

The Healthcare Medicine Institute presents

Safety in Herb-Drug Combinations #2

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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.



Diuretic Drugs with Astringent Herbal Medicines

Diuretic drugs and astringent herbal medicine often, but not always, have opposing functions. Astringent herbal medicines are often contraindicated in cases of excess Fire and damp heat.

Drug

Common diuretics are furosemide, hygroton, and hydrochlorothiazide. They strongly drain water and lower blood pressure but potentially drain potassium (and other electrolytes) which creates the need for potassium supplementation.

Herb

Shan Zhu Yu (Fructus Corni Officinalis) astringes the Kidney & Jing and strengthens the Kidney and Liver. Shan Zhu Yu is both astringent and also exerts a diuretic action. It has been shown to temporarily lower blood pressure without affecting blood sugar levels as a result of inducing diuresis. Shan Zhu Yu also has anti-inflammatory and antibiotic properties.

Sha Yuan Zi (Sha Yuan Ji Li, Tong Ji Li) (Astragali Complanati Semen) warms Kidney Yang without drying, astringes Kidney Jing, and benefits the eyes.

Yi Zhi Ren (Fructus Alpiniae Oxyphyllae) is warm, astringes the Kidney Yang and tonifies the Spleen.

Jin Ying Zi (Fructus Rosae Laevigata) is neutral, astringes Kidney Jing, and stops diarrhea.

Fu Pen Zi (Fructus Rubi Chingii) is warm, astringent, benefits the eyes, and nourishes the Kidney and Liver.

Lian Xu (Nelumbinis Stamen) astringes the Kidney to stop frequent urination, preserves Kidney Jing, and stops bleeding.

Sang Piao Xiao (Ootheca Mantidis) and **Wu Bei Zi** (Galla Chinensis) astringe the Kidney to stop frequent urination and premature ejaculation. Sang Piao Xiao harmonizes Heart and Kidney communication when used in the formula Sang Piao Xiao San. Wu Bei Zi expels Lung heat and promotes the healing of open wounds.

Case I

A 32 year old female complains of frequent, scanty and burning urination. She is taking **hydrochlorothiazide** (diuretic) and **nitrofurantoin** (antibiotic). The frequent urination is every 15 minutes and the patient asked for herbal medicines to slow down the frequency. Her tongue is dark red, dry, and pulse is wiry and weak.

Diagnosis: Lower Jiao damp heat and Kidney Qi deficiency.

She was given **Lian Xu** (Nelumbinis Stamen) and **Shan Zhu Yu** (Fructus corni Officinalis) after which she has less frequent urination but increased burning.

Remarks:

The patient continues to have excess damp heat in Lower Jiao and the astringent herbs trapped the damp heat evil internally. A better approach is to discontinue the astringent herbs entirely and simply reduce the dosage of the diuretic while the antibiotics treat the heat. Additionally, herbs can be used to clear damp heat.

Case II

A 40 year old female has irritation of urinary bladder especially after sex and scanty, burning urination. She took the diuretic drug **hydrochlorothiazide**. Her symptoms gradually fade each time after intercourse with this approach. She also has tinnitus, lower back pain, a red and dry tongue, and a small, wiry and rapid pulse.

Diagnosis: Kidney and Liver Yin deficiency and Qi stagnation.

The patient then took **Shan Zhu Yu** (Fructus corni Officinalis), **Yu Mi Xu** (Maydis Stigma), **Mu Dan Pi** (Cortex Moutan Radicis) and **Bai Shao** (Radix Peoniae Lactiflorae) two weeks before sexual activity and the patient's condition improved significantly.

Remarks:

The patient has a chronic syndrome. **Shan Zhu Yu** (Fructus corni Officinalis) astringes and strengthens the Kidney, **Yu Mi Xu** (Maydis Stigma) promotes urination and drains Fire, **Mu Dan Pi** (Cortex Moutan Radicis) cools blood heat & promotes circulation and **Bai Shao** (Radix Peoniae Lactiflorae) smoothes the Qi and relaxes the muscle.



Mu Dan Pi

Expectorant, Decongestant, and Cough Suppressant Drugs with Phlegm-Resolving and Coughing & Wheezing Herbs

Expectorants, decongestants, and cough suppressants (antitussives) combined with phlegm resolving and coughing & wheezing herbs should be used with caution when combined due to overlapping functions.

Drug

There are several western medications to treat coughing but there are limited therapies to thin phlegm. Guaifenesin is an over-the-counter expectorant used to bring up phlegm from the airways in acute respiratory tract infections. It is sold as pills or in syrups and is in medicines such as Mucinex, Robitussin DAC, Robitussin AC, and Bidex 400. Guaifenesin is thought to increase the volume and reduce the viscosity of secretions in the trachea and bronchi to increase the efficiency of the cough reflex thereby facilitating the removal of sections. However, there is conflicting evidence concerning this mechanism of action.

Guaifenesin is often combined with dextromethorphan (antitussive). Dextromethorphan is commonly found in drugs such as Robitussin, NyQuil, Dimetapp, Vicks, Coricidin, and Delsym.

Many medications used to stop coughing include anti-histamines, anti-inflammatories, bronchodilators (to open airways), and steroids. Loratadine, an antihistamine, is often used for allergic rhinitis (hay fever).

Herb

Ban Xia (Pinelliae Rhizoma Preparatum) strongly dries phlegm in the Lungs, relieves nausea and vomiting, and resolves phlegm nodules. There are some reports of allergic reactions to Ban Xia characterized by bodily itching and redness. Unprocessed raw Ban Xia is toxic.

Bai Fu Zi (Typhonii Rhizoma Preparatum) dispels wind-phlegm in the channels and collaterals to relieve muscle spasms. Bai Fu Zi is toxic and should be used with caution.

Tian Nan Xing (Rhizoma Arisaematis) dries hot phlegm. Unprocessed Tian Nan Xing is toxic and it is usually prepared with Sheng Jiang. Tian Nan Xing is not recommended for pregnant women. Tian Nan Xing has a sedative effect and should be used with caution when combined with drugs that induce drowsiness.

Bai Jie Zi (Semen Sinapsis) strongly penetrates phlegm stagnation.

Case I

A 20 year old male patient has yellow sinus mucous in the morning and a heavy voice. He is taking **loratadine** to dry the mucous and his tongue is red with a dry coating. The pulse is floating and full.

Diagnosis: Upper Jiao and Lung damp heat.

The patient took a simplified version of Er Chen Tang: **Ban Xia** (Pinelliae Rhizoma Preparatum), **Chen Pi** (Pericarpium Citri Reticulatae), **Fu Ling** (Sclerotium Poriae Cocco). The next day the patient complains of nose bleeding and thicker yellow mucous.

Remarks:

The patient is taking an antihistamine to help dry mucous. Clearing the damp heat herbs are appropriate and this patient's herbs are too warming.

Case II

A 50 year old male loves to eat excess amounts of cheese and has sinus mucous. He is taking **loratadine**. Although taking the drug for two months, his index finger joint remains swollen, the tongue is dark with thick white coating, and the pulse is slippery and wiry.

Diagnosis: Qi and phlegm stagnation in the channels

The patient was given **Bai Jie Zi** (Sinapsis Semen), **Fu Ling** (Sclerotium Poriae Coccinea) and **Shen Qu** (Massa Fermentata). Bai Jie Zi penetrates the phlegm stagnation in the joint, Fu Ling drains dampness and balances the water in the body, and Shen Qu moves food stagnation. After two weeks his index finger is no longer swollen and the sinus mucous resolved. Half a year later the patient ate excess amounts of cheese and his index finger swelled again. He used same formula and the condition resolved.

Remarks:

The herbs and the drug have complementary functions to dry the phlegm thereby reducing stagnation and dampness in the channels and Middle Jiao.

Stomach Acid Blockers and Sour Herbs

Use caution with patients who have excess stomach acid when using sour tasting herbal medicines.

Drug

The histamine-2 blocker, ranitidine (Zantac), and the proton pump inhibitor, omeprazole (Prilosec), are routinely used to block stomach acid secretion especially in cases of peptic ulcer disease and gastroesophageal reflux disease (GERD). Other H₂-receptor antagonists include cimetidine, famotidine, and nizatidine. Other proton pump inhibitors include lansoprazole (Prevacid, Levant), esomeprazole (Nexium), pantoprazole (Protonix), and rabeprazole (Zechin). They are commonly used as a short-term therapy of approximately 6-8 weeks to help heal stomach ulcers.

Proton pump inhibitors (PPIs) are commonly used for a wide variety of disorders including: dyspepsia, gastroesophageal reflux disease (GERD), peptic ulcers, and gastritis. Common side effects are headache, diarrhea, fatigue, dizziness, abdominal pain, and nausea. Ranitidine (Zantac) is especially indicated for stress ulcers. Both the use of H₂-receptor antagonists and proton pump inhibitors increase the risk of community-acquired pneumonia. The FDA notes that long term use of PPIs may increase the risk of fractures including those of the hip, spine, and wrist. The FDA notes that the antiplatelet drug clopidogrel (Plavix) should not be taken with PPIs.

Herb

Shan Zha (Fructus Crateigi) promotes digestion, eliminates food stagnation and promotes blood circulation. Shan Zha is particularly indicated for meat stagnation and is often used to treat dyslipidemia, particularly high cholesterol levels. Long term use of Shan Zha is not

recommended for patients who have Spleen and Stomach Qi deficiency. Shan Zha can stimulate gastric acid secretion and should therefore be used with caution in patients with gastritis and stomach ulcers. A better choice would be a non-sour Chinese herbal medicine for this situation. In addition, Shan Zha has a cardiotoxic effect as does the drug digoxin (Lanoxin). Since both Shan Zha and digoxin increase the contractile force of the heart, use caution if a patient is taking this drug or consider an alternate herbal medicine to avoid side effects.

Wu Wei Zi (Fructus Schizandrae Chinensis) reduces acid secretion, astringes the Heart and Kidney meridians, holds the Jing, and stops sweating. Wu Wei Zi is often used to treating coughing due to Lung and Kidney deficiency, sweating and thirst, chronic diarrhea, and for calming the Shen in cases of Heart and Kidney Yin deficiency. Deoxyschisandrine, an active ingredient in Wu Wei Zi, decreases gastric acid secretion and may be used in the treatment of gastric ulcers.

Case I

A 54 year old female patient is taking **omeprazole** to block stomach acid secretion. She has fullness of the stomach region, belching, irritation of the throat, coughing and excessive mucous, a sour taste in the mouth, irritability, and insomnia. She self-administered **Wu Wei Zi** (Fructus Schizandrae Chinensis) to calm her mind after which she is sleeping better but continues to complain of stomach upset and has an increased sour taste in the mouth. The tongue has red sides and a white coating while pulse is wiry and slippery.

Diagnosis:

Liver and Stomach not harmonized and Stomach Qi rebels upwards

Remarks:

Wu Wei Zi (Fructus Schizandrae Chinensis) in raw form is very sour and must be used cautiously when a patient has a sour taste in the mouth. Wu Wei Zi is appropriate for calming the Shen in cases of Heart and Kidney Yin and Blood deficiency. Wu Wei Zi contains the ingredient deoxyschisandrin which inhibits the secretion of gastric acid and is therefore beneficial for the treatment of gastric ulcers. However, Wu Wei Zi is also contraindicated for excess conditions such as heat, damp-phlegm, wind-heat, and Liver Fire and therefore must be used with caution.

Case II

A 20 year male complains of stomach fullness, burping, and a sour taste in the mouth. He loves fast food & greasy food and he does not eat on a regular schedule. The patient took over-the-counter **ranitidine** (Zantac) and his stomach condition improved significantly but he continues to suffer from some stomach fullness and burping, especially after eating. He took **Shan Zha** (Fructus Crateigi) pills to eliminate food stagnation and promote blood circulation. The burping and stomach fullness improved. He has red sides of the tongue with a thick white coating and a wiry and full pulse.

Diagnosis: Liver and Stomach not harmonized and dampness

Remarks: The patient took **Shan Zha** (Fructus Crateigi) in pill form to assist digestion and to promote blood circulation. Shan Zha is especially effective for meat stagnation and is mild when taken in pill form compared with a concentration of the raw herb tea. Common practice for the layperson is to consume Shan Zha pills when self-administering and the risk of side effects is minimized by its administration in pill form. By contrast, ranitidine (Zantac, Zinetac) is also over-the-counter in 75mg and 150mg tablets but is very strong and patients may experience side effects such as dizziness, depression, rash, constipation, diarrhea, arrhythmias, pancreatitis, and leukopenia.

Blood Thinners & Birth Control Medications and Blood Invigorating and Stop Bleeding Herbs

When using promote blood circulation (invigorate blood) and stop bleeding herbal medicines one must be very careful prior to surgery. Otherwise, during the operation the surgeon may have difficulty controlling drug dosages. Strong caution is always advised when a patient is using blood thinners. Promote blood circulation herbs may increase the thinning of blood and they dispel blood stasis.

Stop bleeding herbs may reduce the thinning of blood. Stop bleeding herbs must be used with caution with patients taking birth control pills because oral contraceptives increase the risk of venous thrombosis.

Drug

A. Blood Thinners

Thinning the blood drugs are anticoagulants such as heparin and warfarin (Coumadin) and antiplatelets like aspirin and clopidogrel (Plavix).

Anticoagulants are used for red clots which are comprised of RBCs and fibrin in veins and the heart atria. Anticoagulants are commonly used to prevent thromboses, embolisms, and strokes. Patients with atrial fibrillation and prosthetic heart valves commonly take anticoagulants.

Warfarin (Coumadin) is best suited for anticoagulation in areas of slowly running blood flow. This is typically in veins, pooled blood accumulating behind artificial and natural valves, and pooled blood in dysfunctional cardiac atria. Warfarin functions by interfering with vitamin K metabolism. Warfarin passes through the placental barrier and is therefore contraindicated during pregnancy. The most common side effect of warfarin is hemorrhage. The effects of warfarin can be

reversed with vitamin K. Warfarin interacts with many foods, herbs and spices.

Antiplatelets aspirin and clopidogrel (Plavix) are helpful with white clots in the arteries. They decrease platelet aggregation, inhibit thrombus formation, and are effective in the arteries. Caution is always advised before surgery with these patients and these drugs are typically tapered or stopped prior to a major procedure by the treating MD. Clopidogrel (Plavix) is commonly used to inhibit blood clots in coronary artery disease, cerebrovascular disease, and peripheral vascular disease. The FDA notes that clopidogrel (Plavix) should not be taken with PPIs including Prilosec and Nexium.

B. Contraceptives

Oral contraceptives for females include the combined oral contraceptive pill and the progestogen only pill. The combined oral contraceptive pill (COCP) has both estrogen (oestrogen) and progestin (progestogen). COCPs inhibit follicular development, prevent an LH surge, and prevent ovulation. COCPs also increase the viscosity of cervical mucous which inhibits sperm penetration to the upper genital tract. COCPs may increase coagulation of blood thereby leading to thromboses, embolisms, and myocardial infarction. Smoking increases this risk substantially. COCPs are affected by antibiotics. Antibiotics affect bacterial flora and therefore may diminish absorption of COCPs. The progestogen only pill (POP) contains progestogens. POPs function by thickening cervical mucus and inhibiting follicular development. POPs do not contain estrogen and therefore have a decreased risk of clotting.

Levonorgestrel is a synthetic progestogen. It is used in both COCPs and POPs and is also the active ingredient in intrauterine systems (Mirena) and contraceptive implants (Norplant, Jadelle).

Herb

San Qi (Radix Notoginseng, Tian Qi) and **Pu Huang** (Pollen Typhae) promote blood circulation, stop bleeding, and stop pain. Both have antiplatelet properties and decrease prothrombin time to stop bleeding. San Qi is warming and reduces swelling. Pu Huang is neutral, promotes urination, and is contraindicated in pregnancy because it can stimulate uterine contractions.

Qian Cao (Gen) (Radix Rubiae Cordifoliae) stops bleeding, cools the blood, and promotes blood circulation.

Di Yu (Radix Sanguisorbae Officinalis) stops bleeding in the Lower Jiao, clears heat toxins and damp heat, and cools the blood.

Ce Bai Ye (Cacumen Biotae Oracientalis) cools the blood, stops bleeding, and dissolves hot phlegm.

Bai Mao Gen (Rhizoma Imperatae Cylindrica) stops bleeding in the Upper Jiao, cools the Lung and Stomach heat, and promotes urination.

Zi Zhu (Cao) (Folium Callicarpae Formosanae) and **Xian He Cao** (Herba Agrimony Pilosae) are astringent and stop bleeding. Zi Zhu clears heat toxins. Xian He Cao strengthens the Qi, stops diarrhea, reduces swellings, and kills parasites. Xian He Cao can increase the platelet count to stop bleeding and it contains vitamin K. Warfarin (Coumadin) may be reduced in efficaciousness due to vitamin K present in this herb.

Bai Ji (Rhizoma Bletillae Striatae) is astringent, stops bleeding and promotes the healing of flesh.

Ai Ye (Folium Artemisiae Argyi) stops bleeding and warms the channels. Ai Ye treats gynecological bleeding due to deficiency and cold.

Chuan Xiong (Radix Ligustici Chuanxiong) promotes Qi flow in the blood and effects the surface and upper body.

Dan Shen (Radix Salviae Miltiorrhizae) cools the heat, calms the Heart and promotes blood circulation in the small blood vessels. Dan Shen is both antiplatelet and anticoagulant. Dan Shen can significantly increase the effects of warfarin and should be used cautiously in patients taking this medication.

Yi Mu Cao (Herba Leonuri Heterophylli) and **Zei Lan** (Herba Lycopi Lucidi) promotes blood circulation and promotes urination. They treat gynecological related blood stagnation and edema. Yi Mu Cao clears heat toxins for treating skin disorders. Yi Mu Cao causes uterine contractions and should be used with caution during pregnancy. Zei Lan is often used for treating traumatic injuries.

Chi Shao (Radix Paeoniae Rubrae) cools the blood, reduces swelling and promotes blood circulation.

Hong Hua (Flos Carthami Tinctorii) and **Tao Ren** (Semen Persicae) promote blood circulation and break congealed blood. Hong Hua strongly breaks congealed blood. Tao Ren promotes blood circulation and stays in the bloodstream for a longer duration and moistens the intestines. They are contraindicated during pregnancy and caution must be used for patients taking blood thinning drugs.

San Leng (Rhizoma Sparganii Stoloniferi) and **E Zhu** (Rhizoma Circuma Ezhu) promote blood circulation and very powerfully break blood stagnation masses. They are contraindicated during pregnancy and must be used with caution in patient taking anticoagulant and antiplatelet drugs.

Ru Xiang (Gummi Olibanum) and **Mo Yao** (Myrrha) promote blood circulation, reduce swelling, and heal the skin & ulcerations. Ru Xiang strongly moves and penetrates and is therefore more common in the treatment of musculoskeletal pain and Bi (joint) pain. Mo Yao more strongly breaks blood stasis. They are contraindicated during pregnancy.

Wu Ling Zhi (Excrem. Trogopteri seu Pteromi) promotes blood circulation and stops uterine bleeding due to blood stagnation. It is contraindicated during pregnancy.

Shui Zhi (Hirudo) promotes blood circulation and powerfully breaks blood stasis. It is slightly toxic and some reports of adverse reactions to this animal product have been reported. It is one of the strongest herbs to invigorate the blood and is contraindicated during pregnancy. The drug lepirudin (Refludan) was made based on this herb. Lepirudin is a powerful anticoagulant drug which is a direct thrombin inhibitor made from yeast cells. It is nearly chemically identical to hirudin, the main active ingredient in Shui Zhi. Lepirudin is often used when patients cannot tolerate heparin.

Tu Bie Chong (Di Bie Chong) (Eupolyphaga/Steleophage) promotes blood circulation and blood flow through congealed blood and masses. It very powerfully invigorates the blood and is contraindicated during pregnancy.

Xu Duan (Radix Dipsaci Asperi) strengthens the Yang, tonifies the Liver and Kidneys, benefits the tendons and bones, calms the fetus, and promotes blood circulation.



Tian San Qi

Case I

A 38 year old female patient is taking **levonorgestrel** for birth control. After taking **San Qi** (Radix Notoginseng), she is suffering severe cramps in the lower abdomen and the menstruation was late by one week. The tongue is purple and there is a slippery-wiry pulse.

Diagnosis: Qi and blood stagnation.

Remarks:

With birth control medications, all of the regulate blood herbs may confuse bodily responses. Also, it is important to ask patients whether or not they are taking birth control medications because it is very common.

Case II

A 54 year male is overweight and has blood clot in his right lower leg with pain and tingling to the foot. He took **clopidogrel (Plavix)** for three months and the pain reduced but there is a persistent perception of tingling to the bones of the foot. Administration of **Chuan Xiong** (Radix Ligustici Chuanxiong) and **Dan Shen** (Radix Salviae Miltiorrhizae) to promote Qi and blood circulation in the small blood vessels quickly eliminated the tingling almost entirely.

Diagnosis: Qi and blood stagnation

Remarks:

Adding the herbs reduced the size of the blood clot by 80% within three weeks and therefore the tingling significantly diminished. In cases of obesity, drugs may not be strong enough to dissolve the clot and the herbal medicine's invigorating the blood functions potentiate the effect to remove the clot.

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