Cancer Nanotechnology

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The research trends and future prospects of nanomaterials in breast cancer

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Abstract

Background: Breast cancer is the most common cause of cancer-related deaths among women globally and the most deadly illness for them. New advances in nanotechnology have led to the development of strategies intended to target breast cancer cells more precisely while causing the least amount of damage to healthy cells. We retrieved articles about nanomaterials for the diagnosis and treatment of breast cancer from the Web of Science Core Collection (WoSCC) database between 2008 and 2023. Our research aims to assess publications on the use of nanomaterials for breast cancer treatment and diagnosis to predict future research directions.

Results: A total of 457 papers on nanomaterials in breast cancer were discovered from various nations, with China being the primary source and the United States having the highest H index. The number of papers in this discipline is increasing on an annual basis. The Egyptian Knowledge Bank is an important research center in this sector. The *International Journal of Nanomedicine* has the most papers, and Kesharwani P is the most frequently referenced author. The most quoted article was written by Miele, Evelina of India in 2009. Topics such as drug delivery may be emerging areas of research.

Conclusion: Our findings predict that the use of nanomaterials in medication delivery will become a significant research area in the future, and provide valuable references for scholars investigating the role of nanotechnology in breast cancer.

Keywords: Nanomaterials, Clinical value, Breast cancer, Visualized analysis

Introduction

Breast cancer is the most common malignant tumor among women, with the highest incidence rate (Thomas et al. 2024; Siegel et al. 2023). According to the GLOBACON database, there were 22,968,840 new cases and 666,103 deaths of breast cancer between 2022 and 2024 (8th February). Early diagnosis of breast cancer is challenging due to the limited sensitivity of existing methods in detecting small lesions (Ha et al. 2018). Various therapeutic modalities have been used to treat breast cancer, including the combination of radiotherapy and chemotherapy to inhibit tumor progression and recurrence. However, the low therapeutic efficacy of these drugs is due to their poor target and affinity

(Liu et al. 2023; Zhang et al. 2022). Therefore, new and effective methods for diagnosing and treating breast cancer are needed.

Nanoparticles can interact with a variety of organelles and biomolecules and range in size from 1 to 100 nm (Nikalje 2015). These properties make them suitable for various applications, from chemical reactions to biomedicine (Mujahid et al. 2022). Quantum dots (QDs) and gold nanoparticles are used at the molecular level for cancer diagnosis (Kher and Kumar 2022). Molecular diagnostic techniques based on nanoparticles can be used for biomarker discovery and rapid tumor diagnosis (Yan et al. 2019). The rapid growth of tumors results in the epidermal cell gap of intra-tumor blood vessels being larger than that of normal blood vessels, and the lack of a lymphatic system within the tumor makes it easy for nanoparticles to "leak" into the tumor from the gap in the tumor blood vessels and accumulate in the tumor. Some investigations have shown that nanomaterials can be targeted against the endothelial cells of tumor blood vessels, releasing anti-angiogenic medicines, successfully suppressing tumor blood vessel growth and reducing the oxygen supply. (Chakraborty et al. 2019). The high surface-to-volume ratio of magnetic nanoparticles allows them to assemble with biomolecules or residues, which can enhance the specificity of chemical drug complexes in targeted therapy (Moloudi et al. 2023; Londhe et al. 2023). In addition, nanotechnology-enhanced photodynamic therapy and immunotherapy are emerging as exciting cancer therapeutic methods with significant potential for improving patient outcomes (Jia et al. 2023). The addition of nanomaterials enhances the responsive release, depth of tissue penetration and precise targeting of phototherapy, enabling precise treatment of specific cancer tissues and cells through photodynamic therapy, photothermal therapy and combination therapy (Mosleh-Shirazi et al. 2022). Some studies have indicated that immune checkpoint blockade therapy does not become noticeably more effective when drugs are delivered using nanoparticles. On the other hand, when paired with chemotherapy and other treatments, nanoparticles can enhance anti-cancer immune responses as well as improve medication transport and usage efficiency. However, no bibliometric analysis has been published on the use of nanomaterials in the diagnosis and treatment of breast cancer.

Hence, this study aims to analyze the use of nanoparticles in breast cancer therapy through quantitative methods. Scientometric analyses aid academics in comprehending the effectiveness of nanomaterials in treating breast cancer, familiarising themselves with published research results, and understanding collaborations and links between countries, institutions, and authors. Additionally, we objectively reveal the current status and future directions of nanotechnology in breast cancer; review current research hotspots; and anticipate research trends and future prospects in this field.

Methods

Browse and search

Web of Science is a crucial database for accessing global academic information (Pei et al. 2022). It can rapidly identify high-impact papers, reveal research directions that domestic and foreign authorities focus on, and expose the trend of subject development (Wang and Maniruzzaman 2022). A search was conducted in the WOSCC database for literature related to the use of nanomaterials in breast cancer diagnosis and treatment from 1 January 2008 to 31 December 2023. The search formula used was as follows:

TS = ("nanostructured materials" OR "nanomaterials" OR "nanotechnology") AND TS = ("breast" OR "breast cancer") AND TS = ("treatment" OR "diagnosis" OR "cure" OR "therapy").

Screening procedures

The inclusion criteria are as follows: (1) the full text of the available papers focused on the diagnosis and treatment of nanomaterials in breast cancer; (2) the papers were written in English; (3) only articles and reviews were permitted; (4) the papers were sourced from the Social Science Citation Index (SSCI) and the Science Citation Index Expanded (SCI-E) databases; and (5) the timeframe was from 2008 to 2023. The study's inclusion criteria were as follows: The following criteria were excluded: (1) This paper will focus on nanomaterials that are not related to breast cancer diagnosis and treatment. (2) This study will consider all types of publications, including reports, theses, and conference abstracts.

Data analytics

The publications and citations were exported as plain text for bibliometric analysis and visualization. VOSviewer (version 1.6.19) and CiteSpace (version 6.2) were used to create visualizations. Line graphs were generated using GraphPad Prism (version 9.5.1) to display the number of publications, citations, and h-index per year. To analyze the most prolific/collaborative countries, institutions, authors, co-cited journals, and co-occurring keywords, VOSviewer was used.

CiteSpace can be used to construct keyword timeline charts and keyword bursts. The visualization chart displays dots representing countries, institutions, authors, or journals, which are clustered into different groups based on their collaboration (Liu et al. 2022). The size of the dots corresponds to the number of publications. The thickness of the lines connecting the nodes represents the link strength (LS) and reflects the strength of collaboration between them (Xia et al. 2022). The Total Link Strength (TLS) metric measures the level of collaboration between nodes (Jin et al. 2023). We improved the keyword analysis by excluding irrelevant keywords and merging those with similar meanings to provide a better perspective. The graph generated by CiteSpace shows significant and reasonable clustering, with a modularity value greater than 0.3 and an average silhouette value greater than 0.7.

Results

Selection and characterization of literature

A search for keywords related to breast cancer and nanomaterials in the Web of Science database retrieved a total of 463 papers. In the first stage of selection, 6 articles were excluded due to type restriction. Next, we screened 457 publications published during the decade from 2008 to 2023 to do the study (Fig. 1). The results show an overall increasing trend in the number of annual publications (Fig. 2A), indicating an increased interest in the field of breast cancer and its treatment and nanomaterials. The number of publications peaked in 2022 with 72 publications, which accounted for 16.74% of the total publications (Fig. 2B). The year with the highest number of citations was 2020, with

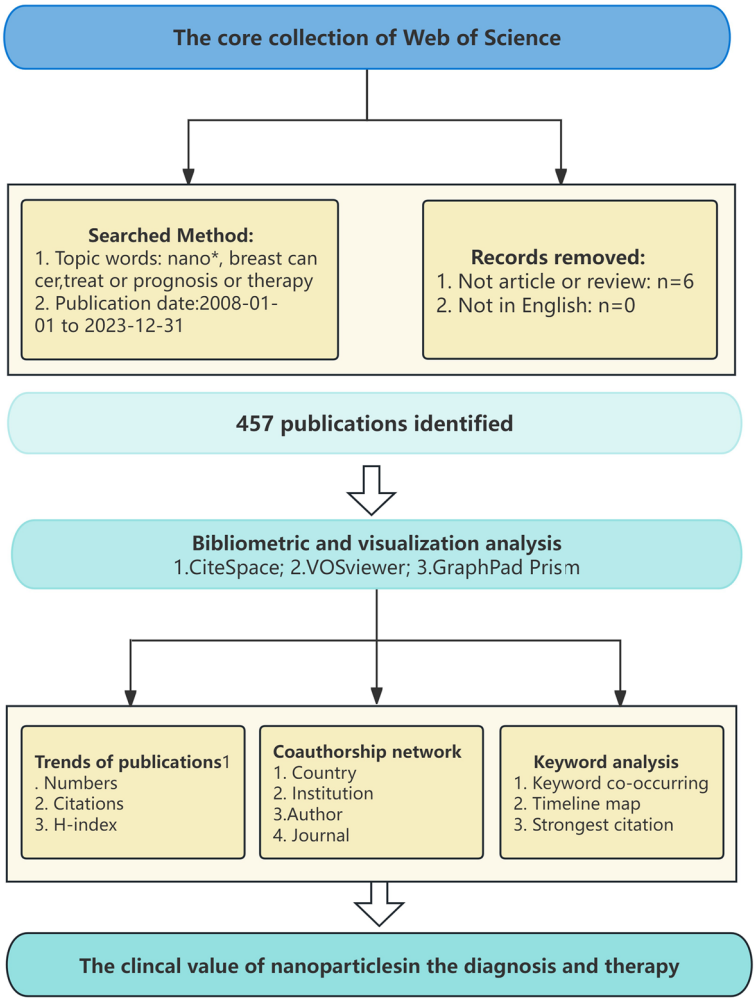

Fig. 1 Flowchart of the literature screening proces

a total of 1269 citations (Fig. 2C). The number of publications has steadily increased from 2008 to 2024. The annual H-index increased from 2 in 2008 to 20 in 2020 (Fig. 2D).

Country/region and institutional analysis of publications

VOSviewer analysis shows that a total of 59 countries/regions have cooperated in this area (Fig. 3A, B). India had the most robust international cooperation network (TLS = 84) and cooperated most closely with Saudi Arabia (TLS = 65). The country with the highest centrality is Iran (0.53), followed by USA (0.34) and India (0.32). The USA (5.9) has the highest burst strength next to Spain (2.85) and South Korea (2.42). Next, we analyzed the top 10 productive countries/regions in terms of number of publications, total citations, and H-index. China published the most papers (109, 22.61%), followed by India (85, 18.53%) and USA (79, 40.14%). In addition, the USA has the highest number of citations (3171) and the highest H-index (30).

The institutional collaboration network diagram is shown in Fig. 3E, which contains 99 institutions. Jamia Hamdard has the strongest total connectivity strength (TLS = 51). Statistically, the institution with the highest centrality is the Egyptian Knowledge Bank

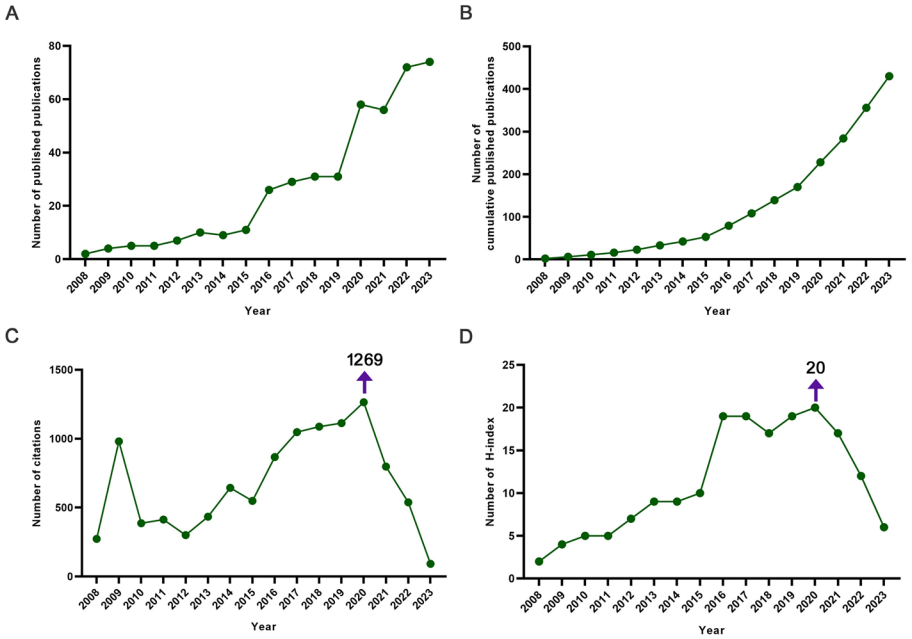

Fig. 2 Publication trends in breast cancer and nanomaterials research. **A**. The number of the publications; **B**. The number of cumulative publications; 15-year publication rate with an exponential trend line, 2008 to 2023. **C**. The total citations of the publications; **D**. The H-index values of the publications

(EKB) (0.14) followed by Islamiv Azda University (IAU) (0.07). Table 1 shows the top 10 most productive institutions. The highest number of published papers was from EKB (20), next to IAU (16). EKB had the highest total number of citations (393) and the highest h-index (10).

Analyzing the authors of publications

The network of inter-authors and collaborative relationships is shown in Fig. 3C, D. In this study, we examined the top ten contributors in terms of posting volume. Kesharwani P (TLS = 60) works most closely with other authors. The highest number of posts is Kesharwani P (11, 25.09%), followed by Chorilli M (7, 5.71%). Kesharwani P has not only the highest number of citations (276), but also has the highest H-index (9).

Analysis of the publication journal

For this study, we selected the top ten most productive journals from the communication network diagram (Fig. 3F, Table 2). The most partnerships with other journals are the *Biomaterials* (TLS = 108,995). The top three journals with the most published research in the field are the *International Journal of Nanomedicine*, the *Journal of Controlled Release*, and the *Journal of Drug Delivery Science and Technology*. The most cited is the *International Journal of Nanomedicine*, which has the highest H-index. Furthermore, the Impact Factor (IF) of journal is a crucial parameter for assessing its worth and that of its published works. *Journal of Controlled Release* has the highest IF (10.8) and JCR category (Q1).

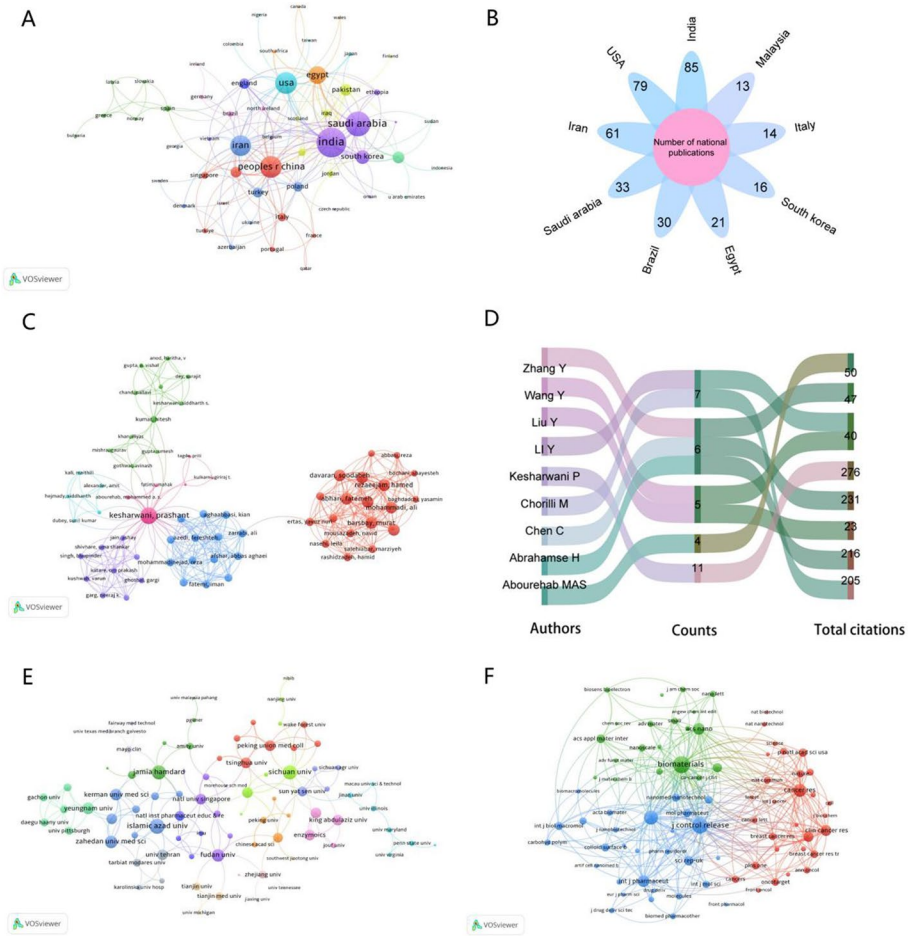

Fig. 3 Diagram of the Nanomaterials and Breast Cancer Collaboration Network. **A-B**. The coauthorship network map of countries; **C-D**. The coauthorship network map of authors; **E**. The coauthorship network map of institutions; **F**. The cocitation network map of journals

Table 1 Top 10 research institutions in terms of publication volume

Rank	Institution	Country	Counts	Percentage	Total citations	H-Index
1	Egyptian gyptian knowledge bank (EKB)	Egypt	20	19.65	393	10
2	Islamiv azda university	Iran	16	10.56	169	9
3	Tabriz university of medical science	Iran	15	21.07	316	9
4	Jamia hamdard university	India	12	16.17	194	7
5	Nationalinstitute of pharmaceutical education research niper	India	11	10.45	115	5
6	Universidade de sao paulo	Brazil	10	15.2	152	6
7	Universidade estadual paulista	Brazil	10	11.6	116	5
8	Mashhad unversity medical science	Iran	9	17.67	159	5
9	Nanjing medcial university	China	9	8.33	75	5
10	Chinese academy of science	China	8	13.25	106	5

Analysis of the most cited articles

The nanomaterials analyzed in the most cited publications of each year during the study period are shown in Fig. 4 (Karathanasis et al. 2008; Eghtedari et al. 2009; Chen et al.

Table 2 The top 10 most productive journals terms of publication volume

Rank	Journal names	Counts	Total citations	H-Index	IF in 2022	JCR category
1	International Journal of Nanomedicine	27	1632	18	8	Q3
2	Journal of controlled release	10	397	9	10.8	Q1
3	Journal of drug delivery science and technology	10	195	8	5	Q3
4	Acs applied materials & interfaces	9	306	8	9.5	Q1
5	Nanomedicine	9	189	6	5.5	Q2
6	Biomaterials	8	755	7	14	Q1
7	Pharmaceutics	8	72	6	5.4	Q2
8	Cancers	7	59	5	5.2	Q2
9	Nanoscale	7	232	6	6.7	Q2
10	Journal of photochemistry and photobiology b-biology	6	126	6	5.4	Q1

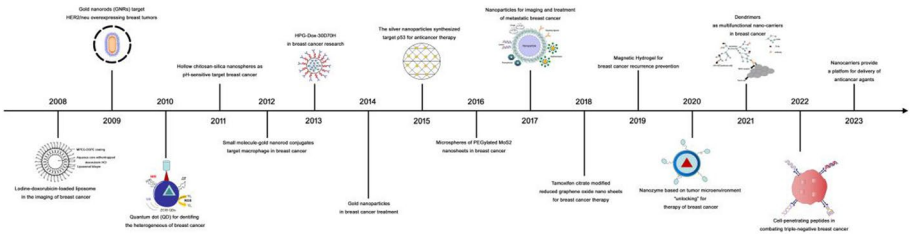

Fig. 4 The timeline of nanomaterials and breast cancer research

2010; Deng et al. 2011; Dreaden et al. 2012; You et al. 2013; Lee et al. 2014; Gurunathan et al. 2015; Kumar et al. 2017; Mu et al. 2017; Zhang et al. 2018; Gao et al. 2019; Wang et al. 2020; Dubey et al. 2021; Fatima et al. 2022; Ashrafizadeh et al. 2023). Gold nanoparticles were commonly used in these studies. Table 3 shows the top 10 most cited articles as of 18 November 2023, along with the information associated with them, which we will examine in the next section. Four of the ten studies are from the USA, two are from India, and the remaining four are from Singapore, China, South Korea, and Italy. The study titled "Albumin-bound formulation of paclitaxel (Abraxane® ABI-007) in the treatment of breast cancer" by Miele E, published in the International Journal of Nanomedicine in Italy in 2009, which was cited 652 times, making it the most cited publication in the field. (Miele et al. 2009).

For the study of keywords and research hotspots

In a paper, keywords can help us get the topic and theme of the research more accurately and quickly (Tang et al. 2023). The division of all keywords into six clusters in Fig. 5A. As shown in Fig. 5B, terms in purple indicate that their average publication year is in 2018 and earlier, while terms in bright yellow indicate that their average publication year is after 2021. "quantum dots", "resistance" and "therapeutics" were the main focus in the early days. Keywords such as "immunotherapy", "nanomaterials" and "anticancer activity" will not start to attract widespread attention until after 2021. The largest clusters are in red and include keywords like "diagnosis" and "metastasis" in breast cancer. The second cluster is in purple and contains keywords such as "nanotechnology",

Table 3 Top 10 cited articles according to number of citations

Author	Title	Journal	Country	Institution	Year	Citation
Miele, Evelina	Albumin-bound formulation of paclitaxel (Abraxane® ABI-007) in the treatment of breast cancer	International journal of nanomedicine	Italy	Univ Roma La Sapienza	2009	652
Al-Mahmood, Sumayah	Metastatic and triple-negative breast cancer: challenges and treatment options	Drug delivery and translational research	USA	Rutgers State Univ	2018	298
Sun, Bingfeng	Multifunctional poly(D,L-lactide-co-glycolide)/montmorillonite (PLGA/MMT) nanoparticles decorated by trastuzumab for targeted chemotherapy of breast cancer	Biomaterials	Singaporean	Natl Univ Singapore,	2008	226
Deng, Ziwei	Hollow chitosan-silica nanospheres as pH-sensitive targeted delivery carriers in breast cancer therapy	Biomaterials	China	Hubei Univ, Key Lab Green	2011	217
Eghtedari, Mohammad	Engineering of hetero-functional gold nanorods for the in vivo molecular targeting of breast cancer cells	Nano letters	USA	Univ Texas Med Branch Galveston	2009	198
Gurunathan, Sangiliyandi	Comparative assessment of the apoptotic potential of silver nanoparticles synthesized by bacillus tequilensis and calocybe indica in MDA-MB-231 human breast cancer cells: targeting p53 for anticancer therapy	International journal of nanomedicine	South Korea	Konkuk Univ	2015	175
Lee, Jihyoun	Gold nanoparticles in breast cancer treatment: Promise and potential pitfalls	Cancer letters	USA	Univ Texas MD Anderson Canc Ctr	2014	174
Singh, Santosh Kumar	Drug delivery approaches for breast cancer	International journal of nanomedicine	USA	Morehouse Sch Med	2017	129
Jain, Vikas	A review of nanotechnology-based approaches for breast cancer and triple-negative breast cancer	Journal of controlled releaes	India	JSS Acad Higher Educ & Res	2020	121

Table 3 (continued)

Author	Title	Journal	Country	Institution	Year	Citation
Vivek, Raju	Multifunctional her2-antibody conjugated polymeric nanocarrier-based drug delivery system for multi-drug-resistant breast cancer therapy	Acs applied materials & interfaces	India	Bharathiar Univ, Prote & Mol Cell Physiol Lab	2014	117

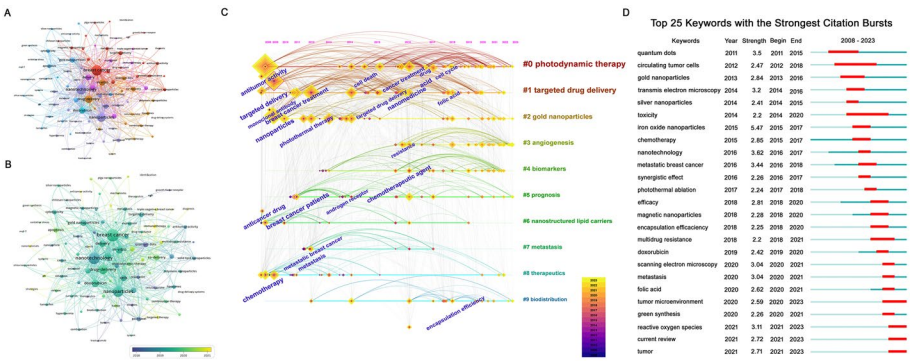

Fig. 5 Keyword analysis of research hotspots. **A-B**. The network A and overlay B of keyword co-occurring; **C**. The timeline map of keyword co-occurring; **D**. The Top 25 keywords with the strongest citation bursts

"nanoparticles" and "cells". The third cluster is in yellow and includes keywords such as "drug delivery", "in vitro" and "co-delivery". The fourth cluster, in blue, contains keywords like "doxorubicin", "apoptosis" and "gold nanoparticles". The fifth cluster in pink contains the keywords "delivery" and "immunotherapy".

In addition, we have used CiteSpace to analyze the similarities and differences in the keywords over time. Until 2014, the main areas of research were breast cancer, metastasis, antitumor therapy, anti-tumour agents and chemotherapy. Breast cancer, photodynamic therapy, resistance and gold nanoparticles continue to be topics of high interest in 2023. The strength of the keyword bursts is another important indicator of the frontiers and hotspots of the study over time. The top ten keywords with the highest outbreak values are iron oxide nanoparticles (5.47), nanotechnology (3.62), quantum dots (3.5), metastatic breast cancer (3.44), transmission electron microscopy (3.2), reactive oxygen species (3.11), scanning electron microscopy (3,04), metastasis (3.04), chemotherapy (2.85), gold nanoparticles (2.84).

Discussion

In recent years, there has been a surge in the bibliometric analysis of articles across various fields (Tang et al. 2023). Tools such as CiteSpace and the VOSviewer enable raw data visualization, offering comprehensive and intuitive data representation (Zhou et al. 2020). Our findings demonstrate an overall increased trend in the number of annual publications in the discipline. 2020 was the most significant year in the field, with the most citations and the highest H-index.

China leads in the number of publications per nation with 109 publications, accounting for 25.35% of the total. It also has the highest number of international partnerships, publications, and citations, as well as the highest h-index. China has a large population base and a large number of researchers and institutions in related fields, resulting in higher literature production. In particular, the efficacy of nanomedicines in breast cancer has been a hot topic of research in recent years. The *International Journal of Nanomedicine*, *Journal of Controlled Release*, and *Journal of Drug Delivery Science and Technology* are widely regarded as the most influential publications in this field. *International Journal of Nanomedicine* has the highest number of published papers, the highest h-index, the highest number of citations and the highest average number of citations of the papers, while *Biomaterials* has the highest JCR category and IF.

Subsequently, we found that one of the most cited papers used nanocarriers to improve the solubility of paclitaxel in water to increase the solubility and stability of the drug, thereby enhancing its efficacy against breast cancer. Furthermore, we have mapped the mechanism of nanomedicine therapy for breast cancer based on this article (Fig. 6). The study points to the development of so-called "third generation" nanocarriers and is based on a multi-stage strategy that addressing all the possible therapies in a more specific manner. The article states that human serum albumin stabilizes the drug particle at an average size of 130 nm (Stinchcombe 2007). This prevents any risk of capillary obstruction and eliminates the need for any particular infusion systems or steroid/antihistamine premedication before the infusion (Okuyama et al. 2021). Preclinical studies have shown that Abraxane® ABI-007 has higher tumor cell penetration and anti-tumor activity compared to equivalent doses of standard paclitaxel (Miele et al. 2009). The most highly cited article published in 2023 focuses on the therapeutic effects of Superparamagnetic Iron-Oxide Nanoparticles (SPIONs) on breast cancer (Dongsar et al. 2023). Controlled drug release from SPIONs can also aid in overcoming non-specific targeting

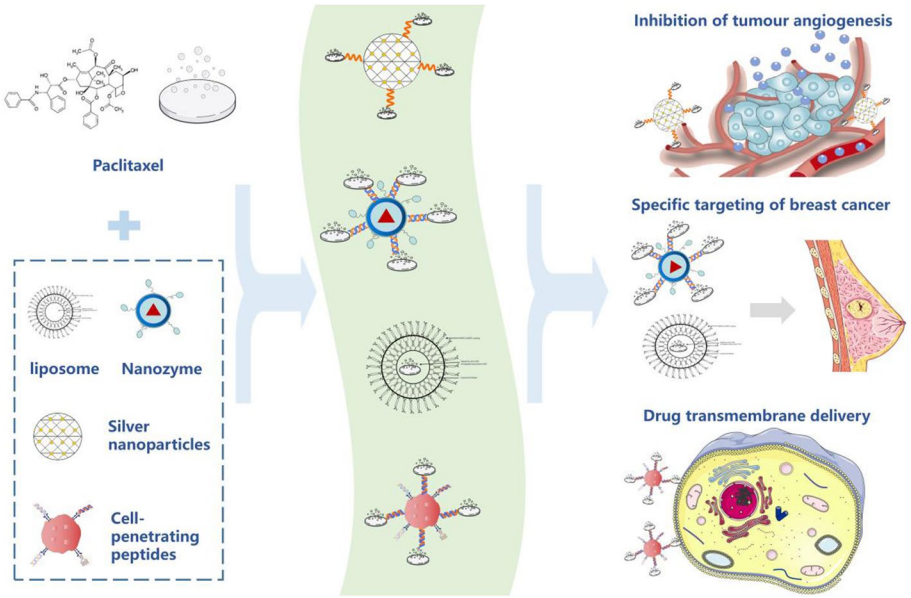

Fig. 6 Mechanistic map of nanochemical combination therapy in breast cancer (represented by the combination of paclitaxel and nanomaterials)

and reducing the need for large therapeutic doses. This is because drug-loaded SPIONs can specifically target certain cells, tissues, or organs, minimizing damage to healthy tissues and improving therapeutic efficacy. (Fakayode et al. 2018). Hoekman et al. demonstrated that liposomes have a stable and robust closed membrane that can carry hydrophilic small molecule drugs, as well as protein, RNA, and DNA drugs within aqueous chambers. This membrane protects the drugs from plasma scavenging and degrading enzymes, prolonging their retention time in the circulation of the body (Xinchen et al. 2023). Overall, by increasing treatment efficacy and lowering harmful side effects, nanocarriers can be a useful drug delivery method.

Moreover, keyword analysis has reviewed the development of nanomaterials in breast cancer. Before 2018, the main focus of research was still on the mechanisms of treatment resistance in people with breast cancer. Loading curcumin into solid lipid nanoparticles promotes the Bax/Bcl-2 ratio but reduces the expression of the cell cycle proteins CyclinD1 and cyclin-dependent kinase 4 (CDK4), which in turn improves the therapeutic outcome of breast cancer (Mitra and Dash 2018). It shows that research on nanomaterials and breast cancer was at a more macroscopic and superficial stage. In the medium term (2018–2021), the research focus gradually expands to the level of magnetic nanoparticles and gold nanoparticles, which have important applications in the diagnosis and treatment of breast cancer. Magnetic nanoparticles can be used in magnetic resonance imaging to help doctors diagnose tumors more accurately (Boosz et al. 2021). On the other hand, gold nanoparticles as the drug carriers can be used to deliver drugs precisely to the tumor site, improving therapeutic effects and reducing side effects (Javan Nikkhah and Thompson 2021). From here, the significance of nanomaterials in detecting and treating breast cancer will become clearer. Nanomaterials will play an important role in the immunotherapy of breast cancer between 2021 and 2024. They can act as carriers for immunomodulators or anticancer drugs, which contribute to increasing the concentration of the drug locally and reducing damage to healthy tissue (Vincenzo et al. 2023). Furthermore, nanomaterials can be designed the specific immunogenic properties that activate the immune system to identify and attack breast cancer cells. Tailored Nano-immunotherapy is expected to enhance therapeutic efficacy and decrease adverse effects in patients with breast cancer.

While there is no denying the importance that nanomaterials play in the detection and management of breast cancer, we think that there are still certain limitations to them. The selectivity and specificity of nanomaterials might have negative effects on cells other than cancer. The usefulness of nanomaterials in therapy and diagnosis may be impacted by their unknown biodistribution and metabolic pathways in vivo (Park et al. 2017). At the same time, not all nanomaterials can be effectively translated into clinical applications, and the process of translating nanomaterials into clinical applications involves extensive clinical trials that demand time and money (Shirwaiker et al. 2013). Additionally, there is still some literature that was not included, such as grey literature and relevant literature that was not included in the WoSCC database. Some recently published articles may receive more citations in the future, which may have led to the exclusion of some high-quality studies from this analysis. And the number of citations does not fully reflect the importance of an article, as some important articles may have few citations and self-citations may introduce bias (Brown et al. 2021).

Conclusion

The findings indicate that the number of publications on this subject increased significantly starting in 2015, with China and the USA exhibiting the highest productivity levels. In the treatment of breast cancer, nanomedicines have demonstrated improved drug uptake and retention, resulting in more effective targeting of the tumor tissue and reduced systemic toxicity. The treatment of metastatic breast cancer may benefit greatly from the use of multifunctional nanotherapeutic medications. Nanotechnology holds the significant potential in improving drug transport, releasing, and targeting, which could lead to higher treatment efficacy and fewer side effects. Targeting nanomaterial-based drugs could have a beneficial effect on breast cancer patients and could be a milestone in the diagnosis and treatment of breast cancer.

Abbreviations

WoSCC	Web of science core collection
QDs	Quantum dots
SSCI	Social science citation index
SCI-E	Science citation index expanded
LS	Link strength
TLS	The total link strength
EKB	Egyptian knowledge bank
IAU	Islamiv Azda University
Abraxane® ABI-007	Albumin-bound formulation of paclitaxel
SPIONs	Superparamagnetic iron-oxide nanoparticles
CDK4	Cyclin-dependent kinase 4

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Author contributions

LY and LXQ performed the literature search and collected the data. LY performed the statistical analysis and wrote the manuscript, and prepared Figs. 1, 2, 3. LAQ and ZJY prepared Figs. 4, 5. LZH revised the manuscript. LY and YY designed the study and conceived and revised the manuscript. All authors contributed to the article and approved the final manuscript.

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Availability of data and materials

All data generated or analyzed during this study are included in this article and additional data are available from the corresponding author upon reasonable request.

Declarations

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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