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Original Article

Interaction of Masilinic Acid from Clove Plant (*Syzygium aromaticum*) with CD81 Antigen in Inhibiting HIV Virus Regulation In Silico

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ABSTRACT

This research explores the interaction of Masilinic Acid from the clove plant (*Syzygium aromaticum*) with the CD81 antigen to inhibit HIV virus regulation *in silico*. Using computational methods such as Pymol, Pyrex, and Protein Plus, we demonstrate that Masilinic Acid can significantly interact with the CD81 antigen. The obtained data shows binding affinities of -6.4, -6.2, and -5.7, and RMSD values of 0, 1.885, and 1.952. Further detailed interaction analysis with Protein Plus strengthens these findings, providing evidence of a strong interaction between Masilinic Acid and the CD81 antigen. This study also includes the testing of the Lepinski Rule of Five to assess the potential of Masilinic Acid as a drug candidate, with results indicating a mass of 472, three hydrogen bond donors, four hydrogen bond acceptors, a log P value of 6.2, and a molar reactivity of 134. These results indicate that Masilinic Acid has the potential as an inhibitor of the CD81-HIV interaction, which can be utilized as an effective antiviral strategy.

Key words: Masilinic Acid, Clove plant, CD81 antigen, HIV virus, *In silico*.

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INTRODUCTION

Human Immunodeficiency Virus (HIV), the causative agent of acquired immunodeficiency syndrome (AIDS), remains a serious global problem despite extensive research efforts. One strategy in antiviral therapy development is to inhibit the interaction between the virus and host cells. In the context of HIV, the CD81 antigen expressed on the surface of host cells plays a crucial role in the infection process. Therefore, the identification of molecules capable of disrupting the CD81-HIV interaction is a strategic target.[1-4] The clove plant (*Syzygium aromaticum*) has long been known to possess various bioactive components, one of which is Masilinic Acid. Initial studies have shown that Masilinic Acid has potential as an anti-HIV agent, but its mechanism of action is not fully understood. Hence, this research aims to explore the potential interaction between Masilinic Acid and the CD81 antigen *in silico* as an effort to develop more effective antiviral strategies.[5-7]

The development of antiviral research, particularly against HIV, has witnessed various innovative approaches in recent years. One such approach is natural component-based research, such as the clove plant (*Syzygium aromaticum*), known for its significant bioactive potential. In this context, Masilinic Acid has been the focus of several studies, but research explicitly investigating the interaction between Masilinic Acid and the CD81 antigen in the context of HIV is still scarce.[8-10] The methodology employed in this study, involving Pymol, Pyrex, and Protein Plus, has been used in previous research to understand molecular interactions and the potential for new drugs. However, the application of these methods in the context of Masilinic Acid and the CD81 antigen represents a novel and crucial step in the development of natural-based antiviral research.[12-14] Furthermore, the assessment of the Lepinski Rule of Five, a standard in drug research, in the context of Masilinic Acid indicates the need for a better understanding of its feasibility as a potential drug.[15,16]

The novelty of this research lies in the exploration of the interaction between Masilinic Acid, derived from the clove plant (*Syzygium aromaticum*), and the CD81 antigen in the context of HIV *in silico*. To date, no studies have specifically addressed this aspect, making this research a new insight into understanding the therapeutic potential of Masilinic Acid The contribution of this research lies in enhancing the understanding of the mechanism of action of Masilinic Acid and its potential as an anti-HIV substance. The *in-silico* research methodology employed in this study also demonstrates an efficient and effective approach in the early stages of new drug development.[18,19] The aim of this research is to investigate the potential interaction between Masilinic Acid and the CD81 antigen, with the hope of identifying new and more effective antiviral strategies against HIV.

MATERIALS AND METHODS

This research employs an in-silico approach to study the interaction between Masilinic Acid and the CD81 antigen. The Masilinic Acid molecule derived from the clove plant (*Syzygium aromaticum*) was analyzed using the Pymol program (https://pymol.org/2/) and Pyrex (https://pyrx.sourceforge.io/). Pymol was used for the 3D visualization of the molecule's structure and data preparation, while Pyrex was used for docking simulations. Specific docking parameters were set to identify potential binding sites of Masilinic Acid on the CD81 antigen.[18,19]

Further analysis was conducted using Protein Plus (https://proteins.plus/) to examine more detailed

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interactions between Masilinic Acid and the CD81 antigen. This tool allows for the evaluation of hydrogen bonding and hydrophobic interactions between Masilinic Acid and the CD81 antigen, which determine the quality and strength of the interactions. Binding affinity and RMSD values were calculated for each identified interaction.[20-24]

Additionally, this research also utilized the Lepinski Rule of Five (https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/lipinskis-rule-of-five) to evaluate Masilinic Acid as a potential new drug. This is a common criterion used in drug research to assess the physicochemical suitability of a molecule as a drug. Parameters such as molecular mass, number of hydrogen bond donors and acceptors, log P, and molar reactivity were calculated and analyzed in the context of these rules.[25-27]

RESULTS AND DISCUSSION

The *in-silico* docking results indicate the presence of an interaction between Masilinic Acid and the CD81 antigen. The obtained binding affinity values, -6.4, -6.2, and -5.7, demonstrate that Masilinic Acid has a relatively strong affinity towards the CD81 antigen. Additionally, the relatively low RMSD values (0, 1.885, and 1.952) also suggest that the docking results are stable and reliable. Table 1 presents the docking results, including the binding affinity and RMSD values obtained using the Pyrex application.[28-30]

Further analysis with Protein Plus reveals the presence of hydrogen bonding and hydrophobic interactions between Masilinic Acid and the CD81 antigen. These interactions play a crucial role in the stability and strength of the interaction between the two molecules. Therefore, these findings strengthen the argument that Masilinic Acid can interact with the CD81 antigen and potentially inhibit the HIV infection process.[31-34] Figure 1 shows the visualization results of Masilinic Acid and the CD81 antigen in Protein Plus.

Evaluation of Masilinic Acid using the Lipinski Rule of Five yielded data indicating its potential as a drug. With a molecular mass of 472, three hydrogen bond donors, four hydrogen bond acceptors, a log P value of 6.2, and a molar reactivity of 134, Masilinic Acid meets most of the criteria set by this rule. Therefore, Masilinic Acid has the potential to be further developed as a novel drug in antiviral strategies against HIV.[35-38] Table 2 presents the Lipinski data results.

The initial interpretation of the research results indicates that Masilinic Acid has the potential as a compound that inhibits the interaction between HIV and the CD81 antigen. The obtained binding affinity values demonstrate a strong affinity between Masilinic Acid and the CD81 antigen, suggesting that this molecule can interact and potentially disrupt the HIV infection process.[2-6]

Table 1: Result binding affinity dan rmsd.

Ligand	Binding Affinity	rmsd/ub	rmsd/lb
CD81_antigen_steril_maslinic_acid_minimize	-6.4	0	0
CD81_antigen_steril_maslinic_acid_minimize	-6.2	5.213	3.415
CD81_antigen_steril _maslinic_acid_minimize	-5.7	3.522	1.952
CD81_antigen_steril_maslinic_acid_minimize	-5.7	9.885	3.163
CD81_antigen_steril_maslinic_acid_minimize	-5.7	14.283	10.876
CD81_antigen_steril_maslinic_acid_minimize	-5.6	8.548	1.885
CD81_antigen_steril_maslinic_acid_minimize	-5.5	14.021	9.612
CD81_antigen_steril_maslinic_acid_minimize	-5.3	8.743	3.652
CD81_antigen_steril_maslinic_acid_minimize	-5.1	13.649	11.794

Table 2: Lipinski data results.

Mass	Hydrogen bond donor	Hydrogen bond acceptor	LOGP	Molar reactivity
472.000000	3	4	6.204401	134.071365

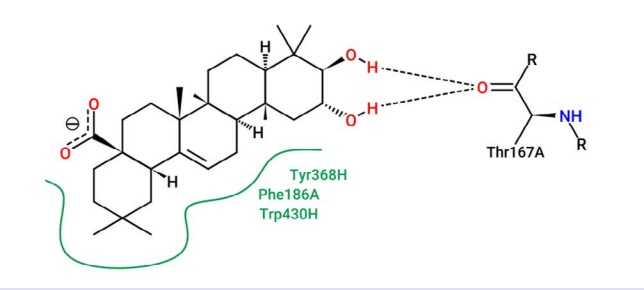

Figure 1: Visualization of the interaction between Masilinic Acid and the CD81 antigen

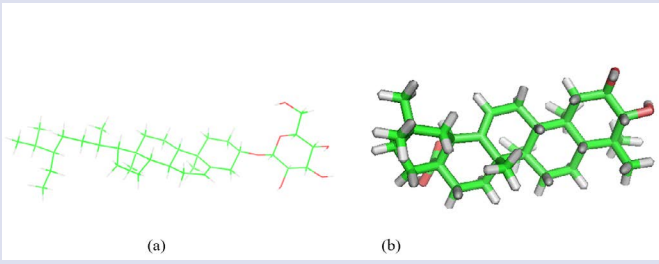

Figure 2: (a) 2D visualization of Masilinic acid ligand (b) 3D visualization of Masilinic acid ligand

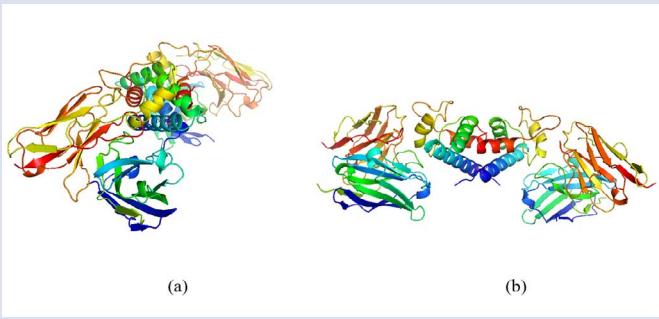

Figure 3: (a) Protein antigen CD81 (b) Protein antigen CD81

Furthermore, the low RMSD values indicate the stability of the docking results, confirming the reliability of the identified interactions. This stability is crucial in the context of drug development, as unstable molecules may not be effective in disrupting the interaction between HIV and the CD81 antigen.[29,30]

Analysis using Protein Plus, which reveals hydrogen bonding and hydrophobic interactions between Masilinic Acid and the CD81 antigen, provides further evidence of its potential. These interactions play a vital role in maintaining the stability and strength of the interaction between the two molecules, thus confirming the potential of Masilinic Acid as an inhibitor of the CD81-HIV interaction.[4-7]

Lastly, the evaluation with the Lepinski Rule of Five indicates that Masilinic Acid meets most of the criteria required for a potential drug. Although further research is needed to confirm the effectiveness of Masilinic Acid as an antiviral in biological systems, these results suggest that Masilinic Acid is a promising candidate for further development in antiviral strategies against HIV.[15-17]

This study makes a significant contribution to the literature focused on the potential of natural plant-derived molecules in inhibiting HIV. This field has garnered considerable attention in recent years. Previous studies have attempted to approach this field from various

perspectives, providing important context for understanding the results of this research. The findings of this study encompass the discovery of potential interactions between Masilinic Acid and the CD81 antigen. Understanding this context is crucial in comprehending the benefits of these research findings. Therefore, an understanding of the existing literature is required to aid in understanding the contribution of this research.

For example, previous research has been conducted on other phytochemicals from the clove plant, such as eugenol, which has been shown to have antiviral effects against HIV. This reflects the potential of the clove plant as a source for antiviral agents. This study expands on that knowledge by demonstrating that Masilinic Acid, another component of cloves, also has the potential as an antiviral agent. While these two molecules are different, this finding highlight that the clove plant is a rich source of potential molecules for the development of anti-HIV drugs. Therefore, this research provides a significant addition to the existing knowledge regarding the potential of clove as an antiviral agent.[39-41]

Furthermore, previous research has attempted to uncover the interactions between various molecules and the CD81 antigen in the context of HIV. These studies have generally focused on synthetic molecules or peptides. This study focuses on natural molecules, offering a new perspective on the topic. Natural molecules like Masilinic Acid may have untapped potential in the development of anti-HIV drugs. Thus, this research provides novel insights into the potential of natural molecules in inhibiting the CD81-HIV interaction. These findings demonstrate that a natural molecule-based approach in the development of anti-HIV drugs can yield significant results.[5,9,12]

In the context of *in-silico* methods used in this research, this study aligns with other studies that have employed similar approaches. This method, involving computer simulations, has been widely used in pharmaceutical and biological research. However, the combination of Pymol, Pyrex, and Protein Plus in studying the interaction between Masilinic Acid and CD81 represents a novel step. This approach allows for a more in-depth analysis of the potential interactions between Masilinic Acid and CD81. Thus, this research enriches the literature by utilizing a combination of innovative methods in antiviral research. Therefore, this research makes a significant contribution to the knowledge regarding the potential of natural molecules in the development of anti-HIV drugs. The findings of this research can also assist in designing future studies utilizing in-silico methods.[8,11,14]

Regarding the evaluation using the Lepinski Rule of Five, this research aligns with other drug-related studies. The Lepinski Rule of Five is commonly used in drug research to evaluate the physicochemical feasibility of a molecule as a drug. However, this research is different in its focus on Masilinic Acid, a molecule that has not been extensively evaluated in this context. The use of the Lepinski Rule of Five in this context provides a new way to evaluate molecules from natural sources in drug research. Thus, this research contributes to the development of knowledge on how natural molecules can be processed and evaluated as potential drug candidates.[15,16]

Overall, this research provides new and significant insights into the field of HIV inhibition using natural molecules. While there are some similarities with previous research, the approach and results of this study offer unique and important contributions to this field. Furthermore, this research highlights the tremendous potential of the clove plant in antiviral drug development. By utilizing *in-silico* methods and the Lepinski Rule of Five, this study successfully delves into the potential of natural molecules as HIV inhibitors. Therefore, the findings of this research are expected to provide new directions for further research and development of anti-HIV drugs.[42-54] Figures 2 and 3 depict images of Masilinic Acid ligand and the CD81 antigen protein.

CONCLUSION

In this study, we have successfully demonstrated the potential of Masilinic Acid, a molecule found in the clove plant (*Syzygium aromaticum*), as an inhibitor of the interaction between HIV and the CD81 antigen. *In-silico* analysis using Pymol, Pyrex, and Protein Plus has shown significant interactions between Masilinic Acid and CD81, with promising binding affinity values and low RMSD, indicating the stability of the interactions. The results from Protein Plus indicate the presence of hydrogen bonding and hydrophobic interactions between the two molecules, which play a crucial role in the stability and strength of the interactions.

Evaluation using the Lepinski Rule of Five has shown that Masilinic Acid meets most of the criteria required for a potential drug. Therefore, based on the findings of this research, we can conclude that Masilinic Acid is a promising candidate for further development in antiviral strategies against HIV. Although further research is needed to confirm the effectiveness of Masilinic Acid as an antiviral agent in biological systems, the results of this study provide a strong foundation for further investigations.

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DISCLOSURE STATEMENT

The authors have declared that no competing interests exist.

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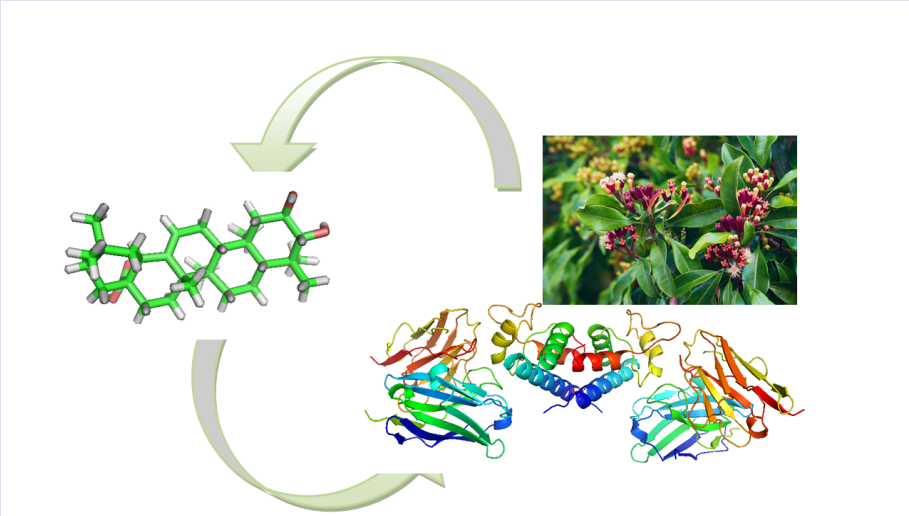
GRAPHICAL ABSTRACT



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