Review Article

Herbal Database Management

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ABSTRACT

Herbal database management is one of the emerging trends nowadays. There are many agencies working on herbal database management. This system helps to overcome many adverse reactions of drugs and their interactions. The safety profile of an herbal is maintained in this database which is very useful for appropriate use of herbal medicine. Here, an attempt is done to enlist various herbal database management agencies and their applications toward the use of herbal drugs for the benefit of mankind.

Introduction

Henriette Kress, known as "cyberspace's herbal archivist," is a well-known Finnish herbalist who has developed one of the most encyclopedic noncommercial web sites on herbal medicine worldwide. It contains archives on several public and non-public herbal forums, a photographic database of 8,000 botanical plant photos, and reprints of 20 major classic herbal works, which had been largely lost to history. The reprints contain information on 4,200 different plants, plus those not yet in the plant name database. (For purposes of comparison, a typical Chinese herbalist might use 300 herbs, an American herbalist 50 - 100, and a native Cherokee medicine man 800).

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History of the herbal web site

Kress has been active on the web since 1992, and published her first FAQ on herbs for the alt.forklore.herbs newsgroup in 1995. After the medicinal herb FAQ got a good start, Larry London (who had a collection on ibiblio) asked if she would do a FAQ for edible herbs as well. So in July 1995 Kress posted the first version of the culinary herb FAQ. Shortly afterward, ibiblio asked Kress to host a noncommercial herbal collection and said that they would provide WWW and FTP space at a time when private ISPs were prohibitively expensive. Henriette's Herbal Homepage was first published on ibiblio in August 1995 where it lasted until 2005, when it became too popular and moved to its current location. It is one of the oldest herbal sites online, with over 36,000 files, 600 MG of information, and 122,000 hits a day as of 2006.[1]

Database management structure

With the aim of capturing data about adverse drug reactions (ADRs) to herbal products in the same system as ADRs to other medicines, the WHO Collaborating Centre for International Drug Monitoring in Uppsala (the Uppsala Monitoring Centre; UMC) has restructured the management of data relating to herbal products. This has mainly involved the structure of information held in the substance register of the WHO Drug Dictionary (WHO-DD). The register identifies the "preferred names" of ingredients of products mentioned on all ADR reports in the global WHO database. The logic

for identifying "preferred names" for herbal substances follows, as far as possible, that for identifying preferred chemical substance names in the WHO-DD. The validity of any scientific name (botanical names) that may be used as a "preferred name" for herbal products is problematic, since such names may be revised during a taxonomic review. It is important to stress that the use of valid Latin binomial (scientific) names in the substance register of the WHO-DD is not for the purpose of providing a botanical reference work. They are the names that UMC has decided to use in order to provide unique names for herbal ingredients equivalent to international nonproprietary names (INN) for chemical ingredients in the global WHO database. The Royal Botanic Gardens, Kew, United Kingdom, has collaborated in ensuring that these names represent unique species. If there are other scientific names, they are regarded as synonyms. The scientific names comprise the Latin binomial (a genus name and a species epithet), the name of the author who described the specific species, and the publication source. To determine which botanical names were synonyms, and to find further information on each medicinal plant, its major chemical constituents/entities and medical uses, the major reference publications that UMC considers relevant were examined. For information on ingredients of reported herbal products, a variety of sources were consulted, including the scientific literature, summaries of product characteristics (SPCs) from national pharmacovigilance centers, and direct input from national pharmacovigilance centers. In addition to the preferred name, the list of ingredients should identify which part of the plant is used and give an indication of how the "active substances" have been extracted. This provides a more complete identification of the "active herbal ingredient." For conventional drugs, all preferred names of single-ingredient medicines are either bases or salts. For all salts, there must be a link to a base, e.g., omeprazole sodium is linked to omeprazole. Herbal products are treated in a similar way, in that the "mother herbs" (medicinal plants) will be the equivalent of bases and the different plant parts (herbal materials) and/or types of extract/herbal preparations are equivalent to the salts. As shown in the herbal substance data links [Figure 1], the herbal ingredients given as valid scientific names of medicinal plants are linked to common names of the plants and also to plant parts and the extracts or other herbal preparations used. So when retrieving information about a specified medicinal plant, starting from any scientific botanical name, vernacular, or common name, it will be easy to find all related substances (chemical 47 WHO guidelines on safety monitoring of herbal medicines in pharmacovigilance system entities) including those where different parts/herbal materials and/or extracts or other herbal preparations are specified, and vice versa.[2]

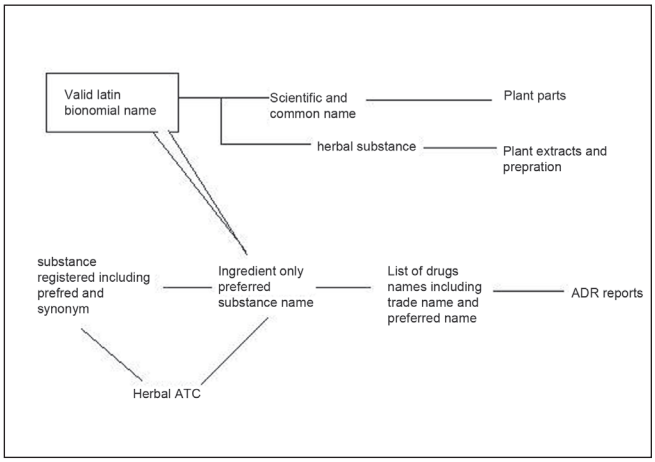

Figure 1: Data links for herbal medicines

Herbal anatomical–therapeutic–chemical classification

The herbal anatomical–therapeutic–chemical classification (HATC) is a classification primarily based on those herbal products that have ADRs reported in the global WHO database and therefore appear in the WHO-DD. They are not necessarily categorized in a medicines category in any particular country. The HATC classification, unlike the regular ATC system, is based on botanical science, pharmacognosy, phytochemistry, literature search, and documented traditional use rather than chemistry and evidence-based medicine. It is linked to botanical synonyms and vernacular names via the substance register of the WHO-DD, which contains all ingredients, herbal and chemical, of medicinal products mentioned on reports in the global WHO database. In addition to the identification by preferred name and information on the plant parts used and methods of preparation, the HATC classification as used in the global WHO database, indicates.

- The suggested anatomical site of the pharmaceutical action
- The range of intended medical uses including traditional therapeutic uses.

The HATC classification is mainly used as an administrative tool for placing groups of herbal products in the coding systems, and to group-related products in signal work and other congregated searches.[3]

The storage and management of safety monitoring information on herbal medicines

Principles of the system

It is often impossible to obtain information on both the traditional product composition and the use of such products by patients. No data management system can capture more than is known, but the combination of the HATC classification and the current global WHO database structure allows any and all information to be entered. The basic philosophy behind the data management of herbal products and traditional medicines is to achieve a system that is capable of handling all levels of information, at the same time being utterly transparent to users over any imprecision, missing data, and the links that are built into the hierarchies in the system. Precision versus uncertainty, for example, can be considered as occurring along several axes:

- identification of the medicinal plant
- itemization of the medicinal plant part (herbal material)
- stipulation of preparation methods (processing including extraction procedures)
- definition of the major chemical constituents extracted
- definition of the major ingredients/herbal materials (name and proportion) in mixture herbal products (complex preparations and products)
- note of any variations in product composition (and dosage form)
- Intended medical use, indicating diseases or symptoms that can be treated.

Detailed descriptions of the HATC classification and the global

WHO database system are available from UMC. ADR terms, and indications, used in ADR reports on herbal products and traditional medicines will often be those recommended for other medicines. However, additions to WHO-ART and MedDRA may be needed to capture differences in expressing ADRs caused by the use of herbal products, especially in the case of traditional medicines, in accordance with particular treatment concepts and/or principles. For example, "increased/decreased Yin" is the possible state of diseases within the Chinese medicine system, a concept unique to this particular type of medicine. Such details will be added to WHO-ART, as required. It is clear that other systems can be devised to accomplish the same ends. The purpose of the data management system described above is specifically for pharmacovigilance, and is specially designed to allow its use alongside pharmacovigilance activities for other medicines. This is an important consideration in view of the increasing likelihood that patients/consumers may use both forms of treatment concurrently. Other systems developed and used for pharmacovigilance should function in a similar way and it should be possible to link them with the global WHO database, to ensure that all international data are pooled for global benefit.[4,5]

Data analysis

The new structure and classification of herbal substances (entities) within the global WHO database will facilitate finding information about finished herbal products containing a specified medicinal plant or just a specific part, herbal materials, or extract or other herbal preparation of the specified medicinal plant. This is crucial in finding and evaluating signals concerning herbal medicines and traditional medicines (more complex than for other medicines), as the following example shows. A company has for years produced a product containing Senna alexandrina Miller, which in the labeling is called "Cassia." Another company markets a product that also lists "Cassia'" as an active ingredient but the product is derived from Senna armata Wats, a different botanical species. Then reports of serious ADRs associated with "Cassia" appear and they are so serious that a withdrawal from the market is considered. It may be that only Senna armata Wats is causing these problems. In this case, the other species, Senna alexandrina Miller, risks being wrongly accused because there is no distinction between the labeled names: "Cassia" is the suspected cause. While the use of the global WHO database and, in particular, the proposed HATC classification does not solve the problem of missing or inaccurate information, it is hoped that it will facilitate proper classification of all herbal product information and, most importantly, show where there is a potential for confusion and/or error. Another linked benefit is that it will be possible to produce a checklist of common and vernacular names covering several different languages, which will be valuable for all those seeking to identify the contents of herbal remedies used nationally. It may also prove useful at poison centers and probably also for pharmaceutical companies in labeling their herbal products. In the end, all involved with herbal products should use the valid scientific names, to avoid any confusion. 49 WHO guidelines on safety monitoring of herbal medicines in pharmacovigilance systems. The use of data-mining tools on pooled international data will be particularly valuable in trying to find useful patterns within such a large volume of heterogeneous data. Much consideration will need to be given to the development of such tools and to the use of international expertise in the interpretation of information. As always, epidemiological studies, where they can be undertaken, will aid the quantification and validation of early signals. However, epidemiological studies on herbal products are difficult because of the problems of ascertaining precise information.[6]

Poison control centers

Poison control centers (PCCs) have been investigated as potential novel sources of ARs for herbal medicinal products (HMPs). In a study of ADRs reported to a PCC in the United States during the period of 2000–2007, dietary supplements, herbs, and homeopathic products combined was one of the highest groups of products associated with hospitalization.[7] In 2002, the total exposures to dietary are to be administered with a view to restoring, correcting, or modifying physiological functions. As such, they are subject to the general regulations for medicines as laid down in the various national medicines laws. A marketing authorization as a HMP is granted based on a "full" dossier in terms of proof of quality, safety, and efficacy in almost all Member States but the Committee on Herbal Medicinal Products (HMPC), part of the EMEA, establishes Community herbal monographs to simplify the authorization of HMPs. With respect to GMP compliance, the EU follows the Pharmaceutical Inspection Cooperation Scheme (PIC/S). The competent authority may carry out announced or unannounced inspections of active substance manufacturers in order to verify compliance with the principles of GMPs for active substances placed on the community market. The marketing authorization holder (MAH) must ensure that they have an appropriate system of pharmacovigilance and risk management in place in order to assure responsibility and liability for its products on the market and to ensure that appropriate action can be taken, when necessary. Specifically, the MAH must have an approved system of reporting adverse reactions. Governmental responsibilities lie with each Member State's agencies. For example, in the United Kingdom, the Medicines and Healthcare Products Regulatory Agency (MHRA) provides transitional provisions where an HMP legally on the UK market as an unlicensed herbal remedy in accordance with the Medicines Act 1968 can continue to be marketed as an unlicensed herbal remedy until April 30, 2011. At that time all manufactured HMPs will be required to have either a Traditional Herbal Registration or a Marketing Authorization based on the European Directive. The Traditional Herbal Registration is a simplified UK registration scheme that began in 2005 with specific standards of safety and quality, agreed indications based on traditional usage, and systematic patient information allowing the safe use of the product.[8]

Surveillance of adverse effects through databases

Regardless of the type of herbalism being practiced, some adverse reactions are more easily recognizable than others. Postulates have been proposed to define if adverse effects are linked to a drug use.[9] In spite of the mode of application, individual differences in physiology may elicit a variety of idiosyncratic local or systemic reactions, including those that are life threatening. Age may also be a factor and those remedies most frequently used by the elderly may elicit varying responses.[10] Similarly, a long-term use can produce predictable reactions or consist of delayed effects such as carcinogenicity and teratogenicity. To better understand the scope of these problems and bring them forward to the public, De Smet

proposed that forms of herbal post marketing surveillances be conducted to "detect serious adverse reactions, quantify their incidence, and identify contributive and modifying factors." Obviously, the success of such endeavors depends on those willing to voluntarily and spontaneously report such events to appropriate health care officials, pharmacologists (http://www.faseb.org:aspet:HandMIG3.htmctop), regulatory bodies (FDA "MEDWATCH" [http://www.vmcfscan.fda.gov:_dms:aems.html]), and responsible parties in the herb trade industry itself, like the American Botanical Council (http://www.herbs.org), who are collating these data for public dissemination. With the number of mixed plant formulations now marketed in the United States alone, it is particularly important to refer to web sites that can provide on an ongoing basis useful information on current adverse reactions. Overall, the United States is still a long way from the development of standardized herbal drugs, called phytopharmaceuticals, which have been formulated (in a fashion) to ensure a reproducible effect by undergoing suitable means of identification and clinical evaluations to achieve international approval. Obviously these are needed steps if allopathic acceptance is to follow. In the interim, information is accumulating that is providing appropriate ways to understand herbal therapies and can be elicited from internet sources like the National Center for Complementary and Alternative Medicine (www.nccam.nih.gov), American Botanical Council (www.herbalgram.org), US Food and Drug Administration (www.fda.gov), and the US Pharmacopoeia (www.U.S.P.org).[11]

China Traditional Chinese Medicine (TCM) Patent Database

The deep indexed China Traditional Chinese Medicine (TCM) Patent Database was established by the State Intellectual Property Office (SIPO) of People's Republic of China. The purpose of creating this database was mainly to meet the need of patent examination. The database has already been put to use in the patent examination department in SIPO since April 2002. The Chinese version of the database covers TCM-related patent applications published from 1985 till today in China. It contains over 19,000 bibliographic records and over 40,000 TCM formulas. In order to present this database to WIPO, an English demo version was created and opened to the world through the WIPO gate. There are 29 search fields in the database that fall into four categories: bibliographic information, subject index terms, uses/effects, and TCM formulas. Rewritten titles and abstracts provide users with more searchable information. The system was built with multiple search features: quick search, advanced search, TCM formula search, and search history tracing function. Moreover, two special features created in the system are very useful for improving searching efficiency: cross-file search based on TCM dictionary and TCM similarity search. The cross-file search enables users to locate a specific TCM in the TCM dictionary file and then cross-file search that name in the patent bibliographic file for relevant records. TCM similarity search enables users to do one-stop searching easily for complex search queries.[12]

Dr. Duke's phytochemical and ethnobotanical databases also known as "Father Nature's Pharmacy"

www.ars-grin.gov/duke/

James A. Duke, Ph.D., the renowned ethnobotanist and retired U.S. Department of Agriculture (USDA) plant economist built this comprehensive database. This is one of the best sites for practitioners because it allows searches in a variety of ways: plant searches, activity searches, chemical searches, and ways to find ethnobotanical uses for particular plants. There is also a solid listing of useful links. A practitioner can also enter a symptom such as "wound" and search for an appropriate remedy. Best of all, there is a caveat for patients who visit this site: "The USDA does not recommend self-diagnosis or self-medication."

American Botanical Council

www.herbalgram.org/

The American Botanical Council (ABC) is a not-for-profit organization (Austin, TX) with a mission to educate the public on the use of herbs and phytomedicinals. The ABC publishes *HerbalGram* jointly with the Herb Research Foundation, and also provides the very useful and informative "HerbClip," a biweekly service summarizing articles drawn from the mainstream and medical media. An extensive Herbal Education Catalog is accessible on the ABC web site. On the opening page, doing a quick search for databases brings up a wealth of links to online herbal databases. This site requires a user to register in order to access some of ABC's resources.

American Herbalists Guild-Health World Online

www.healthy.net/herbalists/

This is a very comprehensive site that allows a variety of searches via specific herbs, health conditions, and health centers. The site is updated frequently and has new information that practitioners and their patients will find helpful. An excellent menu of links includes Herbs and Children's Health, Herbs and Aging, and more.

Herbal Hall – Professional herbalists' discussion list

www.herb.com/herbal.htm

As with similar sites, there is an array of links down the left side of the screen. These include: Features, References, Books, HerbWalk, HerbMail, HerbFiles, Herbs, Herb FAQ, Search, Links, and HerbNews. However, many of the links do not function, and entering oregano, and then kava, into the search box, brought about an error, without any results displayed. This site might be promising in the future because there were many links that seemed to be worth reading, but the web master needs to fix a few things first. In any event, it is a site to watch.

Medline Plus – Health Information

www.nlm.nih.gov/medlineplus/herbalmedicine.html

This essential site contains up-to-date information from a variety of sources, which may be of practical use. Down the center of the screen is an updated list of stories pertaining to herbal applications and usually cautions about the use of specific herbs in certain situations. Sometimes, these stories are from the mainstream media, such as the Associated Press, but others come from research institutions, such as the Mayo Foundation for Medical Education and Research, the National Institute on Aging, and the American Academy of Family Physicians.

Botanical Medicine Information Resources – Directory of databases

www.cpmcnet.columbia.edu/dept/rosenthal/Botanicals.html

As an information database, this site is extremely good. Maintained by the Richard and Hinda Rosenthal Center for Complementary and Alternative Medicine, Columbia University College of Physicians and Surgeons, New York, the site provides a vast, comprehensive listing of searchable databases that relate directly to botanical medicine.

Phytotherapies.org

www.phytotherapies.org/

This site includes editorial content, articles, and an extensive searchable database on current herbal therapeutics. Herbal practitioners are encouraged to register, free of charge, in order to gain full access to the site's massive database. On the left side, after one scrolls down a bit, there is a tantalizing listing of the 20 most popular herbs as selected by site's regular users. Below the list are links to obtaining herbal extracts and other useful information.

MedHerb.com – "where medicine meets the herb"

www.medherb.com/

At the top of the portal page of this site are a series of links, boxed, with a variety of offerings. However, the more interesting contents are a bit further down. These include links such as Adverse Affects, Anatomy, Folk Uses, Plant Pharmacy, and approximately a dozen others. In many cases, these links are related to books that have been written about the topic (i.e., the use of witch hazel in the original formula for Pond's Cold Cream). This site seems inexhaustible, being that following a trail of links can lead you to very interesting books about sixteenth-century herbal preparations.[13]

KUlHerb: Knowledge Unifying Initiator Herbal Information

Knowledge about herbal medicine can be contributed from experts in several cultures. With the conventional techniques, it is hard to find the way with which the experts can build a self-sustainable community for exchanging their information. In this work, the Knowledge Unifying Initiator for Herbal Information (KUlHerb) is used as a platform for building a web community for collecting the intercultural herbal knowledge with the concept of a collective intelligence. Four components are implemented on KUlHerb: accessing information, sharing opinions, providing information, and web site statistics. In the case of multiple opinions, the majority voting will select the most preferable term used in the community. Herb identification, herbal vocabulary, medicinal usages, and a list of experts in herbal medicine can be collected from this system.[14]

Natural Medicines Comprehensive Database

The Natural Medicines Comprehensive Database, one of the most comprehensive and reliable natural medicine resources available, is by Therapeutic Research Faculty, an impressive team of experts. Natural medicines in this context refer to all herbal and nonherbal supplements. Although some of the supplements may not be produced from natural sources, they are included, because they are generally categorized with natural products.[15]

HerbMed®

It is an interactive, electronic herbal database providing hyperlinked access to the scientific data underlying the use of herbs for health. It is an impartial, evidence-based information resource provided by the nonprofit Alternative Medicine Foundation, Inc. This public site provides access to 20 of the most popular herbs.

HerbMed Pro™

It is an enhanced version of HerbMed®, provides access to the entire database (225 herbs) with continuous updating using Dynamic Updates, and is available for subscription and licensing or multiuser subscriptions from the American Botanical Council.[16]

InPACdb – Indian Plant Anticancer Compounds Database

Indian Plant Anticancer Compounds Database (InPACdb) is a web-based open access database of phytochemicals. The objective of this initiative is to project the potential of anticancer phytochemicals from Indian pharmacopoeia in an integrated environment. This database is unique in providing comprehensive information covering cancer type, molecular target, 3D stereochemical structures (tautomers, stereoisomers, conformers, and resonance structures), chemical descriptors, etc. for each entry, enabling effective cheminformatics analysis. The complete dataset of InPACdb encompasses 32 descriptive fields for each entry, and is freely available for download at http://www.inpacdb.org.[17]

Foundation for Revitalisation of Local Health Traditions (FRLHT)

The Foundation has, together with other public interest NGOs working on traditional medical systems, argued forcefully for reorienting public health care policies, at least in India, in the direction of tapping the enormous skills and expertise available with practitioners involved in local or folk health traditions. The same groups have also insisted that more attention be paid to the Indian Systems of Medicine (ISM), notably Ayurveda, Unani, Siddha, and Tibetan Medicine. They point to the example of China, which has continued to treat its indigenous system of medicine on par with the imported Western system. The common point in most of the Asian systems is that they are largely based on plant medicines. The cultures which have given rise to these systems of medicine are also fairly expert in their knowledge of medicinal plants and their collection from the wild or their cultivation in specialized gardens.[18]

Conclusion

Generally herbal drugs are preferred because they are safe, but nowadays adverse effects and drug interactions are observed with herbal drugs. There is a necessity to make a list of such adverse effects and interactions for herbal drugs. In brief, the safety profile of a herbal drug is necessary before using it for therapeutic application. Such adverse effects and interactions are listed by the "herbal database management." Systems which are really useful for the proper application of herbal drugs in treatment of various ailments of mankind.

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