Oncology Database of Drug Interactions between Chemotherapeutic Agents and Anticancer Herbs

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ABSTRACT

Traditional Chinese Medicinal (TCM) herbs and herbal supplements are commonly used by cancer patients to treat or prevent cancer, in conjunction with anticancer treatment. However, herbs and drugs may interact, and when not monitored, could lead to dire consequences. This study aims to create a comprehensive drug-herb database for clinicians and pharmacists in their clinical practice. Searches on drug-herb interactions were done by checking through databases and literature, and the results found are then collated in Microsoft Excel. A total of 70 anticancer herbs were identified. 21\% were found to interact with anticancer drugs to give 47 interactions. 85\% were pharmacodynamic interactions, while the remaining 15\% were pharmacokinetic. Corticosteroids and licorice were found to have the greatest number of interactions, being involved in 35\% and 19\% of them respectively. Hence, most of the interactions found are of pharmacodynamic nature. Pharmacodynamic interactions may result in antagonism with anticancer drugs, and management is needed.

INTRODUCTION

Cancer is a disease involving uncontrolled growth and spread of abnormal cells, which could result in death if not promptly managed. Various treatments, such as surgery, chemotherapy and radiotherapy, are currently available for cancer patients (Alteri, 2008). TCM herbs and herbal supplements are commonly used by cancer patients (Richardson, 2000). However, the effects of many herbs are not well-documented due to the limited studies done on them (Kronenberg, 2002). As a result, many pharmacists and clinicians may not be aware of possible interactions between patients’ prescribed anticancer drugs and any concurrent herbs for cancer therapy (Miller, 1998). Herbs may interact pharmacodynamically or pharmacokinetically with drugs. Drug-herb interactions, when not monitored, can lead to fatal outcomes (Miller, 1998). Hence, this study aims to create a comprehensive drug-herb database for oncology clinicians and pharmacists to detect possible drug-herb interactions. This would also increase their awareness regarding possible drug-herb interactions, so that adjustments can be made to optimize the outcome of cancer therapy.

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METHODOLOGY

Searches on drug-herb interactions were done by checking through various literature and databases such as Micromedex Healthcare Series version 5.1\(^4\) and Drug Digest (Drug Digest, 2008), Drug Information Handbook for Oncology 6\(^{th}\) Edition (Solimando, 2007), British National Formulary 53 (Martin, 2006), PubMed\(^5\) and Science Direct\(^6\).

The information gathered was organized on Microsoft Excel based on herb-related parameters and drug-herb interaction parameters. Qualitative analysis of the data was then performed.

RESULTS AND DISCUSSION

In this study, a total of 70 anticancer herbs were identified and 47 drug-herb interactions were found. 85% of the interactions found were of pharmacodynamic nature, while the remaining 15% were pharmacokinetic. Among the 66 anticancer drugs, corticosteroids were found to have the greatest number of interactions, being involved in 35% of them. Among the anticancer herbs, licorice has the greatest number of interactions with anticancer drugs, taking part in 19% of them.

In the next few sections, the drug-herb interactions are discussed in greater details according to the classes of anticancer drugs.

Corticosteroids

Corticosteroids have immunosuppressant properties, and hence would be antagonized by herbs, including cat’s claw and fenugreek (InteliHealth, 2005), which have immunostimulant properties. Bitter melon is immunomodulatory and may increase activity of corticosteroids (InteliHealth, 2005).

Platinum Analogues

Nephrotoxicity and hepatotoxicity are common side effects of cisplatin (Chemocare.com, 2005). Silymarin in milk thistle has been shown to prevent tubular necrotic effects of cisplatin (Gaedeke, 1996). In an animal study, the administration of the licorice extract together with cisplatin also recovered functional indices in the kidney and liver to almost the control levels (Lee, 2007). Hence, milk thistle and licorice may be useful in preventing cisplatin-induced nephrotoxicity and/or hepatotoxicity.

Furthermore, a combination of emodin, present in sheep sorrel, with cisplatin has been shown to synergistically inhibit the proliferation of lung cancer cells (Zhang, 1996). Therefore, the use of sheep sorrel could possibly enhance the effects of cisplatin in the treatment of lung cancer.

Silibinin, another compound found in milk thistle, has also been reported to exhibit synergy with carboplatin in inhibiting the growth of estrogen-dependent human breast carcinoma. However, such an interaction was not observed in cisplatin or oxaliplatin (Tyagi, 2004). Hence, such an interaction does not apply to the entire class of platinum analogues.

Hormone agonists and antagonists

Soy has estrogen-like properties and has been found to interact with aromatase inhibitors, thereby reducing their therapeutic effects (MedlinePlus, 2007).

Licorice also has estrogen-like properties (UMM, 2008). High doses of licorice may prevent estrogen from attaching to estrogen receptors, thereby reducing estrogen's effects (Drug Digest, 2008). Such an effect may enhance the anti-estrogen effect of the aromatase inhibitors (Chinese Materia Medica, 2008). On the other hand, glabridin found in licorice may displace tamoxifen from estrogen receptors, thereby reducing the latter’s anti-estrogen effect (Tamir, 2000).

Animal studies suggest that low doses of genistein in soy may antagonize the effects of tamoxifen on estrogen-dependent breast cancer, by reversing the inhibitory effects of tamoxifen (Jones, 2000). Therefore, clinicians should take precaution if a patient takes soy products while having tamoxifen.

Topoisomerase inhibitors

Silibinin in milk thistle was reported to exhibit synergism with doxorubicin by inhibiting the growth of human breast carcinomas in vitro (Tyagi, 2004). The combination of emodin, present in sheep sorrel, with doxorubicin or with etoposide was also found to synergistically inhibit the proliferation of lung cancer cells (Zhang, 1996). Therefore, clinicians should practise caution should they find patients taking sheep sorrel and doxorubicin or etoposide concomitantly.

Procarbazine and Thalidomide

Thalidomide is anti-inflammatory and has significant immunomodulatory actions (Lake, 2004). Cat’s claw immunostimulant properties may hence interfere with thalidomide (UMM, 2008).

Fenugreek may potentiate the effect of procarbazine (DIC, 2008). Procarbazine may also interact with Asian and American ginsengs, causing insomnia, tremor, headache, agitation and worsening of depression (Nikaido, 1984). Hence patients should be advised to avoid the use of any ginseng products while on procarbazine.

CONCLUSION

A limited number of anticancer herbs have been found to interact with anticancer drugs. This could be due to the fact that many herbs are not well-studied. Moreover, searches for herb-related information were done on English-language websites. Many of the 70 anticancer herbs are from TCM and are poorly documented in English-language databases and literature. Hence, very little information, if any, could be obtained from these sources.

Based on the data collected from the databases and literature, 47 drug-herb interactions, predominantly pharmacodynamic, have been identified. Most of these interactions involve corticosteroids and licorice. The drug-herb interaction database that will be created using would increase clinicians’ and pharmacists’ awareness of potential drug-herb interactions, so that appropriate management could be done to optimize the anticancer treatment.

REFERENCES


