IJPSR (2017), Vol. 8, Issue 1 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 19 July, 2016; received in revised form, 21 September, 2016; accepted, 26 September, 2016; published 01 January, 2017

MMP DATABASE: ONLINE REPOSITORY PROVIDING INFORMATION REGARDING MMPS AND ITS INHIBITORS

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Keywords:

MMP, Inhibitors, Database, SQL, mmpdatabase, www.mmpdatabase.com

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ABSTRACT: Although technologies are emerging day to day and bioinformatics is also growing with number of databases developed, but being a very important factor in cancer invasion and metastasis, MMPs have no exclusive database. Matrix Metallo-Protienase (MMP) is a major class of proteolytic enzymes that plays a dominant role in ECM degradation. Every time researchers are searching and gathering information from different places and next researcher repeating the same. In this study we developed a database exclusively designed for the MMPs and their inhibitors.

INTRODUCTION: Matrix Metallo-Protienase (MMP) is a major class of proteolytic enzymes that plays a dominant role in ECM degradation. MMPs are regulated by sets of activators and inhibitors so that the integrity of the connective tissue is never compromised.

The extracellular matrix (ECM) is a complex structure that influences the behavior of its resident cells and migrating cells by providing specific contextual information. The ECM remains in a constant state of remodelling i.e, the breakdown of existing and synthesis of new ECM proteins. Thus ECM remodelliing can alter the interaction between the matrix and the cells. There are many factors which control the degradation of ECM.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.8(1).334-38

Article can be accessed online on: www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.8 (1).334-38

Literature survey showed that MMPs playing important role in the metastasis and the invasion and inhibition of their activity might be helpful in treatment of the cancer. Surveys showed that most of the patients are dying due to the invasion and metastasis of the cancer in distal organs. But with advancement of the technology as well as huge amount of data is available online and offline both, despite of all importance there is no exclusive place or database regarding the MMPs and its inhibitors. Every time researchers are searching and gathering information from different places and next researcher repeating the same. In this study we developed a database exclusively designed for the MMPs and their inhibitors.

Methodology: Study was performed with use of all the required facilities at Department of Pharmacology and Therapeutics, King George's Medical University, Lucknow, India. With aim to use important data about MMPs and to avoiding the repetitive experimentation, MMP database was created and is freely available online at www.mmpdatabase.com. Several computational tools were used during the database development.

MySQL Platform: Database created and developed on MySQL that provides easy platform for entering a field name and field data types in each row of the field entry area of the database table interface. MySQL recognizes parent-child relationships and embeds methods to ensure that the integrity of these relationships remains valid during data processing operations. MySQL established integrity rule for one to one or one to many relationships during the creation of the relationship or it can be established when modifying existing tables to establish a relationship.

Database design Process: A design activity involves a combination of a design process and a modeling language. A design process provides a sequence of steps through which the developers proceed when constructing a conceptual model. In the same way as there is no universally accepted notation for conceptual modeling, there is no universally accepted design process (**Fig. 1**; Elmasri et al., 1993; Elmasri et al., 1993; Elmasri et al., 1985).

Conceptual Design/ Database Modeling: A conceptual data model (CDM) provides a notation by which the structuring of data and their relationship from entities has been described more precisely. Many notations have been used for conceptual modeling, but must have two principle notations: entity types and relationships.

Entity-Relationship (ER) Modeling: An ER diagram is graphical representation of following: Entities and their attributes; relationships between entities (and their attributes); constraints on the entities and their relationships.

These are standard techniques for converting ER diagrams to the relational model. A single entity type is expected to have many instances, each of which gives values to the attributes specified in the corresponding type. An attribute specify the properties of an entity. ER attributes can be necessary to set value. A relationship represents an association between two or more entity types. Each entity participates in a given role and roles are represented as a relation between entity and relationships.

Interface Design: Database provides the best performance for storing large, heterogeneous chunks of information. Database is designed for simplifying the process of storing and retrieving information. To display, queries and retrieving information, a number of HTML & PHP pages has been design or constructed. PHP pages are used to connect and communicate with the database. PHP pages has been created using the *Eclipse* IDE, which is a professional editor for design, coding and developing website pages and web application. PHP contains two parts: programming code and embedded HTML.

Access database Using PHP: PHP has a lot of inbuilt functions you can use to manipulate databases. In PHP version 5, a lot more were added as well! Here, we'll stay with the inbuilt functions for versions earlier than PHP 5. But if you have version 5, it's well worth researching the newer database functions.

The approach we'll take has three steps: Open a connection to MySQL itself; Specify the database we want to open; Close the connection.

Reading and Displaying Contents/information: A web interface is able to perform some queries can be found at the address www.mmpdatabase.com. The interface is very simple, using click options and fields to make it possible for the user to select queries and extract the information from the database. Using this interface, it is possible to perform queries such as retrieving all the record data from the database.

RESULTS: The developed database was named as MMPDATABASE and freely available online. The database can be assassed by web-link www.mmpdatabase.com. The interface of database is divided in different web pages. Few web pages are shown here as: "Home Page" is the first webpage of the database, and shows all the related links on it (**Fig.1**). As we were designing the database exclusibly for the information about MMPs, "About MMPs" web page was also designed (**Fig.2**). Process of data mining resulted as different types of MMPs and shown as list in "List of MMPs" web page (**Fig. 3**).

With regards to thesis work focused on the "MMP-2 ihibitors", it is necessary to give a list of all the MMP-2 inhibitors (Natural and Synthetic inhibitors) with respective information (**Fig. 4).** One page of the database is totally dedicated to the related databases from where we gathered the information for our work designed as "Tools and Links" (**Fig.5**). If the user faced any type of problem or query regarding mmpdatabase, he/she can contact by filling the query form or e-mail or by the phone number given on the page "Contact Info" (**Fig.6**).

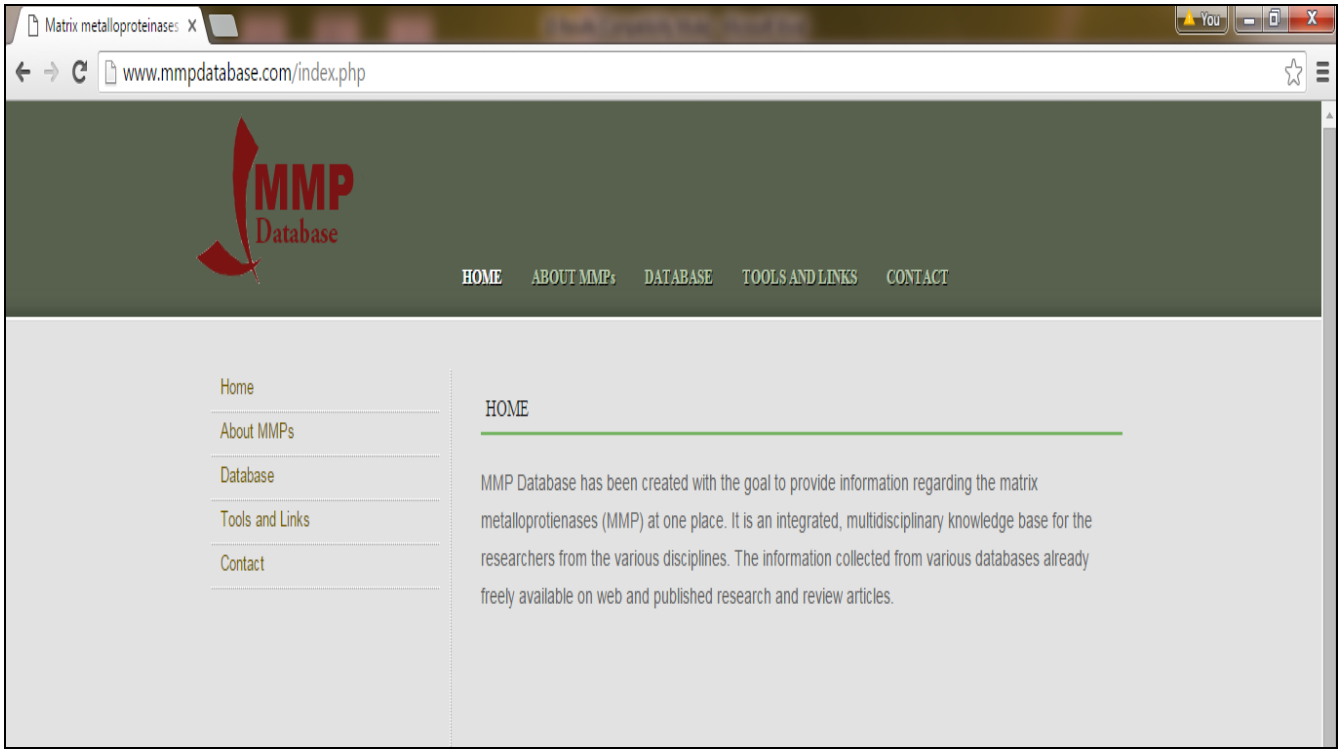


FIG. 1: HOMEPAGE OF MMP DATABASE AS FIRST LOOK ON THE WEB

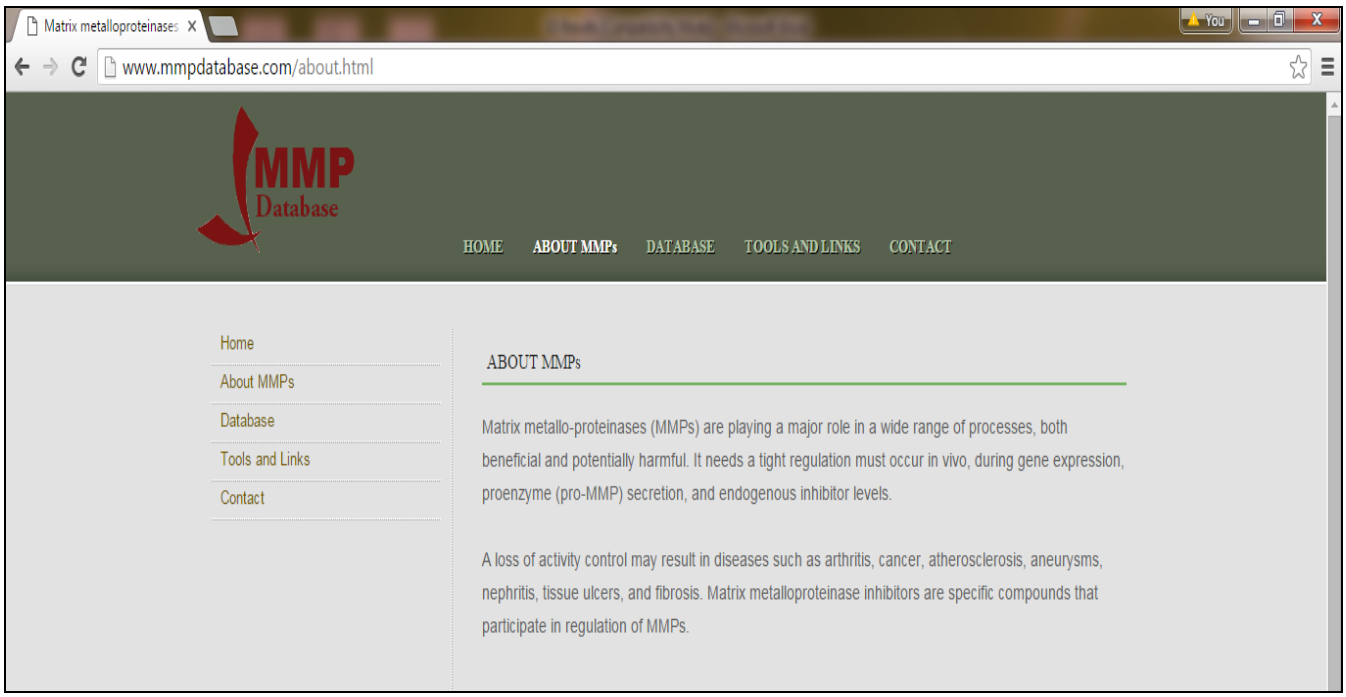
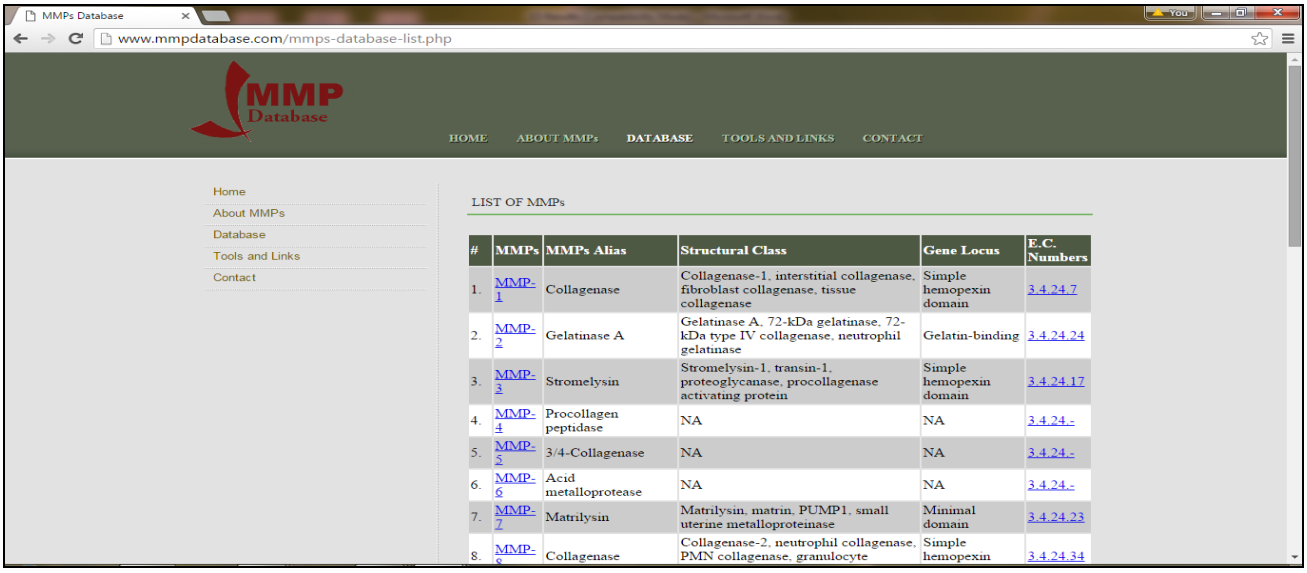
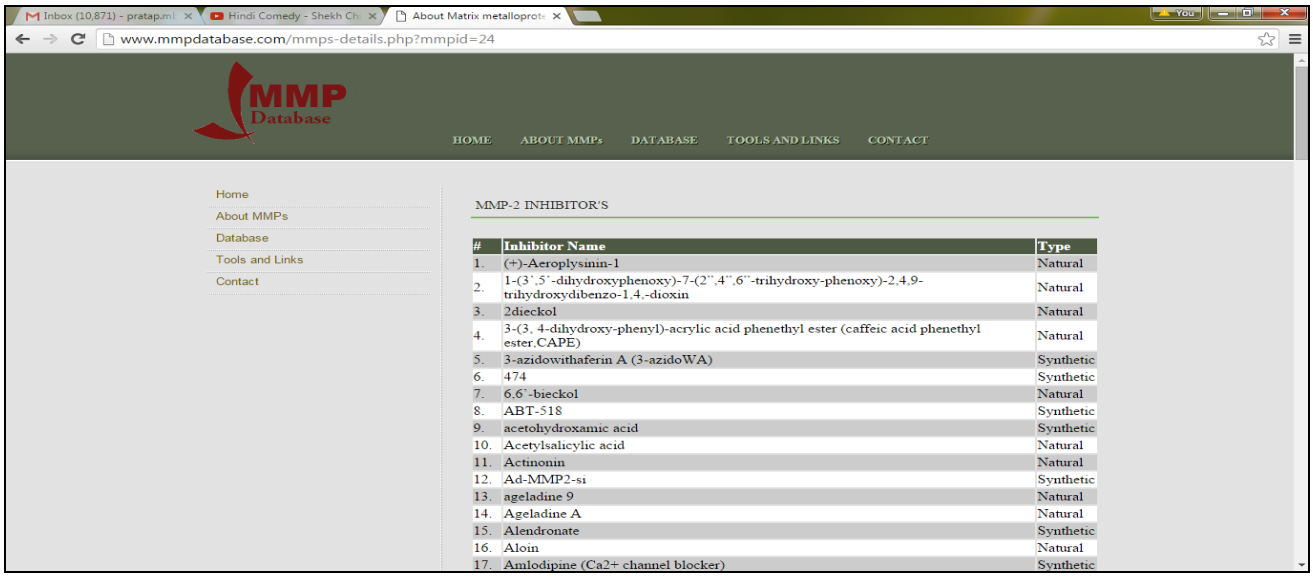


FIG. 2: WEB PAGE OF THE MMPDATABASE SHOWING INFORMATION REGARDING MMPS.



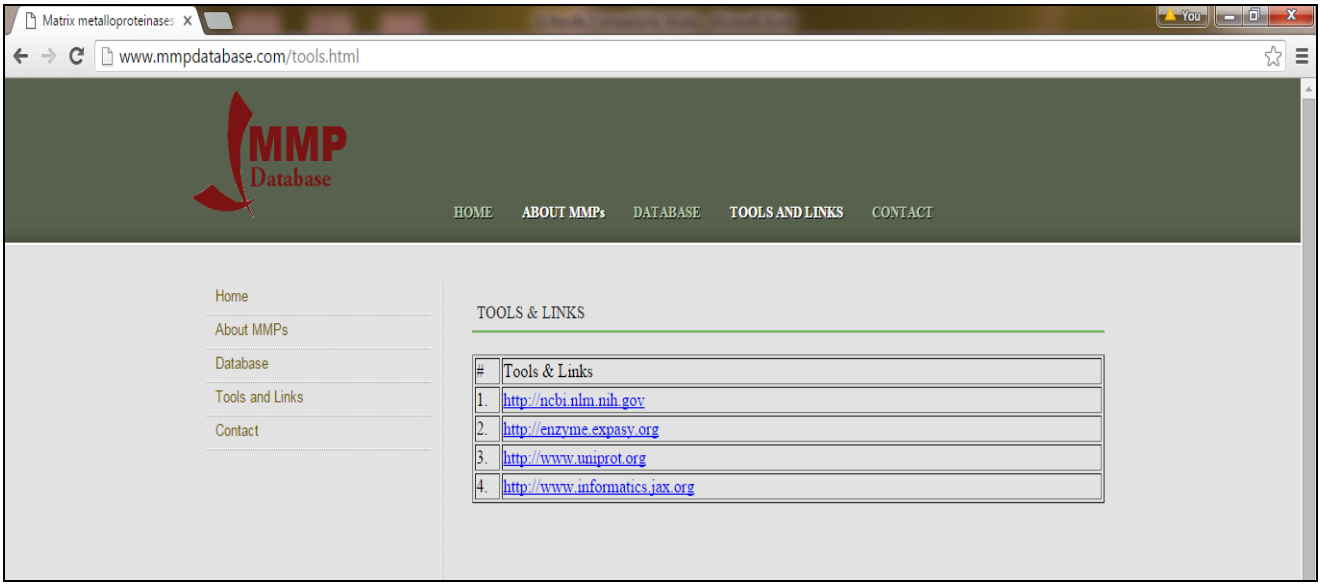
#	MMPs	MMPs Alias	Structural Class	Gene Locus	E.C. Numbers
1.	MMP-1	Collagenase	Collagenase-1, interstitial collagenase, fibroblast collagenase, tissue collagenase	Simple hemopexin domain	3.4.24.7
2.	MMP-2	Gelatinase A	Gelatinase A, 72-kDa gelatinase, 72-kDa type IV collagenase, neutrophil gelatinase	Gelatin-binding	3.4.24.24
3.	MMP-3	Stromelysin	Stromelysin-1, transin-1, proteoglycanase, procollagenase activating protein	Simple hemopexin domain	3.4.24.17
4.	MMP-4	Procollagen peptidase	NA	NA	3.4.24.-
5.	MMP-5	3/4-Collagenase	NA	NA	3.4.24.-
6.	MMP-6	Acid metalloprotease	NA	NA	3.4.24.-
7.	MMP-7	Matrilysin	Matrilysin, matrin, PUMP1, small uterine metalloproteinase	Minimal domain	3.4.24.23
8.	MMP-8	Collagenase	Collagenase-2, neutrophil collagenase, PMN collagenase, granulocyte	Simple hemopexin	3.4.24.34

FIG. 3: WEB PAGE OF THE MMPDATABASE CONTAINING ALL TYPE OF MMPS WITH RELATED INFORMATION.



#	Inhibitor Name	Type
1.	(+)-Aeroplysinin-1	Natural
2.	1-(3',5'-dihydroxyphenoxy)-7-(2'',4'',6''-trihydroxy-phenoxy)-2,4,9-trihydroxydibenzo-1,4,-dioxin	Natural
3.	2dieckol	Natural
4.	3-(3, 4-dihydroxy-phenyl)-acrylic acid phenethyl ester (caffeic acid phenethyl ester,CAPE)	Natural
5.	3-azidowithaferin A (3-azidoWA)	Synthetic
6.	474	Synthetic
7.	6,6'-bieckol	Natural
8.	ABT-518	Synthetic
9.	acetohydroxamic acid	Synthetic
10.	Acetylsalicylic acid	Natural
11.	Actinonin	Natural
12.	Ad-MMP2-si	Synthetic
13.	ageladine 9	Natural
14.	Ageladine A	Natural
15.	Alendronate	Synthetic
16.	Aloin	Natural
17.	Amlodipine (Ca2+ channel blocker)	Synthetic

FIG. 4: WEB PAGE OF MMPDATABASE CONTAINING MMP-INHIBITORS (NATURAL/SYNTHETIC).



#	Tools & Links
1.	http://ncbi.nlm.nih.gov
2.	http://enzyme.expasy.org
3.	http://www.uniprot.org
4.	http://www.informatics.jax.org

FIG. 5: WEB PAGE OF MMPDATABASE WITH WEB RESOURCES OF INFORMATION RETRIEVAL.

FIG. 6: WEB PAGE OF MMPDATABASE WITH CONTACT INFO IN CASE OF ANY ISSUES RELATED TO DATABASE

DISCUSSION: Electronic data publishing is here, and Nobel laureate Walter Gilbert has argued that access to such resources is changing the way biology is done [1]. Scientists must have reliable scientific literature with which to communicate, and this is possible only through the establishment and use of professional editing standards. A primary service provided by a traditional scientific journal is the certification of the results presented in its papers. Scientists are always more willing to accept, or at least to take seriously, findings presented in journals with well-established editorial policies and a reputation for stringent review [3-10].

Ziman argues that the primary goal of scientific literature should be the achievement of consensus. This requires that established standards be maintained, both in editorial policy and in decorum. Words chosen for their rhetorical flourish or their stylistic grace may charm the already convinced, but they are not as effective in generating consensus as words chosen for clarity and precision [2].

As the huge amount of data generated by experiments and other recourses, this data is stored in some places with the manipulations are also done according to the need, it requires a continuous monitoring of the data to prevent the storage of wrong information in databases.

CONCLUSION: The present challenge is to handle a huge volume of data, such as the ones generated by the different researches including the human genome project. There is no doubt that bioinformatics tools for efficient research will have

significant impact in biological sciences and betterment of human lives. The advantage of any database is that the stored information can be used further for research purposes.

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How to cite this article:
Shankar P, Singh DK, Lakhani P, Tutu S, Singh S, Sachan AK and Dixit RK: MMP database: online repository providing information regarding mmps and its inhibitors. Int J Pharm Sci Res 2017; 8(1): 334-38.doi: 10.13040/IJPSR.0975-8232.8(1).334-38.