Journal of Experimental and Clinical Application of Chinese Medicine

ORIGINAL RESEARCH

Open Access

Global Research Hotspots and Publications of *Ganoderma lucidum* (Lingzhi): A Bibliometric Analysis from 1994 to 2024

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DOI: https://doi.org/10.62767/jecacm601.5814

Keywords

Ganoderma lucidum

Network data analysis

Antioxidant

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Received: 16 October 2024

Revised: 4 December 2024

Accepted: 26 December 2024

Published: 2 January 2025

***Journal of Experimental and Clinical Application of Chinese Medicine* 2025; 6(1): 9-22.**

Abstract

Background: Traditional Chinese medicine holds a unique and invaluable position internationally. *Ganoderma lucidum*, a traditional Chinese herbal medicine, is anti-oxidative, anti-aging, anti-tumor, anti-inflammatory, and effective in the treatment of diabetes. However, there is still a lack of systematic bibliometric analysis with regard to *Ganoderma lucidum*. **Objective:** This study uses bibliometric analysis methods to assess the published literature on *Ganoderma lucidum*, determine the current state of *Ganoderma* research, visualize development trends and research hotspots, and provide references for research on the topic. **Methods:** This study searched the Web of Science Core Collection database for literature published between 1994 and 2024, and used WPS Excel, VOSviewer, and CiteSpace to analyze and apply information on authors, institutions, journals, regions, keywords, etc., included in the collection, and construct visual literature collaboration networks. **Results:** A total of 3320 publications were ultimately analyzed. The three most prolific authors in the past 30 years are Ang Ren, Liang Shi and Mingwen Zhao. The Chinese Academy of Sciences is the most outstanding institution in the field of *Ganoderma lucidum* research. And the journal INTERNATIONAL JOURNAL OF MEDICAL MUSHROOMS has made outstanding contributions in the field. China has published the most publications in this field, followed by the United States. In recent years, the pharmacological effects of *Ganoderma lucidum* on regulating the gut microbiota have attracted a lot of attention. **Conclusion:** From 1994 to 2024, research attention to *Ganoderma lucidum* has continued to increase, as such it may be a potential research hotspot in the field of traditional medicine. This study examined the development trends and research hotspots of relevant scholars.

1 Introduction

With constant progress and development in the field of natural medicine, the specific pharmacological effects of medicinal plants have been continuously confirmed through research. *Ganoderma lucidum* (Curtis) P. Karst. belongs to the family *Ganoderma lucidum*, genus *Ganoderma lucidum*, a large fungus of basidiomycete white rot, known for its wide range of therapeutic functions. *Ganoderma lucidum* is widely distributed all over the world, and its resources and species are extremely rich in China, mainly distributed in Anhui, Fujian and other regions. Modern research has confirmed that *Ganoderma lucidum* regulates immune activity [1] and has anti-tumor [2], anti-aging [3], antiviral (HIV) [4], anti-diabetic [5], anti-bacterial [6] and anti-oxidant [7] properties along with other pharmacological effects.

As a medicinal and edible fungus, *Ganoderma lucidum* enjoys the reputation as an "immortal mushroom" in China, Japan, Korea and other East Asian countries [8]. Its fruiting body, spore powder, and mycelium can all be used medicinally. In China, the term "Zhi" originated from *Liezi - Tangwen* of the Zhou Dynasty: "There are Zhi on the rotten soil" [9]. The herbal classic *Shennong's Ben Cao Jing (The Divine Farmers Materia Medica)* includes "Chizhi, Qingzhi, Huangzhi, Baizhi, Blackzhi and Zizhi" as high-grade medicines, and describes in detail the medicinal properties, smell and indications of the six Zhi [10]. Professor Zhibin Lin summarized it as "nourishing the five organs of the heart, liver, lungs, spleen and kidneys", "nourishing essence qi", "calming the nerves", "increasing wisdom", and that "long term consumption prevents aging, extends life, and can make one immortal". He also confirmed that "the six Zhi are non-toxic" [11]. In the Ming Dynasty text, *The Compendium of Materia Medica*, Shizhen Li put forward different opinions about *Ganoderma lucidum* according to the "five colors" and "five elements", and believed that "the five colors of the Zhi correspond with the taste of the five elements, but the taste may not follow the five colors" [12]. Shizhen Li believed the legend that "Zhi" could confer immortality was ridiculous: "Zhi is born of decay and excrescence, just like a tumor. Ancient and modern people think it is an auspicious substance and say consuming it can make one immortal, which is truly absurd" [13]. *The Compendium of Materia Medica* revised the effects of "Zhi", and for the first time denied the theory that "long-term consumption confers immortality".

The pursuit of health has existed since ancient times and is confirmed throughout the Chinese medicine classics; however, the so-called "elixir" may not truly exist. *Ganoderma lucidum* has received extensive attention due to its promising pharmacological effects; therefore, the study of *Ganoderma lucidum* has certain practical and theoretical significance.

The primary purpose of this study is to investigate and discuss the research results of *Ganoderma lucidum* through data analysis and empirical research in known publications, and to verify its pharmacological effects through these research results. Through the analysis of *Ganoderma lucidum* publications, this study will help enrich the theoretical system in related fields and provide new ideas and directions for future research on medicinal plants.

2 Research methods

2.1 Data source and search

An extensive search was conducted in the Web of Science Core Collection (WOSCC) database utilizing terms such as "*Ganoderma*", "*Ganoderma lucidum*", "*Ganoderma lucidum* OR lingzhi", "*Ganoderma lucidum*" OR Abstract "lingzhi", "*Ganoderma lucidum*" OR Abstract "lingzhi" OR Topic "lingzhi" OR Title "lingzhi", "*Ganoderma lucidum* OR reishi" OR Abstract "lingzhi" OR Topic "lingzhi" OR Titlem "lingzhi", published between January 1, 1994 and August 25,

2024. The number of journals is shown in Table 1.

"*Ganoderma lucidum*", "lingzhi" and "reishi" are often used as the English names of *Ganoderma lucidum*, but a direct search of "*Ganoderma lucidum* OR lingzhi" will include "lingzhi" and "ling-zhi" as the content of the study, and in the search results containing only "lingzhi" and "ling-zhi" none of the authors have published research publications on *Ganoderma lucidum*, so they were excluded from the search. Searches were conducted in the primary databases for publications with "*Ganoderma lucidum* OR reishi" or "lingzhi" in abstract or "lingzhi" in subject or "lingzhi" in title. After excluding literature unrelated to *Ganoderma lucidum* research, there are still 3320 publications. The specific search strategy and selection processes are shown in Figure 1.

Table 1 Number of documents included in each search from 1994 to 2024.

Search for content	Database	Number of documents
All fields "Ganoderma"	Web of Science Core Collection	5582
All fields "*Ganoderma lucidum*"	Web of Science Core Collection	4168
All fields "*Ganoderma lucidum* OR lingzhi"	Web of Science Core Collection	7954
All fields "*Ganoderma lucidum*" OR Abstract "lingzhi"	Web of Science Core Collection	4206
All fields "*Ganoderma lucidum*" OR Abstract "lingzhi" OR Topic "lingzhi" OR Title "lingzhi"	Web of Science Core Collection	4251
All fields "*Ganoderma lucidum* OR reishi" OR Abstract "lingzhi" OR Topic "lingzhi" OR Title "lingzhi"	Web of Science Core Collection	4396

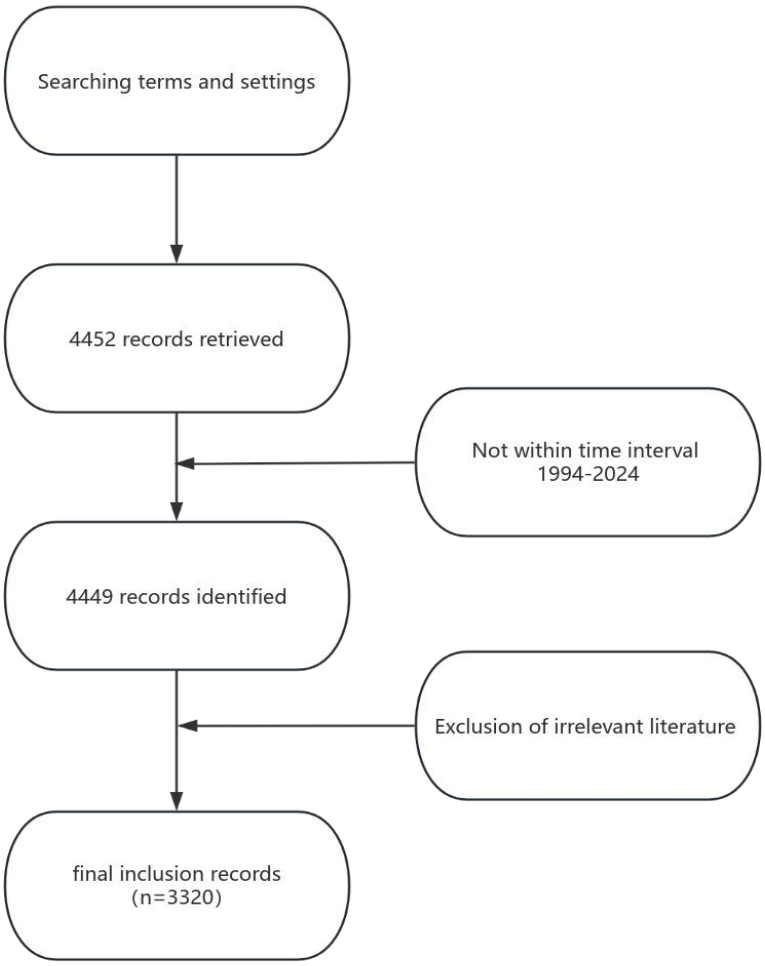

Figure 1 The flowchart of searching and selection process.

2.2 Data analysis

WPS Excel, VOSviewer (version 1.6.20.0) and CiteSpace 6.2.R6 were used to analyze the research data, including regions and institutions of the publications, the keywords of the publications, etc., the synonyms were normalized, and the research hotspots and development trends related to *Ganoderma lucidum* were explored in combination with available references.

The data was entered into WPS Excel and output as a graph. The analysis graphs include the linear relationship of the number of published papers in each year in the past 30 years, the histogram of the category to which the research field belongs, and the proportion of the number of articles published in journals. VOSviewer was used to visualize and analyze the network data of the first author of the article, the regional institution that published the article, and the keywords that frequently appear in both the journal and the full text. VOSviewer map is made up of nodes of different sizes and colors and lines that connect the nodes together. The size of the node is related to the frequency of the occurrence of the word, and the color of the node shows the connection with other nodes of similar color. CiteSpace is a scientific literature analysis tool jointly developed by Professor Chen and others to present the research structure and development trends of disciplinary fields. In this study, it was applied to the visualization analysis of cited publications.

2.3 Exclusion method

In searching the WOS Core Collection database from 1994 to 2024 for "*Ganoderma lucidum* OR reishi", content was excluded that contained the author's name and only the term lingzhi, publications not related to *Ganoderma lucidum* research, and publications that were not available. No restrictions were set for languages. The excluded publications are detailed in Table S1.

3 Result analysis

3.1 Analysis of research trends

As shown in Figure 2A, in general, the number of publications on *Ganoderma lucidum* has been increasing. Since 2008 the number of publications has remained above 100, reaching a level of 300 in 2023, indicating that *Ganoderma lucidum* has received a lot of attention in recent years. The increase in the number of publications marks a joint effort by researchers to uncover the numerous health benefits and biological activities of *Ganoderma lucidum*. There is a significant increase in the published literature on *Ganoderma lucidum* in the WOS Core Collection beginning in 2007. This may be attributed to a combination of factors, including scientific and technological advances, funding for integrative and complementary medicine research, increased interest in natural products, and the expanded global market for herbal supplements. Articles, which make up the majority of the published literature (n = 2932 articles or 86.69% of the published literature) report the research results and experimental data of researchers, providing foundation for understanding the pharmacological effects, mechanisms, and clinical applications of *Ganoderma lucidum*. 197 reviews (5.82%) also played a crucial role. The review provides a comprehensive overview of *Ganoderma lucidum*, highlighting hot topics and indicating future research directions, as shown in Figure 2B.

3.2 Analysis of authors

Using VOSviewer, analyzing the first author, the frequency density of co-occurrence between authors is directly reflected. As shown in Figure 3A, a total of 127 authors have published 10 or more publications. "Ren, Ang", "Shi, Liang", and "Zhao, Mingwen" have the largest nodes, indicating that they have published the most publications. Among them, Ang Ren's publications has been cited up to 1902 times. This high citation frequency is indicative of the research

quality, originality, and relevance of Ren's publications, which have received widespread attention within the academic community.

This VOSviewer analysis offers a comprehensive view of the research, highlighting key individuals and their contributions, while also revealing collaborative trends and areas of focus on the field.

3.3 Analysis of institutions

Figure 3B shows the connections between various institutions. The top 10 most influential institutions are all from China, indicating that China has a dominant position in the research of *Ganoderma lucidum*. Chinese Acad SCI is the institution with the most published papers (190 publications) and the closest relationship with other institutions. Shanghai Jiao Tong University ranks second with 96 published publications and 2879 citations. Although Nanchang University has only published 25 publications, its citation count is 1641 times, indicating the high quality of their research.

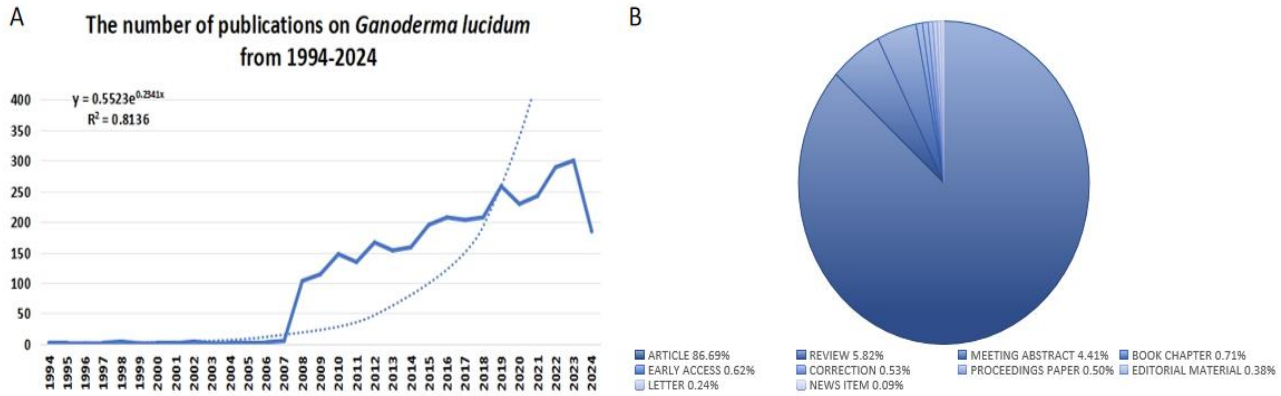

Figure 2 Research trends. (A) The changes in the numbers of global publications between 1994-2024. (B) Proportion of articles by type and number.

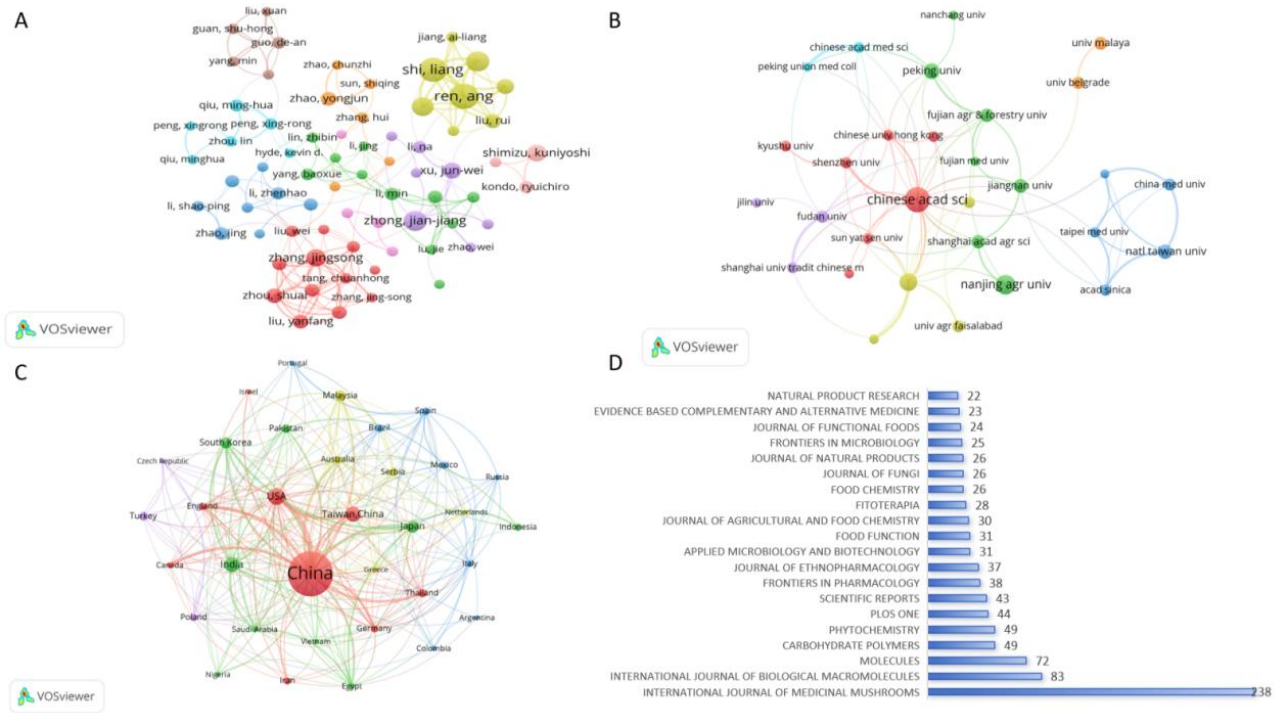

Figure 3 Bibliometric analysis of publications in the field of *Ganoderma lucidum*. (A) Author collaboration network diagram. (B) Institutional collaboration network diagram. (C) Regional collaboration network diagram. (D) The top 20 journals in terms of publication ranking.

3.4 Analysis of regions

According to the collected data, a total of 100 regions have made contributions in the field of *Ganoderma lucidum*, indicating strong research interest in this field worldwide. Figure 3C shows the collaborative network diagram in various regions from 1994 to 2024. Each node represents a region, and the larger the node, the more publications in that region. Among them, China has the highest number of publications, with a total of 1725 publications published; The United States (n = 242), India (n = 205), Taiwan, China (n = 196), Japan (n = 132) and China occupy the top five positions together.

3.5 Analysis of journals

In this study, the search and analysis was conducted on papers published between January 1, 1994 to August 25, 2024. The first publication on *Ganoderma lucidum* was *Lanostanoid triterpenes from Ganoderma applanatum*, published in PHYTOCHEMISTRY in March 1994 [14]. This publication determined the inhibitory effect of *Ganoderma applanatum* triterpenoids on early antigen activation of the virus. As a world-class journal, PHYTOCHEMISTRY has an impact factor of 3.4 in the past five years.

INTERNATIONAL JOURNAL OF MEDICINAL MUSHROOMS is the journal with the largest number of publications on *Ganoderma lucidum*, with an impact factor of 1.5 in the past five years. The top 20 journals in terms of publications are show in Figure 3D.

3.6 Analysis of cited references

Table 2 shows the top 20 *Ganoderma lucidum* publications with the highest number of citations in WOSCC and the journals they published. "Citation" indicates the number of times this publication has been cited, and "cite" indicates how many articles this publication cited. A highly cited paper is one that, as of January/February 2024, has received enough citations to place it in the top 1% of its academic field based on the high citation threshold for the field and year of publication. Through the search, it was found that there were a total of 34 highly cited publications, and 17 of them were studied in this paper, as show in Table 3.

Figure 4A shows the top 25 publications with the strongest citation bursts. "Begin" represents the time when the burst occurred, "end" represents the time when the burst ended, and the red section represents the duration of the burst. The duration of the burst represents the time period during which the publication received significant attention. The earliest publication to emerge was *Ganoderma-A therapeutic fungal biofactory* [15], which is a review that summarizes the research topics on *Ganoderma* species around the world, with a particular emphasis on biomedical related chemicals. *Antitumor, Antimicrobial, Antioxidant, and Antiacetylcholinesterase Effect of Ganoderma Lucidum Terpenoids and Polysaccharides: A Review* [16] is one of the most influential publications since 2019. This review considered the antitumor, antibacterial, antioxidant, and antiacetylcholinesterase effects of compounds isolated from *Ganoderma lucidum*.

Figure 4B shows the clustering analysis of the cited publications. Each color represents a cluster, each distinct color in the visualization represents a cluster, encapsulating publications that share common themes, methodologies or research areas. As can be seen, clusters include "TOXICOLOGY", "POLYMER SCIENCE", "MEDICANE", "RESEARCH & EXPERIMENT", "CHEMISTRY, CHEMICAL", "ONCOLOGY", "CHEMISTRY, MEDICAL", "MYCOLOGY", "BIOTECHOLOGY & APPLIED MICROBIOLOGY". These clusters exhibit the highest number of cited publications and represent the research value and scientific development potential. Cluster analysis measures the similarity between different publications and classifies similar publications into the same cluster. The publications in the "TOXICOLOGY" and "ONCOLOGY" clusters highlight the key role of *Ganoderma lucidum* in pharmacology.

"POLYMER SCIENCE", "CHEMISTRY, CHEMICAL" and "CHEMISTRY, MEDICAL" include publications that focus more on the chemical structure and composition of *Ganoderma lucidum*. The emergence of clusters indicates potential areas for interdisciplinary collaboration, where researchers can utilize research methods from different fields to solve unknown problems. For example, the collaboration between chemists and oncologists can discover the impact of *Ganoderma lucidum* chemical components on tumors.

Table 2 Top 20 most cited publications on *Ganoderma lucidum*.

No.	Title	Journal title	Citation	Cite
1	*Ganoderma lucidum* reduces obesity in mice by modulating the composition of the gut microbiota	NATURE COMMUNICATIONS	815	70
2	Purification, composition analysis and antioxidant activity of a polysaccharide from the fruiting bodies of *Ganoderma* atrum	FOOD CHEMISTRY	514	48
3	Genome sequence of the model medicinal mushroom *Ganoderma lucidum*	NATURE COMMUNICATIONS	401	60
4	The Role of Culinary-Medicinal Mushrooms on Human Welfare with a Pyramid Model for Human Health	INTERNATIONAL JOURNAL OF MEDICINAL MUSHROOMS	372	97
5	Tissue invasion and metastasis: Molecular, biological and clinical perspectives	SEMINARS IN CANCER BIOLOGY	360	542
6	Antioxidative and immunomodulating activities of polysaccharide extracts of the medicinal mushrooms *Agaricus bisporus*, *Agaricus brasiliensis*, *Ganoderma lucidum* and *Phellinus linteus*	FOOD CHEMISTRY	338	51
7	*Ganoderma lucidum*: A Potent Pharmacological Macrofungus	CURRENT PHARMACEUTICAL BIOTECHNOLOGY	311	153
8	Recent developments in mushrooms as anti-cancer therapeutics: a review	3 BIOTECH	293	87
9	Advanced Materials From Fungal Mycelium: Fabrication and Tuning of Physical Properties	SCIENTIFIC REPORTS	289	61
10	Secondary metabolites from *Ganoderma*	PHYTOCHEMISTRY	280	216
11	Anti-HIV-1 and anti-HIV-1-protease substances from *Ganoderma lucidum*	PHYTOCHEMISTRY	277	33
12	Ability of white-rot fungi to remove selected pharmaceuticals and identification of degradation products of ibuprofen by *Trametes versicolor*	CHEMOSPHERE	269	38
13	From 2000 years of *Ganoderma lucidum* to recent developments in nutraceuticals	PHYTOCHEMISTRY	251	110
14	Species Diversity and Utilization of Medicinal Mushrooms and Fungi in China (Review)	INTERNATIONAL JOURNAL OF MEDICINAL MUSHROOMS	244	111
15	Antitumour, Antimicrobial, Antioxidant and Antiacetylcholinesterase Effect of *Ganoderma Lucidum* Terpenoids and Polysaccharides: A Review	MOLECULES	243	102
16	Chemical features of *Ganoderma* polysaccharides with antioxidant, antitumor and antimicrobial activities	PHYTOCHEMISTRY	238	123
17	Characterization and antioxidant activity of two low-molecular-weight polysaccharides purified from the fruiting bodies of *Ganoderma lucidum*	INTERNATIONAL JOURNAL OF BIOLOGICAL MACROMOLECULES	234	38
18	Extraction, purification, characterization and antitumor activity of polysaccharides from *Ganoderma lucidum*	CARBOHYDRATE POLYMERS	232	33
19	Triterpenes from the spores of *Ganoderma lucidum* and their inhibitory activity against HIV-1 protease	CHEMICAL & PHARMACEUTICAL BULLETIN	232	33
20	*Ganoderma lucidum* Polysaccharides: Immunomodulation and Potential Anti-Tumor Activities	AMERICAN JOURNAL OF CHINESE MEDICINE	227	54

Table 3 Highly cited publications on *Ganoderma lucidum*.

No	Title	Journal title	Publication time	Placed in the top 1% in any academic field	Citation
1	*Ganoderma lucidum* reduces obesity in mice by modulating the composition of the gut microbiota	NATURE COMMUNICATIONS	Jun 2015	Clinical Medicine	815
2	Tissue invasion and metastasis: Molecular, biological and clinical perspectives	SEMINARS IN CANCER BIOLOGY	Dec 2015	Clinical Medicine	360
3	Advanced Materials From Fungal Mycelium: Fabrication and Tuning of Physical Properties	SCIENTIFIC REPORTS	Jan 2017	Chemistry	289
4	Secondary metabolites from *Ganoderma*	PHYTOCHEMISTRY	Jun 2015	Plant & Animal Science	280
5	From 2000 years of *Ganoderma lucidum* to recent developments in nutraceuticals	PHYTOCHEMISTRY	Jun 2015	Plant & Animal Science	251
6	Antitumour, Antimicrobial, Antioxidant and Antiacetylcholinesterase Effect of *Ganoderma lucidum* Terpenoids and Polysaccharides: A Review	MOLECULES	Mar 2018	Chemistry	243
7	Chemical features of *Ganoderma* polysaccharides with antioxidant, antitumor and antimicrobial activities	PHYTOCHEMISTRY	Jun 2015	Plant & Animal Science	238
8	Immunomodulatory activities of polysaccharides from *Ganoderma* on immune effector cells	FOOD CHEMISTRY	Mar 2021	Agricultural Sciences	197
9	Herbal Medicine for Cardiovascular Diseases: Efficacy, Mechanisms, and Safety	FRONTIERS IN PHARMACOLOGY	Apr 2020	Pharmacology & Toxicology	191
10	*Ganoderma lucidum* polysaccharide modulates gut microbiota and immune cell function to inhibit inflammation and tumorigenesis in colon	CARBOHYDRATE POLYMERS	Sep 2021	Chemistry	179
11	Molecular mechanisms of bioactive polysaccharides from *Ganoderma lucidum* (Lingzhi), a review	INTERNATIONAL JOURNAL OF BIOLOGICAL MACROMOLECULES	May 2020	Biology & Biochemistry	171
12	Suppression of obesity and inflammation by polysaccharide from sporoderm-broken spore of *Ganoderma lucidum* via gut microbiota regulation	CARBOHYDRATE POLYMERS	Mar 2021	Chemistry	153
13	Identification of existing pharmaceuticals and herbal medicines as inhibitors of SARS-CoV-2 infection	PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA	Feb 2021	Microbiology	129
14	Species diversity of basidiomycota	FUNGAL DIVERSITY	May 2022	Plant & Animal Science	39
15	Species diversity, systematic revision and molecular phylogeny of *Ganodermataceae (Polyporales, Basidiomycota)* with an emphasis on Chinese collections	STUDIES IN MYCOLOGY	Mar 2022	Plant & Animal Science	38
16	A Review of *Ganoderma* Triterpenoids and Their Bioactivities	BIOMOLECULES	Jan 2023	Biology & Biochemistry	35
17	*Ganoderma lucidum* polysaccharide inhibits HSC activation and liver fibrosis via targeting inflammation, apoptosis, cell cycle, and ECM-receptor interaction mediated by TGF-β/Smad signaling	PHYTOMEDICINE	Feb 2023	Pharmacology & Toxicology	24

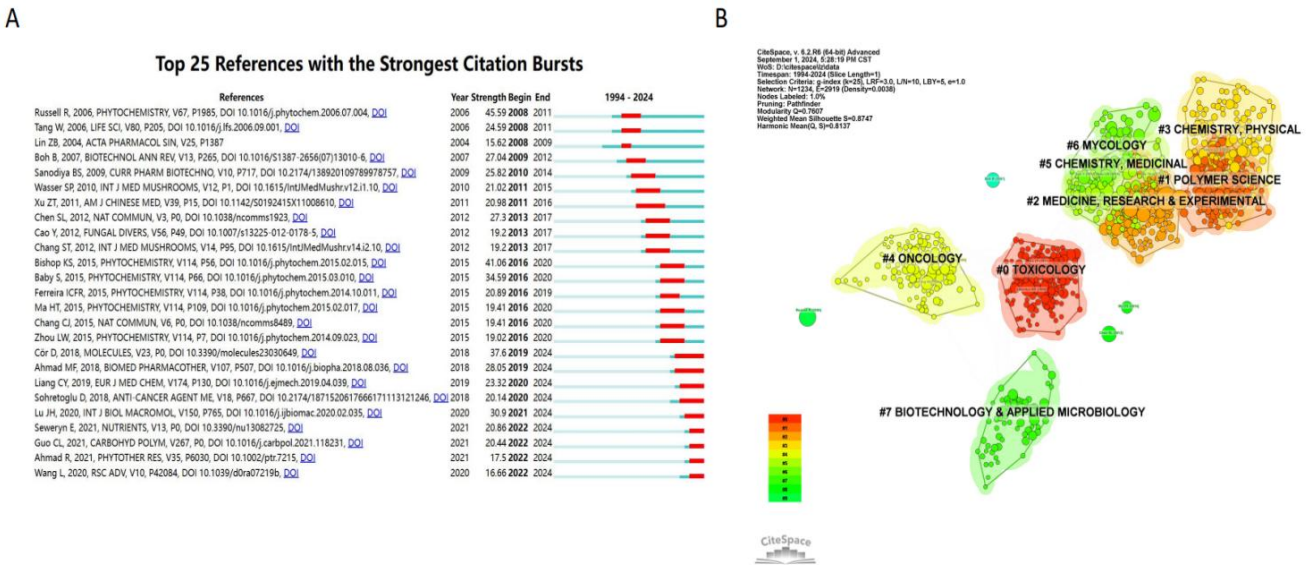

Figure 4 1994-2024 Visualization map of cited bibliometric analysis in the field of *Ganoderma lucidum*. (A) The top 25 cited publications with strong burst in the research domain of *Ganoderma lucidum* during 1994-2024. (B) Cluster analysis of cited publications.

3.7 Analysis of keywords

Keyword analysis, a fundamental tool in bibliometric research, categorizes terms into three distinct groups: "all keywords", "author keywords", and "upgraded keywords". Utilizing VOSviewer to perform coverage visualization analysis on all keywords, filtering out those that are repeated more than 50 times, excluding non-specific keywords such as "mice", "culture", and "cells", as shown in Figure 5A. The top five keywords in the publications are "*Ganoderma lucidum*", "polysaccharides", "medicinal mushrooms", "antitumor", and "antioxidants". This indicates that in the past 30 years, *Ganoderma lucidum* polysaccharides have been the focus of scholars' research, and the antitumor and antioxidant effects of *Ganoderma lucidum* are the most widely studied pharmacological effects. Meanwhile, as shown in the figure, "anti-inflammatory", "gut microbiota", and "metabolism" have received much attention, indicating that these three may be potential research hotspots in the future. The efficacy of different species of *Ganoderma* varies. Figure 5B shows the collinear network diagram of keywords for different species of *Ganoderma*. The two species of *Ganoderma* with the largest nodes, "*ganoderma applanatum* (red)" and "*ganoderma atrum* (green)", indicate that, apart from *Ganoderma lucidum*, these two species have been studied the most. And their antioxidant and anti-tumor properties are hot topics of research for scholars. Figures 5C and 5D indicate that the most studied pharmacological effects of *Ganoderma lucidum* are anti-tumor, antioxidant, and anti-inflammatory, with polysaccharides and triterpenoids being the most studied active ingredients.

4 Discussion

This study analyzed the research hotspots in the field of *Ganoderma lucidum* and conducted a bibliometric analysis of the literature on *Ganoderma lucidum* over the past 30 years. The keywords "triterpenes", "polysaccharides" and other active ingredients have been mentioned frequently. Therefore, in the discussion section, we will analyze the pharmacological activities and clinical applications of various chemical components in *Ganoderma lucidum*.

Studies on the extraction and separation of the

chemical components of *Ganoderma lucidum* have confirmed that there are about 431 secondary metabolites in *Ganoderma lucidum* [17]. Its primary compounds include polysaccharides, triterpenoids, proteins, enzymes, steroids, sterols, nucleotides, fatty acids and other components which have been shown to have a variety of pharmacological activities [18] and potential clinical application.

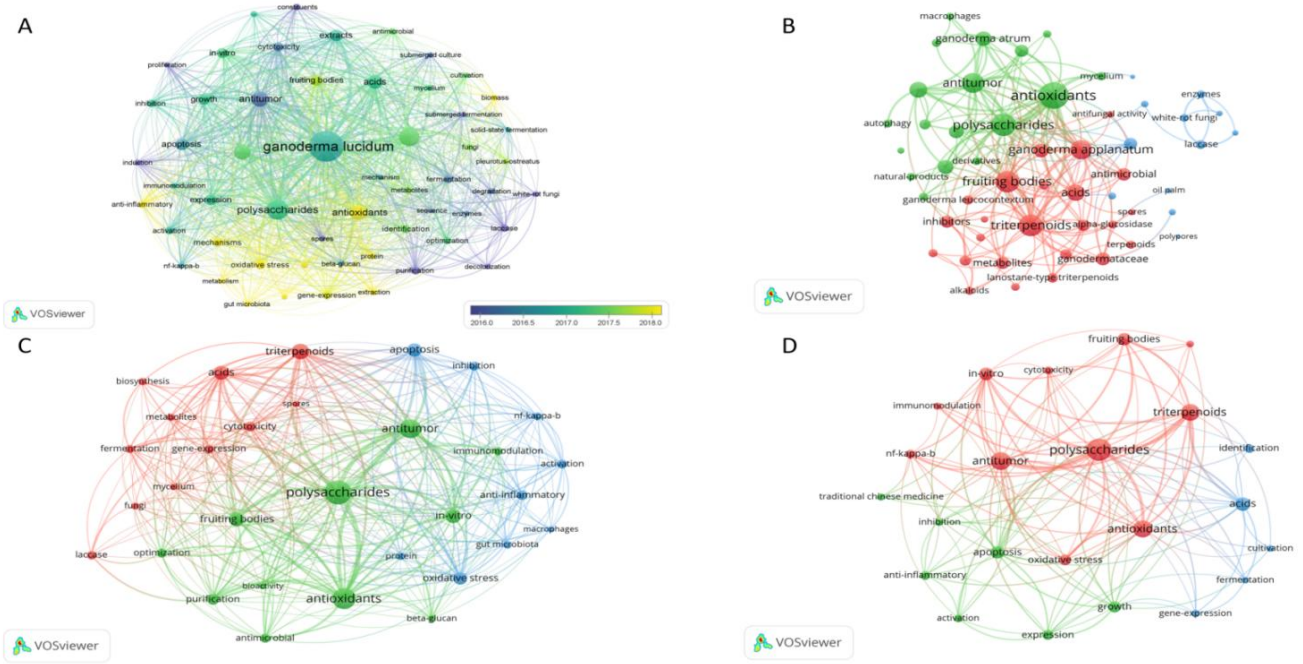

Figure 5 Keywords visualization analysis. (A) All keywords coverage visualization analysis. (B) Network visualization analysis of different types of *Ganoderma* keywords.(C) Network visualization analysis of *Ganoderma lucidum* pharmacological research.(D) Network visualization analysis of *Ganoderma lucidum* clinical research.

4.1 Triterpenoids

Triterpenoids are the primary source of bitterness in *Ganoderma lucidum*, and are also important components that exert pharmacological effects [19,20]. Liu Y et al. and Wu GS et al. found that *Ganoderma lucidum* triterpenoids mainly exert anti-tumor effects by inducing apoptosis and cytotoxicity to tumor cells [21,22]. Ahmad MF et al. found that *Ganoderma lucidum* triterpenoids exert antiviral effects by inhibiting various enzymes such as neuraminidase, HIV protease, DENV2, NS2B-NS3 protease, and HSV proliferation [23]. Zhao C et al. found that *Ganoderma lucidum* triterpenoids exerted pharmacological effects on protecting alcohol-induced liver injury by inhibiting lipid peroxidation, increasing the activity of antioxidant enzymes, and inhibiting apoptosis cell death and immune inflammatory responses [24]. Wang C et al. demonstrated that triterpenoids and aromatic methyl terpenoids have antioxidant and neuroprotective effects [25]. Dudhgaonkar S et al. found that *Ganoderma lucidum* triterpenoids significantly inhibited the secretion of inflammatory cytokines tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6), as well as inflammatory mediators nitric oxide (NO) and prostaglandin E (PGE), in lipopolysaccharide (LPS)-stimulated mouse RAW264.7 cells [26]. Li P et al. found that *Ganoderma lucidum* contained neutral triterpenoid fraction (NTF) and acid triterpenoid fraction (ATF), and the percentages of total triterpenoids in ATF and NTF were 46.7% and 57.6%, respectively. Both reduced the viability of SW480, SW620, and SW1116 cells *in vitro*, with NTF showing a stronger effect than ATF [27].

4.2 Polysaccharide compounds

Polysaccharides have always been one of the most important components in natural product research.

The polysaccharides of *Ganoderma lucidum* belong to fungal polysaccharides, which are a class of compounds formed by the condensation of more than ten kinds of monosaccharides. At present, 220 kinds of polysaccharides have been isolated from *Ganoderma lucidum*, and their monosaccharides are mainly composed of β-glucans. There is a small amount of α -glucan, though it has almost no biological activity [28]. Pharmacological study on *Ganoderma lucidum* polysaccharide (GLP) of Guo C et al. showed that GLP reduced the incidence of colitis and tumorigenesis induced by oxide azomethane/dextran sodium sulfate (AOM/DSS), which was manifested by a significant decrease in disease activity index score, and the total number and size of tumors. In addition, GLP can improve AOM/DSS-induced dysbiosis by inhibiting TLR4/MyD88/NF- κ B signaling, increasing the production of short-chain fatty acids and alleviating endotoxemia [29]. Zhang X et al. found that polysaccharides in plants showed good anti-diabetic effects [30]. Ma HT et al. found that GLP has the effect of lowering blood sugar and controlling diabetes by increasing plasma insulin levels and decreasing plasma sugar levels in mice [31]. Han XQ et al. found that Zizhi polysaccharides induce vigorous proliferation of mouse spleen B cells, which can be engulfed by macrophage-like cell line RAW 264.7 cells, thereby inducing biological responses (such as NO production) [32]. Liu KS et al. demonstrated that the polysaccharide GSP-2 extracted from Zizhi is a Toll-like receptor 4 (TLR4) agonist. GSP-2 dose-dependently induces TLR4 overexpression [33]. Chen Z et al. found that Changbaishan *Ganoderma lucidum* polysaccharide (CGLP) can regulate the expression of inflammatory cytokines IL-1 beta, TNF-α and IL-10 in a concentration-dependent manner, inhibit alveolar bone loss caused by periodontitis, and reduce inflammation [34]. Kao PF et al. found that the water-soluble β -1,3-glucan (LMG) recovered from *Ganoderma lucidum* extract residue has antioxidant capacity against H_2O_2-induced cell death by attenuating intracellular ROS and inhibiting SMase activity [35].

4.3 Other effective compounds in *Ganoderma lucidum*

Qingping Wu isolated ergosterol peroxide from *Ganoderma lucidum*, and it was found that it could eliminate microRNA miR-378-mediated chemotherapy-resistant tumor cells [36]. Jiao C et al. found that *Ganoderma lucidum* spore oil (GLSO) induces apoptosis in breast cancer cells *in vitro* and *in vivo* by activating caspase-3 and caspase-9 [37]. Wu X et al. found that *Ganoderma lucidum* spore oil enhanced the phagocytosis of mouse macrophages and NK cytotoxicity, and induced the structural rearrangement of intestinal microbiota. Its immunomodulatory effects are highly correlated with increased abundance of several bacterial genera (Lactobacillus, Turicibacter, and Romboutsia) and species (*Lactobacillus intestinalis* and *Lactobacillus reuteri*), as well as decreased levels of Staphylococcus and *Helicobacter pylori* [38]. Liu Y et al. found that *Ganoderma lucidum* spore lipophilic component (XF) can maintain the metabolic balance and function of the heart by regulating the expression of some proteins related to cardiovascular disease (Ucp1, Mmpz, Fasn, Nefl, Mtnd5, Mtnd2, S100a8, S100a9 and Bdh1), while *Ganoderma lucidum* spore polysaccharide (DT) can reduce the risk of cardiovascular disease by targeting the intestinal microbiota [39]. Wound healing has always been a worldwide problem, and Jiao C et al. found that *Ganoderma lucidum* spore oil regulates the levels of gram-negative bacteria and gram-positive bacteria, reduces the levels of LPS and TLR4 and some other related inflammatory cytokines, and significantly accelerates the process of skin wound healing. *Ganoderma lucidum* spore oil also improves burn healing by stimulating cell proliferation in skin wounds. In tissues, GLSO may enhance TRPV1

expression, initiate TGF- β /SMAD signaling more quickly, and promote SMAD2/3 nuclear translocation, thereby accelerating the progression from inflammatory to proliferative stages in skin wound healing [40,41].

5 Conclusion

By analyzing the research trends and hot spots of *Ganoderma lucidum* in the last 30 years, it can be expected that research publications on *Ganoderma lucidum* will continue to increase in the future, and that exchanges between institutions in different regions will become more frequent. The biological mechanisms, including anti-oxidative and anti-tumor effects of *Ganoderma lucidum* have been defined through extensive research. Future research may look to expand on the pharmacological effects, toxicology and safety to bring *Ganoderma lucidium* into primary healthcare.

Acknowledgements

Not applicable.

Conflicts of Interest

The authors declare no conflicts of interest.

Author Contributions

Investigation, Y.X. and R.H.; Data collection, Y.X.; Validation, Y.X. and R.H.; Supervision, Q.S. and R.H.; Writing—original draft, Y.X., Q.S., and R.H.; Writing—review and editing, Y.X., Q.S., and R.H. All authors have read and agreed to the published version of the manuscript.

Ethics Approval and Consent to Participate

The manuscript didn't involve any human or animal subjects, therefore no ethical approval was required for this article.

Funding

This research received no external funding.

Availability of Data and Materials

The data presented in this study are available on request from the corresponding author.

Supplementary Materials

The following supporting information can be downloaded at: https://ojs.exploverpub.com/index.php/jecacm/article/view/216/sup. Table S1: Excluded publications, which contained the author's name and only the term lingzhi, which were not related to *Ganoderma lucidum* research, and which were not available.

References

[1] Seweryn E, Ziała A, Gamian A. Health-promoting of polysaccharides extracted from *Ganoderma lucidum*. *Nutrients* 2021; 13(8): 2725.

[2] Liu H, Cheng J, Wang X, et al. Structure Identification of *Ganoderma lucidum* Spore Polysaccharides and Their Antitumor Activity In Vivo. *Molecules* 2024; 29(10): 2348.

[3] Ji C, Yang Y, Fu Y, et al. 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* 2022; 99: 105322.

[4] Cheng PG, Teoh TC, Rizman-Idid M. Chemical compounds and computational prediction of their inhibitory effects on the HIV-1 gp120 receptor by lingzhi or reishi medicinal mushroom, *Ganoderma lucidum* (agaricomycetes), with antler-like morphology of fruiting bodies. *International Journal of Medicinal Mushrooms* 2021; 23(7): 63-77.

[5] Ahmad MF, Ahmad FA, Hasan N, et al. *Ganoderma lucidum*: Multifaceted mechanisms to combat diabetes through polysaccharides and triterpenoids: A comprehensive review. *International Journal of Biological Macromolecules* 2024; 268(Pt 1): 131644.

[6] Tajik A, Samadlouie HR, Salek Farrokhi A, et al. Optimization of chemical conditions for metabolites production by *Ganoderma lucidum* using response surface methodology and investigation of antimicrobial as well as anticancer activities. *Frontiers in Microbiology* 2024; 14: 1280405.

[7] Kolniak-Ostek J, Oszmianski J, Szyjka A, et al. Anticancer and antioxidant activities in *Ganoderma lucidum* wild mushrooms in Poland, as well as their phenolic and triterpenoid compounds. *International Journal of Molecular Sciences* 2022; 23(16): 9359.

[8] Sanodiya BS, Thakur GS, Baghel RK, et al. *Ganoderma lucidum*: a potent pharmacological macrofungus. *Current Pharmaceutical Biotechnology* 2009; 10(8): 717-742.

[9] Lie Y. *Liezi - Tang Wen*; Huayashi Bookstore: Beijing, China, 2002.

[10] Luan Y, Hou W. *Shennong's Herbal*; People's Military Medical Publishing House: Beijing, China, 2010.

[11] Lin Z. Study on the integration of traditional Chinese and western medicine to interpret the discussion on *Ganoderma lucidum* in Shennong's Herbal Classic. *Chinese Journal of Pharmacology and Toxicology* 2019; 33(09): 645-646.

[12] Lin Z. From prehistory to modern times: A brief history of the development of *Ganoderma lucidum* medicine in China. *Mycological Research* 2024; 22(01): 1-8.

[13] Li S. *Compendium of Materia Medica New: Upper and Lower Volumes*; Huaxia Publishing House: Beijing, China, 2004.

[14] Chairul SM, Hayashi Y. Lanostanoid triterpenes from *Ganoderma applanatum*. *Phytochemistry* 1994; 35(5): 1305-1308.

[15] Paterson RRM. *Ganoderma* — A therapeutic fungal biofactory. *Phytochemistry* 2006; 67(18): 1985-2001.

[16] Cör D, Knez Ž, Knez Hrnčič M. Antitumour, antimicrobial, antioxidant and antiacetylcholinesterase effect of *Ganoderma lucidum* terpenoids and polysaccharides: A review. *Molecules* 2018; 23(3): 649.

[17] Baby S, Johnson AJ, Govindan B. Secondary metabolites from Ganoderma. *Phytochemistry* 2015; 114: 66-101.

[18] Ahmad MF. *Ganoderma lucidum*: Persuasive biologically active constituents and their health endorsement. *Biomedicine & Pharmacotherapy* 2018; 107: 507-519.

[19] Wang L, Li J, Zhang J, et al. Traditional uses, chemical components and pharmacological activities of the genus *Ganoderma* P. Karst.: a review. *RSC Advances* 2020; 10(69): 42084-42097.

[20] Galappaththi MCA, Patabendige NM, Premarathne BM, et al. A review of *Ganoderma triterpenoids* and their bioactivities. *Biomolecules* 2022; 13(1): 24.

[21] Liu Y, Wen H, Xu R, et al. Semisynthesis and antitumor activity of endertiin B and related triterpenoids from *Ganoderma lucidum*. *Organic & Biomolecular Chemistry* 2024; 22(24): 4978-4986.

[22] Wu GS, Guo JJ, Bao JL, et al. Anti-cancer properties of triterpenoids isolated from *Ganoderma lucidum*—a review. *Expert Opinion on Investigational Drugs* 2013; 22(8): 981-992.

[23] Ahmad MF, Ahmad FA, Khan MI, et al. *Ganoderma lucidum*: A potential source to surmount viral infections through β -glucans immunomodulatory and triterpenoids antiviral properties. *International Journal of Biological Macromolecules* 2021; 187: 769-779.

[24] Zhao C, Fan J, Liu Y, et al. Hepatoprotective activity of *Ganoderma lucidum* triterpenoids in alcohol-induced liver injury in mice, an iTRAQ-based proteomic analysis. *Food Chemistry* 2019; 271: 148-156.

[25] Wang C, Liu X, Lian C, et al. Triterpenes and aromatic meroterpenoids with antioxidant activity and neuroprotective effects from *Ganoderma lucidum*. *Molecules* 2019; 24(23): 4353.

[26] Dudhgaonkar S, Thyagarajan A, Sliva D. Suppression of the inflammatory response by triterpenes isolated from the mushroom *Ganoderma lucidum*. *International Immunopharmacology* 2009; 9(11): 1272-1280.

[27] Li P, Liu L, Huang S, et al. Anti-cancer effects of a neutral triterpene fraction from *Ganoderma lucidum* and its active constituents on SW620 human colorectal cancer cells. *Anti-Cancer Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Anti-Cancer Agents)* 2020; 20(2): 237-244.

[28] Ren L, Zhang J, Zhang T. Immunomodulatory activities of polysaccharides from *Ganoderma* on immune effector cells. *Food Chemistry* 2021; 340: 127933.

[29] Guo C, Guo D, Fang L, et al. *Ganoderma lucidum* polysaccharide modulates gut microbiota and immune cell function to inhibit inflammation and tumorigenesis in colon. *Carbohydrate Polymers* 2021; 267: 118231.

[30] Zhang X, Wang J, Zhang T, et al. Updated Progress on Polysaccharides with Anti-Diabetic Effects through the Regulation of Gut Microbiota: Sources, Mechanisms, and Structure — Activity Relationships. *Pharmaceuticals* 2024; 17(4): 456.

[31] Ma HT, Hsieh JF, Chen ST. Anti-diabetic effects of *Ganoderma lucidum*. *Phytochemistry* 2015; 114: 109-113.

[32] Han XQ, Yue GL, Yue RQ, et al. Structure elucidation and immunomodulatory activity of a beta glucan from the fruiting bodies of *Ganoderma sinense*. *PLoS One* 2014; 9(7): e100380.

[33] Liu KS, Zhang C, Dong HL, et al. GSP-2, a polysaccharide extracted from *Ganoderma sinense*, is a novel toll-like receptor 4 agonist. *PLoS One* 2019; 14(8): e0221636.

[34] Chen Z, Qin W, Lin H, et al. Inhibitory effect of polysaccharides extracted from Changbai Mountain *Ganoderma lucidum* on periodontal inflammation. *Heliyon* 2023; 9(2): e13205.

[35] Kao PF, Wang SH, Hung WT, et al. Structural Characterization and Antioxidative Activity of Low-Molecular-Weights Beta-1, 3-Glucan from the Residue of Extracted *Ganoderma lucidum* Fruiting Bodies. *BioMed Research International* 2012; 2012(1): 673764.

[36] Wu Q, Xie Y, Deng Z, et al. Ergosterol peroxide isolated from *Ganoderma lucidum* abolishes microRNA miR-378-mediated tumor cells on chemoresistance. *PLoS One* 2012; 7(8): e44579.

[37] Jiao C, Chen W, Tan X, et al. *Ganoderma lucidum* spore oil induces apoptosis of breast cancer cells in vitro and in vivo by activating caspase-3 and caspase-9. *Journal of Ethnopharmacology* 2020; 247: 112256.

[38] Wu X, Cao J, Li M, et al. An integrated microbiome and metabolomic analysis identifies immunoenhancing features of *Ganoderma lucidum* spores oil in mice. *Pharmacological Research* 2020; 158: 104937.

[39] Liu Y, Lai G, Guo Y, et al. Protective effect of *Ganoderma lucidum* spore extract in trimethylamine-N-oxide-induced cardiac dysfunction in rats. *Journal of Food Science* 2021; 86(2): 546-562.

[40] Jiao C, Xie Y, Yun H, et al. The effect of *Ganoderma lucidum* spore oil in early skin wound healing: interactions of skin microbiota and inflammation. *Aging (Albany NY)* 2020; 12(14): 14125.

[41] Jiao C, Yun H, Liang H, et al. An active ingredient isolated from *Ganoderma lucidum* promotes burn wound healing via TRPV1/SMAD signaling. *Aging (Albany NY)* 2022; 14(13): 5376.