

## Q&A Session:

### “Integrative Clinical Pharmacology: Herb-Drug Interactions”

– John K. Chen, PhD, PharmD, OMD, LAc

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1. Should client's resume the Camellia teas in general 2 hours after herbs to avoid the interaction? Or should they be avoided overall while trying to access a formula's effect, especially if prescribed TID?

The interaction happens as the *Cha Ye* (Folium Camelliae) comes in direct physical contact with fat soluble compounds. So the solution to avoid interaction is to avoid direct contact. In pharmacology, an “empty stomach” is defined as one hour before or two hours after meals, so using that logic, I think two hours should be sufficient to avoid any significant interaction.

2. Is there a way to protect kidney function from compromises that may be caused by some prescription drugs perhaps a low dose combination of Chinese herbs (like zhi ke & mu ze)

Yes, there are herbs that have been shown to improve renal function and protect the kidneys. Two herbs that may be helpful to prevent and/or minimize drug-induced renal toxicities are *Huang Qi* (Radix Astragali) and *Dong Chong Xia Cao* (Cordyceps). Please see attached.

3. Will you ever, or have you already, created a database for those of us working in medical institutions to use as a resource when we want to give our patients Chinese formulas and need to help their MD feel safe with our choices?

This, in fact, is the singular focus of my career. I am very fortunate to be in a position where I speak fluent Chinese and English, and have extensive education in Chinese herbology and Western pharmacology. So I dedicated my career to be the “bridge” of Western medicine and traditional Chinese medicine. All my research, teaching and writing are all dedicated to improve the knowledge of Chinese herbal medicine and integrative medicine. These two textbooks are my most significant work: [Chinese Herbology and Pharmacology](#) and [Chinese Herbal Formulas and Applications](#).

4. Do psyllium fiber oral supplements affect absorption/increase elimination of meds/herbs?

I don't believe psyllium fiber has any significant influence on the absorption of drugs and herbs. Stimulant laxatives, on the other hand, may affect the absorption if they cause significant diarrhea.

5. Tea also has tannins which inhibits Fe absorption, does this affect tea drinking with meat-based meals in China?

In theory *Cha Ye* (*Folium Camelliae*) may affect absorption of meat and fat-soluble compounds in food. To what extent I am not sure. But if we zoom out, and consume food and tea in moderation, I don't think there will be significant interaction.

6. Thank you so much for being here Dr. Chen. Recommending herbal formulas to oncology patients can be particularly challenging due to drug herbal interactions. I see some oncologists recommend single herbs such as Korean ginseng for chemo related fatigue. In the hospital setting, where pharmacists don't have training in Chinese herbal medicine, do you think it is more efficacious to recommend single herbs rather than formulas?

The grand round was only one hour, so there is only so much information I can present. I will be doing more seminars/webinars with more indepth analysis if you are interested.

1. [Pacific Symposium](#) in San Diego in November. I speak on Friday morning and afternoon.
2. Lotus Institute.
  - a. Full day class on Herb Drug Interactions.  
<https://www.elotus.org/live/herb-drug-interaction-depth-analysis>
  - b. Four hours class on Herb Drug Interactions specifically for breast cancer to address use of herbs in chemotherapy and herbs with phytoestrogenic effect.  
<https://www.elotus.org/live/herbal-safety-breast-cancer-caution-contraindications-and-interactions>
7. The chart TCM WM very clear. Do you know of a book that would have this type of charting for TCM and WM? Thanks

Not sure which chart you are referring to. But these are my two books on Chinese herbs from an integrative approach. <https://aompress.com/>

8. How much of the adverse effects of herbal usage is due to skill of the practitioner, how much is truly negative interactions? In Integrative TCM hospitals or clinic, lets say in China, herbs and drugs are commonly use.

Our goal is to hopefully educate the practitioners on this topic and avoid the interactions as much as possible. This is a relatively new science / topic, so it is not clear how frequent such events happen.

9. Would eating licorice and dates improve chi (qi) in general?

Yes, *Gan Cao* (Radix et Rhizoma Glycyrrhizae) – licorice, and *Da Zao* (Fructus Jujubae) – dates, do help to improve qi. But they are generally used as an adjunct, and not as the primary herb. To improve qi, I would suggest formulas such as *Si Jun Zi Tang* (Four-Gentlemen Decoction) or *Shen Ling Bai Zhu San* (Ginseng, Poria, and Atractylodes Macrocephala Powder).

10. Thank you for such a wonderful introductory talk! Can you share any resources/databases you'd recommend for use to assess these interactions and learn more about their use and function?

I would suggest attend more webinars and seminars (ie, [Pacific Symposium](#) or [Lotus Institute](#)), and if you have questions on the herbs and formulas mentioned in those classes, then look them up in textbooks at [Art of Medicine Press](#). (They are the best resources in my very biased opinion)

11. Given our new understanding of gut microbiome in herb and drug metabolism, does this change our understanding?

Yes. If there are imbalances in gut microbiome, then that needs to be addressed first. Otherwise, the most accurate diagnosis and the most appropriate herbal treatment are useless if they cannot be absorbed. This is the central thesis in a TCM philosophy / school of thought called *Pi Wei Lun* (Treatise on the Spleen and Stomach) by Li Dong-Yuan.

12. What is the best way for biomedical providers to learn more about herbal medicine? Training, etc.

See #10 above. If you want to go all in, then TCM school may be necessary to be fully trained in TCM. There are many excellent schools throughout the US.

13. Is it possible that a rise in subsaharan African malaria resistance is due to separating out Artemisinin to combat the disease? since traditionally it has been used in synergistic combinations

Resistance is always possible. It happens more to one compound substance (ie, artemisinin), less to one herb (ie, *Qing Hao* (Herba Artemisiae Annuae) where artemisinin comes from), and not likely to one formula (ie, add *Qing Hao* (Herba Artemisiae Annuae) to *Huang Qin Tang* (Scutellaria Decoction) or *Ge Gen Huang Qin Huang Lian Tang* (Kudzu, Coptis, and Scutellaria Decoction)).

14. How can we learn chinese herbal medicine as an MD without becoming acupuncturist?

A wise man in China (Lao Zi) once said a journey of a thousand miles begins with the first step. Everyone in the audience has already taken that first step by attending the Grand Round. Now it is a matter of learning one more herb at a time, or one more formula at a time. Perhaps look up the many herbs or formulas I mention above. Perhaps attend an additional seminar / webinar that is interesting or pertinent to you. All these steps will help. Then, ideally, the UCSF model of integrative medicine can be replicated in more universities and we can all learn from each others to better treat the patients.

15. In which case would you still be concerned with interactions even when herbs/drugs that have potential interactions are given 2 hours apart? Are you concerned with the use of astragalus with chemo to mitigate its side effects?

Taking herbs and drugs two hours apart help to avoid/minimize absorption interactions, but not necessarily others. *Huang Qi* (Radix Astragali) is actually very helpful to alleviate many side effects of chemotherapy. I will present more on this at my seminars. See #6 above. In the meantime, here is my draft on *Huang Qi* (Radix Astragali), attached.

16. As a green tea proponent, what is the magnitude of the alteration induced by *Camilla sinesis*?

*Cha Ye* (Folium Camelliae) has a binding effect and may affect the absorption of fat soluble foods. For drugs, the studies I have read state that tea binds to nadolol and bisoprolol. These are the only two documented to my knowledge. For diet overall, I think as long as the tea and food are consumed in moderation, there are no significant adverse effects.

## **Huáng Qí (Radix Astragali)**

### **黄耆 / 黄芪**

**Pinyin Name:** *Huang Qi*

**Literal Name:** "yellow leader," "yellow length"

**Alternate Chinese Names:** 棉芪 *Mián Qí*, 箭芪 *Jiàn Qí*, 口芪 *Kǒu Qí*

**Original Source:** *Shen Nong Ben Cao Jing* (Divine Husbandman's Classic of the Materia Medica) in the second century

**English Name:** milkvetch root

**Botanical Name:** *Astragalus membranaceus* Bge. var. *mongholicus* (Dge.) Hsiao (蒙古黄芪 *Méng Gǔ Huáng Qí*); *Astragalus membranaceus* (Fisch.) Bge. (荚膜黄芪 *Jiá Mó Huáng Qí*)

**Pharmaceutical Name:** Radix Astragali

**Properties:** sweet, slightly warm

**Channels Entered:** Spleen, Lung

### **CHINESE THERAPEUTIC ACTIONS**

#### **1. Tonifies Qi and Raises Yang**

**Spleen qi deficiency:** *Huang Qi* (Radix Astragali) tonifies the Spleen to enhance its effectiveness in transformation and transportation. Clinical applications include pale or sallow facial appearance, fatigue, tired extremities, decreased food intake, diarrhea, and other conditions of Spleen deficiency.

- Fatigue and tired extremities due to Spleen deficiency: use *Huang Qi* individually, or combine it with *Dang Shen* (Radix Codonopsis) or *Ren Shen* (Radix et Rhizoma Ginseng) for synergistic effect.
- Loose stools or diarrhea due to Spleen deficiency: add it to dry-fried *Bai Zhu* (Rhizoma Atractylodis Macrocephalae), *Fu Ling* (Poria), dry-fried *Shan Yao* (Rhizoma Dioscoreae), dry-fried *Bai Bian Dou* (Semen Lablab Album) and dry-fried *Yi Yi Ren* (Semen Coicis).
- Spleen yang deficiency: use *Huang Qi* with yang tonics.

**Inability of qi to control blood circulation:** Proper flow and production of blood require an adequate supply of qi. In addition, Spleen qi controls the flow of blood and keeps it in the vessels. Deficiency of Spleen qi may lead to secondary blood deficiency and leakage of blood. Clinically, patients may exhibit fatigue, lethargy, shortness of breath, pale face, hematemesis, hematochezia, bruises, uterine bleeding, or other bleeding disorders. In short, patients with Spleen qi deficiency may bleed or bruise easily.

- Qi and blood deficiencies characterized by shortness of breath and pale face: combine *Huang Qi* with *Ren Shen* (Radix et Rhizoma Ginseng), *Bai Zhu* (Rhizoma Atractylodis Macrocephalae), *Dang Gui* (Radix Angelicae Sinensis) and dry-fried *Suan Zao Ren* (Semen Ziziphi Spinosa). **Exemplar Formula:** *Gui Pi Tang* (Restore the Spleen Decoction).
- Hematemesis, hematochezia, and profuse menstrual bleeding caused by deficiency of qi and leakage of blood: use this herb with charred *Jing Jie* (Herba Schizonepetae), charred *Mian Ma Guan Zhong* (Rhizoma Dryopteridis Crassirhizomatis), *San Qi* (Radix et Rhizoma Notoginseng), dry-fried *Hai Piao Xiao* (Endoconcha Sepiae) and *E Jiao* (Colla Corii Asini) in addition to *Gui Pi Tang* (Restore the Spleen Decoction).

**Prolapse of organs:** *Zhong* (central) qi deficiency results in prolapse of internal organs. *Huang Qi* tonifies qi and raises yang to treat prolapse of the stomach, rectum or other organs caused by the inability of qi and yang to hold the organs in the proper place.

- Prolapse of internal organs: use *Huang Qi* with *Ren Shen* (Radix et Rhizoma Ginseng), *Bai Zhu* (Rhizoma Atractylodis Macrocephalae), *Chai Hu* (Radix Bupleuri), and *Sheng Ma* (Rhizoma Cimicifugae). **Exemplar Formula:** *Bu Zhong Yi Qi Tang* (Tonify the Middle and Augment the Qi Decoction). A large amount of *Zhi Qiao* (Fructus Aurantii) may be added to enhance the overall effectiveness of the formula to lift the prolapsed organs.

**Lung and Spleen qi deficiencies:** Clinical manifestations of compromised respiratory and digestive functions include cough, wheezing, shortness of breath, profuse white and watery sputum, pale face, low voice, fatigue, abdominal fullness and diarrhea. *Huang Qi* enters both Lung and Spleen channels to tonify qi. It is the herb of choice for treating qi deficiency of these organs.

- Lung and Spleen qi deficiencies: combine *Huang Qi* with *Dang Shen* (Radix Codonopsis), *Fu Ling* (Poria), *Zi Wan* (Radix et Rhizoma Asteris), and *Chen Pi* (Pericarpium Citri Reticulatae).

**Qi and blood deficiencies:** This imbalance is characterized by sallow facial appearance, dizziness, vertigo, lack of energy, no desire to speak, spontaneous perspiration, palpitations and insomnia. Since qi is the leader of blood, tonification of qi enhances the production of blood.

- Qi and blood deficiencies: pair *Huang Qi* with *Dang Gui* (Radix Angelicae Sinensis). **Exemplar Formula:** *Dang Gui Bu Xue Tang* (Tangkuei Decoction to Tonify the Blood).

**Qi deficiency with deficiency heat symptoms:** Spleen qi deficiency prohibits clear yang from disseminating throughout the body. If yang qi is trapped in the muscle level for a prolonged period of time, symptoms of irritability with low-grade fever or unremitting high fever with fatigue, spontaneous sweating and frequent contraction of exterior conditions will occur. *Huang Qi* treats this deficiency heat condition even though it is warm in nature. **Exemplar Formula:** *Bu Zhong Yi Qi Tang* (Tonify the Middle and Augment the Qi Decoction).

**Cancer with qi deficiency caused by chemotherapy and radiation treatments:** Patients with cancer often receive chemotherapy and radiation treatments that severely damage qi. Use of *Huang Qi* replenishes the qi and decreases the adverse side effects associated with such treatments.

- Qi deficiency due to chemotherapy and radiation: use *Huang Qi* with *Ling Zhi* (Ganoderma), *Nu Zhen Zi* (Fructus Ligustri Lucidi), *Dang Shen* (Radix Codonopsis), *Ren Shen* (Radix et Rhizoma Ginseng), *Dong Chong Xia Cao* (Cordyceps) and *Shan Zhu Yu* (Fructus Corni).

**Sudden qi collapse due to heavy blood loss:** Qi and blood travel together in the vessels. When there is a sudden loss of blood, qi collapses as well. Symptoms include sudden facial pallor, profuse sweating, shortness of breath, and fading pulse. In severe cases, symptoms such as icy extremities, a sudden drop in blood pressure and body temperature, and sweating, may occur.

- Qi and blood collapse: use a large dose of *Huang Qi* (between 60 to 120 grams) with *Dang Gui* (Radix Angelicae Sinensis), *Ren Shen* (Radix et Rhizoma Ginseng), *Fu Zi* (Radix Aconiti Lateralis Praeparata), *Mai Dong* (Radix Ophiopogonis), and *Wu Wei Zi* (Fructus Schisandrae Chinensis).

## **2. Tonifies Wei (Defensive) Qi, Consolidates the Exterior**

**Deficiency of the wei (defensive) qi with spontaneous sweating:** Deficiency of the exterior leads to leakage of body fluids, resulting in spontaneous perspiration. This often leads to a compromised immune system and frequent contraction of exterior pathogenic infections.

- Spontaneous perspiration with aversion to wind, weak pulse, and frequent contraction of bacterial and viral infections: use this herb with *Bai Zhu* (Rhizoma Atractylodis Macrocephalae) and *Fang Feng* (Radix Saposhnikoviae). **Exemplar Formula:** *Yu Ping Feng San* (Jade Windscreen Powder).
- Spontaneous perspiration because of exterior deficiency: use *Huang Qi* with *Mu Li* (Concha Ostreae), *Ma Huang Gen* (Radix et Rhizoma Ephedrae), and *Fu Xiao Mai* (Fructus Triticis Levis). **Exemplar Formula:** *Mu Li San* (Oyster Shell Powder).
- Profuse perspiration and extreme fatigue due to yang deficiency: combine *Huang Qi* with *Fu Zi* (Radix Aconiti Lateralis Praeparata) and *Sheng Jiang* (Rhizoma Zingiberis Recens).
- Night sweating due to qi and yin deficiencies: use it with *Di Huang* (Radix Rehmanniae), *Mai Dong* (Radix Ophiopogonis), *Wu Wei Zi* (Fructus Schisandrae Chinensis), *Fu Xiao Mai* (Fructus Triticis Levis) and *Di Gu Pi* (Cortex Lycii).

## **3. Promotes the Discharge of Pus and Generates Flesh**

**Chronic non-healing ulcers and sores:** *Huang Qi* treats chronic sores and ulcerations with underlying deficiencies of qi and blood. Use of *Huang Qi* facilitates the discharge of pus and abscess, and encourages healing through generation of new flesh.

- Chronic non-ulcerating sores with pus: combine *Huang Qi* with *Dang Gui* (Radix Angelicae Sinensis), *Chuan Xiong* (Rhizoma Chuanxiong), *Chuan Shan Jia* (Squama Manis), and *Zao Jiao Ci* (Spina Gleditsiae). **Exemplar Formula:** *Tou Nong San* (Discharge Pus Powder).
- Chronic sores with underlying deficiency: use this herb with *Ren Shen* (Radix et Rhizoma Ginseng), *Dang Gui* (Radix Angelicae Sinensis), *Chuan Xiong* (Rhizoma Chuanxiong), *Bai Zhi* (Radix Angelicae Dahuricae) and *Fang Feng* (Radix Saposhnikoviae). **Exemplar Formula:** *Qian Jin Nei Tuo San* (Drain the Interior Powder Worthy of A Thousand Gold).

- Flat, chronic sores and non-healing ulcers underlying qi and blood deficiencies: use it with *Dang Gui* (Radix Angelicae Sinensis), *Shu Di Huang* (Radix Rehmanniae Praeparata), *Ren Shen* (Radix et Rhizoma Ginseng), *Bai Zhu* (Rhizoma Atractylodis Macrocephalae), and *Rou Gui* (Cortex Cinnamomi). **Exemplar Formula:** *Shi Quan Da Bu Tang* (All-Inclusive Great Tonifying Decoction).
- Lesions in children with qi deficiency: add *Huang Qi* to *Ren Shen* (Radix et Rhizoma Ginseng), *Rou Gui* (Cortex Cinnamomi), and *Zhi Gan Cao* (Radix et Rhizoma Glycyrrhizae Praeparata cum Melle). **Exemplar Formula:** *Bao Yuan Tang* (Preserve the Basal Decoction).

#### 4. **Regulates Water Circulation, Reduces Edema**

**Edema due to qi deficiency:** Spleen qi deficiency with an inability to carry out the transportation function results in retention of water in the body. *Huang Qi* tonifies qi and promotes normal circulation of water to treat conditions such as facial edema, superficial edema, sensations of heaviness in the body, spontaneous sweating and intolerance of wind. *Huang Qi* tonifies qi, and in turn facilitates the elimination of water. When used individually, the diuretic effect of *Huang Qi* is very mild and should be combined with diuretic herbs for stronger therapeutic results.

However, this is the herb of choice when the patient presents deficiency along with water retention signs and symptoms. When using *Huang Qi* as a diuretic only, the recommended dosage is low, approximately 9 grams.

- Edema, heavy sensations of the body, spontaneous perspiration, and aversion to wind because of accumulation of water with an exterior wind condition: use *Huang Qi* with *Bai Zhu* (Rhizoma Atractylodis Macrocephalae), *Fang Ji* (Radix Stephaniae Tetrandrae), *Gan Cao* (Radix et Rhizoma Glycyrrhizae) and *Sheng Jiang* (Rhizoma Zingiberis Recens). **Exemplar Formula:** *Fang Ji Huang Qi Tang* (Stephania and Astragalus Decoction).
- Superficial edema caused by qi and yang deficiencies: combine this herb with *Gui Zhi* (Ramulus Cinnamomi), *Fu Ling* (Poria) and *Fang Ji* (Radix Stephaniae Tetrandrae). **Exemplar Formula:** *Fang Ji Fu Ling Tang* (Stephania and Poria Decoction).
- Chronic nephritis with edema and proteinuria: use a high dose of *Huang Qi* (60 to 90 grams) with *Dang Shen* (Radix Codonopsis), *Shi Wei* (Folium Pyrosiae), and *Shan Yao* (Rhizoma Dioscoreae) with *Fang Ji Huang Qi Tang* (Stephania and Astragalus Decoction) or *Fang Ji Fu Ling Tang* (Stephania and Poria Decoction).

#### 5. **Relieves Numbness and Pain**

**Numbness:** Numbness of the muscles in this case is due to insufficient nourishment and circulation of qi and blood. *Huang Qi* has a strong effect to tonify qi, which, in turn, helps to generate blood and increase blood flow to the extremities. It tonifies and promotes normal circulation of qi to relieve skin and muscle numbness and pain.

- Skin and muscle numbness and pain caused by qi and blood deficiencies: use this herb with *Gui Zhi* (Ramulus Cinnamomi), *Bai Shao* (Radix Paeoniae Alba), *Sheng Jiang* (Rhizoma Zingiberis Recens) and *Da Zao* (Fructus Jujubae). **Exemplar Formula:** *Huang Qi Gui Zhi Wu Wu Tang* (Astragalus and Cinnamon Twig Five-Substance Decoction).
- Numbness and pain in the extremities due to deficiency at *ying* (nutritive) and *wei* (defense) levels and accumulation of wind and dampness: use *Huang Qi* with *Qiang Huo* (Rhizoma et Radix Notopterygii), *Fang Feng* (Radix Saposhnikoviae), *Jiang Huang* (Rhizoma Curcumae Longae), and *Dang Gui* (Radix Angelicae Sinensis). **Exemplar Formula:** *Juan Bi Tang* (Remove Painful Obstruction Decoctions).

**Stroke Sequelae:** *Huang Qi* is commonly used to treat post-stroke complications, such as hemiplegia and deviation of the eyes and mouth, caused by qi deficiency and blood stasis. It is important to note that *Huang Qi* is only suitable for post-stroke patients who are deficient in nature and the dosage used must be high. Use of *Huang Qi* is not recommended for those who are at risk of stroke due to Liver yang rising, such as in patients with hypertension.

- Post-stroke complications: use a high dose of *Huang Qi* with *Dang Gui Wei* (Extremities Radix Angelicae Sinensis), *Chuan Xiong* (Rhizoma Chuanxiong), *Tao Ren* (Semen Persicae), *Hong Hua* (Flos Carthami) and *Di Long* (Pheretima). **Exemplar Formula:** *Bu Yang Huan Wu Tang* (Tonify the Yang to Restore Five Decoction).

#### 6. **Treats Xiao Ke (Wasting and Thirsting) Syndrome**

**Xiao ke syndrome:** *Huang Qi* tonifies qi, promotes generation of body fluids, and treats *xiao ke* syndrome accompanied by symptoms of thirst and fatigue.

- *Xiao ke* syndrome without interior heat: use *Huang Qi* with *Di Huang* (Radix Rehmanniae), *Shan Zhu Yu* (Fructus Corni), *Shan Yao* (Rhizoma Dioscoreae) and pig pancreas.

- *Xiao ke* syndrome with interior heat: combine this herb with *Zhi Mu* (Rhizoma Anemarrhenae), *Ge Gen* (Radix Puerariae Lobatae), *Tian Hua Fen* (Radix Trichosanthis) and *Shan Yao* (Rhizoma Dioscoreae). **Exemplar Formula:** *Yu Ye Tang* (Jade Fluid Decoction).

#### DOSAGE

9 to 30 grams, up to 120 grams maximum; used decoction, pill and powder forms.

#### TRADITIONAL PREPARATION AND PROCESSING

- 黄芪 *Huáng Qí*, the unprocessed root, has qualities better suited to treat exterior disorders. It tonifies *wei* (defensive) *qi*, stops perspiration, regulates water circulation, reduces edema and promotes generation of flesh.
- 蜜黄芪 *Mì Huáng Qí* (Radix Astragali Praeparata cum Melle), also known as 炙黄芪 *Zhì Huáng Qí*, is the honey-fried root. It is prepared by blending *Huang Qi* [100 kg] with honey water [made from 25 kg of refined *Feng Mi* (Mel) with 8.3 to 12.5 kg of water] in a covered container until the honey water is fully absorbed, followed by parching or tossing it in a heated wok at moderate temperature until it becomes dark yellow in color and not sticky when touched. Sweet, warm and moistening in nature, the honey-fried root has enhanced effect to tonify the middle *jiao*, benefit *qi* and lift yang. The honey-fried *Huang Qi* is commonly used to treat chronic cases of fatigue, diarrhea and organ prolapse due to *qi* and yang deficiencies.

#### CAUTIONS / CONTRAINDICATIONS

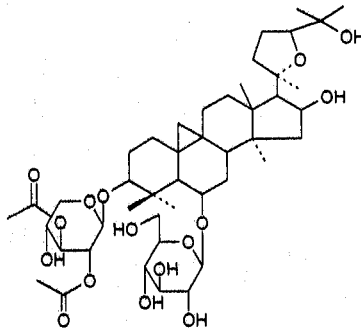
- Use of *Huang Qi* is contraindicated when pathogens are present at exterior levels of the body.
- It is contraindicated in cases characterized by an excess of *qi*, such as found in anger due to Liver *qi* stagnation.
- It is contraindicated in internal heat, excess fire, or deficiency and cold of the lower *jiao*.
- It is contraindicated with sores and lesions caused by heat in the blood.
- It is contraindicated in cases of stagnation.
- Women in the third trimester of pregnancy should use *Huang Qi* with caution. It has a diuretic effect and long-term use may decrease the quantity of amniotic fluid.<sup>1</sup> Furthermore, *Huang Qi* is a tonic herb that may stimulate the development of the muscles and bones of the baby, potentially leading to a difficult labor.<sup>2</sup>
- Hypersensitivity reactions, such as skin itching, redness, swelling and rash, have been observed.<sup>3</sup> Hypersensitivity reactions of the skin may be alleviated with an herbal wash made from *Huang Lian* (Rhizoma Coptidis), *Huang Bo* (Cortex Phellodendri Chinensis) and *Gan Cao* (Radix et Rhizoma Glycyrrhizae).<sup>4</sup>

#### OVERDOSE AND OVERDOSE TREATMENT

Oral ingestion of *Huang Qi* in excess of 60 grams per dose has been associated with a slight increase in blood pressure in 5 of 42 patients.<sup>5</sup> Oral ingestion of *Huang Qi* in excess of 100 grams may cause tremor and pain of the limbs.<sup>6</sup> Most adverse reactions associated with *Huang Qi* are mild and self-limiting and will resolve without treatment.

#### CHEMICAL COMPOSITION

Acetylastragaloside I, astragaloside I-IV, isoastragaloside I-II, agramembrannin II, cycloastragenol, cyclosiversigenin, soyasaponin I, tragacantha, kumatakenin, fomononetin.<sup>7,8</sup>



Astragaloside I



## PHARMACOLOGICAL EFFECTS

- **Immunostimulant:** *Huang Qi* exhibits significant effect to stimulate the nonspecific and specific immune system. The water extract of *Huang Qi* activates macrophages, neutrophils and natural killer cells, promotes the proliferation of T-cells, T-helper cells and B-cells, accelerates antibody production (IgG, IgA and IgM), and elevates interleukin-2 levels.<sup>9,10,11,12,13,14</sup>
- **Immunomodulatory:** Administration of *Huang Qi* shows marked effect to reduce intestinal mucosal damage and promote tissue repair by inhibiting lipopolysaccharide-induced expression of inflammatory cytokines (IL-1 $\beta$ , IL-4, IL-6, IL-8 and TNF- $\alpha$ ).<sup>15</sup> In addition, administration of *Huang Qi* in mice prolongs allograft survival associated with promotion of T<sub>reg</sub> cells (CD4<sup>+</sup> CD25<sup>+</sup>).<sup>16</sup>
- **Immunostimulant and antiviral:** Administration of *Huang Qi* has been shown to stimulate the innate immunity (through regulation of TLR3, TAK1, TBK1, IRF3, and IFN- $\beta$  in the TLR3), which then exerts the antiviral effect, against influenza virus.<sup>17</sup> *Huang Qi* also shows antiviral effect against herpes simplex virus type 1 with low cytotoxicity.<sup>18</sup> Specifically, *Huang Qi* contains polysaccharides with indirect antiviral effect against Epstein-Barr virus by suppressing the lytic cycle of viral reproduction.<sup>19</sup> Furthermore, *Huang Qi* contains isoflavonoids that exhibit antiviral effect against coxsackie virus to treat viral myocarditis.<sup>20</sup> The mechanism of antiviral effect is attributed to the inhibition of RNA replication of coxsackie virus.<sup>21</sup>
- **Immunomodulatory and antitumor:** *Huang Qi* contains polysaccharides that have been shown to effectively inhibit the solid tumor growth of hepatocarcinoma cells (H22) in mice. The mechanism of action is attributed in part to the immunomodulatory effect of *Huang Qi* to increase the secretion of interleukin (IL)-2, IL-12 and tumor necrosis factor- $\alpha$  and decreased IL-10 level in serum.<sup>22</sup> In addition, *Huang Qi* acts as a potential anticancer agent by inducing caspase-dependent apoptosis in chronic myeloid leukemia cell line (K562).<sup>23</sup> Lastly, *Huang Qi* shows *in vitro* and *in vivo* antitumor effects by restoring the impaired T cell functions.<sup>24</sup>
- **Immunomodulatory and antiasthmatic:** Oral ingestion of *Huang Qi* has an inhibitory effect on airway inflammation by modulating the Th<sub>1</sub> and Th<sub>2</sub> immune balance, according to a study in murine model of asthma with excess production of IgE, eosinophilia, cytokines, and bronchial hyperresponsiveness.<sup>25</sup>
- **Hematopoietic:** *Huang Qi* has been shown to induce the differentiation and proliferation of hematopoietic stem cells and promote the hematopoietic functions. Specifically, astragalosides improve the micro-environment of marrow hematopoietic system and enhance the secretion of endogenous hematopoietic factors.<sup>26,27</sup>
- **Metabolic:** Decoction of *Huang Qi* has been shown to increase the basal metabolic rate and cAMP in mice.<sup>28</sup> Decoction of *Huang Qi* is associated with increased cAMP but decreased cGMP in plasma, increased cAMP and cGMP in the spleen, and increased cGMP in the liver.<sup>29</sup>
- **Antifatigue:** *Huang Qi* illustrates antifatigue effects and is an effective ergogenic aid in exercise training. Administration of *Huang Qi* improves physical performance and reduces exercise-induced accumulation of the byproducts blood lactate and ammonia in subjects challenged with exercise performance.<sup>30</sup> Furthermore, use of *Huang Qi* is associated with increased muscle strength, elevated levels of plasma cortisol, and improved tolerance of hypoxia.<sup>31</sup>
- **Hypoglycemic:** According to a study in mice with type 2 diabetes and insulin resistance, use of *Huang Qi* is associated with marked effect to lower plasma glucose levels and alleviate insulin resistance.<sup>32</sup> In addition, the combination of *Huang Qi* and *Fang Ji* (*Radix Stephaniae Tetrandrae*) has synergistic effect to increase blood insulin levels and lower blood glucose levels in mice with streptozotocin-induced diabetes.<sup>33</sup>
- **Antihyperlipidemic:** The water extract of *Huang Qi* has been shown to reduce plasma levels of total cholesterol, triglycerides and low-density lipoprotein. In addition, astragalus polysaccharides decrease lipid deposition in the liver in subjects with hyperlipidemia.<sup>34</sup>
- **Cardiovascular:** *Huang Qi* has numerous influences on the cardiovascular system. *Huang Qi* exerts a regulatory effect on the blood pressure: it lowers blood pressure through its vasodilating and diuretic effect, yet it increases and sustains elevated blood pressure during shock. Furthermore, astragalosides exhibit a stimulant effect on the cardiovascular system to enhance myocardial contractility and increase cardiac output.<sup>35,36,37,38</sup>
- **Anti-ischemic:** *Huang Qi* protects against myocardial and cerebral ischemia and reperfusion-induced injuries. The mechanisms of action are attributed in part to its vasodilating effect to improve blood circulation and anti-inflammatory effect via the inhibition of NF- $\kappa$ B, IL-1 $\beta$ , IL-6 and TNF- $\alpha$ .<sup>39</sup>
- **Hepatoprotective and antifibrotic:** *Huang Qi* and its flavonoids exhibit significant effect to protect the liver from a wide variety of reagents (i.e., thioacetamide, paracetamol, carbon tetrachloride and D-galactosamine) and diseases (i.e., schistosomiasis, toxoplasmosis, obstructive jaundice and endotoxemia). The mechanisms of action include protection of liver cell membrane, relief of lipoperoxidation, and inhibition of hepatic stellate cells.<sup>40,41,42</sup>

In addition, administration of *Huang Qi* and *Bai Shao* (Radix Paeoniae Alba) shows marked protective effect on the liver via reduction of nitric oxide production and suppression of the pro-inflammatory mediator and cytokines production.<sup>43</sup> *Huang Qi* and *Bai Shao* (Radix Paeoniae Alba) also have hepatoprotective and antifibrotic effect to attenuate liver fibrosis induced by carbon tetrachloride or porcine serum.<sup>44,45,46</sup> Furthermore, the combination of *Huang Qi* and *Dan Shen* (Radix et Rhizoma Salviae Miltiorrhizae) has been shown to inhibit liver fibrosis and reduce invasion capacity of HepG2 cells. The beneficial effects include the inhibitory activity on cell proliferation, invasion and collagen synthesis in keloid fibroblast.<sup>47</sup> Lastly, *Huang Qi* shows antitumor and hepatoprotective effects by delaying and suppressing the hepatocarcinogenesis induced by diethylnitrosamine, an industrial by-product with hepatotoxic and carcinogenic effects.<sup>48</sup> The extract of *Huang Qi* and *Bai Shao* (Radix Paeoniae Alba) shows antineoplastic effect to induce apoptosis and inhibit the proliferation, migration and invasion of human hepatoma cell lines.<sup>49</sup>

One study reports six herbs with hepatoprotective effect to liver diseases: *Shui Fei Ji* (Fructus Silybi), *Gan Cao* (Radix et Rhizoma Glycyrrhizae), *Huang Qin* (Radix Scutellariae), *Wu Wei Zi* (Fructus Schisandrae Chinensis), *Dan Shen* (Radix et Rhizoma Salviae Miltiorrhizae) and *Huang Qi*.<sup>50</sup>

- **Nephroprotective and antifibrotic:** Administration of *Huang Qi* via injection is associated with numerous benefits to treat diabetic nephropathy, such as renal protective effect (BUN, SCr, CCr and urine protein) and systemic state improvement (serum albumin level).<sup>51</sup> *Huang Qi* exerts the nephroprotective effect by reducing fasting blood glucose and albuminuria levels, reversing the glomerular hyperfiltration state and ameliorating the pathological changes of early diabetic nephropathy.<sup>52</sup> *Huang Qi* also has beneficial effect to protect renal tubular damage induced by free radicals. The protective effect was superior to the effects of verapamil (Calan).<sup>53</sup> Furthermore, *Huang Qi* treats IgA nephropathy by regulating the immune system and correct the derangement of Th<sub>1</sub> and Th<sub>2</sub>.<sup>54</sup> Lastly, the decoction of *Huang Qi* and *Dang Gui* (Radix Angelicae Sinensis) shows marked effect to treat progressive chronic kidney disease by reducing proteinuria, decreasing the loss of capillaries and improving microstructure dysfunction.<sup>55</sup> The nephroprotective effect is attributed in part to the antifibrotic activity to improve ischemic microvasculature and attenuate interstitial fibrosis.<sup>56</sup>
- **Cardioprotective and antifibrotic:** Administration of *Huang Qi* has been shown to effectively prevent and treat myocardial fibrosis. The mechanism of action is attributed to the regulation of inflammation, oxidant stress, and pro-fibrotic signaling pathways.<sup>57</sup>
- **Neuroprotective:** Astragaloside IV exhibits neuroprotective effect against glutamate-induced neurotoxicity in PC12 cells through Raf-MEK-ERK pathway.<sup>58</sup>
- **Neurological:** According to *in vitro* and *in vivo* studies in subjects with nerve defects, the water extract of *Huang Qi* causes a marked enhancement of the growth of axons in the peripheral nerve. Administration of *Huang Qi* for 8 weeks promotes a relatively more mature structure with larger mean values of myelinated axon number, endoneurial area and total nerve area, when compared with the control group receiving the saline only.<sup>59</sup>
- **Estrogenic:** According to one *in vitro* study, the 70% ethanol extracts of 11 Chinese herbs demonstrated estrogenic activity and showed efficacy for hormone replacement therapy. These 11 herbs, listed from the highest to lowest estrogenic relative potency, are *Hu Zhang* (Rhizoma et Radix Polygoni Cuspidati), *Da Huang* (Radix et Rhizoma Rhei), *Jue Ming Zi* (Semen Cassiae), *Zhi He Shou Wu* (Radix Polygoni Multiflori Praeparata), *Yin Yang Huo* (Folium Epimedii), *Bu Gu Zhi* (Fructus Psoraleae), *Suo Yang* (Herba Cynomorii), *She Gan* (Rhizoma Belamcandae), *Huang Qin* (Radix Scutellariae), *Huang Qi* and *Ge Gen* (Radix Puerariae Lobatae).<sup>60</sup>
- **Phytoestrogenic:** Ten Chinese herbs with phytoestrogen effect were evaluated to determine their safety profile in breast cancer: *Rou Cong Rong* (Herba Cistanches), *Shan Yao* (Rhizoma Dioscoreae), *Huang Qi* (Radix Astragali), *Tu Si Zi* (Semen Cuscutae), *Yin Yang Huo* (Folium Epimedii), *Gan Cao* (Radix et Rhizoma Glycyrrhizae), *Chuan Xiong* (Rhizoma Chuanxiong), *Bu Gu Zhi* (Fructus Psoraleae), *Ren Shen* (Radix et Rhizoma Ginseng) and *Ge Gen* (Radix Puerariae Lobatae). The water extract of two herbs, *Rou Cong Rong* and *Shan Yao*, showed a stimulant effect *in vitro* on breast cancer cells that were estrogen receptor (ER)-positive (MDA-MB-361 and MCF-7) and ER-negative (SKBR3 and MDA-MB-231). In follow up animal studies *in vivo*, no significant differences were noted between the breast tumors in mice treated with these two herbs when compared to the control group. Furthermore, treatments with these two herbs did not stimulate, but rather suppressed, human triple-negative (MDA-MB-231) breast cancer xenografts growth in immunodeficiency mice. In addition, *Rou Cong Rong* and *Shan Yao* exhibited a significant immunomodulatory effect to suppress the growth of breast cancer cells. They increase the Th-1 cytokines (i.e., IL-2 and IFN- $\gamma$ ) which elicit antitumor responses, and decrease Th-3 cytokines (i.e., IL-10) which suppress antitumor immunity and impair host-protective immunity. Finally, no toxic effects were observed in animals treated with these two herbs. Based on these scientific data and evidence, the researchers

concluded that these ten Chinese herbs with phytoestrogen effect, including *Rou Cong Rong* and *Shan Yao*, at Chinese Pharmacopoeia recommended dosages would not be that hazardous for breast cancer growth.<sup>61</sup>

- **Other:** antibacterial, sedative, analgesic and anti-inflammatory.<sup>62,63,64</sup>

#### CLINICAL STUDIES AND RESEARCH

- **Prevention of common colds and influenza:** In one study, 540 patients with past histories of frequent common colds and influenza were divided into two groups and received preventative treatment with *Huang Qi*. One group received 5 grams of *Huang Qi* in pills three times daily, and the other group received 15 grams of *Huang Qi* in decoction every other day. All patients had two courses of 10 days treatment, with 5 days of rest in between courses. The study reported that patients in both groups had similar results. Both had 2.7 times lower risk of infection, and a shortened duration of infection.<sup>65</sup>
- **Prevention of pulmonary tract infection:** An herbal tea of 15 grams of *Huang Qi* and 10 grams of *Da Zao* (*Fructus Jujubae*), given twice daily, demonstrated marked effectiveness in prevention of pulmonary tract infection in 160 patients with past histories of chronic bronchitis, bronchial asthma, and allergic rhinitis.<sup>66</sup>
- **Prevention of upper respiratory tract infection in children:** One report described that 2 ml of *Huang Qi* solution (equivalent to 2 grams of dried herb) given daily, showed 94% effectiveness in prevention of respiratory tract infection in 100 children.<sup>67</sup>
- **Rhinitis:** Local injection of a *Huang Qi* preparation every third day for 10 treatments showed a 93.26% rate of effectiveness in 47 patients with rhinitis.<sup>68</sup>
- **Prevention of asthma and cough:** A *Huang Qi* preparation was injected (equivalent to 1 gram of dried herb) into *Zusanli* (ST 36) bilaterally twice weekly for three months per course of treatment, for a total of 3 to 4 courses of treatment, with 2 weeks of rest between each course. Out of 41 patients, there was significant improvement in 85.4% and moderate improvement in 56.1%. Furthermore, most patients noticed an increase in appetite and energy, improvement in quality of sleep, and fewer episodes of infection.<sup>69</sup>
- **Peptic ulcer disease:** According to one report, patients with gastric ulcers, duodenal ulcers, or both, were treated with intramuscular injections of 2 ml of a *Huang Qi* preparation (equivalent to 2 grams of dried herb) twice daily. Many patients showed symptomatic improvement after 1 week. Most patients showed complete healing or moderate improvement after approximately one month.<sup>70</sup> According to another report, an herbal decoction containing *Huang Qi* 12g, *Bai Shao* (*Radix Paeoniae Alba*) 12g, *Gan Cao* (*Radix et Rhizoma Glycyrrhizae*) 5g, *Gui Zhi* (*Ramulus Cinnamomi*) 10g, *Sheng Jiang* (*Rhizoma Zingiberis Recens*) 3g, *Da Zao* (*Fructus Jujubae*) 5 pieces, and *Yi Tang* (*Maltosum*) 30g, was given in two equally-divided doses twice daily for 25 to 53 days to treat patients with peptic ulcer disease. Out of 43 patients, 22 reported significant improvement, 17 reported moderate improvement, and 4 showed no improvement. The rate of effectiveness was 90.7%.<sup>71</sup>
- **Gastric prolapse:** Patients with gastric prolapse were treated with an herbal preparation of fresh *Huang Qi*, *Sheng Ma* (*Rhizoma Cimicifugae*), *Chai Hu* (*Radix Bupleuri*), and *Wu Wei Zi* (*Fructus Schisandrae Chinensis*). The treatment protocol was to inject the herbs (dosage equivalent to 1 gram of each herb) intramuscularly into *Zhongwan* (CV 12) and *Zusanli* (ST 36) every other day for 1 month. The rate of effectiveness was 84.9% among 42 patients who participated in the study.<sup>72</sup>
- **Rectal prolapse:** Daily administration of an herbal decoction containing 30 to 50 grams of fresh *Huang Qi*, 15 grams of *Dan Shen* (*Radix et Rhizoma Salviae Miltiorrhizae*), 10 grams of *Shan Zha* (*Fructus Crataegi*), 3 grams of *Fang Feng* (*Radix Saposhnikoviae*), and 3 grams of *Sheng Ma* (*Rhizoma Cimicifugae*) showed marked effectiveness for treatment of rectal prolapse.<sup>73</sup>
- **Hepatitis:** In one study, 29 patients with chronic infectious hepatitis were treated with intramuscular injections of *Huang Qi* (equivalent to 4 grams of dried herb) for 1 to 3 months, with marked improvement.<sup>74</sup> Another report described 174 patients with positive HBsAg who were treated with an injection of a 100% *Huang Qi* preparation. The treatment protocol was to administer one injection every three days for a total of 2 months, alternating between two acupuncture points *Zusanli* (ST 36) and *Shenshu* (BL 23). Out of 174 patients, 131 (75.3%) became negative for HBsAg.<sup>75</sup>
- **Immune disorder:** According to one report, 14 patients with low white blood cell counts showed marked improvement with an herbal decoction of 30 grams of fresh *Huang Qi*, 15 grams of *Ren Shen* (*Radix et Rhizoma Ginseng*), and 20 pieces of *Da Zao* (*Fructus Jujubae*).<sup>76</sup>
- **Immune suppression:** In an *in vivo* study, administration of *Huang Qi* was associated with reversal of cyclophosphamide-induced immune suppression.<sup>77</sup>
- **Leukopenia:** Administration of *Huang Qi* was associated with an obvious rise in white blood cell (WBC) counts in 115 patients with leukopenia.<sup>78</sup>

- **Immune restoration:** Administration of *Huang Qi* and *Nu Zhen Zi* (Fructus Ligustri Lucidi) was reported to act as a potent immune stimulant in 19 cancer patients.<sup>79</sup>
- **Nephritis:** Twenty patients with chronic nephritis were treated with 100g of *Huang Qi* in decoction, given in two equally-divided doses twice daily for 15 to 90 days. Out of 20 patients, 7 showed significant improvement, 9 showed marked improvement, and 4 showed no improvement. Most patients reported symptomatic improvement as well as a decrease of protein in the urine.<sup>80</sup>
- **Nephropathy:** *Huang Qi* in large doses has shown beneficial effects against nephropathy in mice and glomerulonephritis in rabbits. Furthermore, large doses of *Huang Qi* are commonly used to treat chronic nephritis in human clinical trials. It increases the volume of urine, and the excretion of chloride and ammonia.<sup>81,82</sup>
- **Idiopathic membranous nephropathy:** A 77-year-old woman with nephrotic syndrome secondary to idiopathic membranous nephropathy was treated for two years without response with drugs such as angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, cyclosporine A, and mycophenolate mofetil. She was then treated with *Huang Qi* at 15 g/day and showed a marked decrease in proteinuria, followed by complete remission of nephrotic syndrome.<sup>83</sup>
- **Glomerulonephritis:** In one study, 56 patients with chronic glomerulonephritis were treated with intramuscular injection of *Huang Qi* (equivalent to 3 grams of dried herb) for 1 month with marked reduction of protein in the urine (effective rate of 61.7%) and improved kidney function.<sup>84</sup>
- **Proteinuria:** One study reported 92.3% rate of effectiveness for treatment of proteinuria using an herbal formula with *Huang Qi* 10-30g, *Ba Ji Tian* (Radix Morindae Officinalis) 10-30g, *Shu Di Huang* (Radix Rehmanniae Praeparata) 10-30g, *Shan Yao* (Rhizoma Dioscoreae) 10-30g, *Shan Zhu Yu* (Fructus Corni) 3-30g, *Fu Ling* (Poria) 3-30g, *Ze Xie* (Rhizoma Alismatis) 3-30g, *Mu Dan Pi* (Cortex Moutan) 3-30g, and others as needed. The treatment protocol was to administer the decoction daily for 60 days per course of treatment. Of 78 cases, 40 had complete stabilization, 12 significant stabilization, 20 had improvement, and 6 had no improvement.<sup>85</sup>
- **Diabetes with microalbuminuria:** Twenty-one type 2 diabetic patients with microalbuminuria were treated with the decoction of *Huang Qi* and *Chuan Xiong* (Rhizoma Chuanxiong) by mouth at 150 mL daily. After six months, there was a significant decrease of urinary albumin excretion and an improvement of endothelial dysfunction.<sup>86</sup>
- **Sarcopenia:** The combination of *Huang Qi* and *Shan Yao* (Rhizoma Dioscoreae) exhibits significant effect to treat sarcopenia in mice with muscle mass loss and a reduction in grip strength induced by senile type 2 diabetes mellitus. The proposed mechanism of action is attributed to their effects on the Rab5a/mTOR pathway and mitochondrial quality control.<sup>87</sup>
- **Psoriasis:** Administration of *Huang Qi* (as powder, decoction, injection or topical cream) was used to treat patients with psoriasis with a 95.6% rate of effectiveness. Out of 204 patients, 42 reported marked improvement, 62 reported moderate improvement, 91 reported slight improvement, and 9 reported no improvement.<sup>88</sup>
- **Pulseless disease (Takayasu's disease):** In one study, 6 patients with this condition were treated with an herbal formula with significant improvement in 3 cases, moderate improvement in 2 cases, and slight improvement in 1 case. The herbal formula contained *Bu Yang Huan Wu Tang* (Tonify the Yang to Restore Five Decoction) with 60 grams of *Huang Qi* and additional blood-activating and blood stasis-resolving herbs.<sup>89</sup>
- **Prostatic hypertrophy:** In one report, 52 patients with prostatic hypertrophy were treated with an herbal decoction taken on an empty stomach. The formula contained 100 grams of fresh *Huang Qi* and 30 grams of *Hua Shi* (Talcum) cooked in decoction, with 3 grams of *Hu Po* (Succinum) added prior to administration. At the conclusion of the study, 38 patients reported complete remission of symptoms, 13 reported improvement in flow rate and reduction in size of the prostate, and 1 reported no improvement.<sup>90</sup>
- **Chronic fatigue syndrome:** According to a randomized, double-blind, controlled clinical trial performed with 36 adults who complained of chronic fatigue, oral administration of *Huang Qi* and *Dan Shen* (Radix et Rhizoma Salviae Miltiorrhizae) decreased the fatigue severity score, when comparing with the herb group against the control group.<sup>91</sup>
- **HIV/AIDS:** Twenty-one patients with HIV/AIDS were treated with 20 grams of an herbal formula orally twice a day for 4 months. The herbal formula contains *Huang Qi*, *Nu Zhen Zi* (Fructus Ligustri Lucidi), *Huang Qin* (Radix Scutellariae), *Tu Bie Chong* (Eupolyphaga seu Steleophaga) and others. After treatment, the study reported that the herbal formula significantly alleviated the symptoms of HIV/AIDS, improved their immune function, inhibited HIV reproduction to a certain extent or keep it stable. Furthermore, no obvious toxic or adverse reaction was seen.<sup>92</sup>
- **Hemorrhagic stroke:** According to a double-blind, placebo-controlled, randomized study, 78 patients with hemorrhagic stroke were treated with 3 grams of *Huang Qi* or 3 grams of placebo three times daily for 14 days. Of

68 patients who completed the study (36 from herb group and 32 from placebo group), *Huang Qi* was shown to enhance recovery of hemorrhagic stroke, though the sample size was relatively small.<sup>93</sup>

#### HERB-DRUG INTERACTION

- **Theophylline:** Astragaloside IV has been shown to inhibit CYP1A2 activity and significantly increase the area under the concentration-time curve (AUC) and decrease the total body clearance for theophylline, a bronchodilator drug.<sup>94</sup>
- **Metoprolol:** Administration of astragaloside IV (3 mg/kg/day for seven days) in rats has been shown to inhibit CYP2D6 activity and reduces the metabolism of metoprolol (27 mg/kg), leading to increased  $C_{max}$  and AUC.<sup>95</sup>
- **Omeprazole:** Pretreatment with astragaloside IV (100 mg/kg/day for 7 days) in rats has been shown to decrease the half-life,  $C_{max}$  and AUC of omeprazole. The exact mechanism of action is not certain, but is attributed to induction of P-gp or CYP3A4 activity.<sup>96</sup>
- **Midazolam:** Concurrent administration of *Huang Qi* and midazolam in rats is associated with greatly increased in the  $C_{max}$  and AUC of midazolam. The proposed mechanism is attributed to the inhibiting effects on the metabolism of CYP3A4.<sup>97</sup>
- **Enalapril:** ACE inhibitors, such as enalapril, reduce renal tubulointerstitial fibrosis but have limited effectiveness. However, the combination of enalapril with *Huang Qi* and *Dang Gui* (Radix Angelicae Sinensis) was significantly more effective to decrease tubulointerstitial fibrosis than treatment with enalapril alone. Therapeutic benefits of the combination included significant reductions in tumor necrosis factor- $\alpha$ , collagen accumulation, activation of fibroblasts, and tubular cell apoptosis.<sup>98</sup>
- **Cyclophosphamide-induced immunosuppression:** Administration of *Huang Qi* exhibited immunomodulating and immunorestorative effects and restored the depressed immune functions in tumor-bearing and cyclophosphamide-treated mice.<sup>99</sup>
- **Cyclophosphamide-induced myelosuppression:** Use of *Huang Qi* via injection promoted myelopoiesis and enhanced hematopoiesis in mice with myelosuppression induced by cyclophosphamide.<sup>100</sup>
- **Daunorubicin-induced cardiotoxicity:** Use of *Huang Qi* significantly attenuated cardiotoxicity induced by daunorubicin by decreasing free radical release and apoptosis in cultured neonatal cardiomyocytes.<sup>101</sup>
- **Aminoglycosides-induced ototoxicity and nephrotoxicity:** In one study, a constituent injection of *Huang Qi* and *Lu Xian Cao* (Herba Pyrolae) in guinea pigs was found to be effective in preventing ototoxicity and nephrotoxicity associated with use of aminoglycosides.<sup>102</sup> [Note: Examples of aminoglycosides include gentamicin, tobramycin, amikacin.]
- **Puromycin-induced nephrosis:** *Huang Qi* and *Dang Gui* (Radix Angelicae Sinensis) are two herbs with antifibrotic effects and have long been used to treat nephrotic syndrome. The combination of these two herbs retarded the progression of renal fibrosis and deterioration of renal function induced by puromycin.<sup>103</sup>
- **Bleomycin-induced pulmonary fibrosis:** Administration of *Huang Qi* via injection has been shown to protect the lung and attenuate bleomycin-induced alveolitis and pulmonary fibrosis. The mechanism of action is attributed in part to the regulation of Th<sub>1</sub>/Th<sub>2</sub> balance.<sup>104</sup>
- **Bleomycin-induced scleroderma:** Administration of *Huang Qi* polysaccharides showed marked effect to inhibit excessive collagen accumulation and treat bleomycin-induced scleroderma. The mechanism of action is attributed in part to its immunomodulatory activities to inhibit transforming growth factor- $\beta$  production.<sup>105,106</sup>

#### TOXICOLOGY

*Huang Qi* has very low toxicity. Oral ingestion of *Huang Qi* decoction (7.5 g/kg) cannot be determined in rats. The LD<sub>50</sub> in mice for intraperitoneal injection is approximately 40 g/kg.<sup>107</sup>

#### AUTHORS' COMMENTS

According to Dr. Zhāng Xiàopíng (张笑平), the combination of *Huang Qi* and *Shan Yao* (Rhizoma Dioscoreae) has excellent effects to lower plasma glucose levels to treat diabetes mellitus patients. These two herbs are especially effective in individuals with diabetes characterized by qi and yin deficiencies.

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# Dōng Chóng Xià Cǎo (Cordyceps)

## 冬蟲夏草 / 冬虫夏草

**Pinyin Name:** *Dong Chong Xia Cao*

**Literal Name:** “winter bug summer herb”

**Alternate Chinese Names:** 虫草 *Chóng Cǎo*, 冬虫草 *Dōng Chóng Cǎo*, 夏草冬虫 *Xià Cǎo Dōng Chóng*

**Original Source:** *Yue Wang Yao Zhen* (Somaratsa) in the 8th centry AD

**English Name:** Chinese caterpillar fungus

**Botanical/Zoological Name:** *Ophiocordyceps sinensis* (Berk.) G.H. Sung et al. [Synonym: *Cordyceps sinensis* (Berk.) Sacc.] (冬虫夏草菌 *Dōng Chóng Xià Cǎo Jūn*); It is usually combined with the larval remains of *Hepialus varians* Staudinger. (绿蝙蝠蛾 *Lǜ Biān Fú É*)

**Pharmaceutical Name:** Cordyceps, Ophiocordyceps

**Properties:** sweet, warm

**Channels Entered:** Lung, Kidney

### CHINESE THERAPEUTIC ACTIONS

#### 1. Tonifies Kidney Yang and Augments Jing (Essence)

**Kidney yang and jing (essence) deficiencies:** This condition is characterized by generalized soreness, lower back and knee weakness and pain, spermatorrhea, frequent urination, nocturnal emissions, impotence, premature ejaculation, tinnitus, forgetfulness, and poor memory. *Dong Chong Xia Cao* (Cordyceps) is also ideal for convalescing patients or those who are extremely weak, with spontaneous sweating.

- Kidney yang and *jing* (essence) deficiencies: add *Du Zhong* (Cortex Eucommiae), *Xu Duan* (Radix Dipsaci), *Lu Jiao Jiao* (Colla Cornus Cervi) and *Gui Ban Jiao* (Colla Plastrum Testudinis).
- Impotence due to Kidney yang deficiency: combine this substance with *Lu Rong* (Cornu Cervi Pantotrichum) and *Yin Yang Huo* (Folium Epimedii).
- Tinnitus due to Kidney yin deficiency: combine it with *Gou Qi Zi* (Fructus Lycii) and *Shan Zhu Yu* (Fructus Corni).
- Spontaneous sweating during recovery from chronic illness: use it with *Huang Qi* (Radix Astragali) to tonify the *wei* (defensive) *qi*. The herbs are cooked as soup with beef, lamb or duck.

#### 2. Tonifies the Lung, Stops Bleeding and Dissolves Phlegm

**Chronic respiratory disorders, cough:** *Dong Chong Xia Cao* treats chronic respiratory disorders with Lung and Kidney deficiencies manifesting in consumptive cough with blood-streaked sputum. It helps to arrest cough, dispel sputum and stop bleeding. Because *Dong Chong Xia Cao* is moderate in its nourishing effect, it is suitable for chronic cough caused by yin or qi deficiency.

- Chronic cough due to Kidney and Lung yin deficiencies manifesting in scanty, blood-streaked sputum: combine it with *Mai Dong* (Radix Ophiopogonis), *E Jiao* (Colla Corii Asini), *Bai He* (Bulbus Lilii), and *Chuan Bei Mu* (Bulbus Fritillariae Cirrhosae).
- Chronic cough due to Kidney and Lung qi deficiencies resulting in manifesting of feeble cough and weakness: add it to *Ge Jie* (Gecko), *Ren Shen* (Radix et Rhizoma Ginseng), and *Wu Wei Zi* (Fructus Schisandrae Chinensis).
- Spontaneous sweating due to Lung deficiency: cook and eat it in stew with chicken, duck, beef or lamb.

### DOSAGE

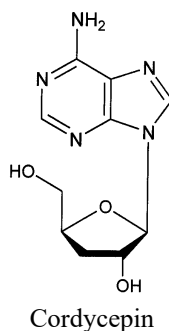
3 to 9 grams.

### CAUTIONS / CONTRAINDICATIONS

- Use *Dong Chong Xia Cao* with caution in exterior conditions.
- Dry mouth and stomach discomfort are two rare side effects associated with use of *Dong Chong Xia Cao*. These side effects are mild and self-limiting, and treatment is unnecessary as the symptoms resolve shortly upon discontinuation.<sup>1</sup>
- Adverse reactions associated with overdosage of *Dong Chong Xia Cao* include headache, irritability, restlessness, edema and swelling of the face and extremities, epistaxis, decreased volume of urine, yellow, greasy tongue coat, and thready, rapid pulse.<sup>2</sup>

## CHEMICAL COMPOSITION

Cordycepic acid 7 to 9%, cordycepin, cordymin, amino acid (approximately 25%), 3-deoxyadenosine, aspartic acid, glutamic acid, serine, histidine, glucine, threonine, lysine, D-mannitol, vitamin A, C; nicotinic acid, nicotinic amide, ergosterol, uracil, adenine nucleoside, ergosterol peroxide, galactomannan, hypoxanthine nucleoside, thymine, guanine, hypoxanthine, adenosine.<sup>3,4,5</sup>



## PHARMACOLOGICAL EFFECTS

- **Testosteronic:** *Dong Chong Xia Cao* has been shown to elevate production of testosterone and cortisol and increase the weight of seminal vesicles, testicles and prostate. Specifically, *Dong Chong Xia Cao* stimulates steroidogenesis in a dose-dependent manner, and the maximal testosterone production is observed between 2 to 3 hour after oral ingestion.<sup>6</sup> Furthermore, *Dong Chong Xia Cao* promotes spermatogenesis to increase both sperm count and sperm motility.<sup>7,8</sup>
- **Estrogenic:** *Dong Chong Xia Cao* has been shown to increase uterine weight, improve uterine structure, elevate follicle-stimulating hormone and luteinizing hormone and induce estradiol production. The mechanism of action is attributed to the increased levels of steroidogenic acute regulatory protein and aromatase expression.<sup>9,10</sup>
- **Adrenocortical:** *Dong Chong Xia Cao* has been shown to stimulate the secretion of adrenal gland hormones in mice.<sup>11</sup>
- **Antifatigue:** Supplementation of *Dong Chong Xia Cao* to diet has been shown to promote exercise endurance capacity by activating skeletal muscle metabolic regulators.<sup>12</sup>
- **Cognitive:** According to *in vivo* and *in vitro* experiments, administration of cordycepin has been shown to significantly alleviate cognitive impairments in neurodegenerative diseases, such as Parkinson's disease. Cordycepin improved cognitive function by regulating the adenosine A<sub>2A</sub> receptors.<sup>13</sup>
- **Immunomodulatory:** The polysaccharides of *Dong Chong Xia Cao* exhibit immunomodulatory effect.<sup>14</sup> On one hand, *Dong Chong Xia Cao* enhances the phagocytic rate, phagocytic index and phagocytic capacity of macrophages.<sup>15</sup> Specifically, cordysinocan activates immune responses in cultured T-lymphocytes and macrophages to signal the cascade and induction of cytokines.<sup>16</sup> On the other hand, cordycepin suppresses T-lymphocyte activity, decreases interleukin-2 expression and increases interleukin-10 expression.<sup>17</sup>
- **Antiosteoporotic:** Administration of *Dong Chong Xia Cao* is associated with many beneficial effects in the management of osteoporosis, such as increases in osteocalcin and estradiol levels, and decreases in serum alkaline phosphatase activity, tartarate-resistant acid phosphatase activity, and interferon-gamma level.<sup>18</sup> In addition, one study shows that the concurrent use of *Dong Chong Xia Cao* and strontium has beneficial effect for the management of postmenopausal osteoporosis in humans. The combination of these two substances decreases bone resorption, increases bone formation, increases in body weight, and enhances 17β-estradiol-production.<sup>19</sup>
- **Antiasthmatic:** Administration of *Dong Chong Xia Cao* extract is associated with marked effect to treat asthma by significantly inhibiting airway inflammation, airway hyperresponsiveness, and the infiltration of eosinophils in the airway. The mechanism of action is attributed to the suppression of nuclear factor-κB in lung cells and cultured airway smooth muscle cells.<sup>20,21</sup> Clinically, *Dong Chong Xia Cao* enhances the effect of adrenaline on the bronchi and exerts a synergistic effect with aminophylline to treat asthma. Furthermore, *Dong Chong Xia Cao* treats obstructive emphysema by improving ventilatory function of the lungs and stopping the deterioration of the lung function.<sup>22</sup>
- **Cardiovascular:** *Dong Chong Xia Cao* exhibits numerous influences on the cardiovascular system. *Dong Chong Xia Cao* contains one polysaccharide that exhibits antihypertensive effect by dilating the blood vessels.<sup>23</sup> *Dong Chong Xia Cao* also decreases in heart rate and blood pressure and reduces oxygen requirement of the cardiac muscles.<sup>24</sup> In addition, the water and ethanol extracts of *Dong Chong Xia Cao* exert antiarrhythmic effect against arrhythmia induced by aconitine, adrenaline and barium chloride.<sup>25</sup> Lastly, *Dong Chong Xia Cao* illustrates

antiplatelet effect to inhibit platelet activation and has high therapeutic potential to treat or prevent cardiovascular diseases.<sup>26</sup>

- **Hypoglycemic and antihyperlipidemic:** Administration of *Dong Chong Xia Cao* extract for 8 weeks to mice with a high-fat diet is associated with numerous benefits. It significantly elevates HDL/LDL ratios, decreases body weight gain, protects pancreatic beta cells, protects the kidney and reduces the accumulation of mesangial matrix and collagen deposition.<sup>27</sup>
- **Nephroprotective:** *Dong Chong Xia Cao* has a significant effect to protect the kidneys. It reduces the occurrence of proteinuria, lowers the amount of blood urea nitrogen and creatinine, and increases creatinine clearance rate. Clinical applications include immunoglobulin A nephropathy, as well as nephritis and renal injury or failure due to chemical agents or ischemia.<sup>28,29</sup>

Administration of *Dong Chong Xia Cao* and *Lei Gong Teng* (*Radix Tripterygii Wilfordii*) is associated with marked effect to alleviate proteinuria and protect and repair podocytes of diabetes nephropathy in rats. The mechanism of action is correlated with up-regulating the expressions of nephrin and podocin. Furthermore, the use of *Dong Chong Xia Cao* increases the efficacy and attenuates adverse reactions of *Lei Gong Teng* (*Radix Tripterygii Wilfordii*).<sup>30</sup>
- **Hepatoprotective:** *Dong Chong Xia Cao* has been shown to treat chronic hepatitis C by improving cellular immune function and hepatic function. *Dong Chong Xia Cao* is also effective to prevent liver injuries and liver fibrosis induced by carbon tetrachloride.<sup>31</sup> In addition, administration of *Dong Chong Xia Cao* is associated with prolonged survival in patients with liver cirrhosis, hepatitis B, hepatitis C and liver metastasis.<sup>32</sup>
- **Antifibrotic:** *Dong Chong Xia Cao* has been shown to effectively treat fibrosis of the lung, liver and kidney. *Dong Chong Xia Cao* postpones the progression of fibrosis in rabbits with artificially-induced silicotic pulmonary fibrosis.<sup>33</sup> In addition, the cultured mycelium of *Dong Chong Xia Cao* exerts hepatoprotective and antifibrotic effect in mice to treat carbon tetrachloride-induced liver inflammation and fibrosis.<sup>34</sup> Lastly, in rats with renal fibrosis due to unilateral ureteral obstruction and subsequent collagen accumulation, *Dong Chong Xia Cao* exhibits a significant effect to prevent and/or treat renal fibrosis.<sup>35</sup>
- **Anticancer:** *Dong Chong Xia Cao* extract exhibits significant anticancer effect on several cancer cell lines: breast cancer (MCF-7), human promyelocytic leukemia (HL-60), human hepatocellular carcinoma (HepG2), promyelocytic leukemia cells (HL-60), lung adenocarcinoma (A549), and colorectal cancer.<sup>36,37,38,39</sup> The mechanism of action includes cytotoxic, antiproliferative, antimetastatic, and others.<sup>40,41</sup> Cordycepin is believed to be one of the main cytotoxic constituents.<sup>42,43</sup>
- **Radioprotective:** The polysaccharides from cultured *Dong Chong Xia Cao* exert protective effect in mice against ionizing radiation by enhancing the immunity, reducing oxidative injury, and modulating the secretion of interleukin (IL)-4, IL-5 and IL-17.<sup>44</sup>
- **Other:** antiaging,<sup>45</sup> antibacterial,<sup>46</sup> anti-inflammatory,<sup>47</sup> antioxidant,<sup>48</sup> sedative and hypnotic.<sup>49</sup>

#### CLINICAL STUDIES AND RESEARCH

- **Sexual dysfunction:** In one study, 197 patients with sexual disorders were treated with 1 gram of *Dong Chong Xia Cao* three times daily for 40 days. The rate of effectiveness was 64.15% in 159 patients who received cultivated *Dong Chong Xia Cao*, and 31.57% in 38 patients who received wild-crafted *Dong Chong Xia Cao*.<sup>50</sup>
- **Chronic kidney disease:** According to a literature review of 22 studies with 1,746 participants with chronic kidney disease but not treated with dialysis, use of *Dong Chong Xia Cao* significantly decreased serum creatinine, increased creatinine clearance, and reduced proteinuria.<sup>51</sup>
- **Kidney impairment:** Compromised renal function in 117 patients was treated with 6 grams of *Dong Chong Xia Cao* three times daily, with good results.<sup>52</sup>
- **Proteinuria:** Daily ingestion of *Dong Chong Xia Cao* at 6 grams three times daily for 30 days per course of treatment effectively reduced protein in the urine from 4.3g to 1.32g in 18 patients with nephritis and proteinuria.<sup>53</sup>
- **Allograft rejection:** *Dong Chong Xia Cao* has been shown to exert an inhibitory effect on allograft rejection to prolong survival time in subjects with heart and kidney transplants.<sup>54,55</sup>
- **Tinnitus:** According to one report, 23 patients with tinnitus were treated with 6 grams of *Dong Chong Xia Cao* three times daily for up to 4 weeks, with good results.<sup>56</sup>
- **Hepatitis B:** One study reported 78.56% rate of effectiveness using *Dong Chong Xia Cao* to treat 33 patients with chronic hepatitis B. The treatment protocol was to administer five pills (0.25g of herb per pill) three times daily for three months per course of treatment.<sup>57</sup>

- **Liver cirrhosis and ascites:** Daily administration of *Dong Chong Xia Cao* was beneficial to treat 40 patients with ascites due to liver cirrhosis. The treatment protocol was to administer 2 to 4 grams of *Dong Chong Xia Cao* two to three times daily before meals with warm water.<sup>58</sup>
- **Arrhythmia:** An effective rate of 64.9% was reported in 57 patients with arrhythmia treated with 0.5 gram of *Dong Chong Xia Cao* three times daily for 2 weeks.<sup>59</sup> Another study reported 88% rate of effectiveness using *Dong Chong Xia Cao* to treat 50 children with arrhythmia (significant improvement in 33 cases, moderate improvement in 11 cases and no effect in 6 cases). The treatment protocol was to administer 2 to 4 pills (0.25g of herb per pill) three times daily for 3 months.<sup>60</sup>
- **Chronic tracheitis:** One study reported 84.4% rate of effectiveness using *Dong Chong Xia Cao* to treat 109 patients with chronic tracheitis.<sup>61</sup>
- **Allergic rhinitis:** Administration of 6 grams of *Dong Chong Xia Cao* three times daily for 4 weeks showed a 93% effective rate in treating 43 patients with allergic rhinitis.<sup>62</sup>
- **Autoimmune disease:** *Dong Chong Xia Cao* has been shown to inhibit the progress of autoimmune disease, including systemic lupus erythematosus, by improving nephritis and lymphadenectasis.<sup>63</sup>
- **Hyperlipidemia:** Administration of 1 gram of *Dong Chong Xia Cao* three times daily showed marked action to decrease LDL and TG and increase HDL in 273 patients with hyperlipidemia. Another study of 204 patients reported that *Dong Chong Xia Cao* decreases LDL but increases TG.<sup>64,65</sup>
- **Low platelet count:** Administration of *Dong Chong Xia Cao* is associated with an 83.3% success rate in raising platelet counts in 30 patients.<sup>66</sup>
- **Cancer:** Malignant tumors in 30 patients were treated with 1.5 grams of *Dong Chong Xia Cao* three times daily for 2 months. The study reported improvement based on symptomatic assessment in 93% of patients.<sup>67</sup> Another study reported marked effect to treat lung cancer in 50 patients using *Dong Chong Xia Cao* three times daily for 30 days.<sup>68</sup>
- **Others:** hypertension, coronary artery disease, prevention of common cold and influenza, and alopecia.<sup>69</sup>

#### HERB-DRUG INTERACTION

- **Cyclosporine:** One study randomly divided 202 patients who received organ transplantation into two groups: control group that received cyclosporine (immunosuppressive regimen) and treatment group that received cyclosporine and *Dong Chong Xia Cao* (1.0 gram three times daily). At 2 to 6 months after transplantation, the use of *Dong Chong Xia Cao* allowed the patients to take decreased dosages and concentrations of cyclosporine without an increased risk of acute rejection. Furthermore, concurrent use of *Dong Chong Xia Cao* with reduced dose cyclosporine led to fewer side effects, such as decrease in proteinuria and a retardation of chronic allograft nephropathy progression.<sup>70</sup>
- **Cisplatin:** The polysaccharides of *Dong Chong Xia Cao* worked synergistically with cisplatin by increasing its cytotoxicity in non-small cell lung cancer cells (H157).<sup>71</sup>
- **Paclitaxel-induced leukopenia:** Use of *Dong Chong Xia Cao* enhanced the recovery of mice from leukopenia caused by paclitaxel treatment. *Dong Chong Xia Cao* protected the hematopoietic progenitor cells directly and the bone marrow stem cell niche through its effects on osteoblast differentiation.<sup>72</sup>
- **Cyclophosphamide-induced immunosuppression:** *Dong Chong Xia Cao* contained a exopolysaccharide that significantly enhanced immune organs and stimulated the release of major cytokines (tumor necrosis factor- $\alpha$  and interferon- $\gamma$ ) in mice to protect against compromised immune functions caused by cyclophosphamide.<sup>73</sup>
- **Doxorubicin-induced toxicity:** Fermented *Dong Chong Xia Cao* had marked protective effect against doxorubicin-induced oxidative stress reactions. The antioxidative stress effect was especially selective to heart and liver, and therefore, may be used to prevent or treat various cardiac and hepatic diseases induced by oxidative stress.<sup>74</sup>
- **Bleomycin-induced pulmonary fibrosis:** The combination of *Dong Chong Xia Cao* with prednisone alleviated pulmonary fibrosis induced by bleomycin in rats. Though *Dong Chong Xia Cao* or prednisone alone was also effective, the combination had synergistic activity and was more effective in treating antifibrous degeneration.<sup>75</sup>
- **Scopolamine-induced memory deficit:** Administration of *Dong Chong Xia Cao* significantly improved the learning and memory impairment in mice induced by scopolamine.<sup>76</sup>
- **Alendronate disuse-induced osteoporosis:** *Dong Chong Xia Cao* has been shown as an alternative therapy for prevention of alendronate disuse-induced osteoporosis in humans. Administration of *Dong Chong Xia Cao* at high doses over an 8-week period prevented osteoporosis due to disuse of alendronate in rats. *Dong Chong Xia Cao* had a positive effect on body weights, mechanical strength, bone mineral density and bone mineral content.

Furthermore, *Dong Chong Xia Cao* decreased markers of bone turnover dose dependently and increased the osteocalcin levels.<sup>77</sup>

#### TOXICOLOGY

*Dong Chong Xia Cao* has an extremely low level of toxicity. Mice have been shown to tolerate up to 45 g/kg of *Dong Chong Xia Cao*, approximately 250 times the therapeutic dosage in humans. The LD<sub>50</sub> in mice via intraperitoneal injection is 21.7 +/- 1.3 g/kg. Symptoms of overdose include generalized inhibition initially followed by generalized excitation, spasms, convulsions and respiratory depression.<sup>78</sup>

#### AUTHORS' COMMENTS

*Dong Chong Xia Cao*, literally “winter bug summer herb,” is commonly referred to as the caterpillar fungus. It begins when the spores from the *Cordyceps sinensis* enters the body of a live moth caterpillar (*Hepialus varians*) while it is in the larval form. After the spores infect the larva, strands of filaments from the spore start to develop inside the caterpillar, eventually leading to its death. The fungus continues to grow, emerges from the insect's carcass, and sprout into a large stalk-like fungal fruiting body. Such natural and wild caterpillar fungus supposedly can only be found in the high mountain regions above 11,000 feet in Tibet, Nepal and Bhutan. There are currently more than 400 documented species of Cordyceps, and they all have similar life cycles. Among them, *Cordyceps sinensis* is the most famous and expensive, has the highest demand but extremely scarce supply. In addition, wild *Cordyceps sinensis* is relatively rare cannot be easily grown in culture. Therefore, most commercial products are cultured cordyceps, and *Cordyceps militaris* is one of the most commonly used.<sup>79</sup>

#### ADDENDUM

##### **Yǒng Chóng Cǎo (Cordyceps Militaris)**

蛹蟲草 / 蛹虫草

**Pinyin Name:** *Yong Chong Cao*

**Alternate Chinese Names:** 北冬虫夏草 *Běi Dōng Chóng Xià Cǎo*, 北虫蛹草 *Běi Chóng Yǒng Cǎo*, 北蛹草 *Běi Yǒng Cǎo*

**Botanical Name:** *Cordyceps militaris*

**Pharmaceutical Name:** Cordyceps Militaris

*Yong Chong Cao* (Cordyceps Militaris) is commonly referred to as the cultivated or man-made cordyceps. *Cordyceps militaris* grows well on grain in a controlled environment, and the harvested materials include both the mycelium and grain substrate. Though not identical, wild *Cordyceps sinensis* and cultured *Cordyceps militaris* have been shown to contain similar composition and have comparable effect to treat diseases.<sup>80,81,82</sup>

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