



## TRADITIONAL MEDICINES : A REMINDER TO REPORT ALL SUSPECTED ADVERSE REACTIONS Berita Ubat-ubatan April 2000

Interest in alternative medicine, especially traditional herbal remedies, is increasing in Malaysia. When pharmaceutical products fail to provide an answer, more and more distraught patients are turning to alternative medicine. Dietary supplements and herbal remedies fill the shelves in supermarkets, pharmacies health food stores and "clinics" of herbal practitioners. Testimonials as well as articles in the newspapers and magazines promote the use of herbs without explaining the dangers and consumers are seldom aware of the fact that just because these are natural preparations it does not imply that they are all that "safe".

Numerous cases of adverse reactions to alternative medicines have been reported, both locally and elsewhere. People may experience an adverse reaction due to:

- An effect of one of the intended constituents of the product
- Contamination or substitution with herbs known to be toxic (such as Magnolia, Aristolochia, Chapparal)
- Contamination with heavy metals
- Illegal inclusion of a drug ( e.g. corticosteroids, analgesics, hypoglycemic agents)

### Herbal Dangers

As many people who use traditional medicines and dietary supplements do not consider them to be a part of their "medication", it is increasingly important that physicians take a thorough medication history of each patient, and that patients be specifically asked if they are currently using any such products.

Cases of adverse drug reactions and interactions between prescription medications and herbals that have been cited in the literature include the following popular herbals:

- **Ginseng:** Ginseng is claimed to be an adaptogen in that it increases the body's resistance to stress and builds up general vitality. Reports have linked ginseng to potential medication interactions with warfarin and digoxin. Hypertension and mastalgia have been documented as side effects of ginseng. Excessive doses of ginseng have been reported to cause agitation, insomnia and raised blood pressure and have been referred to as abuse of the remedy.
- **Ginkgo biloba:** There have been several published incidents of bleeding problems associated with ginkgolide B, a platelet-activating factor inhibitor that is a component of ginkgo biloba. Patients who are on anticoagulant therapy should avoid taking ginkgo due to the possibility of drug interactions. Adverse reactions that have been reported to the WHO include hypertension, leucopenia, thrombocytopenia and hallucinations.
- **Evening Primrose oil (EPO):** EPO has been promoted for a variety of skin ailments as well as for pre-menstrual syndrome. EPO may have the potential to make manifest undiagnosed temporal lobe epilepsy, especially in schizophrenic patients and / or those who are already receiving known epileptogenic drugs such as phenothiazines.

- **St John's Wort:** Extracts of St. John's Wort (*Hypericum perforatum*) is gaining popularity in the west for minor nervous tension, insomnia and is used in cases of slight mood lowering. There have been several reports of decreased warfarin, theophylline and cyclosporin levels in association with the concomitant use of St. John's Wort. Studies are being conducted to determine whether this product may be an inducer of a broad range of drug metabolising enzymes.
- **Echinacea extract :** Echinacea has been promoted for the prophylaxis and treatment of cold and flu symptoms. Allergy-like reactions including bronchospasm, dyspnoea and angioedema have been reported. It is possible that individuals with asthma may be at risk of developing these reactions.
- **Alfalfa :** Alfalfa is said to contain vitamins A,C, E and K as well as calcium, potassium, phosphorus and iron. However, it has been reported that the use of alfalfa can induce systemic lupus erythematosus (SLE) - like syndrome in individuals predisposed to this condition.
- **Comfrey :** This herbal ingredient contain pyrrolizidine alkaloids, compounds known to be hepatotoxic and has been associated with obstruction of blood flow to the liver possibly leading to hepatotoxic reactions. Products containing comfrey should not be taken internally and the topical application of comfrey-containing preparations to broken skin should be avoided.
- **Peppermint Oil :** Products containing this ingredient have been associated with bronchospasm, anaphylactoid reaction and duodenal ulcer perforation.
- **Senna Extract :** Senna is stated to possess cathartic properties and has been used traditionally for constipation. Adverse reactions that have been reported include grand mal seizures, circulatory failure, hypertension and anaphylactic reaction.
- **Silymarin :** Silymarin is widely promoted as a liver tonic. It has been associated with cerebral haemorrhage, hepatic coma and neuropathy.
- **Ispaghula :** Ispaghula is stated to possess demulcent and laxative properties. Adverse reactions reported including bronchospasm, asthma and intestinal obstruction. If swallowed dried, ispaghula may cause oesophageal obstruction.
- **Lobelia** (also known as Indian tobacco) : It is thought to possess respiratory stimulant, antiasthmatic, antispasmodic, expectorant and emetic properties. The possible adverse reactions range from breathing problems at low doses to sweating, rapid heartbeat, low blood pressure and possibly coma and death at higher doses.
- **Chaparral :** This is a traditional American Indian medicine, which has been linked with liver disease. It is claimed to have antioxidant properties used to slow the aging process and as a treatment for skin conditions and other disorders. Chaparral-induced toxic hepatitis has been reported for two-patients in different parts of the USA.

- **Magnolia-Stephania-Aristolochia** : These ingredients which are mainly found in Chinese traditional medicines. Adverse reactions related to kidney disease leading to permanent kidney failure have been reported in Belgium and the UK.
- **Ephedra** (also known as Ma huang, Chinese ephedra and ephedrin) : Adverse reactions reported range from high blood pressure, irregular heartbeat, nerve damage, injury, insomnia, tremor, headaches to seizures, heart attack, stroke, death.

(Chaparral, Magnolia, Stephania, Aristolochia and Ephedra are still found in herbal remedies in various parts of the world but are not allowed to be used in traditional medicines registered in Malaysia.)

### What and how to report

If it is suspected that a patient has suffered an adverse reaction to a traditional medicine, it should be reported to the Malaysian Adverse Drug Reactions Advisory Committee either through the website, through the ADR reporting form or even by a letter. All information on the name of the remedy, its ingredients and source (if known) should be included. In order to facilitate better assessment and to allow further action to be taken, when necessary, please include the label / packaging material of the product where possible. If it is suspected that the product is contaminated with some other medicines such as steroids, painkillers, hypoglycemic agents etc, please include a sample of the product to enable analysis to be performed.

### Further Information

For further information, please contact the Malaysian Adverse Drug Reactions Advisory Committee at:

- its website at <http://www.come.to/madrac/>
- National Pharmaceutical Control Bureau, Ministry of Health Malaysia, P.O. Box 319, Jalan Universiti, 47730 Petaling Jaya (Tel:7573611 ext. 258)

### References:

1. Institute for Safe Medication Practices Medication Safety Alert! June 4 1997 Vol.2 No. 11
2. Herbal Medicines, A Guide for Health Care Professionals
3. The WHO Adverse Drug Reactions Database in Uppsala, Sweden

### Products Containing St. John's Wort: Warning on Drug Interactions

St. John's Wort (*Hypericum perforatum*) is a herb which is gaining increased popularity as it has been claimed to possess mood modifying properties and may help alleviate insomnia. The Drug Control Authority has registered 7 products containing St John's Wort as a single ingredient and 7 other products where it is formulated with other ingredients.

Based on adverse reaction reports to other regulatory agencies and also documented case reports in the literature, it has been found that products containing St. John's Wort may interact with the following drugs:

- Warfarin
- Cyclosporin
- Theophylline
- Oral contraceptives
- Amitriptyline
- Nortriptyline
- Digoxin
- Carbamazepine

The mechanism for the interaction is not yet clearly understood but it is thought that St John's Wort may be an enzyme inducer resulting in reduced plasma concentrations of these drugs.

- **Decision:** The DCA has agreed that any product which contains St. John's Wort should carry a warning on the box stating:-

This product may interact with other medicines. Please consult a doctor/pharmacist before using it.

### Reporting Rate Of Adverse Drug Reactions To Madrac

MADRAC received a total of 875 ADR reports during 1999 which represents a 45.1% increase as compared to 1998. Fig. 1 shows the number of reports submitted by health professionals from the various states in 1999.

