

*The Healthcare Medicine Institute presents*

# Safety in Herb-Drug Combinations #1

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# Herb-Drug Interaction Overview

Drug interactions are both pharmacodynamic and pharmacokinetic. Pharmacodynamics concern the *actions* of two or more drugs and pharmacokinetics concern the *absorption, distribution, metabolism, and/or excretion* of one or more drugs affecting another. Interactions can be additive, synergistic, and antagonistic. Additive interactions are those wherein the effects of two or more chemicals taken together is equal to the sum of taking them separately. Synergistic interactions occur when taking two or more substances together results in a stronger action than the sum of taking them separately. The substances increase each others' effects. Antagonistic interactions are when taking substances together weakens their overall effect.

Chinese Medicine (CM) uses differential diagnosis in determining the appropriate herbs. Herbal choices are based on the functions of the individual herbs and the overall function of a formula. When patients consume western medications with herbs, care must be taken not to alter the effects of the western medicine such that adverse reactions occur. This can happen when the herbal medicine is additive, synergistic, or antagonistic to the effects of the medication. If, however, the medication is of insufficient strength, herbal medicine can potentiate its effects for a better clinical outcome. Herbal medicines are commonly used to protect the patient from the side effects of western medications and to holistically balance the patient's constitution. In general, caution is needed more often in cases of excess rather than deficiency.

Herbal toxicity and herb-drug interactions have not surfaced as a major issue in the USA partially because the list of FDA allowable herbs is highly restricted such that most available herbs do not have harmful reactions with pharmaceuticals. The most common herb-drug interaction concern is that of warfarin (Coumadin). One concern is that herbal medicines may compete with warfarin for absorption. Commonly, the issue is to what extent and which herbs may decrease or increase the efficacy of warfarin. For example, herbs

containing vitamin K may be antagonistic and blood invigorating herbs tend to be additive or synergistic.

Herb-drug interactions are not the only concern. There are food-drug interactions and food-herb interactions. Dietary irregularities often complicate treatment. In the case of a patient who consistently drinks excess amounts of coffee and refuses to curb this behavior, the properties of the coffee affect the usage of herbs- particularly those that raise the Qi, strengthen the Yang, warm the interior, or dry dampness.



Sheng Di Huang

## 1. Allergy Medications and Release Surface Herbs

Allergy drugs suppress allergic reactions and often have an astringent property whereas acrid and warm herbs commonly used in the treatment of allergies open the pores and release the wind.

### Drug

Dimenhydrinate (Dramamine), cetirizine, loratadine, and chlorpheniramine are common over-the-counter antihistamines. Levocetirizine (Xyzal) and fexofenadine (Allegra) are prescription anti-histamines. Anti-histamines are distinguished by degrees of sedation and patients react differently to anti-histamines. Loratadine provides non-sedating, short-term symptomatic relief.

### Herb

**Ma Huang** (Herba Ephedrae) opens the Lung, releases surface and encourages sweating. Ma Huang stimulates the central nervous system (CNS) and the cardiovascular system and therefore should not be combined with drugs of a similar nature such as ephedrine, pseudoephedrine (Sudafed), caffeine, and MAO inhibitors. Ma Huang may also reduce the effects of beta blockers such as metoprolol (Lopressor, Toprol) and propranolol (Inderal) because Ma Huang increases levels of norepinephrine.

**Gui Zhi** (Ramulus Cinnamomi Cassiae) warms the channels to release the surface and causes sweating.

**Fang Feng** (Radix Ledebouriellae Diaricatae) and **Jing Jie** (Schizonepetae Herba) release the surface and cause sweating. Jing Jie more strongly releases the surface and Fang Feng treats internal wind and wind damp Bi pain. Fang Feng detoxifies the body from

multiple substances including heavy metals in the bloodstream and overdoses of Fu Zi. Fang Feng is especially good as an antidote for arsenic poisoning.

**Chan Tui** (*Periosticum Cicadae*) is physically light-weight and expels the wind. Its light-weight characteristic is reflected in its ability to act quickly. Chan Tui may aggravate chronic Yin deficient skin conditions. Chan Tui may induce drowsiness and is a central nervous system (CNS) suppressant. Therefore, use caution when combining with allergy drugs that also induce drowsiness. Chan Tui is anti-spasmodic and tranquilizing but may also impair labor and should therefore be used with caution in pregnant women. From a Chinese Medicine perspective, Chan Tui stops spasms & convulsions due to internal wind. For pregnant women with deficiency, Chan Tui must be used with caution. Therefore, be sure to have a clear diagnosis and limit the dosage where appropriate.

**Sheng Ma** (*Cimicifugae Rhizoma*) lifts the Qi and encourages the Qi to the surface from the interior to the exterior. It treats wind-heat rashes, itching, and incomplete expression of measles.



Gui Zhi

## Case I

A 54 year old male patient has had a skin rash for years. He is under a great deal of stress, wakes early in the morning, and takes **Loratadine**. He has a red tongue with a dry coating and a small, wiry, and rapid pulse.

Diagnosis:

Heart and Liver Yin deficiency with deficiency heat and Qi stagnation.

Treatment:

a. Pushing the Rash Outwards by Releasing the Surface

**Fang Feng** (Radix Ledebouriellae Diaricatae), **Jing Jie** (Schizonepetae Herba) and **Chan Tui** (Periosticum Cicadae) release the toxins outwardly and may worsen the skin rash if the Yin is not protected in cases of Yin deficiency heat.

b. Cool Heat and Benefit Yin to Eliminate Rash

**Sheng Di Huang** (Radix Rehmanniae Galutinosae), **Xuan Shen** (Radix scrophulariae Ningpoensis), **Zhi Mu** (Rhizoma Anemarrhenae Asphodeloidis) and **Mu Dan Pi** (Cortex Moutan Radicis) eliminates the rash by cooling internal heat and benefitting the Yin.

Remarks:

Treatment (a) fails because it pushes the rash outwardly and also depletes the Yin. Treatment (b) succeeds because the rash is eliminating by following the differential diagnosis and therefore protecting the Yin. Although Chan Tui may cause drowsiness with many allergy medications, Loratadine is not a concern in this regard because it does not cause drowsiness.



## Case II

A 43 year old female patient has chicken pox. During the first two weeks she took **cetirizine** and the chicken pox rash persisted but did not fully express. The tongue is puffy with a white coating and the pulse is floating and slippery.

Diagnosis:

Wind damp heat attack.

Treatment:

**Fang Feng** (Radix Ledebouriellae Diaricatae), **Jing Jie** (Schizonepetae Herba,) and **Niu Ban Zi** (Fructus Arctii Lappae). The chicken pox expressed after taking the herbs and began diminishing within two days. Fang Feng and Jing Jie encourage wind dampness to the surface to release damp toxins and Niu Ban Zi releases the surface and clears heat toxins.

Remarks:

The patient had an acute external wind damp attack and used anti-histamines which suppressed and trapped the evil within the body. The anti-histamines did not allow the pathogens to release outwardly. Release surface herbs pushed the pathogens out of body and therefore the chicken pox released and expressed properly.

## 2. Antibiotics, Laxatives, and Antiviral Drugs combined with Clear Heat Toxins, Cool the Blood and Purging Herbs

Antibiotics have a very bitter taste and clear heat toxins may also, however, they may damage the Spleen and Stomach Qi. It may cause diarrhea to use both western antibiotics with Chinese herbs that both have antibiotic effects.

### Drug

#### *Common western antibiotics and uses*

Community-acquired pneumonia:	azithromycin, doxycycline
Urinary tract infection:	nitrofurantoin, ciprofloxacin
Trichomonas:	metronidazole

### Herb

**Sheng Di Huang** (Radix Rehmanniae Galutinosae) cools and nourishes the blood and has a sticky quality that can cause damp stagnation in the Middle Jiao. Sheng Di Huang is contraindicated in patients with diarrhea, abdominal fullness, and Spleen and Stomach Qi and Yang deficiency. Use with caution when patients are taking antibiotics since antibiotics may cause these disorders.

**Ku Shen** (Radix Sophorae flavescens) has a bitter taste and may damage the Spleen Qi. It strongly clears damp heat toxins from the skin.

**Niu Bang Zi** (Fructus Arctii Lappae) clears heat toxin sore throats and is bitter. It is a seed and may cause loose stool.

**Long Dan Cao** (Radix Gentianae Longdancao) clears Liver and GB damp heat, has a very bitter taste and may damage the Spleen Qi. In larger dosages, Long Dan Cao may induce drowsiness therefore use caution when a patient takes medications that cause drowsiness.

**Zhi Zi** (Fructus Gardeniae aJasminoidis) clears heat toxins, cools the blood, mildly promotes blood circulation in the San Jiao and reduces Heart fire irritability. Zhi Zi has a sedative effect and should be used cautiously when patients are taking barbiturates as not to increase sleeping time.

**Yu Xing Cao** (Herba Cum Radice Houltuyniae Cordate) clears damp heat in the Lung and large dosages may cause diarrhea.

**Yin Chen Hao** (Herba Artemisiae Yinchenhao) clears Liver and GB damp heat jaundice and may cause diarrhea for patients with Spleen Qi deficiency. Yin Chen Hao has hepatoprotective properties.

**Shan Dou Gen** (Radix Sophorae Tonkinensis) strongly clears heat toxins from the throat and is very bitter indicating that it may cause diarrhea.

**Da Huang** (Radix Et Rhizoma Rhei) is purging, clears heat toxins, and promotes blood circulation. Da Huang has a broad spectrum antibiotic effect but must be used with caution in patients taking antibiotics as not to cause diarrhea. Da Huang has hepatoprotective and nephroprotective properties.

**Mang Xiao** (Natrii Sulfas) is purging and softens hard stool. Mang Xiao is contraindicated during pregnancy. Mang Xiao is a very powerful purging herb and should not be used in patients with diarrhea due to antibiotic intake.

**Fan Xie Ye** (Sennae Folium) is used for treating difficulty with bowel movements characterized by tenesmus, bloating, and gas. This herb is physically light-weight as compared to Da Huang. Its light-weight character indicates that it acts quickly and on a more surface level

whereas Da Huang acts more deeply and is more appropriate for pushing out deep obstructions.

**Yu Li Ren** (Pruni Semen) purges the bowels, lubricates large intestine Yin and promotes urination.



Zhi Zi

## Case I

A 45 year old male patient had shingles and used the anti-viral drug **valacyclovir (Valtrex)** to treat the herpes zoster infection.

Tongue: red , yellow greasy coating

Pulse: wiry and full

Diagnosis:

Liver and GB damp heat toxins

The use of the loose herb formula Long Dan Xie Gan Tang led to explosive diarrhea- at least ten times per day. The **Long Dan Cao**

(Radix Gentianae Longdancao) and **Zhi Zi** (Fructus Gardeniae Jasminoidis) clear heat toxins but also damaged the Spleen Qi thereby contributing to the diarrhea. Also, **Sheng Di Huang** (Radix Rehmanniae Galutinosae) is sticky and therefore creates damp stagnation in the Middle Jiao.

Remarks:

Lower the dosages of the aforementioned herbs and add warming herbs to benefit the Spleen. This will balance the formula and prevent diarrhea.

## Case II

A 45 year old female has constipation and acute pneumonia. She takes the antibiotics **azithromycin** and **doxycycline** without therapeutic effect for two weeks. The treating MD has been a student of Chinese Medicine (CM) and knows that the Lung and Large Intestine are paired organs. He used **Mang Xiao** (Natrii Sulfas) to cause the patient to have diarrhea four times on the day of the administration of the herb. The next day the fever was gone and the doctor continued the same antibiotics for one week and the patient recovered.

Remarks:

Chinese Medicine (CM) theory guided the doctor to combine Mang Xiao with the antibiotics based on a diagnosis of Yang Ming Fu Organ syndrome.

### 3. Diuretic Drugs with Promote Urination Herbs

Diuretic drugs and promote urination herbal medicines have similar functions therefore use caution with the dosage. Diuretic drugs and promote urination herbs may deplete Yin due to excessive drainage. In this case, combining drugs and herbs with additive and synergistic interactions may lead to a loss of fluids and electrolytes.

#### Drug

Common diuretics are furosemide (Lasix), chlorthalidone (Hygroton), and hydrochlorothiazide (Apo-Hydro, Aquazide H, Microzide). **They strongly drain water and lower blood pressure but may drain potassium which creates the potential need for potassium supplementation to avoid harmful side effects.** Furosemide is widely used for both the treatment of edema, hypertension, and congestive heart failure. Furosemide and many diuretics may cause dehydration and electrolyte depletion marked by a loss of potassium, calcium, sodium, and magnesium. Furosemide has an increased risk of causing electrolyte imbalances when combined with corticosteroids and an increased risk of kidney damage when combined with some antibiotics. Hydrochlorothiazide is commonly used to treat hypertension and congestive heart failure but is also used for the prevention of kidney stones.

Functionally, diuretics lower blood pressure by decreasing cardiac output and reducing plasma and extracellular fluid. The body responds to the diuretics with a homeostatic response that returns these levels to relatively normal or slightly less than normal. However, a reduction in peripheral vascular resistance persists and the blood pressure remains lower.

## Herb

**Fu Ling** (Sclerotium Poriae Cocco) and **Zhu Ling** (Sclerotium Polypori Umbellati) promote urination. Fu Ling is neutral and emphasizes balancing the water in the body. Zhu Ling is cooling and more strongly promotes urination.

**Ze Xie** (Alismatis Rhizoma) promotes urination and drains Kidney excess and deficiency heat.

**Che Qian Zi** (Semen Plantaginis) promotes urination and drains Liver and GB damp heat.

**Hua Shi** (Talcum) promotes urination and sedates Qi level heat and Summer heat.

**(Chuan) Mu Tong** (Caulis Clematidis Armandii) strongly promotes urination, promotes lactation, and treats Bi pain by unblocking blood stagnation in the channels. Chuan Mu Tong treats damp-heat, bloody, and stone dysuria. Chuan Mu Tong contains no aristolochic acid and is therefore considered a safe herb for medicinal use. **Guan Mu Tong (Caulis Aristolochiae Manshuriensis) is toxic because it contains aristolochic acid.**

**Qu Mai** (Herba Dianthi) and **Bian Xu** (Herba Polygoni Avicularis) promote urination and drain Lower Jiao damp heat. Qu Mai emphasizes clearing heat more strongly than dampness. Bian Xu more strongly drains dampness.

**Shi Wei** (Folium Pyrossiae) promotes urination, clears damp heat and stops bleeding.

**Dong Gua Ren (Dong Gua Zi)** (Semen Benincasae Hispidae) drains Upper Jiao damp heat and dissolves phlegm.

**Jin Qian Cao** (Lysimachiae Herba) is one of classic herbs to move urinary stones.

**Guang Fang Ji** (Radix Aristolochiae Fangchi) is cold, bitter, and pungent. It promotes urination and expels wind damp Bi pain. **Guang Fang Ji contains aristolochic acid and is therefore considered toxic and to be avoided.** It is advised to use Fen Fang Ji (Radix Stephaniae Tetandreae) which is not toxic and is regarded as safe for medicinal use.

**Yu Mi Xu** (Maydis Stigma) promotes urination, clears Liver and GB damp heat, and treats edema including edema and dysuria due to nephritis. Yu Mi Xu contains vitamin K. Vitamin K plays a key role in blood coagulation and may block the blood thinning actions of anticoagulants such as warfarin (Coumadin).



Mu Tong

## Case I

An 85 year old female has edema especially on the legs due to her heart condition. She is taking **furosemide** and her tongue is teeth marked with a moist coating and the pulse is slippery and floating.



Diagnosis: Heart and Kidney Qi deficiency and water stagnation

The patient took **furosemide** and used the herbal medicines: **Fu Ling** (Sclerotium Poriae Cocco), **Zhu Ling** (Sclerotium Polypori Unbellati), **Yu Mi Xu** (Maydis Stigma).

Remarks:

After taking the herbs, the patient complains of urinating every hour. Urinating day and night weakens the patient. Use caution and lower the dosage of promote urination herbs when patients are consuming diuretic drugs. In cases of Heart and Kidney Qi deficiency such as with this patient, use strengthening Qi and Yang herbs instead of promoting urination herbs to reduce the edema.

## Case II

A 25 year old female complains of burning and frequent urination. She is taking an antibiotic and a diuretic drug: **nitrofurantoin** and **hydrochlorothiazide**. However, she continues to suffer urgent and scanty urination. Her tongue is red and moist with a wiry and slippery pulse.

Diagnosis: Kidney and Lower Jiao damp heat.

The patient continued drug therapy and used **Jin Qian Cao** (Lysimachiae Herba), **Shi Wei** (Folium Pyrossiae), **Qu Mai** (Herba Dianthi) and **Bian Xu** (Herba Polygoni Avicularis) for four days. All of her symptoms resolved.

Remarks:

The patient has an acute condition and strong Qi therefore it is appropriate to use promote urination and clear damp heat herbs.

## 4. Lower blood pressure drugs - Antihypertensives

Use caution with raising the Qi and Yang herbs when patients are taking medications to control high blood pressure. There are potential synergistic and additive pharmacodynamic interactions.

### Drug

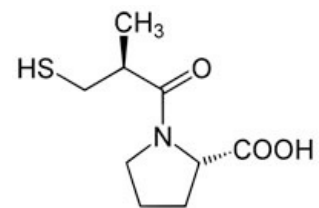
*There are many classes of antihypertensives including:*

#### A.

**ACE inhibitors** (angiotensin converting enzyme inhibitors), these are the "prils": ramipril, enalapril, lisinopril.

Angiotensin converting enzyme (ACE) raises blood pressure by constricting blood vessels and ACE inhibitor drugs prevent constriction by ACE and therefore lower blood pressure. ACE inhibitors are primarily used for hypertension and congestive heart failure. Historically, the discovery of an orally inactive peptide from snake venom led to the development of the first ACE inhibitor, Captopril.

Side effects of ACE inhibitors include hypotension, headache, fatigue, nausea, renal impairment, cough, and hyperkalemia (elevated potassium levels in the blood). For pregnant women, ACE inhibitors can cause serious congenital malformations, still births, and neonatal death.



#### B.

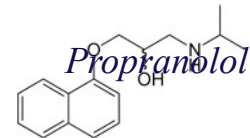
**Calcium channel blockers (CCBs):** nifedipine, diltiazem, amlodipine.

CCBs disrupt calcium channels and most CCBs decrease the force of myocardium (heart muscle) contractility making them valued for the treatment of hypertension. Many CCBs slow the electrical conduction within the heart are therefore used to treat atrial fibrillation and atrial flutter.

### C.

**Beta blockers: metoprolol xl, atenolol, propranolol.**

This class of drugs is commonly used to treat cardiac arrhythmias and hypertension. They are also administered after MI (myocardial infarction, heart attack) for cardioprotection purposes.



Beta blockers are beta adrenergic receptor antagonists and therefore reduce the effects of endogenous catecholamines (including epinephrine 'adrenaline' and norepinephrine) on beta adrenergic receptors. The receptors are part of the sympathetic nervous system and therefore regulate the flight or fight response.

Beta blockers decrease melatonin release which may explain reports of sleep disturbances. They impair bronchial muscle relaxation and should therefore be avoided by asthmatics. Side effects include: nausea, diarrhea, bronchospasm, insomnia, fatigue, dizziness, hair loss, hallucinations, dyspnea, nightmares, depression, sexual dysfunction, and erectile dysfunction.

### D.

**ARBs (angiotensin receptor blockers): Losartan, irbesartan, olmesartan.**

These are the "sartans". Losartan is available generically. They are also referred to as angiotensin II receptor antagonists and are often used to treat hypertension and congestive heart failure. New research suggests that ARBs may be associated with an increased risk of cancer.

*Response to the various classes are individualized and are often dependent on the side effects profile.*

## Herb

**Huang Qi** (Radix Astragali Membranaceus) raises the Qi, encourages Qi to the surface and promotes wound healing.

**Ren Shen** (Radix Ginseng) strengthens source Qi.

**Chai Hu** (Radix Bupleuri) and **Sheng Ma** (Rhizoma Cimicifugae) raise Qi upwards. Chai Hu regulates Liver and GB Qi. Sheng Ma is stronger for raising the Qi upwards.

**Dang Gui** (Radix Angelicae Sinensis) promotes blood circulation and nourishes blood.

**Lu Rong** (Cornu Cervi Parvum) strengthens Kidney Yang and Jing.  
**Ge Jie** (Gecko) strengthens Kidney and Lung Yang for treating asthma and impotence.

**Suo Yang** (Herba Cynomorii Songarici) is warm and astringes the Kidney Yang.

**Yin Yang Huo** (Herba Epimedii) and **Bai Ji Tian** (Rhizoma Bletillae Striatae) warm the Kidney Yang and expel wind damp cold Bi pain. Yin Yang Huo has a faster effective action. **Bai Ji Tian** is maintained in the bloodstream longer.

**Bu Gu Zhi** (Fructus Psoraleae Corylifoliae) warms the Kidney and Spleen Yang for treating morning diarrhea and strengthens the bone marrow.

**Xian Mao** (Rhizoma Curculiginis Orchiodis) warms Kidney Yang. Long term use is discouraged due to its toxicity.

**Gou Ji** (Rhizoma Cibotii Barometz) is warm and strengthens Kidney Yang, especially for spinal pain.

**Xu Duan** (radix Dipsaci Asperi) strengthens Kidney Yang and promotes blood circulation.

**Gu Sui Bu** (Rhizoma Drynariae) strengthens Kidney Yang and heals bone fractures.



Chai Hu

## Case I

A male patient with high blood pressure takes **losartan** to control it. The patient has stress, frustration and pain in the hypochondriac region. The tongue has red sides and the pulse is wiry.

Diagnosis:

Liver Qi stagnation with Yang uprising

After taking **Chai Hu** (Radix Bupleuri) his hands started mildly shaking like a person who drank a lot of coffee and therefore cannot be still or hold on to the cup.

Discussion:

The patient's personality is stressed. This is Liver Qi stagnation leading to Yang rising. **Chai Hu** (Radix Bupleuri) smoothes the Liver and GB Qi while lifting the Qi. The lifting the Qi function of Chai Hu is too strong for this patient at a normal dosage level. To avoid tremors, lower the dosage of Chai Hu and add calming and smoothing the Qi herbs.

## Case II

An 80 year old male patient has high blood pressure. He has a blood clot in the brain and the left side of his body has partial paralysis. He is taking **warfarin**, a blood thinner, and the blood pressure medication **losartan (Cozaar)**. He complains after three months of taking the medications that his thinking is too slow. His tongue is dark red and the pulse is wiry and small.

Diagnosis:

Liver and Heart Yang uprising  
Qi and blood stagnation

He is given **Huang Qi** (Radix Astragali Membranaceus), **Niu Xi** (Radix Achyranthis Bidentatae) and **Mu Li** (Concha Ostrae). Huang Qi promotes Qi flow, Niu Xi promotes blood circulation and descends blood circulation and Mu Li stabilizes the Yang.

After taking the formula for one month, his bodily range of motion improved by 30% on the impaired side. His mental responses are quicker and the blood pressure is controlled to a normal range by the herbs. The lifting, descending, and stabilizing effects of the herbs act to harmonize the patient's condition by restoring balance.

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