

RESEARCH TRENDS AND HOTSPOTS OF THE TRADITIONAL CHINESE MEDICINAL PLANT RHUBARB: A BIBLIOMETRIC ANALYSIS AND VISUALIZATION

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Abstract

Rhubarb is a plant that contains numerous chemical substances and has been found to have a significant curative effect, particularly in the treatment of constipation. The purpose of this study was to utilize bibliometrics based on the Web of Science to explore the research trends and hotspots related to rhubarb. This research focused on rhubarb and utilized a significant number of literature sources published between 2000 and 2021. To comprehensively review these sources, we used CiteSpace, VOSviewer, and R language to examine various aspects, including research fields, publishing institutions, journals, and authors. A total of 1,552 articles were retrieved, indicating a steady increase in the number of published papers. Notably, the largest increase occurred between 2010 and 2021. The research frontiers encompass a range of disciplines, including Pharmacology Pharmacy, Chemistry, Biochemistry Molecular Biology, and Integrative Complementary Medicine. China is at the center of this research, with the Chinese Academy of Sciences making the greatest contribution through the publication of 91 papers. Network analysis of keywords revealed that rhubarb, emodin, and anthraquinones were the most prominent. Co-citation analysis further highlighted that anthraquinones, pharmacokinetics, and emodin were the main research hotspots. Research on rhubarb has taken a diversified perspective, resulting in significant progress in identifying active substances and understanding pharmacological activities. However, the quality control, resource development and utilization of rhubarb are relatively limited. As a result, research on metabolic, anti-inflammatory, oxidative stress, and damage mechanisms will likely become a hot topic in the future.

Key words: Bibliometrics, Research hotspots, CiteSpace, Medicinal Plant, Rhubarb.

Introduction

Rhubarb is a collective name for several perennial plants belonging to the Polygonaceae family that belong to the genus *Rheum* L. (Dai *et al.*, 2021). Rhubarb, a medicinal plant, is endemic to the Qinghai-Tibetan Plateau (Wang & Ren, 2009). *Rheum tanguticum* Maxim. *ex Balf.*, *Rheum palmatum* L. and *Rheum officinale* Baill. are listed as authentic rhubarb by the Chinese Pharmacopoeia (Chinese Pharmacopoeia Commission, 2020). Rhubarb prefers bright light, cold-resistant, and is not suitable for growth in places with high temperatures or humidity. The main phytochemicals from rhubarb are anthraquinones and their glycosides, anthrones and their glycosides, stilbenes, saccharides, tannins and so on. Rhubarb is known for its traditional functions, which include clearing heat and promoting bowel movements, cooling blood and detoxifying the body, and stopping bleeding (Wang *et al.*, 2011). The efficacy and pharmacological effects of a substance are closely tied to its chemical composition. Previous studies have shown that rhubarb has a purging effect, and the active ingredients that produce purging are sennosides, which are anthrones (Wei *et al.*, 2020). The purging and detoxifying effects of rhubarb are attributed to the presence of free anthraquinone compounds such as emodin and rhein. These compounds have been found to inhibit the growth of most gram-positive bacteria, thus exhibiting antibacterial properties (Wei *et al.*, 2021); rhubarb tannins can significantly reduce serum urea nitrogen, thereby playing a role in gallbladder and jaundice reduction (Nishioka *et al.*, 1981; Zhang *et al.*, 2015). In

addition, rhubarb also has anti-inflammatory, antibacterial, hypoglycemic, and antitumor effects (Dong *et al.*, 2016; Yang *et al.*, 2022; Zeng *et al.*, 2021).

Rhubarb is very popular in domestic and foreign markets due to its remarkable medicinal effects (Liu *et al.*, 2020). At present, there are more than 800 kinds of national standard traditional Chinese medicines that use rhubarb, making it one of the few important traditional Chinese medicines with the largest application range and the highest frequency of use in traditional Chinese medicine prescriptions (Yang *et al.*, 2022). Due to the sour taste of rhubarb, the stalks are eaten as vegetables by local people and animals in some regions (Dai *et al.*, 2021). Rhubarb petiole has been developed as a fat-reducing and slimming tea drink (Wang *et al.*, 2022c). Rhubarb has a wide range of uses, covering medicine, daily life, food processing and other aspects. Today, rhubarb is used not only as a medicinal substance, but also for other purposes in different fields. Concurrently, wild resources of rhubarb have declined sharply in recent years as a result of anthropogenic activities and environmental changes. Therefore, understanding the research status and development trends of rhubarb is highly important for exploring its potential value and sustainable utilization of resources. In this context, rhubarb has become a research hotspot in the field of traditional Chinese medicine. In recent years, rhubarb research has been very active, with various research providing a solid theoretical basis for the basic research, development and rational utilization of rhubarb (Shen *et al.*, 2017; Wang *et al.*, 2022b; Wei *et al.*, 2013; Xiong *et al.*, 2021; Xiong *et al.*, 2019). With the progress of research, vertical and horizontal intersecting

research has resulted in a complex literature system, and the large body of literature plays an important role in promoting academic progress.

Bibliometrics is a discipline that takes the literature system and bibliometric characteristics as the research object, uses mathematical and statistical methods to quantitatively analyze the structure and characteristics of literature information, and then uses this information to study the development status of a certain field and predict future research hotspots (Zhang *et al.*, 2022). For example, Qiao Tao *et al.* used bibliometric methods to systematically and comprehensively analyze the related fields of icariin and proposed that improving the poor water solubility of icariin based on advanced drug delivery systems will become a hot research field in the future (Qiao *et al.*, 2021). Based on the measurement and interpretation of the research literature of Ningxia wolfberry in the past 35 years by Fang Zhang, the results showed that China was at the core of this research field and that the research and development of the non-fruit parts of the plant is the limiting factor for the current study of Ningxia wolfberry (Zhang *et al.*, 2022). Therefore, bibliometrics is an effective means to quickly grasp and track the development of the field. However, bibliometric studies on rhubarb have not been reported, leaving rhubarb researchers lacking a comprehensive understanding of the field. Therefore, to clarify the development context and future development trend of rhubarb research, this study used bibliometric analysis to systematically summarize the research on rhubarb over the past 20 years and reveal the research hotspots and future research trends in this field. This study provides a reference point for a better understanding of the current situation and deficiencies in this field and provides valuable insight and broad ideas for the modernization and international development of other Chinese medicinal materials.

In this study, we searched the Web of Science database for literature and conducted a bibliometric analysis of Rhubarb using the Bibliometricx package in R language, CiteSpace and VOSviewer analysis tools to compensate for the lack of previous reviews and comprehensively reviewed the progress of rhubarb research between 2000 and 2021. The purpose of this study is to identify influential countries, institutions, authors and journals along with bursting keywords. In addition, this study aimed to comprehensively and clearly understand the research status, frontier hotspots and development trends in this field to provide reference data for researchers to acquire rhubarb-related knowledge and address scientific issues.

Material and Methods

Literature sources and retrieval strategies: Literature sources: Web of Science Core Database. Search strategy: The search terms used were rhubarb, *Rheum tanguticum*, *Rheum officinale* or *Rheum palmatum*. Literature index date: January 1, 2000, to December 30, 2021. Types of literature: articles and reviews. Literature download content: full records and cited references. Document download format: plain text.

Research methods: The bibliometric analysis software CiteSpace and VOSviewer were used to analyze the retrieved original literature data. CiteSpace software was developed by Professor Chen Chaomei from Drexel University in the

United States based on the Java language. Through the analysis of scientific literature information, a knowledge map is drawn for a specific field, and the knowledge structure is intuitively presented (Chen, 2006). The analysis included the cooperation network of the research subjects (countries/regions, institutions and core authors), the hot research trends, and the visualization of the map of scientific knowledge. Origin software was used to map the number of relevant publications for analysis of the number of publications of countries and institutions and then reveal the cooperative relationships between countries in this field. VOSviewer was developed by VanEck and Waltman at the Leiden University Science and Technology Research Center in the Netherlands in 2009 (van Eck & Waltman, 2010). It is mainly oriented to the literature data and a relational knowledge unit constructed by literature. VOSviewer was used to construct scientific knowledge graphs and show the interrelationships among the rhubarb research literature. A keyword co-occurrence network map was drawn with VOSviewer software. The top 10 papers and journals with both citation frequencies and numbers of publications were used to assist in the analysis of research hotspots and journals related to rhubarb. The original literature data were analyzed in R (version 4.1.0) using the Bibliometricx package (version 3.13). The analysis content included the keyword evolution process map and hotspot prediction map, which were used to study hotspot prediction and future trend research.

Results

Characteristics of published papers: A total of 1,552 papers (research papers and reviews) related to rhubarb were retrieved from the Web of Science database. Figure 1 shows that the cumulative number of published papers from 2000 to 2021 shows a rapid growth trend. The first stage occurred before 2010 and included 427 papers, while the second stage, between 2011-2021, included 1,125 papers, which is 2.6 times greater than that of the previous 10 years. In the first ten years, the growth was relatively stable, and in the second ten years, there was explosive growth. In 2020 alone, 136 articles were published, equivalent to 31.85% of the first stage prior to 2010. It is therefore clear that rhubarb research is receiving increasing amounts of attention from researchers.

The number of papers produced by different countries and the relationships among collaboration networks between countries: The statistical results of the bibliometrics showed that 1,552 studies were from 49 countries or regions. Chinese authors published 987 articles on rhubarb, accounting for 63.6% of all research articles, followed by South Korea (6.6%), Japan (5.3%), the United States (2.8%) and India (2.7%), with more than 40 articles each. The total number of publications from other countries or regions was 293, accounting for 18.8% of the research literature (Table 1). Figure 2 shows that China has close cooperation with other countries or regions. As an ancient civilization with thousands of years of history developing traditional Chinese medicine (TCM), it is unsurprising that China ranks first in the number of publications. However, other countries such as South Korea, Japan and the United States were at the center of the recent increase of literature citations and are influential countries in

the fields of science and technology. In the future, it will be necessary to strengthen cooperation between countries, build on the past and communicate, and place equal emphasis on the contributions of Eastern and Western countries to make further progress in TCM research.

Table 1. The number of papers published by different countries.

Country	Articles	SCP	MCP	Freq	MCP Ratio
China	987	907	80	0.636	0.081
Korea	103	84	19	0.066	0.184
Japan	83	65	18	0.053	0.217
USA	44	33	11	0.028	0.25
India	42	38	4	0.027	0.095
Germany	34	21	13	0.022	0.382
Poland	30	24	6	0.019	0.2
Canada	21	17	4	0.014	0.19
Italy	20	16	4	0.013	0.2
Iran	18	15	3	0.012	0.167

The number of papers published by different research institutions and the collaborative network relationships between institutions:

The Bibliometricx package was used to visualize published research institutions to identify key research institutions working on rhubarb. The top 10 universities and research institutions are shown in Fig. 3. Compared with other countries, China has conducted more extensive research on rhubarb and published the most research results, so the top 10 research institutions or universities are all in China. China Medical University published the most rhubarb-related literature (n = 140), followed by China Pharmaceutical University (n = 82), Nanjing University of Chinese Medicine (n = 71) and Beijing University of Chinese Medicine (n = 54). The analyzed literature was imported into VOSviewer software, the minimum number of institutional publications was set to 5, and then the institutional cooperation network was analyzed visually. The number of nodes was 122. The size of the nodes in the visualization diagram represents the number of publications of institutions, and the connections between institutions reflect the closeness of cooperation. As shown in Fig. 4, major research institutions were identified, with China Medical University, the University of the Chinese Academy of Sciences, the Chinese Academy of Fishery Sciences and Chengdu University of Traditional Chinese Medicine as the centers.

Literature analysis of the top ten most frequently cited articles:

As shown in Table 2, there were 5 articles on the pharmacological effects of emodin, and 4 articles were related to the anticancer, anti-inflammatory and antioxidant effects of rhubarb. One article was related to germplasm genetic variation. The most frequently cited paper was “Anti-cancer properties of anthraquinones from rhubarb”, with an average annual citation frequency of 20.19 times. In 2016, the paper “Emodin: A Review of its Pharmacology, Toxicity and Pharmacokinetics”, which studied the research progress on the pharmacology and toxicity of emodin, was published. This paper has been cited 314 times in the past five years, with an average annual number of citations of 62.8. Liu Bo of Nanjing Agricultural University contributed the most to the publications, and the top 10 authors were from China (Table 3). Therefore, China is at the core of the field of Chinese herbal medicine.

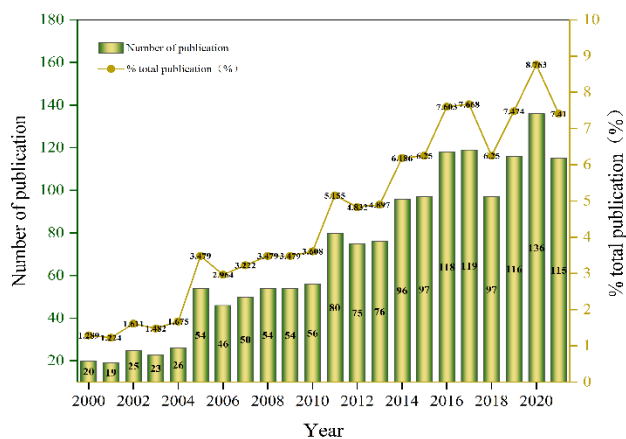


Fig. 1. Annual and cumulative number of documents published on rhubarb in 2000-2021.

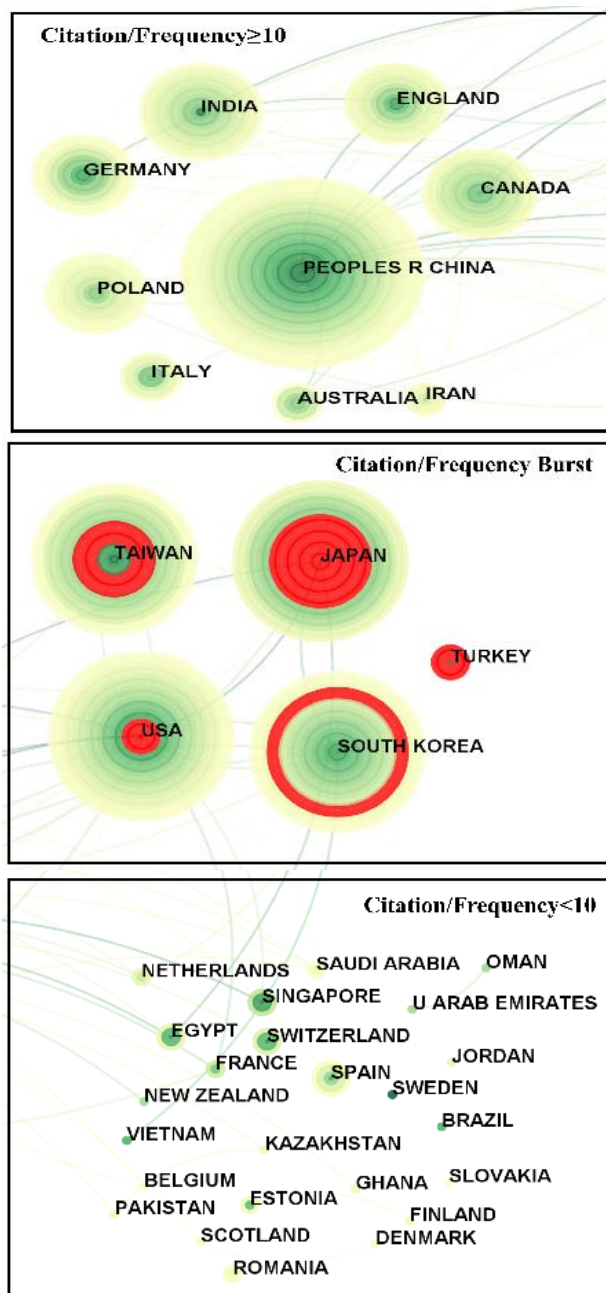


Fig. 2. Cooperation network mapping of national and regional institutions.

Table 2. The top 10 most cited articles related to rhubarb research.

Ranking	Cited number	The title of article	Year	Journal
1.	424	Anti-cancer properties of anthraquinones from rhubarb	2007	Medicinal Research Reviews
2.	353	Multidrug pump inhibitors uncover remarkable activity of plant antimicrobials	2002	Antimicrobial Agents and Chemotherapy
3.	314	Emodin: A Review of its Pharmacology, Toxicity and Pharmacokinetics	2016	Phytotherapy Research
4.	314	Genetic Variation in <i>Rheum palmatum</i> and <i>Rheum tanguticum</i> (Polygonaceae), Two Medicinally and Endemic Species in China Using ISSR Markers	2012	Plos One
5.	282	Emodin blocks the SARS coronavirus spike protein and angiotensin-converting enzyme 2 interaction	2007	Antiviral Research
6.	261	Emodin induces apoptosis in human lung adenocarcinoma cells through a reactive oxygen species-dependent mitochondrial signaling pathway	2005	Biochemical Pharmacology
7.	213	Antioxidant and Anti-inflammatory Activities of Selected Medicinal Plants Containing Phenolic and Flavonoid Compounds	2011	Journal of Agricultural and Food Chemistry
8.	203	Total phenolic contents and antioxidant properties of commonly consumed vegetables grown in Colorado	2006	LWT-Food Science and Technology
9.	194	Emodin induces apoptosis in human promyeloleukemic HL-60 cells accompanied by activation of caspase 3 cascade but independent of reactive oxygen species production	2002	Biochemical Pharmacology
10.	188	Targeted abrogation of diverse signal transduction cascades by emodin for the treatment of inflammatory disorders and cancer	2013	Cancer Letters

Table 3. The top 10 authors ranked by total literature on rhubarb research.

Authors	Documents	Citations	Total link strength	Institutions	Countries
Bo Liu	29	891	153	Nanjing Agricultural University	China
Jun Xie	20	755	116	Chinese Academy of Fishery Sciences	China
Qunlan Zhou	18	685	111	Chinese Academy of Fishery Sciences	China
Xianping Ge	17	665	94	Nanjing Agricultural University	China
Xiaohe Xiao	16	479	89	China Military Institute of Chinese Materia Medica	China
Jiabo Wang	15	442	88	General Hospital of People's Liberation Army	China
Pao Xu	14	711	88	Chinese Academy of Fishery Sciences	China
Yanling Zhao	13	422	78	Tibet Agriculture & Animal Husbandry University	China
Yan Li	12	474	25	Peking University	China
Liangkun Pan	12	556	81	Chinese University of Hong Kong	China

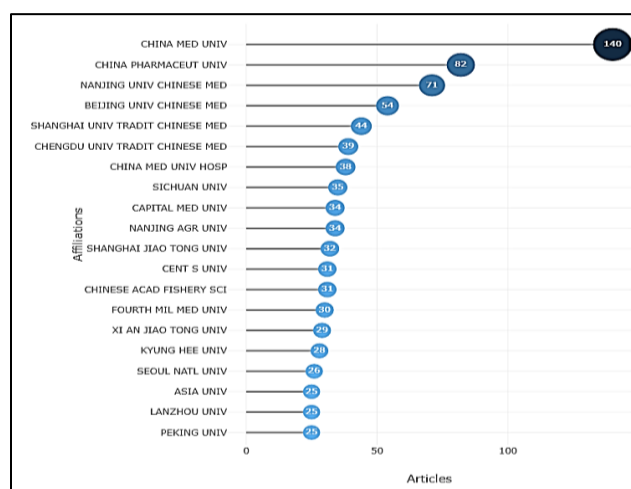


Fig. 3. Number of papers published by different research institutions.

Analysis of keywords and journals: By running the co-occurrence analysis type in the VOSviewer software, the analysis type was chosen to be all keywords, and the minimum frequency of keywords was set to 5. Finally, a visual map with 144 nodes was obtained. As shown in Fig. 5, the literature analyses were all carried out on the basis of rhubarb. These included anthraquinones, emodin, pharmacokinetics, *Rheum palmatum* and traditional

Chinese medicine. The occurrence frequency of rhubarb was 255, while other keywords with high frequency were emodin ($n = 170$), anthraquinones ($n = 86$), apoptosis ($n = 67$), and rhein ($n = 80$) (Fig. 5). The co-occurrence of keywords reflected the main research direction and content of this research field, which has an important guiding role for the research status of rhubarb. Further analysis revealed the 3 journals with the most rhubarb research papers. These journals were the Journal of Ethnopharmacology (67 publications, 4.32%), the Journal of Separation Science (39 publications, 2.51%) and Evidence-Based Complementary and Alternative Medicine (34 publications, 2.19%) (Table 4). The domains covered by these journals were consistent with the co-occurrence of key words, mainly focusing on pharmacological and chemical directions. According to the analysis of the research directions of rhubarb from 2000 to 2021, the top 3 were Pharmacology Pharmacy, Chemistry and Biochemistry Molecular Biology (Fig. 6).

Literature clustering analysis: CiteSpace software was used to perform cluster analysis on the keywords cited in the references, and then the logarithmic likelihood rate (LLR) clustering method was used to construct the keyword clustering map (Fig. 7). In the figure, the modularity Q represents the modularity (Q value) of a network, ranging from 0 to 1 (the closer the value is to 1, the better the clustering effect will be: $Q > 0.3$ indicates that the network clustering structure is significant). The

silhouette represents the contour value (S value), which is an indicator of the homogeneity of the network. The value ranged from -1 to 1 (the closer the S value is to 1 , the closer the connection between nodes in the cluster is, the better the homogeneity is, and the higher the reliability of the clustering results is. $S > 0.5$ indicates a convincing clustering effect). A total of 16 keyword cluster tags were obtained in this study, with clustering $Q = 0.8331 > 0.3$ and $S = 0.9529 > 0.5$, indicating the high reliability of the keyword clustering effect. Figure 7 shows the top 6 classes, where the largest cluster was #0 (anthraquinones), followed by #1 (pharmacokinetics) and #2 (emodin).

Research frontier analysis: Emergent words are keywords whose frequency changes greatly over a certain

period of time. The analysis of emergent words can reflect the research frontier and developments trend in the field. CiteSpace was used to analyze the emergence of literature keywords, and the top 20 emergent words were obtained. The nodes shown in red in Fig. 8 represent emergent words. Tannin and anthraquinone were the two most persistent keywords. From 2000 to 2010, the outbreak themes included rhei rhizoma, rhubarb, separation, stilbene, resveratrol, and induction. This indicated that chemical structure identification and component separation were the main focuses of this stage, among which tannin and anthraquinone are the most studied parts of rhubarb. After 2018, the main research topics related to rhubarb were oxidative stress, metabolism, inflammation, the gut microbiota and mechanisms.

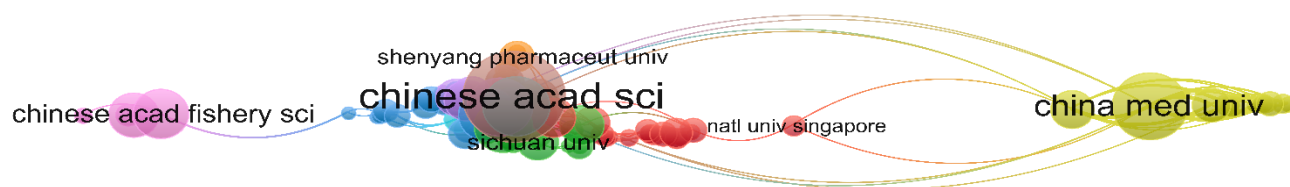


Fig. 4. Institutional cooperation network diagram.

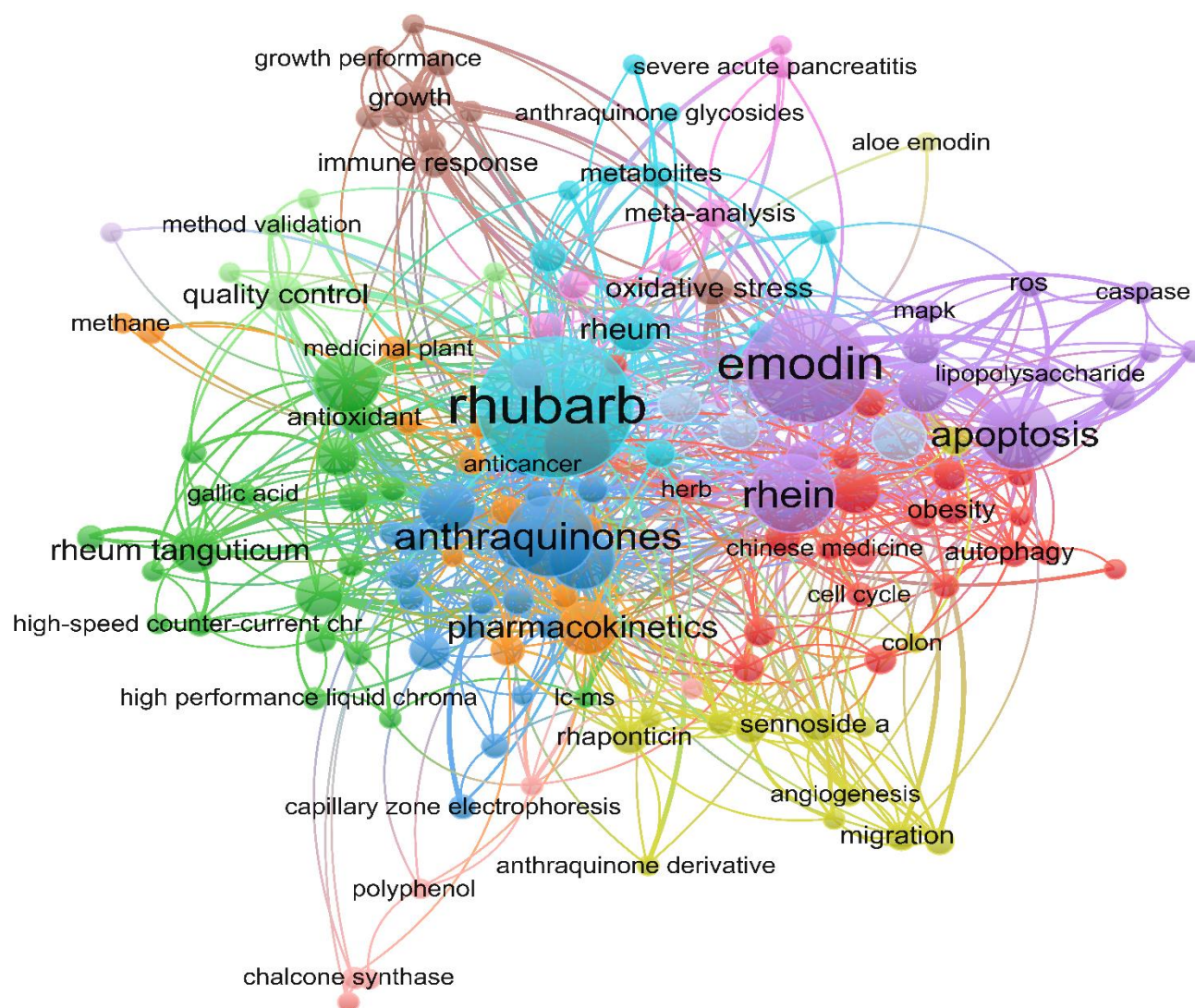


Fig. 5. Network of keywords based on the co-occurrence method for rhubarb research from 2000–2021.

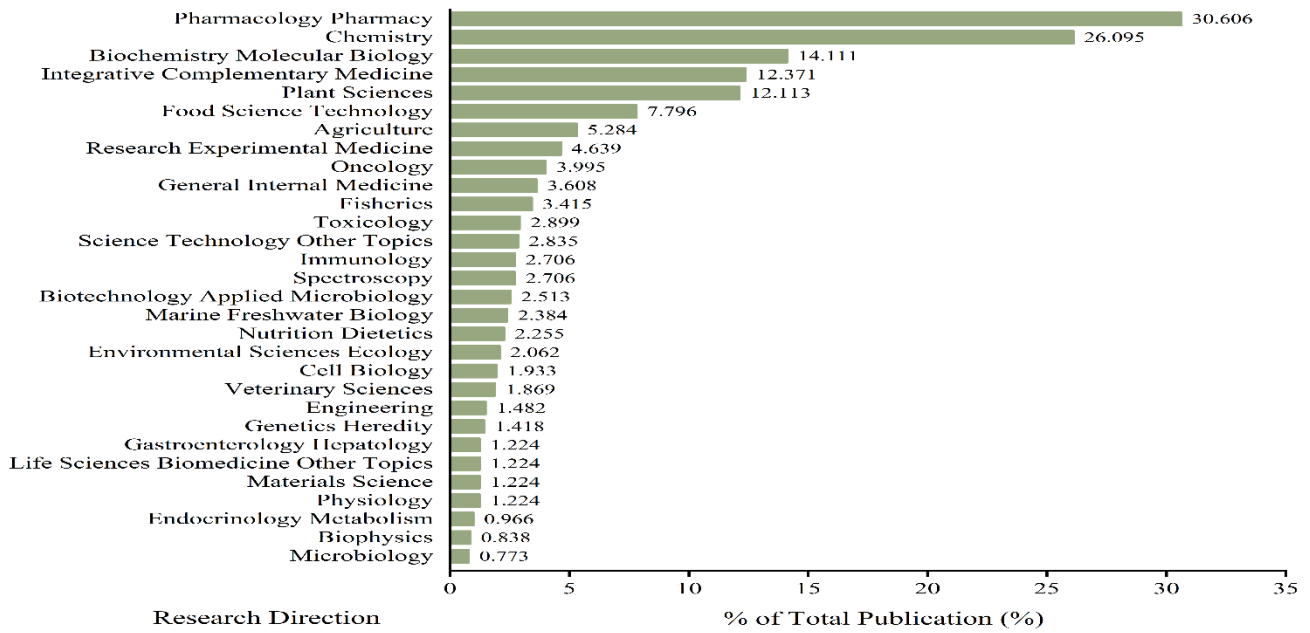


Fig. 6. The top 30 research directions related to rhubarb from 2000 to 2021.

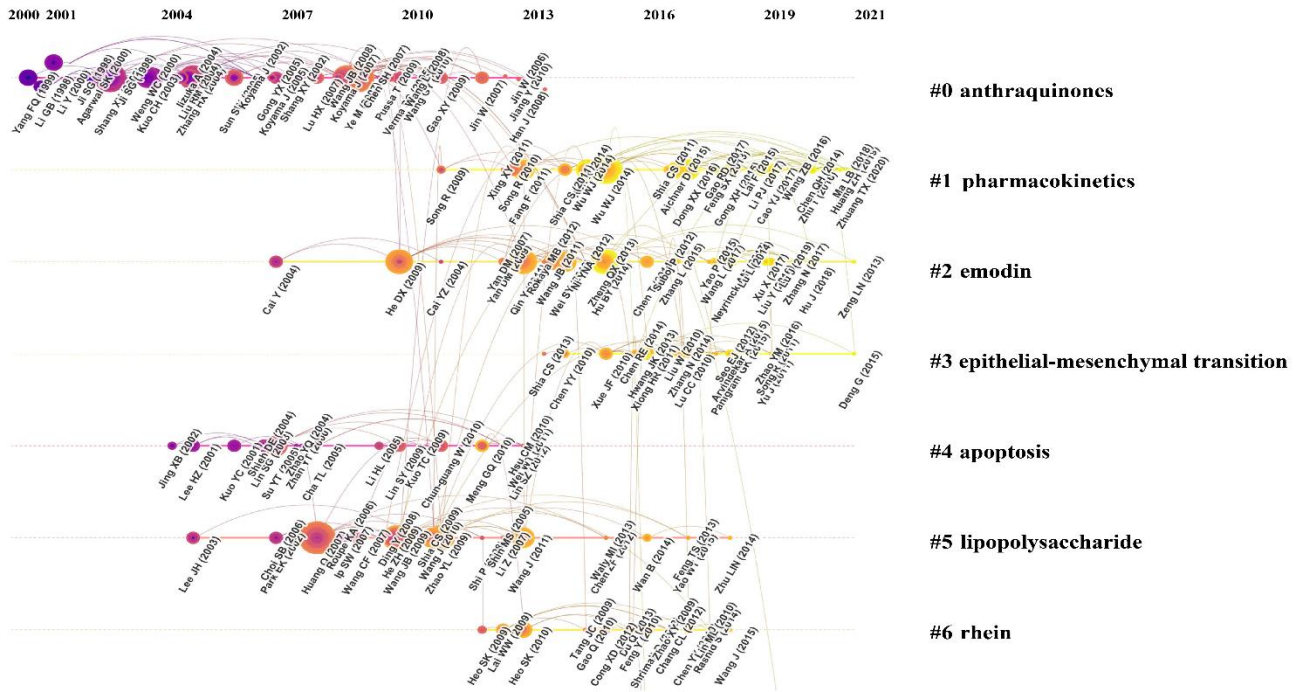


Fig. 7. Time graph of literature joint citations. The horizontal axis represents the year, with each node representing a popular reference, and the size of each node is proportional to how often it is referenced.

Table 4. The top 10 journals related to rhubarb research.

Ranking	Number of publication	% of Total publication	Journal			
			Name	Country/region	Impact factor (2020)	H-Index (2020)
1.	67	4.317	Journal of Ethnopharmacology	Netherlands	4.36	205
2.	39	2.513	Journal of Separation Science	Switzerland	3.645	106
3.	34	2.191	Evidence Based Complementary and Alternative Medicine	USA	2.63	100
4.	30	1.933	Frontiers in Pharmacology	Switzerland	5.811	104
5.	26	1.675	American Journal of Chinese Medicine	Singapore	4.667	67
6.	25	1.611	Phytotherapy Research	England	5.882	140
7.	22	1.418	Fish & Shellfish Immunology	USA	4.581	130
8.	21	1.353	Journal of Chromatography A	Netherlands	4.759	237
9.	20	1.289	Journal of Pharmaceutical and Biomedical Analysis	Netherlands	3.935	133
10.	18	1.16	Biological & Pharmaceutical Bulletin	Japan	2.233	122

Top 20 Keywords with the Strongest Citation Bursts

Keywords	Year	Strength	Begin	End	2000 - 2021
tannin	2000	8.11	2000	2011	[Bar]
anthraquinone derivative	2000	5.62	2001	2012	[Bar]
rhei rhizoma	2000	9.23	2001	2007	[Bar]
rhubarb	2000	8.94	2000	2005	[Bar]
oxidative stress	2000	7.32	2016	2021	[Bar]
separation	2000	7.21	2002	2007	[Bar]
stilbene	2000	4.74	2005	2010	[Bar]
pharmacokinetics	2000	4.16	2013	2017	[Bar]
mass spectrometry	2000	6.15	2014	2017	[Bar]
resveratrol	2000	4.46	2007	2010	[Bar]
metabolism	2000	4.14	2018	2021	[Bar]
inflammation	2000	9.91	2019	2021	[Bar]
rheum officinale baill	2000	5.47	2014	2016	[Bar]
gut microbiota	2000	5.4	2019	2021	[Bar]
mechanism	2000	4.61	2019	2021	[Bar]
plasma	2000	4.61	2013	2015	[Bar]
injury	2000	4.49	2019	2021	[Bar]
induction	2000	4.45	2009	2011	[Bar]
in vitro	2000	4.42	2017	2018	[Bar]
rat	2000	4.15	2014	2015	[Bar]

Fig. 8. Emergent keywords of rhubarb research from 2000 to 2021.

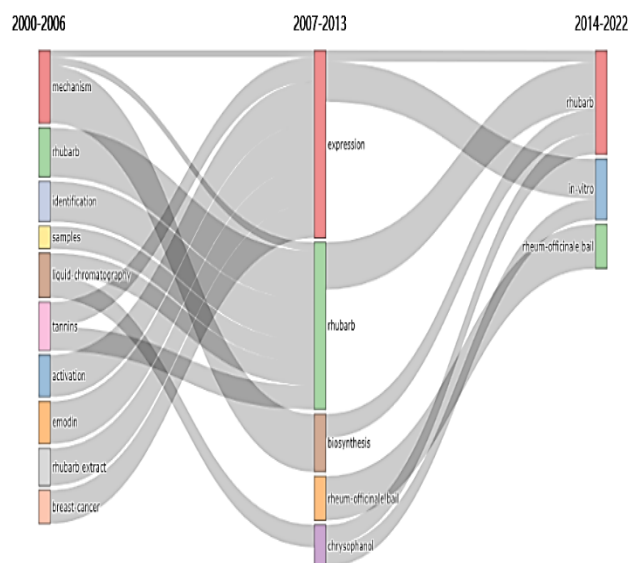


Fig. 9. Keywords evolution map.

Trend Topics

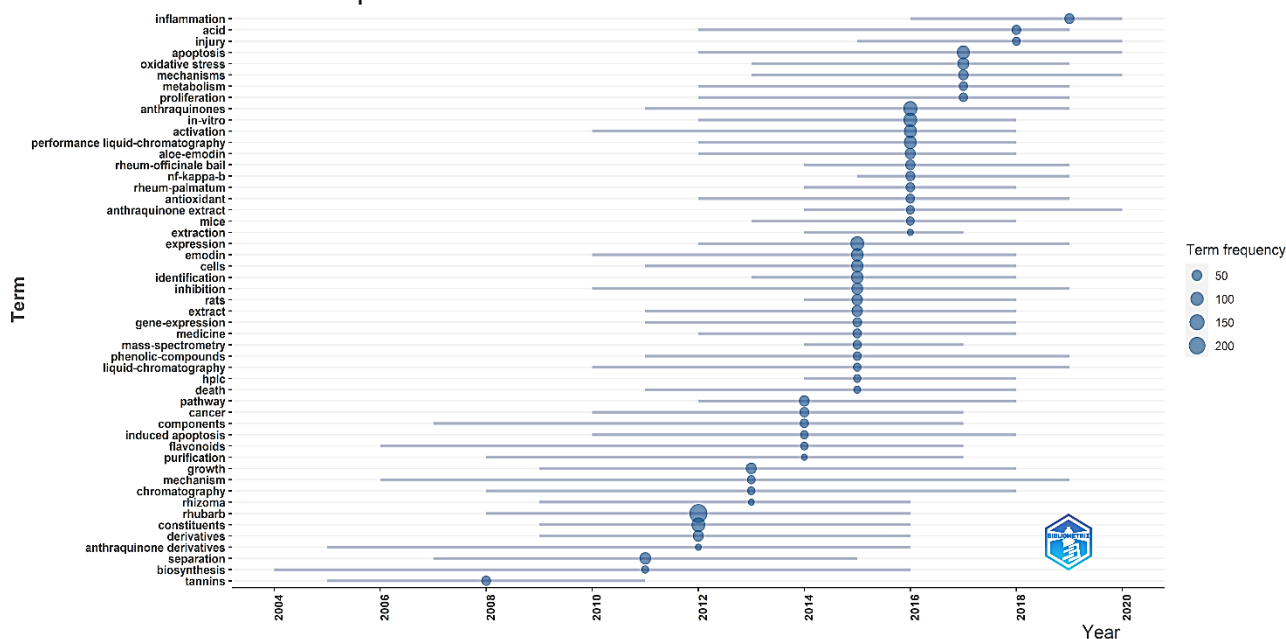


Fig. 10. Prediction of keywords.

We used Bibliometricx, the bibliometricx package, and the "Thematic Evolution" function under the "Conceptual structure" toolbar to visually analyze key word evolution and then establish the dynamic relationship of key word evolution in different time periods. As shown in Fig. 9, in the early stage of rhubarb research, from 2000 to 2006, the most popular keywords were identification, liquid chromatography, tannin, emodin and rhubarb extract. From 2007 to 2013, research on hot keywords showed more specific and in-depth development toward germplasm, biosynthesis and expression, including expression, biosynthesis and rheum officinale baill. The emergence of the keywords rhubarb and chrysophanol indicates that previous studies on the chemical composition of rhubarb are still in progress. In addition, from 2014 to 2021, keywords

focused mainly on rhubarb, *In vitro* and rheum officinale baill, indicating that research on the *In vitro* resistance mechanism of authentic rhubarb has been important to the majority of researchers. The "Trend Topics" function was further used for the visual analysis and prediction of research hotspots related to rhubarb. The analysis period was from 2000 to 2021, the minimum word frequency was set to 25, and the annual number of popular research words was set to 20 to ensure the reliability of the analyzed research hotspots. As shown in Fig. 10, similar to the keyword evolution results, the keyword rhubarb extended from 2012 to 2016. *In vivo* studies of rhubarb from 2014 to 2019 have attracted much attention from researchers. In 2015, there were an increasing number of in-depth studies on gene expression, *In vitro* and *In vivo* tests and component identification of rhubarb. After

2017, studies on the mechanisms underlying the anti-inflammatory, oxidative stress, metabolic and apoptotic effects of rhubarb began to emerge and became a research hotspot. Therefore, the exploration of the effective chemical components involved in the anti-disease mechanism of rhubarb may become a research hotspot in the next few years.

Discussion

CiteSpace and VOSviewer can quickly extract a large amount of literature information and reflect it into a knowledge graph, which has the advantages of comprehensively and objectively evaluating literature progress and predicting hotspots (Gao *et al.*, 2022; Martins *et al.*, 2022). Recently, progress has been made in the separation and identification of the pharmacological and chemical structures of rhubarb (Cao *et al.*, 2017; Huang *et al.*, 2007; Lu *et al.*, 2014; Shrimali *et al.*, 2013), but there are still some areas that need further exploration (Ren *et al.*, 2016; Sun *et al.*, 2016b). Bibliometrics can summarize and interpret past trends and further predict future trends (Wang *et al.*, 2022a; Zhan *et al.*, 2022).

Through visual statistical analysis of 1,552 studies included in the Web of Science, it was found that the cumulative annual number of publications increased gradually before 2010, and the number of publications increased explosively after 2010. From researchers such as Zhongjing Zhang in ancient times to Youyou Tu at present, TCM has been continuously inherited and developed for thousands of years. National collaboration maps showed that rhubarb research was concentrated in Asian countries such as China, Japan and South Korea. In addition, research on rhubarb has increased in the United States and Turkey, further indicating that the use of rhubarb as a traditional Chinese medicine has received increasing attention from researchers around the world. With the deepening of TCM research, a China-centered international exchange and cooperative research platform will be established in the future. The top 10 research institutions in terms of number of publications are all from China, mainly the Chinese Academy of Sciences and medical universities, but there are few exchanges between universities. Therefore, other types of schools should strengthen university cooperation and actively participate in cooperation with medical schools in the future.

The top ten most cited papers have focused on resistance mechanisms, genetic variation, and functional development of other active components of rhubarb. The most frequently cited document was “Anti-cancer properties of anthraquinones from rhubarb”, published by Qing Huang of the National University of Singapore in 2007, which reviewed the toxicity and antitumor potential of anthraquinones in rhubarb (Huang *et al.*, 2007). The main components of rhubarb to inhibit tumor are rhubarb anthraquinone derivatives, rhein, emodin, aloe-emodin and rhubarb polysaccharide, among which emodin can inhibit the growth of various tumor cells such as lung cancer, liver cancer, pancreatic cancer, cervical cancer and prostate cancer. This study is the first to summarize the antitumor mechanism of the pharmacological components of rhubarb, showing that emodin and aloe-emodin can exert antitumor effects by inducing apoptosis (disruption of the mitochondrial membrane potential, cytochrome c release, and activation of

caspase 3) and cell cycle arrest. Other anthraquinone components inhibit the activity of certain key enzymes and transcription factors, such as HER-2/neu, CKII, PKC, and NF- κ B. Therefore, rhubarb may be a promising candidate for the research and development of antitumor drugs. In recent years, research on the anticancer mechanism of anthraquinones has become more detailed and precise. As described in “A Comprehensive and System Review for the Pharmacological Mechanism of Action of Rhein, an Active Anthraquinone Ingredient” (Sun *et al.*, 2016a), “Anti-angiogenic effect and mechanism of rhein from *Rhizoma Rhei*” (He *et al.*, 2011), and “Emodin induced necroptosis in the glioma cell line U251 via the TNF- α /RIP1/RIP3 pathway” have demonstrated the pharmacological mechanism of rhein and emodin (Zhou *et al.*, 2020). Therefore, *In vivo* studies of the resistance mechanisms of plants to rhubarb medicinal ingredients will likely attract increasing attention from researchers in the future.

Keywords are words that have substantial meaning, express the core content of the paper, and are highly concise for the entire study. The results of the keyword co-occurrence network indicated that research in the field of rhubarb has focused on emodin, anthraquinones, and pharmacokinetics. Keyword evolution maps showed that the initial research ideas were derived from the extraction and identification of components and chemical structure separation. Later studies further extended from *In vitro* expression and *In vivo* activity to gut flora and metabolic mechanisms (2014-2021) (Liu *et al.*, 2020; Wu *et al.*, 2020). Research hotspots related to mass spectrometry separation, biosynthesis, and the induction of cell apoptosis have focused on metabolic, anti-inflammatory, and oxidative stress treatment mechanisms (Bajic *et al.*, 2016; Wang *et al.*, 2022b). In summary, the study of the mechanisms of rhubarb medicinal ingredients in resistance against disease may become a new research hot spot in the future.

This is the first study to use CiteSpace and VOSviewer to perform bibliometric analysis and provide a visual display of publications on rhubarb from cooperation among authors, countries, and institutions to hot spots. However, our study has several limitations. Since we analyzed only English studies in the Web of Science, the data may be insufficient. Our results may be inapplicable to research published in other languages. However, our results point out hot research directions for researchers and help to better address scientific questions in the future.

Conclusions

In this study, we used bibliometric methods to analyze the results of studies in the field of rhubarb research from 2000 to 2021. In summary, the amount of related literature is growing rapidly, especially in pharmacology. China is the country with the most published literature, and the Chinese Medical University has published maximum papers. The most influential journal is the Journal of Ethnopharmacology. The lead author is Bo Liu. After more than 20 years of development, the field of rhubarb research has evolved from chemical structure separation and activity verification to metabolic mechanisms, oxidative stress, and *In vivo* activity research, with even broader prospects for future development.

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