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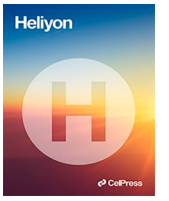

Visualization of the relationship between fungi and cancer from the perspective of bibliometric analysis

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ABSTRACT

The relationship between cancer and microorganisms has been extensively studied, with bacteria receiving more attention than fungi. However, fungi have been shown to play a significant role in cancer development and progression. Understanding the underlying mechanisms is crucial for identifying new avenues in prevention and treatment. To evaluate the current state of research on fungi and cancer, we conducted a comprehensive bibliometric analysis. Using the Web of Science Core Collection database, we searched for English-language articles published between 1998 and 2022. Analyzing the resulting publication data, we identified trends, patterns, and research gaps. Our analysis encompassed co-authorship networks, citation analysis, and keyword co-occurrence analysis. With 8283 publications identified, averaging 331.32 publications per year, our findings highlight China, the United States, India, Japan, and Germany as the top contributing countries. The Chinese Academy of Sciences, Sun Yat-Sen University, and University of São Paulo emerged as the most productive institutions. Key themes in the literature included "cancer," "cytotoxicity," "apoptosis," "metabolites," and "fungus." Recent trends indicate increased interest in keywords such as "green synthesis," "molecular docking," "anticancer activity," "antibacterial," "anti-cancer," and "silver nanoparticles." Our study provides a comprehensive assessment of the current research landscape in the field of fungi and cancer, offering insights into collaborative networks, research directions, and emerging hotspots. The growing publication rate demonstrates the rising interest in the topic, while identifying leading countries, institutions, and research themes serves as a valuable resource for researchers, policymakers, and funders interested in supporting investigations on fungi-derived compounds as potential anti-cancer agents.

1. Introduction

The interplay between microorganisms and cancer has been extensively studied, with bacteria being the primary focus [1–4].

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Despite fungi having a significant impact on cancer, this area has received less attention until recently, with growing research findings that have garnered increased interest [5–7]. Fungi are diverse microorganisms that play crucial roles in ecological and biological processes [8,9]. However, some fungi are pathogenic, causing a range of diseases in plants, animals, and humans [10–13]. These diseases can be superficial or systemic, and they can be especially problematic for immunocompromised individuals such as cancer patients undergoing chemotherapy [14–18]. This immunosuppression increases the risk and severity of fungal infections, which can negatively impact the patient's prognosis [19–23].

In recent times, the relationship between fungi and cancer has gained significant attention, with studies demonstrating the contribution of specific fungal species to cancer development and progression by promoting tumor growth and metastasis [24–28]. Additionally, certain fungi can produce toxins that damage DNA and cellular components, leading to mutations and genomic instability, thereby elevating the risk of cancer [29–31]. The intricate interplay between fungi and cancer involves the immune system, as the immune response to fungal infections plays a crucial role in cancer pathogenesis [32,33]. Fungi stimulate the production of cytokines and other inflammatory mediators, which cause chronic inflammation, a significant risk factor for cancer due to its ability to promote cellular damage and mutation [34–36].

While research advancements have highlighted the significant role of fungi in cancer etiology, the underlying mechanisms governing the interplay between fungi and cancer remain elusive [28,37–40]. Therefore, further scientific inquiry is essential to identify specific fungal species and their associated mechanisms contributing to cancer progression. This will enable the identification of novel therapeutic targets for effective cancer prevention and treatment. Bibliometric analysis, which employs quantitative methods to scrutinize scientific publications and their citation patterns, enables the extraction of valuable insights related to the development and impact of research in a particular field, by examining publication output and citation trends [41–45]. In the study of complex diseases, such as cancer, bibliometric analysis has emerged as a powerful tool to assess research trends and identify knowledge gaps, gaining considerable traction in recent years [46–51].

To this end, bibliometric analysis emerges as a powerful method to assess the current state of research on fungi and cancer, allowing for the identification of critical knowledge gaps that necessitate further exploration. Our research contributes to the existing scholarship on the association between fungi and cancer, providing valuable insights into opportunities for future studies. By uncovering the underlying mechanisms of the interaction between fungi and cancer, we may potentially reveal new targets for prevention and treatment, ultimately improving the outcomes of cancer patients.

2. Material and methods

Data source: We utilized the Web of Science Core Collection (WOSCC) as our database for this study.

Time range: We conducted our search from January 1st, 1998 to December 31st, 2022.

Inclusion criteria: We considered for inclusion all research articles investigating the relationship between fungi and cancer that were published in the English language.

Exclusion Criteria: This study excluded all articles on the topic of fungi and cancer that were not published between 1998 and 2022. Additionally, it excluded articles related to fungi and cancer published in a non-English format and non-research articles between 1998 and 2022.

Search strategy: To identify relevant articles, we used the following search strategy: Topic Search (TS) = (((TS=(Fungus) OR TS=(Fungi, Filamentous) OR TS=(Filamentous Fungi) OR TS=(Filamentous Fungus) OR TS=(Fungus, Filamentous) OR TS=(Molds) OR TS=(Mold)) AND ((TS=(Tumor) OR TS=(Neoplasm) OR TS=(Tumors) OR TS=(Neoplasia) OR TS=(Neoplasias) OR TS=(Cancer) OR TS=(Cancers) OR TS=(Malignant Neoplasm) OR TS=(Malignancy) OR TS=(Malignancies) OR TS=(Malignant Neoplasms) OR TS=(Neoplasm, Malignant) OR TS=(carcinoma) OR TS=(Neoplasms, Malignant))) We exported the search results using the "Plain Text file" format, with the record content selected as "Full Record and Cited References." The downloaded file was saved in the format download_*.txt, facilitating easy access and retrieval of the comprehensive data.

3. Data analysis and visualization

VOSviewer and CiteSpace stand out as the predominant software tools employed for bibliometric analysis. In 2009, a program known as VOSviewer was developed by Eck and Waltman from Leiden University. This software tool serves the purpose of constructing scientometrics networks and visualizing knowledge maps [52]. VOSviewer, renowned for its visual prowess, offers a direct portrayal of collaborative associations among research topics [53]. Node size corresponds to the frequency of co-occurrence, while lines connecting nodes signify their co-occurrence relationships, with colors indicating clustering patterns. CiteSpace, a Java application designed for bibliometric analysis, was developed by Chen Chaomei, CiteSpace excels in aggregating keyword bursts, thereby illuminating emerging trends and dynamic shifts within research hotspots [54].

In this study, we utilized VOSviewer 1.6.19 software to perform visual analysis of authors, institutions, and countries by importing the data as plain text files. VOSviewer is a widely-used software tool that is utilized for bibliometric analysis and visualization. The network visualization maps generated by VOSviewer furnish comprehensive information about the publications originating from diverse countries and institutions, as well as their collaborative relationships. In the generated graph, nodes are employed to represent countries or institutions, with their sizes indicating the number of publications that they have contributed. The larger the size of a node, the greater the number of publications that it has produced. The links in the graph reflect the level of association or collaboration between the countries or institutions. Notably, thicker links denote a stronger degree of collaboration between the respective entities.

For the visual analysis of keywords and dual-map overlay of journals, we employed Citespace 6.2.R3 (64-bit) advanced software.

The parameters set in Citespace software included Time slicing (January 1, 1998–December 31, 2022), Time slicing (n = 1), Pruning (pathfinder, pruning sliced networks, pruning the merged networks), and other parameter settings that adhered to the default configurations of the software.

Using the Dual-map analysis function in CiteSpace 6.2R3, we loaded the citation data of the original literature set onto the base graph layer. The normalization was conducted using Z-Score. Subsequently, we examined the citation relationships between the original and cited literature sets to analyze the knowledge absorption characteristics of fungal research related to cancer. The dual-map overlay of journals shows the citation relationship citing journals (presented on the left) and cited journals (presented on the right), with the colored line connecting them indicating the citation paths. In the path of the double map overlay, z and f represent the node's cluster fraction and literature count, respectively. The z value indicates the density of the cluster in which the node is located along the path. A higher z value suggests that the node is more closely related to other nodes in the path, as the cluster is more densely packed. The f value represents the number of literature corresponding to the node in the whole dataset. A higher f value indicates that the literature corresponding to the node has been cited more frequently, and hence, the node has a greater influence.

4. Process and criteria for literature screening

The literature screening process involved several stages. First, we screened the titles and abstracts of the retrieved studies to exclude irrelevant studies. Next, we read the full-text articles of the remaining studies to assess their relevance to our research question. Three authors (Jiawei Xu, Ying Zeng, and Chengdong Yu) independently searched and screened the articles, and in case of disagreement, they discussed or sought help from the fourth author (Siyi Xu).

5. Result

5.1. Analysis of literature publications

A total of 8283 research articles were selected for inclusion in this study, meeting the stringent criteria of relevance to the investigation of fungi and their correlation with cancer, publication in the English language, and adherence to the criteria depicted in Fig. 1. Through this meticulous and comprehensive selection process, we have ensured the inclusion of articles that offer profound insights into the focal subject matter.

Based on the bibliometric analysis presented in Fig. 2, it can be observed that the number of publications on fungal research related to cancer has increased steadily over the years. Specifically, the number of papers has gradually increased from 101 in 1998 to 796 in 2022. Notably, from 2007, more than 200 articles were published every year, indicating rapid growth in this field. Over the last five years, a total of 3194 papers were published, which accounts for 38.56% of the overall publications (8283).

5.2. Journal analysis

The WoSCC search revealed that the current analysis includes 8283 papers published in 1940 different journals over the last 25 years. VOSviewer was employed to assess the influence of these journals, and the top 10 are listed in Table 1. Among these, seven publishers are based in the USA, while the other three are situated in the United Kingdom and Switzerland. The Journal of natural products, which demonstrated the highest number of total publications (231) with 9432 citations, ranked first in the research field of fungal research related to cancer. Notably, Journal of Antibiotics published 67 papers, yet it only garnered 1686 citations, averaging 25.16 citations per publication.

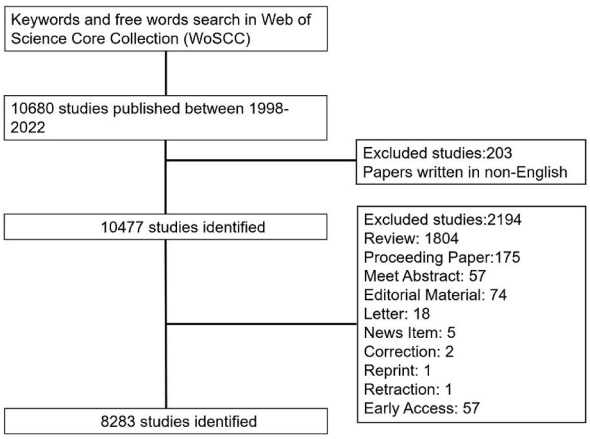

Fig. 1. The flow diagram of the screening process between fungal research related to cancer from the perspective of bibliometric analysis.

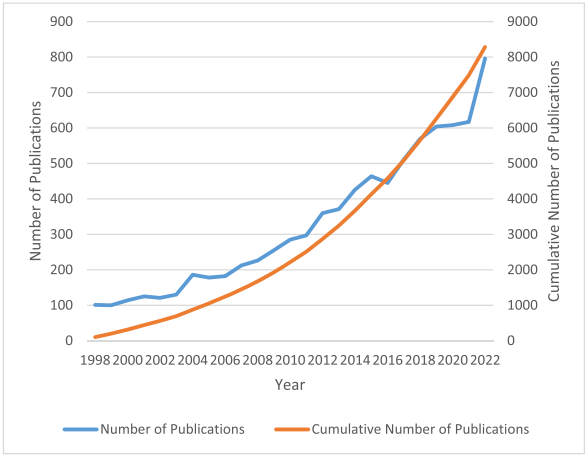

Fig. 2. The increase in the number of publications made in the WoS on fungal research related to cancer for the period 1998 to 2022.

Table 1
Top 10 Journals with the highest number of publications in fungal research related to cancer (1998–2022).

Rank	Journal	Publications	Citations	Average citation per publication
1	Journal of Natural Products	231	9423	40.79
2	Marine Drugs	164	3378	20.60
3	Molecules	152	2051	13.49
4	Natural Product Research	120	1218	10.15
5	PLOS ONE	104	2311	22.22
6	Scientific Reports	87	1722	19.79
7	Medical Mycology	72	1852	25.72
8	Fitoterapia	70	1148	16.40
9	Frontiers in Microbiology	68	792	11.65
10	Journal of Antibiotics	67	1686	25.16

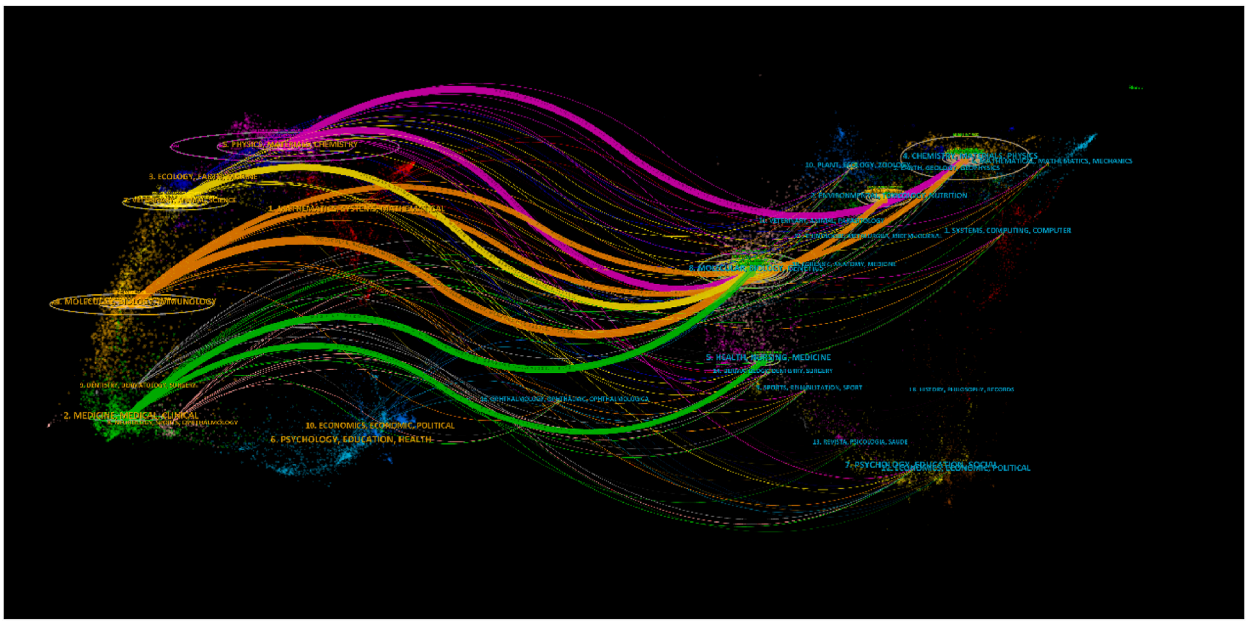

Fig. 3. The dual-map overlay of journals on fungal research related to cancer.

5.3. Dual-map analysis

The citation relationship between journals was unveiled using a dual-map overlay. We meticulously analyzed the comprehensive dataset encompassing original literature from 1998 to 2022, employing the cutting-edge visualization tool CiteSpace 6.2R3. On the left side of the figure, we presented the group of journals in the citing literature set with a paper count of 30 or more, while the right side showcased the group of cited journals with a citation frequency of 5 or more.

For a comprehensive visualization of the citation landscape concerning fungal research linked to Cancer (Fig. 3), we seamlessly integrated and superimposed the biplot overlay of journal citations using a Z-score standardization technique. This innovative methodology enabled us to capture the intricate interrelationships and trends within the citation landscape, shedding light on the scholarly impact and influence of the study spanning the past 25 years.

We identified eight significant citation paths, including two purple paths, one yellow path, three orange paths, and two green paths. The clusters of journals that publish fungal research associated with cancer predominantly lie in the domains of molecular biology, immunology, physics, materials, chemistry, veterinary, animal science, medicine, and clinical research. Conversely, the clusters of journals that assimilate the primary knowledge are concentrated in the realms of molecular biology, genetics, health, nursing, medicine, chemistry, materials, physics, environmental science, toxicology, and nutrition.

A particularly noteworthy citation path is the orange path, which signifies a robust interconnection between molecular biology immunology journals (citing journals on the left) and molecular biology genetics journals (cited journals on the right). The elevated z-value of 9.116112 suggests a dense network of citations and a close relationship between the nodes within this pathway. Moreover, the significant f-value of 24066 indicates that molecular biology genetics journals have garnered substantial citations in the literature, highlighting their significant influence in the field.

5.4. Analysis of literature institutions, and Countries

Bibliometric analysis provides valuable insights into the research landscape and the contributions of various institutions in a specific field. In the context of fungal research related to cancer, the findings presented in Fig. 4a reveal that particular institutions, such as the Chinese Academy of Sciences, Sun Yat-Sen University, and University of Sao Paulo, have emerged as prominent leaders in the domain of fungal research about cancer for the period spanning 1998 to 2022. These institutions have demonstrated remarkable achievements in this area, as is evidenced by the larger node sizes and thicker lines within the data, which are indicative of higher levels of publication numbers and collaboration.

Based on the analysis of the temporal evolution of fungal research related to cancer spanning from 1998 to 2022, as depicted in Fig. 4b, it is apparent that institutions such as Taif University, King Saud University, and Cairo University have experienced a notable surge in their research productivity in this domain in recent times. As a consequence, these institutions warrant particular attention and recognition.

The investigation of fungal research associated with cancer has garnered the interest of multiple academic establishments, encompassing universities, research organizations, and medical centers from all over the world. As illustrated in Table 2, the top 10 institutions in this field include seven located in China, with the remaining institutions situated in Brazil, Saudi Arabia, and Egypt, respectively. Chinese Academy of Sciences, located in China, emerges as a top-ranking academic institution in this list. With a total of 327 publications and an impressive citation count of 6919, the institution has demonstrated its dominance in this research field, with an average of 21.16 citations per publication. It is noteworthy that King Saud University has the lowest average citations in the table at 15.92. However, our careful analysis of their published literature shows a concentration of research output in recent years [55–58]. Therefore, the average citations of King Saud University may significantly increase over time.

As illustrated in Fig. 5a, China has the highest publication output with 2267 articles, followed by the USA with 1685 articles, and

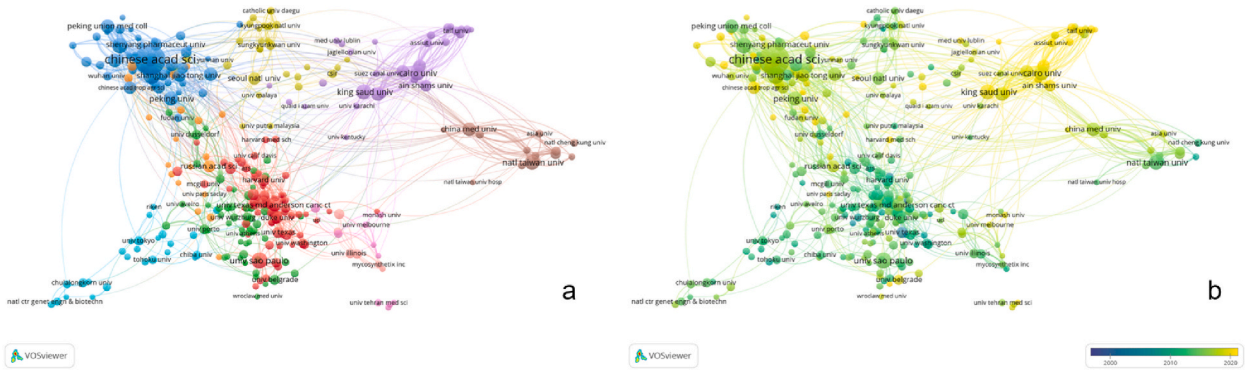

Fig. 4. (a) Collaboration network map of institutions of fungal research related to cancer for the period 1998 to 2022, (b) Temporal evolution of fungal research related to cancer for the period 1998 to 2022. Different colors of the circles indicated the average year of the studies according to the bar in the lower right corner. The color range indicated the average year of publications in each institution. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Table 2
The top 10 institutions of fungal research related to cancer with the highest number of publications for the period 1998 to 2022.

Rank	Institution	Publications	Citations	Average citation per publication	Country
1	Chinese Academy of Sciences	327	6919	21.16	China
2	Sun Yat-Sen University	110	3280	29.82	China
3	University of Sao Paulo	90	2148	23.87	Brazil
4	Chinese Academy of Medical Sciences	84	2143	25.51	China
5	Cairo University	80	2505	31.31	Egypt
6	King Saud University	79	1258	15.92	Saudi Arabia
7	National Taiwan University	76	2196	28.89	China
8	Peking University	70	1955	27.93	China
9	Ocean University of China	66	1368	20.73	China
10	Zhejiang University	66	1150	17.42	China

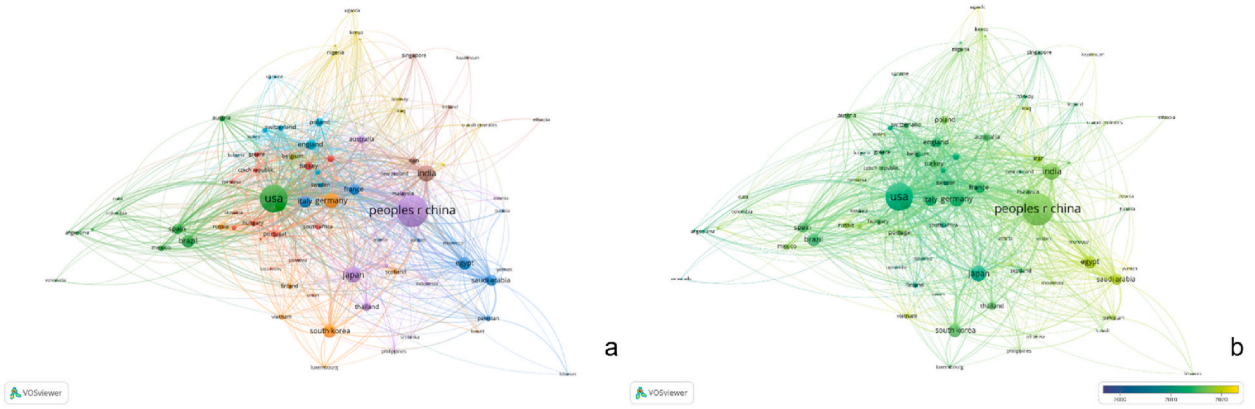

Fig. 5. (a) Collaboration network map of countries of fungal research related to cancer for the period 1998 to 2022, (b) Temporal evolution of fungal research related to cancer for the period 1998 to 2022. Different colors of the circles indicated the average year of the studies according to the bar in the lower right corner. The color range indicated the average year of publications in each country. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

India with 564 articles. Based on the Temporal evolution of fungal research related to cancer presented in Fig. 5b, Egypt, Iran, and Saudi Arabia have demonstrated noteworthy contributions to fungal and cancer-related research in recent years. These countries should be given special attention by scholars engaged in this field of research.

The investigation of fungal research related to cancer is a global research endeavor, as evidenced by the leading countries in Table 3. China has cemented its position at the forefront of this field, with an impressive corpus of 2267 publications. The United States follows closely behind with 1685 publications, positioning it as a strong contender for the top spot. However, India, Japan, and Germany are also making noteworthy contributions to this area of research, with 594, 539, and 502 publications, respectively. In addition, the presence of countries such as South Korea, Brazil, and Egypt within the top ten underscores the worldwide interest and commitment to this critical area of research. The diverse composition of countries in the top ten highlights the importance of international collaboration in expediting research and development. By sharing knowledge and insights, researchers from different countries and cultures can uncover breakthroughs that understand the relationship between fungi and cancer.

Table 3
The top 10 countries of fungal research related to cancer with the highest number of publications for the period 1998 to 2022.

Rank	Country	Publication	Cite	Average citation per publication
1	China	2267	45545	20.09
2	America	1685	82438	48.92
3	India	594	11883	20.01
4	Japan	539	13478	25.01
5	Germany	502	23060	45.94
6	South Korea	392	10245	26.14
7	Brazil	366	8451	23.09
8	Egypt	351	7396	21.07
9	Italy	304	10307	33.90
10	Saudi Arabia	273	4411	16.16

5.5. Authors and co-cited authors analysis

In these 8283 articles, a remarkable 41627 authors have contributed. An analysis of the authorship provides valuable insights into the prominent researchers and key research themes in a given field. As shown in Fig. 6a, a network analysis of authors who have published more than twelve articles reveals the presence of stable collaborative groups, underscoring the significance of collaboration in the field. As depicted in Fig. 6b, the temporal evolution of the number of author publications during this period is presented. Remarkably, Liu Zhaoming, Tan Haibo, Wang Weiyi, Li Saini, and Gao ying have demonstrated sustained activity in this field in recent years. Liu Zhaoming has conducted research on the isolation of novel phenolic and sesquiterpenoid compounds from deep-sea fungi. This involved determining their structures through the use of spectroscopic, X-ray, and total synthesis methods, and evaluating their cytotoxic activities against human cancer cell lines. These compounds exhibit unique skeletal and stereo-configurations, suggesting the potential of deep-sea fungi as a source for new drug development [59–61]. Tan Haibo's work centered on isolating several novel metabolites and ketones from endophytic and deep-sea fungi. These compounds were identified through spectroscopic analysis and subsequently evaluated for their cytotoxic activity against human cancer cell lines. Interestingly, the compounds had unique skeletons and structures, highlighting the vast diversity and innovation of fungi as a source for developing new drugs [62,63].According to the study conducted by author Ying Gao, it has been discovered that Alternaria sp. sb23, an endophytic fungus isolated from the roots of Schisandra chinensis, is capable of producing trichostatin-like compounds. These compounds exhibit cytotoxic activity and enhance TRAIL-induced apoptotic effects. Consequently, they represent promising candidates for cancer therapy [64].

According to the investigations conducted by the aforementioned authors, it is probable that forthcoming research in the field of cancer and fungi will persist in concentrating on the isolation and identification of fresh compounds from diverse fungal sources, along with the assessment of their cytotoxic activities against human cancer cell lines. Given the immense diversity of fungi and their potential as a resource for novel drugs, it is anticipated that research in this area will continue to expand and diversify.

Indeed, it is interesting to observe that the predominant focus of active authors in the field of fungi and cancer research in recent years lies in studying the relationship between marine fungi and cytotoxicity [65–68]. This emphasis can be attributed to several factors, including the distinct properties exhibited by marine fungi, their potential for therapeutic applications, and prior research findings supporting their relevance. it is noteworthy that amidst the prevailing emphasis on marine fungi and their cytotoxic properties, a subset of researchers diligently delve into the exploration of diverse facets pertaining to the intricate interplay between fungi and cancer [69–71]. These scholars engage in the study of different types of fungi or investigate the impact of fungal infections on cancer. These alternative perspectives play a crucial role in enriching our understanding of the overall topic, offering valuable insights into the diverse interactions between fungi and cancer.

Our research on co-citation relationships among authors in the field of fungal research related to cancer revealed a diverse group of highly co-cited authors from various countries and institutions. The top three authors with the most co-citations were Mosmann T (441), Marr KA (384), and Kontoyiannis DP (697), followed by Walsh TJ, Abdel-Rahman IH, Pagano L, Newman DJ, Strobel G, De Pauw B, Nucci M, and Denning DW with high co-citation counts. These authors have made significant contributions to the field and have shaped current research directions. To better understand the co-citation relationships among these influential authors, we created a detailed visualization (Fig. 7) that illustrates the complex interconnections between authors with over 82 co-citations, providing insights into the collaborative networks that have emerged among them.

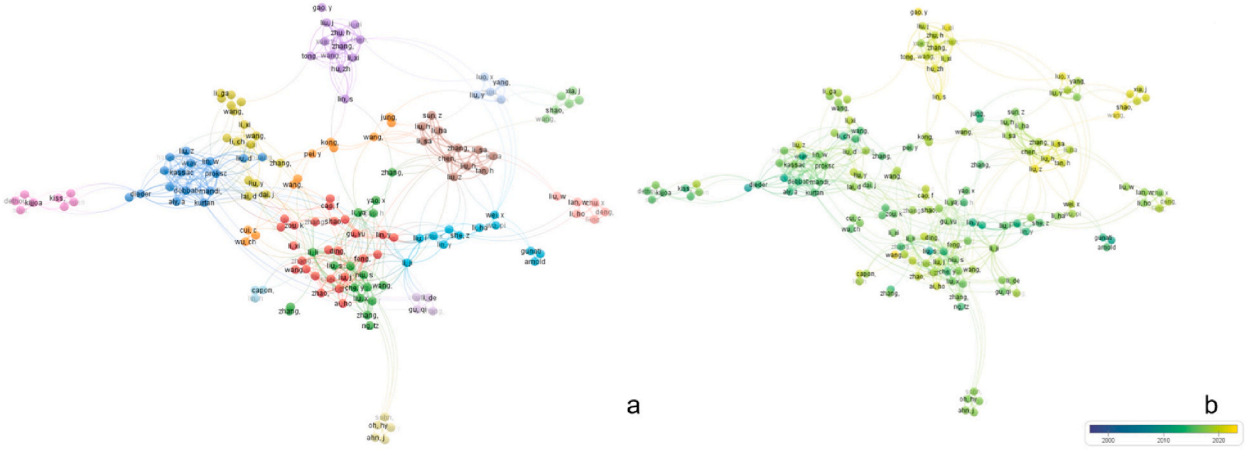

Fig. 6. (a) Collaboration network map of authors of fungal research related to cancer for the period 1998 to 2022, (b) Temporal evolution of fungal research related to cancer for the period 1998 to 2022. Different colors of the circles indicated the average year of the studies according to the bar in the lower right corner. The color range indicated the average year of publications for each author. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

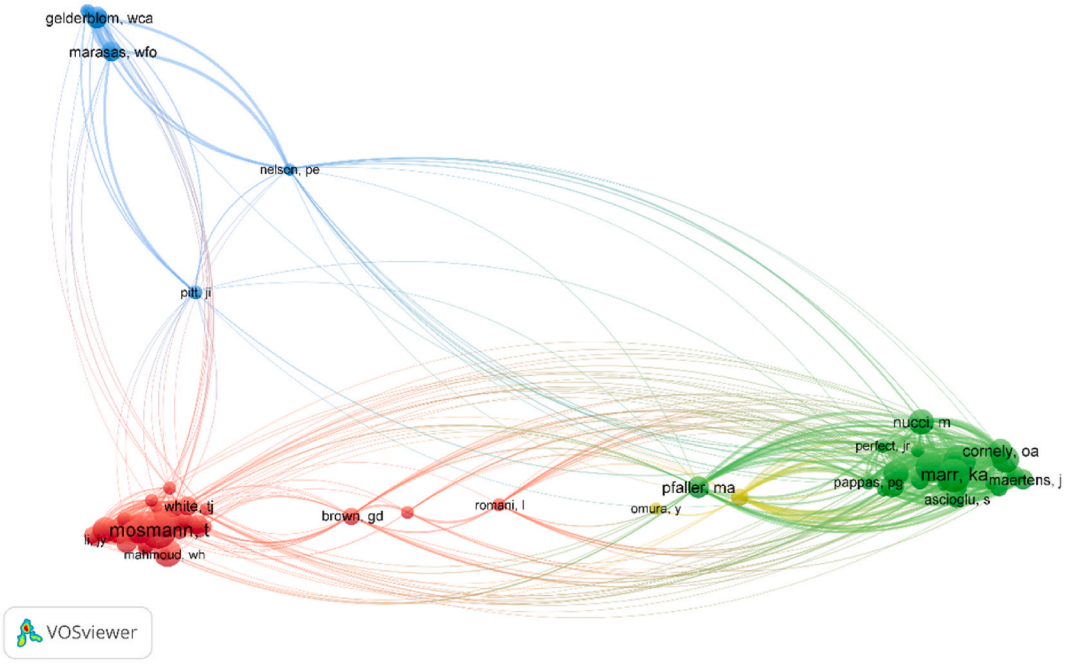

Fig. 7. Co-citation network map of authors of fungal research related to cancer for the period 1998 to 2022.

5.6. *Keywordsanalysis*

Fig. 8a illustrates a network map of keyword co-occurrence for fungal research related to cancer. The primary objective of this analysis was to identify the most frequently occurring terms, which comprised ten keywords: "cancer," "cytotoxicity," "apoptosis," "metabolites," "fungus," "derivatives," "expression," "fungi," "in-vitro," and "growth." The analysis revealed that the keyword "cancer" had the highest frequency, followed by "cytotoxicity," "apoptosis," "metabolites," and "fungus." The findings suggest that the analysis focused primarily on the relationship between fungal research and cancer, specifically in terms of cytotoxicity, apoptosis, and metabolites produced by fungi.

The analysis of the temporal evolution of fungal research related to cancer from 1998 to 2022 unveiled that "anticancer," "antioxidant," and "antioxidant activity" were the most frequent and prominent keywords in recent years (Fig. 8b). These keywords signify the prevailing trend and direction of research in this field. The growing number of publications associated with these keywords over time indicates that the investigation of fungal metabolites as potential anticancer agents has garnered considerable attention in recent years [72–74]. The analysis of literature pertaining to the identified keywords revealed that fungal metabolites possess diverse

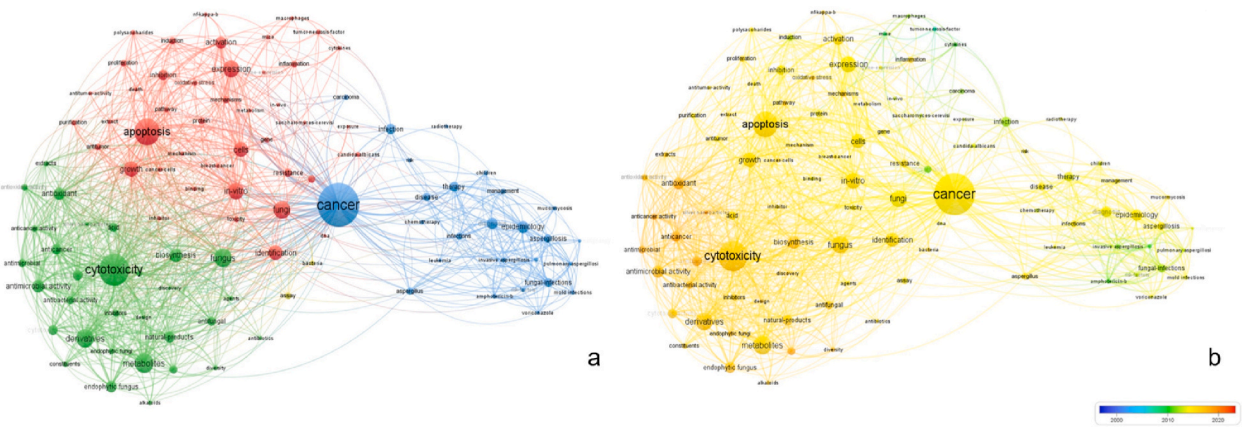

Fig. 8. (a) Collaboration network map of Keywords of fungal research related to cancer for the period 1998 to 2022, (b) Temporal evolution of fungal research related to cancer for the period 1998 to 2022. Different colors of the circles indicated the average year of the studies according to the bar in the lower right corner. The color range indicated the average year of publications in each Keywords. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

biological activities such as anticancer and antioxidant properties [70, 75–80]. However, understanding the complex mechanisms of action and biosynthetic pathways of these metabolites require further investigation [81–83]. Despite the promising potential of fungal metabolites as anticancer agents, no fungal-derived drugs have yet been approved as anticancer drugs. This can be attributed to the lack of in-depth understanding and effective utilization of fungal metabolites in the field of cancer research [72, 74, 84]. Hence, future research should aim to address the challenges associated with fungal resources and promote their development and application. This may entail identifying and characterizing novel fungal metabolites that possess anticancer activity, along with determining their mechanisms of action and biosynthetic pathways. Furthermore, the development of more effective strategies for the isolation, purification, and synthesis of fungal metabolites may be necessary to expedite their development as potential anticancer drugs [85–88].

Keywords with the Strongest Citation Bursts offer a systematic and visual approach to dissecting the bursts of citations associated with specific keywords. This insightful analysis aids researchers in comprehending the focal points, emerging trends, and profound significance within their respective fields of study. By delving into the strength values of these keywords, one can acquire a deep understanding of their research prominence and impact, facilitating the judicious selection of pivotal keywords for further investigation. Such a comprehensive assessment not only informs researchers of the current research climate but also serves as an invaluable compass guiding them towards areas of scholarly exploration that hold the greatest potential for advancement and discovery.

In the realm of fungal and cancer research, the keyword "tumor necrosis factor" experienced an unparalleled citation surge in 1998, boasting an impressive strength value of 34.23. This remarkable figure underscores the widespread attention and scholarly curiosity it has garnered. From 1998 to 2010, its captivating influence continued to captivate researchers, fueling an enduring interest and stimulating a flurry of investigations. During the early stage (1998), the keywords "mycotoxins" and "fusarium moniliforme" emerged with considerable intensity. With respective strength values of 19.31 and 17.96, these keywords signify the extensive exploration of the intricate connection between mycotoxins and specific fungal species with cancer at that pivotal time.

Furthermore, specific time periods witnessed the emergence of bone marrow transplantation and esophageal cancer as hot topics of research, garnering substantial attention from the scientific community. Bone marrow transplantation, with a strength value of 18.71, witnessed a surge in research interest from 1998 to 2007. Similarly, esophageal cancer, with a strength value of 15.01, experienced significant research advancements and breakthroughs between 1998 and 2010. The high citation bursts observed for these keywords, coupled with their notable strength values, further emphasize the importance and impact of the research conducted during those particular periods.

The burst analysis of cancer and fungi-related research reveals that in recent years, the keywords "green synthesis," "molecular

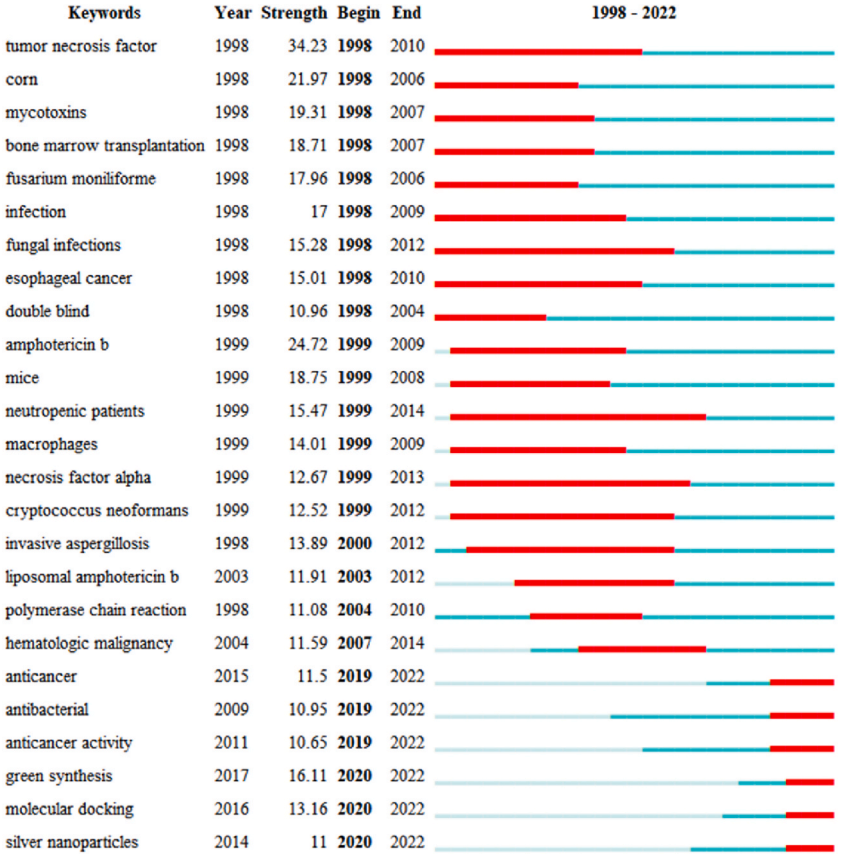

Fig. 9. Keywords bursts of fungal research related to cancer for the period 1998 to 2022.

docking," "anticancer activity," "antibacterial," "anticancer," and "silver nanoparticles" have gained significant attention (Fig. 9). These keywords reflect the growing interest and importance attributed to their respective areas of study. Notably, "green synthesis" holds a strength value of 16.11, "molecular docking" has a strength value of 13.16, "anticancer activity" is at 10.65, "antibacterial" at 10.95, "anticancer" at 11.5, and "silver nanoparticles" at 11. This suggests that research in this field has focused on the development of novel anticancer and antibacterial agents derived from fungi using green synthesis methods, as well as using molecular docking techniques to identify potential anticancer compounds [72,89–96]. Additionally, studies have been conducted on the potential of silver nanoparticles as therapeutic options for cancer treatment [97–101]. Alqaraleh et al. has shown that silver nanoparticles synthesized by fungi have the potential for antibacterial and anticancer treatments, while another study describes a green-based approach for synthesizing silver nanoparticles using the fungal endophyte Penicillium oxalicum. The nanoparticles showed potential inhibitory effects against bacterial and fungal strains, antioxidant activity, and cytotoxic potential against breast cancer cells [97,99]. Although these studies have limitations such as the lack of clinical trials to determine the safety and efficacy of nanoparticles as potential drugs for cancer treatment and the need for further investigation into the mechanisms of action on cancer cells, they suggest that green synthesis methods for producing silver nanoparticles with antibacterial and anticancer properties may be a promising area of research for cancer-related fungi studies.

To examine the historical development of research on the relationship between fungi and cancer, we conducted a co-occurring keywords analysis and organized the results by time zone. The resulting Fig. 10 displays how research hotspots have evolved over time and offers insight into the trajectory of fungal research related to cancer.

6. Discussion

The achievement of a thorough and comprehensive comprehension of the intricate mechanisms that govern the interaction between fungi and cancer is an essential prerequisite for developing innovative therapeutic approaches to combat this multifarious and enigmatic disease. In this regard, bibliometric analysis emerges as a quantitative method that meticulously examines scientific publications and citation patterns, furnishing valuable insights into the trajectory and impact of research within a particular domain [44,46–51,102–105]. Through the rigorous scrutiny of publication output and citation trends, researchers can effectively evaluate the current state of research pertaining to the interplay between fungi and cancer, identify significant gaps in knowledge, and discern domains that require further exploration and analysis. Consequently, the power and potential of bibliometric analysis endow researchers with the ability to precisely determine the scope and direction of future research efforts in this field.

In this study, we conducted a comprehensive bibliometric analysis on the topic of fungi and cancer. Our analysis included a total of 8,283 research articles published between 1998 and 2022. These articles were sourced from 1,940 journals, authored by researchers from 136 different countries and 7,252 institutions, involving a total of 41,627 authors. A total of 29,981 keywords were extracted

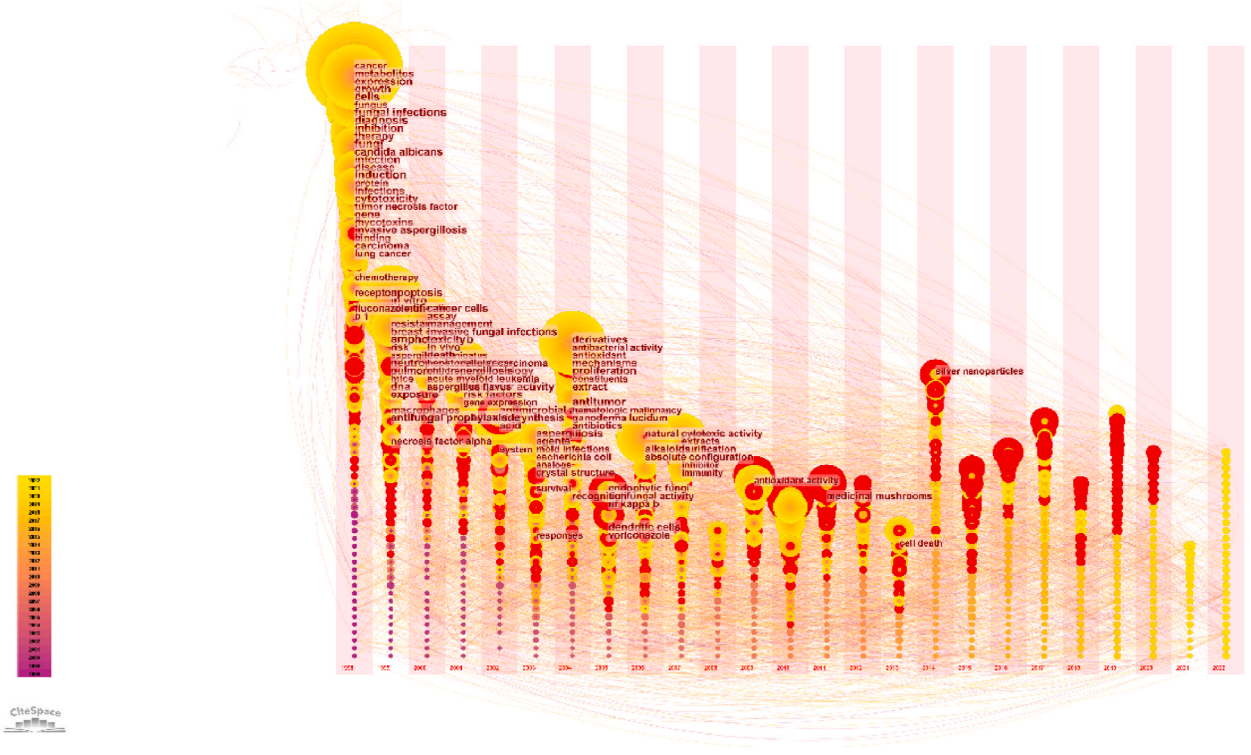

Fig. 10. Keywords time zone of fungal research related to cancer for the period 1998 to 2022.

from the articles for further analysis.

By applying burst analysis to the cancer and fungi-related research, we identified emerging trends and hotspots in the field. Our findings reveal that certain keywords have garnered significant attention in recent years. These keywords include "green synthesis," "molecular docking," "anticancer activity," "antibacterial," "anticancer," and "silver nanoparticles." This analysis suggests that current research in this field has placed emphasis on the development of novel anticancer and antibacterial agents derived from fungi using green synthesis methods. Furthermore, the utilization of molecular docking techniques to identify potential anticancer compounds has also gained substantial interest.

Overall, this study provides a comprehensive compilation of the reported material in the field of fungi and cancer. It sheds light on the current hotspots and emerging trends, guiding authors and researchers in this field towards relevant areas of investigation. The identified keywords reflect the focus on the development of effective therapeutic strategies and the exploration of potential anticancer agents derived from fungi.

The results of this bibliometric analysis indicate that there has been a marked increase in research on the relationship between fungi and cancer during the period 1998 to 2022. The rapid growth in the publication rate indicates that the study of fungi in the context of cancer is an increasingly popular and important area of research, attracting significant interest among researchers. The identification of the top 10 countries with the highest number of publications reveals that China has the highest number of publications, with 2267. Following closely is America with 1685 publications. India, Japan, and Germany also demonstrate a considerable number of publications, with 594, 539, and 502 respectively. Additionally, South Korea, Brazil, Egypt, Italy, and Saudi Arabia make significant contributions, with 392, 366, 351, 304, and 273 publications respectively. This suggests that research in this field is not limited to a particular region.However, it is worth noting that Egypt, Iran, and Saudi Arabia have made noteworthy contributions to fungal and cancer-related research in recent years.

Additionally, our analysis revealed that the Chinese Academy of Sciences is the most productive institution in this field, underscoring the critical role played by Chinese researchers in advancing our understanding of the interaction between fungi and cancer. The co-occurrence analysis, burst detection, and timeline analysis for keywords revealed several research directions and hotspots. The most frequent keywords found in the publications were "cancer," "cytotoxicity," "apoptosis," "metabolites," and "fungus." Moreover, the burst analysis of cancer and fungi-related research indicates that several keywords, such as "green synthesis," "molecular docking," "anticancer activity," "antibacterial," "anticancer," and "silver nanoparticles," have gained significant attention in recent years.

Cancer is a significant cause of morbidity and mortality on a global scale, with incidence rates continuing to rise [106,107]. Therefore, meticulous efforts have been undertaken to delve into the intricacies of cancer development, diagnosis, and treatment, as the human race strives to overcome this obstinate adversary. As research on the relationship between fungi and cancer continues to deepen, there has been a growing interest in exploring this area [5–7,108–110]. Here, we further analyzed the following aspects related to the research on fungi and cancer.

Anticancer activity of fungal metabolites: The study of the anticancer activity of fungal metabolites is a rapidly growing field, involving the evaluation of various compounds from fungal sources, their mechanisms of action, and biosynthetic pathways on cancer cells [72,82,111–116]. Fungi produce a diverse array of bioactive compounds, including, terpenes, polyphenols, and alkaloids, many of which exhibit significant anticancer activity and can serve as candidates or lead compounds for novel anticancer drugs [114, 117–121]. The mechanisms by which fungal metabolites exhibit anticancer activity are diverse, and they affect various signaling pathways and molecular targets of cancer cells. For example, they can impact the cell cycle, induce apoptosis or autophagy, inhibit angiogenesis or metastasis, and more [82]. One study has shown that fungal metabolites can inhibit the receptor tyrosine kinase (RTK) signaling pathway, while another study has shown that fatty acid esters from the marine fungus Aspergillus sp. can inhibit the proliferation and migration of tumor cells by inducing apoptosis and autophagy, offering a promising strategy for cancer therapy [122, 123]. To fully evaluate the potential of fungal metabolites as anticancer agents, a combination of in vitro and in vivo studies is necessary [40,124–126]. Molecular docking techniques can also be employed to predict the potential binding modes and affinity of these compounds to their target proteins [79,82,88]. Recent research has identified and analyzed active compounds from the endophytic fungus *Alternaria alternata* isolated from the medicinal plant Jatropha heynei, which have both antibacterial and anticancer activities [87]. The use of molecular docking techniques provides valuable insights into the mechanisms underlying the anticancer activity of fungal metabolites, facilitating the identification of promising candidates for further development.

Anticancer activity of silver nanoparticles synthesized by fungi: The synthesis of silver nanoparticles (AgNPs) by fungi has gained significant attention as a green alternative to traditional chemical synthesis methods [99,127,128]. Silver nanoparticles exhibit broad-spectrum biological activities, including anticancer properties [129–133]. Fungi can synthesize these nanoparticles through various mechanisms, including extracellular reduction, intracellular reduction, and extracellular secretion [134–140]. Recent studies have demonstrated that silver nanoparticles can be synthesized using the fungal endophyte Penicillium oxalicum associated with the plant Amoora rohituka. These silver nanoparticles, known as POAgNPs, have exhibited potent cytotoxic effects against breast cancer cell lines MDA-MB-231 and MCF-7, inducing apoptosis, inhibiting wound healing, altering nuclear morphology, and affecting the expression of genes related to apoptosis, tumor suppression, and cell cycle arrest [99]. The endophytic fungus Penicillium oxalicum strain LA-1 has been found to synthesize silver nanoparticles (AgNPs) that exhibit potent anticancer activity. These PoAgNPs have been characterized and demonstrated to effectively inhibit the growth of breast cancer cells [141]. This environmentally friendly synthesis method offers potential for enhanced stability and uniformity of nanoparticles, making it an attractive option for future development and investigation [141,142]. However, further research is necessary to fully evaluate the safety and efficacy of these nanoparticles and to understand their underlying mechanisms of action.

Induction of apoptosis by fungal metabolites: The induction of apoptosis by fungal metabolites has become a rapidly growing field in natural product drug discovery with promising potential for cancer prevention and treatment [72,143]. This field focuses on

understanding the compounds produced by fungi that have the ability to induce self-regulated death of cancer cells, as well as their mechanisms of action and biosynthetic pathways [72,82,111–116,144]. The mechanisms by which fungal metabolites induce apoptosis in cancer cells are diverse and involve various signaling pathways and molecular targets. These include the generation of ROS, inhibition of NF-κB signaling, and activation of the mitochondrial pathway of apoptosis. For instance, chaetocin, a fungal compound, induces glioma cell death by increasing reactive oxygen species (ROS), which activates the ATM and JNK pathways [145]. Reduced-gliotoxin, a small molecule derived from marine fungi, induces anoikis in colorectal cancer cells by disrupting integrin-mediated cell detachment and inducing excessive ROS production to activate apoptotic pathways [146]. Additionally, a bioactive metabolite from endophytic Chaetomium globosum modulates p53, BCL-2, and NF-κB pathways to induce apoptosis in cancer cells [147]. Another study reports the anticancer effects of emestrin, a compound isolated from a plant endophytic fungus, on human liver cancer cells by inducing apoptosis through the mitochondrial pathway [148].

Despite the promising potential of fungal metabolites as inducers of apoptosis in cancer cells, there are still challenges and limitations that need to be addressed. For example, the development of more efficient screening assays is necessary to identify novel compounds with potent pro-apoptotic activity. Preclinical and clinical studies are also needed to evaluate the therapeutic potential of these compounds in humans and to determine their optimal dosing and administration regimens.

Overall, the study of the induction of apoptosis by fungal metabolites is a multidisciplinary and multilevel field, with broad application prospects and development potential. With the advancement of science and technology and the emergence of new discoveries, there are still many problems and challenges to be explored and solved in this field.

In conclusion, this comprehensive bibliometric analysis yields valuable insights into the research landscape encompassing the interaction between fungi and cancer. The study unveils a notable surge in research activity in this domain, signifying its burgeoning significance and popularity among researchers worldwide. China, the United States, India, Japan, and Germany emerge as leading contributors to this research, underscoring the global nature of scientific exploration in this realm. The analysis identifies emerging trends and focal points within the field, accentuating the emphasis on developing innovative anticancer and antibacterial agents derived from fungi. Notably, green synthesis methods, molecular docking techniques, and the investigation of silver nanoparticles synthesized by fungi have garnered substantial attention in recent years. These findings underscore the potential of fungal metabolites and nanoparticles as promising candidates for the development of effective therapeutic strategies against cancer.

Moreover, the study underscores the significant role played by fungal metabolites in inducing apoptosis in cancer cells. The diverse mechanisms of action employed by these metabolites, including modulation of signaling pathways and generation of reactive oxygen species, offer promising avenues for targeted cancer therapy. However, further research is necessary to comprehensively evaluate the safety, efficacy, and mechanisms of action of these compounds.

In summary, this study provides a comprehensive overview of the research on fungi and cancer, shedding light on current focal points, emerging trends, and potential directions for future investigations. These findings offer valuable guidance to authors and researchers in this field, facilitating the development of innovative therapeutic approaches and the identification of novel anticancer agents derived from fungi. Continued exploration of the intricate mechanisms underlying the interplay between fungi and cancer will undoubtedly contribute to the advancement of cancer research and the development of improved treatment strategies in the future.

Declarations

Ethical approval

Since all data used were obtained from the Web of Science database, ethical approval was not required.

Author contribution statement

Jiawei Xu: Ying Zeng: Chengdong Yu: Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Siyi Xu: Lei Tang: Xiaoqiang Zeng: Yanxiao Huang: Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

Zhengkui Sun: Bin Xu: Tenghua Yu: Conceived and designed the experiments.

Data availability statement

Data will be made available on request.

Funding statement

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Declaration of competing interest

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

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