Trend on *Epimedium brevicornu* Maxim in Two Decades (from 2003 to 2022): Bibliometric Analysis and Visualization

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Abstract [**Objectives**] *Epimedium brevicornu* Maxim is a well-known plant having the concomitant function of both medicine and foodstuff with the bioactivity of anti-inflammatory and cardiovascular protection. It has important therapeutic effects and health benefits for various chronic diseases. This study aimed to analyze the studies on *E. brevicornu* Maxim from 2003 to 2022 with bibliometric analysis. [**Methods**] Publications related to *E. brevicornu* Maxim was retrieved in Web of Science Core Collection (WoSCC) from January 1, 2003 to November 19, 2022, and analyzed in Microsoft Excle, CiteSpace, and VOSviewer. [**Results**] In total, 1 317 documents were extracted from the WoSCC database. The growth rate of the publications showed a rapid increase from 2017. China provided the most documents, and Chinese Academy of Medical Sciences, Fudan University and Chinese Academy of Sciences contributed more papers. Wang Ying from Chinese Academy of Sciences was the most productive author, and the Journal of Ethnopharmacology was the most co-cited journal. The words "icariin", "activation", "oxidative stress", "apoptosis", "proliferation", "osteogenic differentiation" and "flavonoid" were frequently occurred in the abstract and title of articles. Cluster analysis of keywords demonstrated "hippocampal neuron", "efficient production", "liquid extraction", "bone regeneration" and "leukemia cell growth" were the hot topics from 2003 to 2022. The focus of the research has changed from the liquid extraction of flavonoids to the inflammatory response and metabolism, while cognitive deficit has emerged as a recent research hotspot. [**Conclusions**] The research on *E. brevicornu* Maxim has been expanding, and more studies are related to signaling pathways and metabolism diseases.

Key words Citespace; *Epimedium brevicornu* Maxim; Medicine food homology; Bibliometrics; VOSviewer
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Epimedium brevicornu Maxim has been used as a kind of medicinal and edible material over 2000 years in China[1]. With the development of new technology, more and more active components of *E. brevicornu* Maxim were detected, and the extracts of this genus has shown activity on many diseases such as atherosclerosis[2], and are effective in regulating bone metabolism in osteoporosis[3], alleviating asthma[4], and resisting viruses[5].

Bibliometrics analysis provides an objective assessment of the literatures in quality and quantity with mathematical and statistical methods[6]. This comprehensive analysis of the academic groups and individual studies makes the trends and hotspots in specific field clearly and easy to understanding[7]. Additionally, the frequencies of keywords appearing in the included articles in recent years reflect the future trends in particular field[8].

Citespace is a document visualization analysis software, which is suitable for bibliometrics analysis and data visualization, and could make a visual analysis on scientific studies in our interesting field and uncover the hotspots and directions of the research[9-11]. VOSviewer was developed by Van Eck and Waltman from Leiden University for mapping bibliolmetric analysis results[12]. This software could construct visual network by relationship among the included data. Citespace and VOSviewer are effective methods for evaluating the authors, countries, journals, citations and institutions of the studies and facilitate comprehension among users[13]. The research on *E. brevicornu* Maxim has been increasing rapidly recent years. However, this type of bibliometric study is absent. To fill the research gap, Citespace and VOSviewer were employed to conduct on analysis study based on the Web of Science Core Collection (WoSCC).

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Lei ZHANG (1986 -), male, P. R. China, lecturer, devoted to research about active components of natural drugs and prevention and treatment of cardiovascular diseases.
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Materials and Methods

Search strategy

Literature was obtained from the Web of Science Core Collection (WOSCC). The search formula was Topic = ("*Epimedium brevicornu* Maxim" OR "*Epimedium sagittatum* Maxim" OR "Epimedium pubescens Maxim" OR "Epimedium koreanum Nakai" OR "icariin"). The results of searching were confined by language (English), publication year from January 1, 2003 to November 19, 2022. 1 513 records were identified (Fig. 1) and 1 317 records were included for biblimetric analysis by Citespace (V6.1 R4) and VOSviewer (version 1.6.18). The records were

manually input into Microsoft Excel 2017 for graphical analysis on the numbers of published paper each year (Fig. 2).

Data analysis

All included records were saved as plain text formation, including authors, titles, abstracts, keywords and cited references. And then, CiteSpace was employed to detect and visualize the author, countries/regions and institutions collaboration, keywords co-occurrence, cluster and burst, co-cited references, and citation burst. The time span was set as 2003 – 2022, and 1 year per slice. Network pruning was based on the preliminary analysis results to choose Pathfinder Network (PFNET). VOSviewer was used to identify the institution cooperation among different clusters and authors' relationships in the studies of *E. brevicornu* Maxim and visualization map of co-citation journals.

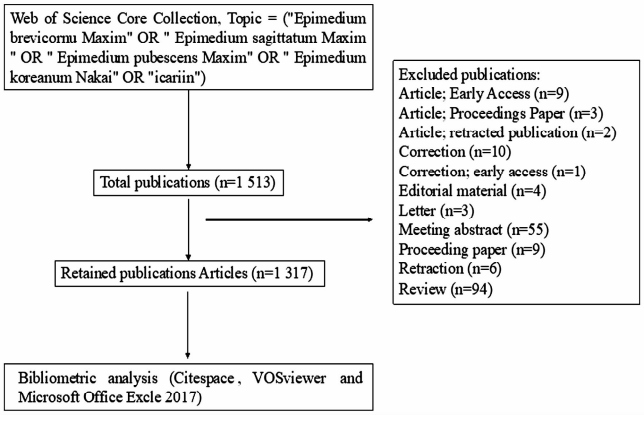


Fig. 1 Flowchart for the publications selection included in this study

Results and Analysis

Publication trends and output

Literature related to *E. brevicornu* Maxim generally showed an upward trend in the past 20 years, and reflected the development profile of *E. brevicornu* Maxim (Fig. 2). Publications about *E. brevicornu* Maxim general started from 2003, and increased slowly before 2011, but after then, a rapid growth appeared from 2012 to 2015, especially after 2016, and the highest value was reached in 2022, with 170 articles.

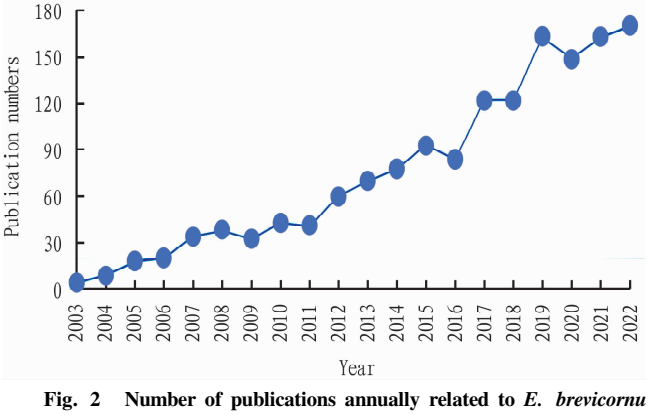


Fig. 2 Number of publications annually related to *E. brevicornu* Maxim (2003 – 2022)

Analysis on collaboration among institutions

A total of 403 institutions were included, and the institutions with more than 10 documents were represented in Fig. 3A. The cooperation clusters were mapped in Fig. 3B, with the size of nodes meaning the number of documents of each institution. The top 25 institutions were represented in Fig. 4. Peking University started the *E. brevicornu* Maxim studies earlier than others, but the documents decreased after 2012. Tianjin Medical University, Wenzhou Medical University, King Abdulaziz University, Zunyi Medical University, Guangzhou University of Chinese Medicine and Nanjing Forestry University have more contributions in recent years. Chinese Academy of Medical Sciences, Fudan University, Peking Union Medical College and Chinese Academy of Sciences have more contact with other institutions.

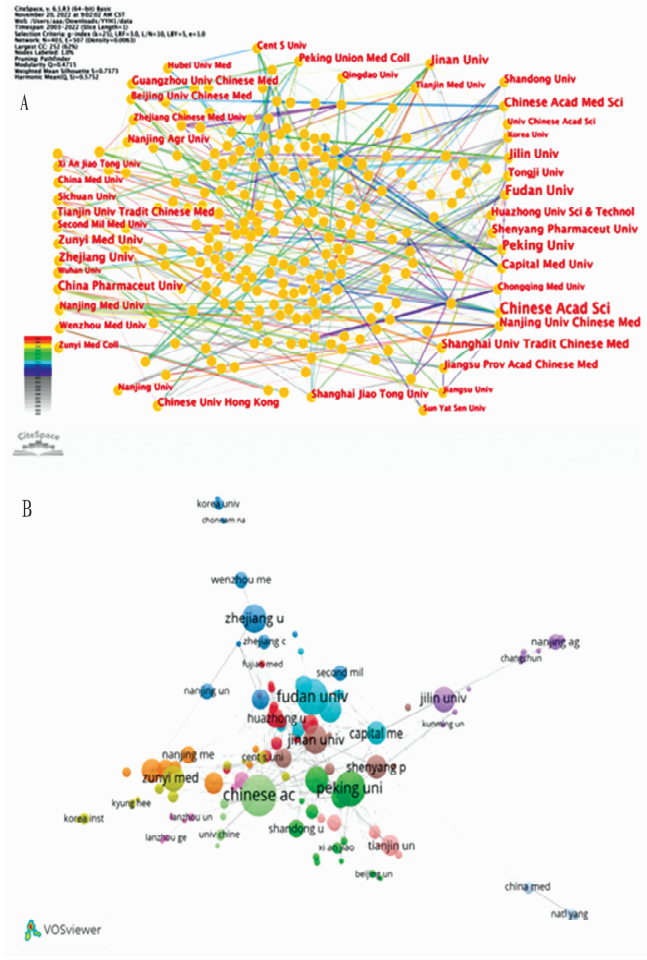


Fig. 3 A visual map of institutions associated with *E. brevicornu* Maxim generated by Citesapce (A) and VOSviewer (B)

In Fig. 3A, the nodes represent institutions; lines connecting the nodes reflect the collaboration network; and each color represent different year (2003 – 2022), and the color changes from gray to red. The thickness of lines between the nodes represent the strength of their cooperation, and thicker lines mean closer and more cooperation. In the Fig. 3B, bigger nodes represent more cooperation with other institutions, and different colors mean cluster of an intimate relationship.

Top 25 Institutions with the Strongest Citation Bursts

Institutions	Year	Strength	Begin	End	2003 - 2022
Peking Univ	2003	6.49	2003	2012	
Zhejiang Univ	2004	5.52	2004	2008	
Chinese Univ Hong Kong	2004	5.05	2004	2012	
Shenyang Pharmaceut Univ	2005	6.48	2005	2011	
Nanjing Univ	2005	4.23	2005	2010	
Natl Yang Ming Univ	2006	3.45	2006	2010	
Chinese Acad Med Sci	2006	3.25	2006	2010	
Peking Union Med Coll	2007	3.21	2008	2009	
Zunyi Med Coll	2005	3.84	2010	2014	
Fudan Univ	2004	4.97	2011	2015	
Jiangsu Prov Acad Chinese Med	2008	5.52	2012	2017	
Dalian Med Univ	2012	3.59	2012	2015	
Tongji Univ	2013	4.01	2013	2019	
Shandong Univ	2014	4.57	2014	2016	
Wuhan Univ	2015	3.23	2015	2019	
Zunyi Med Univ	2015	5.99	2016	2022	
Jinan Univ	2010	4.48	2016	2018	
Guangzhou Univ Chinese Med	2016	3.41	2016	2022	
Beijing Univ Chinese Med	2006	3.3	2016	2018	
Huazhong Univ Sci & Technol	2012	7.39	2017	2020	
Ningbo Univ	2017	3.52	2017	2019	
Tianjin Med Univ	2019	4.77	2019	2022	
Wenzhou Med Univ	2017	4.67	2020	2022	
King Abdulaziz Univ	2020	3.74	2020	2022	
Nanjing Forestry Univ	2020	3.49	2020	2022	

Fig. 4 Top 25 institutions with the strongest citation bursts

Analysis of countries/regions

As presented in Fig. 5, a total of 59 countries were included (supplementary Table 2). China provided the most documents, and Japan, USA, Australia, Saudi Arabia and Iran were the top 5 countries with the strongest citation.

Colors of lines mean different years, from gray to red (2003 – 2022); and the thickness of lines represents the cooperation strength between each other.

Fig. 5 Visualization map of the countries/regions collaboration involved in *E. brevicornu* Maxim research

Analysis of authors

From 2003 to 2022, the authors who published literature related to *E. brevicornu* Maxim are listed in Fig. 6. As shown in Fig. 6A, Wang Ying from Chinese Academy of Sciences is the most productive author with 24 articles, followed by Dong Jingcheng from Fudan University with 20 publications as of November 19, 2022. Other authors with more than 10 publications include Shi Jingshan (14 papers) from Zunyi Medical University, Jia Xiaobin (14 papers) from China Pharmaceutical University, Zhang Feng (11 papers) from Zunyi Medical University, Wu Jinfeng (11 papers) from Fudan University, Sun E (10 papers) from Nanjing Medical University. In Fig. 6B, the relationships among authors are clustered by different colors, with the node size representing the cooperation degree. Fig. 7 shows the top 14 authors with the strongest citation bursts. Liu ZQ had the most citations from 2003 to 2006, while Zhang Feng shows more citation records in recent years.

In Fig. 6A, bigger font of name means more documents, and colors of lines mean different years. In Fig. 6B, bigger nodes represent more documents, and different colors mean cluster of cooperation.

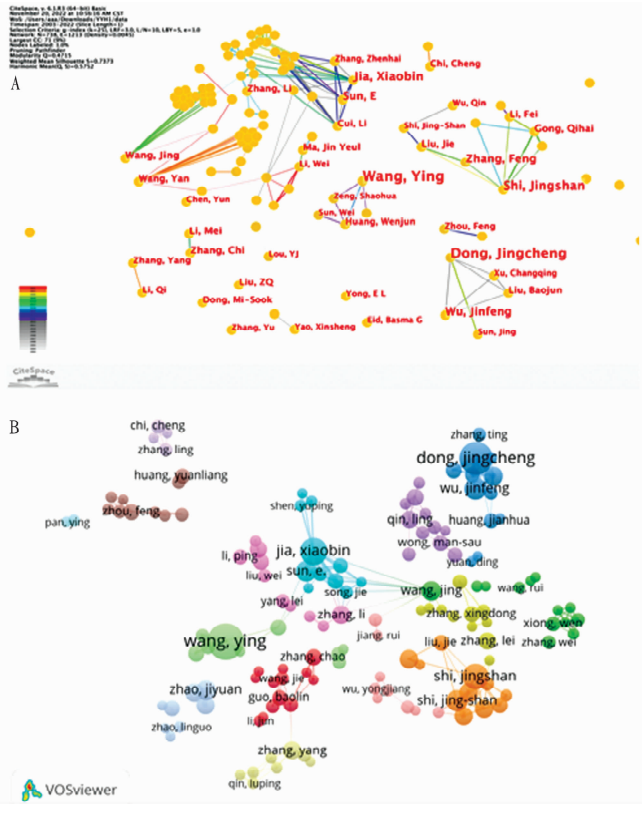


Fig. 6 Inter-author collaborative map conducted by CiteSpace (A, threshold =5) and VOSviewer (B)

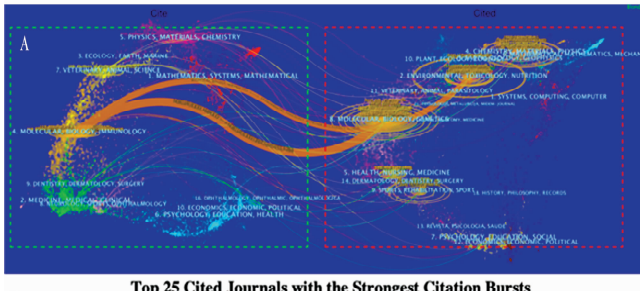
Top 14 Authors with the Strongest Citation Bursts

Authors	Year	Strength	Begin	End	2003 - 2022
Liu, ZQ	2003	4.35	2003	2006	
Lou, YJ	2004	3.25	2004	2005	
Wu, Jinfeng	2011	5.37	2011	2014	
Dong, Jingcheng	2011	3.38	2011	2016	
Sun, E	2012	5.2	2012	2014	
Zhou, Feng	2012	3.11	2012	2014	
Wang, Ying	2008	6.69	2013	2015	
Huang, Wenjun	2013	3.21	2013	2015	
Shi, Jingshan	2016	4.38	2016	2020	
Zhang, Li	2016	3.88	2016	2017	
Yang, Li	2016	3.83	2016	2018	
Gong, Qihai	2016	3.06	2016	2019	
Li, Mei	2017	3.51	2017	2019	
Zhang, Feng	2015	3.62	2018	2020	

Fig. 7 Top 14 authors with the strongest citation generated by CiteSpace

Analysis of journals

The distribution of academic journals related to *E. brevicornu* Maxim studies is illustrated by a dual-map overlay of journals[14] in Fig. 8A. Citing journals are in the green frame on the left, and the cited journals are in the red frame on the right side. Each node in the map represents a journal. The length of each ellipsoid indicates the number of authors in each journal, and the width of the ellipsoid corresponds to the number of papers published in each journal. As displayed in the map, two colored primary citation pathways reveal that *E. brevicornu* Maxim studies published in the molecular, biology, environmental, toxicology, nutritional and genetic fields are cited by researches published in biology and immunology journals. And the journal of ethnopharmacology (875 citations), European journal of pharmacology (825 citations), phytomedicine (853 citations), journal of biology chemistry (616 citations) and Plos one (713 citations) have more cited records (Fig. 9). Fig. 8B lists the top 25 cited journals with strongest citation bursts. Journal of Chromatography A had the most strength in early *E. brevicornu* Maxim research from 2003 to 2006, and the journal of front in pharmacology bursts in recently studies.



B

Top 25 Cited Journals with the Strongest Citation Bursts

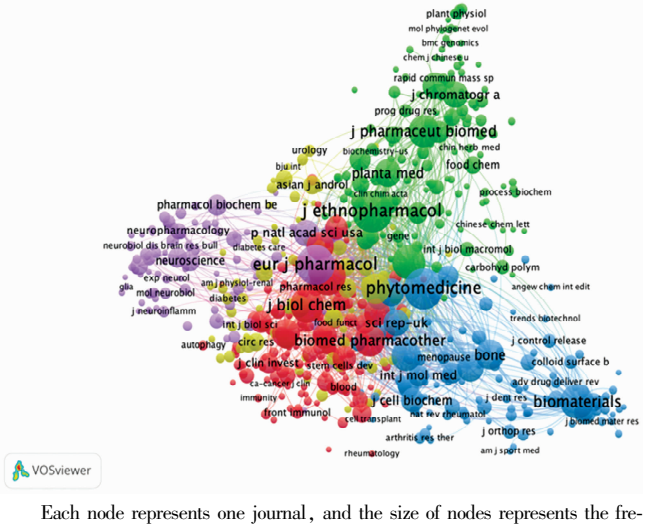
Cited Journals	Year	Strength	Begin	End	2003 - 2022
J CHROMATOGR A	2003	29.68	2003	2013	
ARZNEIMITTELFORSCH	2003	16.66	2003	2012	
J CHROMATOGR SCI	2003	9.87	2003	2015	
PHYTOCHEMISTRY	2004	33.21	2004	2013	
PROG DRUG RES	2004	25.43	2004	2013	
PLANTA MED	2004	24.81	2004	2014	
ZHONGGUO ZHONGYAO ZAZHI	2004	18.96	2004	2014	
ASIAN J ANDROL	2005	14.16	2005	2015	
PHARM PEOPL REP CHIN	2005	13.18	2005	2013	
CHINA J CHIN MAT MED	2005	9.88	2005	2012	
J PHARMACEUT BIOMED	2005	23.3	2007	2013	
PHARMAZIE	2005	19.59	2007	2013	
PHARMACOL BIOCHEM BE	2007	16.5	2007	2016	
UROLOGY	2007	15.33	2007	2016	
FEBS LETT	2007	10.81	2008	2016	
中国中药杂志 CHINA JOURNAL OF CHINESE MATERIA MEDICA	2008	10.32	2008	2013	
BRAIN RES	2007	9.84	2008	2016	
PHYTOMEDICINE	2006	12.26	2009	2014	
CHINESE MED J-PEKING	2003	10.73	2009	2016	
BIOCHEM BIOPH RES CO	2006	10.28	2009	2012	
SCIENCE	2007	12.95	2010	2015	
J SEX MED	2012	9.45	2012	2015	
J PHARM PHARMACOL	2007	9.48	2013	2016	
FRONT PHARMACOL	2017	26.73	2020	2022	
AGING-US	2020	10.18	2020	2022	

A: Dual-map overlay of journals related to *E. brevicornu* Maxim studies, in which citing journals are located on the left, and journals appear on the right, and colored paths represent the citation relationship; B: Top 25 cited journals with the strongest citation bursts from 2003 to 2022 year.

Fig. 8 Distribution of academic journals related to *E. brevicornu* Maxim studies

Analysis of cited references and reference bursts

The authors and related references cited more than 20 times are listed in Fig. 10A, and the top 25 references with the strongest citation bursts are shown in Fig. 10B. The paper authored by Li CR *et al.*[15] is the most highly cited. The paper summarized the literatures related to the pharmacological effects of icariin, such as osteoprotective effect[16], neuroprotective effect[17], cardiovascular protective effect[18-20], anti-cancer effect[21-22], anti-inflammation effect[23-24], immunoprotective effect[25] and reproductive function[26]. And it also discussed the pharmacokinetic properties of bioactive ingredients in Herba Epimedii. The second most cited paper is "The effect of icariin on bone metabolism and its potential clinical application" by *Wang Z et al.* published in 2018[27]. The review provides a comprehensive survey of icariin on its structure and function, effect on bone metabolism[28], and potential for clinical application. The included previous studies in this paper demonstrate that icariin promotes bone formation by stimulating osteogenic differentiation of BMSCs (bone marrow-derived mesenchymal stem cells)[29-30], while inhibiting osteoclastogenic differentiation[31] and the bone resorption activity of osteoclasts[32]. The third most cited article, "The genus *E. brevicornu* Maxim: An ethnopharmacological and phytochemical review" by Ma HP *et al.* published in 2011[33], summarized the ethnopharmacology, the biological activities and the correlated chemical compounds of *E. brevicornu* Maxim species, as well as the anti-osteoporosis, immunological function modulation, anti-oxidation and anti-tumor, anti-aging, anti-atherosclerosis and anti-depressant activities in pharmacological actions.



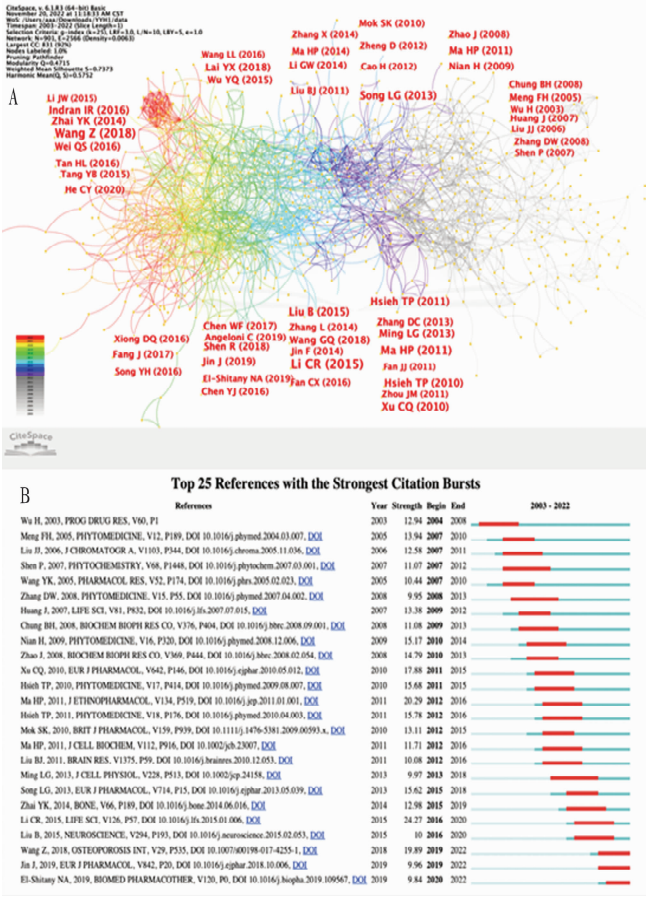
Each node represents one journal, and the size of nodes represents the frequencies of citations.

Fig. 9 Visualization map of co-citation journals devoted to *E. brevicornu* Maxim studies conducted by VOSviewer

Analysis of research hotspots and frontier

Keywords co-occurrence and cluster analysis map was conducted by CiteSpace (Fig. 11A). A total of 571 keywords were extracted, with the the top 10 being "icariin" (273), "expression" (262), "*in vitro*" (206), "cell" (160), "differentiation" (154), "activation" (126), "oxidative stress" (123), "apoptosis" (118), "proliferation" (117), "osteogenic differentiation" (117) and "flavonoid" (101). These keywords reflect the topic of studies related to *E. brevicornu* Maxim focused on the compounds such as icariin and flavonoid, and the research models were cellar and *in vitro*. Related mechanisms involved differentiation, apoptosis and oxidative stress in the formation of bone. Cluster analysis based on the

statistical method of classifying data revealed the research distribution on particular subjects[34]. Fig. 11A displays the top 10 clusters, namely, cluster 0 (hippocamal neruon), cluster 1 (efficient production), cluster 2 (liquid extraction), cluster 3 (gene expression), cluster 4 (osteogenic differentiation), cluster 5 (embryonic stem cell), cluster 6 (bone regeneration), cluster 7 (r2r3-myb transcription factor), cluster 8 (mesenchymal stem cell) and cluster 9 (leukaemia cell growth) from 2003 to 2022. The keywords busts could detect the sudden increase in frequency within a short period, and reflect the research hotspots and trend at that time, and the top 25 keywords with the strongest citation bursts are listed in Fig. 11B.



B

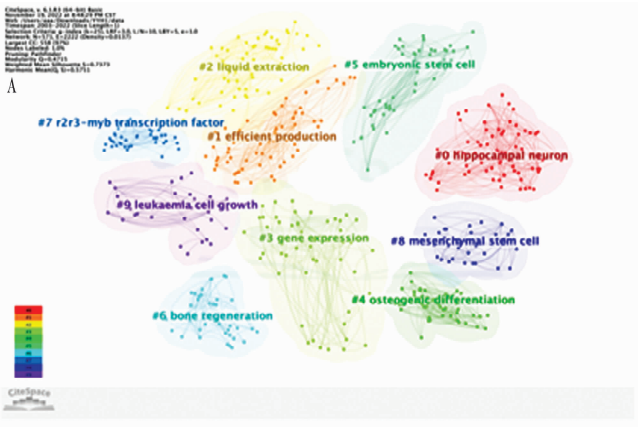
Top 25 References with the Strongest Citation Bursts

References	Year	Strength	Begin	End	2003 - 2022
Wu H, 2003, PROG DRUG RES, V60, P1	2003	12.94	2004	2008	
Meng FH, 2005, PHYTOMEDICINE, V12, P189, DOI 10.1016/j.phymed.2004.03.007, DOI	2005	13.94	2007	2010	
Liu JJ, 2006, J CHROMATOGR A, V1103, P344, DOI 10.1016/j.chroma.2005.11.036, DOI	2006	12.58	2007	2011	
Shen P, 2007, PHYTOCHEMISTRY, V68, P1448, DOI 10.1016/j.phytochem.2007.03.001, DOI	2007	11.07	2007	2012	
Wang YK, 2005, PHARMACOL RES, V52, P174, DOI 10.1016/j.phrs.2005.02.023, DOI	2005	10.44	2007	2010	
Zhang DW, 2008, PHYTOMEDICINE, V15, P55, DOI 10.1016/j.phymed.2007.04.002, DOI	2008	9.95	2008	2013	
Huang J, 2007, LIFE SCI, V81, P832, DOI 10.1016/j.lfs.2007.07.015, DOI	2007	13.38	2009	2012	
Chung BH, 2008, BIOCHEM BIOPH RES CO, V376, P404, DOI 10.1016/j.bbrc.2008.09.001, DOI	2008	11.08	2009	2013	
Nian H, 2009, PHYTOMEDICINE, V16, P320, DOI 10.1016/j.phymed.2008.12.006, DOI	2009	15.17	2010	2014	
Zhao J, 2008, BIOCHEM BIOPH RES CO, V369, P444, DOI 10.1016/j.bbrc.2008.02.054, DOI	2008	14.79	2010	2013	
Xu CQ, 2010, EUR J PHARMACOL, V642, P146, DOI 10.1016/j.ejphar.2010.05.012, DOI	2010	17.88	2011	2015	
Hsieh TP, 2010, PHYTOMEDICINE, V17, P414, DOI 10.1016/j.phymed.2009.08.007, DOI	2010	15.68	2011	2015	
Ma HP, 2011, J ETHNOPHARMACOL, V134, P519, DOI 10.1016/j.jep.2011.01.001, DOI	2011	20.29	2012	2016	
Hsieh TP, 2011, PHYTOMEDICINE, V18, P176, DOI 10.1016/j.phymed.2010.04.003, DOI	2011	15.78	2012	2016	
Mok SK, 2010, BRIT J PHARMACOL, V159, P939, DOI 10.1111/j.1476-5381.2009.00593.x, DOI	2010	13.11	2012	2015	
Ma HP, 2011, J CELL BIOCHEM, V112, P916, DOI 10.1002/jcb.23007, DOI	2011	11.71	2012	2016	
Liu BJ, 2011, BRAIN RES, V1375, P59, DOI 10.1016/j.brainres.2010.12.053, DOI	2011	10.08	2012	2016	
Ming LG, 2013, J CELL PHYSIOL, V228, P513, DOI 10.1002/jcp.24158, DOI	2013	9.97	2013	2018	
Song LG, 2013, EUR J PHARMACOL, V714, P15, DOI 10.1016/j.ejphar.2013.05.039, DOI	2013	15.62	2015	2018	
Zhai YK, 2014, BONE, V66, P189, DOI 10.1016/j.bone.2014.06.016, DOI	2014	12.98	2015	2019	
Li CR, 2015, LIFE SCI, V126, P57, DOI 10.1016/j.lfs.2015.01.006, DOI	2015	24.27	2016	2020	
Liu B, 2015, NEUROSCIENCE, V294, P193, DOI 10.1016/j.neuroscience.2015.02.053, DOI	2015	10	2016	2020	
Wang Z, 2018, OSTEOPOROSIS INT, V29, P535, DOI 10.1007/s00198-017-4255-1, DOI	2018	19.89	2019	2022	
Jin J, 2019, EUR J PHARMACOL, V842, P20, DOI 10.1016/j.ejphar.2018.10.006, DOI	2019	9.96	2019	2022	
El-Shitany NA, 2019, BIOMED PHARMACOTHER, V120, P0, DOI 10.1016/j.biopha.2019.109567, DOI	2019	9.84	2020	2022	

A: Network visualization of co-cited authors and references in each year; B: Top 25 references with the strongest citation.

Fig. 10 Visualization network of co-cited authors and references regarding *E. brevicornu* Maxim

The keywords timeline picture in Fig. 12 illustrates the evolution of high-frequency keywords. As shown in Fig. 12, the hotspots in the studies of *E. brevicornu* Maxim changed in each cluster from 2003 to 2022 year. In the beginning of 2003, studies on *E. brevicornu* Maxim focused on the liquid extraction of flavonoid, bone regeneration, antioxidant and apoptosis *in vitro* experiments. Then, the study hotspots developed to the field of inflammatory response, signaling pathway and stem cell. Metabolism and cognitive deficit have grained significant attention in recent research.



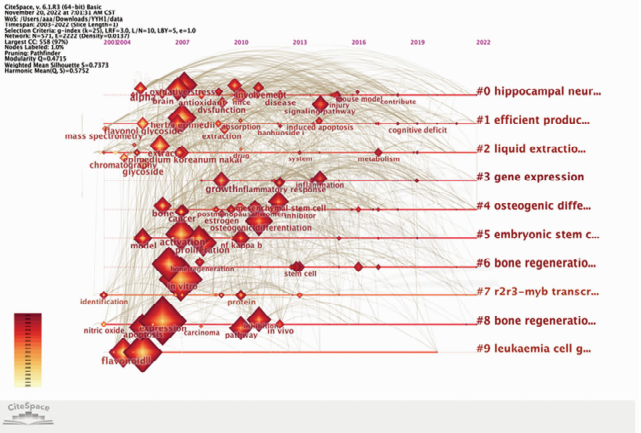
B

Top 25 Keywords with the Strongest Citation Bursts

Keywords	Year	Strength	Begin	End	2003 - 2022
nitric oxide	2003	4.63	2003	2014	
separation	2003	4.11	2003	2010	
chromatography	2004	5.87	2004	2013	
capillary zone electrophoresis	2004	3.72	2004	2009	
flavonol glycoside	2005	8.37	2005	2012	
glycoside	2005	4.53	2005	2009	
rat	2005	4.43	2005	2014	
extract	2006	8.24	2006	2015	
herba epimedii	2007	7.35	2007	2013	
cell	2005	4.1	2007	2011	
embryonic stem cell	2008	4.31	2008	2015	
extraction	2009	4.81	2009	2011	
performance liquid chromatography	2009	3.67	2009	2015	
disease	2012	3.85	2012	2017	
gene	2013	4.61	2013	2015	
mice	2010	4.37	2014	2018	
dysfunction	2009	4.29	2014	2016	
marrow stromal cell	2012	6.97	2016	2018	
stromal cell	2017	4.41	2017	2019	
regeneration	2013	3.92	2017	2020	
pathogenesis	2017	3.9	2017	2018	
protect	2009	4.87	2018	2020	
metabolism	2017	4.38	2018	2022	
osteoarthriti	2019	3.73	2019	2022	
system	2013	3.69	2019	2022	

A: Visualization map of keywords cluster generated by CiteSpace; B: Top 25 keywords with the strongest citation.

Fig. 11 Analysis of keywords in studies related to *E. brevicornu* Maxim



Each horizontal row represents a cluster, and each node on the line denotes a keyword. The keyword relationship between each other is represented as line connecting two nodes, and the size of the node means the frequencies in each year.

Fig. 12 Timeline visualization of keywords clusters

Discussion

In this research, we obtained 1 513 papers on *E. brevicornu* Maxim from 2003 to 2022 based on the web of science core database, and screened manually. Visualization analysis were conducted by CiteSpace 6.1.R4 and VOSviewer (version 1.6.18). Publication distributions, author cooperation, cited references and research trends were evaluated. Hotspots were identified by keyword co-occurrence analysis in each period and demonstrated the evolutionary path of *E. brevicornu* Maxim studies in recently.

General information

In 2003, only four articles focused on *E. brevicornu* Maxim, and the main studies were related to the method of separated and determined the flavonoids in *E. brevicornu* Maxim[35-36], and other biological activity of icariin, such as mechanism of therapeutic action of icariin on erectile dysfunction[37]. And the papers increased slowly before 2011, and the year 2012 was a turning point for this research field, when more and more researchers focused on the *E. brevicornu* Maxim, leading to a rapid upward trend. The number of publications reached 122 in 2017, and the largest number of 170 appeared in 2022.

According to the authors' analysis, the researcher of Wang Ying from Chinese Academy of Sciences (Wuhan Botanical Garden) made the most contributions with 24 papers, followed by Dong Jingcheng from Fudan University (Huashan Hospital) with 20 published articles. Notablely, Wang Ying's work includes the development of an ultrasonic-assisted extraction method for epimedin A/B/C and icariin from Herba Epidmedii[38-39], the investigation on the compatibility of calcinated antler cancellous bone scaffolds with icariin[40], the flavonoid biosynthesis and regulation[41-42] and the bioactive components[43] in *E. brevicornu* Maxim, the discovery of R2R3-MYB transcription factors regulating the flavonoid pathway[44], and isolation of the genes encoding flavonoid 3'-hydroxylase (F3'H) and flavonoid 3', 5'-hydroxylase (F3'5'H) involved in the flavonoid biosynthetic pathway[45-47], the flavonoid absorption and metabolism[48] in osteoporosis rats[49] and zebrafish model[50], and intestinal absorption mechanism[51]. Genetic and environmental variations contribute to the Chemotypic and genetic diversity in *Epimedium sagittatum*[52]. The research on *E. brevicornu* Maxim populations found significant concentration variations in main flavonoids[53]. The medicinal component variation in a specific local geographic accession of *E. sagittatum* was found in Luotian county of Hubei Province (China) which had a much higher content of total flavonoids and polysaccharides[44]. Icariin have benefits in osteoporosis patients through regulating the balance of the EphB4/Ephrin-B2 pathway[54], 12 polymorphic microsatellite loci were developed for epimedium[55], and the genome composition and structure of the *E. sagittatum* genome were demonstrated[56].

Dong's studies focused on the bioactivity of icariin, such as neuroprotective effects by against the apoptosis through blockade of p38 MAPK phosphorylation[57], anti-inflammatory, anti-tumor effects by inhibited the activity of STAT3 and AKT through down-regulate the expression of IL-10, IL-6, S100A8/9 and TNF-α *in vitro* and *vivo*[58-59]. Icariin significantly inhibits social defeat-induced increases of corticosterone and IL-6 levels[17] and anti-depressant-like effects by restoring the negative feedback regulation of the hypothalamic-pituitary-adrenal axis[60], and attenuated the airway hyperreponsiveness and chronic airway inflammatory changes in murine asthma model[4, 23] through regulate the response of Th17/Treg balance[61], anti-cancer effects through cell cycle regulation, apoptosis[62], angiogenesis and metastasis via JAK2-STAT3, MAPK-ERK and PI3K-AKT-mTOR signaling pathways[63], and icariin also displayed the anti-inflammatory effects[64] by inhibiting inducible NO synthase and cyclooxygenase-2 protein expression[65], prevent excessive corticosterone induced cell death via activation of PI3-K/ATK pathway[66], and anti-neuroinflammatory effects via suppressing HMGB1-RAGE and TLR4-XBP1S related NF-κB signaling pathways[67-68]. Icaritin could attenuate cigarette smoke-induced inflammation, airway remodelling[69] and oxidative stress by quenching reactive oxygen species (ROS) and up-regulated glutathione (GSH) through PI3K-AKT-Nrf2-dependent mechanism[70], anti-inflammation in monocytes via the CD14/TLR4 signaling pathway[71]. The icariin quality and quantity were identified in Bu-Shen-Yi-Qi-Fang, a traditional Chinese formula used for asthma[72], which protected the lung injury by enhanced the expression of glucocorticoid receptor α (GRα) and inhibited the expression of NF-κB p65, c-Jun, Stat3, IL-6, and TNF-α in acute lung injury model of mice[73].

China is the most productive country (1 255 articles), and followed by South Korea (83), USA (75), India (30) and Australia (23). Among the top 10 countries/regions, China also has the most cooperative relationships with others, and the highest centrality (0.93) also suggest that Chinese researchers have significant impact in this field and a widely cooperation with others. Chinese academic of science has the most published products (70), and Peking university has the highest centrality (0.24) as demonstrated that more cooperation with other institutions. Three journals, namely, The European Journal of Pharmacology, PHYTO medicine and Journal of Ethnopharmcology, have the most cited counts, over 500 respectively, implying a significant role in this study field.

Hotspots and frontiers

Keywords burst detection reflects the hotspots of the researches in an particular field. The keyword cluster analysis reveals the knowledge structure, and timeline maping illustrates the evolution of new hotspots. These information are also the most valuable in the bibliometric analysis[74]. According to the visualization of keywords-cluster analysis (Fig. 11 A), the top 10 cluster " #1 hippocampal neuron", "#2 liquid extraction", "#3 gene expression", "#4 osteogenic differentiation", "#5 embryonic stem cell", "#6 bone regeneration", "#7 r2r3-myb transcription factor", "#8 mesenchymal stem cell", "#9 leukaemia cell growth"

mainly constructed the knowledge structure.

The studies related to *E. brevicornu* Maxim based on the numbers of publications could be divided into three period: the beginning phase (2003 – 2011), acceleration phase (2012 – 2016) and rapid development phase (2017 – 2022). During the first period, "extract", "flavonoid", "model", "cell", "expression", "activation", "growth", "absorption" and "*in vitro*" were the mainly rising keywords, and reflected that the research were associated with the compounds of *E. brevicornu* Maxim and the preliminary effectiveness of them. In the acceleration period (2012 – 2016), the articles published every year raised from 60 to 120, and the keywords covered "signaling pathway", "injury", "system", "inflammatory response", "stem cell", "*in vivo*", "inhibitor", "protein", "nf kappa b", "mouse model", demonstrating that the research trends are changing to the bioactivity of the compounds. From 2017 to now, the studies of *E. brevicornu* Maxim focused on the "cognitive deficit", "metabolism", "contribute", "osteoarthriti", "system" and so on, and studies on the relationship between *E. brevicornu* Maxim and diseases are becoming new hotspots.

As shown in Fig. 11B, "nitric oxide (NO)" was the most hot study area from 2003, and related articles decreased from 2014, mainly including osteogenic activity related to NO signal pathway and PI3K/AKT pathway[75], therapy of ulcerative colitis[76], protects murine chondrocytes from inflammation response[77], neroprotective effects[78], protection against duck virus hepatitis by antioxidant properties[79] and so on. In the following several years, more studies focused on the "extraction" of *E. brevicornu* Maxim[80], such as the contents of "flavonol glycoside"[81], the method of "performance liquid chromatography"[82-83], and from 2012, the attention of scientists moved to pharmacological effects and pharmacokinetic properties of *E. brevicornu* Maxim in some diseases, such as endothelial cell "dysfunction"[84-85] and bone "regeneration"[86-87], "marrow stromal cell" and "metabolism"[88] in "osteoarthriti"[89-91].

Limitations

In this bibliometric analysis, CiteSpace and VOSviewer were both applied to simultaneously survey the hotspots and cutting-edge metabolomics in the field of *E. brevicornu* Maxim. However, limitations should be explained. First, research data were collected from a single source, and the WOSCC database, some studies published in non-SCI journals or other database were excluded, and only English articles were included which might lead to source bias. Second, literature related to this field is updating continuously and dynamically, and some rapid updating hot topics and research frontiers in *E. brevicornu* Maxim might have been missed. These limitations may slightly impact the analysis results but are unlikely to change the main trends in this paper.

Conclusions

Our study provide a bibliometric analysis for understanding the research topics, hotspots, and development trends in *E. brevicornu* Maxim. Literature information of different countries, institutions, authors, and journals were evaluated in this study. The study of *E. brevicornu* Maxim began to get attention in 2003 and focused on compound extraction, and then explored to pharmacological and related diseases treatment. Our study provides mainly information about *E. brevicornu* Maxim, and current research hotspots showed that flavonol analog benefits in marrow stromal cell may be a potential therapeutic method in osteoarthritis.

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(Continued on page 24)

ensures optimal emergence, and light irrigation is carried out if needed. Precision supplementary seeding is implemented when emergence rate is not high enough.

(2) Weed control. Weeding should be conducted on sunny days between mid-November and mid-December.

(3) Fostering strong seedlings. Strong seedlings are indicated by robust stems, six leaves with one central leaf, and 5 – 7 secondary roots.

(4) Winter irrigation. Watering should be carried out in a manner of spray or micro-spray irrigation from late November to early April.

(5) Frost prevention. Fertilizers and water are applied in early spring to mitigate frost damage and promote recovery.

Spring management

(1) Green-up stage. The growth of wheat seedlings should be closely monitored, and light irrigation is adopted to improve cold tolerance accordingly.

(2) Jointing to flowering stage. It is necessary to ensure adequate nutrition and water, so as to strengthen stalks and increase spike number.

(3) Flowering to grain-filling stage. Root and leaf health should be maintained to avoid early senescence and promote grain filling.

Harvesting Wheat harvesting typically commences in early June, though regional climatic variations and varietal-specific maturation periods dictate precise scheduling. Mechanized harvesting systems enhance operational efficiency while reducing field losses, but they necessitate rigorous post-harvest protocols where immediate drying becomes critical to inhibit mycotoxin formation and preserve germination viability.

Conclusions

Wheat quality and yield significantly influence China's agricultural development. Advanced cultivation techniques and efficient management practices are necessary for high-quality yields. Adopting techniques adapting to local conditions and effectively managing the field are key to successfully cultivating the wheat variety New Century 999 and enhancing disease control measures.

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