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IN-SILICO MOLECULAR DOCKING AND ADMET PROFILING OF SELECTED PHENOLIC COMPOUNDS AS POTENTIAL TYROSINE KINASE INHIBITOR

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ABSTRACT

Tyrosine kinases are really important in how cells signal inside, controlling stuff like growth and when cells die, and when they go wrong, it leads to cancer getting worse. I think targeting them makes sense for new cancer drugs. This study looked at some phenolic compounds to see how they bind to a tyrosine kinase enzyme and what their drug properties might be, all done on a computer. We used software like ChemDraw and ChemSketch to get the ligand structures ready. Then docked them to the protein from PDB ID 3ERT with PyRx and AutoDock. For the interactions between protein and ligand, it was BIOVIA Discovery Studio and this tool called PLIP. SwissADME helped predict if theyd work as drugs, like ADMET stuff. Out of the compounds screened, chlorogenic acid stood out with the best binding, at negative 6.1 kcal per mol. It made stable bonds with active site residues, hydrogen ones, hydrophobic, and even pi pi stacking. That seems pretty solid. The ADMET results showed okay pharmacokinetics, and it followed Lipinskis Rule of Five. So chlorogenic acid could be a good starting point, maybe test it for real as a tyrosine kinase blocker in cancer treatment. Im not totally sure about the next steps, but it feels promising. The whole in silico approach helped narrow it down without lab work yet.

KEYWORDS: Molecular docking; Tyrosine kinase; Chlorogenic acid; In-silico drug design; ADMET; Drug-likeness.

1. INTRODUCTION

Cancer still poses a big health issue globally; in fact, cancer incidence and mortality continue rising, yet improvements in therapy approaches have been witnessed. However, in conventional chemotherapy, lack of selectivity, toxicity, and the emergence of resistance have often been encountered as some of the main drawbacks. Hence, targeted therapies have attracted considerable attention as promising approaches that selectively target molecular pathways in cancer.

Protein tyrosine kinases play a very important role as regulators in cell signaling processes involving proliferation, differentiation, and survival. Tyrosine kinases have been associated with several malignancies, leading to their increased attraction as potential therapeutic targets in anti-cancer drug development. Tyr kinase inhibition has proved successful in managing several malignancies.

In-silico drug discovery methods, especially molecular docking, have emerged as effective resources in the early-stage screening of candidates for potential drugs.

This is because it is possible to predict the affinity of interaction between the ligand and protein molecules.

Phenolics, particularly those isolated from natural sources, display various biological activities, such as antioxidant and anticancer activities. Chlorogenic acid and its phenolic analogs have been reported to possess promising biological activities, but their binding affinity towards the tyrosine kinase target has yet to be investigated by in-silico approaches. This study aimed to determine the molecular interaction and ADMET property of some selected phenolics towards tyrosine kinase by means of in-silico computations.

2. MATERIALS AND METHODS

2.1 Chemicals and Software

All such calculations performed in the course of this study were conducted using various highly accepted and validated tools in the cheminformatics and molecular modeling field.

ChemDraw and **ChemSketch** software packages were utilized in the design as well as depiction of the two-dimensional chemical structural models of the preferred phenolic compounds. The softwares employed in the design of the chemical structural models enabled the creation of precise designs of molecular frameworks, functional groups, as well as bonding arrangements. The designs were employed as inputs in the optimizations prior to the molecular docking analysis.

The **PubChem** database was used as a main resource for searching for the ligand structures and basic physicochemical properties required for the ligands of interest. Furthermore, PubChem ensures the integrity of molecular details for ligands employed in computations.

The three-dimensional crystal structure of target protein tyrosine kinase was taken from the **Protein Data Bank**, which is a repository of experimentally determinated protein structures. For this study, protein structure **3ERT** was chosen because of its relevance to tyrosine kinase function. Protein preparation included the removal of water molecules and crystallized ligands to prevent interference in protein-target binding, and addition of polar hydrogens to facilitate accurate binding.

PyRx was used as a docking and virtual screening tool. PyRx combines the functionality of AutoDock and AutoDock Vina and provides tools for preparation of ligand and protein files, grid box setup, and execution of docking procedures. In this work, PyRx software was used for initial ligand molecule docking and for effective management of ligand and protein interaction.

AutoDock software was employed for detailed molecular docking studies to predict the favored binding orientation and binding affinity of ligands within the active site of the tyrosine kinase enzyme. In this software, the ligand conformations were explored by the use of a Lamarckian Genetic Algorithm, and ligand-protein interactions were calculated based on the binding energy (kcal/mol). From the docking scores, the most potent ligand was determined.

The software used for the interpretation of docked complexes of protein/ligand was **BIOVIA Discovery Studio**. This software allowed for the 2D and 3D representation of binding models. The amino acid residues that take part in binding were identifiable through this software. The important molecular interactions including hydrogen bonding, hydrophobic, and aromatic interactions were also analyzed through this software.

The **Protein–Ligand Interaction Profiler**, named PLIP, was employed to automate the identification and classification of protein–ligand interactions. PLIP offered information on hydrogen bonds, hydrophobic interactions, electrostatic interactions, and π-π stacking, thus aiding in the qualitative evaluation of the results achieved through docking.

SwissADME was employed for making predictions regarding pharmacokinetic properties and drug likeness of the selected chemicals. ADMET parameters were considered, and Lipinski's Rule of Five was used to predict the bioavailability of the ligands in terms of their ability to act as drugs.

2.2 Ligand Preparation

The phenolic compounds of interest for this study have been shortlisted for their significance to biological processes. The chemical structures of these ligands can either be fetched from the PubChem database or can be designed manually using the software of ChemDraw and ChemSketch. These structures have been screened carefully for 2D to assure correct atom representation, connectivity of bonds, and functional groups.

The structures of the prepared ligands were optimized to generate energy-stable conformations that could be used in molecular docking. Energy minimization was carried out to remove steric clashes and to optimize the geometries of the ligands before conducting docking studies. The optimized structures of the ligands were then transformed to the required file formats for use in the docking software.

Hydrogen atoms on the polar sites of the ligands were added, and the use of Gasteiger charges was employed to correctly model the electrostatics during the ligand docking analysis task. Rotatable bonds were set to incorporate the ligand flexibility during the ligand docking analysis task. Files were prepared correctly before being subjected to ligand molecule docking analysis.

This was followed by a ligand preparation method that ensured that all ligands tested were in their suitable and

standardized form, thus enhancing the reproducibility and accuracy of molecular docking outcomes.

2.3 Protein Preparation

The three-dimensional structure of the target protein, tyrosine kinase, was obtained from the Protein Data Bank (PDB) with the accession number 3ERT. This target protein structure was selected depending on how closely associated it is with the activity of tyrosine kinases.

Protein preparation procedures were done to achieve a relevant biologically constrained structural conformation necessary for docking. First, all water molecules initially found within the crystal structural formation were eliminated because such water molecules could potentially inhibit ligand interaction and hence affect dock accuracy. Ligands that were co-crystallized within the enzyme structure were also deleted.

Later, polar hydrogen atoms were incorporated into the protein model in order to effectively model the interaction of hydrogen bonds in the docking process. Finally, appropriate charges were assigned, and the protein model was thoroughly investigated for integrity. This prepared protein model was then saved in the correct file format for usage in the docking tool.

This protein preparation was done systematically to ensure that the target enzyme is prepared in the optimal manner, and this increased the accuracy of the results obtained from the molecular docking calculations.

2.4 Molecular Docking

Molecular docking studies were performed using AutoDock as implemented within the PyRx virtual screening platform to explore the binding affinity and interaction pattern of the selected ligands with the tyrosine kinase enzyme. In the process, PyRx was employed to facilitate ligand and protein preparation, grid box generation, and execution of docking simulations.

A grid box was defined around the active site of the protein to ensure proper accommodation of the ligands within the binding pocket. The parameters of the grid were chosen in such a way that the entire region of the active site would be covered, leaving enough space for ligand flexibility during docking. Docking simulations were then carried out to predict the most favorable orientation of each ligand in binding within the active site of the protein.

AutoDock uses a Lamarckian genetic algorithm for the exploration of possible ligand conformations and estimates the interactions of ligand-protein interactions using a scoring function. Docking results are expressed in terms of binding energy in kcal/mol. More negative binding energy indicates strong binding affinity. From each ligand, the best docking pose is chosen based on lowest binding energy and favorable interaction profile.

This docking protocol enabled the relative assessment of the binding affinity of the selected compounds, thus facilitating identification of the most promising ligand for further interaction studies in ADMET analysis.

2.5 Interaction Analysis

The resulting protein/ligand complexes obtained through docking simulations were analyzed in-depth by BIOVIA Discovery Studio and Protein-Ligand Interaction Profiler (PLIP) software to understand interactions at a molecular level in respect to ligand stabilization in the active site of tyrosine kinase enzymes.

The two-dimensional (2D) and three-dimensional (3D) structures of the docked compounds were generated using BIOVIA Discovery Studio, facilitating easy observation of the orientation of the ligands and the amino acid residues that are responsible for the interactions. The major interactions, such as hydrogen bonding, hydrophobic interactions, and aromatic interactions, were studied to reveal the mode of binding of the ligands in the protein active site.

PLIP was used for automatic binding site detection and classification of protein-ligand interactions. PLIP offered detailed information about hydrogen bonds, hydrophobic interactions, electrostatic interactions, and π-π stacking interactions along with their corresponding interacting amino acid residues. Automatic interaction profiling by PLIP facilitated qualitative interpretation of docking outcomes.

The joint application of BIOVIA Discovery Studio and PLIP facilitated the study of ligand and protein interaction, thus aiding in the determination of stable and relevant ligand-binding modes.

2.6 ADMET Prediction

The pharmacokinetic properties and drug-likeness properties of selected phenolic compounds were studied using the SwissADME online prediction tool. The SwissADME is a valuable tool for estimating the ADMET properties of compounds using a computational approach. ADMET properties are necessary in drug discovery research.

In this study, SwissADME was employed to estimate important physicochemical and pharmacokinetic properties such as molecular weight, lipophilicity, hydrogen bond donor/acceptors, and oral bioavailability. Drug likeliness was examined by employing Lipinski's Rule of Five for evaluating the potential of the molecules for oral intake.

Moreover, the SwissADME tool was employed to predict some pharmacokinetic properties including gastrointestinal absorption. The pharmacokinetic profiles

predicted by SwissADME helped in verifying the docking results as well as in screening candidates showing desired pharmacokinetic profiles.

This ADMET assessment gave a initial glimpse at drug-likeness properties for the selected chemical structure candidates. This helped in picking possible lead molecules.

3. RESULTS

3.1 Molecular Docking Results

The results of molecular docking studies using AutoDock are presented in Table 1. The screened phenolic compounds varied in binding affinity against the tyrosine kinase enzyme, which revealed variations in their binding potential with the active site of target proteins. The binding affinity was measured in terms of binding energy (in kcal/mol), and higher negative values revealed higher binding affinity.

Among all tested compounds, chlorogenic acid (3A) showed the highest binding affinity, having a docking score of -6.1 kcal/mol, indicating strong interaction with the tyrosine kinase active site. The binding affinity was found to be comparable for p-coumaric acid (3C) having a docking score -6.1 kcal/mol, syringic acid (3B), and kaempferol (3G) having a binding energy of -6.0 kcal/mol. The moderate binding affinities were found for luteolin (3H) and quercetin (3F) having docking scores -5.9 and -5.6 kcal/mol, respectively.

On the other hand, Syringaldehyde (3D) and Ascorbic acid (3E) have shown lower binding affinity, with a binding score of –2.1 kcal/mol. Moreover, for Caffeic acid (3I) and Myricetin (3J), binding scores could not be derived under the specified docking conditions and hence, these values have been excluded.

For docking studies, it is determined that chlorogenic acid (3A) is the lead ligand. This is followed by protein-ligand interaction analyses. The subsequent step is ADMET evaluation.

Table 1: Molecular Docking Results of Selected Phenolic Compounds Against Tyrosine Kinase (PDB ID: 3ERT)

Compound Name	Compound Code	Binding Affinity (kcal/mol)
Chlorogenic Acid	3A	-6.1
Syringic Acid	3B	-6.0
p-Coumaric Acid	3C	-6.1
Syringaldehyde	3D	-2.1
Ascorbic Acid	3E	-2.1
Quercetin	3F	-5.6
Kaempferol	3G	-6.0
Luteolin	3H	-5.9
Caffeic Acid	3I	-4.5
Myricetin	3J	-5.3

3.2 Protein–Ligand Interaction Analysis

Protein-ligand analysis of the docked model of chlorogenic acid (3A) and the tyrosine kinase enzyme protein (PDB code: 3ERT) was carried out by PLIP and BIOVIA Discovery Studio. This analysis indicated the presence of several non-covalent bonding interactions to stabilize the protein-ligand complex (Table 2).

Chlorogenic acid made a total of four hydrogen bonds with crucial amino residues ASP83, GLU88, ASN84, and SER80, with the bond lengths ranging from 2.0 to 2.8 Å, representing a high level of favorable interactions between the ligand and amino residues. In addition, one carbon-hydrogen bond was made with ALA82 with a bond length of about 3.7 Å.

Electrostatic interaction was found between the carboxyl group of chlorogenic acid and residue ASP80 with a distance of about 4.4 Å. Additionally, π-π stacking interaction existed between the aromatic ring of chlorogenic acid and TYR88 with a distance of about 3.9 Å, which aided in proving aromatic interaction at the active site.

Hydrophobic interactions were also observed, and these involved amino acids ALA84, LEU86, and VAL81, with distances of 3.5 to 4.2 Å. Hydrophobic interactions increase the stability of the ligand-protein complexes.

The coexistence of several hydrogen bonds, hydrophobic, electrostatic, and π-π stacking interactions reveals a stable binding conformation of chlorogenic acid in the active site of the tyrosine kinase enzyme.

Table 2: Protein–Ligand Interaction Analysis of Chlorogenic Acid (3A) with Tyrosine Kinase (PDB ID: 3ERT)

Interaction Type	No. of Bonds	Protein Residues Involved	Ligand Atom / Group	Distance (Å)
Hydrogen bonding	4	ASP83, GLU88, ASN84, SER80	O–H / O groups	2.0 - 2.8
Carbon–hydrogen bond	1	ALA82	Ring carbon	~3.7
Electrostatic interaction	1	ASP80	Carboxyl group	~4.4
π–π stacking	1	TYR88	Aromatic ring	~3.9
Hydrophobic interaction	3	ALA84, LEU86, VAL81	Aromatic ring hydrogens	3.5 - 4.2

3.3 ADMET Analysis

To assess the pharmacokinetics attributes and drug-likeness scores for the identified lead compound, chlorogenic acid (3A), the SwissADME prediction tool was employed. Per ADMET analysis, chlorogenic acid satisfied the criteria outlined in Lipinski's Rule of Five, implying its ability to act as an orally active drug candidate.

The estimated physicochemical properties such as molecular weight, number of hydrogen bond donors, number of hydrogen bond acceptors, and lipophilicity were well within the allowed limits for an orally active molecule. The prediction by SwissADME also revealed optimal gastrointestinal absorption properties, supporting its potential for bioavailability.

In general, the ADMET data indicate that chlorogenic acid has reasonable pharmacokinetic properties, and this is consistent with the molecular docking and interaction study results. Based on this data, the selection of chlorogenic acid as a candidate drug is justified.

4. DISCUSSION

This study looked at how some phenolic compounds might interact with the tyrosine kinase enzyme. We used molecular docking and other computer methods, plus checking ADMET stuff to see if they could work as drugs. The docking showed different binding strengths for each compound. It really depends on their structures, I guess.

Compounds with lots of hydroxyl groups and those ring systems did better. The hydroxyls can make hydrogen bonds with amino acids in the active site. And the aromatic parts help with hydrophobic stuff and pi-pi stacking. That stabilizes things, making the binding stronger. Its kind of key for how ligands stick to proteins.

Chlorogenic acid came out on top. It had the best affinity and interactions. It formed hydrogen bonds with ASP83, GLU88, ASN84, SER80. Then hydrophobic ones with ALA84, LEU86, VAL81. And pi-pi with TYR88. There was even some electrostatic help. All that together means its probably stable in there.

This matches what other studies say about hydrogen bonds, hydrophobics, and stacking for kinase inhibition. Like, syringaldehyde and ascorbic acid did not do well because they lack those groups. So the structure really matters, as we saw.

ADMET predictions from SwissADME showed chlorogenic acid follows Lipinskis Rule of Five. Its pharmacokinetics look okay. That fits with the docking, so maybe its worth looking into more as a drug candidate.

But these are just computer results. They dont cover everything in real biology. It feels like we need in-vitro and in-vivo tests to really check if chlorogenic acid can inhibit kinases or fight cancer. Some people might think its promising already, but I am not totally sure without experiments.

5. CONCLUSION

This study looks at chlorogenic acid in a computer way, and it seems like it could be a good phenolic compound for targeting the tyrosine kinase enzyme. The molecular docking showed that it had one of the best binding affinities out of the compounds we picked, which means it interacts strongly with the active site of the protein. I think the detailed analysis of how the protein and ligand interact points to stability from non-covalent things, like hydrogen bonds and hydrophobic interactions, plus electrostatic ones and pi-pi stacking with important amino acids that help kinase activity.

Chlorogenic acid has these multiple hydroxyl groups and aromatic rings, and that probably helps a lot with those interactions, making the binding more stable in the active site. It reminds me of what Ive read about structure-interaction relationships for kinase inhibitors, where hydrogen bonding and hydrophobic contacts really matter for how well they bind. Sometimes it gets a bit confusing with all these details.

On top of the docking results, the ADMET predictions from SwissADME say chlorogenic acid fits Lipinskis Rule of Five, and it has okay drug-likeness along with pharmacokinetic properties. Those are important for spotting potential leads that might work orally and go further in development. Not everything is perfect though.

Putting it all together, the docking, interactions, and ADMET stuff suggest chlorogenic acid could be a lead for more research. But these are just computational predictions, so experimental stuff like in-vitro assays for enzyme inhibition, cell-based anticancer tests, and in-vivo evaluations need to happen to really check if its useful as an anticancer agent targeting tyrosine kinase. That part feels like it needs more work to settle.

6. REFERENCE

1. S. G. Ghaleno and S. J. Hosseini, "Therapeutic potential of chlorogenic acid: A review of recent experimental and clinical studies (2022–2024)," Biomed. Pharmacother., Jan. 2024; 170: 116012.
2. Davis, B. J. Walker, and H. G. Miller, "Global resurgence of Coffea liberica: Phytochemical profile and climate resilience," Nature Food, Feb. 2024; 5(2): 112–125.
3. Tan AC, Ashley DM, López GY, Malinzak M, Friedman HS, Khasraw M. Management of glioblastoma: State of the art and future directions. CA Cancer J Clin., 2020; 70(4): 299-312. doi:10.3322/caac.21613.
4. Herbst RS, Morgensztern D, Boshoff C. The biology and management of non-small cell lung cancer. Nature, 2018; 553(7689): 446-454. doi:10.1038/nature25183.
5. Stupp R, Mason WP, Van Den Bent MJ, et al. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. N Engl J Med., 2005; 352(10): 987-996. doi:10.1056/NEJMoa043330.
6. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2022. CA Cancer J Clin., 2022; 72(1): 7-33. doi:10.3322/caac.21708.
7. Pradeep, N. et al. Biological removal of phenol from wastewaters: A mini review. Appl. Water Sci., 2015; **5:** 105–112.
8. Barba FJ, Roohinejad S, Barba FJ, Roohinejad S, Jambrak AR, Granato D, Montesano D, Kovačević DB (2018) Novel food processing and extraction technologies of high-added value compounds from plant materials. Foods, 7(7): 106–106.
9. X-q Sun, Chen L, Y-z Li, W-h Li, Liu G-x, Tu Y-q, et al. Structure-based ensemble-QSAR model: a novel approach to the study of the EGFR tyrosine kinase and its inhibitors. Acta Pharmacol Sin., 2014; 35(2): 301–10.
10. Muchtaridi, M., Dermawan, D., & Yusuf, M. (2018). Molecular docking, 3D structure-based pharmacophore modeling, and ADME prediction of alpha mangostin and its derivatives against estrogen receptor alpha. Journal of Young Pharmacists, Volume 10, Nomor 3: 252–259.
11. Muti'ah R, Rahmawati EK, Dewi TJD, Firdausy AF. In Silico Prediction of The Antiangiogenesis Activity of Heliannuol Lactone sesquiterpenes Compounds from Sunflower (Heliannthus annuus L.). Indones J Cancer Chemoprevention, 2021; 12(2): 90.
12. Mutiah, R., Dewi, T. J. D., Suryadinata, A., & Qonita, K. (2022). Inhibition of Human Epidermal Growth Factor Receptor-2 (HER-2) from Pomelo (Citrus maxima) Flavonoid Compounds: An in-Silico Approach. Indonesian Journal of Cancer Chemoprevention, Volume 12, Nomor 3: 148.
13. Pangribowo, S. 2019. Beban Kanker di Indonesia. Pusat Data Dan Informasi Kementerian Kesehatan RI, 1–16.
14. Pires, D. E. V, Blundell, T. L., & Ascher, D. B. 2015. pkCSM: predicting small molecule pharmacokinetic properties using graph-based signatures (Theory- How to Enterpret pkCSM Result). PKCSM, 5.
15. Zhuang, D.; Ibrahim, A.K. Deep learning for drug discovery: A study of identifying high efficacy drug compounds using a cascade transfer learning approach. Appl. Sci., **2021;** 11: 7772. [**Google Scholar**] [**CrossRef**]
16. Pu, L.; Naderi, M.; Liu, T.; Wu, H.C.; Mukhopadhyay, S.; Brylinski, M. EToxPred: A machine learning-based approach to estimate the toxicity of drug candidates. BMC Pharmacol. Toxicol, **2019;** 20: 2. [**Google Scholar**] [**CrossRef**]
17. Rees, C. The Ethics of Artificial Intelligence. In IFIP Advances in Information and Communication Technology, 1st ed.; Chapman and Hall/CRC; CRC Press/Taylor & Francis Group: Boca Raton, FL, USA, 2020; 555: 55–69. ISBN 9781351251389. [**Google Scholar**]
18. Wess, G.; Urmann, M.; Sickenberger, B. Medicinal Chemistry: Challenges and Opportunities. Angew. Chem. Int. Ed., **2001;** 40: 3341–3350. [**Google Scholar**] [**CrossRef**]
19. Chen, R.; Liu, X.; Jin, S.; Lin, J.; Liu, J. Machine learning for drug-target interaction prediction. Molecules, **2018**; 23: 2208. [**Google Scholar**] [**CrossRef**] [**PubMed**]
20. Gómez-Bombarelli, R.; Wei, J.N.; Duvenaud, D.; Hernández-Lobato, J.M.; Sánchez-Lengeling, B.; Sheberla, D.; Aguilera-Iparraguirre, J.; Hirzel, T.D.; Adams, R.P.; Aspuru-Guzik, A. Automatic Chemical Design Using a Data-Driven Continuous Representation of Molecules. ACS Central Sci., **2018;** 4: 268–276. [**Google Scholar**] [**CrossRef**]
21. Meng X-Y, Zhang H-X, Mezei M, Cui M. Molecular docking: a powerful approach for structure-based drug discovery. Curr computer-aided drug Des., 2011; 7: 146–57.
22. Jorgensen WL. The many roles of computation in drug discovery. Science, 2004; 303: 1813–8.
23. Darvas F, Keseru G, Papp A, Dorman G, Urge L, Krajcsi P (2002) In silico and ex silico ADME approaches for drug discovery. Curr Top Med Chem., 2(12): 1287–1304.
24. Uzoeto HO, Ajima JN, Arazu AV, Ibiang GO, Cosmas S, Durojaye OA (2022) Immunity evasion: consequence of the N501Y mutation of the SARS-CoV-2 spike glycoprotein. J Genet Eng Biotechnol, 20(1): 1–5.
25. Bruno A, Costantino G, Sartori L, Radi M (2019) The in silico drug discovery toolbox: applications in lead discovery and optimization. Curr Med Chem., 26(21): 3838–3873.

26. Becker OM, Marantz Y, Shacham S, Inbal B, Heifetz A, Kalid O, Bar-Haim S, Warshaviak D, Fichman M, Noiman S (2004) G protein-coupled receptors: in silico drug discovery in 3D. Proc Natl Acad Sci U S A, 101(31): 11304–11309.
27. Sacan A, Ekins S, Kortagere S (2012) Applications and limitations of in silico models in drug discovery. In: Larson RS (ed) Bioinformatics and drug discovery (Methods in molecular biology), vol 910. Springer, 87–124. https://doi.org/10.1007/978-1-61779-965-5_6
28. Fadahunsi AA, Uzoeto HO, Okoro NO, Cosmas S, Durojaye OA, Odiba AS (2024) Revolutionizing drug discovery: an AI-powered transformation of molecular docking. Med Chem Res., 33: 2187–2203. https://doi.org/10.1007/s00044-024-03253-9
29. Kharkar PS, Warrier S, Gaud RS (2014) Reverse docking: a powerful tool for drug repositioning and drug rescue. Future Med Chem., 6(3): 333–342.
30. Abraham MJ, Murtola T, Schulz R, et al. GROMACS: High performance molecular simulations through multi-level parallelism from laptops to supercomputers. SoftwareX, 2015; 1: 19–25.
31. Agahi F, Juan C, Font G, et al. In silico methods for metabolomic and toxicity prediction of zearalenone, α-zearalenone and β-zearalenone. Food Chem Toxicol, 2020; 146: 111818.
32. Amadei A, Linssen AB, Berendsen HJ. Essential dynamics of proteins. Proteins, 1993; 17: 412–425.
33. Amir M, Kumar V, Dohare R, et al. Investigating architecture and structure-function relationships in cold shock DNA-binding domain family using structural genomics-based approach. Int J Biolog Macromol, 2019; 133: 484–494.
34. Abraham MJ, Murtola T, Schulz R, et al. GROMACS: High performance molecular simulations through multi-level parallelism from laptops to supercomputers. SoftwareX, 2015; 1: 19–25.
35. G, et al. In silico methods for metabolomic and toxicity prediction of zearalenone, α-zearalenone and β-zearalenone. Food Chem Toxicol, 2020; 146: 111818.
36. Amadei A, Linssen AB, Berendsen HJ. Essential dynamics of proteins. Proteins, 1993; 17: 412–425.
37. Anjum F, Ali F, Mohammad T, et al. Discovery of natural compounds as potential inhibitors of human carbonic anhydrase II: An integrated virtual screening, docking, and molecular dynamics simulation study. OMICS, 2021a; 25: 513–524.
38. Araujo SC, Maltarollo VG, Honorio KM. Computational studies of TGF-βRI (ALK-5) inhibitors: Analysis of the binding interactions between ligand-receptor using 2D and 3D techniques. Eur J Pharm Sci., 2013; 49: 542–549.