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## Concurrent Use of Herbal Medicines and Pharmaceuticals Pharmacokinetic Interactions

by John Chen, Ph.D., Pharm.D., O.M.D., L.Ac..

The practice of medicine is now at a crossroad: countless patients are being treated simultaneously with both Western and Oriental medicine. It is quite common for a patient to seek herbal treatment while taking several prescription medications. According to JAMA, in 1997, an estimated 15 million adults in the United States (representing 18.4% of all prescription pharmaceutical users) took prescription drugs concurrently with herbal remedies and/or vitamins.

As the general public grows increasingly more open to the use of herbs and supplements, both patients and the health professionals who care for them are becoming more alert to the potential for occasional adverse herb-drug interactions. Safety has become a major topic of discussion. Even though herbal remedies are classified as dietary supplements, it must be noted that if used incorrectly, herbs, like any substance, may adversely affect patients. The safest route of access to herbal therapy is through a well-qualified herbalist.

Although Chinese herbal medicine has been prescribed safely by professionals in the West for many years now, and a great deal of research has been amassed in China, there is still a lack of formal studies that are published in the West to document the safety and efficacy of combining herbs with prescription drugs. Some questions posed by Western healthcare professionals or patients are difficult to answer quickly with documented specifics. However, with some general insights into pharmacology, one can foresee possible interactions and take appropriate precautions to prevent incompatible combinations.

The concept of 'interaction' refers to the possibility that, when two (or more) substances are given concurrently, one substance may interact with another, and/or alter its bioavailability or clinical action. The net result may be an increase or a decrease in the effectiveness of one or both substances. It is important to note that interactions may yield positive effects (achieving better therapeutic effects at lower dosage) or negative results (creating unwanted side effects or adverse reactions). Most of the possible interactions may be classified in two major categories: pharmacokinetic and pharmacodynamic.

### Pharmacokinetic Interactions

'Pharmacokinetic interactions' refer to the fluctuation in bioavailability of herb/drug molecules in the body as a result of changes in absorption, distribution, metabolism, and elimination.

### Absorption

Absorption is the term that describes the process of the physical passage of herbs or drugs from the outside to the inside of the body. The majority of all absorption occurs in the intestines where

herbs or drugs must pass through the intestinal wall to enter the bloodstream. Several mechanisms may interfere with the absorption of drugs through the intestines.

The absorption of herbs may be adversely affected if herbs are administered with drugs that may promote binding in the gastrointestinal (GI) tract. Drugs such as cholestyramine (Questran), colestipol (Colestid) and sucralfate (Carafate) may bind to certain herbs, forming an insoluble complex that decreases absorption of both substances. Because of the large size of the insoluble complex, few or no molecules of either substance pass through the intestinal wall.

Herb absorption may be adversely affected in the presence of drugs that change the pH of the stomach. Antacids, cimetidine (Tagamet), famotidine (Pepcid), nizatidine (Axiid), ranitidine (Zantac), and omeprazole (Prilosec) may neutralize, decrease, or inhibit the secretion of stomach acids. With this subsequent decrease in stomach acidity, herbs may not be broken down properly in the stomach, leading to poor absorption in the intestines. To minimize this interaction, herbs are best taken separately from these drugs by approximately two hours.

Drugs that affect gastrointestinal motility may also affect the absorption of herbs. GI motility is the rate at which the intestines contract to push food products from the stomach to the rectum. Slower GI motility means that the herbs stay in the intestines for a longer period of time, thereby increasing the potential absorption. Conversely, more rapid GI motility means that the herbs stay in the intestines for a shorter time, which may decrease absorption. Drugs such as haloperidol (Haldol) decrease GI motility and may increase herb absorption; while drugs such as metoclopramide (Reglan) increase GI motility and possibly decrease herb absorption.

Therefore, it may be necessary to decrease the dosage of herbs when the patient is taking a drug that decreases GI motility and increases overall absorption. Likewise, it is probably helpful to increase the dosage of herbs when the patient is taking a drug that increases GI motility and thus decreases overall absorption.

### Distribution

After absorption, herbs or drugs must be delivered to the targeted area in order to exert their influence. 'Distribution' refers to the processes by which herbs or drugs (once absorbed) are carried and released to different parts of the body. Currently, it appears that the majority of herbs and drugs do not have any clinically-significant interactions affecting distribution, and thus can safely be taken together. The exception seems to be if a drug has a narrow range-of-safety index and is highly protein-bound, in which case interaction with other substances might occur during the distribution phase. Examples of drugs that have both a narrow range-of-safety index and a high protein-bound ratio include warfarin (Coumadin) and phenytoin (Dilantin).

Unfortunately, it is very difficult to predict whether an individual herb will interact with either one of these drugs because there are no known tests or experiments documenting such interactions.

### Metabolism

Once metabolized by the liver, most herbs and drugs become inactive derivatives. The rate at which the liver metabolizes a substance determines the length of time it stays active in the body. If the liver were induced to speed up its metabolic rate, herbs and drugs would be deactivated at a more rapid pace, and the overall effectiveness of ingested substances would be lower. On the other hand, if the liver were made to slow its metabolism, herbs and drugs would be deactivated at a slower pace and the overall impact of the substances would be greater.

In general, drugs that induce greater liver metabolism do not exert an immediate effect. The metabolism rate of the liver changes slowly, over several weeks. Therefore, the effect of accelerated liver metabolism is not seen until weeks after the initiation of drug therapy. Some examples of pharmaceuticals that speed hepatic metabolism are: phenytoin (Dilantin), carbamazepine (Tegretol), phenobarbitals and rifampin (Rifadin). Therefore, herbs given in the presence of one of these products may be deactivated more rapidly, and their overall effectiveness lowered. Under these circumstances, a higher dose of herbs may be required to achieve the desired effect.

In great contrast, drugs that inhibit liver metabolism have an immediate onset of action. The rate of liver metabolism may be greatly impaired within a few days. Pharmaceuticals that slow or inhibit liver metabolism include: cimetidine (Tagamet), erythromycin, ethanol, fluconazole (Diflucan), itraconazole (Sporanox) and ketoconazole (Nizoral), among others. When a patient takes these drugs concurrently with herbs, there is a higher risk of herbal components accumulating in the body, as the ability of the liver to neutralize them is compromised. If the herbs are metabolized more slowly, their overall effectiveness may be prolonged. In this case, one may need to lower the dosage of herbs to avoid unwanted side effects.

Depending on the half-life in the body of drugs that influence liver metabolism, it may be necessary to increase or decrease the dosages of herbs for weeks or even months after discontinuation of the pharmaceutical substance, along with consistent monitoring.

#### Elimination

While the liver neutralizes incoming drugs and herbs, the kidneys are responsible for eliminating the substances and their metabolites from the body. If the kidneys are damaged, then the rate of elimination is slowed, leading to an accumulation of active substances in the body. Important examples of drugs that damage the kidneys include amphotericin B, methotrexate, tobramycin and gentamicin. As a safety precaution, when prescribing herbs for a patient who is currently taking or has recently taken one of these drugs, it may be wise to lower the dose of herbs to avoid unnecessary and unwanted side effects.

#### **Summary of Pharmacokinetic Interactions**

The pharmacokinetic interactions listed above include both theoretical and actual interactions. Though such interactions are possible, the extent and severity of each interaction will vary depending on the specific circumstances, such as the dosages of all substances, the inherent sensitivity of each patient, individual body weight, and metabolic rate.

#### **Summary: Concurrent Use of Herbal Medicines and Pharmaceuticals**

Historically, herbs and drugs have been presumed to be very different treatment modalities that have rarely, if ever, been used together. The line that separates the use of herbs and drugs, however, has blurred in recent decades as the lay public gains increased accessibility to multiple treatment modalities. It is not uncommon for one patient to seek care from several health professionals for an ailment. As a result, a patient may easily be taking multiple drugs, herbs, supplements, and vitamins concurrently. It becomes difficult to predict whether the combination of all these substances will lead to unwanted side effects and/or interactions. It is imprudent to assume that there will be no interactions. On the other hand, it is just as unwise to abandon treatment simply for fear of possible interactions. The solution to this situation is in the understanding of pharmacokinetic and pharmacodynamic herb-drug interactions. By understanding these mechanisms, one can recognize potential interactions and take proper actions to prevent their occurrence.

This article was taken out of Dr. Chen's *Chinese Medical Herbology and Pharmacology*. [Click here](#) to order a copy.

### About the Author

Dr. John Chen is a recognized authority in both western pharmacology and Chinese Herbal Medicine. He teaches at the USC School of Pharmacy, Emperor's College, Yo San University of TCM, OCOM, Five Branches, AOMA and ACTCM. Dr. Chen's most recent published work is *Chinese Medical Herbology and Pharmacology* (2003, AOM Press) and *Chinese Herbal Formulas and Applications* (2008, AOM Press) for which he was lead author.

To learn more about herb-drug interactions and herbal alternatives, Dr. John Chen is speaking on the following topics for Lotus Institute. All classes are approved for 8 CEUs/PDAs by the CA, IL, FL, and TX Acupuncture Boards, and NCCAOM; also approved for 8 pharmacy CME credit hours by CNDA.

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