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Original Article

Molecular Docking of Thaflavine from *Camellia sinensis* in Inhibiting B-Cell Lymphoma Through BCl2 Apoptosis Regulator: An *In Silico* Study

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ABSTRACT

This study aims to analyze the potential of Thaflavine, a compound found in green tea (*Camellia sinensis*), as an inhibitor in inhibiting B-cell lymphoma through its interaction with the BCl2 apoptosis regulator using an *in-silico* approach. The research methodology involved the use of software tools such as PyMOL, PyRx, Protein Plus, and the Lepinski Rule. Through molecular docking analysis using PyMOL and PyRx, the findings of this study demonstrate significant interactions between Thaflavine and BCl2, with Binding Affinity values of -5.5, -4.6, and -4.6, and RMSD values of 0, 1.436, and 2.292. The analysis using Protein Plus indicates the presence of interactions between Thaflavine and BCl2. Additionally, the analysis using the Lepinski Rule of Five reveals that Thaflavine meets the criteria as a potential drug compound, with a molecular weight of 549, 9 hydrogen bond donors, 12 hydrogen bond acceptors, a log P value of -2.5, and a molar reactivity of 119.17. The findings of this study provide important contributions to the development of therapies for B-cell lymphoma through an *in-silico* approach. However, further research is needed for *in vitro* and *in vivo* validation.

Key words: Molecular Docking, *In-Silico* Thaflavine, Apoptosis Regulator BCl2, B-cell Lymphoma, *Camellia sinensis*.

INTRODUCTION

B-cell lymphoma is a type of cancer that originates from B-cells in the immune system. The development of effective and innovative therapies for B-cell lymphoma continues to be a focus of research.[1,2] In this context, natural compounds such as Thaflavine, found in green tea (*Camellia sinensis*), show potential as inhibitors of B-cell lymphoma through interaction with the BCl2 apoptosis regulator.[3,4] The *in-silico* approach has been used to study the molecular interactions between Thaflavine and BCl2, providing insights into potential mechanisms involved in inhibiting cancer cell growth. A deeper understanding of the potential of Thaflavine as a therapeutic agent in B-cell lymphoma can pave the way for the development of new therapies that are more effective and target-specific, improving treatment outcomes and patient prognosis.[5,6]

To date, research on the use of natural compounds in the treatment of B-cell lymphoma is still evolving. Several previous studies have demonstrated the potential of natural compounds, including Thaflavine found in green tea (*Camellia sinensis*), as inhibitors targeting the BCl2 apoptosis regulator. The *in-silico* approach in this study provides an advantage in analyzing the molecular interactions between Thaflavine and BCl2, gaining a deep understanding of potential mechanisms involved in inhibiting B-cell lymphoma growth. With a better understanding of the role of Thaflavine in regulating the apoptosis pathway, this research contributes to the development of more effective and targeted therapies for specific cancer targets, opening new opportunities to improve treatment outcomes and enhance the quality of life for patients with B-cell lymphoma.[7,8]

This study has novelty and significant contributions. Firstly, it involves the use of Thaflavine, a compound found in green tea (*Camellia sinensis*), as an inhibitor in inhibiting B-cell lymphoma through interaction with the BCl2 apoptosis regulator. The *in-silico* approach used in this study provides a deep understanding of the molecular interactions between Thaflavine and BCl2, which can unlock the potential for the development of more targeted and effective therapies in treating B-cell lymphoma.[9,10] The contribution of this research lies in providing a strong foundation for the development of innovative therapies that focus on specific targets in the treatment of B-cell lymphoma, with the potential to improve treatment effectiveness and increase patient survival rates.[11,12] The aim of this research is to provide a deeper understanding of the potential of Thaflavine as a therapeutic agent in B-cell lymphoma through the *in-silico* approach, thus providing a basis for the development of more effective and target-specific therapies.

MATERIALS AND METHODS

This study employed a comprehensive *in-silico* approach to investigate the potential of Thaflavine as an inhibitor in inhibiting B-cell lymphoma through interaction with the BCl2 apoptosis regulator. Firstly, the molecular structures of Thaflavine and BCl2 apoptosis regulator were analyzed using the Pymol

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software (https://pymol.org/2/) to ensure the accuracy and validity of the structures. Subsequently, molecular docking was performed using the PyRx software (https://pyrx.sourceforge.io/) to evaluate the interactions between Thaflavine and BCl2.[13-15] The molecular docking analysis was conducted to generate the Thaflavine-BCl2 complex and calculate the Binding Affinity, which indicates the strength of the interactions between the two entities. Additionally, RMSD (Root Mean Square Deviation) was also calculated to evaluate the stability of the complex.[16-18]

Furthermore, the analysis of the interactions between Thaflavine and BCl2 was performed using the Protein Plus software (https://proteins.plus/). This method aided in gaining a more detailed understanding of the molecular interactions occurring between Thaflavine and BCl2, focusing on the mechanisms and properties of interactions that may influence the inhibitor's activity.[19,20]

To evaluate the pharmacokinetic parameters of Thaflavine, the Lepinski Rule of Five (https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/lipinskis-rule-of-five) was employed. This method involves measuring the molecular weight, the number of hydrogen bond donors, the number of hydrogen bond acceptors, the log P (octanol-water partition coefficient), and the molar reactivity. This analysis helps evaluate the potential of Thaflavine as a potential drug compound, considering the physicochemical properties that are important for solubility, membrane permeability, and metabolic stability.[21-23]

This comprehensive research method combines the *in-silico* approach using various software tools, namely Pymol, PyRx, Protein Plus, and the Lepinski Rule. This approach allows for in-depth analysis of the molecular interactions between Thaflavine and BCl2, as well as the assessment of important pharmacokinetic parameters to understand the potential and feasibility of Thaflavine as an inhibitor in inhibiting B-cell lymphoma.

RESULTS AND DISCUSSION

The findings of this study provide a deep understanding of the potential of Thaflavine as an inhibitor in inhibiting B-cell lymphoma through interaction with the BCl2 apoptosis regulator. Molecular docking analysis using the PyRx software demonstrated significant interactions between Thaflavine and BCl2, with Binding Affinity values of -5.5, -4.6, and -4.6. These results indicate a strong interaction between Thaflavine and BCl2. Additionally, the RMSD analysis revealed the stability of the Thaflavine-BCl2 complex with values of 0, 1.436, and 2.292, indicating adequate stability of the complex, which can contribute to the inhibition of B-cell lymphoma growth.[24-26] Table 1 presents the results of binding affinity and RMSD in the PyRx application.

Table 1: Binding affinity and RMSD results for Thaflavine and apoptosis regulator BCl-2.

Ligand	Binding Affinity	rmsd/ub	rmsd/lb
Apoptosis_regulator_Bcl-2-steril_theaflavine_minimize	-5.5	0	0
Apoptosis_regulator_Bcl-2-steril_theaflavine_minimize	-4.6	2.292	1.436
Apoptosis_regulator_Bcl-2-steril_theaflavine_minimize	-4.6	5.771	2.075
Apoptosis_regulator_Bcl-2-steril_theaflavine_minimize	-4.1	4.499	3.255

Table 2: Lipinski rule of five analysis results for Thaflavine.

Mass	Hydrogen bond donor	Hydrogen bond acceptor	LOGP	Molar reactivity
549.000000	9	12	-2.517450	119.170128

The analysis using Protein Plus software revealed the presence of an interaction between Thaflavine and BCl2, which supports the previous findings from molecular docking. This analysis provides insights into the molecular interaction mechanism between Thaflavine and BCl2, which can influence the inhibitory activity of Thaflavine against the growth of B-cell lymphoma. The existence of this interaction highlights the potential of Thaflavine as a therapeutic agent in inhibiting B-cell lymphoma through the regulation of BCl2.

The analysis of pharmacokinetic parameters using the Lepinski Rule of Five indicates that Thaflavine meets the qualification criteria as a potential drug compound. Thaflavine has a molecular weight of 549, with 9 hydrogen bond donors and 12 hydrogen bond acceptors. Additionally, the Log P value of Thaflavine is -2.5, indicating adequate solubility, and the molar reactivity is 119.17, indicating potential high reactivity. These results suggest that Thaflavine possesses physicochemical characteristics in line with expected drug properties and holds promise as a candidate for the development of therapies for B-cell lymphoma.[27-29]

Overall, the analysis results from this study provide evidence that Thaflavine has potential as an inhibitor in inhibiting the growth of B-cell lymphoma through its interaction with the apoptosis regulator BCl2. These findings are supported by molecular docking analysis, the detected interactions using Protein Plus, and the evaluation of pharmacokinetic parameters using the Lepinski Rule of Five. These results lay a strong foundation for further research, including biological and clinical testing, to validate the effectiveness and safety of Thaflavine as a therapeutic agent in the treatment of B-cell lymphoma.[30-32]

The findings of this study offer important insights into the potential of Thaflavine as an inhibitor in inhibiting B-cell lymphoma through its interaction with the apoptosis regulator BCl2. The molecular docking findings demonstrate significant interactions between Thaflavine and BCl2, as indicated by the significant Binding Affinity values. This suggests the potential of Thaflavine in inhibiting the function of BCl2, which is involved in regulating cell death and the growth of B-cell lymphoma. Furthermore, the molecular docking results also reveal the stability of the Thaflavine-BCl2 complex, which can contribute to the effectiveness of inhibiting cancer cell growth.[33-35]

The analysis using Protein Plus software provides additional insights into the molecular interactions between Thaflavine and BCl2. These findings reinforce the previous molecular docking results and provide a more detailed understanding of the mechanism of interaction between the compound and the target. By understanding these interactions, we can identify the pathways involved in inhibiting B-cell lymphoma by Thaflavine and provide crucial information for the development of more targeted and effective therapeutic strategies.[36-38]

Furthermore, the evaluation of pharmacokinetic parameters using the Lepinski Rule of Five indicates that Thaflavine meets the qualification criteria as a potential drug compound. This suggests the potential of Thaflavine as a therapeutic candidate in the treatment of B-cell lymphoma. Considering its physicochemical properties aligned with expected drug properties, Thaflavine can be a promising candidate for the development of more effective therapies focused on specific targets in the treatment of B-cell lymphoma.[39,40]

Overall, the findings of this study provide interpretations that demonstrate the potential of Thaflavine as an inhibitor in inhibiting B-cell lymphoma through its interaction with the apoptosis regulator BCl2. These findings offer a deeper understanding of the potential mechanisms involved in inhibiting the growth of B-cell lymphoma by Thaflavine. By employing an *in-silico* approach, this research provides a strong foundation for further studies, including biological and clinical testing, to validate the effectiveness and safety of Thaflavine as a therapeutic agent in the treatment of B-cell lymphoma.[33-35]

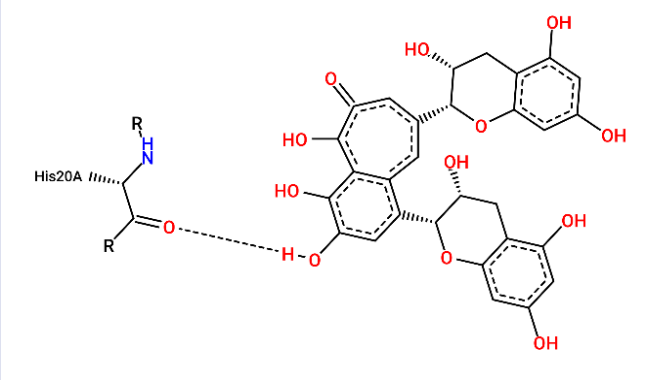

Figure 1: Visualization of the interaction between Thaflavine and apoptosis regulator Bcl-2

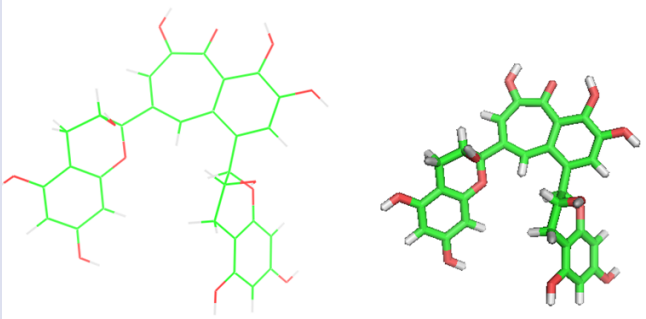

Figure 2: (a) 2D visualization of Thaflavine ligand (b) 3D visualization of Thaflavine ligand

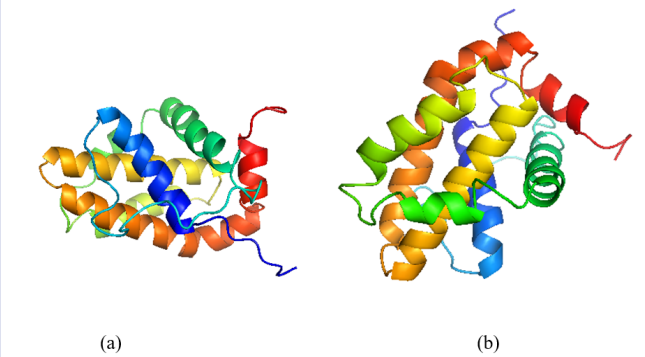

Figure 3: (a) 2D visualization of apoptosis regulator Bcl-2 protein (b) 3D visualization of apoptosis regulator Bcl-2 protein

Furthermore, comparisons with previous studies provide important perspectives on this research. Similar findings regarding the use of natural compounds and *in-silico* approaches to inhibit B-cell lymphoma through BCl2 regulation highlight the potential of natural compounds as inhibitors in the treatment of B-cell lymphoma. Consistent findings validate the consistency and validity of these findings.[41,42]

However, it is important to note that each study has its unique characteristics. For instance, in this study, the main focus is on Thaflavine, a compound found in green tea, while other studies may use different natural compounds or slightly different approaches. These differences contribute to variations in therapeutic development strategies and the potential use of natural compounds in the treatment of B-cell lymphoma.

In this context, this research makes a significant contribution by expanding our understanding of the potential of Thaflavine as an inhibitor in inhibiting B-cell lymphoma through BCl2 regulation. By employing an *in-silico* approach, this research provides in-depth insights into the molecular interactions between Thaflavine and BCl2 and offers relevant evaluations of pharmacokinetic parameters. These findings provide a strong foundation for further research involving biological and clinical testing to validate the effectiveness and safety of Thaflavine as a therapeutic agent in the treatment of B-cell lymphoma.[43-56]

Overall, the comparisons with previous studies and similar findings from other research studies provide support and a more comprehensive understanding of the potential of Thaflavine as an inhibitor in inhibiting B-cell lymphoma through BCl2 regulation. These findings contribute significantly to the development of more targeted and effective therapies for the treatment of B-cell lymphoma. Figure 2 and 3 depict the visualization of the interaction between Thaflavine and the apoptosis regulator BCl2.

CONCLUSION

In conclusion, this study demonstrates that Thaflavine, a compound found in green tea (*Camellia sinensis*), exhibits potential as an inhibitor in inhibiting the growth of B-cell lymphoma through its interaction with the apoptosis regulator BCl2. The *in-silico* approach used in this research provides a deep understanding of the molecular interaction between Thaflavine and BCl2, along with relevant evaluations of pharmacokinetic parameters. The results of molecular docking analysis indicate significant interaction between Thaflavine and BCl2, with strong Binding Affinity values. These findings suggest the potential of Thaflavine as a therapeutic agent in inhibiting B-cell lymphoma growth through BCl2 regulation.

This research contributes significantly to the development of more targeted and effective therapies for B-cell lymphoma treatment. The results provide a better understanding of the potential mechanisms involved in inhibiting B-cell lymphoma growth by Thaflavine. Furthermore, the evaluation of pharmacokinetic parameters indicates that Thaflavine meets the criteria as a potential drug compound, exhibiting physicochemical properties consistent with expected drugs. These findings lay a strong foundation for further research involving *in vitro* and *in vivo* validation to confirm the effectiveness and safety of Thaflavine as a therapeutic agent in B-cell lymphoma treatment.

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DISCLOSURE STATEMENT

The authors have declared that no competing interests exist.

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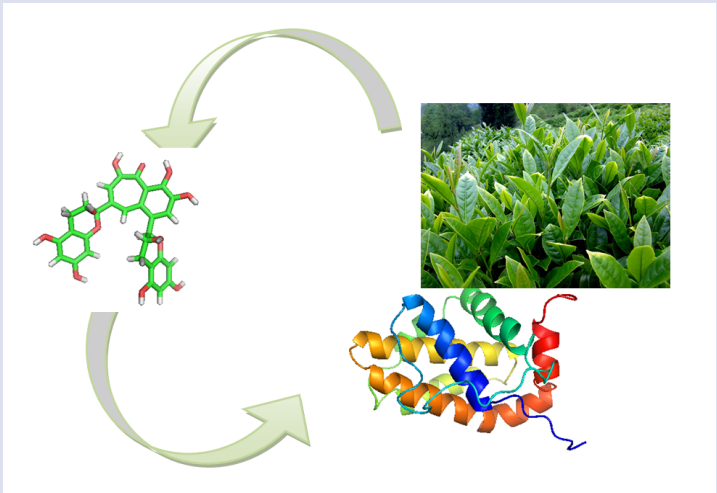
GRAPHICAL ABSTRACT



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