

# Research and Application Prospect of Nanomedicine in Kidney Disease: A Bibliometric Analysis From 2003 to 2024

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**Abstract:** Kidney disease is a major public health concern that has a significant effect on a patient's life span and quality of life. However, effective treatment for most kidney diseases is lacking. Nanotechnology mainly explores the design, characterization, production, and applications of objects in the nanoscale range and has been widely used in the medical field. To date, there has been an increasing amount of research on the application of nanotechnology in kidney disease. However, systematic bibliometric studies remain rare. In this review, data collected from the Web of Science Core Collection database until December 31, 2024, were subjected to a bibliometric analysis. A total of 1179 articles and reviews were included. The publication trends, countries, institutions, authors, co-authorship, co-citations, journals, keywords, and references pertaining to this topic were examined. The results showed that nanotechnology research in kidney disease is increasing. The leading country, organization, and author were China, Sichuan University, and Professor Peng Huang, respectively. ACS APPLIED MATERIALS & INTERFACES was the top journal among the 464 journals in which articles on nanotechnology in kidney disease were published. KIDNEY INTERNATIONAL was the most cited journal in the field. The most significant increases were shown for “acute kidney disease”, “drug delivery”, “oxidative stress”, “diabetic nephropathy”, and “chronic kidney disease”, indicating the current research hotspots. Furthermore, the development prospects and challenges of nanotechnology in kidney disease were discussed in this review. How to achieve precise drug delivery to render kidney-targeting therapy a reality may be problematic in future studies.

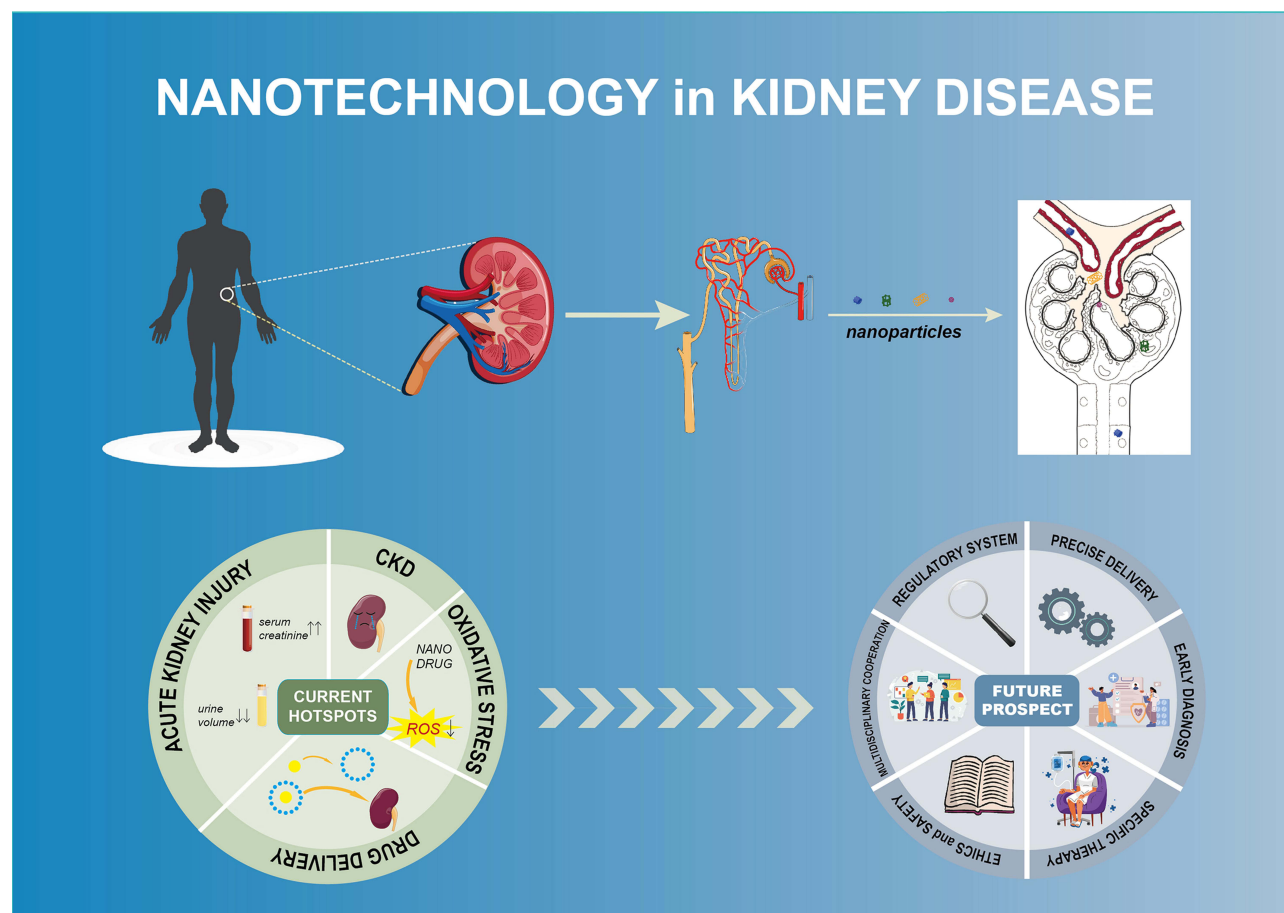
**Keywords:** nanomedicine, kidney disease, bibliometric analysis, drug delivery, diagnosis, therapy

## Introduction

The kidney is an organ that excretes metabolite and keeps the balance of water and electrolyte. It is composed of nephrons, periglomerular organs, interstitium, blood vessels, and nerves. Nephrons, including glomeruli, renal tubules, and renal sacs, are the most primary structural and functional units of the kidney and responsible for filtration, reabsorption, and secretion to ensure body homeostasis. In kidney disease, the above structures and functions are damaged, resulting in internal environment disorders, proteinuria, hematuria, oliguria, edema, hypertension, and other symptoms. Eventually, kidney function is impaired, which can affect other organs and, in severe cases, lead to death.

Kidney disease has been a significant public health concern globally, affecting roughly 10% of the global population, and its prevalence is increasing yearly. In 2019, 1.4 million people died from chronic kidney disease (CKD) and the number of deaths has increased by 30% in the past 10 years.<sup>1</sup> Approximately 10–15% of patients in hospitals suffer from acute kidney injury (AKI) and half are in intensive care units.<sup>2</sup> It has been reported that the mortality rate of AKI was greater than CKD and surpassed the combined rates of diabetes, heart failure, prostate cancer, and breast cancer.<sup>3</sup> In

## Graphical Abstract



addition, patients' quality of life is seriously affected by kidney disease. In patients 50–74 years of age, CKD was the eighth leading cause of disability-adjusted life years (DALYs) worldwide.<sup>4</sup> Patients with end-stage renal disease (ESRD) usually depend on dialysis, which both decreases their quality of life and imposes a significant financial burden on their families and countries.<sup>5</sup> In particular, kidney disease increases the mortality risk of other diseases such as cardiovascular disease.<sup>6</sup> However, there are few effective treatments for kidney disease, and many drugs have poor therapeutic effects due to low bioavailability, short residence time in the kidney, and significant adverse effects. Therefore, developing kidney targeting drugs and improving their bioavailability are of great importance for delaying the progression of kidney disease.

Nanotechnology, which was proposed in 1959, is the engineering and manufacturing of materials at the atomic and molecular scales.<sup>7</sup> In its strictest definition from the National Nanotechnology Initiative, nanotechnology refers to structures roughly in the 1–100 nm size regime in at least one dimension. Despite this size restriction, nanotechnology commonly refers to structures that are up to several hundred nanometers in size and that are developed by top-down or bottom-up engineering of individual components.<sup>8</sup> The study of nanotechnology is based on various subjects such as macrophysics, computer technology, quantum mechanics, and biology. The size of many biological molecules is within the nano or subnano range, thus, nanotechnology is widely applied in biology. The term “nanomedicine” appeared around 2000 and pertains to the use of nanotechnology in maintaining health and improving diseases.<sup>9</sup> Nano-Drug Delivery System (NDDS) refers to a novel approach in the pharmaceutical field, harnessing the potential of nanotechnology for

drug delivery. According to the carrier materials and structures used, NDDS are divided into different categories, including nanosuspensions, nanoliposomes, micelles, microemulsions/self-microemulsions, nanocapsules, and solid lipid nanoparticles.<sup>10</sup> These NDDS can enhance drug stability, increase bioavailability and half-life, improve drug distribution, and reduce adverse reactions by using nanotechnology to deliver drugs.<sup>11</sup> For example, pegylated liposomal doxorubicin (Doxil), the first nanodrug, was approved in 1995 by the United States Food and Drug Administration (FDA).<sup>12</sup> Doxil showed lower heart cardiotoxicity and a longer half-life than doxorubicin alone.<sup>13</sup> In the past decade, the funding for nanomedicine has increased, and nanomedicine has shown significant potential in treating diseases, especially cancer.<sup>14</sup>

Currently, most kidney diseases cannot be cured completely, and some drugs used clinically, especially immunosuppressants, have numerous adverse reactions. For example, glucocorticoids and immunosuppressants are commonly used to treat kidney disease. However, long-term use of glucocorticoids can lead to obesity, necrosis of the femoral head, and even fatal infections. Some immunosuppressants, such as cyclophosphamide, inhibit the hematopoietic system or lead to impaired liver function. These severely limit the clinical application of drugs and bring great trouble to clinicians and patients. Nanotechnology may be effective in solving these problems. Nanoparticles (NPs) are the molecules and atoms engineered by nanotechnology with specific properties that can change drug pharmacokinetics and pharmacodynamics so as to target certain organs or even certain cells.<sup>15,16</sup> Several NPs have shown a potential curative effect in kidney disease mouse models.<sup>14</sup> For example, researchers created myofibroblast-targeting NPs with the antineoplastic agent Sorafenib, which can reduce renal fibrosis in mouse models.<sup>17</sup> For hereditary kidney disease, DNA or RNA may be delivered to target cells by nanogene carriers and provide a therapeutic benefit.<sup>18–20</sup> Ferumoxylol, a superparamagnetic iron oxide nanoparticle coated with a semi-synthetic carbohydrate shell, had a better effect on renal anemia than oral iron in phase III trials, and has been approved by the FDA.<sup>21,22</sup> Nanotechnology can also be used to improve dialysis membranes and adsorbents. It can reduce the size of devices and aid in monitoring blood ion concentration using nanosensors.<sup>23,24</sup> In addition, nanotechnology can aid in the early diagnosis of kidney disease, which is important for improving prognosis. Researchers found microRNA(miR)-21 highly expressed in early-onset AKI.<sup>25</sup> A new type of nanoantenna has been synthesized that can detect miR-21 and diagnose AKI earlier in mice.<sup>26</sup>

As a new interdisciplinary subject, nanotechnology has been paid more and more attention to its application in kidney disease. Although there have been numerous reviews on the study of nanomedicine, many of them lack objective visualized data support and mainly rely on researchers' subjective understanding of the field. Bibliometrics, created by James McKeen Cattell, is a method to count the information of publications and analyze the current state and trend of research.<sup>27,28</sup> Professor Chaomei Chen transformed the statistical results into various visualization maps to simplify comprehension.<sup>29</sup> Bibliometrics can objectively show the development status, research hotspots, and future prospects of a research field through statistical analysis of various characteristics of publications. At present, systematic bibliometric analysis studies on nanotechnology in kidney disease are rare. In this paper, bibliometrics analysis was used to visualize the landscape of publications, countries, organizations, authors, journals, keywords, and references on the topic of nanotechnology in kidney disease to display the research progress of nanotechnology in the diagnosis and treatment of kidney disease over the past 21 years. In addition, the existing problems and potential future research directions were proposed, serving as a valuable resource for scholars new to the field.

## Materials and Methods

### Data Collection

First, the Web of Science Core Collection (WoSCC) database, which is widely used for bibliometric analysis was searched. The database is comprised of several indices including the Science Citation Index-Expanded (SCIE), Social Sciences Citation Index (SSCI), and Arts & Humanities Citation Index (A&HCI).<sup>30–32</sup> The search terms were

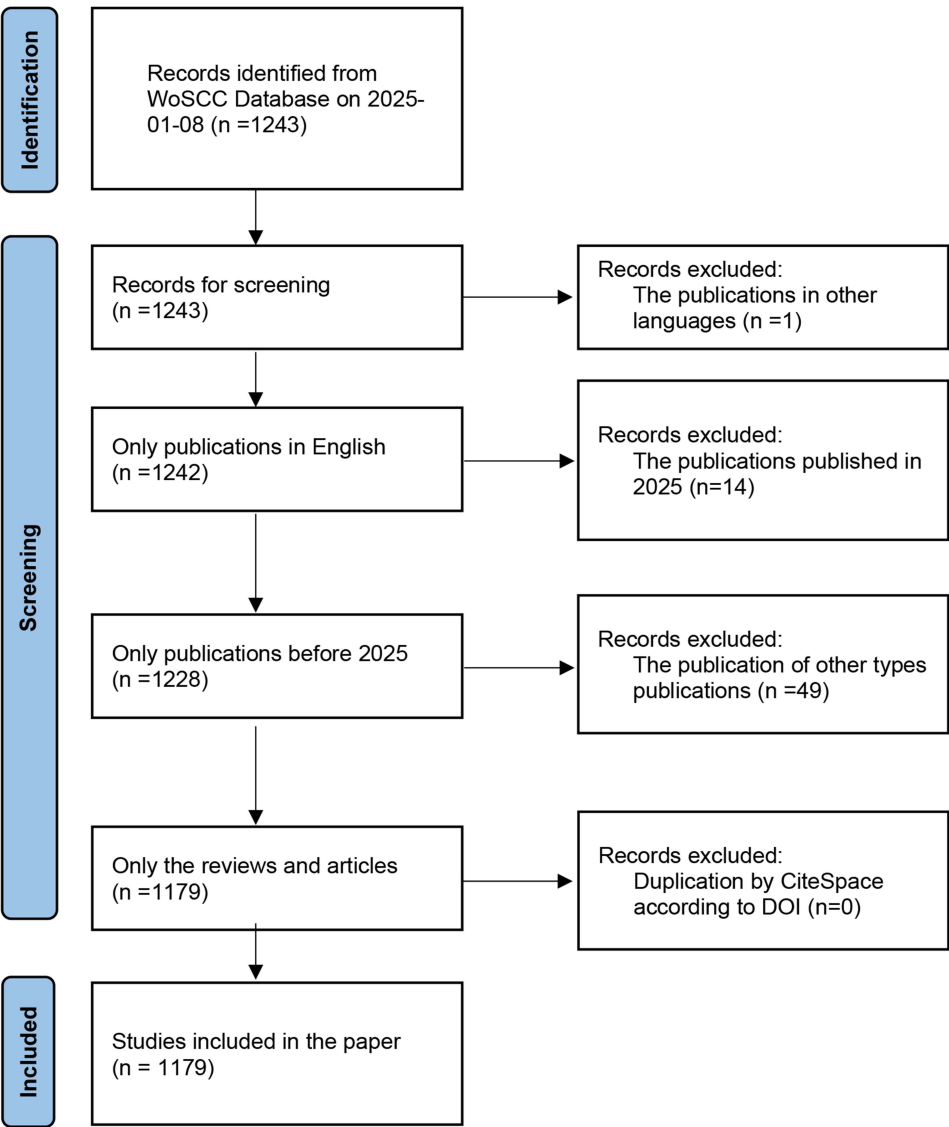
TI=x OR AB=x OR AK=x ('TI', 'AB', and 'AK' represent the field tag of 'title', 'abstract', and 'author keywords', respectively), x=((nanomedicine OR nanoparticle\* OR nanotube\* OR 'nano drug\*' OR nanomaterial\* OR nanocomposite\*)

AND ('Kidney disease\*' OR nephropath\* OR 'renal disease\*' OR nephrosis OR 'renal insufficiency' OR 'renal dysfunction' OR 'kidney dysfunction' OR 'kidney insufficiency' OR 'renal failure' OR 'kidney failure' OR uremia OR 'kidney injury' OR 'renal injury' OR 'renal impairment' OR 'kidney impairment' OR 'CKD' OR 'end-stage renal disease' OR 'ESRD' OR 'end-stage kidney disease' OR 'ESKD' OR 'hemodialysis' OR 'peritoneal dialysis' OR 'renal replacement therapy' OR 'kidney transplant' OR 'AKI' OR 'nephrotic syndrome' OR 'glomerulonephritides' OR 'glomerulonephritis' OR 'nephritis') NOT (cancer OR carcinoma OR tumor OR neopla\*)).

In total, 1243 publications were found.

### Data Filtration

The filtering shown in Figure 1 and the search were performed on the same day (January 8, 2025). Only peer-reviewed reviews and articles published in English before January 1, 2025, were included. Other types of publications or those not written in English or published after January 1, 2025, were excluded. The filtered publication information was then exported as Excel and Plain text files for later analysis using bibliometrics visual analysis software. Finally, the



**Figure 1** The process of publications' filtration.

publications were checked for duplication using CiteSpace 6.3.1 Basic. A total of 1179 publications were ultimately included in this study ([Supplementary Table 1](#)). Two authors independently completed the work.

## Data Analysis

Various bibliometric visualization software was used in the analysis. The VOSviewer 1.6.18 was used for co-authorship analysis of countries, authors, organizations, co-citation analysis of cited authors, and citation analysis of journals.<sup>33</sup> R 4.3.2 with the R package bibliometrix was used for mapping three fields plot, author keywords evolution paths, and finding the core journals based on Bradford's Law.<sup>34</sup> Burst detection, cluster analysis, timeline view, co-occurrence of keywords, and co-cited analysis of references were performed with CiteSpace 6.3.1 Basic.<sup>29</sup> Microsoft Excel 2016 was used for descriptive statistics and producing polynomial trend lines, tables, and figures.

## Results

### The Number of Publications and Citations

This review included 1179 publications on nanotechnology in kidney disease: 1022 articles and 157 reviews. The earliest paper was published in 2003. It explored the influence of different functional groups on latex nanoparticles' surfaces on the protein adsorption from human serum, and the conclusion was useful for the design of hemodialysis devices.<sup>35</sup> The number of publications increased overall from 2003 to 2024 ([Figure 2A](#)) and the annual growth rate was 29.42%. Nearly half of the publications were published in the past 3 years. The number of publications was fitted using a polynomial curve ( $y = 0.0413x^3 - 0.5607x^2 + 2.5506x + 1$ ,  $R^2 = 0.9934$ ) which predicted the future growing trend. These publications were cited a total of 26567 times (average 22.53) prior to our search. The number of citations increased yearly from 2003 to 2024.

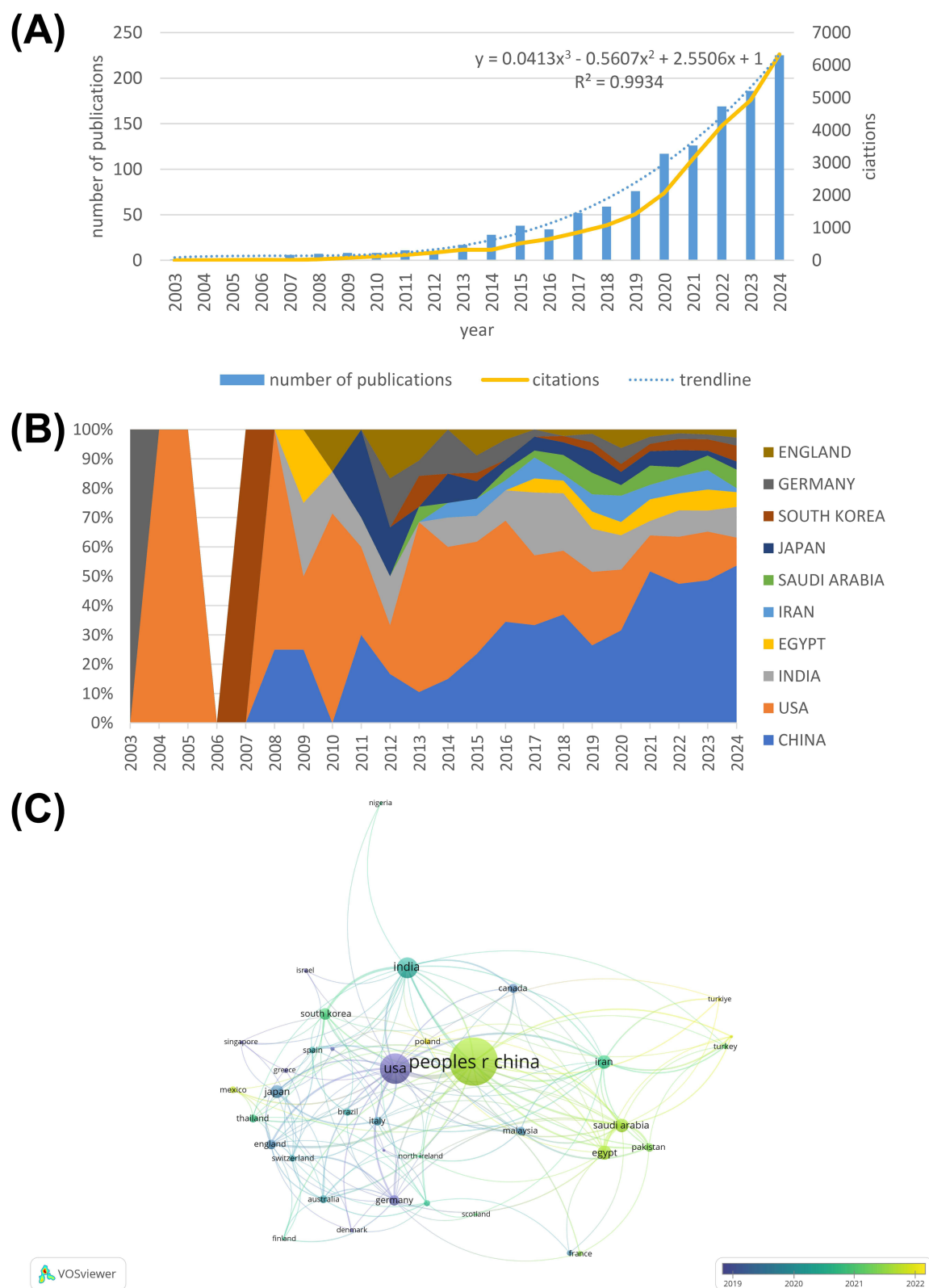
### Distribution

A total of 76 countries made contributions to this field. China was the largest contributor with 456 publications, followed by the United States (210), India (109), Egypt (56), and Iran (52). In the top 10 ([Table 1](#)), 6 countries were from Asia, 2 from Europe, 1 from Africa, and 1 from North America. The top 10 countries published 1085 publications in all, accounting for 92.02% of the total and the proportion is shown in [Figure 2B](#). The United States led the field prior to 2016 and China led thereafter. In addition, China had the most citations (9327). The country with the highest average number of citations was Denmark (80.667). The collocation between countries is shown in [Figure 2C](#). The node color represents the average publication year of all publications on the topic from the country, the node size represents the number of publications from the country, and the thickness of links represents the frequency of cooperation between countries. The United States had the highest total link strength (118) and collaborated closely with other countries, including China, India, Germany, and England.

All literature was from 1643 organizations. The Sichuan University from China contributed the most with 32 publications. All the top 10 organizations ([Table 2](#)) were from China. The publications from Zhejiang University were cited the most (1645). The National Institute of Biomedical Imaging and Bioengineering in the USA and Wuxi People's Hospital in China tied for first place of the average citations because they co-published 1 paper that received 548 citations. [Figure 3A](#) shows the cooperation among organizations. Taif University from Saudi Arabia had the highest total link strength (57).

### Authors

In total, 6888 authors contributed to writing the articles. Only 22 authors produced more than 5 papers in the field ([Table 3](#)). Among these authors, 9 were from China. Professor Peng Huang had the most publications (10) and most citations (653). All authors were classified into 4 clusters by the VOSviewer and were distinguished by colors in the overlay visualization map ([Figure 3B](#)). The authors in the same cluster cooperated more, possibly because the authors in the same cluster were usually from the same organization ([Supplementary Table 2](#)). The relationship of leading countries, organizations, and authors is shown in [Figure 3C](#).



**Figure 2** (A) The number and citations of publications over the years from 2003 to 2024. (B) The publications proportion of the top 10 nations over the years from 2003 to 2024. (C) The overlay visualization map of the co-authorship analysis of countries (including the counties with over 5 publications and cooperation with others).

**Table 1** The Top 10 Countries by Number of Publications

Rank	Country	Number of Publications	Citations	Average (Avg.) Citations	Total Link Strength
1	CHINA	456	9327	20.45	100
2	USA	210	8223	39.16	118
3	INDIA	109	2144	19.67	61
4	EGYPT	56	974	17.39	40
5	IRAN	52	1202	23.12	44
6	SAUDI ARABIA	51	984	19.29	70
7	JAPAN	47	909	19.34	20
8	SOUTH KOREA	39	425	10.90	29
9	GERMANY	34	1220	35.88	34
10	ENGLAND	31	815	26.29	42

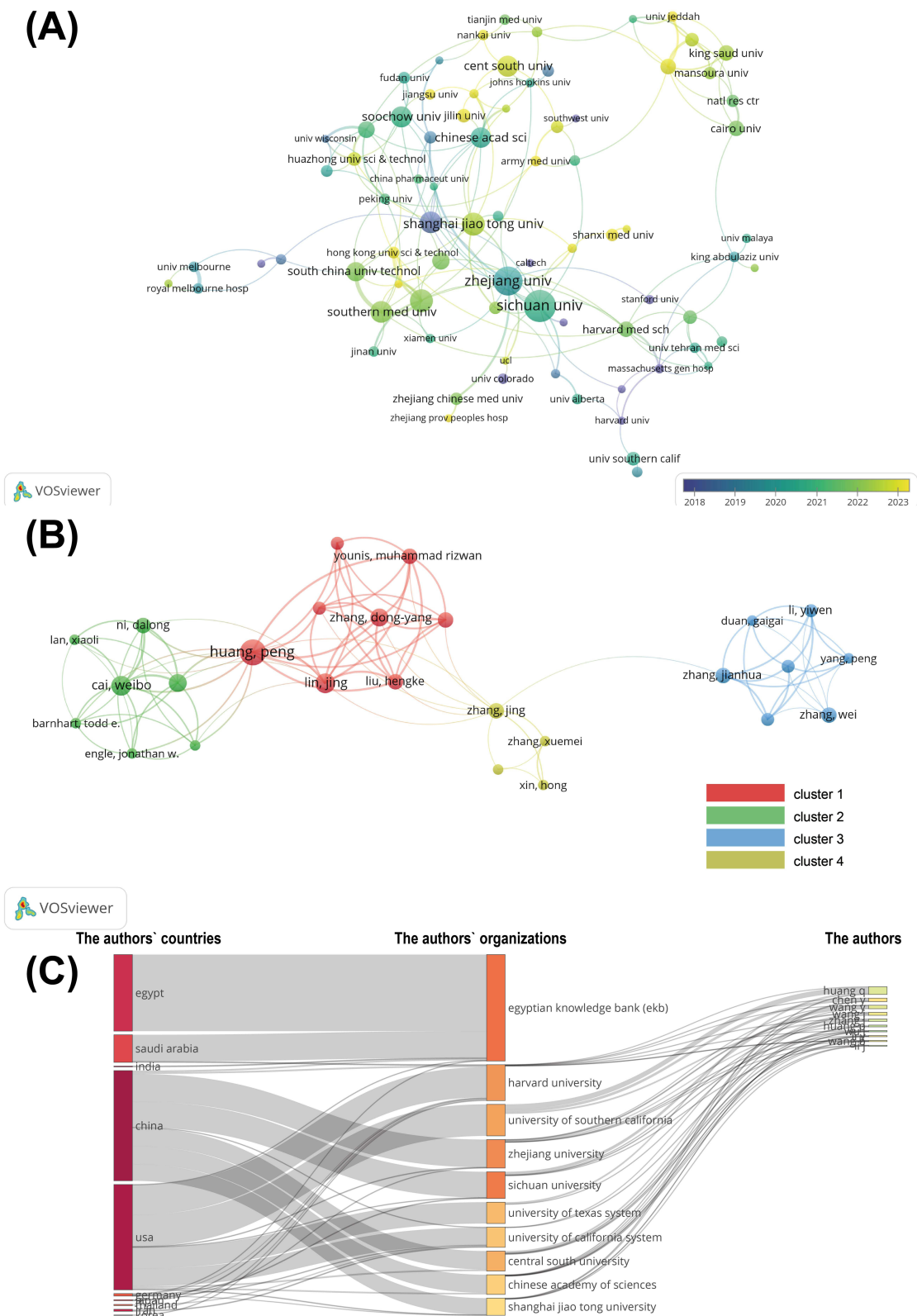
**Table 2** The Top 10 Organizations by Number of Publications

Rank	Organization	Country	Number of Publications	Citations	Avg. Citations	Total Link Strength
1	Sichuan University	China	32	938	29.31	42
2	Zhejiang University	China	28	1645	58.75	44
3	Shanghai Jiao Tong University	China	20	451	22.55	36
4	Sun Yat-sen University	China	20	270	13.50	41
5	Southeast University	China	19	929	48.89	24
6	Southern Medical University	China	19	292	15.37	41
7	Soochow University	China	18	443	24.61	28
8	Central South University	China	18	242	13.44	18
9	Chinese Academy of Sciences	China	17	342	20.12	39
10	South China University of Technology	China	16	290	18.13	24

A co-citation analysis of the cited authors was performed. [Table 4](#) includes a list of the top 20 writers based on citation count. Compared with [Table 3](#), there were 5 cited authors (Ryan M. Williams, Edward R. Smith, Dawei Jiang, Mengxiao Yu, and Dong-Yang Zhang) who wrote more than 5 publications. Rm Williams was the leading author in the references, and his papers were cited 145 times. The co-citation analysis results are shown in [Figure 4A](#). The node size indicates the number of times the author has been cited, and the thickness of the line between authors indicates the number of times that both authors were cited in the same article. The co-citations between cited authors were very common.

## Journals

The 1179 articles in the field were published in 464 journals. The journal in which most of the articles were published was the ACS APPLIED MATERIALS & INTERFACES, with an impact factor of 8.5. Among the top 10 journals ([Table 5](#)), chemistry and nanoscience & nanotechnology were the major areas of interest. Bradford's Law is an important law in bibliometrics. According to the law, journals are divided into three zones: core, middle, and tail. The law is used to estimate the exponentially diminishing returns of searching for references in science journals. For example, when journals in a field are sorted by number of articles into the three zones, each with approximately one-third of all articles, then the number of journals in each zone will be proportional to  $1:n:n^2$  ( $n > 1$ ).<sup>36</sup> Based on Bradford's Law ([Table 6](#)), 34 journals were included in the core journals ([Supplementary Table 3](#)). As shown in [Figure 4B](#), the articles in the CHEMICAL ENGINEERING JOURNAL were mainly published in recent years. The links in [Figure 4B](#) represent the citations between journals. Furthermore, KIDNEY INTERNATIONAL was the most cited journal in the field, which was cited 1605 times in total.



**Figure 3** (A) The overlay visualization map of the co-authorship analysis of organizations (including the organizations with over 5 publications and cooperation with others). (B) The network visualization map of co-authorship analysis of authors (including the authors with over 3 publications and cooperation with others). (C) The three fields plot of countries, organizations, and authors.

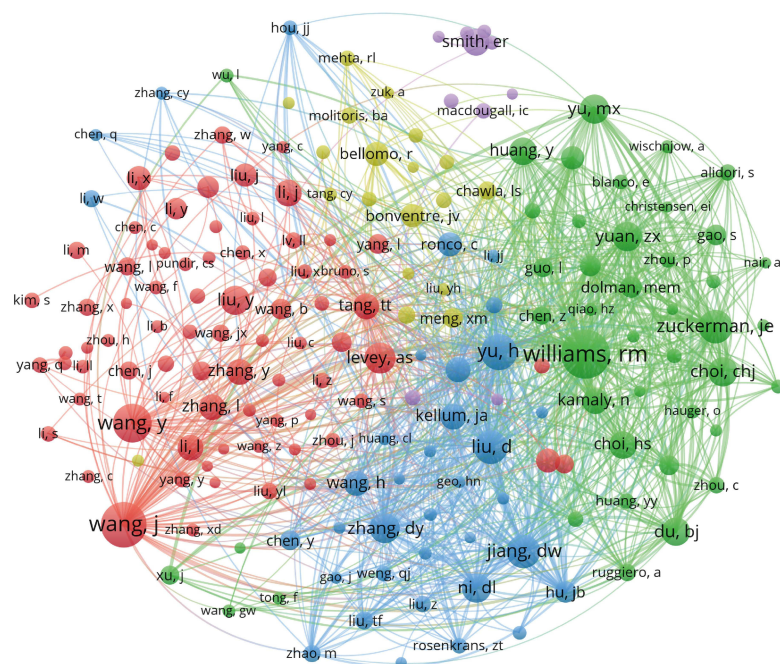
**Table 3** Authors With Over 5 Publications

Rank	Author	Organization	Country	Number of Publications	Citations	Avg. citations	Total Link Strength
1	Peng Huang	Shenzhen University	China	10	653	65.30	82
2	Eun Ji Chung	University of Southern California	USA	9	363	40.33	37
3	Ryan M. Williams	The City College of New York	USA	8	392	49.00	54
4	Makoto Kuro-O	Jichi Medical University	Japan	8	385	48.13	33
5	Zhirong Zhang	Sichuan Univeristy	China	8	342	42.75	50
6	Samuel A. Wickline	University of South Florida	USA	8	281	35.13	53
7	Weibo Cai	University of Wisconsin-Madison	USA	7	457	65.29	60
8	Daniel A. Heller	Memorial Sloan Kettering Cancer Center /Weill Cornell Medical College	USA	7	389	55.57	49
9	Jie Zheng	The University of Texas at Dallas	USA	7	365	52.14	32
10	Jing Lin	Shenzhen University	China	7	360	51.43	57
11	Edward R. Smith	Royal Melbourne Hospital/The University of Melbourne	Australia	7	123	17.57	45
12	Deepak Kukkar	Chandigarh University	India	7	31	4.43	19
13	Andreas Pasch	Johannes Kepler University Linz/Calcsicon AG	Austria/ Switzerland	6	399	66.50	58
14	Dawei Jiang	Huazhong University of Science and Technology / University of Wisconsin-Madison	China / USA	6	393	65.50	55
15	Mengxiao Yu	The University of Texas at Dallas	USA	6	303	50.50	28
16	Dong-Yang Zhang	Guangzhou Medical University	China	6	302	50.33	47
17	Mohd Sohaimi Abdullah	Universiti Teknologi Malaysia	Malaysia	6	183	30.50	48
18	Jianqiang Hu	South China University of Technology	China	6	147	24.50	56
19	Aiqing Li	Southern Medical University	China	6	147	24.50	56
20	Fong-Yu Cheng	Chinese Culture University	China	6	134	22.33	44
21	Jun Wu	The Hong Kong University of Science and Technology	China	6	51	8.50	43
22	Ki-Hyun Kim	Hanyang University	South Korea	6	31	5.17	17

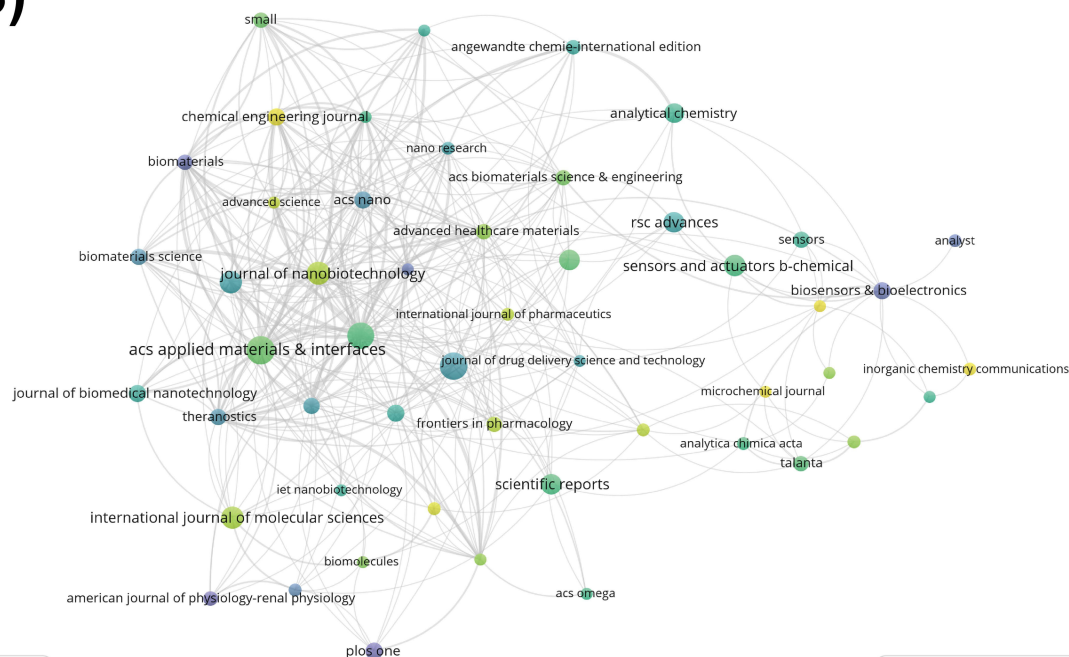
**Table 4** The Top 20 Cited Authors by Citations

Rank	Cited Author	Citations	Rank	Cited Author	Citations
1	Rm Williams	145	11	Zx Yuan	72
2	J Wang	131	12	Chj Choi	72
3	Y Wang	106	13	Mx Yu	71
4	H Yu	94	14	Y Liu	70
5	D Liu	86	15	Bj Du	69
6	Dw Jiang	86	16	Hs Choi,	66
7	Je Zuckerman	86	17	Y Huang	66
8	As Levey	78	18	Er Smith	64
9	Dy Zhang	75	19	J Li	62
10	DI Ni	72	20	Ja Kellum	61

(A)



(B)



**Figure 4** (A) The network visualization map of co-citation analysis of cited authors (including the cited authors with over 20 citations). (B) The overlay visualization map of the co-citation analysis of journals (including journals with over 6 publications and cooperation with others).

## Keywords

The 1179 publications contained 5403 keywords in total, including 2924 Keywords Plus, which were the keywords from the analysis of the WoSCC database, and 2964 author keywords, which were keywords written by the authors. In the co-occurrence analysis of author keywords, 288 were included (selection criteria:  $g\text{-index}$  ( $k = 14$ ),  $LRF = 3.0$ ,  $L/N = 10$ ,  $LBV = 5$ ,  $e = 1.0$ ). The top 20 are shown in Table 7 based on frequency. “Acute kidney injury” (124) occurred the most

**Table 5** The Top 10 Journals by the Number of Publications

Rank	Journal	Number of Publications	Citations	Avg. Citations	Avg. pub. Year	IF (2023)	Publisher	Category Quartile*	Category
1	ACS APPLIED MATERIALS & INTERFACES	23	479	20.83	2021.52	8.5	AMER CHEMICAL SOC	Q1	Materials science, multidisciplinary/ nanoscience & nanotechnology
2	INTERNATIONAL JOURNAL OF NANOMEDICINE	22	697	31.68	2019.45	6.7	DOVE MEDICAL PRESS LTD	Q1	Nanoscience & nanotechnology/ pharmacology & pharmacy
3	JOURNAL OF CONTROLLED RELEASE	21	726	34.57	2021.14	10.5	ELSEVIER	Q1	Chemistry, multidisciplinary/ pharmacology & pharmacy
4	JOURNAL OF NANOBIO TECHNOLOGY	17	207	12.18	2022.29	10.6	BMC	Q1	Biotechnology & applied microbiology/ nanoscience & nanotechnology
5	JOURNAL OF MATERIALS CHEMISTRY B	16	506	31.63	2019.75	6.1	ROYAL SOC CHEMISTRY	Q1	Materials science, biomaterials
6	INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES	16	134	8.38	2022.19	4.9	MDPI	Q1	Biochemistry & molecular biology/ chemistry, multidisciplinary
7	SENSORS AND ACTUATORS B-CHEMICAL	15	507	33.80	2021.07	8	ELSEVIER SCIENCE SA	Q1	Chemistry, analytical/ electrochemistry/ instruments & instrumentation
8	INTERNATIONAL JOURNAL OF BIOLOGICAL MACROMOLECULES	14	290	20.71	2021.36	7.7	ELSEVIER	Q1	Biochemistry & molecular biology/ chemistry, applied/ polymer science
9	SCIENTIFIC REPORTS	14	210	15.00	2021.07	3.8	NATURE PORTFOLIO	Q1	Multidisciplinary sciences
10	RSC ADVANCES	14	182	13.00	2019.79	3.9	ROYAL SOC CHEMISTRY	Q2	Chemistry, multidisciplinary

**Notes:** \*The Category Quartile listed in the table was the higher one if the journal belonged to two different quartiles.

**Table 6** According to Bradford's Law, the Journals Were Divided Into Three Zones, and the Journals in Zone 1 Were the Core

	Number of Journals	Number of Publications	Percentage
Zone 1	34	396	33.59%
Zone 2	103	394	33.42%
Zone 3	327	389	32.99%
Total	464	1179	100.00%

**Table 7** The Top 20 Author Keywords by Frequency

Label	Frequency	Centrality	Sigma	ClusterID
Acute kidney injury	124	0.15	1	4
Chronic kidney disease	79	0.27	1	1
Oxidative stress	69	0.11	1	0
Diabetic nephropathy	44	0.08	1	2
Gold nanoparticles	34	0.08	1	3
Drug delivery	21	0.03	1	0
Renal fibrosis	21	0.02	1	0
Extracellular vesicles	15	0.01	1	1

(Continued)

**Table 7** (Continued).

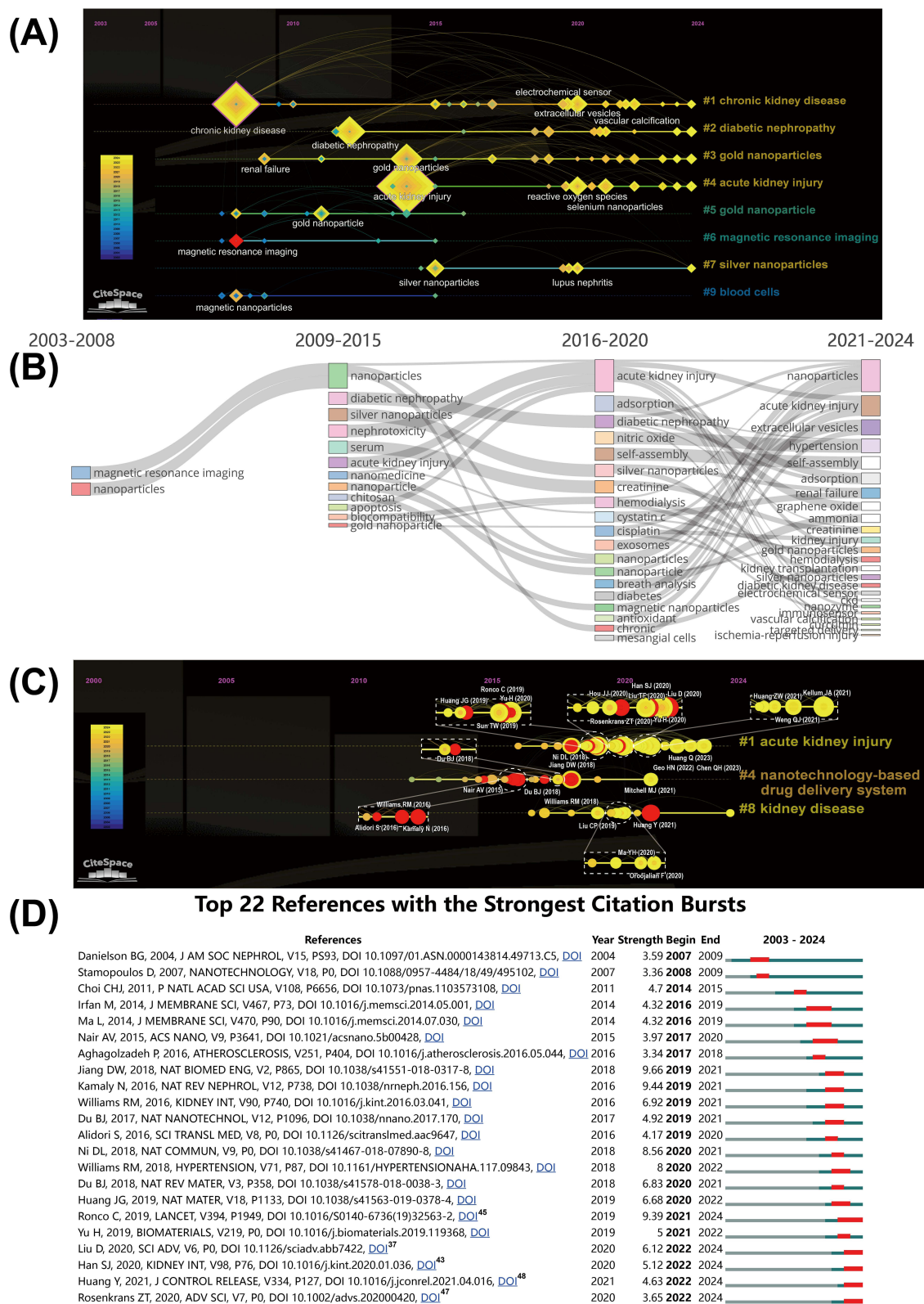
Label	Frequency	Centrality	Sigma	ClusterID
Reactive oxygen species	15	0.01	1	4
Silver nanoparticles	14	0.02	1	7
Kidney disease	14	0.01	1	0
Kidney injury	11	0.02	1	0
Magnetic resonance imaging	10	0.06	1.42	6
Gold nanoparticle	9	0.03	1	5
Selenium nanoparticles	9	0.01	1	4
Electrochemical sensor	8	0	1	1
Magnetic nanoparticles	7	0.04	1	9
Renal failure	7	0.01	1	3
Vascular calcification	7	0.01	1	1
Lupus nephritis	7	0	1	7

and “chronic kidney disease” had the highest centrality (0.27) which represented the extent of interaction between nodes. The higher the centrality of keywords is, the more important the keywords are in the topic. Additionally, both “acute kidney injury” and “oxidative stress” had centrality higher than 0.1. “Magnetic resonance imaging” had the highest sigma values of 1.42, which reflected the novelty. The 295 keywords were divided into numerous clusters using CiteSpace. The major 8 clusters are shown in [Figure 5A](#). The time when the keywords first appeared is indicated by the node position on the horizontal axis, the color represents the time of occurrence, and the purple outline of nodes represents the centrality higher than 0.1. The keywords commonly used in the last few years were included in clusters #1, #2, #3, #4, and #7. In burst detection, only one keyword, “magnetic resonance imaging”, displayed burst (the red nodes in [Figure 5A](#)). It burst from 2008 to 2015 and was also the keywords with the highest sigma values. The evolution of author keywords from 2003 to 2024 is shown in [Figure 5B](#). NP, diabetes nephropathy, and AKI were the persistent hotspots. In addition, the research on CKD, dialysis, and kidney transplantation has increased in recent years.

### References

The co-citation analysis of references was conducted using CiteSpace and 293 references that met the selection criteria (g-index ( $k = 3$ ), LRF = 3.0, L/N = 10, LBY = 5,  $e = 1.0$ ) were included in the analysis. The references with the top 10 citations are listed in [Table 8](#). Among the top 10 citations, 7 were original articles regarding loading certain medications on NPs that could alleviate AKI or renal fibrosis in mice. The 2 reviews by JA. Kellum and C. Ronco, respectively, both comprehensively reviewed the research on AKI.<sup>37,38</sup> In the fifth paper, the safety of mesoscale NPs in mice was proven and was shown to accumulate more markedly in the kidney than in other organs, with a specific target to the proximal tubular epithelial cells.<sup>39</sup> The reference titled “ROS-responsive nano-drug delivery system combining mitochondria-targeting ceria nanoparticles with atorvastatin for acute kidney injury” and “Selective Nanoparticle Targeting of the Renal Tubules” had the highest centrality (0.02).

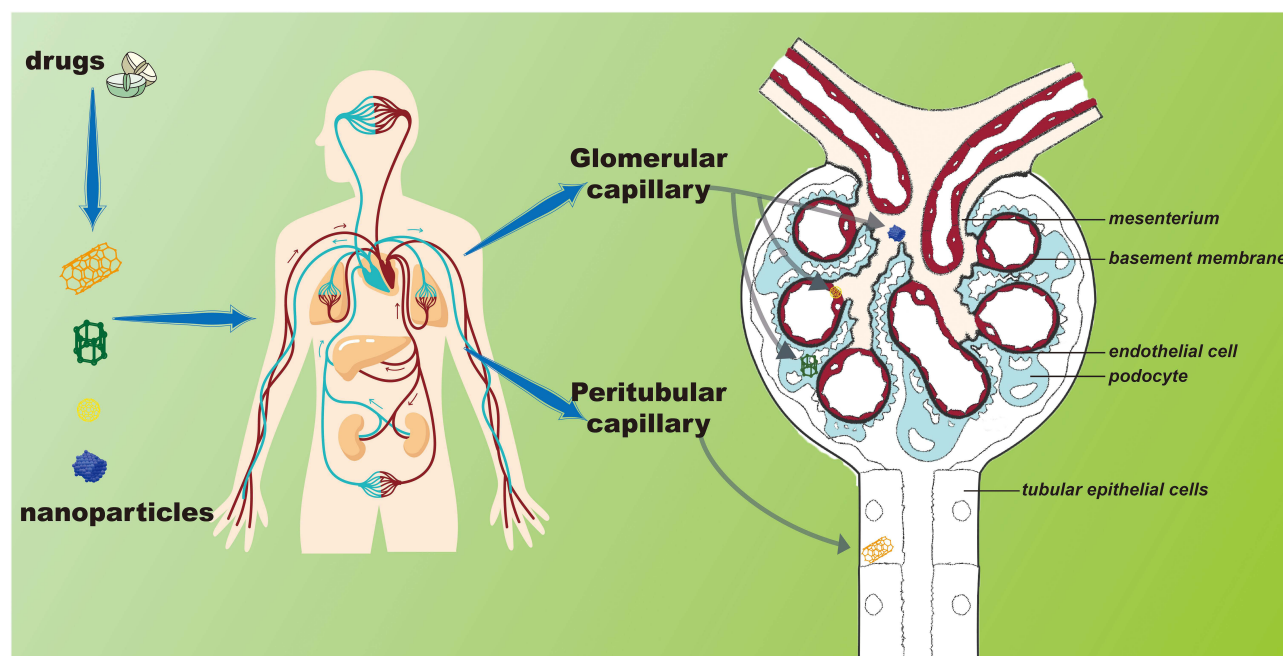
[Figure 5C](#) shows the three major clusters of references and the tendency over time. All of the top 10 references belonged to #1 and #4. The connections between various clusters were minimal. The burstness of 22 references was determined ([Figure 5D](#)). The main content of references that have burst until 2024 was as follows: some NPs, selenium-doped carbon quantum dots, and l-serine-modified chitosan with D-Arg-dimethylTyr-Lys-Phe-NH<sub>2</sub> (SS-31), could selectively accumulate in the kidney and inhibit oxidative stress to alleviate AKI in mice model; a review about AKI; a review about the influence of nanoparticle physicochemical properties on kidney target; the NP with a selective Toll-like receptor 9 (TLR9) antagonist could target renal tubular and attenuate ischemic acute kidney injury in mice.<sup>38,40,44,47,48</sup>



**Figure 5** (A) The major eight clusters' timeline view of author keywords' co-occurrence analysis. (B) The evolution of author keywords from 2003 to 2024. (C) The timeline view of references' co-citation analysis. (D) The references' burstness history view.

**Table 8** The Top 10 References by Citations

Label	Title	Type	Disease	NP/drug	Centrality	DOI	ClusterID	Reference
Liu D (2020)	ROS-responsive chitosan-SS3I prodrug for AKI therapy via rapid distribution in the kidney and long-term retention in the renal tubule	Article	AKI	l-serine-modified chitosan with SS3I	0	10.1126/sciadv.abb7422	1	[40]
Yu H (2020)	ROS-responsive nano-drug delivery system combining mitochondria-targeting ceria nanoparticles with atorvastatin for acute kidney injury	Article	AKI	A type of Ceria nanoparticles modified with triphenylphosphine and coated with ROS-responsive organic polymer with atorvastatin	0.02	10.7150/thno.40395	1	[41]
Yu H (2019)	Size and temporal-dependent efficacy of oltipraz-loaded PLGA nanoparticles for treatment of acute kidney injury and fibrosis	Article	AKI and fibrosis	Poly (lactic-co-glycolic acid) (PLGA) NPs with Oltipraz	0	10.1016/j.biomaterials.2019.119368	1	[42]
Williams RM (2018)	Selective Nanoparticle Targeting of the Renal Tubules	Article	NA	Mesoscale nanoparticles	0.02	10.1161/HYPERTENSIONAHA.117.09843	4	[39]
Kellum JA (2021)	Acute kidney injury	Review	AKI	NA	0	10.1038/s41572-021-00284-z	1	[37]
Ni DL (2018)	Molybdenum-based nanoclusters act as antioxidants and ameliorate acute kidney injury in mice	Article	AKI	Molybdenum-based polyoxometalate (POM) nanoclusters	0	10.1038/s41467-018-07890-8	1	[43]
Han SJ (2020)	Selective nanoparticle-mediated targeting of renal tubular Toll-like receptor 9 attenuates ischemic acute kidney injury	Article	AKI	Mesoscale nanoparticles encapsulated with a selective TLR9 antagonist	0	10.1016/j.kint.2020.01.036	1	[44]
Jiang DW (2018)	DNA origami nanostructures can exhibit preferential renal uptake and alleviate acute kidney injury	Article	AKI	DNA origami nanostructures	0	10.1038/s41551-018-0317-8	1	[45]
Ronco C (2019)	Acute kidney injury	Review	AKI	NA	0	10.1016/S0140-6736(19)32563-2	1	[38]
Sun TW (2019)	A Melanin-Based Natural Antioxidant Defense Nanosystem for Theranostic Application in Acute Kidney Injury	Article	AKI	Ultrasmall Mn <sup>2+</sup> -chelated melanin nanoparticles with polyethylene glycol	0	10.1002/adfm.201904833	1	[46]



**Figure 6** Nanoparticles loading drugs could accumulate in the special location of the kidney.

## Discussion

### General Information

A general understanding exists on the topic of nanomedicine in kidney disease as shown in the above-mentioned analyses. The topic originated in 2003 and shows a noticeable upward tendency to date. The researchers from China and the United States made significant contributions with considerable cooperation between the 2 countries. In addition, organizations in the 2 countries significantly contributed. Notably, although China produced the most publications, the United States had the highest average citations of the top ten countries is vital for this field, having advantages in academia. The leading organization was the Sichuan University in China. Based on the co-authorship analysis of authors and co-citation analysis of cited authors, Professor Peng Huang was the leading author, and 22 authors published more than 5 papers. Rm Williams, J Wang, and Y Wang were always cited, so they contributed significantly to the study of nanotechnology in kidney disease. Furthermore, the research was focused on the chemistry, and nanoscience & nanotechnology fields instead of clinical application based on the analysis results from journals' category.

### Nanotechnology Facilitates Drug Delivery to the Kidney

Drug delivery is a significant field of nanotechnology in kidney disease (Figure 6). In the analysis of keywords as well as references, drug delivery was the leading field. "Drug delivery" was the sixth most frequent keyword and the label of reference cluster #4. Meanwhile, the keyword "gold nanoparticles" was the fifth most frequent keyword and the labels of keyword clusters #3, #5, and #7 were all NP. In addition, drug delivery was the main topic among the leading references and the references burst in recent years. Initially, JJ. Marty et al designed NPs as a drug delivery system in the 1970s.<sup>49</sup> Subsequently, the issues regarding how NPs are delivered to the kidney have attracted attention.

The ability of NPs to target the kidneys depends on physicochemical properties.<sup>48</sup> The size of NPs plays an important role in renal targeting. Researchers found that gold (AU)-based NPs of  $75 \pm 25$  nm in diameter could sufficiently accumulate in the kidney mesangium.<sup>50</sup> Materials can pass through the glomerular filtration barrier and be excreted in the urine if their effective radius is smaller than 4.2 nm. However, AU-based NPs smaller than 1 nm showed less renal clearance because they were trapped by endothelial glycocalyx of the glomerulus.<sup>51</sup> NPs larger than 100 nm could be excreted through secretion instead of filtration.<sup>52</sup> The NPs greater than 250nm, called mesoscale nanoparticles (MNPs), possess special kidney-targeting capacity and slow-release properties. They can specifically accumulate in proximal

tubular epithelial cells by endocytosis of the endothelial cells of peritubular capillaries, thereby realizing kidney-targeting therapy.<sup>53</sup> The glomerular filtration barrier also repels the negatively charged particles because the barrier is negatively charged. Therefore, more negatively charged NPs typically accumulate more in the kidneys than positively charged NPs.<sup>54,55</sup> In addition, the neutral surface charge and zwitterionic coating prevent the opsonin and formation of protein corona, which could prevent NPs from penetrating.<sup>55</sup> The drug delivery is also affected by the shape. Researchers proved that short rod NPs and spherical NPs were initially more distributed in the kidney than long rod NPs; however, a few days later, the results were reversed.<sup>56</sup> The NPs with high molecular weight and high aspect ratio could also penetrate the glomerular filtration barrier, which was important for delivering small interfering RNA (siRNA) to the kidney.<sup>57,58</sup> Furthermore, NPs were made of various materials, like lipid, polymer, protein, nucleic acid, and inorganics, various materials showed different renal accumulations with density being a key factor.<sup>59</sup> NPs made of high-density materials usually accumulated more in the kidney and had lower clearance than low-density materials.<sup>48</sup> However, the above-mentioned studies were based on healthy kidneys. Patients may have a different distribution of NPs because kidney disease can damage the glomerular filtration barrier.

In addition to passive delivery, the ligands including peptides and antibodies in the surface layer of NPs could act as active pathways.<sup>60</sup> For example, the peptide amphiphile micelles assembled with a type of zwitterionic peptide ligand (KKEEE)3K, which bound to the megalin on proximal tubule cells, adequately targeted the kidneys in a mouse model.<sup>55,61</sup> The  $\alpha 8$  integrin was shown expressed in mesangial cells.<sup>62</sup> Using the anti- $\alpha 8$  integrin antibody, liposomes were used to target kidneys in both normal and nephritis mice.<sup>63</sup>

In summary, NPs produced based on nanotechnology could facilitate drug delivery through active or passive methods, and the efficacy of passive delivery was related to the physicochemical properties of NPs such as the size, charge, shape, and density.

## Nanotechnology in AKI

“Acute kidney injury” was the most common keyword and the label of keywords clusters #4 in Figure 5A. Additionally, AKI was the label of reference cluster #1 in Figure 5C and the main content of the top 10 references. AKI was defined as a 50% rise in serum creatinine from baseline level within 7 days, or an increase in creatinine greater than or equal to 0.3 mg/dL during 48 hours, or oliguria for 6 hours.<sup>64</sup> It is well known that the pathogenesis of AKI is related to oxidative stress, inflammation, and mitochondrial dysfunction.<sup>65,66</sup> However, the current management of AKI mainly focuses on symptomatic management, such as removal of induction, correction of ion disorders, hemodynamic management, prohibition of nephrotoxic drugs, and dialysis. Kidney-targeting drugs or methods for causal treatment are quite limited.

Nanotechnology can aid drugs targeting the kidney and reduce adverse reactions of the agents. To date, various NPs have shown kidney benefits in AKI animal models based on different mechanisms. Oxidative stress can aggravate AKI, and several antioxidant drugs have been tried to treat or prevent AKI. Resveratrol is a natural antioxidant; however, its water solubility and bioavailability are low. When it was loaded by NPs, its inhibitory effect on oxidative stress damage became much better than that of resveratrol alone *in vivo*.<sup>67</sup> The accumulation and activation of macrophages in the kidney were important to the inflammatory reaction in AKI induced by severe acute pancreatitis (SAP). Clodronate, able to reduce macrophage in the tissue, has low cytomembrane permeability and a short half-life. Dang et al created superparamagnetic iron oxide (SPIO)-clodronate-liposomes, which could induce apoptosis and decrease the release of inflammatory mediators to improve the AKI induced by SAP.<sup>68</sup> Mitochondrial dysfunction induces cell apoptosis and takes part in the AKI advance.<sup>15</sup> Formoterol, a type of long-acting  $\beta$ -agonist, can promote mitochondrial biogenesis and has a desirable effect *in vitro*. However, the efficacy *in vivo* was limited because of the renal distribution and adverse reaction, NPs could solve those problems and increase the therapeutic effect.<sup>69</sup>

Nanotechnology can also be combined with other therapies to improve AKI, such as stem cell-based therapy and gene therapy.<sup>70</sup> Mesenchymal stem cells (MSCs) participate in the repair process during AKI, and the extracellular vesicles (EVs) from MSCs are essential.<sup>71,72</sup> EVs with a diameter of nanometers participate in cell–cell communication in almost all physiological processes. In addition, EVs from MSCs can be used as a type of nanomedicine and transport biological active molecules such as proteins, lipids, and nucleic acids to target cells.<sup>73</sup> IL-10 mRNA was discovered in vesicles. Human-derived proximal tubule epithelial cells could synthesize IL-10 when co-cultured with EVs, thereby reducing the

inflammatory response, fibrosis, and cell death.<sup>72,74</sup> However, the efficacy in clinical trials was not satisfactory due to low bioavailability and kidney accumulation.<sup>75,76</sup> Zhang et al developed Arg-Gly-Asp peptide nanofibers, which could enhance the stability of EVs and improve the therapeutic effect in mouse AKI model.<sup>77</sup> Several other RNAs also participate in the pathogenesis of AKI.<sup>78,79</sup> Researchers have successfully transfected long non-coding RNA (lncRNA)-OIP5-AS1 with the assistance of NPs to inhibit renal ischemic reperfusion injury in mice.<sup>80</sup> Arginase-2 (Arg-2) leads to tubular injury in contrast-induced AKI, and Arg-2 siRNA can inhibit the transcription and translation, thereby alleviating the renal injury. However, the uptake efficiency of siRNA is poor, which limits its renoprotection in vivo.<sup>81,82</sup> The layer-by-layer assembly of renal-targeted polymeric NPs could solve the above problems and had a protective effect in the contrast-induced AKI mice model.<sup>83</sup> Another RNA, miR-5100, has a low expression in AKI and may be a novel biomarker.<sup>84</sup> Researchers successfully induced miR-5100 overexpression by injecting miR-5100-mimic conjugated with polyethylenimine NPs in the AKI mice and finally achieved the effect of prevention and treatment of AKI.<sup>84</sup>

Furthermore, nanotechnology may be helpful in the early diagnosis and monitoring of AKI. Based on nanotechnology, the detection of biomarkers can be simple and fast. For example, approximately only 5 minutes was necessary to detect neutrophil gelatinase-associated lipocalin in urine using an ultrarapid nanoconfinement-enhanced fluorescence clinical detection platform.<sup>85</sup> NPs also assist in the imageological examination. The SPIO mentioned earlier, can be used as a tracer in MRI and has the potential to detect renal damage in mice.<sup>68</sup> Recently, a nanosystem, platelet membranes-ICG-SS31-poly lactic-co-glycolic acid (PLGA), was developed that could target kidney lesion areas in mice models and be detected by near-infrared rays to aid in early detection and monitoring of AKI.<sup>86</sup> Vesicles can be used for the treatment of AKI and also for the prediction of AKI. It was proven that the lower levels of podocalyxin-like protein 1-positive EVs in urine before surgery, the more serious AKI patients suffered after cardiac surgery.<sup>87</sup>

## Nanotechnology in CKD

According to the latest KDIGO guideline, CKD is defined as abnormalities of kidney structure or function, present for a minimum of 3 months, with implications for health.<sup>88</sup> CKD can be classified into 5 stages based on eGFR. At present, most CKD patients are not diagnosed in time, and the treatment effect is slow or even poor. In particular, effective therapy for advanced-stage CKD is quite limited. While nanotechnology is helpful for the diagnosis and treatment of CKD.

In renal dysfunction, several abnormal metabolites are present in patients and can be excreted through exhalation. Polyaniline NPs can detect ammonia in human breath to provide a cost-effective and noninvasive method for monitoring renal function.<sup>89</sup> Recently, Luo et al created pentyptycene metallopolymer/single-walled carbon nanotube complexes that can more sensitively detect ammonia of CKD patients.<sup>90</sup> Glutathione-coated AU NPs as imaging contrast agents were used to evaluate renal function, which was highly sensitive and noninvasive and could evaluate the unilateral renal function in mice models.<sup>91</sup> Nanotechnology can also improve the detection methods for urinary albumin.<sup>92</sup>

Celastrol (CLT) is the major active component of the herb *tripterygium wilfordii* widely used for the treatment of certain CKDs. However, the toxicity of CLT limits its effect. Wu et al designed peptides coupled with CLT-phospholipid NPs to deliver CLT to endothelial cells and podocytes in the glomerulus and obtained satisfactory anti-inflammatory and kidney-beneficial effects in mouse CKD model.<sup>93</sup> NPs can not only reduce the toxicity but also prolong the duration of drug efficacy. Emodin enema delays the progression of CKD, however, the short retention time and low solubility limit the application. With the polymer NP, better colon adhesion and persistent effects were reached than emodin alone.<sup>94</sup> The EVs from MSCs mentioned above assist in renal repair after AKI and have therapeutic potential for CKD. Recently, Li et al discovered that MSC-derived EVs could ameliorate lupus nephritis by regulating the proportion of T cell subsets, reducing plasma cells and pro-inflammatory cytokines in vivo; however, the exact mechanism remained unclear.<sup>95</sup> In a single-center, randomized, placebo-controlled clinical trial, EV injection was proven to improve the renal function of stage 3–4 CKD patients by regulating inflammatory reactions.<sup>96</sup> With the increasing number of diabetic patients, diabetic nephropathy is gradually replacing primary glomerulonephritis as the major cause of CKD. A nanometal-organic framework containing chromium or selenium and zinc was proven to increase creatinine clearance and decrease urinary albumin in the diabetic nephropathy mouse model.<sup>97,98</sup> In addition to diabetic nephropathy, nanotechnology can also assist in the treatment of other CKDs. For example, lupus nephritis is caused by the immune reaction of anti-dsDNA

antibody which can be inhibited by D-form modified ALW peptide.<sup>99</sup> The polyethylene glycol (PEG)-PLGA NP could improve the stability of ALW peptide and reduce the IgG and C3 deposition in the kidney.<sup>100</sup> Renal fibrosis, the final pathology change of ESRD, was potentially relieved by NPs. It was proven that folic acid-conjugated gold NPs selectively accumulated in the renal tubules of the fibrotic kidney in unilateral ureteral obstruction mice and inhibited the p38 $\alpha$  mitogen-activated protein kinase leading to the relief of tubulointerstitial fibrosis.<sup>101</sup>

Furthermore, nanomedicine can help alleviate complications of CKD. Hyperphosphatemia is a severe and common complication of CKD and may lead to secondary hyperparathyroidism and even increase the risk of mortality. Ma et al synthesized nano-lanthanum hydroxide, which had a higher specific surface area and thus a better phosphorus-binding rate. The safety and efficacy of the synthesized nano-lanthanum hydroxide were also proven in mouse models.<sup>102</sup>

In general, given the unique physicochemical properties, nanomedicine can achieve continuous release and long-lasting efficacy, thereby owing to a broad therapeutic prospect in CKD.

## Nanotechnology and Oxidative Stress

“Oxidative stress” is the third frequency keyword and also the main topic of many references above. Five of the top 10 references indicated nanotechnology could improve AKI through antioxidative effects,<sup>40–43,46</sup> showing that oxidative stress is an important field of nanotechnology in kidney disease. Oxidative stress is caused by the high production of reactive oxygen species (ROS), which can lead to the destruction of proteins, DNA, cytomembranes, and other substances, thereby resulting in cell death and kidney disease.<sup>103–105</sup> Therefore, anti-ROS is an important therapeutic strategy for kidney disease. The application of nanotechnology in anti-ROS therapy mainly manifests in two aspects: inhibition of ROS generation and scavenging excess ROS. It has been reported that H<sub>2</sub>O<sub>2</sub>-responsive nanoparticles loaded with vanillyl alcohol could target ROS over-production sites and inhibit production.<sup>106</sup> Lozano et al designed PLGA nanoparticles encapsulating quercetin, which could maintain the integrity of mitochondrial electron transfer chains, and then reduce ROS production.<sup>107</sup> PLGA nanoparticles combined with Cyclosporin A, an immunosuppressant commonly used in kidney disease, were designed to inhibit mitochondrial permeability transition pore opening, thus reducing ROS damage.<sup>108</sup> Besides inhibiting ROS production, it is equally important to eliminate existing ROS. Nanozymes are enzyme-mimicking nanomaterials with properties of low cost, high stability, and catalytic ability. It has been demonstrated that iron oxide NPs, a kind of metallic nano-enzyme, could mimic peroxidase and scavenge ROS in vivo. Nanotechnology can also deliver antioxidants.<sup>109</sup> The efficacy of antioxidants in clinical treatment is still uncertain. Factors such as low bioavailability and instability may affect its effectiveness. Nano-delivery systems have been a promising solution. For example, researchers have prepared lactate protein-based polylactic acid NPs for the delivery of natural antioxidants. The NPs could improve the water solubility and bioavailability of curcumin and reduce its biotoxicity.<sup>110</sup> Yu et al utilized ROS-responsive nanocapsules to deliver drugs to the kidney in diabetic kidney disease models.<sup>111</sup> In addition, DNA can also play a therapeutic role with nanotechnology aiding. It has been reported that DNA with the origami nanostructure could eliminate ROS and accumulate preferentially in the kidneys.<sup>45</sup> More importantly, the anti-complement component 5a could be loaded into the DNA nanostructure, enabling dual-target therapy.<sup>112</sup> These studies indicate that nanotechnology has broad application prospects in anti-oxidative stress.

## Other Kidney Diseases

Nanomedicine also shows potential for the treatment of hereditary nephropathy. A prevalent hereditary nephropathy is polycystic kidney disease (PKD), which is primarily an autosomal dominant inheritance. Research indicated that folate-conjugated PLGA-PEG NPs loading rapamycin and antioxidants could better control cystic development in vivo than rapamycin alone.<sup>113</sup> In addition to drug loading, NPs can load nucleic acids, which may cure hereditary nephropathy at the genetic level in the future.<sup>18,19</sup> However, the application of nanotechnology in genetic kidney disease involves ethics and supervision, and relevant systems and laws need to be continuously improved for the further development of nanomedicine.

The safety of certain NPs or medications connected to nanotechnology was proven in clinical trials, and several are currently on the market.<sup>114–117</sup> For example, the polymeric NPs with erythropoiesis-stimulating agents have been

approved for renal anemia treatment.<sup>117</sup> A clinical study of domestic polysaccharide SPIO NP injection for renal contrast-enhanced MRI to evaluate renal blood vessels and renal function is currently underway.<sup>118</sup>

Immune response also plays a critical role in the pathogenesis of kidney diseases, particularly in the use of immunosuppressants for the treatment of CKD. However, the application of some immunosuppressants commonly used at present, such as glucocorticoids, is often limited because of obvious side effects. Therefore, it is of great clinical significance to further explore the role of nanomedicines in immune regulation. Several relevant literatures have been reported. For example, dexamethasone (DXM)-loaded IFN- $\gamma$ -treated MHC class I deficient cancer membrane-coated NPs (IM-MNPs/DXM) were fabricated which could utilize the immunosuppressive power of tumor cells for the treatment of lupus nephritis. These particles could evade immune clearance and accumulate in inflammatory organs. The sustained release of DXM can inhibit the production of proinflammatory cytokines in the inflammatory microenvironment, exhibiting significant therapeutic efficacy in ameliorating lupus nephritis as well as decreasing side effects *in vivo*.<sup>119</sup> It has been found that calcium calmodulin kinase IV is increased in podocytes of patients with focal segmental glomerulosclerosis and in mice injected with doxorubicin. Using NPs loaded with a small drug inhibitor of calcium calmodulin kinase IV and tagged with antibodies directed to CD4 can inhibit autoimmunity, thereby alleviating kidney damage.<sup>120</sup> Therefore, developing nanomaterials with immunomodulatory properties could offer new therapeutic approaches for treating immune-mediated kidney diseases.

However, there are still some problems of nanotechnology used in kidney diseases, limiting the wide application of nanomedicine. For instance, commonly used metal NPs may be deposited in other organs, like the liver, spleen, or even the brain, and cause metal poisoning.<sup>121</sup> Although the accelerating degradation rate of nano-drugs can improve the safety, the efficacy may be reduced.<sup>122,123</sup> Doping, a widely used and effective strategy for inorganic NPs, seems to be a method to reduce inorganic NPs' toxicity. It can prevent NPs from dissolution and binding with oxygen.<sup>124,125</sup> However, whether doping may affect the efficacy of NPs still needs to be further explored. Therefore, to keep the balance between effectiveness and safety is necessary.<sup>122</sup> Furthermore, a systematic and detailed safety evaluation as well as a regulatory system for nanomedicine are lacking, and the effects on long-term exposure to nanomedicine remain unclear. Therefore, the long-term observation of the side effects and safety of nanomedicine are essential.<sup>125</sup>

## Conclusion and Future Perspective

In this review, bibliometric methods were used to comprehensively collect and analyze global publications on nanotechnology in kidney disease. The development trend of nanotechnology, high-yield authors and institutions, important literature, and research hotspots were summarized. The results are essential to fully understand the current status of nanotechnology in kidney disease, adjust future research directions, and explore unknown areas. Based on the results of this study, many questions and challenges remain to be solved in this fast-growing field.

First, drug delivery is a significant advantage of nanotechnology and is currently a hot research topic. However, the kidney structure is complex, including various cell types and tissue components. How to achieve precise delivery, such as cell-specific or tissue-specific, to render accurate targeted therapy into reality may be problematic.

Secondly, the current research on the application of nanomedicine in kidney disease is mainly focused on AKI. AKI was the most common keyword in all publications analyzed. In addition, among the 10 most-cited references, 9 were on AKI. Fewer studies were on CKD than AKI. CKD presents as a slowly progressing disease, and the continuity of drug therapy and the persistence of drug effects are important in clinical application. Therefore, the development of sustained- or controlled-release technology in nanomedicine is essential for the treatment of CKD.

Thirdly, the results of this analysis showed that the mechanism of nanomaterials in the treatment of kidney disease is mainly through antioxidative effects. "Oxidative stress" was the third most common among the top 10 keywords. The immune response is also important in the pathogenesis of kidney disease, and immunosuppressive agents are often administered in CKD treatment. Therefore, the development of nanomedicine with immunosuppressive effects should be further investigated.

Finally, the potential side effects and bioaccumulation issues associated with the long-term use of nanomedicines require more attention. These concerns are critical for clinical applications and may become significant research directions in the future. Monitoring the long-term safety and efficacy of nanomedicine has been a great challenge.

In conclusion, due to the continuous progress of nanotechnology and the rapid development of artificial intelligence, early diagnosis, precise treatment, and the possibility of curing kidney disease is becoming a reality based on multi-disciplinary cooperation.

## Abbreviations

CKD, chronic kidney disease; AKI, acute kidney injury; DALYs, disability-adjusted life years; ESRD, end-stage renal disease; NDDS, nanodrug delivery system; FDA, United States Food and Drug Administration; NPs, nanoparticles; miR, microRNA; WoSCC, the Web of Science Core Collection; SCIE, the Science Citation Index-Expanded; SSCI, the Social Sciences Citation Index; A&HCI, the Arts & Humanities Citation Index; TI, title; AB, abstract; AK, author keywords; TLR9, Toll-like receptor 9; AU, gold; MNP, mesoscale nanoparticle; SAP, severe acute pancreatitis; SPIO, super-paramagnetic iron oxide; MSCs, mesenchymal stem cells; EVs, extracellular vesicles; lncRNA, long non-coding RNA; Arg-2, arginase-2; siRNA, small interfering RNA; PLGA, poly lactic-co-glycolic acid; CLT, celastrol; PEG, polyethylene glycol; ROS, reactive oxygen species; PKD, polycystic kidney disease; DXM, dexamethasone.

## Data availability statement

The data presented in this article are available on the WoSCC database using the search query listed in the “Materials and methods” section, further inquiries can be directed to the corresponding authors.

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The authors report no conflicts of interest in this work.

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