Am J Transl Res 2022;14(10):7290-7307
www.ajtr.org /ISSN:1943-8141/AJTR0144773

Original Article

A worldwide bibliometric analysis of triptolide research from 1997 to 2021

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Received June 15, 2022; Accepted September 15, 2022; Epub October 15, 2022; Published October 30, 2022

Abstract: Objectives: In recent years, triptolide has received much attention due to its wide range of pharmacological activities. However, no bibliometric studies have been published on triptolide. This study conducted a bibliometric study to provide scientific and insightful information for further research. Methods: This study performed a bibliometric study of articles published in the Web of Science database from 1997 to 2021. Based on the keywords used in relation to the title of the article containing the word triptolide, 970 publications were searched for further analysis. We used Microsoft Excel for frequency analysis, VOSviewer and CiteSpace for data visualization, and Rstudio for citation metrics and analysis. Results: After analysis, standard bibliometric indicators such as the growth of publications, prolific authors and coauthorship, country distributions, preferred journals, most influential institutions and top cited documents were presented in this study. Conclusions: According to our findings, the number of triptolide-related publications has been increasing since 2009. China was the largest contributor to triptolide research, followed by the USA. *Biomedicine & Pharmacotherapy* was the leading journal related to triptolide research. The most productive authors were Zhang LY (China Pharmaceut Univ) and Jiang ZZ (China Pharmaceut Univ). China Pharmaceutical University was the most influential institution in the field of triptolide research. Our findings suggest that the effective use of triptolide in cancer therapy as well as overcoming its multiorgan toxicity to promote its widespread clinical applications are expected to be hot research topics in the future.

Keywords: Bibliometric analysis, triptolide, VOSviewer, CiteSpace, Rstudio

Introduction

Tripterygium wilfordii Hook F (TWHF) is an herb of the Celastraceae family and is widely distributed in eastern and southern China [1]. Triptolide, a diterpene triepoxide, is the main bioactive component of TWHF extracts [2]. Since it was first isolated and characterized by Kupchan in 1972 [3], it has received increasing attention due to its powerful pharmacological activities, such as anti-inflammatory [4], antioxidant [5], anti-fertility [6], anti-cystogenic [7], immunosuppressive [8], anti-osteoporosis [9], neuroprotective [10], anti-proliferative and pro-apoptotic activities [11]. As a result, triptolide is widely used in the treatment of inflammatory diseases, autoimmune diseases and cancers.

With the global prevalence of inflammatory diseases increasing, the therapeutic activity of anti-inflammatory drugs needs to be urgently improved. Triptolide has potent anti-inflammatory and immunosuppressive properties, which make it a promising drug for the treatment of inflammatory diseases. Studies have been conducted which report that triptolide plays an important therapeutic role in inflammatory diseases such as membranous nephropathy (MN) [12], kidney transplantation [13], inflammatory bowel disease [14], asthma [15], acute lung injury [16], diabetic nephropathy (DN) [17] and autoimmune diseases such as rheumatoid arthritis [18, 19], systemic lupus erythematosus (SLE) [20] and collagen-induced arthritis (CIA) [21]. In addition, triptolide attenuates neuroinflammation and exerts a neuroprotective pharmacological effect, so it has become a potential drug for the treatment of certain neurodegenerative diseases, such as Parkinson's disease [22] and Alzheimer's disease [23].

Triptolide has a therapeutic effect on various cancers, including ovarian cancer [24], pancreatic cancer [25], oral cancer [26], lung cancer [27], breast cancer [28], and chronic myelogenous leukemia [29]. An increasing number of experiments indicate that triptolide regulates autophagy, induces apoptosis [30], inhibits angiogenesis [31], arrests cell cycle progression [32], and suppresses tumor migration, invasion and metastasis [33]. Triptolide exerts its anti-cancer activity by modulating a variety of key molecular mechanisms and signaling pathways, such as XPB, TFIIH [34], RNA polymerase I and II [35], HSP70 [36, 37], Rac1, Jak/Stat3 [38], Bcr-abl [39], NF-kB [40], reactive oxygen species [41], MKP-1, Bcl-2 [42], and caspase 3 [43]. In addition, triptolide not only directly inhibits tumor growth but can also be used in combination with other chemotherapeutic agents to produce synergistic anti-cancer effects [44]. As a result, triptolide has become a broad-spectrum anti-cancer drug capable of multitargeted inhibition of cancer cell proliferation and induction of apoptosis.

Triptolide has promising pharmacological activities, but its poor water solubility and multiorgan toxicity need to be overcome, greatly hindering its clinical applications [45]. Triptolide can cause hepatotoxicity [46], acute myocardial injury [47], reproductive toxicity [48], nephrotoxicity [49], spleen and liver damage [50], and gastrointestinal symptoms [51]. To overcome these drawbacks, triptolide derivatives and delivery methods have been systematically investigated. In the past few decades, the important functional groups of triptolide have been studied and structurally modified in detail so that much important structure-activity relationships (SARs) information has been obtained, leading to the synthesis of a series of derivatives with good water solubility and low toxicity. To date, a number of derivatives of triptolide have progressed in clinical trials; for example, Minnelide is even more effective than the traditional first-line drug gemcitabine in treating pancreatic cancer [52]. In addition to the synthesis of triptolide derivatives, the development of new triptolide-loaded delivery systems is a sensible strategy to overcome the limitations of the clinical application of triptolide. Combining triptolide with certain molecular ligands [53] (such as glucose transporter (GLUTs), megalin receptor, NAD(P)H:quinone oxidoreductase 1 (NQO1), aptamers, and antibodies) or using novel nanodelivery systems [54-56] (such as solid lipid nanoparticles, liposomes, polymeric micelles, microemulsions and nanogels) has achieved targeted delivery of triptolide to diseased cells or tissues, significantly improving the bioavailability of triptolide.

There are no bibliometric studies on triptolide; therefore, it is necessary to provide a comprehensive review of this field. This is the first attempt at bibliometric analysis and mapping based on the Web of Science database, which aims to shed light on publication trends and hot research directions for future research. Specifically, we explored the growth of publications, prolific authors and coauthorship, country distributions, preferred journals, most influential institutions and top cited documents in the field of triptolide from 1997 to 2021.

Materials and methods

Data source and search strategy

As of March 2022, the Web of Science database was used for bibliometric analysis. The search term 'triptolide' included in the article title, was used to search for articles related to triptolide. We focused on the title of the articles because it directly reflects the main subject of the article and helped us to filter out the eligible publications accurately. We refined our search to the publication years 1997 to 2021 to identify the developments and recent trends in triptolide research. The retrieved documents were exported in the form of 'all records and references' and saved as a 'plain text file' using the 'download_txt' extension. **Figure 1** shows our search strategy.

Data extraction and analysis

In this study, we excluded errata documents to avoid double counting and retracted documents that might create false-positive results. All eligible statistics were imported into Microsoft Excel 2019, VOSviewer (version 1.6.17), CiteSpace (version 5.8. R3) and Rstudio for further analysis and visualization.

VOSviewer and CiteSpace, as bibliometric software capable of constructing high-quality knowledge maps, were implemented for the visualization process essentially through com-

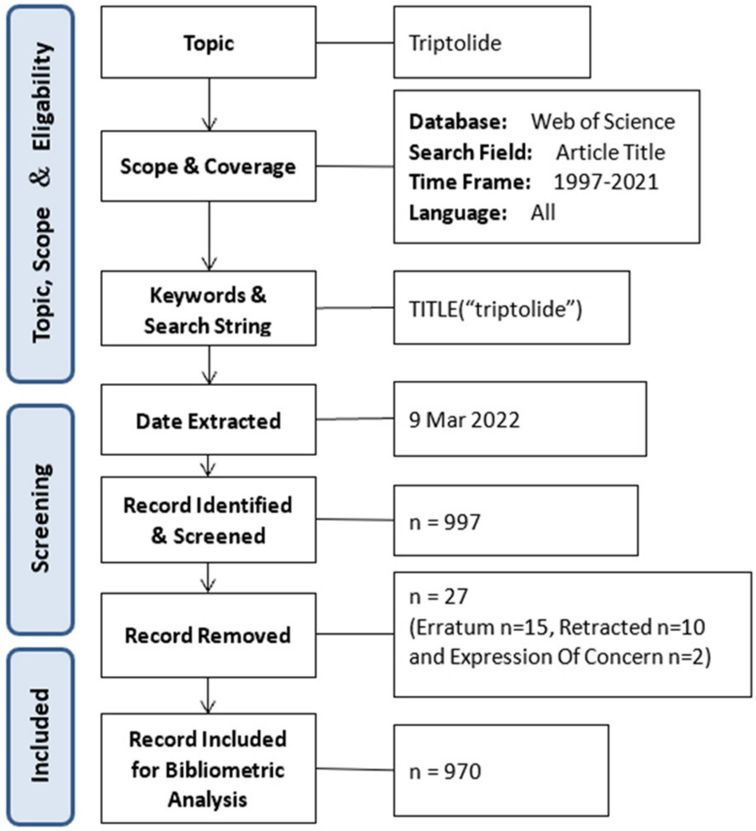

Figure 1. Flow diagram of the search strategy.

Table 1. Types of retrieved documents

Document Type	Total Publications (TP)	Percentage (%)
Article	775	79.90
Meeting Abstract	148	15.25
Review	29	15.25
Proceedings Paper	5	0.52
Letter	5	0.52
Early Access	3	0.31
Editorial Material	3	0.31
Book Chapter	1	0.10
News Item	1	0.10
Total	970	100.00

puter algorithms, and both needed to go through three main steps in the visualization process: standardization of the similarity, clustering, and visualization methods [57, 58]. In the visualization process, the first step was to standardize the imported data, which provides an initial measure of the links between the various data to reveal the interrelated data. The next step was to further analyze the relationships between different data. VOSviewer and CiteSpace both apply cluster analysis to reveal the relationships. Clustering is the process of grouping data objects into multiple classes or clusters, with the principle that objects in the same cluster have better similarity to each other, while objects in different clusters are more distinct from each other. Finally, the construction of knowledge maps based on keywords, authors, institution and country topics is carried out through different visual presentation methods, such as network visualization, density visualization and timeline visualization.

The bibliometrix package in Rstudio offers a suite of programs for quantitative study in bibliometrics and scientometrics [59]. It is programmed by R language and provides an open-source environment. The property of comprehensive statistical algorithms and integrated data visualization makes it available for a wide application in the field of bibliometrics.

We used Microsoft Excel 2019 to calculate the frequencies and percentages of the published materials, VOSviewer and CiteSpace to create and visualize bibliometric networks, and Rstudio to calculate the citation metrics in this study.

Relevant bibliometric indicators

h-index: The *h*-index reflects an author/journal/country that has *h* articles referenced at least *h* times, and the rest of the articles are referenced less than *h* times. It takes the publications and citations into account and has been applied to assess the academic impact of an author/journal/country.

g-index: The *g*-index indicates the most cited *g* articles that have been referenced at least g^2 times.

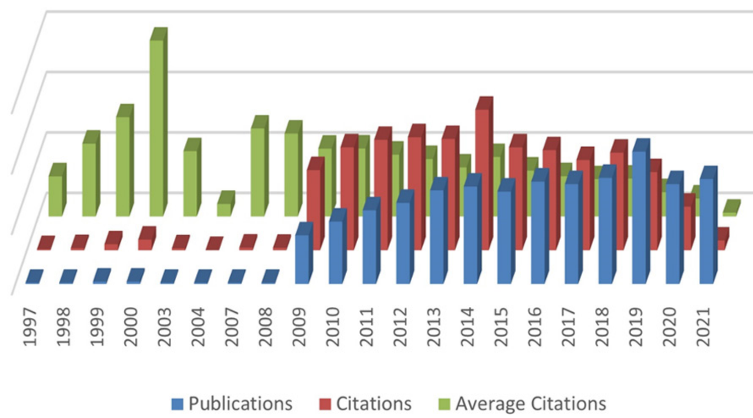

Figure 2. Growth of publications.

$$m\text{-}index = \frac{h\text{-}index}{Y_{academic\ age}} \quad (1)$$

DF: Dominance Factor, the frequency with which an author occupies the first authorship on coauthored articles.

Results

Description of retrieved literature

A total of 970 documents were identified from the Web of Science database based on the document type. The document types include article, meeting abstract, review, proceedings paper, letter, early access, editorial material, book chapter and news item. We summarized the composition of the repertoire according to the type of document (**Table 1**). Original articles accounted for more than three quarters (775, 79.90%) of the total number of documents published, followed by meeting abstracts (148, 15.25%) and reviews (29, 2.99%), and other document types accounted for less than 1% of the total number of documents published.

Growth of publications

Examination of the documents based on year of publication aids the researcher in observing the growth pattern and popularity of the research subject over time. Trends of annual scientific production are represented in **Figure 2**. Since the first article was published in 1997, there have been fewer than 2 articles per year on triptolide in the following 11 years. Until 2009, when an increasing number of academics began to focus on the field, which led to a surge in the number of articles. The highest productivity was observed in 2019, with a total of 106 documents. The citation matrix of the retrieved literature for each year is shown in **Table 2**. The number of citations per publication was highest for documents published in 2000 (70.00 citations per article), while the lowest was for those published in 2021 (1.52 citations per article) due to the short period of time since publication.

Prolific authors and coauthorship

A total of 10 (1.03%) documents were single-authored publications, while the remaining documents (439; 98.97%) were multiauthored publications. The maximal author count of a single article was 19, and most articles were accomplished by 5-8 authors. Therefore, the prevalence of team collaboration or the degree of research cooperation among triptolide researchers was 98.97%. Using VOSviewer technology, authors with a minimum productivity of 5 documents were visualized, as shown in **Figure 3**. This map includes 118 circles, each of which represents an author. The 118 authors were divided into 23 clusters, which suggests that the active authors in the triptolide research field have good research collaboration.

According to our data, a total of 3474 authors published publications in the field of triptolide from 1997 to 2021. We listed the 10 most prolific authors during the study period. Zhang LY (China Pharmaceut Univ) was the most productive author with the highest number of publications (44 publications), as shown in **Table 3**. Jiang ZZ (China Pharmaceut Univ) and Banerjee S (Univ Minnesota) were tied for the second place with a total of 42 publications. Li H (China Pharmaceut Univ) was the most productive first author, with a total of 7 publications (DF=0.292).

The most influential authors ranked by total citations are listed in **Table 4**. Zhang LY (China Pharmaceut Univ) was the most influential author in triptolide research, with a total of 1100 citations, which was also proven by the *h*-index, *g*-index and *m*-index of Zhang LY. Jiang

Table 2. Annual number of publications and citation matrix

Year	Total Publications (TP)	Total Citations (TC)	Average Citations (AC)
1997	1	16	16.00
1998	1	29	29.00
1999	2	79	39.50
2000	2	140	70.00
2003	1	26	26.00
2004	1	5	5.00
2007	1	35	35.00
2008	1	33	33.00
2009	39	1053	27.00
2010	50	1353	27.06
2011	59	1452	24.61
2012	65	1486	22.86
2013	75	1463	19.51
2014	78	1847	23.68
2015	74	1353	18.28
2016	82	1316	16.05
2017	80	1186	14.83
2018	85	1282	15.08
2019	106	1028	9.70
2020	80	573	7.16
2021	84	128	1.52

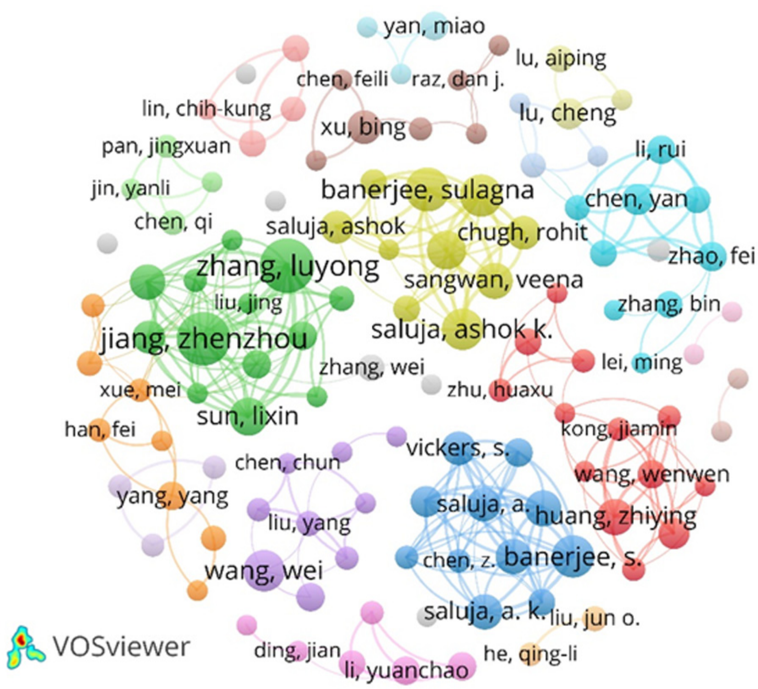

Figure 3. Network visualization map of coauthorship in triptolide research.

ZZ (China Pharmaceut Univ) won Rank 2 with a total of 1088 citations.

Geographical distribution of publications and citations

Researchers from 23 different countries were involved in the publication of the retrieved literature. The top 10 countries that contributed to the publications are listed in **Table 5**. China ranked first, with 761 documents (684 documents were single country publications), followed by the USA, with a total of 117 publications. The other countries published fewer than 10 articles. Furthermore, China also ranked first, with a total of 12469 citations, followed by the USA, with a total of 2196 citations, and the country with the highest average number of article citations was Germany. The results of country distribution based on single country publications and multiple country publications are shown in **Figure 4**.

Subfields and hotspots of triptolide research

Subfields: The keyword co-occurrence network of triptolide was structured by VOSviewer software (**Figure 5**). The size of the nodes represents the weights of the nodes and words. The larger the node is, the greater the weight is. The line between two keywords indicates that they have emerged together. The thicker the line is, the more frequently they appear together. The top 10 keywords along with their frequencies and total link strengths are shown in **Table 6**.

The strength of the link between two nodes represents the frequency of co-occurrence. The node “triptolide” has thicker lines with “apoptosis”, “hepatotoxicity”, “inflammation”, “nf-kappa b”,

Table 3. Top 10 most productive authors

Author's Name	Affiliation	Country	TP	Single-Authored	Multi-Authored	First-Authored	DF	Rank by DF
Zhang LY	China Pharmaceut Univ	China	44	0	44	0	0	7
Jiang ZZ	China Pharmaceut Univ	China	42	0	42	2	0.048	6
Banerjee S	Univ Minnesota	America	42	0	42	5	0.119	4
Dudeja V	Univ Minnesota	America	34	0	34	4	0.118	5
Saluja AK	Univ Minnesota	America	33	0	33	0	0	7
Liu Y	Chinese Acad Sci	China	31	0	31	6	0.194	2
Sangwan V	Univ Minnesota	America	30	0	30	4	0.133	3
Saluja A	Univ Minnesota	America	25	0	25	0	0	7
Vickers SM	Univ Minnesota	America	25	0	25	0	0	7
Li H	China Pharmaceut Univ	China	24	0	24	7	0.292	1

Table 4. Top 10 most cited authors

Author's Name	Affiliation	Country	TP	TC	AC	*h*	*G*	*m*	PY_start
Zhang LY	China Pharmaceut Univ	China	44	1100	25.00	20	32	1.43	2009
Jiang ZZ	China Pharmaceut Univ	China	42	1088	25.90	20	32	1.43	2009
Saluja AK	Univ Minnesota	America	33	759	23.00	13	17	0.93	2009
Vickers SM	Univ Minnesota	America	25	575	23.00	11	12	0.79	2009
Sangwan V	Univ Minnesota	America	30	563	18.77	10	11	0.77	2010
Dudeja V	Univ Minnesota	America	34	529	15.56	10	14	0.71	2009
Li YC	Chinese Acad Sci	China	13	510	39.23	12	13	0.86	2009
Wang Y	Chinese Acad Med Sci	China	21	509	24.24	11	19	0.92	2011
Chugh R	Univ Minnesota	America	22	499	22.68	9	10	0.64	2009
Liu L	China Pharmaceut Univ	China	21	484	23.05	11	18	0.85	2010

PY_Start: the year that researcher published his first article during the investigated period.

Table 5. Top 10 countries contributed to the publications

Country	TP	TC	AC	SCP	MCP	MCP_Ratio
China	761	12469	16.39	684	77	0.10
USA	117	2196	18.77	103	14	0.12
Korea	20	255	12.75	20	0	0.00
Japan	6	49	8.17	6	0	0.00
France	4	146	36.50	2	2	0.50
Canana	3	83	27.67	2	1	0.33
Germany	3	205	68.33	2	1	0.33
India	3	27	9.00	3	0	0.00
Singapore	3	159	53.00	2	1	0.33
Australia	2	61	30.50	1	1	0.50

SCP: Single Country Publications, MCP: Multiple Country Publications.

"autophagy", "oxidative stress", "rheumatoid arthritis", "pancreatic cancer", "toxicity", "p53", and "proliferation". The relationships between "triptolide" and "inflammation" and "rheumatoid arthritis" indicate that the subfield of triptolide is anti-inflammation. The relationships between "triptolide" and "apoptosis", "autophagy", "nf-kappa b", "p53", "proliferation" and "pancreatic cancer" indicate that the subfield of triptolide is anticancer. The relationships between "triptolide" and "hepatotoxicity", "oxidative stress", and "toxicity" reflect that the subfield of triptolide is toxic.

Hotspots: We can make timeline (**Figure 6**) and burstness (**Figure 7**) views of keywords by the CiteSpace software. **Figure 6** shows that keywords related to inflammation, such as "inflammatory bowel disease", "collagen-induced arthritis" and "rheumatoid arthritis", mainly appeared from 2009 to 2013. However, keywords related to anti-cancer (such as "chemotherapy", "cycle arrest", "angiogenesis") as well as toxicity (such as "oxidative stress", "cytotoxicity", "acute lung injury") and novel drug delivery methods (such as "nanoparticle", "transdermal delivery", "(5R)-5-hydroxyrhyncholine") are not only widely distributed between 2009 and 2021, but also have become hotspots in recent years. The same

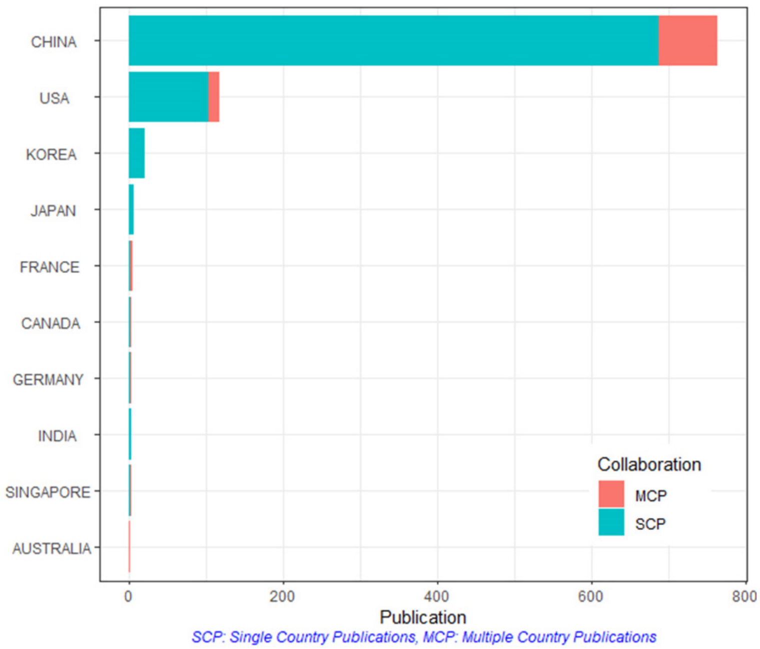

Figure 4. Country distribution based on single and multiple country publications.

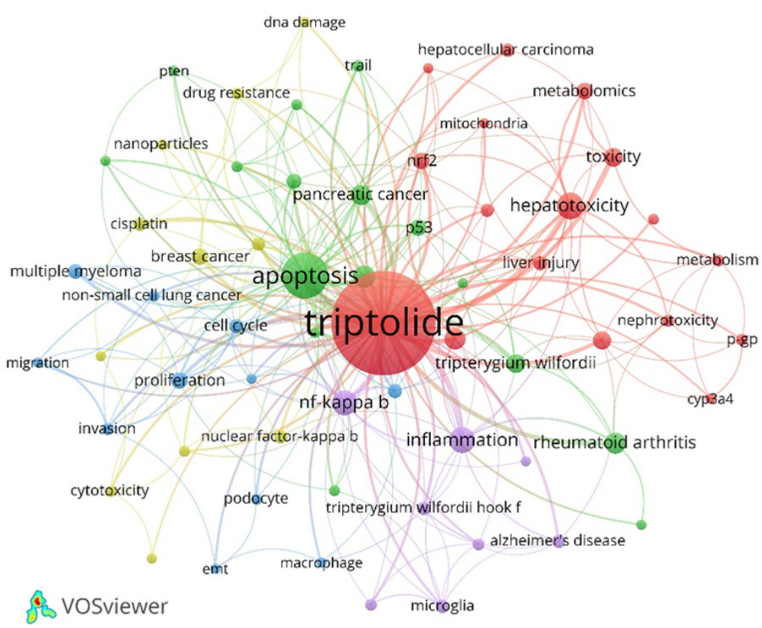

Figure 5. Network visualization map of the author keywords.

results can be found in the burstness view that keywords related to anti-cancer as well as toxicity and novel drug delivery methods appeared in the past 5 years.

Preferred journals

We listed the top 10 journals on triptolide research in **Table 7**. *Pancreas* ranked first with 27 documents, followed by *Biomedicine & Pharmacotherapy* (24 documents). The journal with the greatest total citations is *International Immunopharmacology*, with a total of 418 citations, followed by *Biomedicine & Pharmacotherapy*, with 345 citations. The highest *h*-index, *g*-index and *m*-index were found in *Biomedicine & Pharmacotherapy* (**Figure 8**). The publication year of relevant articles published in the top 10 preferred journals is represented in **Figure 9**.

Top cited documents

The top 10 most highly cited articles in the field of triptolide are listed in **Table 8**. The article that received the highest citation "XPB, a subunit of TFIIH, is a target of the natural product triptolide" was published in *Nature Chemical Biology* in 2011; it received a total of 288 citations and was the most influential article. The second most cited article, "Triptolide and its expanding multiple pharmacological functions", which was published in *International Immunopharmacology* in 2011, received a total of 237 citations.

Most influential institutions

The most influential institutions are listed in **Table 9**. China Pharmaceutical University was the most productive institution and ranked first, with a total of 127 publications and 1263 citations, followed by Sun Yat-sen University (89,1182) and Minnesota University (82,837). Most of the influential research institutions were from China. The annual publication number of the top ten most influential institutions is shown in **Figure 10**. Using VOSviewer technology, institutions with a minimum productivity of 5 documents were visualized, as shown in **Figure 11**.

Table 6. The top 10 keywords of the triptolide-related publications

Author Keywords	Frequencies	Total Link Strength
Triptolide	638	679
Apoptosis	113	220
Hepatotoxicity	36	66
Inflammation	34	60
Nf-kappa B	31	61
Autophagy	24	53
Oxidative Stress	23	46
Rheumatoid Arthritis	22	29
Pancreatic Cancer	20	38
Toxicity	18	30

The map shows 75 institutions distributed in 12 different clusters, each with a different color.

Discussion

Bibliometrics is a trans-disciplinary science that uses mathematical and statistical approaches to quantitatively analyze all carriers of knowledge. It can help us review the development of certain fields and provide scientific and insightful information to carry out further research. In this paper, we conducted a bibliometric study of triptolide-related publications from 1997 to 2021 in the Web of Science database. The analysis revealed some interesting results, which can be summarized as follows:

First, the number of triptolide-related publications remained extremely low from 1997 to 2008. However, after 2009, the number of publications increased rapidly. The upward trend in the number of publications indicates that triptolide research is attracting increasing attention.

Second, Zhang LY was the most prolific author, with 44 publications. Jiang ZZ and Banerjee S were tied for the second most prolific authors with 42 publications. However, the top 10 most prolific authors all had relatively low DFs. Zhang LY and Jiang ZZ were also the most cited authors, tied for the first place in the *h*-index, the *g*-index and the *m*-index. They were both from China Pharmaceut Univ and jointly published the third most cited article in the *Journal of Ethnopharmacology*, "Triptolide: Progress on research in pharmacodynamics and toxicology". Thus, Zhang LY and Jiang ZZ were the most influential authors in the field of triptolide.

Third, *Pancreas* published the most publications, but its total citations were very low. However, the *h*, *g* and *m* index of *Biomedicine & Pharmacotherapy* were all Rank 1; at the same time, its publications and total citations were Rank 2. Moreover, there have been no triptolide-related publications published by the *Pancreas* since 2016. In contrast, *Biomedicine & Pharmacotherapy* has many and constant publications. Therefore, *Biomedicine & Pharmacotherapy* was considered to be the most influential journal.

Fourth, China Pharmaceutical Univ, Sun Yat-sen Univ and Minnesota Univ were the most prolific institutions and received the highest total citations. However, Minnesota Univ had not published triptolide-related publications since 2018. As a result, we focus more attention on the China Pharmaceutical University and Sun Yat-sen University. China had the most publications, the largest number of citations worldwide, and most of the influential institutions were from China, which means that China was the leader in this field. It was followed by the United States.

Finally, through keyword analysis, we found that the main research fields of triptolide focused on its anti-inflammatory and anti-cancer pharmacological effects as well as its toxicity. However, the research hotspots are currently more focused on its anti-cancer activity and toxicity.

Cancer is a disease that mankind has not yet been able to completely conquer. The ability of triptolide to inhibit the proliferation of cancer cells and induce their apoptosis in a multitargeted manner makes it a promising anticancer drug for development.

Triptolide has attracted much attention due to its unique structure and rich pharmacological activities, but its clinical application is greatly hindered by its multiorgan toxicity and poor water solubility. To further promote the clinical use of triptolide, we also need to make breakthroughs in the following aspects:

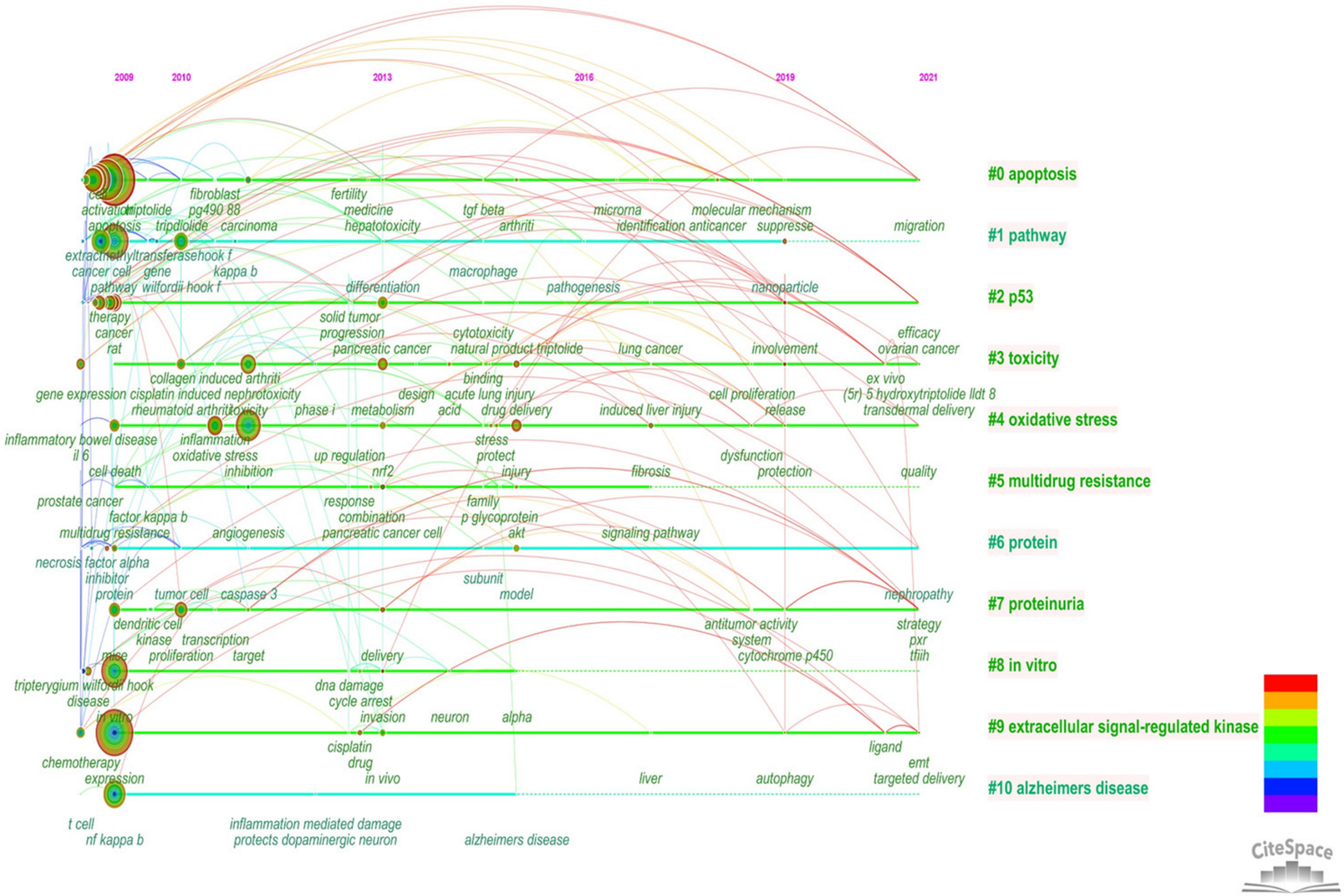

Figure 6. The timeline view of keywords.

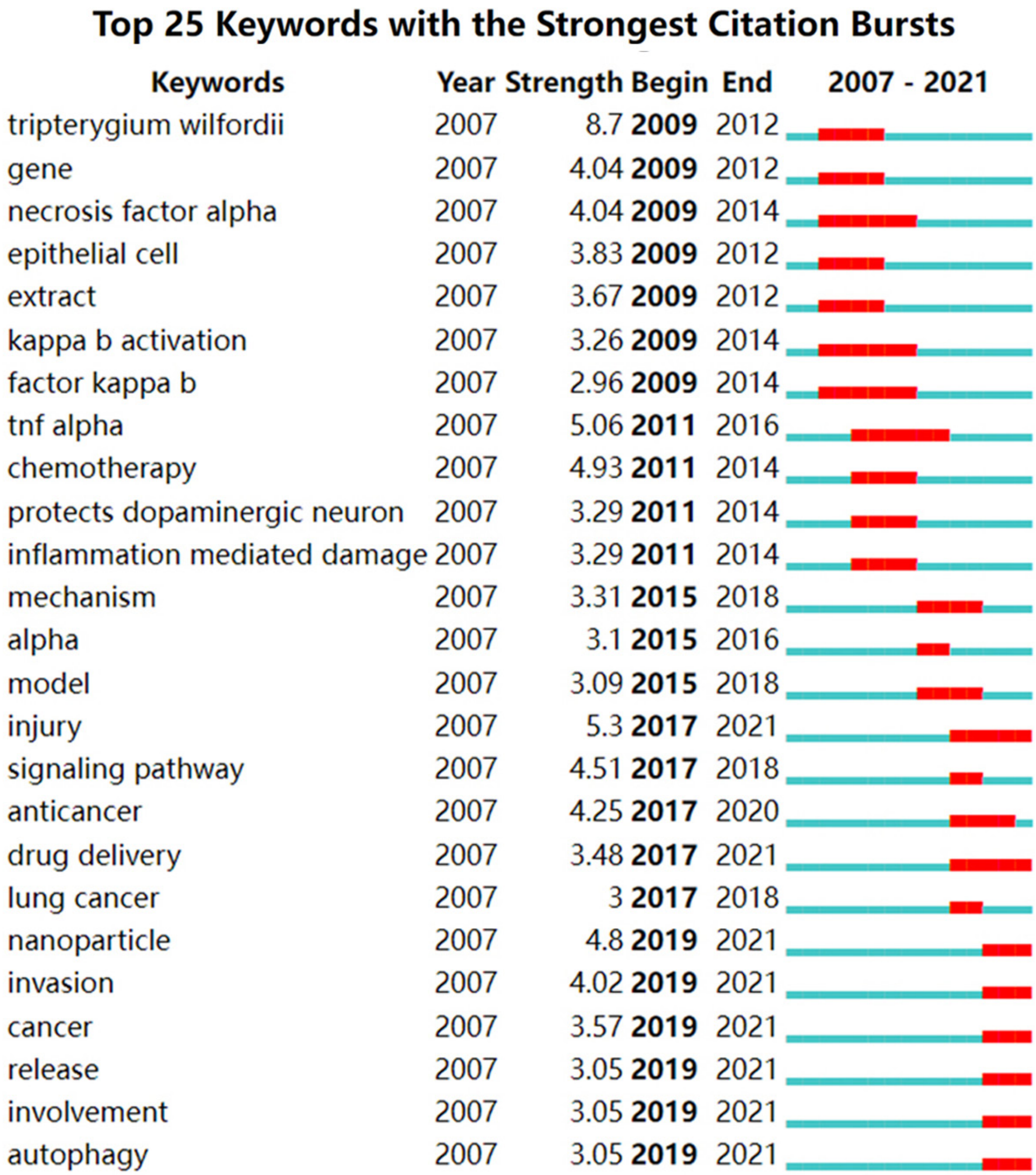

Figure 7. The burstness view of keywords.

(1) To further explore the structure-activity relationships (SARs) of triptolide and rationally design new derivatives with higher water solubility, more potent bioactivity and fewer side effects and toxicity.

(2) The signaling pathways and molecular targets for the action of triptolide have not yet been fully identified, so we need to design new molecular probes to further identify the unknown targets of action [60]. In addition, it has been shown that triptolide-induced toxicity is closely related to certain molecular targets. For example, activation of the Nrf2 signaling pathway counteracts oxidative stress and attenuates triptolide-induced kidney injury [61]. These efforts provide new perspectives for alleviating triptolide-induced toxicity.

Table 7. Top 10 publishing journals on triptolide research

Source Title	TP	TC	*h*	*g*	*m*	PY_start	Categories
Pancreas	27	60	3	4	0.27	2012	Toxicology
Biomedicine & Pharmacotherapy	24	345	11	18	1.57	2016	Medicine, Research & Experimental; Pharmacology & Pharmacy
Cancer Research	18	83	2	6	0.18	2012	Oncology
Frontiers in Pharmacology	17	328	10	13	1.43	2016	Medicine, Research & Experimental
Experimental and Therapeutic Medicine	17	184	7	13	0.70	2013	Pharmacology & Pharmacy
International Immunopharmacology	16	418	9	15	0.75	2011	Immunology; Pharmacology & Pharmacy
Molecular Medicine Reports	16	244	9	15	1.00	2014	Oncology; Medicine, Research & Experimental
Toxicology Letters	15	336	9	13	0.69	2010	Oncology
Acta Pharmacologica Sinica	15	245	10	12	0.77	2010	Gastroenterology & Hepatology
Oncology Reports	14	289	10	14	0.71	2009	Chemistry, Multidisciplinary; Pharmacology & Pharmacy

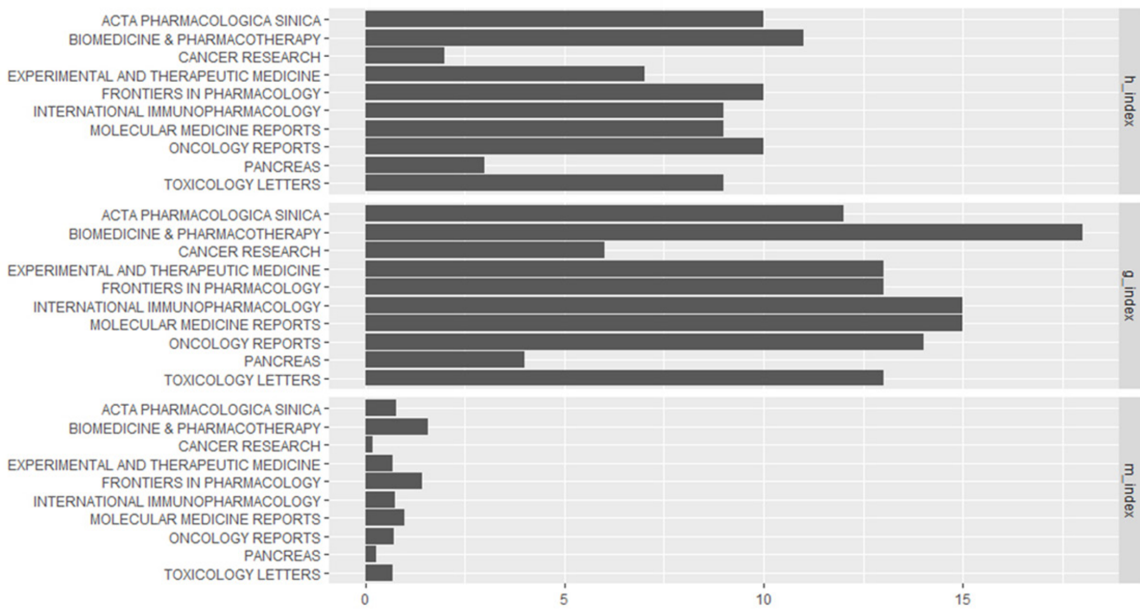

Figure 8. The *h*-index, *g*-index and *m*-index of top 10 journals.

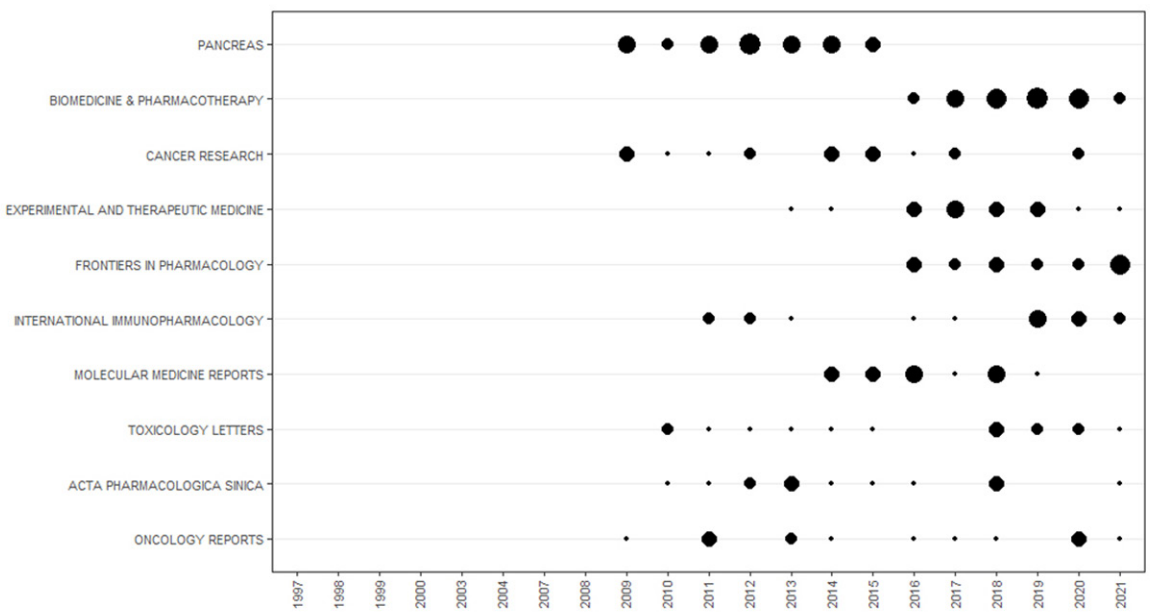

Figure 9. The published year of relevant articles published in top 10 journals.

(3) The development of highly effective triptolide-targeted delivery systems is an effective strategy to achieve targeted drug delivery and reduce systemic toxicity. We can design nanoparticles or conjugated ligands that target tumor microenvironments [62] or certain molecular targets that are overexpressed or selectively expressed on pathological tissues or cells to achieve selective delivery of triptolide and reduce systemic toxicity [63].

(4) The development of triptolide in combination with other drugs would be a practical strategy. Combining drugs has many advantages, including synergistic effects to improve efficacy, delaying or reducing the incidence of drug resis-

Table 8. Top 10 highly cited articles in triptolide research

	Title	Journal	Authors	Year	TC	TC PerYear
1	XPB, a subunit of TFIIH, is a target of the natural product triptolide	Nature Chemical Biology	DV Titov, B Gilman, QL He, S Bhat, WK Low, YJ Dang, M Smeaton, AL Demain, PS Miller, JF Kugel, JA Goodrich, JO Liu	2011	288	24.00
2	Triptolide and its expanding multiple pharmacological functions	International Immunopharmacology	QY Liu	2011	237	19.75
3	Triptolide: Progress on research in pharmacodynamics and toxicology	Journal of Ethnopharmacology	XJY Li, ZZ Jiang, LY Zhang	2014	216	24.00
4	Triptolide: structural modifications, structure-activity relationships, bioactivities, clinical development and mechanisms	Natural Product Reports	ZL Zhou, YX Yang, J Ding, YC Li, ZH Miao	2012	185	16.82
5	A Mechanistic Overview of Triptolide and Celastrol, Natural Products from Tripterygium wilfordii Hook F	Frontiers in Pharmacology	SR Chen, Y Dai, J Zhao, LG Lin, YT Wang, Y Wang	2018	135	27.00
6	Triptolide Induces Cell Death in Pancreatic Cancer Cells by Apoptotic and Autophagic Pathways	Gastroenterology	N Mujumdar, TN Mackenzie, V Dudeja, R Chugh, MB Antonoff, D Borja-Cacho, V Sangwan, R Dawra, SM Vickers, AK Saluja	2010	128	9.85
7	Triptolide is an inhibitor of RNA polymerase I and II-dependent transcription leading predominantly to down-regulation of short-lived mRNA	Molecular Cancer Therapeutics	S Vispe, L DeVries, L Creancier, J Besse, S Breand, DJ Hobson, JQ Svejstrup, JP Annereau, D Cussac, C Dumontet, N Guilbaud, JM Barret, C Bailly	2009	106	7.57
8	Triptolide in the treatment of psoriasis and other immune-mediated inflammatory diseases	British Journal of Clinical Pharmacology	R Han, M Rostami-Yazdi, S Gerdes, U Mrowietz	2012	105	9.55
9	Toxicity of triptolide and the molecular mechanisms involved	Biomedicine & Pharmacotherapy	C Xi, SJ Peng, ZP Wu, QP Zhou, J Zhou	2017	104	17.33
10	Triptolide reverses hypoxia-induced epithelial-mesenchymal transition and stem-like features in pancreatic cancer by NF-jB downregulation	International Journal of Cancer	L Liu, AV Salnikov, N Bauer, E Aleksandrowicz, S Labsch, C Nwaeburu, J Mattern, J Gladkich, P Schemmer, J Werner, I Herr	2014	100	11.11

Table 9. Top 10 most influential institutions

Affiliation	Country	TP	TC	AC
China Pharmaceut Univ	China	127	1263	9.94
Sun Yat Sen Univ	China	89	1182	13.28
Univ Minnesota	America	82	837	10.20
Capital Med Univ	China	51	483	9.47
Nanjing Univ	China	49	712	14.53
Fourth Mil Med Univ	China	42	440	10.48
Nanjing Univ Chinese Med	China	40	254	6.35
Nanjing Med Univ	China	37	389	10.51
Shanghai Inst Mat Med	China	35	795	22.71
Zhejiang Univ	China	35	424	12.11

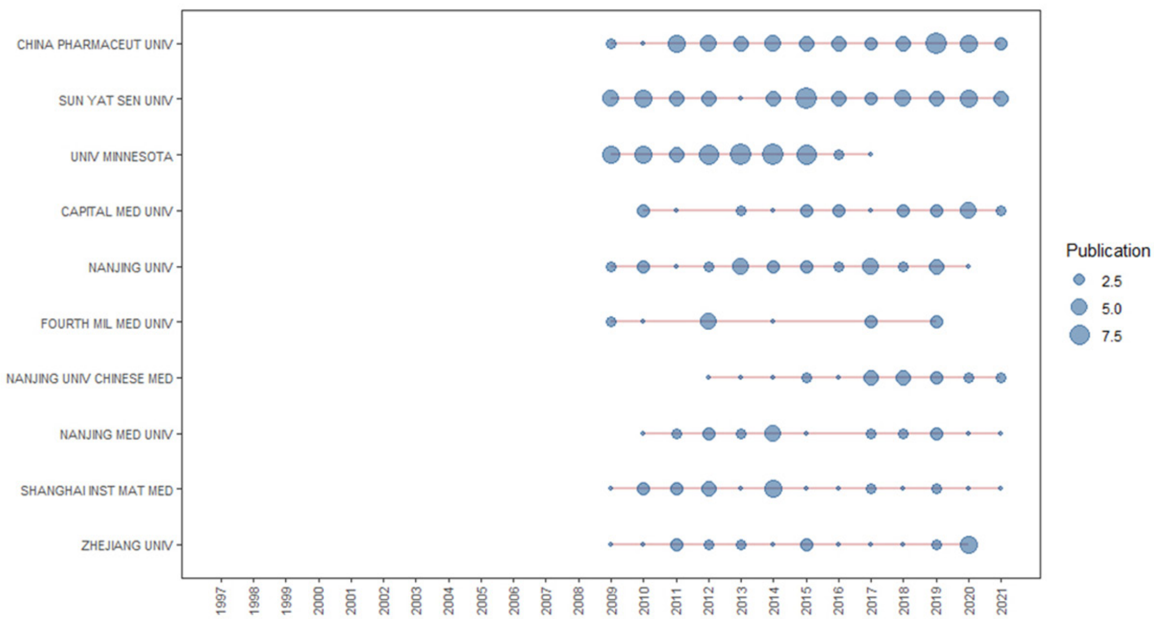

Figure 10. The annual publication numbers of top 10 institutions.

tance and reducing the dose of individual drugs to reduce toxic side effects. For example, the combination of triptolide and cisplatin inhibited the growth of gastric cancer cells better than both alone, synergistically promoting apoptosis without significant side effects [64].

Strengths and limitations

The strengths of this study include a detailed analysis of keywords, preferred journals and influential institutions in a timeline dimension. The keywords were analyzed using CiteSpace software for both timeline and burstness views, clearly showing the evolution of the field of triptolide and current research hotspots. The top 10 journals and institutions on triptolide research were visualized using Rstudio software to provide a visual representation of their annual publications, which helped us to predict the most authoritative journals and institutions in the future. This bibliometric study also has some limitations. First, the documents studied were limited to the Web of Science database and only included partial samples of global production in this field. Second, we might have neglected some articles on triptolide if the authors did not put our research keywords in the title of the publication, resulting in an inaccurate analysis.

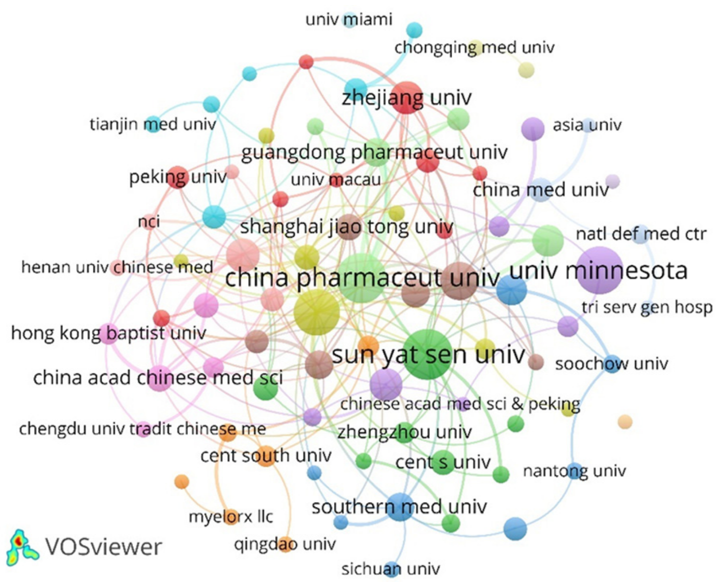

Figure 11. The institute coauthorship network of triptolide-related publications.

Conclusion

China was the largest contributor to triptolide research, followed by the USA. *Biomedicine & Pharmacotherapy* was the leading journal related to triptolide research. China Pharmaceutical University was the most influential institution in the field of triptolide research. Zhang LY (China Pharmaceut University) and Jiang ZZ (China Pharmaceut University) are authoritative researchers in the field. The effective use of triptolide in cancer therapy and overcoming its multiorgan toxicity to promote its widespread clinical applications are expected to be hot research topics in the future.

Acknowledgements

This work was supported by the National Key R&D Program of China [2019YFA0111900]; National Natural Science Foundation of China [81874030, 81902203, 82072506, 82272611]; Provincial Clinical Medical Technology Innovation Project of Hunan [2020SK53709]; Science and Technology Innovation Program of Hunan Province [2021RC3025]; the Administration of Traditional Chinese Medicine of Hunan Province [2021075]; Innovation-Driven Project of Central South university [2020CX045]; the program of Health Commission of Hunan Province [202204074879]; National High Level Hospital Clinical Research Funding Elite Medical Professionals Project of China-Japan Friendship Hospital [ZRJY2021-QM21].

Disclosure of conflict of interest

None.

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