








RESEARCH ARTICLE

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Pluronic F-127 Hydrogel for Delivering Antimicrobial Agents: A Bibliometric Analysis using Scopus Database

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Abstract

Infectious diseases caused by pathogenic microorganisms pose significant threats to public health globally. The emergence of antibiotic-resistant bacteria has further complicated the treatment of these infections, necessitating the exploration of alternative therapeutic strategies. Among these strategies, the use of hydrogels as delivery systems for delivering antimicrobial agents has gained considerable attention. This paper presents a comprehensive bibliometric analysis of the utilization of Pluronic F-127 (PF-127) hydrogel for delivering antimicrobial agents. The aim of this study is to explore the current research landscape, identify key trends, influential authors, and prominent journals in this field. The analysis is based on a systematic search conducted using the Scopus database. The analysis covered publication trends, geographic distribution, influential authors, and key journals in the field of PF-127 hydrogel-based antimicrobial agent delivery. The results revealed the growing interest in this field, with a focus on countries such as India, the United States, and Egypt. The analysis also identified top authors, institutions, and journals contributing to the research. The findings reveal the growth of research in this area, highlighting the potential of PF-127 hydrogel as a promising vehicle for antimicrobial agent delivery. It highlights the need for further research to optimize formulation parameters, explore combination therapies, conduct in vivo studies, and promote collaboration to maximize the therapeutic potential of PF-127 hydrogel-based delivery systems in combating infectious diseases and antimicrobial resistance. This paper provides valuable insights into the existing literature and serves as a reference for future research and development in the field.

Keywords: Poloxamer 407, Research Trends, PF-127, Scopus Database, Thermoresponsive Hydrogel, Antimicrobial Agent, Antibacterial Activity

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Citation: Sharun K, Banu SA, Nair SS, et al. Pluronic F-127 Hydrogel for Delivering Antimicrobial Agents: A Bibliometric Analysis using Scopus Database. *J Pure Appl Microbiol.* 2023;17(3):1516-1531. doi: 10.22207/JPAM.17.3.14

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INTRODUCTION

Infectious diseases caused by pathogenic microorganisms pose significant threats to public health globally. The use of antimicrobial agents is essential in addressing the challenges posed by infectious diseases and antimicrobial resistance.¹ However, the effectiveness of these agents is often limited by factors such as poor bioavailability, rapid clearance, and the emergence of resistant strains. The emergence of antibiotic-resistant bacteria has further complicated the treatment of these infections, necessitating the exploration of alternative therapeutic strategies. Among these strategies, the use of hydrogels as delivery systems for antimicrobial agents has gained considerable attention.² Hydrogels offer a three-dimensional (3D) network capable of encapsulating and releasing drugs in a controlled and sustained manner.² Pluronic F-127 (PF-127) hydrogel, in particular, has emerged as a promising candidate due to its unique properties and potential to combat microbial infections.³

PF-127 hydrogel has emerged as a promising vehicle for delivering antimicrobial agents in various biomedical applications. It is a block copolymer composed of poly(ethylene oxide) (PEO) and poly(propylene oxide) (PPO) segments.⁴ This amphiphilic nature of PF-127 enables it to self-assemble into micelles at low temperatures and undergo sol-gel transition at physiological temperatures.⁵ This transition behavior has been extensively exploited in drug delivery applications, as it allows for convenient gelation at room temperature, facilitating ease of administration. The unique properties of PF-127, including its thermosensitivity, biocompatibility, and ability to sol-gel transition, make it an attractive choice for controlled and sustained release of antimicrobial agents.^{6,7} This hydrogel system offers several advantages, such as localized drug delivery, prolonged drug release, and the ability to create an optimal environment for wound healing while combating infections.⁸ PF-127 hydrogel lacks intrinsic antimicrobial activity against *Staphylococcus aureus* and *Escherichia coli*, but its antiadhesive properties and biocompatibility make it a promising neutral carrier system for antibiotics and antimicrobial compounds in biomedical applications.⁷ Its antiadhesive properties indirectly

contribute to preventing microbial infections by inhibiting bacterial adhesion. PF-127 hydrogel reduces the likelihood of bacterial colonization and subsequent infection.⁹

PF-127 hydrogel provides a promising solution by encapsulating and releasing antimicrobial agents in a controlled manner, thereby maximizing their therapeutic potential.⁴ Understanding the interplay between the hydrogel and the loaded agents is crucial for optimizing the therapeutic efficacy and ensuring controlled release profiles.¹⁰ A deeper understanding of the release mechanisms will aid in the design and development of hydrogel-based delivery systems with tailored release profiles for specific.¹¹

This paper aims to provide a comprehensive overview of the current state of research on PF-127 hydrogel for delivering antimicrobial agents. It encompasses a bibliometric analysis using the Scopus database to explore publication trends, geographic distribution, influential authors, and key journals in this field. Understanding the literature landscape and the advancements made in PF-127 hydrogel-based antimicrobial agent delivery will enable researchers to identify knowledge gaps, potential areas for further investigation, and emerging trends in the field. Moreover, this analysis will facilitate collaboration and knowledge sharing among researchers, leading to accelerated advancements and the development of more effective strategies for antimicrobial agent delivery. The present study explores the current research landscape, identify key trends, influential authors, and prominent journals associated with evaluating the potential of PF-127 as a carrier of antimicrobial agents.

MATERIALS AND METHODS

Search strategy and data collection

The literature search was performed on May 23, 2023, using the Scopus database. The search strategy aimed to collect data on journal articles published until 2022 while excluding certain publication types such as reviews, editorials, conference papers, book chapters, books, letters, notes, short surveys, erratum, reports, and retracted papers. Only articles published in English were considered, excluding publications in other languages. The following

search query was employed:

TITLE-ABS-KEY ((poloxamer 407 OR "Pluronic F-127" OR pf-127 OR pluronic-f-127 OR "Pluronic™ F-127" OR "Plutonic F127" OR pf127 OR "Pluronic® F-127" OR "Pluronic® F127") AND (antibiotic* OR antimicrobial* OR antifungal* OR antiviral* OR anti-biofilm)) AND (LIMIT-TO (DOCTYPE, "ar")) AND (LIMIT-TO (LANGUAGE, "English")) AND (LIMIT-TO (SRCTYPE, "j")) AND (EXCLUDE (PUBYEAR, 2023))

By employing the above search strategy, a focused and comprehensive dataset of journal articles related to Pluronic F-127 hydrogel for delivering antimicrobial agents was obtained, adhering to the specified criteria for publication type, language, and publication year. This search query focuses on articles that mention the specific term "Pluronic F-127" and its modifications in conjunction with different keywords corresponding to different antimicrobial agents. The use of the operator "OR" broadens the search to include different variants of PF-127 and antimicrobial agents.

Analysis of variables and visualization

The metadata was analyzed using R Studio and the bibliometrix package, which is a powerful open-source tool specifically designed for conducting comprehensive science mapping analysis within the R statistical programming language.¹² The extracted data was further analyzed and interpretation was done under the following titles: overview of publication trends, geographic distribution of research, most cited articles, analysis of keywords, identification of top authors and institutes, identification of influential journals, and evaluation of collaboration networks. In addition, the data was visualized using network visualization software VOSviewer (version 1.6.17).¹³

RESULTS AND DISCUSSION

Scopus offers a vast collection of scholarly literature, including journals, conference papers, patents, and book series, from various disciplines. It covers a wide range of subject areas, making it suitable for multidisciplinary research.¹⁴ Web of Science might have limited coverage of literature, particularly in some emerging or specialized

Table 1. Basic characteristics of the analyzed data on Pluronic F-127 hydrogel research for delivering antimicrobial agents

Description	Results
Main information	
Timespan	1981:2022
Sources (Journals, Books, etc.)	161
Documents	325
Annual growth rate %	10.01
Document average age	6.31
Average citations per doc	23.02
References	13643
Document contents	
Keywords Plus (ID)	3354
Author's keywords (DE)	1023
Authors	
Authors	1678
Authors of single-authored docs	4
Authors collaboration	
Single-authored docs	4
Co-authors per doc	5.96
International co-authorships %	20
Document types	
Article	325

fields. However, this can be due to the fact that Web of Science maintains strict inclusion criteria, ensuring the quality and reliability of the indexed publications.¹⁵ This database is renowned for its rigorous selection process, which minimizes the risk of including low-quality or predatory journals in the analysis.^{14,15} It is important to note that both Scopus and Web of Science have their strengths and weaknesses when it comes to bibliometric analysis. Researchers should consider their specific research needs, disciplinary focus, and intended analysis goals while selecting the most appropriate database for their bibliometric studies.

Overview of Publication Trends

This paper provides a comprehensive overview of research on PF-127 hydrogel for delivering antimicrobial agents, covering a period from 1981 to 2022 (Table 1). The analysis is based on 161 sources (journals) resulting in a total of 325 documents. The field has shown an annual growth rate of 10.01%. The average age of the documents is 6.31 years, while the average number of citations per document is 23.02. The collected data includes a total of 13,643 references. The document contents consist of 3,354 keywords Plus

Table 2. Characteristics of the top ten most cited papers in Pluronic F-127 hydrogel research for delivering antimicrobial agents

No. Paper	Total Citations	TC per Year	Normalized TC
1. Kelly HM, Deasy PB, Ziaka E, et al. Formulation and preliminary in vivo dog studies of a novel drug delivery system for the treatment of periodontitis. <i>Int J Pharm.</i> 2004;274(1-2):167-83. doi: 10.1016/j.ijpharm.2004.01.019.	184	9.20	1.47
2. Veyries ML, Couarraze G, Geiger S, et al. Controlled release of vancomycin from poloxamer 407 gels. <i>Int J Pharm.</i> 1999;192(2):183-93. doi: 10.1016/s0378-5173(99)00307-5	162	6.48	1.00
3. Ding A, Nagarsenker M. Formulation and evaluation of fast dissolving films for delivery of triclosan to the oral cavity. <i>AAPS PharmSciTech.</i> 2008;9(2):349-56. doi: 10.1208/s12249-008-9047-9047	156	9.75	1.75
4. Chang JY, Oh YK, Kong HS, et al. Prolonged antifungal effects of clotrimazole-containing mucoadhesive thermosensitive gels on vaginitis. <i>J Control Release.</i> 2002 Jul 18;82(1):39-50. doi: 10.1016/s0168-3659(02)00086-x	149	6.77	1.51
5. Bilensoy E, Rouf MA, Vural I, et al. Mucoadhesive, thermosensitive, prolonged-release vaginal gel for clotrimazole:beta-cyclodextrin complex. <i>AAPS PharmSciTech.</i> 2006;7(2):E38. doi: 10.1208/pt070238	130	7.22	1.24
6. Liu Y, Zhu YY, Wei G, et al. Effect of carrageenan on poloxamer-based in situ gel for vaginal use: Improved in vitro and in vivo sustained-release properties. <i>Eur J Pharm Sci.</i> 2009;37(3-4):306-12. doi: 10.1016/j.ejps.2009.02.022	125	8.33	2.51
7. Mou D, Chen H, Wan J, et al. Potent dried drug nanosuspensions for oral bioavailability enhancement of poorly soluble drugs with pH-dependent solubility. <i>Int J Pharm.</i> 2011;413(1-2):237-44. doi: 10.1016/j.ijpharm.2011.04.034	117	9.00	4.45
8. Bromberg L, Alakhov V. Effects of polyether-modified poly(acrylic acid) microgels on doxorubicin transport in human intestinal epithelial Caco-2 cell layers. <i>J Control Release.</i> 2003;88(1):11-22. doi: 10.1016/s0168-3659(02)00419-4	105	5.00	1.86
9. Chudasama B, Vala AK, Andhariya N, et al. Highly bacterial resistant silver nanoparticles: synthesis and antibacterial activities. <i>Journal of Nanoparticle Research.</i> 2010;12:1677-85.	103	7.36	3.38
10. El-Housiny S, Shams Eldeen MA, El-Attar YA, et al. Fluconazole-loaded solid lipid nanoparticles topical gel for treatment of pityriasis versicolor: formulation and clinical study. <i>Drug Deliv.</i> 2018;25(1):78-90. doi: 10.1080/10717544.2017.1413444	102	17.00	4.08

and 1,023 author's keywords. In total, there are 1,678 authors associated with these documents, and 4 of the documents are single-authored. The collaboration among authors shows an average of 5.96 co-authors per document, with international co-authorships accounting for 20% of the total.

The subject areas under which articles in Pluronic F-127 hydrogel research for delivering antimicrobial agents are classified in the Scopus database are illustrated in Figure 1. The major subject areas include Pharmacology, Toxicology and Pharmaceutics¹ (92 documents), Biochemistry, Genetics and Molecular Biology (74), Materials Science (67), Chemistry (60), Medicine (54), Chemical Engineering (49), Engineering (36), Physics and Astronomy (26), Immunology and Microbiology (15), Agricultural and Biological Sciences (7), Dentistry (7) to name a few. Line diagram illustrating the publication trend of articles in Pluronic F-127 hydrogel research for delivering antimicrobial agents from 1981 to 2022 is inserted as Figure 2. In addition, the line diagram illustrating the mean total citations per year (MeanTCperYear) is inserted as Figure 2.

Geographic Distribution of Research

Scientific production on the use of Pluronic F-127 hydrogel for delivering antimicrobial

agents varies across different countries (Figure 3). India has the highest number of articles with 112 publications, followed closely by the United States with 107 articles. Egypt has contributed 85 articles, while Brazil and China have 83 and 82 articles, respectively. Spain has published 51 articles, Turkey 49, and Thailand 42. France and the United Kingdom have comparatively lower numbers of publications, with 33 and 31 articles, respectively, on this topic. The map representing Country Scientific Production (worldwide data) is inserted as Figure 3a. The map illustrating the country collaboration analysis is inserted as Figure 3b. The USA was found to be the country with the broadest collaboration network which includes active scientific relationships with 16 other countries. This was followed by India and United Kingdom as second and third active scientific collaborations (8 and 7 countries).

Most Cited Articles

The characteristics of the top ten most cited papers in Pluronic F-127 hydrogel research for delivering antimicrobial agents are given in Table 2. Among the 10 papers, three highly cited papers were published in the International Journal of Pharmaceutics, Two each in AAPS PharmSciTech journal and Journal of Controlled Release. In

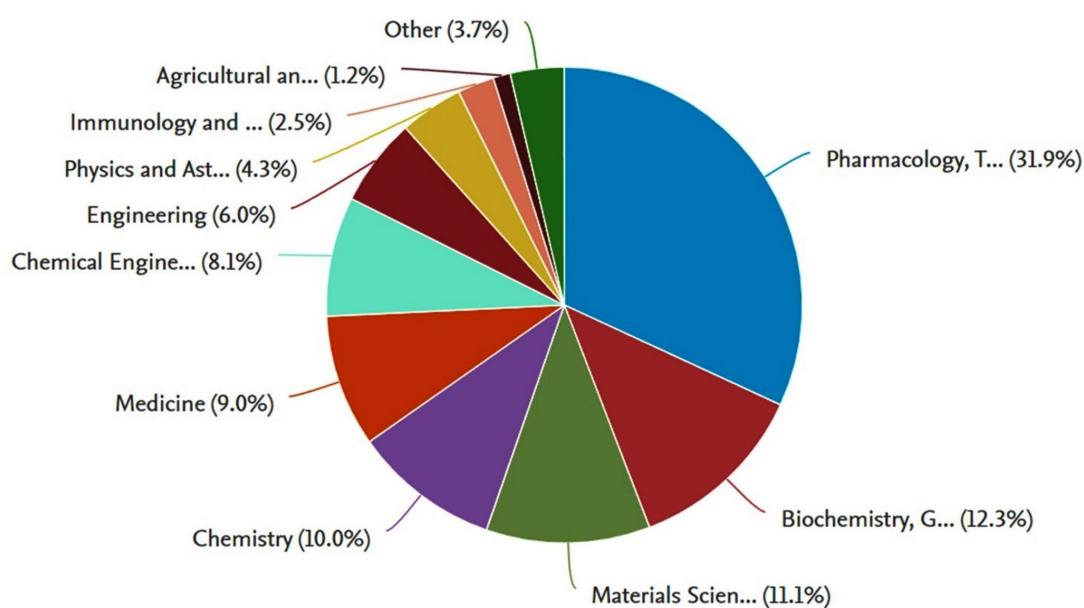


Figure 1. Pie chart illustrating the subject areas under which articles in Pluronic F-127 hydrogel research for delivering antimicrobial agents are classified in the Scopus database

addition, one paper was published in Journal of Nanoparticle Research, European Journal of Pharmaceutical Sciences and Drug Delivery Journal.

The salient findings of the top 10 most cited papers in Pluronic F-127 hydrogel research for delivering antimicrobial agents are as follows:

- A drug delivery system for periodontitis treatment was developed using

tetracycline-loaded halloysite coated with chitosan. Poloxamer 407 was used as a thermoresponsive polymer, with the gelling temperature modified by PEG 20,000.¹⁶

- Poloxamer 407 25% (w/w) formulations were developed to prolong the residence time of vancomycin for high-risk infection sites. The formulations underwent reversible thermal gelation upon injection, maintaining

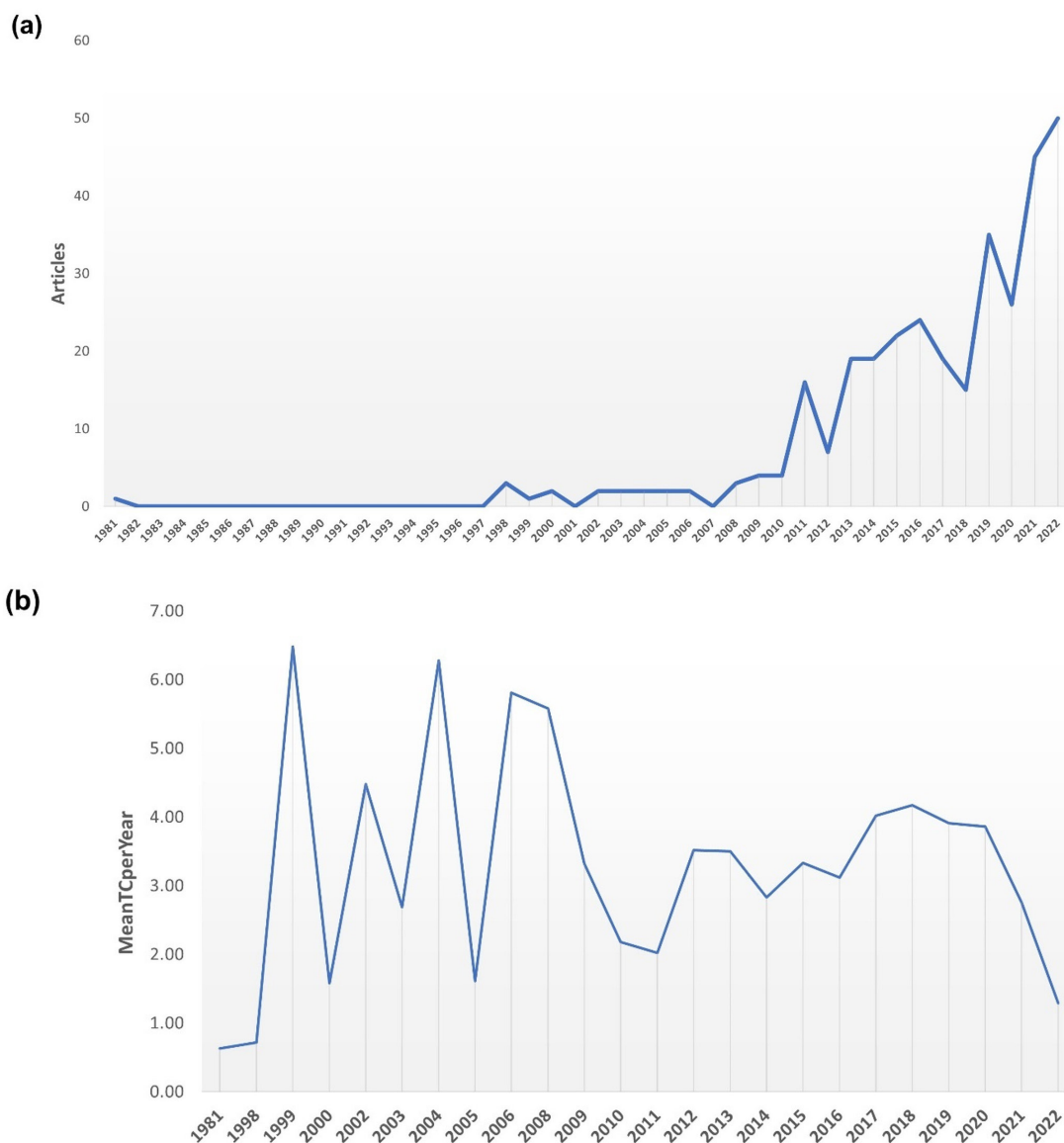


Figure 2. (a) Line diagram illustrating the publication trend of articles in Pluronic F-127 hydrogel research for delivering antimicrobial agents from 1981 to 2022. (b) Line diagram illustrating the mean total citations per year (MeanTCperYear) of articles published from 1981 to 2022

- the rheological properties and antibacterial activity of vancomycin. Poloxamer 407 shows promise as a vancomycin delivery vehicle for local infection prophylaxis, particularly in prosthetic surgery.¹⁷
- Triclosan (TC) fast dissolving films for oral delivery were formulated using poloxamer 407. The addition of poloxamer 407 and hydroxypropyl- β -cyclodextrin (HPBCD) enhanced TC solubility. Films with TC-Poloxamer 407 showed improved dissolution profile and antimicrobial activity compared to TC-HPBCD complex films.¹⁸
 - Mucoadhesive thermosensitive gels containing clotrimazole were developed for vaginal candidiasis treatment. Formulations with poloxamers 407, 188, and polycarbophil (PC) showed enhanced mucoadhesiveness.¹⁹
 - Clotrimazole (1%) was complexed with beta-cyclodextrin to enhance solubility and achieve controlled release. The gel formulation with clotrimazole:beta-cyclodextrin (1%:1) in Pluronic F127 (20%) with hydroxypropylmethylcellulose (0.2%) exhibited prolonged release above MIC values, offering potential for enhanced

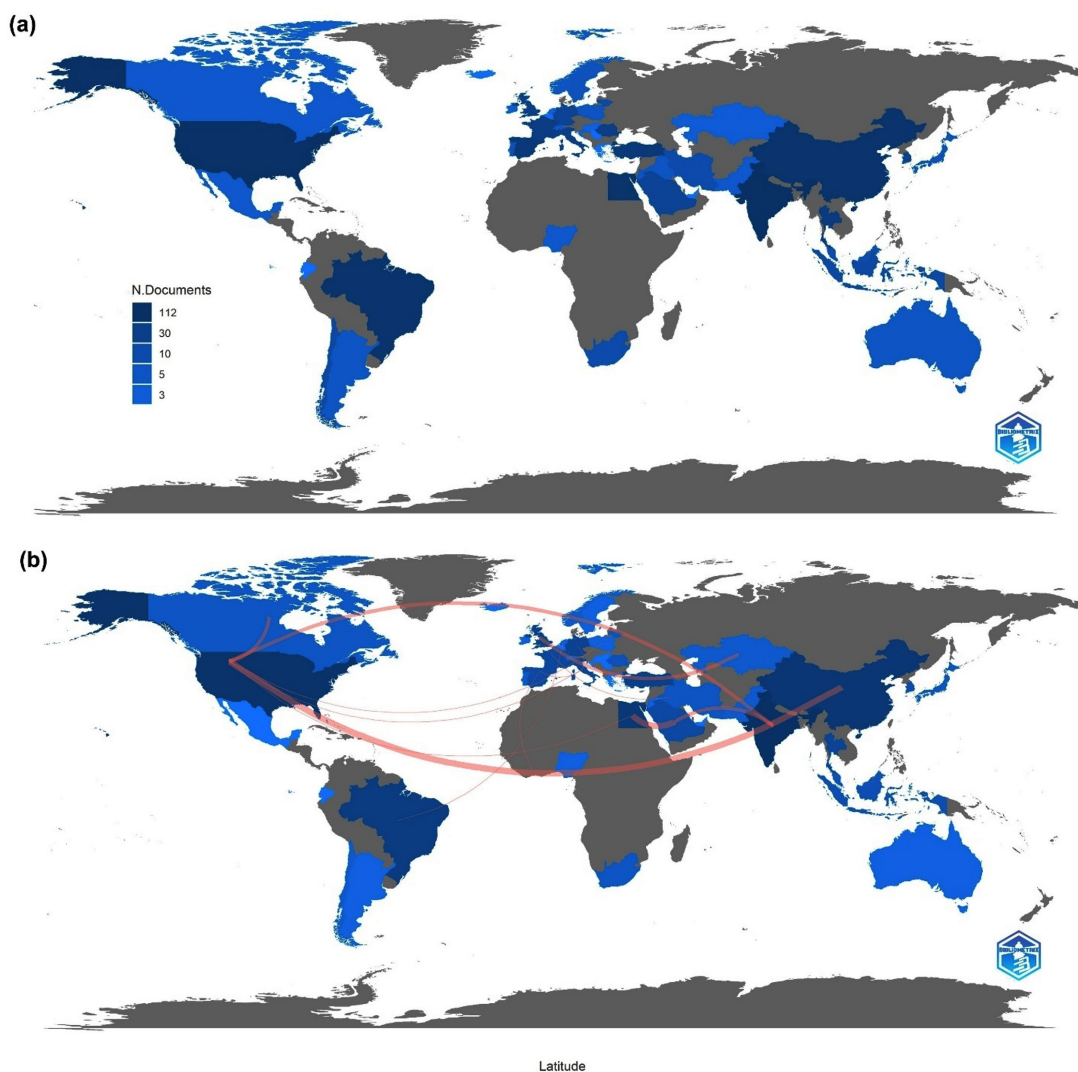
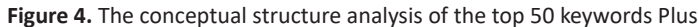


Figure 3. (a) Map representing Country Scientific Production across the globe. (b) Map illustrating the country collaboration analysis



- therapeutic efficacy and patient compliance.²⁰
- Carrageenan was found to enhance the sustained-release properties of poloxamer 407-based vaginal in situ gel. It reduced the release rate of acyclovir, slowed gel erosion, and prolonged drug residence locally. The combination of carrageenan and poloxamer 407 holds promise for the development of improved vaginal drug delivery systems with prolonged local residence and enhanced clinical outcomes.²¹
- Dried nanosuspensions of itraconazole (ITZ) were prepared using poloxamer 407 or HPMC as stabilizers. The spray-dried ITZ nanosuspensions showed preserved high dissolution rates. This formulation may be a promising approach to enhance the oral bioavailability of poorly soluble drugs with pH-dependent solubility.²²
- Microgels composed of cross-linked copolymers of poly(acrylic acid) and Pluronics, specifically Pluronic L61, L92, and F127, were evaluated as permeation enhancers for doxorubicin transport in Caco-

2 cell monolayers. The microgels inhibited P-glycoprotein-mediated efflux and enhanced the passive influx of doxorubicin, resulting in increased cell absorption.²³

- A rapid synthesis route using oleylamine was employed to produce uniform hydrophobic silver nanoparticles. Pluronic F127 was utilized for phase transfer to enhance dispersal in water. The hydrophilic silver nanoparticles showed excellent antimicrobial activity against various bacteria, surpassing commercially available antibacterial agents.²⁴
- This study aimed to enhance the topical delivery of Fluconazole (FLZ) for treating Pityriasis Versicolor (PV) by formulating FLZ-loaded solid lipid nanoparticles (SLNs) topical gel. The use of Poloxamer 407 as a stabilizer in SLNs resulted in smaller particle size compared to other surfactants.²⁵

Analysis of Keywords

The Multiple Correspondence Analysis (MCA) was employed to analyze the keywords in our dataset. It condenses vast data with multiple

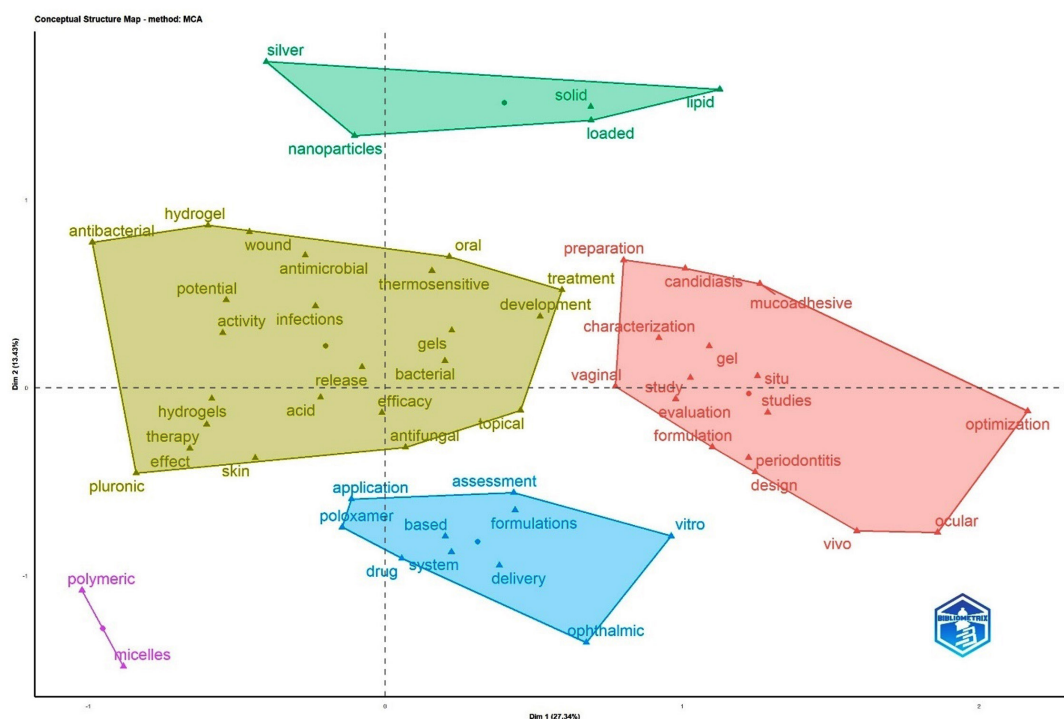


Figure 6. The conceptual structure analysis of the top 50 keywords in titles

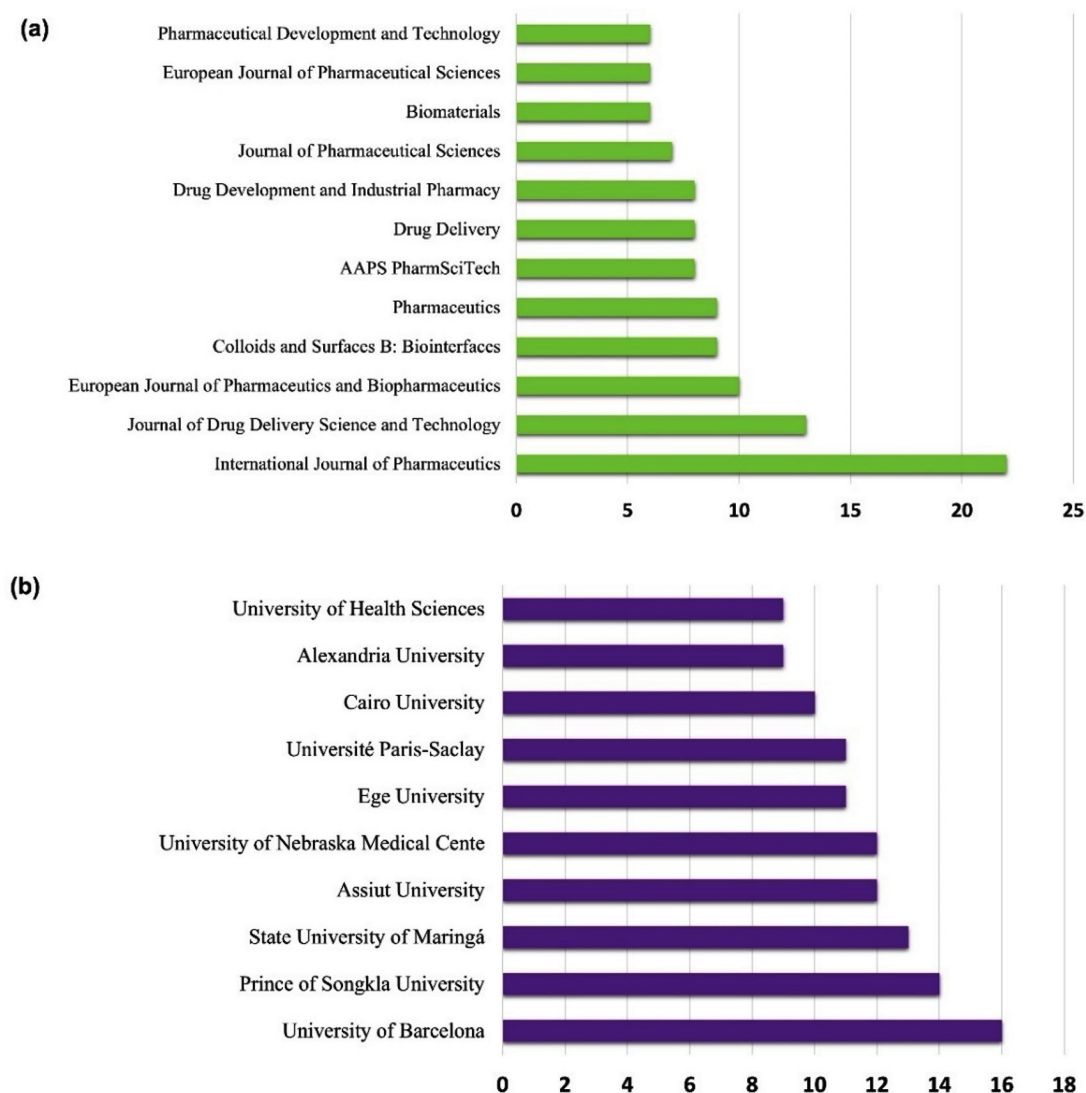
approach the center point indicate a higher level of attention in recent. The interpretation of the results is based on the positions of the points and their distribution along the dimensions. The closer words are represented on the map, the more

[illegible]

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similar their distribution is years.²⁶ The conceptual structure analysis of the top 50 keywords Plus, author keywords, and keywords in titles is given in Figure 4. The top 50 keywords Plus were divided into five clusters: Cluster 1 (anti-bacterial agents, anti-infective agent), Cluster 2 (human, drug effect, humans, chemistry), Cluster 3 (drug carriers, animal, male, female, gels, hydrogel, unclassified drug, priority journal, drug carrier, animals), Cluster 4 (animal tissue, animal model, animal experiment, in vivo study), and the remaining were clubbed as Cluster 5. Similarly, the top 50 author keywords and keywords in titles were clustered into five groups as given in Figure 5 and 6.

The WordCloud illustrating the top 100 most frequent Keywords Plus is given as Figure 7a. The general terms such as poloxamer (450), article (262), nonhuman (195), controlled study (191), chemistry (142), and in vitro study (139), were the top five most frequent Keywords Plus identified in this study. Similarly, Figure 7b presents the WordCloud of top 100 authors keywords used in their publications. Among the identified keywords, the highest occurrences include poloxamer 407 (51), poloxamer (28), pluronic f127 (17), chitosan (15), nanoparticles (15), in situ gel (14), and antimicrobial (12).



(c)

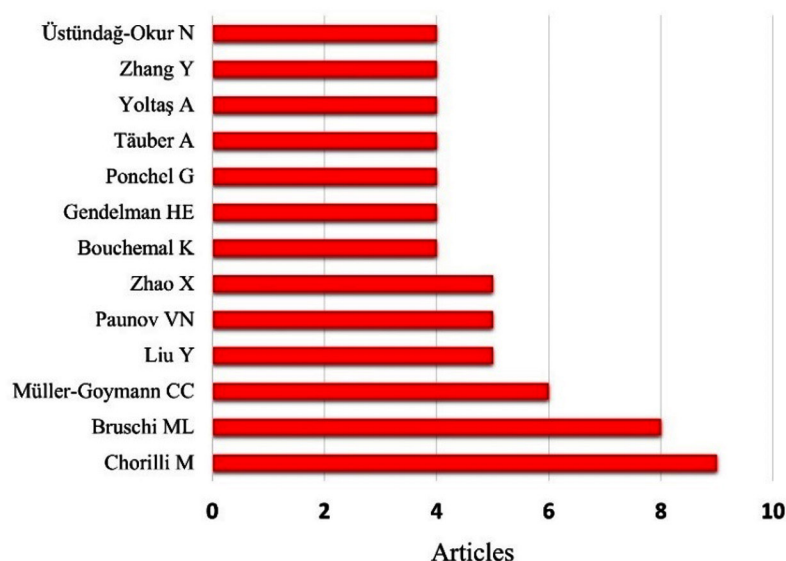


Figure 8. (a) Bar diagram illustrating the top journals publishing articles in Pluronic F-127 hydrogel research for delivering antimicrobial agents. (b) Bar diagram illustrating the top productive universities/institutes publishing articles in Pluronic F-127 hydrogel research for delivering antimicrobial agents. (c) Bar diagram illustrating the top productive authors publishing articles in Pluronic F-127 hydrogel research for delivering antimicrobial agents

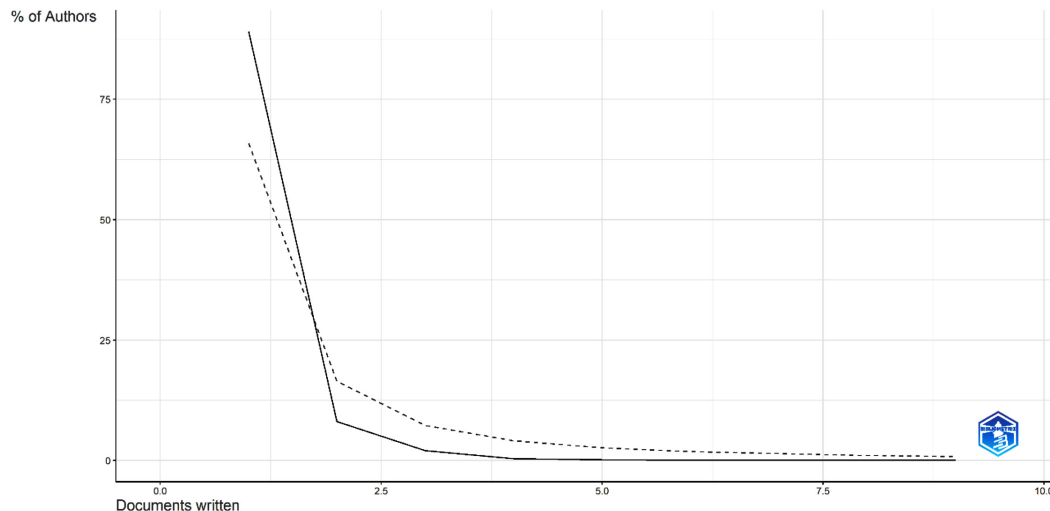


Figure 9. Author productivity through Lotka's law

Identification of Top Authors and Institutes

Bar diagram illustrating the top productive authors publishing articles in Pluronic F-127 hydrogel research for delivering antimicrobial agents is inserted as Figure 8. According to Lotka's law, 1494 authors (89.03%) among the total 1678 identified are considered occasional authors

whereas 48 authors were identified as the core authors (who published ≥ 3 articles in the present case). Lotka's law characterizes the distribution of authorship in a specific field, stating that the frequency of authors publishing a certain number of articles follows an approximate inverse-square relationship. According to Lotka's law, the ratio of

authors who publish a specific number of articles to the number of authors who publish only one article remains relatively constant. Additionally, Lotka's law confirms that as the number of

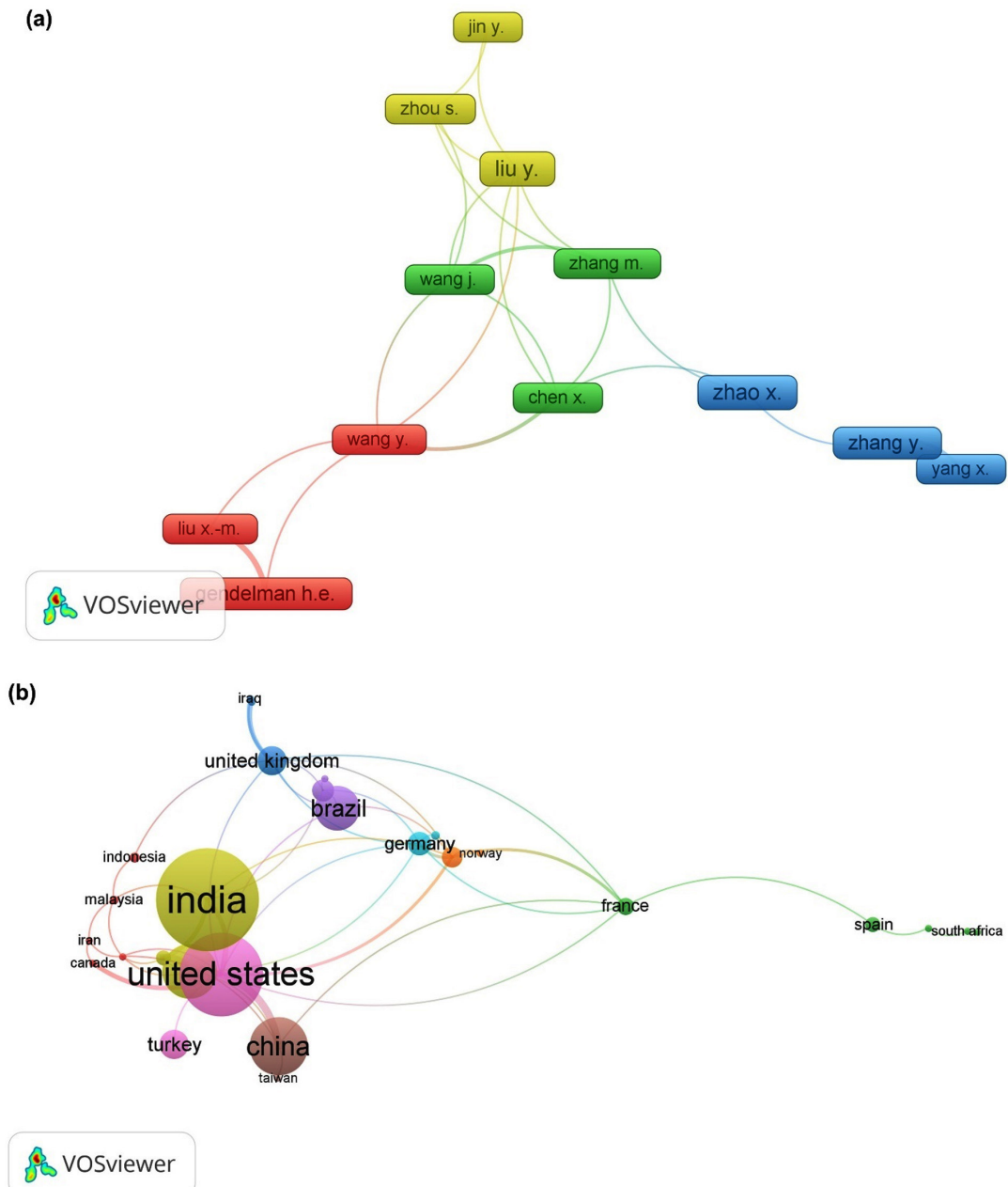


Figure 10 The network visualization map indicating the connections between authors and countries. Specifically, authors with a minimum of three documents (a) and countries with a minimum of three documents (b) were selected for inclusion in the map. The size of each circle/frame in the map represents the total number of published articles, with larger circles indicating a higher publication count. On the other hand, the width of the lines in the map signifies the strength of the links, with wider lines indicating stronger connections. The distance between two circles in the map reflects the degree of relatedness between the corresponding nodes

articles published increases, authors who produce that many publications become less common (Figure 9).

Bar diagram illustrating the top productive universities/institutes publishing articles in Pluronic F-127 hydrogel research for delivering antimicrobial agents is inserted as Figure 8. Among the 541 entries of universities/institutes identified, the following were selected as the most productive: University of Barcelona, Prince of Songkla University, State University of Maringá, Assiut University, University of Nebraska Medical Center, Ege University, Université Paris-Saclay, Cairo University, Alexandria University, and University of Health Sciences.

Identification of Influential Journals

The top journals publishing articles in Pluronic F-127 hydrogel research for delivering antimicrobial agents included International Journal of Pharmaceutics (22 documents), Journal of Drug Delivery Science and Technology (13), European Journal of Pharmaceutics and Biopharmaceutics (10), Colloids and Surfaces B: Biointerfaces (9), Pharmaceutics (9), AAPS PharmSciTech (8), Drug Delivery (8), Drug Development and Industrial Pharmacy (8), Journal of Pharmaceutical Sciences (7), Biomaterials (6), European Journal of Pharmaceutical Sciences (6), and Pharmaceutical Development and Technology (6) (Figure 8).

Among the 161 journal (sources) that published 325 documents, 12 journals (International Journal of Pharmaceutics, Journal of Drug Delivery Science and Technology, European Journal of Pharmaceutics and Biopharmaceutics, Colloids and Surfaces B: Biointerfaces, Pharmaceutics, AAPS PharmSciTech, Drug Delivery, Drug Development and Industrial Pharmacy, Journal of Pharmaceutical Sciences, Biomaterials, European Journal of Pharmaceutical Sciences, and Pharmaceutical Development and Technology) were included in the Zone 1 of the three zones. These Zone 1 journals together published 112 articles of the total 325 (34.46%). According to the Bradford's law, Zone 1 is considered the nucleus (core zone) of journals particularly devoted to the given subject.

Evaluation of Collaboration Networks

The network visualization map indicating the connections between authors and countries. Specifically, authors and countries with a minimum of three documents were selected for inclusion in the map. Although 43 authors met this threshold, some of them were not connected and therefore the largest set of connected items constituting of 12 authors were illustrated (Figure 10). Similarly, 27 countries of the total 29 countries that met the threshold were illustrated since they formed the largest network (Figure 10). The size of each circle/frame in the map represents the total number of published articles, with larger circles indicating a higher publication count. On the other hand, the width of the lines in the map signifies the strength of the links, with wider lines indicating stronger connections. The distance between two circles in the map reflects the degree of relatedness between the corresponding nodes.²⁷

CONCLUSION

PF-127 hydrogel holds significant potential for delivering antimicrobial agents. Through a comprehensive bibliometric analysis, this paper has provided insights into the current research landscape, key trends, influential authors, and prominent journals in this field. The findings highlight the growing interest in PF-127 hydrogel as a versatile platform for antimicrobial agent delivery. Future research should focus on addressing the remaining challenges, optimizing formulation parameters, exploring combination therapies, conducting in vivo studies, and promoting collaboration to realize the full potential of Pluronic F-127 hydrogel-based delivery systems in clinical applications. The insights gained from this analysis will contribute to the development of innovative approaches for combating infections and addressing the growing threat of antimicrobial resistance.

ACKNOWLEDGMENTS

The authors would like to thank Director, ICAR-Indian Veterinary Research Institute, Izatnagar, Bareilly, India, and the All-India Network Program on Diagnostic Imaging and Management

of Surgical Conditions in Animals (AINP-DIMSCA) for providing the necessary research facilities to carry out this work.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTION

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

FUNDING

None.

DATA AVAILABILITY

All datasets generated or analyzed during this study are included in the manuscript.

ETHICS STATEMENT

Not applicable.

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