Information for Community Pharmacists About Herbal Medicines

Key points

- The phrases 'natural', 'herbal' and 'derived from plants' do not give any assurance that a product is 'safe'.
- Herbal products have potential to interact with prescription and over the counter medicines.
- The safety of herbal products would be better understood if any suspected side effects were reported through the Yellow Card Scheme.

Background

The Medicines and Healthcare products Regulatory Agency's key objective is to protect public health. To help achieve this, the Agency wishes to inform consumers, companies and practitioners about herbal medicines that may pose a risk to human health. Not all herbal products are medicines. However, any substance or combination of substances aimed at treating or preventing disease in people or which may be administered to people with a view to making a diagnosis or restoring, correcting or modifying a physiological function is classified as a medicine[1].

Herbal medicines, as with any other medicine, are likely to have an effect on the body and should be used with care. There may be the perception in some quarters that the herbal medicines pose few safety issues, however many pharmaceutical medicines, ranging from aspirin to digoxin, have their origins in the isolation of active chemical constituents in particular plants.

It is important to note that the Medicines and Healthcare products Regulatory Agency (MHRA) is interested in reports for all prescription and over the counter (OTC) medicines, as well as herbal preparations (licensed or unlicensed). Many herbal remedies are still unlicensed and are purchased from outlets other than pharmacies, including Ayurvedic and Traditional Chinese Medicines (TCM). The MHRA would ask you to consider this possibility when patients seek advice on potential side effects. Also it is always worthwhile to consider interactions between herbal preparations (i.e. drug/food, drug/disease and drug/drug) and other medicines, which can possibly lead to side effects.

Always remind consumers that the phrases 'natural', 'herbal' and 'derived from plants' do not necessarily mean 'safe'. Among consumers there is the perception that **natural equates to safe** and, therefore, many herbal medicine users would not realise that a herbal remedy may be responsible for symptoms they have experienced.

Survey evidence shows that most people do not tell their doctor that they are taking a herbal remedy (and most doctors do not ask) and so the **doctor would have no reason to suspect that ill health was linked to consumption of a herbal remedy**; survey evidence also shows that patients are much less likely to report to their doctor the suspected side effect of a medicine if they believe it may be linked to a herbal medicine [2].

The safety of many herbal medicines has not been established in certain key groups, including:

- pregnant women
- breastfeeding mothers
- children
- anyone with a history of liver or kidney complaints
- the elderly

Surveys show that the use of herbal medicines by older patients is increasing and that typically more than one herbal product is used at a time, often concomitantly with prescription medicines[2]. Older patients are often reluctant to tell their doctor that they are taking herbal products and so are at risk of potential drug-herb interactions.

Quality assurance of herbal products

There is an international trade in poor-quality, unregulated and unlicensed herbal products. Some of these have been found to contain banned pharmaceutical ingredients or heavy metals which are poisonous. Products may also contain harmful herbs that are not permitted in the UK, and you should be aware that unlicensed herbal medicines manufactured outside the UK may not be subject to any form of effective regulation. See Table 1 for further detail on the possible regulatory routes by which a medicine may reach the consumer. Real examples[2] include:

- **Adulteration** with **pharmaceutical** substances. (This is a frequent occurrence and has involved potent medicines such as anti-diabetics (glibenclamide), drugs for erectile dysfunction (sildenafil), appetite suppressants (sibutramine) etc)
- **Addition of analogues of pharmaceutical substances.** (This is a growing activity where a chemical derivative of a known pharmaceutical substance is included in a product e.g. nitrosofenfluramine, sildenafil (Viagra) analogues (homosildenafil, acetildenafil). The analogue is often more toxic than the parent molecule (e.g. nitrosofenfluramine) or is of unknown toxicity as in the case of many of the sildenafil derivatives)
- **Addition of heavy metals/toxic elements as ingredients** (e.g. TCM product found with 117,000 times level of mercury permitted in foods, leading to a number of hospital admissions. TCM and Ayurveda traditionally use heavy metals and other toxic elements as ingredients. These include realgar (arsenic sulphide), cinnabaris (mercuric sulphide), calomelas (mercurous chloride), hydrargyri oxydum rubrum (red mercuric oxide). The current Chinese Pharmacopoeia includes 48 products containing at least one of these ingredients.
- **Contamination** during manufacturing process (e.g. poor control on use of pesticides, mycotoxins, microbiological loads)

Table 1: Licensing and regulation of herbal medicines in the UK

There are three possible regulatory routes by which a herbal remedy can reach the consumer. These are as:

1. **Licensed herbal medicines.**
   Some herbal medicines in the UK hold a product licence or marketing authorisation. These are marked with a nine digit Product Licence (PL) number and are required to demonstrate safety, quality and efficacy (or effectiveness) and be accompanied by the necessary information for safe usage.
2. **Registered traditional herbal medicines.**
   A simplified registration scheme, the Traditional Herbal Medicines Registration Scheme, began on 30 October 2005. Products are required to meet specific standards of safety and quality and be accompanied by agreed indications, based on traditional usage, and systematic patient information allowing the safe use of the product.
3. **Unlicensed herbal remedies.**
   These products don't have to meet specific standards of safety and quality; standards can vary widely and there are no requirements to supply safety warnings and contraindications. By April 2011 all manufactured herbal medicines will be required to have either a traditional herbal registration or a product licence.

The use of some herbal ingredients in medicines are restricted or prohibited due to their toxicity or potency. Some such as Fangji and Mu tong are not permitted in any unlicensed medicines, while others such as Digitalis (foxglove) or Mandrake can only be made available via a prescription from a registered doctor or dentist.

The main areas of risk with herbal medicines

The MHRA currently receives about 70 suspected adverse drug reaction reports relating to herbal medicines each year[2]. This is believed to represent only a small proportion of cases. The expectation is that over time with better publicity and with the extension of the reporting scheme to patients, self reporting will increase. Real examples[2] include:

- **Delay in effective treatment** for serious condition e.g. TCM practitioner advertising that herbal remedy will obviate need for coronary artery bypass graft.
- **Interference with vital treatment** e.g. Ayurvedic clinic advising patient to discontinue antipsychotic medication and take alternative Ayurvedic remedies.
- **Exploitation of vulnerable groups such as children and the seriously ill** e.g. parents wanting baby/child to have "natural" cream for eczema, unaware that the products supplied actually contain undeclared steroids; patients with cancer have been prescribed large quantities of TCM.
- **Overloading patient with multiple medications** e.g. 16 year boy with acne on over 100 TCM tablets a day for several months; patient hospitalised with serious unexplained abdominal pain.
- **Unexpected rare but serious liver toxicity of plants** e.g. Kava Kava, Black cohosh leading to liver transplants in some cases.
- **Toxic plants used** e.g. Senecio species used in TCM which may cause liver toxicity or liver cancer.
- **Side effects** as with any other medicine.
- **Interactions** with other medicines e.g. St John's Wort can interact with many prescribed medicines including contraceptive pill and immunosuppressant medicines. This has resulted in unwanted pregnancies and rejection of transplanted organs; gingko biloba can interfere with the action of anaesthetics.
- **Wrong, toxic,** plant used either accidentally due to lack of expertise or intentionally due to practice in TCM of substituting one ingredient for another believed to have a similar action.
- **Confusion over standards** in TCM sector over whether traditional formulae have or have not had known toxic ingredients removed.
- **Weak or missing information** about safe use of products or other poor practices such as over labelling list of ingredients on product with a different list.
- **Communications** - Inability of practitioner to communicate in English to find out whether patient has a serious medical condition, such as diabetes, is on other medication, or is pregnant, breastfeeding.

Patient reporting of Adverse Drug Reactions

Patient reporting of Adverse Drug Reactions (ADRs) was launched in the UK in February 2008, which allows any member of the public to report a possible side effects via the patient Yellow Card for themselves, a child for whom they are responsible; or if someone else asks them to report on their behalf.

Reports from healthcare professionals are vital in gaining clinical information and perspective on suspected Adverse Drug Reactions (ADRs). However, patient reporting of ADRs complements healthcare professional reporting in a number of ways, as described below:

1. Patients report directly, cutting out the 'middle man'. That is, for a healthcare professional to consider a Yellow Card report, they must first be informed of a side effect that the patient is experiencing. After discussion with the patient the healthcare professional will then decide if the side effect warrants reporting. If they do decide to report they must then report without changing the meaning of the patient's concerns.
2. Patients tend to report ADRs earlier than their healthcare professional(s), which is particularly important for serious ADRs that require prompt action from the MHRA.
3. Patients provide a more detailed description of side effect(s) and how it affects their quality of life; this is often not provided in reports from healthcare professionals.

What can a community pharmacist do to help?

For patient Yellow Card reporting to be successful patients need to be aware that they are able to report. As one of the most accessible of the healthcare professionals, community pharmacists are well placed to inform patients about the Yellow Card Scheme. Pharmacists have a professional responsibility to advise patients on the reporting of any suspected side effects associated with their medicines including over the counter (OTC) medicines and herbal products.

Patients can be encouraged to complete as much of the Yellow Card report they can before sending to the MHRA, however, patients should be reassured that the lack of any particular piece of information should not prevent reporting. Some patients may appreciate help in the completion of Yellow Cards. The advice you can offer patients includes helping to think about whether a possible side effect could be due to a patient's medicine; whether the possible side effect meets the MHRA criteria for reporting; and what details to include on the report (see Table 2).

Community pharmacists should remember, however, that patient reporting is in addition to healthcare professional reporting. Therefore community pharmacists should continue to report ADRs via the Yellow Card Scheme as per the MHRA criteria (i.e. all suspected ADRs for new medicines and vaccines; and all serious suspected ADRs for established medicines and vaccines. The MHRA are specifically interested in any ADRs in children and the elderly. In addition, the MHRA is interested in reports for all prescription and over the counter (OTC) medicines, as well as herbal preparations (licensed or unlicensed). Remember that there is no need to worry about duplicate reports from community pharmacists and patients since the MHRA can identify these.

Table 2: Essential Information to Include on a Yellow Card Report

Suspected medicine(s)	The suspected medicine(s), brand name(s) and batch number for vaccines (if known), route of administration, dosage, dates of administration and indication. For herbal products the information required (if available) is: (i) the ingredient(s) (ii) source or supplier (iii) the use to which the remedy was being put. Retention of a sample of the product would be helpful in case an analysis is required.
Suspected reaction(s)	A description of the reaction(s) and any treatment given, together with the dates the reaction started and stopped and whether the reaction was considered to be serious. There are also tick boxes to give information on the outcome, and, if and why the reaction was considered to be serious.
Patient details	Patient's sex and age and their weight (if known). Information that would identify the patient should not be used (for reasons of confidentiality) although their initials and a local identification number are helpful in case it is necessary to refer back to the patient's records. It is not necessary to obtain the patient's consent to report on an ADR.
Reporter details	Name and full address of the reporter, so that the report can be acknowledged and contact made for further information, if necessary.

YellowCard
Helping to make medicines safer

1 MHRA. Guidance for Retailers, Wholesalers, Importers and Manufactures on Registering Herbal Medicine under the THMR scheme. Available from: http://www.mhra.gov.uk/Howweregulate/Medicines/Herbalmedicines/PlacingaherbalmedicineontheUKmarket/con2030651. Last accessed 5 November 2010.

2 MHRA. Public Health Risk with Herbal Medicines: An Overview. 2008. Available from: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON023163&RevisionSelectionMethod=Latest. Last accessed 30 September 2010.