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# Drug and herb interactions

## Searching the web

### Background

Australian patients spend large sums of money on complementary medicine and therapy each year. General practitioners are often asked questions about whether prescribed medications will interact with complementary medications. What current internet resources can be accessed to assist in answering these questions?

### Objective

This article looks at current internet resources that can assist GPs to answer patient questions about interactions between prescribed and complementary medicines.

### Discussion

Many of the websites found in this study provided limited information and limited searchability. We found seven websites out of 100 that met our selection criteria. A web portal, with risk categorisation of mild, moderate and severe for drug-herb interactions, can assist doctors in clinical decision making. Maximum benefits could be obtained by working corroboratively with the Therapeutic Goods Administration.

■ **There are misconceptions that most herbs are 'natural' and 'safe'.<sup>1</sup> It is not surprising, given this misconception of safety, that potentially up to billions of dollars are spent by patients on complementary medicines (CM).<sup>2</sup> All herbs have actions that may interact with drugs patients may be taking. The risk of drug and herb interactions may be especially severe for the elderly, frail or those taking multiple medications for chronic diseases. There are many reports, papers and websites that discuss information on drug and herb interactions.**

### Study methods

In Australia, it has been shown that between 2003 and 2006, 67.3% of general practitioners used the internet or email in their practice.<sup>3</sup> The most commonly used website has been found to be 'Google'.<sup>4</sup> The search strategy used the Google search engine with the term 'drug and herb interaction'. Specific medicine related databases or websites (eg. Medline, Medline Plus, eMedicine) were excluded. A search in March 2009 obtained 351 000 results, from which the first 100 links were evaluated by the inclusion criteria listed in *Table 1*. The arbitrary number of 100 was selected, as it was considered that many doctors would not have the time to continue a search beyond this point. Websites meeting the inclusion criteria were included, even if they required subscription.

### Study results

All 100 websites were initially reviewed by all authors. The final selection was discussed among all authors to cross check compliance to the inclusion criteria. Seven websites met the inclusion criteria. The remaining 93 links were subdivided into four groups based on their reason for exclusion (*Table 2*).

### Natural Medicines Comprehensive Database

Natural Medicines Comprehensive Database (*Figure 1*) provides information on drugs and natural medicines including safety, effectiveness, adverse reactions, dosage, administration, and interactions with drugs, herbs and food. The 'Natural product/drug interaction checker' can produce a report by browsing a menu or

entering the drugs and natural products. Available at [www.naturaldatabase.com/home.aspx?tab=2](http://www.naturaldatabase.com/home.aspx?tab=2).

Interactions are rated as minor, moderate or severe and highlighted in different colours, based on the possibility of the interaction and the severity of the outcome based on literature reports. The occurrence and level of evidence are clearly pointed out. This allows users to rapidly gain an idea of how severe the interaction might be and how reliable the statement is. Further descriptions of the potential adverse reactions are provided in paragraphs that require navigation.

Natural Medicines Comprehensive Database is updated daily and designed for health care professionals. A consumer version provides patient information based on the professional version. The major negative is that this website requires subscription.

**DrugDigest**

DrugDigest (*Figure 2*) contains extensive information about drugs, vitamins, herbs and supplements and offers an interactive database that covers a wide range of potential interactions with drugs, herbs, food and alcohol. An advantage is the ability to check two or more drug-herb interactions. Available at [www.drugdigest.org/wps/portal/ddigest](http://www.drugdigest.org/wps/portal/ddigest).

Users can either type the drug name or select from a menu list. The possible interaction is easy to read and understand, particularly for the general public. The interaction severity is classified as minor, moderate, or severe; with the level of evidence provided as poorly or well documented. The last update date is provided

Figure 1. Natural Medicines Comprehensive Database website

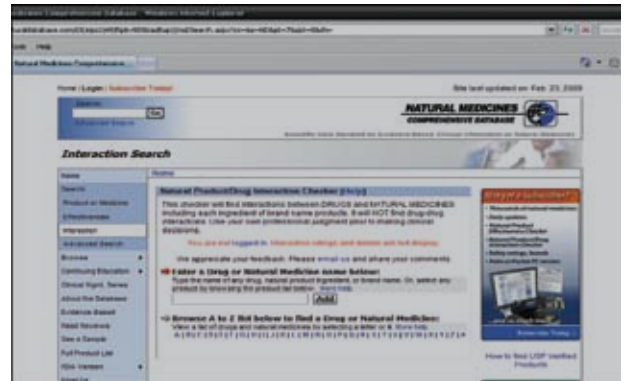
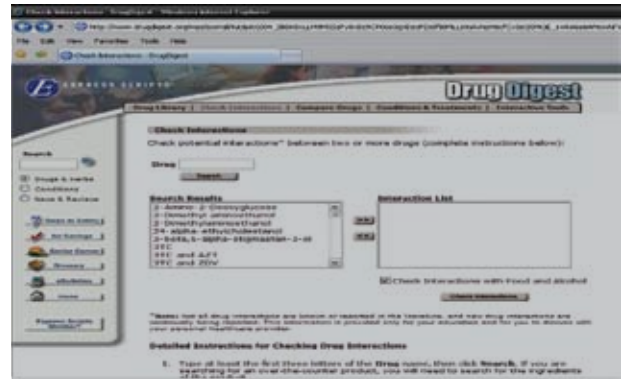


Figure 2. DrugDigest website



allowing assessment of the information currency. It does not require subscription, enhancing accessibility. The main drawback is the lack of reference lists to prove the reliability of the drug-herb interactions, although DrugDigest declares the information materials provided are evidence based.

**HerbMed**

HerbMed (*Figure 3*) is a public website that focuses on herbs and includes data such as the scientific/common/family name, mechanism of action (eg. efficacy and activity), adverse effects and toxicity, interactions, contraindications, formulas and cultivation, conservation, and ecology of the herbs. Users gain a comprehensive understanding of the herbs. Available at [www.herbmed.org/](http://www.herbmed.org/).

HerbMed also acts as a search engine allowing the user to check drug-herb interactions by entering the herb or browsing the menu. HerbMed differs in providing links to journal abstracts using PubMed instead of providing an information precis. This hyperlink access allows users to review the literature and obtain up-to-date and reliable information.

Nevertheless, this key feature could limit its use as HerbMed does not provide direct 'answers' (ie. what interactions would this herb cause if taking with that drug?) to users. Reading and absorbing the information in scientific journal articles may be too difficult for the general public. For all except the most common herbs, the details are accessible only on subscription.

Table 1. Inclusion criteria

<b>Content</b>
<ul style="list-style-type: none"> <li>• Relevant to 'drug and herb interaction'</li> <li>• Reliable and evidence based (ie. the website should provide reference or evidence to support the materials, or may belong to certain association, organisation, university, or government)</li> <li>• Current (ie. the website was updated/revised/established between 2000–2009)</li> </ul>
<b>Design</b>
<ul style="list-style-type: none"> <li>• Precise, uncluttered and easy to read (ie. the information on the website should be presented clearly)</li> <li>• Interactive and searchable</li> </ul>
<b>Other</b>
<ul style="list-style-type: none"> <li>• Accessible (ie. the website should be available and free of charge during the time of review or should be accessible with membership or subscription)</li> </ul>

Table 2. Classifications of the links not included in the discussion (N=93)

Category	Number (%)
Not relevant to 'drug and herb interaction'	17 (18.3)
Journal articles	25 (26.9)
Commercial websites (eg. pharmaceutical company, bookstore) or personal websites	32 (34.4)
Others (eg. online books, lecture notes, online tutorial, PDF/ Word files for unknown purposes, encyclopaedia, news)	19 (20.4)

### IMgateway.net

Integrative Medicine Gateway (Figure 4) is the only Australian internet based resource that integrates both CM and conventional medicines. It is developed by Unity Health Pty Ltd with a stated research methodology and consulting committee of academics in the field.<sup>5</sup> It provides data on herbs, drugs, supplements and medical conditions. Available at [www.imgateway.net/page.jsp?demoProfRef=ProfLookups\\_Herbs](http://www.imgateway.net/page.jsp?demoProfRef=ProfLookups_Herbs).

To find drug-herb interactions, users can select either 'herb or supplement interactions with drugs' or 'drug interactions with herbs/supplements'. If searching by drug name, the possible herbs or supplements that may interact with this drug are listed, and further details can be reached by clicking on 'herb/supplements'. If searching by herbs/supplements, the interactions with drugs are presented in text format with the use of subtitles (ie. drug names). All materials are well referenced and continuously updated by the editors. Patient information sheets are available and easy to understand. IMgateway requires subscription.

### Comprehensive and Interactive Medical Reference

Comprehensive and Interactive Medical Reference (Figure 5) contains two useful tools: 'complementary and alternative medicine index' and 'drug interaction checker'. Available at [www.umm.edu/medref/index.htm](http://www.umm.edu/medref/index.htm).

The website includes numerous drugs, herbs, supplements, medical conditions and treatment options. In particular, a list of herbs

Figure 3. HerbMed website



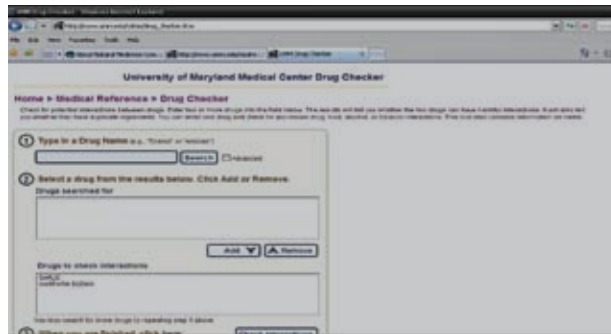
Figure 4. IMgateway website



Figure 5. Comprehensive and Interactive Medical Reference website



Figure 6. 'Drug interaction checker'



and their interactions with medications is available by selecting the herb from a menu. Drug interaction checker allows users to enter drugs and herbs to find out potential interactions (Figure 6). The severity of the interaction is illustrated by an 'interaction image'. There is also a description of the interaction, providing an understanding of why and how the interaction may occur.

Both tools are easy to navigate and written in consumer friendly language. This website requires no subscription and users can access the resources without difficulty. The only shortcoming is that although all materials have been recently reviewed by the editors, there is no reference shown on the website to support its reliability and accuracy.

### MerckManuals Online Medical Library

MerckManuals Online Medical Library (Figure 7) provides 'medicinal herbs and nutraceuticals' in the drug section and offers basic information on herbs. Available at [www.merck.com/mmhe/sec02/ch019/ch019a.html](http://www.merck.com/mmhe/sec02/ch019/ch019a.html).

Instead of searching the database for drug-herb interactions, users can click on the herb to obtain further information about it, such as background and possible side effects. The contents are easy to read, presented precisely and written in plain language suitable for the general public. The drug-herb interactions are also well summarised in a table after the introduction so users can get instant ideas about drug-herb interactions.

It only covers 18 herbs, so does not have enough information for users and is not as practical as other websites. In addition, although it is updated periodically with new information, the editors do not provide references.

Figure 7. MerckManuals Online Medical Library website

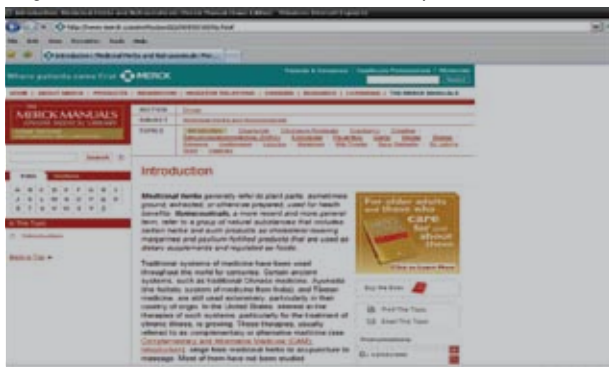
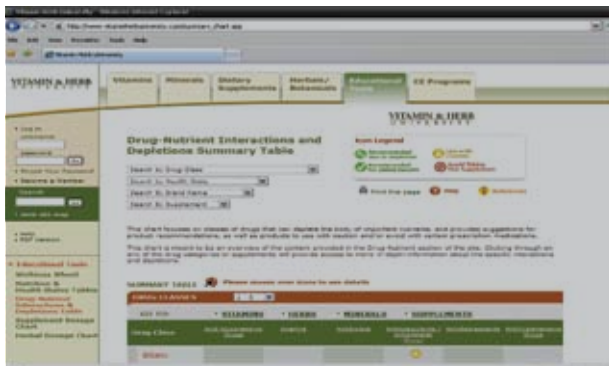


Figure 8. Vitamin &amp; Herb University website



### Vitamin & Herb University

Vitamin & Herb University (*Figure 8*) serves as an information resource for pharmacists to obtain herb/supplement information and includes evidence based information on mechanism of action, dosage, benefits, toxicity, and drug-herb interactions. Available at [www.vitaminherbuniversity.com/drug\\_intro.asp](http://www.vitaminherbuniversity.com/drug_intro.asp).

It offers an interactive educational tool, the 'drug-nutrient interaction and depletion database' and allows users to check potential drug-herb interactions or depletion that can occur with drugs. Interactions can be found by searching drug class, health state, brand name or supplement. Information is then categorised with different subtitles (eg. recommended due to depletion, recommended for added benefit, use with caution and avoid taking this supplement), and is easy to read. A summary table contains all key messages and provides an overview of contents in drug-nutrient interaction section. All materials are accessible. Information in 'drug-nutrient interaction and depletion database' is not referenced, although other sections (eg. herb information, dietary supplement information) have scientific evidence to ensure the reliability of the resources. In addition, there is no indication of the last date of update in the interaction database, so users are not able to assess the currency of the information.

### Discussion

Many websites found in our search provided only a quick reference table with a few common drug-herb interactions listed, with no

interactive search function nor evidence based material to support claims. Of the 351 000 hits, we found seven websites from the first 100 sites which satisfied our selection criteria. It is important to note that often the sponsored commercial websites are listed at the top of the search results, however there were no sponsored links from this search. Therefore, we believe the first 100 listed websites from a Google search should represent the most commonly searched sites by the public or health professionals.

A recent National Prescribing Service study also identified the need to improve the awareness and availability of CM information among Australian health professionals and consumers.<sup>6</sup> This comprehensive study reviewed 52 CM information resources, including free websites, subscription databases, books and e-books. It evaluated these resources according to accessibility and currency, content, transparency, coverage and accuracy. An in-depth review of the short listed CM information resources was performed to examine three domains of quality: technical quality, content quality, and clinical utility. Of 52 resources, five of our 7 websites were included (Natural Medicines Comprehensive Database, DrugDigest, HerbMed, IMGateway, and Comprehensive and Interactive Medical Reference). Only Natural Medicines Comprehensive Database was considered as being of the highest quality, ranking second overall. The remaining six resources were not classified as either the highest (tier 1) or high quality (tier 2) resources. It should also be noted that the vast majority of resources ranked as tiers 1 and 2 were internet based; however, eight of these 9 resources were not included in our study. This was primarily because of our search strategy used Google and the keywords 'drug and herb interactions'; this simple search strategy missed resources found by specific databases. For example, Medline Plus, one of our exclusions, was rated in tier 1.

There are several limitations to our analysis. First, the information from these websites is being taken on face value without evaluating accuracy. Second, using only Google without combining the search results from other medical databases such as PubMed may miss good evidence based drug and herb information. Third, selected websites might not provide the most up-to-date interactions information. Finally, for practitioners wanting to search for a particular herb, more information may be obtained by performing a specific search rather than a general search in as our study.

The National Prescribing Service currently recommend that tier 1 and tier 2 resources should be available in various formats, such as web based information resources.<sup>6</sup> However, they also recommended the necessity of assessing the usability and 'real life' utility for both health professionals and consumers in order to select the most appropriate resource.<sup>6</sup> Based on our findings, we believe a web portal with risk categorisation of mild, moderate and severe for drug-herb interactions can assist doctors in clinical decision making. In addition, it may help practitioners adjust dosage of medications or herbs to minimise any potential side effects and to increase the cost effectiveness of a combined integrative treatment. It is

likely there will be more reports of severe side effects and adverse interactions.<sup>7</sup> Maximum benefits could be obtained by working collaboratively with the Therapeutic Goods Administration so that it could receive reports about drug-herb interactions in a similar way to how it receives information on adverse medication reactions. In this way, practitioners may benefit from the uniform up-to-date information provided by easily accessible and evidence based websites.

Conflict of interest: none declared.

## References

1. Dunne F. The 'natural health service': natural does not mean safe. *Adv Psychiatr Treat* 2009;15:49–56.
2. Bensoussan A, Lewith G. Complementary medicine research in Australia: A strategy for the future. *Med J Aust* 2004;181:331–3.
3. Henderson J, Britt H, Miller G. Extent and utilisation of computerisation in Australian general practice. *Med J Aust* 2006;185:84–7.
4. Sim M, Khong E, Jiwa M. Does general practice Google? *Aust Fam Physician* 2008;37:471–4.
5. UnityHealth Pty Ltd. Integrative Medicine Gateway. 2004; Available at [www.imgateway.net/page.jsp?demoProfRef=ProfLookups\\_Herb](http://www.imgateway.net/page.jsp?demoProfRef=ProfLookups_Herb) [Accessed 16 June 2009].
6. McGuire T, Walters J, Dean A, et al. Review of the Quality of Complementary Medicines Information Resources: Summary Report. 2009. Available at [www.nps.org.au/\\_\\_data/assets/pdf\\_file/0005/69656/CMsInfoSummary.pdf](http://www.nps.org.au/__data/assets/pdf_file/0005/69656/CMsInfoSummary.pdf) [Accessed 1 May 2009].
7. Pan C, Morrison R, Ness J, Fugh-Berman A, Leipzig R. Complementary and alternative medicine in the management of pain, dyspnea, and nausea and vomiting near the end of life: A systematic review. *J Pain Symptom Manage* 2000;20:374–87.