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Global Scientific Evolution and Knowledge Mapping of Research on Emerging Extended-Spectrum Beta-Lactamase Inhibitors: A Scientometric Analysis

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Abstract: Antimicrobial resistance (AMR) represents a major global public health challenge and has stimulated substantial scientific interest in the development and evaluation of β-lactam/β-lactamase inhibitor strategies against resistant Gram-negative bacteria. However, the scientific literature on emerging extended-spectrum β-lactamase (ESBL) inhibitors has not been comprehensively characterized from a scientometric perspective. This study aimed to map and characterize the global scientific literature on emerging ESBL inhibitors by analyzing publication trends, citation patterns, influential authors and institutions, leading journals, international collaboration networks, and emerging research themes. This study was designed as a bibliometric and scientometric mapping analysis rather than a pharmacological, chemical, or laboratory investigation of ESBL inhibitors. Bibliographic records were retrieved from the Scopus and Dimensions databases. A total of 2,086 records were identified, of which 503 publications met the predefined eligibility criteria and were included in the analysis for the period 2013–2023. Bibliographic data were analyzed and visualized using RStudio and VOSviewer to assess publication productivity, citation patterns, collaboration networks, and keyword co-occurrence and evolution. The United States demonstrated the highest research productivity, with 445 publications and 15,889 citations, followed by France and China. Antimicrobial Agents and Chemotherapy was the leading journal, with 171 publications and the highest citation count. Indiana University Bloomington and Case Western Reserve University were among the leading institutions, while Robert Bonomo was the most prolific author and Karen Bush had the highest citation impact. Keyword analysis identified taniborbactam, xeruborbactam, enmetazobactam, VNRX-5236, and imipenem-relebactam as prominent emerging research themes. Overall, this scientometric analysis provides a structured overview of the development and knowledge landscape of research on emerging ESBL inhibitors, identifies major contributors and collaboration patterns, and highlights evolving research priorities that may guide future investigations.

Key words: Antimicrobial Resistance; β-Lactamase Inhibitors; Extended-Spectrum β-Lactamase (ESBL); Knowledge Mapping Scientometric and bibliometric Analysis.

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الاتجاهات العالمية للتطور العلمي وبنية المعرفة البحثية حول المثبطات الناشئة لإنزيمات بيتا-لاكتاماز ممتدة الطيف: تحليل سينتومتري

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ملخص البحث

يمثل مقاومة مضادات الميكروبات (AMR) تحديًا رئيسيًا للصحة العامة على مستوى العالم، وقد حفّزت اهتمامًا علميًا كبيرًا بتطوير وتقييم استراتيجيات البيتا–لاكتام/مثبطات البيتا–لاكتاماز (β–lactam/β–lactamase inhibitors) الموجهة ضد البكتيريا سالبة الغرام المقاومة. ومع ذلك، لم تتم دراسة الأدبيات العلمية المتعلقة بمثبطات إنزيمات البيتا–لاكتاماز ممتدة الطيف (ESBL) الناشئة بصورة شاملة من منظور التحليل العلمِيّ المقاييسي (Scientometric). هدفت هذه الدراسة إلى رسم خريطة للأدبيات العلمية العالمية المتعلقة بمثبطات ESBL الناشئة وتوصيفها، وذلك من خلال تحليل اتجاهات النشر، وأنماط الاستشهادات المرجعية، والمؤلفين والمؤسسات الأكثر تأثيرًا، والمجلات العلمية الرائدة، وشبكات التعاون الدولي، والموضوعات البحثية الناشئة. صُممت هذه الدراسة بوصفها تحليلًا ببليومتريًا ورسمًا علميًا مقاييسيًا للمعرفة(Bibliometric and Scientometric Mapping Analysis) ، وليس دراسة دوائية أو كيميائية أو مختبرية لمثبطات ESBL. وقد جرى استرجاع السجلات الببليوغرافية من قاعدتي بيانات Scopus و Dimensions. وتم تحديد ما مجموعه 2,086سجلًا، استوفى 503منشورات منها معايير الأهلية المحددة مسبقًا، وأُدرجت في التحليل للفترة من 2013إلى 2023. جرت معالجة البيانات الببليوغرافية وتحليلها وتمثيلها بصريًا باستخدام RStudio وVOSviewer، بهدف تقييم إنتاجية النشر، وأنماط الاستشهادات المرجعية، وشبكات التعاون، والتشارك في ظهور الكلمات المفتاحية وتطورها. أظهرت الولايات المتحدة الأمريكية أعلى إنتاجية بحثية، بواقع 445منشورًا و15,889 استشهادًا، تلتها فرنسا والصين . وكانت مجلة Antimicrobial Agents and Chemotherapyالمجلة الرائدة، بواقع 171منشورًا وأعلى عدد من الاستشهادات. وكانت Indiana University Bloomington وCase Western Reserve University من بين المؤسسات البحثية الرائدة، في حين كان Robert Bonomo المؤلف الأكثر إنتاجية، بينما حققت Karen Bushأعلى تأثير من حيث الاستشهادات. وقد حدد تحليل الكلمات المفتاحية كلًا من taniborbactam، وxeruborbactam، وenmetazobactam، وVNRX–5236، وi mipenem–relebactam بوصفها من أبرز الموضوعات البحثية الناشئة. وبوجه عام، يوفر هذا التحليل العلمِيّ المقاييسي عرضًا منظمًا لتطور البحث العلمي وخريطة المعرفة المتعلقة بمثبطات ESBL الناشئة، ويحدد أبرز المساهمين وأنماط التعاون البحثي، كما يسلط الضوء على الأولويات البحثية المتطورة التي قد توجه الدراسات المستقبلية.

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الكلمات المفتاحية: التحليل العلميّ المقاييسي والببليومتري، إنزيمات البيتا–لاكتاماز ممتدة الطيف، رسم خرائط المعرفةESBL) ، مثبطات البيتا–لاكتاماز، مقاومة مضادات الميكروبات.

Introduction

Antimicrobial resistance (AMR) has emerged as one of the major global public health challenges, threatening the effectiveness of antimicrobial therapy and placing increasing pressure on healthcare systems worldwide (Antimicrobial Resistance Collaborators, 2022). The increasing prevalence and global dissemination of resistant bacterial pathogens have stimulated extensive scientific efforts to identify effective therapeutic strategies. Among the important mechanisms contributing to antimicrobial resistance in Gram-negative bacteria is the production of β-lactamases, including extended-spectrum β-lactamases (ESBLs), which can hydrolyze a broad range of β-lactam antibiotics (Bush & Bradford, 2019; Livermore, 2008).

ESBL-producing organisms, particularly members of the Enterobacterales, represent an important clinical concern because they can substantially limit available treatment options. Major ESBL families include TEM, SHV, and CTX-M, with CTX-M enzymes becoming the predominant ESBL family in many regions worldwide. ESBL-producing organisms have been associated with both healthcare-associated and community-acquired infections, contributing to significant challenges in antimicrobial selection and infection management (Livermore, 2008; Rodríguez-Baño et al., 2018; Tamma et al., 2021). Consequently, considerable scientific attention has been directed toward β-lactamase inhibitors and β-lactam/β-lactamase inhibitor (BL/BLI) combinations as potential strategies for addressing infections caused by β-lactamase-producing bacteria (Bush & Bradford, 2019; Yahav et al., 2020).

The development of β-lactamase inhibitors has generated a rapidly expanding body of scientific literature encompassing different research approaches, including experimental studies, clinical investigations, molecular and computational studies, and evaluations of β-lactam/β-lactamase inhibitor combinations (Bush & Bradford, 2019; Yahav et al., 2020). In parallel, several reviews, systematic reviews, and meta-analyses have examined specific clinical, microbiological, pharmacological, and therapeutic aspects of ESBL-producing organisms and β-lactamase inhibitor combinations (Harris et al., 2015; Rodríguez-Baño et al., 2018; Yahav et al., 2020). These publications provide important information regarding individual scientific questions and therapeutic approaches; however, they do not necessarily provide a quantitative overview of how the scientific literature in this research area has developed over time.

Bibliometric and scientometric analyses provide complementary approaches for quantitatively examining the development, structure, and evolution of scientific knowledge. These approaches can identify publication trends, citation patterns, influential researchers and institutions, leading journals,

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collaboration networks, and changes in research themes and keywords. Such analyses can therefore provide a broader perspective on the development of a research field and identify areas of increasing scientific attention (Aria & Cuccurullo, 2017; van Eck & Waltman, 2010). VOSviewer, in particular, provides tools for constructing and visualizing bibliometric maps based on relationships such as co-citation, bibliographic coupling, and keyword co-occurrence (van Eck & Waltman, 2010).

Despite the growing body of literature concerning ESBL inhibitors, a comprehensive scientometric mapping of the global research landscape remains limited. In particular, there is a need to characterize how research output has evolved, which countries, institutions, authors, and journals have contributed most substantially, how international and institutional collaborations have developed, and which research themes have emerged over time.

Therefore, the present study focuses specifically on the **scientific literature concerning emerging ESBL inhibitors**, rather than on the chemical properties, pharmacological activity, therapeutic efficacy, or laboratory evaluation of individual inhibitors. The study was designed as a **bibliometric and scientometric mapping analysis** to characterize the global development and structure of this research field. Bibliographic records published between 2013 and 2023 were retrieved from the Scopus and Dimensions databases and analyzed using VOSviewer and RStudio. The analysis examined publication and citation trends, influential countries, authors, institutions, and journals, collaboration patterns, keyword co-occurrence, and emerging research themes.

By providing a quantitative map of the scientific literature, this study aims to clarify the development and knowledge structure of research on emerging ESBL inhibitors and to identify major contributors, collaborative networks, and emerging research priorities. Importantly, the study does not seek to evaluate the pharmacological or laboratory performance of ESBL inhibitors; rather, it provides a scientometric overview of how research in this field has evolved and where future scientific attention may be directed.

Materials and Methods

Data Search

Digital searches were conducted using the Dimensions (https://app.dimensions.ai/) and Scopus (https://www.scopus.com) databases. The search terms used were 'ESBL OR ESBL enzyme OR Inhibitor OR Nacubactam OR Zidebactam OR Vaborbactam OR Taniborbactam OR Durlobactam OR Clavulanic Acid OR Sulbactam OR Tazobactam OR Avibactam OR Relebactam OR Nacubactam' in the title and abstract.

Titles, summaries, and abstracts of relevant articles were carefully reviewed for inclusion. A total of 2,086 papers were retrieved, of which 503 were selected based on relevance and suitability (Figure 1). Ethical approval was not sought, as no human or animal subjects were involved in the

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study.

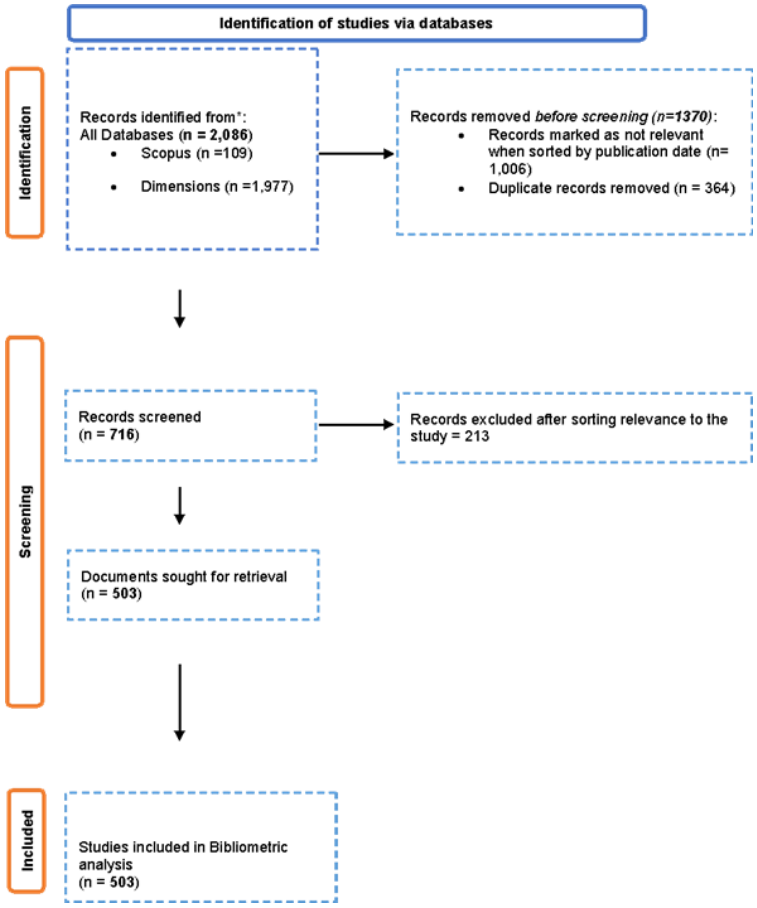

Figure 1. Database search and article selection process.

Inclusion Criteria

A publication was eligible for inclusion if it met the following criteria:

1. It was published in English between 2013 and 2023.
2. It addressed ESBLs, β-lactamase inhibitors, or emerging β-lactam/β-lactamase inhibitor strategies within the scope of the present bibliometric analysis.
3. The publication was indexed in either the Scopus or Dimensions database.
4. The publication contained sufficient bibliographic information for scientometric analysis.

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Exclusion Criteria

The following records were excluded:

1. Newspaper articles and editorials.
2. Conference proceedings.
3. Publications outside the predefined study period (2013–2023).
4. Records that did not meet the predefined relevance criteria for ESBL inhibitor research.
5. Duplicate records identified during the data screening and cleaning process.

Data Analysis

After document selection, data were extracted from the Dimensions and Scopus databases in XLS and CSV formats. The outcomes from the digital search were analyzed using VOSviewer (version 1.6.18; Leiden University, The Netherlands) and RStudio software (version 2023.03.0-daily+82.pro2). VOSviewer was employed to visually depict networks of collaborations among the analyzed variables and terms (Huang et al., 2020; van Eck & Waltman, 2011).

In the visualizations, the size of each bubble represented the quantity of publications, whereas the distance between two bubbles indicated the relatedness between terms. The color of each bubble represented the connections between different research themes (van Eck & Waltman, 2010).

Ethical Considerations of the Study

Ethical approval was not sought, as no human or animal subjects were involved in the study. The research primarily involved the collection and analysis of publicly available data from digital databases such as Dimensions and Scopus. As the study did not involve any direct interaction with human participants or animals, nor did it require the collection of personal or sensitive information, ethical review was not necessary. Additionally, all data used were non-personal, anonymized, and publicly accessible, adhering to the ethical guidelines for secondary data analysis in research.

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Results

The findings of this study indicated that from 2013 to 2023, the number of articles available on new inhibitors for ESBL enzymes was significant (Figure 2). In 2021, 26 research articles were published, while in 2022 and 2023, 135 and 107 papers were published, respectively, demonstrating that the scientific community had developed a strong interest in this research topic. The highest citation count occurred in 2016, with an average citation rate of 159.

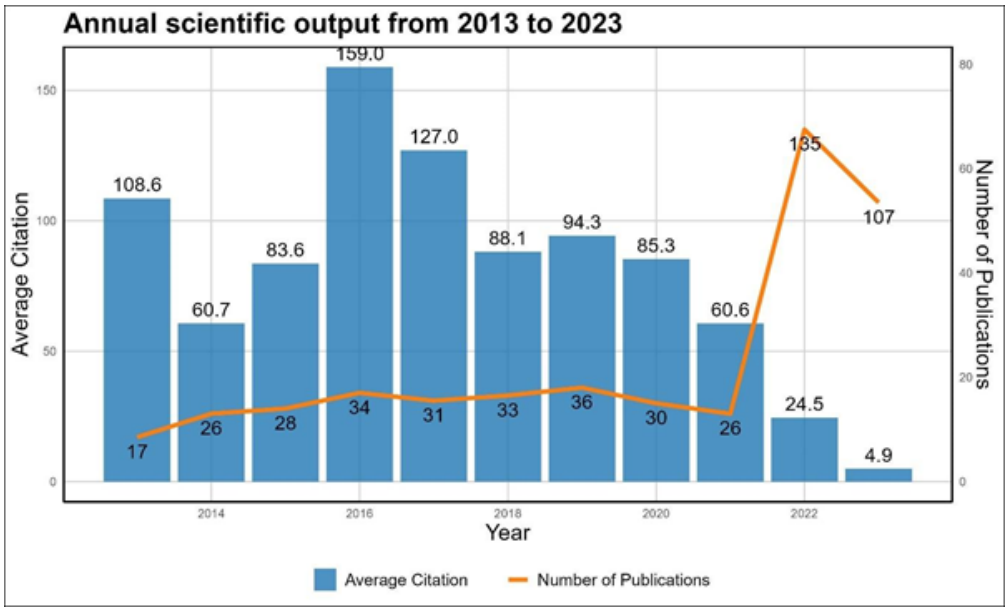

Figure 2. Publication trends and citation analysis for ESBL inhibitor research.

To provide a more detailed temporal analysis, keyword trends were examined across different years. The results indicate that in 2013-2016, the most frequently occurring keywords included "β-lactamase inhibitors," "resistance genes," and "CTX-M." From 2017 onwards, emerging terms such as "taniborbactam," "xeruborbactam," and "VNRX-5236" began to appear more frequently, highlighting the shift towards novel inhibitor research. Additionally, 2020 onwards saw an increased focus on combination therapies involving β-lactamase inhibitors, demonstrating a diversification in research approaches. Keyword co-occurrence networks illustrated that terms such as "resistance mechanisms," "novel inhibitors," and "clinical efficacy" have become more prominent in the past five years, reflecting a broader understanding of ESBL inhibitor applications.

Table 1 depicts the top countries that published the most papers related to new inhibitors for the ESBL enzyme. The United States (U.S.) led in both the number of articles (445) and citations (15,889), followed by France and China, which published 209 and 157 articles, respectively. In terms of citations, France (1,543) and China (740) garnered the most citations after the U.S.

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among countries involved in research on new inhibitors for the ESBL enzyme. The U.S. and France exhibited the highest level of collaboration among the countries.

Table 1. Major countries with highest publications related to inhibitors for ESBL enzyme.

Country	Documents	Citations	Total link strength
United States	445	15889	3333
France	209	5650	1543
China	157	2246	740
Japan	146	1977	625
India	137	2624	454
Spain	127	3584	1430
United Kingdom	115	2425	753
Germany	114	3259	1073
Italy	100	2816	1127
Switzerland	100	2720	764

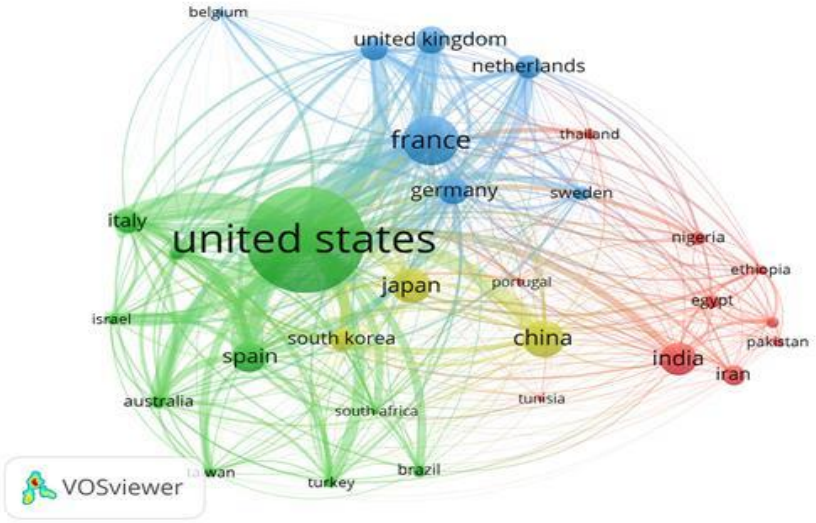

Figure 3. Network of country collaborations.

Table 2 shows the high-impact journals (sources) with the most publications in the domain of new inhibitors for the ESBL enzyme. Antimicrobial Agents and Chemotherapy and PLOS One published 171 and 86 papers, respectively, receiving 7,556 and 2,238 citations. Figure 4 illustrates the prominent journals in the field of new ESBL enzyme research.

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Table 2. Top journals on new inhibitors for ESBL enzyme.

Sources	Documents	Citations	Total link Strength
Antimicrobial Agents and Chemotherapy	171	7556	824
Plos One	86	2238	467
Microbial Drug Resistance	78	1069	267
International Journal of Antimicrobial Agents	68	1412	320
Journal Of Global Antimicrobial Resistance	57	692	202
Microbiology Spectrum	45	209	108
Antimicrobial Resistance & Infection Control	42	1040	298
BMC Infectious Diseases	41	948	263
Journal of Infection and Chemotherapy	38	744	123
Diagnostic Microbiology and Infectious Disease	36	521	166

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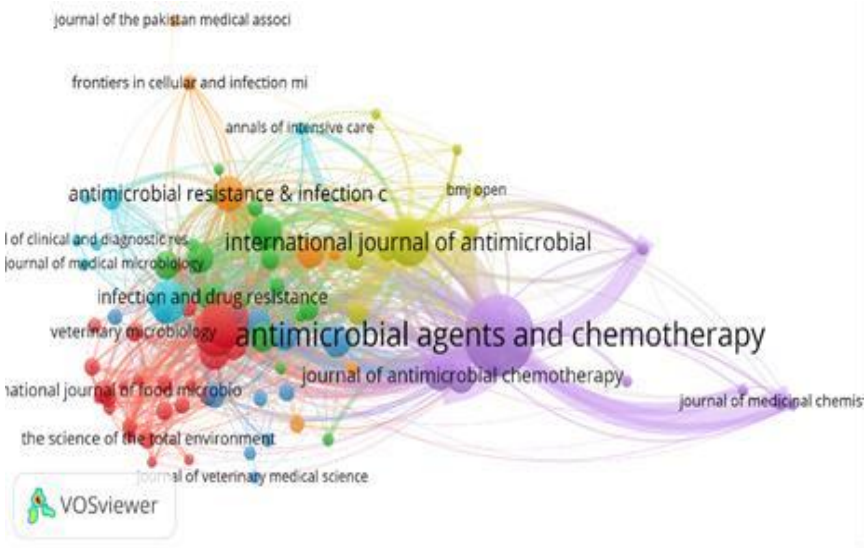

Figure 4. Lead journals on new inhibitors for ESBL enzyme.

Table 3 shows the leading organizations that published the most in the field of new inhibitors for ESBL. Indiana University Bloomington (U.S.) published 7 papers with 1,955 citations, followed by Case Western Reserve University (also from the U.S.), with 34 papers and 1,887 citations. Indiana University Bloomington received the highest number of citations.

Table 3. Top organization that published papers linked to new inhibitors for ESBL enzyme.

Organization	Documents	Citations	Total Link Strength
Indiana University Bloomington	7	1955	1
Case Western Reserve University	34	1887	59
Louis Stokes Cleveland Va Medical Center	23	1189	43
Utrecht University	27	1172	53
University Medical Center Utrecht	31	1169	86
Astrazeneca (United States)	18	1127	24
Hospital Universitario Virgen Macarena	17	1093	56
University Of Manitoba	15	1089	27
University Of Siena	15	1083	29
Hôpital Bichat-Claude-Bernard	18	1057	38

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Table 4 indicates the top authors who published articles on new inhibitors for the ESBL enzyme. Robert Bonomo published 23 papers, followed by Mariana Castanheira, who published 20 articles. The most-cited author was Karen Bush, with 1,955 citations, followed by Robert Bonomo with 1,518 citations, and Paul-Louis Woerther with 1,120 citations.

Table 4. Top authors in research on new inhibitors for ESBL enzymes.

Author (Institution)	Documents	Citations	Total Link Strength
Bush, Karen	7	1955	2
Bonomo, Robert	23	1518	44
Woerther, Paul-Louis	8	1120	13
Karlowsky, James A.	7	1054	19
Hoban, Daryl J.	8	949	19
Lomovskaya, Olga	14	931	49
Andremont, Antoine	9	917	14
Castanheira, Mariana	20	845	56
Dudley, Michael N.	5	722	23
Rodríguez-Baño, Jesús	6	697	0

Table 5 presents the most highly cited original papers on new inhibitors for ESBL enzymes. Among these, a paper by Kaushik et al. (2019) received the highest number of citations (36). The next most highly cited article was authored by Docobo-Pérez et al. (2013), which received 53 citations, followed by the work of Levasseur et al. (2015), with 49 citations.

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Table 5. Highly cited original articles on new inhibitors for ESBL enzyme.

Publication (DOI)	Times cited[1]	Recent citations[2]	RCR[3]	FCR[4]
10.1128/AAC.02623-18	59	25	3.19	11.92
10.1128/AAC.02190-12	53	13	1.97	7.8
10.1128/AAC.04218-14	49	7	2.18	7.99
0.1128/AAC.00164-17	47	10	2.28	9
10.1128/AAC.02596-17	42	11	2.5	7.72
0.1128/AAC.04920-14	36	13	1.66	3.31
10.1093/jac/dku237	30	5	1.36	4.74
0.1128/AAC.00757-20	30	19	2.42	7.14
10.1093/cid/ciw743	30	7	1.3	5.48

[1]Number of citations (references from other publications in Dimensions), [2]Number of citations within the past two years, [3]Relative Citation Ratio, [4]Field Citation Ratio.

Similarly, Table 6 shows the most highly influential papers on new inhibitors for ESBL enzymes. An article by Rodríguez-Baño et al. (2018) garnered the highest number of citations (531). Other highly cited articles include one by van Duin and Bonomo (2016), which received 449 citations, and a paper by Zhanel et al. (2013), which received 365 citations (Table 6).

Table 6. Highly influential papers on new inhibitors for the ESBL enzyme.

Publication (DOI)	Tims cited[1]	Recent citations[2]	RCR[3]	FCR[4]
10.1128/CMR.00079-17	531	201	30.62	114.63
10.1093/cid/ciw243	449	142	21.54	82.72
10.1007/s40265-013-0013-7	365	75	12.88	37.55
10.1038/s41579-019-0159-8	340	151	20.66	45.75
10.1007/s40265-017-0851-9	300	111	17.54	40.77
10.1128/CMR.00115-20	291	235	23.42	78.6
10.1128/AAC.01443-17	266	83	13.43	43.49
10.1101/cshperspect.a025239	205	76	8.64	37.44
10.1021/acs.jmedchem.9b01518	192	104	14.89	48.04
10.1007/s10156-013-0640-7	191	34	6.92	40.95

[1]Number of citations (references from other publications in Dimensions), [2]Number of citations within the past two years, [3]Relative Citation Ratio, [4]Field Citation Ratio.

Many keywords (Figure 5a) have been used in the field of inhibitors for the ESBL enzyme. The dominant keywords identified in the current analysis, based on their frequency of occurrence, were patients (2,492), blaCTX-M (836), treatment (788), ESBL (727), carbapenem (646), and tazobactam (477). In terms of research direction, works related to new inhibitors for ESBL enzymes can be divided into three groups based on the results of keyword clusters: (1) Clinical and Epidemiological Aspects of ESBL Infections, (2) Therapeutic Strategies and Biochemical Mechanisms, and (3) Genetic and Molecular Epidemiology of ESBL Resistance (Figure 5A).

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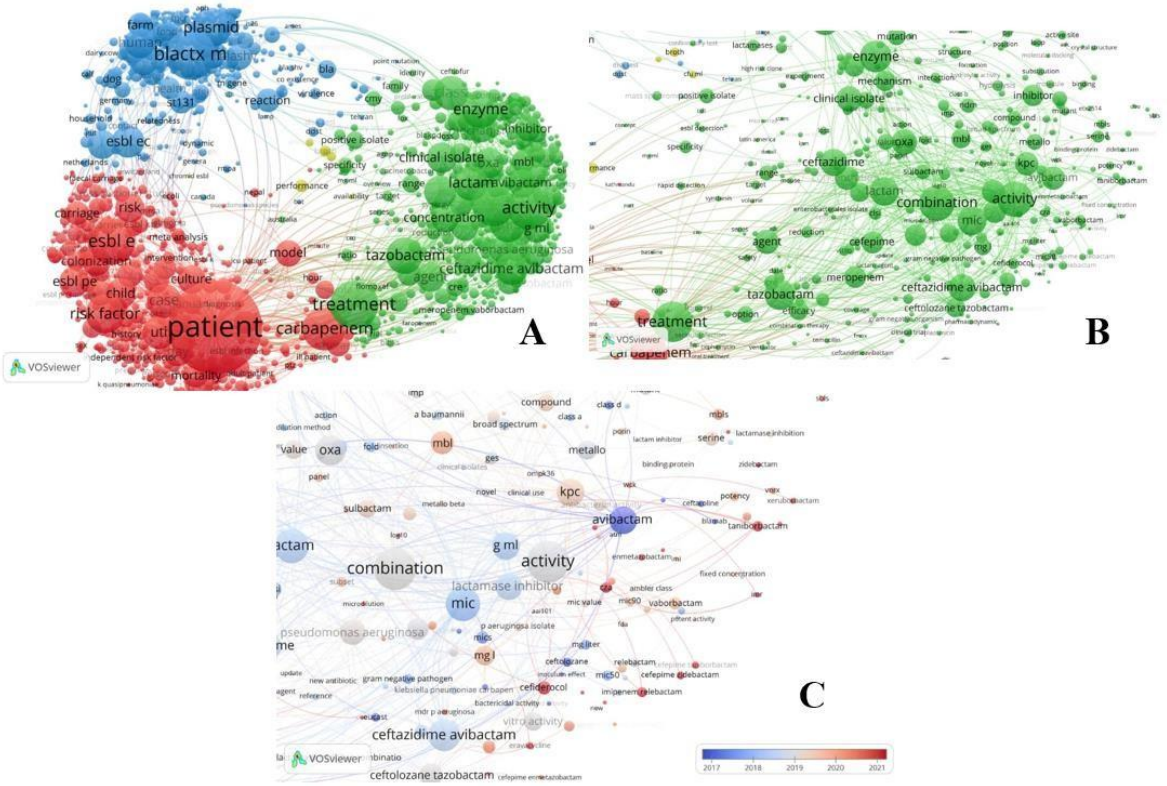

Figure 5. The co-occurrence network of the top keywords in new inhibitors for ESBL enzyme, 2013–2023.

Clinical and Epidemiological Aspects of ESBL Infections (red circle): Frequently used keywords included "patients," "risk factors," "ESBL," "mortality," "colonization," "carbapenem," "transmission," "intervention," "carriage," and "UTI."

Therapeutic Strategies and Biochemical Mechanisms (green circle): Frequently used keywords included "treatment," "concentration," "activity," "meropenem-vaborbactam," "combination," "molecular docking," "potency," "ceftazidime," "avibactam," "ceftolozane-tazobactam," "vaborbactam," "taniborbactam," and "zidebactam" (Figure 5A, B).

Genetic and Molecular Epidemiology of ESBL Resistance (blue circle): Frequently used keywords included "plasmid," "blaCTX-M," "ESBL-EC," "ST131," "m gene," "blaSHV," "pair," "water," "mcr," "virulence," and "co-existence."

Different keywords were assessed over time to create a distribution map of research priorities. Figure 5C shows that "taniborbactam," "xeruborbactam," "enmetazobactam," "VNRX-5236," and "imipenem-relebactam" are emerging research hubs in the field of new inhibitors for the ESBL enzyme (Figure 5C).

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Discussion

To the best of our knowledge, this bibliometric analysis is the first to focus specifically on new inhibitors for ESBL enzymes published from 2013 to 2023. Various factors, such as leading organizations, countries, journals, keywords, and contributions by authors, were analyzed using science mapping (Adeiza & Shuaibu, 2022). Scientometric analysis aids in visualizing the evolving aspects of scientific fields, enhancing understanding of specific scientific domains, and identifying potential research hotspots and future trends (Aria & Cuccurullo, 2017; Islam et al., 2023).

A rise in the number of research outputs was observed from 2021 to 2023, likely reflecting increasing scientific recognition of the need for newer inhibitors targeting β-lactamase-mediated resistance. This development may be particularly important in the context of the continuing emergence of antimicrobial resistance and the limited availability of effective therapeutic options (Suleiman et al., 2022). The analysis showed that the United States, France, and China led this field, with the United States emerging as the leader in both publication output and citations. Similar patterns of geographical concentration of scientific productivity have been reported in bibliometric studies conducted in dental medicine, regenerative endodontics, endodontics, and dental implant research (Adnan & Ullah, 2018; Shamszadeh et al., 2019; dos Santos et al., 2023). The availability of research funding, together with substantial scientific communities and established research infrastructure in these countries, may contribute to their high scientific productivity and the production of highly cited research (Sweileh & Mansour, 2020).

Indiana University Bloomington and Case Western Reserve University from the United States were the most prolific organizations, publishing the highest number of papers. This finding is consistent with previous bibliometric studies showing that universities and research institutions in the United States frequently contribute substantially to scientific publication output (Huang et al., 2020; Bang et al., 2019). Interestingly, Karen Bush and Robert A. Bonomo, who were affiliated with Indiana University Bloomington and Case Western Reserve University, respectively, were among the highly cited authors in this research area. Their contributions highlight the important role of these institutions in research concerning β-lactamases and β-lactamase inhibitors.

A notable finding of this analysis was that many publications were concentrated on established scientific journals with substantial citation impact, suggesting that research published in widely recognized journals may achieve greater visibility and citation influence (Adeiza & Shuaibu, 2022). In this analysis, *Antimicrobial Agents and Chemotherapy* and *PLOS ONE* had the highest records in terms of publication output and citations. Additionally, collaborative papers involving researchers from different countries tended to have higher citation counts, further emphasizing the potential importance of international collaboration in advancing research in this field (O'Leary et al., 2024).

Regarding the top-cited original paper by Kaushik et al. (2019), the authors examined the antibacterial activity of β-lactamase inhibitors, including relebactam and vaborbactam, in combination with β-

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lactam antibiotics against *Mycobacterium abscessus* complex clinical isolates through an in vitro study. Their findings indicated that vaborbactam and relebactam could enhance the activity of several carbapenems and cephalosporins against *M. abscessus* complex isolates, supporting further investigation of these combinations in preclinical and clinical studies (Kaushik et al., 2019).

The second highly cited paper was by Docobo-Pérez et al. (2013), who examined the inoculum effect on the efficacy of amoxicillin-clavulanate, piperacillin-tazobactam, and imipenem against *Escherichia coli* isolates in an experimental murine sepsis model. The isolates included both ESBL-producing and non-ESBL-producing strains. Their results supported the hypothesis that the inoculum effect could contribute to reduced efficacy of β-lactam/β-lactamase inhibitor combinations against high bacterial loads. The findings highlighted the importance of considering bacterial inoculum when evaluating the effectiveness of antimicrobial agents against ESBL-producing organisms (Docobo-Pérez et al., 2013).

Rodríguez-Baño et al. (2018), in their highly cited publication, reviewed treatment options for infections caused by ESBL-, AmpC-, and carbapenemase-producing Enterobacteriaceae. The authors discussed the role of different antimicrobial strategies and emphasized that treatment decisions should be individualized according to the susceptibility profile, resistance mechanism, infection severity, and host characteristics. The review also discussed newer antimicrobial agents and β-lactam/β-lactamase inhibitor combinations, including ceftazidime-avibactam and other emerging therapeutic options (Rodríguez-Baño et al., 2018).

Many authors have studied the role of new inhibitors targeting β-lactamases. Among the highly cited publications identified in the present analysis, Bush and Bradford (2019) reviewed the relationship between β-lactamases and newly developed β-lactamase inhibitors. Their review discussed clinically relevant inhibitor combinations, including avibactam and vaborbactam, which belong to the diazabicyclooctane and cyclic boronic acid inhibitor classes, respectively. These compounds represent important advances in β-lactamase inhibitor development and provide opportunities for the design of future inhibitor strategies.

Similarly, van Duin and Bonomo (2016) discussed second-generation β-lactam/β-lactamase inhibitor combinations, particularly ceftazidime-avibactam and ceftolozane-tazobactam, with emphasis on their antimicrobial spectra and available clinical evidence. The authors also highlighted the importance of antimicrobial stewardship in preserving the effectiveness of these agents and emphasized the need to consider pre-existing resistance mechanisms before their widespread clinical implementation.

Keywords help researchers and readers identify and retrieve relevant studies and can provide an indication of the major themes within a research field. In bibliometric and scientometric analyses, keyword co-occurrence can therefore be used to identify emerging research topics and conceptual clusters (Eshima et al., 2024). In the current analysis, "taniborbactam," "xeruborbactam," "enmetazobactam," "VNRX-5236," and "imipenem-relebactam" were identified as emerging research hotspots.

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Regarding the limitations of the current analysis, bibliometric analysis primarily uses quantitative approaches; therefore, the methodological quality and scientific validity of individual publications were not independently evaluated (Adeiza & Shuaibu, 2022). Only the Dimensions and Scopus databases were selected, and publications not written in English were excluded, which may have introduced selection bias. Furthermore, the data extraction process was performed manually. Despite careful checking of the databases, some errors or inconsistencies may remain. Therefore, the findings should be interpreted within the context of these methodological limitations.

Conclusion

A rise in annual scientific output in recent years has been observed to significantly influence the citation count of each paper. Among the countries focusing on research related to new inhibitors for ESBL enzymes, the U.S. produced the most papers and received the highest number of citations. Indiana University Bloomington and Case Western Reserve University stood out among all institutions. The majority of the articles were published in Antimicrobial Agents and Chemotherapy, which also received the highest number of citations. Among the authors, Karen Bush garnered the most citations, while Robert Bonomo published the most papers. The most cited paper was authored by Rodríguez-Baño et al. and published in Clinical Microbiology Reviews. This bibliometric analysis serves as a valuable tool for researchers, clinicians, and pharmaceutical developers to identify emerging trends, key collaborations, and potential drug candidates. The growing research interest in β-lactam/β-lactamase inhibitor combinations highlights the need for enhanced treatment strategies to address antimicrobial resistance effectively. By emphasizing the importance of continued surveillance, early resistance detection, and interdisciplinary research, this study contributes to shaping the future direction of ESBL inhibitor development and its application in clinical settings.

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