



# Herbs and Cytotoxic Drugs: Recognizing and Communicating Potentially Relevant Interactions

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Drug interactions are an unending concern in the pharmacologic management of many acute and chronic conditions, including cancer. More than 100,000 deaths per year in the United States can be attributed to fatal acute drug reactions, making drug reactions the sixth-leading cause of death (Lazarou, Pomeranz, & Corey, 1998). For patients with cancer, cytotoxic drugs often are a component of their treatment plans. When patients take herbs simultaneously with cytotoxic drugs, the pharmacologic dynamics of the interactions are not well understood and may remain clinically unknown in the short term. The impact of drug interactions between herbs and cytotoxic drugs on a patient's course of therapy can be overdosing or undertreatment, and this occurrence or series of occurrences can have wide range of clinical consequences (Beijnen & Schellens, 2004; Brater, 2005). As consistent care providers, oncology nurses are on the forefront of assessing, observing, and documenting events associated with cytotoxic drugs across multiple settings. Also, as more assessments include an over-the-counter medication history, knowledgeable nurses can recognize potential overlaps between herb use and anticipated cytotoxic drug administration before interactions occur. This article will present the mechanisms of drug interactions with a specific focus on several top-selling herbs, in addition to a discussion on communicating potentially relevant interactions to patients, families, and healthcare providers.

## Classification of Drug Interactions

Drug interactions can be classified as pharmaceutical, pharmacodynamic, or pharmacokinetic in nature.

Pharmaceutical interactions may occur as a result of physical or chemical incompatibility. An example is when taxanes precipitate in diluted infusion fluids possessing low pH. Pharmacodynamic interactions may occur as a result of additive, synergistic, or antagonistic effects, such as when cytotoxic drugs are given in combination regimens.

Pharmacokinetic interactions may occur as a result of variations in drug absorption, distribution, metabolism, or elimination. Often, metabolizing enzymes or drug transports are involved. The hepatic enzyme cytochrome P450 is the most important drug-metabolizing system, the predominant site of most drug metabolism, and the site for most drug-drug interactions. More than 100 substrates (also known as isoenzymes or isoforms) of cytochrome P450 exist, and nomenclature is based on and named for the amino acid or enzyme involved in the pharmacokinetic pathway. Enzymes responsible for the largest part of drug metabolism are CYP3A (50%), CYP2D (25%), and CYP2C (20%) (Sparreboom, Cox, Acharya, & Figg, 2004; Zhou et al., 2003).

Specifically, drug interactions arise when drugs are given simultaneously and one drug alters the metabolic clearance of the second drug in inhibition or induction of specific isoenzymes (Zhou et al., 2003). Cytotoxic agents are metabolized through the cytochrome P450 pathways involving predominantly enzyme CYP3A. Some herbs also are metabolized through the same pathway and can either induce or inhibit activity of the CYP isoenzymes on a cellular level in the liver or the intestinal epithelium (see Table 1). Herbs also may induce enzymes and transporters in tumor cells and cause

resistance to some cytotoxic agents or lessen therapeutic responses to other cytotoxic agents (Sparreboom et al., 2004). Because multiple CYP isoenzymes in the P450 pathway are involved in drug metabolism in general and especially with cytotoxic agents, the concurrent use of some herbs with cytotoxic drugs may have clinical and toxicologic implications. Most cancer treatment regimens are complex (e.g., multiple cytotoxic agents, antiemetics, analgesics, and corticosteroids). Given the complexity of most treatment regimens, relatively few specific data are available to guide clinicians beyond general avoidance of herbs with known or suspected interactions in connection with cytotoxic agents.

## Herb Use by Patients With Cancer Undergoing Cytotoxic Therapy

Several researchers have assessed herbal use by patients with cancer undergoing cytotoxic therapy. McCune et al. (2004) conducted a sample investigation examining

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