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A Review on Computational Drug Designing and Discovery

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Abstract

Novel Drug discovery and the development of new medicine is a time-consuming, complex, costly and highly risky process. This is the reason computer-aided drug design (CADD) approaches are widely used in the pharmaceutical industry to accelerate the procedure and the hit rate of novel drug compounds, as it uses a much more targeted search than the traditional HTS. On an average of 10 to 15 years and US $500-800 million to introduce a drug into the market along with the synthesis and testing of lead compounds. Therefore, it is beneficial to apply computational tools in hit-to-lead optimization to cover a wider chemical space while reducing the compounds to synthesize and test in vitro. Homology modeling is used for the prediction of three-dimensional structure of the protein, whereas molecular docking is been performed to study the interaction of a drug molecule with the protein. The best orientation of docked structure (ligand-protein) obtained based in the overall minimum energy. In silico methods are used to identify potential drugs for various diseases. Thus, computer-aided drug designing has played an integral part of the drug discovery process. The main purpose of this review article is to give a glimpse about the part Computer Aided Drug Design has played in present medical science and the scope it conveys in the near future, in the service of designing newer drugs along with lesser expenditure of time and money.

Keywords: Drug discovery; Autodock; Malaria; Flaviviruses; Tuberculosis; ligand; Zikavirus; Dengue

Introduction

Drugs are basic for the prevention and treatment of disease. Thus, ideal drugs are in great demand. Few approaches are required, which would form the basis of Computer Aided or in silico Drug Designing [1]. The use of computational methods in drug discovery and development process is gaining popularity, implementation and appreciation nowadays. The computational optimization of a hit compound involves a Structure-Based Drug Design and Ligand-Based Drug Design. Structure-based involves in the analysis of docking poses and energy profiles for hit analogs, whereas ligand-based screening of compounds with similar chemical structure to know the improved predicted biological activity or prediction of affinity,

optimize the drug based on metabolism and pharmacokinetics (DMPK) or to know potential for toxicity using absorption, distribution, metabolism, excretion, and the (ADMET) properties [2,3].

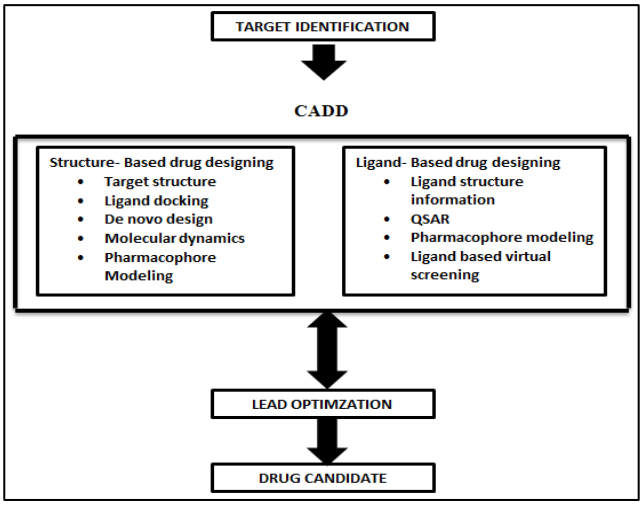

FIG. 1. **Drug designing and discovery pipeline**

FIG. 1 shows the drug discovery pipeline mainly deals with screening of large number of compounds with reference to a native ligand that is present in the viral protein. The structure-based methods shows increasing utility for the discovery of lead compounds, and especially for the refinement of lead compounds and for the re-engineering of drugs to overcome certain types of resistance. The structure-based methods are becoming quite important in part of rapid growth in structural data, and in particularly high speed with which structures can be determined as part of a focused drug-discovery effort with a well-determined target [4].

Target Identification and Validation

The primary stage in the drug discovery pipeline is identification of targets and its validation, which is still a challenging task. Various technologies for addressing the targets have developed, whereas genomic and proteomic approaches are the major tools for target identification and few of the databases shown in TABLE 1. A proteomic approach involves the comparison of protein expression profiles for a given cell in the presence or absence of the given molecule for identification of binding proteins for a given small molecule, it is not been proved very successful in target discovery as it is laborious and much time consuming. Hence, complementary to it, a series of computational (in-silico) tools have developed for target identification that is categorised into sequence-based approach and structure-based approaches [5-7].

TABLE 1. **Few Drug target identification databases**

UTILITY	**URL**
In silico target identification	http://www.dddc.ac.cn/pdtd/
Pathway analysis	http://www.genome.jp/kegg/
	http://www.geneontology.org
	http://www.reactome.org
	http://www.pantherdb.org

	http://www.biocarta.com
	http://www.ingenuity.com/
Chemogenomic data	http://www.ebi.ac.uk/chembldb
	http://pubchem.ncbi.nlm.nih.gov
Drug target database	http://www.drugbank.ca
Protein data bank	http://www.pdb.org
Disease specific target database	http://thomsonreuters.com/metacore
Pharmacogenomic data	http://www.pharmgkb.org
Multi-level drug data	http://r2d2drug.org/DMC.aspx
Comparative toxicogenomic database	http://ctdbase.org
Target-toxin database	http://www.t3db.org
Protein expression information	http://www.proteinatlas.org
Therapeutics target database	http://bidd.nus.edu.sg/group/cjttd/

Sequence-based approach includes the processes of target identification by providing functional information related to targets and the positioning information to biological networks. The diseases caused by external pathogens such as bacteria and viruses, for those unique targets are mainly found in the pathogens by comparing functional genomics from humans with the corresponding genomics from pathogens.

Disease specific examples of drug discovery attempts using Computational tools

Malaria

Malaria is a devastating infectious disease that characterized by intermittent high fevers caused by the protozoan parasites of the genus *Plasmodium* and it is characterized by intermittent high fevers. The re-emergence of drug-resistant *Plasmodium falciparum*, the most fatal human malarial parasite that is been focused on the Shikimate pathway [8,9]. Shikimate pathway is seven-step metabolic process that mainly found only in microorganisms and plants. First step includes the glycolytic intermediate phosphoenol pyruvate and the pentose phosphate pathway intermediate erythrose- 4-phosphate is been condensed to a seven-carbon six-membered heterocyclic compound, 3-deoxy-o-arabino-heptulosonate Fphosphate (DAHP), which is formally which is 2-deoxy-~-glucose-6-phosphate derivative as shown in FIG 2. The ring oxygen is been exchanged for the exocyclic C7 of DAHP to form a highly substituted cyclohexane derivative, 3-dehydroquinate in the second step. The other remaining five steps serve to introduce a side chain and two of the three double bonds that convert cyclohexane into the benzene ring. DAHP synthase, 3-dehydroquinate synthase, 3-dehydroquinate dehydratase, shikimate dehydrogenase, shikimate kinase, EPSP synthase and chorismate synthase are seven different enzymes involved in the pathway. This pathway connects the metabolism of carbohydrates to biosynthesis of aromatic compounds through seven metabolic steps. Phosphoenolpyruvate (PEP) and erythrose 4-phosphate is converted to chorismate, which is the precursor for synthesising a series of aromatic compounds, naphtoquinones, menaquinones, and mycobactins [10-14].

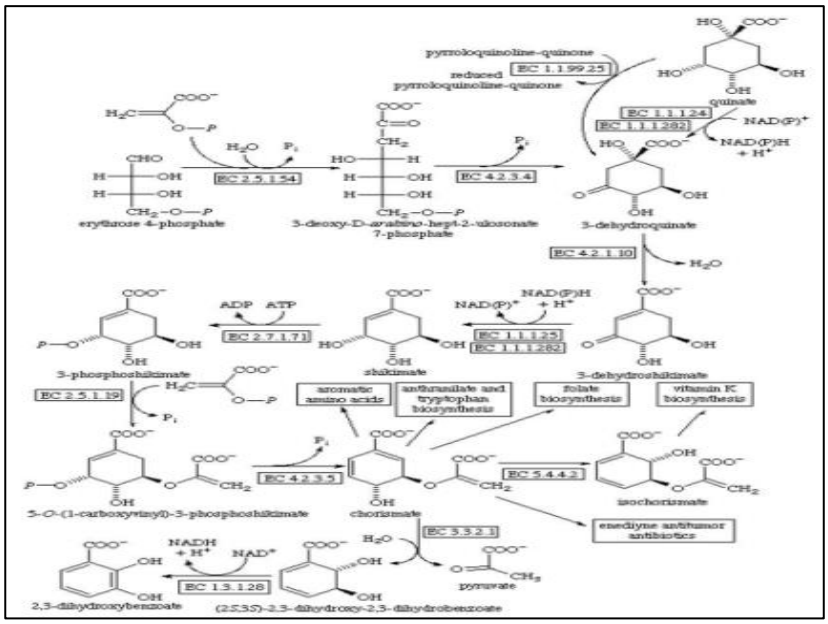

FIG. 2. **The sequence of seven metabolic steps in the shikimate pathway, from phosphoenolpyruvate and erythrose 4-phosphate to chorismate** [**Source:** IUBMB, 2002] [15]

Chorismate Synthase is the key enzyme of the pathway which helps in conversion of 5-enolpyruvylshikimate 3-phosphate to Chorismate via a 1,4-trans elimination of phosphate. The PfCS structure along with cofactor FMN was been predicted by homology modeling by using the crystal structure of Helicobacter pylori chorismate synthase. PDB code 1UM0 as shown in FIG 3, whose sequence length is 365 residues. The structure includes 32% helical (12 helices; 118 residues) and 23% beta sheet (28 strands; 87 residues) [16].

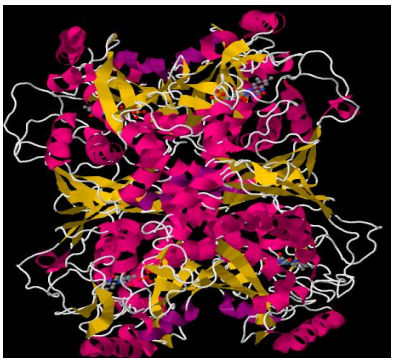

FIG.3. **Secondary structure of 1UM0** [**Source:** Ahn HJ et al. 2004] [17]

Further, the enzyme was catalysed using online and off-line bioinformatics tools like PHYLO_WIN tool to construct the phylogenetic tree, PROCHECK, Eukaryotic Linear Motif, SOPMA tool, etc. The outcome provided a deep insight about the detailed structure and function of Chorismate Synthase and aid in rational drug designing [18-20].

HIV(Human Immunodeficiency Virus)

Acquired immunodeficiency syndrome (AIDS) is an immunosuppressive disease caused by human immunodeficiency virus (HIV) which mainly affects the $CD4^+$ T cells and dendritic cells in the human immune system. Out of three key enzymes, HIV-1-reverse transcriptase plays a vital role in the virion development. The two classes of RT inhibitors are nucleoside RT inhibitors (NRTIs) and the non-nucleoside transcriptase inhibitors. The primary target for antiretroviral drugs is HIV-1 enzyme RT [16]. Reverse Transcriptase is a heterodimer composed of two 560 and 440 amino acid residues subunits which are referred to as p66 and p51[3]. These subunits share the same amino acid sequences. Subunit p51 lacks the catalytic activity and whereas RNase H domain is performing a structural role. Unlike p51, p66 has the more flexible structure and contains polymerase and RNase H active sites as shown in FIG 4. All the commercially available RT-targeting drugs affect the polymerase activity by inhibiting its function, some RNase H inhibitors are designed recently and studied [21,22].

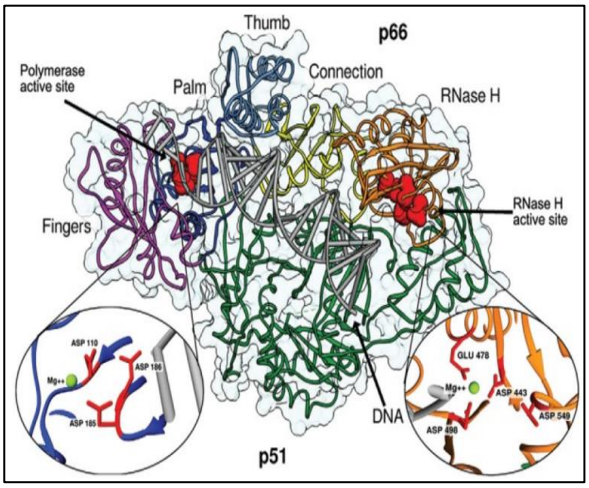

FIG. 4. **(PDB:1T05) Structure of human immunodeficiency virus-1 reverse transcriptase (HIV-1 RT) in complex with DNA** [**Source**: Lucianna HS et al. 2015] [23]

The RNase H domain is located at the p66 C-terminus, RNase H active site contains a DDE motif comprising residues of carboxylates ASP443, GLU478, ASP498 and ASP549 that can coordinate as a divalent Mg2+ ion.

Receptor and ligand preparation of HIV-1-RT, anti-HIV alkaloid was considered for *in silico* docking. The Active site prediction was done using Q-Site Finder, 12 alkaloids were considered from a medicinal plant *Toddalia asiatica* for its probabilistic binding with the active site of the HIV-1-reverse transcriptase, Molecular docking study was carried out using Autodock v4.0,where toddanol, toddanone, and toddalenone found to be potent inhibitors of HIV-1-RT. ligand-enzyme complex simulation was performed using GROMACS 4.5.5 software, alkaloid toddanol could aid in efficient for HIV-1 drug discovery [24].

Tuberculosis

Tuberculosis (TB) is an infectious illness caused by bacteria called Mycobacterium tuberculosis, which is the second leading cause of death. Mycobacterium tuberculosis (MTb) is a gram-positive organism spread through the persons through Air. The rapid increase of multidrug-resistant tuberculosis has resulted in an urgent need to develop new drug targets for Mtb.

FIG 5 demonstrates the first step in the fatty acid synthesis, which is the production of malonyl-COA. It is been produced from the carboxylation of acetyl CoA by the catalytic action of Acetyl-CoA carboxylase. Acetyl-CoA carboxylase is a multi-

subunit catalyst having three dissimilar domains: Biotin Carboxyl Carrier Protein (BCCP), biotin carboxylase component, and transcarboxylase component. Active holo Biotin Carboxyl Carrier Protein (BCCP) plays a vital role in promoting the initiation and elongation of fatty acid [25]. Biotin protein ligase catalyzes the transfer of biotin to BCCP, ApoBCCP is biotinylated by Biotin Protein Ligase (Bpl) to form holo BCCP. Hence targeting this biotin protein ligase (Bpl) will stop the synthesis of fatty acids, ultimately it leads to death of the organisms [26].

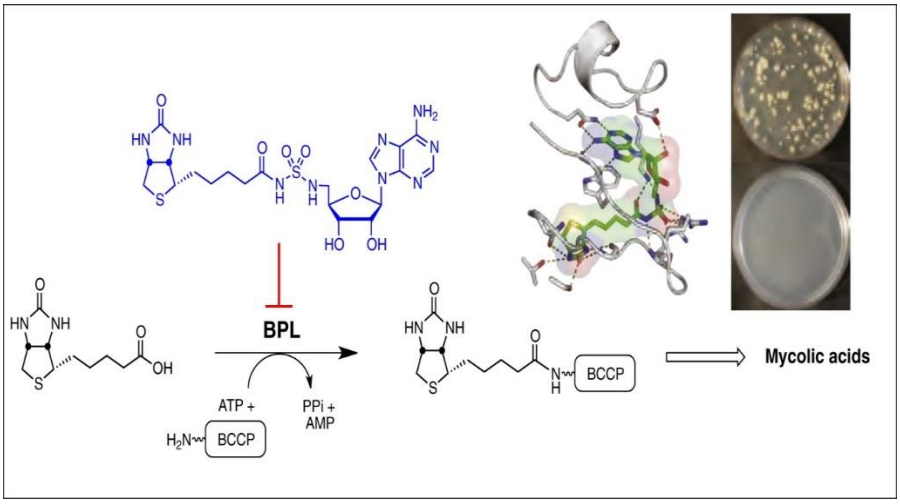

FIG. 5. **Fatty acid synthesis** [**Source**: Courtney CA, 2011] [27]

The crystal structure of biotin-protein ligase BirA from Mycobacterium tuberculosis which is in complex with an acylsulfamide bisubstrate inhibitor (PDB Code: 3RUX), whose sequence length is 270 and the secondary structure consists of 30% helical (11 helices; 83 residues) and 32% beta sheet (17 strands; 87 residues) as shown in FIG 6.

FIG. 6. **PDB Code: 3RUX: Secondary structure** [**Source**: Duckworth BP, 2011] [28]

MGL tools are used for docking preparation and Autodock Vina was used for calculation of binding energy. The docking site was analysed virtually by Pymol [29]. The Discovery Studio 4.0 was used to perform the computational screening methods. Screening of large number of compounds from Enamine REAL database and further conformations of the compounds generated using the Build 3D Database protocol. Docking KAPA and ACM, a known substrate and inhibitor of BioA was performed using CDOCKER docking protocol. Out of the mentioned number of compunds, seventeen compounds were assayed through microtiter and other four compounds, 7((Z)-N-(2-isopropoxyphenyl)-2-oxo-2-((3-(trifluoromethyl)

cyclohexyl) amino) acetimidic acid) displayed inhibitory activity against the growth of the *Mtb* H37Ra strain. The TOPKAT (Toxicity Prediction by Komputer Assisted Technology) protocol was used to predict the toxicity of compounds [30-32].

Yersinia

Plague is a bacterial zoonotic disease which infects both human beings and animals. Yersinia pestis is the causative agent of bubonic, pneumonic, and septicemic plague. It is always been recognized as one of the classical biological warfare or bioterrorism agents [33]. Shikimate pathway, seven steps metabolic route that is responsible for the synthesis of chorismate. Shikimate Kinase catalyzes the phosphorylation of shikimate to form shikimate 3 phosphates and ADP [34]. Shikimate Kinase is been studied extensively along with other important drug targets of pathogens as it is considered as a promising drug target [35,36]. FIG 7 shows the four structures are 1E6C from *Erwinia chrysanthemi* whose sequence length is 173, 1KAG from *Escherichia coli* whose sequence length is 214, 1L4U from *Mycobacterium tuberculosis* whose sequence length is 161 and 1VIA from *Campylobacter jejuni* whose sequence length is 167 as a templates for the target sequences.

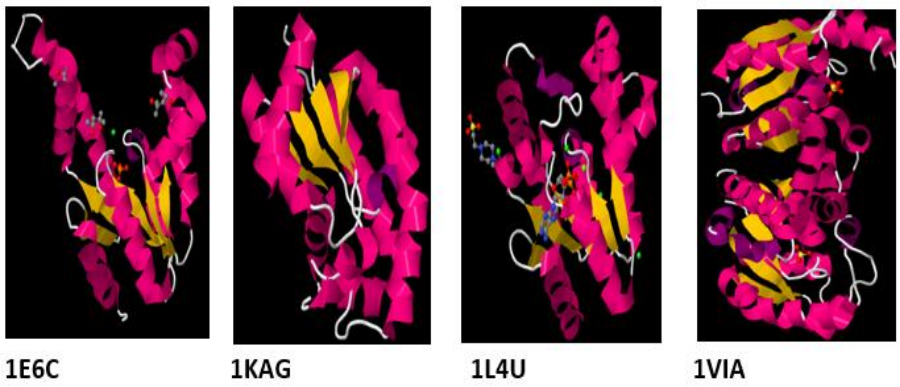

FIG. 7. **Secondary structure of 1E6C, 1KAG, 1L4U, 1VIA** [**Source**: Krell T, et al. 2001. Romanowski MJ, 2002. Gu Y, 2002. Badger J, 2005] [37-40]

The enzyme of KFB61218.1, EFA47400.1 and WP_016255950.1 considered as SK1, Sk2 and Sk3. Further, the important physicochemical properties are calculated. The secondary structures (Alpha helix, extended strand, Beta turn, Random coil and Ambiguous states) are predicted for SK using NPS server. Result shows that that random coils and alpha helices were predominant. The number of helices and turns were found to be 10 and 5 in modelled structures of SK1, SK2, and SK3. SK1 showed only 13 strands, whereas 15 strands were present in SK2 and SK3. Total H bonds present in SK1, SK2 AND SK3 were 117, 111 and 139 respectively [41]. Template search performed using the Modeller; template-target sequence alignment obtained using ClustalX. MODELLER9v3 is used to generate the models. SAVES server was used to evaluate the stereochemical quality by employing PROCHECK, WHATCHECK, VERIFY 3D and ERRAT program. PROSA is used to the stability of generated structures. Further these models were subjected for the identification of active sites using CASTp (Computed Atlas of Surface Topology of Proteins) [42-44].

Flaviviruses

The Flaviviridae are a family, Genus: Flavivirus of positive, single-stranded, enveloped RNA viruses. Flaviviruses are transmitted to hosts by arthropod vectors, mosquitoes in which they actively replicate. Over half of known flaviviruses have

been associated with human disease, including the human pathogens like yellow fever virus, dengue virus, Zika virus, Japanese encephalitis virus, West Nile virus, tick-borne encephalitis virus, etc. [45-48].

Dengue

Dengue infection is one of the most significant mosquito transmitted infection. This virus contains four antigenically distinct viral serotypes named as DEN-1, DEN-2, DEN-3 and DEN-4 which are transmitted by mosquitoes of the Aedes genus, primarily *Aedes aegypti* and *Aedes albopictus*. The core nucleocapsid C protein, envelope (E) glycoprotein and the membrane (M) protein are widely studied [49-55]. The glycoprotein E so-called precursor membrane protein, prM was also studied in details represented in various literature sources. It passes through the secretory pathway, where prM is cleaved to M in a late trans-Golgi compartment by furin-like protease. Most of the ectodomain of prM is removed in the cleavage, further releases a constraint on E and primes the particle for low-pH-triggered membrane fusion. E, which mediates both receptor binding and fusion, is a so-called ‘‘class II’’ viral fusion protein [56, 57]. The three-domain structures of dengue virus sE dimer includes Domain I, the 8-stranded central beta-barrel which organizes the structure. Its beta-strands are denoted as B0–I0 along with the short amino-terminal strand (A0) which is parallel to strand C0. The elongated domain II is formed by the insertions between strands D0 and E0 and strands H0 and I0, at the tip it bears the fusion peptide (Fig. 1B). Domain II contains mainly 12 beta-strands which are denoted as a–l, and 2 alpha-helices, alpha A and alpha B. Domain III contais ten beta-strands (Figure 8). Beta-strands predominate in all the three domains (1OAN) [58-62].

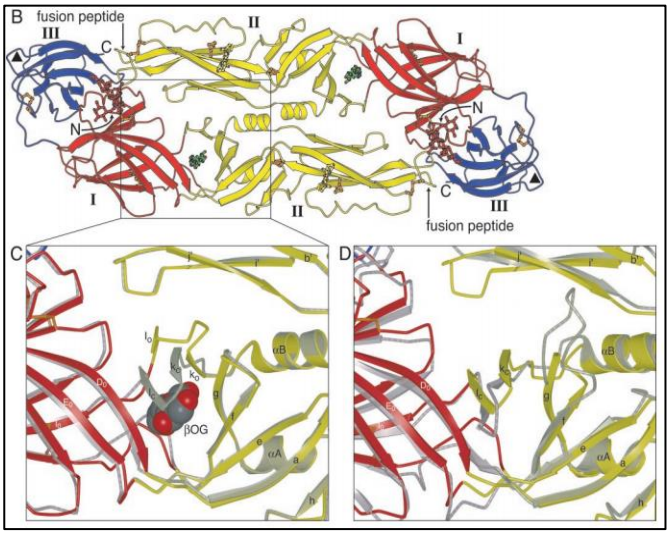

FIG.8. Dengue E protein and its ligand-binding pocket [**Source**: Stephen C. Harrison, 2003] [63]

Number of compounds having same drug like properties were selected for molecular studies and those are optimized using bioinformatics tools ChemBioDraw Ultra 13.0 and HyperChem professional 8.0.10. Docking was performed with the receptor 2FOM structure using AutoDock 4.2. LigandScout software is used for creating the three-dimensional (3D) pharmacophore models. The docked complexes were analyzed closely using Visual Molecular Dynamics (VMD) [64].

West Nile virus

The 2B and 3(NS2B–NS3) are the non-structural proteins of West Nile Virus (WNV) which mainly constitutes the proteolytic complex further mediates both the cleavage and processing of the viral polyprotein. NS3 initiates NS2B and NS5 proteins to

direct the protease and replication activities. NS3 alone triggers the apoptotic pathways involving both caspases-8 and -3. Test results from use of caspase specific inhibitors and caspase-8 siRNA showed that the initiation of apoptotic signaling in NS3-expressing cells is done by the activation of caspase-8. It was experimented that expressions of protease and helicase domains are sufficient to trigger apoptosis generating an insight into the apoptotic pathways which are triggered by NS3 from WNV [65].

2FP7 is a crystal structure of NS2B/NS3protease of West Nile Virus which in complex with the Bz-Nle-Lys-Arg-Arg-H whose length is 54; the replication of flaviviruses requires the correct processing of their polyprotein by the viral NS3 protease (NS3pro). It consists of 31% beta sheet (4 strands; 17 residues), essential for the activation of NS3pro is a 47-residue region of NS2B**.**

Non-structural 3 protease (NS3pro) acts as a target for the development of drug against West Nile virus. the Compound Libraries are prepared using the program CHARMM, program DAIM (Decomposition and Identification of Molecules) is used for the Decomposition of each molecule of the library and the fragment docking with electrostatic solvation evaluation is done by th e program SEED (Solvation Energy for Exhaustive Docking). Flexible docking of each compound of the library using the position and orientation of its fragments is anchored by the program FFLD (Fragment-based Flexible Ligand Docking) [66].

Zika Virus

The Zika infection is an member from the flavivirus family, ZIKV is a positive-sense, single-stranded RNA infection whose structural proteins of genome [mature capsid protein (C), premembrane protein (prM), envelope protein (E)] and the non-structural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5) and the non-structural peptide 2K [67]. NS4A-Induced Cell Hypertrophy and Growth Delay are interceded through the Rapamycin-Mediated Cellular-Stress Response Pathway target as the NS4A induces cellular oxidative stress. NS4A protein was communicated by means of the nmt1 inducible promoter in wild-sort, Tor1-deletion (ΔTor1) and type 2A phosphatase activator Tip41-cancellation (ΔTip41) mutant strains.

The primary protein in TOR pathway is Tor1 protein; it is required for cell reactions and it manages cell development and the control of cell measure. The Tip41 protein likewise is associated in cellular responses to nitrogen starvation, and it adversely manages the TOR signalling pathway in maturing yeast. The Tip41deletion had no reasonable impact on cell size and development as the TIP41 is produced by yeast cells fission, as the induced cell hypertrophy by NS4A was largely abolished.

As indicated by the colony-forming assay, the development of cells. The NS4A protein expression in the ΔTip41 cells worsened NS4A-induced growth.

The outcome proposed that NS4A-actuated hypertrophy and the delay in development are mediated by the TOR cellular stress-response pathway via Tor1 and Tip41 [68-70]. FIG 9 demonstrates the structure of the ZIKV helicase180– 617 in complex with ATP/Mn2+, in the structure of the ZIKV helicase172– 617 in complex with 7-mer RNA, the single-stranded RNA goes through Domain II to Domain I in an expanded adaptation with the bases stacked against each other, isolating these two areas from Domain III. The ssRNA 3′ end binds to Domain I, while the 5′ end binds with Domain II. [71].

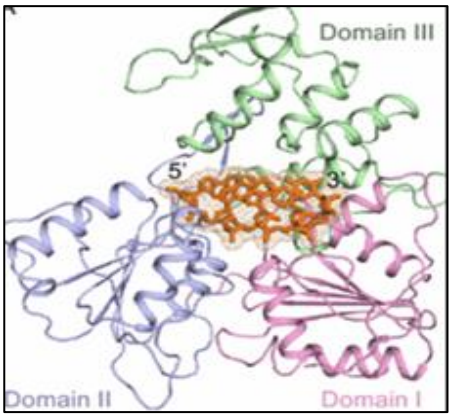

FIG. 9. **Structure of the ZIKV helicase in complex with RNA** [**Source**: Haitao Yang, 2016] [72]

The coordinates are deposited in PDB under accession number 5GJB and 5GJC. 5GJC has 31% helical (18 helices; 139 residues) and 18% beta sheet (19 strands; 80 residues). The sequence length is 442 residues. The sequence of NS4A protein was retrieved and Phyre2 servers was used predict the three-dimensional (3D) structure of a protein sequence. Server also helps to predict and analyse protein structure, function and mutations. ProSA program (Protein Structure Analysis) is used for the protein structures refinement and validation. ProQ is a neural system used to anticipate the nature of protein demonstrates. Additionally refined model is been checked utilizing ERRAT server which helps in confirming protein structures dictated by crystallography. PubChem database is utilized to recover the Chemical structures of ligands and SDF records are transported in utilizing open babel of PyRx. The last ligands were subjected to docking utilizing Autodock Vina in PyRx 0.8 [73].

Yellow fever virus

The causative agent of Yellow fever disease is yellow fever virus, NS2B-NS3 protein complex has protease activity required for viral replication. The YFV genome encodes a polyprotein from a single open-reading frame that is cleaved by host and virus proteases into 10 polypeptides. The structural proteins C, prM/M and E are encoded by the 5′ end of the genome, while the remaining encodes non-structural (NS) proteins NS1, NS2A, NS2B, NS3, NS4A, NS4B and NS5 which are associated with virus-host interactions, viral assembly and replication [74-76]. Activation of the MEK1/2 [mitogen-activated protein kinase (MAPK) extracellular signal-regulated kinase (ERK) kinase]/ERK1/2 signaling pathway is involved in cellular responses such as motility, proliferation, differentiation and survival. Research study provides evidence on both in vitro and in vivo that the pharmacological inhibitor of MEK1/2 in U0126 shows an antiviral efficacy against other flavivirus, YFV. MEK1 is a member of the MAPK signal transduction pathway that responds to growth factors and cytokines. PDB ID 3EQH shows X-ray structure of the human mitogen-activated protein kinase kinase 1 (MEK1) in a ternary complex with U0126, ADP and MG2P. It consists of 40% helical (16 helices; 146 residues) shares the residues (44-58), (65-67) and 11% beta sheet (9 strands; 43 residues) [77]. NS2B/NS3 complex model is been built by Modeller software package (mod9v7) and is further SAVES server for evaluation of its quality using PROCHECK. The residues of the complex were mutated using BioEdit. NS2B/NS3 complex was studied using CCP4 packages to understand the stability of complex, hydrogen bonds. The docking studies were performed using Autodock 4.0.1 using Genetic algorithm and Lamarckian genetic algorithm methods [78].

TABLE 2: **Some of the popular structure prediction tools, methods of prediction and their availability**.

TOOL	METHOD
Homology	
3D-JIGSAW	Fragment -based assembly
MODELLER	Satisfaction of spatial restraints
HHpred	Pairwise comparison of profile HMMs
RaptorX	Single/multi-template threading, alignment quality prediction
Swiss model	Fragment based assembly and local similarity
Phyre 2	Advanced remote homology detection, effect of amino acid variants
Fold Recognition	
MUSTER	Profile-profile alignment with multiple structural information
GenTHREADER	Sequence alignment, threading evaluation by neural networks
I-TASSER	Iterative template fragment assembly
Ab initio	
QUARK	Replica-exchange MC and optimized knowledge based force field
Rosetta/Robetta	Fragment assembly, simulated annealing
I-TASSER	Fragment assembly
CABS-FOLD	User provided distance restraints from sparse experimental data
EV fold	Calculate evolutionary variation by co-evolved residue pairs

Denovo drug designing and QSAR are the two most extensively used computational drug designing methods. These two methods have significantly added the rationalization in the traditional hit and trial method of drug designing. With rapid computational advancements and continuously improving algorithms, it seems to assist the drug designing more efficiently in near future. Some of the popular tools used for the prediction are shown in Table 2. The future of computer-aided drug design is promising; molecular dynamics simulations are likely to play an increasingly important role [79].

Benefits of CADD

CADD methods and Bioinformatics tools offer significant benefits for drug designing programs. Cost Savings. Many biopharmaceutical companies use computational methods and Bioinformatics tools to reduce the cost burden. CADD helps drug research programs to choose only the most promising drug candidates. By focusing drug research on specific lead candidates, biopharmaceutical companies can get drugs to market more quickly. The non-quantifiable benefits of CADD and the use of Bioinformatics tools help researchers to acquire about drug-receptor interactions. When the new molecular models of putative drug compounds, its protein targets and their binding affinity is shown to researcher, they often come up with new ideas on the improvement and modification of the drug compounds.

Conclusion

In the present world, the development and applications of Computer Aided Drug Design has made significant impact in both academics and industries. CADD approach provides information on the identification of target and its validation, lead selection and optimization process. Comparative protein modeling plays a vital role during the rational design of drug molecules. New drug molecules can still be designed by modifying the molecular structure of conventional drugs which

benefits in resistance and by improving patient compliance. The newly designed molecules can be used as probe for further research.

Secondary structure elements followed by alpha helix, extended strand and beta turns. The active sites were explored for determining important residues. Apart from structural aspects, dynamics and binding affinity of the ligand molecules can be well estimated through this cost effective protocols.

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