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Review article

# Unveiling the future: Bibliometric analysis on the application of nanomaterials in osteoarthritis (2006–2023)

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ABSTRACT

*Background:* As the population ages, the socio-economic impact of osteoarthritis (OA) is becoming increasingly significant. In recent years, there has been a growing focus on the design and development of nanomaterials for diagnosing and treating OA. This study aims to comprehensively evaluate the current status and trends in the application of nanomaterials in OA through bibliometric analysis and provide a review.

*Methods:* Studies on nanomaterials and OA were sourced from the Web of Science Core Collection (WoSCC) database, with relevant articles selected based on predefined inclusion criteria. Quantitative and visual analyses of the included publications were conducted using tools such as VOSviewer, and GraphPad Prism 9.5.0.

*Results:* A total of 532 publications were included in this study. The number of annual publications has increased steadily from 2006 to 2023. China, the United States, and South Korea are the leading countries in this field. Shanghai Jiao Tong University and Li Zheng are recognized as the most influential institutions and authors, respectively. Biomaterials is the most frequently published and cited journal. Current research primarily focuses on drug delivery and the anti-inflammatory and antioxidant properties of nanomaterials. Recent research hotspots include mesoporous silica nanoparticles, electrostatic interaction, and injectable hydrogels.

*Conclusion:* In this study, we summarised the annual publication trends and identified the most influential countries, institutions, authors, journals, and current research and development trends in the application of nanomaterials for OA.

List of abbreviations

| | |
|---|---|
| CS | Chitosan |
| DNA | Deoxyribonucleic acid |
| EMA | Electromagnetic actuation |
| IF | Impact factor |
| IGF-1 | Insulin-like growth factor 1 |
| LS | Link strength |
| MMP-13 | Matrix metalloproteinase-13 |
| NIR | Near-infrared |
| OA | Osteoarthritis |

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| | |
|---|---|
| PAMAM | Polyamidoamine |
| PCL | Polycaprolactone |
| PEG | Polyethylene glycol |
| PEI | Polyethylene imine |
| PGC-1α | Peroxisome proliferator-activated receptor gamma coactivator 1-α |
| PLGA | Poly(lactic-co-glycolic acid) |
| RNS | Reactive nitrogen species |
| ROS | Reactive oxygen species |
| SCI-E | Science citation index-expanded |
| SIRT1 | Sirtuin 1 |
| SPION | Superparamagnetic iron oxide nanoparticles |
| SSCI | Social sciences citation index |
| TGF-β1 | Transforming growth factor-β1 |
| TLS | Total link strength |
| TNF-α | Tumor necrosis factor-α |
| WoSCC | Web of science core collection |

## 1. Introduction

Osteoarthritis ( OA ) is a chronic degenerative condition and ranks among the most prevalent joint diseases [1]. It primarily involves the wear and degeneration of articular cartilage [2], leading to joint deformation, pain, and dysfunction, especially in the knees [3], hip [4], spine [5], and feet. Various factors contribute to the onset of OA, including age [6], genetics [7,8], joint injuries, obesity [9], and other joint-related conditions. The main symptoms of OA encompass joint pain, stiffness, limited function, deformation, and swelling [1]. Current treatment options for OA include drug therapy [10,11], physical therapy, and surgery [12]. Additionally, daily life measures such as weight control, moderate exercise, and maintaining healthy lifestyle habits can help alleviate symptoms and prevent the progression of OA [13]. In recent years, with the rapid advancement of nanotechnology, an increasing amount of research has been directed towards exploring the application of nanomaterials in the treatment of osteoarthritis.

Nanomaterials, due to their small size, large specific surface area, and excellent biocompatibility, are particularly effective at penetrating joint cartilage and synovial fluid. This allows them to act directly on affected areas, thereby more effectively alleviating the symptoms of osteoarthritis [14,15]. Research has demonstrated that nano drugs, nano biomaterials, and nano gene therapy can have significant impacts on treating osteoarthritis, reducing inflammation, promoting cartilage repair, and enhancing joint function [16].

For instance, certain nanomedicines can alleviate symptoms of osteoarthritis by inhibiting inflammation and enzyme activity that leads to cartilage degradation. Additionally, nano biomaterials, such as nanogels [17] and nanofibers can mimic the microstructure of natural cartilage, providing an optimal environment for the repair of damaged tissue. Song and colleagues [18] developed a cartilage-targeted dual-drug delivery platform that utilizes near-infrared (NIR) targeting to release drugs and activate the sirtuin 1 (SIRT1)-peroxisome proliferator-activated receptor gamma coactivator 1-α (PGC-1α) signaling pathway. This stimulation enhances the mitochondrial energy metabolism of chondrocytes, effectively delaying cartilage degeneration. Furthermore, nano gene therapy approaches can enhance the living environment and functionality of joint cells by regulating gene expression [19].

In this study, we aim to review the development of nanomaterials in the treatment of osteoarthritis, analyze current research hotspots, and offer predictive analyses of future main fields.

Bibliometric analysis, which employs statistical and econometric methods to analyze scientific literature, is a crucial scientific research method. It uncovers laws and trends in scientific research by analyzing data from scientific publications. Additionally, it supports and guides the evaluation of scientific research, the study of disciplinary development, the formulation of scientific policies, and significant scientific data research [20].

However, there remains a significant gap in research utilizing bibliometric analysis to evaluate the application of nanomaterials in the field of osteoarthritis. In this study, we aim to obtain an overview of the treatment of OA using nanomaterials through bibliometric analysis and to analyze the research hotspots and trends within this field.

## 2. Materials and methods

### *2.1. Data sources and search strategy*

All data for this paper were sourced from the Web of Science Core Collection (WoSCC) database for bibliometric analysis. The reasons for selecting the WoSCC database include (1) High-quality literature; (2) Broad subject coverage; (3) Comprehensive citation data; (4) Advanced data analysis tools; and (5) Esteemed academic reputation.

The search strategy employed was: "TS = ((osteoarthritides OR osteoarthrosis OR osteoarthroses OR osteoarthritis OR osteoarthrosis deformans OR osteoarthropathy) AND (nanomedicine OR nanocarrier OR nanomaterial OR nanoencapsulation OR nanoparticles OR nanostructures OR nanotechnology OR nanocomposites OR nanofibers OR nanotubes OR nanowires OR nanocrystal OR nanoscience OR nanosheets) AND (treat OR treatment OR therapy OR disease management OR therapeutic OR remedy))."

### 2.2. Screening criteria and data extraction

After conducting the data search, the following criteria were used to filter the obtained literature: (1) The publication language is "English"; (2) The reference type selected is "article"; (3) The publication period spans from 2006 to 2023; (4) The publications are sourced from the Science Citation Index-Expanded (SCI-E) and the Social Sciences Citation Index (SSCI) within the WoSCC (Fig. 1).

From the selected publications, we extracted data including the title, authors (along with their institutional affiliations), keywords, number of published papers, citation frequency (total and average citations), journal (including the journal's H-index), and the five-year impact factor.

### 2.3. Data analysis

The collected data was analyzed using VOSviewer, and GraphPad Prism 9.5.0.

Specifically, VOSviewer was utilized to map collaboration networks among institutions, authors, and countries, as well as to conduct keyword cluster analysis. In the VOSviewer data graph, the size of each node (circle) represents the number of publications, while the link strength (LS) are depicted by the thickness of the lines between nodes, indicating the strength of collaboration. The total link strength (TLS) reflects the comprehensive nature of the cooperation relationships. GraphPad Prism 9.5.0 was employed to create charts showing the annual changes in institutional publications.

## 3. Results

### 3.1. Overview of global publication distribution and citations

Through meticulous search and filtering, as illustrated in Fig. 2, we retrieved 532 articles from WoSCC. From 2006 to 2023, the annual number of published papers displayed an upward trend, with the highest growth rate occurring in 2020, which saw an increase of 44.44 % compared to 2019. The year 2023 recorded the highest number of publications with 108 articles, marking a slight increase from 2022 (Fig. 2aandb). As of the retrieval date for this study, these publications have accumulated a total of 10846 citations, averaging 20.39 citations per article. Since 2020, the citation frequency of publications in this field has remained high, with more than 1000 citations annually: 1097 in 2020, 1739 in 2021, 2538 in 2022, and 3011 in 2023 (Fig. 2c). The H-index for this field is 52, which was relatively low until 2011 (H-index<5). From 2012 to 2020, the H-index experienced volatile growth, peaking at 26 in 2020, and showing a slight downward trend from 2021 to 2023 (Fig. 2d).

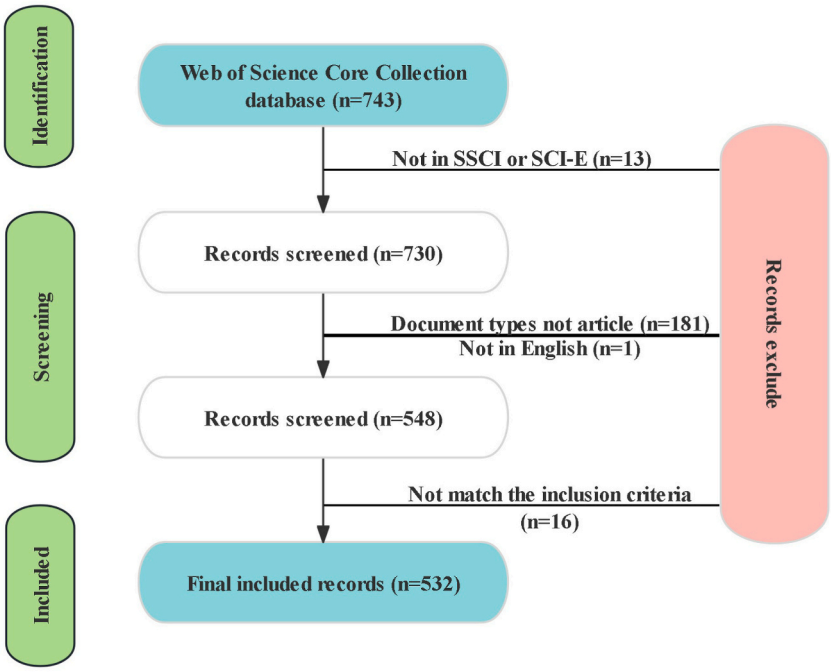


**Fig. 1.** Flowchart of the literature screening process.

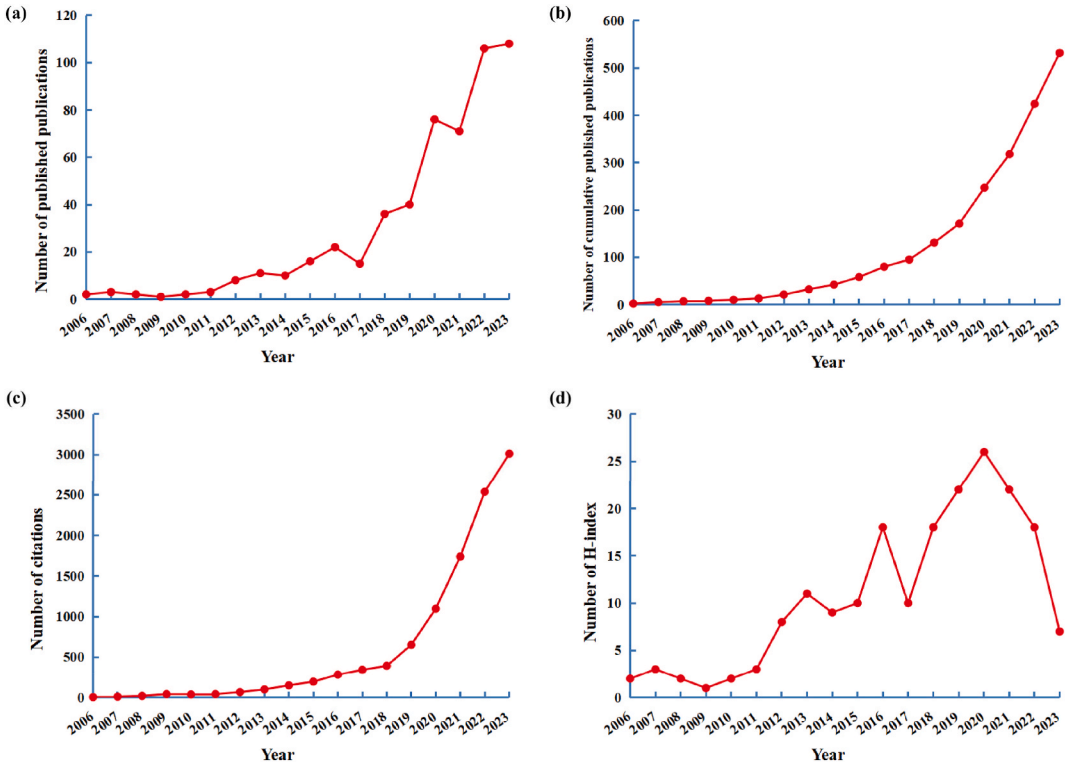


**Fig. 2.** (a) The global annual number of publications. (b) The global yearly number of cumulative publications. (c) The international annual number of citations of the publication. (d) The global yearly H-index of the publications.

### *3.2. Journal and institutional contributions*

A total of 532 papers were published across 222 journals, with 128 of these papers, or 24.06 % of the total, appearing in the top 10 journals. The journals Biomaterials (1340 citations), International Journal of Pharmaceutics (438 citations), and Journal of Nanobiotechnology (346 citations) are the three most frequently cited. On average, Biomaterials (58.26 citations per paper), Drug Delivery (30.89 citations per paper), and ACS Applied Materials & Interfaces (29.82 citations per paper) had the highest citation rates (Table 1).

In Table 2, we highlighted the top 10 articles with the highest citation counts. The most frequently cited article, titled "Stretchable Heater Using Ligand Exchange Silver Nanocomposite for Wearable Art Thermotherapy," has garnered 417 citations. Additionally, we introduce a relatively new metric, Altmetric, to assess the social impact of these articles to a certain extent. Altmetric primarily measures the level of attention and sharing of academic papers online. Unlike traditional metrics such as the Impact Factor, Altmetric more effectively captures the real-time online influence and social engagement of academic papers. The value of Altmetric lies in providing insights into how widely documents are shared, downloaded, read, and discussed online, as well as the extent to which they are recognized. Among the top ten articles by citation count, the article "Cartilage generating nanocarriers improve delivery and efficiency of growth factor treatment of osteoarthritis" achieved the highest Altmetric score (208).

Out of 855 institutions, 38 have published five or more papers. Shanghai Jiao Tong University leads with 41 publications, followed by the Chinese Academy of Sciences with 25, and Guangxi Medical University with 24, ranking second and third, respectively (Fig. 3a).

**Table 1**
The top 10 most productive journals regarding nanomaterials and osteoarthritis research from 2006 to 2023.

| Rank | Publication Titles | Record Count | Percentage | Times Cited | Average per item | H-index | IF |
|---|---|---|---|---|---|---|---|
| 1 | Biomaterials | 23 | 4.291 | 1340 | 58.26 | 18 | 13.8 |
| 2 | Journal of Nanobiotechnology | 18 | 3.385 | 346 | 19.22 | 11 | 11.5 |
| 3 | International Journal of Pharmaceutics | 17 | 3.172 | 438 | 25.76 | 11 | 5.8 |
| 4 | Pharmaceutics | 12 | 2.239 | 79 | 6.58 | 5 | 6 |
| 5 | ACS Applied Materials & Interfaces | 11 | 2.052 | 328 | 29.82 | 8 | 9.6 |
| 6 | Frontiers in Bioengineering and Biotechnology | 11 | 2.052 | 68 | 6.18 | 4 | 6.2 |
| 7 | Journal of Controlled Release | 10 | 1.866 | 341 | 34.1 | 9 | 10.2 |
| 8 | Drug Delivery | 9 | 1.679 | 278 | 30.89 | 8 | 6.5 |
| 9 | International Journal of Nanomedicine | 9 | 1.679 | 174 | 19.33 | 5 | 8.1 |
| 10 | ACTA Biomaterialia | 8 | 1.493 | 189 | 23.63 | 6 | 9.9 |

**Table 2**
The top 10 most cited references regarding nanomaterial and osteoarthritis research from 2006 to 2023.

| Rank | Title | Authors | Journal | Citations | Altmetric |
|---|---|---|---|---|---|
| 1 | Stretchable Heater Using Ligand-Exchanged Silver Nanowire Nanocomposite for Wearable Articular Thermotherapy | Suji Choi, Taeghwan Hyeon, Dae-Hyeong Kim et al. | ACS Nano | 417 | 41 |
| 2 | Intra-articular delivery of kartogenin-conjugated chitosan nano/microparticles for cartilage regeneration | Mi Lan Kang, Ji-Yun Ko, Ji Eun Kim et al. | Biomaterials | 180 | 3 |
| 3 | Cartilage-penetrating nanocarriers improve delivery and efficacy of growth factor treatment of osteoarthritis | Brett C. Geiger et al. | Science Translational Medicine | 156 | 208 |
| 4 | Development and characterization of a novel drug nanocarrier for oral delivery, based on self-assembled β-casein micelles | Michal Bachar, Amitai Mandelbaum et al. | Journal of Controlled Release | 121 | 3 |
| 5 | Novel hyaluronic acid-chitosan nanoparticles as non-viral gene delivery vectors targeting osteoarthritis | Hua-Ding Lu, Hui-Qing Zhao et al. | International Journal of Pharmaceutics | 118 | 9 |
| 6 | Human adipose-derived mesenchymal stem cell-based medical microrobot system for knee cartilage regeneration in vivo | Gwangjun Go et al. | Science Robotics | 114 | 70 |
| 7 | Curcumin slows osteoarthritis progression and relieves osteoarthritis-associated pain symptoms in a post-traumatic osteoarthritis mouse model | Zhang, Z., Leong, D.J., Xu, L. et al. | Arthritis Research & Therapy | 111 | 7 |
| 8 | Manganese dioxide nanoparticles protect cartilage from inflammation-induced oxidative stress | Sharma, Blanka et al. | Biomaterials | 110 | 2 |
| 9 | Dexamethasone-containing PLGA superparamagnetic microparticles as carriers for the local treatment of arthritis | Nicoleta Butoescu, Christian A. Seemayer et al. | Biomaterials | 107 | 3 |
| 10 | Chitosan-Graft-Polyethylenimine/DNA Nanoparticles as Novel Non-Viral Gene Delivery Vectors Targeting Osteoarthritis | Lu H, Dai Y, Lv L et al. | Plos One | 106 | 4 |

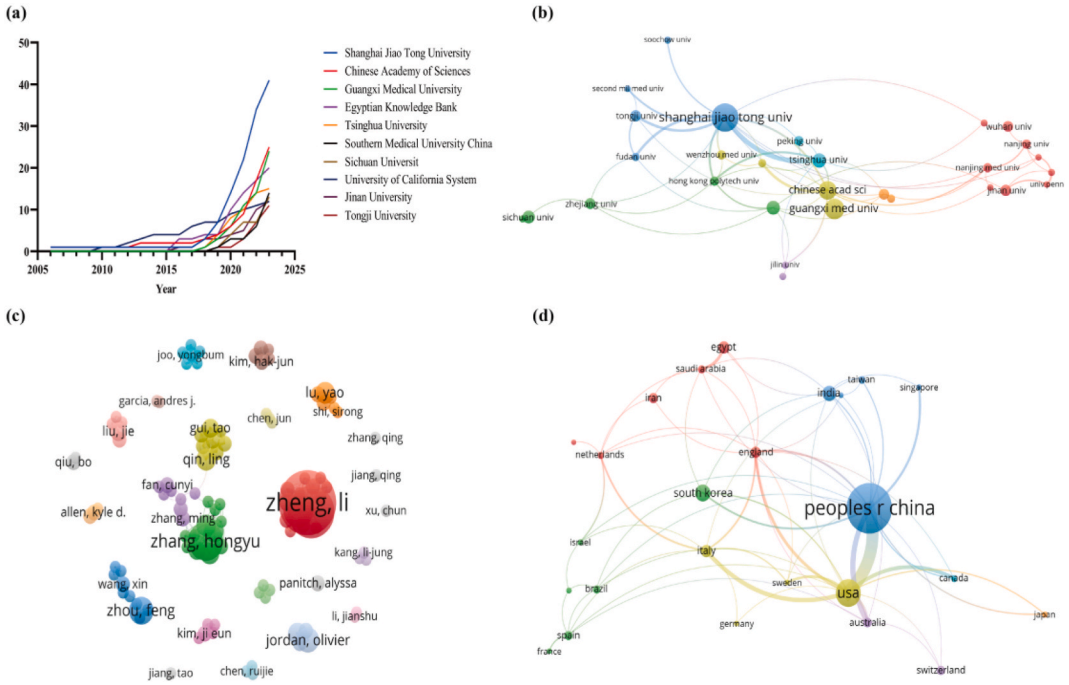


**Fig. 3.** (a) Cumulative number of publications by the top 10 institutions per year. (b) The co-authorship network map of institutions. (c)The co-authorship network map of authors. (d) The co-authorship network map of countries.

Using VOSviewer to analyze the co-authorship relationships among these institutions, Shanghai Jiao Tong University shows the most robust collaboration network, with other institutions (15 LS, TLS 35). Tsinghua University is closely linked with Shanghai Jiao Tong University. The Chinese Academy of Sciences (12 LS, TLS 20) and Tsinghua University (8 LS, TLS 17) are the second and third most actively collaborating institutions, respectively (Fig. 3b).

### *3.3. Authors contributions*

A total of 3425 authors have contributed to the publications under review. The co-authorship network diagram, which includes authors with three or more publications, is depicted in Fig. 3c. Li Zheng is at the forefront of collaborative activities, with the most

robust connections (14 LS, TLS 68). Other notable authors include Zhiliang Cheng (7 LS, TLS 26), Hongyu Zhao (10 LS, TLS 35), Xin Wang (5 LS, TLS 7), Cunyi Fan (4 LS, TLS 9), and Jieli Chen (4 LS, TLS 10). These authors form several densely interconnected collaboration networks.

### 3.4. Countries contributions

A total of 51 countries are involved in the publications under review. Collaborative analysis was conducted on countries with at least five publications. Among these, 25 countries have established relatively close cooperative relationships. China leads in terms of collaboration frequency (16 LS, TLS 55), with countries like the United States and South Korea among those closely collaborating with China (Fig. 3d).

### 3.5. Keyword analysis

Keyword cluster analysis involves grouping different topics within a research field by analyzing keywords and their associations. These topics represent various research directions or hotspots in OA research, and each direction possessing its own unique importance and characteristics (Fig. 4).

Cluster 1 (Red): Cartilage regeneration and repair. Keywords include cartilage regeneration, cartilage repair, osteoarthritis, and regenerative medicine. This cluster concentrates on the mechanisms and methods of cartilage regeneration and repair, emphasizing the application of biomaterials such as chitosan and hyaluronic acid, gene therapy, and stem cell therapy to provide regenerative medicine solutions for osteoarthritis treatment.

Key researchers like Cuixi Wu, Yao Lu, Jieli Chen, and Yu Cai have pioneered several new technologies including a supramolecular hydrogel that quickly binds tumor necrosis factor-α (TNF-α) to alleviate arthritis symptoms, copper-sulfur nanoparticles for removing senescent chondrocytes and promoting cartilage regeneration, and biomimetic nanoparticles carrying transforming growth factor-β1 (TGF-β1) plasmid deoxyribonucleic acid (DNA) to enhance mesenchymal stem cell therapy effectiveness. Additionally, carboxymethyl chitosan-assisted manganese oxide nanoparticles have been developed for simultaneous MRI and therapeutic interventions to achieve cartilage regeneration and repair [21–24].

Cluster 2 (Green): Osteoarthritis inflammation and drug treatment. Keywords include arthritis, celecoxib, curcumin, dexamethasone, intra-articular delivery, knee osteoarthritis, and nanomedicine. This cluster delves into the pathophysiology of osteoarthritis, particularly in managing knee pain and inflammation. It explores various strategies to mitigate osteoarthritis symptoms through inflammation control, which is pivotal in developing new anti-inflammatory treatments that could substantially enhance patients'

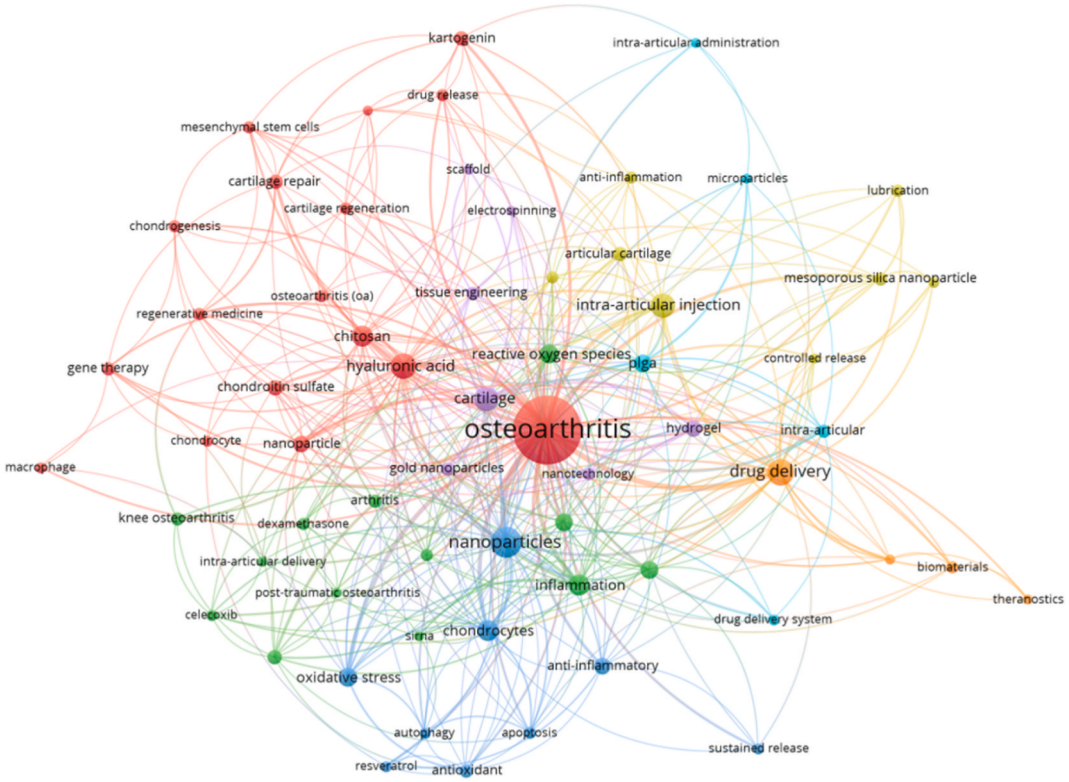


**Fig. 4.** Map of keyword co-occurrence.

quality of life.

Cluster 3 (Blue): Anti-inflammatory and antioxidant. Keywords include anti-inflammatory, antioxidant, and oxidative stress. This cluster focuses on employing anti-inflammatory and antioxidant approaches in osteoarthritis treatment, with keywords like anti-inflammatory, antioxidant, and oxidative stress. It investigates the impact of different drugs and antioxidants on the disease process at a molecular level, aiming to discover novel therapeutic avenues for osteoarthritis.

The research within these two clusters overlaps significantly, particularly in areas concerning inflammation management and drug development. Researchers such as Xianfang Jiang, Jinmin Zhao, Li Zheng, Dan Kai, and Zainen Qin have extensively collaborated to innovate in this space. They have developed reactive oxidative species (ROS)-responsive nanofibers and metal-polyphenol nanoformulations that provide both anti-inflammatory and antioxidant functions. Additionally, they've created polycaprolactone (PCL) and lignin copolymer nanofibers using electrospinning technology, noted for their excellent biocompatibility and therapeutic effects. Moreover, dopamine melanin nanoparticles have emerged as a novel antioxidant solution, significantly reducing inflammation and offering cartilage protection by scavenging ROS and reactive nitrogen species (RNS) [25–28].

Cluster 4 (Yellow): Lubrication and local treatment. Keywords include hydration lubrication, intra-articular injection, lubrication, and mesoporous silica nanoparticles. This cluster emphasizes advancements in joint lubrication and local treatment strategies aimed at mitigating joint pain and inflammation in OA. The use of hydration lubrication, intra-articular injections, and mesoporous silica nanoparticles are key to these strategies, which focus on local drug release and lubrication technology to directly reduce mechanical stress and pain associated with OA.

Prominent researchers such as YuLong Sun, Jing Luo, and Hongyu Zhang have led significant efforts in addressing OA through enhanced joint lubrication and local drug delivery. Their innovative approaches include the use of dopamine methacrylamide and poly (2-methacryloyloxyethyl phosphorylcholine) copolymers, synthesized through biomimetic strategies, to enhance joint lubrication and precisely control the release of anti-inflammatory drugs. Additionally, they have engineered a friction-induced nanovalve system that is activated by high temperatures in damaged joint areas, enabling targeted drug release.

Their work also extends to the development of thermosensitive bifunctional nanospheres, fabricated through electrospinning technology, which utilize a hydration lubrication mechanism for local drug delivery. Furthermore, they have created polyelectrolyte-coated mesoporous silica nanoparticles through photopolymerization techniques, demonstrating exceptional lubrication and wear resistance properties. These nanoparticles effectively reduce the friction coefficient within the joint and ensure sustained drug release [29–34].

Cluster 5 (Purple): Biomaterials and tissue engineering. Keywords include electrospinning, gold nanoparticles, hydrogel, nanotechnology, scaffold, and tissue engineering. This cluster focuses on the application of biomaterials and tissue engineering in the treatment of osteoarthritis, highlighting the use of biomaterials and nanotechnology to promote tissue repair and regeneration. These studies have fostered the development of new tissue engineering technologies and biomaterials, offering advanced solutions for osteoarthritis treatment.

Cluster 6 (Light Blue): Drug delivery system. Keywords include drug delivery system, intra-articular, intra-articular administration, microparticles, PLGA. This cluster primarily explores the application of drug delivery systems in osteoarthritis treatment, emphasizing the enhancement of drug delivery efficiency and therapeutic effects through microparticles and nanomaterials. These studies contribute to the development of new drug delivery platforms to improve the targeting and efficiency of treatment, such as using poly (lactic-co-glycolic acid) (PLGA) nanoparticles for biodegradability and specific cartilage tissue binding [35], and hyaluronic acid/-chitosan nanoparticles to enhance gene delivery transfection efficiency [36].

Cluster 7 (Orange): Molecular imaging and diagnostic-therapeutic integration. Keywords include molecular imaging and theranostics. This cluster studies advanced diagnostic and therapeutic technologies in osteoarthritis, emphasizing molecular imaging and theranostic technologies to enhance diagnostic accuracy and therapeutic efficacy. These studies contribute to the development of new diagnostic and therapeutic technologies, enhancing diagnostic accuracy and therapeutic efficacy.

Proteolytic enzymes such as matrix metalloproteinase-13 (MMP-13) may serve as crucial biomarkers for early OA diagnosis. Zhao et al. optimized MMP-13 for sustainable drug release in acidic OA conditions [37]. Clarke, Emily J. et al. successfully demonstrated the potential of using Raman spectroscopy and photothermal infrared spectroscopy to analyze plasma-derived extracellular vesicles in equine osteoarthritis, with photothermal infrared spectroscopy showing high accuracy in distinguishing healthy from diseased samples, providing a novel diagnostic tool for future clinical diagnosis [38]. However, a comprehensive diagnostic and therapeutic system has not yet been developed, presenting substantial room for future research in this area.

The above research clusters are not isolated from each other. There are potential connections between the clusters and the possibility of future mergers. They can establish links with each other through interdisciplinary research and integrated treatment strategies. For example, combining biomaterials (Cluster 5) with stem cell therapy (Cluster 1) can develop new treatments. Linking the study of inflammatory mechanisms (Clusters 2 and 3) with cartilage regeneration (Cluster 1) may lead to the discovery of new treatment strategies. Combining biomaterials (Cluster 5), drug delivery systems (Cluster 6) and molecular imaging diagnostics (Cluster 7) may lead to the development of more effective integrated treatment plans, etc.

In the future, as research develops and interdisciplinary collaboration increases, these existing clusters may merge due to shared technologies or common research goals to form new and broader research directions. For example, the combination of cartilage regeneration and stem cell therapy: With the development of regenerative medicine, Clusters 1 and 5 may merge to form an innovation cluster focusing on the combined treatment of osteoarthritis using stem cells and biomaterials.

## 4. Discussion

To the best of our knowledge, this article is the inaugural bibliometric analysis employing the WoSCC database to examine the application of nanomaterials in OA treatment. We analyzed a total of 532 publications in this field. Our results suggest that research on nanomaterials for OA treatment is evolving from its nascent phase to a peak of interest. The statistical trends of annual publications and citations suggest continued growth in this research area in the foreseeable future. The year 2020 was particularly significant, witnessing the highest growth rate in publications and achieving the largest H-index. The observed decline in the H-index in recent years may be related to the proximity of data collection.

We also analyzed the most influential countries, authors, institutions, and journals in the field. Among all countries, China stands out with the most international collaborations, the highest number of publications and citations, and the largest H-index, establishing it as the country with the most significant global influence in this domain. Biomaterials emerges as the most influential journal, boasting the highest number of articles, citations, H-index, and impact factor among all journals. Institutionally, Shanghai Jiao Tong University is identified as the most influential institution, with the highest number of publications and H-index. It also holds a central position in the institutional cooperation network, facilitating close collaborations with other institutions. Key researchers such as Li Zheng, Jinmin Zhao, and Zainen Qin have published extensively and collaborated closely, positioning them as leaders in the field.

Additionally, we analyzed the top 10 most cited publications in the field. Highly cited research papers are generally regarded as the most significant and influential works in their respective areas. The most cited publication in this dataset explored a wearable and stretchable heater for joint hyperthermia therapy using nanocomposites. In this study, the researchers utilized silver nanowires and thermoplastic elastomers, combined through ligand exchange reactions, to create highly conductive and uniform nanocomposites [39]. This material employed a serpentine grid structure to facilitate effective heat transfer, optimizing its application for therapeutic heating of joints.

On one hand, heat therapy can improve blood circulation in the skin and joints, helping to alleviate muscle spasms. On the other hand, the use of elastic materials can reduce discomfort for patients and enhance their compliance with treatment protocols. Consequently, this approach holds high feasibility and significant potential for enhancing the therapeutic effects of existing medical devices. This study aligns with the prevailing trend in family medicine, emphasizing the practical application of treatments. Moreover, it advocates for expanding the use of nanomaterials beyond in vivo applications to include the enhancement of in vitro medical devices. As scientific research progresses, the focus is not solely on discovering new phenomena but, crucially, on applying research findings to clinical practice and facilitating the translation of scientific discoveries into practical applications.

The remaining nine articles concentrate on drug delivery. One study particularly innovative in its integration of nanorobots with medicine. Gwangjun Go and his colleagues [40] designed a medical microrobot system utilizing human fat and mesenchymal stem cells. This system employs electromagnetic actuation （EMA） and magnets to precisely target and anchor the robot at the lesion site, addressing the challenge of actively targeting cells for knee joint cartilage regeneration. Nanorobots represent a cutting-edge topic in modern medicine, striving to deliver precise and substantial medical assistance. They are extensively researched for applications in drug delivery, diagnostic testing, tissue engineering, nanosurgery, and biological imaging. However, as highlighted in the study, these technologies encounter a significant limitation: the absence of effective and reliable methods for body injection. Ironically, despite the advancements in in vivo treatment techniques, they still depend on more primitive methods of intervention, presenting a paradox in the application of such advanced technologies.

One study explored drug delivery systems leveraging the self-assembly properties of the nanomaterials. Michal Bachar et al. [41,42] utilized β-casein, which can self-assemble into nano core-shell micelles, to encapsulate drugs for osteoarthritis treatment. This approach aims to address the challenges associated with hydrophobic drugs, such as low water solubility and poor oral bioavailability, while also extending the shelf life of the drugs. Encapsulation is a widely used strategy to enhance the stability, safety, and efficacy of pharmaceuticals.

β-casein, known for its high nutritional value and physiological functions, is extensively utilized in the food industry. Similarly, the self-assembled nanomedicine based on β-casein exhibits significant potential in drug delivery, gene therapy, and other medical fields. Its properties allow for potential enhancements, such as combining it with other drugs or modifying its surface, to improve the control over drug release. These modifications could potentially optimize therapeutic outcomes by tailoring the release profiles and targeting capabilities of the drug delivery system.

Two studies have introduced innovative non-viral gene delivery vectors for OA gene therapy by targeting genes to chondrocytes and synovial cells [43,44]. Chitosan (CS) is considered an effective non-viral gene vector due to its biocompatibility and biodegradability. Polyethylene imine (PEI), another promising cationic non-viral vector, offers protection for DNA against degradation by nucleases and facilitates the intracellular release of complexes via the proton sponge effect [45]. The cationic nature of PEI also potentially enhances the penetration of nanocarriers within the joint microenvironment. In one notable study, Yuhu Dai et al. [43] engineered a novel non-viral gene nanoparticle carrier by grafting PEI onto CS/DNA complexes, which significantly reduced cellular toxicity and enhanced the transfection efficiency in chondrocytes and synovial cells, presenting a more efficient approach for gene therapy in OA.

One study focused on using nanomaterials to inhibit oxidative stress, thereby protecting cartilage and treating osteoarthritis. Lu H et al. [46] developed manganese dioxide nanoparticles known for their reactive oxygen species (ROS) scavenging capabilities. Manganese dioxide effectively clears free radicals and provides cellular protection. Additionally, polyethylene glycol is incorporated to enhance the penetration of these nanoparticles into cartilage, increase their residence time in the joint, and enable the nanoparticles to remain within the joint space of the scaffold, thus continuously combating oxidative stress. This approach represents a promising strategy for mitigating the degenerative effects of osteoarthritis through targeted oxidative stress reduction.

Four studies have evaluated the effectiveness of nano-drug delivery systems in enhancing drug penetration and extending retention time within joints. Superparamagnetic iron oxide nanoparticles (SPION) have the double advantage of synovial cell internalization and prolonged drug action due to magnetic properties that increase the residence time of the particles in the joint [47]. Encapsulated curcumin nanoparticles have proven more effective at relieving OA-related pain than oral curcumin [48]. Chondrocytes, which are deeply embedded in dense anionic cartilage tissue, can be effectively targeted using cationic nanocarriers coupled with growth factors. These nanocarriers are designed for targeted delivery directly to chondrocytes and are retained within the articular cartilage following intra-articular injection. They leverage reversible electrostatic interactions with the anionic cartilage tissue, enhancing tissue binding, penetration, and residence time of the therapeutic agents [49,50]. The Altmetric index of the article titled "Cartilage generating nanocarriers improve delivery and efficiency of growth factor treatment of osteoarthritis" significantly surpasses that of other highly cited articles. This high index reflects the considerable societal interest and extensive media coverage the study has received, indicating its impact beyond the academic community. In their study, Brett C. Geiger et al. [49] prepared an optimal charge cationic nanocarrier by coupling polyamidoamine (PAMAM) dendrimers with polyethylene glycol (PEG), and loaded it with insulin-like growth factor 1 (IGF-1), which greatly reduced the loss of injection of IGF-1 and prolonged its residence time in the joint. The drug is non-toxic, and the required dosing interval aligns well with actual medication needs, which is of great significance for the clinical application development of OA treatment drugs.

In summary, the use of nanomaterials in the treatment of osteoarthritis offers significant advancements through various mechanisms. These include enhancing the efficacy and comfort of medical devices, improving drug release efficiency, and boosting drug targeting capabilities. Additionally, developing an effective intervention method to facilitate drug delivery from outside to inside the body is crucial. During the treatment, increasing the protection of cartilage and rescuing cartilage degeneration are important focuses that cannot be ignored. The rapid clearance of drugs within the joint space and the dense, avascular nature of cartilage tissue pose significant challenges in current treatments. PEG may serve as an effective targeting and penetration agent.

Keyword co-occurrence analysis shows that the included keywords can be roughly divided into seven categories, namely: (1) Cartilage regeneration and repair; (2) Osteoarthritis inflammation and drug treatment; (3) Anti-inflammation and antioxidant; (4) Joint lubrication; (5) Biomaterials and tissue engineering; (6) Drug delivery systems; (7) Molecular imaging and theranostics. These seven categories fully demonstrate the current main focus of this research field.

The application of nanomaterials in treating OA offers significant advantages, particularly in enhancing drug delivery systems. By precisely controlling their size, shape, and surface characteristics, nanomaterials enable targeted drug delivery directly to affected areas. This targeted approach not only improves the effectiveness and bioavailability of drugs but also minimizes side effects, making treatments more efficient and patient-friendly [51]. Furthermore, nanomaterials can significantly enhance tissue repair, particularly in bone-related applications. By mimicking the structure and function of bone tissue, these materials can stimulate the proliferation and differentiation of bone cells, thereby accelerating the regeneration and repair processes [52]. Nanomaterials also have good biocompatibility and biodegradability, which can reduce adverse effects and side effects on the human body [53–56]. For instance, gold nanoparticles can enhance the proliferation and differentiation of articular chondrocytes and promote cartilage regeneration [57]. Gold nanoparticles also play a significant role in inhibiting the activity of inflammatory cells and reducing the symptoms of arthritis [58]. Carbon nanotubes have shown potential in enhancing the proliferation of articular chondrocytes and boosting their ability to synthesize collagen. This capability makes them excellent candidates for creating scaffolds that support the regeneration and repair of chondrocytes and cartilage. These scaffolds provide a structured environment that mimics natural tissue architecture, promoting effective tissue repair and regeneration in damaged or diseased joints, thereby offering promising advances in treatments for conditions like osteoarthritis [59,60].

While the potential of nanomaterials in medical applications is promising, several challenges must be addressed before their widespread adoption in clinical settings can occur.

Firstly, safety concerns arise due to the unique physical and chemical properties of nanomaterials, which may adversely affect the human body through toxicity and immunogenicity. Consequently, rigorous safety assessment and continuous monitoring are imperative for the application of nanomaterials. Secondly, there is an absence of long-term effect evaluations. Current research often lacks comprehensive assessments of the sustained impacts and safety of nanomaterials in treating osteoarthritis, underscoring the necessity for more extensive clinical trials and extended follow-up studies. Lastly, there are technical and cost constraints. The production and application of nanomaterials typically involve complex and costly technologies, limiting their accessibility and practicality in routine clinical practice. Overcoming these challenges is crucial for the successful translation of nanomaterial-based therapies from the laboratory to clinical settings.

Despite our efforts to conduct this study scientifically and comprehensively, several limitations remain. First, our literature search was confined to the SCI-E and SSCI indices within the WoSCC database, which, while extensive and comprehensive, may not encompass all relevant literature. Nonetheless, the WoSCC database is among the most globally recognized sources for bibliometric analysis and provides a robust dataset adequate for reflecting the current research landscape in this field. Second, our study included only publications in English, potentially overlooking significant contributions published in other languages. This language restriction might limit the scope of our analysis by excluding diverse perspectives and findings. Third, despite meticulous efforts to design our search strategy with comprehensive and carefully selected keywords, some relevant topics or terms may have been inadvertently omitted, possibly skewing the comprehensiveness of the retrieved data. Lastly, while we rigorously reviewed and screened the initially retrieved publications, there remains a possibility of selection bias, where some less relevant publications might have been included, or potentially pivotal studies inadvertently excluded. These factors could affect the overall findings and interpretations of our bibliometric analysis.

In conclusion, this article employs bibliometric analysis to provide a comprehensive overview of research on the application of

nanomaterials in OA from 2006 to 2023. It delves into the current research status, identifies hotspots, and forecasts future trends in this field. Undoubtedly, nanomaterials hold substantial potential for treating OA, offering innovative approaches to enhance therapeutic efficacy. However, their practical application still confronts several challenges. These challenges, including safety concerns, long-term effectiveness, and technical and economic barriers, necessitate further research and development to harness the full potential of nanomaterials in clinical settings effectively.

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## Ethics approval and consent to participate

Not applicable.

## Consent for publication

Not applicable.

## Data availability

Has data associated with your study been deposited into a publicly available repository?Response: No. Data will be made available on request.

## CRediT authorship contribution statement

**Chunxi Shu:** Writing – original draft, Visualization. **Xinyang Yin:** Writing – original draft, Software, Data curation. **Qin Zhong:** Validation, Software. **Ming Cheng:** Writing – review & editing, Supervision, Resources, Methodology, Investigation, Funding acquisition.

## Declaration of competing interest

None.

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