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STRUCTURE BASED DRUG DESIGN METHOD: MOLECULAR DOCKING STUDY ON ANDROGENIC RECEPTOR AND PROSTATE SPECIFIC ANTIGEN WITH POTENTIAL LEAD MOLECULES

K Ganesh Kadiyala[1]
K. Jagadeesh
Ch. Geetika
I. Lakshmi Lavanya
B. Kanaka Durga
J. Suresh Kumar
Bachina Kiran
B. N. Suresh Varma Dendukuri

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A B S T R A C T

Molecular docking simulations were conducted to analyze the interactions between eight lead molecules with AR and PSA proteins. The lead molecules included Enzalutamide, Abiraterone, Docetaxel, Apalutamide, Cabazitaxel, Bicalutamide, Curcumin, Galeterone, Resveratrol, and Darolutamide. For the Androgen Receptor (AR), Enzalutamide displayed the most favorable docking energy of -10.96Kcal/mol, followed by Galeterone (-10.52Kcal/mol) and Darolutamide (-9.97Kcal/mol). The binding affinities of these compounds to AR suggest potential inhibitors. On the other hand, resveratrol exhibited the strongest interaction with the AR protein (-8.02Kcal.mol) among the natural compounds studied (Resveratrol and Curcumin). In the case of Prostate Specific Antigen (PSA), Abiraterone showed a docking energy of -9.14 kcal/mol, indicating a potential interaction with PSA. The docking results suggest that Enzalutamide, Galeterone, and Darolutamide, hold promise as potential inhibitors for the Androgen Receptor in prostate cancer treatment. Abiraterone, Enzalutamide, Apalutamide ligands shown a significant interaction on Prostate Specific Antigen, hinting at its potential as a dual-target agent.

1. INTRODUCTION

Prostate cancer stands as one of the most prevalent and clinically challenging malignancies affecting men worldwide, with an estimated 1.4 million new cases diagnosed in 2020 alone (Bray et al., 2018). Despite significant advancements in diagnostic tools and therapeutic strategies, the quest for targeted and efficacious

[1] Corresponding author: K Ganesh Kadiyala,
E-mail: kganeshkadiyala@gmail.com

treatments remains an ongoing pursuit. This complex disease arises from its heterogeneous nature, encompassing various molecular subtypes and intricate signaling pathways (Abeshouse et al., 2015). As a result, precision medicine approaches that selectively target aberrant signalling cascades while sparing healthy tissues have become increasingly crucial (Manzari et al., 2021).

The relationship between PSA (prostate-specific antigen) and the androgen receptor is interdependent within the realm of prostate health and pathology (Saxena et al., 2012; Kim & Coetzee 2004). Prostate-specific antigen (PSA) serves as an indicator of androgen receptor activation and is frequently employed in the screening and surveillance of prostate cancer (Balk et al., 2003). The androgen receptor, however, plays a crucial role in the regulation of prostate function and is frequently the focus of therapeutic interventions for prostate cancer aimed at impeding the advancement of the illness (Ahmed et al., 2014). The inclusion of these two elements is of utmost importance when examining, controlling, and addressing prostate-related ailments, specifically prostate cancer (Koochekpour, 2010).

In recent years, the field of prostate cancer research has seen a surge in the application of computational methods, particularly molecular docking, in the discovery of novel therapeutic agents (Ongaba et al., 2022). Molecular docking, rooted in structural biology, enables researchers to predict and analyse the interactions between small molecules and the three-dimensional structures of target proteins (Kitchen et al., 2004) (Rajendra Prasad et al., 2013). By simulating the binding process, docking studies hold the promise of identifying novel drug candidates (Reddy et al., 2014) that can disrupt pivotal cellular pathways driving prostate cancer progression (Durrant & McCammon 2011) . It is imperative to acknowledge that although the utilization of PSA testing has proven beneficial in many instances for the timely identification of prostate cancer, (Thompson & Ankerst 2007) it has also resulted in the excessive diagnosis and treatment of the condition. Hence, the determination to undergo prostate-specific antigen (PSA) testing and any consequent medical interventions have to be predicated upon a comprehensive dialogue between the patient and their healthcare practitioner, taking into account individual circumstances and preferences.

The exponential growth in available protein structures and computational resources has fueled the application of docking research in prostate cancer drug discovery. This approach offers a streamlined way to identify potential drug candidates with enhanced specificity and reduced adverse effects (Lavecchia & Giovanni 2013) . Moreover, molecular docking plays a pivotal role in elucidating protein-ligand interactions, assessing binding affinities, and guiding the optimization of lead compounds (Shoichet & Kuntz 1991). The utilization of docking software enables the anticipation of drug molecule polarity (Kadiyala et al., 2015) and the bonding contact between ligands and the active site of proteins. As the field of prostate cancer drug discovery continues to evolve, harnessing the power of molecular docking offers a compelling avenue for the identification of innovative therapeutic agents (Meng et al., 2020).

This study aims to make a significant contribution to the expanding field of docking research in prostate cancer. Its objective is to advance precision medicine and enhance the quality of life for individuals impacted by this intricate disease. This research paper provides a comprehensive overview of the existing state of docking research in prostate cancer therapeutics. Further, this study aims to investigate the substantial impact of molecular docking techniques in the elucidation of protein-ligand interactions involving the Androgen receptor and Prostate cancer Antigen. It will involve the evaluation of binding affinities and the utilization of these findings to facilitate the optimization of lead compounds (ligands). Furthermore, an exploration of the obstacles and constraints associated with docking studies will be undertaken, with a particular focus on the significance of including experimental validation to effectively transform computational discoveries into practical clinical applications (Huang et al., 2010).

2. MATERIALS AND METHODS

2.1 Determination of target receptors and the lead ligands

The protein obtained from the Protein Data Bank (PDB) possesses a fully assigned charge. Therefore, prior to the docking process utilizing Auto Dock Software, we included polar hydrogens and Kollman charges into the macromolecule. The outcomes of the macromolecule docking process may exhibit variability when water molecules are present. Water molecules were eliminated from the macromolecule in order to mitigate any undesired protein behavior during the execution of docking tests.

The protein Androgen Receptor, sourced from the Protein Data Base (PDB), is associated with a distinct ligand known as metribolone (R1881) (NCBI 2023, CID 261000). During the process of docking with other ligands, these ligands are displaced from their binding sites in order to investigate the behavior of the selected ligand in a more focused manner. The employed structure entails a crystal structure that is bound to ligand(s). Consequently, in order to successfully dock the intended ligand onto the protein at that specific location, it is necessary to eliminate the associated ligand by eliminating the heteroatoms from the PDB file. The precise location of the active site inside the protein remains undetermined. Blind docking was employed in this study, wherein the full protein surface was chosen for the purpose of protein-ligand interaction.

After establishing the grid box for blind docking, the protein is subsequently stored in the PDBQT format.

2.2 Target protein preparation for docking studies using autodock

Androgen Receptor (AR)

The protein taken from Protein Data Base (PDB) does have the complete charge assigned to it. Hence, we added polar hydrogens and Kollman charges to the macromolecule prior to the docking process using the Auto Dock Software. The results of the docking of the macromolecule may vary when it has water molecules. Water molecules from the macromolecule were removed to avoid any unwanted behavior of the protein while performing docking studies. The protein Androgen Receptor taken from the PDB has a unique ligand metribolone (R1881). This ligand is deleted while performing docking with other ligands to study the behavior of the selected ligand more specifically. The structure utilized in this context is a crystal structure that is complexed with ligands. Consequently, in order to perform docking of the intended ligand with the protein at the specified position, it is necessary to eliminate the attached ligands by removing the heteroatoms from the PDB file. The active site for the protein is unknown. So, we chose blind docking by selecting the entire protein surface for the protein ligand interaction. Once the grid box for blind docking is set, the protein is saved in PDBQT format.

Prostate Specific Antigen (PSA)

The protein taken from PDB does have the complete charge assigned to it. Hence, we added polar hydrogens and Kollman charges to the macromolecule prior to the docking process using Auto Dock Software. The results of the docking of the macromolecule may vary when it has water molecules. So, we removed water molecules from the macromolecule to avoid any unwanted behavior of the protein while performing docking studies. The employed structure entails a crystal structure that is bound to the ligand(s). Consequently, in order to successfully dock the intended ligand onto the protein at that specific location, it is imperative to eliminate the associated ligand by eliminating the heteroatoms from the PDB file. The active site for the protein is unknown. So, we chose blind docking by selecting the entire protein surface for the protein ligand interaction. Once the grid box for blind docking is set, the protein is saved in PDBQT format.

Collection of Ligands from sources and Preparation for docking studies using auto dock

All the ligands are taken from PubChem. The ligands from PubChem are taken in .SDF format. Open Babel software is used to convert the .SDF format to PDBQT format as auto dock supports. PDBQT format. Using Auto Dock software, the root of the ligand is detected and choose. The ligand must also be saved in PDBQT format along with the target protein using Auto Dock software. The ligands used for docking with both the proteins are Enzalutamide (NCBI 2023, CID 15951529), Abiraterone (NCBI 2023, CID 132971), Apalutamide (NCBI 2023, AID 2375), Bicalutamide (NCBI 2023, CID 67171867), Darolutamide (NCBI 2023, CID 9854073), Galeterone (NCBI 2023, CID 11188409), Resveratrol (NCBI 2023, CID 445154), and Curcumin (NCBI 2023, CID 969516). We intend to compare the docking simulations using these ligands to evaluate their effectiveness in binding to the active sites of the PSA and AR receptors.

Analysis of the docking results

The .DLG file which is obtained after running the auto grid and auto dock processes is studied to obtain the values of docking energy, RMSD, which measures the difference between the native ligands' positions before docking and after redocking, total internal energy, Inhibition Constant (CI), which play an important role in defining the ligand and protein. All these values for the 10 unique ligands are tabularized for finding the best protein-ligand pairs. We used Discovery studios software to analyse the results in 3-D and 2-D format. The images talk about the position of the ligand on the surface of the protein in 3-D f and 2-D formats. It also tells us the interactions like van der Waals, pi-lone pair, alkyl, pi-alkyl, and conventional hydrogen bond etc. between the atoms of protein and the ligand.

3. RESULTS AND DISCUSSION

The evaluation of the docking interactions involving the receptors PSA and AR and the selected lead ligands has been conducted, and the resulting findings have been documented in Table 1, correspondingly. The binding affinity between a ligand and the active site of a protein is positively correlated with the number of interactions. Consequently, an increase in the number of interactions leads to an improvement in binding affinity, ultimately resulting in the development of a favorable docking score. The inhibition constant (IC) is a measure of the concentration of the ligand needed to effectively inhibit the activity of the corresponding protein. If the IC value is lower for a specific ligand, it indicates that the ligand is superior and exhibits a strong affinity at the active site for the specific protein.

The ligand Enzalutamide (depicted in Figures 1.1 and 2.1) has exhibited a docking score of -10.96 Kcal/mol and -7.95 Kcal/mol, in addition to an inhibitory constant (IC) of 9.23 nm and 1.49 µM on the androgen receptor (AR) and prostate-specific antigen (PSA) receptors, respectively. The ligand Enzalutamide has demonstrated over 15 distinct bonding interactions, including Van der Waals forces, conventional hydrogen bonding, pi-sigma contacts, pi-pi stacking, alkyl interactions, and pi-alkyl interactions, inside the active region of the androgen receptor protein. While coming to the PSA the ligand has shown less than 8 distinct bonding interactions, including

van der Waals, conventional hydrogen bonding, pi-sigma and pi-alkyl interactions.

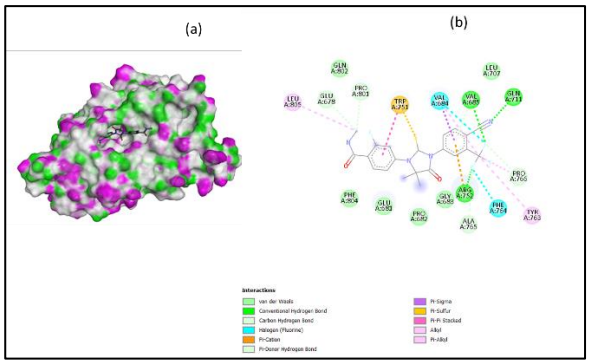

Figure 1.1 (a): 3-D representation of AR protein and Enzalutamide ligand interaction, (b): 2-D representation of AR protein and Enzalutamide ligand interaction.

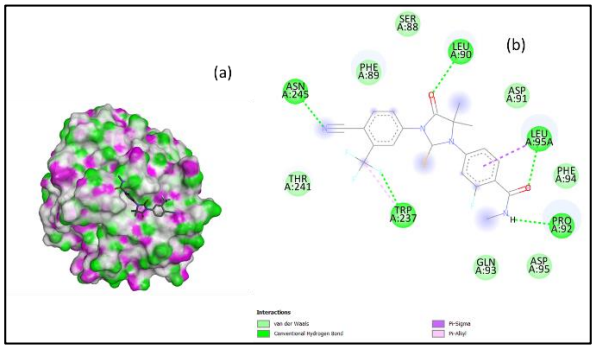

Figure 2.1. (a): 3-D representation of PSA protein and Enzalutamide ligand interaction, (b): 2-D representation of PSA protein and Enzalutamide ligand interaction.

The compound Galeterone, represented by Figures 1.2 and 2.2, has exhibited a docking score of -10.52 Kcal/mol and -1.78 Kcal/mol for the androgen receptor (AR) and prostate-specific antigen (PSA) receptors, respectively. Additionally, it has demonstrated inhibitory constants (IC) of 19.35 nm and 300 µM for the AR and PSA receptors, respectively.

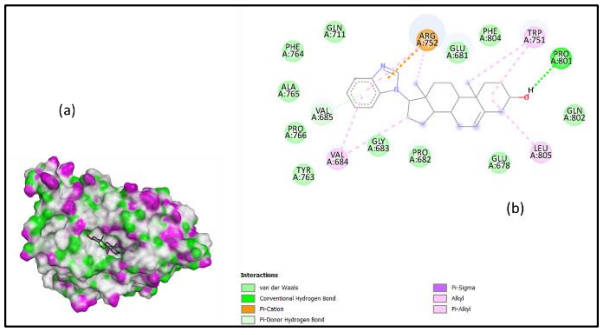

Figure 1.2. (a): 3-D representation of AR protein and Galeterone ligand interaction, (b): 2-D representation of AR protein and Galeterone ligand interaction.

Galeterone has demonstrated a total of eight distinct interaction sites with the androgen receptor (AR). These sites encompass a range of intermolecular forces, such as Van der Waals forces, conventional hydrogen bonding, pi-sigma contacts, pi-pi stacking, alkyl interactions, and pi-alkyl interactions. These interactions occur inside the active region of the androgen receptor protein. Among the identified eight ligands, galeterone has minimal interactions with the prostate-specific antigen (PSA) (Figure 2.2).

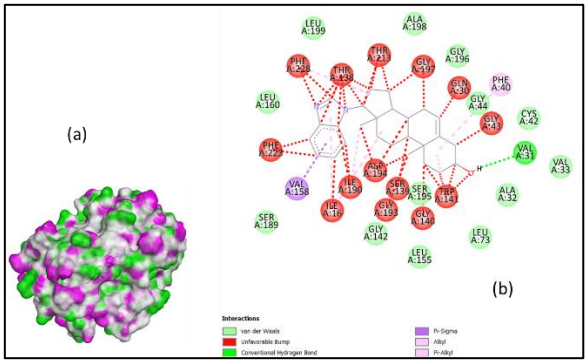

Figure. 2.2. (a): 3-D representation of PSA protein and Galeterone ligand interaction, (b): 2-D representation of PSA protein and Galeterone ligand interaction.

The ligand Darolutamide (Figures 1.3 and 2.3) has exhibited a docking score of -9.97 Kcal/mol and -6.89 Kcal/mol, as well as an inhibitory constant (IC) of 49.02 nm and 8.95 µM on the androgen receptor (AR) and prostate-specific antigen (PSA) receptors, respectively.

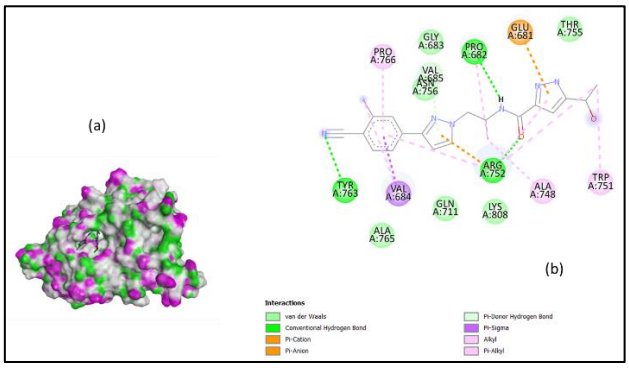

Figure 1.3. (a): 3-D representation of AR protein and Darolutamide ligand interaction, (b): 2-D representation of AR protein and Darolutamide ligand interaction.

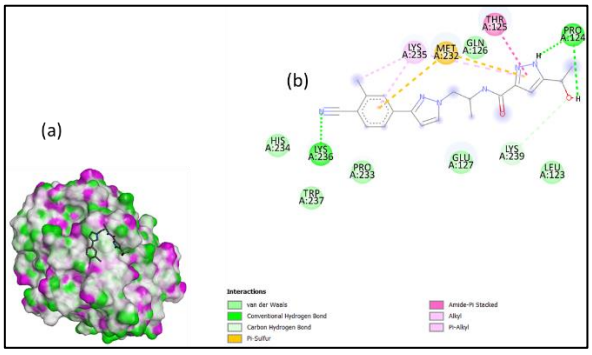

Figure 2.3. (a): 3-D representation of PSA protein and Darolutamide ligand interaction, (b): 2-D representation of PSA protein and Darolutamide ligand interaction.

The ligand darolutamide exhibited interactions with over 14 interactions at the active site on the androgen receptor (AR). Specifically, darolutamide demonstrated 10 interactions with the prostate-specific antigen (PSA) protein at its active site. The findings indicate that darolutamide exhibits favorable interactions with the androgen receptor (AR) in comparison to prostate-specific antigen (PSA).

The ligand Bicalutamide, as depicted in Figures 1.4 and 2.4, has exhibited a docking score of -9.84 Kcal/mol and -6.36 Kcal/mol for the androgen receptor (AR) and prostate-specific antigen (PSA) receptors, respectively.

Additionally, it has demonstrated inhibitory constants (IC) of 67.35 nm and 21.61 µM for the AR and PSA receptors, respectively. Bicalutamide has demonstrated over nine contacts at the active site of the androgen receptor (AR) and over 15 interactions at the active site of the prostate-specific antigen (PSA), indicating a strong binding affinity with both receptors. These interactions encompass a variety of types, highlighting the robust nature of the binding.

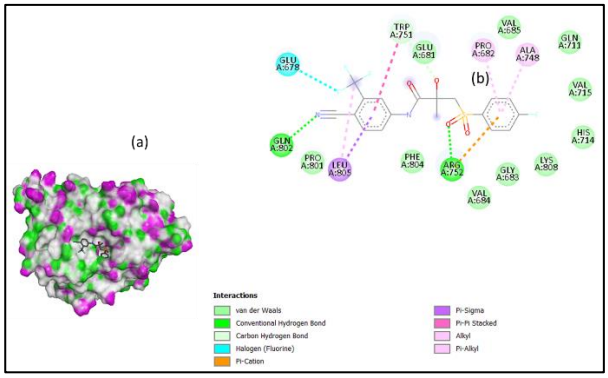

Figure 1.4. (a): 3-D representation of AR protein and Bicalutamide ligand interaction, (b): 2-D representation of AR protein and Bicalutamide ligand interaction.

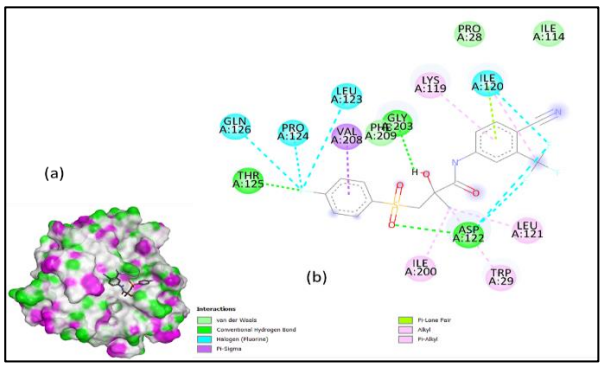

Figure 2.4. (a): 3-D representation of PSA protein and Bicalutamide ligand interaction, (b): 2-D representation of PSA protein and Bicalutamide ligand interaction.

The ligand Abiraterone (Figures 1.5 and 2.5) has exhibited a docking score of -8.68 Kcal/mol and -9.14 Kcal/mol, as well as an inhibitory constant (IC) of 434.41 nm and 201.19 nM on the androgen receptor (AR) and prostate-specific antigen (PSA) receptors, respectively. Abiraterone is one of the eight ligands that have been chosen due to their significant bonding interactions with both proteins. Abiraterone exhibits a higher binding affinity towards the prostate-specific antigen (PSA) in comparison to seven other ligands. This enhanced affinity is attributed to the appropriate interactions that occur at the active site.

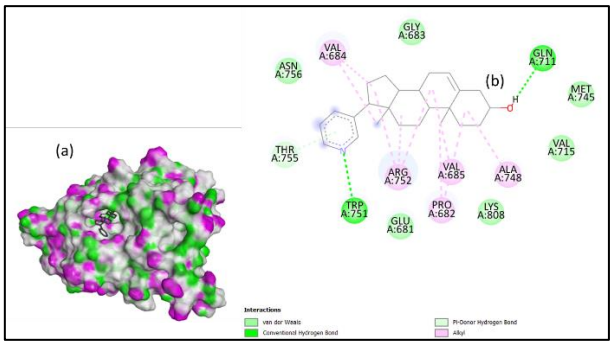

Figure 1.5. (a): 3-D representation of AR protein and Abiraterone ligand interaction, (b): 2-D representation of AR protein and Abiraterone ligand interaction.

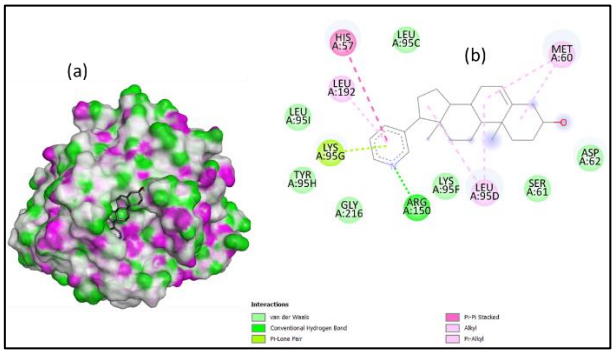

Figure 2.5. (a): 3-D representation of PSA protein and Abiraterone ligand interaction, (b): 2-D representation of PSA protein and Abiraterone ligand interaction.

The ligand Apalutamide (refer to Figures 1.6 and 2.6) has exhibited a docking score of -8.50 Kcal/mol and -7.41 Kcal/mol, in addition to an inhibitory constant (IC) of 584.63 nM and 3.71 uM on the androgen receptor (AR) and prostate-specific antigen (PSA) receptors, respectively. Among the eight selected ligands following Abiraterone, the Apalutamide ligand had a favorable interaction with the prostate-specific antigen (PSA).

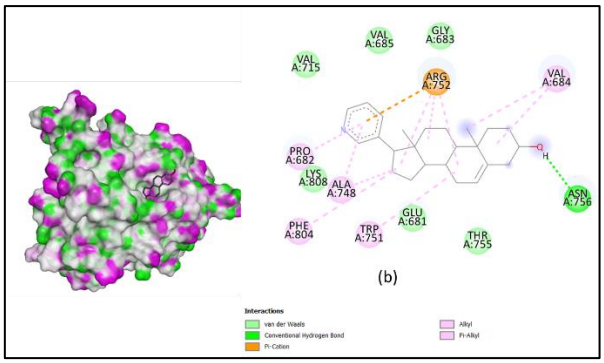

Figure 1.6. (a): 3-D representation of AR protein and Apalutamide ligand interaction, (b): 2-D representation of AR protein and Apalutamide ligand interaction.

Furthermore, Apalutamide displayed a strong binding affinity with the active sites of the androgen receptor (AR).

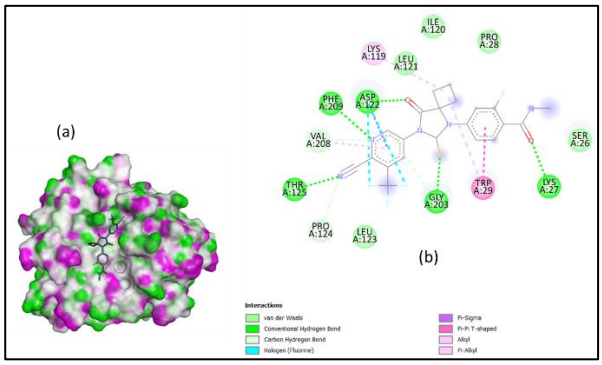

Figure 2.6. (a): 3-D representation of PSA protein and Apalutamide ligand interaction, (b): 2-D representation of PSA protein and Apalutamide ligand interaction.

The ligand Resveratrol, as depicted in Figures 1.7 and 2.7, has exhibited a docking score of -8.02 Kcal/mol and -6.03 Kcal/mol for the androgen receptor (AR) and prostate-specific antigen (PSA) receptors, respectively. Additionally, Resveratrol has demonstrated inhibitory constants (IC) of 1.33 uM and 38.13 uM for the AR and PSA receptors, respectively.

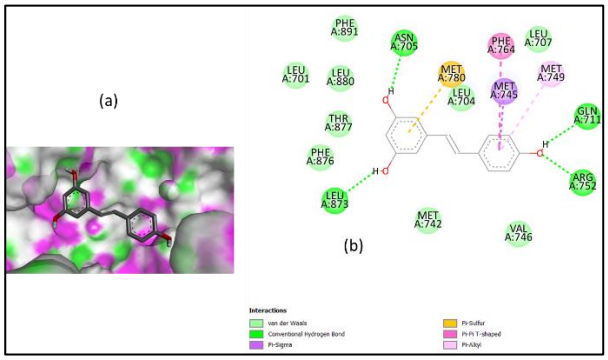

Figure 1.7. (a): 3-D representation of AR protein and Resveratrol ligand interaction, (b): 2-D representation of AR protein and Resveratrol ligand interaction.

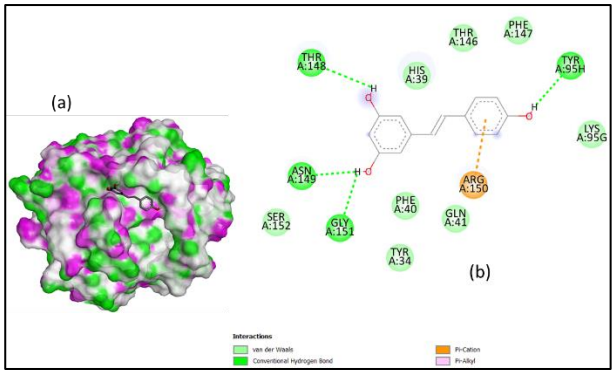

Figure 2.7. (a): 3-D representation of PSA protein and Resveratrol ligand interaction, (b): 2-D representation of PSA protein and Resveratrol ligand interaction.

Resveratrol has demonstrated over seven distinct binding interactions with the androgen receptor (AR) in its active site, including van der Waals forces, covalent hydrogen bonding, Pi-sigma contacts, Pi-stalk interactions, Pi-pi shaped interactions, and pi-alkyl interactions. Simultaneously, the active site of PSA has exhibited over five interactions, including van der Waals forces, typical hydrogen bonding, pi-cation interactions, and pi-alkyl interactions.

The ligand Curcumin, depicted in Figures 1.8 and 2.8, has exhibited a docking score of -5.96 Kcal/mol and -5.51 Kcal/mol, as well as an inhibitory constant (IC) of 43.01 uM and 91.40 uM on the androgen receptor (AR) and prostate-specific antigen (PSA) receptors, respectively. Curcumin exhibits a multitude of interactions, exceeding nine in number, at the active sites of the androgen receptor (AR). These interactions include van der Waals forces, conventional hydrogen bonding, Pi-sigma contacts, Pi-pi, T-shaped interactions, alkyl interactions, and pi-alkyl interactions. Curcumin exhibits over ten distinct interactions at the active site of the prostate-specific antigen (PSA), including van der Waals forces, typical hydrogen bonding, pi-sigma interactions, alkyl interactions, and pi-alkyl interactions.

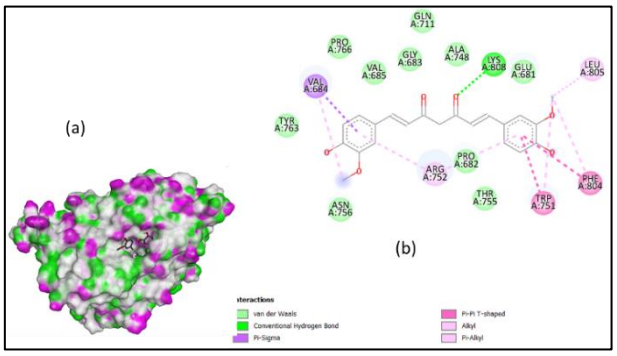

Figure 1.8. (a): 3-D representation of AR protein and Curcumin ligand interaction, (b): 2-D representation of AR protein and Curcumin ligand interaction.

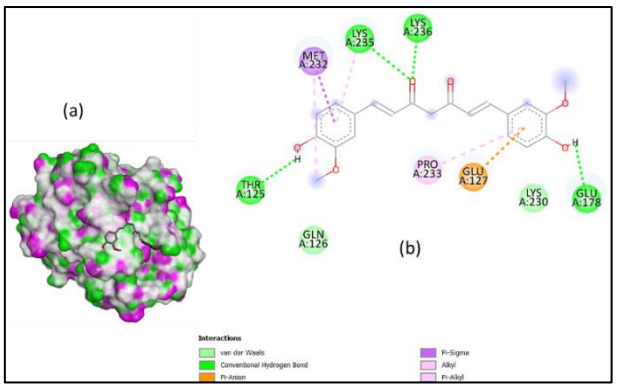

Figure 2.8. (a): 3-D representation of PSA protein and Curcumin ligand interaction, (b): 2-D representation of PSA protein and Curcumin ligand interaction.

Among the examined set of eight ligands, Enzalutamide has demonstrated a favorable binding affinity towards the Androgen-Receptor (AR), as evidenced by a docking score of -10.96 Kcal/mol. Additionally, Enzalutamide has exhibited a notable inhibitory constant of 9.23 nM. Regarding the case of prostate-specific antigen (PSA), it has been observed that the Abiraterone ligand has a favorable binding affinity, as evidenced by a docking score of -9.14 Kcal/mol and an inhibition constant value of 201.9 nM. Apalutamide has also shown a good binding score and exhibited a good binding affinity with -7.41 Kcal/mol with PSA with inhibition constant value of 3.71 μM followed by Abiraterone (shown in Table 1).

Table 1. Comparing of the Docking results of multiple ligands (Lead Ligands) interaction on the Androgen Receptor (AR) and Prostate Specific Antigen (PSA)

S.No	Lead Molecule	Target Protein	Docked Energy (Kcal/mol)	Inhibition Constant (IC)	Target Protein	Docked Energy (Kcal/mol)	Inhibition Constant (IC)
1.	Enzalutamide	Androgen-Receptor (AR)	-10.96	9.23 nM	Prostate Specific Antigen (PSA)	-7.95	1.49 μM
2.	Galeterone	Androgen-Receptor (AR)	-10.52	19.35 nM	Prostate Specific Antigen (PSA)	-1.78	300 μM
3.	Darolutamide	Androgen-Receptor (AR)	-9.97	49.02 nM	Prostate Specific Antigen (PSA)	-6.89	8.95 μM
4.	Bicalutamide	Androgen-Receptor (AR)	-9.84	61.35 nM	Prostate Specific Antigen (PSA)	-6.36	21.61 μM
5.	Abiraterone	Androgen-Receptor (AR)	-8.68	434.41 nM	Prostate Specific Antigen (PSA)	-9.14	201.19 μM
6.	Apalutamide	Androgen-Receptor (AR)	-8.50	584.63 nM	Prostate Specific Antigen (PSA)	-7.41	3.71 μM
7.	Resveratrol	Androgen-Receptor (AR)	-8.02	1.33 μM	Prostate Specific Antigen (PSA)	-6.03	38.13 μM
8.	Curcumin	Androgen-Receptor (AR)	-5.96	43.01 μM	Prostate Specific Antigen (PSA)	-5.51	91.40 μM

4. CONCLUSION

The receptors PAS and AR are the primary target receptors implicated in the context of prostate cancer. In this study, we have selected eight lead ligands or medications to conduct a comparative analysis of their docking scores and Inhibition constant values. The objective is to predict the binding affinity of these ligands towards specific receptors known to be associated with prostate cancer.

Enzalutamide, one of the eight lead ligands, has demonstrated a favorable binding affinity with a docking score of -10.96 Kcal/mol and an IC value of 9.23 nM on AR. The analysis of the docking poses revealed that the ligand Enzalutamide exhibited favorable van der Waals interactions, hydrogen bonding, and carbon-hydrogen bonding within the binding pocket of the androgen receptor (AR). Regarding the matter of PSA, it is noteworthy that half of the lead ligands (specifically, 4 out of 8) did not exhibit a favorable binding affinity during the docking process. However, it is worth mentioning that among the chosen ligands, the Abiraterone ligand demonstrated a docking score of -9.14 Kcal/mol and an IC value of 200.119 nM. The binding pocket of the prostate androgen receptor demonstrated positive interactions with abiraterone, including van der Waals contacts, conventional hydrogen bonding, pi-pi stacking interactions, and alkyl interactions. Based on the findings, it may be inferred that Enzalutamide and Abiraterone exhibit favorable binding affinity as ligands towards the androgen receptor (AR) and prostate-specific antigen (PSA), respectively, as compared to the other selected lead ligands. Resveratrol has demonstrated favorable binding affinity on androgen receptor (AR) and prostate-specific antigen (PSA) compared to curcumin, both of which are natural ligands.

Hence, out of the eight lead ligands that were chosen, four to five ligands have demonstrated favorable binding interactions with the specified proteins, namely PSA and AR with good docking energy and less inhibition constant value.

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References:

Abeshouse, A., Ahn, J., Akbani, R., Ally, A., Amin, S., Andry, C. D., ... & Lolla, L. (2015). The molecular taxonomy of primary prostate cancer. *Cell*, *163*(4), 1011-1025. doi:10.1016/j.cell.2015.10.025

Ahmed, A., Ali, S., & Sarkar, F. H. (2014). Advances in androgen receptor targeted therapy for prostate cancer. *Journal of Cellular Physiology*, *229*(3), 271–276. doi:10.1002/jcp.24456

Balk, S. P., Ko, Y. J., & Bubley, G. J. (2003). Biology of prostate-specific antigen. *Journal of Clinical Oncology*, *21*(2), 383–391. doi:10.1200/JCO.2003.02.083

Bray, F., Ferlay, J., Soerjomataram, I., Siegel, R. L., Torre, L. A., & Jemal, A. (2018). Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: A Cancer Journal for Clinicians*, *68*(6), 394–424. doi:10.3322/caac.21492

Durrant, J. D., & McCammon, J. A. (2011). Molecular dynamics simulations and drug discovery. *BMC Biology*, *9*, 71. doi:10.1186/1741-7007-9-71

Huang, S. Y., Grinter, S. Z., & Zou, X. (2010). Scoring functions and their evaluation methods for protein-ligand docking: Recent advances and future directions. *Physical Chemistry Chemical Physics*, *12*(40), 12899–12908. doi:10.1039/c0cp00151a

Kadiyala, K. G., Tyagi, T., Kakkar, D., Chadha, N., Chuttani, K., Roy, B. G., Datta, A. (2015). Picolinic acid based acyclic bifunctional chelating agent and its methionine conjugate as potential SPECT imaging agents: Syntheses and preclinical evaluation. *RSC Advances*, *5*(43), 33963–33973. doi:10.1039/C4RA13690J

Kim, J., & Coetzee, G. A. (2004). Prostate specific antigen gene regulation by androgen receptor. *Journal of Cellular Biochemistry*, *93*(2), 233–241. doi:10.1002/jcb.20228

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. doi:10.1038/nrd1549

Koochekpour, S. (2010). Androgen receptor signaling and mutations in prostate cancer. *Asian Journal of Andrology*, *12*(5), 639–657. doi:10.1038/aja.2010.89

Lavecchia, A., & Di Giovanni, C. (2013). Virtual screening strategies in drug discovery: A critical review. *Current Medicinal Chemistry*, *20*(23), 2839–2860. doi:10.2174/09298673113209990001

Manzari, M. T., Shamay, Y., Kiguchi, H., Rosen, N., Scaltriti, M., & Heller, D. A. (2021). Targeted drug delivery strategies for precision medicines. *Nature Reviews. Materials*, *6*(4), 351–370. doi:10.1038/s41578-020-00269-6

Meng, X., Cui, L., Song, F., Luan, M., Ji, J., Si, H., Zhai, H. (2020). 3D-QSAR and Molecular Docking Studies on Design Anti-Prostate Cancer Curcumin Analogues. *Current Computer-Aided Drug Design*, *16*(3), 245–256. doi:10.2174/1573409914666181029123746

National Center for Biotechnology Information. (2023). PubChem Bioassay Record for AID 2375, Panel results of Cell based ELISA Assessing Activation of Cdc42 and Rac1, Source: NMMLSC. Retrieved from https://pubchem.ncbi.nlm.nih.gov/bioassay/237.

National Center for Biotechnology Information. (2023). PubChem compound summary for CID 11188409, galeterone. Retrieved from https://pubchem.ncbi.nlm.nih.gov/compound/Galeterone.

National Center for Biotechnology Information. (2023). PubChem compound summary for CID 132971, abiraterone.

National Center for Biotechnology Information. (2023). PubChem compound summary for CID 445154, resveratrol. Retrieved from https://pubchem.ncbi.nlm.nih.gov/compound/Resveratrol.

National Center for Biotechnology Information. (2023). PubChem compound summary for CID 67171867, darolutamide. Retrieved from https://pubchem.ncbi.nlm.nih.gov/compound/Darolutamide.

National Center for Biotechnology Information. (2023). PubChem compound summary for CID 969516, curcumin. Retrieved from https://pubchem.ncbi.nlm.nih.gov/compound/Curcumin.

National Center for Biotechnology Information. (2023). PubChem compound summary for CID 9854073, cabazitaxel. Retrieved from https://pubchem.ncbi.nlm.nih.gov/compound/Cabazitaxel.

National Center for Biotechnology Information. (2023). PubChem compound summary for CID 15951529, enzalutamide. Retrieved from https://pubchem.ncbi.nlm.nih.gov/compound/Enzalutamide.

National Center for Biotechnology Information. (2023). PubChem compound summary for CID 261000, methyltrienolone. Retrieved from https://pubchem.ncbi.nlm.nih.gov/compound/Methyltrienolone.

Ongaba, T., Ndekezi, C., & Nakiddu, N. (2022). A Molecular Docking Study of Human STEAP2 for the Discovery of New Potential Anti-Prostate Cancer Chemotherapeutic Candidates. *Frontiers in Bioinformatics*, *2*, 869375. doi:10.3389/fbinf.2022.869375

Rajendra Prasad, V. V. S., Deepak Reddy, G., Appaji, D., Peters, G. J., & Mayur, Y. C. (2013). Chemosensitizing acridones: In vitro calmodulin dependent cAMP phosphodiesterase inhibition, docking, pharmacophore modeling and 3D QSAR studies. *Journal of Molecular Graphics and Modelling*, *40*, 116–124. doi:10.1016/j.jmgm.2012.12.009

Reddy, G. D., Kumar, K. P., Divya, R., Kumar Reddy, K. P., & Prasad, V. V. S. R. (2014). Quantum polarized molecular docking, pharmacophore modeling and 3D-QSAR studies of pyrido-indole containing JAK2 inhibitors. *Journal of Receptors and Signal Transduction*, *13*, 23–34.

Retrieved from https://pubchem.ncbi.nlm.nih.gov/compound/Abiraterone.

Saxena, P., Trerotola, M., Wang, T., Li, J., Sayeed, A., Vanoudenhove, J., Languino, L. R. (2012). PSA regulates androgen receptor expression in prostate cancer cells. *Prostate*, *72*(7), 769–776. doi:10.1002/pros.21482

Shoichet, B. K., & Kuntz, I. D. (1991). Protein docking and complementarity. *Journal of Molecular Biology*, *221*(1), 327–346. doi:10.1016/0022-2836(91)80222-g

Thompson, I. M., & Ankerst, D. P. (2007, June 19). Prostate-specific antigen in the early detection of prostate cancer. *CMAJ*, *17*6(13), 1853–1858. doi:10.1503/cmaj.060955

K Ganesh Kadiyala
Department of Chemistry, Shri Vishnu Engineering College for Women, Bhimavaram-534202, Andhra Pradesh, India.
kganeshkadiyala@gmail.com
ORCID 0000-0001-7357-0504

K. Jagadeesh
Department of Chemistry, Shri Vishnu Engineering College for Women, Bhimavaram-534202, Andhra Pradesh, India.
kadali.jc@gmail.com
ORCID 0000-0002-3805-4931

Ch. Geetika
Department of CSE, Shri Vishnu Engineering College for Women, Bhimavaram-534202, Andhra Pradesh, India.
geetikachukkaa@gmail.com

I. Lakshmi Lavanya
Department of CSE, Shri Vishnu Engineering College for Women, Bhimavaram-534202, Andhra Pradesh, India.
lavanyaimmaneni12@gmail.com

B. Kanaka Durga
Shri Vishnu Engineering College for Women, Bhimavaram-534202, Andhra Pradesh, India
kanakadurga1711@gmail.com
ORCID 0009-0009-4571-430X

J. Suresh Kumar
Department of Engineering Chemistry, Sagi Rama Krishnam Raju Engineering College, Bhimavaram-534204, Andhra Pradesh, India.
jayanthigitam@gmail.com
ORCID 0009-0008-8135-2337

Bachina Kiran
Department of Physics, B.V. Raju College, Bhimavaram, 534202, Andhra Pradesh, India,
kiran.b@bvricedegree.edu.in
ORCID 0000-0002-7374-4698

B. N. Suresh Varma Dendukuri
Department of Chemistry, Shri Vishnu Engineering College for Women, Bhimavaram-534202, Andhra Pradesh, India.
sureshvarma60@gmail.com
ORCID 0000-0002-9921-9461