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Research Article

Development of a Docking-Based QSAR and ADMET Analysis of White Radish (*Raphanus sativus* L.) Compounds as Potential Anti Insomnia Agents

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Abstract

Raphanus sativus L. (white radish) contains various bioactive compounds that may have potential as anti-insomnia agents. This study aimed to evaluate the structure–activity relationship and pharmacokinetic properties of white radish compounds using Quantitative Structure–Activity Relationship (QSAR) modeling and ADMET prediction. Fourteen compounds previously identified through molecular docking studies against the GABA receptor were analyzed. Binding affinity values from previous docking studies were used as the dependent variable, while lipophilicity (logP), topological polar surface area (TPSA), and hydrogen bond donor (HBD) were selected as molecular descriptors. QSAR modeling was performed using multiple linear regression and validated through Leave-One-Out Cross Validation (LOOCV), multicollinearity analysis, and residual diagnostics. The final QSAR model showed good statistical performance with an adjusted R^2 of 0.820 and Q^2LOO of 0.756. LogP and HBD were identified as the most influential descriptors, whereas TPSA did not significantly contribute to the model. ADMET prediction revealed considerable variation in pharmacokinetic properties among the investigated compounds. Glucobrassicin exhibited the strongest predicted binding affinity, while ledol and nerolidol demonstrated more favorable pharmacokinetic profiles, including blood–brain barrier permeability and high gastrointestinal absorption. These findings suggest that glucobrassicin, ledol, and nerolidol are promising candidates for further development as natural product-based anti-insomnia agents.

Keywords: ADMET, anti insomnia, molecular descriptor, QSAR, *Raphanus s*ativus L.

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1 Introduction

Insomnia remains one of the most prevalent sleep disorders globally and is characterized by persistent difficulties in initiating, maintaining sleep continuity, or experiencing restorative sleep despite adequate opportunity for rest. According to the World Health Organization (WHO), sleep disorders affect 16–25% of the global population, with adults in Indonesia facing a prevalence rate of approximately 10% [1]. insomnia not only impairs daily functioning and quality of life but is also strongly associated with cognitive decline, mood disturbances, cardiovascular disorders, anxiety, and depression. Consequently, insomnia has become an important public health concern due to its multifactorial impact on both physical and psychological wellbeing [2], [3], [4]

Pharmacological management of insomnia commonly involves benzodiazepines, non-benzodiazepine hypnotics, melatonin receptor agonists, and sedative antidepressants. Although these agents may improve sleep onset and duration, their prolonged use is frequently associated with undesirable adverse effects, including daytime sedation, tolerance, dependence, cognitive impairment, rebound insomnia, and psychomotor dysfunction [5]. Several reports have also highlighted the increased risk of falls, memory impairment, and withdrawal-related complications following long-term sedative use. These limitations underscore the urgent need for safer and more effective therapeutic alternatives, particularly those derived from natural products with lower toxicity profiles [1], [6], [7].

In recent years, medicinal plants have gained increasing attention as potential sources of novel neuroactive compounds for central nervous system disorders. Among these, white radish (Raphanus sativus L.) has emerged as a promising candidate due to its rich composition of bioactive secondary metabolites, such as flavonoids, phenolic compounds, glucosinolates, and sulfur-containing molecules. Several of these compounds possess structural features that may enable interactions with neurotransmitter-related targets involved in sleep regulation. Previous molecular docking studies have demonstrated that several phytochemicals from white radish exhibit favorable binding affinity toward the gamma-aminobutyric acid (GABA) receptor, suggesting their potential as anti-insomnia agents [8], [9], [10], [11] The γ-aminobutyric acid type A (GABAA) receptor was chosen because it represents the primary molecular target of most clinically used hypnotic agents, including benzodiazepines and non-benzodiazepine tranquilizers. Enhanced GABAergic neurotransmission enhances neural inhibition, facilitating sleep initiation and maintenance. Therefore, compounds capable of interacting with GABAA receptors are considered promising candidates for anti-insomnia drug discovery [6] [5].

Despite the promising molecular docking results, the structural factors responsible for the observed receptor-binding affinity remain poorly understood. Furthermore, information regarding the pharmacokinetic behavior and safety characteristics of these compounds is still limited. Understanding the relationship between molecular structure and biological activity is essential for identifying key physicochemical properties that contribute to receptor interaction and for guiding future optimization of candidate compounds [1].

Quantitative Structure–Activity Relationship (QSAR) modeling represents an important computational approach for establishing mathematical relationships between molecular descriptors and biological activity. In situations where experimental bioactivity data are unavailable, molecular docking-derived binding affinity may serve as a surrogate endpoint for preliminary QSAR investigations. Nevertheless, because molecular docking scores represent computational estimates rather than experimentally measured biological activity, the resulting models should be interpreted as exploratory docking-based QSAR models intended for virtual screening and hypothesis generation rather than conventional QSAR models [12], [13]. Through this approach, QSAR analysis can identify molecular characteristics associated with stronger receptor interactions and provide predictive models useful for virtual screening and lead optimization. In addition, Absorption, Distribution, Metabolism, Excretion, and Toxicity (ADMET) prediction offers valuable insights into the pharmacokinetic properties and safety profiles of candidate compounds prior to experimental validation [13], [4], [5].

To date, studies integrating QSAR modeling and ADMET evaluation of white radish phytochemicals for anti-insomnia applications remain limited. Therefore, the present study aimed to

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investigate the relationship between selected molecular descriptors and GABA receptor binding affinity of white radish compounds using QSAR analysis. Furthermore, ADMET prediction was performed to evaluate the pharmacokinetic and toxicity profiles of the identified compounds and to prioritize compounds for future experimental validation and drug development.

2 Method

2.1 Compound Selection

All the chemical structures of compounds of Raphanus sativus L. included in this study were selected based on previously published molecular docking study and supporting literature reports [11]. The selected compounds consisted of 4-hydroxyglucobrassicin, glucobrassicin, glucoiberin, glucoraphanin, squalene, ledol, neophytadiene, sulforaphane, erucin, benzyl isothiocyanate, 4-methylthio-3-butenyl isothiocyanate, nerolidol, progoitrin, and methyl linolenate. The two-dimensional (2D) chemical structures of all compounds were retrieved from the PubChem database. PubChem was selected because it is a freely accessible and publicly available chemical database containing manually curated molecular information and compound annotations [14]. The binding affinity values against the gamma-aminobutyric acid (GABA) receptor were obtained from previously reported molecular docking study and used as the dependent variable in QSAR analysis.

2.2 Docking-based QSAR Model Development and Validation

A dataset consisting of fourteen phytochemical compounds from R. sativus L. was used for docking-based QSAR model development. Molecular descriptors were calculated using PaDEL-Descriptor and SwissADME website. The selected descriptors included lipophilicity (logP), topological polar surface area (TPSA), and hydrogen bond donor (HBD). These descriptors were chosen based in their relevance to ligand-receptor interactions, blood-brain barrier permeability, and pharmacokinetic characteristics of central nervous system-active compounds.

Docking-based QSAR analysis was performed using the Multiple Linear Regression (MLR) method implemented in RStudio version 2025 (4.5.2). Prior to model construction, descriptor preprocessing was conducted, including correlation analysis, descriptor selection, regression model development, and statistical validation of the generated model. The initial docking-based QSAR model was developed using all selected descriptors. Descriptor significance was evaluated using regression coefficients and p-values, and non-significant descriptors were excluded to obtain the final model [15], [16].

TDescriptor significance was evaluated using regression coefficients and p-values, and non-significant descriptors were excluded to obtain the final model [17], [18]. Model validation included internal validation using Leave-One-Out Cross Validation (LOOCV), residual diagnostic analysis, variance inflation factor (VIF), Shapiro–Wilk normality test, Breusch–Pagan heteroscedasticity test, Durbin–Watson autocorrelation test, applicability domain analysis using Williams plot, and Y-randomization with 100 random permutations to evaluate the model's robustness to chance correlation. Model robustness was further assessed using empirical p-values and Roy's cRp^2 parameter.

2.3 ADMET and Toxicity Prediction

The pharmacokinetic and toxicity profiles of the selected compounds were evaluated using SwissADME, pkCSM, and ADMETlab 3.0 web servers. The evaluated parameters included gastrointestinal absorption, blood–brain barrier permeability, hepatotoxicity, acute toxicity, and Lipinski's rule of five. These computational tools were selected due to their comprehensive predictive models and recent updates that improve the prediction accuracy for natural-product-derived compounds [19], [20].

The predicted ADMET profiles were subsequently integrated with the QSAR results to identify compounds exhibiting favorable binding affinity, pharmacokinetic properties, and safety characteristics. This integrated approach was used to prioritize potential anti-insomnia candidates from R. sativus L. for further investigation [12]

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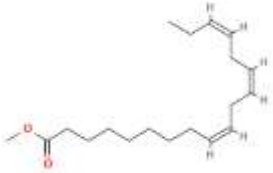
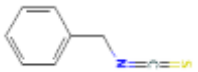
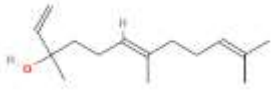
3 Result and Discussion

Fourteen active compounds from white radish (Raphanus sativus L.) were used to develop a docking-based QSAR model based on binding affinity values obtained from previous molecular docking study against the GABA receptor associated with insomnia (Table 1). Binding affinity was used as an activity parameter because experimental biological activity data, such as IC50, Ki, or EC50, were not yet available for these compounds.

The molecular descriptors analyzed included lipophilicity (logP), topological polar surface area (TPSA), and hydrogen bond donor (HBD), selected based on their relevance to ligand-receptor interactions and the pharmacokinetic characteristics of the active compounds in the central nervous system [21]. They were obtained through calculations using the PaDEL-Descriptor and SwissADME platforms. Although the dataset consisted of only fourteen compounds, the ratio between the number of observations and descriptors remained within the generally accepted range for preliminary QSAR studies [18]. Therefore, the model was considered adequate for exploratory virtual screening rather than definitive predictive applications.

The initial modeling stage was performed using multiple linear regression with these three descriptors included as independent variables. The analysis results showed that the TPSA descriptor did not provide a significant contribution to the model ($p = 0{,}890$), while logP and HBD showed a significant relationship to the binding affinity value ($p < 0{,}001$). Therefore, TPSA was eliminated to obtain a simpler model with better predictive capabilities.

Table 1 Active compounds of *Raphanus sativus* L. used and their binding affinity values

No.	Compound	Binding Affinity ΔG (kcal/mol)	No.	Compound	Binding Affinity ΔG (kcal/mol)
1	4-methylthio-3-butenyl isothiocyanate 	-4,52	8	Ledol 	-7,27
2	4-OH glucobrassicin 	-9,73	9	Methyl linolenate 	-6,86
3	Benzyl isothiocyanate 	-5,34	10	Neophytadiene	-7,11
4	Erucin 	-4,43	11	Nerolidol 	-6,3

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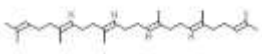
5	Glucoiberin		-7,31	12	Progoitrin		-6,68
6	Glucobrassicin		-9,38	13	Sulforaphane		-5,14
7	Glucoraphenin		-7,74	14	Squalene		-9,13

Table 2 Molecular descriptor of the test compound

Compound	Descriptor		
	logP	TPSA	HBD
4-methylthio-3-butenyl isothiocyanate	2,356	69,75	0
4-OH glucobrassicin	-0,738	235,81	7
Benzyl isothiocyanate	2,2894	44,45	0
Erucin	2,2324	69,75	0
Glucoiberin	-2,028	236,07	5
Glucobrassicin	-0,180	215,58	6
Glucoraphenin	-1,604	236,07	5
Ledol	3,4657	20,23	1
Methyl linolenate	5,7489	26,30	0
Neophytadiene	7,1677	0	0
Nerolidol	4,239	20,23	1
Progoitrin	-1,379	220,02	6
Sulforaphane	0,306	80,73	0

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Squalene	11,0844	0	0

Description:
Lipophilicity (logP); topological polar surface area (TPSA); hydrogen bond donor (HBD).

The results of the correlation analysis between variables (Figure 1) indicate that the HBD descriptor has a stronger relationship with binding affinity (BA) than the other descriptors. The logP and TPSA descriptors exhibit a relatively weaker negative correlation with BA. However, the regression analysis indicates that logP still makes a significant contribution to the final docking-based QSAR model. Meanwhile, TPSA, although theoretically known to play a role in blood-brain barrier permeability, did not contribute significantly to the final docking-based QSAR model in this study. This is likely due to the structural diversity of the compounds used in the study, making the influence of molecular polarity less dominant than the lipophilicity and hydrogen bond donor descriptors.

Lipophilicity is crucial for compounds targeting the central nervous system because adequate lipophilicity facilitates passive diffusion across the blood-brain barrier. Hydrophobic interactions also stabilize ligand binding within the hydrophobic pocket of the GABAA receptor. Therefore, the negative coefficient obtained for logP indicates that compounds with higher lipophilicity tend to exhibit stronger predicted receptor binding, provided that excessive lipophilicity does not compromise pharmacokinetic properties. Hydrogen bond donor groups facilitate specific interactions with amino acid residues located in the receptor binding pocket. These interactions increase the stability of the ligand-receptor and contribute to a decrease in the binding free energy during molecular docking simulations.

The final docking-based QSAR equation obtained in this study is expressed as follows:.

$$\text{Binding Affinity} = -4{,}183 - 0{,}435(\text{logP}) - 0{,}777(\text{HBD})$$

A negative regression coefficient indicates that increasing logP and HBD values tend to result in more negative binding affinity values. Although the logP regression coefficient appears numerically smaller than that of the HBD, it should not be compared directly because each molecular descriptor is expressed on a different numerical scale. Therefore, statistical significance rather than coefficient magnitude provides a more accurate measure of the importance of the descriptor. Furthermore, the statistical test results indicate that its contribution to the model is significant. In molecular docking studies, a more negative binding affinity value indicates a stronger binding affinity. Therefore, lipophilicity and hydrogen-bond-donor capacity appear to be important determinants of the interaction between the compounds and the GABA receptor [22].

Table 3 Statistical parameters of the docking-based QSAR model

Parameter	Value	Parameter	Value
Multiple R^2	0,844	p-value	$3{,}19 \times 10^{-5}$
Adjusted R^2	0,816	PRESS	9,453
Residual standard error	0,7242	Q^2LOO	0,750
F-statistic	30,62	VIF	1,98
Mean Random R^2	0,153	RMSE	0,650
Maximum Random R^2	0,642	MAE	0,524
Empirical p-value	0,0099	cRp^2	0,763

The obtained docking-based QSAR model (Table 3) demonstrated good statistical performance, with a Multiple R^2 value of 0,844 and an adjusted R^2 value of 0,816, indicating that the model was able to explain 81,6% of the variation in compound binding affinity. The residual standard error of 0.7242 indicates that the model has a relatively low level of prediction error. The overall regression model also demonstrated high statistical significance, as indicated by an F-statistic of 30,62 with a probability of 3,19

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x 10-5. In exploratory QSAR studies involving natural products, an adjusted R^2 value greater than 0,70 is generally considered acceptable for virtual screening and early-stage candidate prioritization.

The model's predictive ability was evaluated using the Leave-One-Out Cross Validation (LOOCV) method. The validation results showed a PRESS value of 9,453 and a Q^2LOO value of 0,750. A Q^2LOO value greater than 0,50 indicates a good predictive ability for the model, while a Q^2LOO value above 0,70 is generally considered indicative of strong internal predictive performance. Therefore, the model can be considered to possess good internal predictive reliability [23].

To evaluate the possibility of overfitting, the Multiple R^2 and Q^2LOO values were compared. The resulting difference is:

$$R^2 - Q^2 = 0,844 - 0,750 = 0,094$$

This value is indicating good agreement between model fitting and predictive performance. The small discrepancy suggests that the model is unlikely to be overfitted and possesses satisfactory internal predictive reliability [23], [24].

Multicollinearity analysis yielded a Variance Inflation Factor (VIF) value of 1,98 for both descriptors, indicating the absence of problematic multicollinearity because the obtained values were well below the commonly accepted threshold of 5 (VIF < 5). The low VIF values suggest that each descriptor contributes distinct information to the model and independently explains variations in compound activity, thereby improving model interpretability and robustness [22], [25].

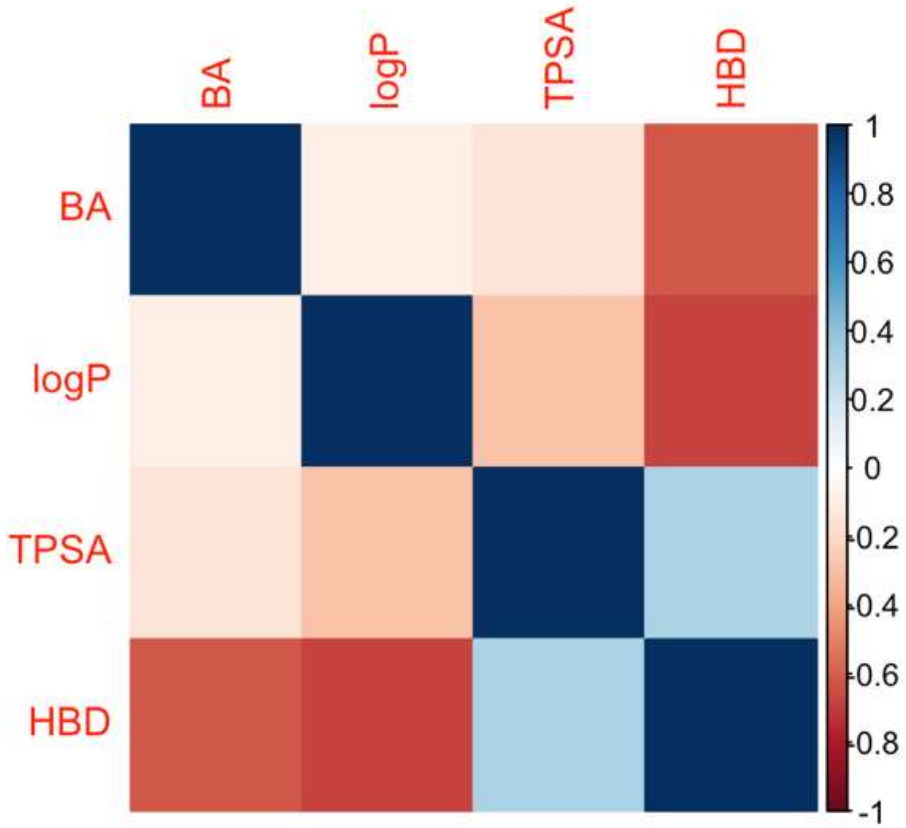

Figure 1 Descriptor correlation test

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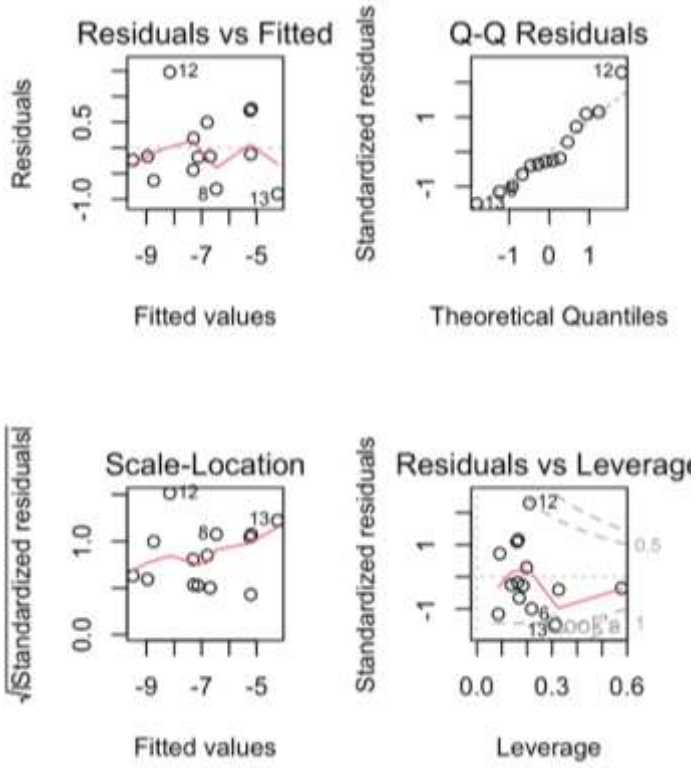

Figure 2 Diagnostic plots of the final docking-based QSAR model

The validity of the regression model was further evaluated through residual diagnostic analysis, including Residuals vs. Fitted, Normal Q-Q, Scale-Location, and Residuals vs. Leverage plots (Figure 2). The Residuals vs. Fitted plot showed that the residuals were randomly distributed around the zero line without forming a clear systematic pattern. This result indicates that the relationship between molecular descriptors and biological activity can be adequately explained using a linear regression approach. The Normal Q-Q plot showed that most of the observation points followed the diagonal line, indicating that the residuals approximated a normal distribution. Although there were slight deviations at some extreme points, the overall residual distribution was still acceptable. The Scale-Location plot showed a relatively uniform distribution of residuals throughout the predicted range. No significant heteroscedasticity patterns were found, thus meeting the assumption of homogeneity of residual variance. Meanwhile, the Residuals vs. Leverage plot showed that no observations exceeded the Cook's Distance limit [26]. This indicates that no compounds exerted an excessive influence on model formation, and the model appears to be reasonably stable and robust [23].

The applicability domain was further evaluated using a Williams plot (Figure 3). All investigated compounds displayed standardized residuals within ±3 and leverage values below the warning leverage threshold (h* = 0,643). Consequently, no structural or response outliers were detected, indicating that all compounds fall within the applicability domain of the developed model, and therefore, the obtained predictions can be considered reliable for the investigated chemical space.

Model robustness was further examined through Y-randomizing using 100 random permutations of the dependent variable. The original model showed an R^2 value of 0,844, while the randomized model produced a significantly lower average R^2 value of 0,153. Furthermore, the empirical p-value was 0,0099, and the calculated cRp^2 reached 0,763, exceeding the recommended threshold of 0,50. These findings indicate that the developed docking-based QSAR model is unlikely to result from chance correlation and has acceptable statistical robustness.

Despite satisfactory internal validation, the developed docking-based QSAR model should be considered an exploratory computational model because it was built using a limited dataset and docking-

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derived binding affinity values, rather than experimentally determined biological activity. Furthermore, external validation was not possible due to dataset limitations. Therefore, further research using a larger dataset and experimental biological data is needed to improve the predictive reliability and generalizability of the model.

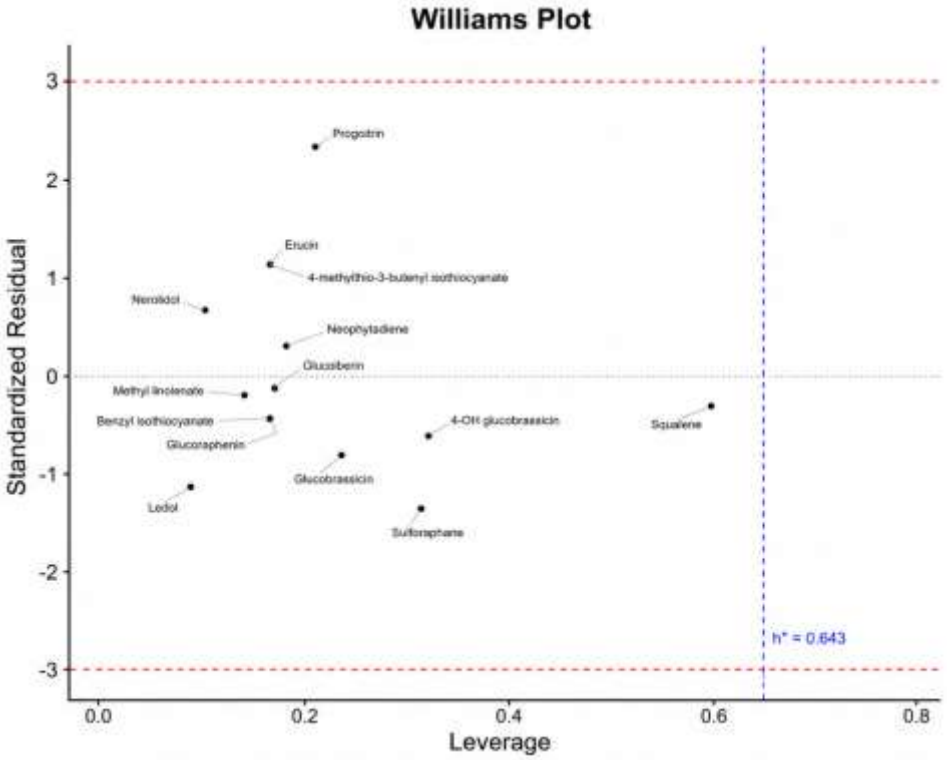

Figure 3 Williams Plot

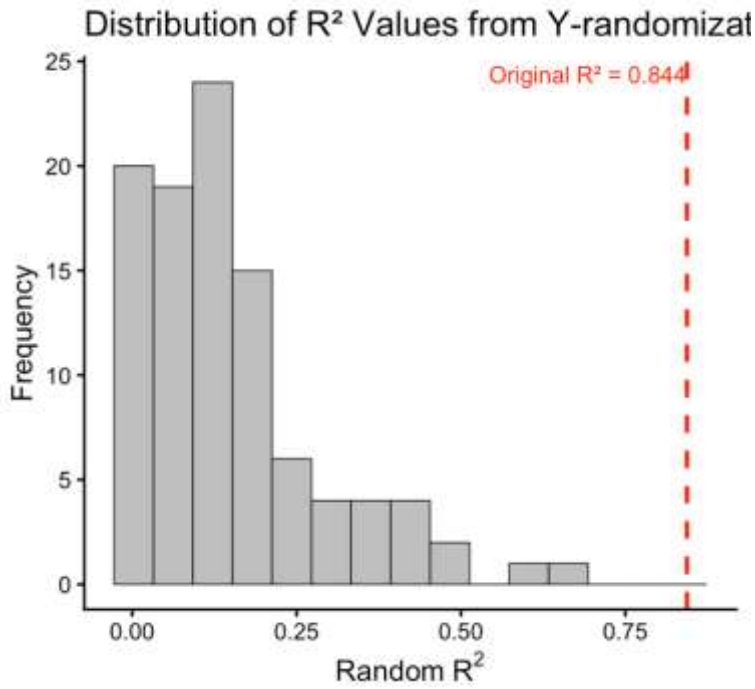

Figure 4 Histogram of Y-randomization

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QSAR analysis results suggest that lipophilicity and hydrogen donor capacity are among the most influential factors affecting the interaction of white radish tuber compounds with the insomnia protein target (GABA). The logP descriptor indicates the level of lipophilicity of a molecule. A negative regression coefficient indicates that increasing lipophilicity tends to result in stronger binding affinity. This finding aligns with the role of hydrophobic interactions in stabilizing the ligand-receptor complex. Furthermore, lipophilicity is a crucial parameter in the development of drugs that act on the central nervous system because it is related to the molecule's ability to penetrate the blood-brain barrier (BBB) [21], [27].

The HBD descriptor also significantly contributes to binding affinity. Hydrogen-bond-donor capacity enables compounds to establish hydrogen-bond-interactions with amino acid residues in the receptor's active site. This interaction contributes to increased stability of the ligand-receptor complex and ultimately increases binding affinity [28], [29].

In contrast, TPSA did not significantly contribute to the final docking-based QSAR model under the conditions and dataset used in this study. Although this descriptor is often associated with membrane permeability and BBB penetration, its effect on binding affinity in this study was relatively small. This is likely due to the high structural and polarity variation of the compounds used, reducing the relative contribution of TPSA to binding affinity prediction compared to logP and HBD [21], [30].

Additional validation was performed using applicability domain analysis (Williams plot) and Y-randomization. The Williams plot confirmed that all compounds were placed within the applicability domain with no structural or response outliers. In addition, Y-randomization yielded an average random R^2 of 0,153 compared to the original R^2 of 0,844, with an empirical p-value of 0,0099 and a cRp^2 of 0,763, indicating that the model was not generated by chance correlation. Moreover, the developed model demonstrated satisfactory internal validation performance. Consequently, this model should be interpreted as an exploratory computational model rather than a fully validated predictive docking-based QSAR model [17], [24]. The validation strategy adopted in this study follows widely accepted recommendations for QSAR model development, including internal validation, applicability domain assessment, and robustness evaluation.

Furthermore, the ADMET prediction results in Table 4 indicate that the compounds studied have diverse pharmacokinetic characteristics. Several isothiocyanate and terpenoid compounds, such as erucin, ledol, and nerolidol, exhibit favorable ADMET profiles, with high gastrointestinal absorption, the ability to penetrate the blood-brain barrier, no potential hepatotoxicity, and compliance with Lipinski's rule. These properties suggest favorable oral bioavailability and an increased likelihood of reaching targets within the central nervous system [31], [32].

Table 4 Predicted ADMET profiles of white radish compounds generated using SwissADME, pkCSM, and ADMETlab 3.0.

Compound	Properties				
	GA	BBB	Hepatotoxicity	Acute oral toxicity	Lipinski's rule
4-methylthio-3-butenyl isothiocyanate	High	Yes	No	High	Yes
4-OH glucobrassicin	Low	No	Yes	Low	No
Benzyl isothiocyanate	High	Yes	No	Medium	Yes
Erucin	High	Yes	No	Medium	Yes
Glucoiberin	Low	No	No	Low	Yes
Glucobrassicin	Low	No	Yes	Low	No

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Glucoraphenin	Low	No	No	Medium	Yes
Ledol	High	Yes	No	Low	Yes
Methyl linolenate	High	Yes	No	Low	Yes
Neophytadiene	Low	No	No	Low	Yes
Nerolidol	High	Yes	No	Low	Yes
Progoitrin	Low	No	No	Low	No
Sulforaphane	High	No	No	High	Yes
Squalene	Low	No	No	Low	Yes

Information:
Gastrointestinal Absorption (GA); blood-brain barrier (BBB). Acute toxicity classification was based on the predicted oral LD50 values generated by ADMETlab 3.0 and pkCSM.

In contrast, glucosinolate compounds such as glucobrassicin and 4-OH glucobrassicin exhibit excellent binding affinity toward the GABA receptor, but showed several pharmacokinetic limitations. Both compounds were predicted to have low gastrointestinal absorption, lack blood-brain barrier permeability, exhibit potential hepatotoxicity, and violate Lipinski's rule of five. Although these compounds demonstrated strong receptor-binding potential, their unfavorable physicochemical and pharmacokinetic characteristics may limit their effectiveness as central nervous system drug candidates. Therefore, structural modification or advanced drug-delivery strategies may be necessary to enhance their bioavailability and central nervous system exposure. Potential strategies include prodrug design, PEGylation, nanoformulation, liposomal encapsulation, or polymeric nanoparticles to improve BBB permeability while maintaining receptor affinity. These strategies remain hypothetical and require experimental validation.

Furthermore, the high polarity generally associated with glucosinolate compounds may contribute to their limited membrane permeability and BBB penetration [21], [33].

Interestingly, terpenoid compounds such as ledol and nerolidol demonstrate a better balance between pharmacokinetic properties and safety. Both compounds have high gastrointestinal absorption, are able to penetrate the blood-brain barrier, do not exhibit potential hepatotoxicity, and have low acute toxicity. Therefore, in addition to considering binding affinity values, the ADMET profile should also be a key factor in the selection of natural product-based anti-insomnia candidates [21], [31].

Overall, the results of the integration of QSAR and ADMET suggest that glucobrassicin exhibited the strongest predicted receptor affinity among the compounds evaluated, whereas ledol and nerolidol emerged as prioritized candidates for subsequent experimental validation due to their balanced combination of predicted activity and favorable pharmacokinetic properties.

Since the proposed model is built from binding affinity values derived from docking using a limited number of phytochemicals, these findings should be interpreted as exploratory computational evidence that requires further validation through experimental biological assays and larger QSAR datasets.

4 Conclusion

This study employed docking-based QSAR modeling integrated with ADMET prediction to identify bioactive compounds from Raphanus sativus L. with favorable computational characteristics for further anti-insomnia drug discovery. The developed QSAR model showed good statistical performance (R^2 = 0,844; Adjusted R^2 = 0.816) and suggested that lipophilicity (logP) and hydrogen bond donor capacity (HBD) are among the most influential molecular descriptors associated with the binding affinity of the compounds toward the GABA receptor.

Among the investigated compounds, glucobrassicin exhibited the strongest predicted binding affinity, while ledol and nerolidol showed more favorable pharmacokinetic profiles, including blood-brain barrier permeability, high gastrointestinal absorption, and low predicted toxicity. These findings identify glucobrassicin, ledol, and nerolidol as promising candidates for further experimental investigation rather than confirmed anti-insomnia agents.

Because the developed model was derived from docking scores obtained from a limited number of compounds, the findings should be interpreted as exploratory and require confirmation using experimental biological activity data. Further in vitro and in vivo studies are required to validate their biological activity and safety.

5 Declarations

5.1 Author contributions

Noer Fauziah Rahman: Writing – original draft, software, methodology, data curation, conceptualization, formal analysis. **Wahyuni Agus**: Writing – review and editing.

5.2 Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

5.3 Funding Statement

There are no sources of funding.

6 Bibliography

[1] L. Waters, K. R. Manchester, P. D. Maskell, C. Haegeman, and S. Haider, "The use of a quantitative structure-activity relationship (QSAR) model to predict GABA-A receptor binding of newly emerging benzodiazepines," Science & Justice, vol. 58, no. 3, pp. 219–225, May 2018, doi: 10.1016/J.SCIJUS.2017.12.004.

[2] P. Rios et al., "Comparative effectiveness and safety of pharmacological and non-pharmacological interventions for insomnia: an overview of reviews," Systematic Reviews 2019 8:1, vol. 8, no. 1, pp. 281-, Nov. 2019, doi: 10.1186/S13643-019-1163-9.

[3] W. W. IsHak et al., "Quality of Life in Patients Suffering from Insomnia," Innov. Clin. Neurosci., vol. 9, no. 10, p. 13, Oct. 2012, Accessed: May 29, 2026. [Online]. Available: https://pmc.ncbi.nlm.nih.gov/articles/PMC3508958/

[4] X. Huang, Y. Wu, Y. Ni, H. Xu, and Y. He, "Global, regional, and national burden of type 2 diabetes mellitus caused by high BMI from 1990 to 2021, and forecasts to 2045: Analysis from the Global Burden of Disease Study 2021," Frontiers in Public Health, vol. 13, Art. no. 1515797, 2025, doi: 10.3389/fpubh.2025.1515797.

[5] F. De Crescenzo *et al.*, "Comparative efficacy and acceptability of pharmacological treatments for insomnia in adults: a systematic review and network meta-analysis," *Cochrane Database Syst. Rev.*, vol. 2016, no. 9, p. CD012364, Sep. 2016, doi: 10.1002/14651858.CD012364.

[6] L. Wang et al., "Simulating dynamic interaction between diazepam and ethanol targeting the GABAA receptor via in silico model," Neurotoxicology, vol. 95, pp. 136–143, Mar. 2023, doi: 10.1016/J.NEURO.2023.01.012.

[7] D. T. Maust, L. A. Lin, and F. C. Blow, "Benzodiazepine use and misuse among adults in the United States," ., vol. 70, no. 2, pp. 97–106, Feb. 2019, doi: 10.1176/APPI.PS.201800321;ISSUE:ISSUE:DOI.

[8] A. Manivannan, J. H. Kim, D. S. Kim, E. S. Lee, and H. E. Lee, "Deciphering the nutraceutical potential of raphanus sativus—A comprehensive overview," *Nutrients*, vol. 11, no. 2, 2019, doi: 10.3390/nu11020402.

[9] M. Gamba *et al.*, "Nutritional and phytochemical characterization of radish (Raphanus sativus): A systematic review," *Trends Food Sci. Technol.*, vol. 113, pp. 205–218, Jul. 2021, doi: 10.1016/J.TIFS.2021.04.045.

[10] L. Y. Hernández-Sánchez et al., "Antinociceptive effects of Raphanus sativus sprouts involve the opioid and 5-HT1A serotonin receptors, cAMP/cGMP pathways, and the central activity of sulforaphane," Food Funct., vol. 15, no. 9, pp. 4773–4784, Feb. 2024, doi: 10.1039/D3FO05229J.

[11] N. F. Rahman, N. Wahyuddin, and M. Marwati, "Studi In-silico Senyawa Umbi Lobak Putih (Raphanus sativus L.) sebagai Kandidat Anti Insomnia," Majalah Farmasi dan Farmakologi, vol. 27, no. 4, pp. 10–14, 2023.

[12] L. G. Ferreira, R. N. Dos Santos, G. Oliva, and A. D. Andricopulo, "Molecular Docking and Structure-Based Drug Design Strategies," Molecules, vol. 20, no. 7, p. 13384, Jul. 2015, doi: 10.3390/MOLECULES200713384.

[13] K. M. T. Islam and S. Mahmud, "In-silico exploring pathway and mechanism-based therapeutics for allergic rhinitis: Network pharmacology, molecular docking, ADMET, quantum chemistry and machine learning based QSAR approaches," Comput. Biol. Med., vol. 187, p. 109754, Mar. 2025, doi: 10.1016/J.COMPBIOMED.2025.109754.

[14] P. M. Khan and K. Roy, "Current approaches for choosing feature selection and learning algorithms in quantitative structure-activity relationships (QSAR)," Expert Opin. Drug Discov., vol. 13, no. 12, pp. 1075–1089, Dec. 2018, doi: 10.1080/17460441.2018.1542428.

[15] A. Rácz, D. Bajusz, and K. Héberger, "Intercorrelation Limits in Molecular Descriptor Preselection for QSAR/QSPR," Mol. Inform., vol. 38, no. 8–9, p. 1800154, Aug. 2019, doi: 10.1002/MINF.201800154.

[16] S. Shayanfar and A. Shayanfar, "Comparison of various methods for validity evaluation of QSAR models," BMC Chemistry 2022 16:1, vol. 16, no. 1, pp. 63-, Aug. 2022, doi: 10.1186/S13065-022-00856-4.

[17] P. M. Khan and K. Roy, "Current approaches for choosing feature selection and learning algorithms in quantitative structure–activity relationships (QSAR)," Expert Opin. Drug Discov., vol. 13, no. 12, pp. 1075–1089, Dec. 2018, doi: 10.1080/17460441.2018.1542428.

[18] K. Otmanine et al., "Anti-malarial evaluation of some bioactive plant compounds: An integrated computational approach combining QSAR and molecular docking," Comput. Biol. Chem., vol. 123, p. 108956, Aug. 2026, doi: 10.1016/J.COMPBIOLCHEM.2026.108956.

[19] N. F. Rahman, "Potensi Ekstrak Daun Jambu Biji (Psidium guajava L.) sebagai Inhibitor Tirosinase: Studi In Silico dan Prediksi ADMET," ILLEA: Journal of Health Sciences, Public Health and Medicine, vol. 1, no. 3, pp. 100–108, 2025.

[20] A. Cherkasov et al., "QSAR modeling: where have you been? Where are you going to?," J. Med. Chem., vol. 57, no. 12, pp. 4977–5010, Jun. 2014, doi: 10.1021/JM4004285.

[21] A. Daina, O. Michielin, and V. Zoete, "SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules," Scientific Reports 2017 7:1, vol. 7, no. 1, pp. 42717-, Mar. 2017, doi: 10.1038/srep42717.

[22] S. Shayanfar and A. Shayanfar, "Comparison of various methods for validity evaluation of QSAR models," BMC Chemistry 2022 16:1, vol. 16, no. 1, pp. 63-, Aug. 2022, doi: 10.1186/S13065-022-00856-4.

[23] N. Chirico and P. Gramatica, "Real External Predictivity of QSAR Models: How To Evaluate It? Comparison of Different Validation Criteria and Proposal of Using the Concordance Correlation Coefficient," *J. Chem. Inf. Model.*, vol. 51, no. 9, pp. 2320–2335, Sep. 2011, doi: 10.1021/CI200211N.

[24] J. H. Kim, "Multicollinearity and misleading statistical results," *Korean J. Anesthesiol.*, vol. 72, no. 6, p. 558, Dec. 2019, doi: 10.4097/KJA.19087.

[25] N. Shrestha, "Detecting Multicollinearity in Regression Analysis," *Am. J. Appl. Math. Stat.*, vol. 8, no. 2, pp. 39–42, Jun. 2020, doi: 10.12691/AJAMS-8-2-1.

[26] C. Camilleri, U. Alter, and R. A. Cribbie, "Identifying Influential Observations in Multiple Regression," *Quant. Method. Psychol.*, vol. 20, no. 2, pp. 96–105, Jul. 2024, doi: 10.20982/TQMP.20.2.P096.

[27] T. T. Wager, X. Hou, P. R. Verhoest, and A. Villalobos, "Central Nervous System Multiparameter Optimization Desirability: Application in Drug Discovery," *ACS Chem. Neurosci.*, vol. 7, no. 6, pp. 767–775, Jun. 2016, doi: 10.1021/ACSCHEMNEURO.6B00029.

[28] L. G. Ferreira, R. N. Dos Santos, G. Oliva, and A. D. Andricopulo, "Molecular Docking and Structure-Based Drug Design Strategies," Molecules 2015, Vol. 20, Pages 13384-13421, vol. 20, no. 7, pp. 13384–13421, Jul. 2015, doi: 10.3390/MOLECULES200713384.

[29] N. S. Pagadala, K. Syed, and J. Tuszynski, "Software for molecular docking: a review," Biophys. Rev., vol. 9, no. 2, pp. 91–102, Apr. 2017, doi: 10.1007/S12551-016-0247-1.

[30] O. A. Raevsky, D. E. Polianczyk, and O. E. Raevskaja, "Binary Classification of Blood-Brain Barrier Penetration by the Logistic Regression Method," Biomedical Chemistry: Research and Methods, vol. 1, no. 3, pp. e00065–e00065, Sep. 2018, doi: 10.18097/BMCRM00065.

[31] G. Xiong et al., "ADMETlab 2.0: an integrated online platform for accurate and comprehensive predictions of ADMET properties," Nucleic Acids Res., vol. 49, no. W1, pp. W5–W14, Jul. 2021, doi: 10.1093/NAR/GKAB255.

[32] D. E. V. Pires, T. L. Blundell, and D. B. Ascher, "pkCSM: Predicting Small-Molecule Pharmacokinetic and Toxicity Properties Using Graph-Based Signatures," J. Med. Chem., vol. 58, no. 9, pp. 4066–4072, May 2015, doi: 10.1021/ACS.JMEDCHEM.5B00104.

[33] I. Blažević et al., "Glucosinolate structural diversity, identification, chemical synthesis and metabolism in plants," Phytochemistry, vol. 169, Jan. 2020, doi: 10.1016/j.phytochem.2019.112100.