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Research Article

IN SILICO STUDIES OF PREDNISOLONE ACETATE DERIVATIVES FOR THE TREATMENT OF DRY EYE DISEASE

Shweta Mittal*[1], Ishita Kathuria[2], Meenakshi K Chauhan[1]

[1]*Department of Pharmaceuticsa, Delhi Institute of Pharmaceutical Sciences and Research, (DPSR University) Pushp Vihar, Sector-3, M.B Road, New Delhi, India*

[2]*School of Pharmaceutical Sciences, (DPSR University) Pushp Vihar, Sector-3, M.B Road, New Delhi, India*

**Corresponding author: shwetamittal489@gmail.com*

ABSTRACT

An attempt was made to find a potential cure for the dry eye syndrome affecting millions of people around the globe eventually leading to inflammation, blurry vision, irritation, redness, and ocular pains. In this condition, the tears are unable to provide enough lubrication either due to the lack of adequate tears or generation of poor-quality tears. The pressing need to find a cure to this chronic disease led to the search for a potential anti-inflammatory drug with the help of molecular studies. Molecular docking studies were used to find the potential anti-inflammatory drug. The study used the glucocorticoid receptor in the eye (PDB Id: 6DXK) as our target protein and A HJ4 801 as our ligand for the binding studies. The CRESSET Flare software was used for the *in-silico* studies of 152 derivatives and the target glucocorticoid protein receptor. Further, ADMET screening was performed to evaluate parameters like lipophilicity, polarity, solubility, Lipinski rule, and bioavailability score. Swiss ADME, web-based software was used to perform these studies, and further strengthen our result. Out of 152 compounds that were studied for molecular docking, 18 compounds namely Deprodone propionate, Methylprednisolone aceponate, Prednisolone valerate acetate, Methylprednisolone hemisuccinate, and pred forte, etc. were found to possess a better score than prednisolone acetate. All the molecules were found to have molecular size (<500 Da), aqueous solubility (soluble, moderately soluble), lipophilicity scores (<5) that serve as a good candidate for ocular permeability. The toxicity studies also showed no ocular irritation or corrosion. The high binding affinity of the target glucocorticoid protein receptor with the ligands can be seen as a potential treatment for dry eye disease. It serves as the basis for introducing better compounds that act as an efficient anti-inflammatory agent by inhibiting the glucocorticoid receptor and having a high binding affinity. The ADME studies showed significant bioavailability and permeability across the cornea. The top five molecules pursued properties necessary to be a good candidate for ocular absorption. Screening more compounds from various databases and performing clinical trials can be an effective strategy to further validate the results eventually leading to the discovery of less toxic and efficacious compounds for curing dry eye syndrome.

Keywords: In-Silico, Prednisolone, Dry Eye Disease

1. INTRODUCTION

Dry eyes or dry eye disease/syndrome is medically referred to as keratoconjunctivitissicca (KCS) [1]. It is a chronic condition in which the tears are unable to provide enough lubrication to the eyes either due to lack of adequate tears or generation of poor-quality tears, causing multiple visionary problems [2, 3]. It is a global problem affecting more than 344 million people every year [4, 5] and is one of the reasons for frequently visiting an eye care practitioner [4]. The prevalence of dry eye ranges from 5-50% and increases with age according to the global mapping undertaken by the Tear Film and Ocular Surface Society (TFOS). It was observed that women have a higher prevalence of dry eye disease than men. The risk factor was found to be consistent with the Asian ethnicity and not just served as an economic burden but also impacted the vision, work productivity, and quality of life. In the year 1995, with the release of the report of 'Workshop on Clinical Trials in Dry Eye' by the National Eye Institute/Industry, the initial focus on the dry eye syndrome shifted. It became the first formal attempt to classify and define dry eye disease [6]. After almost 20 years, another definition was released by TFOS Dry Eye Workshop II which

included terms like hyperosmolarity, homeostasis, and neurosensory abnormalities to further refine the definition [7]. Dry eye is often accompanied by ocular pain, dryness, irritation, foreign debris sensation, redness in eyes, stinging, burning, and light sensitivity. Corneal neuropathic pain characterized as stinging or burning sensation, dull or sharp ache is also observed [8, 9]. Some other consequences include notably blurry and fluctuating vision, visual symptoms, etc [10]. The therapeutic strategies which are used for treating dry eyes include increasing the amount of liquid on the eye surface, increasing the lubricity or lipid content of tears, and decreasing the tear evaporation [11]. Numerous topical lubricants such as drops, ointments, and gel formulations containing artificial tears are also available in the market to provide symptomatic relief [12]. The inflammation in moderate to severe cases can be decreased by using prescription-based topical applications such as glucocorticosteroidsimmuno modulatory agents. As the ocular inflammation is decreased, tear production is increased [13]. In some cases, tear duct plugs can also be used if the tears drain out too quickly from the eye. These tear ducts are called puncta plugs and help in retaining the tears in the eyes [2]. Lifestyle changes and altering dietary approaches can also help in disease management. Moderating alcohol, using protective eyewear, avoiding forced-air heating and air conditioners, using humidifiers to lessen the dryness in the air, reducing screen time, taking adequate fluid, avoiding environmental triggers and sufficient amount of sleep can help manage this disease better [2,14,15]. Includingfatty acids and essential supplements in a regular diet have been seen to enhance the quality and production of tears [13, 16].

A 1% solution of prednisolone acetate is currently marketed for the treatment of moderate to severe dry eye. Prednisolone acetate is a corticosteroid and shows anti-inflammatory action through signal transduction by their nuclear receptor, the glucocorticoid receptor (GR) when applied to the eye. In the current study, docking analysis is performed with prednisolone acetate derivatives with the PDB: 6DXK which is a glucocorticoid receptor with the co-crystallized ligand A HJ4 801. Further ADME studies were also conducted to evaluate parameters like lipophilicity, polarity, solubility, Lipinski rule, and bioavailability score.

2. MATERIAL AND METHODS

Molecular docking is the most well-known method in structure-based drug design. The term 'docking' is being widely used since the early 1980s [17]. This virtual screening method is useful for predicting the structure of the ligand-protein complex and the binding affinity of protein and ligand with each other. This helps in lead optimization, leading to drug discovery and development [18]. It is mainly performed between a small molecule known as ligand and a target macromolecule known as protein and, therefore, is referred to as ligand-protein docking [19]. Two basic steps involved in molecular docking are assessing the binding affinity and predicting the ligand conformation, its orientation, and position within sites which are referred to as pose [20]. Absorption Digestion Metabolism Excretion Toxicology also known as ADMET are important parameters for drug discovery and development. These parameters are essential in determining the fate of the drug candidates whether they will be terminated, advanced, or held [21], therefore, ADMET properties were also screened to ensure the selection of bioactive ligands possessing drug safety and pharmacokinetic properties. Here, the PDB 6DXK was considered for the anti-inflammatory studies [22].

2.1. Software Validation

Software validation becomes extremely important in a computational study like docking as a change in software can lead to variation in results. As each PDB possesses its active site and co-crystallized ligand, software validation is ensured by re-docking the co-crystallized ligand. The orientation and conformational changes obtained can be studied by performing these steps which ultimately help in stabilizing the repeatability.

2.2. Retrieval of target protein structure

These anti-inflammatory studies were made possible by targeting the glucocorticoid receptor in the eye with the PDB ID: 6DXK [22]. This 3D structure was extracted from the RCSB Protein Data Bank [23] as it is the only collection of biological macromolecules' structural data around the globe [24]. Wizard was used to prepare the protein. This protein consists of 2 chains "A, B". Docking was performed in reference to chain A. A copy of the protein was made to save it as dry protein. Water molecules present on the active site were deleted and all the possible amino acids residues were shown.

2.3. Identification of Binding Site

It is essential to identify the target binding site as it will help in the post-dock dynamics. Also, it provides

information on the phenomenon involved in the interaction of ligand-protein, the free energy of the complex, and hydrogen bond formation which in turn helps in the identification of the most suitable ligand [25]. In this case, for the proposed target the binding site was found to be A HJ4 801 that is the co-crystallized ligand.

2.4. Preparation of the Ligand

The prednisolone acetate and its derivative were made available through PubChem in its 3D form and saved in SDF format. PubChem is a large repository, containing various types of structures (2D and 3D), physical and chemical properties, pharmacology, toxicology, metabolism, bioactivity data, etc [26].152 derivatives were used to perform the docking studies to check their conformation with the target site of our protein responsible for the anti-inflammatory activity.

2.5. Protein-Ligand Molecular Docking

Free energies of binding and bound conformations can be predicted through docking for both, small molecule ligands and macromolecular targets [27]. The anti-inflammatory activity of the 152 ligands with the target glucocorticoid receptor was checked using the Flare module. The trial version of the module offered by CRESSET software was used on Micromax Intel ® Core ™ i3-5005U CPU @ 2.00 GHz,2 Core (s), 6.00 GB RAM, 4 Logical processors, x64 based processor, 64-bit Operating System. Further, the protein was prepared, minimized, and then, according to the binding information the grid box was defined to dock the ligands with the protein's active site. The docking process continued and calculations were performed in the normal mode with default settings in the CRESSET Flare software. Finally, the bond interactions like hydrophobic and hydrophilic bonds, attachment affinities were analyzed, and then the minimal docking score was used to choose the best potential candidates with high efficacy as anti-inflammatory drugs.

2.6. ADMET Screening

The ADMET screening was performed for all 152 derivatives via Swiss ADME. It is a freely available web-based tool for analyzing pharmacokinetics, physiochemical properties, lipophilicity, and various other parameters. Initially, for all the compounds canonical SMILES were listed in the web-based tool and then the software was run. After the process completion, the results were downloaded in form of an MS Excel workbook. Lastly, the screening of ADMET profiles took place for parameters like lipophilicity, polarity, solubility, Lipinski rule, and bioavailability score.

3. RESULTS AND DISCUSSION

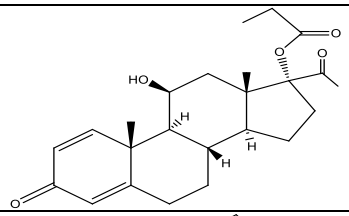
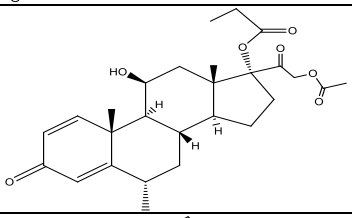
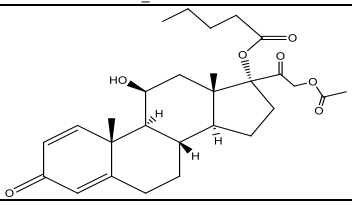
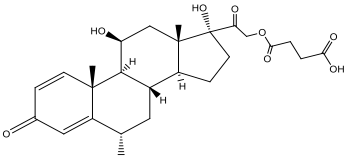
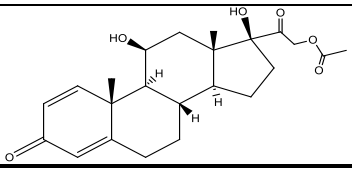
- Classification: Transcription
- Organism:*Homo sapiens*
- Expression System: *Escherichia coli*
- Resolution: 3.05 Å
- Name : (8S,11R,13S,14S,17S)-11-[4-(dimethy-lamino) phenyl]-17-(3,3-dimethylbut-1-yn-1-yl)-17-hydroxy-13-methyl-1,2,6,7,8,11,12,13,14,15,16,17-dodecahydro-3H-cyclopenta[a]phenanthren-3-one (non-preferred name)
- Formula: C_{32} H_{41} N O_2

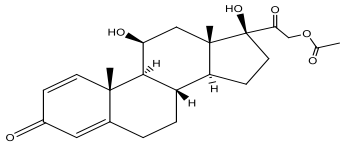
The results are summarized in Table 1.

Glucocorticoid receptor in the eye from *Homo sapiens* was chosen as the target protein. The CRESSET FLARE's protocols were used to perform molecular docking with the target protein and ligands by utilizing the extended electron distribution (XED), polarizable force field. The anti-inflammatory effect was studied for all 152 compounds by checking the inhibition of the glucocorticoid receptor in response to the compounds by performing molecular docking. These 152 compounds were then prepared for docking, as ligands. Substantial binding was seen for various ligands as a result of the screening performed and many compounds showed the binding affinity better than prednisolone acetate. The best inhibitor for our target protein 6DXK was found to be Deprodone propionate ([(8*S*,9*S*,10*R*,11*S*,13*S*,14*S*,17*R*)-17-acetyl-11-hydroxy-10,13-dimethyl-3-oxo-7,8,9,11,12,14,15,16-octahydro-6*H*-cyclopenta[a]phenanthren-17-yl] propanoate). A significant docking score was found to be -10.781. Key amino acid residues which played a major role in binding with the ligand were found to be A ARG 611, A MET 604, A LEU 563. Strong hydrogen bond interaction was observed with the A ARG 611 residue (bond length 1.8 Å), Van der Waals interaction with the A MET 604, and A LEU 563 residues showing 2.9 Å and 3.0 Å respectively. Methylprednisolone aceponate ([(6*S*,8*S*,9*S*,10*R*,11*S*,13*S*,14*S*,17*R*)-17-(2-acetyloxy-acetyl)-11-hydroxy-6,10,13-trimethyl-3-oxo-7,8,9,11,12,14,15,16-octahydro-6*H*-cyclopenta[a]phenanthren-17-yl] propanoate) with the docking score of -10.381 was the second best inhibitor. 5 key amino acid residues

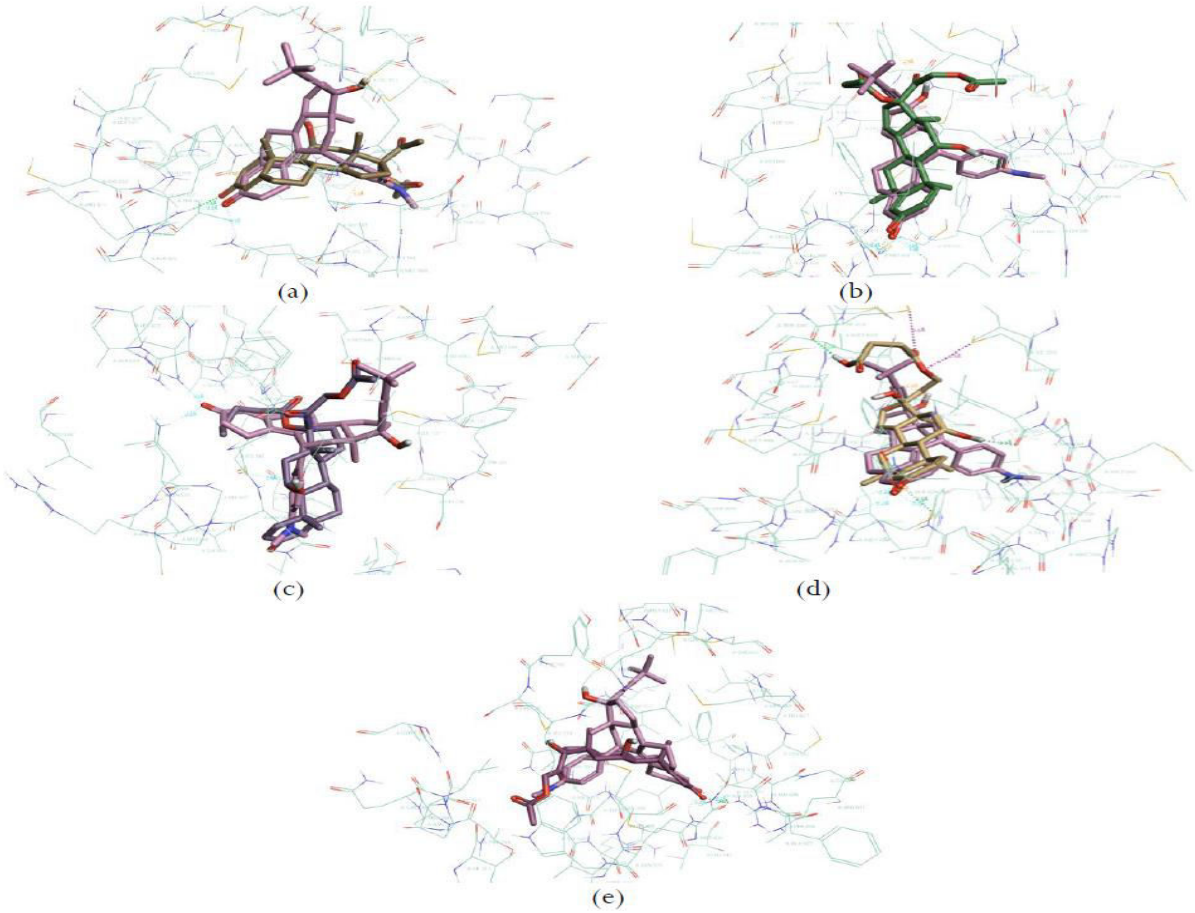
namely A TYR 735, A LEU 536, A ARG 611, A PHE 623, A GLN 570 played a significant role in binding with the target protein. A TYR 735 and A PHE 623 residues formed Van der Waals interaction with the bond length as 2.9 Å and 2.7 Å respectively. Strong hydrogen bond interactions were seen with the A LEU 536 residue (bond length 2.3 Å) and 2 other residues, A ARG 611 and A GLN 570 having bond lengths 2.4 Å and 2.6 Å respectively showed weak hydrogen bond interactions. Another ligand viz Prednisolone valerate acetate ([(8*S*,9*S*,10*R*,11*S*,13*S*,14*S*,17*R*)-17-(2-acetyloxyacetyl)-11-hydroxy-10,13-dimethyl-3-oxo-7,8,9,11,12,14,15,16-octahydro-6*H*-cyclopenta[a]phenanthren-17-yl] pentanoate) also showed a significant docking score of -10.187 when screened. A MET 646 residue with a bond length of 4.1 Å showed cation-pi interaction whereas A LEU 563 with a bond length of 2.8 Å showed a weak hydrogen bond. -10.175 docking score was found to be for the compound Methylprednisolone hemisuccinate (4-[2-[(6*S*,8*S*,9*S*,10*R*,11*S*,13*S*,14*S*,17*R*)-11,17-dihydroxy-6,10,13-trimethyl-3-oxo-7,8,9,11,12,14,15,16-octahydro-6*H*-cyclopenta[a]phenanthren-17-yl]-2-oxoethoxy]-4-oxobutanoic acid), therefore, making it one of the best inhibitors for the target protein.

Table 1: contains the summary of docking score, hydrophilic and hydrophobic interactions of the above-mentioned compounds.

S. No	CID	COMPOUND	DOCKING SCORE	INTERACTION WITH AMINO ACID	BOND DISTANCE (Å)	TYPE OF BOND
1	443972		-10.781	A ARG 611 A MET 604 A LEU 563	1.8 2.9 3.0	Strong hydrogen bond Van der Waals interaction Van der Waals interaction
2	63019		-10.381	A TYR 735 A LEU 536 A ARG 611 A PHE 623 A GLN 570	2.9 2.3 2.4 2.7 2.6	Van der Waals interaction Strong hydrogen bond Weak hydrogen bond Van der Waals interaction Weak hydrogen bond
3	5284612		-10.187	A MET 646 A LEU 563	4.1 2.8	Cation-pi interaction Weak hydrogen bond
4	16923		-10.175	A MET 639 A MET 560 A TYR 735 A LEU 563 A GLN 570 A ARG 611 A PHE 623	2.0 3.6 3.3 3.0 2.3 2.3 2.4 2.8	Strong hydrogen bond Cation-pi interaction Cation-pi interaction Van der Waals interaction Strong hydrogen bond Strong hydrogen bond Weak hydrogen bond Van der Waals interaction
5	657238		-10.004	A ARG 611	2.0	Strong hydrogen bond

S. No	CID	COMPOUND	DOCKING SCORE	INTERACTION WITH AMINO ACID	BOND DISTANCE	TYPE OF BOND
1	5834 Prednisolone Acetate		-9.387	A GLN 570 A MET 560	2.0 3.8	Strong hydrogen bond Cation-pi interaction

LIGAND NAME	DOCKING SCORE	INTERACTION WITH AMINO ACID	BOND DISTANCE	TYPE OF BOND
A HJ4 801 Ligand		A ARG 611	2.2	Weak hydrogen bond
		A GLN 570	2.2	Weak hydrogen bond
A HJ4 801 (1)_D Docked Ligand	-12.462	A ARG 611	2.6	Weak hydrogen bond
		A GLN 570	2.9	Weak hydrogen bond



(a) ([(8S,9S,10R,11S,13S,14S,17R)-17-acetyl-11-hydroxy-10,13-dimethyl-3-oxo-7,8,9,11,12,14,15,16-octahydro-6H-cyclopenta[a] phenanthren-17-yl] propanoate. (b)([(6S,8S,9S,10R,11S,13S,14S,17R)-17-(2-acetyloxyacetyl)-11-hydroxy-6,10,13-trimethyl-3-oxo-7,8,9, 11,12,14,15,16-octahydro-6H-cyclopenta[a]phenanthren-17-yl] propanoate). (c) ([(8S,9S,10R,11S,13S,14S,17R)-17-(2-acetyloxyacetyl)-11-hydroxy-10,13-dimethyl-3-oxo-7,8,9,11,12,14,15,16-octahydro-6H-cyclopenta[a]phenanthren-17-yl] pentanoate). (d) (4-[2-[(6S,8S,9S,10R, 11S,13S,14S,17R)-11,17-dihydroxy-6,10,13-trimethyl-3-oxo-7,8,9,11,12,14,15,16-octahydro-6H-cyclopenta[a]phenanthren-17-yl]-2-oxoethoxy]-4-oxobutanoic acid). (e) ([2-[(8S,9S,10R,11S,13S,14S,17S)-11,17-dihydroxy-10,13-dimethyl-3-oxo-7,8,9,11,12,14,15,16-octahydro-6H-cyclopenta[a]phenanthren-17-yl]-2-oxoethyl] acetate)

Fig. 1: Interactions of the selected compounds with the best binding score values with amino acid residues in the Glucocorticoid receptor binding pocket

Out of the 7 key amino acid residues, light strong hydrogen bond and cation-pi interaction were observed with A MET 639 (bond length 2.0 Å and 3.6 Å respectively), cation-pi interaction was observed with A MET 560(bond length 3.3 Å), Van der Waals interaction with A TYR 735 (bond length 3.0 Å) and A PHE 623 (bond length 2.8 Å), strong hydrogen bond interactions with A LEU 563(bond length 2.3 Å) and A GLN 570(bond length 2.3 Å) and weak hydrogen bond interactions with A ARG 611(bond length 2.4 Å). Another ligand, that showed significant binding with the target protein was Pred forte ([2-[(8*S*,9*S*,10*R*,11*S*,13*S*,14*S*,17*S*)-11,17-dihydroxy-10,13-dimethyl-3-oxo-7,8,9,11,12,14,15,16 -octahydro-6*H*-cyclopenta[a]phenanthren-17-yl]-2-oxoethyl] acetate). Its docking score was found to be -10.004 through molecular docking and strong hydrogen bond interactions were seen with A ARG 611(bond length 2.0 Å) residue.

Fig. 2: Interactions of the reference compound, Prednisolone Acetate ([2-[(8*S*,9*S*,10*R*,11*S*,13*S*, 14*S*,17*R*)-11,17-dihydroxy-10,13-dimethyl-3-oxo -7,8,9,11,12,14,15,16-octahydro-6*H*-cyclopenta [a]phenanthren-17-yl]-2-oxoethyl]acetate) with amino acid residues in the Glucocorticoid receptor binding pocket

A HJ4 801, the ligand showed weak hydrogen bond interaction with both A ARG 611(bond length 2.6 Å) and A GLN 570(bond length 2.9 Å). Binding interactions were investigated by the docking studies. The A HJ4 801 with the target protein, glucocorticoid receptor, and the docking score was found to be -12.462 Å. The result of our studies suggests that 18 compounds showed enhanced binding properties in comparison to the A HJ4 801 whereas 133 compounds were seen to have weaker binding properties. Out of these 18 derivatives, the marketed formulation that is Pred forte ([2-[(8*S*,9*S*,10*R*,11*S*,13*S*,14*S*,17*S*)-11,17-dihydroxy-10,13-dimethyl-3-oxo-7,8,9,11,12,14,15,16 -octahydro-6*H*-cyclopenta[a]phenanthren-17-yl]-2-oxoethyl] acetate) was found to differ isomerically from Prednisolone acetate ([2-[(8*S*,9*S*,10*R*,11*S*,13*S*,14*S*,17*R*) -11,17-dihydroxy-10,13-dimethyl-3-oxo-7,8,9,11,12, 14,15,16-octahydro-6*H*-cyclopenta[a]phenanthren-17-yl]-2-oxoethyl] acetate). The R configuration in Prednisiolone acetate was replaced by the S configuration in Pred forte, eventually leading to the higher binding efficacy of the later in docking.

3.1. Drug-likeness and ADMET studies

Most of the drug candidates don't reach their ultimate destinations of becoming marketed drugs due to various reasons involved. It becomes extremely important to predict the drug-likeness through computational methods to improve the success of the drugs being discovered, developed, and marketed [28]. Drug-likeness studies refer to the molecule's probability to serve as an oral drug about its bioavailability. The interaction of an enzyme and inhibitor cannot be the sole assurer of its appropriateness as a drug; the results of docking were further strengthened by performing in silico ADMET screening. The web tool Swiss ADME was used for performing these studies [29]. Predicting these properties becomes essential in the designing of the drug as poor ADMET properties can often lead to failed clinical trials in approximately 60% of new chemical entities [30]. The early estimation of these properties can thus lead to fewer failures related to pharmacokinetics in clinical studies [31]. In silico techniques also establishes as a more attractive option for the prediction of ADMET properties rather than using the conventional experimental assay due to the less cost and time involved and the availability of testing a large number of designed and real compounds. Therefore, the Swiss ADME web tool becomes a valuable and reliable tool [30].

Non-uniform pharmacokinetics of the drug molecule takes place in the ocular tissues. Several factors play a crucial role in the ADME of the eye. Size plays an important role in the distribution throughout the vitreous. The diffusion of large ones is highly restricted throughout the vitreous whereas the small ones can rapidly distribute. Other factors that influence the distribution of the drug are physiochemical properties such as solubility, structure, logP, and stability of the

administered drug. The molecular weight and the surface charge also affect the distribution of our drug across the ocular tissues [32].

The molecular weight of all the top 152 compounds was found to be less than 500 Daltons thus, it can be said that they would easily permeate and distribute evenly in the eye through passive diffusion [33]. All the molecules were found to follow Lipinski rule of five that is Molecular mass less than 500 Dalton, Highlipophilicity (expressed as LogP less than 5), Less than 5 hydrogen bond donors, Less than 10 hydrogen bond acceptors, TPSA (Total Polar Surface Area) less than 140 Å. It can thus be predicted that all the molecules could show better absorption and permeation through the oral route. The optimum lipophilicity of a molecule for corneal absorption is 10-100 n'octanol partition coefficients. An increase in lipophilicity leads to increased binding of the drug to the lipid membrane of the cornea and thus decreased drug diffusion through the cornea. All the top five molecules had optimum lipophilicity [34]. The ESOL and Silicos-IT aqueous solubility revealed soluble to moderately solubility for all the molecules and thus can exhibit much solubility in tear fluid that would help the drug to permeate more through the cornea. The results of ADME studies for the top five molecules and Prednisolone acetate is depicted in table 2.

The toxicity of the top five compounds and prednisolone acetate was predicted using the admetSAR online tool. The results of toxicity prediction are presented in Table 3. No compound exhibited carcinogenicity. None of the compounds caused eye irritation and eye erosion. All the top five molecules are safe from Ames mutagenesis.

These results dispense essential information about the toxicological profile of the tested compounds and might be useful in choosing the preferred dosage form and route of administration. Since different values of probability were reported, this indicates the preliminary nature of the studies, and experimental data is needed to confirm them.

Table 2: ADME results of top five molecules and prednisolone acetate

MOLECULE	MW	Fraction Csp3	Rotatable H bonds	H-bond acceptors	H-bond donors	TPSA	XLOG P3	Lipinski # violations	ESOL Class	Silicos-IT class
1	400.51	0.71	4	5	1	80.67	3.56	0	Moderately soluble	Soluble
2	472.57	0.7	7	7	1	106.97	3.77	0	Moderately soluble	Soluble
3	486.6	0.71	9	7	1	106.97	4.34	0	Moderately soluble	Moderately soluble
4	474.54	0.69	7	8	3	138.2	2.16	0	Soluble	Soluble
5	402.48	0.7	4	6	2	100.9	2.4	0	Soluble	Soluble
19	402.48	0.7	4	6	2	100.9	2.4	0	Soluble	Soluble

Table 3: Toxicity prediction for compounds 1-5 and 19

Compounds	1	2	3	4	5	19
Carcinogenicity (binary)	0.9143	0.9143	0.9143	0.9286	0.9429	0.9429
Eye corrosion	0.9949	0.9933	0.9933	0.9940	0.9940	0.9940
Eye irritation	0.9610	0.9444	0.9517	0.9534	0.9708	0.9708
Ames mutagenesis	0.9100	0.8500	0.9300	0.8200	0.9200	0.9200

4. CONCLUSION

Dry eyes disease affects millions of people around the world leading to ocular pains, blurry vision, and dryness, itchy and burning sensation, inflammation, and so on. This leads to an urgent need for the development of treatments with higher efficacy and lesser side effects. Here, we have tried to do the same. This study showed the presence of compounds having more efficacy than the previously available compounds. 152 compounds were tested with molecular docking and among them, 18 compounds including Deprodone propionate, Methylprednisolone aceponate, Prednisolone valerate acetate, Methylprednisolone hemisuccinate, and Pred forte showed a better score than Prednisolone acetate. Therefore, this study acts as a basis for introducing better compounds that could serve as an efficient anti-inflammatory agent by inhibiting the glucocorticoid receptor and having a high binding affinity. These

compounds can be seen as potential treatment options for dry eyes. To validate this study further, clinical studies need to be performed. Also, more compounds and their derivatives need to be screened and investigated from different databases. This study could open doors for the discovery and eventual use of efficacious and less toxic compounds that can inhibit this target protein and serve as a treatment for dry eye syndrome.

Declarations

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Financial and non-financial Interests

The authors have no relevant financial or non-financial interests to disclose.

Conflict of Interest

The authors have no conflicts of interest to declare that are relevant to the content of this article.

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