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Mapping the Relationship Between Selenium and Bone: A Bibliometric Analysis Covering 1980-2023

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Abstract

Background: Selenium, an indispensable trace element in the human body, has been the subject of growing research that highlights its significant association with bone health. This project aims to employ the Bibliometrics method to comprehensively understand the research status of selenium and bone between 1980 and 2023. By utilizing visualizations to identify research hotspots and trends, we strive to shed light on the current state of knowledge in this field. ***Methods:*** Relevant articles on the topic of selenium and bone were retrieved from the Network Science Core Collection (WoSCC). Statistical and visual analysis was conducted using CiteSpace and VOSviewer. This analysis encompassed various aspects, including annual publication output, active countries, prolific institutions, authors, and keyword analysis. ***Results:*** A total of 864 relevant articles were retrieved for analysis, comprising 746 articles and 118 reviews. The number of publications in the field of selenium and bone has demonstrated a consistent upward trend over time. Notably, China emerged as the leading contributor in terms of publication output, with 195 articles, followed closely by the United States with 177 articles, and Germany with 50 articles. Among the institutions, Huazhong University of Science and Technology stood out as a core institution, while K. Sandeep Prabhu emerged as a prominent core author. The analysis of keyword frequency revealed the most frequently occurring terms in the publications. Selenium, with a count of 415, topped the list, followed by Bone (101), oxidative stress (91), zinc (87), osteoporosis (70), metabolism (66), copper (63), toxicity (62), supplementation (57), and nanoparticles (55). Notably, the emergence of Selenium nanoparticles and Scaffolds indicates novel research trends within the field. ***Conclusions:*** The research demonstrates an increasing number of publications focusing on the association between selenium and bone health in recent years, with China leading in terms of article output. Furthermore, prominent keywords such as selenium, bone, and oxidative stress indicate recurring themes in the literature, while emerging trends like selenium nanoparticles and scaffolds have gained significant attention.

Keywords: selenium, bone, bibliometric

1. Introduction

Selenium is an essential micronutrient in the human body, widely distributed and possessing crucial physiological functions (Prasad R. & Shivay Y.S., 2022). Research indicates a positive correlation between increased selenium levels and improved femoral bone density, decreased FRAX scores, and a lower incidence of previous fractures (Wu C.-C. et al., 2021). Selenium is actively involved in cartilage collagen synthesis and metabolism, regulating the process of fracture healing and playing a key role in maintaining bone health. Inadequate selenium levels can impact cartilage collagen synthesis and structure, leading to cartilage abnormalities and functional impairments (Ren F.L. et al., 2007). This can manifest as cartilage degradation, joint pain, and even contribute to the development of conditions such as osteoarthritis, characterized by chondrocyte nuclear degeneration, endoplasmic reticulum ballooning, and reduced bone density (Sasaki S. et al., 1994). Furthermore, selenium's participation is crucial in the fracture healing process. It stimulates protein synthesis in chondrocytes, accelerating fracture healing and promoting bone tissue regeneration. Selenium also exhibits antioxidant properties, mitigating oxidative stress-induced damage to bone cells and safeguarding them against harm from reactive oxygen species, thereby facilitating bone tissue recovery and repair (Wu C.-C. et al., 2021; Zhang Z., Zhang J. & Xiao J., 2014). Essential antioxidant selenium proteins, including glutathione peroxidase (GPx) and thioredoxin reductase (trxR), play a pivotal role in maintaining skeletal homeostasis and preventing bone loss (Zhang Z., Zhang J. & Xiao J., 2014). Moreover, selenium proteins are vital for maintaining bone health. They actively participate in regulating thyroid hormone metabolism, influencing cell growth and bone metabolism processes (Wang F. et al., 2023). Hence, selenium plays a significant role in the human skeletal system. Dietary selenium supplementation has been demonstrated to increase skeletal muscle mitochondrial volume density and bone density (Wesolowski L.T., Semanchik P.L. & White-Springer S.H., 2022).

By leveraging scientific knowledge graphs, a comprehensive, real-time, and dynamic analysis of a large corpus of literature can be conducted, thereby eliminating subjectivity and bias in the reading and summarization process. VOSviewer is a commonly used visualization software for clustering analysis. CiteSpace, developed by Professor Chaomei Chen, is a visualization tool that facilitates knowledge graph construction and offers functionalities such as bibliometric analysis, clustering analysis, and collaboration network analysis. Both software tools have gained wide popularity and application in the field of medicine. In this study, a combined application of these two tools was employed to visually present the results of selenium and bone-related literature, uncovering prolific countries, authors, research institutions, collaboration networks, research hotspots, and frontiers. Furthermore, a summary of the current research status and future trends was provided, serving as a reference for future studies.

2. Methods

2.1 Data Retrieval and Analysis

Web of Science Core Collection (WoSCC) was utilized as the data source for retrieval, covering the period from the establishment of the database to June 7, 2023. The search query was formulated as follows: TS = Selenium and TS = bone*. Inclusion criteria were defined as follows: relevant literature on the topic, including complete content with titles, abstracts, and keywords, without restriction on study type. Only English-language articles were included. The document types were limited to Article or Review. The search process is depicted in Figure 1. The identified literature was imported into Excel 2016, CiteSpace, and VOSviewer software, generating networks of authors, country collaborations, co-occurrence of keywords, and visualization maps of significant terms.

Figure 1. Literature search process

3. Results

3.1 Publication and Citation Analysis

Through the search process, a total of 864 relevant articles were retrieved, including 746 articles and 118 reviews. As shown in Figure 2, the number of publications exhibited an increasing trend, with fluctuations around 10 publications per year prior to 2004. However, since 2004, the number of publications has been consistently rising, reaching its peak in 2021 with 79 articles. Similarly, the citation count has been steadily increasing, with a total of 18,993 citations. The highest citation count was observed in 2021, with 2,319 citations. The upward trend in both publication and citation counts signifies the growing interest in the relationship between selenium and bone health within the academic community.

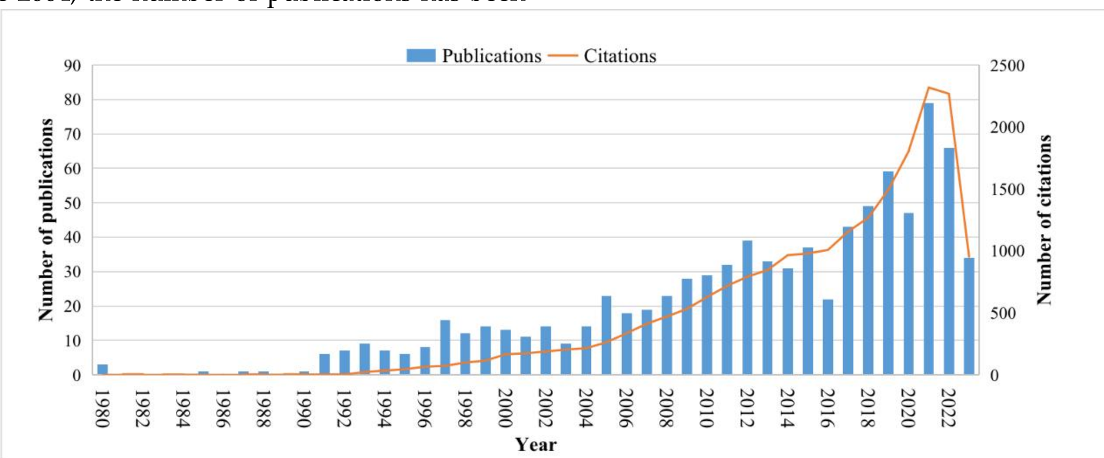


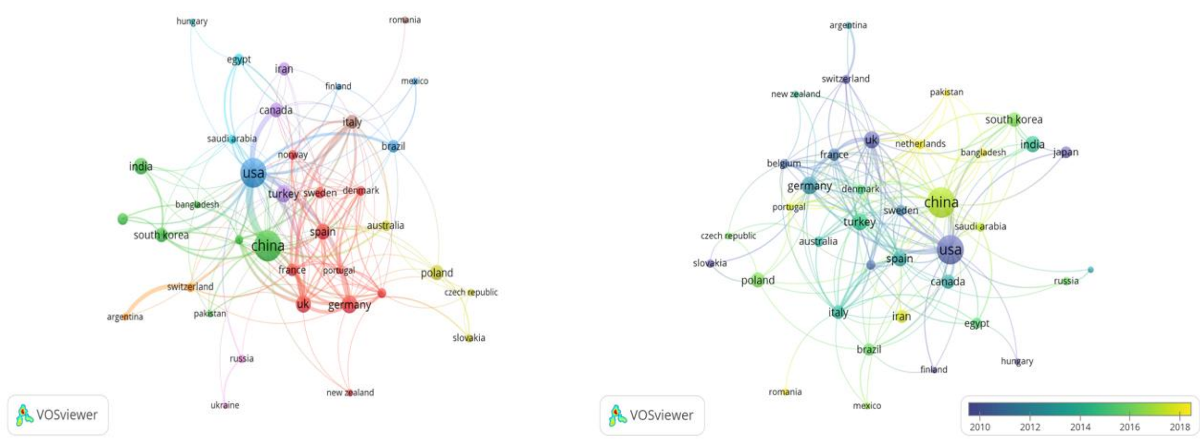
Figure 2. The annual number of publications and citations related to selenium and bone

3.2 Country Analysis

A total of 61 countries contributed to research on selenium and bone health. China emerged as the leading country in terms of publication output with 195 articles, followed by the United States with 177 articles and Germany with 50 articles. The top ten countries in terms of productivity are listed in Table 1. In terms of citation count, the top three countries were the United States (6,315 citations), China (3,058 citations), and Germany (1,709 citations). The collaboration network among countries is illustrated in Figure 3A, highlighting the close collaboration between China, the United States, and Canada. Figure 3B depicts the network with node size representing publication output and color indicating average publication time, with yellow indicating later publication dates. It can be observed that countries such as the United States, the United Kingdom, and Japan had earlier average publication times, while countries like China, the Netherlands, Bangladesh, Pakistan, and Iran had relatively later average publication times.

Table 1. Distribution of publications different countries

Rank	Country	Documents	Citations
1	China	195	3058
2	USA	177	6315
3	Germany	50	1709
4	Turkey	49	539
5	UK	48	1704
6	India	44	701
7	Spain	39	1030
8	Poland	37	542
9	Canada	34	826
10	South Korea	31	456



(A) (B)

Figure 3. Co-authorship analysis of countries

(A) Cooperation networks across countries. **(B)** Overlay Visualization of countries.

3.3 Institution Analysis

A total of 1,280 institutions have contributed to research on selenium and bone health. The top three institutions are Xian Jiao Tong University, Huazhong University of Science and Technology, and The Pennsylvania State University. Among the top ten productive institutions, six are from China, two are from the United States, one is from Poland, and one is from Germany, as shown in Table 2. The institutional collaboration network, as depicted in Figure 4A, reveals close collaborations among institutions within the same country. Notably, Huazhong University of Science and Technology exhibits the strongest collaboration intensity, indicating its pivotal role in selenium and bone-related research. Figure 4B illustrates the average publication time of institutions, revealing that institutions from China tend to have relatively later publication dates, while institutions from Europe and the United States have earlier publication dates.

Table 2. Distribution of publications different institution

Rank	Institution	Country	Documents	Citations
1	Xian Jiao tong university	China	22	345
2	Huazhong University of Science and Technology	China	20	500
3	The Pennsylvania State University	USA	17	635
4	Sichuan University	China	12	345
5	Medical-University-of-Warsaw	Poland	11	176
6	Chinese academic of sciences	China	10	296
7	Soochow university	China	9	99
8	Shanghai Jiao tong university	China	8	157
9	Cornell university	USA	7	156
10	University Wurzburg	Germany	7	7773

Figure 4. Co-authorship analysis of institutions

(A) Cooperation networks across institutions. **(B)** Overlay Visualization of institutions.

3.4 Author Analysis

A total of 4,247 authors have contributed to research on selenium and bone health. The top ten productive authors are presented in Table 3. The three most productive authors are K. Sandeep Prabhu (14 publications), Kolmas, Joanna (9 publications), and Webster, Thomas J (9 publications). In terms of citation count, the top three authors are K. Sandeep Prabhu (620 citations), Jakob, Franz (713 citations), and Webster, Thomas J (336 citations). The H-index rankings indicate that K. Sandeep Prabhu and Webster, Thomas J hold the top two positions. Figure 5 depicts the author collaboration network, revealing that K. Sandeep Prabhu ranks first in terms of publication count, citation count, and H-index. This signifies the central role of K. Sandeep Prabhu as a key author in selenium and bone-related research.

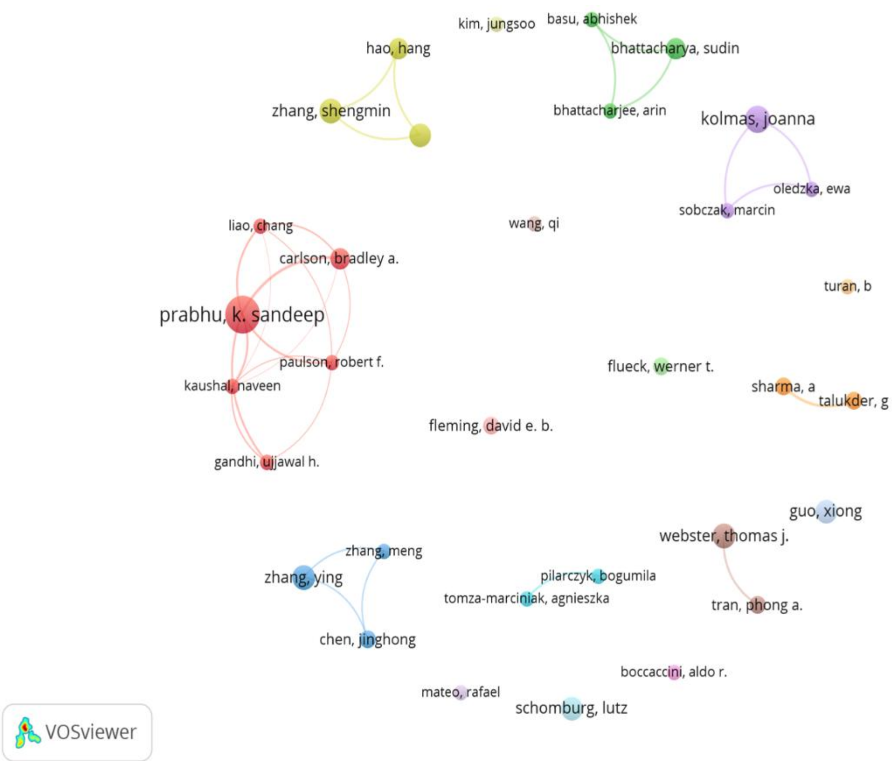


Figure 5. Co-authorship analysis of authors

Table 3. The top 10 productivity authors

Rank	Author	Documents	Citations	H-Index
1	K. Sandeep Prabhu	14	620	10
2	Kolmas, Joanna	9	164	7
3	Webster, Thomas J.	9	336	8
4	Zhang, Shengmin	8	344	6
5	Liu, Yi	8	129	6
6	Schomburg, Lutz	7	77	7
7	Tran, Phong	7	269	6
8	Hao, Hang	7	193	5
9	Bhattacharya, Sudin	7	205	7
10	Jakob, Franz	6	713	6

3.5 References Analysis

The top five cited references are presented in Table 4. The first three ranked references are as follows: "Selenium deficiency-induced growth retardation is associated with impaired bone metabolism and osteopenia" (Moreno-Reyes R. et al., 2001). Zeng et al. (2013) provided an overview of the research progress on the functional role of selenium in bone health. "Bone turnover and bone mineral density are independently related to selenium status in healthy euthyroid postmenopausal women" (Hoeg A. et al., 2012). Figure 6 illustrates the citation bursts of the referenced articles. Among them, the publication by Wang et al. (2016) titled "In Vitro and in Vivo Mechanism of Bone Tumor Inhibition by Selenium-Doped Bone Mineral Nanoparticles" has the highest citation burst value of 10.55.

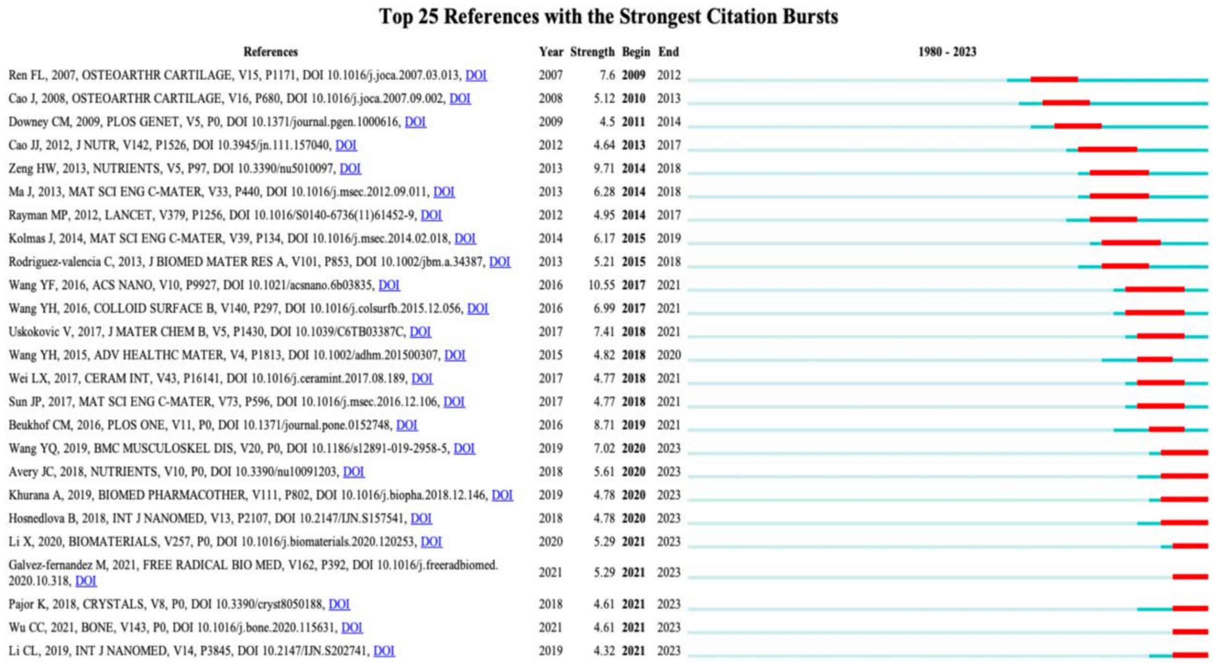


Figure 6. The top 25 references with the strongest citation bursts

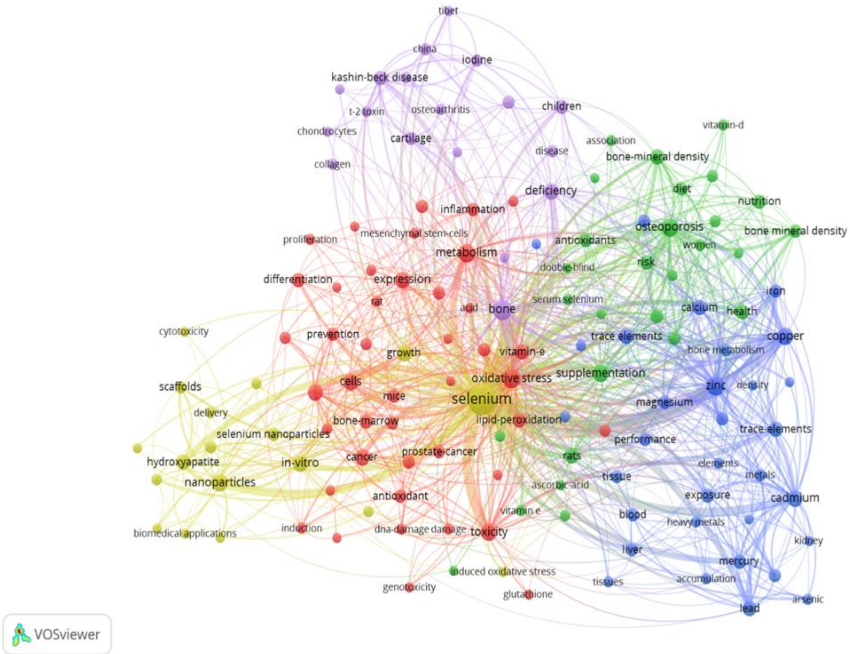
Table 4. The top 5 cited references

Rank	References	Type	DOI	Citations
1	Selenium deficiency-induced growth retardation is associated with an impaired bone metabolism and osteopenia	article	10.1359/jbmr.2001.16.8.1556	82
2	Selenium in bone health: roles in antioxidant protection and cell proliferation	review	10.3390/nu5010097.	60
3	Bone turnover and bone mineral density are independently related to selenium status in healthy euthyroid postmenopausal women	article	10.1210/jc.2012-2121	43
4	Selenium deficiency decreases antioxidative capacity and is detrimental to bone microarchitecture in mice	article	10.3945/jn.111.157040	32
5	Selenium Status Is Positively Associated with Bone Mineral Density in Healthy Aging European Men	article	10.1371/journal.pone.0152748	27

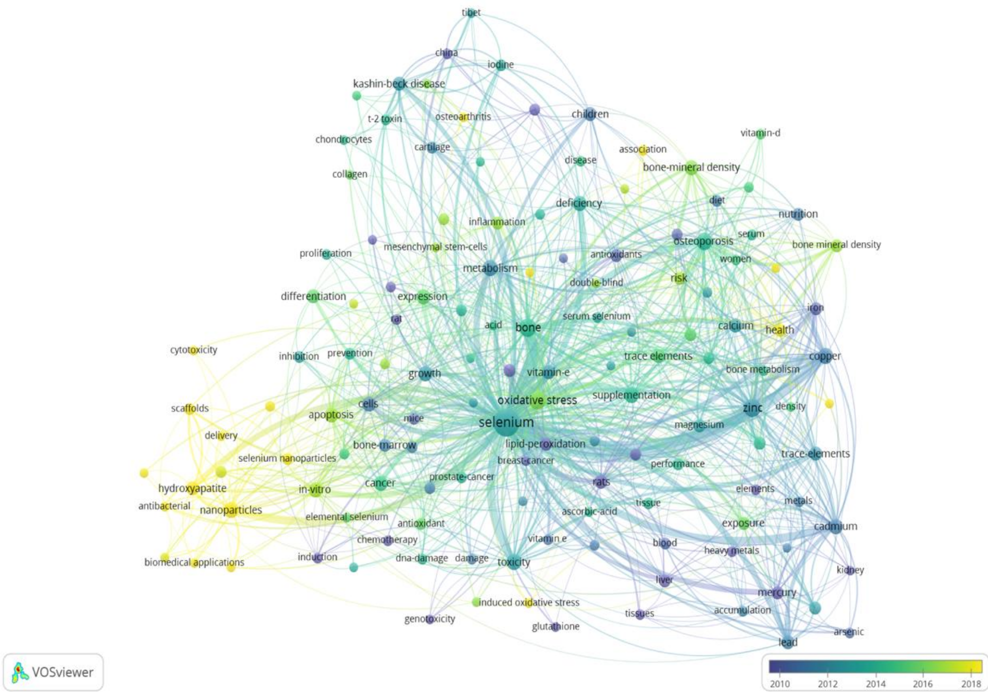
3.6 Keywords Analysis

A total of 4,779 keywords were extracted, with 139 keywords appearing more than ten times and 63 keywords appearing more than twenty times. Table 5 displays the co-occurrence terms of the top 20 keywords. Selenium (415), Bone (101), oxidative stress (91), zinc (87), osteoporosis (70), metabolism (66), copper (63), toxicity (62), supplementation (57), and nanoparticles (55) emerge as core themes in selenium and bone research. As depicted in Figure 7A, we can observe clusters represented by yellow, red, purple, green, and blue colors, corresponding to five distinct research directions.

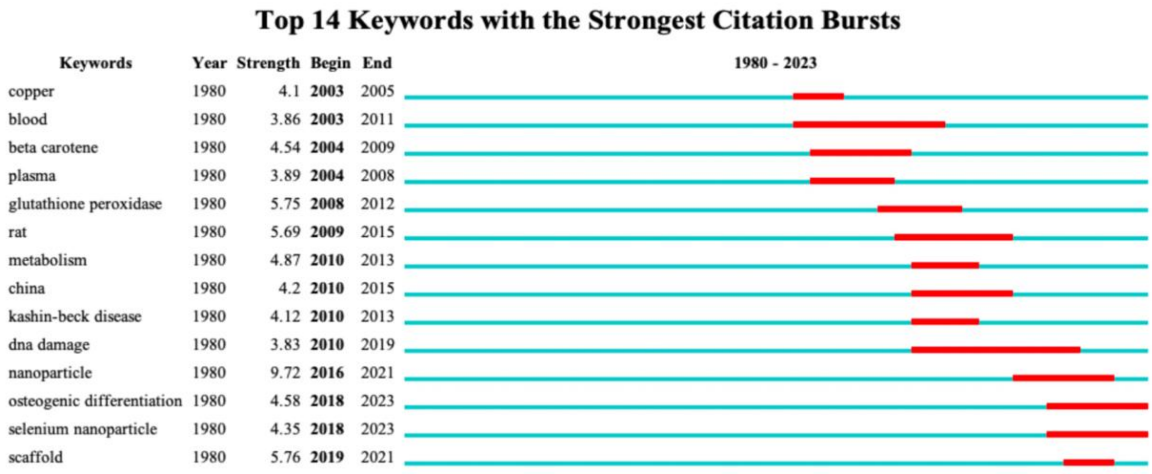
The yellow cluster primarily focuses on selenium research, with major keywords being selenium, nanoparticles, and in vitro. The red cluster revolves around mechanisms linking selenium and bone, emphasizing oxidative stress, differentiation, expression, cells, and related aspects. The purple cluster pertains to bone-related studies. The green cluster primarily concentrates on selenium and osteoporosis research, encompassing keywords such as osteoporosis, bone density, antioxidants, and supplementation. The blue cluster encompasses research on other trace elements, including zinc, cadmium, copper, calcium, among others. Figure 7B presents the top 14 keywords with the strongest citation bursts. It is noteworthy that inflammation, autophagy, type 1 diabetes, risk, microRNA, type 2 diabetes, maturation, and dedifferentiation persist until 2022. The Venn diagram (Figure 7C) reveals emerging areas highlighted in yellow, such as selenium nanoparticles and scaffolds.



(A)



(B)



(C)

Figure 7. **(A)** Cooperation networks across keywords. **(B)** Overlay Visualization of keywords. **(C)**The top 14 keywords with the strongest citation bursts.

Table 5. The top 20 keywords

Rank	Keywords	Occurrences	Rank	Keywords	Occurrences
1	selenium	415	11	cadmium	50
2	bone	101	12	deficiency	49
3	oxidative stress	91	13	cells	48
4	zinc	87	14	expression	48
5	osteoporosis	70	15	in-vitro	48
6	metabolism	66	16	apoptosis	46
7	copper	63	17	growth	46
8	toxicity	62	18	cancer	43
9	supplementation	57	19	bone-mineral-denesity	42
10	nanoparticles	55	20	vitamin-e	41

4. Discussion

4.1 General Information

In this study, we conducted a bibliometric analysis of selenium and bone-related publications over the past 40 years. To the best of our knowledge, this is the first bibliometric analysis in the field of selenium and bone research. The annual publication count exhibited an upward trend from 1980 to 2023. China emerged as the leading country in terms of publication output in selenium and bone research. Among the top ten productive institutions, seven are based in China. Similarly, six out of the top ten productive authors are affiliated with Chinese institutions. K. Sandeep Prabhu ranked first in terms of publication count, citations, and H-index, indicating that he is a key author in selenium and bone-related research. However, Chinese researchers and their publications are less involved in citation frequency and collaborative exchanges with authors from other countries. Therefore, Chinese researchers should focus on improving the quality of their research and publication content, rather than solely pursuing quantity. It is crucial for them to engage in close communication and collaboration with authors from different countries, regions, and institutions to enhance the impact of their research.

4.2 Research Hotspots

4.2.1 Selenium Nanoparticles

Selenium nanoparticles possess advantages such as high absorption rate, high bioactivity, and low toxicity, and can be directly absorbed by the human body and converted into organic selenium. Gradually, selenium nanoparticles are replacing traditional selenium supplements and hold broad prospects in the food and pharmaceutical industries. Selenium nanoparticles exhibit antibacterial, anti-aging, anticancer, and antitumor effects (Zhang T. et al., 2023). Nanoscale selenium regulates osteoblast differentiation (Hou J. et al., 2022). Additionally, selenium peptides have significant anticancer effects with low toxicity. The anticancer mechanism of selenium-doped hydroxyapatite nanoparticles (SeNPs) involves inducing ROS generation, DNA damage, cell cycle arrest, and mitochondrial dysfunction (Li Q. et al., 2023). Se-hANs induce tumor cell apoptosis via the intrinsic caspase-dependent apoptotic pathway, which is further validated through in vivo animal assessment, where Se-hANs greatly induce tumor apoptosis, inhibit tumor growth, and reduce systemic toxicity (Wang Y. et al., 2016). Moreover, SeNPs can significantly reduce the expression of major inflammatory factors, inducible nitric oxide synthase (iNOS), and cyclooxygenase-2 (COX-2), thereby exhibiting a protective effect in osteoarthritis (Li Y. et al., 2023). In the case of osteoporosis, low concentrations of SeNPs may enhance the survival and osteogenic potential of human mesenchymal stem cells by regulating oxidative stress and activating the JNK/FOXO3 pathway, thereby enhancing bone formation (Fatima S. et al., 2021). Nanoscale selenium in bioactive wound dressings enhances collagen synthesis, re-epithelialization, and rapid wound closure after fractures (Ruan Q. et al., 2023). Therefore, the exploration and application of selenium nanoparticles in understanding the mechanisms of fractures, arthritis, and osteoporosis remain future research priorities.

4.2.2 Scaffolds

Numerous selenium-containing compounds exhibit broad biological activities, making them promising scaffolds in medicinal chemistry (Domínguez-Álvarez E. et al., 2022). Bacterial infection poses a significant clinical risk for any implanted biomaterial. Selenium nanoparticles (Se0), as a promising antibacterial biomaterial with no cytotoxicity to tissue cells, hold great potential in applications such as bone regeneration scaffolds or orthopedic implants. For instance, selenium nanoparticle-phosphate coating inhibits the planktonic growth and biofilm formation of key bacteria, Staphylococcus aureus, and promotes bone formation in rat calvarial defects (Vaquette C., Bock N. & Tran P.A., 2020). Selenium nanoparticle coatings as anti-infective implants are effective against methicillin-resistant Staphylococcus aureus and epidermis infections in trauma orthopedics (Tran P.A. et al., 2019). Additionally, selenium-modified calcium phosphate cement (Se-CPC) scaffolds demonstrate rapid repair of femoral condyle defects (Li T.-L. et al., 2021). Therefore, the future exploration of selenium nanoparticles in conjunction with scaffolds for bone regeneration scaffolds or orthopedic implant applications will be a prominent research area.

5. Conclusion

In this study, we conducted a systematic and visual analysis of selenium and bone using bibliometric analysis. We anticipate that research and attention in this field will continue to increase. China emerged as the most prominent contributor in the field of selenium and bone. Huazhong University of Science and Technology stood out as a core institution. K. Sandeep Prabhu emerged as a key author in selenium and bone-related research. Selenium nanoparticles and scaffolds were identified as important research directions in the field of selenium and bone.

6. Limitations

Our study has certain limitations and shortcomings. The WOSCC database served as the sole source of our original data, thereby potentially excluding publications and articles from other databases. Additionally, we only included English articles, as English serves as the universal language. However, we believe that our study still presents an overall picture and development trends in this field.

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