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Review Article

ADVANCED DRUG DESIGNING SOFTWARES AND THEIR APPLICATIONS IN MEDICAL RESEARCH

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ABSTRACT

Drug designing softwares has potential role to design novel proteins or drugs in biotechnology or pharmaceutical field. The drug designing softwares are used to analyze molecular modeling of gene, gene expression, gene sequence analysis and 3D structure of proteins. In addition, drug designing area has important role in the diagnosis of diseases such as lung cancer, brain cancer, breast cancer and Alzheimer disease. This review article summarizes the structure based drug designing and ligand based drug designing softwares and their applications in the field of medical research.

Keywords: Drugdesignsoftwares,Medicalresearch

INTRODUCTION

Drug design is a process which involves the identification of a compound that displays a biological profile and ends when the biological profile and chemical synthesis of the new chemical entity are optimized[1]. Drug designing is otherwise known as rational drug design and it is a method of finding new medications based on the biological receptors and target molecules. It involves the designing of small molecules which is complementary to the biological receptor to which they bind and interact to cause the pharmacological actions [2]. Modern method of drug designing is done with the aid of computers and hence the process is known as Computer Assisted/Aided Drug Design (CADD). It uses computational chemistry to study about the drugs and related biological active molecules. The major aim is to find whether the given molecule bind to the target and causes pharmacological actions or not. The basic steps involved in CADD are:

- Hit identification using virtual screening.
- Hit-to-lead optimization of affinity and selectivity.
- Lead optimization of other pharmaceutical properties maintaining affinity.

In the present article, we discussed about structure based drug designing and ligand based drug designing softwares and their therapeutic potential in the field of medical research[3].

DRUG DESIGNING SOFTWARES

A computer needs software for its functions such as programs. This software makes our work simpler and faster. Various companies such as Accelrys, Schrodinger, Auto Dock and Argus Lab offering drug designing softwares.

Accelrys

Accelrys is a software company with its headquarters in US, along with its organization in Europe and Japan. It provides softwares especially for drug discovery and materials science. Their products and technologies create solutions for several stages in the drug discovery and developmental process[4]. The different softwares produced by Accelrys are:

- Insight II
- Pipeline Pilot
- Discovery Studio
- Materials Studio
- Accord

Insight II

Insight II is a graphical molecular modeling program. Using this software we can build and manipulate virtually any class of molecules or molecular systems. Some of these insight II computational engines have the capacity to restart calculations from informations in the saved files[5].

Pipeline Pilot

Pipeline Pilot datas are based on powerful client-server platform that leads to construct graphical workflows for data retrieval, filtering, analysis, and reporting. Data modeling in this software is done by modeling tools, statistical filters and clustering components optimized for large real-world data sets. One can create additional components using various technologies such as Perl, Java, SOAP and basic command line access. This software is used for sequence analysis, gene expression, in cheminformatics to study the ADME properties of the drug and check the toxic constituents present in the drugs[6].

Discovery Studio

Discovery studio is the advanced software solutions for life science researchers and is easy to use, a graphical interface for powerful drug design and protein modeling, sequence analysis, pharmacophore analysis and it is a structure based designing software. Discovery studio provides a visualizing tool ActiveX control, which provides 3D molecular structures and sharing scientific results. The sequence analysis is done by using tools such as BLAST (Basic Local Alignment Search Tool) and protein modeling by DS Modeller. It can be operated in different operating system applications such as Linux and Windows based environment[7].

Materials Studio

Materials studio software is the most advanced technology and is used to solve the problems in R&D process. It is designed for structural and computational researchers in chemicals and materials R&D. Materials studio provides tools for modeling crystal structure and crystallization processes; property prediction for molecules, polymers, catalysts and for determining the structure activity relationship. They provide various ranges of quantum mechanics based tools for predicting structures, density functional methods, linear scaling and semi-empirical tools. QSAR integration in the Materials studio has wide range of descriptors such as topological

and electro-topological descriptors, these helps the calculation process easier[8].

Accord

Accord is software specially designed for cheminformatics. They can capture, manage, analyze, and mine chemical data. Accord is oracle based software used for storage, retrieval, analysis of chemical structures and related biological, chemical and inventory data. Accord is user friendly and is powered by Robust and well proven chemistry engine that can be used for any type of chemistry[9].

Schrodinger

Schrodinger software provides accurate, reliable and high performance computational technology and provides facilities to solve problems in life science research. It was used for molecular modeling and well suited for drug designing both structure based and ligand based methods. Most of the pharmaceutical companies, biotechnology companies, government agencies, universities and supercomputing centers are using this software[10]. The various products of Schrodinger are:

- Glide
- Prime
- Jaguar
- Macro Model

Glide

Glide offers a complete solution for ligand-receptor docking with speed and accuracy. Glide works with HTVS- High Throughput Virtual Screening mode in which it can retrieve million compound libraries, to Standard Precise (SP) mode in which it docks hundreds to thousands of ligands with high accuracy. From SP it switches to XP Extra Precision where the false results are changed by advanced scoring. They can also exhibit excellent range of docking accuracy across diverse range of receptors. This makes the glide universally applicable[11].

Prime

Prime is a package used for protein structure predictions. It is user friendly. Prime provides users complete control over calculational settings to increase the accuracy of the result, they provide accurate receptor models for structure based drug design. Homology modeling and fold recognition can be done using prime. Comparative modeling is used to generate accurate homology models for further structure based studies. Threading and fold recognition techniques are used in cases of low or no sequence identity. Prime allows the users to specify and adjust parameters to optimize the quality of predictions[12].

Jaguar

Jaguar is a high performance ab-intio package for both gas and solution phase recreation, with particular strength in treating metal containing systems. Jaguar proceeds faster than the other conventional methods and it makes more possible to carry out more calculations at a single time. Jaguar computes a comprehensive array of molecular properties such as NMR, IR, pKa, partial charges, electron density, electrostatic potential and NBO analysis. It also generates potential energy surface with respect to differences in the internal co-ordinates[13].

Macro Model

Macro Model is a complete molecular modeling packaging suitable using leading force fields which provides accurate results. Force-field molecular modeling is used to examine molecular conformations, molecular motions and inter molecular interactions such as ligand-receptor complex. It can also perform molecular dynamics at constant temperatures using mixed Monte Carlo algorithm and stochastic dynamics. They help wide range of searching methods and handling systems in the range of small molecules to entire proteins. Different types of force fields such as MM2, MM3, AMBER, AMBER 94, MMFF, and OPLS-AA are supported by Macro Model to do a wide range of research applications[14].

Auto Dock

Auto Dock is a pack of automated docking tools which is designed to dock small molecules, like how substrates or drug candidate binds to the receptor of a known 3D structure. It consists of two programs:

1. Auto Dock – it performs docking of the ligand with the target molecule which is a protein.
2. Auto Grid- pre calculates this binding of the ligand with the target molecule.

This type of study can help in designing better binders. Auto Dock Tools (ADT) has been developed to set up which type of bonds is rotatable in the ligand to analyze the docking. Auto Dock has several applications in[15]

- X-ray crystallography
- Structure-based drug design
- Lead Optimization
- Virtual Screening (HTS)
- Combinational library design
- Protein-Protein docking
- Chemical mechanism studies.

Argus lab

Argus lab is molecular modeling software that runs on windows. It is free software and can be easily accessed by the public. It consists of a user interface that displays the graphical structure of the molecules and runs quantum mechanics calculation using Argus Computing Server[16]. By using Argus lab we can able to build an atom, build molecules using templates, to change the structure of an atom and bond types, and to build new structures from the pre-existing structures[17].

Table1: List of Drug designing softwares and their therapeutic potential

Drug Designing Software	Types	Therapeutic potential
Insight II	Structure based	Graphical molecular modeling
Pipeline Pilot	Structure based	Gene sequence analysis
Discovery Studio	Structure based	Protein modeling
Materials studio	Structure based	Modeling crystal structures
Accord	Structure based	Cheminformatics
Glide	Ligand based	High Throughput Virtual Screening
Prime	Structure based	Protein structure prediction
Jaguar	Structure based	Gas and solution phase reaction

Macro Model	Ligand based	Docking of ligand and target molecule
Argus lab	Ligand based	Build molecules using templates

CONCLUSION

The drug designing softwares such as Insight II, Discovery Studio, Materials Studio, Accord, Prime and Jaguar are used for structure based drug designing and drug designing softwares such as Glide, Macro Model, Auto-dock and Argus lab are used for ligand based drug designing. In addition, structural based drug designing softwares are used for molecular modeling, protein modeling and gene sequence analysis. In case of ligand based drug designing softwares are mainly used for docking the ligand with target drug molecules. Therefore, these structure based and ligand based drug designing softwares have potential applications in the pharmaceutical or biotechnology field to design novel drugs.

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