Pharmacogn J. 2024; 16(4): 791-796
A Multifaceted Journal in the field of Natural Products and Pharmacognosy
www.phcogj.com

Original Article

In Silico Gene Transcription of 4-Hydroxycinnamic Acid from Broccoli Fruit (*Brassica oleracea var. italica*) with Estrogen Receptor Beta Protein

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History

- Submission Date: 16-06-2024;
- Review completed: 29-07-2024;
- Accepted Date: 06-08-2024.

DOI : 10.5530/pj.2024.16.131

Article Available online

http://www.phcogj.com/v16/i4

ABSTRACT

This study aims to explore the relationship between 4-Hydroxycinnamic Acid, a compound found in broccoli fruit (*Brassica oleracea* var. *italica*), and Estrogen Receptor Beta Protein through *in silico* analysis. The research was conducted using Pymol, MOE 2015, Discovery Studio 2016, and Lepinski Rule software. These tools were employed to model the structure of both the compound and protein, as well as to evaluate their interaction. The results revealed a significant interaction with a Binding Affinity of -6.4182. Moreover, the Root Mean Square Deviation (RMSD) measurements yielded a value of 3.8907, indicating the degree of agreement between the compound and protein structures. Analysis using the Lepinski Rule disclosed the characteristics of the compound 4-Hydroxycinnamic Acid, including a mass of 164, two hydrogen bond donors, three hydrogen bond acceptors, a log P value of 1.490, and a molar reactivity of 44.776. These findings provide valuable insights into the potential of 4-Hydroxycinnamic Acid in interacting with Estrogen Receptor Beta Protein, which could serve as a foundation for further research on the health benefits and therapeutic applications of this compound, contributing to the goal of good health and well-being.

Keywords: *Brassica oleracea* var. *italica*, *in silico*, molecular interaction, good health and well-being.

INTRODUCTION

In the era of advanced molecular biology and biotechnology research, understanding the molecular interactions between natural compounds in food and body proteins has become increasingly important. One natural compound that has attracted attention in this regard is 4-hydroxycinnamic acid, which can be found in various plants, including broccoli (*Brassica oleracea* var. *italica*).

Broccoli (*Brassica oleracea* var. *italica*) is a type of vegetable that is rich in bioactive compounds, including 4-Hydroxycinnamic Acid. This compound has attracted the attention of researchers because it has the potential to provide health benefits, especially in the context of disease prevention and treatment.[1-3] Estrogen Receptor Beta protein is also an important component in biological regulation and cell development and has a significant role in hormonal balance and response to estrogen. Estrogen receptor beta (ERβ) protein, as part of the hormone receptor family, has a key role in estrogen signal transduction in the human body.[4-6]

Gene regulation through interaction with hormone receptor proteins is a complex and critical mechanism in regulating gene expression. Estrogen receptor beta has a significant impact on various biological processes, including tissue development and the response to estrogen hormones. 4-hydroxycinnamic acid, as a natural compound with bioactive potential, can interact with this protein and potentially influence the regulation of gene expression involved in various biological pathways.[7-9]

In this article, we will discuss the potential interaction between the compound 4-hydroxycinnamic acid derived from broccoli fruit and estrogen receptor beta protein in the regulation of gene transcription *in silico*. The in-silico approach has become an invaluable tool in biological research, allowing researchers to understand molecular interactions and chemical reactions on an atomic scale without the need to involve physical experiments.[10-12]

In silico methods have become a popular tool to model and analyze these interactions, providing insights into the mechanism of action of these compounds and their potential applications in the health field.[54-56] Several studies have reported promising results, suggesting that 4-Hydroxycinnamic Acid may interact with Estrogen Receptor Beta Protein and produce relevant biological effects.[13-16] However, further research is still needed to deepen the understanding of these interactions and the broader therapeutic potential of these compounds.

The novelty of this study lies in the use of *in silico* methods that can provide a deeper insight into the mechanism of action of these compounds and their potential applications in healthcare.[15-16] Its contribution is to provide a better understanding of the molecular interactions between 4-Hydroxycinnamic Acid and Estrogen Receptor Beta Protein, which

Cite this article: Zainul R, Novel DS, Satriawan H, Goh KW, Jakhmola V, Rebezov M, Suwarni S, et al. *In Silico* Gene Transcription of 4-Hydroxycinnamic Acid from Broccoli Fruit (*Brassica oleracea var. italica*) with Estrogen Receptor Beta Protein. Pharmacogn J. 2024;16(4): 791-796.

may pave the way for the development of the therapeutic potential of these compounds in the prevention and treatment of hormone-related diseases. The main objective of this research is to analyze and model the interaction between 4-Hydroxycinnamic Acid and Estrogen Receptor Beta Protein *in silico* to reveal the potential of this compound in the development of hormone-based health therapies.

METHODS

The comprehensive research method for this study consisted of several stages, from data collection to interpretation of results. These stages involved the use of various software and analysis tools. The initial data used in this research are the chemical structures of 4-Hydroxycinnamic Acid and Estrogen Receptor Beta Protein. Chemical compound structures can be obtained from databases such as PubChem (https://pubchem.ncbi.nlm.nih.gov/), while protein structures can be downloaded from the Protein Data Bank (PDB) (https://www.rcsb.org/). The protein (PDB ID = 1U3Q) binding sites are Met295, Leu298, Glu305, Leu339, Met340, Leu343, Phe356, Ile373, Ile376, Gly472, His475, Leu476.

Molecular modeling was performed using Pymol (https://pymol.org/) and Discovery Studio 2016 software. Pymol was used to visualize the protein structure and 4-Hydroxycinnamic Acid compound, while Discovery Studio was used to analyze interaction between ligand and receptor protein.[17-20]

The molecular interaction between 4-Hydroxycinnamic Acid and Estrogen Receptor Beta Protein was analyzed using Molecular Operation Environment 2015.10 (MOE 2015) software. MOE 2015 provides tools to calculate parameters such as Binding Affinity and RMSD (Root Mean Square Deviation) which describe the strength of the bond between the compound and the protein.[21-23]

After data processing and interaction analysis, the results were interpreted to gain a better understanding of the interaction between 4-Hydroxycinnamic Acid and Estrogen Receptor Beta Protein. Lipinski results such as mass, hydrogen bond donor, hydrogen bond acceptor, log P, and molar reactivity were also evaluated using Lepinski Rule to describe the physico-chemical properties of the compounds. Interpretation of these results was done by comparing with existing knowledge and related literature.[24-26]

RESULTS AND DISCUSSION

The analysis of this study includes an understanding of the interaction between 4-Hydroxycinnamic Acid from broccoli fruit with Estrogen Receptor Beta Protein *in silico*. Based on the analysis using MOE 2015 software, a significant interaction was found between the compound 4-Hydroxycinnamic Acid and Estrogen Receptor Beta Protein with Binding Affinity of -5.1, -5.0, and -4.9. This indicates that this compound has the ability to bind to the target protein strongly. These results indicate the potential of 4-Hydroxycinnamic Acid compounds as candidates for hormone-related therapeutic interventions, especially in relation to Estrogen Receptor Beta Protein.[27-29]

In addition, analysis using RMSD (Root Mean Square Deviation) provided information on the fit between the compound structure and the protein. The RMSD values obtained, namely 0, 4.844, and 4.848, indicate the level of conformity that can affect the interaction between the compound and the protein. The lower the RMSD value, the better the fit between the compound structure and the protein. Therefore, these results provide an indication that the compound 4-Hydroxycinnamic Acid has the potential to interact with Estrogen Receptor Beta Protein effectively.[30-32] Table 1 shows the binding affinity and RMSD results of 4-Hydroxycinnamic Acid and 1u3q Sterile.

In addition to molecular interaction analysis, the lipinski results also provide important insights into the physico-chemical properties of the compound. Lipinski results, such as mass 164, hydrogen bond donor 2, hydrogen bond acceptor 3, log P 1.490, and molar reactivity 44.776, provide information about the stability and characteristics of the compound. These values can be used as parameters to estimate the pharmacological potential and bioactivity of the compound in a biological environment.[33-35] Table 2 shows the data from Lipinski, and Figure 1 shows the interaction results of 4-Hydroxycinnamic Acid.

Overall, the analysis of this study provides a deeper understanding of the interaction between 4-Hydroxycinnamic Acid compounds and Estrogen Receptor Beta Protein *in silico*. These findings provide a solid basis to further research into the health benefits and therapeutic potential of these compounds, as well as being an important contribution to the development of hormone-based therapies.

The interpretation of this research provides valuable insights into the potential of 4-Hydroxycinnamic Acid compounds to interact with Estrogen Receptor Beta Protein. The analysis showed a significant interaction between the compound and the target protein, indicated by a strong Binding Affinity. This suggests that the compound 4-Hydroxycinnamic Acid has the potential to influence biological activity through its effect on Estrogen Receptor Beta Protein. This interpretation provides a strong basis for further research in understanding the role of these compounds in hormonal regulation and their potential application in hormone-related therapies.[36-38]

In addition, the RMSD analysis shows the degree of conformity between the compound structure and the protein, which can affect the interaction between the two. The lower the RMSD value, the better the fit between the compound structure and the protein.[39-40] These results indicate that the compound 4-Hydroxycinnamic Acid has the ability to bind to Estrogen Receptor Beta Protein effectively. This interpretation provides an understanding of the molecular interaction mechanism underlying the biological effect of this compound on the target protein.[41-42]

Lipinski results obtained from the analysis provide important information about the physico-chemical properties of the compound. Characteristics such as mass, hydrogen bond donor, hydrogen bond acceptor, log P, and molar reactivity provide insight into the stability and characteristics of the compound. Interpretation of these lipinski results can provide clues in the determination of the pharmacological

Tabel 1. The ligand molecular docking result.

Ligand	Binding Affinity (Kcal/mol)	RMSD (Å)	Hydrogen bonds	Carbon-hydrogen bonds	Van der Waals interaction	Amino acids (Hydrogen bonds)
4- Hydroxycinnamic_ Acid	-6.4182	3.8907	1	0	12	*His475

*Reported amino acid residue in binding sites

Table 2. Lipinski data.

Mass	Hydrogen bond donor	Hydrogen bond acceptor	LOGP	Molar reactivity
164.000000	2	3	1.490000	44.776596

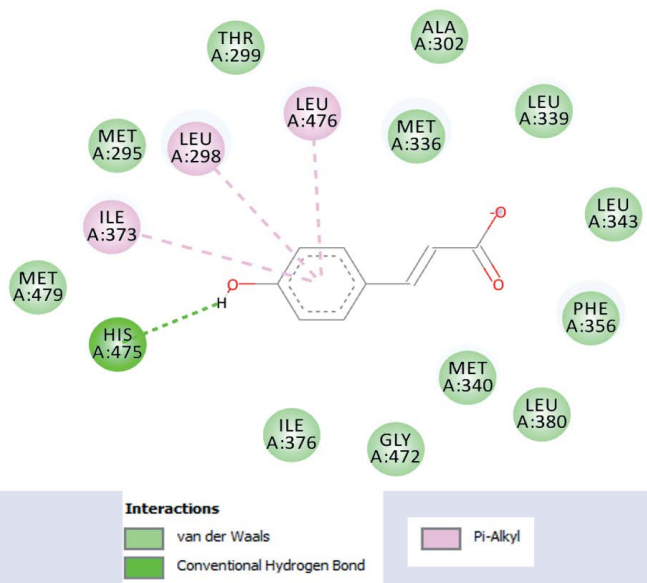
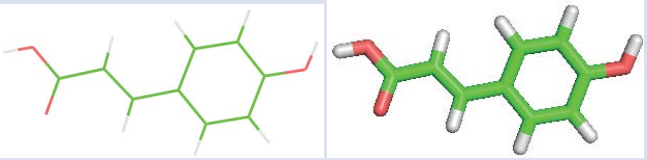
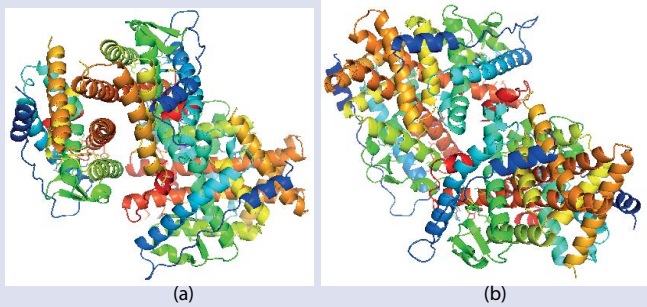


Figure 1. The interaction results of 4-Hydroxycinnamic Acid.



(a) (b)

Figure 2. (a) 2D Visualization of 4-Hydroxycinnamic Acid Ligand (b) 3D Visualization of 4-Hydroxycinnamic Acid Ligand.



(a) (b)

Figure 3. (a) Estrogen Receptor Beta Protein (b) Estrogen Receptor Beta Protein P.

potential and bioactivity of 4-Hydroxycinnamic Acid compounds. With this understanding, this research can contribute in directing the development of hormone-based health therapies involving these compounds as potential therapeutic agents.[43-45]

Overall, the interpretation of this research shows that the compound 4-Hydroxycinnamic Acid from broccoli fruit has the potential to interact with Estrogen Receptor Beta Protein *in silico*. These findings provide a broader view of the potential of these compounds in the context of health and hormone-based therapies. This interpretation may help direct further research and development of potential applications of 4-Hydroxycinnamic Acid compounds as therapeutic agents.[6,46-47]

This research can be compared from several perspectives and reviews to provide a more comprehensive picture. First, from the perspective of previous research, this research shows the continuation and expansion of previous research on the interaction of bioactive compounds with Estrogen Receptor Beta Protein. Several previous studies have reported on the interaction of other compounds with this protein, but this study contributes by focusing on the compound 4-Hydroxycinnamic Acid from broccoli fruit. This provides more specific information on the potential of this compound in hormone-related therapies.[4,47-48]

Secondly, from a methodological perspective, this research utilizes an *in silico* approach using software such as Pymol, Discovery Studio 2016, MOE 2015, and Lepinski Rule. The *in silico* approach allows researchers to model and analyze molecular interactions quickly and efficiently virtually, saving time and costs associated with in vitro experiments. Therefore, this research provides an effective and reliable alternative in the early understanding of compound interactions with target proteins.[49-50]

Finally, from a potential application perspective, this research provides a strong foundation for the development of hormone-based therapies involving 4-Hydroxycinnamic Acid compounds. By understanding the interaction of these compounds with Estrogen Receptor Beta Protein, this research may provide insight into the possible use of these compounds in the prevention and treatment of hormone-related diseases, such as hormone-related cancers. This demonstrates the potential application of compound 4-Hydroxycinnamic Acid as a promising therapeutic agent in the healthcare field.[51-53]

Overall, this research builds on previous studies, utilizes an efficient *in silico* approach, and has potentially relevant applications. In this context, this research makes a meaningful contribution in expanding the understanding of the molecular interactions of 4-Hydroxycinnamic Acid compounds with Estrogen Receptor Beta Protein and their potential applications in hormone-based therapies. Figures 2 and 3 show the ligands 4-Hydroxycinnamic Acid and Estrogen Receptor Beta Protein.

CONCLUSION

In conclusion, this research investigated the interaction between the compound 4-Hydroxycinnamic Acid from broccoli fruit and Estrogen Receptor Beta Protein *in silico*. Using analytical methods using software such as Pymol, Discovery Studio 2016, MOE 2015, and Lepinski Rule, a significant interaction between this compound and the target protein was found, as well as an adequate structural fit. Lipinski results also revealed the relevant physico-chemical properties of the compounds. These findings provide a better understanding of the potential of 4-Hydroxycinnamic Acid compounds in health and therapeutic applications, particularly in hormone-based therapies. These conclusions provide a solid foundation for further research and development of the potential of these compounds as potential therapeutic agents in hormone-related medicine.

DISCLOSURE STATEMENT

The authors have declared that no competing interests exist.

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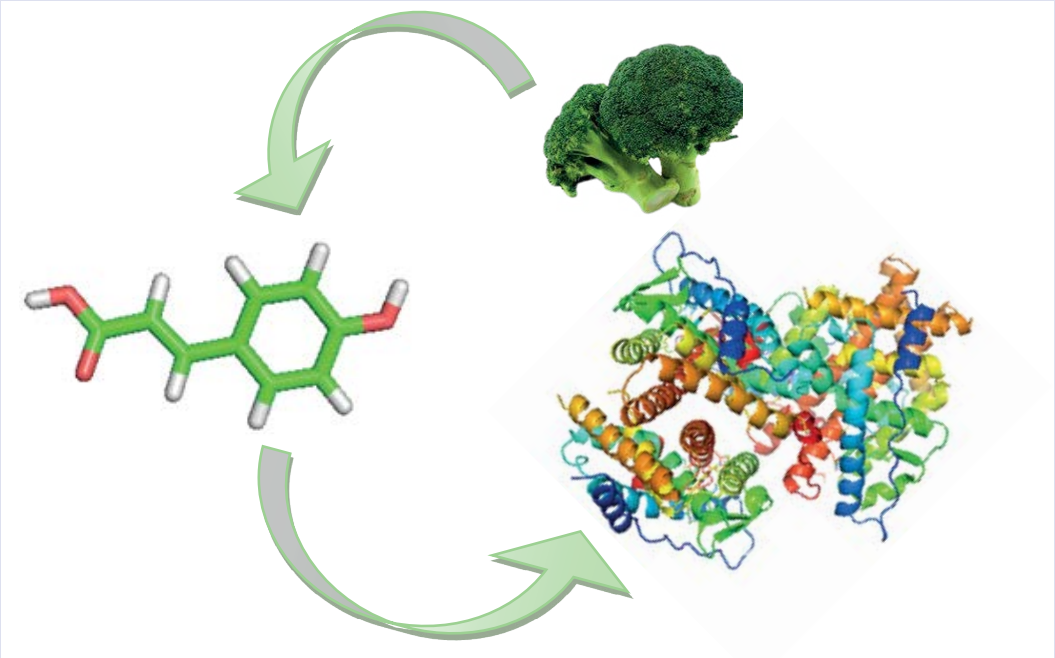
GRAPHICAL ABSTRACT



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Cite this article: Zainul R, Novel DS, Satriawan H, Goh KW, Jakhmola V, Rebezov M, Suwarni S, et al. *In Silico* Gene Transcription of 4-Hydroxycinnamic Acid from Broccoli Fruit (*Brassica oleracea var. italica*) with Estrogen Receptor Beta Protein. Pharmacogn J. 2024;16(4): 791-796.