (ug/g)
(2002)食 B2114h1-1310	0.053	0.16	0.066	6.2	38.3	23.1	0.033	37.8
(2002)食 B2114h2-1310	0.056	0.15	0.068	6.3	40.1	23.7	0.040	43.7
(2002)食 B2114h3-1310	0.034	0.11	0.072	6.3	39.4	24.7	0.042	37.4

	原花青素 (g/100g)	吡啶甲酸铬 (mg/g)	总黄酮 (以芦丁计) (mg/100g)	崩解时间 (min)	亮兰 (g/kg)	柠檬黄 (g/kg)	批号
(2002)食 B2114h1-1310	8.5	1.0	26.8	11.0	0.0077	0.019	20020501
(2002)食 B2114h2-1310	8.3	1.1	24.6	10.0	0.0081	0.017	20020502
(2002)食 B2114h3-1310	8.9	1.0	25.8	13.0	0.0075	0.017	20020503

以下空白

检测机构(盖章) 北京市疾病预防控制中心 检测检验专用章

本报告仅对送检样品负责

签发者

2003 年 1 月 20 日

北京市卫生防疫站
卫生检测结果报告

(2000)量认(京)字(S0220)号

编　　号: (2002)食B2114f1-3
收样日期: 2002年07月31日
检验日期: 2002年07月31日

样品名称:	北京玺圆环球生物胰岛素	委托单位:	北京玺圆环球生物医药技术有限公司
检验目的:	卫生学	生产单位:	北京玺圆环球生物医药技术有限公司
检验编号:	(2002)食B2114f1-3-0939	检验依据:	GB4789.15-94
样品数量:	150g×3批	样品性状:	胶囊
检验项目:	霉菌酵母计数	保存条件:	常温

检验结果:

样品编号	(2002)食B2114f1-0939	(2002)食B2114f2-0939	(2002)食B2114f3-0939
样品名称	北京玺圆环球生物胰岛素	北京玺圆环球生物胰岛素	北京玺圆环球生物胰岛素
样品批号	20020501	20020502	20020503
酵母(cfu/g)	<5	<5	<5
霉菌(cfu/g)	<5	<5	<5

以下空白

报告日期: 2002年08月12日
最终审核日期: 2002年08月12日
检测单位负责人:

本检验报告仅对送检样品负责

北京市卫生防疫站
卫生检测结果报告

(2[illegible])京(S0220)号

编　　号: (2002)食B2114m1-3
收样日期: 2002年07月31日
检验日期: 2002年07月31日

样品名称:	北京玺圆环球生物胰岛素	委托单位	北京玺圆环球生物医药技术有限公司
检验目的:	卫生学	生产单位:	北京玺圆环球生物医药技术有限公司
检验编号:	(2002)食B2114m1-3-2158	检验依据:	GB4789.2-5.10-11-94
样品数量:	150g×3	样品性状:	胶囊
检验项目:	菌落总数、大肠菌群、致病菌	保存条件:	常温

检验结果:

样品编号	(2002)食B2114m1-2158	(2002)食B2114m2-2158	(2002)食B2114m3-2158
样品名称	北京玺圆环球生物胰岛素	北京玺圆环球生物胰岛素	北京玺圆环球生物胰岛素
样品批号	20020501	20020502	20020503
菌落总数(cfu/g)	60	20	30
大肠菌群(MPN/100g)	<30	<30	<30
致病菌			
金黄色葡萄球菌	未检出	未检出	未检出
沙门氏菌	未检出	未检出	未检出
志贺氏菌	未检出	未检出	未检出
溶血性链球菌	未检出	未检出	未检出

以下空白

报告日期: 2002年08月09日
最终审核日期: 2002年08月[illegible]日
检测单位负责人: [illegible]

检测检验专用章

本检验报告仅对送检样品负责

北京市疾病预防控制中心
稳定性实验报告

检验产品：北京璧阖环球生物胰岛素
送检单位：北京璧阖环球生物医药技术有限公司
生产单位：北京璧阖环球生物医药技术有限公司
检测单位：北京市疾病预防控制中心
保存条件：37-40℃，相对湿度 75%
检测时间：2002 年 07 月--2003 年 01 月(保温实验)
检验结果：见下表.

表 1.北京璧阖环球生物胰岛素稳定性实验检测结果

检测项目及检测时间	产品批号	20020501	20020502	20020503
菌落总数 (cfu/g)	保温前	60	20	30
	保温一月	<10	<10	10
	保温二月	20	30	10
	保温三月	20	20	30
大肠菌群 (MPN/100g)	保温前	<30	<30	<30
	保温一月	<30	<30	<30
	保温二月	<30	<30	<30
	保温三月	<30	<30	<30
致病菌（沙门氏菌、志贺氏菌、金黄色葡萄球菌、溶血性链球菌）	保温前	未检出	未检出	未检出
	保温一月	未检出	未检出	未检出
	保温二月	未检出	未检出	未检出
	保温三月	未检出	未检出	未检出
酵母 (cfu/ g)	保温前	<5	<5	<5
	保温一月	<5	<5	<5
	保温二月	<5	<5	<5
	保温三月	<5	<5	<5
霉菌 (cfu/ g)	保温前	<5	<5	<5
	保温一月	<5	<5	<5
	保温二月	<5	<5	<5
	保温三月	<5	<5	<5
总黄酮（以芦丁计）(mg/g)	保温前	26.8	24.6	25.8
	保温一月	26.4	24.9	25.2
	保温二月	26.1	25.1	25.7
	保温三月	26.6	24.8	25.5

表 2 北京望圆环球生物胰岛素稳定性实验检测结果（续表 1）

检测项目及检测时间	产品批号	20020501	20020502	20020503
砷 (mg/kg)	保温前	0.053	0.056	0.034
	保温一月	0.069	0.075	0.052
	保温二月	0.092	0.089	0.082
	保温三月	0.088	0.089	0.093
铅 (mg/kg)	保温前	0.16	0. 15	0.11
	保温一月	0.10	0.10	0.12
	保温二月	0.17	0.10	0.14
	保温三月	0.12	0.10	0.11
汞 (mg/kg)	保温前	0.066	0.068	0.072
	保温一月	0.043	0.043	0.047
	保温二月	0.053	0.048	0.062
	保温三月	0.038	0.041	0.033
水分 (g/100g)	保温前	6.2	6.3	6.3
	保温一月	6.3	6.5	6.4
	保温二月	6.5	6.4	6.7
	保温三月	6.5	6.7	6.6
灰分 (g/100g)	保温前	38.3	40.1	39.4
	保温一月	39.7	39.5	40.2
	保温二月	40.0	40.7	39.9
	保温三月	40.1	40.3	40.4
钙 (g/100g)	保温前	23.1	23.7	24.7
	保温一月	23.6	24.7	25.7
	保温二月	24.5	24.9	24.5
	保温三月	25.4	25.1	25.5
吡啶甲酸铬 (mg/g)	保温前	1.0	1.1	1.0
	保温一月	1.1	1.0	0.99
	保温二月	1.1	1.2	1.1
	保温三月	1.2	1.1	1.0
原花青素 (g/100g)	保温前	8.5	8.3	8.9
	保温一月	8.0	7.9	8.1
	保温二月	8.1	8.4	8.2
	保温三月	7.9	8.2	8.1

病预防 检验专用

表 3 北京至圆环球生物胰岛素、稳定性实验检测结果（续表 2）

检测项目及检测时间	产品批号	20020501	20020502	20020503
镉 (mg/kg)	保温前	0.033	0.040	0.042
	保温一月	0.052	0.055	0.054
	保温二月	0.061	0.021	0.036
	保温三月	0.038	0.018	0.032

结论：北京济世堂中医药保健研究所、聊城市绿源蜂胶科贸有限公司送检的聊城市绿源蜂胶科贸有限公司生产的济世慈航牌蜂胶糖泰胶囊(生产时间为:20020501，20020502，20020503)，在 37-40℃，75%相对湿度下进行三月保温实验，经理化、微生物检验，提示所检指标质量稳定。

检测单位负责人：

2002年01月21日

申报资料 4

治病及原理

北京玺圃环球生物医药技术有限公司

1 蜂胶

蜂胶内含丰富的黄酮类，萜烯类及各种氨基酸，维生素，钙、镁、钾，锌，铬等有益于人体的物质。

蜂胶中的 B 族维生素，是制造胰岛素的原料。蜂胶中含有的胰蛋白梅等活性酶和其它抗病毒物质（如黄酮类，萜烯类物质）对恢复胰脏机能有明显作用，蜂胶中的一些黄酮类，萜烯类等物质具有促进利用外源性葡萄糖合成肝糖元的作用，可促进人体对葡萄糖的利用。

2 富铬酵母（C_r^{3+}）

三价铬（C_r^{3+}）是改善葡萄糖耐受因子（GTF）的主要物质，三价铬（C_r^{3+}）的缺少可以损坏β细胞，并抑制、阻挠降低了胰岛素的分泌，排运和受体结合的环节。

3 苦瓜

苦瓜，苦寒，主治除邪热，解劳乏，清心明目。子，益气。现代研究表明，其有降低血糖的作用。

4 葡萄籽提取物（OPC）

葡萄籽提取物是迄今发现的植物来源的最高效的抗氧化剂之一，体内和体外试验表明，葡萄籽提取物的抗氧化效果，是维生素 C 和维生素 E 的几十倍，超强的抗氧化效率具有清除自由基，提高人体免疫力的强大效果。

5 虫草提取物

虫草内含丰富的氨基酸类，环肽类，多糖类等。现代研究表明，其有降低血糖、增强免疫力的作用。

6 生姜提取物

生姜解表散寒，温中止呕，化痰止咳。

纵观全方，以蜂胶，苦瓜的主要原料，佐以富铬酵母，虫草提取物，葡萄籽提取物，生姜提取物。使其中的有效成份相辅相成，协同增强，符合中医的辩证组方理论，因此该方是较为科学、完善，保健功能较为明显。

申报资料 5

毒理报告

北京玺圃环球生物医药技术有限公司

首都医科大学毒理研究室

检验报告书

样品受理编号： 2002041

样 品 名 称： 北京圣面环球生物胰岛素

送 检 单 位： 北京圣面环球生物医药技术有限公司

发 送 日 期： 2002 年 11 月 20 日

首 都 医 科 大 学

毒 理 学 检 验 报 告

共 11 页 第 1 页

样品编号: 200202041 样品批号: 20020501

受试物名称: 北京玺圃环球生物胰岛素 样品数量: 3.0kg

送样单位: 北京玺圃环球生物医药技术有限公司

生产单位: 北京玺圃环球生物医药技术有限公司

收样日期: 2002年 8 月 29 日 报告日期: 2002 年 11 月 20 日

检测目的: 毒理学安全性评价

检测项目: 1. 急性毒性试验
2. 三项致突试验
3. 30 天喂养试验

实验依据: 《食品安全性毒理学评价程序和方法》GB15193－94

实验结果与判断:

急性毒性试验: 经口 LD50,Wistar 大鼠及昆明种小鼠均大于 10g/kgBW 动物活动正常,未发现任何症状,属实际无毒物质.

三项致突试验: Ames 试验、小鼠骨髓 PCE 微核试验和小鼠精子畸变试验为阴性。

30 天喂养试验: 实验结果表明,该受试物于 3.30、2.48、1.65g/kgBW 剂量(相当于人群推荐量 0.0 33g/kgBW 的 100、75 和 50 倍)时,对生长发育、血液系统,肝、肾功能,蛋白、脂肪、糖的代谢,以及主要脏器的组织学改变,均无明显影响。

(试验方法及结果见附件)

本检验仅对送检样品负责

技术负责人 薄[illegible]

附件 1 急性毒性半数致死量(LD50)实验报告 第 2 页

样品编号：2002041 样品批号：20020501
受 试 物：北京玺圃环球生物胰岛素 推 荐 量：2.0g/日（0.033g/kgBW）
送检单位：北京玺圃环球生物医药技术有限公司
生产单位：北京玺圃环球生物医药技术有限公司
实验动物：Wistar 种大鼠，体重 180～200g，ICR 种小鼠，体重 18～22g 均由首都医科大学实验动物部提供 SPF 级合格动物（合格证号医动字 01-4059）随机分入各组每组动物 10 只，雌雄各半，
饲养环境：SPF 级合格动物室（合格证号医动字 01-4059）室温 22±2℃，相对湿度 60%RH 真空包装饲料由北京九江口饲料公司提供(合格证号 052)。
样品处理：称取样品 50g 加蒸馏水至 100ml，10g 相当于 20ml，灌胃量 2ml/100gBW，灌胃浓度分别为 50% 、23.2%、10.75%、5%
实验方法：霍恩氏法，受试物经口灌胃给予，灌胃前停食 16 小时，连续观察 1 周，并纪录动物中毒症状及死亡情况。
实验结果：

Wistar 大鼠

剂量	雄鼠 动物数	雄鼠 死亡数	雌鼠 动物数	雌鼠 死亡数
10.0g/kg	5	0	5	0
4.64g/kg	5	0	5	0
2.15g/kg	5	0	5	0
1.00g/kg	5	0	5	0

ICR 种小鼠

剂量	雄鼠 动物数	雄鼠 死亡数	雌鼠 动物数	雌鼠 死亡数
10.0g/kg	5	0	5	0
4.64g/kg	5	0	5	0
2.15g/kg	5	0	5	0
1.00g/kg	5	0	5	0

在实验期间各组动物活动均正常，毛色光泽度良好，未发现任何症状。经口半数致死量（LD50 g/kg）> 10g/kg。

结论：受试物以急性毒性半数致死量毒性分级，均属实际无毒物质，

实验者：陈振良 吴 涛
复核者：苏忆兰

技术负责人：蒋致诚

首都医科大学毒理研究室
2002 年 9 月 10 日

附件 2 **微 核 试 验 报 告** 第 3 页

样品编号：2002041 样品批号：20020501
受 试 物：北京玺圃环球生物膜品紫 推 荐 量：2.0g/日（0.033g/kgBW）
送检单位：北京玺圃环球生物医药技术有限公司
生产单位：北京玺圃环球生物医药技术有限公司
实验动物：ICR 种小鼠，体重 24~28g 由首都医科大学实验动物部提供 SPF 级合格动物（合格证号医动字 01-4059）。按体重分层随机分入各组，每组动物 10 只，雌雄各半。
饲养环境：SPF 级实验动物室（合格证号医动字 01-4059）室温 22±2℃，相对湿度 60%RH 群笼喂养 5 只/笼，真空包装饲料由北京九江口饲料公司提供（合格证号 052）。
样品处理：称取样品 10g 加蒸馏水至 20ml 灌胃量 0.2ml/10gBW 灌胃浓度分别为 50% 25%和 12.5%
剂量分组：按急性毒性试验最大剂量 10g/kgBW 为最高剂量，以下分别设 1/2（5.0g/kgBW）及 1/4（2.5g/kgBW）二个剂量组，另设阳性对照组（环磷胺 35mg/kg）及阴性对照组，均经口灌胃 给予，灌胃浓度分别为 50%、25%、12.5% 。
实验方法：连续给予受试物二天（间隔 24 小时）于末次给药后 6 小时，动物颈椎脱臼处死，取胸骨骨髓，按常规制片、染色、镜检。每只动物观察 1000 个 PCE，记录含微核 PCE 数，计算微核率。
统计方法：泊松分布 U 检验
实验结果：

组别	动物数 雄鼠	观 察 PCE 数	含微核 PCE 数	微核率 (‰)	动物数 雌鼠	观 察 PCE 数	含微核 PCE 数	微核率 (‰)
10.0g//kg	5	5×1000	5	1.00±0.71	5	5×1000	5	1.00±0.71
5.0g/kg	5	5×1000	4	0.80±0.45	5	5×1000	4	0.80±0.84
2.5 g/kg	5	5×1000	3	0.60±0.55	5	5×1000	3	0.60±0.55
CP35mg/kg	5	5×1000	102	20.40±1.82	5	5×1000	103	20.60±2.51
阴性对照组	5	5×1000	3	0.60±0.55	5	5×1000	3	0.60±0.55

各剂量组与阴性对照组相比，均未发现有显著性差异（P>0.05），阳性对照组与阴性对照组相比有非常显著的差异（P<0.01）。实验结果表明在本实验剂量范围内，该受试物不诱发微核率的增加。

实验者：沈家琴 褚金花
复核者：苏忆兰

技术负责人：薛松城

首都医科大学毒理研究室
2002 年 11 月 2 日

附件 3

精子畸变试验报告

样品编号：2002041　　样品批号：20020501

受试物：北京盟固环球生物膜品素　　推荐量：2.0g/日（0.033g/kgBW）

送检单位：北京盟固环球生物医药技术有限公司.

生产单位：北京盟固环球生物医药技术有限公司

实验动物：雄性 ICR 种 SPF 级小鼠，体重 24～28g 由首都医科大学实验动物部提供（合格证号医动字 01-4059）按体重分层随机分入各组，每组动物 5 只。

饲养环境：SPF 级实验动物室（合格证号医动字 01-4059）室温 22±2℃，相对湿度 60% RH. 群笼喂养 5 只/笼。真空包装饲料由北京九江口饲料公司提供（合格证号 052）.

样品处理：称取样品 20g 加蒸馏水至 40ml，灌胃量 0.2ml/10gBW，灌胃浓度分别为 50%、25%、及 12.5%。

剂量分组：以急性毒性试验最大剂量 10g/kgBW 为最高剂量,以下分别设 1/2 (5.0g/kgBW) 及 1/4 (2.5g/kgBW) 二个剂量组，另设阳性对照组（环磷酰胺 35mg/kg）及阴性对照组均经口灌胃给予。

实验方法：连续给予受试物五天于第一次给予后的第 35 天处死，取双侧附睾按常规制片染色和镜检，每只动物观察 1000 个精子，记录畸变精子数,计算畸变率.

统计方法：以秩和检验检测显著性.

实验结果：

组别	动物数（只）	观察精子数	精子畸变类型 不定型	香蕉	无钩	胖头	卷折尾	双尾	畸变精子数（个）	畸变率 %
10.0g/kg	5	5×1000	49	7	0	0	0	0	56	1.12±0.19
5.0g/kg	5	5×1000	48	3	0	1	2	0	54	1.08±0.13
2.5g/kg	5	5×1000	50	5	0	2	0	0	57	1.14±0.18
CP 35mg/kg	5	5×1000	321	72	62	65	69	0	589	11.78±0.56
阴性对照组	5	5×1000	47	5	1	2	3	0	58	1.16±0.15

经秩和检验各剂量组与阴性对照组相比，均未发现有显著性差异（P>0.05），阳性对照组与阴性对照组相比有非常显著的差异（P<0.01）。实验结果表明该受试物在本实验剂量范围内，未发现对生殖细胞有诱变作用。

实验者：冯　亚　张　杰

复核者：苏忆兰

技术负责人：薛毅阳

首都医科大学病理研究室

2002 年 10 月 25 日

Ames 试验报告

样品编号：2002041 样品批号：20020501

受 试 物：北京玺圃环球生物胰岛素 推 荐 量：2.0g/日（0.033g/kgBW）

送检单位：北京玺圃环球生物医药技术有限公司

生产单位：北京玺圃环球生物医药技术有限公司

实验菌株：TA97a、TA98 为移码型突变株，TA100、TA102 为碱基置换型突变株，由美国加州大学 Ames 教授惠赠。

(1) 四株的五个遗传特性鉴测定都符合其规定标准。

(2) 实验前，取 20ul -80℃保存的菌液接种到 10mlNO.2 营养肉汤培养基中，37℃ 12—16 小时水浴振荡培养，得到大约 2×10^8 菌悬液。

使用方法：平板预先温浴法：

S-9 或 PBS（非 S9 对照）0.5ml，被测物 100ul，菌液 100ul。阳性对照（标准致突变物），阴性对照（样品溶剂）混合后 37℃水浴振荡 20 分钟。再加 2ml 顶面琼脂（0.5mM 组氨酸/生物素），快速倒板均匀铺平 37℃孵育 48 小时看结果.

样品处理：称取样品 0.5 克,溶于毫升 DMSO 中，用水稀释成所需浓度。预实验中 1.0mg/皿以上浓度出现抑菌，故以 1mg/皿为最大剂量向下稀释。

样品浓度：根据药品及食品法规定，最大受试浓度及杀菌浓度/皿，实验浓度选定为 0.5mg/皿、0.25m g/皿、0.1mg/皿、0.05mg/皿、0.01mg/ 皿、五个测试浓度。

阳性对照：2-AF（2-氨基芴）10ug/皿、MMS（甲基甲烷磺酸酯）2ul/皿、芴酮（2,4,7-三硝基 9 芴酮.）0.2ug/皿、2AA 12ug/皿。

实验参数：(1) Aroclo-1254 诱导的大鼠肝匀浆，蛋白含量 33mg/ml。

(2) 按照 83 年 Ames Test 修订方法，S-9 加入量 20ul/皿。

(3) 实验结果的数据为三个平皿的均数。

实验结果：实验中我们选用了四株两种突变类型的菌株对样品进行五个浓度的测试，在有代谢活化+S9 或无代谢活化-S9 系统的条件下，被测物对四种突变株没有明显的诱导作用。

结 论：在本实验的条件下，我们选择的剂量范围内，该样品对四种菌株未见明显的诱导突变作用。

实验者 刘 毅 冯亚

复核者 苏忆兰

技术负责人 蒋验诚

首都医科大学毒理研究室
2002 年 9 20 日

附件 4～2

Ames Test 结果（平板预先溶温法）

受试物 mg/ml	TA97a +S9	TA97a -S9	TA98 +S9	TA98 -S9	TA100 +S9	TA100 -S9	TA102 +S9	TA102 -S9
北京强国环球生物圆岛素				第一次				
1.00	90.00	67.00	32.33	18.67	131.33	137.00	293.00	184.67
	±29.46	±22.63	±5.03	±4.73	± 8.14	±9.85	±18.36	±37.07
0.50	138.33	127.33	30.67	26.67	128.67	132.33	312.00	246.00
	±39.88	± 2.52	±4.61	±3.79	± 6.43	±10.69	± 8.54	±12.49
0.25	130.67	136.00	31.67	30.67	141.00	139.67	298.33	254.33
	±16.07	±13.75	±5.03	±3.06	± 7.94	±13.43	±11.50	± 4.73
0.1	137.33	150.33	36.67	31.00	139.50	131.00	313.67	253.67
	± 8.08	±24.13	±3.61	±4.00	±12.02	± 4.36	±20.21	±16.50
0.05	132.33	129.33	33.33	28.67	136.67	137.33	298.00	258.67
	±20.55	± 4.51	±4.62	±2.52	±16.26	±7.51	±19.31	±14.01
0.01	134.33	133.00	30.67	30.33	137.67	135.33	300.67	263.33
	± 3.51	± 8.19	±3.06	±3.06	± 8.02	±6.03	±14.22	±7.09
His-(PBS+0.1mlDMSO)								
	139.67	138.00	33.67	29.67	132.67	125.67	281.33	260.33
	± 7.51	± 6.56	±4.73	±3.51	± 9.29	±9.07	±13.2	± 8.50
				第二次				
0.50	130.00	127.33	29.67	28.33	142.33	137.33	312.67	268.67
	± 9.64	± 5.33	±2.52	±3.06	± 14.01	±8.50	±10.26	±13.42
0.25	139.33	136.67	33.67	33.33	128.67	133.33	307.33	254.33
	± 9.07	±10.69	±2.52	±5.03	± 3.51	±8.74	±14.22	±10.41
0.1	131.67	133.33	32.33	32.67	139.67	134.00	298.33	264.67
	± 7.37	± 3.51	±4.16	±5.69	± 13.2	±12.00	±19.86	±10.97
0.05	142.67	128.67	34.33	29.67	145.67	135.33	301.33	255.00
	±13.50	± 4.51	±3.21	±3.21	± 14.57	± 8.02	±10.69	±18.52
0.01	136.00	131.33	30.33	31.33	140.67	136.67	292.33	248.33
	±14.53	± 4.04	±3.79	±3.06	±8.33	±9.45	±9.45	±13.05
His-(PBS+0.1mlDMSO)								
	127.67	133.00	31.33	31.67	134.33	132.33	313.00	250.67
	± 5.69	± 6.24	±5.69	±5.03	± 9.29	±10.97	±14.18	±17.9

阳性对照（ug/ml）

2-AF	10	1461±94.75		2688±271.53				
丙酮	0.2		2724±130.11		2182±93.34			
2-AF	10					1512±90.51		
MMS	2ul						1993±188.09	3412±265.87
2AA	12						1326±138.59	

(97)京认(药)字(50292)号 附件 S-1

30 天喂养实验报告

样品编号： 2002041　　样品批号：20020501

1.受 试 物：北京金圆环球生物胰岛素 为蜂胶、吡啶甲酸铬、葡萄籽提取物及珍珠粉混合制成。人群推荐量 2.0g/日，按成人 60kg 体重计为 0.033g/kgBW。

1.送样单位：北京金圆环球生物医药技术有限公司

3 生产单位：北京金圆环球生物医药技术有限公司

4.实验动物：由首都医科大学实验动物部提供 Wistar 种体重 61~70g SPF 级断乳大鼠及动物实验室，（合格证号医动字 01-4059 号）喂饲粉状基础饲料（北京市九江口饲料公司提供真空包装无菌饲料，合格证号 052）3 天后，按体重分层随机分入各组。室内温度 22±2℃，相对湿度 60%。

5.剂量分组：以人群推荐量(0.033g/kgBW)的 100、75 和 50 倍设三个剂量组，即 3.3g/kgBW、2.48g/kgBW 及 1.65g/kgBW。另设阴性对照组（粉状基础饲料）共四组，每组动物雌、雄各 10 只。

6.给予途径：掺入饲料，自由摄入。

7.饲料配制：以大鼠体重 10%作为饲料摄入量，按剂量配制含不同济世慈航牌蜂胶糖萝胶素浓度的饲料，即 3.3%、2.48%、1.65%。

8.观察指标：

8.1 每日观察动物的活动情况、毛色、摄食及排泄情况，症状及出现的时间，出现死亡时要进行尸体解剖，肉眼观察脏器的病理改变，必要时作病理切片作组织学观察。

8.2 生长发育及食物利用率：实验前及实验期间每周称量体重、饲料加入量及剩余量，计算食物利用率。

8.3 血液学指标：Hb、RBC、PLT、WBC 及分类。

8.4 生化指标： ALT、AST、TP、ALB、GLB、A/G、BUN、CRE、GLU、TC、TG。

8.5 脏器系数：心、肝、脾、肾、胃、胰、睾丸或卵巢。

8.6 病理检查： 常规制片、染色、光学显微镜检查心、肝、脾、肾、胃、十二指肠、胰、睾丸或卵巢的组织学改变。

9.统计分析：方差分析。

10.实验结果：

各组动物在实验期间活动正常，毛色光泽度好，摄食及排泄正常，未发现有症状出现。

10.1 生长发育情况：各组动物在实验前和实验期间各周的体重情况见表 1。

附件 5～2

表 1 各组动物实验前及实验期间各周体重（X±sd）

组 别	动物数	实验前	第一周	第二周	第三周	第四周
北京堡圃环球生物胰岛素			雄	鼠		
3.30g/kg	10	65.80±2.90	109.70±11.60	159.70± 9.19	207.10±8.95	255.50±11.19
2.48g/kg	10	65.70±2.98	112.40±11.41	160.20±11.63	209.80±8.88	258.20± 7.18
1.65g/kg	10	66.00±2.75	110.30± 8.93	158.80± 8.24	206.10±7.75	252.40± 6.54
阴性对照	10	65.80±3.01	111.30± 5.48	163.40± 6.85	211.20±9.40	259.40± 8.93
			雌	鼠		
3.30g/kg	10	66.00±2.11	105.80±6.41	134.80±5.79	161.00±8.82	188.20±7.83
2.48g/kg	10	66.10±1.91	100.70±5.68	135.30±5.62	163.30±7.56	188.90±6.17
1.65g/kg	10	66.10±1.91	101.40±4.65	132.20±5.33	162.20±4.75	188.30±5.96
阴性对照	10	66.20±1.99	101.80±5.86	132.40±4.17	157.90±8.50	183.10±8.16

由表 1 可见三个剂量组动物实验前和实验期间各周体重与阴性对照组相比，均未发现有显著性差异（P>0.05）。

10.2 食物利用率： 各组动物的增重和食物利用率见表 2。

表 2 各组动物的增重（g）和食物利用率（x±SD）

组别	雄鼠 增重	雄鼠 总入量	雄鼠 食物利用率	雌鼠 增重	雌鼠 总入量	雌鼠 食物利用率
北京堡圃环球生物胰岛素						
3.30g/kg	189.70±10.31	504.40±14.32	37.59±1.05	122.20±8.20	454.60±29.70	26.94±1.88
2.48g/kg	192.50± 6.43	512.30±10.21	37.58±0.97	122.80±5.92	470.10±16.37	26.14±1.43
1.65g/kg	186.40± 6.45	495.50±23.53	37.67±1.64	122.20±6.76	448.90±21.01	27.25±1.42
阴性对照	193.60± 8.82	501.90±14.76	38.57±1.06	116.90±6.54	445.00±18.42	26.27±0.94

由表 2 可见三个剂量组动物的增重及食物利用率与阴性对照组相比，各组间均未发现有显著性差异（P>0.05）。

附件 5～3

10.3 血液指标： 各组动物血液学指标测定结果见表 3。

表 3 各组动物血液学指标测定结果 （x±SD）

组别	Hb (g/L)	RBC ($x10^{12}$/L)	WBC ($x10^{9}$/L)	PLT ($x10^{9}$/L)	淋巴 (%)	中性 (%)	其他 (%)
北京堡圆环球生物膜品素			雄	鼠			
3.30g/kg	143.40±16.05	5.94±0.62	15.85±2.50	379.60±118.11	81.70±1.16	14.20±1.23	4.10±0.74
2.48g/kg	145.10±14.46	6.02±0.57	15.77±3.45	320.40±141.86	80.90±1.45	15.20±0.92	3.90±0.74
1.65g/kg	146.00±13.91	5.88±0.49	17.01±4.66	351.90±164.01	81.30±1.70	15.00±1.15	3.70±0.82
阴性对照	146.30± 9.24	5.93±0.44	16.72±1.72	378.90± 89.17	81.00±1.70	15.30±1.34	3.70±0.67
			雌	鼠			
3.30g/kg	152.80±10.04	6.51±0.80	15.34±3.45	296.80±101.58	82.00±1.25	14.50±1.35	3.50±0.53
2.48g/kg	153.70±16.56	6.60±0.56	16.66±2.70	404.20±108.38	82.60±0.79	13.50±0.97	3.70±0.82
1.65g/kg	158.70±19.52	6.35±0.79	17.04±3.14	353.70±126.21	83.10±1.29	13.70±1.15	3.20±0.42
阴性对照	149.00± 7.97	6.43±0.42	15.86±3.79	418.70±137.48	81.60±1.69	15.00±1.41	3.20±0.42

由表 3 可见三个剂量组动物的各项血液学指标与阴性对照组相比，均未发现有显著性差异(P>0.05)。

10.4 生化指标： 各组动物生化指标测定结果见表 4、5。

表 4 各组动物生化指标测定结果 （x±SD）

组 别	ALT U/L	AST U/L	TP g/L	ALB g/L	GLB g/L	A/G
北京堡圆环球生物膜品素		雄	鼠			
3.30g/kg	27.30±6.19	136.42±7.80	65.80±2.00	31.94±0.69	33.86±2.23	0.95±0.07
2.48g/kg	23.21±4.64	137.99±9.42	66.44±1.93	31.66±0.62	34.78±1.94	0.91±0.05
1.65g/kg	25.95±4.87	144.16±9.06	66.63±2.04	32.06±0.76	34.57±1.89	0.93±0.05
阴性对照	23.74±6.29	148.24±9.60	66.34±2.00	32.14±0.96	34.20±2.45	0.95±0.09
		雌	鼠			
3.30g/kg	21.57±6.39	135.55± 8.80	66.88±2.58	32.24±0.96	34.64±2.86	0.94±0.09
2.48g/kg	18.56±4.28	140.48±12.18	67.80±2.48	32.05±0.71	35.75±2.21	0.90±0.06
1.65g/kg	23.44±5.21	142.79± 9.19	67.01±2.31	31.84±0.73	35.17±2.17	0.91±0.06
阴性对照	22.85±4.53	146.49± 9.33	67.33±2.18	32.31±0.91	35.02±2.96	0.93±0.10

表 5 各组动物生化指标测定结果 (x±SD)

组 别	CRE umol/L	BUN mmol/L	GLU mmol/L	TC mmol/L	TG mmo/L
北京塑圆环球生物胰岛素		雄	鼠		
3.30g/kg	44.30± 9.85	5.14±0.58	4.59±0.21	1.53±0.17	0.72±0.14
2.48g/kg	45.78±14.69	5.19±0.60	4.47±0.30	1.57±0.10	0.75±0.17
1.65g/kg	44.30±13.92	5.19±0.57	4.47±0.14	1.58±0.14	0.70±0.13
阴性对照	47.25± 6.23	4.83±0.90	4.41±0.13	1.61±0.19	0.75±0.16
		雌	鼠		
3.30g/kg	39.87± 7.13	4.74 ±0.80	3.73±0.27	1.46±0.09	0.49±0.10
2.48g/kg	39.87± 7.13	4.61 ±0.84	3.85±0.34	1.46±0.08	0.51±0.10
1.65g/kg	39.87± 7.13	4.56 ±0.68	3.89±0.33	1.37±0.09	0.57±0.14
阴性对照	47.25±13.57	4.80 ±0.69	4.10±0.43	1.51±0.10	0.53±0.14

由表 4、5 可见三个剂量组动物的各项生化指标测定结果与阴性对照组相比，均未发现有意义的显著性差异。

10.5 脏器系数： 各组动物的主要脏器系数见表 6。

表 6 各组动物的主要脏器系数

组 别	心	肝	脾	肺	肾	胃	睾丸(卵巢)
北京塑圆环球生物胰岛素			雄	鼠			
3.30g/kg	0.31±0.01	2.83±0.10	0.23±0.02	0.17±0.02	0.72±0.02	0.51±0.02	0.91±0.05
2.48g/kg	0.31±0.01	2.96±0.14	0.23±0.01	0.16±0.01	0.72±0.02	0.53±0.03	0.89±0.03
1.65g/kg	0.31±0.01	2.86±0.09	0.23±0.02	0.17±0.02	0.72±0.02	0.51±0.05	0.89±0.06
阴性对照	0.31±0.02	2.98±0.17	0.24±0.02	0.17±0.02	0.73±0.01	0.51±0.03	0.91±0.05
			雌	鼠			
3.30g/kg	0.32±0.02	2.87±0.14	0.24±0.02	0.19±0.02	0.72±0.03	0.56±0.02	0.062±0.008
2.48g/kg	0.31±0.01	2.87±0.12	0.25±0.02	0.17±0.01	0.73±0.02	0.54±0.03	0.057±0.007
1.65g/kg	0.32±0.02	2.80±0.10	0.25±0.02	0.17±0.02	0.72±0.03	0.56±0.03	0.057±0.006
阴性对照	0.33±0.01	2.91±0.19	0.26±0.02	0.18±0.02	0.74±0.03	0.58±0.03	0.061±0.006

由表 6 可见三个剂量组动物的各主要脏器系数与阴性对照组相比，均未发现有显著性差异（P>0.05）。

10.6 病理组织学观察：

大体解剖所见肝脏的颜色正常，边缘锐利，其他脏器均未见异常。病理组织学观察，除各组均有部分动物的肝细胞出现轻度点状坏死（高剂量组 5/20、中剂量组 2/10、低剂量组 2/10、对照组 5/20）外，其他脏器心、脾、肾、胃、肠、胰、卵巢或睾丸均结构正常，未见明显病理改变。

10. 结论：

由实验结果表明该受试物在本实验剂量范围内（1.65g～3.30g/kgBW），对实验动物的生长发育、食物利用率、血液系统、肝、肾功能、生殖系统，以及蛋白、脂肪、糖的代谢无明显影响。

实验者： 陈振良 冯亚 等

复核者： 苏忆兰

技术负责人： 蒋政诚

首都医科大学毒理研究室

2002 年 12 月 20 日

申报资料 6

批准证书

北京玺圃环球生物医药技术有限公司

NO.Y.05—1

卫生许可证

副本

昌工食监字[2002]第-2805号

单位名称：北京玺圃环球生物医药技术有限公司

法定代表人：王文斌

地　　址：昌平镇科技园区振兴路9号

许可项目：玺圃胰岛营养素委托加工销售

发证机关

2002年11月15日

有效期限：2002年11月15日至2004年11月14日

12.FEB.2003 13:22 FAX 01 WING WAI TAD. CO. +852 23344665 NO.907 P.18
010 64947998

北京市产品标准登记注册证

登记注册号: CP0450

企业名称: 北京盟卿环球生物医药技术有限公司

注册地址: 北京市昌平区科技园区振兴路9号

法人代表: 王文斌

机构代码: 80266437-8

产品类别:

食品　特种食品

登记注册有效期限: 自 2002 年 11 月 19 日
至 2007 年 11 月 19 日

登记注册机关: 北京市质量技术监督局