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Review Article

Medicinal Plant Informatics- An Insight

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ABSTRACT: The renaissance on traditional usage of medicinal plants as drugs for various human ailments has increased interest in the search for information on plant medicinal systems. A demand by the pharma-industry on the sources and availability of the lead compounds from plants has inculcated the research across the globe. This has proportionately provided us with a wealth of data which needs a classical and a dedicated approach for easy identification. Based on this view, many different databases have emerged that contain enormous amounts of information on the phyto-constituents, biological properties of various plant species and the possible strategies that could be adopted to extract and explore these in an effective manner. Since this information is stored as mixture of online and commercial resources, identifying them become a difficult task. Hence the approach outlined in this review is useful to comprehend the surplus data available on these web resources so that any reader could be aware on the specific database as well as the information system that it carries for a better understanding and exploration in the future.

KEYWORDS: databases, exploration, medicinal plants, pharma-industry, phyto-constituents.

INTRODUCTION

In recent years, due to growing recognition of natural products and process in sustaining human and environmental health, the economic as well as environmental importance of the medicinal plant resources have increased tremendously. Medicinal plants are used at the household level and by the practitioners of classical traditional systems of medicine such as Ayurveda, Chinese medicine and the Japanese Kampo. A report by an "All India Ethno-biological Survey" carried out by the Ministry of Environment and Forests, Government of India, revealed that there are over 8000 species of plants being used by the people of India alone for its wide application in pharmaceutical, cosmetic, agricultural and food industry (http://www.hindu.com/herbalcerpa.org/hn.2.5.06.c.doc). A survey by World Health Organization (http://www.idrc.ca/en/ev-21245-201-1-DO_TOPIC.html) revealed that over 80% of the worlds population (4.3 billion people) rely upon traditional plant-based systems of medicine for primary health care, as they are non-toxic without notable side-effects and are easily available at affordable prices. Allopathic medicine also owes a tremendous debt to medicinal plants as one in four prescriptions filled are either a synthesized form of a plant constituent, or derived directly from plant materials.[1]

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Plants may be described as biosynthetic laboratories for a multitude of compounds including glycosides, alkaloids etc., which exert physiological and therapeutic effects. Among the plants that furnish products for the crude-drug trade are common weeds, popular wild flowers, and important forest trees. The data available from International Trade Centre reveals that the import of plant materials from India has increased from USD 52.9 million to USD 71.2 million, with a steady annual growth rate of approximately 5-7% during the most recent decades.[2] This indicates several major global opportunities for India, a country unrivaled in terms of diversity of medical systems and practices, in addition to being a major storehouse of biological diversity, with 2 of the 14 megabiodiversity areas of the world located within its borders.[3]

Role of herbs as a potential target for human dysfunctions

With the onset of research in medicine, the biological activities of herbs have been realized and are reported to contain active principles, which are responsible for curative action against pathogens and thus are therapeutically active.

Notable examples include aconitine, atisine, lobeline, nicotine, strychnine, digoxin, atropine and morphine. Moreover, some herbal products such as *Artemisia annua* (artemesinin),[4] *Taxus baccata* (taxol) and *Silybum marianum* (silymarin),[5] *Hypericum perforatum* for depression (hypericin and hyperforin) and *Ginkgo biloba* for tinnitus, *Chrysanthemum parthenium* for migraine (sesquiterpenes lactones called parthenolides) have established their remedial activities by controlled studies. Likewise, plants such as *Allamanda cathratica* [allamandin], *Elephatopus elatus* [elephantpoin], *Helenium autmnale* [helenalin] *Vernonia hymenlepis*, *Heliotropium indicum* [Indicine-N-oxide], *Daphne mezereum* (mezerien) and *Stereospermum suaveolans* [laphacol] are proven to have significant tumor inhibiting effects.[6]

The effects of medicinal herbs on the immune system are evidenced based on the scientific knowledge. Plant polysaccharides have been reported to stimulate immune responses and anti-tumor effects. Research on anti-inflammatory and chemo-preventive effects of medicinal plants are gaining increased interest because inflammation serves a protective function in controlling infections and promoting tissue repair. However, uncontrolled and excessive inflammation results in tissue damage and diseases including rheumatoid arthritis, inflammatory bowel disease, psoriasis, cancer etc. There are many researches undertaken to identify anti-inflammatory phytocompounds /extracts by targeting activities of pro-inflammatory cytokine promoters and inflammation-induced transcription factors (NF-kB) especially from *Lithospermum erythrorhizon, Bidens pilosa* and species of *Echinacea* (http://abrc.sinica.edu.tw/E_www/).

Phyllanthus amarus has been used as a traditional medicine to treat jaundice, diabetes, gonorrhea, irregular menstruation, tachycardia, dysentery, spasmodic cough, itchiness, arthritis, otitis, swelling, skin ulcer and weakness of male organ. Infusion of their leaves, stem and roots are used in Brazilian folk medicine for treating kidney problems, intestinal infection, liver problems and for inducing labour, in the treatment of oedema, feverish pain, sore throat, female sterility, oliguria and vaginitis.[7] In India and in numerous other parts of the world, its aqueous preparations are used as a safe tonic along with native food to eliminate waste from the body, restore the activity of the liver and build up blood and innate defense system.[8] A number of plant derivatives such as michellamine-b (*Ancistrocladus korupensis),*[9] calanolide-a (*Caulophyllum langigerum*),[10] costatolide-a (*Caulophyllum teymani*),[11] prostratin (*Homalanthus nutans*) and concurvone (*Conospermum* sp.)[12] have been employed in the African countries as a suitable cure for HIV/AIDS. Furthermore, its extracts containing tannins, phenols and other phytochemicals have been associated with antimicrobial properties and protective effects on the acetaminophen induced hepatotoxicity in rats.[13] Indeed, this continuous research on medicinal plants has provided us enormous amount of data , that could be surfed under many different databases, depending on the properties or its function.

Diabetes mellitus (the fifth deadliest disease of the world) is reported to affect approximately 20.8 million people worldwide, amounting to 7 % of the world's total population. Of these, about 6.2 million people are undiagnosed (http://www.cdc.gov/diabetes/pubs/estimates05. *Ajuga reptens*, *Galagea officinalis* (galagine), *Bougainvillea spectabilis* (pinitol),[14] *Momordica charantia* (chirantin),[15] *Gymnema sylvestre* (gymnemic acid)[16] and extract of *Tecoma stans* (tecomonine)[17] are some medicinal herbs that have shown effectiveness in non-insulin dependent diabetes. Arthritis is another disorder where no satisfactory answer has yet been discovered by modern medicine., Whilst allopathic anti-arthritis drugs exist, these all have undesirable side effects. In contrast, *Commiphora mukul* (guggulsterones), *Boswellia serrata* [boswellic acid],[18] *Withania somnifera* (withanolides),[19] *Ruscus aculeatus* (ruscogenin), *Harpagophytum procumbens* (harpagoside)[20] are some prominent plants reported with anti-arthritic activity which appear promising as natural therapeutics. The hepatoprotective action of certain botanicals also deserves attention. *Sedum sarmentosum* (sarmentosin), and *Schisandra chinensis* (waweizichun and schisantherin)[21,22] have shown an ability to lower the elevated levels of some liver enzymes during hepatitis. Similarly, *Croton sublyratus* (plaunotol)[23] has been reported to have wide spectrum anti-peptic ulcer action.

The role of antioxidants is receiving immense recent attention and research has shown a number of herbal derivatives as an excellent antioxidants. *Bacopa monnieri* containing bacosides A and B act as a strong antioxidant, reducing several steps of free radical damage[24] *Coleus forskohlii* (forskolin), Grape seed (proanthocyanidins), *Camellia sinensis* (polyphenols),[25] *Huperzia serrata* (huperzine) and *Pinus maritima* (Pycnogenol),[26] *Borago officinalis* (gamma linoleic acid), *Vinca minor* (Vinpocetine)[27] and *Enicostemma littorale*[28] are a selection of plants with potential antioxidant properties.

Transition from Biotechnology to Bioinformatics- an efficient measure of characterization:

Plant genomes vary tremendously in genome size, chromosome number and chromosome morphology.[29] One of the most direct ways of dissecting complex biological processes in plants is the generation and analysis of genetic mutants which is viably performed by T-DNA activation tagging where random insertion of a T-DNA carrying constitutive enhancer elements causes transcriptional activation of flanking plant genes. Subsequently the activated plant gene is rescued from saluted mutant transformants for further functional analysis. In addition to measuring mRNA levels of sizable gene collections, it has been adapted for genotyping,[30] screening for transposon insertions[31] and proteinprotein or proteinligand interactions.[32] Although the physiological changes in plant development are due to a number of genes, the molecular methods such as reverse transcription PCR and microarray analysis allows only analysis of rare or special cells.

BIOINFORMATICS AS A POTENTIAL EXPLORER OF PLANT FUNCTIONS:

Role of genomics

Genomics have developed a wide range of tools and bioinformatics have revolutionized gene expression analysis especially for genome wide discovery of genes to decipher their function and to characterize them by simultaneous profiling methods for indefinite genes that are represented by hundreds of tissue samples exposed to different treatments or conditions associated with the experiment.[33] Thus, it unravels the networks of coordinated gene expressions, which allows the genome of an organism to respond dynamically to physiological and environmental changes, permitting a deeper understanding of how the transcriptome functions. In recent times, perhaps much of the excitement surrounding genomics is the promise that genomics provide a systematic discovery of gene by cloning and characterizing genes controlling agronomic traits. Relating individual genes and alleles to agronomic traits were once considered a challenge but today, many statistical methods including association analysis employing molecular biology and bioinformatics relative to natural variation and candidate genes with agronomic phenotypes in plants, have provided very high resolution and evaluated a wide range of alleles rapidly.[34, 35]

Quantitative Trait Locus (QTL) analysis has been a mainstay approach for obtaining a genetic description of complex agronomic traits for plants. QTL gives information on the structure, organization and gene functions of plant genomes, including the development of high density molecular marker maps.[36] Thus, a myriad of information on a individual gene that regulates a particular pathway and Expressed Sequence Tags (ESTs) or the fragments of mRNA that dynamically identifies new proteins expressed in a particular cell (or under particular circumstances) [37] help in evolving the physical maps. With the accessibility to bioinformatics tools, this may identify and address the problems associated with agronomic traits. Thus the plant research community now, with the substantial support of full genome sequences of both dicot (*Arabidopsis thaliana)* and monocot (*Oryza sativa L.*) models have attempted to investigate the cloning and characterization of QTLs for many plant systems. *Lycopersicon* sp. has revealed the identification of fw 2.2 QTL (major QTL fruit weight in tomato) which was found to be a regulatory protein encoding a RAX family protein. Similarly, in ricethe Hd1 locus was identified to encode a zinc finger domain protein which is presumed to be a transcription factor with similarity to the photoperiod sensitive gene CONSTANS of *Arabidopsis*. On the other hand, Hd6 locus encodes for a subunit of protein kinase CK2Y that was believed to function in the signal transduction pathway leading to flowering. [38]

Proteomics as a functional genomic tool

Compared to the genome which is an almost unchangeable part of an organism, the transcriptome and proteome are highly variable, depending on the conditions and activities of the organism. It complements transcriptomics by providing information about the time and place of the protein synthesis and accumulation, as well as identifying those proteins and their post-translational modifications (PTMs). It helps the networks involved between gene products and metabolites, by studying the biosynthetic pathways leading to secondary metabolites, where many enzymes are involved and often work in close collaboration to catalyze cascades of reactions. Hence proteomics is as a big task, where, many studies have been concentrated to establish the proteomes of model plants eg., *Arabidopsis thaliana,*[39] the legume *Medicago truncatula,*[40] rice,[41] tobacco[42] and maize.[43]

However Microarray technology (also called the transcriptome) is the dynamic link between the genome and the proteome where the entire genome of several organisms could be fully sequenced, thus becoming increasingly useful in measuring expression levels of a large number of genes at the levels of mRNA.[44] They have been used for a variety of studies including developmental controls,[45] biotic and abiotic stress response,[46] nutrient response[47] and gene family surveys.[48] Hence, Genome sequencing efforts have uncovered a large number of open reading frames (ORF), whose functions could be predicted based on the homology. However, in many cases ORF sequences alone fail to provide any clue with respect to their function. Therefore, functional genomics approaches in plants have been necessitated (i) virus-induced gene silencing (VIGS) in which post transcriptional gene silencing (PTGS) mechanism are adopted by the use of several tobacco mosaic virus (TMV)[49] (ii) potato virus vector X(PVX) (iii) tomato golden mosaic virus (TGMV) and (iv) tobacco rattle virus (TRV)[50] are employed to target and degrade RNA in a sequence specific manner which silences the expression of a gene in the whole plant so as to determine its biological function and RNA interference (RNAi).[51]

In addition, t proteome analyses have been used in medicinal plants studies globally (Table 1) which focus on diverse and agronomically or pharmacologically important species mainly: (i) providing markers for genetic and phylogenetic analysis relative to the environmental conditions, with the aim to identify candidate genes for traits like drought or

Table 1: Globally available medicinal plants databases.

Name of the database	Information retrieval system	Important constituents
Plants For A Future	http://www.pfaf.org/user/default.aspx	A resource and information centre for edible and otherwise useful plants
American Herbal Pharmacopeia	http://www.herbal-ahp.org	Mostly organizational information: status report on monographs, how to get involved, contributor information,
American Herbal Products Association	http://www.ahpa.org	Promotes responsible commerce of products which contain herbs and which are used to enhance health.
Botanical.com	http://www.botanical.com	educates/informs on herbal medicine and related issues.
CAB Database of Plant Science	http://www.cabi.org/	Contains abstracts of internationally published scientific research literature.
Central Institute of Medicinal and Aromatic Plants	http://sunsite.sut.ac.jp/asia/india/jitnet/india/csir/cimap.html	Research into plant based products and their processes.
Chinese Plants and Medicine	http://flora.huh.harvard.edu/china/	
Dr Duke's Phytochemical and Ethnobotanical Database	http://www.ars-grin.gov/duke/	Includes medicinal plant searches, chemical searches, and ethnobotanical searches
Herb Research Foundation	http://www.herbs.org	The Herb Research Foundation (HRF) is a nonprofit research and educational organization focusing on herbs and medicinal plants. They help to educate the press, the public, scientists, doctors, legislators and the herb industry about all aspects of botanicals.
Herbs and Aromas	http://world.std.com/~krahe/	Good terminology and preparations information
Medicinal and Poisonous Plant Databases	http://www.biologie.uni-hamburg.de/b-online/ibc99/poison/	Includes information lists on herbs, chemistry, and molecular modeling. Some major sections include pharmacognosy, extensive mistletoe information, and poisonous plants. There are interesting links to resources on Cancer and HIV
National Center for the Preservation of Medicinal	http://www.ncpmh.org	Informative and interesting site with information on biodiversity issues, herb trivia, conservation practices, the Center, and even something for children.
Plantas Medicinais	http://www.ciagri.usp.br/planmedi/planger.html	to create a database of the medicinal plants of Brazil
U.S. Pharmacopeia	http://www.usp.org	The USP promotes public health by establishing and disseminating officially recognized quality standards and authoritative information for the use of medicines and other healthcare technologies by health professionals, patients, and consumers.
A database of medicinal plants of Assam	http://www.assamplants.com	Ethanobotanical information intended for research and conservation only.

pathogen resistance;[52] (ii) for studying the transcription factors which are emerging as a powerful tool that allow the simultaneous activation of multiple genes in a pathway, overcoming the limitations of flux constraints, metabolite channeling and homeostatic control and metabolic pathways[53] (iii) for understanding and exploiting secondary metabolism[54] and iv) for nodulation of plants by nitrogen fixing bacteria.[55]

Thus, several different sources serve as public distribution points for genomic and proteomic resources of plants and are supported to the public as stock centers (Table 1 and 2). The relationship between bioinformatics and medicinal plants have contributed to new approaches and have given enough scope (i) to study the resources of medicinal plants (ii) to distinguish different medicinal plants and analyze their phylogenetics by alignment of amino acid sequences or DNA sequences through megablast or gene bank, (iii) to analyze single nucleotide polymorphisms, iv) to predict protein primary, secondary and tertiary structure with accuracy below 80%. Increasingly, problems might be discovered and solved in the research of medicinal plants, especially on genome projects, with the tools of bioinformatics.

CONCLUSION

There has been resurgence in the consumption and demand for medicinal plants. With onset of scientific research in herbals, it is becoming clearer that the medicinal herbs have a potential in today's synthetic era, as numbers of medicines are becoming resistant. Although, only 20% of the plant flora has been studied, around 60% of synthetic medicines owe their origin to plants and are being used as pharmaceuticals, neutraceuticals, cosmetics and food supplements. Biomedical informatics and communication activities have assumed greater significance in recent years, highlighting the potential of herbs in many different forms. As traditional source of medicines, plants continue to play pivotal roles. Ancient knowledge coupled with scientific principles could provide us with powerful remedies to eradicate numerous diseases and health issues.

Table 2: Digital inventory of medicinal plants available through the world.

S. No	Databases	Constructors
1	Arabidopsis Biological Resource Centre (ABRC)	(i) National Science Foundation (NSF) (ii) Ohio State University (iii) Nottingham Arabidopsis Stocks Centre (NASC) (iv) Biotechnology & Biological Sciences Research Council (BBSRC)
2	Maize Genetic Cooperation	(i) United States Dept. of Agriculture (USDA).
3	Arabidopsis Information Resource (TAIR)	(i) Carnegie Institution of Washington Department of Plant Biology (ii) National Centre for Genome Resources (NCGR) (iii) National Science Foundation, USA
4	Arabidopsis thaliana Database (MATDB)	(i) European Scientists Sequencing Arabidopsis (ESSA)
5	USDA-NCC Carotenoid Database for U.S. Foods	University of Minnesota –updated 1993 http://www.nal.usda.gov/fnic/foodcomp/Data/car98/car98.html. Holden et al., 1999. Carotenoid Content of U.S. Foods: An Update of the Database. J. Food Comp. Anal. 12:169-196
6	Kohler's Medicinal Plants	Missouri Botanical Garden http://www.mobot.org/default.asp
7	3D-Database of Pharmaceutically Active Chemicals	2005-2007 Karl Harrison http://www.3dchem.com/atoz.asp
8	Office of Dietary Supplements (IBIDS)	The International Bibliographic Information on Dietary Supplements database provides access to bibliographic citations and abstracts from published, international, and scientific literature on dietary supplements http://ods.od.nih.gov/Health_Information/IBIDS.aspx
9	Dr. Jim Duke's Phytochemical Databases	Plant, Chemical, Activity and Ethonobotany searches - Mary Jo Bogenschutz http://www.ars-grin.gov/duke/index.html Phytochemistry and Pharmacognosy Research Group at Middlesex University
10	Phytopharmacognosy listserv archives	Commercial research of Herbal Sciences International Ltd focusing on the scientific aspects of herbal medicines.Dr John A Wilkinson http://www.phytochemistry.freeserve.co.uk/frames/password.htm
11	Dietary Supplements (Food and Nutrients Information Centre)	American Society for Nutrition. Information and resources on individual macronutrients, phytonutrients, vitamins and minerals. http://fnic.nal.usda.gov/nal_display/index.php?tax_level=1&info_center=4&tax_subject=274
12	Search Clinical Research Studies Protocol Database(NIH)	Consortium of National Health Centres http://clinicalstudies.info.nih.gov/
13	People and Plants Online	Xishuangbanna Tropical Botanical Garden, Yunnan http://peopleandplants.org/
14	Flowering Plant Family Identification	World Wide Flowering Plant Family Identification, Family Listing Information about this, Identification Process, Sample Data and Description of the Search Algorithm, CGI Source Code http://www.colby.edu/info.tech/BI211/PlantFamilyID.html
15	Dictionary of Botanical Epithets Internet Directory for Botany	The epithets are largely taken from alpine plants and found in the seed lists of the North American Rock Garden Society's seed list, alpine plant nursery catalogs and alpine references http://www.winternet.com/~chuckg/dictionary.html
16	Michael Moores' Botanical Images (Genus)	Focusing on clinical and constitutional herbalism, and Materia Medica. http://www.swsbm.com/HOMEPAGE/HomePage.html
17	Ohio State University Online Image Database	Department of Horticulture and Crop Science http://www.hcs.ohio-state.edu/plants.html
18	Antibiotic Guide	The University of Wisconsin School of Medicine and Public Health-Department of Biostatistics and Medical Informatics (analyses of laboratory, clinical, and epidemiologic studies and clinical trials in a variety of biomedical disciplines). http://www.biostat.wisc.edu/
19	Hardin Meta Directory-Pharmacology	University of Iowa http://www.lib.uiowa.edu/
20	Center for Drug Evaluation and Research	US Food and Drug Adminstration. http://www.fda.gov/cder/

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