DEREPLICATIONS CAN AMPLIFY THE EXTENT AND WORTH OF TRADITIONAL PHARMACOPEIAS.

Memory Elvin-Lewis

Washington University, Box 1137
St. Louis MO 63130
E-mail: elvin@biology.wustl.edu

Abstract

As aculturization and globalization continues, there is an urgent need to carefully record and delineate traditional pharmacopeias so that their true worth is understood and protected and any possible benefits related to their commercial development are equitably distributed. In the past most of these endeavors resulted in a list of plants with their associated uses without providing further explanations as to the extent of this knowledge within the traditional group, or if this knowledge was known elsewhere. This practice tended to generate the notion of finite exclusivity without providing proof that this was actually the case. Moreover, since the talents and methods of those conducting these initial studies varied widely, little effort was made to provide adequate information on how selective processes and preferences as well as modes of collection, preparation and use were achieved. Without these data, the potential of their clinical worth, bioreactive capacities or chemical compositions were often compromised. This frequently led to expending much time, effort and treasure on a pharmacopeia's evaluation without guidance on how these efforts could be optimized to achieve its best possible medicinal potential. This paper will review how types of dereplications and other techniques are helpful in amplifying this process.

Introduction

Before appropriate dereplications can be applied to a traditional pharmacopeia it is important to know how these data were acquired and by whom. The worth of this information is dependant upon the expertise of not only those involved in the acquisition of the data but also those that examine its worth. Nowadays to corroborate and/or exploit the medicinal value of a traditional-based pharmacopeia it is important to utilize the talents of many expert scientists. Such endeavors should be viewed as a team effort, with data evolved by one type of investigator providing insights to others along the validation process.

In the past it was not unusual for medicinal plant inventories pertaining to a specific traditional pharmacopeia to be conducted by individuals who were limited in their expertise. This often generated a list of plants and/or local names associated with some, but not necessarily all of their uses. I have observed that depending on the extent of the study, this occasionally results in incomplete or erroneous information being recorded regarding the true nature of the malady or remedy or the correct identification of the plant itself. In the latter instance, when accompanying plant vouchers were not provided, or inappropriately prepared without fruit and/or flowers, misidentifications could be made in a variety of ways. Sometimes this has meant depending on local names to guide determinations without understanding if one or more disparate taxa were associated with this epithet e.g., Akan designation of "tweapea" for *Garcinia afzellii* and *G. epunctata* (Adu-tutu. et al 1979; Elvin-Lewis, 1980, Elvin-Lewis, 1982). There was also a tendency to list plants for a use without citing when and how the plant was collected, what plant part might be used, how it might be stored and prepared, and if it was used alone, sequentially or in combination with other plants or other substances.

Also, without knowledge of the local language or medical terms that were locally applied or conventionally known, medical descriptors could be so vague as to refer to the incorrect disease syndrome, or eliminate particular details, which could have further aided in the diagnosis. This is particularly true in cases of those with multiple etiologies. For example, detailed descriptions of symptoms are frequently critical to an appropriate diagnosis and/or etiological identification of gastrointestinal, dermatological or pulmonary infections. Thus, in one ethnopharmacology Amazonian study related to traditional treatments for viral diarrheas among the Kayapó of Brazil, information regarding the duration of the illness and the nature of the stools was considered trivial and not recorded. These omissions were unfortunate since it is generally recognized in the medical community that a short acute illness is more likely to be viral in origin and the color and consistency of fecal excrement is often indicative of the cause of the problem at least at the level of whether or not it is bacterial or parasitic in nature. Appreciating these differences would have been useful in prioritizing the evaluations that were executed. In spite of this exclusion, the authors did conduct sufficient chemical and ethnobotanical dereplications so they were able to determine that "most of the genera employed included species that contained classes of compounds relevant to antiviral activity, or are related to species

doi: 10.4314/ajtcam.v8i5S.12

used by other peoples for viral diseases or gastrointestinal troubles" (Elisabethsky and Posey, 1994). Causes of pulmonary infections are particularly difficult to assess unless one understands the types of disease that are regionally recognized, if they are acute or chronic, seasonal or perennial, primarily affect one age group or another, or if any unique symptoms (nature of sputa, cough etc) are related to a certain condition. Adding this type of information is particularly valuable when additional in vitro studies are used to evaluate their worth such as for certain bacterial infections like tuberculosis, viral infections like influenza, or parasitic infestations, which cause lung involvement.

Understanding the nature and epidemiology of diseases, which are prominent in the study area is useful in distinguishing what might be expected and what might be unusual. This is true for numerous infectious diseases as it is or certain medical ailments with circumscribed regional distributions. For example, confusion of what is meant by a medical descriptor may relate to how it is interpreted by the translator or in translation from one language to another. For instance, an ethnomedical study in Polynesia described the treatment of "yellow fever" by *Homalanthus nutans* (Euphorbiaceae) (Cox, 1991). Since this virus was unknown to the locality I questioned those familiar with the Samoan language and the study and asked them how the ailment had been described. Apparently the descriptor meant "yellowing eyes" inferring that the patient had jaundice, possibly due to hepatitis B (HBV) which is endemic to the region. These made sense since additional studies indicated its prostratin was inhibitory against Human Immunodeficiency viruses (HIV) and these viruses and HBV both possess reverse transcriptases (RT) (Lewis and Elvin-Lewis, 2003). Of note, many plant compounds can elicit this interesting cross sensitivity. Also, during the time I was involved in conducting a medicinal plant inventory of an indigenous Amazonian tribe our translator referred to a skin rash as being small pox. As an infectious disease microbiologist this did not seem logical to me since there was a lack of variola-scarring in the populace. In questioning the informant regarding the symptoms being reported it was apparent that the individual was referring to measles (rubeola) that was known to occur in the region.

To treat certain diseases several disparate groups have utilized the "doctrine of signatures" to select certain of their medicinal plants according to their shape or color etc., with the notion that these indicators provide some sort of cosmic clue as to their usefulness. While many of these signs have little value, one cannot totally disregard all of these interesting secondary selective criteria. Perhaps the best example is its application in identifying plant parts useful in the treatment of hepatitis and jaundice. For example, in studying Amazonian hepatitis remedies a significant number of those selected fell into this category (Elvin-Lewis et al., 2002). In these cases as well as in other pharmacopeias I have examined worldwide, identifiable efficacious yellow compounds such as antioxidant and antiviral flavonoids have often been associated with the yellow fruits, roots, flowers and/or barks found in these formulations. Another example related to leaf shape was the use of the Penobscot Amerindians of Mayapple (*Podophyllum spp*) to treat venereal warts (*Condyloma acuminata*). This plant has serrated and multi-lobed leaves, which are similar in shape to these anal lesions. In the latter instance, this led to the identification of its bioreactive podophyllotoxins and the semi-synthesis of the topisomerase inhibitors, teniposide and etoposide useful in the treatment of cancers such as leukemia, lymphomas, as well as brain and bladder cancers (Lewis and Elvin-Lewis, 2003).

The quality of data that is acquired during the initial interviewing process is but one aspect to be considered. Pivotal to the process of understanding a traditional-based pharmacopeia is to determine the type of medicinal practices that are involved, and if the knowledge is widespread and practiced among members of a community or only known to circumscribed healers. These differences will depend upon the number of individuals that should be interviewed within a neighborhood or regionally so a realistic consensus of what is valued and by whom can be generated. Within this context one must be mindful of the fact that there are numerous selective processes at play as to how these remedies are chosen including a variety of social parameters together with those preferences based on gender, tribe or religion. The contents of these remedies and prescribed uses may be rigidly adhered to or vary even within family units. However, when significant data are garnered from both practitioners and/or users alike, these perceptions of value can be applied to affirm their merit. This is particularly true when a large number of specific treatments are known for a specific condition and when there is a critical need to identify those of value to the health of a community or region. Detailed studies associated with chewing-stick use in Ghana (Adu-tutu et al., 1979, Elvin-Lewis et al., 1980) and Amazonian hepatitis remedies in Peru (Elvin-Lewis et al., 2002), called "ethnomedical focusing" provided insights into the worth of this type of effort. In both instances, favored species proved to have significant relevant bioreactivities when laboratory studies were conducted, clinical verifications made, and appropriate ethnobotanical and/or chemical dereplications were executed.

Access to secondary information was limited in the past since academic libraries and the like rarely had sufficient collections of published data, access to government reports, theses from other nearby institutions etc. to provide investigators with information about related and/or regional pharmacopeias. Also, when published in local languages, these were limited to those with the necessary linguistic expertise. The process of retrieving prior information from written reports could be painstaking whenever these sources failed to have adequate indices to facilitate the process. Similarly, only large herbaria were likely to have large enough collections to provide a comprehensive overview of the distribution of the taxa, or have specimens with labels indicating ethnomedical uses. Presently, because of the need to protect traditional knowledge as "know how", it is likely that some recent collections will indicate that ethnomedical data has been redacted from the herbarium label but is available through access to a defensive database (Elvin-Lewis, 2006; Elvin-Lewis 2007a; Elvin-Lewis 2007b; Christian, 2009).

doi: 10.4314/ajtcam.v8i5S.12

Today, many of these past problems have been overcome through information being readily retrieved from a wide range of electronically-based databases in ethnobotany, botany, biomedicine, pharmacognosy, chemistry, and clinical medicine including the process of meta-analytical and relevant patent pending or patented items from national and global patent agencies. Aside from these specialized and professional resources, the internet is replete with additional information (accurate or otherwise) on subjects pertaining to medicinal plants and their uses. These dereplication processes are invaluable in revealing what is already known, and how studies should proceed to optimize the worth of a traditional pharmacopeia as well as being helpful in revealing new avenues for research that might not otherwise be apparent.

Ethical Considerations

The issue of protecting traditional knowledge is an ongoing process as is evident by the ongoing draft revision of the WHO 1993 guidelines related to the conservation of medicinal plants, national and regional conferences on the subject, in addition to recent reports (Christian, 2009). Since the object of this paper is to provide ways in which pharmacopeias can be validated for their worth and/or commercial potential it is important that all future studies comply with these ethical guidelines and are sensitive to global, regional and national policies and laws which would impact on such endeavors. Readers may also refer to discussions on how both collective (CK) and traditional knowledge (TK) are defined, how claims of ownership can vary and can be utilized if in the public domain, in addition to ways circumscribed TK might be protected through defensive databases, trade secrets, sui generis laws, and the "requirement" associated with TK-associated genetic resources (Elvin-Lewis 2006, Elvin-Lewis 2007a, 2007b).

Ethnobotanical/Ethnomedical Dereplication

The challenges to utilizing a unified approach when addressing the complexities of ethnobotanical research and applying bioinformatics are continuing and have yet to be resolved. However practical solutions are likely to emerge as information technologies evolve and become more user friendly (Thomas, 2003).
Until a consensus evolves these tasks may be pain-staking because of the lack of standardization and the myriad of ways this information is available. Nonetheless these efforts are worthwhile if the full value of a traditional pharmacopeia is to be realized.

Ethnobotanical/ Ethnomedical dereplications are useful in determining the derivation of a remedy, whether or not it is ethnically specific, if it has been introduced from elsewhere through migration of populations or otherwise, if the use of the remedy is widespread because of its popularity or the distribution of the species, if it is used alone or as a mixture, and if treatment criteria gives a clue as to its value. This technique is also useful in identifying related species, when sourcing issues demand alternate supplies. An understanding how this might be achieved has already been addressed in detail (Elvin-Lewis 2005a, Elvin-Lewis, 2005b, Elvin-Lewis, 2010). To emphasize the value of this and related methodologies a number of aspects will be reiterated throughout this paper.

Applying this knowledge is essential to identifying those remedies worthy of additional study. For example, in today's evolving paradigm it is becoming evident that medicinal plants, already preselected by empirical methods, are more likely to elicit positive "hits" when screened for a particular bioreactivity than those studied from plant libraries representing random collections of local or regional floras. This is particularly true if the assay methods are complementary to mechanisms associated with "targeted" diseases.

However, this was not always the case. Up until the late 20th century both the U.S. National Cancer Institute (NCI) and Industry believed that mass screening of randomly collected plants was more likely to yield unique and interesting compounds, than when their ethnomedical uses were taken into consideration. Using this approach a small number (2-8%) of active compounds was isolated from 32,000 species of flowering plants screened worldwide between 1956-81(WHO, 1989). A shining example of this effort was the discovery of the complex anticancer molecule, paclitaxel (taxol) from the North American Yew, *Taxus brevifolia* . However, retrospective ethnomedical dereplication conducted several years later indicated that indeed an ethnomedical linkage existed in that the First Nation Tsimshian of Northern British Columbia and Alaska had used *T. brevifolia* 's wood for the treatment of cancers (Moerman 1991). Moreover, when alternative sources were needed to satisfy the growing need for paclitaxel, an examination of other species for this compound or precursor molecules was initiated. Among these was the Himalayan anticancer plant *T. walachiana*, cited in the Bower Manuscript written between 1893 and 1912. It is noteworthy that in the early days of paclitaxel's development this association was known to NCI but not considered relevant (Hartwell, 1967). It was only when this species and the European yew, *T. baccata* was identified as the potential source of the precursor molecule, baccatin III, needed to produce the semi-synthetic analog docetaxel, that a better appreciation of the worth of ethnomedical knowledge began to evolve. (Lewis and Elvin-Lewis, 2003).

At this time a number of other studies were beginning to indicate that screening of medicinal plants, which had been essentially disbanded, was once again becoming a worthwhile endeavor. This was particularly true when collaborative efforts evolved between those still utilizing their pharmacopeias and expert scientists that were able to accurately evaluate their worth. Optimal correlative results clearly depended upon the specificity of the assays and clinical evaluations that were being applied.

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In one study involving the NCI, HIV Screening program, a significant number of hits (15-25%) was elicited when medicinal plants from Belize, Central America were evaluated. Most of these contained bioreactive compounds with the ability to react with a number of target sites as is often the case with highly complex polyphenolics or flavonoids (Balick, 1990). On the whole these types of compounds, while not considered to be pharmaceutically viable, have the potential to become useful phytopharmaceuticals.

Additional unpublished data generated in 1992 through collaboration with the NCI HIV screening laboratories and those of Dr. Walter Lewis and I also affirmed this observation. Crude extracts of 25 plant collections prescreened by traditional medicinal use for anti-infectivity activity, and representing 23 genera in 19 families of terrestrial plants from four continents, were submitted to the NCI HIV screening program. Of the 50 aqueous and solvent extracted samples, which were tested 15-30% proved weakly to strongly active against HIV *in vitro.* When these results were compared with 16,886 extracts of primary anti-HIV screens our prescreened selected samples proved significantly different (X2=20.9, df 1; P = 0.001). Using aqueous and solvent extractions, noteworthy differences were also obtained between selected collections and random collections: 25 aqueous-extracted samples gave 10 active against HIV (40%) compared to NCI's 8,443 samples and 1,174 active (13.9%) (X2 = 8.7, df 1; P = 0.01; and 25 solvent-extracted samples gave 5 active (20%) compared to NCI's 8,443 samples and 255 active (3%) (X2 = 4.9, df 1; P = 0.05).

For example, our studies in the Peruvian Amazon indicated that the selection of many plants used to treat viral hepatitis and malaria could be therapeutically verified in a number of ways. Because of confidentiality agreements these data will only be reported as an overview since at this time the identity of taxa or any of their compounds remain proprietary. Within this context bioreactivity was not only identified by in vitro studies, but for hepatitis was also clinically established in the context of use (Elvin-Lewis et al., 2002). In addition, on going ethnobotanical dereplications associated with these hepatitis remedies are proving to be particularly valuable in both identifying those taxa which are unique to a group or region but also to others, which are much more widely used for the same purpose elsewhere. Many investigations identified in this latter process have also identified bioreactive components that are germane to their therapeutic value.

Also, within the context of the (International Collaborative BioDiversity Group-Peru (ICBG-Peru) Project, 91% (78/85) extracts from plants used to treat malaria were found active in functional tests against both chloroquine-sensitive and chloroquine –resistant *Plasmodium falciparum*. Significant activity was also elicited by a number of alkaloids belonging to taxa from two distinctly related families when they were tested in the *P. vinckei* mouse model at concentrations found in therapeutic formulations (Lewis et al., 2004).

When targeted candidates have been tested for cross-sensitivity to related organisms interesting new avenues of research have evolved. This concept was first tested in preliminary studies conducted in my laboratory in the 1990's utilizing secondary sources to identify some North Amerindian hepatitis remedies from our plant extract library. When approximately 40% of those tested were found to inhibit HIV-reverse transcriptase activity additional studies were evolved using plants derived from primary data.

In this case, the proportion of correlative hits was significantly higher when plants were identified in the Peruvian Amazon from populations who participated in studies to categorize and validate the worth of viral hepatitis plant remedies. Not only did many of these plants, as DMSO extracts, inhibit the processes of Hepatitis B (HBV) replication, but many proved to be clinically effective when validated in the context of use (Elvin-Lewis et al., 2002; Elvin-Lewis, 2010). In addition, all of those that inhibited HBV replication and were submitted to NCI for HIV screening proved to be active to one degree or another. Whereas some taxonomic relatedness was evident at the order, family or generic level (3 families, 5 genera) others proved unique. These results were dependant upon the way specimens were prepared with activity being identified in 10 of 14 samples or 71.4% (7 aqueous, 3 solvent). Compared to the random NCI collections, this group of specific extracts was significantly different (X2 = 37.6, df 1; P = 0.001. Following these studies, Dr. J. Cardellina, who coordinated these investigations at NCI, remarked that "he had never seen such a high proportion of "hits" from a group of terrestrial plant specimens". These initial studies indicated that the more valid the ethnobotanical and clinical data the more likely are plants able to be identified that possess this unique cross reactivity. My recent studies into evaluating the conceptual similarities of hepatitis remedies worldwide are also indicating that while not all plants used in the treatment of generic and/or viral hepatitis are likely to react similarly, many have proven to possess comparable cross sensitivities to HIV (Elvin-Lewis, in manuscript). Hopefully this potential will be assessed further, particularly in developing countries where access to conventional treatments for AIDS is unavailable.

Preliminary studies conducted under the auspices of the ICBG-Peru project have also shown that testing for cross-sensitivity is a valid process. Extracts were tested by the NIAID evaluation laboratories for *Cryptosporidium* at Tufts University and for *Toxoplasma* at the Research institute, Palo Alto medical Foundation, headed by Saul Tzipori and Fausto Arauj, respectively. Seven species, shown to be active in either functional or in vivo antimalarial assays as described above, were tested as DMSO extracts at 0.2 µg/mL concentrations for their ability to inhibit a number of apicoplexan protozoa causing AIDS associated diseases. When compared with Paromomycin at 2 mg/mL in DMSO. Five of these elicited inhibition of *Cryptosporidium parvum* at ranges comparable to, or exceeding that of Paromomycin, whereas the remainder was less active. When the same extracts were studied for their ability to inhibit the RH strain of *Toxoplasma gondii* only moderate activity was seen at 25µg/mL. In the majority of cases these activities were associated with some degree of host cell toxicity. Coincidental with this research were studies with 9 West African antimalarial plants. Inhibitory activity was obtained with *Veronia colorata* at >10µg/mL, with an IC50 of 16.310µg/mL

doi: 10.4314/ajtcam.v8i5S.12

Table 1. Index of Ethnobotanical Data Bases, URL Designations or Contact Information

Category	Subject	URL or Web Address
Worldwide	EthnobotDB	ukcrop.net/perl/ace/search/EthnobotDB
	ETHMED	http://ww.toyama-mpu.ac.jp
	HERBMED	www.herbmed.org/
	Plants for a Future	http://pfaf.org
	SEPASAL	www.rbgkew.org.uk/ceb/sepasal/ceb.html
Regional	Greater Southwest of U.S.A.	www.anthro.fortlewis.edu/ethnobotany/database.htm
	Peruvian Amazon	www.biopark.org/Plants-Amazon.html
	Prelude: Africa	www.metafro.be/prelude
	PROSEA: SE Asia	www.prosea.nl
	PROTA: Africa	www.database.prota.org/
	South Florida, U.S.A.	www.fig.cox.miami.edu/7Escofield/sofl.
	TRAMIL: Caribbean & Latin America	www.funredes.org/tramil/english/indice.html
	WIP0: China, India, Korea	www.wipo.or/ipd/en
National	Bangladesh	www.ethnobotanybd.com
	Brazil	http://www.ciagri.usp.br/planmedi/planger.htm
	Brunei Dusan	Lucy.ukc.ac.uk/Brunei.html (Filemaker Pro download)
	China (TCM)	cmmrc@cuhk.edu.hk
	Hawaii	www2.bishopmuseum.org/Ethnobotanydp/index
	India -MEDFLOR (Andrha Pradesh)	www.biomedexperts.com/MEDFLOR
	NATTS	cdrilk@sirnet.ernet.in
	INMEDPLAN	http:/ece.iisc.ernet.in/ernet-members/frlht.html
	AYUSH	www.ccras.nic.in/
	TKDL (CSIR)	htp://www.indianmedicine.nic.in
	Indonesia	www.oybkuc,uastate,edy/~CYBERSTACKS/hyb.r.2htm
	Papua New Guinea	Wau Ecology Institute Herbarium
	Madagascar	www.luneroughe.org/ilerouge/produits/prod01.e.htm
	Malta	Royal University of Malta, Msida, Malta
	Samoa	www.dittmar.dusnet.de/english/
	Russia (FLORIN Medicinal Plants)	www.florin.ru/eng
	Thailand (Medplant Pharmdatabase)	www.medplant.mahidol.ac.th/index.asp
	Tibet	www.home.t-online.de/home/5200978994-001/yuthog/frameset/plants.html
	Turkey (FLOTURK)	http://www.anadolu.edu.tr/anadolu/tbam/index.html
Ethnic Groups	Australian Aboriginal	http://www.anbg.gov.au/aborig; www.scribd.com/.../CMKb; www.chem.mq.edu.au/~jjamie/ethnopharm.htm.
	Canadian Gwich'in	http://gwichin.ca/
	Maya of Central America	www.ecosur.mx
	Quijos-Quichua Shamen of Andes	www.public.iastate.edu/~cbutter/ethnofra.htm
	Native American & First Nations of North America	Herb.umd.umich.edu
U.S. Government	ARICOLA (Agriculture)	agricola.nal.usda.gov/
	Phytochemical & Ethnobotanical Database	www.ars-grin.gov/duke/plants.html
	IBIDS (Dietary Supplements)	ods.od.nih.gov/health_information/ibids.aspx
	USPTO	www.uspto.gov
American Academy of Science	TEK*PAD	ip.aaas.org

doi: 10.4314/ajtcam.v8i5S.12

and its organic solvent fractions with IC50 of 1.7, 2.6 and 2.9 10μg/mL for dichloromethane, acetone and ethanol extracts, respectively (Benoit-Vical et al, 2000). Cross sensitivities have also been demonstrated for a Colombian Annonaceae species, selected for their ethnobotanical uses or chemotaxonomic relationships. These were inhibitory against chloroquine sensitive and resistant strains of *P. falciparum* and promastigotes of three *Leishmania* species and epimastigotes of *Trypanosoma cruzi* (Osorio et al., 2007).

Ethnobotanical dereplications have also indicated the many novel compounds with the potential of being utilized for the treatment of tuberculosis were used to treat respiratory or other antiinfective ailments. Unfortunately these structures were published before sufficient work was conducted to verify their bioreactive spectra or clinical potentials (Okunade and Elvin-Lewis, 2009).

Altogether these examples indicate the value of utilizing both ethnobotanical dereplications and chemotaxonomic relationships for identifying new therapeutic leads.

Dereplication methods are useful in identifying which aspects of a pharmacopeia are unique, or known throughout the region as well as elsewhere. This is an essential aspect when dealing with issues of benefit sharing and claims of ownership. While initially these data might be perceived as circumscribed traditional knowledge (TK), additional dereplications may prove otherwise and thus designate these as regional or collective knowledge (CK). In order to protect any TK during this process herbarium labels may indicate that any ethnomedical information linked to the specimens are only available through access to a defensive databases (Elvin-Lewis, 2006, Elvin-Lewis 2007a). However, when this information is already in the public domain ethnobotanical dereplications can be accomplished by referring to secondary data found in published material, on herbarium sheets, or part of relevant electronic journals and data-bases etc. Specific data bases relevant to Ethnobotany and use of Medicinal Plants are cited in Table 1. In addition, there are a number of tertiary resources, which are available only on CD-ROM or other types of offline electronic publications and these are listed in Table 2. Regardless of the source it should be emphasized that there is likely to be a wide variation in the value of this type of information with more credence given to those data, which have been scientifically validated and published in peer reviewed journals.

Numerous databases associated with the use and value of medicinal plants can be elicited through referring to lists provided by the Alternative Medicine Resources at http://www.pitt.edu/~cbw/database.html. as well as others cited by Thomas (2003).The current Medicinal Plant Database of K.K. Bhat (http://joyppkau.tripod.com/-WordFiles/MP.doc) provides considerable detail concerning the nature of these sites. Several additional databases associated with Complementary and Alternative Medicine (CAM) can be found by eliciting http://www.rosenthal.his.columbia.edu/Databases.html. or others cited by Wooten (1997) and Allias et al. (2000).

Of significant value are those databases that include sources acquired world wide, such as the United Kingdom's, EthnobotDb, and SEPASAL(Survey of Economic Plants for Arid and Semi-Arid Lands) maintained by the Royal Botanic Gardens, Kew. The latter is limited to those plants growing in dry tropical and subtropical climates. Also useful for medicinal foods is the British, *Plants for a Future* database. An excellent resource for scientific studies related to medicinal herbs is the American-based website HerbMed® developed by the Alternative Medicine Foundation. Under development is the Japanese database, ETHMED, which is being compiled at the Takko Kaiseki Center (Analytical Research Center for Ethnomedicine) and the Institute of Wakan-Yaku (Traditional Sino Japanese Medicines) associated with Toyama University. This project involves providing comprehensive biological, chemical and taxonomic data based on their world wide medicinal plant herbarium collections and the 20,000 crude "drug" samples held at the Museum Materia Medica of the Institute.

Table 2: For Fee, Membership, eBooks and CD Rom Format Databases: Alternative Medicine, Medicinal Plants

Category	Organization	Address: URL, Web Address or CD-ROM
Africa	AHA	https://apps.who.int/hlt/otherdata/English/african.htm; CD-ROM
Asia-Pacific	AHEAD	3 disc CD-ROM
	APINMAP	CD-ROM; http://www.pchrd.dost.gov.ph/apinmap/
Caribbean & Latin America	TRAMIL	www.funredes,org/tramil/english/ CD-R0M and Electronic Books
France	PASCAL	http://www.inist.fr
	PLANTES MEDICINALES	CD-ROM
Korea	TRADIMED	CD-ROM
United Kingdom	CABI Medicinal Plant	www.cabi.org
	Hom-Inform	hominform.soutron.com/
	GREEN MEDICINE (Chinese Herbal Medicine)	Hopkins Technology CD-ROM
U.S.A.	HerbMedPro™	www.herbmed.org/members/
	Biosis Previews	http://www.biosis.org and CD-ROM
	MANTIS	www.healthindex.com/
	HERBALIST	http://www.hoptechno.com/ and CD-ROM
	TCM & Pharmacology	http://www.hoptechno.com/ and CD-ROM

doi: 10.4314/ajtcam.v8i5S.12

Other comprehensive databases of specific regions, countries or populations may represent general compellations of an individual, specific group or organization. Their usefulness is variable because of the quality and quantity of data presented. Utilization of these may be free or require a fee or membership to an organization.

Regionally based databases include those assembled from the traditional medicinal systems of Asia as generated by World Intellectual Property Organization (WIPO) member states of China, India and Korea. PROSEA (Plant Resources of South-East Asia) is a collaborative effort of participating organizations in Indonesia, Malaysia, Papua New Guinea, Phillipines, Thailand, VietNam with publishing offices in Wageningen, Netherlands). For Africa, Prelude Medicinal Base of African ethnobotany and ethnomedicine encompasses information used by humans and for veterinarian purposes gleaned from the colonial period until today. These data are correlated with current information related to taxonomic and biomedical research. PROTA, available in either English or French is another database, which identifies useful plants of tropical Africa. Medicinal plants of the Caribbean and Latin America can be found in TRAMIL which has generated an ebook on the Caribbean pharmacopeia in addition to a CD-ROM on conservation. Some databases attributed to uses in the Peruvian Amazon, the greater southwest and South Florida of the U.S. may be limited in scope.

Those of national origin include Bangladesh, Brazil, Brunei, China (Chinese Medicinal Material Research Center (CMMRC), India (MEDFLOR, NATTS, INMEDPLAN,AYUSH,TKDL), Hawaii, Indonesia, Papua New Guinea, Madagascar, Malta, Samoa, Russia (Florin Medicinal Plants), Spain, Thailand, Tibet and Turkey (FLOTURK).

Additional sources may be restricted to circumscribed groups such as the Gwich'in of Northern Canada, the Aboriginal people of Australia, Maya of Central America, the Quijos of the Andes, or those in India that practice specialized medicinal systems such as Aryurveda (Unnikrishnan, 2005) or AYUSH (Aryurveda, Yoga, Unani, Naturopathy, Siddha and Homeopathy). Alternately, the Native American Ethnobotany Database describes uses of indigenous Amerindian tribes/1st Nations in both the U.S. and Canada, respectively.

Noteworthy among the free databases generated by the U.S. government is one for agriculture called ARICOLA with over 3 million records of post 1970 publications and those found in the Phytochemical and Ethnobotanical databases compiled by J. Duke. Others related to medicinal plants such as The International Bibliographic Information on Dietary Supplements (IBIDS) (a PubMed dietary supplement subset), the U.S. Patent and Trade Office (USPTO). Additional American private or institution generated databases include HerbMed^{TM} , the online Archive of American Folk Medicine and the Traditional Ecological Knowledge Prior Art Database (TEK*PAD) concerning indigenous knowledge and plant uses, which is maintained by the American Association for the Advancement of Science.

Specialized for fee databases include in the U.S. Biosis Previews, which is considered the world's largest database on medical and biological subjects with over 12 million citations. Access is available on line or through CD-ROM distributors. In addition membership fees to the American Botanical Council are required to elicit HerbMedPro^{TM},a more professional version of HerbMed$^{®}$. This is an interactive herbal database developed by the Alternative Medicine Foundation linking scientific evidence underlying the use of herbs for health. Another fee based database is called MANTIS (Manual, Alternative and Natural Therapy Index), which utilizes ChiroACCESS;(the online Chiropractic community), Dialog Corporation, Health Index and OVID Technologies, Inc. Currently it cites about 417,000 references obtained from over a thousand, mostly peer reviewed journals.

United Kingdom-based for fee databases include the CABI Medicinal Plant Database, which comprises aspects of human health and nutrition, the Hom-Inform Database produced by the British Homeoepathic Library at Glasgow Homoepathic Hospital and the Society of Homeopaths, Treuherz Collection, and the Index to Chiropractic Literature. In France, the large multilingual bibliographic data base, PASCAL compiled by the Institute de l'Information Scientifique et Technique (INIST) can be accessed both online and offline and cites over 500,000 records in science and technology.

Regional for fee or membership databases, may also be for sale in a CD- ROM format. In Asia, these include the Korean and Chinese TradiMed, The Chinese TCM Database and Chinese Materia Medica, the Japanese JICSR-EPlus, and FRLHT (Bio-informatics on Medicinal Plants and Traditional Knowledge) based in India. The latter is a compilation of 7,500 botanical names associated with local traditional uses. The UNESCO-sponsored project, The Asian Pacific Information Network on Medicinal and Aromatic Plants (APINMAP) is a consortium of countries (Australia, People's Republic of China, India, Indonesia, Republic of Korea, Malaysia, Nepal, Pakistan, Papua New guinea, the Philippines, Sri Lanka, Thailand, Turkey and Vietnam) with a Secretariat based in the Philippines. Its database contains bibliographic and factual information on medicinal plants in addition to contact information and the activities of member scientists conducting research in this discipline. Another Asian collaborative effort called the Asian Health, Environmental and Allied Databases (AHEAD) between India, Thailand, Philippines, Malaysia, Singapore and Bangladesh is sponsored by the International Development Research Center of Canada. Coordinated in New Delhi by the National Institute of Science Communication (NISCOM) a 3 disc CD-ROM series has been developed on the Environment, Health and Wealth of Asia. Incorporated into the latter disc is the entire *Medicinal and Aromatic Plants* bibliographic database in addition to the plant and mineral resources listed in the *Wealth of India*. The African Health Anthology, produced by the National Information Services Corporation (NISC) South Africa, represents a compilation of comprehensive databases related to African health issues from 1924 to the present, including those related to alternative and complementary medicine. Traditional Medicinal Plants of the

doi: 10.4314/ajtcam.v8i5S.12

Caribbean and Latin America (TRAMIL) is an interdisciplinary collaboration of Caribbean institutions to study their traditional popular medicines. Within this context they have published in electronic book form both English and Spanish versions of the Caribbean Herbal Pharmacopeia 2nd Ed (Germosén-Robineau, 2006) in addition to a booklet Plantas Medicinales Caribeñas para la Atención Primaria (Cuba) and a CD-ROM on conservation. Two multimedia CD-ROMs are available from Hopkins Technology of Hopkins, Minnesota. *The Herbalist* by David Hoffman is an encyclopedia of western herbal medicine and cites the uses of 170 plant species and the *Traditional Chinese Medicine and Pharmacology* describes the use of 322 medicinal herbs.

Access to medicinal traditional knowledge in other countries will depend if these have been evolved from secondary information or as primary data are placed into defensive databases with for fee and restricted access as is the BioZulua of Venezuela (Elvin-Lewis 2006, Elvin-Lewis, 2007a). Whatever the source, utilizing these whenever possible and practical is invaluable to understanding the relative value of a particular ethnic group's medicinal plant knowledge and whether or not these data are either unique or known elsewhere.

Botanical Dereplication

Most countries with national herbaria are useful reference sources for information regarding the nature and distribution of taxa within a nation and adjacent territories. Moreover large herbaria with collections ranging from about 5-9 million collections are likely to have comprehensive representations from around the world and especially from countries where their interests are now presently, or have been in the past. These include in order of the number of specimens in their collections the Muséum National d'Histoire Naturelle (P), Paris; Royal Botanic Gardens, Kew (K), London, England; New York Botanical Garden (NY), New York, USA , the Komarov Herbarium (LE), St. Petersburg, Russia Conservatoire et Jardin botaniques de la Ville de Genève (G), Geneva Switzerland, The Nationaal Herbarium Nederland (NHN)(L, U, WAG); The National History Museum formerly The British Museum of Natural History (BM); London, England the Missouri Botanical Garden (MO) St Louis MO, USA, and Harvard University Herbaria (GH,A, AMES,ECON,FH), Cambridge Mass, USA. In addition, the United States National Herbarium (BCI) at the Smithsonian National Museum of Natural History (DC) with its 4.5 million specimens is particularly rich in type specimens (90,000). These institutions are also likely to have specialist botanists that can aid in the determination of difficult to identify or unknown taxa. Reference to their collections and current taxonomic determinations of this material can be made by accessing their websites in Table 3.

Reference to the International Plant Names Index (www.ipni.org/) would also be helpful. Access to the professional botanical literature for additional check lists, floras, and monographs etc. is also valuable for understanding what is known botanically regarding the species in question, if they are taxonomically defined, and which taxa are more closely allied to them. Another important resource for ethnobotanical and ethnomedical information are citations on herbarium labels, albeit often annotated by individuals of limited medical knowledge.

Table 3: Website/URL Addresses of Botanical Institutions

Institution	Web Address /URL
Conservatoire et Jardin botaniques de la Ville de Genève	www,ville-ge.ch
Harvard University Herbaria	asaweb.huh.harvard.edu:8080/databases/specimen_index.html).
Komarov Herbarium	www.biodiversitycollectionsindex.org/collection/view/.../15844
Missouri Botanic Garden's Tropicos	http://tropicos.org
Muséum National d'Histoire Naturelle	www.biodiversitycollectionsindex.org/collection/view/.../15763
Nationaal Herbarium Nederland	data.gbif.org/datasets/resource/1085
National History Museum	www.nhm.ac.uk/research-curation/collections/.../index.html
NY Botanic Garden's C.V. Starr Virtual Herbarium	www.nybg.org/bsci/hcol
Royal Botanic Gardens, Kew	www.kew.org/collections/herbcol.html
Smithsonian National Museum of Natural History	botany.si.edu/dcflora/dcherbarium.htm

doi: 10.4314/ajtcam.v8i5S.12

Biomedical/Pharmacognosy Dereplication

Prior to the development of medical and biological library search engines in the 1950's these types of studies were particularly time consuming and depended on the library acquisitions available to the investigator. While clearly biomedical research has evolved since then, these older acquisitions are still an invaluable resource for those wishing to identify the basis for some studies that are now being conducted. A useful way to identify these types of relevant references is to look at current publications for these types of early citations. Be aware that the titles themselves may be misleading as to the types of plants or plant parts that have been studied or the nature of bioassays that have been applied.

Today a number of major biomedical bibliographic databases exist that are invaluable to the biomedical investigator (Table 4). Of these, Pub Med of the National Library of Medicine (NLM), USA is perhaps the most utilized, since it is free and available by public web access. Going back to 1950, the database contains over 15 million references from 5,000 journals in 37 languages. Keywords are indexed as MeSH terms. Also the official publication of Pharmacognosy network provides free access to Caspur, DOAJ, EBSCO Publishing's Electronic Databases, Excerpta Medica / EMBASE, Google Scholar, Index Copernicus, OpenJGate, PrimoCentral, ProQuest, SCOLOAR, SCOPUS, SIIC databases, Summon by Serial Solutions, and Ulrich's International Periodical Directory. Also a free ebook pdf of Pharmacognosy theses is useful in finding unpublished information on these subjects.

Several subscription-based, for fee online databases also exist, for example, Embase produced by Elsevier Science BV of the Netherlands incorporates extensive data on both pharmacological as well as biomedical and drug research and also allows access to selected MEDLINE records. The Qigong Database provides 2,050 citations on various aspects of clinical and experimental research. Also within this category is the relational database, NAtural PRoducts ALERT (NAPRALERT), which is described in full under the section on Chemistry.

Table 4: Major Website/URL Addresses on Biomedical/Pharmacognosy Subjects

Type	Web Address or URL
PubMed	www.ncbi.nlm.nih.gov/pmc/
Pharmacognosy network	www.phcogres.com
Unpublished theses and dissertations on pharmacognosy	www.ebookpdf.net/database-of-pharmacognosy-thesis ebook.html .
EMBASE	Embase.com
Qigong	www.qigonginstitute.org/html/database.php
NAPRALERT	www.napralert.org/

Table 5: Free Major URL or Website Addresses of Clinical Studies

Type	Web Address or URL
CUGH	www.cugh.org
CenterWatch	www.centerwatch.com
Cochran Collaboration	www.cochrane.org
Cochran CAM Field	www.compmed.umm.edu/cochrane_about.asp
U.S. Government	www.clinicaltrials.gov/
CAM	www.cam.nih.gov/research/clinicaltrials/factsheet/clinicaltrials.pdf
CRISP	http://report.nih.gov/crisp/
NLM	www.nlm.nih.gov/news/expanded_clinicaltrials.html
FDA Poisonous Plant Database	www.accessdata.fda.gov/scripts/plantox/index.cfm
PUBMED	http://www.ncbi.nlm.nih.gov/entrex/query.fcgi
Bandolier	www.medicine.ox.ac.uk/bandolier/bandlink.html
CISCOM	www.rccm.org.uk/ciscom/CISCOM_intro.aspx
DATADIWAN	www.datadiwan.de/index_e.htm

doi: 10.4314/ajtcam.v8i5S.12

Clinical Studies

Information regarding relevant clinical studies can be elicited by accessing either free (Table 5) and "for fee" databases (Table 6). For individuals wishing to determine the global or regional distribution of specific diseases, referral to national Communicable Disease Centers and/or the World Health Organization websites are reliable resources. Regional medical centers and/or national medical schools are likely to be helpful as are certain University Medical Schools or Institutes with interests in global medicine such as those, which are apart of the Consortium of Universities for Global Health (CUGH).

Free databases describing clinical trials include the global CenterWatch which is categorized according to therapeutic and geographic regions and reports ongoing industry and government-sponsored studies. In the U.S. the Cochrane Collaboration, and the Cochrane CAM Field maintains and updates a registry of randomized controlled trials; US government-based databases include the Complementary and Alternative Medicine (CAM) and the National Institute of Health's, NLM Databases accessed through PubMed, ClinicalTrials.gov, and CRISP (Computer Retrieval of Information on Scientific Projects) describing the National Institutes of Health (NIH) sponsored biomedical research on natural medicine, herbal medicines, and dietary supplements and the Poisonous Plant Database of the U.S. Food and Drug Administration (FDA). In the United Kingdom, Bandolier is a tertiary compilation of evidence-based database describing published research and clinical trails on specific treatments whereas the CISCOM Database (The Centralized Information Service for Complementary Medicine) represents a large database regarding complementary therapies and clinical trials. In Germany, the holistic medicine database, DATADIWAN (Pattienteninformation fur Naturheilkunde: Patient information for natural therapies) links research institutions and organizations worldwide with over 6,000 bibliographic entries and addresses.

The for-fee database, AMED (Allied and Complementary Medicine Database) is produced by the British Library Health Care Information Service and contains primarily European references including many not found in MEDLINE or EMBASE. For fee access is also required for The Natural Standard, which is a global collaborative endeavor highlighting evidence-based, consensus-based, and peer-reviewed data on herbal medicine, supplements, conditions and alternative modalities. An interactive database on the *Poisonous plants in Britain and Ireland* is available in CD-ROM form.

Additional alternative medicine resources which are likely to illustrate the therapeutic value of medicinal plants include ACUBASE by the Bibliothèque Universitatire de Médicine de Nîmes with over 17,000 French and English references, including conference proceedings on acupuncture and Traditional Chinese Medicine (TCM), AltHealthWatch of EBSCO Information Services.

Chemical Dereplication and Patent Databases

Within the context of utilizing chemical dereplication it is essential to understand that a herbal remedy may consist of plants containing one or more compounds with complementary or different activities or a group of plants taken together (polyherbal) or sequentially to optimize the effects of the treatment. Variances in the chemical composition of each plant can depend upon the climate and soil compositions in which it was grown, the season in which it was harvested, the method of harvest and preparation, as well as how it was stored and prepared. Moreover within the range of its distribution one species may be represented by a number of chemotypes, which can vary in the proportion of bioreactive component/s such as the fraction of bioreactive to non reactive isomers they might contain. Obviously these inconsistencies would be directly related to how these chemotypes are valued in a particular region. Chemical analysis is apt to yield a number of bioreactive ubiquitous compounds along with others that are unique to the species or shared among closely allied species or genera. Understanding these possibilities is useful in identifying particular taxa that may have greater therapeutic potential or others that serve sourcing needs.

On the whole most medicinal plants, in the context of traditional use, are valued because they are moderate in potency and toxicity. When toxicities are known, parameters of use, including the nature of the formulations are often carefully delineated to avoid any problematical outcome elicited by over-dosage. Usually these medications are taken for circumscribed short periods of time to treat acute illnesses rather than for prolonged periods needed for chronic conditions. They rarely meet the criteria for pharmaceutical development because their bioreactive compounds are likely to be structurally complex containing numerous chiral centers in addition to representing mixtures of active and non reactive isomers. It is commonplace for one plant to contain a number of related compounds, which can synergistically or in complementary ways elicit the optimal therapeutic goal. Within the commercial arena of Western herbal medicine these medicinal plants are sometimes standardized by the chemical "fingerprinting" of their bioreactive ingredients into reliable phytopharmaceuticals. Only rarely is a candidate identified with pharmaceutical potential such as being highly potent, low in toxicity and molecular weight, structurally simple, user friendly, and if necessary readily semi-synthesizable to enhance its therapeutic value. Of course if development is to go forward, issues of availability must be rationally addressed such as identifying practical ways for resource management of the species itself, or identifying others with the same compound that are more easily grown or with precursor molecules that through semi-synthesis can provide the active molecule. Ideally, the pharmaceutical industry prefers those compounds that can be practically synthesized, since this method overcomes issues related to utilizing the natural resource. Another alternative method is related to the discovery that many compounds are the result of endophytic (systemic fungal) infections e.g., paclitaxel (Lewis and Elvin-Lewis, 2003). This aspect continues to be explored to ensure that bioculture can provide yields of a particular compound sufficient enough to be usefully applied.

A number of other strategies have also been proposed to achieve these goals. These not only utilize biodiversity to identify new chemical entities but are also associated with identifying additional disease-associated molecular targets so that new treatments can be realized. One useful review paper (Basso et al., 2005) describes mechanistic-based strategies to identify natural compounds from ethnobotanical and chemotaxonomic studies, which may have therapeutic potential in the treatment of malaria, tuberculosis, and chronic degenerative diseases. The authors' primary criteria for selecting natural products over those evolved through combinatorial chemistry, is because their structural diversity is more likely to identify biologically active compounds by interacting with a wide variety of proteins and biological targets. Unlike their synthetic or combinatorial counterparts they are represented by a broader distribution of molecular properties, which includes molecular size, octanol-water partition coefficients, and diversity of ring systems. This broad screening approach, which is considered cost effective, describes the evaluation of plant extracts as well as pure substances for their ability to inhibit targeted mechanisms such as pathway enzymes so as to identify those with selective toxicities related to their specific chemotherapeutic potential. Expanding on this concept is what is referred to as "reverse pharmacognosy" (from diverse molecules to plants) coupled with pharmacognosy (from biodiverse plants to molecules), which combines the use of high throughput screening, virtual screening and knowledge databases associated with the traditional uses of plants (Do and Bernard, 2004; Blandeau et al., 2010).

The use of a number of chemical databases dealing with pharmacognosy and natural product's chemistry are invaluable in understanding the therapeutic bases for any pharmacopeia (Corley and Durley, 1994). Reference to these should provide information substantiating the nature of phytochemicals of interest or others related to them. Additional studies associated with the basis of their bioreactivies toxicological profiles, or other medicinal parameters of worth are also likely to become evident.

In order to facilitate the rapid characterization of known compounds, chemical dereplications have become an important asset. To expedite the process these databases may be available for non commercial purposes in an open access format, or may require permission or use for a fee from the provider should they be used for commercial purposes. This is true of the SuperNatural database (generated by the Oxford University Press, which requires permission and/subscription from industry. Among these is a recently developed database for the dereplication of natural product mixtures in bioassay-guided protocols called NAPROC-13. Through analysis of over 6000 natural products, structural information associated with chemical substructures, spectral features, chemical shifts and multiplicities are provided. Also accessed according to the standard classification of natural compounds are searches for trivial and semi-systematic names, molecular forms, families, types and groups of compounds (López-Perez et al., 2007).

Other "for fee" databases can be accessed by academic researchers through institutional subscription. Among these is ChemnetBase representing a comprehensive structure database whereby one can elicit online versions of the *Handbook of Chemistry and Physics*, *Polymers*: *a Property Database, Properties of Organic Compounds, Combined Chemical Dictionary*, in addition to a number of subject-based Dictionaries for organic compounds, drugs, inorganic and organometallic compounds, commonly cited compounds, marine natural products, food compounds, carbohydrates, and natural products. Also accessed through this search engine is The Chapman and Hall/CRC database, which was once available in hard copy or in CD-ROM and is now updated every six months in its online version.

Chemical Abstracts markets a number of relevant databases including Scifinder Scholar, which focuses on current chemical and related biological research as well as patents and patent applications. Included within this database are numerous patent applications, which have not received full patent status. These usually represent polyherbal formulae from Asian countries. The data that are provided are nonetheless useful in identifying ways in which medicinal plants, their compounds and derivatives are being promoted. Reference to the collection of 180 databases found in the Scientific and Technical Network International (STN) provides for the rapid characterization of known compounds such as their formula weight, carbon count, structure fragments, bioactivity and taxonomy. Of these CA, REGISTRY, BEILSTEIN, SPECINFO, MEDLINE, EMBASE, JICST, and BIOSIS and NAPRALERT are most often used by natural products chemists. The latter, is a relational database from the University of Illinois, which surveys the worldwide literature on natural products and secondary metabolites and includes ethnomedical, pharmacological/biochemical, clinical studies and plant distribution studies. Its over 200,000 records encompass data from 1650 to the present, with more comprehensive coverage found between the years 1975-2003. Linked to this is DEREP (DEREPlication) which contains data on the physical constants of natural products. Additional Natural Products databases include Berdy's antibiotic database known as the Bioreactive Natural Products Database (BNPD) developed in collaboration with the U.S. National Cancer Institute. Additional for fee databases relevant to chemistry can be accessed by referring to Chemistry and Engineering Databases through Universities or similar institutions that subscribe to these products.

doi: 10.4314/ajtcam.v8i5S.12

Table 6: URL or Website Addresses of Clinical Studies: Fee or CD-ROM

Type	Web Address or URL
ACUBASE	www.acubase.org/index.asp
AltHealthWatch	http://www.epnet.com/eptech/
AMED	www.ebscohost.com/academic/amed
Natural Standard	www.naturalstandard.com/
Poisonous Plants in Britain and Ireland (CD-ROM)	http://194.128.652/publicat/titles/plants/plants.htm

Table 7: Chemical Dereplication and Patent Databases

Type	URL or Website Address
SuperNatural	http://bioinformatics.charite.de/supernatural journal.permissions@oxfordjournals.org
Chapman and Hall/CRC	library.dialog.com/bluesheets/html/bl0303.html
ChemnetBase	www.chmnetbase.com
STN	www.stn-international.de/database.html?&tx ptgsashop
BNPD	www.bio.net/mm/bio-www/1998-January/000703.html
WIPO GOLD	www.wipo.int/ipdl/en/
WTMPD	www.intellogist.com/.../World_Traditional_Natural_Medicine_ Patent_Database http://www.wtmpd.com

Throughout the nations of the world there are variances on how patent law can be applied to the utilization of natural products and their compounds as linked to traditional knowledge (Elvin-Lewis, 2006, 2007). Within this context, it is possible to identify relevant plant derived compouds or their derivatives from numerous global, regional or national Patent Databases (wiki.piug.org) (Table 7). Of these the World Intellectual Property (WIPO) database referred to as WIPO GOLD provides access to online intellectual property databases hosted by WIPO and member states. Free access is possible to The Canadian Patent Database, The State Intellectual Property Office of the People's Republic of China, the European Patent Organization, and The United States Patent and Trademark Office Patent Database. For Western and South East Asian Countries access to patents in the natural medicine/traditional field are identified through The World Traditional/Natural Medicine Patent Database. Currently it represents over 400,000 documents, which can be elicited by classification and keyword, full texts are unavailable. It also supports a chemical structure query interface as well as a Chinese medicine formula similarity search. Also available is the" for fee" China TCM Patent Database, which includes a subset of formulas from 1985 to the present in English.

Discussion

Suitable dereplications are useful in validating pharmacopeias in many ways. Numerous databases have been evolved to aid in these endeavors and should be employed in addition to other sources whenever possible. Without these references the worth of ethnobotanical data related to medicinal uses is limited at best.

For example, it is only human nature for those that still utilize and value their medicinal plants to believe that its content is uniquely circumscribed. It is therefore important that before initiating medicinal plant inventories, when prior informed consent is elicited, that those who are custodians of this traditional knowledge and the informants they designate are aware that the process will include differentiating those aspects that are novel from those that are not. This should mollify any unrealistic expectations of worth, since clearly exclusive information is likely to have greater value to them than others known generally.

From the onset it is critical to emphasize how these data will be managed during the verification process and which aspects are expected to benefit them directly. Clearly botanical dereplications are required to accurately access the identity of any medicinal plant and its relationship to other taxa that might be known regionally. By using ethnobotanical dereplications the exclusivity of certain plant remedies are likely to become evident, as are those that are more widely valued.

Understanding the spectrum of these uses is also helpful to those wishing to investigate the mechanistic and chemical basis of these remedies. If optimal results are to be achieved the application of disease-targeted assays is preferred, since these can also be used in biodirected isolations of the active compounds. Clearly the value of these results can be amplified if related plants or target diseases are tested to identify additional potential uses. Reference to the myriad of databases on these subjects is not only important in selecting the appropriate assay tools, but also in understanding the therapeutic role of compounds already isolated from related taxa. Evaluating certain remedies in the context of use is only justified once a critical need has been identified to warrant the expenditure of time and

doi: 10.4314/ajtcam.v8i5S.12

treasure. In addition to the utilization from basic science databases, reference to those describing relevant clinical studies or patents is worthwhile.

Overall it is important to emphasize that it would be a rare event to identify from ethnobotanical sources potential pharmaceutical compounds, which are novel, potent and safe. More than not, most plant remedies contain compounds that are moderate in efficacy and toxicity, and are too complex or ubiquitous to be categorized in this manner. However, there are some plants or plant mixtures which merit consideration for use as botanicals or phytopharmaceuticals. It is these approaches that are more likely to be pursued once basic studies have been completed in evaluating an indigenous pharmacopeia. It is within this context that reference to known information is so very relevant and where benefit -sharing with those that are custodians of the original traditional knowledge are more likely to be achieved.

Acknowledgements

I would like to express my appreciation to Dr. Walter Lewis for providing unpublished preliminary data elicited in our laboratories, as well as under the auspices of the ICBG-Peru Project. I am indebted to the number of U.S. government sponsored laboratories involved in the screening of plants and other substances against specific disease entities that collaborated in eliciting need preliminary data. These included NCI-AIDS screening laboratory at Camp Dietrick, Maryland, the NIAID screening laboratories for hepatitis at Georgetown University, for *Cryptosporidium* at Tufts University, and for *Toxoplasma* at the Research Institute, Palo Alto Medical Foundation under the directorships of Drs. J.Cardellina, John Gerin, Saul Pzipori and Fausto Araui, respectively. I acknowledge as well the contributions Dr. Daniel E Goldberg and his associates at Washington University School of Medicine who conducted the antimalarial screening assays during the ICBG-Peru project. The help of Dr. Will McClatchey in clarifying the Samoan descriptor for hepatitis is also appreciated as are the invaluable insights provided by Drs. Steve Caspar of the FDA, Edward Kennelly of Lehman College, SUNY and Robert McGill of the Missouri Botanical Garden who reviewed the manuscript.

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doi: 10.4314/ajtcam.v8i5S.12