Trop J Nat Prod Res, August 2025; 9(8): 3430 - 3441 ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

Tropical Journal of Natural Product Research

Available online at https://www.tjnpr.org

Review Article

Transforming Oral Drug Delivery: A Thrilling Journey of Three Decades of Innovation and Breakthroughs

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ARTICLE INFO

Article history:
Received 05 April 2025
Revised 09 July 2025
Accepted 18 August 2025
Published online 01 September 2025

ABSTRACT

Oral Drug delivery systems (ODDS) play a crucial role in modern pharmacotherapy, enhancing the efficacy and safety of drug treatments. This study presents a comprehensive bibliometric analysis of drug delivery system (DDS) research trends over the past 32 years (1992–2024), providing new insights into the evolution of this field. Using a dataset of 437 documents from 161 journals, books, and conference proceedings, bibliometric methods were applied to identify influential authors, key research themes, and international collaboration patterns. Co-citation analysis revealed the significant impact of prominent contributors such as Attwood D, Miyazaki S, Kubo W, and Liu Y on advances in DDS. Keyword clustering analysis revealed dominant research themes, including nanoparticles, polymers, oral bioavailability, and targeted delivery. International collaborations accounted for 24.49% of the total co-authorship, reinforcing the international nature of DDS research. This review also offers a critical examination of publication growth, highlighting emerging trends such as nanotechnology and personalized medicine, while addressing gaps in clinical translation, mechanistic understanding, and drug resistance. Unlike previous bibliometric studies, this study offers a longitudinal perspective on DDS research, mapping both historical evolution and contemporary developments. The bibliometric methods employed ensure quantifiable information on the trajectory of the field, guiding future research directions and fostering collaborative advances. By synthesizing trends and identifying strategic gaps, this study provides a valuable reference for researchers and policymakers, facilitating evidence-based decision-making to improve drug delivery technologies and therapeutic outcomes

Keywords: Oral Drug Delivery Systems, Bibliometric Analysis, Nanoparticles, Targeted Delivery, Personalized Medicine, Global Collaboration..

Introduction

Oral Drug delivery systems (ODDS) play a crucial role in modern pharmacotherapy, enhancing the efficacy and safety of drug treatments. Drug delivery refers to the technologies and methods used to administer therapeutic agents in a controlled and targeted manner.[1–6] This include a range of technologies, from tablets and capsules to nanoparticles and implantable devices. Numerous bibliometric studies have been conducted on drug delivery systems, including the studies of Peng *et al*. (2022)[7] on DDS applied to ocular delivery and Chen *et al*. (2024)[8] on drug delivery systems in periodontitis. Additional studies have been completed, and more are underway, demonstrating the importance of DDS and rapid growth of research in this field.[9,10] The oral route is the most common route of drug administration due to its convenience, patient acceptability, and relatively low cost. However, with respect to drug delivery systems, the oral route presents unique challenges, including enzymatic degradation in the gastrointestinal tract and variability in absorption due to physiological conditions.

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Citation: Fekrouni M, Benomar A, Ameggouz M, Mojemmi B, Chakkor S. Transforming Oral Drug Delivery: A Thrilling Journey of Three Decades of Innovation and Breakthroughs. Trop J Nat Prod Res. 2025:9(8):3430 – 3441 https://doi.org/10.26538/tjnpr/v9i8.1

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Nevertheless, it also offers significant opportunities for innovation.[1] Oral DDS include formulations such as extended-release tablets, gastro-resistant capsules, and nanoparticles designed to improve the solubility and stability of poorly soluble drugs. Controlled and targeted release technologies play a crucial role in orally administered medications, as they enable the modulation of drug release profiles, decrease the frequency of administration, and minimize adverse effects.[11,12]

Biopharmaceutics is a branch of pharmacy that studies the interaction between the physical and chemical properties of drugs, dosage forms, and pharmacological response. Bioavailability refers to the proportion of a drug that reaches systemic circulation and is available to exert its therapeutic effect.[13] DDS are essential for optimizing bioavailability by controlling the drug's release, dissolution, and absorption within the body.[8] Advances in biopharmaceutics enable the design of DDS to overcome physiological barriers and maximize therapeutic efficacy.[14]

Advanced technologies, particularly nanotechnologies, play an increasingly vital role in drug delivery systems. Nanotechnologies facilitate the development of nanoparticles that can specifically target diseased cells, thereby enhancing treatment efficacy and minimizing side effects.

Drug delivery systems based on nanotechnologies offer several advantages: Nanoparticles can penetrate biological barriers more easily, reaching treatment sites more effectively.[15] The functionalization of nanoparticles allows precise targeting of diseased cells, thereby reducing the impact on healthy cells. Nanoparticles can be designed to release drugs in a controlled and prolonged manner, thereby improving bioavailability and therapeutic efficiency.[16-18]

The objectives of this study were to analyze research trends, international collaborations, and gaps in the field of drug delivery. Various bibliometric parameters were used to understand the field's

intellectual, social, and conceptual structure. The study also aims to identify existing gaps and propose future research directions. Understanding the trends and developments in the field of DDS is essential to guide future research and collaborations. The results of this study will provide valuable insights to researchers, practitioners, and policymakers, contributing to the improvement of drug treatments and technological innovation.

Materials and Methods

To conduct a comprehensive bibliometric analysis of research trends in drug delivery systems (DDS), a dataset of 437 documents were aggregated from scientific databases, spanning a 32-year period (1992–2024). These documents were extracted from 161 journals, books, and conference proceedings, highlighting the multifaceted importance of DDS research.

Data collection and processing

The dataset was compiled from the Web of Science database, selected for its high-quality, peer-reviewed scientific literature and robust citation metadata. The search query was formulated as follows:

("oral drug delivery system" OR "oral drug delivery") AND
("sustained release" OR "controlled release") AND
("nanoparticles" OR "microspheres" OR "bioavailability")
AND NOT (biomedical OR biochemistry OR biophysics OR agri-food OR veterinary),

excluding entries from 2025. This search yielded a final dataset of 437 documents used for the bibliometric synthesis.

Bibliometric analysis tools

VOSviewer (version X.X) and the R package Bibliometrix (version X.X) were used for bibliometric visualization and analysis, applying the following techniques:[13,19]

Co-citation analysis - Identification of influential authors and references in DDS research.

Keyword co-occurrence analysis - Definition of dominant research themes in the dataset.

Analysis of collaboration networks - Mapping of global scientific partnerships and co-authorship trends.

Temporal trends in publications - Tracking the evolution of DDS research topics over time.

Validation and systematic approach

To ensure methodological rigor and reproducibility, this approach followed established bibliometric protocols.[20,21] The following data processing flowchart (Figure 1) illustrates the systematic methodology, from document identification to analysis, providing a structured framework for trend assessment and thematic exploration.

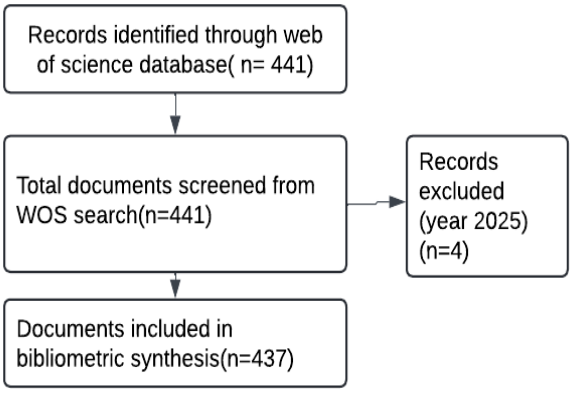

Figure 1: Data Processing Flowchart

This improved methodology enables a comprehensive understanding of advances in DDS research, thus guiding future scientific research and clinical applications.[19,22]

Results and Discussion

Basic statistics

The field of drug delivery systems has witnessed considerable growth and evolution over the years, as reflected in key statistical indicators. The data from 1992 to 2024 encompasses 437 documents aggregated from 161 diverse publications. The annual growth rate stands at an impressive 11.21%, alongside an h-index of 72, highlighting dynamic and rapidly advancing nature of DDS research. On average, documents were cited 45.69 times, indicating high impact scholarship and relevance in this area. The average age of the documents was 7.6 years, showcasing a blend of both recent innovations and foundational studies. Keyword analysis revealed a substantial volume of Keywords Plus (1404) and Author's Keywords (1287), reflecting the diversity and complexity of explored research topics. Furthermore, a total of 2030 authors have contributed to this domain, with only 11 single-authored documents, underscoring the inherently collaborative nature of DDS research. This analysis elucidated the role of international partnerships in propelling advancements in DDS technologies. Beyond the primary objectives, this study elucidated the existing gaps within the current research landscape and suggests pathways for future exploration to advance drug delivery systems (DDS) technologies. By comprehensively analyzing research trends and collaboration dynamics, the study aimed to offer critical insights for researchers, pharmaceutical companies, and healthcare professionals seeking innovative DDS solutions. Table 1 presents a comprehensive overview of the main information, document contents, authors, collaborations, and document types in drug delivery systems (DDS) research from 1992 to 2024.

Intellectual structure

The evaluation of the literature in drug delivery systems (DDS) revealed a substantial upward trajectory in publication volume over time, specifically from 1992 to 2024. The annual growth rate stands at 11.21%. A notable acceleration in this growth occurs post-2010, indicating a surge in innovation and scholarly interest, culminating in a peak publication year of 2021 (Figure 2).

This trend underscores the continued endeavors of researchers to enhance therapeutic efficacy, mitigate adverse effects, and refine delivery mechanisms. Research outputs originated from diverse 161 sources, encompassing journals, monographs, and other publication mediums. The leading journals—such as the International Journal of Biological Macromolecules, International Journal of Pharmaceutics, and Journal of Controlled Release served as critical venues for disseminating groundbreaking research and technological advancements, thereby providing practitioners and researchers access to cutting-edge findings and clinical insights (Figure 3).

Publishing in these esteemed journals reinforces the establishment of research standards and best practices within the domain of DDS. Furthermore, the analysis of authorship revealed pivotal contributors among a total of 17,051 authors. A selected subset of 44 individuals emerged as particularly influential based on publication frequency and citation metrics. Attwood D established a significant corpus on polymers and solid dispersion techniques. Miyazaki S work is recognized in the realms of controlled release systems and nanotechnology, while Kubo W is lauded for his investigations into nanoparticles and targeted delivery systems. Liu Y has also made considerable strides in oral drug delivery systems and the development of polymeric nanoparticles (Figure 4). In conclusion, this in-depth analysis delineates drug delivery systems research progressive evolution and growing significance.

The publication patterns, authorship contributions, and citation dynamics elucidate the research ecosystem and its tangible impact on clinical applications. The innovations emerging from this field possess transformative potential for medical therapies, enhancing patient care and paving the way for personalized medicine approaches

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

Table 1: Summary of Data on Drug Delivery Systems (DDS) Research (1992-2024)

Description	Result
MAIN INFORMATION ABOUT DATA	
Timeline	1992 - 2024
Sources (Journals, Books, etc)	161
Documents	437
Annual Growth Rate %	11,21
h-index	72
Document Average Age	7.6
Average citations per doc	45.69
References	24463
DOCUMENT CONTENTS	
Keywords Plus (ID)	1404
Author's Keywords (DE)	1287
AUTHORS	
Authors	2030
Authors of single-authored docs	11
AUTHORS COLLABORATION	
Single-authored docs	11
Co-Authors per Doc	5,35
International co-authorships %	24,49
DOCUMENT TYPES	
article	323
article; early access	4
article; proceedings paper	2
article; retracted publication	2
proceedings paper	4
review	100
review; book chapter	1
review; early access	1

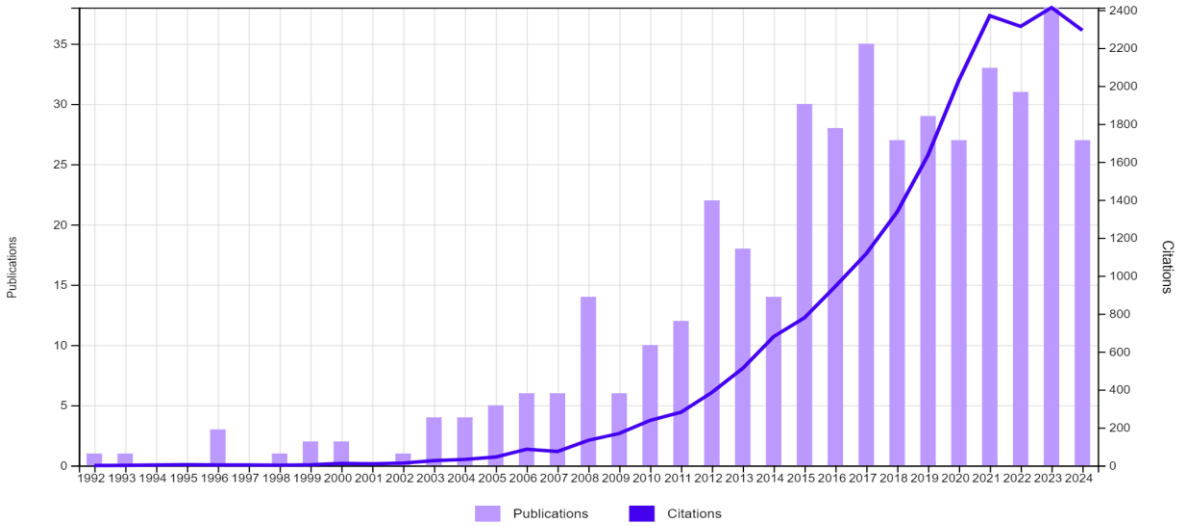

Figure 2: Publication and Citation Trends in Drug Delivery Systems (DDS) Research (1992-2024)

ISSN 2616-0684 (Print)
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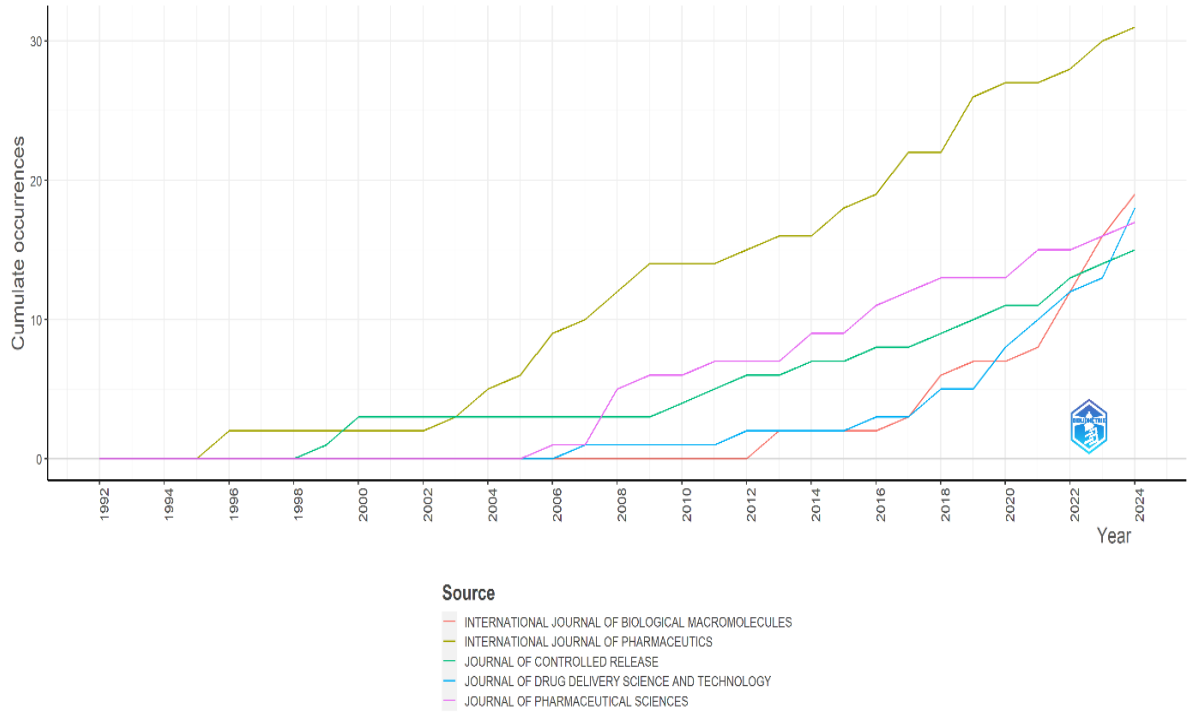

Figure 3: Cumulative Occurrences of Articles from Selected Journals (1992-2024)

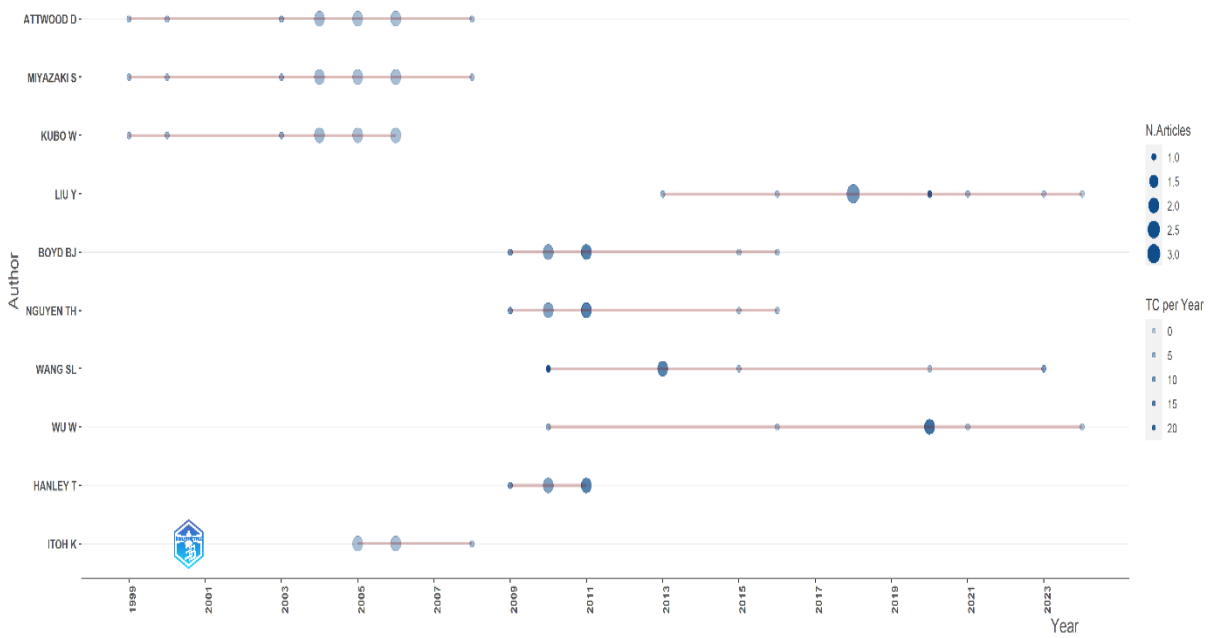

Figure 4: Author Productivity Over Time in Drug Delivery Systems (DDS) Research (1999-2023)

Figure 5 presents a combined bar and line graph illustrating the evolution of publication and citation metrics within the drug delivery systems (DDS) domain from 1992 to 2024. The x-axis delineates the years, while the left y-axis quantifies the annual number of publications (ranging from 0 to 35), and the right y-axis quantifies the citation counts (ranging from 0 to 2400). Publications are represented by light purple bars, with the line graph in dark purple tracking represents total annual citation. This line graph depicts the cumulative tally of published articles from five distinguished journals from 1992 to 2024. The x-axis captures the years, and the y-axis reflects the cumulative occurrence count for each journal, facilitating a comparative analysis of publication output across selected avenues in DDS research. The scatter plot elucidates the publication output of various authors within the DDS field over the span of 1999 to 2023. The x-axis spans the years, while the y-axis delineates individual authors: Attwood D, Miyazaki S, Kubo W, Liu Y, Boyd BJ, Nguyen TH, Wang SL, Wu W, Hanley T, and Itoh K. Each plotted point corresponds to the annual article count per author, where the dot size indicates the number of articles published (N. Articles) and colour intensity reflects total citations (TC per Year).
The correlation of larger and darker dots signifies more published articles and citation metrics.

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

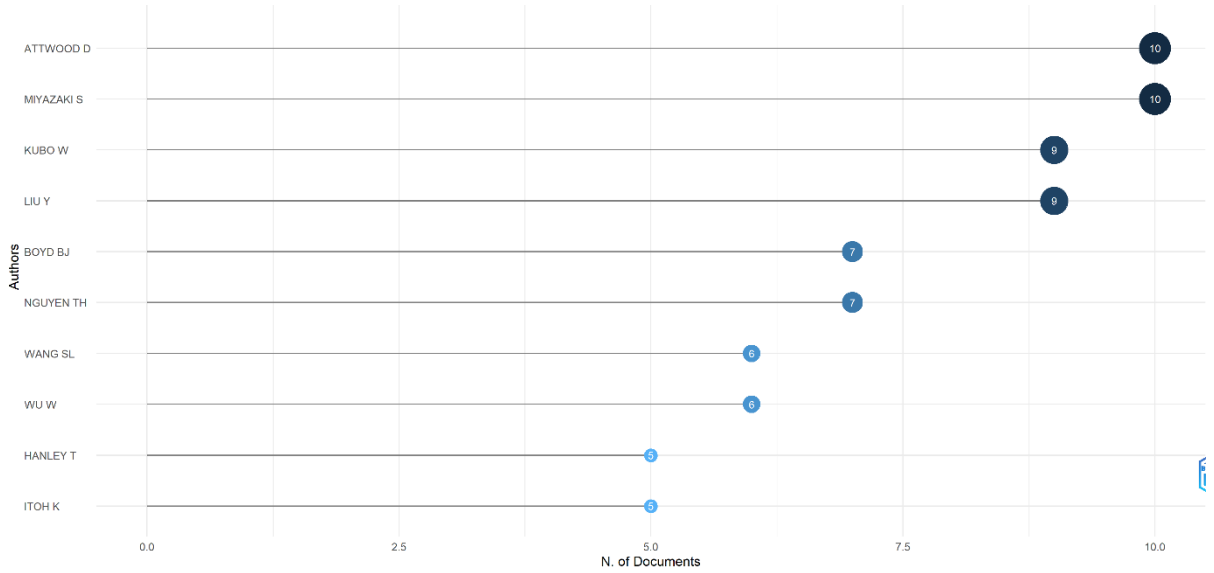

Figure 5: Author Productivity in Drug Delivery Systems (DDS) Research (1999-2023)

The bar chart presented quantitatively delineates the document output of individual contributors within the drug delivery systems (DDS) research domain from 1999 to 2023. The y-axis enumerates authors, while the x-axis depicts their corresponding document counts, thereby elucidating the productivity distribution among the key contributors in the field (Figure 5).

Social structure

Analyzing the social structure of DDS research unveiled the pivotal role of author co-citation and collaborative interactions that catalyze innovation in this discipline. Notable figures such as Attwood D, Miyazaki S, Kubo W, and Liu Y exhibited substantial co-citation frequencies, underscoring their influence on advancing DDS methodologies. Foundational documents that attain high co-citation rates have significantly redefined the research terrain, serving as cornerstones for subsequent studies. Collaboration is integral to this research landscape, with international partnerships constituting 24.49% of all co-authorships, highlighting the inherently global fabric of DDS research. The United States, China, and India emerged as dominant players in these collaborative efforts, fostering an environment conducive to knowledge transfer and resource sharing. Distinct research clusters have been identified, focusing on themes such as polymers and solid dispersions, nanotechnology and targeted delivery, and oral bioavailability. These clusters reflect concentrated scholarly efforts and specialization within particular facets of DDS research. A comprehensive understanding of these dynamics is essential for decision makers and researchers as it pinpoints influential studies and enhances collaboration by identifying active research clusters and key partners. Furthermore, awareness of widely cited works can lead to improved research quality (Figure 6).

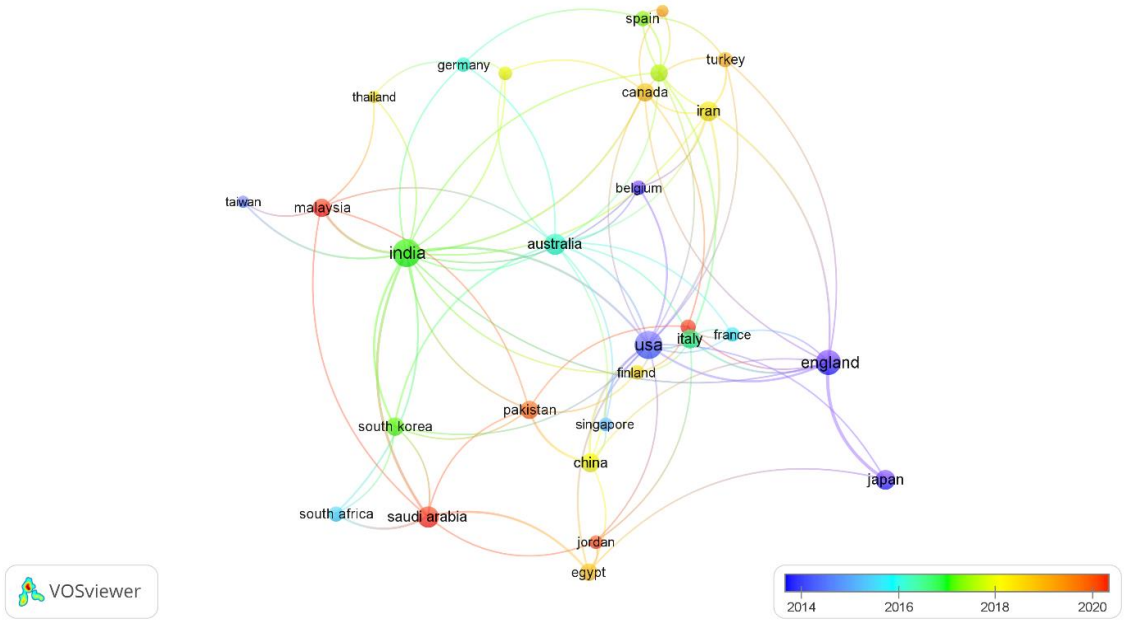

Figure 6: International Collaboration Network in Drug Delivery and Controlled Release Research

Co-citation network analyses revealed intricate interrelationships among authors and their contributions, allowing for a deeper understanding of the collaborative ecosystem. Prominent research strands, such as polymers and solid dispersions associated with Attwood D and Liu Y, as well as nanotechnology and targeted delivery linked to Miyazaki S and Kubo W, are distinctly characterized in these networks. The analysis also showcased the substantial extent of international collaboration, especially among the U.S., China, and India, which is crucial for the advancement of innovative DDS technologies. These collaborative efforts help disseminate knowledge and enable sharing of cutting-edge technologies across borders (Figures 7 and 8). Overall, this intricate overview of the social structure in DDS research accentuated the critical contribution of leading authors, foundational documents, and collaborative strategies, which are pivotal in propelling the field forward and ultimately guiding future research and clinical applications. This figure encapsulates the comprehensive data on drug delivery systems (DDS) research amassed from 1992 to 2024, highlighting key parameters such as document types, authorship patterns, and collaboration networks. This visualization employs VOSviewer to illustrate the citation dynamics of scholarly articles in the realms of drug delivery and controlled release.

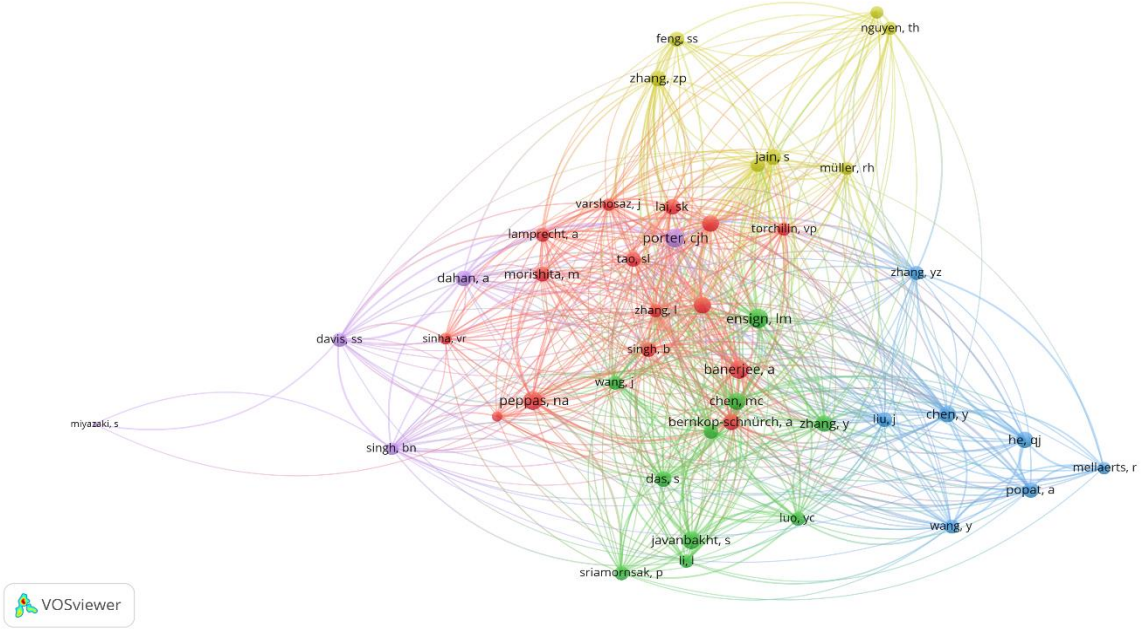

Figure 7: Main Information about Drug Delivery Systems (DDS) Research Data (1992-2024)

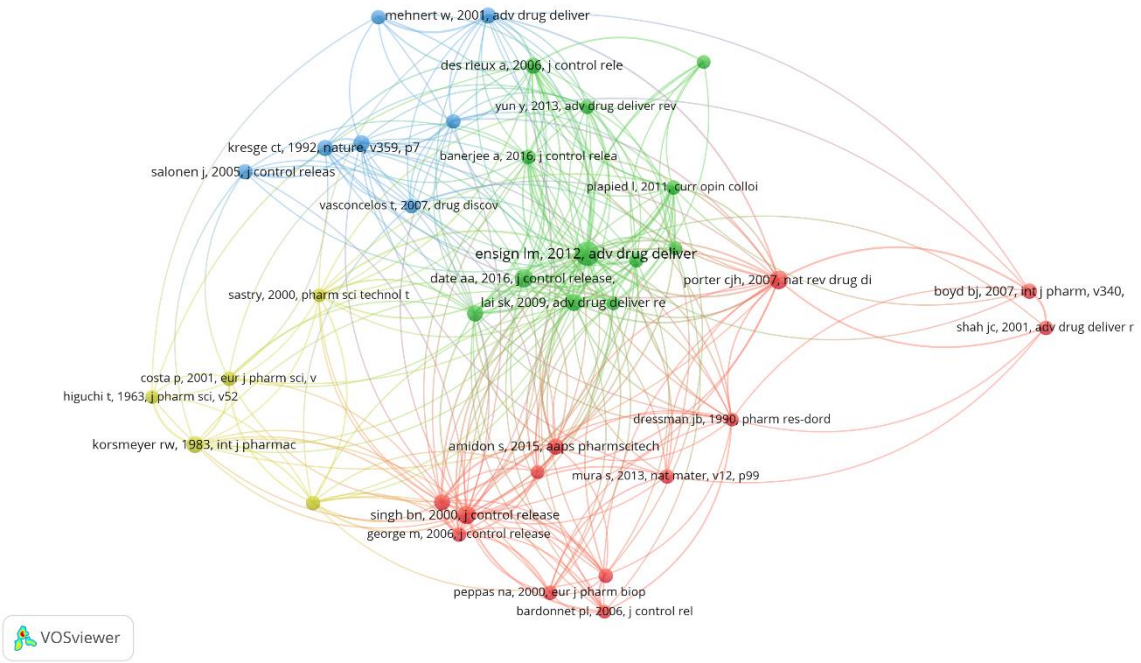

Figure 8: Citation Network in Drug Delivery and Controlled Release Research

Each node denotes an individual paper, while the edges represent citation links between them. The colour-coding of nodes denotes clusters based on citation relationships, indicating groups of papers with frequent cross-citations. The size of the nodes correlates with the citation volume each paper has accumulated, and the edge thickness indicates the intensity of citation connections. The use of VOSviewer portrayed the international collaboration landscape in drug delivery and controlled release research. Each node signifies a country, with lines illustrating collaborative partnerships. The colour gradient, reflecting a timeline from 2014 to 2020, indicates evolving collaboration trends. Node size varies proportionately to the number of connections, indicating countries of greater significance within the network.

Conceptual structure

Analysis through keyword co-occurrence clustering revealed predominant research themes and focus areas (Figure 9a):

1. Nanoparticle Cluster: Keywords such as "nanoparticles," "nanotechnology," and "nanocapsules" characterized this cluster, which centers on the development of nanoparticle-based delivery systems that enhance drug targeting and controlled release. Nanoparticles are engineered to improve solubility, stability, and bioavailability, positioning them as critical assets across a spectrum of therapeutic applications.

2. Polymer Cluster: This cluster is defined by keywords such as "polymers," "PLGA," and "hydrogels." Research efforts concentrated on employing polymeric materials to formulate sustained-release mechanisms and enhance drug stability. Polymers like PLGA and hydrogels are favoured for their biocompatibility and efficacy in controlled-release formulations.

3. Bioavailability Cluster: Focusing on terms such as "oral bioavailability," "dispersions," and "solubility," this cluster targets the enhancement of drug solubility and absorption in oral administration contexts. Techniques like solid dispersions and emulsions are pivotal for improving the oral bioavailability of poorly soluble compounds and optimizing therapeutic effectiveness.

4. Targeted Delivery Cluster: This cluster includes keywords such as "targeted delivery," "controlled release," and "site-specific delivery." The research here is dedicated to engineering systems that facilitate precise drug delivery to the site of action, thereby amplifying therapeutic efficacy while minimizing adverse effects. These targeted delivery systems are designed to mitigate drug exposure to non-target tissues, enhancing overall treatment outcomes.

The investigation of topic trends and keyword clusters within drug delivery systems (DDS) research revealed insights into the progression of scientific inquiry. By analyzing keyword frequency and co-occurrence across different time frames, dominant research trajectories, emerging paradigms, and shifts in investigative focus within the field can be discerned (Figure 9a).

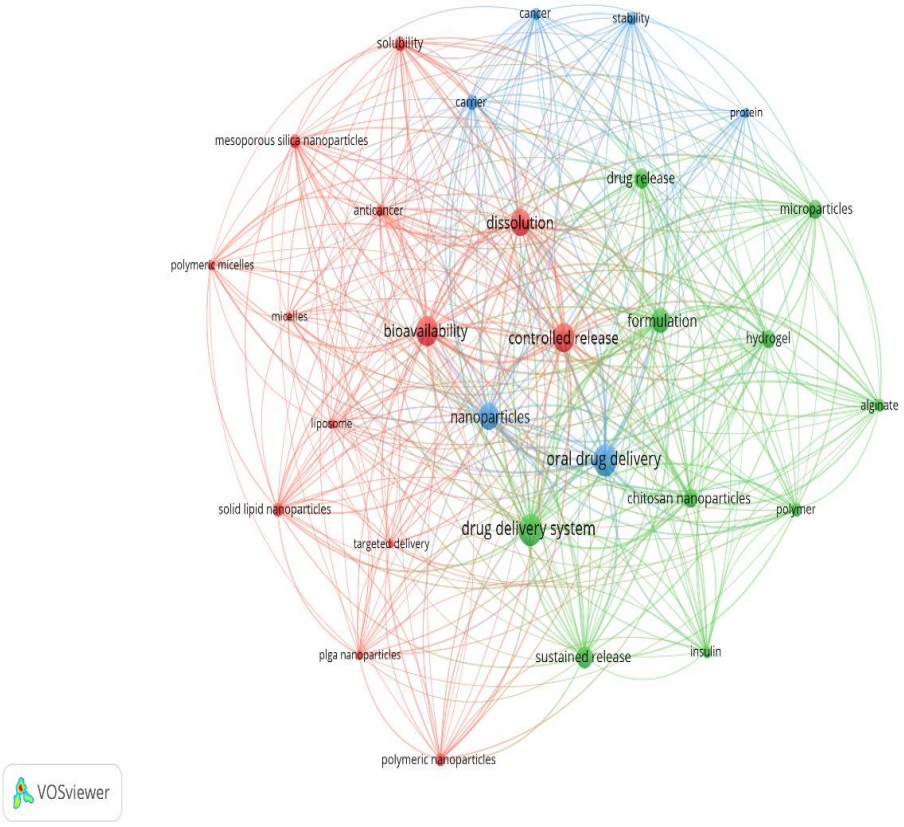

Figure 9a: Trends in Research Topics in Drug Delivery Systems (DDS) and Nanotechnology (1995-2025)

1990s-2000s: Initial Endeavors in Polymer-Based Controlled Release Systems

During the 1990s and early 2000s, the Drug Delivery Systems (DDS) domain was primarily centered around polymeric materials and controlled release mechanisms.[1] Key terminologies of this era included "polymers," "encapsulation," and "controlled release".[23,24] The primary objective was to engineer materials capable of sustaining drug release over prolonged durations, thereby enhancing patient compliance and optimizing therapeutic outcomes.[1,15] Techniques such as encapsulation, utilizing biodegradable polymers like PLGA (polylactic-co-glycolic acid), were pivotal in advancing the field, facilitating the development of systems that could modulate drug release kinetics effectively.[23,25]

2000s-2010s: Emergence and Advancement of Nanotechnology

The early 2000s heralded a transformative phase in DDS research, characterized by the integration of nanotechnology. Terminologies such as "nanoparticles," "nanotechnology," and "nanocapsules" gained traction in scholarly discourse. This period witnessed substantial

advancements in the design and implementation of nanoscale drug delivery systems, which offered remarkable precision in targeting specific cellular and tissue environments. The incorporation of nanoparticles not only improved drug solubility and stability but also enhanced bioavailability, rendering them highly suitable for diverse therapeutic applications. Consequently, this shift towards nanotechnology facilitated significant innovations in targeted delivery frameworks and controlled release mechanisms.[23,25]

2010s-2020s: Advancement of Smart Delivery Systems and Enhancement of Oral Bioavailability

In the past decade, research in DDS has progressed towards developing smart delivery systems and augmenting oral bioavailability.[26]

Terms such as "smart delivery," "bioavailability," and "dispersions" have become increasingly prominent in the literature. A critical focus has emerged on engineering intelligent delivery systems that respond to specific physiological stimuli, including pH-sensitive and temperature-responsive mechanisms. Concurrently, enhancing the oral bioavailability of poorly soluble pharmacological compounds has gained attention, driving the exploration of innovative formulation techniques such as solid dispersions, emulsions, and lipid-based delivery systems. This evolution illustrates a concerted effort to optimize drug delivery while addressing inherent solubility challenges associated with specific therapeutic agents.[15,25]

2020s-2024: Innovations in Personalized Medicine and Smart Nanocomposites in Drug Delivery Systems.

In recent years, significant progress has been made in personalized medicine and the application of smart nanocomposites within drug delivery systems (DDS). Concepts such as "personalized treatment," "smart nanocomposites," and "targeted delivery" have emerged as focal points in contemporary research. The objective is to engineer drug delivery platforms that are precisely tailored to individual patients' unique genetic, environmental, and lifestyle profiles. Smart nanocomposites, which integrate multiple functionalities, encompassing targeting, imaging, and therapeutic action are at the forefront of DDS innovation.[26] These advancements are designed to enhance the efficacy and safety profiles of drug delivery mechanisms. The trends identified in the present investigations aligned closely with existing literature, reflecting a unified and comprehensive understanding of the field's trajectory. Key studies provided a robust overview of the implications and significance of these trends in the evolution of DDS.

Elevated Significance of Nanotechnology and Polymers

Smith (2024)[27] emphasized the rising influence of nanotechnology and polymer-based systems in DDS. Their review delineates the transformative potential of nanoparticles for achieving precise targeting and controlled drug release.[26] They noted that nanoparticles' superior solubility, stability, and bioavailability position them as optimal candidates for various therapeutic interventions. The integration of biodegradable polymers, such as poly(lactic-co-glycolic acid) (PLGA), has been crucial in developing sustained-release formulations. These materials do not only enhance drug stability but also facilitate meticulous control over release kinetics, ultimately reducing dosing frequency and improving patient adherence to therapeutic regimens.[28]

2020s-2024: Advancements in Personalized Medicine and Smart Nanocomposites

In recent years, there has been a growing emphasis on personalized medicine and the use of smart nanocomposites in DDS. Keywords related to "personalized treatment," "smart nanocomposites," and "targeted delivery" have emerged as trending topics. The goal is to develop delivery systems tailored to individual patient needs, considering genetic, environmental, and lifestyle factors. Smart nanocomposites, which combine multiple functionalities such as targeting, imaging, and therapy, represent the cutting edge of DDS research. These advancements aim further to enhance the efficacy and safety of drug delivery.[29]

The trends observed in the present analyses aligned closely with the findings reported in the existing literature, indicating a coherent and consistent understanding of evolution in the field. Several key studies provided a comprehensive overview of the significance and impact of these trends on the advancement of drug delivery systems (DDS).[30]

Growing Importance of Nanotechnology and Polymers

Smith (2024)[27] highlighted the increasing prominence of nanotechnology and polymer-based systems in DDS. Their review underscores the transformative potential of nanoparticles in achieving targeted and controlled drug delivery. They pointed out that nanoparticles-enhanced solubility, stability, and bioavailability make them ideal candidates for various therapeutic applications.[31] The integration of polymers, particularly biodegradable ones like PLGA, has been pivotal in developing sustained release formulations.[27] These materials improve drug stability and allow for precise control over the release kinetics, reducing dosing frequency and improving patient compliance.[31] The present analysis indicates a marked escalation in the prevalence of terms such as "nanoparticles," "nanotechnology," and "polymers" over the past two decades, corroborating the insights presented by Smith.[27]

Advancements in Intelligent Delivery Systems

According to Kim *et al*. (2019),[32] significant progress has been made in the realm of intelligent drug delivery systems (DDS).[30] Their research highlights an increasing focus on smart delivery mechanisms capable of responding to specific physiological triggers, including pH variations, temperature fluctuations, or enzymatic activities. These systems are designed to enhance therapeutic efficacy by enabling localized and timely drug release. The rising prominence of keywords like "smart delivery," "controlled release," and "site-specific delivery" in recent literature reflects a robust interest in refining DDS technologies.[31] In addition, Kim *et al*.[32] have emphasized methodologies aimed at improving oral bioavailability, particularly for therapeutics exhibiting poor solubility. The present analysis corroborates this shift, revealing an uptick in the focus on terms such as "oral bioavailability," "dispersions," and "solubility," highlighting the critical nature of these advancements.[29]

Emerging Trends in Personalized Medicine

The transition towards personalized medicine represents another pivotal trend documented in the literature. Research conducted by Choudhary *et al*., (2021)[33] illustrated that personalized drug delivery systems are increasingly tailored to meet individual patient profiles, factoring in genetic, environmental, and lifestyle variables.[30] This approach aspires to optimize therapeutic outcomes while mitigating adverse effects. The recent emergence of terms such as "personalized treatment" and "smart nanocomposites" underscores the sector's movement towards individualized and patient-centric DDS solutions.[31] The present analysis aligns with these observations, showcasing a heightened emphasis on keywords pertinent to personalized medicine, suggesting that this domain is poised for considerable evolution in the near future.[30]

Clinical and Practical Implications

The trends identified in the present analysis, which aligned with existing literature, carry significant clinical and practical ramifications. The emergence of advanced drug delivery system (DDS) technologies, particularly those utilizing nanoparticle-based platforms and smart delivery mechanisms, presents the opportunity to transform pharmacotherapy. These innovations can enhance therapeutic efficacy, mitigate adverse effects, and bolster patient adherence to treatment regimens.

For researchers, a comprehensive understanding of these trends is essential for directing future investigations and promoting innovation within the realm of DDS technologies. Pharmaceutical enterprises can utilize these insights to inform the design and development of novel products that effectively tackle contemporary drug delivery challenges. Clinicians stand to benefit from integrating the latest advancements into treatment protocols, thereby enhancing clinical outcomes, especially in the context of personalized medicine.[22,31]

In conclusion, findings from the present study underscore the evolving research themes in DDS, reflecting a sustained focus on nanotechnology, intelligent delivery systems, and personalized

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

treatment strategies. This dynamic evolution do not only signifies potential advancements in medical therapies and patient care but also equips stakeholders with crucial guidance for future research endeavours, product development, and clinical application. Ultimately, these insights are pivotal for the continuous enhancement of drug delivery technologies and therapeutic efficacy.

Figure 9b illustrates twelve-line graphs, each representing the longitudinal trends of distinct scientific terms or technologies from 1995 to 2025. The y-axis denotes the "Count," while the x-axis represents "Year." Figure 9c presents a network visualization crafted using VOSviewer, illustrating the interconnectivity of numerous terms pertinent to drug delivery systems. Each node signifies a distinct term, while the edges between them denote their relationships. The nodes are categorized into colour-coded clusters that reflect groups of related concepts.[22] For instance, terms such as "bioavailability," "controlled release," and "dissolution" are aggregated in a red cluster, whereas "oral drug delivery," "drug delivery system," and "sustained release" form a green cluster. Other clusters identified include "cancer," "stability," and "drug release" in blue, and "microparticles," "hydrogel," and "polymer" in green.

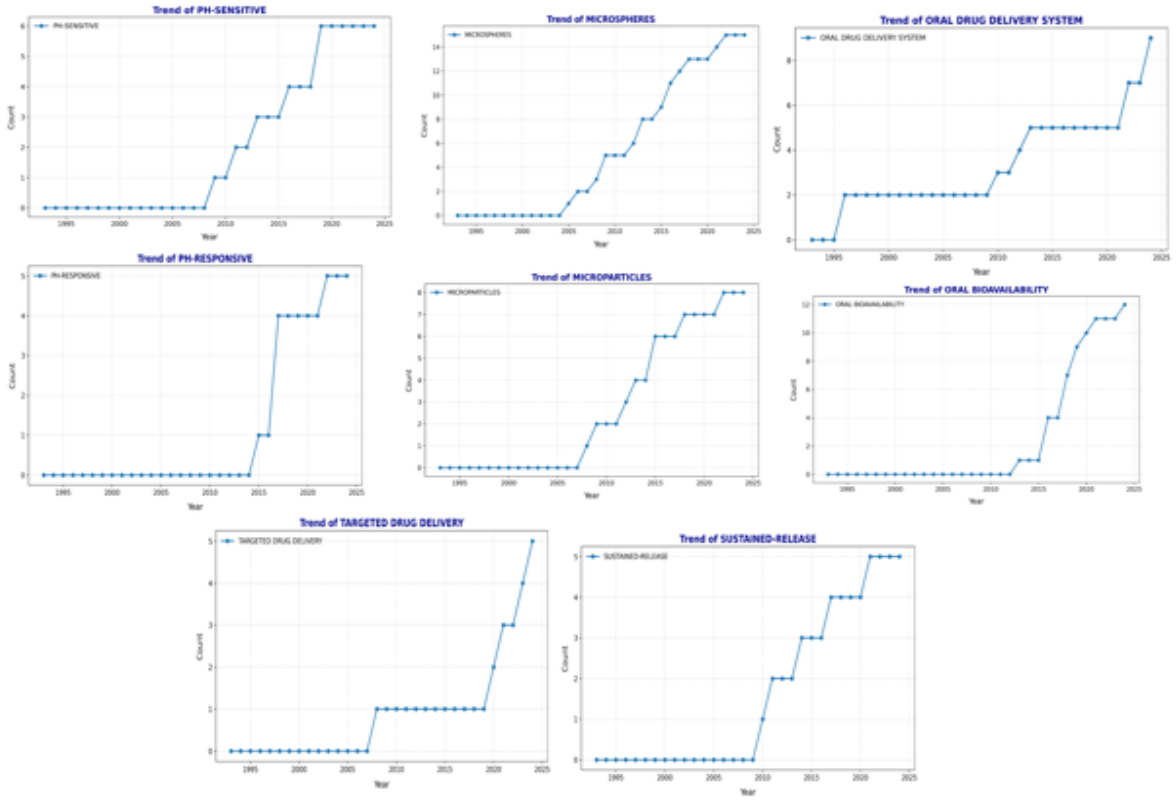

Figure 9b: Trends in Research Topics in Drug Delivery Systems (DDS) and Nanotechnology (1995-2025)

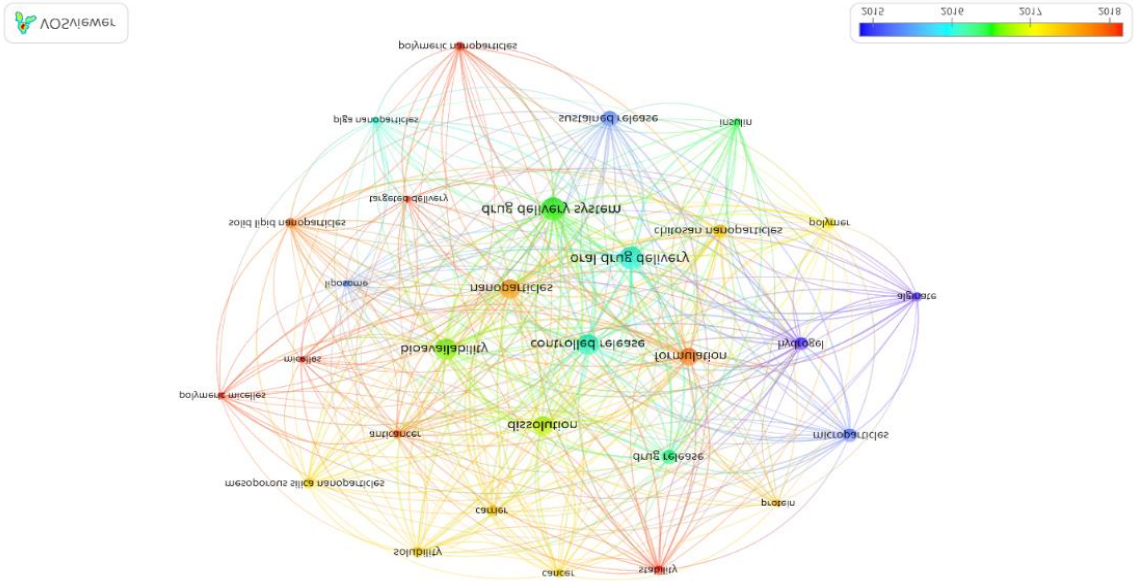

Figure 9c: Trends in Drug Delivery Systems (DDS) and Related Terms (1995-2025)

Future Directions and Identified Gaps in Drug Delivery Systems Evolution

The evolution of drug delivery systems (DDS) has been marked by significant advancements and breakthroughs over the past few decades. However, as the field continues to progress, it is essential to identify future directions that can further enhance DDS technologies and address the existing gaps that may hinder their clinical translation and widespread adoption. By exploring these future directions and acknowledging the identified gaps, researchers, pharmaceutical companies, and healthcare practitioners can focus their efforts on developing innovative solutions that improve therapeutic outcomes and patient care. The future of DDS research holds immense potential for advancing medical treatments through the development of cutting-edge technologies. Key areas of focus include advanced nanotechnology applications, personalized medicine, smart drug delivery systems, enhanced oral bioavailability, and the use of biodegradable and biocompatible materials. These future directions aim to address current limitations and offer more effective, targeted, and patient-specific drug delivery solutions.

1. Advanced Nanotechnology Applications: The integration of nanotechnology will remain pivotal in the evolution of drug delivery systems (DDS). Investigations into novel nanoparticle types, such as quantum dots and dendrimers, are at the forefront, offering exceptional properties for targeted delivery and imaging. The development of multifunctional nanoparticles that facilitate integrated therapeutic and diagnostic capabilities (theranostics) represents a promising trajectory, potentially yielding enhanced treatment modalities for cancers, neurodegenerative disorders, and multifaceted medical conditions.[28,34]

2. Personalized Medicine: The momentum toward personalized medicine is set to intensify, focusing on devising drug delivery systems illustrates the interconnections among various terms associated with drug delivery systems in the scientific literature. Each node corresponds to a distinct term, while the edges depict the co-occurrence and relationships between these terms.[29,35] Node size reflects term frequency, and a colour gradient indicates publication year, ranging from blue (2015) to red (2018). Prominent terms in this visualization include "dissolution," "bioavailability," "controlled release," "oral drug delivery," and "drug delivery system".[36] These terms connect to a range of related concepts, such as "nanoparticles," "polymeric nanoparticles," "micelles," "liposomes," "hydrogels," and "sustained release," highlighting their relevance and interrelations within drug delivery and pharmaceutical research. The visualization captures key concepts and their evolving relationships in the DDS field, emphasizing emerging trends and focal areas in recent studies.[14,37]

Identified Gaps

Despite the progress made, several gaps remain in the field of DDS that need to be addressed to ensure the successful translation of research findings into clinical practice. These gaps include limited clinical translation of promising technologies, a need for a deeper understanding of the mechanisms of action, challenges in addressing drug resistance, high costs and accessibility issues, and a lack of long-term safety and efficacy data. By identifying and addressing these gaps, the research community can work towards overcoming the barriers that hinder the full potential of DDS technologies.

1. Limited Clinical Translation: Despite notable advancements in DDS research, a significant divide remains between laboratory findings and clinical implementation. Promising technologies often stall at preclinical stages due to scalability, regulatory approval, and manufacturing challenges. To bridge this gap, enhanced standardized protocols, robust regulatory frameworks, and collaborative efforts between academia and industry are essential for translating research into viable clinical applications.

2. Understanding Mechanisms of Action: A comprehensive understanding of various DDS mechanisms is still lacking. Further investigations are needed into how different delivery systems interact with biological tissues, their biodistribution, and chronic effects. Comprehensive pharmacokinetic and pharmacodynamic studies are crucial for optimizing DDS design and ensuring both safety and efficacy.

attuned to the unique requirements of individual patients. This entails leveraging genetic and biomarker data to engineer tailored drug delivery strategies. Personalized DDS can optimize clinical outcomes by addressing interindividual variability in pharmacokinetics, therapeutic response, and adverse effects. Additionally, researchers are delving into 3D printing technologies to manufacture patient-specific drug delivery devices and implants.[29,34,35]

3. Smart Drug Delivery Systems: The advent of smart drug delivery systems that are responsive to specific physiological parameters, such as pH, temperature, or enzymatic activity marks a significant advancement. These systems offer controlled drug release mechanisms that enhance effectiveness while minimizing adverse effects. Innovations in stimuli-responsive materials and nanorobotics are laying the groundwork for sophisticated next-generation DDS capable of executing complex functions within the body.[28,34]

4. Oral Bioavailability Enhancement: Enhancing the oral bioavailability of poorly soluble pharmaceuticals remains a formidable challenge. Future investigations will prioritize novel formulation strategies, including self-emulsifying drug delivery systems (SEDDS) and nanocrystal formulations. Such approaches aim to improve drug solubility and absorption, thus facilitating more effective and convenient oral administration.[28,35]

5. Biodegradable and Biocompatible Materials: Research into biodegradable and biocompatible materials for DDS is progressing actively. Future efforts will focus on exploring innovative materials that provide superior safety profiles and reduce adverse reactions. The development and application of natural polymers such as chitosan and alginate, alongside their derivatives, are expected to gain prominence due to their biocompatibility and versatility across various drug delivery contexts.[14,28] This network visualization, generated with VOSviewer,

3. Addressing Drug Resistance: Drug resistance presents a significant obstacle, particularly in oncology and infectious disease treatments. Future research must prioritize the development of DDS that effectively navigate resistance mechanisms, such as efflux pumps and drug-degrading enzymes. This effort may include exploring combination therapies and the co-delivery of multiple agents to enhance therapeutic efficacy.

4. Cost and Accessibility: The high cost associated with advanced DDS technologies often hinder patient access, especially in low- and middle-income countries. To improve affordability and access, it is imperative to focus on developing cost-effective delivery systems and scalable manufacturing techniques. Partnerships with global health organizations can be instrumental in ensuring that innovative treatments reach underserved populations.

5. Long-Term Safety and Efficacy: New DDS technologies frequently lack robust long-term safety and efficacy data. Comprehensive long-term studies and post-marketing surveillance are required to assess these systems' sustained performance.[22] Understanding potential risks and adverse effects is critical for ensuring patient safety and facilitating regulatory approval. Addressing existing gaps and exploring future avenues is crucial for advancing drug delivery systems (DDS) and realizing their full potential in clinical settings. Researchers can devise innovative solutions that improve patient care and therapeutic efficacy by prioritizing personalized medicine, intelligent delivery systems, and enhancing bioavailability. Effectively overcoming the hurdles associated with clinical translation, elucidating mechanisms of action, and ensuring the development of cost-effective and safe DDS will facilitate the emergence of next-generation drug delivery technologies.[22,37]

Conclusion

This comprehensive bibliometric analysis provided valuable insights into the evolution of drug delivery systems (DDS) over the past 32 years (1992–2024). By reviewing 437 documents from 161 separate publications, we mapped the intellectual structure, identified key contributors, and analyzed global collaboration patterns within this dynamic field. These findings provide essential guidance for researchers, pharmaceutical companies, and healthcare professionals seeking to advance DDS technologies. Understanding the evolution of research themes and interdisciplinary partnerships allows stakeholders

to drive innovation, refine drug formulation techniques, and improve patient outcomes. Moving forward, the future of DDS research will be shaped by emerging trends, such as Advanced nanotechnology applications → Enabling highly precise targeted therapies; Personalized Drug Delivery → Harnessing AI-driven personalization based on genetic profiling. Intelligent DDS Mechanisms → Integrating stimuli-responsive and theranostic features. Biodegradable and Biocompatible Systems → Optimizing drug safety and efficacy. Improving Clinical Translation → Bridging the gap between laboratory advances and real-world applications. As DDS research continues to evolve, addressing key gaps and refining next-generation delivery strategies will be critical to maximizing therapeutic impact and driving global healthcare innovation. This study provides a comprehensive reference, guiding future research, pharmaceutical developments, and clinical applications in the field of DDS.

Conflict of interest

The author declares no conflicts of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

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