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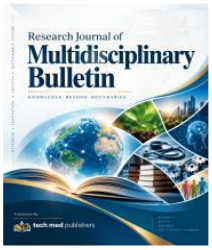

Review Article

FROM NETWORK TO DYNAMICS: A COMPREHENSIVE IN – SILICO REVIEW ON NETWORK PHARMACOLOGY, MOLECULAR DOCKING AND MOLECULAR DYNAMIC

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ABSTRACT

To increase complexity, cost and time in conventional drug discovery the computation approach used in drug discovery. In case of Modern drug discovery, the Network pharmacology, Molecular docking and Molecular dynamic is powerful in-Silco approach. So, by integrating this approach it provides compressive framework for target identification, mechanism exploration, virtual screening, lead optimization. The Network pharmacology help to identify bioactive compound, potential target. Molecular docking is used to identify ligand-protein interaction and binding affinity. While molecular dynamic evaluates stability and behavior of protein- ligand complex. By using this type of approach used to identify herbal candidates. This review identifies the methodology, Application of computational tool for drug discovery. Then by this type of study we can validate methodology by in-vitro experimental studies.

Key words: MD, CADD, Network Pharmacology, Molecular docking, Diabetes.

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1. INTRODUCTION

In novel medicine the drug discovery and development are complex, expensive and lengthy so to speed up the process of design and devolvement the computer aided drug design is commonly used in pharmaceutical industries[1].Due to CADD lead optimization phase of drug design has economical advantage. The computational drug design contains the various software and algorithms which is used to predict the properties of various drug molecules, potential target prediction, optimization of drug for therapeutics properties and used for low-cost drug designing and development[1]. CADD approaches are divided in two categories such as: structure-based drug design (SBDD) and ligand-based drug design (LBDD). In case of three-dimensional structure of target protein SBDD design is used and in case of absence of receptor 3D information and to gain knowledge about bind of biological target LBDD design is used[1-2].

In silico design is used in biomedical industry for optimization of parameter like absorption, distribution, metabolism, and excretion and their toxicity profile. In SADD the target structure needs to be known which obtained by X- ray crystallography or NMR when it is not available the computational methods like homology modeling used to predicts three-dimensional structure of target. By knowing the structure screen is done and then docking method apply on drug targets. Then filtering and optimization of drug molecules done and after that final selected lead molecules are tested in vitro for identifying their activity[1-3].

2. CLASSIFICATION OF COMPUTATIONAL METHOD FOR DRUG DESIGN:

2.1 Structure Based Drug Design
2.2 Ligand Based Drug Design

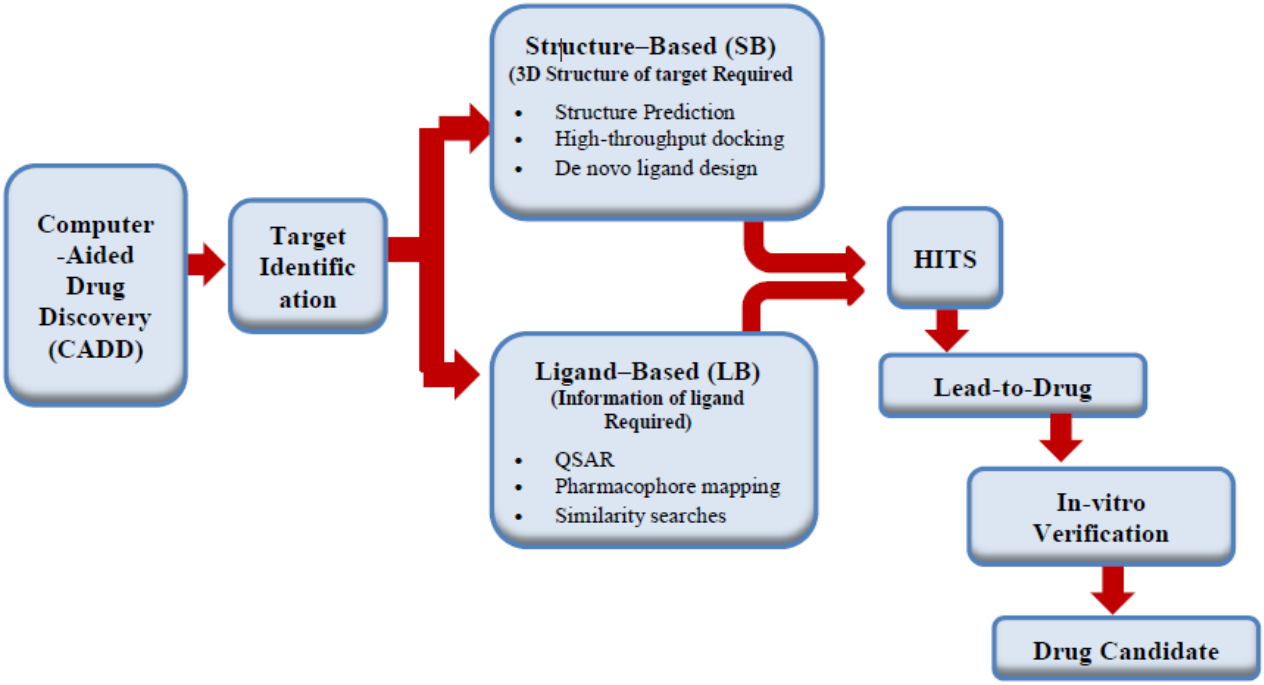

Fig.1 Classification of Computational Method for Drug Design

2.1 Structure Based Drug Design (SBDD):

Structure based drug design (SBDD) is used in virtual screening and de novo drug design. It is used as effective tools for drug discovery and development. Structure based virtual screening, molecular docking and molecular dynamic are used in SBDD for effective and rapid lead discovery and their optimization because they are mostly related to 3D structure of target protein[2-3]. The SBDD it has contributed to many compounds for the clinical trials and get FDA approve. HIV-1 protease is a drug target for anti-AIDS therapeutics. In 1990s many approved HIV protease inhibitors were developed to target HIV infections using structure-based molecular docking[4]. Saquinavir is first drug for HIV-1 protease to reach the market. Amprenavir is another drug that was developed to target HIV-1 protease as target that was also developed by using SBDD[3-4].

2.1.1. Basic steps of SBDD:

A. Target Protein Structure Prediction and Identification of Ligand Binding Site:

Structure-Based Drug Design (SBDD) involves identification of biological targets like enzymes, receptors, or ion channels that are important factors in disease development. The various advanced techniques like genomics, proteomics, and bioinformatics are used to identify these targets[5]. This target is then validated by using various animal modal. Due to structural evaluation techniques such as x-rays and NMR increasingly more protein systems had been solved and stored within the PBD format. However accurate structure of a protein is essential to understand their biological function. It uses Amino acid information to generate 3-D atomic fashions by multiple Threading alignments and iterative structural meeting simulations[4-5]. The characteristic of the protein is then inferred by structurally Matching the 3D fashions with different proteins. Even by offer disulfide bonding modes, secondary and tertiary systems, and purposeful annotations on ligand binding websites, however it takes a quite long term to build complicated systems[5-6].

B. Scoring Function:

The scoring function helps us to calculate the binding affinity between protein and ligand functions. It is divided into force field, empirical, knowledge-based, and machine learning. the binding energy of ligands to receptors is given by Bohm[6].

C. Molecular Docking:

Molecular docking is computational technique used to predicted the interaction between a ligand and target protein. Its help in determining the binding affinity and stability of ligand protein complex. It is widely used in drug discovery and design for screening bioactive compound. Molecular docking used for identifying the behavior of small molecules at the binding site of the target protein. It involves two basic steps - the estimation of ligand conformation and binding of the ligand within the target active site with accuracy, so that it is used in structure-based drug design (SBDD)[7-8].

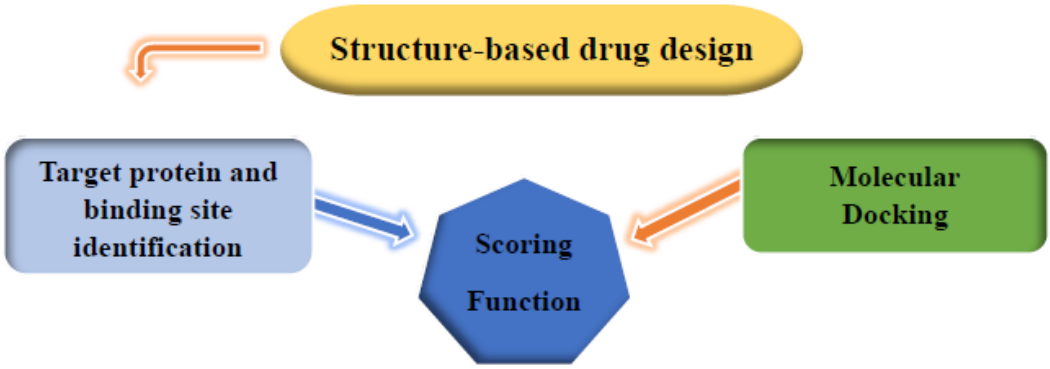

Fig No. 2 Structure based Drug Design

Table 1. Software for Structure-Based Drug Designing (SBDD)

Stages	Tools used	Brief Description	link
1. Target modelling	Swiss Model	Homology modelling	https://swissmodel.expasy.org /
	Modeler	Homology Modelling	https://salilab.org/modeller/
	Phyre And Phyre2	Template detection alignment as well as 3D modelling	http://www.sbg.bio.ic.ac.uk/phyre2/html/page.cgi?id=index
2. Binding site	Castp	Binding site prediction	http://sts.bioe.uic.edu/castp/index.html?2011
	Active Site Prediction Tool	Active site prediction	http://www.scfbio iitd.res.in/dock/ActiveSite.jsp
3.Molecular Docking	Auto Dock Vina	Molecular docking and virtual screening	https://vina.scripps.edu/
	Schrodinger	Maestro	https://www.schrodinger.com/products/maestro

2.2 Ligand Based Drug Design (LBDD):

In absence of receptor 3D information, the Ligand-based drug design is an approach used and relies on knowledge of molecules that bind to the biological target of interest[7]. The 3D quantitative structure activity relationships (3D QSAR) and pharmacophore modelling are the most important tools for LBDD[7]. They can provide predictive models for lead identification and optimization. It consists of information of molecules that bind to the desired target site. These molecules can be used to derive a Pharmacophore model. A pharmacophore model is defined as a molecule with the necessary structural abilities to bind to a desired target site[6,7]. After identification of Pharmacophore it is determined whether it is suitable for the receptor, otherwise the Pharmacophore is further modified to make a potential drug[6-9].

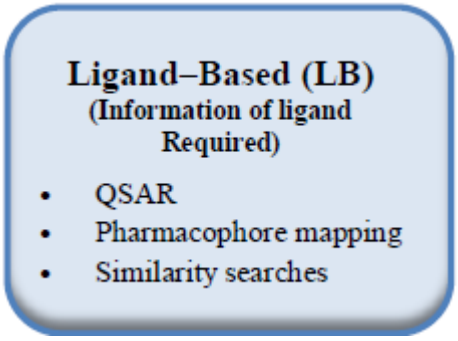

Fig No. 3 Ligand Based Drug Design

2.2.1. Quantitative Structure Activity Relationships:

The interactions between small organic molecules and biological macromolecules the QSAR used as quantitative study. It contains a correlation between calculated properties of molecules and their experimentally determined biological activity. If the structure of receptor is not known then then QSAR method is most accurate and

effective method for drug design[8]. In 1980's 3D structural information was introduced into the QSAR method, called as 3D-QSAR[9,10].

2.2.2. Pharmacophore mapping:

Pharmacophore used to describe the biological activity of molecule. It is also used in understanding the ligand – protein interaction. If the structure of target is not available then pharmacophore models can be generated by using the structural information about the active ligands that bind to the target known as the ligand-based pharmacophore modelling[10].

3. DRUG DESIGNING BY USING NETWORK PHARMACOLOGY, MOLECULAR DOCKING AND MOLECULAR DYNAMIC:

- **Network Pharmacology:**

Network pharmacology is types of drug discovery used to studies how your drug
molecules interact with multiple biological target and pathway at same time[11].

Methodology of network pharmacology:

1. Identification of bioactive compounds:

Firstly, the selected medicinal plant will find to investigated bioactive constituents by using literature and various database like PubChem, ChEMBL[12].

2. Screening of bioactive compounds:

Then the identified compound will be screened regarding their pharmacokinetics, drug likeness characteristics, oral bioavailability, drug likeness, molecular weight and
lipophilicity[12-13].

3. Prediction and collection of compound-related targets:

After that potential targets of selected compound will identify using database and various computational platforms such as Swiss Target Prediction, STITCH, Drug Bank, Binding DB, ChEMBL and BATMAN-TCM[13].

4. Target standardization:

The identified targets then standardized using uniport or by using protein or gene database. Then the duplicate targets will be removed and protein name will be converted into standardized gene symbols or uniport ID prepared.

5. Identification of disease-associated targets:

By using multiple database Disease related gene or target is collected such as Gene card, OMIM, DisGeNET, Comparative Toxicogenomics Database (CTD) and DrugBank[14].

6. Identification of common targets:

To identify overlapping of protein the compound related targets and disease associated targets are comparing.

7. Construction of the compound–target network:

By using cytoscape the compound target can be constructed. Network analysis allows identification of compounds interacting with multiple targets and targets associated with multiple compounds[14].

8. Protein–Protein Interaction (PPI) network construction:

To obtained protein -protein interaction information the common targets are submitted to STRING database. Then resulting data base will be imported to Cytoscape for visualization and for next analysis. The PPI network help to identify hub targets[14].

9. Gene Ontology (GO) enrichment analysis:

The hub targets that are identified will subjected to Gene ontology (GO) enrichment analysis and provide biological function associated with targets[15].

10. KEGG pathway enrichment analysis:

To identify the signaling and metabolic pathways KEGG pathway enrichment analysis will perform. The biological characterized is identified by using this analysis. It includes PI3K–Akt, MAPK, NF-κB, apoptosis, JAK–STAT and TNF signalling[15].

11. Molecular docking analysis:

In molecular docking the protein structured given from PDB websites and ligand structure by PubChem or another database. Then ligand protein interaction can be analyzed by using molecular docking[15].

12. Molecular dynamics simulation:

For investigation of complex stability molecular dynamic stimulation is performed.
Parameters may include root mean square deviation (RMSD), root mean square fluctuation (RMSF), radius of gyration (Rg), hydrogen bonds, solvent-accessible surface area (SASA) and binding free-energy estimation where appropriate.

13. Experimental validation:

By using in – vitro studies we can validate computational predication like network pharmacology, docking and Molecular docking. In-vitro studies may include cell viability assay, enzyme inhibition assay, ROS estimation, ELISA, Western blotting, qRTPCR and protein-expression analysis[15].

- **MOLECULAR DOCKING:**

Molecular Docking Methodology:

1. Selection of Target Protein:

The protein targets can be identified through network pharmacology depending upon the hub gene, and then molecular docking can be studies. The three-dimension structure of protein can be selected by PDB websites[16].

2. Preparation of Target Protein:

The selected protein structure will be required to prepared before docking which required removing of

water molecules, adding of missing hydrogen atom and atomic charges.

3. Preparation of Ligands:

By using network pharmacology, the bioactive compound obtained will be used as ligands for molecular docking. Their chemical structured can be obtained from PubChem and it is then converted into Three-dimension structure. The ligands will be subjected to structural optimization, addition of hydrogen atoms, assignment of appropriate charges and definition of rotatable bonds before docking[17].

4. Identification of Binding Site:

To identify the site banding of selected protein the experimental reporting the active site residues, literature data or computational binding pocket prediction is used.

5. Selection of Molecular Docking Software:

Molecular docking will perform by using software such as Auto Dock vina or Auto Dock 4.

6. Definition of Grid Box:

For selecting binding site of target grid box will be used by using grid box the binding pocket is covered and it gives space for ligand movement[17].

7. Molecular Docking:

The target which is selected will bind to the binding site of protein. During docking process scoring function will check so by using binding affinity and binding orientation the affinity of ligand with protein can be identify[17]

8. Evaluation of Docking Score:

In Auto dock, it indicates more negative predicted binding energy value generally indicated more interaction in scoring model but it has some limitation.

9. Analysis of Protein–Ligand Interactions:

So, by using hydrogen bonding, hydrophobic interaction, π–cation interactions, electrostatic interactions and van der Waals interactions will can analysed best ranked docking pose.

10. Comparison with Reference Ligand:

To check whether the binding mode of test compound will match with known ligand we select the docking result. The docking result includes the binding energy, binding orientation and interaction active site residue[18].

11. Validation of Docking Protocol:

After that docking protocol shall be validated to all possible outcome. It can be analyzed by compared with RMSD and value should be around or below 2 Å. It is used to check the reliability of docking methodology[18].

12. Visualization of Docking Results:

Then the PyMoL used to visualized the docked protein and ligand complex.

13. Selection of Potential Lead Compounds:

By using relevant interaction of all favorable compound with biological site can be consider as lead compound.

14. Integration with Network Pharmacology:

For predicting compound target relationship, the docking result will be integrated with network pharmacology. It is type of computational investigation[18,19].

15. Molecular Dynamics Simulation:

For studying dynamics stability of compound for that the Molecular dynamic studies are done which includes RMSD, RMSF, radius of gyration, hydrogen bond interaction may be evaluated[19].

16. Experimental Validation:

For computational validation the experimental validation used containing in – vitro test performed like enzyme inhibition assay, cell-based assay, western blotting, ELISA or suitable in – vivo study1[19,20].

- **Molecular Dynamic:**

1. Preparation of protein ligand complex:

By assigning appropriate protonation states, atomic charge and molecular parameter molecular dynamic stimulation study after docking.

2. Energy Minimization and Equilibration:

The solvated system will undergo various energy minimization by removing unfavorable steric contact for obtaining stable configuration. Also, equilibrium done by NVT and NPT condition to stabilize temperature, pressure and density before production run.

3. Production molecular Dynamic Stimulation:

After equilibrium is achieved in protein – ligand complex it is subjected to production of molecular dynamic stimulation. In which various type of packages are used to record the data at regular interval[23,24].

4. Binding free energy analysis:

By using MM-PBSA OR MM-GBSA approach the binding stability of selected complex may be investigated[24,25].

REFERENCE

[1]. Niazi, S. K., & Mariam, Z. (2023). Computer-Aided Drug Design and Drug Discovery: A Prospective Analysis. Pharmaceuticals, 17(1), 22.

[2]. Sumudu, P. (2016). Computational methods in drug discovery (12-13).

[3]. Batool, M., Ahmad, B., & Choi, S. (2019). A Structure-Based Drug Discovery Paradigm. International Journal of Molecular Sciences, 20(11), 2783.

[4]. Raghuvanshi, U. R., Gupta, N. G., Jhala, A. J., Patidar, N. P., & Gavande, P. G. (2026). A Review on Structure-Based Drug Design and Its Role in

Modern Medicinal Chemistry. Indian Journal of Pharmaceutical Chemistry and Analytical Techniques, 64–76.

[5]. Syriopoulou, A., Markopoulos, I., Tzakos, A. G., & Mavromoustakos, T. (2021). Ligand Receptor Interactions and Drug Design. In Methods in molecular biology (Clifton, N.J.) (Vol. 2266, pp. 89–104). PubMed. https://doi.org/10.1007/978-1-0716-1209-5_5

[6]. Meng, X.-Y., Zhang, H.-X., Mezei, M., & Cui, M. (2011). Molecular Docking: A Powerful Approach for Structure-Based Drug Discovery. Current Computer Aided-Drug Design, 7(2), 146–157.

[7]. Kalaimathi, K., Thiyagarajan, G., Vijayakumar, S., Bhavani, K., Karthikeyan, K., Maria Jancy Rani, J., Dass, K., Sureshkumar, J., & Prabhu, S. (2021). Molecular docking and network pharmacology-based approaches to explore the potential of terpenoids for Mycobacterium tuberculosis. Pharmacological Research - Modern Chinese Medicine, 1, 100002.

[8]. Noor, F., Tahir ul Qamar, M., Ashfaq, U. A., Albutti, A., Alwashmi, A. S. S., & Aljasir, M. A. (2022). Network Pharmacology Approach for Medicinal Plants: Review and Assessment. Pharmaceuticals, 15(5), 572.

[9]. Álvaro Cortés-Cabrera, Sánchez, P. A., Morreale, A., & Gago, F. (2015). - Ligand-Based Drug Discovery and Design. CRC Press eBooks, 116–139. https://doi.org/10.1201/b18799-9

[10]. Hopkins, A. L. (2008). Network pharmacology: the next paradigm in drug discovery. Nature Chemical Biology, 4(11), 682–690.

[11]. Noor, F., Tahir ul Qamar, M., Ashfaq, U. A., Albutti, A., Alwashmi, A. S. S., & Aljasir, M. A. (2022). Network Pharmacology Approach for Medicinal Plants: Review and Assessment. Pharmaceuticals, 15(5), 572.

[12]. Luo, T., Lu, Y., Yan, S., Xiao, X., Rong, X., & Guo, J. (2019). Network Pharmacology in Research of Chinese Medicine Formula: Methodology, Application and Prospective. Chinese Journal of Integrative Medicine, 26(1), 72–80.

[13]. Wu, Z., Li, W., Liu, G., & Tang, Y. (2018). Network-Based Methods for Prediction of Drug-Target Interactions. Frontiers in Pharmacology, 9.

[14]. Burle, S. S., Gupta, K. R., Jibhkate, Y. J., Hemke, A. T., & Umekar, M. J. (2023). Insights into molecular docking: A comprehensive view. International Journal of Pharmaceutical Chemistry and Analysis, 10(3), 175–184.

[15]. Morris, G. M., Huey, R., Lindstrom, W., Sanner, M. F., Belew, R. K., Goodsell, D. S., & Olson, A. J. (2009). AutoDock4 and AutoDockTools4: Automated docking with selective receptor flexibility. Journal of Computational Chemistry, 30(16), 2785–2791.

[16]. Paggi, J. M., Pandit, A., & Dror, R. O. (2024). The Art and Science of Molecular Docking. Annual Review of Biochemistry.

[17]. Meng, X.-Y., Zhang, H.-X., Mezei, M., & Cui, M. (2011). Molecular Docking: A Powerful Approach for Structure-Based Drug Discovery. Current Computer Aided-Drug Design, 7(2), 146–157.

[18]. Trott, O., & Olson, A. J. (2009). AutoDock Vina: Improving the Speed and Accuracy of Docking with a New Scoring function, Efficient optimization, and Multithreading. Journal of Computational Chemistry, 31(2).

[19]. Kitchen, D. B., Decornez, H., Furr, J. R., & Bajorath, J. (2004). Docking and scoring in virtual screening for drug discovery: methods and applications. Nature Reviews Drug Discovery, 3(11), 935–949.

[20]. Case, D. A., Cheatham, T. E., Darden, T., Gohlke, H., Luo, R., Merz, K. M., Onufriev, A., Simmerling, C., Wang, B., & Woods, R. J. (2005). The Amber biomolecular simulation programs. Journal of Computational Chemistry, 26(16), 1668–1688.

[21]. Yao, T., Wang, Q., Han, S., Lu, Y., Xu, Y., & Wang, Y. (2022). Potential Molecular Mechanisms of Ephedra Herb in the Treatment of Nephrotic Syndrome Based on Network Pharmacology and Molecular Docking. BioMed Research International, 2022(1).

[22]. Zhang, L., Han, L., Wang, X., Wei, Y., Zheng, J., Zhao, L., & Tong, X. (2021). Exploring the mechanisms underlying the therapeutic effect of Salvia miltiorrhiza in diabetic nephropathy using network pharmacology and molecular docking. In Bioscience

[23]. Shahzadi, Z., Yousaf, Z., Anjum, I., Bilal, M., Yasin, H., Aftab, A., Booker, A., Ullah, R., & Bari, A. (2024). Network pharmacology and molecular docking: combined computational approaches to explore the antihypertensive potential of Fabaceae species. In Bioresources and bioprocessing (Vol. 11, Issue 1, p. 53).

[24]. Yao, T., Wang, Q., Han, S., Lu, Y., Xu, Y., & Wang, Y. (2022). Potential Molecular Mechanisms of Ephedra Herb in the Treatment of Nephrotic Syndrome Based on Network Pharmacology and Molecular Docking. BioMed Research International, 2022(1).

[25]. Ye, J., Li, L., & Hu, Z. (2021). Exploring the Molecular Mechanism of Action of Yinchen Wuling Powder for the Treatment of Hyperlipidemia, Using Network Pharmacology, Molecular Docking, and Molecular Dynamics Simulation. BioMed Research International, 2021(1).