

**Review Article**

# Bibliometrics Research on Immune of Traditional Chinese Medicine

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**Abstract:** Bibliometrics analysis is increasingly used for situation analysis in a certain field. We aimed to analyze the immunological aspects of traditional Chinese medicine (TCM) from 1995 to the present, such as study countries, institutions, journals, and hotspots. The web of science core collection was used to retrieve the articles related to TCM-Immune from 1995 to 2018, and the statistical analysis of those projects by the Excel, VOS viewer software. A total of 4005 kinds of literature on TCM-Immune were retrieved. It was found that the total number of papers published in recent years had increased rapidly, with China being the country with the largest number of publications, followed by the United States, South Korea, India, and Japan. Top 10 institutions except Kyung-hee University are based in China, and so are the authors of the top three. VOS viewer software divided the keywords into four clusters, the first cluster is immune in vitro, the second cluster is immune in vivo, the third cluster is TCM-Immune resistance, the fourth cluster is the mechanism of immune, the analysis shows that inflammation, oxidative stress, signal pathway, the mechanism of action is new hotspots in the future.

**Keywords:** Bibliometric Citation, Traditional Chinese Medicine, Immune, Hotspots

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## 1. Introduction

Traditional Chinese medicine was widely used to prevent and treat human or animal diseases in China. In the theory of traditional Chinese medicine (TCM) or traditional Chinese veterinary medicine (TCVM), strengthening the body resistance is one of the basic principles of preventing and treating diseases [1]. With the progress of society, people pay more attention to human sub-health [2-4] and the development of proprietary Chinese medicine for human or animal use. Chinese medicine has rich experience in the prevention and treatment of the disease, especially in the immunity of traditional Chinese medicine. There are many reports have shown that immunity is related to disease [5-7], such as

non-small cell lung cancer [8], cutaneous lupus erythematosus [9], systemic sclerosis [10], et al.

Bibliometrics refers to the quantitative analysis of all knowledge carriers by mathematical and statistical methods. VOS viewer is a free bibliometric analysis software developed by Nees Jan van Eck and Ludo Waltman of Leiden University in the Netherlands to construct and view bibliometric maps, which can draw scientific maps of various fields. It has been applied to the analysis of document information in many natural sciences. Compared with other Bibliometrics software, VOS viewer pays special attention to the graphical representation of bibliometrics map [11].

The objective was attempted to provide all-around insights on the current state of global TCM-Immune research. The distribution of the publications was analyzed as well as keywords and references to better understand the global trend

of research and to discover the hotspots in this field.

## 2. Materials and Methods

### 2.1. Bibliometric Dates and Search Strategy

A comprehensive bibliographic retrieval was performed online using the Web of Science Core Collection on 15 September 2018. In order to avoid errors caused by daily updates, the retrieval is completed in one day.

The retrieval strategy was: TS = (Traditional Chinese medicine\* OR Herb\* OR TCM\*) AND TS = (immunology\* OR Immunity\* OR Immune\*). Language was selected as English. Articles and reviews that were normally peer-reviewed were included, but all others were excluded.

### 2.2. Date Collection

The original data downloaded from the web of science firstly imported into Microsoft Excel 2016, and then validated and evaluated by two independent researchers. Disagreement is United through discussion. Finally, the number of papers, citations and H-index bibliometric parameters were extracted. The collected data are imported into Microsoft Excel 2016 and VOS view software for quantitative and qualitative analysis.

### 2.3. Bibliometric Analysis

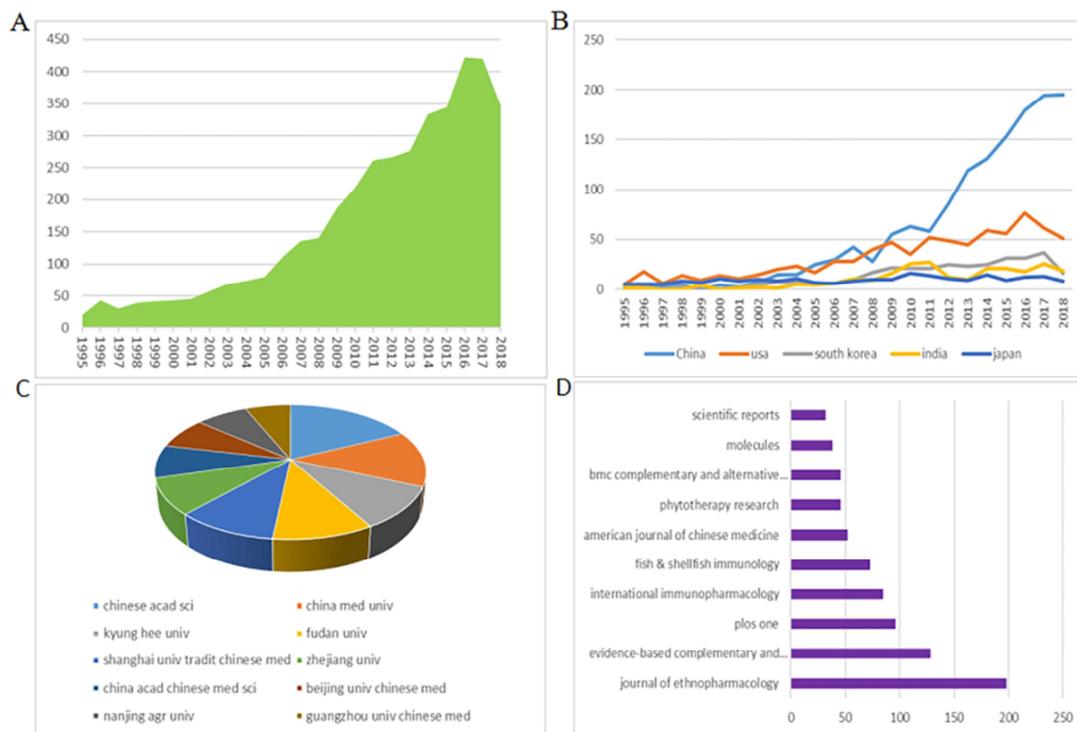
Firstly, Microsoft Excel 2016 is used to analyze the time trend of the number of publications, which can predict the future trend of the literature to a certain extent, in which the

X-axis represents the time and Y axis to represent the amount of literature produced in the corresponding year. VOS viewer can be used for keyword mapping and clustering, and the frequency of hotspots [11].

## 3. Results

### 3.1. Contributions of Countries and Regions to Global Publications

Both the quantity and quality of publications were measured to evaluate the contributions of different countries and regions. A total of 4152 articles from 1995 to 2018 met the search criteria. After screening, a total of 4005 articles are available for analysis. We can see that TCM-Immune related articles have increased rapidly in recent years from Figure 1 A. Figure 1 B shows the trend of publications in five countries with the largest number of articles on TCM-Immune in recent years. China has the fastest growth and the largest number of papers since 2011. Although the number of papers issued by the United States, South Korea, India, and Japan has increased, there is still a big gap with China in this field, which may be related to national history, the cultural background and so on. The above-detailed information is shown in Table 1. People R China had the first place when ranking for the number of publications (1408, 35.16%), followed by USA (763, 19.05%) and the South Korea (313, 7.82%). The USA had the most citations with a number of 25158. People R China ranked 2nd with the citation number of 19154.



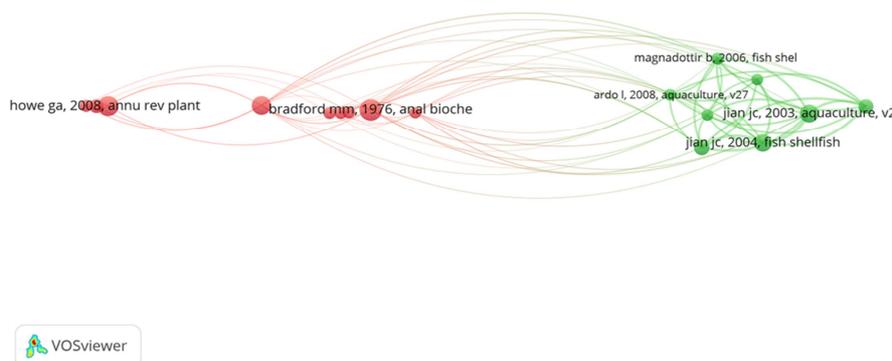
**Figure 1.** Contributive characteristics of TCM-Immune research. A Time-trend in the number of published documents in the studied field. B The total publications worldwide and five most productive countries in TCM-Immune. C The number of publications on TCM-Immune research from the top 10 contribution institutes. D The number of publications of the top 10 popular journals on TCM-Immune research.

**Table 1.** Publications in the 10 most productive countries.

Country	N	%	Total citations
People R China	1408	35.16	19154
USA	763	19.05	25158
South Korea	313	7.82	4278
India	239	6.017	4003
Japan	224	5.97	4350
Taiwan	191	4.844	2926
Germany	188	4.77	7126
Canada	126	3.15	3110
Iran	108	2.69	1094
Australia	95	2.37	2409

### 3.2. Journals Publishing TCM-Immune Research

After analysis the publication's research on TCM-Immune by VOS viewer software, we know a journal of Ethnopharmacology published the most studies with 198 publications. There were 128 articles in evidence-based complementary and alternative medicine, 96 articles in PLoS one and 85 articles in international immunopharmacology on TCM-Immune research. The top 10 journals that published the most studies are listed in Figure 2.



**Figure 2.** Analysis of the top 17 references. Mapping of the top 17 co-cited references of 4055 publications on TCM-Immune research.

### 3.3. Institutes Publishing TCM-Immune Research

Publications from top 10 institutes accounted for 13.51% of all articles on TCM-Immune research. As can be seen from Figure 1 C, Chinese Academy of Sciences had the highest number of publications with a total of 97, thereby accounting

for 2.42% of all published literature in this field, followed by China Medical University, Kyung Hee University, Fudan University and so on. Similarly, we can find that in the top 10 of the institutions, besides Kyung Hee University, they all belong to People R China (Table 2).

**Table 2.** Top 10 of institution engaging in research on TCM-Immune by frequency.

Institution	Country	N	%	Total citations
Chinese Acad Sci	People R China	97	2.42	1586
China Med Univ	People R China	73	1.82	834
Kyung Hee Univ	South Korea	55	1.37	931
Fudan Univ	People R China	55	1.37	477
Shanghai Univ Tradit Chinese Med	People R China	55	1.37	312
Zhejiang Univ	People R China	47	1.17	580
China Acad Chinese Med Sci	People R China	43	1.07	473
Beijing Univ Chinese Med	People R China	41	1.02	193
Nanjing Agr Univ	People R China	40	0.99	738
Guangzhou Univ Chinese Med	People R China	35	0.87	133

### 3.4. Authors Publishing TCM-Immune Research

**Table 3.** The top 10 authors with the most publications related to TCM-Immune research.

Author	N	Country	Total citations
Wang, Y	100	People R China	814
Li, J	78	People R China	1094
Li, X	75	People R China	1045
Zhang, Y	69	People R China	817
Wang, J	63	People R China	860
Wang, X	62	People R China	575
Chen, J	53	People R China	720
Wang, H	50	People R China	473
Zhang, X	43	People R China	381
Zhang, L	43	People R China	531

A total of 593 publications were from the top 10 authors, accounting for 14.81% of all publications related to the field. The 3 authors who published the most research was Wang, Y with 100 publications on TCM-Immune, followed by Li, J with 78 publications and Li, X with 75 publications (Table 3).

### 3.5. Analysis of References in TCM-Immune Publications

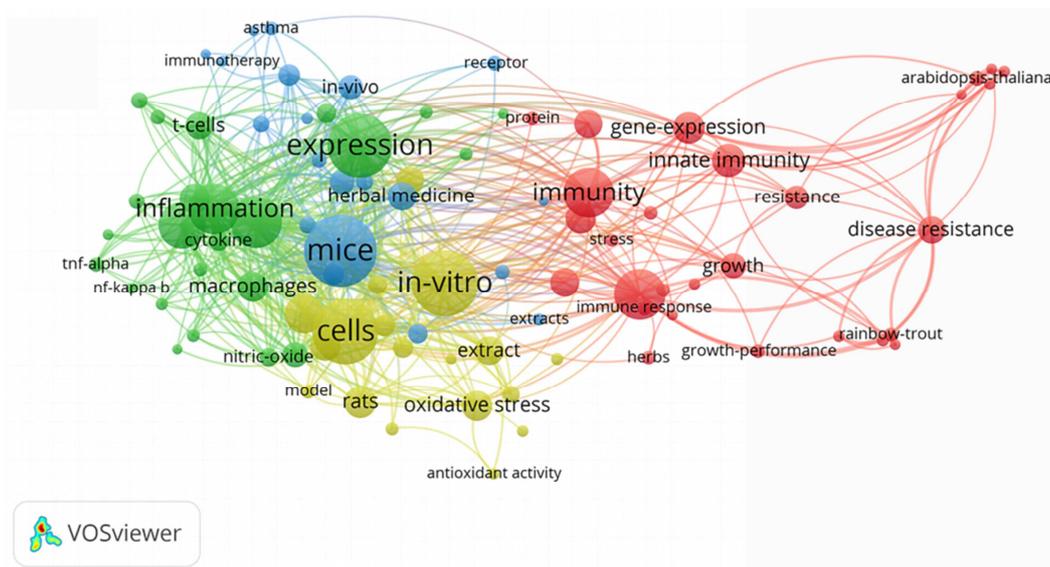
Reference analysis is used to examine the relationship both references and classify them. The top 17 references with more than 50 citations were selected for analysis of references by VOS viewer. Eventually, 17 papers were divided into two clusters. The first cluster consisted of 9 papers, mainly focusing on specific immunity of TCM, and the second cluster consisted of 8 papers, mainly focusing on innate immunity of TCM.

### 3.6. Analysis of Keywords in TCM-Immune Publications

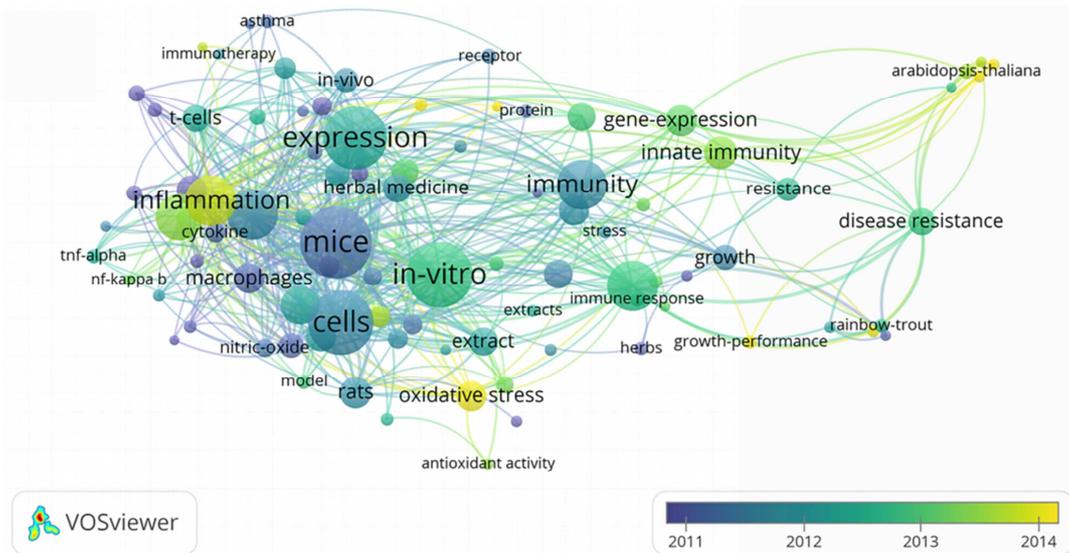
The analysis of keywords can infer hotspots, and provide directions for future research. We cluster analysis on 90 keywords that appear at least 50 times in VOS viewer. 90 keywords were divided into four clusters: “Immune in vitro”, “Immune in vivo”, “TCM-Immune resistance” and “The mechanism of immune”. In “Immune in vitro” cluster, frequency keywords were: in-vitro (370 times), cells (364 times) and rats (167 times); In “Immune in vivo” cluster, frequency keywords were: mice (405 times), herbal medicine (149 times) and in-vivo (127 times). In “TCM-Immune resistance” cluster, frequency keywords were traditional Chinese medicine (281 times), immunity (273 times) and innate immunity (173 times). In “The mechanism of immune” cluster, frequency keywords were an expression (358 times), inflammation (279 times) and activation (277 times). The

results indicate that there are four main directions in the research of traditional Chinese medicine immunity.

The statistic of keyword appearance time is done under the operation of VOS viewer software. Blue means that the keyword appeared earlier and red means that this keyword appears late (Figure 3). Before 2011, in the early stage of TCM-Immune research, the main popular hotspots were: cytokines, macrophages, induction and in-vivo, et al. According to Figure 4, we can know the latest trends, the newest keywords of the first cluster were oxidative stress, mechanism research; the second cluster included regulatory T cells; the third cluster involved herbivorous insects, Arabidopsis, growth performance, *Aeromonas hydrophila*, and the fourth cluster main included inflammation and signaling pathways. Clearly knowing these hotspots is of guiding significance for the subsequent research.



**Figure 3.** Distribution of keywords according to their time of appearance. The blue colour means the early appearance and red coloured keywords appeared later.



**Figure 4.** Mapping of the keywords in TCM-Immune research. The key words were divided into 4 groups according to different colours generated by default.

## 4. Discussion

China has the largest number of TCM-Immune publications in the world. In the early stage of TCM-Immune research, the United States has the largest number of papers, but since 2009, China has always maintained the number of the first, which is related to the history of China and the scientific research conditions at that time. After China, the United States, South Korea, India, and Japan, which also have more research on the TCM-Immune, are sending more papers. The quantity of TCM-Immune is the first in China, but the frequency of citation is the second, which is related to the policy of the evaluation system of Chinese scientific research [12], thus the quantity increases, but the quality is not very high [13].

More articles on TCM-Immune have been published in Journal of Ethnopharmacology, Evidence-based complementary and alternative medicine, Plos one and International Immunopharmacology. It is speculated that the new findings in this field will be published in these journals.

The research institutes and universities of China are the leading organizations in the research of TCM-Immune, which is closely related to the cultural and historical background of Chinese traditional medicine. Nine of the top 10 organizations, except Kyung Hee University, are based in China. This shows that China establishment of a world-class university is fundamental to improving the country scientific research capabilities [14].

Wang Y, Li Y, and Li X are three of the most published

articles on TCM-Immune. Wang Y is from Northwest University of Agriculture and Forestry Science and Technology, Li Y from the Dalian University of Technology, Li X from Nanjing University of Traditional Chinese Medicine. They mainly studied the mechanism of immunomodulation [15-17] and anti-inflammation [18-20] of traditional Chinese medicine. Keeping an eye on the three authors new articles will obtain an update on the immunological research of traditional Chinese medicine (TCM).

According to bibliometrics analysis, we found the top 10 references. Plant immunity to insect herbivores [21] written by Howe GA was the most frequently cited, followed by Hormonal Modulation of Plant Immunity [22], Signal signature and transcriptome changes of Arabidopsis during pathogen and insect attack [23], Glucosinolate Metabolites Required for an Arabidopsis Innate Immune Response [24], Central memory self/tumor-reactive CD8(+) T cells confer superior antitumor immunity compared with effector memory T cells [25], Jasmonate Passes Muster: A Receptor and Targets for the Defense Hormone [26] Jasmonate passes muster: a receptor and targets for the defense hormone, et al. In recent years, inflammation [27], oxidative stress [28], signal pathway [29], mechanism of action [30], regulatory T cells [31-33] have been the focus of research (Table 4).

**Table 4.** The top 10 TCM-Immune research papers with the most citation frequency.

Title	First author	Journal	Year	Citations
Plant immunity to insect herbivores	Howe GA	Annual Review of Plant Biology	2008	951
Hormonal Modulation of Plant Immunity	Pieterse	Annual Review of Cell and Developmental Biology	2012	657
Signal signature and transcriptome changes of Arabidopsis during pathogen and insect attack	De Vos	Molecular plant-microbe interactions	2005	527
Glucosinolate Metabolites Required for an Arabidopsis Innate Immune Response	Clay	SCIENCE	2009	507
Central memory self/tumor-reactive CD8(+) T cells confer superior antitumor immunity compared with effector memory T cells	Klebanoff	Proceedings of the national academy of sciences of the united states of america	2005	484
Jasmonate Passes Muster: A Receptor and Targets for the Defense Hormone	Browse	Annual review of plant biology	2009	443
Health-promoting properties of common herbs	Craig	American journal of clinical nutrition	1999	366
The scientific rediscovery of an ancient Chinese herbal medicine: Cordyceps sinensis Part I	Zhu	Journal of alternative and complementary medicine	1998	312
Induced Systemic Resistance by Beneficial Microbes	Pieterse	Annual review of phytopathology	2014	303
Pesticide mixtures, endocrine disruption, and amphibian declines: Are we underestimating the impact?	Hayes	Environmental health perspectives	2006	302

Bibliometrics method was used to analyze the development trend of TCM-Immune, and analyze the countries, institutions, authors, and magazines that have the most frequently published papers in this field and has important guiding significance for subsequent research. At the same time, this method also has some limitations. Firstly, the source of the literature comes from the web of the science core collection, not all databases. Second, the source of the literature is only English, and the literature of other languages is not statistically analyzed. Therefore, the source of literature on TCM-Immune is not comprehensive. In short, this study can provide very important guidance for future

researchers in TCM-Immune.

## 5. Conclusion

At present, the research scope of TCM immunity is mainly focused on immune in vitro, immune in vivo, the TCM-Immune resistance, and the mechanism of immune. Through the analysis of this review shows that inflammation, oxidative stress, signal pathway, the mechanism of action is new hotspots in the future.

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## Statement of Ethics

Not Applicable.

## Conflict of Interest

The authors have no conflicts of interest to declare.

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## Author Contributions

Dongdong Bai conducted the study and contributed to study design, data analysis, and preparation of the manuscript, Zhen Dong participated in the writing of the article and the revision and proofreading of the article. Xinpu Li, Jinyin Luo, Xurong Wang guide the writing. Hongsheng Li provided funding for the article. All authors gave their final approval of the manuscript.

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