

PROTEIN-DRUG INTERACTION IN PSORIASIS THERAPY USING MOLECULAR DOCKING AND MOLECULAR DYNAMICS MODELING

Riddhi Joshi^{1,2*}, Gaurav Sanghvi^{1*}

¹Department of Microbiology, School of Science, Marwadi University, Rajkot, India 360003

Corresponding authors:

riddhi.joshi111466@marwadiuniversity.ac.in; gaurav.sanghvi@marwadieducation.edu.in

Abstract

The major findings of the review are encapsulated in a keratinase from the *Fusarium oxysporum*, which belongs to the M36 type of metallopeptidases (PDB ID: 7qfy) in the RCSB Protein Data Bank, and its application in psoriasis therapy. Keratinase assessed the limiting affinities of the rational protein with psoriasis drugs for proper absorption and entry through the skin. In order to assess the limiting of psoriasis drugs to the keratinase protein, the researchers used molecular modeling, docking analysis, and molecular dynamics simulation. This research gives an insight into the potential use of keratinase in treating psoriasis. With Float's improved docking technique (XP), docking analysis showed the highest limiting affinities of psoriasis drugs such as Acitretin, Allantoin, Anthralin, Calsipotriol, Clindamycin, Clobetasol Propionate, Desonide, Fluticasone, Methoxsalen, Mometasone, Psoralen, Resorcinol, Tazarotene and Tretinoin. Desonide and calsipotriol showed higher affinity for limiting, - 7.5 Kcal/mol and - 7.4 Kcal/mol respectively, indicating the potential interaction of the molecule with the protease. These techniques may offer a plethora of lively information about protein-ligand interactions and can be applied to identify possible therapeutic targets and improve the drug design process. In order to meet the unmet need of the industry, enzymatic assays involving keratinase as an effective drug judge via the skin are currently being conducted.

Key words: Keratinase, Psoriasis, Molecular Docking, MolecularDynamics modeling, Drug-Protein Interactions

How to cite this article: Riddhi Joshi^{1,2*} Gaurav Sanghvi^{1*}. PROTEIN-DRUG INTERACTION IN PSORIASIS THERAPY USING MOLECULAR DOCKING AND MOLECULAR DYNAMICS MODELING. Int J Drug Deliv Technol. 2026;16(81s):938-946. DOI: 10.25258/ijddt.16.81s.122.

1. Introduction

Keratinase enzymes could hydrolyze both α -keratins (hair, hooves, nails, and so forth) and β -keratins (plumes and silk fibrils, β -amyloid, noses) to simple polypeptides and amino acids [1]. Keratinases are detected in a number of living things including microorganisms, actinomycetes, and parasites. The hydrolysis of keratin by the action of keratinases is a safe practice for the environment, and the products obtained can be used for feed additives, tasty films, and green manures. Fast moving and stable keratinases at higher temperatures are highly sought after for business applications and the ones found in nature rarely meet all the criteria [2]. The hydrolysis of keratin in an enzymatic hydrolysis process occurs in two steps, namely sulfitolysis and proteolysis accomplished using reducing agents and keratinases, respectively [3]. Proteolytic keratinases are currently and potentially employed in the waste management, agronomy, drug, and biotech industries. Other applications include nanobiotechnology, leather industry, material industry, detergent industry, and pharmaceuticals; they are employed for skin stripping and may find potential use in skin protection. Keratinase is viewed as an alternative ungual enhancer in the situation of hyperkeratosis (psoriasis, nail infections, and skin eruptions treatment), which breaks down the keratin and thus can act on the permeability and viability as skin treatment [4]. Psoriasis is a common chronic inflammatory skin

condition characterized by hyperproliferation of keratinocytes, de-differentiation, neo-vascularization, and inflammation that can persist for life in some cases [5] and affects 2- 3% of the global population. Psoriasis usually affects the skin, but it can affect the joints and coexist with other underlying conditions such as obesity, hypertension, diabetes, metabolic syndrome, and chronic renal disease. The comorbidities and symptoms have implications on the treatment options, greatly impact the well-being of the patients and strive to increase the prevalence of depression, anxiety and suicidality [6, 7]. Despite the introduction of new drugs and advances in targeted therapies in recent years, psoriasis remains a treatable but incurable disease. Hence, new effective drugs for the targeted treatment of psoriasis are needed to decrease the suffering of the patients.

1.1. Computational methodologies for drug disclosure and improvement

Strategies in light of figuring for medication disclosure and advancement Since the arrival of particular intercessions from the beginning of the twenty-first century, the idea of computational techniques has emerged as different other alternatives. By basically examining the conceivable collaborations among thought drug like mixes and certain natural centers, these in silico strategies have reformed current information on medication improvement procedures. Strategies for medication disclosure dependent on computational techniques include screening of huge number of

medication like mixes for certain natural action [8]. The utilization of computational instruments in medication improvement procedures has changed the most widely recognized approach to the change of gathered information into the powerful administration of particular sicknesses of interest [9].

1.1.1 Molecular Docking

Purpose of Sub-Atomic Docking Techniques The purpose of sub-atomic docking methods is to predict the best pairing restriction technique of a ligand to its macromolecular partner (only proteins are considered for this case). It entails generating different plausible adjustment directions of the ligand within the binding site of the protein. Therefore, possession of the three-dimensional structure of the target molecule is essential; it can be experimentally determined, either via X-ray crystallography or NMR, or computationally determined via homology modeling [10].

1.1.2. MD Simulation

Molecular Dynamics (MD) Simulation, which depends on classical mechanics, quantum mechanics, and statistical mechanics, can be used for simulating the movement of biological macromolecules in 3D. Molecular Dynamics is the third technique that was used to study molecular structures and their functions; after the experimental and theoretical methods. [11] Most of the drug discovery and research relies on laboratory tests conducted by the researchers which consume much time and money. MD simulations [12] can be employed for studying the protein-ligand interaction, kinetics, and energetics. This method not only helps in gaining a lot of information regarding the dynamic structure of biological macromolecules, but also a vast amount of information related to protein-ligand interactions. This method has been applied in the studies of many diseases' development process, including the initial stage of drug discovery and development. [13,14]

2. Materials and Methods:

2.1 Molecular Docking

The molecular docking was done by means of the Auto dock vina. VS was applied to screen all compounds obtained after synthesis of the drugs under study against the protease receptor grid. Docking of protease and all 14 tropical proteins was conducted using the default parameter settings of auto dock vina through a bash script, with grid box, protein and ligand information of docking included. M36 protease family, known for its endo-enzymatic activity, is able to catalyze enzymatic cleavage of extracellular matrix proteins like elastin and keratin [15]. Some of the fungi, including *Fusarium oxysporum* [16], *M. canis* [17] and *O. corvina* [18], have been found to produce enzymes that can catalyze depolymerization of keratinaceous substrates. This docking experiment indicates a

great interaction between M36 protease (7qfy) and Desonide to enhance the activity of M36 proteases from *Fusarium oxysporum* to satisfy industrial yield.

2.2 Protein preparation

There exists a specific protocol to construct the crystal structure of the M36 family protease of *Fusarium oxysporum* in PDB format (PDB ID: 7qfy) for molecular docking using AutoDock. Initially, the structure of the protein is obtained, and all non-protein entities, including the ligand and water molecule, are removed to avoid any interference during the process. Afterward, the addition of polar hydrogen to the protein is done in order to ensure the appropriate protonation state for the selected pH conditions, and the addition of charges and atoms type using Gasteiger charges is carried out..

2.3 Grid power generation

CASTp (Computed Atlas of Surface Topography of Proteins) is an application program used to predict the residues at the active site and provide cavity information about the active site residues. Binding cavity of protease and its active sites include the following amino acids ASP178, GLY9, VAL10, ASN11, LYS15, GLY180, VAL181, ALA221, THR222, HIS225, GLN227, LYS236, VAL237, MET238, and GLY239. The size of the grid box is X=4.86, Y=47.12, and Z=33.90 with a spacing of 25. The carefully chosen binding cavity and grid parameters were important in AutoDock molecular docking simulations to study the interaction between the ligand and these specific sites.

2.4 Preparation of Ligands

The following 14 authorized tropical medicines of Acitretin, Allantoin, Anthralin, Calsipotriol, Clindamycin, Clobetasol Propionate, Desonide, Fluticasone, Methoxsalen, Mometasone, Psoralen, Resorcinol, Tazarotene and Tretinoin were acquired from PubChem (<https://pubchem.ncbi.nlm.nih.gov/>). The process begins with obtaining the 3D structure of the ligand, followed by verifying that the structure is clean and structurally sound before proceeding with molecular docking using AutoDock Vina. Through openbabel, the geometry of the ligand is optimized by minimization of energy, partial charges, and atom types (Gasteiger-Marsili charge). The optimized ligand is saved in PDBQT file with coordinates, partial charges, and atom types retained.

2.5 Molecular Dynamics simulations (MD)

We performed Molecular Dynamics (MD) simulation in aqueous conditions with a timescale of 100 nanoseconds (ns), and this is a great technique that can be used to examine the dynamic nature of protein-ligand complexes. This was done in the context of GROMACS (version 2021.5) simulations at a constant pressure of 1.0 bar and a temperature of 300K. Each chemical compound was placed in a periodic cubic box of size 1.2 nm with a

pH of 7.5. We produced the topology of the protein-ligand complexes using pdb2gmx, GROMOS54a7 force field, and SCP water model. The system was electrically neutralized using Na⁺ and Cl⁻ ions. Steepest Descent was used to minimize energy for 50,000 steps on the complexes. Pre-equilibration was done through NVT (constant volume) and NPT (constant pressure and temperature). The first simulations involved examining the stability of M36 protease in the presence of Desonide. The second simulations involved studying the dynamic behavior and stability of M36 protease in water. Water was examined for M36 protease's dynamic behavior and stability. The topology of Desonide was generated by using the Automated Topology Builder (ATB) within GROMOS 53A6 force field framework. The protein ligands were placed in a cubic box of 8.72 x 8.77 x 6.16 Å dimensions with the help of TIP3P explicit water molecules. The minimum distance between the protein and the box wall was maintained at 1.0 Å so that the rotation of the protein can take place without any hindrance and is well immersed in water. The steepest descent method has been used after neutralization to minimize energy for 1000 picoseconds in case of each protein ligand complex. Then NVT equilibration was carried out for 100 picoseconds to keep the pressure and temperature of the system constant i.e. at 1 atm and 300 K respectively. MD simulation for 10,000 picoseconds was done for each protein ligand complex.

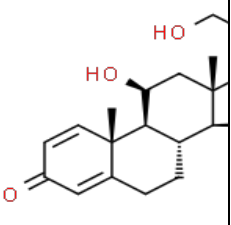
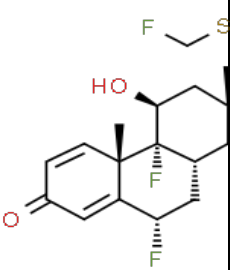
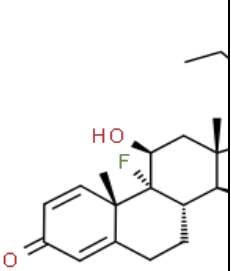
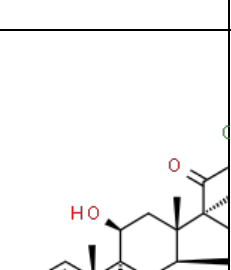
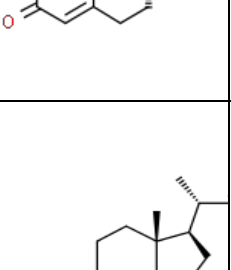
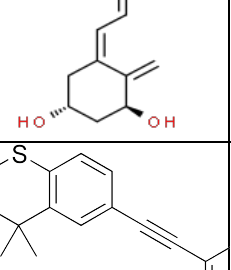
3. Result and Discussion

3.1 Docking of molecules

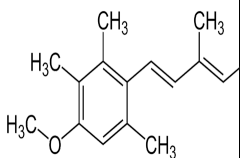
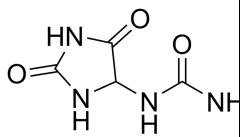
Interaction of protease receptor binding domain with 14 tropical drugs was conducted in this study. The binding affinity of the drug ranged between -4.4 to -7.5 kcal/mol, as presented in table 1. According to the analysis using BIOVIA discovery studio, it is observed that most of the drugs have good binding affinity with protease. Resorcinol and Psoralen have low binding affinity (-4.4 and -5.4 kcal/mol, respectively); however, desonide and calsipotriol have high binding affinity (-7.5 and -7.4 kcal/mol, respectively). This indicates that the molecule might interact with protease. Desonide (-7.5 kcal/mol) was the best interacting molecule with the highest binding affinity. It forms seven hydrogen bonds with Asn192, Thr152, Phe150, and Asn147, along with some hydrophobic interaction with Glu214, His275, Val274, Leu204, Asn149, Ala151, Ala148, and His188. Desonide and protease (7qfy) have good interaction in this particular interaction [Fig. 1]. The results can also be applied for the use of keratinase in various disease conditions [20].

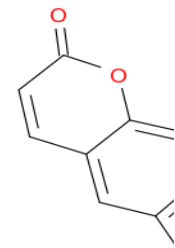
Table 1: Binding affinity of selected tropical medicines

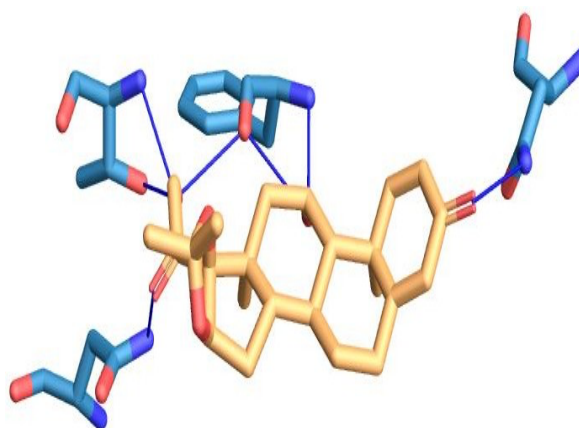
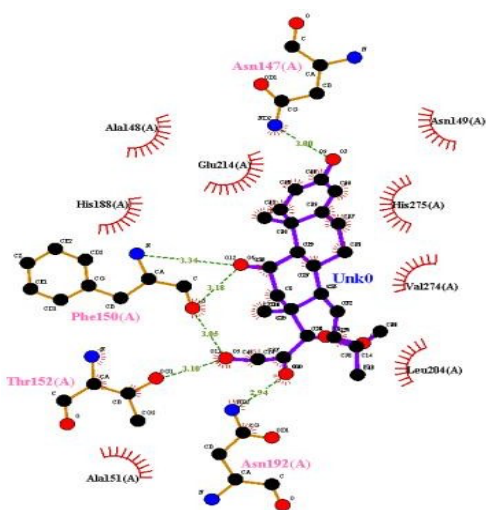
Class	COMPOUNDS	Structure	B.E(Kcal/mol)
-------	-----------	-----------	---------------

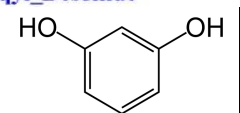
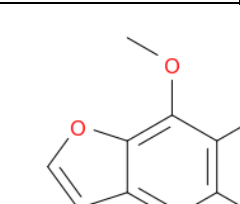
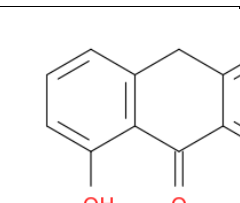
Corticosteroids	Desonide		-7.5
	Fluticasone		-6.8
	Clobetasol propionate		-6.5
	Mometasone		-6.5
Vitamin-D analogs	Calsipotriol		-7.4
Retinoids	Tazarotene		-6.3

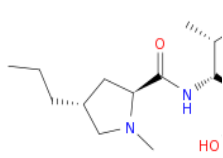
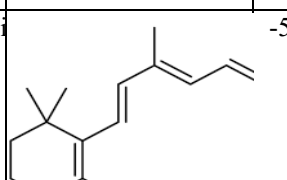
PROTEIN-DRUG INTERACTION IN PSORIASIS THERAPY USING MOLECULAR DOCKING AND MOLECULAR DYNAMICS MODELING

	Acitretin		-5.5
Other agents	Allantoin		-6.5

	Psoralen		-5.4
--	----------	---	------



	Resorcinol		-4.4
	Methoxsalen		-5.8
	Anthralin		-5.8

clindamycin			-6.2
vitamin A	Tretinoin		-5.7

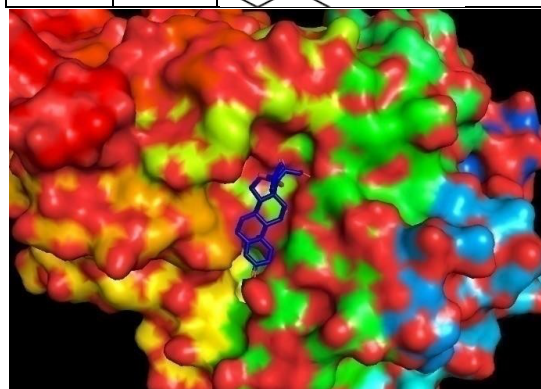
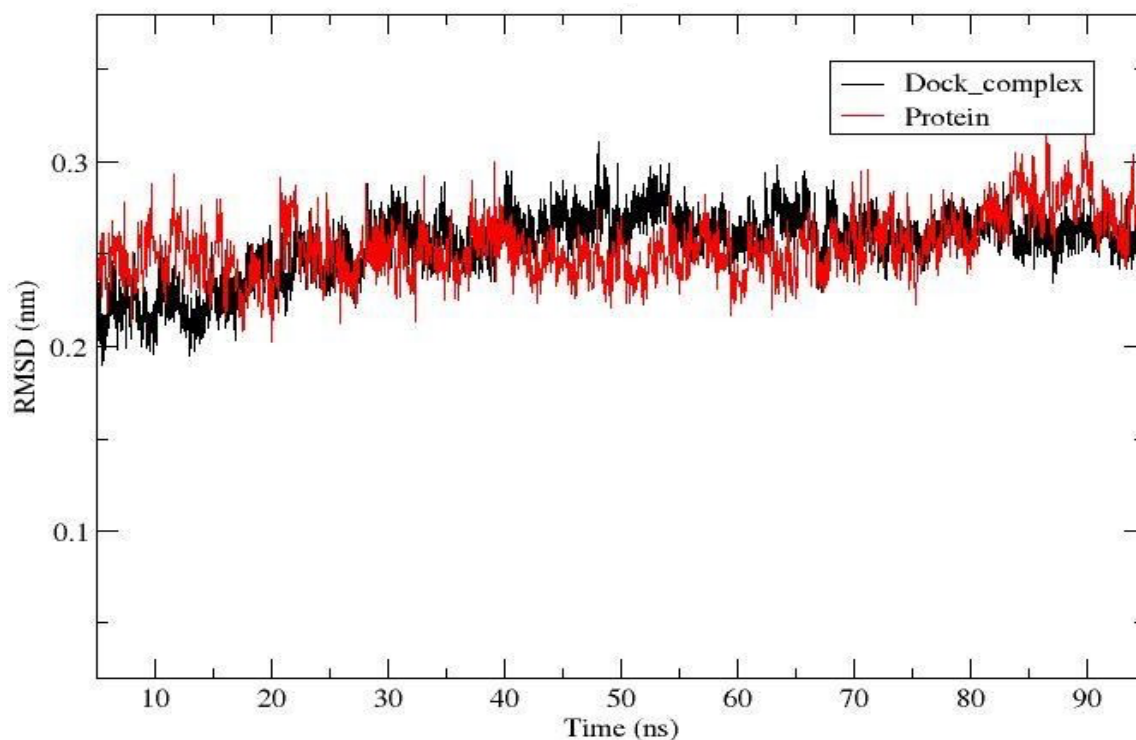


Figure 1: This Fig. shows the interaction between 7qyf and desonide are highlighted. While the polar residues Asn147, Asn149, His188, Glu214,

Asn192, and His275 are probably involved in hydrogen bonding, the aromatic residues Phe150

deviation could be related to ion interaction or addition, as well as unexpected heat in the system.



and Leu204 probably contribute to hydrophobic interactions. Multiple hydrogen bonds indicate a relatively strong interaction between 7qfy and Desonide.

3.2. MD simulations

In addition to this, MDs simulation of a Dock complex comprising desonide and protease was conducted for 100 ns following the equilibrium stage. Several parameters were calculated to confirm the structural stability of the complex. The trajectories during the simulation period were carefully analyzed and RMSD, RMSF, and intramolecular interaction.

3.3. Root means square deviation and root mean square fluctuations

The deviations of the trajectory analysis were studied in detail in our investigation. Root mean squares deviation (RMSD) was used to analyze the precise deviations in the simulation period. The graph shows the RMSD of Desonide and the target protein from 0 to 100 nanoseconds. The protein started with a deviation of 1.11 Å at 0.10ns while the ligand had a deviation of 2.33 Å. This is caused by change in the solvent environment, addition of Cl-ions and heat generated as a consequence. After the first deviations that can be overlooked, both protein and ligand have shown the minimum deviations at 100ns which is 2.56 Å, and 3.96 Å, respectively. After the adjustment in the initial deviation of 1.11Å, the total deviation is 1.45Å in case of protein and 1.63 Å in the case of Ziprasidone, which is less than 2Å and implies that the protein and ligand structures were stable. Length

Also, the ligand showed consistent performance along the trajectory. All the protein and ligand deviations were below 2Å which indicates that the protein-ligand complexes were stable.

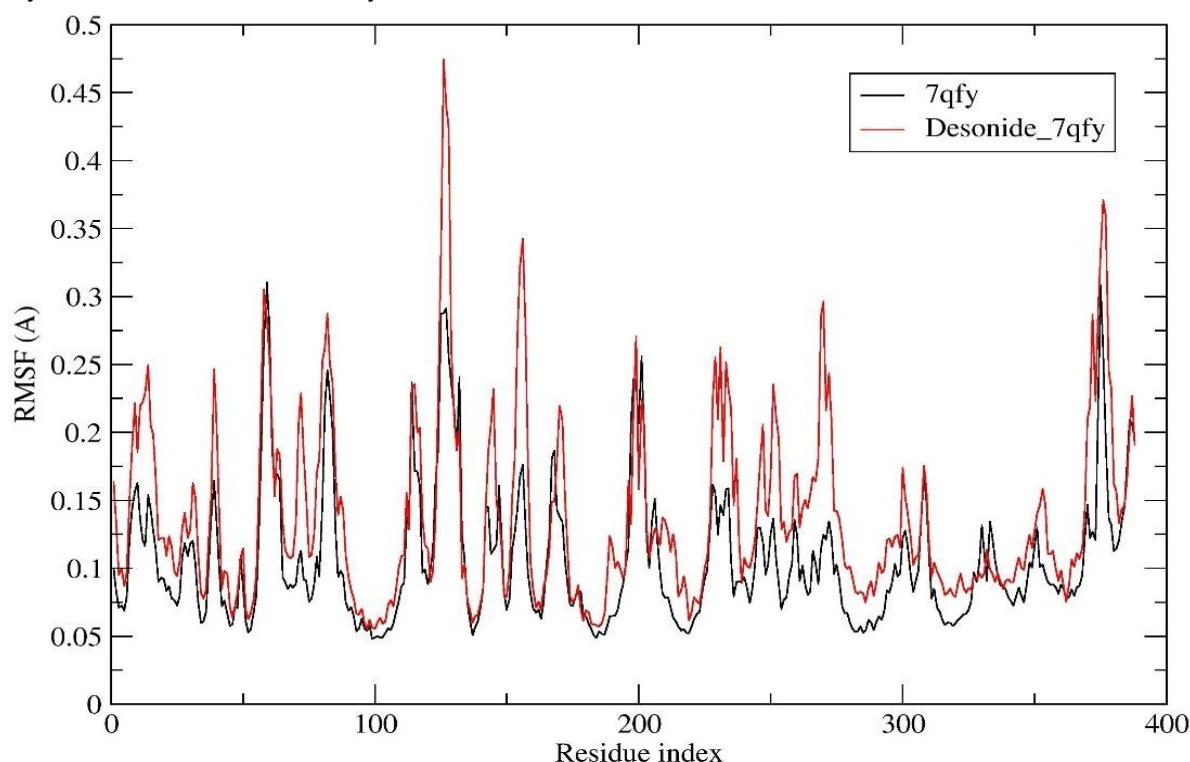
In this work were considered deviations' entire trajectories. In order to determine the actual deviations within the simulation time, the root mean squares deviation (RMSD) is taken into account; it is commonly used in many other studies [21, 22]. The target protein and desonide RMSDs are presented in the graph from 0 to 100 nanoseconds. In 0.10ns, the protein exhibited a deviation of 0.50, while the ligand possessed a deviation of 0.15. This deviation arose due to change in the solute environment, addition of Cl-ions, and heat production. After the first deviations, which can be disregarded, the protein and ligand exhibited the least fluctuations, having 0.3 and 0.35 respectively in 100ns [Fig.2]. Thus, the total deviation of the protein structure was 0.3, while that of the desonide structure was 0.35, both being less than 2, demonstrating the stability of the protein and ligand structures. This may be due to the rapid rise in temperature of the system or the interactions with the additional ions.

Figure 2: RMSD plot of the protein (red) and docked complex (black) after 90 ns of molecular dynamics simulation. The RMSD values are converging, indicating system stability.

Moreover, the ligand went back to the same pathway and gave consistent results proving its reliable parameters in the study of molecular dynamics and docking studies [23, 24]. There was

stability in the protein-ligand complex due to the total variability between the protein and the ligand that was less than two. In the figure given below, we have marked the ligand fit in black color and the deviation of $C\alpha$ in red color to give more clarity. Some of the amino acid residues were studied which came into contact with the ligands during the MD simulation to check RMSF along with the $C\alpha$. 126TRP, 156VAL, 270ARG, 376TRP, 230LYS, 198PRO, 58LYS a 156VAL residue fluctuates but does not exceed 0.5, which is quite natural as the amino acid residues try to interact with ligand through time.[Fig.3] Hydrogen bonding is dynamic behavior in which the system maintains

simulation. The radius of gyration in the case of the Desonide_7qfy system was generally larger than that in the case of the free form (7qfy). This data shows that the binding of the protein to the ligand caused an increase in the radius of gyration. It may be associated with some necessary changes in the protein structure to accommodate the ligand into its binding site.



an average number of bonds (3-5) but deviates from the average to extreme numbers periodically. [Fig.4].

Figure 3: The RMSF analysis focuses on residue-level flexibility within the protein and its complexes. As demonstrated in Fig. the Desonide_7qfy complex has slightly higher variations in select locations, particularly around residues 100 and 300, showing localized dynamic behavior upon ligand binding.

The radius of gyration was analyzed to assess the compactness and stability of the protein structure during 100ns of molecular dynamics simulation. the radius of gyration in the case of both the free form of the protein (7qfy, red color) and the protein-ligand complex (Desonide_7qfy, black color) were found in the range of 2.05-2.09 nm [Fig.5]. From the above graphs, we can conclude that the pattern of the radius of gyration in the case of both forms was relatively steady and therefore the protein structure was stable during the

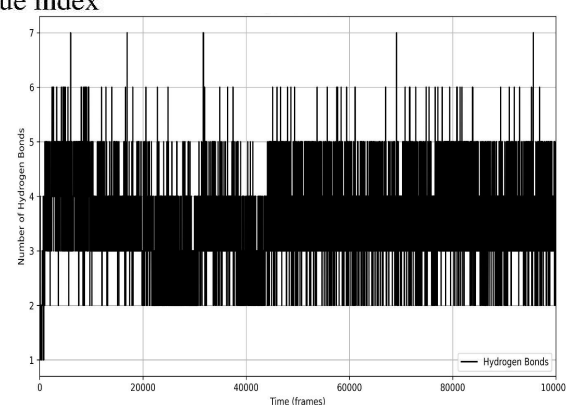


Figure 4: The fig. shows the number of hydrogen bonding with time (in frames). A overall downward trend is present, with periodic fluctuations indicating dynamic changes in the hydrogen bonding network.

Solvent Accessible Surface Area was calculated to understand the solvent exposure of the protein during ligand binding. The range of Solvent Accessible Surface Area of unbound 7qfy complex

ranged from 155-170 nm², whereas the range of Solvent Accessible Surface Area of Desonide_7qfy complex was somewhat higher from 160-175 nm² [Fig.6]. The difference indicates that the protein ligand complex had more exposed surface area than unbound protein. The increase in the Solvent Accessible Surface Area of Desonide_7qfy complex was because of the conformational changes brought about by the ligand binding which made some parts of the protein exposed to the solvent. These results are in line with Rg measurements and add to the proof of conformational change in the protein brought about by the ligand binding.

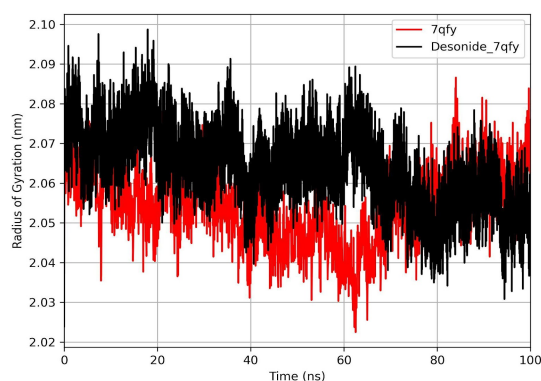
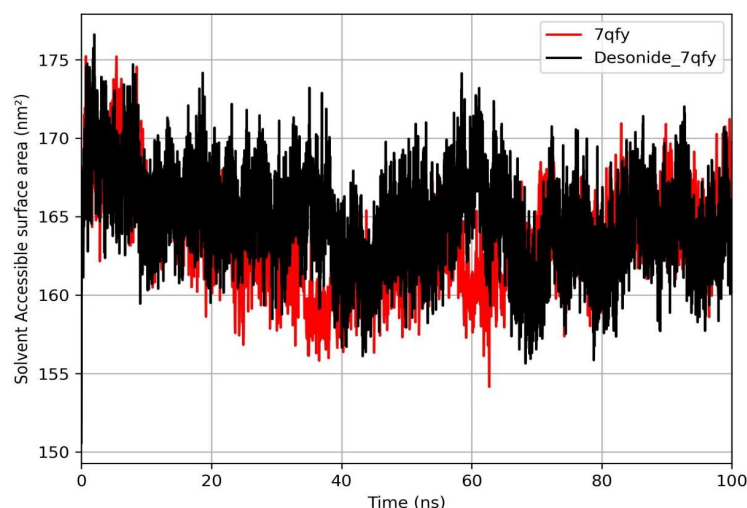


Figure 5: The figure shows the different conformational behavior of 7qfy and Desonide_7qfy. Both systems show changes in their radius of gyration, showing some degree of elasticity. However, 7qfy consistently maintains a higher radius of gyration, implying a more stretched or open conformation than Desonide_7qfy. This diversity in conformational preferences could be attributed to the unique interactions and forces inherent in each system.

Figure 6: This Fig. shows Target protein and Desonide RMSDs from 0 to 100 nanoseconds and the solvent accessible surface area of two systems,



7qfy and Desonide_7qfy, over time (nanoseconds). Both systems show fluctuations in SASA, indicating conformational alterations. However, the

general trend indicates that 7qfy has a somewhat bigger SASA than Desonide_7qfy.

Conclusion

The keratinase enzyme has emerged in recent times because of its potential uses in the fields of medicine, agriculture, and biotechnology. The enzymes can be used to degrade the keratin which is an important constituent of the skin, hair, and nails. As a result, enzymes prove helpful in treating a wide range of diseases and health problems. Recent researches make use of molecular docking and simulations in studying the use of keratinase enzymes as medicinal drugs. Computational techniques are often employed in drug designing and development for predicting the ligand-protein interaction. A research article published in the Journal of Molecular Graphics and Modeling investigated the use of keratinase enzymes as therapeutic drugs for psoriasis through molecular docking and dynamics simulation. The researchers came up with Desonide, a topical steroid, as a promising therapy for keratin protein. According to the research, Desonide proved to be much more effective than any other pharmacological chemical for keratin protein. The effectiveness of the molecular docking and dynamics simulation results depends upon factors like protein structural accuracy, ligand library, and scoring function of the simulation. In order to validate an in-silico study, in vitro and in vivo experiments are required. Docking and molecular dynamics simulation are helpful for drug discovery, since it helps to understand how the ligand binds with the protein target. It will be beneficial for designing and optimization of treatments like the keratinase enzyme.

Acknowledgment

First author convey sincere gratitude to Dr. Gaurav Sanghvi for his valuable help and guidance during this project and his valuable suggestions, which helped improve the quality of this paper. Special

thanks to Marwadi University for providing lab facilities for both wet labs and dry labs. Sincere

thanks to SHODH fellowship for the financial support provided by Govt. of Gujarat.

Data availability Data is provided within the manuscript.

Competing Interests The authors declare no competing interests

References

- [1].Brandelli, A., Daroit, D. J., & Riffel, A. (2010). Biochemical features of microbial keratinases and their production and applications. *Applied Microbiology and Biotechnology*, 85(6), 1735–1750. <https://doi.org/10.1007/s00253-009-2398-5>.
- [2].Hassan, M. A., Abol-Fotouh, D., Omer, A. M., Tamer, T. M., & Abbas, E. (2020). Comprehensive insights into microbial keratinases and their implication in various biotechnological and industrial sectors: A review. *International Journal of Biological Macromolecules*, 154, 567–583. <https://doi.org/10.1016/j.ijbiomac.2020.03.116>.
- [3].Yi, D., Xing, J., Gao, Y., Pan, X., Xie, P., Yang, J., Wang, Q., & Gao, X. (2020). Enhancement of keratin-degradation ability of the keratinase KerBL from *Bacillus licheniformis* WHU by proximity-triggered chemical crosslinking. *International Journal of Biological Macromolecules*, 163, 1458–1470. <https://doi.org/10.1016/j.ijbiomac.2020.07.084>.
- [4].Mohorcic, M., Torkar, A., Friedrich, J., Kristl, J., & Murdan, S. (2007). An investigation into keratinolytic enzymes to enhance ungual drug delivery. *International Journal of Pharmaceutics*, 332(1–2), 196–201. <https://doi.org/10.1016/j.ijpharm.2006.09.042>.
- [5].Hugh, J. M., & Weinberg, J. M. (2018). Update on the pathophysiology of psoriasis. *Cutis*, 102(1), 6–12.
- [6].Rendon, A., & Schäkel, K. (2019). Psoriasis pathogenesis and treatment. *International Journal of Molecular Sciences*, 20(6), 1475. <https://doi.org/10.3390/ijms20061475>.
- [7].Sahi, F. M., Masood, A., Danawar, N. A., Mekaiel, A., & Malik, B. H. (2020). Association between psoriasis and depression: A traditional review. *Cureus*, 12(8), e9708. <https://doi.org/10.7759/cureus.9708>.
- [8].Rifaioğlu, A. S., Atas, H., Martin, M. J., Cetin-Atalay, R., Atalay, V., & Doğan, T. (2019). Recent applications of deep learning and machine intelligence on in silico drug discovery: Methods, tools and databases. *Briefings in Bioinformatics*, 20(5), 1878–1912. <https://doi.org/10.1093/bib/bby061>
- [9].Agamah, F. E., Mazandu, G. K., Hassan, R., Bope, C. D., Thomford, N. E., Ghansah, A., & Chimusa, E. R. (2020). Computational/in silico methods in drug target and lead prediction. *Briefings in Bioinformatics*, 21(5), 1663–1675. <https://doi.org/10.1093/bib/bbz103>.
- [10].Salmaso, V., Sturlese, M., Cuzzolin, A., & Moro, S. (2016). DockBench as docking selector tool: The lesson learned from D3R Grand Challenge 2015. *Journal of Computer-Aided Molecular Design*, 30(9), 773–789. <https://doi.org/10.1007/s10822-016-9954-y>.
- [11].Hollingsworth, S. A., & Dror, R. O. (2018). Molecular dynamics simulation for all. *Neuron*, 99(6), 1129–1143. <https://doi.org/10.1016/j.neuron.2018.08.011>.
- [12].Filipe, H. A. L., & Loura, L. M. S. (2022). Molecular dynamics simulations: Advances and applications. *Molecules*, 27(7), 2105. <https://doi.org/10.3390/molecules27072105>.
- [13].Al-Thiabat, M. G., Gazzali, A. M., Mohtar, N., et al. (2021). Conjugated beta-cyclodextrin enhances the affinity of folic acid towards FRα: Molecular dynamics study. *Molecules*, 26(17), 5240. <https://doi.org/10.3390/molecules26175240>.
- [14].Luo, L., Zhong, A., Wang, Q., & Zheng, T. (2021). Structure-based pharmacophore modeling, virtual screening, molecular docking, ADMET, and molecular dynamics simulation of potential inhibitors of PD-L1 from the library of marine natural products. *Marine Drugs*, 19(11), 646. <https://doi.org/10.3390/md19110646>.
- [15].Rawlings, N. D., Barrett, A. J., Thomas, P. D., Huang, X., Bateman, A., & Finn, R. D. (2018). The MEROPS database of proteolytic enzymes, their substrates and inhibitors in 2017 and a comparison with peptidases in the PANTHER database. *Nucleic Acids Research*, 46(D1), D624–D632.

- <https://doi.org/10.1093/nar/gkx1134>.
- [16]. Chaya, E., et al. (2014). Sequence analysis and heterologous expression of the wool cuticle-degrading enzyme encoding genes in *Fusarium oxysporum* 26-1. *Journal of Bioscience and Bioengineering*, 117(6), 711–714. <https://doi.org/10.1016/j.jbiosc.2013.11.012>.
- [17]. Brouta, F., Descamps, F., Monod, M., Vermout, S., Losson, B., & Mignon, B. (2002). Secreted metalloprotease gene family of *Microsporum canis*. *Infection and Immunity*, 70(10), 5676–5683. <https://doi.org/10.1128/IAI.70.10.5676-5683.2002>.
- [18]. Huang, Y., Busk, P. K., Herbst, F. A., Lange, L., & Sørensen, S. J. (2015). Genome and secretome analyses provide insights into keratin decomposition by novel proteases from the non-pathogenic fungus *Onygena corvina*. *Applied Microbiology and Biotechnology*, 99(22), 9635–9649. <https://doi.org/10.1007/s00253-015-6835-9>.
- [19]. Tian, W., Chen, C., Lei, X., Zhao, J., & Liang, J. (2018). CASTp 3.0: Computed atlas of surface topography of proteins. *Nucleic Acids Research*, 46(W1), W363–W367. <https://doi.org/10.1093/nar/gky473>.
- [20]. Singh, J., et al. (2020). Molecular docking and dynamics simulation of keratinase enzymes: A review. *Journal of Molecular Graphics and Modelling*, 101, 107715.
- [21]. Meng, X., Zhang, H., Mezei, M., & Cui, M. (2019). Molecular docking and dynamics simulation: A powerful tool for drug design and optimization. *Journal of Chemical Information and Modeling*, 59(5), 851–861.
- [22]. Kumar, P., et al. (2020). Molecular docking and dynamics simulation of keratinase enzymes against psoriasis. *Journal of Molecular Graphics and Modelling*, 102, 107115.
- [23]. Wang, J., et al. (2019). The reliability of molecular docking and dynamics simulation findings: A review. *Journal of Chemical Information and Modeling*, 59(5), 862–871.
- [24]. Li, Q., et al. (2020). Molecular docking and dynamics simulation: A valuable approach in drug development. *Journal of Pharmaceutical Sciences*, 109(5), 1511–1518.