A DATABASE ON THE BIO-MINERALIZATION PROCESS IN LIVING ORGANISMS.

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CERTIFICATE

This is to certify that the work entitled, "A Database on the Biomineralization Process in Living Organisms" submitted by Jaapna Dhillon - 031515 and Manu Shrivastava - 031506 in partial fulfillment for the award of degree of Bachelor of Technology in Bioinformatics of Jaypee University of Information Technology has been carried out under my supervision. This work has not been submitted partially or wholly to any other University or Institute for the award of this or any other degree or diploma.

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[Dr. C. Tandon]

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We are extremely grateful to Dr. C. Tandon (Asst. Prof., Dept. of Biotechnology & Bioinformatics), under whose guidance and supervision we could complete the project. This work familiarized us with the different physiological and pathological Biomineralization process occurring in living organisms. It also helped us improve our knowledge and skills of the general aspects of creating a biological database like collecting, assorting and managing data and the technical intricacies as well, to finally producing a user-friendly database.

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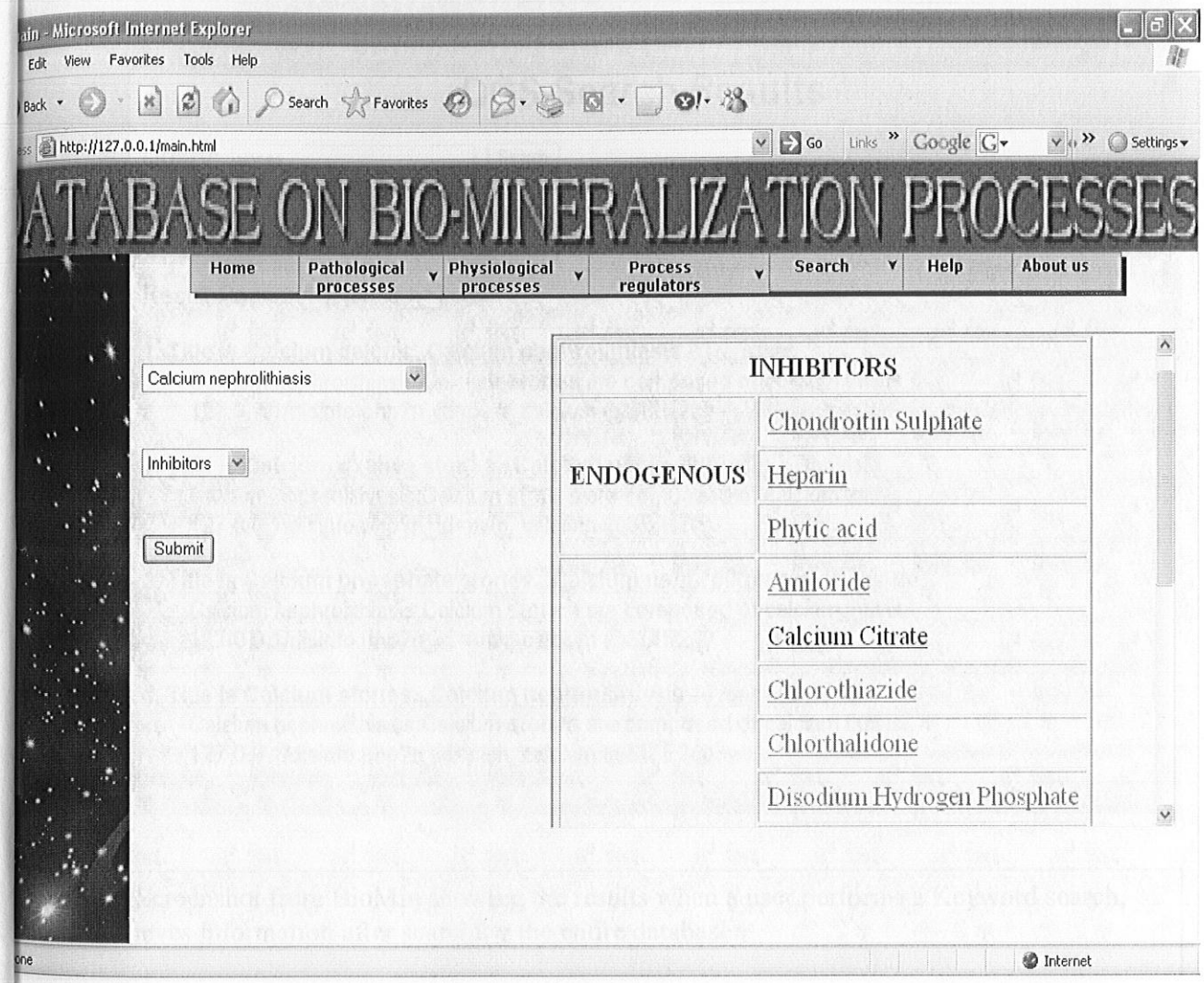

igure 1: Screenshot from BioMin showing the results when a user selects a particular process of iomineralization and selects to view only its inhibitors.

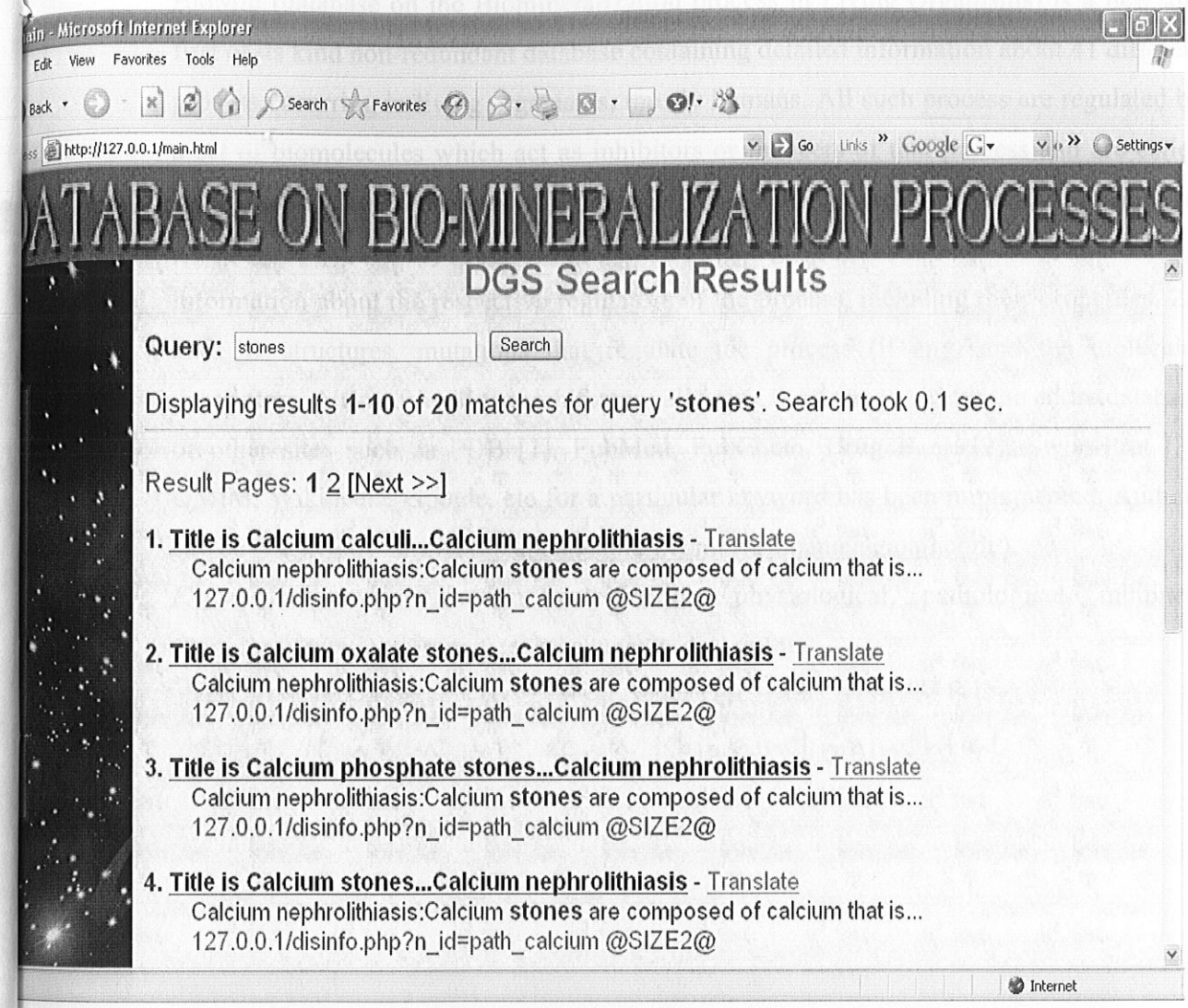

Figure 2: Screenshot from BioMin showing the results when a user performs a Keyword search, which retrieves information after searching the entire database.

ABSTRACT

BioMin (database on the Biomineralization process in Living Organisms) is a new and first of its kind non-redundant database containing detailed information about 41 different process occurring in living organisms, mostly humans. All such process are regulated by a set of biomolecules which act as inhibitors or inducers of that process and are called 'regulators'. The physiological process are regulated by certain biomolecules and the pathological process by biomolecules and some drugs. The database provides descriptive information about the respective regulators of the process, including their properties, 2D and 3D structures, mutations that regulate the process (if any) and the molecular descriptors. A user-friendly search feature allowing the users to search the entire database or other sites such as PDB [1], PubMed, PubChem, Drug Bank [2], Swiss-Prot [3], OMIM, Wikipedia, Google, etc for a particular keyword has been implemented. Authors can be reached by E-mail (djaapna@gmail.com, shri.manu@gmail.com).

Keywords: biomineralization, calcification, physiological, pathological, inhibitor, promoter, mutation, properties, mechanism, descriptors

The database can be visited at the URL:
http://www.juit.ac.in/biomin/main.html

INTRODUCTION

At present, there are many known bio-mineralization [4, 5] process which occur in living organisms ranging from unicellular prokaryotes to multicellular eukaryotes, but very few have been properly studied so far and many of the forms are perhaps not discovered as yet. One of the most recent researches in the field of biological sciences are focusing on discovering the various types and to study their mechanism. But the data lies scattered all over. We have made an attempt to consolidate all the relevant information of each process into a single database.

"Bio-mineralization" is the deposition of ions in the form of a mineral phase in or on to the matrix. It occurs under both physiological and pathological conditions in organisms varying from multicellular animals and plants to unicellular organisms as well.

Under **physiological conditions**, which is healthy biomineralization, come the normal processes of Bone [6-9] and Teeth [10, 11] Calcification (formation) in vertebrates, Shell formation in mollusks [12, 13], Calcium oxalate formation in plants [14] especially in cacti [15], Silicon and Carbonate formation in a variety of plants and diatoms [16], eggshell [17] formation, accumulation of iron [18] and carbon [19], etc.

The **pathological conditions**, which is unhealthy biomineralization, comprises the formation of minerals which lead to various diseases and disorders or deformities in living cells and organisms. The most commonly formed minerals in this case are Ca ions and PO_4 ions. Their deposition in soft tissues of the body causes them to malfunction.

For example, mineralization of Aorta [20, 21], urinary tract [22-30], kidney [31-38], gall bladder [39-41] and many collagenous soft tissues like skin [42], tendons [43]. Some pathological conditions in mineralization lead to dissolving away of the inorganic matrix for example, in certain bone diseases [44-46].

Bio-mineralization is like any other biochemical process and hence attributes many factors affecting its occurrence and the rate of formation of the minerals and these are called 'regulators'. The regulators can be classified as **Inducers** [27, 44, 46] and **Inhibitors** [20, 22-24, 29, 35, 38, 43, 47, 48]. The former help in the promoting the process and the latter inhibit. Each process has its own set of inducers and inhibitors and these vary with the organisms.

The regulators are usually biomolecules in case of physiological process and comprise of biomolecules and drugs [41] in case of pathological process but for many such process the regulators are still unknown. We have tried to collect all the information about the regulators like their synonyms, function, sequence, 2D and 3D structures, mutations (if any) [34, 44, 45] and we have also calculated their molecular descriptors.

By providing all the information on a single palate and the links to popular online databases, BioMin serves as an encyclopedia for the researchers working in this field and in bioinformatics research, as it provides valuable information about the proteins and drugs like their properties and molecular descriptors. It would help initiating new research with promising applications in pharmacology as the analysis of the regulators' information would lead to better understanding of the pathological process and their cure.

METHODS

BioMin includes most of the bio-mineralization process that have been discovered and documented so far and for which any kind of information is available either online or in the journals. The regulators affecting these process are also included and all the details regarding their properties, function, etc are incorporated. The sequence, 2D and 3D structures of the regulators have been collected from online databases like Swiss-Prot, PDB, Modbase and DrugBank. The regulators for which the structures were not available have been modeled using software MOE (Molecular Operating Environment).

The molecular descriptors of the regulators were calculated using MOE, which is an interactive, windows-based chemical computing and molecular modeling tool with a broad base of scientific applications in Bioinformatics, Cheminformatics, High Throughput Discovery, Structure Based Design, Protein Modeling and Molecular Modeling and Simulations.

MOE QuaSAR-Descriptor

The purpose of QuaSAR-Descriptor is to calculate properties of molecules that serve as numerical descriptions or characterizations of molecules in other calculations such as QSAR, diversity analysis or combinatorial library design. In principle, because any molecular property may be used as a molecular descriptor, there is no single calculation

procedure for QuaSAR-Descriptor. Rather, QuaSAR-Descriptor is a forum for the calculation of many descriptors.

A QuaSAR-Descriptor calculation proceeds as follows. Given a molecular database with a molecule field, a set of numerical properties will be calculated for each molecule and stored in the database. Every descriptor is given a unique name, or code, which identifies the descriptor. These codes are used as database field names. QuaSAR-Descriptor will overwrite fields with names identical to descriptor codes.

Descriptors are partitioned into *classes*. Each class indicates what is assumed by the descriptor calculators about the molecule presented:

- **2D**. 2D descriptors only use the atoms and connection information of the molecule for the calculation. 3D coordinates and individual conformations are not considered.
- **i3D**. Internal 3D descriptors use 3D coordinate information about each molecule; however, they are invariant to rotations and translations of the conformation.
- **x3D**. External 3D descriptors also use 3D coordinate information but also require an absolute frame of reference (e.g., molecules docked into the same receptor).

The database has been modeled on the relational model and has been built using MySQL 5.0 as the back end, PHP 5.2 as the front end and the Apache 2.0 server. A universal relation with all the attributes of the database was created and was then normalized into various sub relations.

UNIVERSAL RELATION

UN_R (name, defn, cause, symptoms, treatment, prevention, composition, alternative names, extrinsic factors, intrinsic factors, inhibitors/promoters, name, 2D structure, 2D image, 3D structure, function, category, synonyms, sequence, IUPAC name, formula, M.W,CAS no, melting point, smiles string, physical properties, subdivided surface areas, atom counts and bond counts, kiers hall connectivity and kapper shape indices, adjacency and distance matrix descriptors, pharmacophore feature descriptors, partial charge descriptors, potential energy descriptors, surface area, volume and shape descriptors, conformation dependent charge descriptors)

Set of Normalized Relations

1)Path_phys (n_id, name, defn, cause, composition)
primary key(n_id)

2) Path (n_id, symptoms, treatment, prevention)
primary key(n_id)
foreign key (n_id) references primary key (n_id) of Path_phys

3) Path_phys_an (n_id, alternative names)
primary key(n_id, alternative names)
foreign key (n_id) references primary key (n_id) of Path_phys

4) Ip (n_id, ip_id,type,fac)
foreign key (n_id) references primary key (n_id) of Path_phys
foreign key (ip_id) references primary key (ip_id) of Gen_pop

5) Ip_syn (ip_id, synonyms)
primary key(ip_id, synonyms)
foreign key (ip_id) references primary key (ip_id) of Gen_prop

6) Gen_prop (ip_id, name, gene, org, 2D structure, 2D image, 3D structure, function, category, sequence, mutations, IUPAC name, formula, M.W,CAS no, melting point, smiles string)
primary key(ip_id)

7) Physical (ip_id , physical properties)
primary key(ip_id)
foreign key (ip_id) references primary key (ip_id) of Gen_prop

8) Sub_surface (ip_id , subdivided surface areas)
primary key(ip_id)
foreign key (ip_id) references primary key (ip_id) of Gen_prop

9) Counts (ip_id , atom counts and bond counts)
primary key(ip_id)
foreign key (ip_id) references primary key (ip_id) of Gen_prop

10) Indices (ip_id , kiers hall connectivity and kapper shape indices)
primary key(ip_id)
foreign key (ip_id) references primary key (ip_id) of Gen_prop

11) Matrix (ip_id , adjacency and distance matrix descriptors)
primary key(ip_id)
foreign key (ip_id) references primary key (ip_id) of Gen_prop

12) Pharmacophore (ip_id , pharmacophore feature descriptors)
primary key(ip_id)
foreign key (ip_id) references primary key (ip_id) of Gen_prop

13) Partial_charge (ip_id , partial charge descriptors)
primary key(ip_id)
foreign key (ip_id) references primary key (ip_id) of Gen_prop

14) Potential (ip_id , potential energy descriptors)
primary key(ip_id)
foreign key (ip_id) references primary key (ip_id) of Gen_prop

15) Surf_vol_shp(ip_id , surface area, volume and shape descriptors)
primary key(ip_id)
foreign key (ip_id) references primary key (ip_id) of Gen_prop

16) Conformation (ip_id , conformation dependent charge descriptors)
primary key(ip_id)
foreign key (ip_id) references primary key (ip_id) of Gen_prop

FRONT – END

PHP

PHP stands for Hypertext Preprocessor and is a server-side language. This means that the script is run on your web server, not on the user's browser, so you do not need to worry about compatibility issues. PHP is relatively new (compared to languages such as Perl (CGI) and Java) but is quickly becoming one of the most popular scripting languages on the internet. PHP is a server-side scripting language. This means that, although your users will not need to install new software, you web host will need to have PHP set up on their server. It should be listed as part of your package but if you don't know if it is installed you can find out using the first script in this tutorial. If you server does not support PHP you can ask your web host to install it for you as it is free to download and install. If you need a low cost web host which supports PHP then try HostRocket. Writing PHP on your computer is actually very simple. You don't need any special software, except for a text editor (like Notepad in Windows). Run this and you are ready to write your first PHP script. PHP is a server-side scripting language. If you've seen ASP, you'll be familiar with embedding code within an HTML page. Like ASP, PHP script is processed by the Web server. After the server plays with the PHP code, it returns plain old HTML back to the

browser. This kind of interaction allows for some pretty complex operations. PHP supports a host of other features right at the technological edge of Internet development. These include authentication, shared memory support, and dynamic PDF document creation to name but a few. If that's not enough, PHP is easy to extend, so you can roll your own solution if you're programming savvy.

- PHP stands for **P**HP: **H**ypertext **P**reprocessor
- PHP scripts are executed on the server
- PHP supports many databases (MySQL, Informix, Oracle, Sybase, Solid, PostgreSQL, Generic ODBC, etc.)
- PHP is an open source software (OSS)
- PHP files may contain text, HTML tags and scripts
- PHP files are returned to the browser as plain HTML
- PHP combined with MySQL are cross-platform (means that you can develop in Windows and serve on a Unix platform)
- PHP runs on different platforms (Windows, Linux, Unix, etc.)
- PHP is compatible with almost all servers used today (Apache, IIS, etc.)

BACK - END

MYSQL

SQL is an ANSI (American National Standards Institute) standard computer language for accessing and manipulating database systems. SQL statements are used to retrieve and update data in a database. SQL works with database programs like MS Access, DB2, Informix, MS SQL Server, Oracle, Sybase, etc. There are many different versions of the SQL language, but to be in compliance with the ANSI standard, they must support the same major keywords in a similar manner (such as SELECT, UPDATE, DELETE, INSERT, WHERE, and others).

SQL is a standard computer language for accessing and manipulating databases.MySQL is an SQL based relational database management system (DBMS) that runs under a broad array of operating systems. MySQL is frequently used by PHP and Perl scripts. The SQL commands discussed in this tutorial apply to MySQL operating under all operating

systems. Only the installation instructions are Windows specific. The focus is on Windows XP Professional and Windows 2000 Professional machines.

MySQL is cross-platform open source database server software. It is used extensively in web-development. It is a multithreaded, multi-user, SQL (Structured Query Language) relational database server (RDBMS) with an estimated six million installations. **MySQL** is open source software available either under the GNU General Public License (GPL) or under other licenses when the GPL is inapplicable to the intended use. Unlike projects such as Apache, **MySQL** is owned and sponsored by a single for-profit firm, the Swedish company MySQL AB. The company develops and maintains the system, selling support and service contracts, as well as commercially-licensed copies of MySQL, and employing people all over the world who work together via the Internet.

PHP - MYSQL COMBINATION

The PHP-MySQL combination is also cross-platform, which means you can develop in Windows and serve on a Unix platform. Also, PHP can be run as an external CGI process, a stand-alone script interpreter, or an embedded Apache module.
PHP also supports a massive number of databases, including Informix, Oracle, Sybase, Solid, and PostgreSQL - as well as the ubiquitous ODBC.Its necessary to install apache before installing php. Apache server helps to formulate php scripts.

HOW TO START?

- Install an Apache server on a Windows or Linux machine
- Install PHP on a Windows or Linux machine
- Install MySQL on a Windows or Linux machine

CONCLUSION

In the present release of BioMin, we have covered 41 process and all their regulators with detailed description. We shall continue to include more data in the future as and when new process are discovered and more regulators are found and studied.

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