Scientific Research Publishing

Advances in Aging Research, 2025, 14(5), 101-114
https://www.scirp.org/journal/aar
ISSN Online: 2169-0502
ISSN Print: 2169-0499

Exploring the Mechanism of the Anti-Aging Effects of *Ganoderma lucidum* Based on Network Pharmacology and Molecular Docking II

Peixuan Hu[1,2*], Jiangwei Tian[3*], Hua Wu[1#]

[1]Department of Nutrition, Nanjing University of Chinese Medicine, Nanjing, China
[2]Nanjing Foreign Language School, Nanjing, China
[3]School of Traditional Chinese Pharmacy, China Pharmaceutical University, Nanjing, China
Email: 170589@njucm.edu.cn

How to cite this paper: Hu, P.X., Tian, J.W. and Wu, H. (2025) Exploring the Mechanism of the Anti-Aging Effects of *Ganoderma lucidum* Based on Network Pharmacology and Molecular Docking II. *Advances in Aging Research*, **14**, 101-114.
https://doi.org/10.4236/aar.2025.145008

Received: July 25, 2025
Accepted: August 24, 2025
Published: August 27, 2025

Abstract

Ganoderma lucidum (Lingzhi) is traditionally recognized for its potential to delay aging, although its precise molecular mechanisms remain unclear. This study employed network pharmacology and molecular docking to investigate the material basis and mechanisms underlying the anti-aging effects of *Ganoderma lucidum*. Active components of *Ganoderma lucidum* and their potential targets were identified using the TCMSP database. Aging-related targets were retrieved from the GeneCards, OMIM, and Disgenet databases. The Venny 2.1 online tool was utilized to obtain common targets shared between the drug and the disease (aging). A "Drug-Components-Aging-Targets" network was constructed using Cytoscape 3.8.2, and a Protein-Protein Interaction (PPI) network was generated via the STRING database. Functional enrichment analysis of Gene Ontology (GO) terms and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways for the drug-disease intersection targets was performed using the DAVID database, with results visualized via the Weishengxin website. Finally, molecular docking validation of the binding affinity between key active components and core targets was conducted using SYBYL-X 2.1.1 software. The results identified 29 active components in G. lucidum, 819 aging-related targets, and 98 overlapping targets. Molecular docking demonstrated strong binding activity between core anti-aging components (including ganoderic acid, ganoderenic acid, and ganodermanondiol) and key targets (such as CYP19A1, NR3C1, and HMGCR). This

*First authors.
#Corresponding author.

study indicates that the anti-aging effects of *Ganoderma lucidum* involve synergistic actions through multiple components, targets, and pathways. These findings provide a theoretical foundation for further exploration of its anti-aging mechanisms.

Keywords

Ganoderma lucidum, Anti-Aging, Network Pharmacology, Molecular Docking, Signaling Pathway

1. Introduction

Aging is a complex biological process characterized by the progressive decline of organismal functions and serves as a primary risk factor for numerous chronic diseases [1], constituting a central cause of human mortality. The global population aged 65 and over currently exceeds 700 million and is projected to reach 1.5 billion by 2050. Within this trend, China's elderly population is expected to surpass 480 million, positioning it as the country with both the highest degree of aging and the largest elderly population worldwide [2]. The mechanisms underlying aging are not yet fully elucidated, with most scholars attributing its onset to factors such as oxidative stress [3], telomere shortening [4], and mitochondrial dysfunction. Existing anti-aging interventions offer limited efficacy and may be accompanied by adverse effects. Consequently, the pursuit of novel therapeutic targets and agents is becoming increasingly critical.

Ganoderma lucidum (Lingzhi), a highly valued medicinal fungus, belongs to the genus *Ganoderma* within the Polyporaceae family of the Basidiomycota phylum. Its use in China dates back centuries, with its properties documented in the ancient pharmacopeia *Compendium of Materia Medica* (Ben Cao Gang Mu), which records its ability to "benefit heart qi, tonify the middle, enhance wisdom, and promote lightening of the body and longevity with prolonged consumption". Revered as a "superior grade" (Shang Pin) herb by generations of physicians, *Ganoderma lucidum* has been confirmed by modern research to contain over 150 active constituents, including triterpenoids, polysaccharides, and adenosine [5]. It exhibits a broad spectrum of pharmacological activities, such as delaying aging [6], modulating immunity, improving metabolism [7], and protecting neural functions [8] [9]. Particularly noteworthy is its ability to activate the SIRT1 longevity protein pathway, scavenge free radicals, and mitigate aging-related inflammation. Its bioactive triterpenoids have been shown to significantly extend the lifespan of model organisms [10] and ameliorate aging-associated cognitive dysfunction [11].

Despite confirmed anti-aging effects and significant research progress, the precise molecular mechanisms through which *Ganoderma lucidum* exerts its anti-aging actions remain incompletely understood. Therefore, this study aims to uti-

lize network pharmacology and molecular docking techniques to investigate these mechanisms, aiming to shed light on the underlying processes and provide a reference for further research.

2. Materials and Methods

2.1. Screening of Active Components and Target Proteins of *Ganoderma lucidum*

The active components of *Ganoderma lucidum* (Lingzhi) were retrieved from the Traditional Chinese Medicine Systems Pharmacology Database and Analysis Platform (TCMSP, https://old.tcmsp-e.com/tcmsp.php) using "*Ganoderma lucidum*" as the search term. The screening criteria were set as oral bioavailability (OB) ≥ 30% and drug-likeness (DL) ≥ 0.18 [1] [12]. OB ≥ 30% ensures adequate absorption and system exposure of the components, and DL ≥ 0.18 ensures screening of molecules with good druggability. This combination provides a reliable candidate molecule for subsequent network pharmacology studies. Potential target proteins for the identified active components were predicted using the Swiss Target Prediction database (http://www.swisstargetprediction.ch/). The species was restricted to *Homo sapiens*, and only targets with a prediction probability greater than zero were retained. Finally, duplicate targets were removed to generate the list of *Ganoderma lucidum* active component-related targets.

2.2. Screening of Aging-Related Targets and Construction of a Common Target Database

Aging-related targets were identified by querying three databases: GeneCards (https://www.genecards.org/), Online Mendelian Inheritance in Man (OMIM, http://www.omim.org/), and DisGeNET (https://disgenet.com/), using "Aging" as the search keyword. From GeneCards, only genes with a relevance score greater than 10 were selected. After removing duplicates, the list of aging-related targets was compiled. The *Ganoderma lucidum*-related targets and the aging-related targets were then uploaded to the Venny 2.1 online tool (https://bioinfogp.cnb.csic.es/tools/venny/) to identify their intersection (common targets). A Venn diagram was generated for visual representation of the overlapping targets.

2.3. Protein-Protein Interaction (PPI) Network Construction and Key Target Screening

The common targets identified in Section 2.2 were imported into the STRING database (https://www.string-db.org/). The "Multiple proteins" option was selected, the species was set to *Homo sapiens*, and a PPI network was constructed. The interaction data in TSV format were downloaded and imported into Cytoscape software (version 3.8.2). The "Centiscape2.2" plug-in was used to automatically calculate the network features, and the thresholds of degree, betweenness centrality and closeness centrality were obtained, and the key targets of *Ganoderma lucidum* anti-aging were screened according to the thresholds.

2.4. Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) Pathway Enrichment Analysis

The common targets identified in Section 2.2 were submitted to the DAVID database (https://david.ncifcrf.gov/) for GO functional enrichment analysis (covering biological process, molecular function, and cellular component) and the Kyoto Encyclopedia of KEGG pathway enrichment analysis. The results were visualized as enrichment bubble plots using the Bioinformatics platform Weishengxin website (http://www.bioinformatics.com.cn/).

2.5. Molecular Docking of *Ganoderma lucidum* Active Components with Key Targets

Based on the preceding network analysis results, the top nine active components ranked by Degree value were selected as ligand molecules. Their 3D structures were downloaded in SDF format from the PubChem database (https://pubchem.ncbi.nlm.nih.gov/) and energy-minimized using Chem3D software (version 23.1.1). The optimized structures were saved in MOL2 format. The top three core targets ranked by Degree value (CYP19A1, NR3C1, HMGCR) were selected as receptor proteins. Their crystal structures were retrieved from the RCSB Protein Data Bank (PDB, https://www.rcsb.org/) in PDB format. Molecular docking simulations were performed using the SYBYL-X software suite (version 2.1.1). The procedure included: preparing the receptor proteins by adding hydrogen atoms and repairing side-chain defects; automatically identifying the binding pocket/active site; and performing the docking analysis using the "Dock Ligand" module.

3. Results

3.1. Screening of *Ganoderma lucidum* Active Components and Target Identification

Screening the TCMSP database yielded 61 *Ganoderma lucidum* active components that met the criteria outlined in Section 2.1. The SMILES structures of these 61 components were submitted to the Swiss Target Prediction database for target prediction, which identified 398 potential disease-related targets. Since some active ingredients did not have targets with a predictive probability greater than 0, they were eliminated, and then 29 active ingredients with key targets were screened out among the remaining active ingredients (e.g., Ganoderenic acid E, MOL011256). Details are presented in Table 1.

Table 1. Active components of *Ganoderma lucidum.*

MOL ID	Chemical Components
MOL000279	Cerevisterol
MOL000282	ergosta-7,22E-dien-3beta-ol
MOL000358	beta-sitosterol
MOL011125	(+)-Ganoderic acid Mf

Continued

MOL011129	methyl (4R)-4-[(5R,10S,13R,14R,17R)-4,4,10,13,14-pentamethyl-3,7,11,15-tetraoxo-2,5,6,12,16,17-hexahydro-1H-cyclopenta[a] phenanthren-17-yl] pentanoate
MOL011137	campesta-7, 22E-dien-3beta-ol
MOL011156	epoxyganoderiol A
MOL011157	epoxyganoderiol B
MOL011159	ergosta-4,6,8(14),22-tetraene-3-one
MOL011160	ergosta-4,7,22-trien-3,6-dione
MOL011162	Ergosta-7,22-dien-3beta-yl palmitate
MOL011172	ganoderan B
MOL011183	(E,6R)-6-[(3S,5R,7S,10S,13R,14R,17R)-3,7-dihydroxy-4,4,10,13,14-pentamethyl-11,15-dioxo-2,3,5,6,7,12,16,17-octahydro-1H-cyclopenta [a]phenanthren-17-yl]-2-methylhept-2-enoic acid
MOL011189	Ganoderic acid DM
MOL011215	(E,5S,6S)-5-acetoxy-6-[(3R,5R,10S,13R,14R,17R)-3-hydroxy-4,4,10,13,14-pentamethyl-2,3,5,6,12,15,16,17-octahydro-1H-cyclopenta [a]phenanthren-17-yl]-2-methylhept-2-enoic acid
MOL011221	ganoderic acid V
MOL011225	Ganoderic acid Y
MOL011229	Ganoderic aldehyde A
MOL011235	Ganoderiol F
MOL011241	Ganodermanondiol
MOL011251	(5R,10S,13R,14R,17R)-17-[(E,2R)-7-hydroxy-6-methylhept-5-en-2-yl]-4,4,10,13,14-pentamethyl-1,2,5,6,12,15,16,17-octahydrocyclopenta[a]phenanthren-3-one
MOL011256	ganolucidic acid E
MOL011258	ganosporelactone B
MOL011266	Lucialdehyde A
MOL011267	Lucialdehyde B
MOL011268	Lucialdehyde C
MOL011270	(4R)-4-[(5R,7S,10S,13R,14R,17R)-7-hydroxy-3,11,15-triketo-4,4,10,13,14-pentamethyl-1,2,5,6,7,12,16,17-octahydrocyclopenta [a] phenanthren-17-yl] valeric acid
MOL011287	Lucidone A
MOL011309	methyl (4R)-4-[(5R,7S,10S,13R,14R,15S,17R)-7,15-dihydroxy-4,4,10,13,14-pentamethyl-3,11-dioxo-2,5,6,7,12,15,16,17-octahydro-1H-cyclopenta[a]phenanthren-17-yl] pentanoate

3.2. Screening of Aging-Related Targets and Identification of *Ganoderma lucidum*-Aging Common Targets

Screening the three databases (GeneCards, OMIM, DisGeNET) as described in

Section 2.2 resulted in 819 unique aging-related targets following duplicate removal. Intersection analysis of the 398 *Ganoderma lucidum* component targets and the 819 aging-related targets using the Venny 2.1 tool identified 98 common targets (Figure 1).

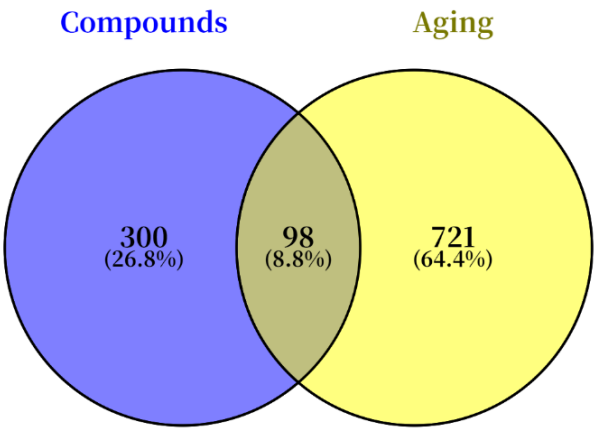

Figure 1. Venn diagram illustrates the intersection between *Ganoderma lucidum* active component targets and aging-related targets.

3.3. Construction of the Protein-Protein Interaction (PPI) Network and Screening of Key Targets

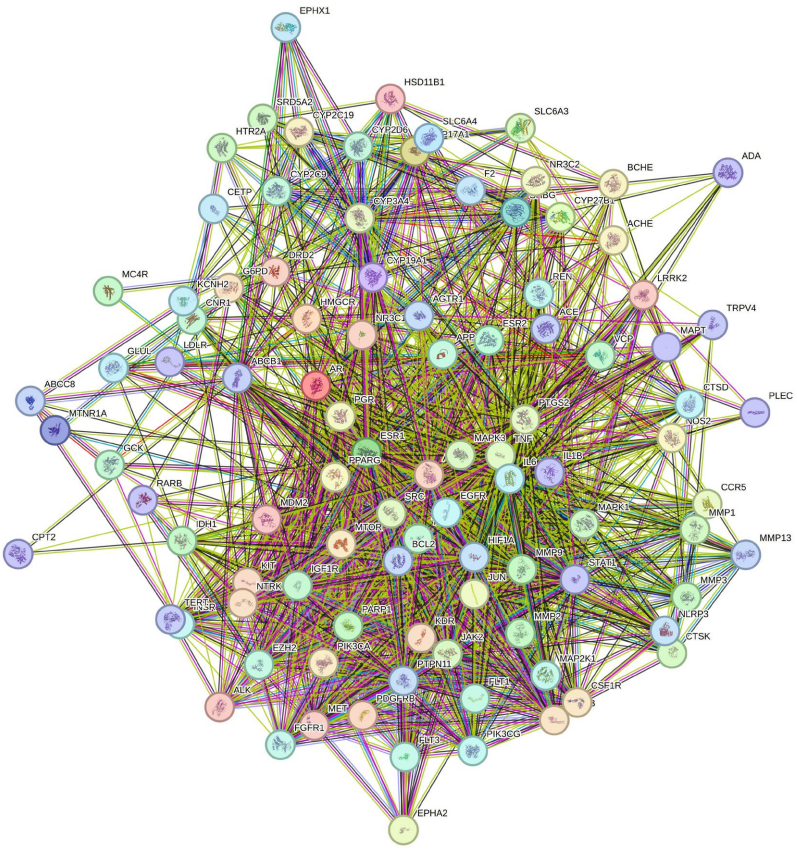

Figure 2. PPI network of common targets shared between *Ganoderma lucidum* and aging.

The 98 common targets were imported into the STRING database to construct a PPI network (Figure 2). Visualization and analysis using Cytoscape 3.8.2 revealed a network comprising 98 nodes and 1,427 edges. Key targets were identified based on network topology parameters (degree, betweenness centrality, and closeness centrality) using the CytoHubba plugin. Nodes exceeding the established thresholds for all three parameters (≥29.1224 for degree, ≥72.2653 for betweenness centrality, and ≥0.006024 for closeness centrality) were designated as key targets. This screening yielded 24 key targets implicated in the anti-aging effects of *Ganoderma lucidum*. Ranked in descending order of degree centrality, the top targets included Cytochrome P450 19A1 (CYP19A1), Nuclear Receptor Subfamily 3 Group C Member 1 (Glucocorticoid Receptor, NR3C1), and 3-Hydroxy-3-Methylglutaryl-CoA Reductase (HMGCR) (Figure 3).

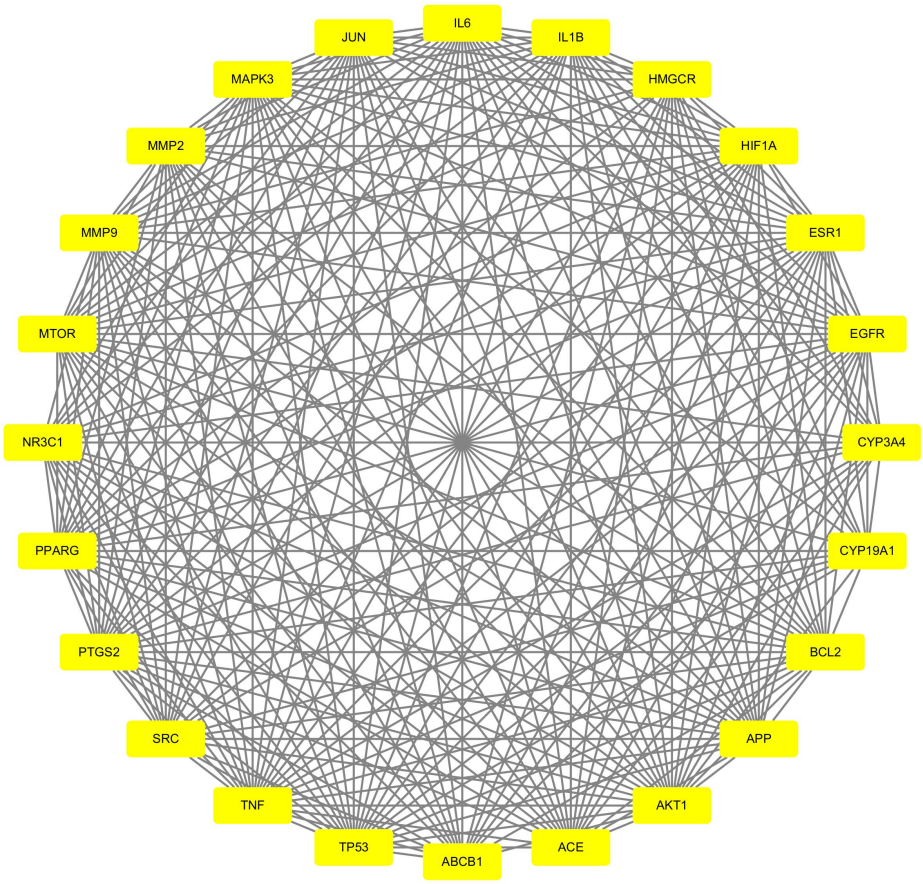

Figure 3. Screening results of key anti-aging targets of *Ganoderma lucidum* based on network topology analysis.

3.4. Construction of the "Active Components-Key Targets" Network

The network relationship between the 29 active components of *Ganoderma lucidum* and the 24 key targets identified in Section 3.3 was visualized using Cytoscape 3.8.2. The resulting network consisted of 53 nodes and 145 edges (Figure 4).

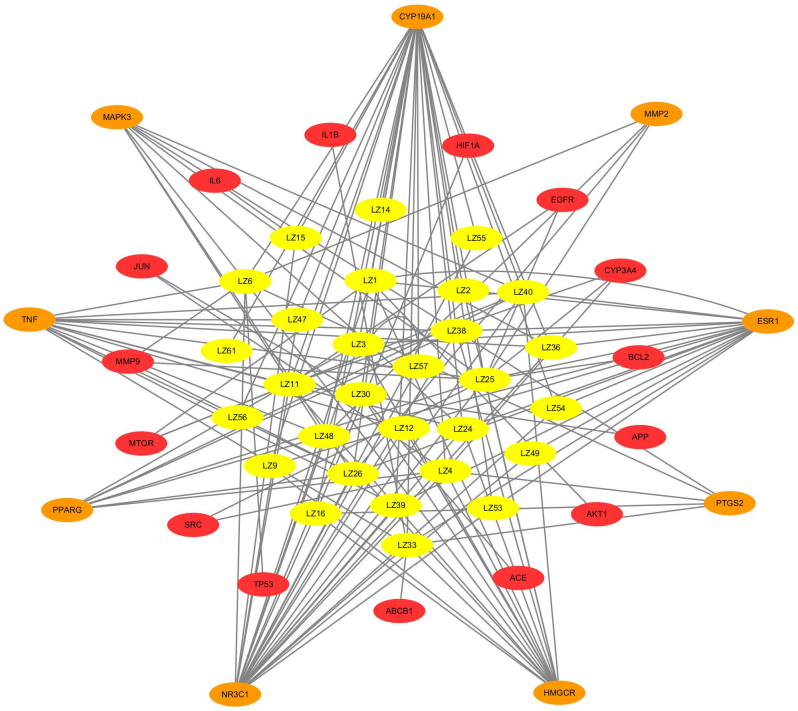

Figure 4. Interaction network depicting the relationships among *Ganoderma lucidum* active components, key targets, and aging.

3.5. GO and KEGG Pathway Enrichment Analysis

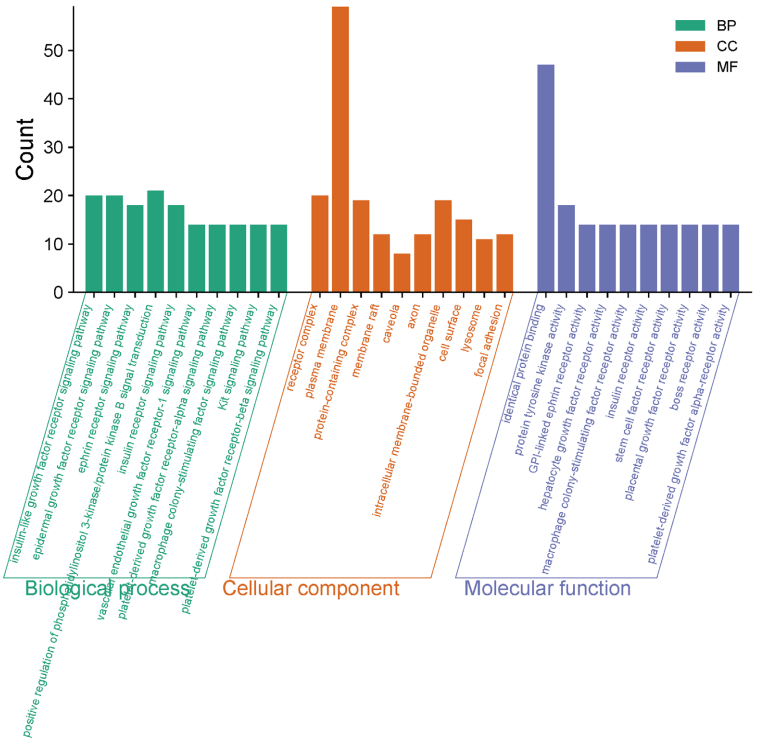

Figure 5. GO functional enrichment analysis of common targets shared between *Ganoderma lucidum* and aging.

To elucidate the anti-aging mechanisms of *Ganoderma lucidum* active components, systematic GO functional and KEGG pathway enrichment analyses were performed on the 98 common targets using the DAVID database. For GO analysis, the top 10 significantly enriched terms (p-value < 0.05) in each category—Biological Process (BP), Cellular Component (CC), and Molecular Function (MF), were selected for detailed analysis (Figure 5). Key enriched functions included identical protein binding (MF) and protein tyrosine kinase activity (MF). KEGG pathway enrichment analysis (Figure 6) revealed significant enrichment in pathways such as the PI3K-Akt signaling pathway and the MAPK signaling pathway, suggesting their potential roles in mediating the anti-aging effects.

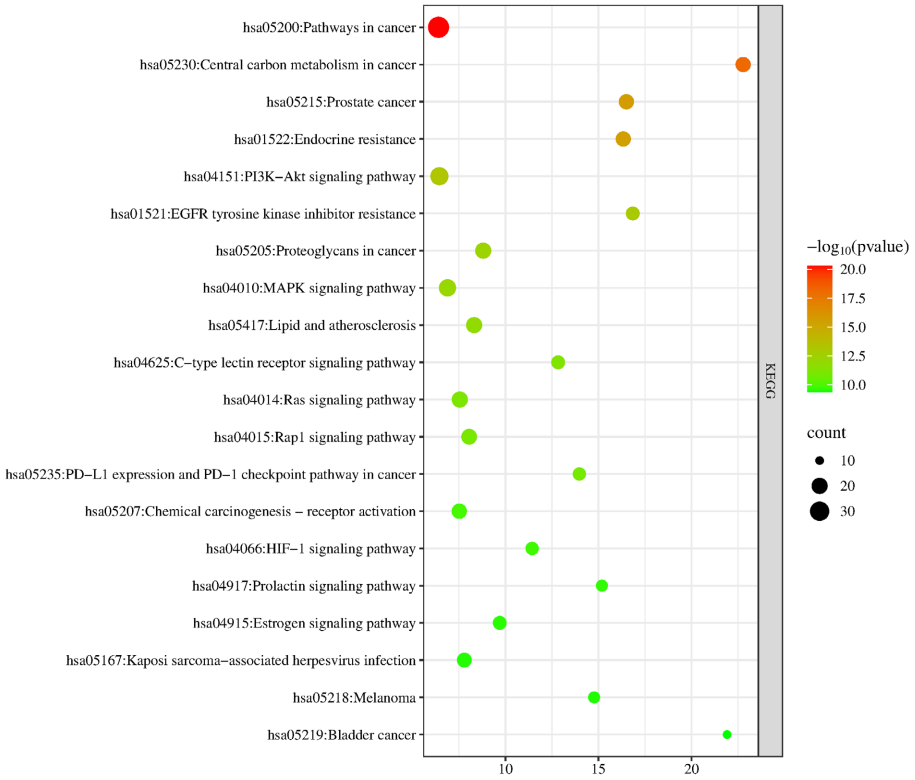

Figure 6. KEGG pathway enrichment analysis of common targets shared between *Ganoderma lucidum* and aging.

3.6. Molecular Docking Results

Based on degree centrality rankings from Section 3.3, the top 3 key targets (CYP19A1, NR3C1, HMGCR) and the top 9 core active components (MOL000279, MOL000358, MOL011125, MOL011160, MOL011189, MOL011225, MOL011235, MOL011241, MOL011256) were selected for molecular docking validation. The docking complexes exhibiting favorable binding poses are illustrated in Figure 7. Docking scores (Total Score) for each ligand—receptor pair are presented in Figure 8. Interactions with a Total Score ≥ 7.0 were considered indicative of stable binding, based on the scoring function within SYBYL-X. The results suggest that CYP19A1 and NR3C1 may play crucial roles in the anti-aging activity of *Ganoderma lucidum*.

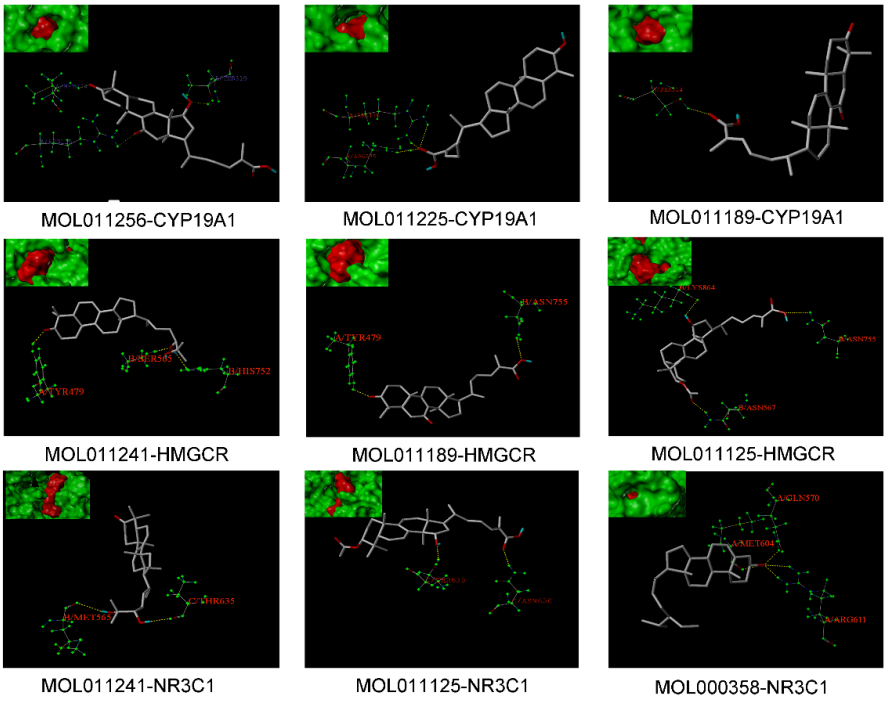

Figure 7. Visualization of molecular docking poses between core *Ganoderma lucidum* active components and key targets.

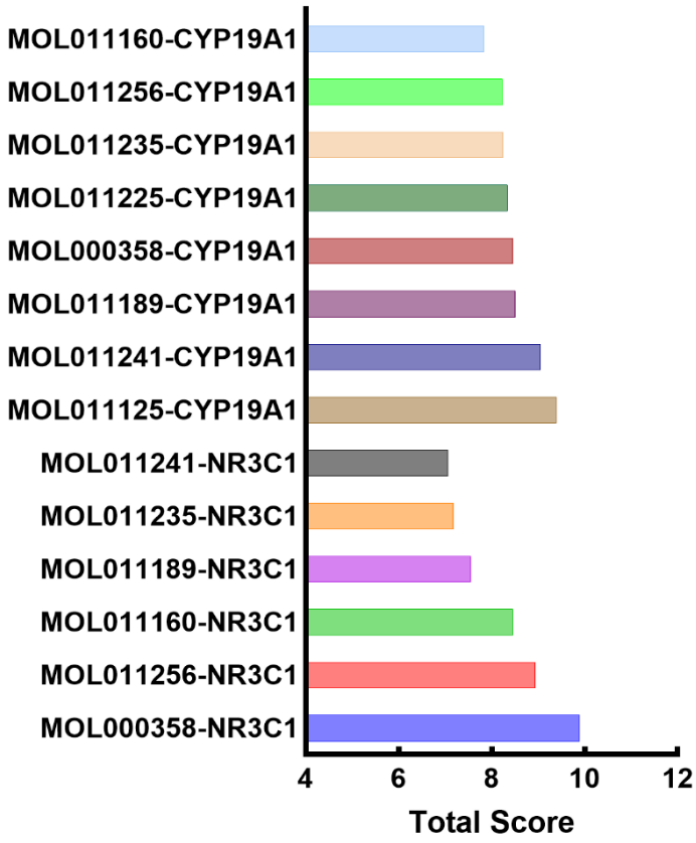

Figure 8. Docking scores for the interactions between the core *Ganoderma lucidum* active components and key targets.

4. Discussions and Conclusions

Ganoderma lucidum, a fungus with a long history of medicinal use, has garnered significant attention in recent years for its potential anti-aging properties. This study employed a network pharmacology approach to systematically investigate the multi-target and multi-pathway mechanisms underlying the anti-aging effects of *Ganoderma lucidum* active components.

The results indicate that *Ganoderma lucidum* may exert anti-aging effects by modulating key molecular targets [13] [14] (including CYP19A1 and NR3C1) through its bioactive components [15]-[17] (such as ganoderic acids, ganoderenic acids, ganodermanondiol, and β-sitosterol), consequently influencing critical signaling pathways including PI3K-Akt and MAPK cascades. These targets and pathways are closely related to known molecular mechanisms of aging: CYP19A1 involved in estrogen synthesis, while decreased estrogen levels have been shown to be associated with cellular senescence, increased oxidative stress, and mitochondrial dysfunction [18] [19]; NR3C1 regulates metabolic homeostasis, and its abnormal activation can accelerate aging-related inflammatory responses (such as NF-κB signal upregulation) and apoptosis [20]; the PI3K-Akt pathway is the core regulatory network of aging, affecting cell proliferation, autophagy, and antioxidant defense [21] [22]; the MAPK pathway, especially p38 and ERK signaling, is closely related to cellular senescence, telomere shortening, and inflammasome activation [23] [24].

From the perspective of Traditional Chinese Medicine (TCM) theory, aging is closely linked to the depletion of kidney essence (*Shen Jing Kui Xu*) and insufficiency of the marrow sea (*Sui Hai Bu Zu*). *Ganoderma lucidum*, known to target the heart, lung, liver, and kidney meridians, possesses properties that enrich kidney essence and nourish the heart to calm the spirit. This aligns with the TCM anti-aging principle of "tonifying the kidney and replenishing the marrow" (*Bu Shen Yi Sui*). Modern research corroborates that polysaccharides and triterpenoids from *Ganoderma lucidum* confer neuroprotection [25] [26], potentially delaying brain aging by inhibiting inflammatory cytokines (e.g., IL-6), reducing oxidative damage, and modulating neurotransmitters (e.g., serotonin, dopamine). Furthermore, *Ganoderma lucidum* extracts may mitigate age-associated neurodegenerative pathologies by suppressing CASP3-mediated apoptosis and downregulating PTGS2-related neuroinflammation [27].

While this study provides initial insights into the potential molecular mechanisms of *Ganoderma lucidum*'s anti-aging effects, several limitations should be acknowledged. These include the need to validate the *in vivo* metabolism of the active components, elucidate the precise signaling pathways of target regulation, and confirm clinical efficacy. Future research should integrate animal models and clinical trials to further delineate the specific mechanisms by which *Ganoderma lucidum* retards aging and related disorders (e.g., Alzheimer's disease). Such investigations will provide a stronger scientific foundation for developing *Ganoderma lucidum* into effective anti-aging therapeutics or nutraceuticals.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Ghanem, A.S., Nguyen, C.M., Mansour, Y., Fábián, G., Rusinné Fedor, A., Nagy, A., *et al.* (2023) Investigating the Association between Sociodemographic Factors and Chronic Disease Risk in Adults Aged 50 and above in the Hungarian Population. *Healthcare*, **11**, Article 1940. https://doi.org/10.3390/healthcare11131940

[2] Dong, B. and Ding, Q. (2009) Aging in China: A Challenge or an Opportunity? *Journal of the American Medical Directors Association*, **10**, 456-458. https://doi.org/10.1016/j.jamda.2009.06.007

[3] Shan, J., Mo, J., An, C., Xiang, L. and Qi, J. (2024) *β*-Cyclocitral from *Lavandula angustifolia* Mill. Exerts Anti-Aging Effects on Yeasts and Mammalian Cells via Telomere Protection, Antioxidative Stress, and Autophagy Activation. *Antioxidants*, **13**, Article 715. https://doi.org/10.3390/antiox13060715

[4] Gleichmann, U., Gleichmann, U. and Gleichmann, S. (2011) Von der kardiovaskulären Prävention zur Anti-Aging-Medizin: Einfluss auf Telomere und Zellalterung. *DMW—Deutsche Medizinische Wochenschrift*, **136**, 1913-1916. https://doi.org/10.1055/s-0031-1286363

[5] Liu, J., Zhang, B., Wang, L., Li, S., Long, Q. and Xiao, X. (2024) Bioactive Components, Pharmacological Properties and Underlying Mechanism of *Ganoderma lucidum* Spore Oil: A Review. *Chinese Herbal Medicines*, **16**, 375-391. https://doi.org/10.1016/j.chmed.2023.09.007

[6] Wang, J., Cao, B., Zhao, H. and Feng, J. (2017) Emerging Roles of *Ganoderma lucidum* in Anti-Aging. *Aging and disease*, **8**, 691-707. https://doi.org/10.14336/ad.2017.0410

[7] Ding, W., Zhang, X., Yin, X., Zhang, Q., Wang, Y., Guo, C., *et al.* (2022) *Ganoderma lucidum* Aqueous Extract Inducing PHGPx to Inhibite Membrane Lipid Hydroperoxides and Regulate Oxidative Stress Based on Single-Cell Animal Transcriptome. *Scientific Reports*, **12**, Article No. 3139. https://doi.org/10.1038/s41598-022-06985-z

[8] Kumar, H., Bansal, S., Chaudhary, R., Sharma, S., Gupta, S. and Choudhary, S. (2024) Amelioration of Neuronal Deficits in Aged Rats via *Ganoderma lucidum* Extract Alone and Combination with *α* Lipoic Acid. *Journal of Pharmacology and Pharmacotherapeutics*, **16**, 77-91. https://doi.org/10.1177/0976500x241288673

[9] Wang, A., Xiao, C., Zheng, J., Ye, C., Dai, Z., Wu, Q., *et al.* (2020) Terpenoids of *Ganoderma lucidum* Reverse Cognitive Impairment through Attenuating Neurodegeneration via Suppression of PI3K/Akt/mTOR Expression *in Vivo* Model. *Journal of Functional Foods*, **73**, Article ID: 104142. https://doi.org/10.1016/j.jff.2020.104142

[10] Cuong, V.T., Chen, W., Shi, J., Zhang, M., Yang, H., Wang, N., *et al.* (2019) The Anti-Oxidation and Anti-Aging Effects of *Ganoderma lucidum* in *Caenorhabditis elegans*. *Experimental Gerontology*, **117**, 99-105. https://doi.org/10.1016/j.exger.2018.11.016

[11] Ji, C., Yang, Y., Fu, Y., Pu, X. and Xu, G. (2022) Improvement of *Ganoderma lucidum* Water Extract on the Learning and Memory Impairment and Its Mechanism in D-Galactose-Induced Aging Mice. *Journal of Functional Foods*, **99**, Article ID: 105322. https://doi.org/10.1016/j.jff.2022.105322

[12] Zhang, G., Xue, P., Zhao, H., Guan, T. and Ma, Z. (2024) Network Pharmacology and Molecular Docking Reveal the Antioxidant Potential of Mangiferin from Mango Peel.

Letters in Drug Design & Discovery, **21**, 1263-1273. https://doi.org/10.2174/1570180820666230403090658

[13] Furth, P.A., Wang, W., Kang, K., Rooney, B.L., Keegan, G., Muralidaran, V., *et al.* (2023) ESR1 but Not CYP19A1 Overexpression in Mammary Epithelial Cells during Reproductive Senescence Induces Pregnancy-Like Proliferative Mammary Disease Responsive to Anti-Hormonals. *The American Journal of Pathology*, **193**, 84-102. https://doi.org/10.1016/j.ajpath.2022.09.007

[14] Appleton, A.A. (2025) A Polyepigenetic Glucocorticoid Exposure Score and HPA Axis-Related DNA Methylation Are Associated with Gestational Epigenetic Aging. *Epigenetics*, **20**, Article ID: 2471129. https://doi.org/10.1080/15592294.2025.2471129

[15] Zhang, X., Ji, C., Fu, Y., Yang, Y. and Xu, G. (2024) Screening of Active Components of *Ganoderma lucidum* and Decipher Its Molecular Mechanism to Improve Learning and Memory Disorders. *Bioscience Reports*, **44**, Article No. 7. https://doi.org/10.1042/bsr20232068

[16] Wang, S., Wang, L., Shangguan, J., Jiang, A. and Ren, A. (2024) Research Progress on the Biological Activity of Ganoderic Acids in *Ganoderma lucidum* over the Last Five Years. *Life*, **14**, Article 1339. https://doi.org/10.3390/life14101339

[17] Chen, L., Wu, B., Mo, L., Chen, H., Yin, X., Zhao, Y., *et al.* (2025) High-Content Screening Identifies Ganoderic Acid a as a Senotherapeutic to Prevent Cellular Senescence and Extend Healthspan in Preclinical Models. *Nature Communications*, **16**, Article No. 2878. https://doi.org/10.1038/s41467-025-58188-5

[18] Li, S., Li, L., Zhang, C., Fu, H., Yu, S., Zhou, M., *et al.* (2023) $PM_{2.5}$ Leads to Adverse Pregnancy Outcomes by Inducing Trophoblast Oxidative Stress and Mitochondrial Apoptosis via KLF9/CYP1A1 Transcriptional Axis. *eLife*, **12**, e85944. https://doi.org/10.7554/elife.85944

[19] Wang, Q., Zhang, L., Han, X., Wang, D., Ding, M., Cheng, D., *et al.* (2023) 2,3',4,4',5-pentachlorobiphenyl Induces Mitochondria-Dependent Apoptosis Mediated by AhR/Cyp1a1 in Mouse Germ Cells. *Journal of Hazardous Materials*, **445**, Article ID: 130547. https://doi.org/10.1016/j.jhazmat.2022.130547

[20] Wu, T., Shao, Y., Li, X., Wu, T., Yu, L., Liang, J., *et al.* (2023) NR3C1/Glucocorticoid Receptor Activation Promotes Pancreatic β-Cell Autophagy Overload in Response to Glucolipotoxicity. *Autophagy*, **19**, 2538-2557. https://doi.org/10.1080/15548627.2023.2200625

[21] Gong, P., Wang, D., Cui, D., Yang, Q., Wang, P., Yang, W., *et al.* (2021) Anti-Aging Function and Molecular Mechanism of *Radix astragali* and *Radix astragali* Preparata via Network Pharmacology and PI3K/Akt Signaling Pathway. *Phytomedicine*, **84**, Article ID: 153509. https://doi.org/10.1016/j.phymed.2021.153509

[22] Li, Y., Liu, Z., Yan, H., Zhou, T., Zheng, L., Wen, F., *et al.* (2025) Polygonatum Sibiricum Polysaccharide Ameliorates Skeletal Muscle Aging and Mitochondrial Dysfunction via PI3K/Akt/mTOR Signaling Pathway. *Phytomedicine*, **136**, Article ID: 156316. https://doi.org/10.1016/j.phymed.2024.156316

[23] He, D., Wu, H., Xiang, J., Ruan, X., Peng, P., Ruan, Y., *et al.* (2020) Gut Stem Cell Aging Is Driven by mTORC1 via a P38 MAPK-p53 Pathway. *Nature Communications*, **11**, Article No. 37. https://doi.org/10.1038/s41467-019-13911-x

[24] Yuan, W., Weaver, Y.M., Earnest, S., Taylor, C.A., Cobb, M.H. and Weaver, B.P. (2023) Modulating P38 MAPK Signaling by Proteostasis Mechanisms Supports Tissue Integrity during Growth and Aging. *Nature Communications*, **14**, Article No. 4543. https://doi.org/10.1038/s41467-023-40317-7

[25] Ding, L., Shangguan, H., Wang, X., Liu, J., Shi, Y., Xu, X., *et al.* (2025) Extraction, Purification, Structural Characterization, Biological Activity, Mechanism of Action and Application of Polysaccharides from *Ganoderma lucidum*: A Review. *International Journal of Biological Macromolecules*, **288**, Article ID: 138575. https://doi.org/10.1016/j.ijbiomac.2024.138575

[26] Wang, T., Xie, Z., Huang, Z., Li, H., Wei, A., Di, J., *et al.* (2015) Total Triterpenoids from *Ganoderma lucidum* Suppresses Prostate Cancer Cell Growth by Inducing Growth Arrest and Apoptosis. *Journal of Huazhong University of Science and Technology* [*Medical Sciences*], **35**, 736-741. https://doi.org/10.1007/s11596-015-1499-x

[27] Rahman, M.A., Hossain, S., Abdullah, N. and Aminudin, N. (2020) Lingzhi or Reishi Medicinal Mushroom, *Ganoderma lucidum* (Agaricomycetes) Ameliorates Spatial Learning and Memory Deficits in Rats with Hypercholesterolemia and Alzheimer's Disease. *International Journal of Medicinal Mushrooms*, **22**, 93-103. https://doi.org/10.1615/intjmedmushrooms.2020033383