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Herbs and Liver Enzymes

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Complementary and herbal medications are growing markets in Australia. An estimated 57% of the Australian population use some form of complementary medicine. Unfortunately, the majority of these people do not disclose this information to their healthcare providers. This poses a challenge to healthcare professionals as many herbal preparations can affect pharmaceutical agents through herb-drug interactions or induction of side effects.

Despite the common assumption that natural therapies are a safe alternative to pharmaceuticals, complementary medications can have serious adverse effects. A [recent U.S. study](#) demonstrated a significant increase in the proportion of liver injury attributed to natural therapies. Between 2004 and 2013, the incidence of hepatic injury from herbal and dietary supplements increased from 7% to 20%. It was also found that the resultant hepatic injury was more severe than with conventional medicines, as indicated by rates of death and liver transplantation.

Another concern posed by the use of herbal medications is the potential for herb-drug interactions. An example of a herb known to be responsible for herb-drug interactions is St. John's wort (*Hypericum perforatum*). St John's wort is a potent inducer of hepatic [cytochrome P450](#) enzymes; CYP3A4 in particular. It has also been shown to induce the intestinal efflux transporter, P-glycoprotein. Clinically significant drug interactions attributable to enzyme induction have been identified with cyclosporin, oral contraceptives, warfarin, digoxin and theophylline, amongst others. Particular caution needs to be exercised with this herb as it also inhibits synaptic reuptake of serotonin and the activity of monoamine oxidase. For this reason, St John's wort is not recommended to be taken with antidepressants or other medications that increase serotonin

activity. Coadministration with such medications may enhance side effects and contribute to the development of the potentially fatal [serotonin syndrome](#).

Ginkgo biloba is commonly used by traditional Chinese medicine (TCM) practitioners for improving memory. Although there is little evidence to support this claim, ginkgolides are proven to inhibit platelet activating factor (PAF). This property lends weight to claims of improving circulation, however, it also raises possible concerns of increased bleeding risk. Ginkgo appears to inhibit P-glycoprotein and may induce or inhibit CYP1A2, CYP2D6, and CYP3A4; although evidence is conflicting. Extracts contain a number of naturally present compounds in differing proportions which may explain this inconsistency. Natural variation in the ratio of active ingredients is to be expected in herbal preparations. However, this phenomenon may produce unpredictable effects on drug metabolism. The *Therapeutic Goods Administration* (TGA) [investigated](#) this issue in 2009 with the intention of refining quality standards for ginkgo products available in Australia. [New guidance](#) has been developed to address the issue of equivalence in herbal medicines.

Garlic, *Allium sativum*, is used in both Eastern and Western herbal medications. Its purported benefits include stimulation of the immune system, protection of the liver, improved lipid and blood sugar profiles, and reduced blood pressure. It is also said to possess antibacterial, antiplatelet, and anticancer effects. Allicin, the main active phytochemical of garlic, demonstrates *in vitro* inhibition of CYP2C9, CYP2C19, CYP3A4, CYP3A5, and CYP3A7 activity. The risk of significant drug interactions with garlic is thought to be low. However, caution should be exercised in patients taking saquinavir or isoniazid as reduced therapeutic levels have been reported with these combinations. Studies showing the effect of garlic on P-glycoprotein are inconclusive.

Ginseng (*Panax ginseng*) extract is commonly used in TCM. The recommended dose is 200mg per day of standardised ginseng, which contains 4% ginsenosides. Ginseng is used medicinally for hypertension, hyperlipidaemia, and improving concentration and energy. Some *in vitro* tests demonstrate inhibition of CYP1A1, CYP1A2, CYP1B1, and P-glycoprotein, however, not all studies have been able to replicate these results. For this reason, caution should be exercised when *Panax ginseng* is used with medications metabolised by these pathways, particularly if they have a narrow therapeutic index.

Although many herbs used in Eastern and Western herbal medicine are also used in everyday cooking, the amount of active ingredient is lower than what is found in supplements and the active ingredients are usually destroyed by cooking. Therefore, consumption of herbs in the diet does not affect liver enzymes to the extent of the purified extracts used in herbal medicine. There is currently a paucity of evidence surrounding the extent of interactions with herbal medicines, and often the evidence is contradictory. For this reason, more research is required to show the safety and efficacy of herbal medications used in conjunction with other medications. As people are increasingly seeking natural alternatives, patients should be counselled on the importance of checking the safety of any herbal medications with their healthcare professional prior to administration.

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