

REVIEW

# Research Trend and Future Perspectives of Traditional Chinese Medicine for Atopic Dermatitis from 2004 to 2023: A Bibliometric Analysis

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**Aim:** The application of bibliometric analysis gives insights into research trend and future perspectives. This paper aims to understand the current status of studies on traditional Chinese medicine (TCM) in the treatment of atopic dermatitis (AD), and to investigate the cooperation network, hotspots and trends in the field.

**Methods:** The original data were retrieved from the Web of Science Core Collection by searching for the topic "atopic dermatitis" and "traditional Chinese medicine" with the time span of 2004–2023. Microsoft Excel was used to create statistical tables and charts, whereas CiteSpace and VOSViewer were applied for knowledge mapping.

Results: In total, 252 publications were identified and downloaded. Current research on TCM treating AD is in the steady growth period. China has the largest number of publications, whereas the USA has the greatest international influence. Notably, the Arab Emirates, Malaysia, India and Bangladesh all have a high research impact but with a low amount of publications. Universities in Hong Kong China have the largest number of publications, but their interaction with other institutions is very poor. The top three most productive authors are all from Hong Kong, having a strong collaboration network with each other. The popular research topics in this field are "children" "cell" "activation" "nf kappa b" "inflammation" "asthma" "extract" "management" and "cytokine". According to the analysis of leading co-cited journals and authors, "J ETHNOPHARMACOL" has the largest amount of citations whilst "AM J CHINESE MED" the strongest academic influence. The largest number of co-cited authors comes from "Hon Karn-Lun Ellis", a well-known scholar from Hong Kong.

**Conclusion:** TCM has been widely used in AD treatment, honored for its individualized therapeutic concepts of evidence-based treatment. The academic community must form a continuous and deep-going pattern to achieve higher international influence and a stronger research degree in this field.

Keywords: atopic dermatitis, traditional Chinese medicine, bibliometrics, knowledge mapping, visual analysis

#### Introduction

Atopic dermatitis (AD) is a common clinical skin disease characterized by an eczema-like rash with intense itching and recurrent flare-ups, often accompanied by other allergic diseases such as food allergies, asthma, rhinitis, etc.<sup>1</sup> It is reported that some patients also suffer from sleep deprivation, social embarrassment, depression and other disorders.<sup>2,3</sup> It seriously affects the quality of life of patients and their families.

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In recent years, dupilumab, a representative biological agent, has become an accepted mainstream treatment that can significantly improve the condition of patients with moderate-to-severe AD. However, some inevitable disadvantages are gradually exposed, for instance, its treatment cost is relatively high. Therefore, it is difficult for some patients with moderate-to-light severity AD to bear this cost. In addition, patients receiving this medication still require other drugs for maintenance treatment and daily care after the condition of the patient is stabilized, and the drug is discontinued. In clinical practice, most patients are simultaneously treated with topical emollients, corticosteroids, calcium-modulated phosphatase inhibitors for external application, antihistamines, hormonal drugs, or immunosuppressants for oral administration.<sup>4</sup> However, these treatments are usually associated with adverse effects and drug tolerance.<sup>5</sup>

Traditional Chinese medicine (TCM) intervention has become a mainstream complementary and alternative therapeutic option and has been widely used in the clinical treatment of various dermatological diseases, honored for its individualized therapeutic concepts of evidence-based treatment. Moreover, TCM can be applied both internally and externally with fewer adverse drug reactions.<sup>6-8</sup> For example, Liangxue Qushi Zhiyang Decoction was applied to treat atopic dermatitis patients with TCM syndrome of blood-heat and dampness accumulation with significant efficacy and the clinical efficacy continued to improve with the increase in the course of treatment. It's also reported that a combined treatment of TCM and western medicine was designed to treat AD, which enhanced the efficacy of the treatment by regulating the peripheral blood T-cell subpopulations and lowering the serum total IgE level. 10,11 More relevant studies have pointed out that the external application of TCM could enable the drugs to reach the interstices of the flesh through heat, effectively preventing the loss of skin moisture, promoting the recovery of the skin barrier function, and inhibiting the abnormal immune-inflammatory response, which further promotes the improvement of clinical symptoms. 12-18 Based on ancient books of TCM, it is written in the "The Golden Mirror of Medicine" that "four bends wind, born in the bends of the legs and the bends of the feet, occurring once a month, in the shape of ringworm, its itch is boundless, scratching through the exudation, in the shape of damp-type dermatitis." These symptom descriptions were consistent with self-conscious symptoms, skin lesions and recurrent episodes of atopic dermatitis. However, AD has not yet been clearly identified in ancient TCM books. Therefore, it is of great significance to search and screen the literature in detail and quantitatively analyze the research status and hotspots of TCM interventions in the treatment of AD.

Bibliometric analysis is a quantitative analysis of literature information based on mathematical and statistical methods. It is widely used in many fields.<sup>20</sup> In the past decades, kinds of software and tools have been explored and applied for bibliometric analysis. Citespace and VOSViewer are two of them. This study aims to use these two software programs to conduct a comprehensive and extensive analysis of the literature on TCM treating AD over the past 20 years to evaluate the current status, hotspots and research trends in this field.

### **Methods**

# Data Source and Retrieval Strategy

The data source and retrieval strategy play an important role in bibliometric analysis. In the pre-retrieval phase, three databases were applied and compared, including Web of Science Core Collection (WOSCC), Scopus, and PubMed. By setting "Atopic Dermatitis and Traditional Chinese Medicine" as the search topic and the time span of 2004–2023, these three databases exported 189, 193, and 79 outcomes, respectively. Firstly, PubMed was not considerable as the data source because of the low amount of publications (79). WOSCC and Scopus barely differed in terms of the number of search outcomes. It is noteworthy that CiteSpace, one of the bibliometric analysis tools in this paper, shows the most powerful feature while WOSCC as the data source.<sup>21</sup> Moreover, taking WOS as a single data source would help us explore research hotspots and future trends more efficiently based on keyword analysis. Therefore, WOSCC was selected as the data source for this study.

First of all, MeSH (Medical Subject Headings) database (free available at <a href="https://www.ncbi.nlm.nih.gov/">https://www.ncbi.nlm.nih.gov/</a>) was employed in the extension of subject words. In this paper, "Atopic Dermatitis" and "traditional Chinese Medicine" are two key subject words in this paper. After searching "Atopic Dermatitis" in MeSH, concept, subheadings, MeSH unique ID, entry terms and MeSH categories of Atopic Dermatitis were illustrated and based on these, "Atopic Dermatitis" were extended into nine terms: Atopic Dermatitis, Neurodermatitis Atopic, Atopic Neurodermatitis,

Neurodermatitis Disseminated, Disseminated Neurodermatitis, Eczema Atopic, Atopic Eczema, Eczema Infantile and Infantile Eczema. Senior researcher Feng, who majors in dermatology, analyzed and narrowed them down to the following five terms: atopic dermatitis, atopic dermatitis, atopic eczema, and eczema. Same operation was carried out for "traditional Chinese Medicine" and in the end eight terms were determined: Medicine Chinese Traditional, Traditional Chinese Medicine, Chung I Hsueh, Hsueh Chung I, Traditional Medicine Chinese, Zhong Yi Xue, Chinese Traditional Medicine and Chinese Medicine Traditional.

The detailed retrieval formulae were: TS = (Dermatitis Atopic OR Atopic Dermatitis OR Eczema Atopic OR Atopic Eczema OR Eczema) AND TS = (Medicine Chinese Traditional OR Traditional Chinese Medicine OR Chung I Hsueh OR Hsueh Chung I OR Traditional Medicine Chinese OR Zhong Yi Xue OR Chinese Traditional Medicine OR Chinese Medicine Traditional) AND DT = (Article OR Review) AND LA = (English). The publication date was settled from 2004-01-01 to 2023-12-31 with a time span of 20 years.

At last, the selected publications were exported to "Plain Text File" in the format of "Full Record and Cited References" and saved as data samples for analysis in CiteSpace (Supplementary File 1: Original data for CiteSpace), while to "Tab Delimited File" in the format of "Full Record and Cited References" for analysis in VOSViewer (Supplementary File 2: Original data for VOSViewer). Those two Supplementary Files are accessible for data analysis and verification.

## Data Analysis and Visualization

Microsoft Excel was used to create statistical tables and charts. For bibliometric analysis CiteSpace 6.2.6 (free available at <a href="http://cluster.ischool.drexel.edu/~cchen/citespace/download/">http://cluster.ischool.drexel.edu/~cchen/citespace/download/</a>) and VOSViewer 1.6.20 (free available at <a href="https://www.vosviewer.com/download">https://www.vosviewer.com/download</a>) were both employed for knowledge mapping of TCM in the treatment of AD. These tools help us visualize cooperation networks of countries, institutions, and authors, but also examine co-citation and co-occurrence patterns. Based on bibliometric analyses, keyword co-occurrence, clustering and timeline maps were drawn, which provided an efficient way to understand the research status, hotspots and future trends of TCM in the treatment of AD.

#### Results

#### Inclusion of Publications

According to the flowchart shown in Figure 1, 252 results were identified as TCM-intervening-AD-related publications and downloaded for analysis on Jan. 30th Jan. 2024. These 252 articles were published in 133 journals and authored by 1204 researchers affiliated with 365 institutions in 24 countries/regions.

#### Trends in the Growth of Publications

The results of the number of annual publications and cumulative annual publications in the field of TCM in the intervention of AD are shown in Figure 2, with data sourced from the WOSCC database. Overall, the number of annual publications has almost quintupled in the past 20 years, increasing from 6 in 2004 to 28 in 2023. According to the results, the output of publications in the first nine years, namely from 2004 to 2012, exhibited a low account, with the maximum number of annual publications being less than 10. It showed considerable growth in 2013, with 21 published articles. The cumulative annual publication curve increased significantly over the next nine years (2013–2021), although the number of annual publications increased and decreased, bouncing between 13 and 23. It has demonstrated promising and steady growth since 2022 although only two-year-data collected, with 25 and 28 articles published in 2022 and 2023, respectively, and the number of cumulative annual publications exceeded 250 by the end of 2023. Accordingly, the period 2004–2012 is described as the slow growth period of TCM-treating-AD research development, 2013–2021 as the fluctuating growth period and 2022–2023 as the steady growth period.

Details of development trends in the field of TCM-intervening-AD were acquired by comparing differences in Web of Science categories, countries/regions, and authors. During the slow growth period (2004–2012), the top category was "dermatology", with the following three closely related to integrative medicine and pharmacology. "Allergy" got its only chance to hit the top-5 list, which was replaced by other categories in the other two periods, such as "Chemistry

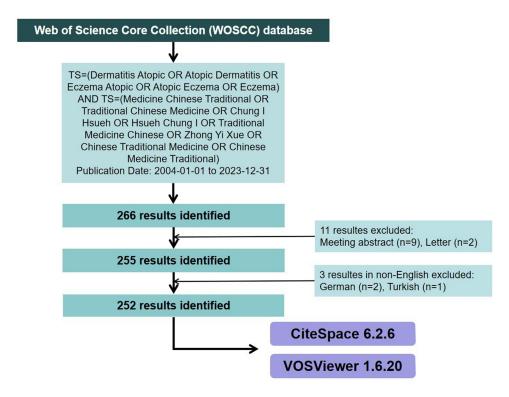


Figure I Detailed flowchart of data search and exclusion criteria for TCM-intervening-AD-related publications.

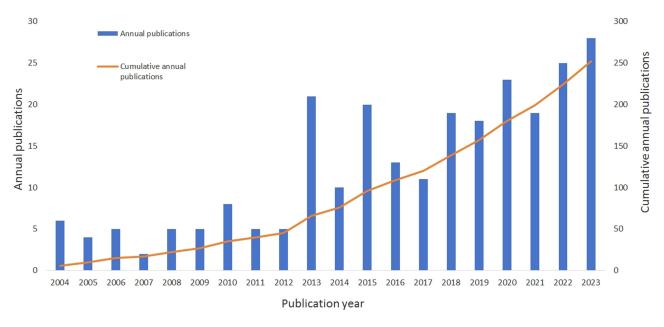


Figure 2 Trend graph of the growth of annual and cumulative annual publications on TCM treating AD.

Pharmacy" "Plant Science" "Biochemistry Molecular Biology" and so on. It offered us a reasonable guess, researchers deviated the emphasis from "TCM can treat AD" to "which kind of TCM treats AD more efficiently and why" which meant in the steady growth period more and more attentions were paid to figure out the chemicals and mechanism of TCM. Further studies are needed to verify this hypothesis. For instance, sorting the 252 results by "Date: newest first" in WOSCC database, the first three published articles were all studied the mechanism of TCM intervening AD based on a specific target or signal pathway, for example, "Oral administration of vermicompost tea ameliorates eczema skin

inflammation via regulation of Th2 immune response." However, the precise research hotspots and development patterns of keywords during different periods remain unclear.

## Cooperation Network Analysis

The results of countries/regions and author rankings by publication number show that the top list differed significantly in different periods. China was ranked first in all three periods, with percentages of 55% (25 records), 68% (107 records) and 89% (47 records), respectively. However, those in the second and third places changed from Japan and the USA, the USA and South Korea to South Korea and England. Obviously, this field has attracted an increasing number of international studies from China to England and from Asia to Europe. In the perspective of author analysis, "Leung Ting-Fan" (10 records) and "Leung Ping-Chung" (13 records) occupied the first place in the slow and fluctuating growth periods, respectively, and those two authors are all from Hong Kong China. Unexpectedly, in the steady growth period, in the top-10 list, almost all authors were affiliated with institutions in mainland China and none from Hong Kong. It could not provide us with more detailed information about the cooperation situation of countries and authors until the cooperation network was performed. Therefore, a visualization analysis based on knowledge mapping was conducted to enlighten us.

#### Country/Region Cooperation Network Analysis

A cooperation network analysis was performed by applying CiteSpace, with country as the node type (Figure 3A; N = 24; E = 40; Density = 0.1449). A relatively strong international collaboration among countries/regions is illustrated in Figure 3A, where the size of the node represents the number of publications and a larger node indicates more publications. The largest node came from China, emerging as the leading contributor with 145 publications, followed by the USA (30), South Korea (22), Taiwan (21) and Japan (15) (Table 1). From the perspective of publication quantity, China published much more articles than the others, almost fivefold as many as the second-ranked the USA. However, in terms of centrality, the highest value is from the USA, indicating that it currently has the most international influence in this field.

Computed according to the centrality value, the outermost rose pink ring of each circle represents the research impact and a thicker ring indicates a higher research impact. The top six countries/regions with the greatest impact were China, the USA, South Korea, the U Arab Emirates, Malaysia and India, all with significant rose pink rings. It is noteworthy that the Arab Emirates currently hold the second-highest research impact, with only two publications. As interesting as the Arab Emirates, there are other countries/regions with high impact, but with a low amount of publications, such as Malaysia, India and Bangladesh.

The difference in color of nodes represents the difference in the year of publication, the darkest the oldest, and the brightest the newest. Among the top five countries/regions in terms of publications, the darkest area is Japan and China; in other words, the earliest studies came from these two. However, Japan has barely been published in the last five years because of a lack of bright colors. The brightest zone appears in China and South Korea, which means that the latest research has been implemented in these two countries/regions. Of the latest 28 articles published in 2023, 25 were from China and 3 from South Korea. Chinese authors in this field are very active, innovative and productive, with the highest number of publications.

#### Institution Cooperation Network Analysis

Setting institution as the node type, a knowledge graph of the institution cooperation network was obtained based on CiteSpace (Figure 3B; N = 270; E = 380; Density = 0.0105). The collaboration intensity of institutions was not as strong as that of the countries/regions. The node size of Chinese University Hong Kong is the largest, with 33 records, but with only two partners: Hong Kong Polytechnic University and Macau Science & Technology. It also contains a light-gray zone, which means that the earliest research came from this university. Nevertheless, it shows no yellow, orange, or red colors, which means that there have been no publications in the last three years.

A close-knit group appeared in 2013 (purple zone) with more than 20 members, such as Chang Gung University, China Med University, and Natural Yang Ming University. However, this group did not include

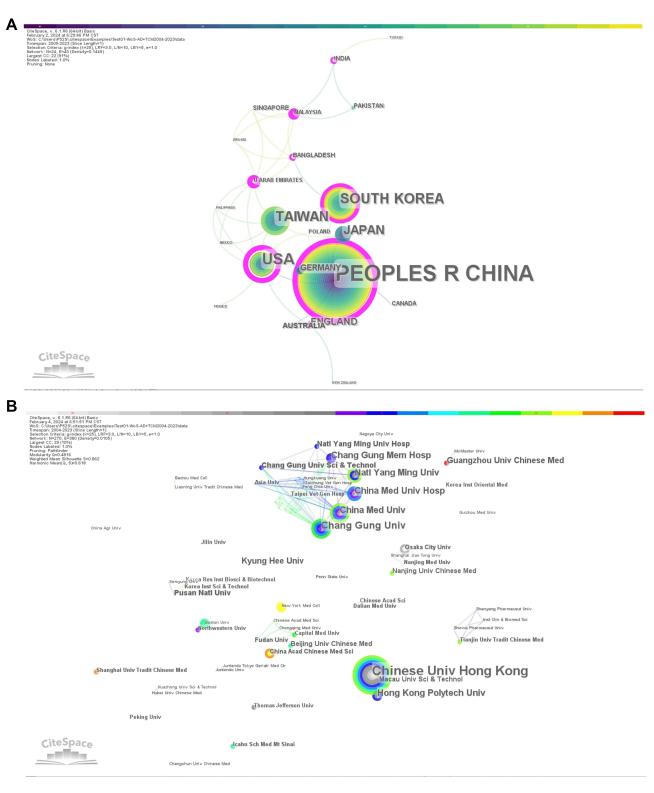


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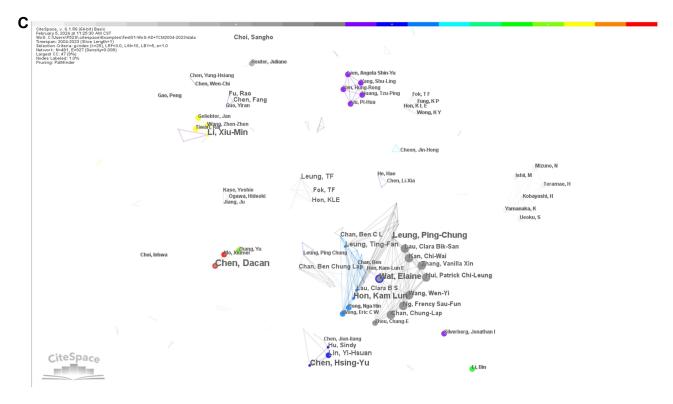


Figure 3 Cooperation network for TCM treating AD studies ((A) Countries/regions; (B) Institutions; (C) Authors).

the most recent articles. The yellow, orange and red nodes cover only four institutions: Guangzhou University Chinese Med, Shanghai University Chinese Med, China Acad Chinese Med Sci and New York Med Coll. Guangzhou University Chinese Medicine had only one partnership with McMaster University, and Shanghai University Chinese Medicine did not cooperate with any other institutions. Although the other two, China Acad Chinese Med Sci and New York Med Coll, did not show a direct connection with each other, they were both in the same cooperative network with five other institutions: Beijing University Chinese Med, Fudan University, Capital Med University, Chongqing Medical University and Chinese Acad Med Sci.

#### Author Collaboration Network Analysis

According to the analysis results of the authors based on source data from the WOSCC, the top two authors in terms of the number of publications were Leung Ping-Chung (20 records) and Leung Ting-Fan (15 records), both affiliated with the Chinese University of Hong Kong. Hon Karn-Lun Ellis from Hong Kong Children's Hosp took third place, with 12 records. Figure 3C (N = 481; E = 927; Density = 0.008), it shows relatively poor international cooperation, especially across countries. Authors in this field tend to collaborate with colleagues or scholars from the same area or country. For example, researchers from Hong Kong, such as Leung Ping-Chung, Hon Karn-Lun Ellis, Chan Ben C L, and so on, collaborated with each other closely in the slow growth period (being greyed in Figure 3C) and also in the fluctuating growth period (being blued in Figure 3C) but did not look for international cooperation. Meanwhile, a purple group of authors from South Korea did not cooperate abroad. Only one or two types of colors indicate that the group did not have a continuous research pattern. The latest publications with yellow and red nodes are from Li Xiu-Min (New York Medical College) and Chen Dacan (Guangdong Prov Hosp Chinese Medical Center). After examining their publications, both their teams had strong overseas partnerships. Therefore, authors from different countries should strengthen their communication and cooperation to explore innovative, high-level research in this field.

**Table 1** Top 15 Countries/Regions in Terms of Publications on TCM Treating AD

No.	Countries/Regions	Publications	Percentage (%)	Centrality
I	PEOPLES R CHINA	145	60.92%	0.43
2	USA	30	12.61%	0.7
3	SOUTH KOREA	22	9.24%	0.11
4	TAIWAN	21	8.82%	0.08
5	JAPAN	15	6.30%	0.04
6	ENGLAND	7	2.94%	0.16
7	GERMANY	5	2.10%	0.01
8	AUSTRALIA	4	1.68%	0
9	INDIA	3	1.26%	0.16
10	BANGLADESH	3	1.26%	0.14
П	CANADA	3	1.26%	0
12	PAKISTAN	3	1.26%	0
13	SINGAPORE	3	1.26%	0
14	U ARAB EMIRATES	2	0.84%	0.63
15	MALAYSIA	2	0.84%	0.43

According to Price's theory,<sup>26</sup> formula (1) describes the method of calculating the number of articles by the core author:

$$N = 0.747 (N_{\text{max}})^{1/2} \tag{1}$$

N: minimum number of articles that the core author should publish.

N<sub>max</sub>: number of articles by top 1 author in terms of publications in the statistical year;

Therefore, the core authors in this field should publish more than 3.3 articles according to Formula (1). Based on the source data for this research, only 45 authors have published at least 4 papers. Hence, among 1204 authors in the field of TCM treating AD, the percentage of core authors was only 3.7%.

## Research Hotspots and Trends

Co-occurrence analysis, co-occurrence clustering analysis and timeline visualization and burst analysis of keywords could vividly give us insights into research hotspots and trends, which all could be operable and achieved in CiteSpace.

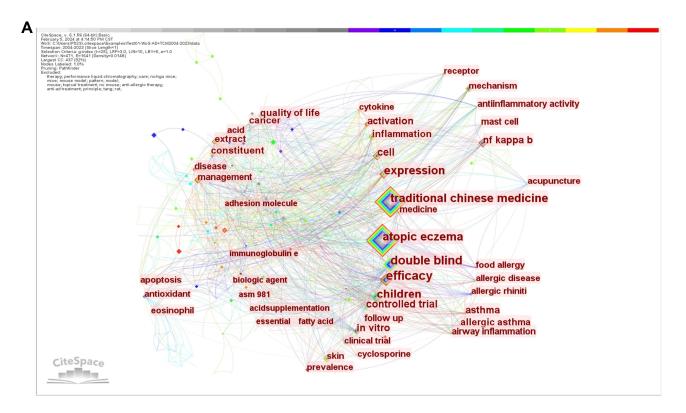
It was unavoidable that one concept would come up with various expressions. For example, when related to the concept of traditional Chinese medicine, different phrases were used, such as Chinese herbal medicine, Chinese medicinal plants, and Chinese patent medicine.

It is necessary to merge them before conducting further research on keyword co-occurrence, clustering, and burst analysis, which is practical in CiteSpace, by editing the ALIAS file. Subsequently, the concept of traditional Chinese medicine was profiled from 70 to 121 records, containing 32 different phrases. Likewise, the count of atopic eczema ranged from 135 to 166 by merging 17 different phrases such as atopic dermatitis, allergic contact dermatitis, atopic eczema topic eczema, etc.

In addition, words such as mice, rats, models, and care were of no practical meaning for this research and were eliminated by adding them to the EXCLUSION file.

#### Keyword Co-Occurrence Analysis

Using keyword as the node type, a keyword co-occurrence network was obtained (Figure 4A; N = 471; E = 1641; Density = 0.0148). It was very tightly structured, with the most frequent occurrence being "atopic eczema" (166 counts),



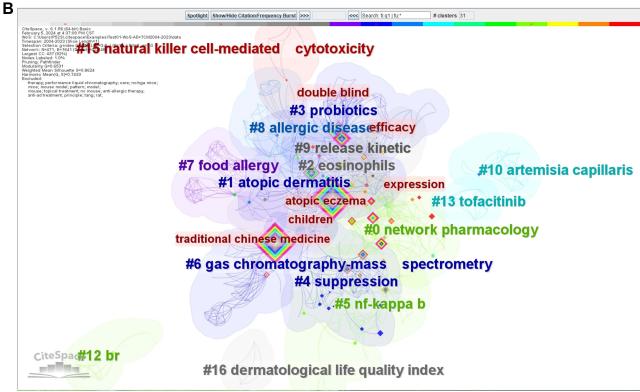


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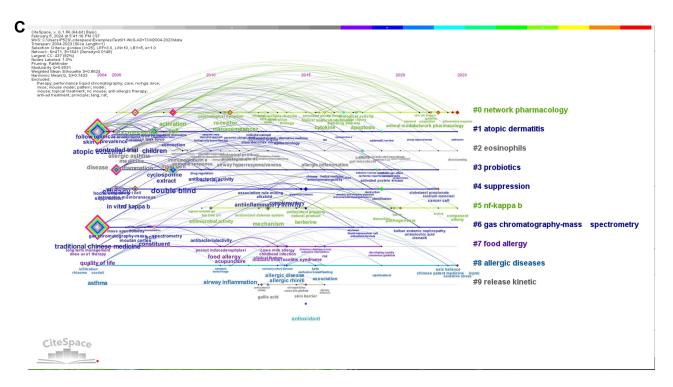


Figure 4 Knowledge mapping of keyword co-occurrence analysis in the field of TCM treating AD ((A) Keyword co-occurrence network; (B) Keyword co-occurrence clustering analysis; (C) Timeline visualization of keyword co-occurrence clustering analysis).

followed by "traditional chinese medicine" (121 counts), "double blind" (34 counts), "efficacy" (28 counts), "children" (25 counts) and "expression" (19 counts). There were 11 keywords with centrality greater than 0.1, namely "cell" "controlled trial" "in vitro" "activation" and "extract", in addition to the words mentioned above. Keywords such as "traditional chinese medicine" "double blind" "efficacy" "controlled trial" "in vitro" and "disease" covered topics too broad to accurately figure out the popular research trends in this field. On the contrary, there are keywords that help us determine the hotspots, including "children" "cell" "activation" "nf kappa b" "inflammation" "asthma" "extract" "management" and "cytokine."

#### Keyword Co-Occurrence Clustering Analysis and Timeline Visualization

Co-occurrence clustering analysis was performed using keywords as the node type, the 16 most popular and active clusters are shown in Figure 4B. The value of Modularity Q (0.6531) was higher than 0.3, indicating that the cluster structure divided by the keyword was significant. The first cluster (#0 network pharmacology) was the most dominant cluster with the largest area. The second largest cluster is #1 atopic dermatitis, and so on. Table 2 summarizes the main characteristics of the ten keyword clusters. It is easy to notice that all silhouette values are higher than 0.7, indicating that these clusters are all compelling.

Then, a timeline visualization of keyword co-occurrence clustering analysis was performed to explore the historical growth rules of the clusters over time, as illustrated in Figure 4C. Among these 10 clusters, studies on network pharmacology, nf-kappa b and allergic diseases are popular. The development of network pharmacology originated in 2005 and has remained active in recent years, with green and red lines. Although "nf-kappa b" did not attract researchers' attention until 2010, it showed good momentum. There are new directions in these three popular trends: the inflammatory response, pathogenesis and oxidative stress.

#### Keyword Burst Analysis

The analysis of keyword bursts provided insights into hot trends in keywords and their temporal distribution. Figure 5 depicts an emerging map of the frequency of occurrence of the top 20 keywords with the strongest citation, where the light blue line segment indicates that a paper has not yet been published, and the dark blue line indicates the publication

Cluster ID LLR Label(s) Size Silhouette Mean (Year) 0 60 0.793 2016 Network pharmacology Τ 58 0.848 2010 Atopic dermatitis 2 Eosinophils 48 0.857 2011 3 0.882 2013 **Probiotics** 46 42 2013 Suppression 0.859 5 40 0.745 2017 nf-kappa b 6 Gas chromatography-mass spectrometry 33 0.94 2011 7 32 0.869 2010 Food allergy 27 0.914 2012 8 Allergic diseases 9 15 0.924 2013 Release kinetic

 Table 2 The Characteristics Summary of Keywords Clusters

of a paper. The red line indicates the burst cycle, and its starting point marks the beginning of the burst cycle, whereas its end point marks the end of the burst cycle. The begin and end year of the keyword burst were listed next to the line segments, for instance, the keyword "prevalence" had its burst from 2011 to 2014 with a strength of 1.92. Keywords with a greater strength value have attracted more attention from researchers in this field.

As shown in Figure 5, "follow up" "inflammation" and "expression" were the top three keywords with the highest strength values. The difference is that the former appeared in 2008 and ended in 2008, when the latter two were active in the last three years, from 2021 to 2023. The keywords primarily included "follow up" "remedy" "controlled trial" "mast cell" and "prevalence", which experienced their burst in the slow growth period from 2004 to 2012. Between 2013 and 2020, researchers began to discuss the complication of AD, to explore the active chemical components of TCM for AD treatment and to conduct pharmacological study, such as "allergic rhiniti" "antioxidant" "gallic acid" "constituent" and "animal model". Among them, some keywords like "management" "activation" and "cell" were still popular in recent years. During the last period (2021–2023), keywords were closely related to pathogenesis and mechanism research, including "inflammation" "expression" and "cytokine".

## Research Frontiers from the Perspective of Citation

The number of citations is an important metric that shows the quality and academic impact of publications. However, a certain amount of time is required for publications to accumulate higher citations. In this paper, the average citation per year (ACY) score was employed to eliminate the time bias for a fairer comparison and reliable conclusions.<sup>27</sup> Formula (2) shows the way to calculate ACY.

$$ACY = total \ citation/(2023 - publication \ year + 1)$$
 (2)

#### Most-Cited Publications Analysis

The top 20 most-cited publications are listed in Table 3 and are sorted in descending order according to the number of citations. The greatest number of citation, 198, comes from the publication titled "Coptidis Rhizoma: a comprehensive review of its traditional uses, botany, phytochemistry, pharmacology and toxicology" with the corresponding authors from Chengdu Univ Tradit Chinese Med, Sichuan, China, followed by "Sophora flavescens Ait.: Traditional usage, phytochemistry and pharmacology of an important traditional Chinese medicine" (189 citations)<sup>29</sup> and "IL33: Roles in Allergic Inflammation and Therapeutic Perspectives" (162 citations).<sup>30</sup> Those three articles are also the top 3 in terms of ACY, higher than 18 while the fourth ACY is only 8.73. The journals and their impact factors (IF) in 2022 are summarized in Table 3. The JOURNAL OF THE AMERICAN ACADEMY OF DERMATOLOGY has the highest IF

#### Top 20 Keywords with the Strongest Citation Bursts Keywords Year Strength Begin End 2004 - 2023 2004 3.28 **2004** 2008

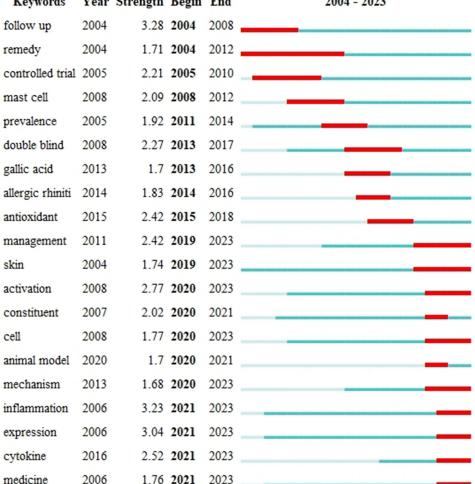


Figure 5 Knowledge map of top 20 keywords with the strongest citation bursts.

(13.8), and the JOURNAL OF ETHNOPHARMACOLOGY has the most publications (4). There are seven reviews on different herbal medicines, such as "Coptidis Rhizoma", "Sophora flavescensi", "Psoralea Corylifoliai", "Phellodendri Cortex" and so on, which were all applied in the treatment of AD.

#### Leading Co-cited Journals and Authors Analysis

A co-citation map was created using VOSViewer based on bibliographic data. Choosing "Cited sources" and "Cited authors" as the unit of analysis, respectively, the knowledge map of leading co-cited journals and authors analysis was obtained (Figure 6). As shown in Figure 6A, "J ETHNOPHARMACOL" "J ALLERGY CLIN IMMUN" and "BRIT J DERMATOL" had the largest number of citations, namely 130, 128, and 122, respectively (Table 4). However, from the perspective of centrality value, the greatest value comes from "AM J CHINESE MED" (0.17), followed by "ACTA DERM-VENEREOL" (0.14) and "BIOL PHARM BULL" (0.13). It is worth mentioning that "LANCET" ranked at fourth with 90 citations in this field.

As shown in Figure 6B, "hon kle" (Hon Karn-Lun Ellis) was the leading author who contributed the most citations. There are three other authors also played important roles in this field, including "sheehan mp" (Sheehan Michael Patrick), "leung dym" (Leung Donald Ym), and "chen hy" (Chen Hsing-Yu). However, "sheehan mp" was related to "hon kle" in

Table 3 Top 20 Most-Cited Publications on TCM Treating AD

Rank	Articles	Citations	ACY	Торіс	Journal	IF (2022)
I	Wang J, Wang L, Lou G H, Zeng H R, Hu J, Huang Q W, Peng W, Yang X B (2019). Coptidis Rhizoma: a comprehensive review of its traditional uses, botany, phytochemistry, pharmacology and toxicology. Pharmaceutical Biology, 57(1): 193–225	198	33	Review on TCM	PHARMACEUTICAL BIOLOGY	3.8
2	He X R, Fang J C, Huang L H, Wang J H, Huang X Q (2015). Sophora flavescens Ait.: Traditional usage, phytochemistry and pharmacology of an important traditional Chinese medicine. Journal of Ethnopharmacology, 172: 10–29	189	18.9	Review on TCM	JOURNAL OF ETHNOPHARMACOLOGY	5.4
3	Chan B C L, Lam C W K, Tam L S, Wong C K (2019). IL33: Roles in Allergic Inflammation and Therapeutic Perspectives. Frontiers in Immunology, 10: 11	162	27	Others	FRONTIERS IN IMMUNOLOGY	7.3
4	Reuter J, Merfort I, Schempp C M (2010). Botanicals in Dermatology An Evidence-Based Review. American Journal of Clinical Dermatology, 11(4): 247–267	131	8.73	Review on TCM	AMERICAN JOURNAL OF CLINICAL DERMATOLOGY	7.3
5	Hon K L E, Leung T F, Ng P C, Lam M C A, Kam W Y C, Wong K Y, Lee K C K, Sung Y T, Cheng K F, Fok T F, Fung K P, Leung P C (2007). Efficacy and tolerability of a Chinese herbal medicine concoction for treatment of atopic dermatitis: a randomized, double-blind, placebo-controlled study. British Journal of Dermatology, 157(2): 357–363	116	6.44	Prevention and treatment	BRITISH JOURNAL OF DERMATOLOGY	10.3
6	Deng C H, Yao N, Wang B, Zhang X M (2006). Development of microwave-assisted extraction followed by headspace single-drop microextraction for fast determination of paeonol in traditional Chinese medicines. Journal of Chromatography A, 1103(1): 15–21	111	5.84	Others	JOURNAL OF CHROMATOGRAPHY A	4.1
7	Leung D Y M, Nicklas R A, Li J T, Bernstein I L, Blessing-Moore J, Boguniewicz M, Chapman J A, Khan D A, Lang D, Lee R E, Portnoy J A, Schuller D E, Spector S L, Tilles S A (2004).  Disease management of atopic dermatitis: an updated practice parameter. Annals of Allergy Asthma & Immunology, 93(3): S1-S21	110	5.24	Others	ANNALS OF ALLERGY ASTHMA & IMMUNOLOGY	5.9
8	Tsang M S M, Jiao D L, Chan B C L, Hon K L, Leung P C, Lau C B S, Wong E C W, Cheng L, Chan C K M, Lam C W K, Wong C K (2016). Anti-Inflammatory Activities of Pentaherbs Formula, Berberine, Gallic Acid and Chlorogenic Acid in Atopic Dermatitis-Like Skin Inflammation. Molecules, 21(4): 21	99	11	Pharmacological research	MOLECULES	4.6
9	Alam F, Khan G N, Bin Asad M H H (2018). <i>Psoralea corylifolia</i> L: Ethnobotanical, biological, and chemical aspects: A review. Phytotherapy Research, 32(4): 597–615	86	12.29	Review on TCM	PHYTOTHERAPY RESEARCH	7.2
10	Tan H Y, Zhang a L, Chen D C, Xue C C, Lenon G B (2013). Chinese herbal medicine for atopic dermatitis: A systematic review. Journal of the American Academy of Dermatology, 69 (2): 295–304	83	6.92	Review on TCM	JOURNAL OF THE AMERICAN ACADEMY OF DERMATOLOGY	13.8
П	He H, Zang L H, Feng Y S, Chen L X, Kang N, Tashiro S, Onodera S, Qiu F, Ikejima T (2013). Physalin A induces apoptosis via p53-Noxa-mediated ROS generation, and autophagy plays a protective role against apoptosis through p38-NF-κB survival pathway in A375-S2 cells. Journal of Ethnopharmacology, 148(2): 544–555	74	6.17	Pharmacological research	JOURNAL OF ETHNOPHARMACOLOGY	5.4

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Table 3 (Continued).

Rank	Articles	Citations	ACY	Торіс	Journal	IF (2022)
12	Krishna P M, Rao K N V, Sandhya S, Banji D (2012). A review on phytochemical, ethnomedical and pharmacological studies on genus <i>Sophora</i> , Fabaceae. Revista Brasileira De Farmacognosia-Brazilian Journal of Pharmacognosy, 22(5): 1145–1154	70	5.38	Review on TCM	REVISTA BRASILEIRA DE FARMACOGNOSIA-BRAZILIAN JOURNAL OF PHARMACOGNOSY	1.6
13	Sun Y, Lenon G B, Yang a W H (2019). Phellodendri Cortex: A Phytochemical, Pharmacological, and Pharmacokinetic Review. Evidence-Based Complementary and Alternative Medicine, 2019: 45	65	10.83	Review on TCM	EVIDENCE-BASED COMPLEMENTARY AND ALTERNATIVE MEDICINE	2.65
14	Chan B C L, Hon K L E, Leung P C, Sam S W, Fung K P, Lee M Y H, Lau H Y A (2008). Traditional Chinese medicine for atopic eczema: PentaHerbs formula suppresses inflammatory mediators release from mast cells. Journal of Ethnopharmacology, 120(1): 85–91	65	3.82	Pharmacological research	JOURNAL OF ETHNOPHARMACOLOGY	5.4
15	Cheng H M, Chiang L C, Jan Y M, Chen G W, Li T C (2011). The Efficacy and Safety of a Chinese Herbal Product (Xiao-Feng-San) for the Treatment of Refractory Atopic Dermatitis: A Randomized, Double-Blind, Placebo-Controlled Trial. International Archives of Allergy and Immunology, 155(2): 141–148	63	4.5	Prevention and treatment	INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY	2.8
16	Gao B B, Wang R J, Peng Y, Li X B (2018). Effects of a homogeneous polysaccharide from Sijunzi decoction on human intestinal microbes and short chain fatty acids in vitro. Journal of Ethnopharmacology, 224: 465–473	62	8.86	Pharmacological research	JOURNAL OF ETHNOPHARMACOLOGY	5.4
17	He H, Feng Y S, Zang L H, Liu W W, Ding L Q, Chen L X, Kang N, Hayashi T, Tashiro S, Onodera S, Qiu F, Ikejima T (2014). Nitric oxide induces apoptosis and autophagy; autophagy down-regulates NO synthesis in physalin A-treated A375-S2 human melanoma cells. Food and Chemical Toxicology, 71: 128–135	59	5.36	Pharmacological research	FOOD AND CHEMICAL TOXICOLOGY	4.3
18	Gao X K, Fuseda K, Shibata T, Tanaka H, Inagaki N, Nagai H (2005). Kampo medicines for mite antigen-induced allergic dermatitis in NC/Nga mice. Evidence-Based Complementary and Alternative Medicine, 2(2): 191–199	58	2.9	Pharmacological research	EVIDENCE-BASED COMPLEMENTARY AND ALTERNATIVE MEDICINE	2.65
19	Kobayashi H, Ishii M, Takeuchi S, Tanaka Y, Shintani T, Yamatodani A, Kusunoki T, Furue M (2010). Efficacy and Safety of a Traditional Herbal Medicine, <i>Hochu-ekki-to</i> in the Long-term Management of Kikyo (Delicate Constitution) Patients with Atopic Dermatitis: A 6-month, Multicenter, Double-blind, Randomized, Placebo-controlled Study. Evidence-Based Complementary and Alternative Medicine, 7(3): 367–373	57	3.8	Prevention and treatment	EVIDENCE-BASED COMPLEMENTARY AND ALTERNATIVE MEDICINE	2.65
20	Hon K L E, Ma K C, Wong Y, Leung T F, Fok T F (2005). A survey of traditional Chinese medicine use in children with atopic dermatitis attending a paediatric dermatology clinic. Journal of Dermatological Treatment, 16(3): 154–157	57	2.85	Prevention and treatment	JOURNAL OF DERMATOLOGICAL TREATMENT	2.9

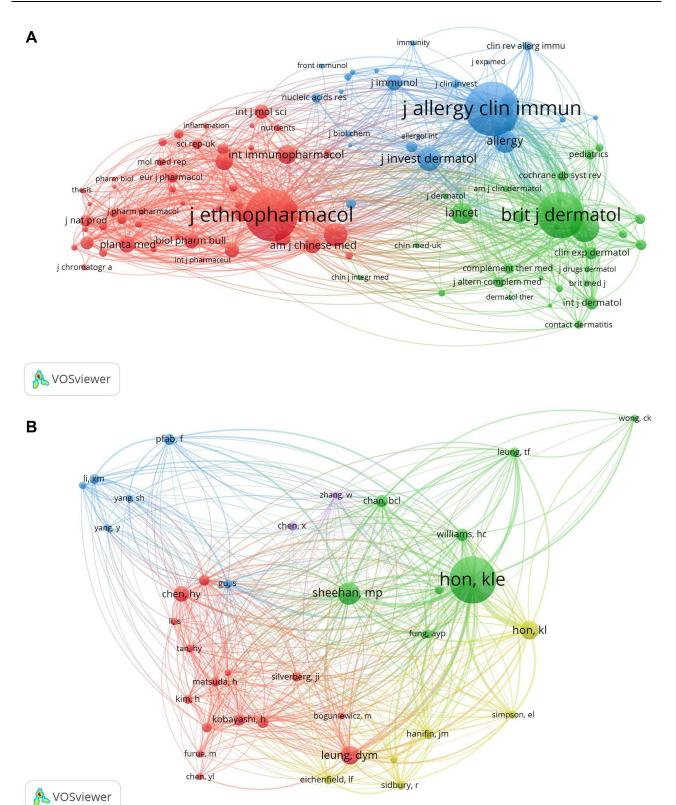


Figure 6 Knowledge map of leading co-cited journals and authors analysis ((A) Journals; (B) Authors).

Table 4 Top 15 Most-Cited Journals

Rank	Journals	Citations	Centrality	
1	J ETHNOPHARMACOL	130	0.01	
2	J ALLERGY CLIN IMMUN	128	0.03	
3	BRIT J DERMATOL	122	0.02	
4	ALLERGY	91	0.09	
5	LANCET	90	0.07	
6	J AM ACAD DERMATOL	84	0.02	
7	J INVEST DERMATOL	71	0.03	
8	EVID-BASED COMPL ALT	70	0.05	
9	INT IMMUNOPHARMACOL	68	0.02	
10	PLOS ONE	63	0.05	
11	MOLECULES	57	0.02	
12	ACTA DERM-VENEREOL	53	0.14	
13	AM J CHINESE MED	50	0.17	
14	PHYTOTHER RES	47	0.03	
15	BIOL PHARM BULL	46	0.13	

the academic community, sharing the same green network. The green network also had other important contributors, such as "chan bel" (Chan Ben Chung-Lap), "Williams he" (Williams Hywel C), and "leung tf" (Leung Ting-Fan).

#### Discussion

Several limitations should be discussed for the improvement of further research. First, while conducting data retrieval, only one database, WOSCC, was utilized in this investigation, potentially resulting in the exclusion of other important and valuable sources, such as Scopus. In addition, data retrieval was completed in January 2024, and some of the latest publications may not have been included in our research, which indicates that some research outcomes related to TCM treating AD may have been overlooked. Second, the search and collection of documents are always in a balance of completeness and accuracy. In this study, although it turns out to be practical and effective to improve the accuracy and completeness of subject-term retrieval by applying MeSH database, the lack of an unified expression of TCM and the diversity of TCM intervention means could still directly result in poor completeness and accuracy. All in all, in the future, more databases should be used for data retrieval, and more bibliometric tools should be applied.

Taking second thought of the results of country/region cooperation network analysis, there are some countries/regions with high impact, but with a low amount of publications, such as U Arab Emirates, Malaysia, India and Bangladesh. This gave us an unneglectable hint that studies from these countries/regions are worth investigating. For example, as one of the only two articles tagged to U Arab Emirates, the research titled "Epidemiology, Diagnosis, and Treatment of Atopic Dermatitis in the Developing Countries of Asia, Africa, Latin America, and the Middle East: A Review" was published in 2019. It was first proposed that patients with AD from different countries or areas should be treated differently because some features of AD may be more or less prominent in patients with darker skin owing to the lack of consistent diagnostic criteria and consistent treatment guidelines. In addition, this study explored the topic of drug pharmacokinetics in varying ethnicities and adverse effects in different skin physiologies, which at the time was referentially valuable for other scholars conducting research related to TCM treating AD.

Furthermore, the whole concept mentioned above is highly consistent with TCM theory of "treatment based on syndrome differentiation". In other word, different patients, even those suffering from the same disease, should be given unique and customized treatments. Most importantly, AD itself is a highly heterogeneous disease. Therefore, the individual diagnosis and treatment system and the flexible prescription and intervention profile no doubt enable TCM remarkable advantages in treating AD.

In the actual clinical application, the independent use of a single Chinese herbal medicine in the treatment of AD still has certain limitations. Taking examples of three kinds of Chinese herbs as mentioned above, namely "Coptidis Rhizoma", "Sophora flavescensi", and "Phellodendri Cortex", are all significantly effective for relieving itching, thanks for their TCM efficacies of clearing heat, drying dampness, purging fire and detoxifying. However, long-term and independent clinic use of them not only results in poor patient compliance owing to the bitter taste but also faces the risk of damage the transport function of spleen and stomach. The other kind of Chinese herbs, for instance "Psoralea Corylifoliai", its oral administration has the effect of warming kidney, and strengthening Yang whilst its external application has the effect of dispelling wind and eliminating spots. Nevertheless, long-term and independent clinic use could probably endanger the liver. Therefore, it is much safer and more effective to prescript a TCM formula containing more than only one single Chinese herb in the treatment of AD, which is also more consistent with the high heterogeneity of AD.

For example, when treating AD patients with TCM syndrome of blood vacuity and wind dryness, Danggui Yinzi (containing ten kinds of TCM decoction pieces), one of the famous TCM formula, had the TCM efficacy of nourishing blood, moistening dryness, dispelling wind and relieving itching. Although "Polygoni Multiflori Radix" in this formula has certain pharmacological toxicity, its clinic use in the form of TCM formula has a long history and reliable experience in human drug application.

It is worthy mention that even those famous TCM formula still have their limitations. They should not be used identically in every case, because at present the etiology and pathogenesis may be more complicated than before. Moreover, patient groups from different regions or of different ages may differ in TCM syndromes, in which individualized treatment based on syndrome differentiation should be considered so as for a more accurate treatment plan.

Besides, when it comes to the treatment of special groups, including infants, pregnant women, breastfeeding women and other patients with special physiological conditions, the TCM intervention method would change accordingly, such as pediatric massage, ear point pressure bean, acupuncture, fire needle and so on. Among those, pediatric massage and ear point pressure bean are both non-invasive, which are easier to accept by infants and children.

#### **Conclusion**

TCM intervention has become a mainstream complementary and alternative therapeutic option and has been widely used in the clinical treatment of AD, honored for its individualized therapeutic concepts of evidence-based treatment. Based on this research, those following topics are profiled for future study: (1) to explore the treatment guidelines and management systems of integrated Chinese and Western medicine, especially in the treatment of refractory atopic dermatitis, (2) to develop TCM external preparations for infantile acute paroxysmal rash and TCM internal preparations for children's allergy improvement, and (3) to clarify the advantages of TCM characteristic technologies in the treatment of AD and obtain high-level evidence-based clinic data, including pediatric massage, acupuncture, fire needle, moxibustion, cupping and so on.

# **Data Sharing Statement**

The original contributions of this study are included in the article and <u>Supplementary Files</u>. Further inquiries can be directed to the corresponding authors.

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#### **Disclosure**

The authors declare that this research was conducted in the absence of any commercial or financial relationships that could be construed as potential conflicts of interest.

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