An exhaustive Data Mining of Medicinal Plants using MySQL for Biotechnology Research

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Submitted by

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Certificate

This is to certify that the thesis entitled, "An exhaustive Data Mining of Medicinal Plants using MySQL for Biotechnology Research" submitted by Satyavikash Bhuyan in partial fulfillment of the requirement for the award of Bachelor of Technology degree in Biotechnology Engineering at National Institute of Technology, Rourkela is an authentic work carried out by him under my supervision and guidance. To the best of my knowledge the matter embodied in the thesis has not been submitted to any other University/Institute for award of any Degree/Diploma.

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Satyavikash Bhuyan

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Abbreviations:

API: Active Pharmaceutical Ingredient

SQL: Structured Query Language

PHP: Hypertext Preprocessor

RDMS: Related Database Management Systems

HTML: Hyper Text Markup Language

XML: Extensible Markup Language

NCBI: National Center for Biotechnological Information

FRLHT: Foundation for Revitalizations of Local Health Traditions

FDA: Food and Drugs Administration

XAMPP: Cross Platform, Apache, MySQL, PHP, Perl

Abstract:

Vital pieces of information related to medicinal plants are exhaustive but scattered. A plant database centering on the Active Pharmaceutical Ingredients (APIs) responsible for therapeutic value of plants is not available in the literature. So it is prudent to make a curated database comprising of information on APIs viz. name of plants with taxonomical hierarchy, Useful parts of the plants, name of generic drugs and recent findings of their therapeutic use. The current project aims to assemble a vast array of information on medicinal plants from different sources and to perform a systematic data mining for simple and effective retrieval for end user. Briefly, the methods used for implementing the database was 1)Extracting information from standard books, journals, existing databases, from databases of abstracts and from Gray literature, 2)Storing the information in Related Database Management System (RDBMS) like MySQL server and 3) Retrieving the information through an interactive webpage using web scripting language PHP. The Database resulted in providing plant related information through two ways. One is drop down menu of APIs and another is through a search box introduced in the webpage. After successful implementation of the methodologies it was concluded that the database could fulfill its purpose of providing unique and organized information of essentiality to the scientific fraternity with proper references. In future this database can be scaled up with more plant related information and more APIs.

Key words: Active pharmaceutical Ingredients, MySQL, RDBMS, PHP, web interface, Gray literature

Chapter 1

Introduction

Introduction:

Medicinal plants and plant derived medicines are widely used in traditional cultures all over the world and they are becoming increasingly popular in modern society as natural alternative to synthetic medicine. In fact due to mild side effect, plant derived medicine is the best preferred choice provided the desired compound is identified first and extracted to the maximum purity before it could be used therapeutically. In old days, people used to utilize different parts of a plant or the whole plant for therapeutic use; but now a days instead of the whole part of the plant active pharmaceutical ingredients (APIs)present in those parts of the plant are being formulated for the same so that proper doses can be administered and the drug will be more effective in its pharmacokinetics and pharmacodynamics.

1.1 Active Pharmaceutical Ingredients:

Active Pharmaceutical Ingredients (APIs) are of a class of organic chemicals that are responsible for therapeutic action of the plant as a whole.. APIs extracted from plants are mainly alkaloids. [Encyclopedia Britannica] In his book "Plant Alkaloids: A Guide to Their Discovery and Distribution", Robert F. Raffauf wrote that 10,000 types of alkaloids are known to human by 1990.[1] As more and more natural remedies, natural products are being synthesized and discovered day by day , enormous amount of data pertaining to these plant alkaloids are being produced. Other chemicals of this class include Flavanoids, Anthracene derivatives, Glycosides , Coumarins and Cannabinoids. Apart from enormity of data available on these, they are scattered at different sources e.g. books, journals, periodicals etc. Research activity is also going on most

of these compounds for better understanding of their various therapeutic actions. Hence there is a need to make a user friendly, accurate and scientific database of all the related information of plant compounds and recent research going on them.

1.2 Data mining:

With the advancement of computing technologies we have many methods of storing and retrieving data. Data mining constitutes of one or more of the following functions, namely, classification, regression, clustering, summarization and functional dependencies, rule extraction etc. and is one of the primary methods in which we can store huge amounts of data. Today in biological research field there has been many research on medicinal plants and many articles regarding them has been published. So by using different data mining techniques, data about medicinal plants has to be extracted and stored.

In response to current advances in technology and research scope, massive amounts of data are routinely deposited in public and private databases. In parallel, there is a proliferation of computational algorithms and analysis tools for data analysis and visualization. Because most databases are accompanied by specific computational algorithms or tools for analysis and presentation and vice versa, we use the term data source to refer to a database or computational analysis tool or both. Scientific literature, images and other text documents are generally stored in unstructured or semi-structured formats (plain text files, pdf, jpg, HTML, XML or php files, binary (files) which are to be stored in a database using data mining techniques.

Data mining (sometimes called data or knowledge discovery) is the process of analyzing data from different perspectives and summarizing it into useful information - information that

can be used to increase revenue, cuts costs, or both. Data mining software is one of a number of analytical tools for analyzing data. It allows users to analyze data from many different dimensions or angles, categorize it, and summarize the relationships identified. Technically, data mining is the process of finding correlations or patterns among dozens of fields in large relational databases. [2]

Presently an enormous wealth of information is available on the Web. The Web is a huge collection of documents that comprises (i) semi structured (HTML, XML) information, (ii) hyper-link information, and (iii) access and usage information and (iv)is dynamic; that is, new pages are constantly being generated. The Web has made cheaper the accessibility of a wider audience to various sources of information. Web mining refers to the use of data mining techniques to automatically retrieve, extract, and evaluate (generalize or analyze) information for knowledge discovery from Web documents and services. [3]

1.3 MySQL:

MySQL is a very fast, robust Relational Database Management System (RDMS). A database enables you to efficiently store, search, sort and retrieve data. The MySQL server controls access to your data to ensure that multiple users can work concurrently to provide fast access to it and to ensure that only authorized person can get access to it. Hence MySQL is a multi user and multi threaded server. It uses SQL (Structured Query Language), the standard database query language worldwide. MySQL has been publicly available since 1996 but has a development history going back to 1976. [4] MySQL is used by some big organizations like Google, Facebook, NCBI etc.

1.4 Objective:

1. To decide which plant related information to be stored in the database. For this literature survey to be done to ensure that intended type of database does not exist already.

2. To design SQL table for storing, searching and retrieving of data.

3. Exhaustive data mining for extracting desired valuable information from literature and various primary databases.

4. Presenting the information to prospective users in an interactive and user friendly way.

1.5 Scheme of the project:

In the flow chart given below scheme of the project has been given to accomplish the above mentioned objectives.

Flowchart 1: Scheme of the project

| Books | Primary Database | Journal |

Data mining

APIs

| Existing drug Database | Book | Database of Abstracts |

Data mining

| Plant Hierarchy | Plant part | Mode of Action | Generic drug | Therapeutic findings |

SQL Database

Interactive portal

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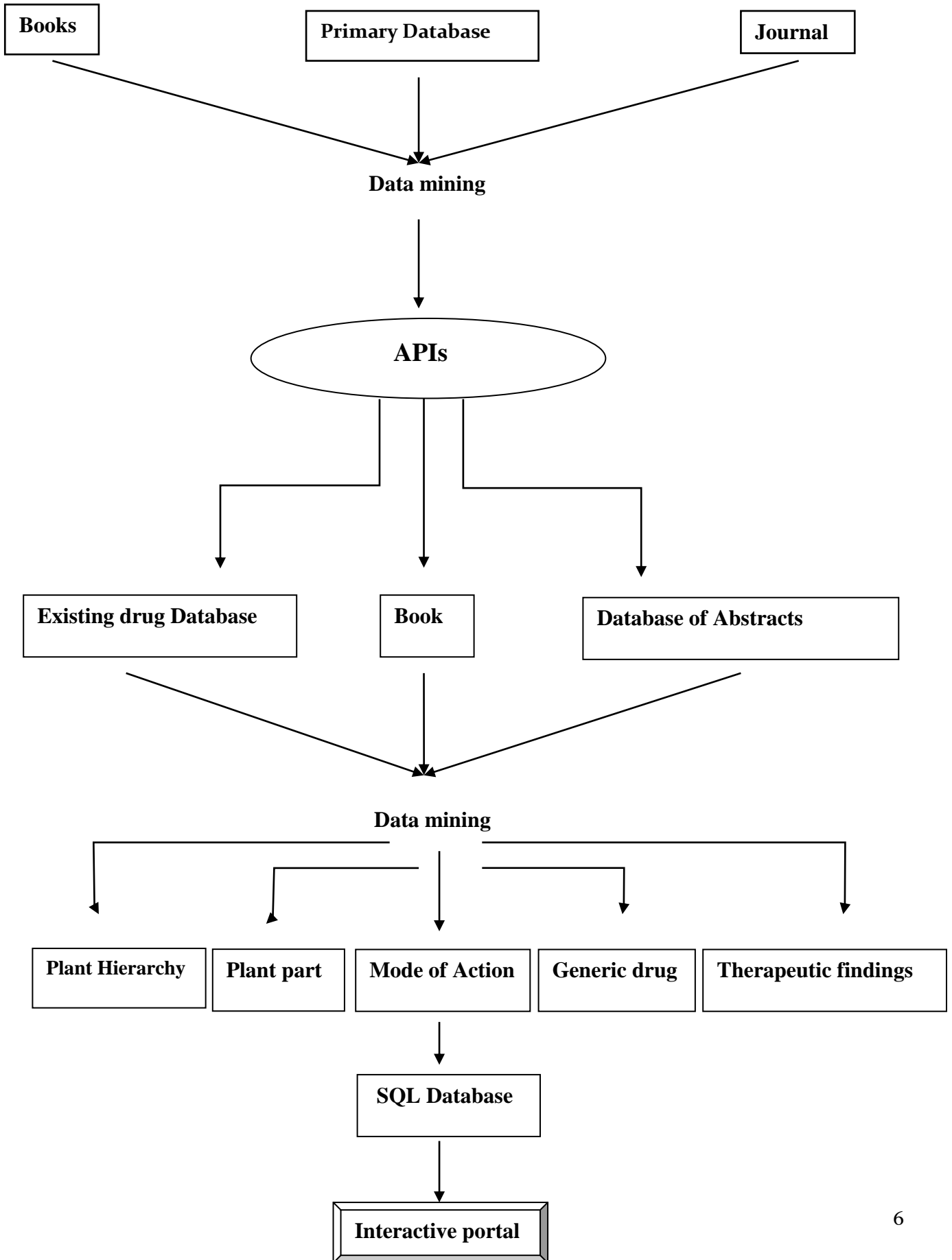
Chapter 2

Literature Review

Literature review:

A number of databases containing plant related information already exist in the literature by various national and international organizations. They provide different categories of information viz. taxonomical hierarchy of plants, their geographical distribution, therapeutic use as a whole, pharmacopoeia of the generic drug extracted from them etc. Given in Table-1 is the list of some databases that stores plant related information.

Foundation for Revitalizations of Local Health Traditions (FRLHT) is registered trust. It is also designated as "ENVIS Centre on Medicinal Plants" by Ministry of Environment Affairs, Govt. of India. It has got an exhaustive database of Indian plants containing information on their vernacular synonyms. [5]

"The Plant List" is a list of all known plant species and it is the largest database of its kind. It is supported by Royal Botanic Gardens, Kew and Missouri Botanical Garden. It contains taxonomical information of all medicinal plant hierarchy. [6]

US Food and Drug Administration (FDA) has got its database of dugs it approves. Most of the drugs are synthesized ones that are used in chemotherapy. [7]

The DrugBank database combines detailed drug data with comprehensive drug target information. The database contains drug entries which are FDA-approved small molecule drugs. It is supported by David Wishart, Departments of Computing Science & Biological Sciences, University of Alberta and "The Metabolomics Innovation Centre". [8]

The PLANTS Database, supported by Natural Resources Conservation service, US Department of Agriculture provides standardized information about the vascular plants, mosses, liverworts, hornworts, and lichens of the U.S. [9]

A relational and annotated database has been created for multiple drug resistant genes as potential drug target so that an user can find a particular gene as well as its putative homologues.[10]

A new database for plants of medicinal interest MEDPHYT® is being created funded by the Beilstein Institute (Frankfurt/Main, Germany).It aims to include European medicinal plant information in its first stage.[11]

After going through the existing resources on plant drug information it was found out that no single database provides the detailed information about the Active Pharmaceutical Ingredients such as Alkaloids, Flavanoids, Anthracene derivatives, Glycosides, Coumarins and Cannabinoids. As these compounds extracted from different parts of plants are extremely important for both therapeutic actions of plant derived generic drugs and research activities in the field of Biotechnology and pharmacy, it was thought prudent to focus on this area of plant information in my intended database.

Table 1: Databases containing plant related information

	Url of information provider	Name of Organization	Information type	Location of publication
1	http://nmpb.nic.in	National Medicinal Plants Board	Medicinal plant information	India
2	http://www.ccras.nic.in	Central Council for Research in Ayurvedic Sciences	Ayurvedic pharmacopoea	India
3	http://envis.frlht.org	Foundation for Revitalization of Local Health Traditions	Plant information with vernacular synonyms	India
4	http://plants.usda.gov	United States Department of Agriculture	Exhaustive database of medicinal plants	USA
5	http://www.pfaf.org	Plants for a future	Plant related information	USA

6	http://www.drugbank.ca/	David Wishart, University of Alberta	Pharmaceutical drug info	Canada
7	http://www.rain-tree.com	Raintree Nutrition, Inc.	plant drug from rainforests: not exhaustive	USA
8	www.erowid.org/	EROWID	plant drug, psychoactive drugs	USA
9	http://www.plant-medicine.com	SustainCare Community Interest Company	Plant medicines	UK
10	http://www.theplantlist.org	Royal Botanic Gardens, Kew and Missouri Botanical Garden	comprehensive database of plants(taxonomy)	Europe, USA

Chapter 3

Materials & Methods

3.1 Materials:

3.1.1 Apache http server:

It is a feature-rich HTTP server software package and very popular in public Internet market. It is a free software and managed by the Apache Group, a geo-graphically distributed group of volunteers. [12] The software is downloadable at http://httpd.apache.org/ .

3.1.2 MySQL:

The MySQL database has also become the world's most popular open source database because of its high performance, high reliability and ease to use features. It is now owned by Oracle Corporation and can be downloaded at http://www.mysql.com/ .

3.1.3 PHP:

PHP is a widely-used general-purpose scripting language and specially suited for Web development which can be embedded into HTML language. HTML language elements are basic building blocks for developing a webpage. This software is downloadable at http://www.php.net/.

3.1.4 XAMPP:

XAMPP is a small and light cross platform Apache distribution containing the most common web development tools in a single stack package. It is an acronym and here X stands for cross platform, A for Apche server language, M for MYSQL, P for PHP and other P for pearl language. Its contents, small size, and portability make it the ideal tool for students developing and testing applications in PHP and MySQL. As this software package fulfills the purpose of this

project completely and it is also free downloadable hence it was downloaded and installed in the PC form the website http://www.apachefriends.org/.

3.1.5 Endnote:

Endnote is a software tool for publishing and managing bibliographies. As the intended database extensively deals with publication references for various therapeutic findings of plant chemicals, Endnote was installed.

For data mining purposes the following materials were used.

3.1.6 Books:

Plant Drug analysis by Wagnar and Bladt. [11] Medicinal Plants of the World: An Illustrated Scientific Guide to Important Medicinal Plants and Their Uses. [12]

3.1.7 Databases and search engines:

Pubmed (Abstracts and citations database)- http://www.ncbi.nlm.nih.gov/pubmed/

Pubchem (database of chemical molecules and information)- http://pubchem.ncbi.nlm.nih.gov/

Scopus (Abstracts and citations database)-- http://www.scopus.com

Google scholar (Bibliographic database)- http://scholar.google.co.in/

Drug database-http://www.drugbank.ca/

3.2 Methods:

3.2.1 XAMPP installation:

As previously mentioned XAMPP was obtained from http://www.apachefriends.org/ and installed in the PC. To check if server is running http://localhost/ was typed in the address bar of browser. The following Figure 1 suggested that XAMPP has been installed properly.
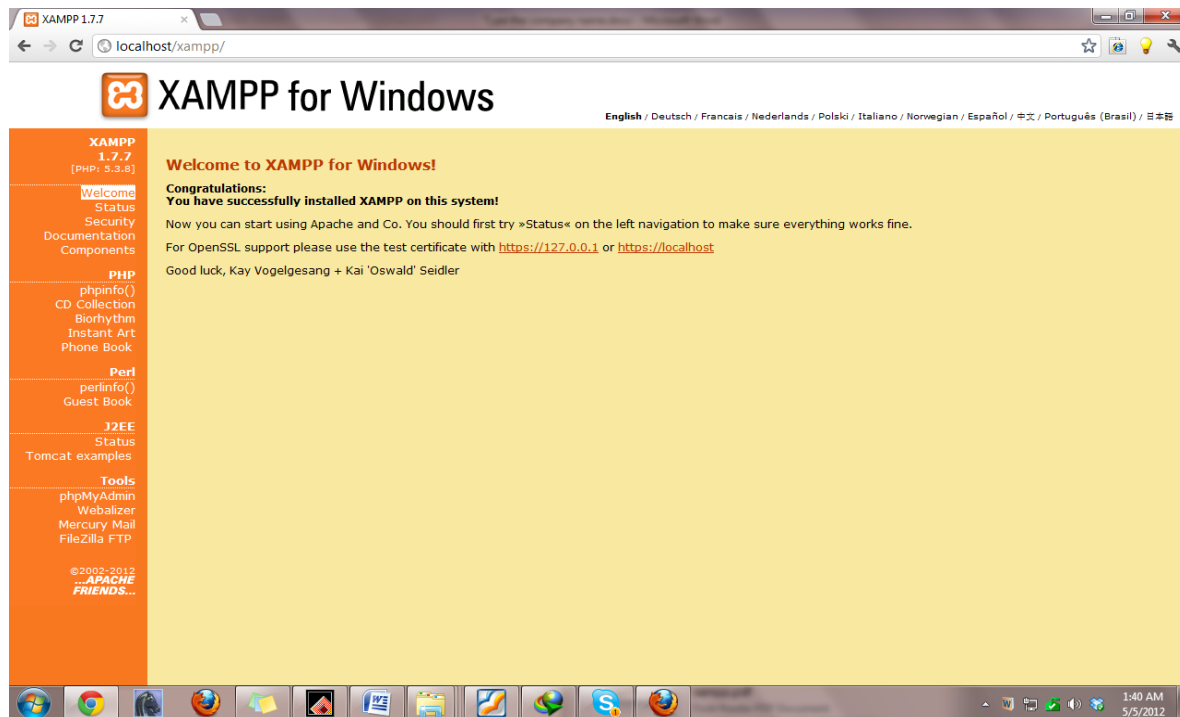
Figure 1: View of XAMP workbench

3.2.2 Running MySQL:

For creating a MySQL database the following steps was followed. Open localhost> Go to tools and click on 'phpMyadmin' > click on 'databases'> give the name of database in box(say mplant) > then click on 'create'. At this stage the interface would look like Figure 2.
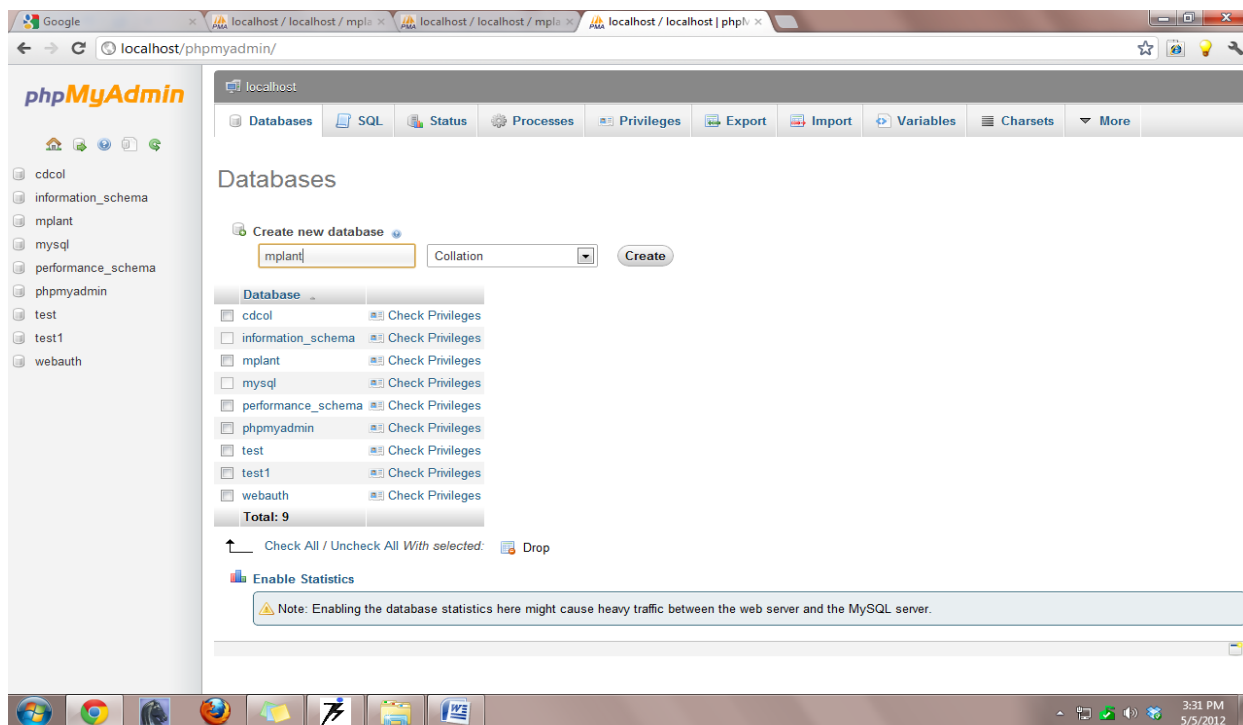
Figure 2: Create database in MySQL

3.2.3 Designing the database:

The database was conceived to consist of following plant related information. They are :

1. Name of API

2. Source plants

3. Plant parts used for extraction

4. Name of the generic drug

5. Therapeutic category of the API

6. Mechanism of action

7. Taxonomical hierarchy(family of the plant)

8. Recent therapeutic findings

9. References.

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To store the above information, two tables were created within the database previously created using MYSQL. One is for first eight type of information (Name of API to Recent therapeutical findings) and other is for References only. The reason for creating a special table is that reference needs not be explicitly displayed to user while retrieving the data and only to be produced if user categorically wants them.

For creating tables in the database the database "mplant" which was created earlier was opened. By clicking on "Create Table" and adding table name as well as column names with their characteristics like Data type, length etc. the tables were created. (Figure 3)
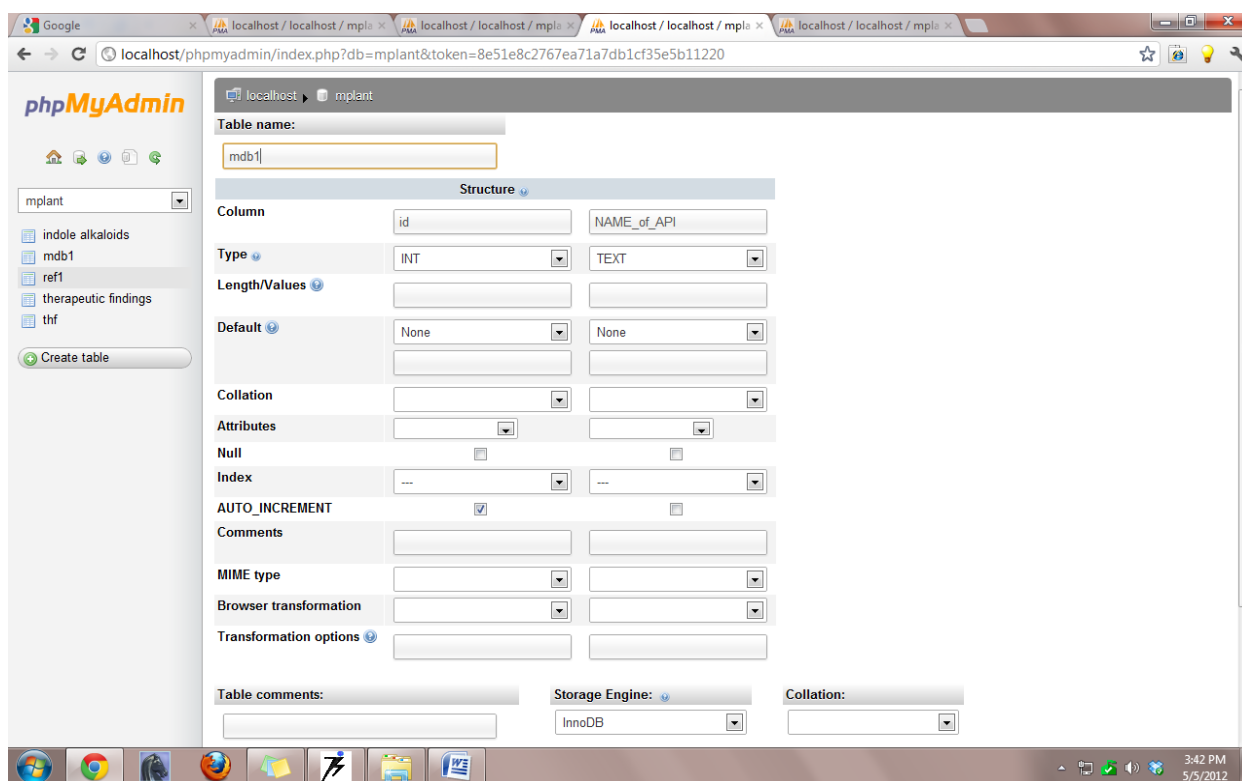
Figure 3 : Inserting data into MySQL table

3.2.4 Data mining of Plants:

Various Plant chemicals, which are used as Active agent in different drugs or could be potentially used for therapeutic purposes, were identified from different published and peer reviewed print materials. Each individual Plant chemical was searched in various databases of abstracts and citations like Pubmed and Scopus, existing primary database like Pubchem and in existing drug databases. In addition to the above material, help of some standard books for taxonomical information and important plant parts used was taken to compile desired information about Active Ingredients of plants. Some typical search results for API 'Berberine' is shown in Figure 4.

The search resulted in a number of academic publication or accomplished research data. Exhaustive reading of all these material was undertaken to find out relevant information and to curate the available information which are scattered at different sources.

While searching for therapeutic findings, in some cases large number of search results obtained in the range of thousand. Going through all the results is practically impossible. So research papers submitted three years ago were not taken into account which also satisfies the objective that "Recent Therapeutic findings" to be included in the database.

As making the database deals with a large number of publication references, help of Bibliographic content management system was thought indispensable. For this reason EndNote software was used. Each piece of information of relevance was put to appropriate field of the SQL table and stored in it.

A special folder for plant related images was created. By giving the url of each image, retrieval of images at appropriate field was made possible.

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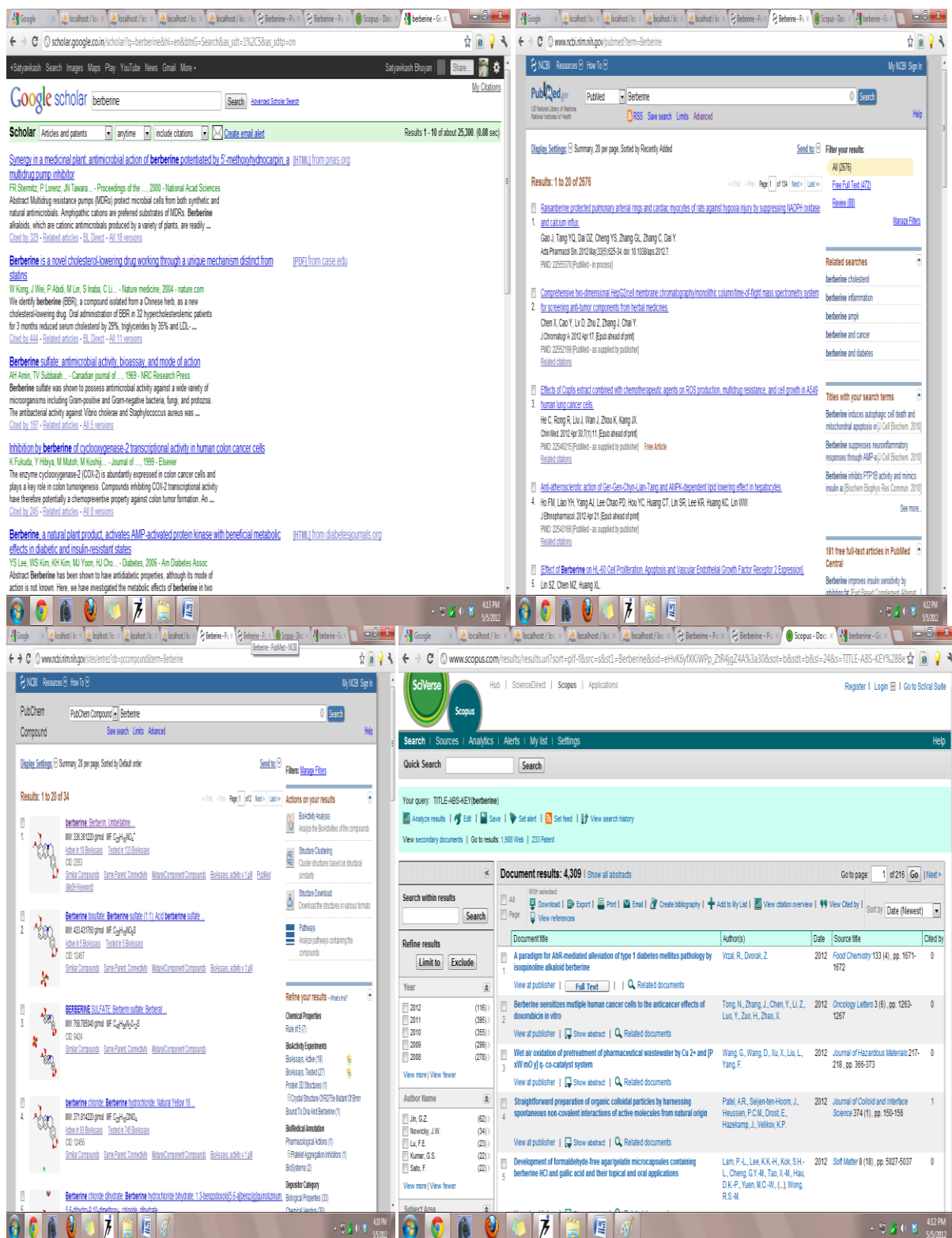
Figure 4 : search results of Berberine from (from upper left in clockwise direction) 1-Google scholar, 2- Pubmed, 3-Scopus, 4- Pubchem

3.2.5 Data retrieval:

Data retrieval is important for two reasons. One is to obtain the data already stored for further use and another is to present it to the user in an interactive and effective way. As mentioned before that MySQL is a fast, easy-to-use Relational Database Management System(RDBMS) used for databases on many Web sites. The MySQL software consists of the MySQL server and this server is the manager of the database system. MySQL server communicates to the end user for accepting and retrieving data through Structured Query Language(SQL) which is a standard language understood by many RDBMSs. Here PHP acts as bridge communicating SQL to MySQL server. PHP also retrieves the status message of database which is also a SQL and present it to user. Hence PHP is a data mover and is particularly strong in its ability to interact with databases in this mechanism.PHP is an embedded scripting language which is used in Web pages. This means that PHP code is embedded in HTML code.

There are several steps which are involved by pairing between MySQL and PHP for data retrieval.

3.2.5.1 Making a Connection:

The function mysql_connect()is used to create a live database connection through which an user may communicate. After this connection is made, sending, retrieving and manipulation of data is possible.The following PHP code segment used for making connection.

```
<? php
$db = mysql_connect("localhost","root", "")
    or die("Unable to connect to SQL server");

?>
```

Once connection to the database server is made successfully, it must be determined to which database queries should be sent. The mysql_select_db() function is for this purpose only. By passing in two parameters—one to declare the connection resource and another to declare which database to connect, all subsequent queries can be sent to that database which was selected by this function.

```
$db_select  = mysql_select_db("mplant", $connection)

if(!$db_select)

   {

die("Database selection failed:".mysql_error());

   }
```

3.2.5.2 Querying the Database:

There is no point in connecting to a database without being able to send and retrieve information from it. Hence there are some specific MySQL functions used for this purpose.

Function mysql_query() passes the query along and processes it theough the mysql connection previously created.

```
$term=$_POST["mol1"];

    $op=$term;
```

```
         $result = mysql_query("SELECT * FROM mdb1 WHERE
id={$op} ", $connection);

         if (!$result){

          die("Database query failed: " . mysql_error());

          }
```

The function mysql_fetch_array() returns a row from the database as an associative array and/or a numeric array and it gets a row from the mysql_query() function and returns FALSE upon failure or when there are no more rows or an array on success.

```
while($row=mysql_fetch_array($result)){

     echo "<strong>Name of Alkaloid : </strong> $row[1]";

     echo "<br/><strong>Name of plant : </strong> $row[2]";

     echo "<br/><strong>Parts used : </strong> $row[3]";

     echo " <br/><strong>Name of drug : </strong>$row[4]";

     echo " <br/><strong>Therapeutic category:</strong> $row[5]";

     echo " <br/><strong>Mode of action :</strong> $row[6]";

     echo " <br/><strong>Family :</strong> $row[7]";

      echo " <br/><strong>Recent Therapeutic findings :</strong>
$row[8]";}

     echo " <br/><strong>Reference :</strong> $row[9]";
```

3.2.5.3 Creating the web interface:

For effective data retrieval an interactive web interface was designed having drop down menu of Plant APIs and also search option. Methods of searching the database has already been explained. The code segment for creating interface with drop down menu is given as follows:

```html
<div>

   <form name="form1" action="database1.php" method="post">

    <h2>Select   the   molecule   you   want   to   see   information
about</h2>

    <select name="mol1">

        <option value="1">Reserpine</option>

        <option value="2">Rescinnamine</option>

        <option value="3">epi-rauwolscine</option>

        <option value="4">serpentine</option>

        <option value="5">ajmaline</option>

        <option value="6">serpentinine</option>

        <option value="7">raupine</option>

                  </select>

    <input type="submit" />
```

Chapter 4

Results

And

Discussion

4.1 Results:

The approach of this database is looking, analyzing and getting information about medicinal plants from the perspective of those active compounds which are responsible for therapeutic actions of the plant medicine.

The primary entry of the database is an Active Pharmaceutical Ingredient(API) and all other information is based on this and revolve around this compound only. At the initial level the medicinal database containing 45 entries in terms of Active Pharmaceutical Ingredients and their related information is created. To show the results of establishing the database at its various level, let us take the example of one API named Berberine. Through this example the making and operation of the database can be illustrated immaculately.

Image of the structure of the chemical compound and image of the source plant were taken from standard plant databases and Pubchem respectively. Image results for Berberine is given in Figure 5.

Figure 5 : (clockwise from upper left corner) 1- *Chelidonium majus L, 2-*Berberine molecule 3- *Mahoria acquifolium, 4-Berberis vulgaris L, 5- HydrastisCanadensis L*

With the help of Gray Literature, various information of importance for Berberine viz. Part of the plant it was extracted, its therapeutic category and mechanism of action was found out. Name of source plant, its taxonomical information and name of generic drug it is used in were extracted from standard text books and existing plant databases. For Berberine the information collected is give in Table 2.

Table 2: Information for Plant alkaloid Berberine

Plant Name	1-*Chelidonium majus L* 2-*Berberis vulgaris L* 3-*HydrastisCanadensis L* 4-*Mahoria acquifolium*
Name of Family	1-papaveraceae(*Chelidonium majus L*) 2-berberidaceae(*Berberis vulgaris L* and *Mahoria acquifolium*) 3-Ranunculaceae(*HydrastisCanadensis L*)
Parts used	1-Whole herb(*Chelidonium majus L*) 2-Root bark(*berberis vulgaris L*) 3-Golden seal root(*HydrastisCanadensis L*) 4-Mahonia bark, grape root(*Mahoria acquifolium*)
Drug Name	1-Chelidonii herba(*Chelidonium majus L*) 2-Berberidis radicis cortex(*Berberis vulgaris L*) 3-Hydrastis rhizoma(*HydrastisCanadensis L*) 4-Mahoriae radicis cortex(*Mahoria acquifolium*)
Therapeutic Category	Relatively toxic, used orally for various parasitic and fungal infections and as antidiarrheal. [PubChem]
Mode of Action	The mechanism of pharmacologic actions of berberine includes metabolic inhibition of some organisms, inhibition of formation of bacterial enterotoxin , inhibition of intestinal fluid accumulation and ion secretion, inhibition of smooth muscle contraction, reduction of inflammation, platelet aggregation inhibition, platelet count elevation in certain types of thrombocytopenia, stimula-tion of bile and bilirubin secretion, and inhibi-tion of ventricular tachyarrhythmias.

4.2 Recent Therapeutic Findings for Berberine:

For therapeutic use of the plant alkaloid Berberine, exhaustive reading of Pubmed and Scopus search results was done. Recently added research papers within two years of duration gave the following information.

Berberine can potentially act as an anti-inflammatory, anti-angiogenic, anti-cell proliferative and apoptosis inducing agent in 7,12-dimethylbenz(a)anthracene(DMBA) induced oral carcinogenesis. [13]

While studying intestinal absorption of berberine in-situ it was found out that absorption may be affected by compatibility of compounds and berberine has got a wide absorption window, better absorption rate in colon. [14]

Berberine creates an ameliorative effect on renal damage in rats in diabetes induced by high-fat diet and streptozotocin.[15]

Berberine improves insulin sensitivity of human by inhibiting fat store and adjusting adipokine profile in preadipocytes and metabolic syndrome patients. [16]

Berberine is a potent agent for chemoprevention and chemotherapy for human colon cancer by targeting Wnt-catenin and inactivating Wnt-catenin signaling. [17]

Endothelial microparticles(EMP) induced upregulation of Nox4 expression may enhance Reactive Oxygen species(ROS) production in human umbilical vein endothelial cells(HUVECs).Berberine improves endothelial function in this case. [18]

Berberine inhibits expression of inflammatory cytokines in ARPE-19 cells and inhibitory effect is mediated by down-regulation of the p38, extracellular signal-regulated kinase(ERK1/2), and c-Jun N-terminal kinase(JNK) pathways.[19]

Berberine was found to Inhibit Myofibroblast Differentiation in Nasal Polyp-Derived Fibroblasts via t p38 Pathway. [20]

Traditional Chinese medicine(TCM) containing Berberine may be a useful tool to unravel genome regulation and expression in complex diseases. [21]

Berberine could reduce norepinephrine-induced apoptosis in neonatal rat cardiomyocytes through inhibition of the reactive oxygen species (ROS)-Tumor necrosis factor (TNF)-caspase signaling pathway. [22]

Berberine Suppresses the TPA(a tumor promoter)-Induced MMP-1 and MMP-9 Expressions through the inhibition of PKC in Breast Cancer Cells. hence it can be used in inhibition of metastasis of human breast cancer. [23]

Berberine can inhibit proliferation through a cell cycle arrest in ovarian carcinoma cell lines. It may be a new anticancer drug for ovarian cancer treatment. [24]

Berberine lowers blood cholesterol and triacylglycerols and improves moderately glucose homeostasis in (streptozotocin)STZ-induced diabetic rats in association with multiple factors related to insulin resistance. [25]

Berberine is a potential antitumor agent as it suppresses of nuclear factor(NF)-?B which is a molecular target for treating Primary effusion lymphoma (PEL) [26]

Berberine inhibits proliferation of thyroid cancer cell lines 8505C and TPC1 through apoptosis and/or cell cycle arrest. [27]

Berberine promotes neuronal extension and axonal regeneration in injured nerves of the peripheral nervous system(PNS). [28]

Berberine activates the chloride channels that are sensitive to tamoxifen and the changes of cell volume in human colorectal carcinoma cells. [29]

Antiangiogenic activity shown by berberine is mediated through the inhibition of various proinflammatory and pro-angiogenic factors. [30]

Berberine may protect hippocampal neuronal damage from transient global ischemia by reducing matrix metalloproteinase-9 (MMP-9) activity. [31]

Benzenediol-berberine hybrid can act as a multifunctional agent for Alzheimer's disease.[32]

Berberine shows decrease in waist circumference and waist-to-hip ratio , total cholesterol , triglycerides , and low-density lipoprotein cholesterol and increase in high-density lipoprotein cholesterol and sex hormone-binding globulin in women with polycystic ovary syndrome in comparison to metformin. [33]

Berberine inhibits lung metastasis produced by intravenous injection of B16F-10 melanoma cells. [34]

Repeated administration of berberine decreases cytochromes P450 in humans. [35]

4.3 Interacting with Data base though webpage:

For data retrieval an interactive and dynamic webpage was designed. A drop down menu of all APIs was created. Also a search box was inserted in the home page for searching key words of three different field of information, namely API, Plant name and Parts used.(Figure 6)
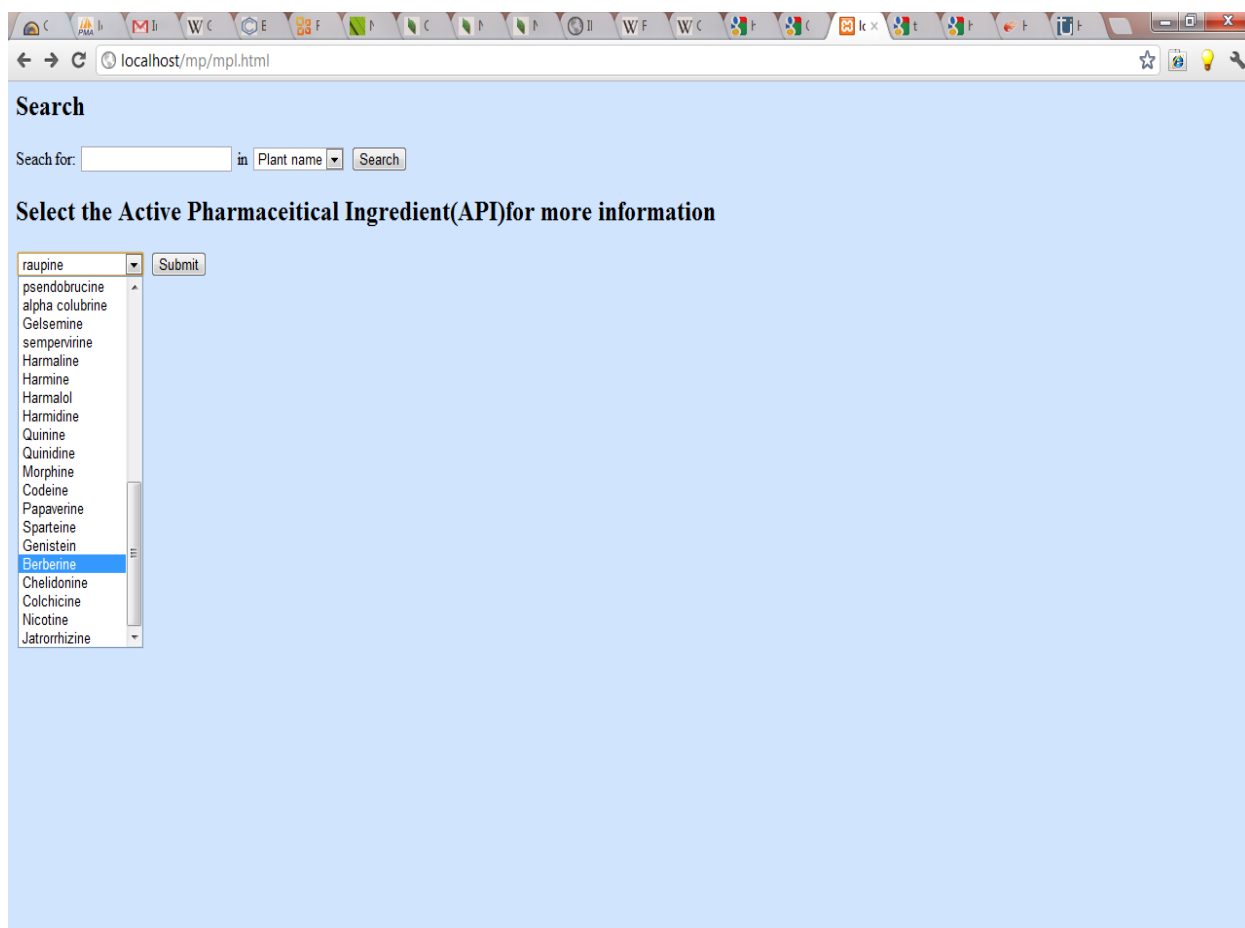

Figure 6 : Home page of webpage with search box and dropdown menu

Name of Alkaloid : Berberine

Name of plant : 1-Chelidonium majus L 2-Berberis vulgaris L 3-Hydrasis canadis L 4-Mahoria acquifolium

Parts used : 1-Whole herb(Chelidonium majus L) 2-Root bark(berberis vulgaris L) 3-Golden seal root(Hydrasis canadis L) 4-Mahonia bark, grape root(Mahoria acquifolium)

Name of drug : 1-Chelidonii herba(Chelidonium majus L) 2-Berberidis radicis cortex(Berberis vulgaris L) 3-Hydrastis rhizoma(Hydrasis canadis L) 4-Mahoriae radicis cortex(Mahoria acquifolium)

Therapeutic category: Relatively toxic parenterally, used orally for various parasitic and fungal infections and as antidiarrheal. [PubChem]
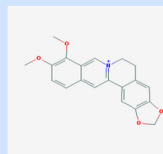
Mode of action : The mechanism of pharmacologic actions of berberine includes metabolic inhibition of some organisms, inhibition of formation of bacterial enterotoxin , inhibition of intestinal fluid accumulation and ion secretion, inhibition of smooth muscle contraction, reduction of inflammation, platelet aggregation inhibition, platelet count elevation in certain types of thrombocytopenia, stimula-tion of bile and bilirubin secretion, and inhibi-tion of ventricular tachyarrhythmias.[1][2]

Family : 1-papaveraceae(Chelidonium majus L) 2-berberidaceae(Berberis vulgaris L and Mahoria acquifolium) 3-Ranunculaceae(Hydrasis canadis L)

Recent Therapeutic findings : Berberine inhibits HL-60 cell proliferation and induce apoptosis of HL-60 cell. The expression of mRNA and proteins of Vascular Endothelial Growth Factor Receptor 2(VEGFR2) decreased after treatment with berberine.[3]

Berberine hydrochloride enhances bactericidal activity in serum of grass carp Ctenopharyngodon idella by activating the complement system and hence indicates of being a potential agent in the prevention or treatment of fish diseases.[4]

Berberine can potentially act as an anti-inflammatory, anti-angiogenic, anti-cell proliferative and apoptosis inducing agent in 7,12-dimethylbenz(a)anthracene(DMBA) induced oral carcinogenesis.[5]

while studying intestinal absorption of berberine in-situ it was found out that absorption may be affected by compatibility of compounds and berberine has got a wide absorption window, better absorption rate in colon.[6]

Berberine creates an ameliorative effect on renal damage in rats in diabetes induced by high-fat diet and streptozotocin.[7]

Berberine improves insulin sensitivity of human by inhibiting fat store and adjusting adipokine profile in preadipocytes and metabolic syndrome patients.[8]

berberine is a potent agent for chemoprevention and chemotherapy for human colon cancer by targeting Wnt/?-catenin and inactivating Wnt/?-catenin signaling.[9]

Endothelial microparticles(EMP) induced upregulation of Nox4 expression may enhance Reactive Oxygen species(ROS) production in human umbilical vein endothelial cells(HUVECs).Berberine improves endothelial function in this case.[10]

Berberine inhibits expression of inflammatory cytokines in ARPE-19 cells and inhibitory effect is mediated by down-regulation of the p38, extracellular signal-regulated kinase(ERK1/2), and c-Jun N-terminal kinase(JNK) pathways.[11]

Berberine was found to Inhibit Myofibroblast Differentiation in Nasal Polyp-Derived Fibroblasts via t p38 Pathway.[12]

Traditional Chinese medicine(TCM) containing Berberine may be a useful tool to unravel genome regulation and expression in complex diseases.[13]

Berberine could reduce norepinephrine-induced apoptosis in neonatal rat cardiomyocytes through inhibition of the reactive oxygen species (ROS)-Tumor necrosis factor (TNF)-caspase signaling pathway.[14]

Berberine Suppresses the TPA(a tumor promoter)-Induced MMP-1 and MMP-9 Expressions through the inhibition of PKC-? in Breast Cancer Cells. hence it can be used in inhibition of metastasis of human breast cancer.[15]

Berberine can inhibit proliferation through a cell cycle arrest in ovarian carcinoma cell lines. It may be a new anticancer drug for ovarian cancer treatment.[16]

Berberine lowers blood cholesterol and triacylglycerols and improves moderately glucose homeostasis in (streptozotocin)STZ-induced diabetic rats in association with multiple factors related to insulin resistance.[17]

Berberine is a potential antitumor agent as it suppresses of nuclear factor(NF)-?B which is a molecular target for treating Primary effusion lymphoma (PEL)[18]

Berberine inhibits proliferation of thyroid cancer cell lines 8505C and TPC1 through apoptosis and/or cell cycle arrest.[19]

Berberine promotes neuronal extension and axonal regeneration in injured nerves of the peripheral nervous system(PNS).[20]

Berberine activates the chloride channels that are sensitive to tamoxifen and the changes of cell volume in human colorectal carcinoma cells.[21]

aAntiangiogenic activity shown by berberine is mediated through the inhibition of various proinflammatory and pro-angiogenic factors.[22]

Berberine may protect hippocampal neuronal damage from transient global ischemia by reducing matrix metalloproteinase-9 (MMP-9) activity.[23]

Benzenediol-berberine hybrid can act as a multifunctional agent for Alzheimer's disease.[24]

Berberine shows decrease in waist circumference and waist-to-hip ratio , total cholesterol , triglycerides , and low-density lipoprotein cholesterol and increase in high-density lipoprotein cholesterol and sex hormone-binding globulin in women with polycystic ovary syndrome in comparison to metformin.[25]

Berberine inhibits lung metastasis produced by intravenous injection of B16F-10 melanoma cells.[26]

Repeated administration of berberine decreases cytochromes P450 in humans.[27]

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Figure 7 : The result displayed for alkaloid Berberine

Chapter 5

Conclusion

&

Future work

5.1 Conclusion:

All the methods were applied scrupulously to implement the database as intended. At the end a productive database was developed in house using SQL and PHP. From this database, the plant information especially recent therapeutic findings of Active Pharmaceutical Ingredients are helpful for Biotechnology Research as the information is accumulated at one place. Search box in the web page enables the user to gather all the information related to a key word searched by the end user. For example the key word "root" would return all APIs extracted from root of the plants and similar results would come for other key words.

5.2 Future Work:

Future work includes-

1. Increasing the size of database by adding more entries
2. Introducing feature so that user can enter new research finding with reference so that the database would not be outdated after some time.
3. Adding more field of information related to plant chemicals for example it can be linked to useful bioinformatics tool.

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