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Autophagy in Traditional Chinese Medicine: Knowledge Structure, Hotspots, and Future Directions

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ABSTRACT

This study aims to examine the key research hotspots and emerging trends in autophagy within Traditional Chinese Medicine (TCM), offering a valuable reference for researchers working in this area. Using visual analysis tools and bibliometric methods, relevant literature on the application of autophagy in Traditional Chinese Medicine (TCM) was analyzed from the Web of Science Core Collection. By examining authorship, keywords, research contexts, hotspots, and emerging trends, this study systematically explored the current status and development directions of autophagy research in TCM. This study analyzed 916 publications, with Beijing University of Chinese Medicine leading in research output, followed by Shanghai University of Traditional Chinese Medicine and Guangzhou University of Chinese Medicine. Key research themes included apoptosis, activation and inhibition of pathways, oxidative stress, proliferation, NF-κB, cancer, and mTOR. The field of autophagy in TCM has grown steadily in recent years, focusing on its role in treating malignancies, atherosclerosis, and Alzheimer's disease, as well as its regulation of signaling pathways such as PI3K/AKT/mTOR, TLR4, Nrf2, and NF-κB. Emerging areas of interest are likely to include the use of TCM in overcoming chemotherapy resistance, the modulation of mitophagy, activation of autophagy-related functions, and the therapeutic potential of TCM components like luteolin in diseases including cancer, asthma, and myocardial injury.

Keywords: Autophagy, Traditional chinese medicine (TCM), Bibliometrics analysis, CiteSpace, Visualized analysis

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Introduction

Autophagy is a highly conserved process of intracellular catabolism and recycling in eukaryotic cells, responsible for degrading non-essential proteins, organelles, and macromolecules. It serves as a protective mechanism, maintaining cellular homeostasis by removing damaged structures under environmental or internal stressors. Autophagy can be triggered by hypoxia, nutrient deprivation, and oxidative stress; however, both insufficient and excessive autophagy can lead to energy deficits and ultimately autophagic cell death. This dual role in cellular protection and death parallels the Traditional Chinese Medicine (TCM) concepts of viscera deficiency, healthy qi deficiency, and pathogenic excess, reflecting the yin-yang balance at a micro level. These associations provide a theoretical basis for exploring the mechanisms by which TCM exerts its effects through autophagy.

Autophagy has been implicated in the pathogenesis of various diseases, including cancer, myopathy, neurodegenerative disorders, infections, and cardiovascular diseases. Over the past decade, TCM has contributed significantly to uncovering new pharmacological mechanisms and therapeutic applications, particularly in relation to autophagy. For example, active components from Bupleurum, Ligusticum chuanxiong, Andrographis, turmeric, and Salvia miltiorrhiza have been shown to regulate cancer, neurodegenerative, and cardiovascular diseases

through autophagic pathways. The multi-component, multi-target, and multi-pathway nature of TCM underlies its complex biological effects, making autophagy a key focus of current research.

Despite the growing number of studies on autophagy in TCM, bibliometric analyses remain scarce. Scientific knowledge mapping offers a promising approach to visualize and quantify research landscapes, enabling researchers to identify knowledge structures, trends, and emerging hotspots more efficiently. In this study, we applied knowledge mapping techniques to classify authors, institutions, keywords, research status, and the developmental trajectory of autophagy in TCM. This analysis highlights current research hotspots and future directions, providing a valuable reference for researchers in the field.

Materials and Methods

Data sources

The literature on autophagy in Traditional Chinese Medicine (TCM) was retrieved from the Web of Science Core Collection (WOS). The search strategy used the terms: "traditional Chinese medicine," "Chinese herbal medicine," "Chinese herbology," "Chinese medicine," or "Chinese herb" in combination with "autophagy", covering publications from January 1, 1985, to December 31, 2022. Initially, 921 records were identified. After filtering to include only research articles and reviews, 916 studies were retained for analysis. The full bibliographic records along with cited references were exported in TXT format to facilitate subsequent bibliometric and visualization analyses.

Data processing

CiteSpace 5.8.R3 was employed for bibliometric analysis in this study. The time span was set from January 2009 to December 2022, as the earliest studies on autophagy in TCM were published in 2009, with a time slice of one year. Node types included authors, institutions, and keywords. For authors and institutions, the threshold was set to the top 25 per slice with no pruning applied. For keywords, the top 25 per slice were selected, and the network was refined using pathfinder and merged network pruning. Based on these parameters, visual analyses were conducted to generate knowledge maps of author and institution collaborations, as well as co-occurrence, emergence, clustering, and timeline visualizations for keywords.

The WOS-retrieved literature, recorded as "full records and cited references," was exported in plain text format and imported into VOSviewer 1.6.18. Full counting was applied, and thresholds were adjusted according to each analysis type. Using this approach, collaborative networks and visual bibliometric maps were constructed to provide insights into research patterns, hotspots, and trends in the field.

Results and Discussion

Publication trend

Research on the application of autophagy in Traditional Chinese Medicine (TCM) first appeared in 2009. Cheng CY *et al.* [1] investigated the in vitro effects of Sanchong Kuijian Decoction (SJKJT) on colon cancer cells and found that SJKJT could upregulate MAP-LC3-II protein expression in colon 205 cells in a time- and dose-dependent manner. This induction of autophagy was identified as one of the biochemical mechanisms by which SJKJT inhibits the proliferation of colon 205 cells, providing foundational evidence for TCM's therapeutic potential via autophagy.

Since this initial study, research in this area has been published annually and has gradually emerged as a hotspot. The publication trends can be divided into three stages. From 2009 to 2015, studies appeared each year but in limited numbers, showing a fluctuating upward trend. Between 2016 and 2022, the annual number of publications increased steadily, surpassing 100 studies per year during 2019–2021. In 2022, publications peaked at over 200 studies. These trends indicate a growing interest and promising prospects for the application of autophagy in TCM, suggesting continued expansion of research in the coming years **(Figure 1)**.

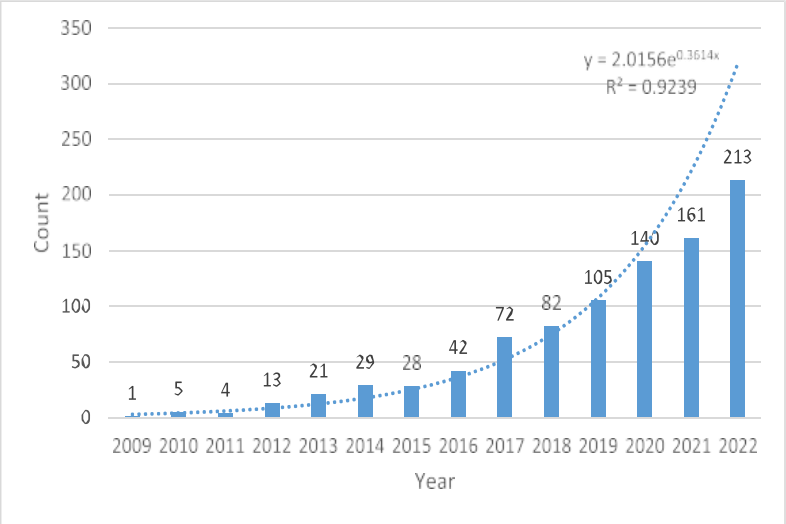


Figure 1. Growth trajectory of published studies on autophagy applications in Traditional Chinese Medicine from 2009 to 2022.

Author collaboration network and co-citation

Figure 2 presents the author collaboration network generated using CiteSpace. The network consists of 426 nodes and 578 links, with a density of 0.0064. Each node represents an individual author, while the connecting lines indicate collaborative relationships; thicker lines denote stronger collaboration [2]. Analysis shows that the team led by Ping Li primarily focuses on the mechanisms through which TCM modulates autophagy to treat conditions such as diabetic nephropathy, Alzheimer's disease, and atherosclerosis. The team led by Wei Wang concentrates on the use of TCM extracts in treating heart failure via autophagy pathways and on the protective effects of TCM against chemotherapy-induced cardiotoxicity. Overall, the author collaboration network appears relatively sparse, suggesting limited interaction between research groups, likely due to differences in research focus or target diseases. **Table 1** lists the top 10 authors and co-cited authors in this field.

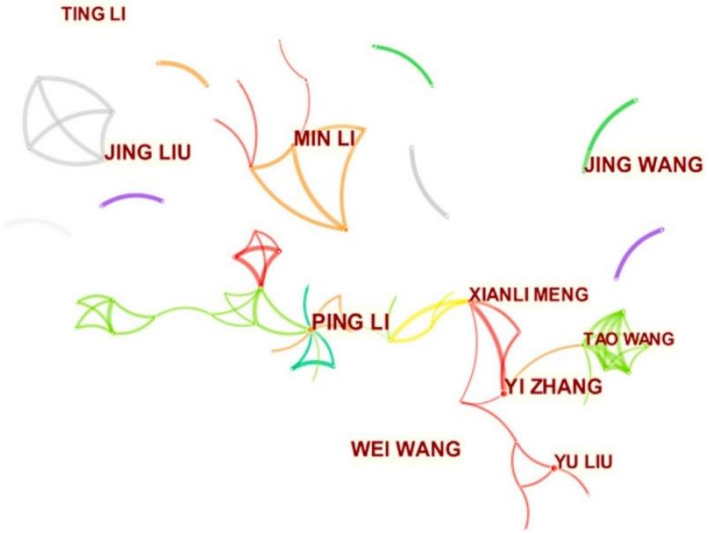


Figure 2. Network map of core authors in TCM autophagy research, showing collaborative links and dominant research clusters.

Table 1. Ranking of the top 10 authors and co-cited authors in TCM autophagy studies, highlighting prominent figures in the field.

No	Author	Count	Year	No	Source	Citations	Total link strength
1	Ping Li	9	2017	1	Mizushima,n	190	1417
2	Wei Wang	8	2017	2	Wang,y	132	2121
3	Yi Zhang	7	2021	3	Zhang,y	120	2036

4	Jing Liu	7	2011	4	Liu,j	106	1547
5	Min Li	7	2019	5	Wang,j	101	1333
6	Jing Wang	7	2015	6	Levine,b	97	841
7	Xianli Meng	6	2020	7	Klionsky,dj	96	680
8	Ting Li	6	2018	8	Li,y	94	1470
9	Yu Liu	6	2021	9	Li,j	92	1394
10	Tao Wang	5	2019	10	Zhang,l	92	1066

Figure 3. Collaboration network of institutions publishing research on autophagy in Traditional Chinese Medicine, highlighting key contributors and inter-institutional connections.

Table 2. Ten most productive institutions in TCM autophagy research, showing publication output and centrality within the field.

NO	Count	Centrality	Year	Institutions
1	46	0.15	2014	Beijing Univ Chinese Med
2	42	0.17	2012	Shanghai Univ Tradit Chinese Med
3	39	0.09	2015	Guangzhou Univ Chinese Med
4	38	0.28	2011	China Med Univ
5	31	0.2	2016	China Acad Chinese Med Sci
6	31	0.05	2014	Capital Med Univ
7	28	0.06	2019	Chengdu Univ Tradit Chinese Med
8	26	0.1	2016	Tianjin Univ Tradit Chinese Med
9	26	0.04	2017	Zhejiang Univ
10	24	0	2017	Nanjing Univ Chinese Med

Fund support
Table 3 summarizes the ten most frequently cited funding sources for research on autophagy in Traditional Chinese Medicine. All top ten funding agencies are based in China, collectively supporting 709 studies, which accounts for 77.4% of the total. Notably, the National Natural Science Foundation of China funded 499 studies, representing more than half of the total, highlighting China's emphasis on fundamental research in TCM.

Table 3. Major funding sources for research on autophagy in Traditional Chinese Medicine, ranked by number of supported studies.

Fund-supporting organization	Quantity	Percentage
National Natural Science Foundation Of China	499	54.48%
China Postdoctoral Science Foundation	39	4.26%
National Natural Science Foundation Of Guangdong Province	32	3.49%
Beijing Natural Science Foundation	23	2.51%
Natural Science Foundation Of Zhejiang Province	23	2.51%
Fundamental Research Funds For The Central Universities	22	2.40%
Ministry Of Science And Technology Taiwan	20	2.18%
National Key R D Program Of China	18	1.97%
National Key Research And Development Program Of China	17	1.86%
Natural Science Foundation Of Jiangsu Province	16	1.75%

Keywords analysis

Keywords co-occurrence analysis

Keywords provide a high-level summary of a study's core topics. Co-occurrence analysis, which visualizes the relationships among keywords, is represented by nodes (keywords) and connecting lines (co-occurrence relationships). In this study, CiteSpace was used to perform visual analysis of the included literature, generating a network of 484 nodes and 986 links, with a density of 0.0084. The top 20 keywords are listed in **Table 4**, while the keyword co-occurrence network for autophagy in TCM is shown in **Figure 4**, illustrating the main research focus in this field.

The studies primarily focus on mechanisms such as apoptosis, activation, inhibition, proliferation, and oxidative stress, with key signaling pathways including NF-κB, mTOR, and AKT. Tumor cells are the main research objects. Using VOSviewer, a keyword co-occurrence network **(Figure 5a)** and an overlay visualization map **(Figure 5b)** were generated. From 3,976 keywords, 291 were selected based on a minimum occurrence threshold of six and grouped into eight clusters: Cluster 1 (96 items): Role of TCM autophagy in tumors Cluster 2 (46 items): TCM autophagy in nervous system diseases Cluster 3 (44 items): TCM autophagy in ischemia-reperfusion injury of cardiovascular and cerebrovascular diseases Cluster 4 (33 items): Autophagy-related signaling pathways Cluster 5 (28 items): TCM autophagy in endocrine and renal diseases Cluster 6 (20 items): Mechanisms of TCM autophagy in atherosclerosis and lipid metabolism Cluster 7 (18 items): Autophagy mechanisms in angiogenesis Cluster 8 (6 items): Autophagy-mediated cell death

The overlay visualization **(Figure 5b)** incorporates a temporal dimension, with colors representing the time of keyword emergence. Earlier appearing keywords are shown in green, while more recent keywords are depicted in warmer colors, providing insight into the evolution of research trends in TCM autophagy.

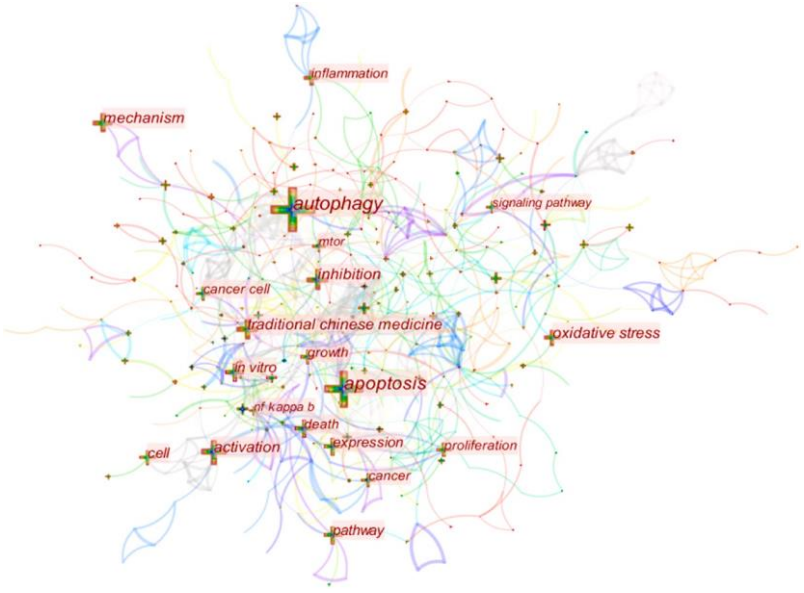
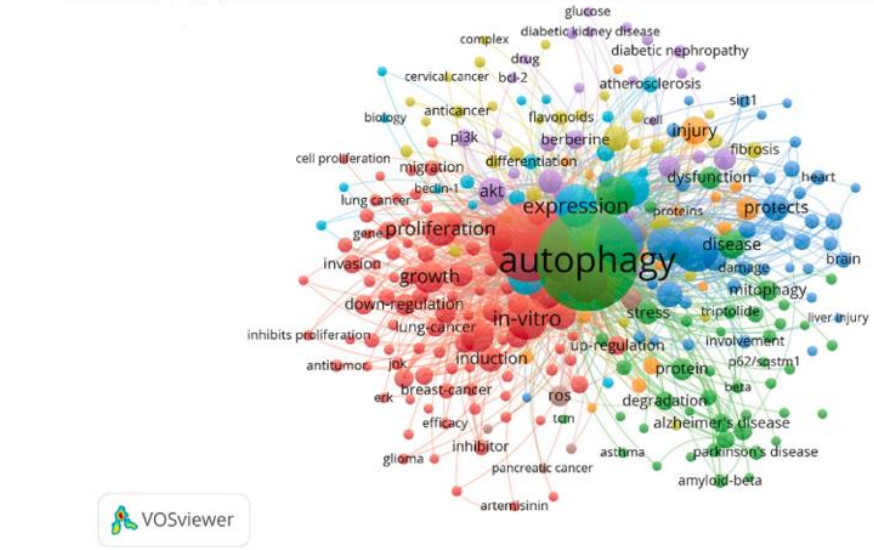
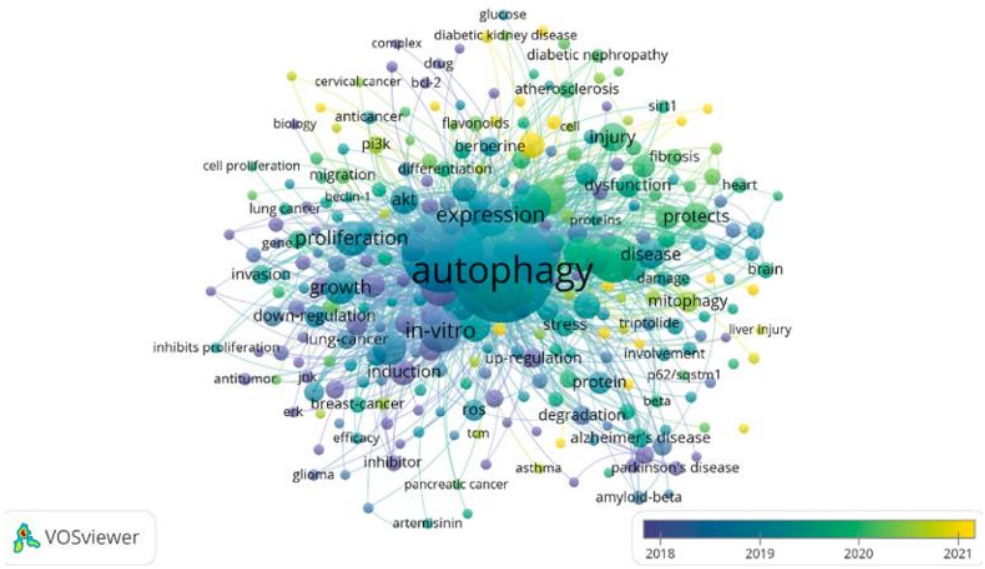


Figure 4. Keywords co-occurrence network diagram based on CiteSpace.



a)



b)

Figure 5. Visualization of keyword co-occurrence in autophagy research within Traditional Chinese Medicine. (a) Cluster map showing grouping of keywords across different research topics. (b) Overlay map illustrating the temporal evolution of keywords according to their average year of appearance.

Table 4. Top 20 keywords in terms of frequency.

Serial number	Frequency	Centrality	Year	Key words	Serial number	Frequency	Centrality	Year	Key words
1	630	0.03	2009	autophagy	11	91	0.01	2012	cell
2	393	0.02	2010	apoptosis	12	90	0.16	2010	death
3	144	0.09	2011	activation	13	76	0.04	2015	inflammation
4	119	0	2015	oxidative stress	14	73	0.07	2013	proliferation
5	118	0.06	2011	inhibition	15	69	0.01	2012	cancer
6	114	0.04	2012	traditional chinese medicine	16	61	0.04	2013	growth
7	112	0	2013	mechanism	17	61	0.06	2012	cancer cell

8	108	0	2013	expression	18	55	0.07	2013	nf kappa b
9	108	0.19	2010	in vitro	19	52	0.05	2012	mtor
10	97	0.04	2013	pathway	20	52	0.06	2014	signaling pathway

Keywords cluster analysis

Keyword clustering analysis was conducted using Carrot2 software, and the resulting map is shown in **Figure 6**. The analysis highlights current research hotspots in TCM autophagy, including the mechanisms by which TCM affects tumor cells via autophagic pathways, the identification of mitophagy and autophagy-related genes, investigations of the PI3K/AKT/mTOR signaling pathway, and studies on the role of TCM in liver diseases through autophagy.

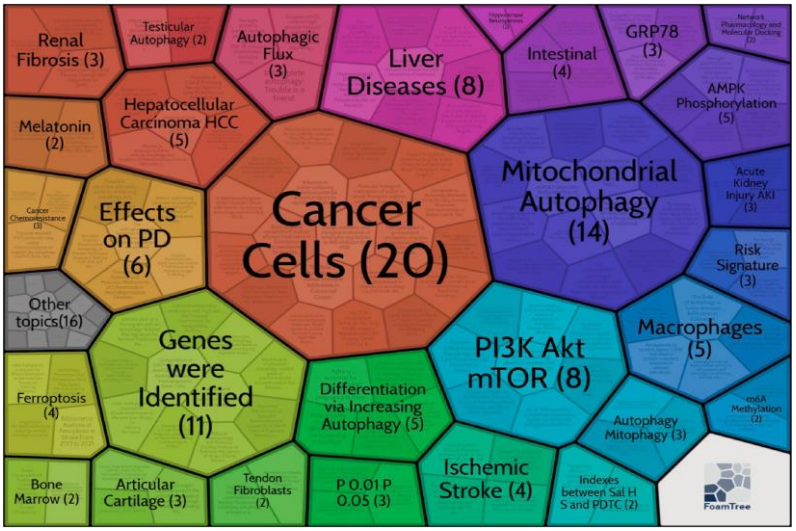


Figure 6. Research status of autophagy in TCM Keyword analysis.

Keywords emergence analysis

"Keyword emergence" refers to a sudden and significant increase in the frequency of a keyword, reflecting emerging research frontiers and hotspots. **Figure 7** presents the analysis of keyword emergence for autophagy-related TCM literature, using parameters of R = 1.0 and minimum duration = 1, which identified 20 emergent keywords. The findings indicate that research on autophagy in TCM began relatively late, with notable activity starting around 2010. Early studies primarily focused on the role of TCM in autophagy-mediated treatment of hepatocellular carcinoma, pancreatic cancer, prostate cancer, and other tumor cells.

In 2015, the degradation pathways of autophagy emerged as a key research hotspot. Following the award of the 2016 Nobel Prize in Physiology or Medicine to Yoshinori Ohsumi for his discovery of autophagy-related genes [3], the field experienced a marked increase in activity. That year, research emphasized TCM's role in Parkinson's disease and hepatocellular carcinoma via autophagy pathways, the regulatory effects of TCM on autophagy, and autophagy-mediated modulation of chemotherapy resistance. During 2017–2018, studies increasingly focused on matrine-induced autophagy and the application of TCM in treating pancreatic, prostate, and other malignant tumors. Since 2021, emerging research has concentrated on the autophagic effects of luteolin and the application of network pharmacology to explore the mechanisms of TCM-mediated autophagy.

Top 20 Keywords with the Strongest Citation Bursts

Keywords	Year	Strength	Begin	End	2009 - 2022
death	2009	8.42	2010	2017	
inhibition	2009	7.28	2011	2015	
bufalin	2009	3.55	2011	2014	
alpha-synuclein	2009	3.12	2011	2017	
induction	2009	6.49	2012	2015	
cancer cell	2009	4.67	2012	2017	
inhibitor	2009	2.92	2012	2016	
p53	2009	4.31	2014	2018	
survival	2009	3.89	2014	2016	
kinase	2009	3.08	2014	2016	
degradation	2009	4.3	2015	2018	
parkinsons disease	2009	3.28	2016	2019	
hepatocellular carcinoma	2009	2.99	2016	2019	
modulation	2009	2.95	2016	2019	
chemotherapy	2009	2.9	2016	2018	
matrine	2009	3.75	2017	2019	
pancreatic cancer	2009	3.03	2017	2018	
prostate cancer	2009	2.79	2018	2018	
network pharmacology	2009	6.09	2021	2022	
luteolin	2009	2.76	2021	2022	

Figure 7. Emergent map of keywords.

The temporal dynamics and relationships of literature clusters were analyzed using the "timeline" function, resulting in the timeline map shown in **Figure 8**. The figure demonstrates that clusters #1, #2, and #8 have ceased evolving, whereas clusters #0 (asthma), #3 (autophagy), #4 (mitophagy), #5 (network pharmacology), #6 (activation), #7 (TLR4), #9 (Traditional Chinese Medicine), and #10 (angiogenesis) span a relatively long time period and remain active to the present. These clusters represent sustained research topics and can be considered long-term hotspots in the field.

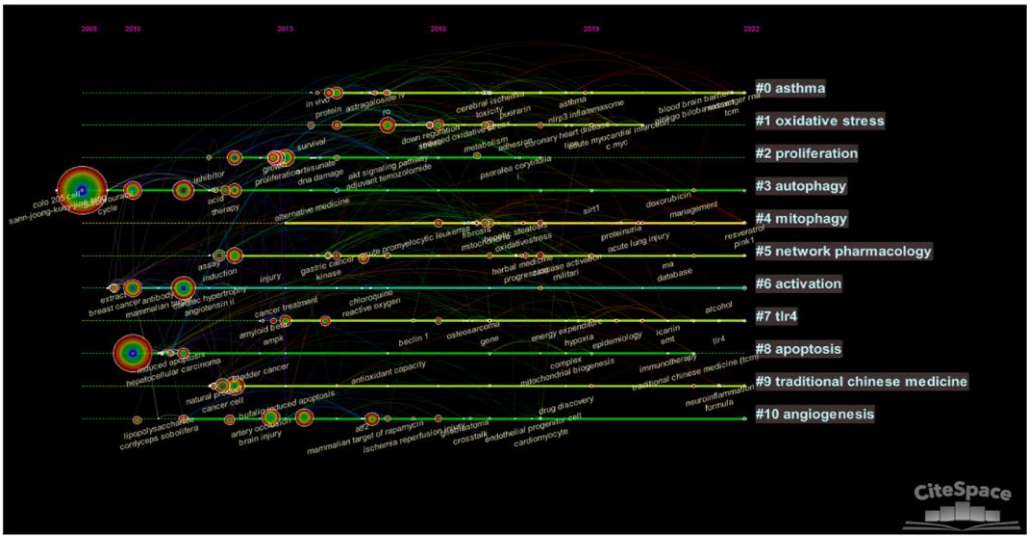


Figure 8. Keyword timeline.

Top ten cited documents and co-cited documents

Table 5 lists the ten most frequently cited studies in the field. Among them, two papers have been cited over 200 times: Tillhon Micol's 2012 article, *"Berberine: new perspectives for old remedies"* (IF = 6.1), and Efferth Thomas' 2017 Cancer Biology Symposium paper, *"From ancient herbs to modern drugs: Artemisia annua and artemisinin for the treatment of tumors"* (IF = 15.707) [4]. Tillhon systematically reviewed the pharmacological properties and therapeutic applications of berberine, highlighting its potential as an anticancer lead compound. Efferth's study provided a comprehensive review of artemisinin's multiple anti-tumor mechanisms over the past two decades, including its role in autophagy-mediated cell death. Both berberine and artemisinin, as representative compounds of TCM, have been shown to exert anti-cancer effects via autophagy pathways, attracting widespread scholarly attention.

A common characteristic among the top ten cited studies is their focus on the application of TCM in anti-tumor therapy—targeting cancers such as colon cancer, osteosarcoma, liver cancer, and non-small cell lung cancer—through autophagy mechanisms. This underscores the broad recognition and importance of autophagy-mediated TCM interventions in cancer research.

Table 5. Top 10 cited documents.

Rank	Study	First Author	Year	Total Citations	Average Citations per Year
1	Berberine: New perspectives for old remedies	Tillhon, Micol	2012	296	24.7
2	From ancient herb to modern drug: Artemisia annua and artemisinin for cancer therapy	Efferth, Thomas	2017	285	40.7
3	Bufalin induces autophagy-mediated cell death in human colon cancer cells via ROS generation and JNK activation	Xie, Chuan-Ming	2011	197	15.2
4	Pharmacological basis and new insights of quercetin in anticancer effects	Tang, Si-Min	2020	196	49.0
5	Celastrol induces apoptosis and autophagy through ROS/JNK signaling in human osteosarcoma cells: in vitro and in vivo study	Li, H-Y	2015	196	21.8
6	Naturally occurring anticancer compounds from Chinese herbal medicine	Luo, Hua	2019	186	37.2
7	Arenobufagin, a natural bufadienolide, induces apoptosis and autophagy in human hepatocellular carcinoma cells via PI3K/Akt/mTOR inhibition	Zhang, Dong-Me	2013	162	14.7
8	Toxicity of triptolide and underlying molecular mechanisms	Xi, Chen	2017	142	20.3
9	Isorhynchophylline promotes alpha-synuclein degradation in neuronal cells through autophagy induction	Lu, Jia-Hong	2012	129	10.8
10	Polyphyllin VI induces caspase-1-mediated pyroptosis via ROS/NF-κB/NLRP3/GSDMD pathway in non-small cell lung cancer	Teng, Jin-Feng	2020	118	29.5

VOSviewer was subsequently used to analyze co-cited references, focusing on the ten most frequently cited studies to construct a co-citation network **(Figure 9)**. The top ten co-cited publications are summarized in **Table 6**. These highly cited studies were predominantly published in high-impact journals. The most frequently co-cited paper was Bray F's 2018 study, *"Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries"* [5]. The second most co-cited work was Levine B's *"Autophagy in the Pathogenesis of Disease"* [6], which systematically reviewed the role of autophagy as a lysosomal degradation pathway in the development and prevention of various human diseases, including infections, cancer, neurodegenerative disorders, aging, and cardiovascular disease. An in-depth examination of the most co-cited literature was further conducted using a pennant plot, as shown in **Figure 10**.

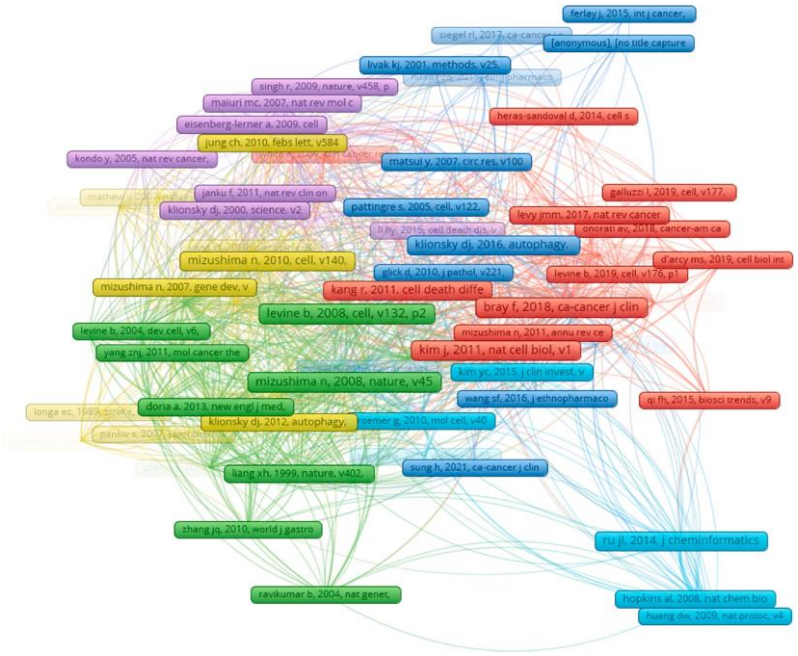


Figure 9. Document Co-citation network.

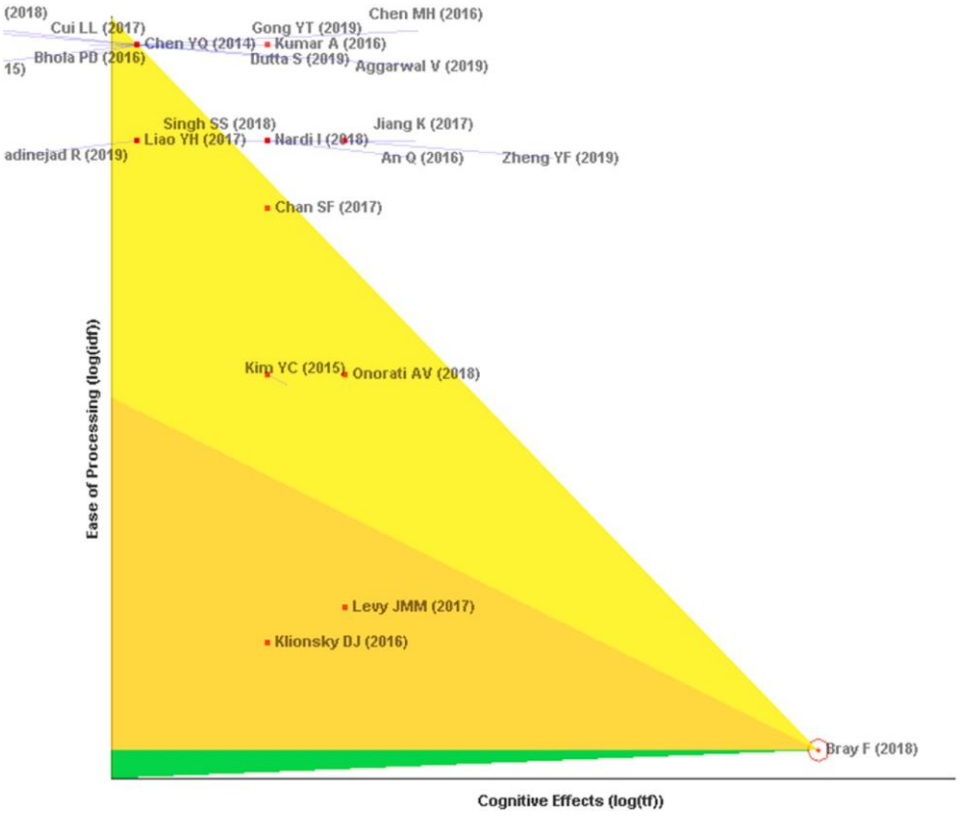


Figure 10. Diagrams of the highest co-cited literature pennants.

Table 6. Top 10 co-cited references.

Rank	Title	First Author	Year	Journal	2022 IF	Citation Count	Total Link Strength
1	*Global Cancer Statistics 2018: GLOBOCAN estimates of incidence*	Bray F	2018	CA: A Cancer Journal for Clinicians	286.13	39	80

	and mortality for 36 cancers in 185 countries						
2	*Autophagy in the Pathogenesis of Disease*	Levine B	2008	Cell	66.85	38	129
3	*AMPK and mTOR regulate autophagy via direct Ulk1 phosphorylation*	Kim J	2011	Nature Cell Biology	28.21	38	100
4	*Autophagy fights disease through cellular self-digestion*	Mizushima N	2008	Nature	69.50	36	111
5	*Autophagy: renovation of cells and tissues*	Mizushima N	2011	Cell	66.85	32	86
6	*TCMSP: Systems pharmacology database for herbal drug discovery*	Ru JL	2014	Journal of Cheminformatics	8.49	30	48
7	*LC3, a mammalian homolog of yeast Apg8p, localizes in autophagosome membranes*	Kabeya Y	2000	EMBO Journal	14.01	28	74
8	*Guidelines for monitoring autophagy assays: use and interpretation*	Klionsky DJ	2016	Autophagy	13.39	28	64
9	*The Beclin 1 network in autophagy and apoptosis regulation*	Kang R	2011	Cell Death & Differentiation	12.07	27	67
10	*Techniques for mammalian autophagy research*	Mizushima N	2010	Cell	66.85	26	58

Leading journals and co-cited journals

Table 7 presents the top ten journals in which studies on autophagy in Traditional Chinese Medicine were published, comprising a total of 259 articles, or 37.66% of all included studies. The journal with the highest output was Frontiers in Pharmacology (89 articles, 9.72%), which primarily publishes pharmacological research on TCM and its mechanisms involving autophagy across a range of diseases. The second most productive journal was Evidence-Based Complementary and Alternative Medicine (52 articles, 5.68%), followed by Journal of Ethnopharmacology (49 articles, 5.35%). Both journals mainly focus on TCM, complementary and alternative medicine, and ethnopharmacology research.

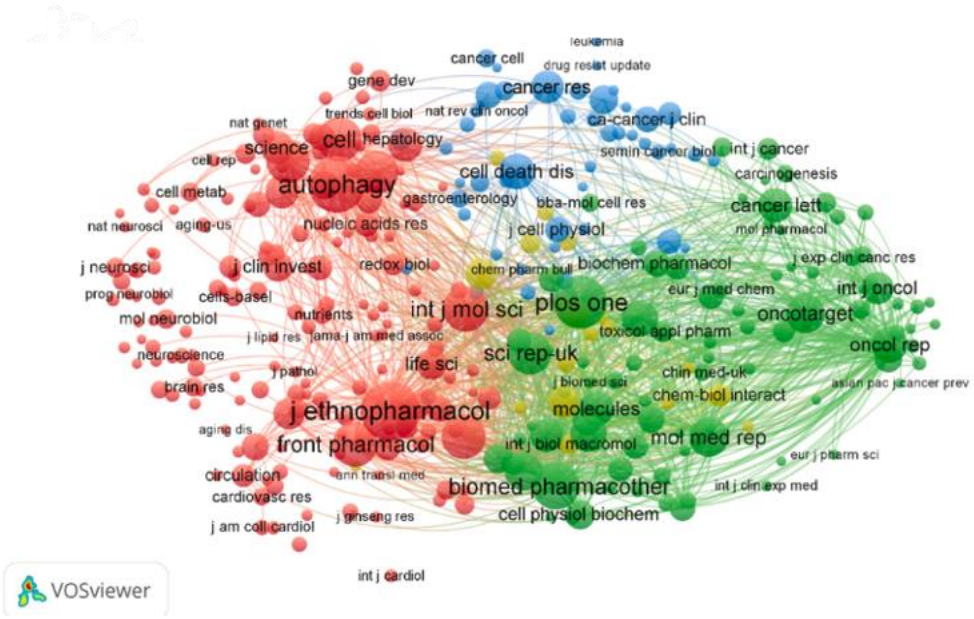
Table 7. The top 10 journals.

Rank	Journals	Count	%	IF2022（JCR）
1	Frontiers In Pharmacology	89	9.72%	5.988（Q1）
2	Evidence-based Complementary And Alternative Medicine	52	5.68%	2.650（Q3）
3	Journal Of Ethnopharmacology	49	5.35%	5.195（Q1）
4	Biomedicine & Pharmacotherapy	46	5.02%	7.419（Q1）
5	Phytomedicine	29	3.17%	6.656（Q1）
6	Molecular Medicine Reports	20	2.18%	3.423（Q3）
7	Oxidative Medicine And Cellular Longevity	16	1.75%	7.310（Q2）
8	American Journal Of Chinese Medicine	15	1.64%	5.928（Q1）
9	Experimental And Therapeutic Medicine	15	1.64%	2.751（Q4）
10	International Journal Of Molecular Sciences	14	1.53%	6.208（Q1）

The most influential journals driving research on autophagy in Traditional Chinese Medicine were identified through co-citation analysis. In the resulting network, the size of a node reflects the number of citations, while the thickness of the connecting lines indicates the strength of co-citation relationships. Among 4,945 journals that published studies in this field, 326 journals were selected for analysis using a threshold of at least 30 citations. The citation counts and link strengths of the top ten journals are summarized in **Table 8**. The results indicate that *Autophagy*, *Journal of Ethnopharmacology*, *PLOS ONE*, *Cell*, and *Nature* are the most influential journals among the analyzed sources.

Cluster analysis of the co-citation network revealed four major groups **(Figure 11a)**. The largest cluster (red, 167 items) includes leading international journals such as *Autophagy*, *Journal of Ethnopharmacology*, *Cell*, and *Nature*. The second cluster (green, 91 items) mainly consists of multidisciplinary journals like *PLOS ONE*, *Biomedicine & Pharmacotherapy*, and *Oncotarget*. The third cluster (blue, 48 items) is composed primarily of oncology-focused journals, including *Cancer Research*, *Cancer Cell*, and *Cell Death & Disease*. The fourth cluster (yellow, 20 items) comprises journals emphasizing natural products and phytotherapy, such as *Phytotherapy Research*, *Food and Chemical Toxicology*, and *Free Radical Biology & Medicine*.

Figure 11b presents the journal co-citation density map. In this visualization, each point's color represents the local citation density: areas with a high concentration of closely related journals appear yellow, indicating strong influence, whereas points with fewer neighboring journals are shaded blue, reflecting lower density. The map provides a visual representation of the distribution and relative impact of journals in the field.



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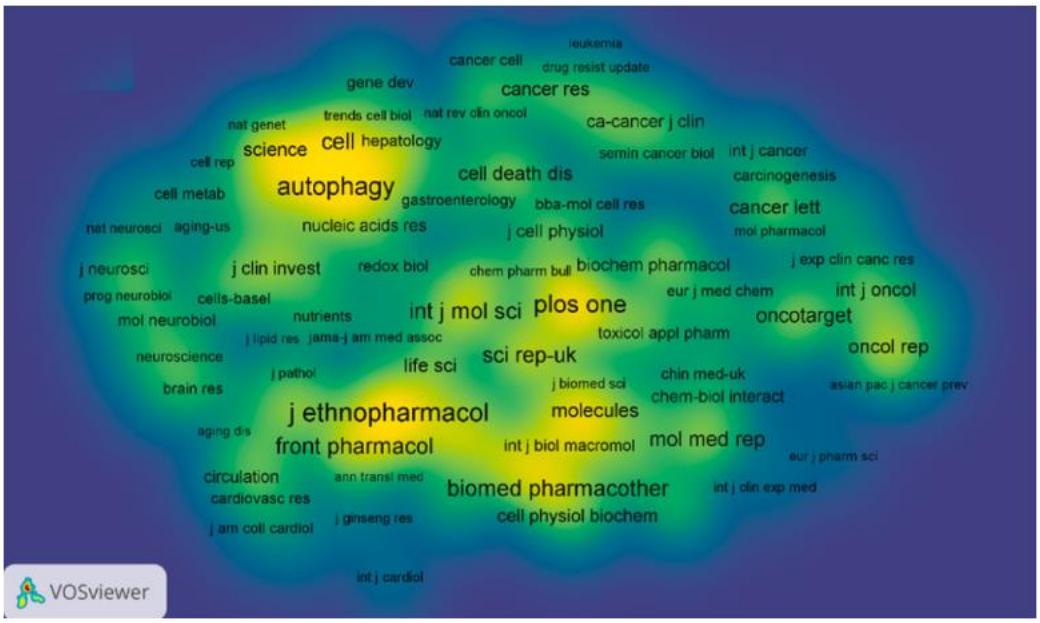

b)

Figure 11. (a) Co-citation network diagram of journals, (b) Co-citation density of journal..

Table 8. Top 10 cited journals.

Rank	Source	Citations	Total link strength
1	Journal Of Ethnopharmacology	1020	66580
2	Antophagy	928	39955
3	Plos one	827	70778
4	Biomed pharmacother	652	60452
5	International Journal Of Molecular Sciences	614	51573
6	Frontiers in Pharmacology	595	41201
7	Cell	588	33390
8	Evidence-based Complementary And Alternative Medicine	570	38173
9	Nature	561	33961
10	Scientific Reports	545	43498

Dual-map overlay

Double overlay mapping is used to illustrate the overall scientific relationships and contributions within a research field. By superimposing two maps, the interactions between citing and cited journals can be visualized [7]. This approach allows publications and citations to be represented at the disciplinary level. Using the CiteSpace overlay function, a citation network was constructed, in which the left side represents the citing journals and the right side represents the cited journals. Curved lines indicate citation links, showing how knowledge flows from one field to another **(Figure 12).**

Analysis based on Z-scores reveals that the most frequently represented disciplines include Molecular Biology and Immunology. Additionally, these fields are influenced by contributions from Physics, Materials Science, Chemistry, and related domains, reflecting the interdisciplinary nature of research on autophagy in Traditional Chinese Medicine.

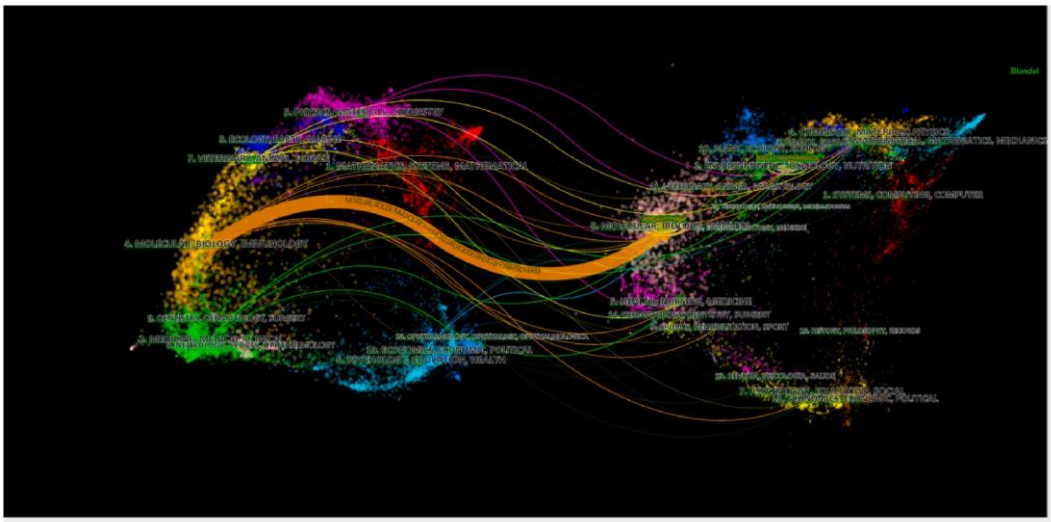

Figure 12. Overlay of double spectra of literatures.

The global recognition of Traditional Chinese Medicine (TCM) has increased significantly in recent years, notably after Professor Tu Youyou was awarded the Nobel Prize in Physiology or Medicine in 2015 for her work in TCM research. The outbreak of COVID-19 in 2019 further highlighted the potential of TCM, attracting increasing international attention. Similarly, Yoshinori Ohsumi's Nobel Prize in 2016 for elucidating the mechanism of autophagy spurred widespread interest in this cellular process. Consequently, the intersection of TCM and autophagy has emerged as a prominent area of scientific inquiry.

A growing number of studies have demonstrated that TCM can modulate autophagy to treat various diseases, particularly malignant tumors. Highly cited studies frequently focus on how TCM promotes autophagy to manage colorectal cancer, hepatocellular carcinoma, and non-small cell lung cancer. Abnormal autophagy is a critical factor in tumor treatment resistance, as tumor cells exploit multiple autophagic pathways to evade therapy [8]. Recent research has concentrated on the potential of TCM to overcome chemotherapy resistance via autophagy, establishing this as a hot topic. Beyond oncology, diseases such as atherosclerosis and Alzheimer's disease (AD) are also emerging research foci. Evidence indicates that autophagy enhances cellular efflux, promotes cholesterol clearance, and reduces apoptosis and inflammation, making autophagy induction a promising strategy for atherosclerosis treatment [9, 10]. In AD, autophagy defects appear in early disease stages, affecting β-amyloid metabolism and Tau assembly, and modulating autophagy through mTOR-dependent and independent pathways may offer novel therapeutic opportunities [11–13].

Pathway analyses reveal that TCM-mediated autophagy primarily involves the PI3K/AKT/mTOR, Nrf2, TLR4, and NF-κB signaling pathways. Key regulators such as mTOR, AKT, and PI3K are central to autophagy initiation and progression in various pathologies, including malignancies, and natural products targeting PI3K/AKT/mTOR-mediated autophagy have shown anti-tumor effects [14–16]. TLR4 signaling has been implicated in the cardioprotective effects of TCM formulas via PDE5A-AKT and TLR4-NOX4 pathways in isoproterenol-induced heart failure [17]. The Nrf2/Keap1 pathway, a major antioxidant stress response route, is involved in tumor protection and chemotherapy resistance [18]. NF-κB, a key transcription factor, regulates inflammation and apoptosis and has been linked to autophagy suppression [19–21]. Autophagy-related genes (ATGs) also contribute to autophagic regulation via the AMPK-mTOR pathway, which TCM can modulate to treat various diseases [22–24].

This study has some limitations. Only the Web of Science (WoS) database was used as the data source, while other databases such as Embase, Medline, and Scopus were not included. Nevertheless, WoS remains one of the most comprehensive and organized bibliographic databases, and the use of tools like VOSviewer and CiteSpace allows for efficient and reliable bibliometric analysis.

Conclusion

Traditional Chinese Medicine (TCM) employs a wide array of therapeutic strategies with significant clinical value, involving multiple components, targets, and biological pathways. Autophagy has been shown to play a critical role in the development and progression of numerous diseases, making its regulation an important focus for clinical research. By integrating the two prominent research areas of TCM and autophagy, this study aimed to identify current research hotspots and anticipate future trends in the application of autophagy mechanisms within TCM.

Current studies have primarily concentrated on the role of TCM in modulating autophagy in conditions such as malignant tumors, atherosclerosis, and Alzheimer's disease. The regulation of key autophagy-related signaling pathways—such as PI3K/AKT/mTOR, TLR4, Nrf2, and NF-κB—has emerged as a central theme in this field. Looking forward, research is expected to focus on several key directions: the therapeutic potential of TCM in chemotherapy-resistant tumor cells via autophagy modulation, the role of TCM in mediating mitophagy and activating autophagic functions, and the effects of bioactive TCM components, such as luteolin, on diseases including cancer, asthma, and myocardial injury through autophagy pathways.

Overall, this study aims to provide researchers with novel insights and directions for future exploration, with the ultimate goal of enhancing the clinical application of TCM by elucidating its mechanisms in regulating autophagy and supporting more effective treatment strategies for human diseases.

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Conflict of Interest: None

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