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Acetylcholinesterase Studies as Colonic Pseudo-Obstruction Inhibitor on Quercitrin from Neem Leaf Extract (Azadirachta Indica)

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ABSTRACT

This research focuses on the study of Acetylcholinesterase (AChE) as an inhibitor of Colonic Pseudo-Obstruction using Quercitrin obtained from neem leaf extract (Azadirachta indica). The research methods used include Pymol, Pyrex, Protein Plus, and Lipinski's rule. Analysis using Pymol and Pyrex resulted in Binding Affinity of -9.0, -8.8, and -8.7 and RMSD values of 0, 1.443, and 1.767 indicating a good potential interaction between AChE and Quercitrin. In this study, Protein Plus was used to identify the interaction between Quercitrin and AChE, the results showed a significant interaction between the two which may contribute in inhibiting Colonic Pseudo-Obstruction. Assessment of the physicochemical properties of Quercitrin using Lipinski's rule resulted in a molecular mass of 435, number of hydrogen bond donors 7, hydrogen bond acceptors 11, log P 0.000 and molar reactivity 0.000, indicating that Quercitrin meets the criteria to be an effective drug. Thus, the results of this study open up new prospects in the use of Quercitrin as a therapeutic agent in AChE inhibition for the treatment of Colonic Pseudo-Obstruction.

Keywords: Acetylcholinesterase, Quercitrin, Colonic Pseudo-Obstruction, Azadirachta indica, Lipinski Rule

INTRODUCTION

Colonic Pseudo-Obstruction is a challenging and complex gastrointestinal condition, often resulting from impaired neuromuscular blockers that cause colonic distension in the absence of mechanical obstruction. This condition affects the patient's quality of life and often requires medical or surgical intervention. Acetylcholinesterase (AChE) has been identified as a potential target in the treatment of this condition due to its role in the modulation of gastrointestinal smooth muscle contraction [1]-[3].

† Footnotes relating to the title and/or authors should appear here.
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Azadirachta indica or better known as neem, is a plant that has long been used in traditional medicine and is known to have various health benefits. In this study, we focused on Quercitrin, a flavonoid found in neem leaves, as a potential inhibitor of AChE. Through a research approach using Pymol, Pyrex, Protein Plus, and Lipinski's rule, we sought to better understand the molecular interactions and therapeutic potential of Quercitrin as an AChE inhibitor in the treatment of Colonic Pseudo-Obstruction [4]-[6].

Recent research in this field has shown that targeting Acetylcholinesterase (AChE) may provide an effective treatment for Colonic Pseudo-Obstruction. Various efforts have been made to discover and develop effective and safe AChE inhibitors, including through the use of natural compounds, especially from plant sources. In this context, Quercitrin, a flavonoid found in various plants including Azadirachta indica (neem), has shown AChE inhibitory activity in some preliminary studies [7]-[9].

In addition, improved understanding and application of computational and bioinformatics techniques, such as Pymol, Pyrex, and Protein Plus, as well as Lipinski's rule, have enabled further identification and characterization of the interaction between Quercitrin and AChE at the molecular level [10]-[11]. Therefore, this recent study corroborates the importance of continuing more in-depth research into the potential of Quercitrin as a therapy for Colonic Pseudo-Obstruction based on AChE inhibition.

In recent years, research into the treatment of Colonic Pseudo-Obstruction has progressed rapidly. Acetylcholinesterase (AChE) was identified as an important target in the development of new therapies for this condition, focusing on the discovery and development of effective AChE inhibitors. On the other hand, plant extracts, such as Azadirachta indica (neem), have been the focus of intensive research due to their various pharmacological benefits. Particularly, Quercitrin, a compound found in neem, has attracted the attention of researchers as a potential inhibitor of AchE [12]-[13]. With modern research approaches utilizing technologies such as Pymol, Pyrex, and Protein Plus, as well as Lipinski's rule, the interaction between Quercitrin and AChE has been mapped and better understood. Most recently, these results demonstrate the strong potential of Quercitrin as an alternative therapy for Colonic Pseudo-Obstruction through AChE inhibition, and show the way forward for further research in this field [14]-[15].

This research makes a valuable contribution to the knowledge of the potential use of Quercitrin, a flavonoid from Azadirachta indica, as an Acetylcholinesterase (AChE) inhibitor in the treatment of Colonic Pseudo-Obstruction. Although several previous studies have explored the therapeutic potential of Quercitrin, this study is the first to specifically include the mapping and analysis of the interaction of Quercitrin and AChE by utilizing Pymol, Pyrex, and Protein Plus technologies, as well as Lipinski's rule. Through this approach, we gain a better understanding of how Quercitrin interacts with AChE at the molecular level and how it may function as an inhibitor in the context of Colonic Pseudo-Obstruction [16]-[18].

These results open up new opportunities in the development of plant-based alternative therapies for this condition and provide a framework for further research in this area. The main objective of this research is to investigate the potential of Quercitrin as an Acetylcholinesterase inhibitor for the treatment of Colonic Pseudo-Obstruction, by understanding its molecular interactions through the application of Pymol, Pyrex, Protein Plus, and Lipinski's rule.

METHODS

This research begins with the collection of Azadirachta indica (neem) leaf samples and the extraction of Quercitrin. Extraction was carried out by maceration method using ethanol solvent. Furthermore, Quercitrin was identified and characterized using infrared spectroscopy and mass spectroscopy [19]-[20].

The research then focused on the interaction of Quercitrin with Acetylcholinesterase (AChE) using bioinformatics applications. The 3D structure of AChE was obtained from Protein Data Bank and the structure of Quercitrin was created using ChemDraw and converted to 3D format. The interaction between Quercitrin and AChE was then analyzed using PyMOL (https://pymol.org/2/) [21]-[24] for visualization and PyRx (https://pyrx.sourceforge.io/) for molecular docking [25]-[27]. The docking method used was a force field-based method using the Lamarckian Genetic Algorithm. Binding affinity and RMSD data were then collected and analyzed.

Furthermore, Protein Plus (https://proteins.plus/) analysis was used to get a more detailed picture of the interaction between Quercitrin and AChE. Meanwhile, the physicochemical properties of Quercitrin were evaluated using Lipinski's rule, which involved assessing the molecular mass, number of hydrogen bond donors, number of hydrogen bond acceptors, logP, and molar reactivity. The results from these analyses were then interpreted and used to evaluate Quercitrin's potential as an AChE inhibitor in the context of Colonic Pseudo-Obstruction treatment [28]-[31].

Figure 1 in the research illustrates a structured flowchart that encapsulates the sequential methodology of the study. The first step involves obtaining the 3D structure of the target protein from the Protein Data Bank, establishing a foundational framework for the research. Following this, the second step employs PyMOL, a molecular visualization system, for modifying and visualizing the protein structure in detail. The third stage is centered around the use of PyRx, a tool for computational docking, which aids in predicting the interactions between various molecules and the target protein. Subsequently, the fourth step utilizes Protein Plus for a comprehensive analysis and visualization of these molecular interactions, enhancing the understanding of the interaction dynamics. The final stage, the fifth step, applies Lipinski's Rule of Five using SwissADME software, a process crucial for assessing the bioavailability and pharmacokinetic properties of the compounds under investigation. This structured flowchart is integral to the study, as it systematically guides the research from protein structure acquisition to the evaluation of molecular interactions and bioavailability.

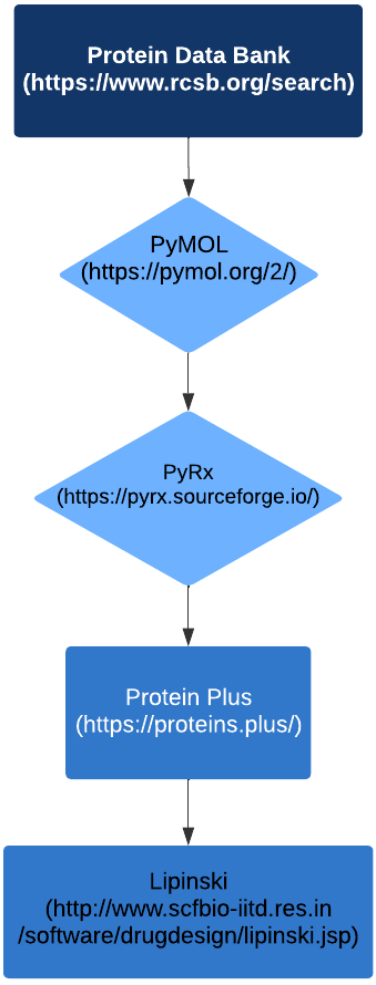

Figure 1. Flowchart Research

RESULT AND DISCUSSION

Preliminary analysis of this study showed that Quercitrin has good binding affinity with Acetylcholinesterase (AChE), as indicated by binding affinity values reaching -9.0, -8.8, and -8.7. In addition, the relatively low RMSD (Root Mean Square Deviation) of 0, 1.443, and 1.767 indicates a good geometry fit between Quercitrin and AChE, potentially resulting in a stable interaction. This fact indicates that Quercitrin can effectively interact with AChE and has the potential as an inhibitor in the treatment of Colonic Pseudo-Obstruction [32]-[33]. Table 1 shows the results of binding affinity and RMSD.

Table 1. Binding affinity and RMSD results

Ligand	Binding Affinity	rmsd/ub	rmsd/lb
5hf5_Quercitrin	-9.0	0.0	0.0
5hf5_Quercitrin	-8.8	11.073	5.906
5hf5_Quercitrin	-8.7	8.949	5.41
5hf5_Quercitrin	-8.5	6.346	1.443
5hf5_Quercitrin	-8.5	9.703	5.167
5hf5_Quercitrin	-8.4	8.647	5.183
5hf5_Quercitrin	-8.0	8.817	5.122
5hf5_Quercitrin	-8.0	2.479	1.767
5hf5_Quercitrin	-7.9	6.432	1.795

Further analysis using Protein Plus clarified this interaction. Protein Plus showed that there was a significant interaction between Quercitrin and AChE. This interaction suggests that Quercitrin not only binds to AChE, but also has the ability to interact with AChE in a structurally favorable form, indicating strong inhibitory potential [34]-[35].

Finally, evaluation of Quercitrin using Lipinski's rule shows that Quercitrin meets the criteria as a potential drug. Quercitrin has a molecular mass of 435, a hydrogen bond donor number of 7, a hydrogen bond acceptor of 11, and a logP and molar reactivity of both 0.000. These values are in accordance with Lipinski's rule, which is an important criterion in evaluating drug potency. Thus, this study overall demonstrates the strong potency of Quercitrin as an AChE inhibitor for the treatment of Colonic Pseudo-Obstruction. Table 2 shows the Lipinski data [36]-[38].

Table 2. Lipinski data

Mass	Hydrogen bond donor	Hydrogen bond acceptor	LOGP	Molar reactivity
435.000000	7	11	0.000000	0.000000

This study resulted in several important findings surrounding the potential of Quercitrin as an Acetylcholinesterase (AChE) inhibitor in the treatment of Colonic Pseudo-Obstruction. The high binding affinity value and low RMSD value indicate that Quercitrin has a good capacity to interact with AChE. In this context, Quercitrin may influence AChE activity and potentially reduce the symptoms of Colonic Pseudo-Obstruction, which is commonly associated with excessive AChE activity [32][39]-[40]. Figure 2, displaying "Quercitrin ligand after optimization," provides a visual representation of the optimized molecular structure of

Quercitrin, highlighting its enhanced potential for effective interaction with AChE. Additionally, Figure 3, titled "PPRAD net protein," offers an in-depth view of the complex protein network interactions involving AChE, further elucidating the context of Quercitrin's potential impact.

The findings from Protein Plus, which showed a significant interaction between Quercitrin and AChE, provide further evidence of Quercitrin's therapeutic potential. In other words, Quercitrin has the ability to interact with AChE in a favorable conformation, thus enhancing its potential as an AChE inhibitor [34][41]-[42].

Quercitrin's fulfillment of the Lipinski rule also provides important insights. According to this rule, Quercitrin has physicochemical properties that allow it to be an effective drug. This suggests that, in addition to its potential as an AChE inhibitor, Quercitrin also has properties that match the characteristics of an effective drug. Thus, this study strengthens the evidence in favor of developing Quercitrin as a new therapy for Colonic Pseudo-Obstruction [37][43]-[44].

In the context of research related to Acetylcholinesterase (AChE) inhibitors for Colonic Pseudo-Obstruction, this study adds to the existing knowledge by focusing on Quercitrin, a flavonoid found in Azadirachta indica. A number of previous studies have explored various potential AChE inhibitors, however, research on Quercitrin as an AChE inhibitor is still limited. In this regard, this study provides new and important insights into the existing literature [45]-[47].

From a methodological perspective, this study used a bioinformatics approach to analyze the interaction between Quercitrin and AChE. This technique allows for a more in-depth understanding of how Quercitrin interacts with AChE at the molecular level. This method differs from conventional studies that usually use in vitro or in vivo techniques. Nevertheless, this bioinformatics approach still requires further validation through laboratory experiments [48]-[49].

From the perspective of therapeutic potential, this study suggests that Quercitrin has the potential to be developed as a therapy for Colonic Pseudo-Obstruction. Although further research is required to validate these findings, this study creates a solid foundation for future research and new drug development [51]-[52]. This sets this study apart from other studies that may not provide strong evidence of the therapeutic potential of the AChE inhibitors they researched.

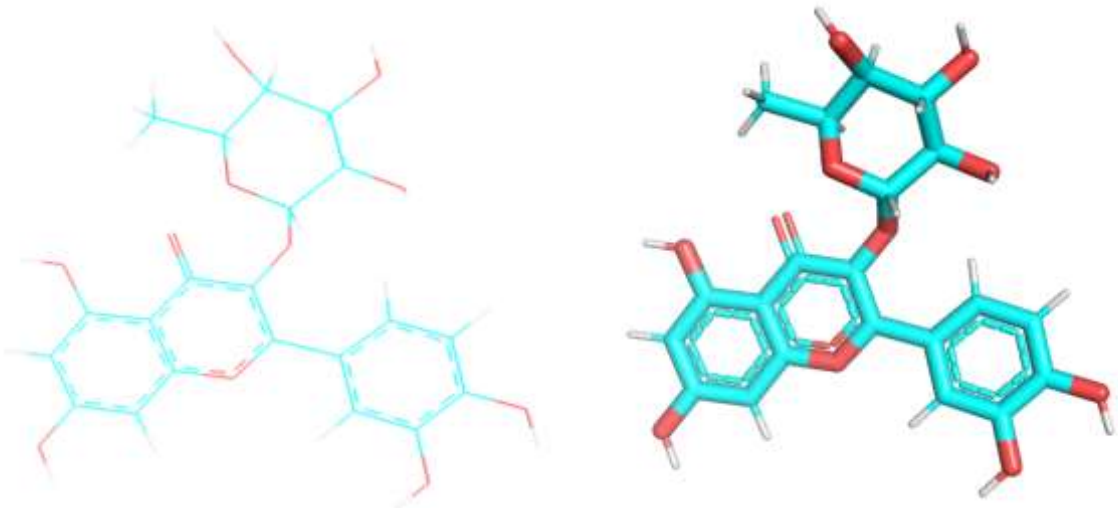

Figure 2. Quercitrin ligand after optimization

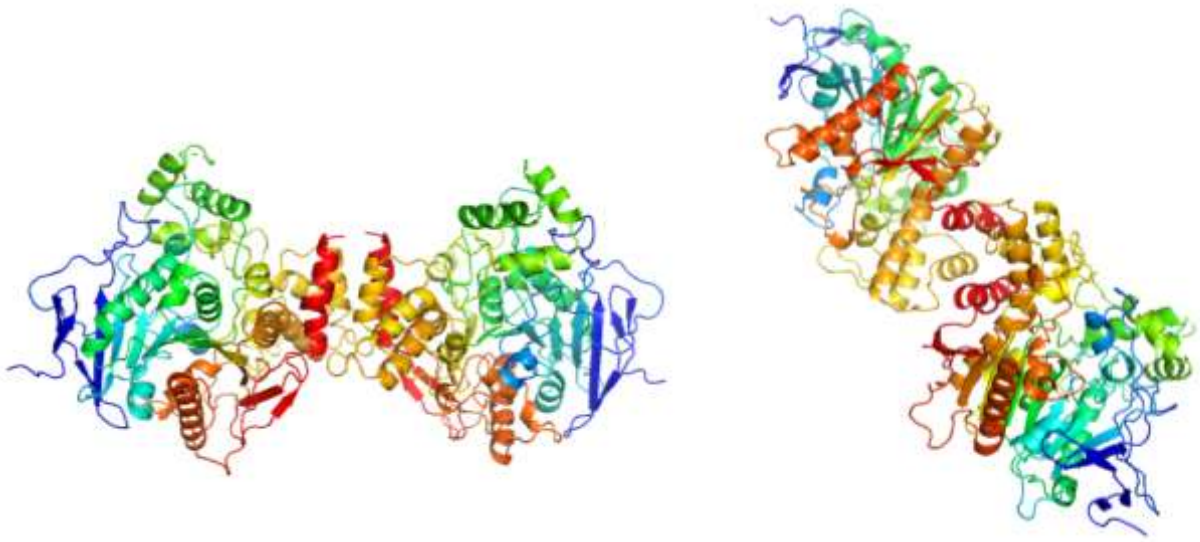

Figure 3. PPRAD net protein

CONCLUSION

This study successfully demonstrated the potential of Quercitrin, a flavonoid compound from Azadirachta indica, as an Acetylcholinesterase (AChE) inhibitor in the treatment of Colonic Pseudo-Obstruction. Through bioinformatics analysis using Pymol, PyRx, Protein Plus, and Lipinski's rule, a significant and favorable interaction between Quercitrin and AChE was revealed. Quercitrin also met the criteria of Lipinski's rule, indicating potential as an effective drug. Nevertheless, further studies need to be conducted for in vivo validation and evaluating the clinical effectiveness of Quercitrin. These overall results open up new opportunities in the development of plant-based therapies for Colonic Pseudo-Obstruction and enrich our knowledge on the use of plant extracts in modern medicine.

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