The Trend of *Ganoderma Lucidum* Research (1936–2019)

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Abstract

Ganoderma lucidum, as the symbol of traditional Chinese medicine, is one of the most economically important medicinal fungi and has received attention worldwide. The number of scientific research publications about *G. lucidum* increased rapidly. However, there have been few research reviews concerning the research trend of *G. lucidum.* Here we used Biblioshiny to analyze 3,286 documents from 1936 to 2019. These documents were screened and analyzed using four software tools: R-package bibliometrix, HisCite, Citespace, and Bibliometric Online Analysis Platform. We presented the performance of relevant sources, authors, institutions, and countries. We analyzed the most highly cited documents of *G. lucidum* to define the research hotspots and research trends in this field.

2.1 Introduction

As the public becomes more aware of drug safety, people prefer natural medicinal products derived from plants and fungi because they have the distinct advantage of being less toxic and having fewer side effects (Tan et al. 2011). Biological natural products are secondary metabolites from living organisms. These sources can be complex mixtures derived from raw materials or single compounds (Lyu et al. 2020; Liu et al. 2020). Several *Ganoderma* species, represented by *Ganoderma lucidum* (Curtis) P. Karst. are well-known medicinal fungi. They have greater advantages over other chemical drugs. *Ganoderma* comes from the Greek word, "gano" meaning shiny, and "derma" meaning skin. For the first time, the mushroom was called *Ganoderma* by mycologist Petter Adolf Karsten in Finland in 1881 (Karsten 1881). *Ganoderma* species is widely distributed in tropical and subtropical regions of Africa, America, Asia, Oceania, and Europe (Zhou et al. 2016; Sun et al. 2020). There are more *Ganoderma* species in southern China, especially in the south of tropical and subtropical regions (Zhao et al. 2018). It mainly regulates human immune function, prolongs life span, has antitumor and neuroprotective functions (Batra 2019). This is one of the reasons for the growing demand for *Ganoderma* products. The main medicinal part of *Ganoderma* is the fruiting body, but its spore powder and mycelium can also be used medicinally. In the United States, *Ganoderma* is available as a dietary supplement and is listed in the United States Pharmacopoeia of Dietary Supplements and Herbs (Nishita et al. 2017; Paterson et al. 2006). With the industry's development, the

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spores and mycelium of *Ganoderma* have been used as new medicinal ingredients. *Ganoderma* spores have been shown to have good antitumor and antioxidant activity (Min et al. 1998; Heleno et al. 2012). The main compounds from *Ganoderma* species include triterpenes, polysaccharides, terpenoids, sesquiterpenoids, steroids, and alkaloids. Across different countries, triterpenes and polysaccharides are considered the main active ingredients (Soccol et al. 2016; Gao et al. 2003a). The fruit bodies, cultured mycelia, and spores of *G. lucidum* have been reported to have therapeutic effects on chronic liver disease, hypertension, hyperglycemia, and neonatal disease (Franz 1989; Furusawa et al. 1992; Shiao et al. 1994). The main active ingredients of *G. lucidum* are triterpenoid and polysaccharides (Paterson et al. 2006; Shaoping et al. 2013).

Literature reviews document and quantify trends in scientific publications. Bibliometrics is a scientific, objective, and convenient literature review method. Pritchard first proposed bibliometrics in 1969 as a pattern-based quantitative method for research and development (Pritchard 1969). It is defined as a mathematical and statistical method that quantitatively analyzes trends across multiple scientific disciplines. This method is often used as a powerful tool to evaluate many scientific publications in different research areas (Ge et al. 2017; Torres et al. 2015; Barbero-Sierra et al. 2015). Its scope extends from the statistical analysis of the single relationship among countries, institutions, authors, and other variables to revealing potential multivariable relationships by establishing and analyzing contact networks (Zhang et al. 2017; Yu et al. 2017; Li et al. 2017).

Several sophisticated software tools have been developed for bibliometrics analysis, including HistCite (Li et al. 2016; Wanqi et al. 2018), Citespace (Gao et al. 2016; Wanqi et al. 2017) and Bibliometrics Online Analysis Platform (BOAP, https://bibliometric.com/). These tools can be used for qualitative and quantitative analysis of data collected from many publications. Histsite allows users to analyze citations in an unfamiliar field to quickly map the trends in this field, identify the most frequently researched research issues, and reveal relevant geographic regions, institutions, and specific research scientists who are leaders in the research field. CiteSpace allows users to understand the history and trends of the field through visual analysis of published research. BOAP is a web application for identifying metrics related to bibliometric analysis. CiteSpace and BOAP have similar functionality, but the former has more modules, and the latter is faster and easier to use. R-package bibliometrix is a bibliometrics analysis tool based on the R language (Aria and Cuccurullo 2018). Bibliometrix provides a workflow that can be used automatically. The bibliometrix is flexible and can be integrated with other R-packages. After successful installation, it provides a web interface based on Biblioshiny, through which users can obtain basic statistics of literature information and the cooperation of various indicators. It is easy to use and fast to produce results. Because these tools have complementary theoretical and functional modules, multiple tools should be used together for the most comprehensive literature analysis.

The health-promoting effects of *G. lucidum* have attracted international research interests on diverse subjects. Related publications have rapidly increased in recent years. However, there are no studies that carried out a comprehensive review on this field. In this study, we use sophisticated tools to carry out a bibliometric analysis. Here, we analyze the past development history and identify future research directions from the following aspects: global publication output, country, author, journal, most local citation references, the conceptual structure, the intellectual structure, and the social structure.

2.2 Data Collection and Analytical Method

Data were retrieved from the Web of Science Core Collection database, using "*Ganoderma lucidum*" as the keywords. We set the retrieval time from 1900 to 2019. A total of 3286 records were obtained between 1936 and 2019. Every record contains the authors' information, title,

source, abstract, keywords, and cited references. The data were analyzed using the four software tools described below.

The manually processed data were visually analyzed using the R-package bibliometrix. Besides, Histsite and Citespace are used for analyzing comprehensive indicators. BOAP is used for cooperative relationship analysis.

2.3 Results

2.3.1 Descriptive Analysis (Country, Author, Source)

The 3,286 documents from 1936 to 2019 include 381 sources, 25.34 average citations per document, 2.727 average citations per year per document, 79,529 references, 9,339 authors, 17,734 author appearances, 9,263 authors of multi-authored documents, 76 authors of single-authored documents. Documents also contain 6,898 author's keywords (DE) and 6,074 keywords plus (ID). The number of documents per author is 0.352. The number of authors per document is 2.84. The majority of these papers are articles (3,021 records, 91.94%), and the remaining ones are reviews (265 records, 8.06%).

As shown in Fig. 2.1, the number of publications increases gradually, and the annual growth rate is 4.73%. It can be divided into three stages, which are stage I: 1936–1992; stage II: 1993–2007; and stage III: 2008–2019. Stage I (1936–1992) was the initial period when less than ten papers were published annually except 1986, 1988, and 1991 which have 12, 15, and 12 publications, respectively. Stage II (1993–2007) is the rising period; the number of papers is higher than before, but not more than 100. Stage III (2008–2019) is the rapid development period that more scholars began to focus on *G. lucidum* research.

During 1936–2019, a total of 87 countries contributed to publications. Figure 2.2 shows the geographical distribution of the country's scientific production and the total publications (TP), total citations (TC), and average citations (AC) of the top 10 most productive countries by the corresponding authors. China produced the most studies with 1,653 publications, account for more than 50%. In contrast, India ranks in second place, has a much smaller number than China. And China shows the highest TC of 41,214. Although China has the highest number of publications and total citations, the average citation is lower than other countries, only 24.93. It indicated that the number of published articles in China is high, but the number of high-level articles is relatively small, and the research field's influence is relatively weak. In terms of the number of publications, Korea ranks the last, but its average citation is in the first place of the top 10 productive countries with 34.64. The USA with 31.93 is second only to Korea.

Figure 2.3a presents the top 10 productive authors in the *G. lucidum* research area. The most productive author is Zhong JJ, with 58 publications from 2002 and has the highest total citations, 2591 and H-index 28. We analyzed the numbers of articles published yearly by these ten prolific authors (Fig. 2.3b). The most productive author Zhong JJ published articles cover the longest time, from 2002 to 2018. And Zhong JJ has published most articles and obtained the highest citations in 2010, 10 and 36.08, respectively. Besides, Shi L and Chen Y started *G. lucidum* research earlier in 1997. Their articles have been published continuously since 2008. It's worth noting that Chen Y at the 10th productive author but has the most articles per year and the highest citations among all authors listed. In 2012, Chen (2012) published 12 articles per year. Besides, Chen Y only published five articles in 2015, but got the highest citations per year: 59.57. Among them, the title "*Ganoderma lucidum* reduces obesity in mice by modulating the composition of the gut microbiota" is a highly cited paper. This research suggested that *G. lucidum* and its high molecular weight polysaccharides can be used as prebiotic agents to prevent intestinal disorders and obesity-related metabolic disorders in obese individuals (Chang et al. 2015).

A total of 3,286 papers were published in 831 different sources by 2019. The top 10 journals account for 20.48% of the total articles analyzed

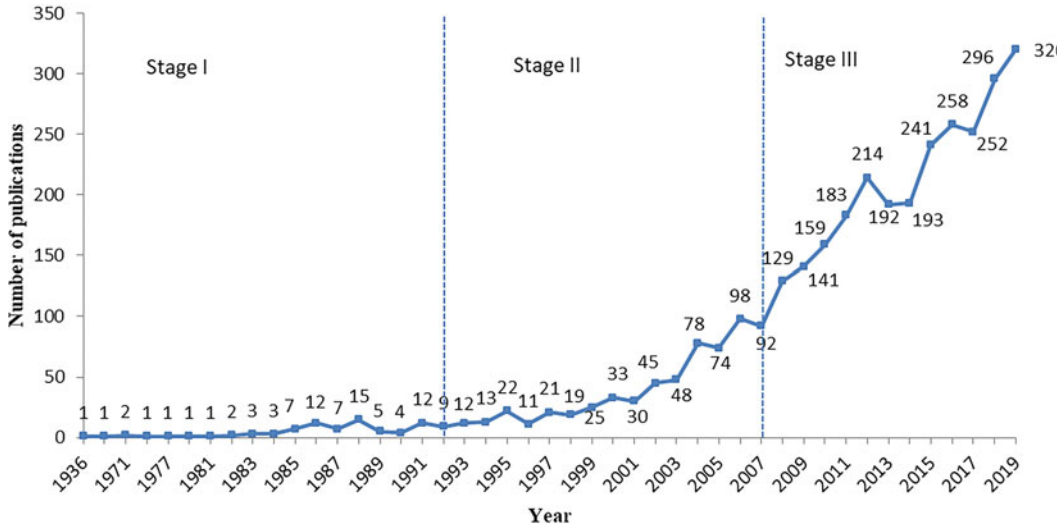

Fig. 2.1 Annual publications in the *Ganoderma lucidum* research area from 1936 to 2019

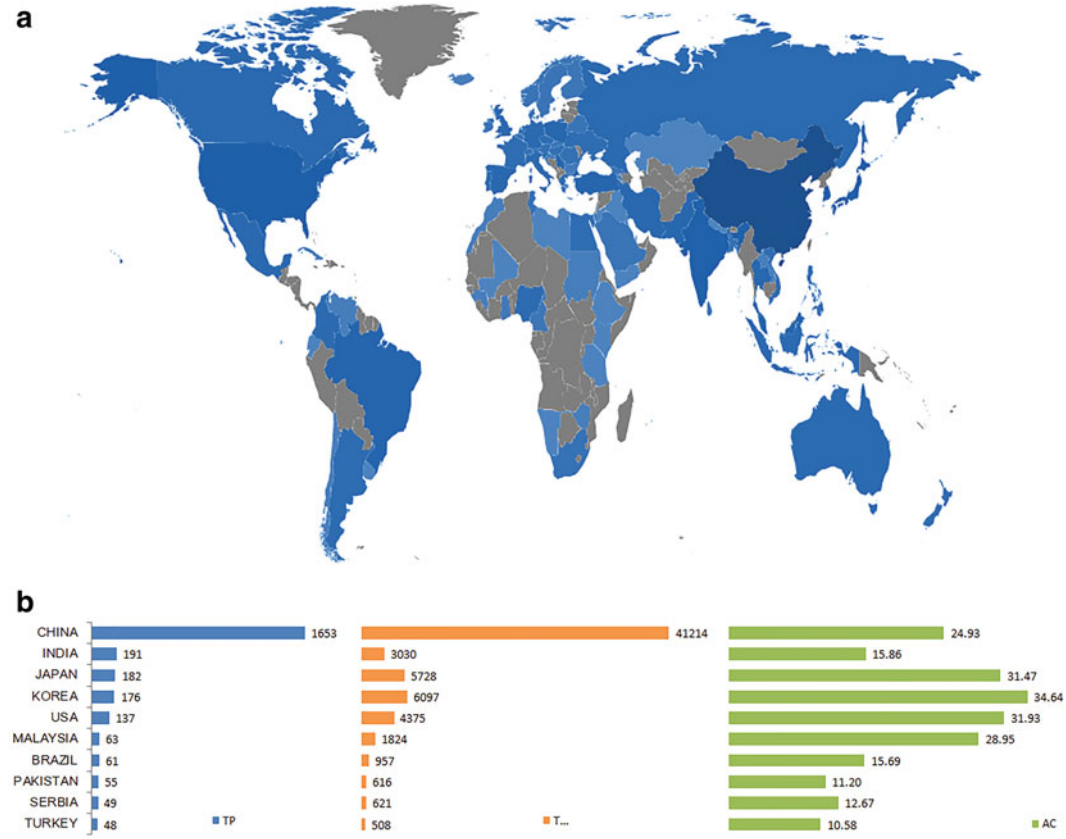

Fig. 2.2 Characteristics of countries/regions in *Ganoderma lucidum* research area from 1936 to 2019. **a** Geographical distribution of research countries/regions. **b** The top 10 relevant countries by the corresponding author

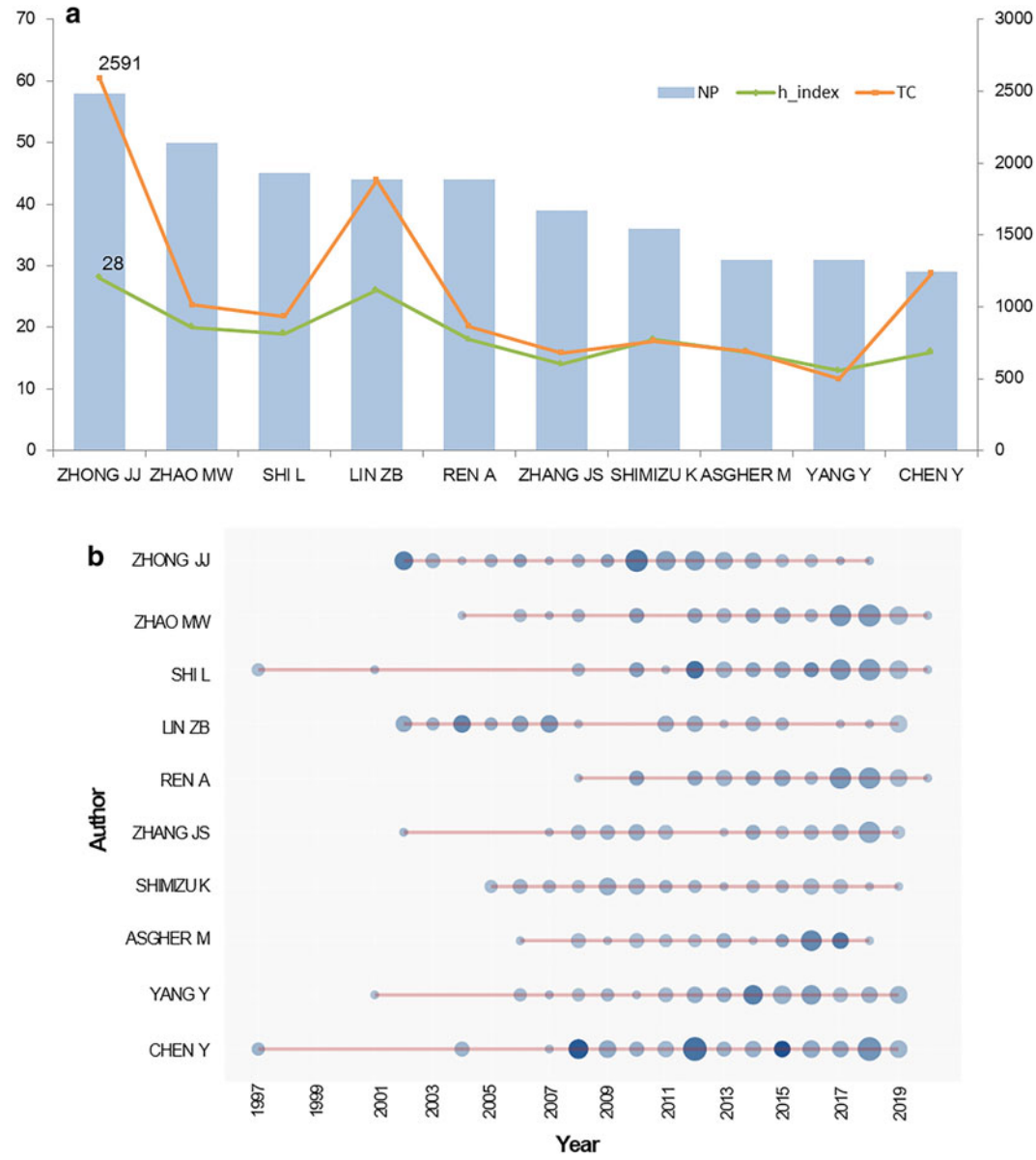

Fig. 2.3 The performance of the authors in *G. lucidum* research from 1936 to 2019. **a** The top 10 productive authors in the *G. lucidum* research area. **b** Top-authors' production over time. The size of the circle represents the number of articles. The depth of the color of the circle represents the number of citations per year

(Table 2.1). Most of the impact factors are $\geq$ 3.0 (7 in 10), and half of them have H-index $\geq$ 25. "International Journal of Medicinal Mushrooms" is the most productive journals with 203 publications related to *Ganoderma lucidum* research. But it's TC and H-index is not the highest, with 2,751 and 20, respectively. "Carbohydrate Polymers" ranks in the second place, and has the highest TC, H-index, and IF of 4120, 36, and 7.182, respectively.

Besides, we analyzed the keywords plus of 3,286 publications. The word cloud is shown in

Table 2.1 Top 10 most productive sources during 1936–2019

Rank	Source	TP	TC	H_index	IF (2019)
1	International Journal of Medicinal Mushrooms	203	2751	20	1.423 (2018)
2	Carbohydrate Polymers	84	4120	36	7.182
3	International Journal of Biological Macromolecules	79	2010	26	5.162
4	Phytochemistry	59	3189	29	3.044
5	Molecules	49	858	17	3.267
6	Journal of Agricultural and Food Chemistry	43	1815	27	4.192
7	Journal of Ethnopharmacology	43	1707	26	3.69
8	Food Chemistry	40	2066	25	6.306
9	Plos One	37	863	19	2.74
10	Process Biochemistry	36	1296	20	2.952

Fig. 2.4. The word minimum frequency is chosen as 5. "*Ganoderma lucidum*" was recorded 844 times in 2013, and "Polysaccharides" had 334 records in 2014. Besides, the records of "lucidum," "in-vitro," "growth," "cells," "expression," and "acid" are more than 200 between 2012 and 2015, indicating that this period is a rapid-growth stage in *G. lucidum* research.

2.3.2 Thematic Analysis

Thematic analysis is used to define the conceptual structure of the topic. The thematic map exploits the Keywords Plus field. Those keywords are associated with Thomson Reuters editorial experts supported by a semi-automated algorithm. They review all references' titles and highlight additional relevant but overlooked keywords that the authors did not list. Different

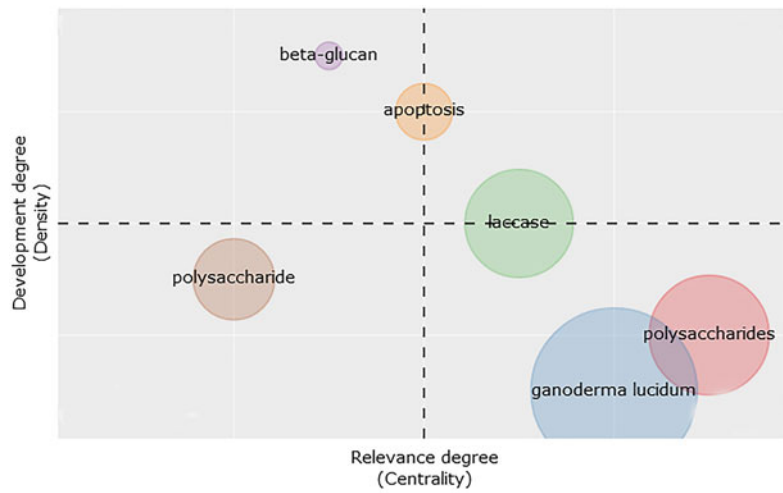

Fig. 2.4 Thematic map. The x-axis represents centrality, and the y-axis represents density

from the authors' keywords, the Keywords Plus field is normalized. Keywords Plus terms can differentiate content with greater depth and variety.

Applying a clustering algorithm on the keyword network makes it possible to highlight a given domain's different themes. Each cluster can be presented on a particular plot. Centrality measures the importance of the subject in the entire research field. In contrast, density measures the theme's development.

Thematic mapping allows visualization of six different types of subjects, as shown in Fig. 2.4. Each bubble represents a network cluster. The bubble name is the word belonging to the cluster, with the higher occurrence value. The bubble size is proportional to the cluster word occurrences. The bubble position is set according to the cluster centrality and density.

The upper-right quadrant shows the "motor themes." They are characterized by both high centrality and density. Regarding the upper-left quadrant, it shows high-density themes. Still, unimportant external links are of only limited importance for the field (low centrality). The main theme is on "beta-glucan." This theme is connected with different concepts, such as "antitumor," "basidiomycetes," and "grifola frondosa." In the lower-left quadrant are the emerging or declining themes. We then analyzed the frequency of the keyword using wordcloud (Fig. 2.5), the theme of "polysaccharide" is emerging. Besides, "antioxidant activity," "antitumor activity," and "structure" are also involved in this theme. Finally, the lower-right quadrant shows the themes that are basic and transversal. These themes concern general topics transversal to the different research areas of the field. In this area, the appearing themes are "*Ganoderma lucidum*" and "polysaccharides." Besides, "laccase" is between motor theme and basic theme, And "submerged culture," "mushrooms," and "response surface methodology" also in this cluster. This shows that the research work on glucan, antitumor effects of Lingzhi are in foucs and it is likely that there will be literatures related to these topics in the future. Active ingredients, such as laccase, polysaccharides, and triterpenoids, have been the research hotspot recently.

2.3.3 Co-Word Analysis

2.3.3.1 Keyword Co-Occurrence

The keywords co-occurrence network is shown in Fig. 2.6a. Among them, words such as Ganoderma-lucidum, polysaccharides, in vitro, growth, lucidum have higher centrality in the whole network, appear more frequently and have a more substantial influence. The above keywords are connected with other keywords, such as antitumor, expressions, fruiting bodies, apoptosis, and purification. These results reflect the wide variety of topics of *G. lucidum* that are currently under study.

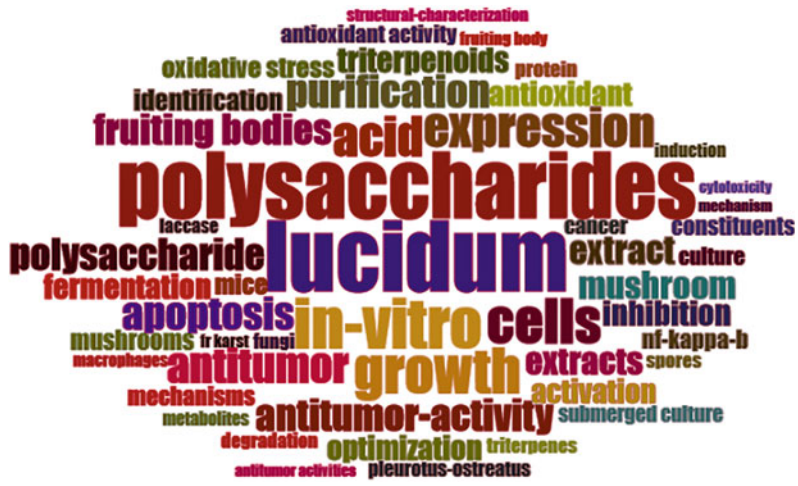

Fig. 2.5 The WordCloud of the keywords in *G. lucidum* research from 1936 to 2019

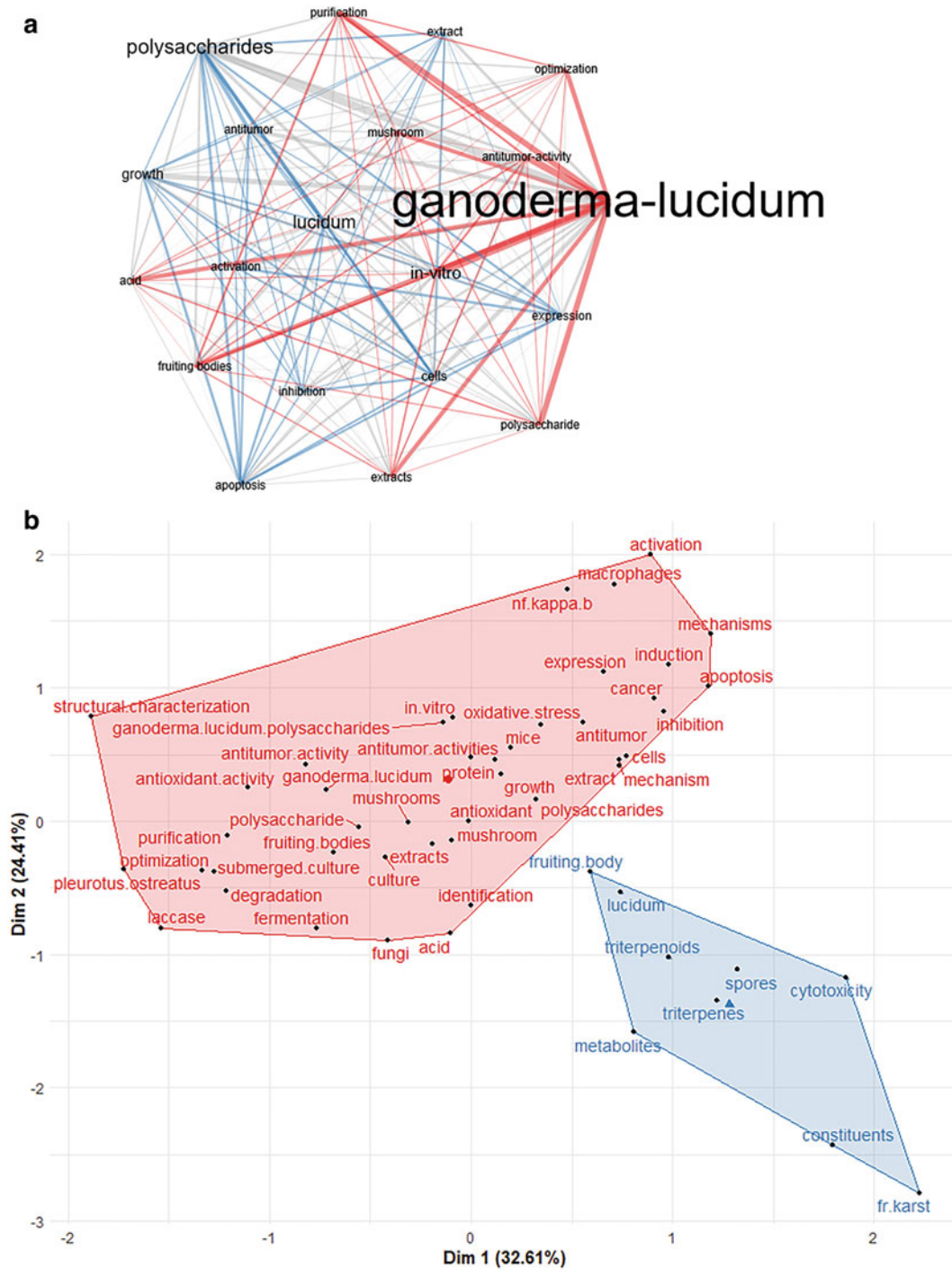

Fig. 2.6 Conceptual structure. **a** Keyword co-occurrence network. **b** Multiple correspondence analysis

2.3.3.2 Correspondence Analysis

The conceptual structure–function in Bibliometrix uses the Multivariate Correspondence Analysis (MCA) to draw the research area's conceptual structure. The k-means clustering method is used to cluster the literature. As shown in Fig. 2.6b, each color represents a cluster of a word. Cluster I in red has the keywords such as structural characterization, optimization, laccase, mechanisms, activation, etc. Cluster II in blue has the keywords such as metabolites, constituents, cytotoxicity, etc.

2.3.4 Co-Citation Analysis

2.3.4.1 Papers Co-Citation Analysis

In the co-citation network (Fig. 2.7a), 20 articles are divided into two clusters with red and blue. The most influential paper is Paterson et al. (2006) with the title of "Ganoderma—A therapeutic fungal biofactory." This review collates the publications detailing activities and compounds by representative species whilst considering the most valid claims of effectiveness.

2.3.4.2 Sources Co-Citation Analysis

In the sources co-citation network (Fig. 2.7b), 20 sources are divided into 3 clusters. Phytochemistry, life science, Journal of Ethnopharmacology, Journal of Natural Products, Phyototherapy Research, Planta Medica and Chemical & Pharmaceutical Bulletin form cluster I in red. Applied Microbiology and Biotechnology, PLOS one, Biochemical and Biophysical Research Communication, Journal of Biological Chemistry and Proceeding of the National Academy of Sciences of the United States of America form cluster II in blue. Journal of Agricultural and Food Chemistry, Food Chemistry, Carbohydrate Polymers, International Journal of Medicinal Mushrooms, Internal Journal of Biological Macromolecules, Food and Chemical Toxicology and International Immunopharmacology form cluster III in green. Phytochemistry, Journal of Ethnopharmacology, and Journal of Agricultural and Food Chemistry correlate with other sources.

2.3.5 Collaboration Analysis

2.3.5.1 Author Collaboration Network

In total, 9,339 authors published a total of 3,286 papers by 2019. In the author collaboration network (Fig. 2.8a), 50 authors are listed, and 18 clusters are formed. Zhao mw, Ren a, and Shi l have more cooperative relationships. Besides, authors Zhang js, Yang y, Tang qj, Liu yf, and Zhou s also have a special collaborative relationship.

2.3.5.2 Institution Collaboration Network

A total of 3,286 papers were published from 2,406 institutions by 2019. In the institutions' collaboration analysis (Fig. 2.8b), National Taiwan University, National Yang-Ming University, Academia Sinica, China Medical University, Taipei Medical University, and National Chung Hsing University have many contacts in *G. lucidum* research. Besides, Shanghai Jiao Tong University and East China University of Science and Technology, Kunming Institute of Botany, and University of Chinese Academy of Sciences also have a cooperative relationship.

2.3.5.3 Country Collaboration Network

Academic cooperation in different countries/regions is vital. Scholars can communicate with one another, exchange novel opinions, and determine ideal solutions through international collaboration. Figure 2.8c shows a clear cooperative relationship between countries/regions. Each color represents a different country/region, and the thickness of the connecting lines denotes the strength of cooperation. China takes first place for *G. lucidum* related international collaboration, especially with the USA and Japan. China is the country with the most abundant *G. lucidum* resources and has established cooperative relations with the United States and Japan, which are technologically advanced at the time of the collaborations.

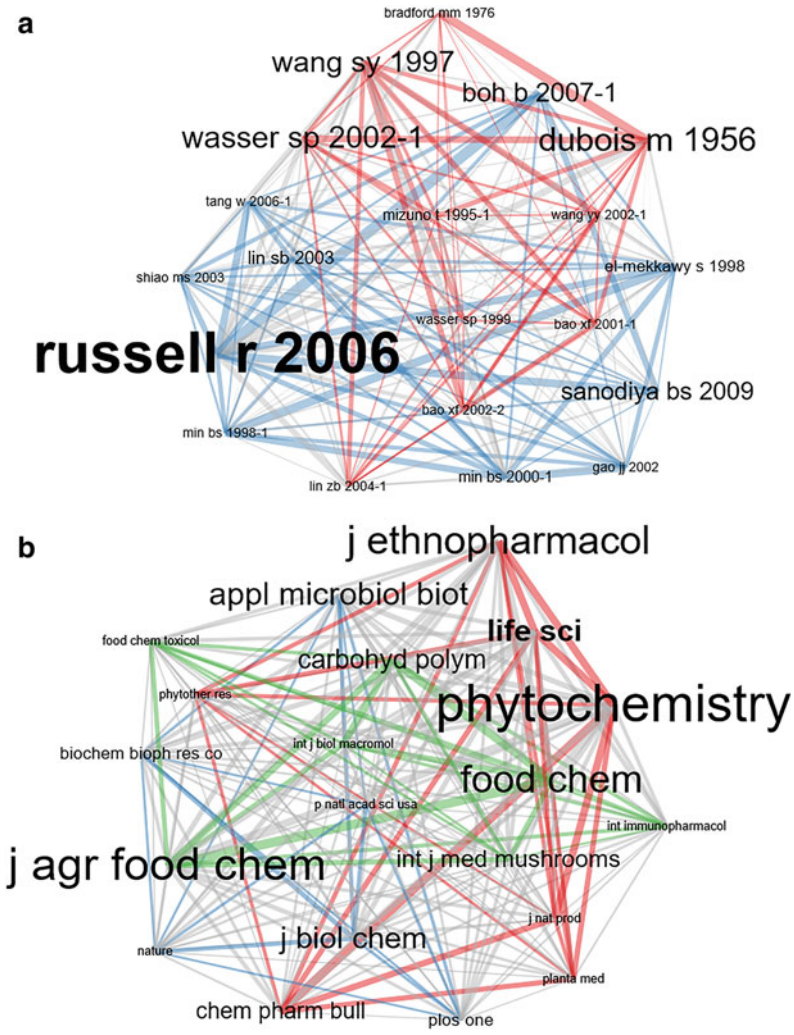

Fig. 2.7 Intellectual structure. **a** Papers co-citation network. **b** Sources co-citation network

2.3.6 Keyword Detection and Analysis

Detection of keywords can be used to identify *G. lucidum* research trends (Chen et al. 2014). Burst detection is a method of detecting dramatic changes in events, measured by a burst intensity parameter, measured by a score calculated by Kleinberg J algorithm (Kleinberg 2003). After importing data into Citespace, eight keywords bursts continued into 2017 and 2019 (Fig. 2.9). The keyword with the largest burst strength score of 9.37 was "lingzhi," followed by "structural characterization" with 8.9. The keywords of "reishi medicinal mushroom" and "meroterpenoid" ended in 2019. Therefore, future research directions may aim to determine the structural feature and meroterpenoid of Lingzhi.

2.3.7 Most Highly Cited Papers Analysis

We analyze the most highly cited articles to define the research hotspots (Table 2.2). The most highly cited paper is a review titled "Antioxidative peptides from food proteins: A review," published in Peptides in 2010 (Sarmadi and Ismail 2010). It has been cited 765 times ever since. This paper reviews bioactive peptides

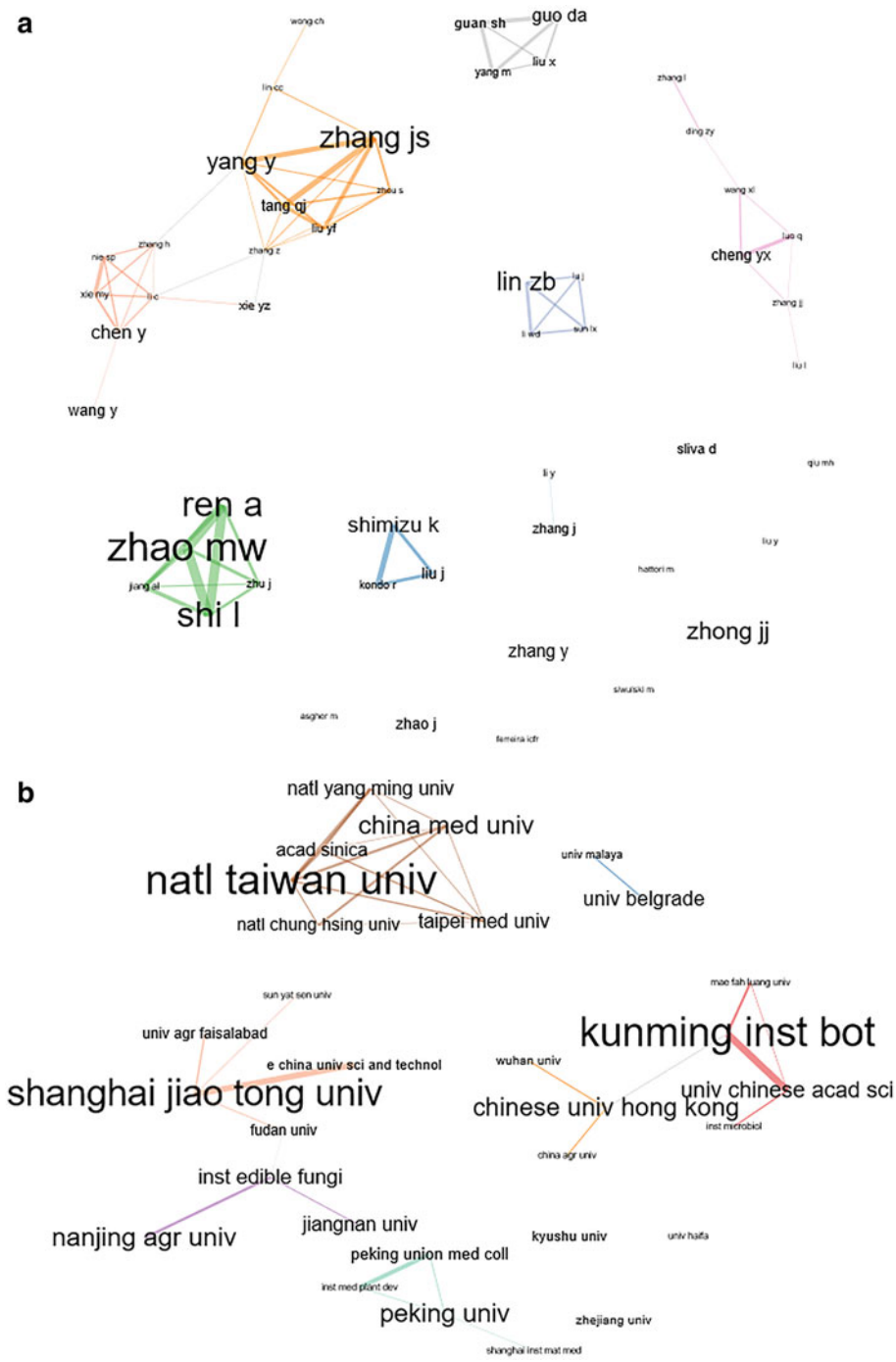

Fig. 2.8 Collaboration network. **a** Authors collaboration network. **b** Institutions collaboration network. **c** Countries collaboration network

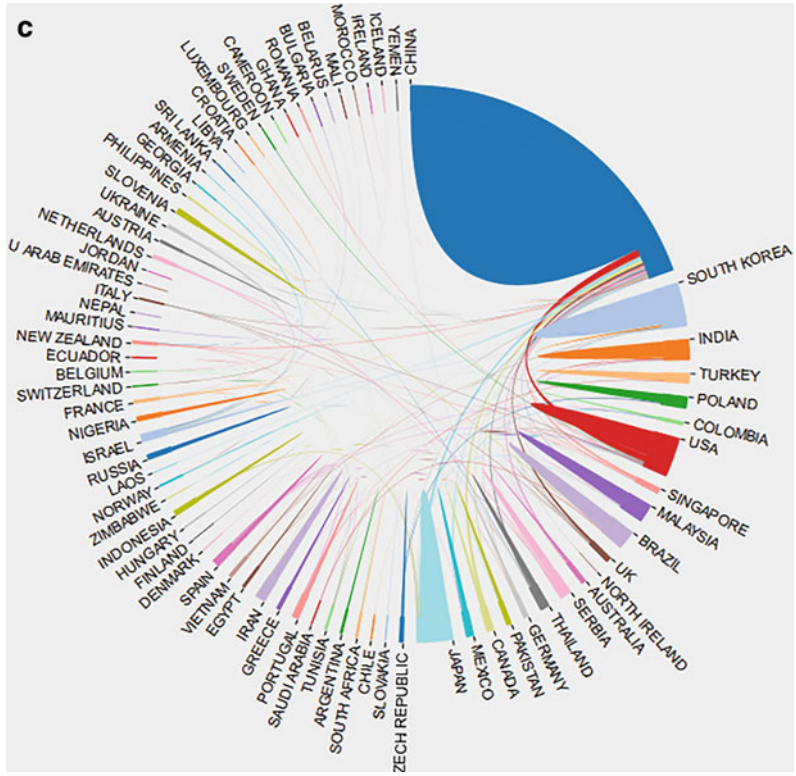

Fig. 2.8 (continued)

Fig. 2.9 Results of keyword burst continuing to 2017 and 2019

Key words	Strength	Beign	End	1936-2019
resistance	7.62	2013	2017	
phanerochaete chrysosporium	6.8	2013	2017	
purification	7.26	2014	2017	
potent	7.65	2015	2017	
reishi medicinal mushroom	6.79	2015	2019	
meroterpenoid	6.3	2015	2019	
lingzhi	9.37	2017	2019	
structural characterization	8.9	2017	2019	

from food sources concerning their antioxidant activities. The properties of active antioxidant peptides, enzymatic production, antioxidant capacity evaluation methods, bioavailability, and safety are also reviewed. Similarly, Mau et al. (2002) studied the antioxidant properties of methanolic extracts from the medicinal mushrooms in Taiwan, namely, *G. lucidum* (Ling-chih), *G. tsugae* (Sung-shan-ling-chih), and *Coriolus versicolor* (Yun-chih). Overall, the antioxidant capacity, reducing capacity, chelation scavenging capacity, and total phenolic content were found higher in *G. lucidum* and *G. tsugae*.

The pharmacologic action of *G. lucidum* is the mostly studied topic studied. For instance, Wang et al. (1997) isolated polysaccharides (PS) from fresh seeds of *G. lucidum* (PS-G) for enhancing cytokine production by human monocyte-

Table 2.2 Summary of the most highly cited articles

Rank	Title	TC	PY	Summary
1	Antioxidative peptides from food proteins: A review	765	2010	This paper reviews bioactive peptides from food sources concerning their antioxidant activities. Then, it reviewed the specific characteristics of antioxidative bioactive peptides, enzymatic production, and methods to evaluate antioxidant capacity and bioavailability. Lastly, safety concerns of peptides were discussed
2	*Ganoderma*—A therapeutic fungal biofactory	549	2006	This review collates the publications detailing activities and compounds by representative species whilst considering the most valid claims of effectiveness
3	The pharmacological potential of mushrooms	521	2005	This review describes pharmacologically active compounds from mushrooms.
4	Medicinal Mushroom Science: History, Current Status, Future Trends, and Unsolved Problems	476	2010	This review summarized the data on mushroom polysaccharides for approximately 700 species of higher Hetero- and Homobasidiomycetes. It discussed the chemical structure of polysaccharides. Furthermore, their connection to antitumor activity was investigated. These include possible ways of chemical modification, experimental testing, and clinical use of antitumor or immunostimulating polysaccharides.
5	Purification, composition analysis and antioxidant activity of a polysaccharide from the fruiting bodies of *Ganoderma atrum*	413	2008	A water-soluble protein-bound polysaccharide was extracted from the fruiting bodies of *Ganoderma atrum* and isolated by gel-filtration chromatography. Its primary structural features and molecular weight were characterized by infrared spectrometry, gas chromatography, size exclusion chromatography, amino acid analyzer, and high-performance liquid chromatography (HPLC). The results suggest the polysaccharides' strong DPPH free radical and superoxide anion radical scavenging activities. The purified polysaccharides could potentially be used as natural antioxidants.
6	The antitumor effect of *Ganoderma lucidum* is mediated by cytokines released from activated macrophages and T lymphocytes	371	1997	The present study was to ascertain the immunomodulating and antitumor effects of *Ganoderma lucidum.*
7	*Ganoderma lucidum* reduces obesity in mice by modulating the composition of the gut microbiota	369	2015	Here, the authors show that a water extract of *Ganoderma lucidum* mycelium (WEGL) reduces body weight, inflammation, and insulin resistance in mice fed a high-fat diet (HFD). They further show that high molecular weight polysaccharides (>300 kDa) isolated from the WEGL extract produce similar anti-obesity and microbiota-modulating effects. Our results indicate that

(continued)

Table 2.2 (continued)

Rank	Title	TC	PY	Summary
				G. lucidum and its high molecular weight polysaccharides may be used as prebiotic agents to prevent gut dysbiosis and obesity-related metabolic disorders in obese individuals.
8	The Role of Culinary-Medicinal Mushrooms on Human Welfare with a Pyramid Model for Human Health	295	2012	This review presents a pyramid model for mushroom uses (industries), like food, dietary supplements (tonic), and medicine. A regular intake of mushrooms can make us healthier, fitter, and happier and help us live longer. The sense of purpose and vision for the mushroom industries is also briefly discussed.
9	Antioxidative and immunomodulating activities of polysaccharide extracts of the medicinal mushrooms Agaricus bisporus, Agaricus brasiliensis, *Ganoderma lucidum*, and Phellinus linteus	232	2011	Partially purified polysaccharides were obtained from four medicinal mushroom species, Agaricus bisporus, Agaricus brasiliensis, Phellinus linteus, *Ganoderma lucidum*, by hot water extraction, followed by ethanol precipitation. EC50 values of the DPPH scavenging activity of the polysaccharides from *G. lucidum* spores and *P. linteus* fruiting bodies were found to be particularly low, i.e., EC50 < 0.1 mg/ml. EC50 values of the antioxidant activity were 7.07 mg/ml for *G. lucidum*, EC50 values of ferrous ions' chelating activity ranged from 0.59 mg/ml for *G. lucidum*
10	Genome sequence of the model medicinal mushroom *Ganoderma lucidum*	231	2012	Here we report its 43.3-Mb genome, encoding 16,113 predicted genes. Twenty-four physical CYP gene clusters are identified. Moreover, 78 CYP genes are coexpressed with lanosterol synthase, and 16 of these show high similarity to fungal CYPs that specifically hydroxylate testosterone, suggesting their possible roles in triterpenoid biosynthesis
11	Antitumor and immunoregulatory activities of *Ganoderma lucidum* and its possible mechanisms	229	2004	This review summarized *G. lucidum* modulate many components of the immune system. The water extract and the polysaccharides fraction of *G. lucidum* exhibited a significant antitumor effect in several tumor-bearing animals. Besides, the alcohol extract or the triterpene fraction of *G. lucidum* possessed an antitumor effect, which seemed to be related to the cytotoxic activity against tumor cells directly. A preliminary study indicated that the antiangiogenic effect might be involved the antitumor activity of *G. lucidum*

(continued)

Table 2.2 (continued)

Rank	Title	TC	PY	Summary
12	Antioxidant properties of several medicinal mushrooms	215	2002	Three species of medicinal mushrooms are commercially available in Taiwan, namely, *Ganoderma lucidum* (Ling-chih), *Ganoderma tsugae* (Sung-shan-ling-chih), and *Coriolus versicolor* (Yun-chih). Methanolic extracts were prepared from these medicinal mushrooms and their antioxidant properties studied. Overall, *G. lucidum* and *G. tsugae* were higher in antioxidant activity, reducing power, scavenging and chelating abilities, and total phenol content
13	Structural features of immunologically active polysaccharides from *Ganoderma lucidum*	196	2002	Three polysaccharides, two heteroglycans (PL-1 and PL-4) and one glucan (PL-3) were extracted from the fruit bodies, followed by anion-exchange and gel-filtration chromatography. Their structural features were elucidated by glycosyl residue and glycosyl linkage composition analyses, partial acid hydrolysis, acetolysis, periodate oxidation, 1D and 2D NMR spectroscopy, and ESI–MS experiments.
14	Triterpenes from the spores of *Ganoderma lucidum* and their inhibitory activity against HIV-1 protease	189	1998	Two new lanostane-type triterpenes, lucidumol A and ganoderic acid beta, were isolated from the spores of *Ganoderma lucidum*, together with a new natural one and seven that were known. Of the compound isolated, ganoderic acid beta, (24S)-lanosta-7,9(11)-diene-3 beta,24,25-triol (called lucidumol B), ganodermanondiol, ganodermanontriol, and ganolucidic acid A showed significant anti-human immunodeficiency virus (anti-HIV)-1 protease activity.
15	Studies on the immuno-modulating and antitumor activities of *Ganoderma lucidum* (Reishi) polysaccharides: functional and proteomic analyses of a fucose-containing glycoprotein fraction responsible for the activities	187	2002	A fucose-containing glycoprotein fraction that stimulates spleen cell proliferation and cytokine expression has been identified from the water-soluble extract of *Ganoderma lucidum*. Proteomic analysis of mouse spleen cells treated with this glycoprotein fraction showed up to a 50% change of the proteome. Further studies indicate a polysaccharide fraction is responsible for stimulating the expression of cytokines.
16	Triterpene-enriched extracts from *Ganoderma lucidum* inhibit the growth of hepatoma cells via suppressing protein kinase C, activating mitogen-activated protein kinases and G2-phase cell cycle arrest	182	2003	In this report, we studied the anticancer mechanism of triterpene-enriched extracts from *G. lucidum*. Our findings suggest that the triterpenes contained in *G. lucidum* are potential anticancer agents.

(continued)

Table 2.2 (continued)

Rank	Title	TC	PY	Summary
17	Effects of Ganopoly (R) (A *Ganoderma lucidum* polysaccharide extract) on the immune functions in advanced-stage cancer patients	178	2003b	This study aimed to investigate the effects of Ganopoly(R), the polysaccharides fractions extracted from *G. lucidum*, on advanced-stage cancer patients' immune function. Thirty-four advanced-stage cancer patients were entered into this study and treated with 1800 mg Ganopoly(R), three times daily orally before meals for 12 weeks. The present study indicates that Ganopoly enhanced the immune responses in patients with advanced-stage cancer. Clinical evaluations of response and toxicity are ongoing.
18	Fed-batch fermentation of *Ganoderma lucidum* for hyperproduction of polysaccharide and ganoderic acid	173	2002	A process was developed for simultaneous efficient production of ganoderic acid (GA) and polysaccharides by fed-batch fermentation. Sucrose as a carbon source was suitable for the extracellular polysaccharide (EPS) production, although the cells could not grow well. Lactose was beneficial for the cell growth and production of GA and intracellular polysaccharide (IPS).
19	Extraction, purification, characterization, and antitumor activity of polysaccharides from *Ganoderma lucidum*	172	2010	Ultrasonic-aid extraction (UAE) was applied to extract polysaccharides from *Ganoderma lucidum*. Then the crude polysaccharides were purified by filtration, DEAE cellulose-52 chromatography, and Sephadex G-100 size-exclusion chromatography in that order.
20	Structural and immunological studies of a major polysaccharide from spores of *Ganoderma lucidum* (Fr.) Karst	172	2001	A polysaccharide isolated from *Ganoderma lucidum* spores was found to be a complex glucan. Its conformational in aqueous solution was analyzed. And the immunological activities of the native and degraded glucans were also investigated.

macrophages and T lymphocytes. The results had shown that the levels of interleukin (IL)-1 beta, tumor necrosis factor (TNF)-alpha, and IL-6 in macrophage cultures treated with PS-G (100 mu g/ml) were 5.1-, 9.8-, and 29-fold higher, respectively, than those of untreated controls. Lin and Zhang (2004) reviewed that the aqueous extract and polysaccharide fraction of *G. lucidum* exhibited significant antitumor effects in several tumor-bearing animals, mainly through its immune-enhancing activity. Recent studies have also shown that the alcoholic extract or triterpene parts of *G. lucidum* have antitumor effects, directly related to their cytotoxic activity against tumor cells. Preliminary studies suggest that the antiangiogenic effect of *G. lucidum* may be associated with the antitumor activity. Gao et al. (2003b) investigated the effect of Ganopoly(R), a polysaccharide fraction of *Ganoderma lucidum*, on immune function in patients with advanced cancer. Thirty-four patients with advanced cancer participated in this study and received 1800 mg Ganopoly(R) orally three times daily before meals for 12 weeks. Immune function was assessed in 30 patients. This study demonstrates that Ganopoly enhances the immune response in patients with advanced cancer. Clinical evaluation of efficacy and toxicity is ongoing. Lin et al.

(2003) prepared the triterpene-rich component WEES—G6 from mycelium of *G. lucidum*. They found that WEES-G6 inhibited the growth of human carcinoma Huh-7 cells, but not normal human hepatocytes. Their findings suggest that the triterpenes contained in *G. lucidum* are potential anticancer agents. Wang et al. (2002) identified a fucose-containing glycoprotein fraction that stimulates spleen cell proliferation and cytokine expression from the water-soluble extract of *G. lucidum*. The active ingredients of *G. lucidum* include polysaccharides and triterpenes. They have attracted scholars' attention at home and abroad.

Besides, research on *G. lucidum* extract methods is common. Firstly, Min et al. (1998) isolated two new lanolin-type triterpenes and a new natural triterpene from spores. Secondly, Bao et al. (2002) identified three polysaccharides, two heteroglycans, and one glucan from the fruit bodies. Thirdly, Bao et al. (2001) found a complex glucan from *G. lucidum* spores. Forthly, Tang and Zhing (2002) developed a process for the simultaneous and efficient production of bioactive ganoderic acid (GA) and polysaccharides using supplement fermentation. Fifthly, Zhao et al. (2010) applied ultrasonic-aid extraction (UAE) to extract polysaccharides from *G. lucidum*. Then the crude polysaccharides were purified by filtration, DEAE cellulose-52 chromatography, and Sephadex G-100 size-exclusion chromatography in that order. Lastly, Kozarski et al. (2011) extraction of partially purified polysaccharides from three medicinal mushrooms, *Agaricus bisporus, Agaricus brasiliensis*, and *G. lucidum*, by hot water extraction and ethanol precipitation. More and more advanced extraction methods have been proposed, conducive to the full utilization of active ingredients of *G. lucidum*.

Most recently, genetic studies of *G. luciudm* become a hot area. Chen et al. (2012) reported a 43.3-Mb genome of *G. lucidum* encoding 16,113 predicted genes, which was obtained using next-generation sequencing and optical mapping methods. The genome also encodes the most abundant set of wood-degrading enzymes of all sequenced Streptomyces. In total, the authors identified 24 physical CYP gene clusters. Moreover, 78 CYP genes are coexpressed with lanosterol synthase. 16 of them showed high similarity to hydroxylate testosterone, suggesting their possible triterpenoid biosynthesis roles. Therefore, the genomic information of *G. lucidum* has been improved, allowing researchers to have a better understanding of *G. lucidum* at the molecular level.

2.4 Conclusion and Discussion

We have conducted a comprehensive bibliometric analysis on "*Ganoderma lucidum*" based on 3286 publications collected from the WOS core collection database from 1936 to 2019. To sum up, the number of publications on *G. lucidum* has been growing rapidly. Geographically, China is the most active region for *G. lucidum* research. The journal "International Journal of Medicinal Mushrooms" is the most productive source. The keyword analysis identified the following most frequently used keywords "polysaccharides," "in-vitro," "expression," and "antitumor-activity". Based on the most cited papers, we found a large number of papers focused on the pharmacologic actions and composition of the active components of *G. lucidum*, followed by papers studying the genetics of *G. lucidum*. China has a long history of using *G. lucidum* for health-promotion. It will likely continue to play a leading role in this area. Increasing cooperation among countries, organizations cooperation, and international exchange will be the inevitable trend. In the past, studies have focused on the pharmacological effects and active ingredients of *G. lucidum.* We think genetic engineering studies of *G. lucidum* will be the focus of further research.

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