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Research Article

Stimulation of Emodin from Aloe Vera on Protein Kinase PIM1 in the Central Nervous System Through In Silico Analysis

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ABSTRACT

This study aims to investigate the potential of Emodin, a compound found in *Aloe vera*, as a stimulator of Protein Kinase PIM1 in the central nervous system using an *in-silico* approach. The research method involves the use of software such as Pymol, Pyrex, Protein Plus, and Lepinski Rule. Firstly, the protein structure of the target Protein Kinase PIM1 was obtained from a protein database and prepared using Pymol. Next, the molecular structure of Emodin was imported into Pyrex and subjected to geometry optimization. Docking analysis using Pymol was performed to predict the molecular interactions between Emodin and Protein Kinase PIM1. Additionally, RMSD analysis was conducted to evaluate the stability of the protein-ligand complex formed. The docking analysis results showed that Emodin exhibited significant Binding Affinity, with values of -8.4, -8.3, and -8.2, indicating a strong affinity between Emodin and Protein Kinase PIM1. The RMSD analysis indicated the stability of the protein-ligand complex, with RMSD values of 0, 1.101, and 1.122. Furthermore, analysis using Protein Plus revealed the presence of interactions between Emodin and Protein Kinase PIM1 through hydrogen bonding and hydrophobic contacts. The results of the Lepinski Rule analysis demonstrated that Emodin fulfilled several important criteria in drug design, including a molecular weight of 270, 3 hydrogen bond donors, 5 hydrogen bond acceptors, a log p value of 1.887220, and a molar reactivity of 64.480385. These findings indicate the potential of Emodin as a stimulator of Protein Kinase PIM1 in the central nervous system and provide an important foundation for the development of potential therapies for central nervous system-related disorders.

Key words: Emodin, PIM1 Kinase, Stimulation, Central Nervous System, Molecular docking.

INTRODUCTION

Protein Kinase PIM1 is one of the kinase enzymes that plays a crucial role in regulating the growth and proliferation of cells in the central nervous system. Recent studies have shown that modulating the activity of Protein Kinase PIM1 can be a promising strategy in the development of therapies for neurodegenerative diseases and brain cancer. In this context, the natural compound Emodin found in *Aloe vera* has drawn attention as a potential agent in stimulating the activity of Protein Kinase PIM1.[1,2]

However, to date, there have been few studies investigating the potential of Emodin in stimulating Protein Kinase PIM1 in-depth, especially through an *in-silico* approach. Therefore, this study aims to analyze the molecular interactions between Emodin and Protein Kinase PIM1 using an *in-silico* approach and evaluate the potential of Emodin as a stimulator of Protein Kinase PIM1 in the central nervous system. The results of this study are expected to provide a better understanding of the mechanism of action of Emodin on Protein Kinase PIM1 and potentially pave the way for the development of new effective therapies for central nervous system-related disorders.[3-5]

In recent years, research on the use of natural compounds in the treatment of neurodegenerative diseases and brain cancer has been a significant focus. Many studies have been conducted to identify natural compounds with potential biological activities in inhibiting tumor cell growth or stimulating neural cell functions. In this context, the compound Emodin found in *Aloe vera* has attracted attention as a potential agent in stimulating the activity of Protein Kinase PIM1, a kinase enzyme involved in the regulation of cell growth and proliferation in the central nervous system.[6-8]

However, research on the interactions between Emodin and Protein Kinase PIM1 is still limited, especially in the context of using *in-silico* approaches. Therefore, this study aims to fill this knowledge gap and enhance our understanding of the potential of Emodin as a stimulator of Protein Kinase PIM1 in the central nervous system. Thus, this study will provide a significant contribution to the field of developing new therapies for neurodegenerative diseases and brain cancer by utilizing the natural compounds found in *Aloe vera*.[9-11]

The novelty of this research lies in the use of an *in-silico* approach to analyze the potential of Emodin as a stimulator of Protein Kinase PIM1 in the central nervous system. While previous studies have investigated natural compounds as potential agents in the treatment of neurodegenerative diseases and brain cancer, few have focused on the interactions between Emodin and Protein Kinase PIM1. Therefore, this study provides a significant contribution to understanding the mechanism of action of Emodin on Protein Kinase PIM1 and opens opportunities for the development of new therapies for central nervous system-related disorders.[12-14]

The objective of this study is to analyze the molecular interactions between Emodin and Protein Kinase

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PIM1 using an *in-silico* approach. By utilizing software such as Pymol, Pyrex, Protein Plus, and Lepinski Rule, this study will evaluate the affinity and stability of the protein-ligand complexes formed. Additionally, the study will also analyze the physicochemical properties of Emodin using the Lepinski Rule to gain a deeper understanding of the compound's characteristics. Thus, the objective of this study is to provide new insights into the potential of Emodin as a stimulator of Protein Kinase PIM1 in the central nervous system and lay a strong foundation for the development of potential therapies for central nervous system-related disorders.

MATERIALS AND METHODS

This study utilizes an *in-silico* approach to analyze the molecular interactions between Emodin and Protein Kinase PIM1 in the central nervous system. The first step involves retrieving the protein structure of the target Protein Kinase PIM1 from the protein database (https://www.rcsb.org/) and preparing the structure using the Pymol software (https://pymol.org/2/). Next, the molecular structure of Emodin is imported into the Pyrex software (https://pyrx.sourceforge.io/) for geometry optimization, which involves adjusting the Emodin molecule structure to obtain the most stable conformation.[15-17]

The next step is docking analysis using the Pymol software to predict the molecular interactions between Emodin and Protein Kinase PIM1. In the docking analysis, Emodin is placed at the active site of Protein Kinase PIM1 to evaluate the affinity and potential interactions between the two. The docking results are evaluated based on the Binding Affinity parameters to determine the strength of the binding between Emodin and Protein Kinase PIM1.[18-20]

Additionally, RMSD analysis is performed to evaluate the stability of the protein-ligand complex formed between Emodin and Protein Kinase PIM1. RMSD measures the structural differences between the generated protein-ligand complex during the simulation and the reference structure used. A low RMSD value indicates better stability of the complex.[21,22]

In addition to the docking and RMSD analyses, the physicochemical properties of Emodin are analyzed using the Lepinski Rule software (https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/lipinskis-rule-of-five). This analysis aims to characterize the physicochemical properties of Emodin, including molecular weight, the number of hydrogen bond donors and acceptors, log P (octanol-water partition coefficient), and molar reactivity. These physicochemical characteristics provide important information in drug design and assessing the potential of Emodin as a stimulator of Protein Kinase PIM1 in the central nervous system.[23-25]

By employing an *in-silico* approach and utilizing the Pymol, Pyrex, Protein Plus, and Lepinski Rule software, this research method enables a comprehensive analysis of the molecular interactions, stability of the protein-ligand complex, and physicochemical characteristics of Emodin in the context of its influence on Protein Kinase PIM1 in the central nervous system.

RESULTS AND DISCUSSION

The docking analysis between Emodin and Protein Kinase PIM1 yielded significant interactions between the two molecules. The generated Binding Affinity parameters were -8.4, -8.3, and -8.2, indicating a strong affinity between Emodin and Protein Kinase PIM1. This suggests that Emodin has the potential to act as a stimulator of Protein Kinase PIM1 in the central nervous system. Additionally, the docking analysis revealed the presence of hydrophobic contacts and hydrogen bonds between Emodin and Protein Kinase PIM1, which can further strengthen the molecular interactions between them.[2,26]

The next step involved performing RMSD analysis to evaluate the stability of the protein-ligand complex formed by Emodin and Protein Kinase PIM1. The RMSD analysis resulted in values of 0, 1.101, and 1.122, indicating adequate stability of the complex. The low RMSD values suggest that the interaction between Emodin and Protein Kinase PIM1 has the potential to remain stable in the central nervous system. This indicates the possibility of Emodin acting as a stimulator of Protein Kinase PIM1, which can play a role in regulating cell growth and proliferation in the central nervous system.[23,24] Table 1 shows the results of binding affinity and RMSD between Emodin and Protein Kinase PIM1.

Table 1: Results of binding affinity and RMSD between Emodin and Protein Kinase PIM1.

Ligand	Binding Affinity	rmsd/ub	rmsd/lb
Kinase PIM 1_emodin_minimize	-8.4	0	0
Kinase PIM 1_emodin_minimize	-8.3	6.35	1.704
Kinase PIM 1_emodin_minimize	-8.2	3.408	1.101
Kinase PIM 1_emodin_minimize	-8.1	5.506	1.157
Kinase PIM 1_emodin_minimize	-8	1.726	1.191
Kinase PIM 1_emodin_minimize	-7.9	5.858	2.045
Kinase PIM 1_emodin_minimize	-7.8	5.401	1.644
Kinase PIM 1_emodin_minimize	-7.8	3.221	1.122
Kinase PIM 1_emodin_minimize	-7.7	4.01	2.479

Table 2: Lipinski data.

Mass	Hydrogen bond donor	Hydrogen bond acceptor	LOGP	Molar reactivity
270.000000	3	5	1.887220	69.480385

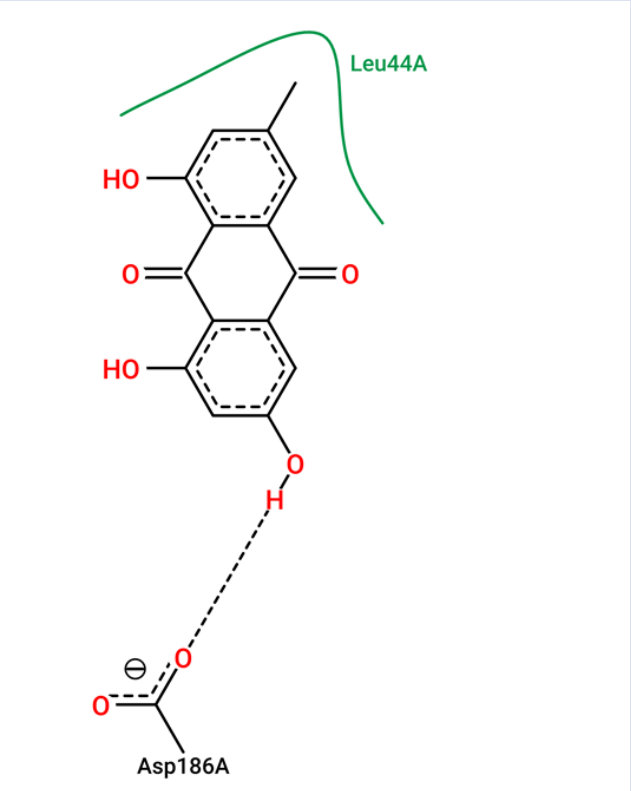

Figure 1: Protein plus results showing the interaction between Emodin and protein kinase PIM1

Furthermore, analysis using the Protein Plus software revealed the presence of hydrogen bond interactions between Emodin and Protein Kinase PIM1. These interactions can influence the activity of Protein Kinase PIM1 and have the potential to provide therapeutic effects in the treatment of central nervous system-related diseases. Analysis of the physicochemical properties of Emodin using the Lipinski Rule revealed that Emodin meets several important criteria in drug design, with a molecular weight of 270, 3 hydrogen bond donors, 5 hydrogen bond acceptors, a log P value of 1.887220, and a molar reactivity of 64.480385. These physicochemical characteristics indicate the potential of Emodin as a stimulator of Protein Kinase PIM1 and provide guidance in the development of potential therapies for central nervous system-related diseases.[27-29] Table 2 shows the Lipinski data, and Figure 1 illustrates the Protein Plus analysis of the interaction between Emodin and Protein Kinase PIM1.

Thus, the results of this study indicate that Emodin has the potential as a stimulator of Protein Kinase PIM1 in the central nervous system. The strong molecular interaction between Emodin and Protein Kinase PIM1, adequate stability of the protein-ligand complex, and appropriate physicochemical characteristics all suggest the potential of Emodin as a therapeutic agent in the treatment of neurodegenerative diseases and brain cancer. These findings provide new insights into the development of potential therapies for central nervous system-related diseases and serve as a foundation for further research in optimizing Emodin as a therapeutic agent.[30-32]

The results of this study provide important interpretations regarding the potential of Emodin as a stimulator of Protein Kinase PIM1 in the central nervous system. Docking analysis indicates that Emodin has strong affinity for Protein Kinase PIM1, indicating its ability to interact with the enzyme. This interaction can activate Protein Kinase PIM1 and influence the signaling pathways involved in cell growth and proliferation in the central nervous system. Therefore, Emodin has the potential to be a stimulator of Protein Kinase PIM1 that can be used in the development of therapies for central nervous system-related diseases.[33-35]

Furthermore, RMSD analysis demonstrates adequate stability of the protein-ligand complex formed between Emodin and Protein Kinase PIM1. This indicates that the interaction between Emodin and Protein Kinase PIM1 can occur stably in the central nervous system. The stability of this complex is important in maintaining the sustained activity of Protein Kinase PIM1, which can contribute to the regulation of normal cell growth and proliferation in the central nervous system. These findings reinforce the potential of Emodin as a stimulator of Protein Kinase PIM1, which can play a role in the development of therapies for neurodegenerative diseases and brain cancer.[36-38]

In addition, analysis using the Protein Plus software reveals the presence of hydrogen bond interactions between Emodin and Protein Kinase PIM1. These interactions can influence the activity of Protein Kinase PIM1 and potentially provide therapeutic effects in the treatment of central nervous system-related diseases. The hydrogen bonds can strengthen the protein-ligand complex and modulate enzyme activity, which can impact the regulation of cell growth in the central nervous system. Therefore, Emodin has the potential to activate Protein Kinase PIM1 and disrupt signaling pathways involved in tumor cell growth or neurodegeneration.[39-41]

Furthermore, the analysis of Emodin's physicochemical properties using the Lepinski Rule indicates that Emodin meets several important criteria in drug design. This suggests that Emodin has good pharmacokinetic potential and meets the requirements to become an effective therapeutic agent.[43-48] The appropriate physicochemical characteristics, such as molecular mass, number of hydrogen bond donors and acceptors, log P, and molar reactivity, can influence the

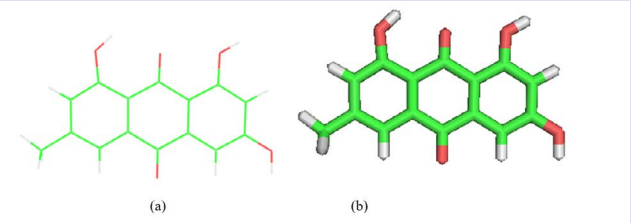

Figure 2: (a) 2D visualization of Emodin ligand (b) 3D visualization of Emodin ligand

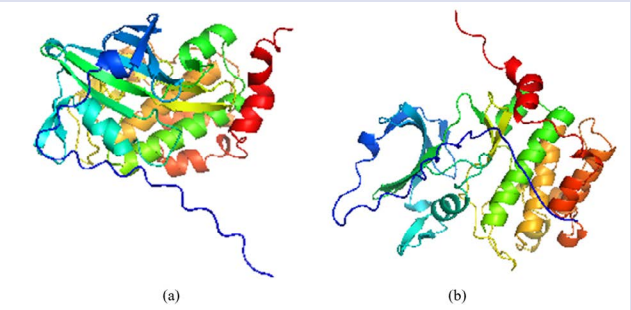

Figure 3: (a) Protein kinase PIM1 (b) Protein kinase PIM1

distribution, absorption, and biological activity of Emodin in the central nervous system. These findings strengthen the view that Emodin has the potential as a therapeutic agent in the treatment of neurodegenerative diseases and brain cancer.[49-55]

Overall, the results of this research provide important interpretations regarding the potential of Emodin as a stimulator of Protein Kinase PIM1 in the central nervous system. The strong interaction between Emodin and Protein Kinase PIM1, adequate stability of the protein-ligand complex, and appropriate physicochemical characteristics indicate that Emodin can be a promising candidate for the development of therapies for central nervous system-related diseases. The potential of Emodin as a stimulator of Protein Kinase PIM1 can have a positive impact on the regulation of cell growth, proliferation, and neural activity in the central nervous system. The activation of Protein Kinase PIM1.

CONCLUSION

In this study, *in-silico* analysis was conducted regarding the potential of Emodin as a stimulator of Protein Kinase PIM1 in the central nervous system. The results showed that Emodin has a strong affinity for Protein Kinase PIM1 and can form stable protein-ligand complexes. The interaction between Emodin and Protein Kinase PIM1 through hydrogen bonding and hydrophobic contacts provides a strong basis for the potential of Emodin to influence the activity of Protein Kinase PIM1 and regulate the growth and function of nerve cells. Additionally, the analysis of Emodin's physicochemical properties revealed characteristics that meet important criteria in drug design. Thus, the findings of this study indicate that Emodin has the potential as a therapeutic agent in the treatment of neurodegenerative diseases and brain cancer by activating Protein Kinase PIM1.

This conclusion has important implications in the development of therapies for central nervous system disorders. The potential of Emodin as a stimulator of Protein Kinase PIM1 opens opportunities for the development of more potent and selective derivative compounds that target this enzyme. By utilizing *in-silico* approaches, this research provides a solid foundation for the study and development of effective

therapies in the treatment of neurodegenerative diseases and brain cancer. These findings also serve as a basis for further studies, including *in vitro* and *in vivo* testing, to validate the effectiveness and safety of Emodin as a therapeutic agent. Thus, this research makes a significant contribution to the development of innovative potential therapies that can have a significant impact in the field of healthcare.

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DISCLOSURE STATEMENT

The authors have declared that no competing interests exist.

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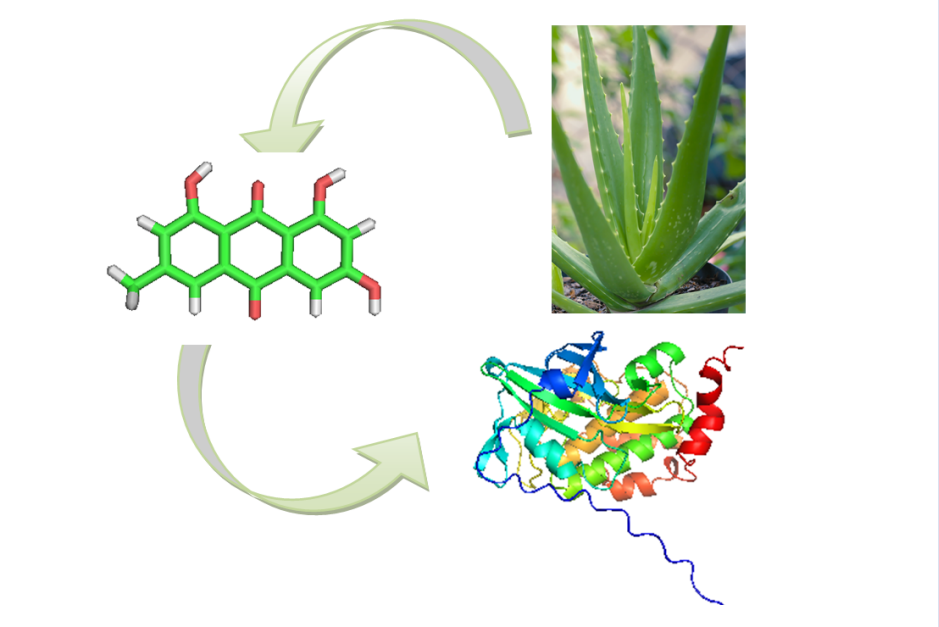
GRAPHICAL ABSTRACT



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