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Article

# MOLECULAR DOCKING OF LION'S MANE BIOACTIVE COMPOUNDS AS BETA-SECRETASE INHIBITORS FOR ALZHEIMER'S DISEASE

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**ABSTRACT**

**Objectives:** Lion's Mane is a medicinal mushroom that has attracted significant interest due to its proposed neuroprotective activity. This has led to research into its potential uses in neurological diseases such as Alzheimer's. Alzheimer's disease is a neurodegenerative disease characterized by a progressive decline in mental function. Pathologically, the disease is associated with the deposition of amyloid-beta plaques and neurofibrillary tangles within the brain. Beta-secretase is a key enzyme in the amyloid genesis pathway. Therefore, beta-secretase is considered a promising therapeutic target to halt the development and progression of Alzheimer's disease.

**Purpose:** This research aims to explore the effect of the active compounds hericinone present in Lion's Mane mushroom as a beta-secretase inhibitor by performing the docking process using Molegro Virtual Docker.

**Methods:** This study conducted a docking study of beta-secretase and some hericinones. Among them, the optimal binding energy of hericinones B was determined after meeting the drug-drug similarity criteria.

**Results:** The binding energy of the target beta-secretase to hericinone B was calculated to be −168 kcal/mol. This energy compares favorably with the binding energy of known ligand complexes to the target, which is −164 kcal/mol. The docking process involving the selected beta-secretase enzyme (Protein Data Bank ID-5QCU) was performed using Molegro. This process is consistent with the five Lipinski guidelines and demonstrates the drug's likelihood and bioavailability.

**Conclusion:** Hericinone B was found to be the best compound that achieved better inhibition energy than the basic ligand. This is due to its chemical structural characteristics, its combination of lipophilic and polar regions, its hydrogen bonding ability, and the specific spatial arrangement of functional groups, which likely allows it to bind to a specific target.

**Keywords:** Lion's mane, Alzheimer's disease, Beta-secretase, Hericenone, Molegro virtual docker.

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## INTRODUCTION

Alzheimer's disease is not just a disease; it is a tragic experience for millions of people around the world. It is a degenerative brain disease that leads to loss of memory, thinking, social, and behavioral abilities. It is considered the leading cause of dementia.

The mechanism of Alzheimer's disease is multifactorial, including the accumulation of tau protein, where the tau protein accumulates abnormally in nerve cells, forming neurofibrillary tangles. This disrupts the internal structure of the cell and leads to cell death. Another cause is the formation of amyloid plaques, where amyloid plaques consist of a protein called beta-amyloid that accumulates between nerve cells. These plaques interfere with cellular communication and lead to neuronal damage. Chronic inflammation has also been shown to play a role in Alzheimer's disease. Alzheimer's patients experience delays in diagnosis, making it imperative to develop new medications and therapeutic strategies to improve clinical response and treatment outcomes [1,2].

Previous studies have shown that the enzyme beta-secretase plays a role in the pathogenesis of Alzheimer's disease. This enzyme, also known as BACE1, is one of the proteins that break down amyloid precursor protein. This breakdown leads to the production of protein fragments, such as beta-amyloid, which causes the deposition of amyloid plaques characteristic of Alzheimer's disease. Several studies reveal that increased beta-secretase activity leads to the production of higher levels of beta-amyloid, increasing the risk of Alzheimer's disease. Because beta-secretase is involved in the formation of amyloid plaques, inhibiting it is a target for therapeutic intervention in Alzheimer's disease [3,4].

Lion's Mane Mushroom has a funny name that belies a natural marvel that can be the key to recovering from most diseases, especially the nasty Alzheimer's disease. The lion's mane mushroom has a set of strange characteristics that have made it the focus of researchers and physicians [5].

Experiments have shown that compounds such as hericenones in lion's mane mushrooms improve the growth of nerve cells and the formation of new connections between them, improving memory and mental function. It has antioxidants that help protect nerve cells against free radical damage, which is key to the creation of Alzheimer's disease. Lion's mane mushrooms may help increase blood flow to the brain, providing oxygen and nutrients the brain needs for healthy function [6,7].

Therefore, this research will explore the effect of hericenone active compounds of the lion's mane mushroom as a beta-secretase enzyme inhibitor by performing a docking procedure using the Molegro virtual docker program.

## METHODS

### Enzyme preparation

The 3D structure of beta-secretase enzyme (protein data bank [PDB] ID-5QCU) was retrieved from the PDB with a resolution factor of 1.95 Å. We defined the active site of based on the X-ray complex structure of beta-secretase enzyme (BACE) and BMC022[(2R,4S)-N-butyl-4-[(5S,8S,10R)-5,10-dimethyl-3,3,6-trioxo-3lambda~6~-thia-7-azabicyclo[11.3.1]heptadeca-1(17),13,15-trien-8-yl]-4-hydroxy-2-methylbutanamide] (Fig. 1) [8].

### Ligand preparation

Chemical structures were retrieved from PubChem database. The mol2 structural formats of all the 10 components were generated from the Marvin Sketch program.

The set of ligand molecules selected for this study was 9 hericenone compounds from lion's mane mushroom and which have been selected after an extensive literature survey that was performed to hunt for hericenone that promotes nerve growth factor (NGF) synthesis *in vitro* through PubMed site [9].

Hericenones have aroused considerable interest recently due to their potential beneficial effects on stimulating NGF, potential protection against neurodegenerative diseases, and possible aid in nerve regeneration.

They also have been reported to have anti-microbial, anti-inflammatory, and anti-oxidant activities [10], and hericenone displays low toxicity and no serious adverse effects in most human trials [11,12].

Table 1 shows the chemical structure of 9 hericenone with the references. These phytochemicals were screened in silico for their inhibitory activity against the selected enzyme molecules, beta-secretase enzyme.

Therefore, we found a natural compound that has the inhibitory properties of the enzyme (BACE) and with properties better than BMC022. It is considered safer for the human body.

### Docking

In this research, we use the Molegro program, which was used in various previous research, and it is available for free.

#### *Molegro virtual docker 6.0*

Molegro virtual docker stands out as a sophisticated software solution for *in silico* drug design, primarily focusing on accurate and efficient molecular docking. The program incorporates advanced algorithms, including the MolDock Score and GRID scoring functions, to predict ligand-protein interactions with high reliability. Beyond docking, Molegro provides functionalities for virtual screening, ligand library management, and visualization of molecular complexes, empowering researchers to identify and prioritize potential drug leads Table 2.

Molegro virtual docker generates enzyme–compound interaction profiles of electrostatic (E), hydrogen-bonding (H), and Van der Waal's (V) interactions. Based on these profiles and compound structures, Molegro virtual docker infers the pharmacological interactions, and Table 2 shows the parameters used in the modeling process [23].

The link energy according to the function MolDock is calculated from the following formula:

$$Etotal=Einter+Eintra$$

#### *Active pocket identification*

The enzyme pockets were identified by MVD software. The selected pocket with a basic ligand was E51-401 and selected pocket size was 2866.18 Å3(Fig. 2) .

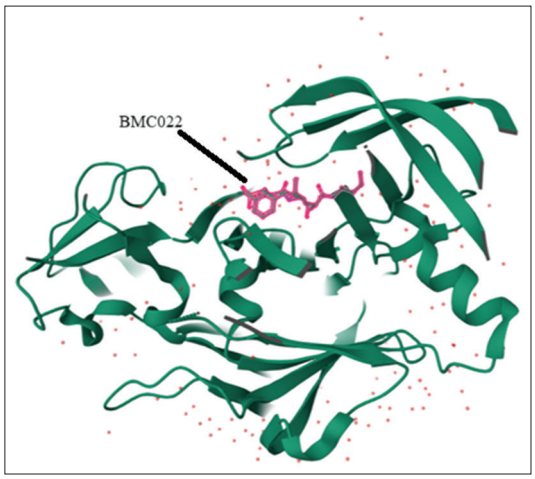



**Fig. 1: Crystal structure of BACE complex with BMC022**

## RESULTS AND DISCUSSION

### Post docking analysis

*In silico*, docking studies were carried out using Molegro. The results showed that all the selected hericenones presented binding energy ranging from −113 kcal/mol to −168 kcal/mol compared to the reference (−164 kcal/mol). Therefore, these molecular docking analyses could lead to further development of potent beta-secretase enzyme inhibitors for the prevention and treatment of Alzheimer's disease caused by beta-amyloid accumulation.

Table 3 summarizes the results of the docking study based on binding energies. The molecular docking procedure identified the energy representing the best binding energy of inhibitors of this enzyme.

It was found that compound hericenone B gave the best binding energy among the hericenones, as its binding energy was better than that of the reference compound. Fig. 2 shows the binding of the reference compound within the active pocket. We note that it formed hydrogen bonds with the amino acids Thr232, Thr231, Gln73, Gly11, and van der Waals bonds with Gly230, Gly11, while Fig. 3 shows compound hericenone B formed hydrogen bonds with Gln73 and van der Waals bonds with the amino acids Thr72, Thr231, Tyr72, Asp32, Leu30, Gly230, and Gln73.

### Lipinski's guidelines

The ability to predict the pharmacological properties of compounds based on their structure is important. Some specific rules apply to predict activity. Lipinski's guidelines of five are a refinement of drug-likeness and are used to predict whether a chemical compound will have pharmacological or biological activity as an orally active drug in humans. This rule was formulated by Christopher A. Lipinski in 1997, based on the observation that most medication drugs are relatively small, lipophilic molecules. The Lipinski "guidelines of five" states that compounds are likely to have good absorption and permeation in

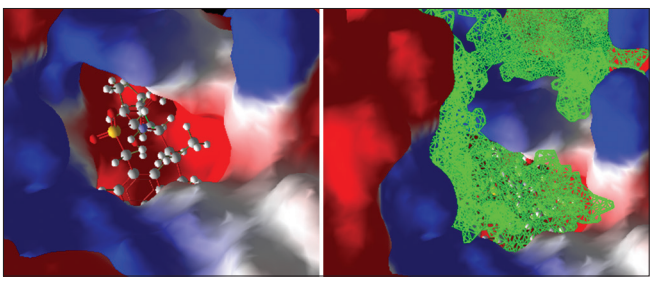
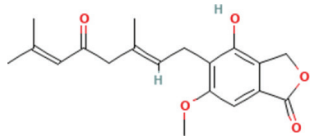
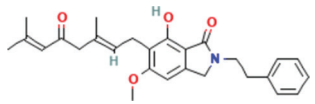
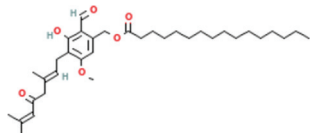
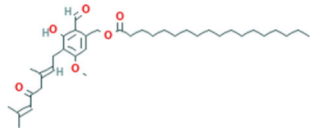
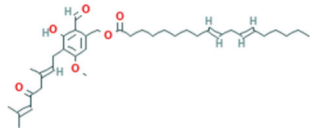
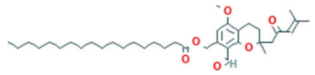
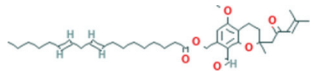
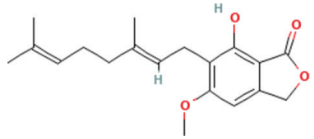


**Fig. 2: Active pocket inside the basic ligament ligand**

**Table 1: The structure of hericenone compounds used in this study**

| S. No. | Chemical name | IUPAC name | Compound structure | References |
|---|---|---|---|---|
| 1. | Hericenone A | 5-[(2*E*)-3,7-dimethyl-5-oxoocta-2,6-dienyl]-4-hydroxy-6-methoxy-3*H*-2-benzofuran-1-one |  | [13] |
| 2. | Hericenone B | 6-[(2*E*)-3,7-dimethyl-5-oxoocta-2,6-dienyl]-7-hydroxy-5-methoxy-2-(2-phenylethyl)-3*H*-isoindol-1-one |  | [14] |
| 3. | Hericenone C | [4-[(2*E*)-3,7-dimethyl-5-oxoocta-2,6-dienyl]-2-formyl-3-hydroxy-5-methoxyphenyl] methyl hexadecanoate |  | [15] |
| 4. | Hericenone D | [4-[(2*E*)-3,7-dimethyl-5-oxoocta-2,6-dienyl]-2-formyl-3-hydroxy-5-methoxyphenyl] methyl octadecanoate |  | [16] |
| 5. | Hericenone E | [4-[(2*E*)-3,7-dimethyl-5-oxoocta-2,6-dienyl]-2-formyl-3-hydroxy-5-methoxyphenyl] methyl (9*E*,12*E*)-octadeca-9,12-dienoate |  | [17] |
| 6. | Hericenone G | [8-formyl-5-methoxy-2-methyl-2-(4-methyl-2-oxopent-3-enyl)-3,4-dihydrochromen-7-yl] methyl octadecanoate |  | [18] |
| 7. | Hericenone H | [8-formyl-5-methoxy-2-methyl-2-(4-methyl-2-oxopent-3-enyl)-3,4-dihydrochromen-7-yl] methyl (9E,12*E*)-octadeca-9,12-dienoate |  | [19] |
| 8. | Hericenone J | 6-[(2*E*)-3,7-dimethylocta-2,6-dienyl]-7-hydroxy-5-methoxy-3*H*-2-benzofuran-1-one |  | [20] |

(*Contd...*)

**Table 1: (*Continued*)**

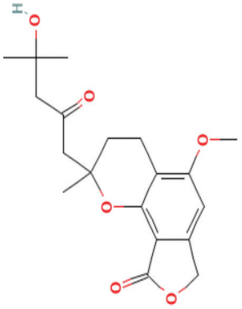
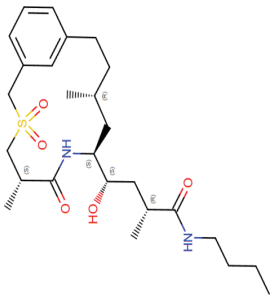
| S. No. | Chemical name | IUPAC name | Compound structure | References |
|---|---|---|---|---|
| 9. | Hericenone K | 2-(4-hydroxy-4-methyl-2-oxopentyl)-5-methoxy-2-methyl-4,7-dihydro-3*H*-furo[3,4-h] chromen-9-one |  | [21] |
| 10. | Ligand with Enzyme | (2R,4S)-N-butyl-4-[(5S,8S,10R)-5,10-dimethyl-3,3,6-trioxo-3lambda~6~-thia-7-azabicyclo[11.3.1] heptadeca-1 (17),13,15-trien-8-yl]-4-hydroxy-2-methylbutanamide |  | [8, 22] |

**Table 2: Parameters of Molegro virtual docker**

| Parameters | Value |
|---|---|
| Scoring function | MolDock (GRID) |
| Grid resolution (A°) | 0.80 |
| Binding site radius (A°) | 17 |
| Searching algorithm | MolDock optimizer |
| Number of runs | 10 |
| Max iterations | 2000 |
| Max population size | 50 |
| Energy threshold | 100 |
| Simplex evaluation (max steps) | 300 |
| Neighbor distance factor | 1 |

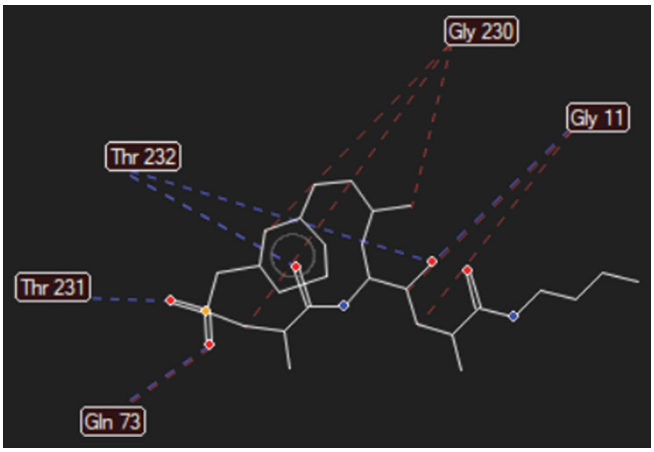



**Fig. 3: Binding of the reference compound within the active pocket of the active site by hydrogen bonds (blue) and van der Waals bonds (red) in the active site**

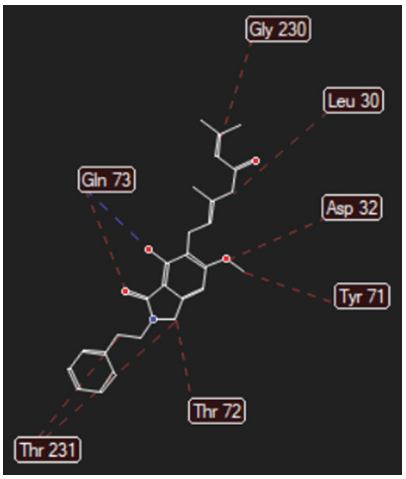



**Fig. 4: Binding of the hericenone B compound within the active pocket of the active site by hydrogen bonds (blue) and van der Waals bonds (red) in the active site**

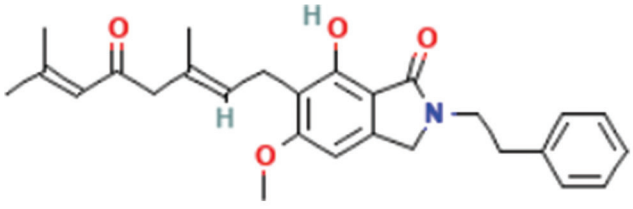


**Fig. 5: The structure of hericenone B**

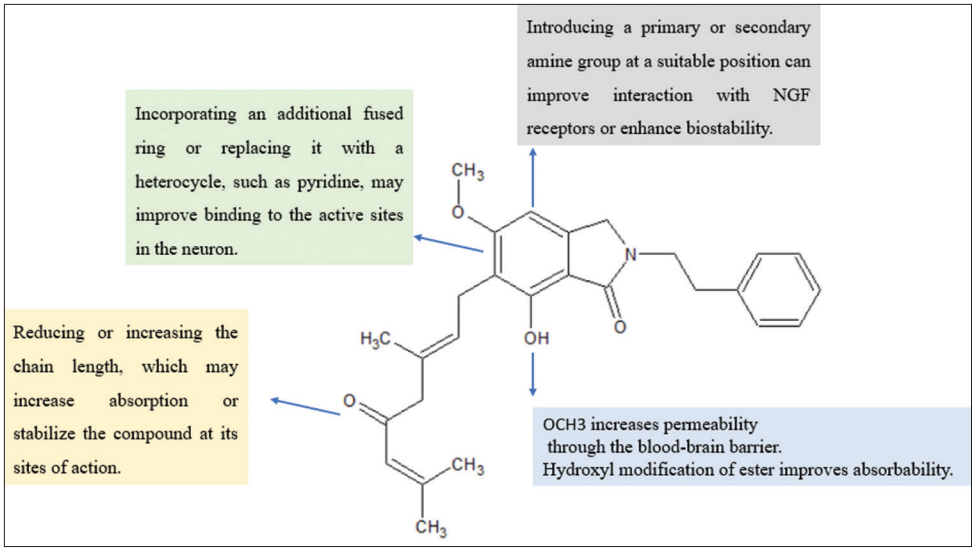



**Fig. 6: Modifications to the chemical structure of hericenone B are proposed to improve efficacy**

**Table 3: The result of the ten compounds**

| Ligand | Van der Waals interaction | H-BOND | Energy docking |
|---|---|---|---|
| Ligand with Enzyme | Gly230, Gly11 | Thr232, Thr231, Gln73, Gly11 | −164 (Kcal/mol) |
| Hericenone A | Gly13, Gly 230, Iie118 | Gln73 | −130 (Kcal/mol) |
| Hericenone B | Thr72, Thr231, Tyr72, Asp32, Leu30, Gly230, Gln73 | Gln73 | −168 (Kcal/mol) |
| Hericenone C | Thr232, Gly11m Tyr71m Gly34, Tyr198, Thr72, Thr231 | Asp32, Thr72, Thr231 | −113 (Kcal/mol) |
| Hericenone D | Thr232, Gly11, Tyr71, Gly34, Tyr198, Thr72, Thr231, Trp115, Ile110 | Thr72 | −120 (Kcal/mol) |
| Hericenone E | Val69, Gly 230, Tyr71, Gly34, Tyr198, Gln12, Thr231, Ile110 | Gly156 | −139 (Kcal/mol) |
| Hericenone G | Ala157, Val361, Glu339, Gln303 | Gln73, Arg235 | −121 (Kcal/mol) |
| Hericenone H | Asp317, Pro308, Glu310, Ser169 | Asp131 | −138 (Kcal/mol) |
| Hericenone J | Tyr72, Iie118, Asp32, Val69, Gln73 | Gln73 | −139 (Kcal/mol) |
| Hericenone K | Asp228, Tyr71 | Thr232, Thr231, Gln73, Arg235, Thr72 | −144 (Kcal/mol) |

biological systems and are more likely to be successful drug candidates if they meet the following criteria:

1. The molecular weight is <500 mg/mol.
2. Has a high lipophilicity (log p<5).
3. Hydrogen bond donors <5.
4. Hydrogen bond acceptor is <10.

The rule describes molecular properties important for pharmacokinetics in the human body, including their absorption, distribution, metabolism, and excretion ("ADME"). The rule is important for drug development where a pharmacologically active lead structure is optimized step-wise for increased activity, selectivity, and drug-like properties as described by Lipinski's guidelines [24-26].

**Veber rule**

In particular, compounds that meet only the two criteria of

a. Rotatable bond count ≥10.
b. Polar surface area equal to or <140° A2 is predicted to have good oral bioavailability [24-26]. The molecules were prioritized to follow Lipinski's guidelines of five, and Veber rule, based on the drug-like properties, are listed in Table 4.

From Table 4, it is clear that compound hericenone B fulfills all the properties of Lipinski and Veber. This makes compound B a promising compound for use in treating and preventing the occurrence and development of Alzheimer's disease, as it has good pharmacokinetics in the body.

**Chemical structure of hericenone B**

Hericenone B features a complex polycyclic structure with several key functional groups and structural motifs such as isoindolone ring system, 7-Hydroxy and 5-Methoxy Substituents, and 6-[(2E/Z)-3,7-dimethyl-5-oxoocta-2,6-dienyl] Side Chain [27,28], as shown in Fig. 5.

**Relationship between structure and effect hericenone B to inhibit the beta-secretase enzyme**

The ability of hericenone B to inhibit beta-secretase enzyme is likely a result of the molecule's overall three-dimensional structure and the specific arrangement of its functional groups, allowing it to interact with the target involved in the Alzheimer's disease progression. While the exact mechanism is not fully elucidated, we can infer some potential structure-activity relationships:

*Lipophilicity and membrane permeability*

The presence of the phenylethyl group and the isoprenoid side chain contributes to the overall lipophilicity of hericenone B, as indicated by its high logP value. This lipophilicity is crucial for its ability to potentially cross cell membranes, including the blood-brain barrier (BBB), to reach its targets within the nervous system.

*Hydrogen bonding potential*

The hydroxyl group (-OH) on the isoindolone ring can act as both a hydrogen bond donor and acceptor, which is important for specific interactions with amino acid residues in the binding site of its target. The carbonyl groups (both in the isoindolone ring and the side chain) can act as hydrogen bond acceptors, while the carbonyl oxygen of the lactam in the isoindolone ring could theoretically participate in hydrogen bonding as an acceptor.

*Specific spatial arrangement*

The overall shape and the spatial arrangement of the different functional groups are critical for fitting into the binding pocket of its

**Table 4: The Lipinski's and Veber properties of the hericenone compounds**

| Chemical name | Molecular formula | MW g/mol 500< | X Log *P* 3-5 | HD 5< | HA 10< | RB 10< | (PSA) Å² 140< |
|---|---|---|---|---|---|---|---|
| Hericenone A | $C_{19}H_{22}O_5$ | 330.4 | 3.6 | 1 | 5 | 6 | 72.8 |
| Hericenone B | $C_{27}H_{31}NO_4$ | 433.5 | 5.7 | 1 | 4 | 9 | 66.8 |
| Hericenone C | $C_{35}H_{54}O_6$ | 570.8 | 11.2 | 1 | 6 | 24 | 89.9 |
| Hericenone D | $C_{37}H_{58}O_6$ | 598.9 | 12.3 | 1 | 6 | 26 | 89.9 |
| Hericenone E | $C_{37}H_{54}O_6$ | 594.8 | 10.7 | 1 | 6 | 24 | 89.9 |
| Hericenone G | $C_{37}H_{58}O_6$ | 598.9 | 11.2 | 0 | 6 | 24 | 78.9 |
| Hericenone H | $C_{37}H_{54}O_6$ | 594.8 | 9.5 | 0 | 6 | 22 | 78.9 |
| Hericenone J | $C_{19}H_{24}O_4$ | 316.4 | 5.3 | 1 | 4 | 6 | 55.8 |
| Hericenone K | $C_{19}H_{24}O_6$ | 348.4 | 1.5 | 1 | 6 | 5 | 82.1 |
| Ligand with Enzyme | $C_{26}H_{42}N_2O_5S$ | 494.687 | 3.5 | 3 | 5 | 7 | 121 |

PSA: Polar surface area, MW: Molecular weight, HD: H bond donor, HA: H bond acceptor, RB: Rotatable bonds, MR: Molar refractivity. Calculated by https://pubchem.ncbi.nlm.nih.gov/search/search.cgi. Calculated by ACD (available chemical directory)

biological target. The rigidity provided by the isoindolone core and the specific geometry of the side chain (including the double bonds and ketone) likely contribute to its specific interactions [29-32].

**Modifications to the chemical structure of hericenone B proposed to improve efficacy**

Hericenone B is a natural compound extracted from the *Hericium erinaceus* fungus. It is known for its potential neuroprotective effects, particularly in stimulating NGF. To enhance its efficacy, the following modifications to its chemical structure may be considered, based on drug design principles:

*Substitution or modification of hydroxy groups (OH)*

For example, replacing the OH group on the aromatic ring with a methoxy group ($-OCH_3$) may increase permeability through the BBB, which is critical for neuroprotection.

*Addition of an amino or alkyl group*

Introducing a primary or secondary amine group at a suitable position can improve interaction with NGF receptors or enhance biostability.

*Modification of the long (oleophilic) side chain*

Reducing or increasing the chain length according to the balance between hydrophilicity and lipophilicity may increase absorption or stabilize the compound at its sites of action.

Alternatively, some carbons in the chain can be replaced with unsaturated double bonds or rings to reduce metabolic degradation.

*Modifying the aromatic core*

Incorporating an additional fused ring or replacing it with a heterocycle, such as pyridine, may improve binding to the active sites in the neuron.

*Converting it to a prodrug derivative*

Hericenone B is attached to a hydrolysable group (such as an ester) to improve absorption, and the active compound is subsequently released [29-32].

Thus, according to the proposed expectations, by modifying the chemical structure, we can obtain a compound with better activity and greater inhibition of the enzyme.

## CONCLUSION

By studying the effect of several hericenone compounds as beta-secretase enzyme inhibitors using the Molgro program, it was found that compound hericenone B is the best compound that achieved better inhibition energy than the basic ligand. This is due to its chemical structure's properties, its combination of lipophilic and polar regions, hydrogen bonding capabilities, and specific spatial arrangement of functional groups, which likely allows it to bind to a particular target involved. By studying the effect of some modifications to the chemical structure according to the rules of drug design, we recommend the following studies: To study the effect of these modifications on the chemical structure as an inhibitor of the enzyme beta-secretase, and to move toward synthesizing the best chemical formula and further research is needed to elucidate the precise molecular mechanisms of action.

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## AUTHORS' CONTRIBUTIONS

Conceptualization: Noura Berakdar. Data Curation: Noura Berakdar. Formal analysis: Noura Berakdar. Funding Acquisition: Sundus J Yaseen. Methodology: Noura Berakdar. Software: Noura Berakdar. Supervision: Noura Berakdar and Sundus J Yaseen. Validation: Noura Berakdar, and Azhar Malek. Writing-Original draft: Noura Berakdar, Writing-review and editing: Azhar Malek, and Mohmad Eiad Alraai.

## CONFLICTS OF INTEREST

There are no known conflicts of interest associated with the publication, and there has been no significant financial support for this work that could have influenced its outcome.

## REFERENCES

1. Kocahan S, Doğan Z. Mechanisms of Alzheimer's disease pathogenesis and prevention: The brain, neural pathology, N-methyl-D-aspartate receptors, tau protein and other risk factors. Clin Psychopharmacol Neurosci 2017;15:1-8.
2. Ju Y, Tam KY. Pathological mechanisms and therapeutic strategies for Alzheimer's disease. Neural Regen Res 2022;17:543.
3. Cole SL, Vassar R. The Alzheimer's disease Beta-secretase enzyme, BACE1. Mol Neurodegener 2007;2:22.
4. Hampel H, Vassar R, De Strooper B, Hardy J, Willem M, Singh N, *et al*. The b-secretase BACE1 in Alzheimer's disease. Biol Psychiatry 2020;89:745-56.
5. Banerjee S, Gupta S, Raj R, Gupta M. Unlocking the potential of Lion's mane mushroom (*Hericium erinaceus*). J Appl Natural Sci 2024;16:39-50.
6. Cha S, Bell L, Shukitt-Hale B, Williams CM. A review of the effects of mushrooms on mood and neurocognitive health across the lifespan. Neurosci Biobehav Rev 2024;158:105548.
7. Contato AG, Conte-Junior CA. Lion's mane mushroom (*Hericium erinaceus*): A neuroprotective fungus with antioxidant, anti-inflammatory, and antimicrobial potential-a narrative review. Nutrients 2025;17:1307.
8. Available from: https://www.rcsb.org/structure/5qcu
9. Kawagishi, H, Ando M, Shinba K, Sakamoto H, Yoshida S, Ojima F, *et al*. Chromans, hericenones F, G and H from the mushroom *Hericium erinaceum*. Phytochemistry 1992;32:175-8.
10. Ma BJ, Shen JW, Yu HY, Ruan Y, Wu TT, Zhao X. Hericenones and erinacines: Stimulators of nerve growth factor (NGF) biosynthesis in

*Hericium erinaceus*. Mycology 2010;1:92-8.
11. Lee LY, Li IC, Chen WP, Tsai YT, Chen CC, Tung KC. Thirteen-week oral toxicity evaluation of erinacine A enriched lion's mane medicinal mushroom, *Hericium erinaceus* (*Agaricomycetes*), mycelia in sprague-dawley rats. Int J Med Mushrooms 2019;21:401-11.
12. Muhanna M, Lund I, Bromberg M, Wicks P, Benatar M, Barnes B, *et al*. ALSUntangled #73: Lion's Mane. Amyotroph Lateral Scler Frontotemporal Degener 2023;25:420-3.
13. Available from: https://pubchem.ncbi.nlm.nih.gov/compound/hericenone-a#section=structures
14. Available from: https://pubchem.ncbi.nlm.nih.gov/compound/hericenone-b
15. Available from: https://pubchem.ncbi.nlm.nih.gov/compound/hericenone-c
16. Available from: https://pubchem.ncbi.nlm.nih.gov/compound/hericenone-d#section=computed-descriptors
17. Available from: https://pubchem.ncbi.nlm.nih.gov/compound/hericenone-e
18. Available from: https://pubchem.ncbi.nlm.nih.gov/compound/hericenone-g#section=3d-status
19. Available from: https://pubchem.ncbi.nlm.nih.gov/compound/hericenone-h
20. Available from: https://pubchem.ncbi.nlm.nih.gov/compound/hericenone-j
21. Available from: https://pubchem.ncbi.nlm.nih.gov/compound/hericenone-k
22. Available from: https://pubchem.ncbi.nlm.nih.gov/compound/69007077#section=computed-properties
23. Bitencourt-Ferreira G, De Azevedo WF Jr. Molegro virtual docker for docking. Methods Mol Biol 2019;2053:149-67.
24. Thomas G. Medicinal Chemistry. 2nd ed. England: University of Portsmouth; 2015. p. 9-10.
25. Kerns EH, Di L. Drug-like Properties: Concepts, Structure Design and Methods: from ADME to Toxicity Optimization. Amsterdam: Academic Press is an Imprint of Elsevier; 2015. p. 6-120.
26. Lipinski CA, Lombardo F, Dominy BW, Feeney PJ. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Adv Drug Deliv Rev 2001;46:3-26.
27. Lin G, Liu W, Zhang F, Linhardt RJ, Wang X. Bioactive substances in *Hericium erinaceus* and their biological properties: A review. Food Sci Hum Wellness 2024;13:1825-44.
28. Kobayashi S, Tamanoi H, Hasegawa Y, Segawa Y, Masuyama A. Divergent synthesis of bioactive resorcinols isolated from the fruiting bodies of *Hericium erinaceum*: Total syntheses of hericenones A, B, and I, hericenols B-D, and erinacerins A and B. J Org Chem 2014;79:5227-38.
29. Diling C, Tianqiao Y, Jian Y, Chaoqun Z, Ou S, Yizhen X. Docking studies and biological evaluation of a potential β-secretase inhibitor of 3-hydroxyhericenone F from *Hericium erinaceus*. Front Pharmacol 2017;8:219.
30. Hunt CE, Turner AJ. Cell biology, regulation and inhibition of beta-secretase (BACE-1). FEBS J 2009;276:1845-59.
31. De Oliveira AM, Rudrapal M. Introduction to drug design and discovery. In: Computer Aided Drug Design (CADD): From Ligand-Based Methods to Structure-Based Approaches. Netherlands: Elsevier; 2022. p. 1-15.
32. Wermuth CG, Ganellin CR, Lindberg P, Mitchard M. Textbook of Drug Design and Discovery. 5th ed. United States: CRC Press; 2016.