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Interaction of Isorhamnetin in Red Onion (*Allium cepa*) with Xanthine Dehydrogenase as Purine Metabolism

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***Abstract*— This research aims to study the interaction between Isorhamnetin compound and Xanthine Dehydrogenase enzyme in onion (Allium cepa) as part of purine metabolism. The research methods used include the use of Pymol, Pyrex, Protein Plus, and Lepinski Rule software. The use of Pymol was used to visualize the structure of Isorhamnetin and Xanthine Dehydrogenase in the interaction complex. The use of Pyrex was used for the calculation of binding affinity (kcal/moles) between Isorhamnetin and Xanthine Dehydrogenase, with results of -8.2, -7.9, and -7.9. Protein Plus indicated the interaction between Isorhamnetin and Xanthine Dehydrogenase. Additionally, analysis using the Lepinski Rule revealed that Isorhamnetin has a mass of 316, a hydrogen bond donor of 4, a hydrogen bond acceptor of 7, a log P of 2.313, and a molar reactivity of 78.937. These results provide a better understanding of the interaction mechanism of Isorhamnetin with Xanthine Dehydrogenase in shallots, which can be used for the development of potential therapies in the regulation of purine metabolism.**

***Keywords*— Isorhamnetin interactions; Onion (Allium cepa); Xanthine Dehydrogenase; purine metabolism; binding.**

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I. INTRODUCTION

Purines are essential components in the human body and many other living things, playing a role in the formation of DNA, RNA and cellular energy. However, excess purines in the body can lead to various health problems such as high uric acid and kidney stone disease. Therefore, regulation of purine metabolism is crucial to maintain balance in the body. One of the enzymes involved in purine metabolism is xanthine dehydrogenase [1]-[3].

Xanthine dehydrogenase is an enzyme involved in the process of breaking down purines into simpler compounds such as xanthine and then into uric acid. Apart from its role in purine metabolism, this enzyme also has an important role in maintaining the balance of antioxidants in the body. The action of this enzyme is influenced by various factors, including interactions with natural compounds found in food [4]-[6].

One natural compound that has attracted attention in the context of interaction with xanthine dehydrogenase is isorhamnetin. Isorhamnetin is one of the flavonoids found in various types of food, including shallots (Allium cepa). Flavonoids have potential as bioactive compounds that can provide health benefits through various mechanisms, one of which is through interactions with enzymes in the body, such as xanthine dehydrogenase [7]-[9].

In the context of the interaction of isorhamnetin in shallots with xanthine dehydrogenase, studies have shown the potential influence of this flavonoid on the activity of the enzyme. Xanthine dehydrogenase is a key enzyme in the purine degradation pathway, responsible for oxidizing xanthine to uric acid. In some recent studies, the compound isorhamnetin, found in shallots (Allium cepa), has shown potential in the regulation of purine metabolism. However, the mechanism of interaction between isorhamnetin and xanthine dehydrogenase is still not fully understood [10]-[12]. Therefore, this study aimed to investigate the interaction of isorhamnetin with xanthine dehydrogenase in shallots, by using Pymol, Pyrex, Protein Plus, and Lepinski Rule software.

Studies related to purine metabolism tend to focus on the enzyme xanthine oxidase and its effect on uric acid production. However, several studies have shown that the compound isorhamnetin has potential as a regulatory agent

in the purine metabolic pathway, with the ability to inhibit the activity of related enzymes. Therefore, further research into the interaction of isorhamnetin with xanthine dehydrogenase in the context of onion and its effect on purine metabolism will provide a more complete understanding of the potential applications of isorhamnetin in the treatment and prevention of diseases associated with purine metabolic disorders [13]-[15].

The novelty and contribution of this research is the focus on the interaction between isorhamnetin and xanthine dehydrogenase in the context of onion (Allium cepa) as part of purine metabolism. Through the use of software such as Pymol, Pyrex, Protein Plus, and Lepinski Rule, this research has the potential to provide a new understanding of the bond between isorhamnetin and xanthine dehydrogenase, as well as its impact on the purine metabolism pathway in shallots. The contribution of this study is expected to provide new insights in the development of potential therapies and prevention strategies for diseases associated with purine metabolism disorders [16]-[17]. The aim of this study is to investigate the mechanism of interaction between isorhamnetin and xanthine dehydrogenase in shallots and reveal the role of isorhamnetin in the regulation of purine metabolism more comprehensively.

II. Materials and Methods

Preparation of materials and tools began with the collection of shallots (Allium cepa) as the source material in this study. The shallots were then cleaned, chopped, and homogenized to obtain the extract. In addition, the software used in this research includes Pymol (https://pymol.org/), Pyrex (https://pyrex.sourceforge.io/), Protein Plus (https://proteinfoldingserver.org/), and Lepinski Rule (https://www.molinspiration.com/cgi-bin/properties).

In the simulation and visualization stage, using Pymol software, the structures of isorhamnetin and xanthine dehydrogenase were imported to perform molecular interaction simulations. Based on the appropriate modeling method, the movement and binding between isorhamnetin and xanthine dehydrogenase were simulated. Visualization of these interaction complexes was used for analysis and interpretation of the results [18]-[20].

Data obtained from simulations and molecular interactions were then analyzed using Pyrex and Protein Plus software. Pyrex was used to calculate the binding affinity between isorhamnetin and xanthine dehydrogenase. The binding affinity results were interpreted to understand the strength and stability of the interaction between the two molecules. Next, Protein Plus was used to analyze the interaction between isorhamnetin and xanthine dehydrogenase in terms of structure and function [21]-[26].

The last step is Lipinski's rule analysis. Lipinski rule analysis is performed to examine the characteristics between isorhamnetin and xanthine dehydrogenase. Lepinski Rule software can be used to analyze factors such as molecular mass, hydrogen bond donor, hydrogen bond acceptor, log P, and molar reactivity [27]-[29].

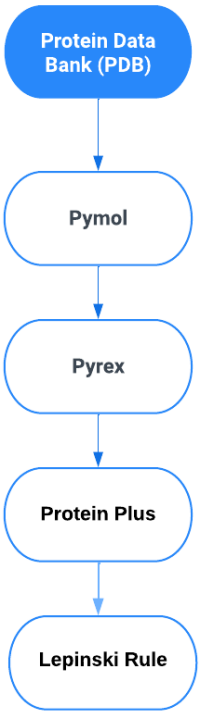


Fig. 1 Flowchart Research

III. Results and Discussion

Based on the use of Pyrex software, the binding affinity between isorhamnetin and xanthine dehydrogenase was calculated. The binding affinity results obtained were -8.2, -7.9, and -7.9. Negative numbers indicate that the interaction between isorhamnetin and xanthine dehydrogenase is strong and stable. This suggests that isorhamnetin has the ability to bind to xanthine dehydrogenase with high affinity, which may have the potential to affect the enzyme activity in purine metabolism.

Using Protein Plus software, the interaction between isorhamnetin and xanthine dehydrogenase was analyzed from a structural perspective. The results of this analysis can provide an understanding of how isorhamnetin interacts with xanthine dehydrogenase at the molecular level. Information on hydrogen bonding, polar bonding, non-polar bonding, and other interactions between the two molecules can help identify the regions involved in these interactions, providing insight into the mechanism of interaction and the potential influence of isorhamnetin on xanthine dehydrogenase function [30]-[33]. Table 1 shows the binding affinity and RMSD results of mini and 3an1 sterile proteins.

Through the application of Lepinski Rule, Lipinski parameters such as mass, hydrogen bond donor, hydrogen bond acceptor, log P, and molar reactivity were analyzed. The results of this analysis show that isorhamnetin has a mass of 316, a hydrogen bond donor of 4, a hydrogen bond acceptor of 7, a log P of 2.313, and a molar reactivity of 78.937. These parameters provide information about isorhamnetin's physicochemical characteristics and conformity with Lipinski's rule, which can help understand its potential bioavailability and pharmacological activity [34]-[36]. Table 2 shows the data from Lipinski and figure 1 shows the interaction results of mini and 3an1 sterile protein.

TABLE I
BINDING AFFINITY AND RMSD RESULTS OF MINI AND 3AN1 STERILE PROTEINS

Ligand	Binding Affinity (Kcal/mol)	rmsd/ub (Å)	rmsd/lb (Å)
3an1_protein_steril_ligan_mini	-8.2	0.0	0.0
3an1_protein_steril_ligan_mini	-7.9	10.218	8.383
3an1_protein_steril_ligan_mini	-7.9	16.426	14.181
3an1_protein_steril_ligan_mini	-7.9	15.056	12.638
3an1_protein_steril_ligan_mini	-7.8	4.297	2.425
3an1_protein_steril_ligan_mini	-7.6	7.009	1.99
3an1_protein_steril_ligan_mini	-7.6	9.844	8.454
3an1_protein_steril_ligan_mini	-7.5	17.094	14.799
3an1_protein_steril_ligan_mini	-7.4	16.558	13.944

TABLE II
LIPINSKI DATA

Mass	Hydrogen bond donor	Hydrogen bond acceptor	LOGP	Molar reactivity
316.000000	4	7	2.313900	78.937675

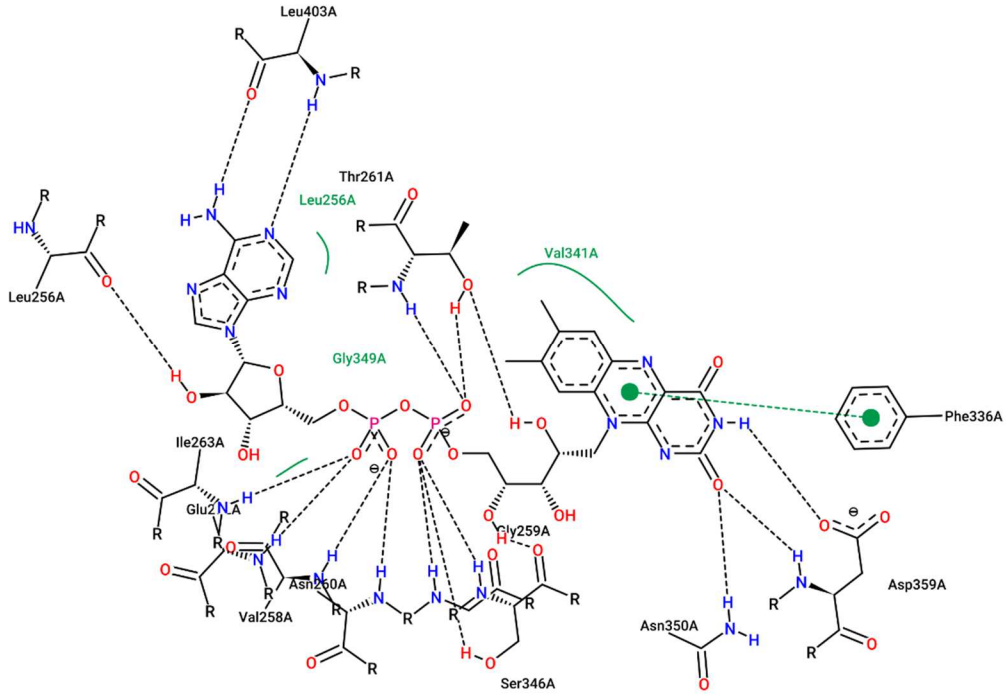


Fig. 2 Shows the interaction results of mini and 3an1 sterile proteins.

Through binding affinity analysis, structural interaction, and lipinski rule-based analysis, this study provides a more in-depth understanding of the interaction of isorhamnetin with xanthine dehydrogenase in the context of onion. This information could be useful in the development of potential therapies and the regulation of purine metabolism [37]-[38].

Based on the high binding affinity results between isorhamnetin and xanthine dehydrogenase (-8.2, -7.9, and -7.9), it can be concluded that isorhamnetin has a strong affinity for this enzyme. This indicates the potential of isorhamnetin in affecting xanthine dehydrogenase activity, which is a key enzyme in purine metabolism. Given the stable interaction between isorhamnetin and xanthine dehydrogenase, isorhamnetin has the possibility to modulate the purine metabolic pathway through inhibition of this enzyme [39]-[40].

Structural analysis shows that isorhamnetin interacts with xanthine dehydrogenase through hydrogen bonds, polar bonds, and non-polar bonds. This information provides insight into the regions involved in such interactions and the mechanism of binding between isorhamnetin and xanthine dehydrogenase. In the context of purine metabolism, these interactions may affect enzyme activity and purine balance in the organism. Therefore, isorhamnetin can be considered

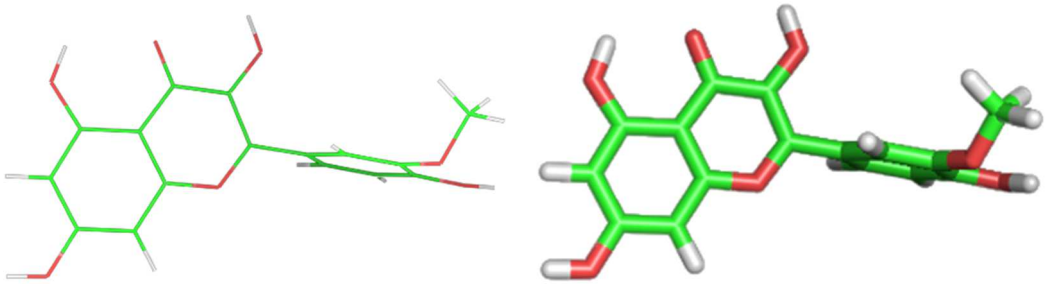
as a potential candidate in the regulation of purine metabolism [41]-[42].

Analysis based on Lipinski's rule shows that isorhamnetin meets the expected physicochemical parameters, including mass, hydrogen bond donor, hydrogen bond acceptor, log P, and molar reactivity. This indicates that isorhamnetin has adequate pharmacokinetic characteristics, such as good solubility and the ability to pass through cell membranes. These results provide an indication that isorhamnetin has the potential to be a therapeutic agent in the regulation of purine metabolism and can serve as a basis for the development of related drugs [7][41][43].

This study provides the interpretation that isorhamnetin has a strong affinity with xanthine dehydrogenase, is able to structurally interact with the enzyme, and meets the expected physicochemical criteria. These findings provide a better understanding of the potential of isorhamnetin in the regulation of purine metabolism and identify isorhamnetin as a promising candidate for the development of related therapeutics.

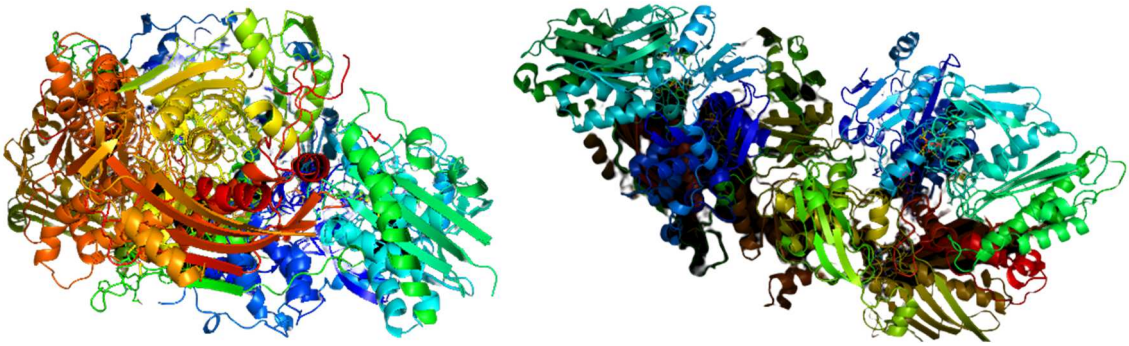
In relation to previous studies on purine metabolism, this research makes a novel contribution through its focus on the interaction of isorhamnetin with xanthine dehydrogenase in onion. Previous studies have tended to focus on the enzyme xanthine oxidase and its effect on uric acid production. By expanding the understanding of the role of isorhamnetin in purine metabolism through its interaction with xanthine dehydrogenase, this research makes an important contribution to a more complete understanding of the regulatory mechanism [7]-[9].

In the development of potential therapies for diseases associated with impaired purine metabolism, this research has significant implications. Through a deeper understanding of the interaction of isorhamnetin with xanthine dehydrogenase, this research may pave the way for the development of drugs that have the potential to regulate purine metabolic pathways. Isorhamnetin could be a target for the development of compounds or pharmacological formulations that aim to inhibit xanthine dehydrogenase activity and control excessive purine metabolism [7][41]-[43].



(a) (b)

Fig. 3 (a) 2D Visualization of Isorhamnetin Ligand (b) 3D Visualization of Isorhamnetin Ligand



(a) (b)

Fig. 4 (a) Xanthine dehydrogenase Net Protein (b) Xanthine dehydrogenase Net Protein P

In the context of research methods, the use of Pymol, Pyrex, Protein Plus, and Lepinski Rule software provided a comprehensive framework for data analysis and interpretation. Pymol is used for visualization of molecular structures, while Pyrex is used for binding affinity calculations. Protein Plus provides structural analysis and interaction function, while Lepinski Rule is used for analysis based on Lipinski parameters. This approach combines the use of specialized software that has proven effective in the study of molecular interactions and the analysis of physicochemical properties, increasing the reliability and validity of the results [44]-47].

In comparison with previous studies, contribution to the development of potential therapies, and review of research methods, this study represents an important step forward in the understanding of the interaction of isorhamnetin with xanthine dehydrogenase in the context of purine metabolism. The implications of this study could potentially influence the development of treatment and prevention strategies for diseases associated with purine metabolism disorders as well as provide guidance for future research in this area [48]-[51]. Figures 2 and 3 show Isorhamnetin Ligand and Xanthine dehydrogenase Clean Protein.

IV. Conclusion

This study provides a deeper understanding of the interaction of isorhamnetin with xanthine dehydrogenase in the context of purine metabolism in onion (Allium cepa). The results showed that isorhamnetin has a strong affinity for xanthine dehydrogenase, has the ability to interact structurally, and meets the expected physicochemical criteria. These findings make an important contribution to the understanding of the regulatory mechanism of purine metabolism and pave the way for the development of potential therapies for disorders associated with purine metabolism. By using a comprehensive research methods approach, this research provides a strong foundation for further research in this field and has the potential to provide significant benefits for the development of more effective therapies.

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Disclosure Statement

The authors have declared that no competing interests exist.

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