

Research Article

Research on Herbal Therapies for Osteoarthritis in 2004–2022: A Web of Science-Based Cross-Sectional Bibliometric Analysis

Weijiang Song ¹, Jiaqi Chen,^{2,3} Guoyan Yang,⁴ Jiahe Liao,^{2,3} Hongbo Shen,¹ Sai Li,¹ Ning Ding,¹ and Dong Li ¹

¹Traditional Chinese Medicine Department, Peking University Third Hospital, Beijing, China

²Graduate School, Beijing University of Chinese Medicine, Beijing, China

³Traditional Chinese Medicine Department of Rheumatism, China-Japan Friendship Hospital, Beijing, China

⁴NICM Health Research Institute, Western Sydney University, Sydney, Australia

Correspondence should be addressed to Dong Li; lidong6512@sina.com

Weijiang Song and Jiaqi Chen contributed equally to this work.

Received 25 April 2022; Accepted 21 June 2022; Published 30 July 2022

Academic Editor: Xing Liao

Copyright © 2022 Weijiang Song et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Objective. The extent, range, and nature of available research in the field of herbal therapies for osteoarthritis (OA) have not been systematically analyzed. This study aimed to map the literature available on herbal therapies for OA and identify global hotspots and trends in this field. **Methods.** Studies on herbal therapies for OA published between 2004 and 2022 were searched from the Web of Science Core Collection. Microsoft Excel, SPSS Statistics, and CiteSpace software were used to analyze and visualize the quantity and citations of publications, and the research hotspots and trends in research on herbal therapies for OA. **Results.** A total of 1649 publications mainly from 76 countries/regions and 270 institutions were included in this study. From 2004 to 2022, there is an upward trend in the publications of herbal therapies for OA. China ranked first in the number of publications ($n = 568$, 34.45%), followed by the USA ($n = 353$, 21.41%), South Korea ($n = 187$, 11.34%), Germany ($n = 85$, 5.15%), and England ($n = 79$, 4.79%). Kyung Hee University ($n = 46$), Xianxiang Liu ($n = 25$), and *Evidence-Based Complementary and Alternative Medicine* ($n = 74$) were the most prolific affiliation, author, and journal, respectively. Felson DT ($n = 185$) and *Arthritis and Rheumatism* ($n = 1173$) held the record for the most cited papers by an author and journal, respectively. Currently, the hot keywords in the field of herbal therapies for OA include knee OA, traditional Chinese medicine (TCM), differentiation, rosa canina, inflammation, oxidative stress, stem cell, and regenerative medicine. The emerging research trends in herbal therapies for OA are herbal medicinal product, chronic knee pain, mesenchymal stem cell, and clinical pharmacology. **Conclusions.** Research on herbal therapies for OA is flourishing, but communication among countries/regions should be strengthened. Current research on herbal therapies for OA mainly focuses on knee OA, TCM, differentiation, rosa canina, inflammation, oxidative stress, stem cell, and regenerative medicine. The research frontiers are herbal medicinal product, chronic knee pain, mesenchymal stem cell, and clinical pharmacology.

1. Introduction

Osteoarthritis (OA) is the most common degenerative joint disorder that affects one or more diarthrodial joints and is often accompanied by joint pain, stiffness, dysfunction, and structural damages [1]. Age, obesity, genetics, sex, and joint biomechanics are generally considered risk factors for OA [2]. With the ageing and increasing obesity in the global population and the increasing numbers of joint injuries, OA

is prevalent, with a worldwide estimate suggesting that 250 million people are currently affected [3]. Moreover, according to the *Global Burden of Disease Study 2019*, OA is the leading cause of disability and source of societal cost in older adults [4].

Recent research has revealed that the mechanism of OA is closely related to inflammation, oxidative stress, apoptosis, and energy metabolism, and these factors can interact with each other [5]. However, the pathogenesis of OA has not

been understood fully, and further research is still needed. To date, no disease-modifying OA drug has received regulatory approval yet. For the main symptoms of joint pain, nonsteroidal anti-inflammatory drugs (NSAIDs), analgesics, and corticosteroids are available as optional drugs. Even so, the cardiovascular and digestive safety issues often surround NSAIDs, and the addictive nature of central analgesics are also concerns of clinicians and patients [6, 7]. Recent case series suggested that negative structural outcomes including accelerated OA progression, subchondral insufficiency fracture, complications of osteonecrosis, and rapid joint destruction may be observed in patients receiving intra-articular corticosteroid injections [8]. Therefore, there is a need to explore effective and safer treatments. Herbs or herbal products have a long history in treating OA and show great potential to generate less adverse events than pharmaceutical drugs [9, 10]. Furthermore, researchers have discovered that herbal therapies can slow down the progression of OA via several mechanisms [11]. At present, there are a large number of literature on herbal therapies for OA, and a bibliometrics is needed.

Bibliometrics is a cross-science that uses mathematical and statistical methods to study documents and bibliometric characteristics [12, 13], such as countries/regions, institutions, journals, authors, and citations. [14]. So far, there are few bibliometric studies on traditional medicine in treating OA, and the majority of them focused on nondrug treatments, such as Tai Chi and acupuncture [15, 16]. However, no bibliometric study has been published on herbal therapies for OA to inform the volume, breadth, and characteristics of research in this area. Hence, we aimed to analyze publications on herbal therapies for OA from 2004 to 2022 and discussed the current hotspots and trends in research.

2. Materials and Methods

2.1. Data Collection. We searched the Web of Science Core Collection (WoSCC) from its inception until 10 February 2022. The search terms were centered on OA and herbs (Figure S1). Articles and reviews reporting herbal therapies in treating OA were eligible for inclusion irrespective of language. Early access, conference proceedings, letters, editorial materials, corrections, book chapters, retracted publications, and editorial materials were excluded. Two authors independently screened all titles and abstracts of the records. The full texts were retrieved for further identification in accordance with eligibility criteria. All uncertainties or discrepancies were resolved through discussion. A total of 1,743 records were identified, of which 94 records were excluded because they did not meet the eligibility criteria. Finally, 1,649 papers were included in this bibliometric study (Figure S1).

2.2. Data Analysis. All included papers retrieved from WoSCC were imported into Microsoft Excel 2019 (Microsoft Corp, Redmond, Washington, USA), which was used to analyze the number of papers published in the year and journal. SPSS Statistics 20 (IBM, Armonk, New York, USA) was used for trend analysis of the number of publications. A

$p < 0.05$ was considered statistically significant. CiteSpace V5.8.R3 (Chaomei Chen, Philadelphia, Pennsylvania, USA) was used to perform visual analysis, including the distribution of countries/regions, institutions, authors, co-cited authors, cocited journals, cocited references, keyword cluster, and timeline viewer. CiteSpace is a widely used visualization analysis software, which can combine information visualization methods, bibliometrics, and data mining algorithms in an interactive visualization tool for extraction of patterns in citation data [17, 18] to analyze the structure and distribution of scientific knowledge and the visualizing trends in scientific literature [19].

3. Results

3.1. The Trend of Publication Outputs. A total of 1,649 papers involving 1,285 articles and 364 reviews published between January 2004 and February 2022 were included for analysis in this study. From 2004 to 2022, the total number of published papers on herbal therapies for OA increased year by year (Figure S2, $p < 0.001$). Since 2017, the number of outputs in the field of herbal therapies for OA has exceeded 100, and the number of publications increased significantly in 2020, with a total number of 235 (14.3%). Compared with 2020, the number of publications in 2021 had a slight decrease. However, till February 10, 2022, 19 papers on herbal therapies for OA have been published in 2022, which was similar to a year of outputs in 2006.

3.2. Distribution of Countries/Regions and Institutions. The 1,649 included papers were published mainly by 76 countries/regions involving 270 institutions. As shown in Table 1, China ranked first in the number of publications ($n = 568$, 34.45%), much higher than other countries/regions, followed by the USA ($n = 353$, 21.41%), South Korea ($n = 187$, 11.34%), Germany ($n = 85$, 5.15%), and England ($n = 79$, 4.79%). Kyung Hee University was the most prolific institution ($n = 46$, 2.79%), followed by Shanghai University of Traditional Chinese Medicine ($n = 42$, 2.55%), Fujian University of Traditional Chinese Medicine ($n = 39$, 2.37%), Beijing University of Chinese Medicine ($n = 32$, 1.94%), and Zhejiang University ($n = 27$, 1.64%).

Figure 1 showed the visualization map of publications related to herbal therapies for OA from different countries/regions. Each node represents a country. The lines between two nodes suggest the communication capability between two countries, and the denser lines indicate closer communication. Overall, the centrality of nodes in the knowledge map measures the importance of node position and reflects the communication capability of the nodes, and each node with high centrality has an outer purple circle. Our results showed that among the top 10 countries with the highest number of publications, 6 countries (USA, Italy, England, Canada, Australia, and Germany) had a centrality of more than 0.1, suggesting these are important bridge countries having strong

TABLE 1: Distribution of publications in the field of herbal therapies for OA from different countries/regions and institutions.

Rank	Country/region	Year	Centrality	Count (%)	Institution	Year	Centrality	Count (%)
1	Peoples R China	2004	0.04	568 (34.45)	Kyung Hee Univ	2005	0.06	46 (2.79)
2	USA	2004	0.51	353 (21.41)	Shanghai Univ Tradit Chinese med	2011	0.14	42 (2.55)
3	South Korea	2004	0.05	187 (11.34)	Fujian Univ Tradit Chinese med	2010	0.02	39 (2.37)
4	Germany	2004	0.12	85 (5.15)	Beijing Univ Chinese med	2015	0.03	32 (1.94)
5	England	2004	0.23	79 (4.79)	Zhejiang Univ	2012	0.06	27 (1.64)
6	India	2004	0.08	71 (4.31)	Shanghai Jiao Tong Univ	2011	0.01	25 (1.52)
7	Australia	2004	0.19	67 (4.06)	Peking Univ	2009	0.07	24 (1.46)
8	Italy	2004	0.31	67 (4.06)	Chinese Univ Hong Kong	2004	0.15	24 (1.46)
9	Canada	2004	0.15	57 (3.46)	Univ Sydney	2011	0.08	23 (1.39)
10	Taiwan	2007	0.05	47 (2.85)	Korea Inst Oriental med	2006	0.05	23 (1.39)

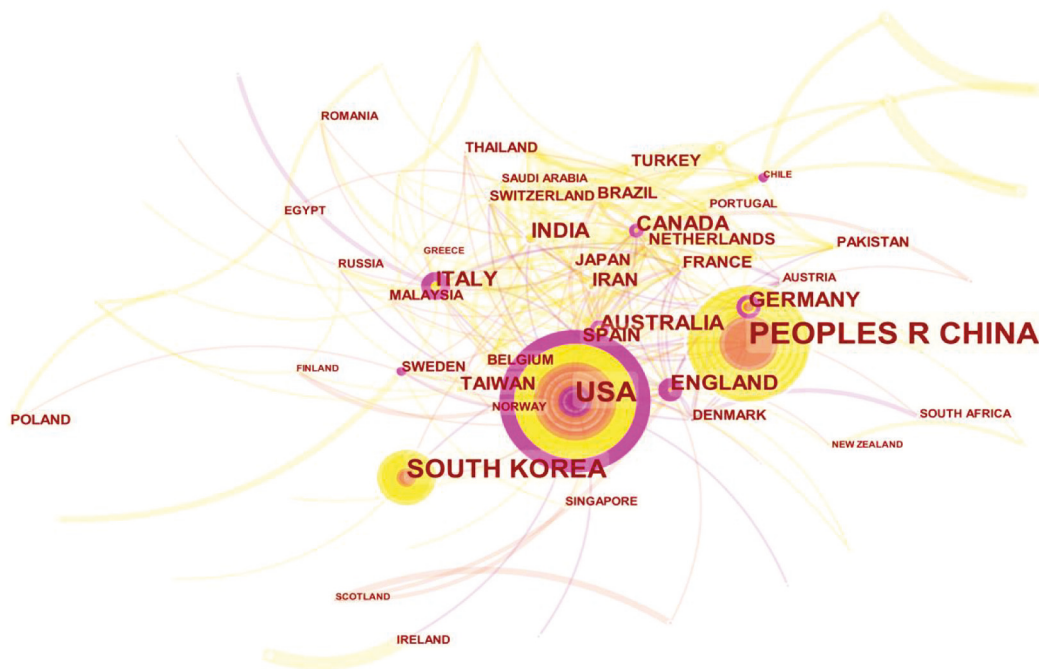


FIGURE 1: CiteSpace visualization map of publications in the field of herbal therapies for OA from different countries/regions.

communication power all over the world in the field of herbal therapies for OA.

3.3. *Authors and Co-Cited Authors.* There were 2,038 major authors involved in the 1,649 papers in this study. As shown in Table 2, Xianxiang Liu was the most prolific author in the number of publications on herbal therapies for OA ($n = 25$, 1.52%), followed by Hongzhi Ye ($n = 22$, 1.33%), and Xihai Li ($n = 20$, 1.21%). Cocited authors are two or more authors who are cited by another literature at the same time. There were 1,848 cocited authors in this study. Among these cocited authors, 9 had a frequency of citation over 100 times, and Felson DT was the top cocited author ($n = 185$), followed by Zhang W ($n = 157$).

3.4. *Journals and Cited Journals.* A total of 586 journals were involved in the 1,649 articles in this study. As shown in Table 3, *Evidence-Based Complementary and Alternative*

Medicine was the top journal in the number of publications on herbal therapies for OA ($n = 74$, 4.49%), followed by the *Journal of Ethnopharmacology* ($n = 56$, 3.40%) and *Medicine* ($n = 49$, 2.97%). Cocited journals are two or more journals that are cited simultaneously. Among 924 cocited journals, 5 were cited over 500 times. *Arthritis and Rheumatism* was the top cocited journal, followed by *Osteoarthritis and Cartilage* ($n = 888$), and *Annals of The Rheumatic Diseases* ($n = 667$).

3.5. *The Hotspots of Keywords.* Keywords often reflect the research topics, and their analysis can indicate the research hotspots in a specific field. The keywords ($n \geq 80$) related to herbal therapies for OA are shown in Table S1. Among these keywords, OA had the highest frequency ($n = 447$), followed by knee OA ($n = 438$), double-blind ($n = 202$), rheumatoid arthritis ($n = 187$), expression ($n = 170$), and pain ($n = 159$). OA, knee OA, and double-blind had a high centrality (>0.10), indicating a great influence of these keywords in the research of herbal therapies for OA.

TABLE 2: Top authors ($n \geq 10$) and co-cited authors ($n \geq 80$) related to herbal therapies for OA.

Rank	Author	Year	Centrality	Count (%)	Cocited author	Year	Centrality	Citation
1	Xianxiang Liu	2009	<0.01	25 (1.52)	Felson DT	2004	<0.01	185
2	Hongzhi Ye	2009	<0.01	22 (1.33)	Zhang W	2004	0.04	157
3	Xihai Li	2011	0.01	20 (1.21)	Anonymous	2005	<0.01	153
4	Chunsong Zheng	2011	0.01	15 (0.91)	Hochberg MC	2004	0.03	151
5	Dongsuk Park	2008	<0.01	11 (0.67)	Bellamy N	2004	0.01	145
6	Yonghyeon Baek	2008	<0.01	11 (0.67)	Goldring MB	2005	<0.01	143
7	Peijian Tong	2014	<0.01	11 (0.67)	Altman R	2004	0.01	142
8	Jaedong Lee	2008	<0.01	10 (0.61)	Altman RD	2004	<0.01	125
9	Guangwen Wu	2011	0.01	10 (0.61)	Mcalindon TE	2004	0.01	121
10	Xueyong Shen	2013	<0.01	10 (0.61)	Loeser RF	2008	0.01	98
11	Qi Jia	2010	<0.01	10 (0.61)	Ernst E	2004	<0.01	95
12	Ling Zhao	2013	<0.01	10 (0.61)	Hunter DJ	2008	<0.01	88
13	Huifeng Xu	2011	<0.01	10 (0.61)	Lawrence RC	2004	<0.01	82

TABLE 3: Top 10 journal and cocited journals related to herbal therapies for OA.

Rank	Journal	Count (%)	Cocited journal	Citation
1	Evidence-Based Complementary and Alternative Medicine	74 (4.49)	Arthritis and Rheumatism	1,173
2	Journal of Ethnopharmacology	56 (3.40)	Osteoarthritis and Cartilage	888
3	Medicine	49 (2.97)	Annals of the Rheumatic Diseases	667
4	Phytotherapy Research	29 (1.76)	Journal of Rheumatology	555
5	BMC Complementary and Alternative Medicine	24 (1.46)	Lancet	502
6	Trials	23 (1.39)	Arthritis Research & Therapy	474
7	Frontiers in Pharmacology	21 (1.27)	Rheumatology	431
8	Chinese Journal of Integrative Medicine	20 (1.21)	PloS One	429
9	Osteoarthritis and Cartilage	19 (1.15)	Journal of Ethnopharmacology	421
10	Phytomedicine	19 (1.15)	Annals of Internal Medicine	379

The strong citation burst of keywords represents sharp changes in the number of citations for keywords, which can reflect the rise or fall of research hotspots. As shown in Figure 2, among the top 25 keywords related to herbal therapies for OA, NSAIDS, controlled clinical trial, placebo, and complementary and alternative medicine were popular keywords from 2004 to 2017. Since 2011, interleukin-1 β has been a hot keyword. Since 2018, pathogenesis, inflammation, network pharmacology, stem cell, oxidative stress, traditional Chinese medicine (TCM), and differentiation have been hotspots studied in herbal therapies for OA.

The timeline mapping of keywords is the summarization and classification of research keywords, which can show the characteristics of research over time. As shown in Figure 3, keywords on herbal therapies for OA were classified into the following 6 clusters: inflammation, knee OA, celecoxib, rosa canina, scaphoid, and regenerative medicine. Since 2004, inflammation, knee OA, and rosa canina have been in the spotlight. Celecoxib and scaphoid boomed in 2004 but declined in 2010 and 2007, respectively. Regenerative medicine began to garner attention in 2010 and has continued to develop in recent years.

3.6. The Research Frontiers of Herbal Therapies for OA. Cocited papers mean two papers appear in the reference list of another paper, and cocitation analysis can mine the cocitation relationships of papers in the repository. A total

of 1,373 articles were cited in papers on herbal therapies for OA in this study, of which 10 papers were cited more than 20 times (table S2). The paper ranked at the top of citations was *OARSI guidelines for the non-surgical management of knee osteoarthritis*. The strongest citation bursts of references, just as the strongest citation bursts of keywords, can reflect changes in research hotspots over a period of time. Figure 4 showed the top 25 references with the strongest citation bursts involved in herbal therapies for OA. Up to now, nearly half of the references remain research hotspots.

On the basis of cocitation analysis, we used CiteSpace to extract cluster labels from papers by cluster analysis, showing the research frontiers in the field of herbal therapies for OA. Silhouette score can evaluate the effect of clustering. When the silhouette score is >0.7, the clustering result is convincing. As shown in Table S3, the following 7 main cluster labels were obtained in the field of herbal therapies for OA: network pharmacology, chronic disorder, mesenchymal stem cell, clinical pharmacology, herbal medicinal product, biological basis, and chronic knee pain.

4. Discussion

4.1. General Information. This is the first bibliometric analysis identifying the global research hotspots and trends in the field of herbal therapies for OA. Our results indicated that the number of publications on herbal therapies for OA

Top 25 Keywords with the Strongest Citation Bursts					
Keywords	Year	Strength	Begin	End	2004 - 2022
non-steroidal anti-inflammatory drug	2004	10.02	2004	2017	
controlled clinical trial	2004	8.78	2004	2017	
celecoxib	2004	7.9	2004	2010	
placebo	2004	7.71	2004	2017	
complementary and alternative medicine	2004	6.33	2004	2017	
double blind	2004	6.18	2004	2010	
herbal remedy	2004	5.74	2004	2010	
therapeutic arthritis research	2004	5.59	2004	2010	
low back pain	2004	5.56	2004	2010	
clinical trial	2004	4.99	2004	2017	
alternative medicine	2004	4.7	2004	2017	
rosa canina	2004	4.54	2004	2010	
aqueous extract	2004	4.41	2004	2010	
rofecoxib	2004	4.3	2004	2010	
disability	2004	5.75	2011	2017	
medicine	2004	5.02	2011	2017	
interleukin-1 beta	2004	4.8	2011	2022	
women	2004	4.47	2011	2017	
pathogenesis	2004	6.73	2018	2022	
inflammation	2004	5.99	2018	2022	
network pharmacology	2004	5.69	2018	2022	
stem cell	2004	5.68	2018	2022	
oxidative stress	2004	5.13	2018	2022	
traditional chinese medicine	2004	4.93	2018	2022	
differentiation	2004	4.87	2018	2022	

FIGURE 2: CiteSpace visualization map of top 25 keywords with the strongest citation bursts involved in herbal therapies for OA.

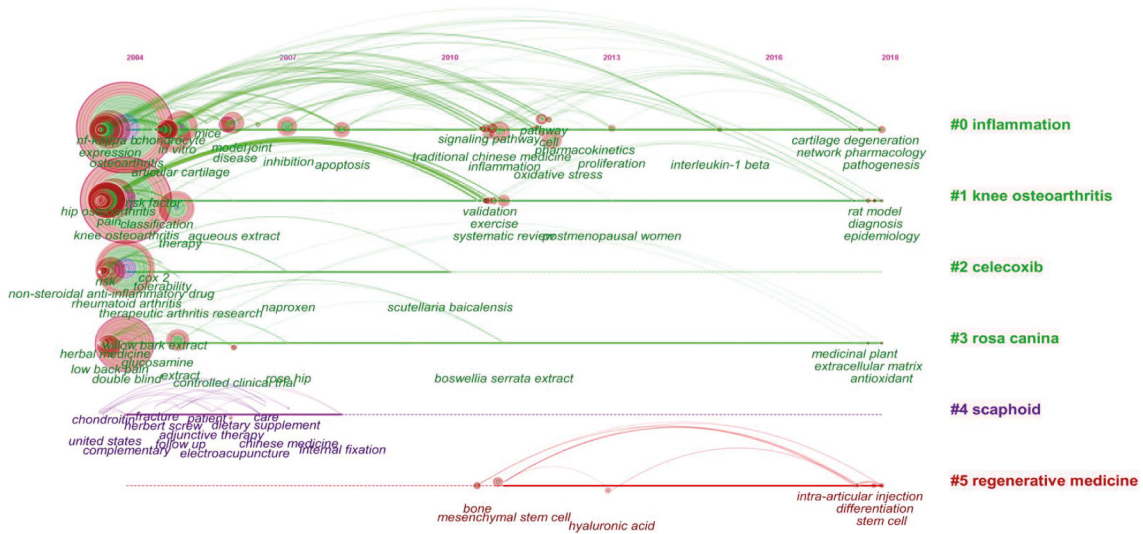


FIGURE 3: CiteSpace visualization map of timeline viewer related to herbal therapies for OA.

presented an overall upward trend in the field of herbal therapies for OA from 2004 to 2022, suggesting that research on herbal therapies for OA is flourishing. Between 2004 and 2016, the number of publications grew slowly. Since 2016, the growth had accelerated, especially in 2020, suggesting that herbal therapies for OA is attracting increasing attention in recent years.

We found that China ranked first in the number of publications on herbal therapies for OA, followed by the USA, South Korea, Germany, and England. Meanwhile, the centrality of the USA was significantly higher than other countries, indicating that the USA played a bridging role in international cooperation. Seven of the top 10 institutions in the number of publications were from China, with Shanghai

Top 25 References with the Strongest Citation Bursts

References	Year	Strength	Begin	End	2004 - 2022
Clegg DO, 2006, NEW ENGL J MED, V354, P795, DOI 10.1056/NEJMoa052771, DOI	2006	8.76	2006	2017	
Zhang W, 2008, OSTEOARTH CARTILAGE, V16, P137, DOI 10.1016/j.joca.2007.12.013, DOI	2008	8.3	2008	2017	
Berman BM, 2004, ANN INTERN MED, V141, P901, DOI 10.7326/0003-4819-141-12-200412210-00006, DOI	2004	7.74	2004	2010	
Schniter TJ, 2004, LANCET, V364, P665, DOI 10.1066/S0140-6736(04)16893-1, DOI	2004	6.96	2004	2010	
Lawrence RC, 2008, ARTHRITIS RHEUM, V58, P26, DOI 10.1002/art.23176, DOI	2008	6.78	2008	2017	
Silverstein FE, 2000, JAMA-J AM MED ASSOC, v284, P1247, DOI 10.1001/jama.284.10.1247, DOI	2000	6.71	2004	2010	
Ezzo J, 2001, ARTHRITIS RHEUM, V44, P819, DOI 10.1002/1529-0131(200104)44:4<819::AID-ANR138>3.3.CO;2-G, DOI	2001	6.37	2004	2010	
Brinkhaus B, 2006, ARCH INTERN MED, V166, P450	2006	5.88	2006	2017	
McAlindon TE, 2014, OSTEOARTH CARTILAGE, V22, P363, DOI 10.1016/j.joca.2014.01.003, DOI	2014	19.05	2014	2022	
Hochberg MC, 2012, ARTHRIT CARE RES, V64, P465, DOI 10.1002/acr.21596, DOI	2012	16.47	2012	2017	
Cross M, 2014, ANN RHEUM DIS, V73, P1323, DOI 10.1136/annrheumdis-2013-204763, DOI	2014	12.36	2014	2022	
Bijlsma JWJ, 2011, LANCET, V377, P2115, DOI 10.1016/S0140-6736(11)60243-2, DOI	2011	8.18	2011	2017	
Zhang W, 2010, OSTEOARTH CARTILAGE, V18, P476, DOI 10.1016/j.joca.2010.01.013, DOI	2010	7.6	2011	2017	
Kuptniratsaikul V, 2014, CLIN INTERV AGING, V9, P451, DOI 10.2147/CIA.S58535, DOI	2014	7.37	2014	2017	
Wojdasiewicz P, 2014, MEDIAT INFLAMM, V2014, P0, DOI 10.1155/2014/561459, DOI	2014	7.35	2014	2022	
Kapoor M, 2011, NAT REV RHEUMATOL, V7, P33, DOI 10.1038/nrrheum.2010.196, DOI	2011	7.28	2011	2017	
Hinman RS, 2014, JAMA-J AM MED ASSOC, V312, P1313, DOI 10.1001/jama.2014.12660, DOI	2014	6.5	2014	2022	
Glyn-Jones S, 2015, LANCET, V393, P1745, DOI 10.1016/S0140-6736(14)60802-3, DOI	2015	16.33	2018	2022	
Hunter DJ, 2019, LANCET, V393, P1745, DOI 10.1016/S0140-6736(19)30417-9, DOI	2019	16.23	2019	2022	
Bannuru RR, 2019, OSTEOARTH CARTILAGE, V27, P1578, DOI 10.1016/j.joca.2019.06.011, DOI	2019	13.52	2019	2022	
TANG X, 2016, ARTHRITIS RHEUMATOL, V68, P648, DOI 10.1002/ART.39465, DOI	2016	11.1	2018	2022	
Kolasinski SL, 2020, ARTHRITIS RHEUMATOL, V72, P220	2020	10.12	2020	2022	
Chen D, 2017, BONE RES, V5, P0, DOI 10.1038/boneres.2016.44, DOI	2017	9.2	2018	2022	
Robinson WH, 2016, NAT REV RHEUMATOL, V12, P580, DOI 10.1038/nrrheum.2016.136, DOI	2016	6.64	2018	2022	
Losser RF, 2016, NAT REV RHEUMATOL, V12, P412, DOI 10.1038/nrrheum.2016.65, DOI	2016	5.9	2018	2022	

FIGURE 4: CiteSpace visualization map of top 25 references with the strongest citation bursts involved in herbal therapies for OA.

University of Traditional Chinese Medicine and the Chinese University of Hong Kong showing a high level of collaboration. Two Korean institutions, named Kyung Hee University and Korea Institute of Oriental Medicine, were on the top 10 lists, with less international collaboration. Xianxiang Liu and *Evidence-Based Complementary and Alternative Medicine* were the most prolific author and journal, respectively. Simultaneously, Felson DT and *Arthritis and Rheumatism* were the most influential author and journal by holding the most cited papers, respectively. There was no overlap in the top 10 publications and citations by authors and journals, revealing that we still lack author and journal with a high impact on herbal therapies for OA. The *OARSI guidelines for the non-surgical management of knee osteoarthritis* [20] published in 2019 was the most cited reference, while a new guideline published in 2020 named the *2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee* may be a new focus in the future [21].

4.2. The Hotspots and Frontiers

4.2.1. Role of Herbal Therapies for OA.

In research on herbal therapies for OA, our results indicated that knee OA has been a research hotspot for a long time (since 2004), and TCM and differentiation also became a research hotspot in 2018. All these suggested that traditional Chinese herbal medicine are research hotspots in the field of herbal therapies for OA. In TCM theories, differentiation refers to syndrome identification, which means the classification of syndrome into a variety of unbalance conditions [22]. Patients with OA could have distinct syndrome classification that dictates different treatment strategies. In this case, traditional Chinese herbal medications will be tailored to the individual patient, which may result in better effects and fewer side effects. However, due to the individualized

characteristics of the syndrome, it is difficult to conduct randomized controlled trials and placebo-controlled trials for traditional Chinese herbal medicine. This may account for the decline in randomized placebo-controlled trials since 2018. Due to a lack of high-quality clinical evidence, Chinese herbal medications are often considered complementary or alternative therapies for patients with OA.

Herbal medicinal products and chronic knee pain are research frontiers in herbal therapies for OA. As one of the major symptoms of OA, chronic knee pain seriously impairs the quality of life for patients [23]. Many studies have indicated that herbal therapies can improve pain and slow the progression of OA [24]. Some researchers aim at transforming herbs with potential therapeutic effects into established herbal medicinal products or new clinical medicines. However, the selection of herbs for the treatment of OA is largely empirical, is time-consuming, and lacks high-quality evidence to support it. The complex composition of herbs makes it difficult to explore the exact active ingredient. Furthermore, the interactions between herbal medications with each other are not fully understood. Therefore, there is a long way to elucidate the mechanisms and determine the efficacy and role of herbal therapies for OA.

4.2.2. Main Types of Herbal Therapies for OA.

There is a wide range of herbs available for the treatment of OA. Our results showed that *rosa canina*, a European traditional herb, has been extensively studied since 2004 [25]. A recent meta-analysis included randomized controlled trials that showed that *rosa canina* powder can alleviate the pain of OA [26], and its mechanism of action is related to antioxidant and anti-inflammatory [27]. TCM mainly includes herbal compounds and herb extracts and has been used in China for over 2,500 years for chronic pain and OA. A famous

TCM compound named *Duhuo Jisheng Tang*, which was invented in the Tang Dynasty, is considered beneficial and widely used in treating OA in China. In addition to compound herbal medicine, many single herbs also showed effects on attenuating symptoms of OA and may be potential therapeutic agents for OA, such as *rhizoma drynariae*, *icariin*, and *curcuma longa* [28–30]. However, current herbal medicines are primarily used as complementary or alternative therapies for OA due to limited evidence [31]. Further long-term, large-sample, high-quality evidence is warranted to support the application of herbal medicines for the treatment of OA.

4.2.3. Mechanisms of Herbal Therapies for OA. For the mechanisms of herbal therapies in treating OA, our results showed that inflammation, oxidative stress, stem cell, regenerative medicine, and network pharmacology were important research hotspots; mesenchymal stem cell and clinical pharmacology were major research frontiers. Understanding the mechanisms of herbal therapies is helpful to maximize the therapeutic effects and develop therapeutic agents. Network pharmacology and clinical pharmacology are research methods aiming at exploring pharmacological actions and therapeutic mechanisms of herbal medicines for OA. It is worth noting that network pharmacology must be analyzed in conjunction with experimental validation to generate trusted evidence.

Inflammation, interleukin-1 β , and oxidative stress have been research hotspots in the mechanism study of herbal therapies for OA for a long time. As a proinflammatory factor, interleukin-1 β can induce joint inflammation and seems to be associated with cartilage destruction [32]. Interleukin-1 β is now often used as a stimulator in cellular experiments. Oxidative stress has been proposed as a driver of the catabolic and anabolic signaling imbalance in cartilage that results in progressive matrix degradation [33]. In addition, oxidative stress can induce senescence in joint cells [34]. There was a correlation between increased oxidative stress and the induction of senescence in cartilage, which might drive OA [33]. Some herbs, such as *curcuma longa*, *vernonia amygdalina*, and *icariin*, can suppress inflammation, decrease oxidative stress, and reduce local symptoms of joints in OA [29, 35, 36].

Stem cell was a research hotpot, and mesenchymal stem cell and regenerative medicine were research frontiers in herbal therapies for OA. Regenerative medicine is an emerging research field in recent years. Recent studies suggested that bone mesenchymal stem cell therapy can relieve local pain and partially repair injured cartilage, with the therapeutic goal of joint regeneration [37]. Some herbs (such as *andrographolide* and *honokiol*) have been shown to improve cell survival and chondrogenesis of mesenchymal stem cells [38, 39], which may be a major potential therapeutic mechanism of herbal therapies for OA.

4.3. Limitations. There are certain shortcomings in this study. Firstly, since we used CiteSpace software for data analysis, which removed some components that were

calculated to be insignificant during the analyses, our results may miss some interesting data. Secondly, we only searched one comprehensive English database that could not cover all studies in herbal therapies for OA, so potential bias may exist in the results. Thirdly, as this is a bibliometric analysis, we did not evaluate the methodological quality of included studies and critically analyze the effects of herbal therapies for OA; our results were based majorly on the quantity of publications and citations and may use as a start point for research in this area.

5. Conclusion

Research on herbal therapies for OA is flourishing, but communication among countries should be strengthened. China ranked first in the number of publications, followed by the USA, South Korea, Germany, and England. Current research on herbal therapies for OA mainly focuses on knee OA, TCM, differentiation, *rosa canina*, inflammation, oxidative stress, stem cell, and regenerative medicine. The emerging research trends in herbal therapies for OA are herbal medicinal product, chronic knee pain, mesenchymal stem cell, and clinical pharmacology.

Data Availability

Data sharing is not applicable to this article as no new data were created in this study. These datasets were derived from the following public domain resources: <https://www.webofscience.com/wos/woscc/advanced-search>.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this article. The funding agencies had no roles in the study design, collection, analysis, and interpretation of the data, in the report's writing, and in the decision to submit the paper for publication.

Authors' Contributions

Conceptualization was done by D.L.; W.S. and J.C. contributed to the methodology; G.Y., J.L., H.S., S.L., and N.D. investigated the study; W.S. and J.C. wrote the manuscript; and G.Y. and D.L. critically revised the manuscript. W.S. and J.C. contributed equally to the work and share the first authorship.

Acknowledgments

The authors would like to thank Citespace software developers. This work was supported by National Natural Science Foundation of China (81804042).

Supplementary Materials

Figure S1 Flowchart of literature search and selection. Figure S2 Trends of publications in the field of herbal therapies for OA from 2004 to 2022. Table S1 Top keywords ($n \geq 80$) related to herbal therapies for OA. Table S2 Top 10

references related to herbal therapies for OA. Table S3 The clusters of cocited references in herbal therapies for OA. (*Supplementary Materials*)

References

- [1] J. Martel-Pelletier, A. J. Barr, F. M. Cicuttini et al., "Osteoarthritis," *Nature Reviews Disease Primers*, vol. 2, no. 1, Article ID 16072, 2016.
- [2] S. Glyn-Jones, A. J. R. Palmer, R. Agricola et al., "Osteoarthritis," *Lancet*, vol. 386, no. 9991, pp. 376–387, Jul. 2015.
- [3] D. J. Hunter and S. Bierma-Zeinstra, "Osteoarthritis," *Lancet*, vol. 393, no. 10182, pp. 1745–1759, 2019.
- [4] GBD 2019 Diseases and Injuries Collaborators, "Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019," *Lancet*, vol. 396, no. 10258, 2020.
- [5] R. Liu-Bryan and R. Terkeltaub, "Emerging regulators of the inflammatory process in osteoarthritis," *Nature Reviews Rheumatology*, vol. 11, no. 1, pp. 35–44, Jan. 2015.
- [6] B. R. da Costa, T. V. Pereira, P. Saadat et al., "Effectiveness and safety of non-steroidal anti-inflammatory drugs and opioid treatment for knee and hip osteoarthritis: network meta-analysis," *BMJ*, vol. 375, Article ID n2321, 2021.
- [7] A. O. Leopoldino, G. C. Machado, P. H. Ferreira et al., "Paracetamol versus placebo for knee and hip osteoarthritis," *Cochrane Database of Systematic Reviews*, vol. 2, no. 2, Article ID CD013273, 2019.
- [8] A. Guermazi, T. Neogi, J. N. Katz et al., "Intra-articular corticosteroid injections for the treatment of hip and knee osteoarthritis-related pain: considerations and controversies with a focus on imaging-radiology scientific expert panel," *Radiology*, vol. 297, no. 3, pp. 503–512, Dec. 2020.
- [9] M. Cameron and S. Chrubasik, "Oral herbal therapies for treating osteoarthritis," *Cochrane Database of Systematic Reviews*, vol. 2014, no. 5, Article ID CD002947, 2014.
- [10] M. Cameron, J. J. Gagnier, C. V. Little, T. J. Parsons, A. Blumle, and S. Chrubasik, "Evidence of effectiveness of herbal medicinal products in the treatment of arthritis. Part I: Osteoarthritis," *Phytotherapy Research*, vol. 23, no. 12, pp. 1647–1662, 2009.
- [11] A. Wang, D. J. Leong, L. Cardoso, and H. B. Sun, "Nutraceuticals and osteoarthritis pain," *Pharmacology & Therapeutics*, vol. 187, pp. 167–179, Jul. 2018.
- [12] S.-Q. Wang, J.-X. Wang, C. Zhang et al., "What you should know about osteoarthritis rehabilitation: a bibliometric analysis of the 50 most-cited articles," *Geriatr. Orthop. Surg. Rehabil.*, vol. 11, Article ID 215145932097319, 2020.
- [13] J.-Q. Chen, Q. He, B.-H. Jiang et al., "Research on primary Sjögren's syndrome in 2004–2021: a Web of Science-based cross-sectional bibliometric analysis," *Rheumatology International*, 2022.
- [14] Y. Zhao, L. Huang, M. Liu, H. Gao, and W. Li, "Scientific knowledge graph of acupuncture for migraine: a bibliometric analysis from 2000 to 2019," *Journal of Pain Research*, vol. 14, p. 1985, 2021.
- [15] G.-Y. Yang, L.-Q. Wang, J. Ren et al., "Evidence base of clinical studies on Tai Chi: a bibliometric analysis," *PLoS One*, vol. 10, no. 3, Article ID e0120655, 2015.
- [16] R. Li, J. Sun, H. Hu et al., "Research trends of acupuncture therapy on knee osteoarthritis from 2010 to 2019: a bibliometric analysis," *Journal of Pain Research*, vol. 13, pp. 1901–1913, 2020.
- [17] M. B. Synnestevedt, C. Chen, and J. H. Holmes, "CiteSpace II: visualization and knowledge discovery in bibliographic databases," *AMIA Annual Symposium Proceedings*, vol. 2005, pp. 724–728, 2005.
- [18] C. Chen, F. Ibekwe-SanJuan, and J. Hou, "The structure and dynamics of cocitation clusters: a multiple-perspective cocitation analysis," *Journal of the American Society for Information Science and Technology*, vol. 61, no. 7, pp. 1386–1409, 2010.
- [19] C. Chen, "Searching for intellectual turning points: progressive knowledge domain visualization," *Proceedings of the National Academy of Sciences of the United States of America*, vol. 101, no. 1, pp. 5303–5310, 2004.
- [20] R. R. Bannuru, M. C. Osani, E. E. Vaysbrot et al., "OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis," *Osteoarthritis and Cartilage*, vol. 27, no. 11, pp. 1578–1589, 2019.
- [21] S. L. Kolasinski, T. Neogi, M. C. Hochberg et al., "2019 American College of rheumatology/arthritis foundation guideline for the management of osteoarthritis of the Hand, hip, and knee," *Arthritis & Rheumatology*, vol. 72, no. 2, pp. 220–233, 2019.
- [22] A. Lu, M. Jiang, C. Zhang, and K. Chan, "An integrative approach of linking traditional Chinese medicine pattern classification and biomedicine diagnosis," *Journal of Ethnopharmacology*, vol. 141, no. 2, pp. 549–556, Jun. 2012.
- [23] T. Neogi, "The epidemiology and impact of pain in osteoarthritis," *Osteoarthritis and Cartilage*, vol. 21, no. 9, pp. 1145–1153, 2013.
- [24] L. Long, K. Soeken, and E. Ernst, "Herbal medicines for the treatment of osteoarthritis: a systematic review," *Rheumatology*, vol. 40, no. 7, pp. 779–793, 2001.
- [25] L. F. Haas, "Rosa canina (dog rose)," *Journal of Neurology, Neurosurgery & Psychiatry*, vol. 59, no. 5, p. 470, 1995.
- [26] R. Christensen, E. M. Bartels, R. D. Altman, A. Astrup, and H. Bliddal, "Does the hip powder of Rosa canina (rosehip) reduce pain in osteoarthritis patients: a meta-analysis of randomized controlled trials," *Osteoarthritis and Cartilage*, vol. 16, no. 9, pp. 965–972, 2008.
- [27] J. Gruenewald, R. Uebelhack, and M. I. Moré, "Rosa canina—rose hip pharmacological ingredients and molecular mechanics counteracting osteoarthritis—a systematic review," *Phytomedicine*, vol. 60, Article ID 152958, 2019.
- [28] G.-Y. Chen, J.-Q. Chen, X.-Y. Liu et al., "Total flavonoids of rhizoma drynariae restore the MMP/TIMP balance in models of osteoarthritis by inhibiting the activation of the NF- κ B and PI3K/AKT pathways," *Evidence-based Complementary and Alternative Medicine*, vol. 2021, Article ID 6634837, 14 pages, 2021.
- [29] L. Pan, Y. Zhang, N. Chen, and L. Yang, "Icariin regulates cellular functions and gene expression of osteoarthritis patient-derived human fibroblast-like synoviocytes," *International Journal of Molecular Sciences*, vol. 18, no. 12, p. 2656, 2017.
- [30] Z. Wang, G. Jones, T. Winzenberg et al., "Effectiveness of curcuma longa extract for the treatment of symptoms and effusion-synovitis of knee osteoarthritis: a randomized trial," *Annals of Internal Medicine*, vol. 173, no. 11, pp. 861–869, 2020.
- [31] G. J. Macfarlane, P. Paudyal, M. Doherty et al., "A systematic review of evidence for the effectiveness of practitioner-based complementary and alternative therapies in the management of rheumatic diseases: osteoarthritis," *Rheumatology*, vol. 51, no. 12, pp. 2224–2233, 2012.

- [32] M. Kapoor, J. Martel-Pelletier, D. Lajeunesse, J.-P. Pelletier, and H. Fahmi, "Role of proinflammatory cytokines in the pathophysiology of osteoarthritis," *Nature Reviews Rheumatology*, vol. 7, no. 1, pp. 33–42, 2011.
- [33] R. F. Loeser, "The role of aging in the development of osteoarthritis," *Transactions of the American Clinical & Climatological Association*, vol. 128, pp. 44–54, 2017.
- [34] P. R. Coryell, B. O. Diekman, and R. F. Loeser, "Mechanisms and therapeutic implications of cellular senescence in osteoarthritis," *Nature Reviews Rheumatology*, vol. 17, no. 1, pp. 47–57, 2021.
- [35] S. Srivastava, A. K. Saksena, S. Khattri, S. Kumar, and R. S. Dagur, "Curcuma longa extract reduces inflammatory and oxidative stress biomarkers in osteoarthritis of knee: a four-month, double-blind, randomized, placebo-controlled trial," *Inflammopharmacology*, vol. 24, no. 6, pp. 377–388, 2016.
- [36] I. N. Madzuki, S. F. Lau, R. Abdullah, N. I. Mohd Ishak, and S. Mohamed, "Vernonia amygdalina inhibited osteoarthritis development by anti-inflammatory and anticollagenase pathways in cartilage explant and osteoarthritis-induced rat model," *Phytotherapy Research*, vol. 33, no. 7, pp. 1784–1793, 2019.
- [37] J. J. Hwang, Y. A. Rim, Y. Nam, and J. H. Ju, "Recent developments in clinical applications of mesenchymal stem cells in the treatment of rheumatoid arthritis and osteoarthritis," *Frontiers in Immunology*, vol. 12, Article ID 631291, 2021.
- [38] T. Kulsirirat, S. Honsawek, M. Takeda-Morishita et al., "The effects of andrographolide on the enhancement of chondrogenesis and osteogenesis in human suprapatellar fat pad derived mesenchymal stem cells," *Molecules*, vol. 26, no. 7, p. 1831, 2021.
- [39] H. Wu, Z. Yin, L. Wang, F. Li, and Y. Qiu, "Honokiol improved chondrogenesis and suppressed inflammation in human umbilical cord derived mesenchymal stem cells via blocking nuclear factor- κ B pathway," *BMC Cell Biology*, vol. 18, no. 1, p. 29, 2017.