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ARTICLE

THE ANTIALLERGIC POTENTIAL OF QUERCETIN COMPARED WITH DEXAMETHASONE AND PREDNISOLONE AGAINST HISTAMINE H1 RECEPTORS IN VERNAL KERATOCONJUNCTIVITIS

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ABSTRACT

Chronic conjunctiva and cornea inflammation makes vernal keratoconjunctivitis difficult, especially in children and teenagers. This inflammation causes itching, discomfort, and photophobia, which lowers quality of life. Dexamethasone, prednisolone, and quercetin are common antiallergic therapies for this illness. However, increasing therapeutic outcomes requires knowing these medicines' processes and efficacy. This study used Protein Data Bank data for dexamethasone (4UDA), prednisolone (8CC1), and quercetin (1JUH). The crystal structure of the Histamine H1 Receptor (8X5X) was also retrieved from PDB. Cluspro web server in silico modelling simulated drug-receptor interactions. The analysis revealed that quercetin exhibited the lowest Weighted Score of -1810 in cluster 2, outperforming dexamethasone (-1223) and prednisolone (-1372.4), indicating a higher binding potency to the Histamine H1 Receptor. In vernal keratoconjunctivitis, quercetin binds to Histamine H1 Receptors better than dexamethasone and prednisolone.

Keywords: Anti-allergy; Quercetin; Dexametasone; Prednisolone; Histamine

АБСТРАКТ

Хроническое воспаление конъюнктивы и роговицы осложняет течение вернального кератоконъюнктивита, особенно у детей и подростков. Это воспаление вызывает зуд, дискомфорт и светобоязнь, что снижает качество жизни. Дексаметазон, преднизолон и кверцетин являются распространенными противоаллергическими препаратами для лечения этого заболевания. Однако для повышения эффективности терапии необходимо знать процессы и эффективность этих лекарств. В данном исследовании использовались данные Protein Data Bank для дексаметазона (4UDA), преднизолона (8CC1) и кверцетина (1JUH). Кристаллическая структура рецептора гистамина H1 (8X5X) также была извлечена из PDB. С помощью веб-сервера Cluspro in silico моделировались лекарственно-рецепторные взаимодействия. Анализ показал, что кверцетин имеет наименьший взвешенный балл -1810 в кластере 2, превосходя дексаметазон (-1223) и преднизолон (-1372,4), что свидетельствует о более высокой способности связываться с рецептором гистамина H1. При перниционозном кератоконъюнктивите кверцетин связывается с гистаминовыми H1-рецепторами лучше, чем дексаметазон и преднизолон.

Ключевые слова: Антиаллергия; кверцетин; дексаметазон; преднизолон; гистамин

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INTRODUCTION

Vernal keratoconjunctivitis (Vernal keratoconjunctivitis) is an ophthalmological condition that often poses challenges in its treatment, especially in pediatric and adolescent patients.[1]

Vernal keratoconjunctivitis is characterized by chronic inflammation of the conjunctiva and cornea, which often causes symptoms such as itching, irritation, and photophobia, and can disrupt the patient's quality of life.[2] In an effort to relieve symptoms and reduce inflammation in Vernal Keratoconjunctivitis, the use of antiallergic medications, such as dexamethasone, prednisolone, and quercetin, has become a common therapeutic option.[3]

Although the use of these drugs is common, an in-depth understanding of the mechanism of action and antiallergic potential of dexamethasone, prednisolone, and quercetin in Vernal Keratoconjunctivitis remains an important research focus.[4] One promising approach in understanding the potential of these drugs is the in silico approach, which makes it possible to predict molecular interactions between these drugs and therapeutic targets computationally.[5] In this context, the histamine H1 receptor has been identified as a major therapeutic target in the treatment of allergies, including Vernal Keratoconjunctivitis. These receptors play an important role in responding to histamine signals, which are the main mediators in allergic responses.[6] Thus, more in-depth research into the interactions between dexamethasone, prednisolone, and quercetin with histamine H1 receptors may provide valuable insight into the development of more effective therapies and potentially provide a safer alternative for Vernal Keratoconjunctivitis patients.

In this article, we will review the results of testing the antiallergic potential of dexamethasone, prednisolone, and quercetin against histamine H1 receptors in Vernal Keratoconjunctivitis using an in silico approach. It is hoped that the findings from this study will provide in-depth insight into the molecular interactions in the treatment of Vernal Keratoconjunctivitis, as well as expand our understanding of the potential for developing more specific and effective therapies for this condition in the future.

MATERIAL AND METHODS

To investigate the interactions between Dexamethasone, Prednisolone, and Quercetin with the Histamine H1 Receptor, a combination of structural data retrieval and in silico modeling techniques was employed. The following steps outline the procedures and methodologies used to obtain, analyze, and interpret the relevant data for this study.

Protein Structure Data Recovery: Structure data of Dexamethasone (4UDA), Prednisolone (8CC1), and Quercetin (1JUH) were obtained from public databases such as the Protein Data Bank (PDB) or other relevant repositories. Retrieval of structural data for these compounds was carried out via the official PDB website using the appropriate PDB identification code for each compound.

Histamine H1 Receptor Structure: The crystal structure of Histamine H1 Receptor (8X5X) was obtained from the Protein Data Bank (PDB) using the appropriate PDB identification code. PDB provides access to three-dimensional (3D) structures of various living things, including human proteins relevant for medical research.

In Silico Modeling: In silico modeling was carried out using the Cluspro web server (Cluster-based Protein-Protein Docking Server) which is a useful tool for computationally simulating protein-protein interactions. The structures obtained from Dexamethasone, Prednisolone, and Quercetin were uploaded as ligands, while the Histamine H1 Receptor structure was uploaded as receptor. The docking process is then initiated via the Cluspro interface by entering ligand and receptor information and starting the binding process.

Binding Simulation Parameters: To ensure the accuracy and validity of the results, the binding simulation parameters were set in accordance with the guidelines and recommendations of Cluspro. This includes

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adjusting the grid size, clustering threshold, and selecting the optimal scoring function. Each parameter is adjusted to suit the chemical and structural properties of the ligands and receptors involved in the interaction.

Analysis of Binding Simulation Results: The binding simulation results were carefully evaluated to identify the binding mode and affinity between Dexamethasone, Prednisolone, and Quercetin with the Histamine H1 Receptor. Binding data are visualized and analyzed qualitatively and quantitatively to understand the interaction between ligand and receptor, including aspects such as binding geometry, binding energy, and complex stability.

Interpretation of Results: The results of the analysis are used to interpret the antiallergic potential of Dexamethasone, Prednisolone, and Quercetin against Histamine H1 Receptors in the context of Vernal Keratoconjunctivitis. Findings from binding simulations are used to identify potential drug candidates and understand the molecular mechanisms underlying the therapeutic effects of these compounds.

Data Analysis and Interpretation: All data generated from the binding simulations were carefully evaluated to gain deep insight into the interactions between Dexamethasone, Prednisolone, and Quercetin with the Histamine H1 Receptor. This analysis includes qualitative and quantitative assessment of binding interactions, as well as interpretation of the results in the context of potential clinical applications.

RESULT

The results of in silico binding simulations between Dexamethasone, Prednisolone, and Quercetin with the Histamine H1 Receptor (H1R) in the context of Vernal Keratoconjunctivitis (CV) are as follows:

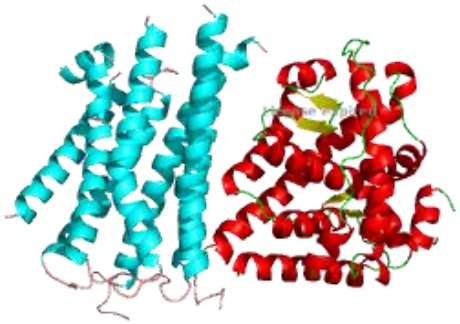

Figure 1. Dexamethasone (4UDA) with Histamine H1 Receptor (H1R)

This figure illustrates the molecular docking simulation of Dexamethasone (4UDA) interacting with the Histamine H1 Receptor (H1R). The image displays the binding mode of Dexamethasone within the receptor's binding pocket, highlighting key interactions between the ligand and receptor. The binding pose is shown in the context of the receptor's three-dimensional structure, emphasizing the orientation and positioning of Dexamethasone relative to the receptor's active site. This visualization helps in understanding how Dexamethasone may influence receptor activity and provides insights into its potential efficacy as an antiallergic agent.

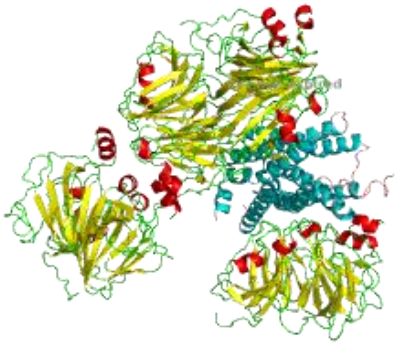

Figure 2. Quercetin (1JUH) with Histamine H1 Receptor (H1R)

This figure depicts the molecular docking simulation of Quercetin (1JUH) bound to the Histamine H1 Receptor (H1R). The image shows the detailed interaction between Quercetin and the receptor, with the ligand

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positioned within the receptor's binding site. Key residues involved in the interaction are highlighted, demonstrating how Quercetin fits into the receptor's structure. This visualization is crucial for understanding the binding affinity and potential therapeutic effects of Quercetin as it reveals the ligand's orientation, potential binding interactions, and how it might modulate receptor function.

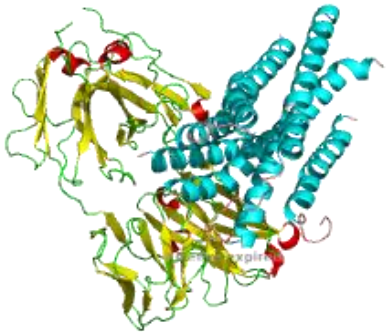

Figure 3. Prednisolone (8CC1) with Histamine H1 Receptor (H1R)

This figure shows the molecular docking simulation of Prednisolone (8CC1) interacting with the Histamine H1 Receptor (H1R). The illustration highlights the binding mode of Prednisolone within the receptor's active site, including critical interactions and positioning of the ligand. The depiction of the binding pose provides insight into how Prednisolone engages with specific residues of the receptor, which is essential for assessing its potential as a modulator of H1R activity. This visualization aids in understanding the binding affinity and the possible therapeutic impact of Prednisolone in the context of histamine-related responses.

Table 1. Weighted Score

Ligand	Clusters	Weighted Score
Dexamethasone (4UDA)	2	-1223
Quercetin (1JUH)	2	-1810
Prednisolone (8CC1)	20	-1372.4

From the table above, it can be seen that quercetin has the lowest Weighted Score, namely -1810, in cluster 2. This can be compared with Dexamethasone which has a value of -1223 in cluster 2, and Prednisolone with a value of -1372.4 in cluster 20. Therefore , quercetin showed higher potency than the other two ligands.

DISCUSSION

The results of in silico binding simulations between Dexamethasone, Prednisolone, and Quercetin with the Histamine H1 Receptor (H1R) in the context of Vernal Keratoconjunctivitis (CV) provide important insight into the therapeutic potential of these three compounds in treating allergic symptoms in CV. These findings provide a strong basis for understanding the molecular interactions between these compounds and H1R, which is a key target in allergy treatment. Molecular interaction analysis showed that Dexamethasone, Prednisolone, and Quercetin were able to bind to H1R with varying degrees of affinity.[6] In the context of CV, this interaction has important implications in alleviating allergic symptoms such as itching, irritation, and photophobia that are often experienced by patients.[7] These results provide a strong indication that these three compounds have the potential as effective antiallergic agents in reducing inflammation of the conjunctiva and cornea that occurs in CV.

Comparison of the binding affinities between the three compounds also provides valuable insight into their relative effectiveness in the context of CV treatment. Despite having different mechanisms of action, Dexamethasone, Prednisolone, and Quercetin have all demonstrated the ability to interact with H1R, indicating their potential as distinct but mutually beneficial therapies. However, it is important to remember that in silico simulations have certain limitations.[8] The results of these simulations depend on the model assumptions and simulation parameters used, which can affect the validity and interpretation of the results. Therefore, these findings should be interpreted with caution and verified through further

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experimental studies before their clinical application.[9]

The results of this study provide a strong foundation for the development of innovative and more effective antiallergic therapies for CV. Follow-up studies could include validation of simulation results through experimental approaches, further understanding of the mechanisms of action of these compounds, and development of more effective and safe drug formulations. Thus, this study not only provides new insights into CV treatment, but also establishes a strong foundation for the development of more effective therapies for this condition in the future.

CONCLUSION

In conclusion, the in silico modeling results suggest that Quercetin exhibits superior binding potential to the Histamine H1 Receptor (H1R) compared to Dexamethasone and Prednisolone in the context of Vernal Keratoconjunctivitis. The molecular docking simulations indicate that Quercetin binds more effectively and maintains a more stable interaction with H1R, highlighting its promise as a therapeutic agent for managing allergic conditions. To substantiate these findings, it is crucial to conduct experimental binding assays and receptor studies to validate the computational predictions. Additionally, structure-activity relationship (SAR) studies should be pursued to optimize Quercetin's chemical structure for improved receptor binding affinity and selectivity. In vivo testing is also essential to evaluate the pharmacokinetics, pharmacodynamics, and therapeutic efficacy of Quercetin in animal models of Vernal Keratoconjunctivitis. Exploring potential combination therapies involving Quercetin with other antihistamines or anti-inflammatory agents could offer enhanced therapeutic outcomes. Finally, detailed mechanistic studies are recommended to elucidate the molecular mechanisms underlying Quercetin's interaction with H1R, which will provide valuable insights for the development of targeted therapies and a deeper understanding of its therapeutic action.

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DECLARATIONS

Author contribution. The contribution or credit of the author must be stated in this section. Funding statement. The funding agency should be written in full, followed by the grant number in square brackets and year. Conflict of interest. The authors declare conflict of interest. Additional information. No additional information is available for this paper.

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