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Nanomaterials in Rheumatoid Arthritis Over Two Decades: A Bibliometric Study of Inflammatory Pathways and Emerging Therapeutic Strategies

Muhammad Amin Nasution[1], Muhammad Andry[2*], Nia Novranda Pertiwi[3], Hindri Syahputri[4], Syilvi Rinda Sari[4], Aqmal Ramadhan Pasaribu[1]

[1] Department of Pharmacy, Faculty of Mathematics and Natural Sciences, Universitas Syiah Kuala, Banda Aceh 23111, Indonesia.
[2] Department of Pharmacy, Faculty of Mathematics and Natural Sciences, Universitas Sriwijaya, Sumatera Selatan 30662, Indonesia
[3] Department of Pharmacognosy and Medicinal Chemistry, faculty of pharmacy, Universitas Mulawarman 75119, Samarinda, Indonesia.
[4] Faculty of Pharmacy, Universitas Muslim Nusantara Al-Washliyah, Medan 20147, Indonesia.

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Corresponding Author:
Muhammad Andry
andry@unsri.ac.id

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Abstract: The rapid expansion of nanomaterial-based rheumatoid arthritis (RA) research has produced a fragmented body of literature, limiting clear recognition of major journals, influential contributors, collaboration patterns, and shifting research priorities. This study presents a two-decade bibliometric mapping of nanomaterials in RA with an inflammation-focused perspective. English-language publications from 2005 to 2025 were collected from Scopus using a nanomaterial–RA–inflammation search strategy, yielding 5,110 initial records. Data were refined in OpenRefine through deduplication, author-name harmonization, and keyword normalization. Following eligibility screening, 720 articles were retained for core bibliometric analysis. Biblioshiny, supported by the Bibliometrix R package, was used to measure annual publication trends, productive sources, leading authors, institutional output, and collaborative networks. Conceptual development was assessed through keyword co-occurrence analysis and thematic mapping, with network visualizations generated in VOSviewer. Results indicate accelerated publication growth in the recent period, with outputs concentrated in drug delivery and biomaterials-related journals. Scientific productivity was driven by a limited group of countries and institutions, reflecting hub-based knowledge production. Keyword and thematic analyses identified targeted drug delivery and macrophage polarization as motor themes, while PI3K–AKT and Hedgehog signaling emerged as developing topics. Overall, the field shows rapid growth and organized thematic evolution.

Keywords: Bibliometric analysis; Inflammatory pathways; Nanomaterials; Rheumatoid arthritis

Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease that primarily affects synovial joints, characterized by persistent synovitis, pannus formation, cartilage destruction, and progressive bone erosion (Jahid et al., 2023; Komatsu et al., 2022) clinical manifestations of RA include not only joint pain and stiffness, but also fatigue, reduced functional capacity, and an increased risk of cardiometabolic comorbidities due to systemic inflammation. From a pathobiological perspective, RA is driven by a complex network of interactions between immune cells (macrophages, T cells, B cells) and stromal cells (fibroblast-like synoviocytes/FLS), which produce pro-inflammatory mediators such as tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), and interleukin-1β (IL-1β), while also inducing oxidative stress, synovial

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angiogenesis, and tissue remodeling. This complexity helps explain why RA often requires long-term therapy and approaches that not only suppress symptoms but also target layered inflammatory mechanisms (Kondo et al., 2021; Ye et al., 2025; Yue et al., 2025).

Over the past two decades, the therapeutic landscape of RA has advanced rapidly through the use of csDMARDs (e.g., methotrexate), biologics, and targeted therapies such as JAK inhibitors (Tanaka, 2021). Although many patients achieve remission or low disease activity, therapeutic responses remain heterogeneous and are often constrained by adverse effects, cost, and the need for intensive monitoring (Fatima et al., 2025). Another frequently overlooked challenge is the limited ability to deliver drugs selectively to the inflamed synovial microenvironment. Many drug molecules undergo broad systemic distribution, rapid metabolism, or have low solubility, so effective concentrations in target tissues are not achieved optimally. As a result, dose escalation may increase toxicity risk without guaranteeing improved efficacy. This gap has driven research toward more precise and target-oriented drug delivery strategies (Emami et al., 2019; Li et al., 2023; Wu et al., 2024).

Nanomaterials and nanomedicine approaches have emerged as one of the most promising strategies to address these limitations. By engineering size, charge, surface properties, and stimulus-responsive designs acidic pH, reactive oxygen species/ROS, or enzymes), nanocarriers can improve drug solubility and stability, prolong circulation time, and enable controlled/triggered release (Alsawaftah et al., 2022; Majumder et al., 2021). In the RA context, nanomaterial design can be optimized to enhance accumulation in hyperpermeable synovial tissue, modulate macrophage phagocytosis, or target FLS that play major roles in joint destruction. Pharmacologically, nano-platforms also enable co-delivery of multiple agents anti-inflammatory and antioxidant compounds), reduce systemic exposure, and improve the therapeutic index (Kalashnikova et al., 2020; X. Zhang et al., 2025). In addition, certain nanomaterials depending on their composition and architecture, may act as passive/active immunomodulators by shifting macrophage polarization (from pro-inflammatory M1 to anti-inflammatory M2), reducing cytokine expression, or dampening inflammatory pathways that drive tissue damage (Batool et al., 2021; Galindo et al., 2024; Wang et al., 2025).

Nevertheless, the rapid growth of publications on nanomaterials in RA has produced a large, multidisciplinary body of literature, making it difficult for researchers to understand the field's knowledge structure, the most influential publication channels, key actors, and topic evolution over time. Traditional narrative reviews often select only subsets of the literature and are vulnerable to selection bias, whereas the current needs of the field demand more systematic mapping (Jia et al., 2025; Xie et al., 2025). Bibliometrics offers a quantitative and reproducible framework to assess scientific performance (productivity, citations, growth) while also enabling science mapping through keyword co-occurrence analysis, thematic mapping (centrality–density), and identification of core journals (Bradford's law) and leading contributors (Kuytu, 2025; Moral-Muñoz et al., 2020). By integrating bibliometric findings with pharmacological interpretation, we can build a logical continuity: dominant thematic clusters in keyword maps can be translated into mechanistic hypotheses regarding the most frequently targeted inflammatory pathways and the therapeutic strategies currently gaining momentum (Chen et al., 2025; Radu et al., 2025).

Beyond mapping productivity and collaboration structures, bibliometric approaches also enable identification of "centers of gravity" in research—namely countries, institutions, and authors that function as hubs of knowledge production—and how core journals serve as channels consolidating scientific discourse. Thus, the results of this study are expected not only to describe the current state of the field, but also to provide a quantitative basis for positioning future research agendas, including the need for keyword/terminology standardization, stronger international collaboration, and sharper focus on the themes most central to the field's evolution (Adeosun et al., 2026; Mikhaylov et al., 2020).

This study presents a comprehensive bibliometric analysis entitled "Nanomaterials in Rheumatoid Arthritis Over Two Decades: A Bibliometric Study of Inflammatory Pathways and Emerging Therapeutic Strategies" over the period 2005–2025, with a primary emphasis on bibliometric mapping (~70%) and a directed pharmacological synthesis (~30%). Specifically, we aim to: (1) describe the dataset profile, author collaboration, and dynamics of scientific output; (2) identify core journals, influential authors, and the most productive organizations; (3) map country contributions and indications of international collaboration; and (4) extract conceptual hotspots through keyword co-occurrence networks and thematic maps to interpret shifts in research focus toward nanomaterial-based therapeutic strategies targeting synovial inflammation.

Method

Source of Documents

The main source of documents for this study is Scopus, chosen for its wide coverage, consistent metadata, and support for citation analysis and keyword

mapping. The search was conducted using a combination of keywords related to nanomaterials, rheumatoid arthritis (RA), and inflammation. The search query was: ("nanomaterial" OR "nanoparticle" OR "nanocarrier" OR "nanomedicine" OR "nano drug delivery" OR "nanostructured material") AND ("rheumatoid arthritis") AND ("inflammation" OR "inflammatory response" OR "synovi" OR "synovial inflammation" OR "pro-inflammatory" OR "anti-inflammatory"). Data was collected on November 26, 2025, to ensure the dataset was a snapshot at a specific time and could be replicated.

Indicators of Bibliometric

Bibliometric indicators used in this study include annual scientific production, identification of key journals and productive publication sources using the Bradford approach, and mapping author contributions based on productivity and local impact. Additionally, productive organizations/affiliations, country contributions, and international collaboration were identified. Other metrics analyzed include citations per document and keywords in the publications (Cano et al., 2024).

Keywords and Search Strategy

The keywords used in the search included terms related to nanomaterials, nanotechnology therapy for rheumatoid arthritis, and inflammation aspects related to the disease. The keywords were designed to capture documents that focus on RA as the primary disease context, nanomaterials in therapeutic or drug-delivery contexts, and their effects on inflammation or inflammatory microenvironments (Nasra et al., 2022).

Data Extraction and Bibliometric Parameters

Data was extracted from Scopus in CSV format, compatible with bibliometric analysis. Key metadata such as publication year, title, abstract, keywords (Author Keywords and Keywords Plus), author names, affiliations, countries, sources/journals, references, and citation metrics were collected. After data collection, filtering was performed to select documents relevant to RA and nanomaterials related to inflammation, ensuring a high-validity dataset for analysis (Ejaz et al., 2022).

Data Management and Data Analysis

Data management involved ensuring the consistency and completeness of the extracted metadata. Selected data were then grouped for further analysis. Bibliometric analysis was conducted using two main approaches: performance analysis and science mapping. Performance analysis included measuring annual scientific output, identifying key journals, and mapping author, organization, and country contributions. Science mapping was done through keyword co-occurrence analysis to identify conceptual clusters and inter-topic relationships (Alsulaiman et al., 2025).

Co-occurrence network visualizations were used to identify dominant thematic centers in the field, while density-centrality thematic maps were used to classify research themes. All analyses were done using the Bibliometrix/Biblioshiny (R package) for dataset summaries, trend visualizations, and identifying the most productive sources, authors, and affiliations. Keyword network visualization was done using VOSviewer to explore clustering structures and co-occurrence relationships (Nasution et al., 2025).

The analysis resulted in outputs such as tables summarizing the dataset characteristics, author collaboration, core journals, key contributors, annual production trends, keyword co-occurrence maps, thematic maps, and country contributions. The analysis resulted in outputs such as tables summarizing the dataset characteristics, author collaboration, core journals, key contributors, annual production trends, keyword co-occurrence maps, thematic maps, and country contributions (Nasution et al., 2025).

Result and Discussion

Types of Documents and Primary Information

Based on available information, research in this field has been ongoing from 2005 to 2025, indicating a significant increase in interest in this topic, particularly in relation to therapeutic strategies involving nanomaterials for rheumatoid arthritis (RA) shown in Table 1.

During this period, the number of documents produced reached 720 articles sourced from 253 journals, books, and other academic platforms. This figure shows that research on nanomaterials in RA is widely spread across various credible sources, reflecting that this topic has received considerable attention from various disciplines. In addition, the annual growth rate of documents of 27.31% reflects that this research is developing rapidly, along with the emergence of new insights into inflammatory pathways and nanomaterial-based therapies (Jia et al., 2025; Xie et al., 2025).

In terms of collaboration, only 9 documents were written by a single author, indicating that this research was highly collaborative. The average number of authors per document was 7.58, demonstrating the importance of interdisciplinary collaboration in this research. In addition, 21.67% of documents involved international collaboration, indicating that this research was conducted globally to address common health issues (Jia et al., 2025; Xie et al., 2025).

Table 1. Main Information about Data and Authors Collaboration

Descriptions	Results	Descriptions	Results
Main Information About Data		Authors Collaboration	
Timespan	2005-2025	Single-authored docs	9
Sources (Journals, Books, etc)	253	Co-Authors per Doc	7.58
Documents	720	International co-authorships %	21.67
Annual Growth Rate %	27.31	Document Types	
Document Average Age	3.95	article	720
Average citations per doc	33.24		
References	5223		
Document Contents			
Keywords Plus (ID)	6907		
Author's Keywords (DE)	1772		
Authors			
Authors	3276		
Authors of single-authored docs	9		

With an average of 33.24 citations per document, this research has significantly influenced its field. The articles contribute greatly to the understanding of rheumatoid arthritis (RA) and the potential role of nanomaterials in treating this condition. The analysis of keywords highlights a strong emphasis on nanomaterials, inflammatory pathways, and RA, further emphasizing the focus of this research on developing therapeutic strategies based on nanomaterials. In summary, this study reflects the swift progress in nanomaterial research for rheumatoid arthritis, characterized by strong international collaboration and a significant impact on the advancement of new treatment options for the disease (Jia et al., 2025; M. Zhang et al., 2022).

Publication Growth and the Geographical Distribution of Research

The development of nanomaterials research for rheumatoid arthritis (RA) therapy over the 2005–2025 period shows a clear growth pattern with accelerating momentum in recent years. In general, the early phase (approximately 2005–2013) was characterized by a relatively low and stable number of publications, reflecting an initial exploratory stage in applying nanomaterial platforms to pharmacokinetic challenges, solubility limitations, and drug delivery in RA. Entering the mid-phase (approximately 2014–2018), publications began to increase gradually alongside broader adoption of biomaterials-based drug-delivery approaches and growing interest in targeting the synovial microenvironment. The late phase (approximately 2019–2025) shows the most pronounced surge, indicating that the field entered a period of rapid expansion and topical diversification—ranging from nanocarrier design optimization and controlled release to multifunctional combination platforms. This pattern is visualized in Figure 1, underscoring the acceleration of scientific output, particularly in the latter half of the study timeframe (Wang et al., 2021; Xie et al., 2025).

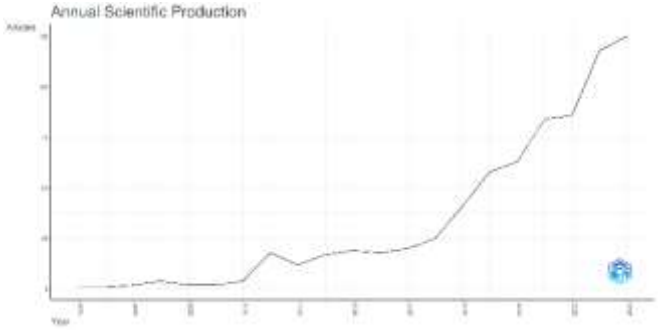

Figure 1. Annual scientific production of nanomaterial research in rheumatoid arthritis therapy

Beyond temporal dynamics, the geographical distribution of research output demonstrates a concentrated pattern in which contributions cluster within specific countries. Based on the mapping of the most relevant countries, publication volume is dominated by nations with strong productivity in nanomedicine and biomaterials, with the largest contribution coming from Asia—particularly China—which consistently ranks first in publication volume. Following China, several other countries emerge as significant contributors, including India, the United States, South Korea, and Pakistan, indicating that nanomaterial development for RA is a global research area but remains characterized by strong productivity hubs in particular regions. From a bibliometric perspective, such concentration typically reflects differences in research capacity (infrastructure, funding continuity, and established publication pipelines), and it suggests that knowledge production is "hub-driven" rather than evenly distributed. This hub structure also implies a practical outlook for the field: as publication capacity becomes concentrated within leading countries, the next stage of maturation will likely depend on

strengthening cross-country collaboration networks to improve reproducibility, broaden validation, and reduce fragmentation across parallel research streams. A summary of country contributions and the ranking of the most relevant countries is presented in Figure 2, which can be used to narratively position the top 10 countries by publication count within the analyzed corpus (Jia et al., 2025; Xie et al., 2025).

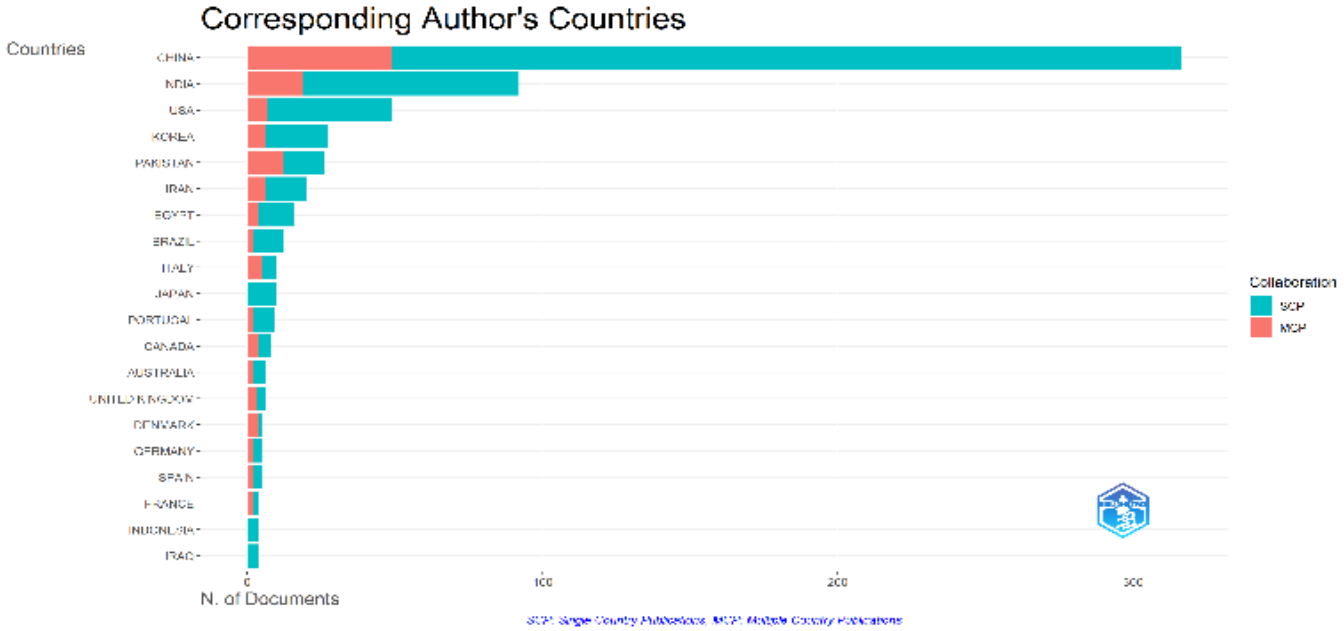

Figure 2. Most relevant countries in nanomaterial-based rheumatoid arthritis research

Core Publication Sources and Key Contributors

To understand the publication structure in nanomaterial-based therapeutic research on rheumatoid arthritis (RA), a bibliometric analysis was conducted on publication sources (journals) and author contributions. Identifying core sources is important because it highlights the primary channels through which knowledge is disseminated, while also reflecting the disciplinary orientations shaping the field. Based on publication-volume rankings, article output is most concentrated in journals with strong profiles in drug delivery, biomaterials, and nanomedicine. This pattern aligns with Bradford's law, whereby a small set of core journals accounts for a large proportion of publications within a given domain. Accordingly, mapping core sources not only indicates where research is published, but also suggests that nanomaterial development for RA sits at the intersection of materials science, drug-delivery technology, and applied pharmacy. The top 10 core journals by publication volume are summarized in Table 2 (Jia et al., 2025; Laha et al., 2024; Logesh et al., 2023).

In addition to publication channels, author contributions were mapped to identify the key actors driving both productivity and impact in this field. In bibliometrics, author ranking can be assessed using productivity indicators (number of publications) and citation-based impact indicators. In this study, author impact is reported using the local H-index, defined as the H-index calculated within the analyzed dataset (within-dataset) rather than the author's global H-index across all publications indexed in Scopus/Google Scholar. Reporting the local H-index helps evaluate an author's role and influence specifically within the nanomaterial–RA domain, making the interpretation more directly aligned with the study focus. From an ecosystem standpoint, the emergence of a small set of recurrent high-impact contributors typically signals a hub-driven intellectual structure, where stable research groups repeatedly shape the corpus through both output volume and within-field citation influence. The top 10 contributors based on local H-index are summarized in Table 3 (Abulimiti et al., 2025; Jia et al., 2025).

Table 2. Top 10 Core Journals by Publication Volume

Journal	Rank	Freq	cumFreq
Journal of Controlled Release	1	34	34
Journal of Nanobiotechnology	2	23	57
International Journal of Nanomedicine	3	22	79
International Journal of Pharmaceutics	4	20	99
Biomaterials	5	18	117
Colloids and Surfaces B: Biointerfaces	6	16	133
ACS Applied Materials and Interfaces	7	14	147
International Journal of Biological Macromolecules	8	14	161
Acs Nano	9	13	174
Advanced Healthcare Materials	10	12	186

Overall, the findings in this subsection indicate that nanomaterials research for RA is not evenly distributed across journals, but instead is concentrated within a set of core journals oriented toward drug-delivery technologies and biomaterials. At the same time, the presence of several authors with relatively high local H-indices suggests the existence of a group of researchers who consistently contribute to the advancement of the field, both through productivity and citation influence within the corpus. In combined Results and Discussion terms, this dual concentration (core journals + recurrent key contributors) supports the interpretation that RA–nanomaterials has moved into a phase of consolidation, where publication venues and leading actors jointly shape the field's dominant methodological norms and thematic priorities. These findings provide an important basis for interpreting the linkage between publication structure (core journals) and the field's intellectual dynamics, before the analysis proceeds to the institutional/organizational level and the conceptual structure of research themes (Abulimiti et al., 2025; Xie et al., 2025).

Table 3. Leading Contributors in RA Nanomaterial Research

Rank	Authors	H-Index
1	Liu Y	16
2	Chen Y	15
3	Wang Y	15
4	Zhang Z	15
5	Li C	14
6	Zhang Y	14
7	Chen X	13
8	Liu L	13
9	Zhao Y	13
10	Li Y	12

Most Productive Organizations and the Conceptual Structure of Research Themes

Mapping institutional productivity is necessary to identify the most active research centers in the development of nanomaterials for rheumatoid arthritis (RA), while also revealing how research capacity is concentrated within specific affiliations. Based on publication counts, institutional contributions show the dominance of several organizations that consistently produce articles in this area.) This pattern suggests that progress in the field is driven not only by individual authors but also by institutional ecosystems, including materials research facilities, collaboration networks, and research program priorities that enable nanomedicine platform development through preclinical evaluation. The top 10 most productive organizations, along with their publication counts, are summarized in Table 4 (Ren et al., 2024).

Beyond identifying "who is most productive," this study also maps "what is most frequently discussed" by analyzing the conceptual structure through keyword co-occurrence. A keyword co-occurrence network visualization depicts relationships among topics through nodes (keywords) and link strength (co-occurrence intensity), enabling the identification of dominant thematic clusters that form the field's intellectual framework. In the RA–nanomaterial context, the network map typically highlights anchor keywords that serve as connectivity hubs (e.g., disease terms, nano-platforms, and drug-delivery terminology), which then branch into clusters representing methodological approaches and biological–inflammatory focal points. Accordingly, this visualization functions as a "concept map," reinforcing that the field has evolved in a multidisciplinary manner—integrating materials and drug-delivery terminology with synovial inflammation and immune-response aspects. The keyword co-occurrence network structure is presented in Figure 3 (Lozano et al., 2019; Ozek et al., 2023).

Table 4. Top 10 Most Productive Organizations

Rank	Institutional Affiliation	Publication Count
1	Sun Yat-Sen University	34
2	Faculty of Pharmacy	27
3	Army Medical University	25
4	Luzhou Medical College	23
5	Southern Medical University	22
6	University of Agriculture	22
7	Xuzhou Medical University	22
8	Sichuan University	19
9	Southwest Jiaotong University	17
10	Shanghai University of Traditional Chinese Medicine	16

To complement the network mapping, thematic evolution was analyzed using a thematic map based on two main dimensions: centrality (the degree to which a theme is connected to the overall field structure) and density (the internal cohesion/maturity of a theme). This map classifies themes into four quadrants: (1) motor themes (high centrality, high density), representing mature themes that function as primary drivers of the field; (2) basic themes (high centrality, low density), reflecting fundamental themes with broad scope but still developing internally; (3) niche themes (low centrality, high density), indicating specialized and well-developed themes that are less connected to the mainstream; and (4) emerging/declining themes (low centrality, low density), capturing either newly emerging topics or themes that are losing momentum. In this study, the thematic map was used to assess shifts in research focus and to position key topics within the two-decade development context. This thematic positioning is consistent with recent bibliometric and visual analyses

in RA nanomaterials that use science-mapping outputs to distinguish consolidated research streams from emerging directions. The thematic map visualization summarizing theme positions and the field's conceptual dynamics over 2005–2025 is presented in Figure 4 (Jia et al., 2025; Xie et al., 2025).

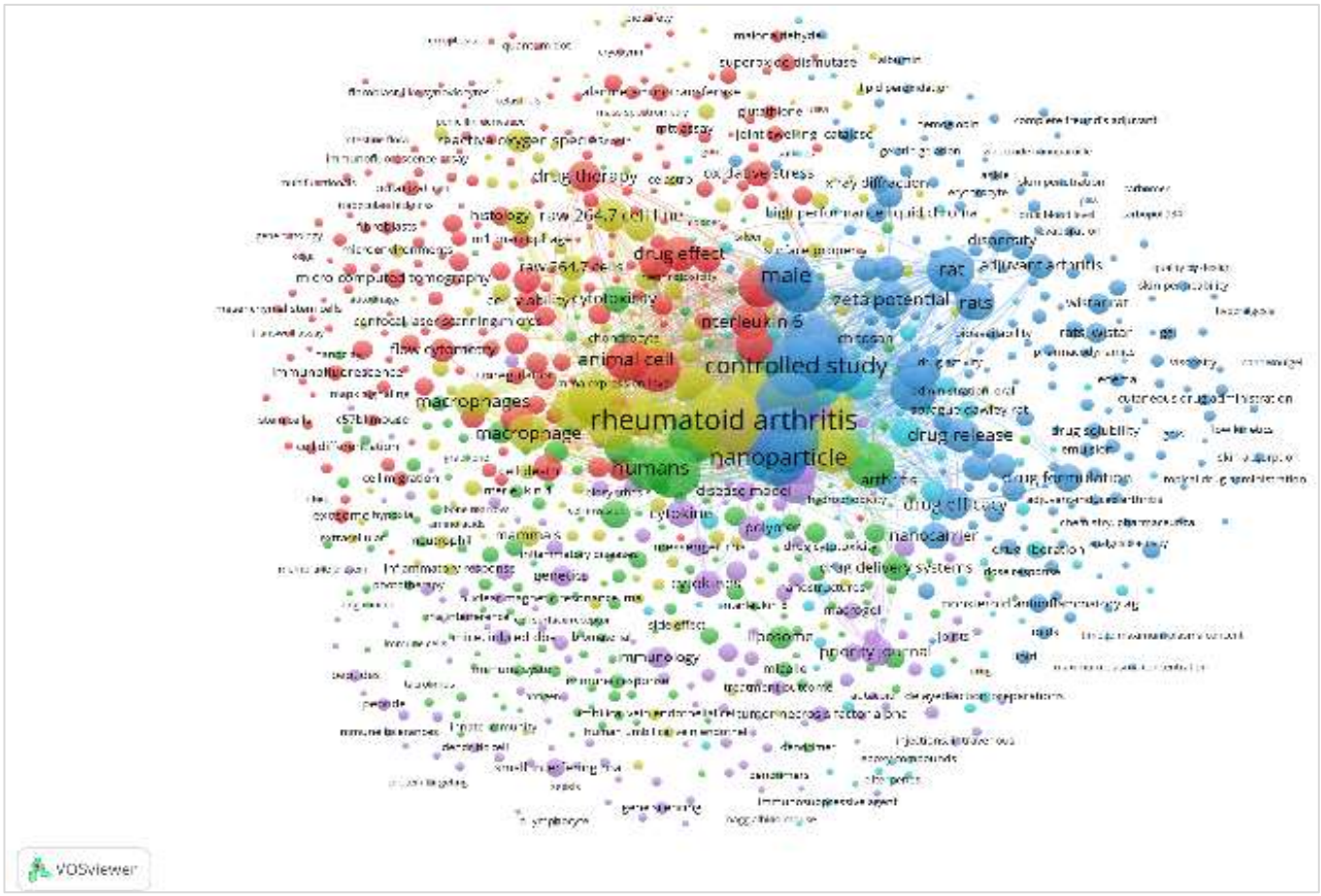

Figure 3. Network visualization of keyword co-occurrence in nanomaterial-based rheumatoid arthritis research (VOSviewer)

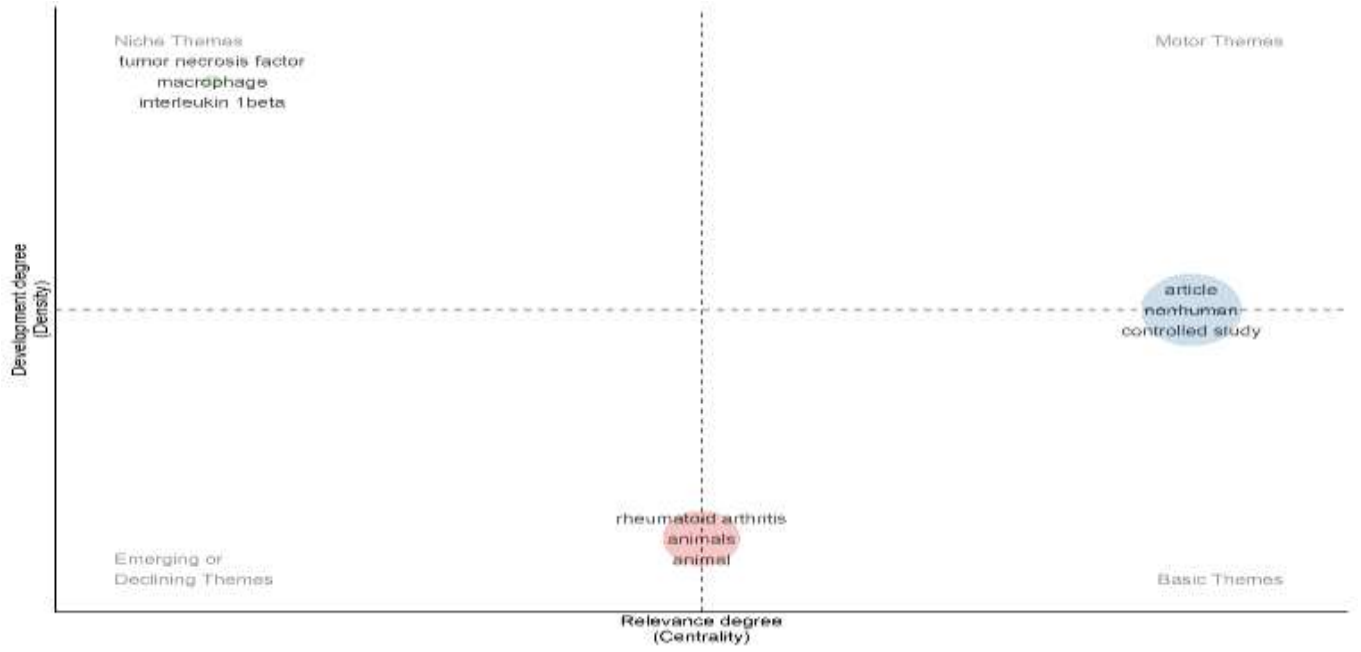

Figure 4. Thematic map based on density and centrality highlighting the evolution of research themes (2005–2025)

Overall, the findings of this subsection confirm that nanomaterials research in RA is supported by a strong institutional base, with dominant contributions from a number of the most productive organizations, while also exhibiting a conceptual structure that can be systematically mapped through keyword co-occurrence networks and thematic maps. In combined Results and Discussion terms, the concurrence of institutional hubs (Table 4) and consolidated conceptual clusters (Figures 3–4) indicates that field growth is increasingly structured, with recognizable hotspots and evolving thematic priorities that are shaped by recurring centers of knowledge production (Jia et al., 2025; Xie et al., 2025).

Conclusion

This bibliometric mapping of RA–nanomaterials research (2005–2025) indicates that the field is transitioning from rapid expansion toward a phase where progress will be defined by consolidation, comparability, and translational readiness. Over the next five years, a central challenge will be overcoming the hub-driven structure of knowledge production—currently concentrated in a limited set of countries, institutions, and recurring author groups—by strengthening cross-country collaboration to enable multi-site validation, reproducibility across models, and broader generalizability of findings. In parallel, the consolidation of dissemination within core drug delivery/biomaterials journals suggests that future impact will increasingly depend on standardized and transparent reporting (e.g., harmonized terminology, consistent physicochemical characterization, and comparable outcome metrics), allowing robust benchmarking across nanoplatforms rather than incremental platform novelty. Conceptual mapping further implies that "what's next" is a shift from generating new carriers to resolving translational bottlenecks: establishing more predictive and standardized preclinical evaluation frameworks, prioritizing comparative studies that clarify relative advantages among leading approaches, and integrating manufacturability, scale-up considerations, and safety/reproducibility requirements earlier in development. Collectively, these priorities—expanded international networks, improved standardization, and translation-oriented study designs—represent the most actionable pathway to convert the field's thematic maturation into clinically meaningful progress in RA nanotherapeutics over 2026–2030.

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Author Contributions
Conceptualization, M.A.N.; A.R.P and M.A; methodology, M.A.N and N.N.P.; software, M.A.N and A.R.P.; validation, M.A. and M.A.N.; formal analysis, S.R.S. and M.A.N.; investigation, H.S.; resources, M.A.N.; data curation, A.R.P.; writing—original draft preparation, M.A.N. A.R.P.; writing—review and editing, M.A.N.; M.A, N.N.P visualization, A.R.P.; H.S; S.R.S supervision, M.A.N.; project administration, M.A.N. All authors have read and agreed to the published version of the manuscript.

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Conflict of Interest
The authors declare no conflicts of interest.

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