# BIOINFORMATICS AND ADME DATABASES ARE USED IN CAAD

Pragya Yadav, Manoj Kumar Yadav, Piyush Yadav, Shashikant Maury, Ravikant Vishwakarma

Prasad Institute of Technology, Jaunpur, UP, India

(Department of Pharmacy)

**ABSTRACT:-**

Bioinformatics is an important area because it has allowed scientists to map the entire human genome computationally. A large amount of biological data can be stored in bioinformatics databases and retrieved using biological tools. Its application in medicine is the creation of drugs that only target diseased genes. ADME database also contains the updated & comprehensive data on interactions of substances with drug metabolising enzymes & drug transporters. It is intended for use in drug research & development, including drug-drug interactions & ADME studies.

**KEYWORDS:-**

CADD, Bioinformatics, SBDD, LBDD, Software, ADME, Database

**INTRODUCTION:-**

CADD(Computer Aided Drug Design) is a modern computational technique used in the drug discovery process to identify and develop a potential lead. CADD includes computational chemistry, molecular modeling, molecular design and rational drug design. CADD is being used to optimize identified leads. CADD techniques are gaining popularity and appreciation in both academic circles as well as in pharmaceutical industries. CADD approach saves time; it is fast and cost-effective.[1]

CADD approach can be utilized in 4 phases:-[2]

1. Screen small molecule library against the target using virtual screening (VS) protocol to identify hits/leads.
2. Investigate specificity of the selected hits from VS using molecular docking in the active site of other known targets.
3. Predicting ADME properties of the selected hit using in silico techniques and the promising hits are called as lead.
4. Helps to optimize the leads by designing better molecules for synthesis and testing. Based on the availability of the 3D structure of the target protein.

CADD techniques are grouped into either of two types –[3]

**a)** Structure-based drug design (SBDD)

**b)** Ligand-based drug design (LBDD)

**(a)STRUCTURE-BASED DRUG DESIGN:-**

Structure-based CADD seeks the knowledge of the target protein structure in the determination of interaction levels of all compounds being examined.[3]

**(b)LIGAND-BASED DRUG DESIGN:-**

Ligand-based CADD relies on the chemical similarity criteria, and the predictive, quantitative structure–activity relationship (QSAR) models that it creates from the molecules to determine the known active and inactives.[3]

**BIOINFORMATICS:-**

The concept bioinformatics was coined by Paulien Hogeweg and Ben Hesper in 1970 as "the study of informatics processes in biotic systems". Paulien Hogeweg is a Dutch theoretical biologist and complex systems researcher researching biological systems as dynamic information processing systems at many interconnected levels.[4]

Bioinformatics describes any use of computers to handle biological information. In practice, the definition used by most people is narrower; bioinformatics to them is a synonym for "computational molecular biology"- the use of computers to characterize the molecular components of living things. Bioinformatics is the unified discipline formed from the combination of biology, computer sciences, and informational technology. It is the use of computer for the acquisition, management, and analysis of biological information.[5]

**BJECTIVE OF BIOINFORMATICS:-**

- At its most basic level, bioinformatics organises data so that researchers can access existing data and send new entries as they are created.[6]

  **e.g.**

  The Protein Data Bank for 3D macromolecular structures.
- It is to develop tools and resources that aid in the analysis of data. The analysis and interpretation of various types of data including nucleotide and amino acid sequences, protein domains, and protein structures.[6]

- It is the creation and implementation of tools that allow efficient access and management of various types of information, or it is the use of these tools to analyse data and interpret the results in a biologically meaningful manner.[6]

**BIOINFORMATICS SOFTWARE:-**

Bioinformatics is done with sequence search programs like BLAST, sequence analysis programs, like the EMBOSS and Staden packages, structure prediction programs like THREADER or molecular imaging/modeling programs like RasMol and WHATIF.[7]

More:

- NetSurfP - Protein Surface Accessibility and Secondary Structure Predictions.
- NetTurnP - Prediction of Beta-turn regions in protein sequences
- MODELLER - Used for homology or comparative modeling of protein three-dimensional structures
- AutoDock - Suite of Automated Docking Tools
- Gromacs - A molecular dynamics package primarily designed for biomolecular systems such as proteins and lipids
- OrfPredictor - The OrfPredictor (ORF-Predictor) server is designed for ORF prediction and translation of a batch of EST or cDNA sequences.

**USES OF BIOINFORMATICS:-**

Bioinformatics used in various field-

a) Medicine-
   - Drug discovery
   - Personal medicine
   - Preventive medicine
   - Gene therapy

b) Microbial Genome-
   - Waste cleanup
   - Climate change

**ADME DATABASES:-**

A database, in the most general sense, is an organized collection of data. It is an electronic system that allow data to be easily accessed, manipulated & updated. Many organization uses database as a method of storing, managing& retrieving information. Modern databases are managed using a database management systems.[8]

Absorption, Distribution, Metabolism, Excretion (ADME) are acronyms for Absorption, Distribution, Metabolism, Excretion. The prediction of ADME properties is critical in the drug design process because these properties are responsible for about 60% of all drug failures in clinical trials. Whereas in the past, ADME methods were used towards the end of the drug development process, today ADME is used at the beginning of the process to exclude molecules with weak ADME properties from the drug development pipeline, resulting in substantial research and development cost savings.[8]

ADME database also contains the updated & comprehensive data on interactions of substances with drug metabolising enzymes & drug transporters. It is intended for use in drug research & development, including drug-drug interactions & ADME studies. The information is provided by category, drug name, enzyme, reaction & type. It is supported by chemical / metabolite structures as well as kinetic values mention in the literature.

The contents of the database were collected & organized according to the Human $P_{450}$ and Transporter Metabolism Database. The database is accessible and completely searchable by keywords or chemical structures. Advanced searches are also obtainable to support investigational studies on drug-drug interactions. ADME Database contain more than 26,000 substances, several natural products and preparations, in addition to others factors affecting Drug metabolizing enzymes activity. The data collected from more than 18,000 citations.[8]

**FEATURE OF HUMAN DRUG METABOLIZING ENZYME DATABASES:-**

It provides information on CYP enzymes (Cytochrome P450) and their variants, which are used to research xenobiotic and endobiotic metabolism in humans. Based on interactions with substrate, inhibitor, inducer, and activator, it provides information on substances that affect CYP behaviour (as well as a variety of natural products and other factors).[9]

The database gives other enzymes information also such as Esterases, UDP-glucuronosyl transferases, sulphotransferases, Glutathione S-transferases, Flavin-containing Monooxygenases.

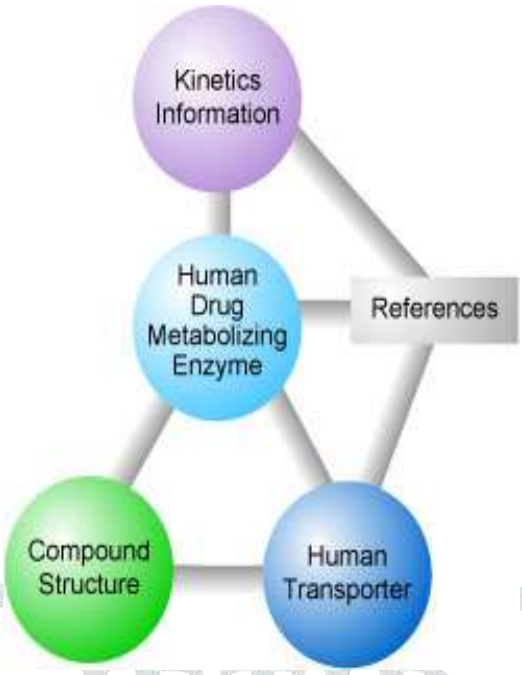


**Fig. ADME database**

**KINETICS INFORMATION DATABASES:-**

It also contains supporting entries from the Human Drug Metabolizing Enzyme Database, which provide numerical data on key kinetic parameters useful in drug development and analysis.

It provides information about in vitro assay used,$K_m$, $V_{max,}$ $k_{i,,}$ k.inactivataion, cooperativityn, $IC_{50}$, $EC_{50}$, $t_{1/2}$ The kinetic database is accessible only when it is joined with Human Drug Metabolizing Enzyme Database.[9]

**HUMAN DRUG TRANSPORTER DATABASES:-**

It contains information on transporters involved in transport of drugs, physiological compounds, nutrients, and other chemicals and metabolites. It is featured with ABC Transporters, Organic Ion Transporters , Nucleotide Transporters, etc.

Apart from above mentioned database, a number of databases describing specific classes of ADME-associated proteins have appeared. A new database, ADMW-associated proteins(ADME-AP), is introduced to give complete information about all classes of ADME-associated proteins illustrated in the literature including physiological function of each ligang/protein, ADME classification, pharmacokinetic effect direction and driving force of disposition, location and tissue distribution, synonyms, substrates, gene name and protein availability in other species. Cross-links to other database are also provided to help the access of information about the sequence, function, 3D structure, genetic disorders, polymorphisms, nomenclature, ligand binding properties and related literatures of each protein. ADME-AP at present has entries for 321 proteins and 964 substrates.[9]

**ACKNOWLEDGEMENT:-**

Computer-aided drug design (CADD) has been used in almost every phase of the drug development process. Over the last few years, there has been a lot of progress in the creation and implementation of novel

approaches. Bioinformatics refers to the use of computers to process biological data. In fact, most people use a narrower definition; bioinformatics is a synonym for "computational molecular biology," which involves using computers to classify the molecular components of living things. The revised and detailed data on interactions of substances with drug metabolising enzymes and drug transporters can also be found in the ADME database. It's designed for drug discovery and testing, including drug-drug interactions and ADME studies. The data is broken down into categories, drug names, enzymes, reactions, and types.

**CONCLUSION:-**

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