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Metronidazole Research: Historical Developments and Future Directions

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Abstract: Metronidazole is widely used around the world to treat anaerobic, parasitic, and bacterial infections. Yet, despite its significance, a comprehensive review that weaves together its historical Breakthroughs and charts a course for future research is still missing. This study used bibliometric analysis to comprehensively examine the global landscape of Metronidazole research, based on publications from the Scopus database between 1960 and 2024. Data were analyzed using R software, VOS viewer, and Cite Space to explore qualitative and quantitative trends. Results: The first article published in 1960, the number of scientific publications has increased, especially after 1985. 6,172 publications were identified with 160,000 citations, showing a steady annual growth rate of 6.26%, reflecting a vibrant and steadily growing field. Notably, publication rates soared after 2024. WANG was the most prolific author, while China and the United States led in productivity, with 13% international collaboration. The Journal of Antimicrobial Chemotherapy is the leading journal in terms of publication venue. Network analysis spotlighted Metronidazole, tetracycline, and vancomycin as central antibiotics. Highly cited studies focused on Clostridium difficile infection, Helicobacter pylori eradication, and bacterial vaginosis. Over time, research themes have shifted from traditional pharmacology and microbiology to innovative areas such as nanotechnology, biosensing, computational modeling, and green chemistry. The research on Metronidazole shifting into four promising directions for future exploration: harnessing artificial intelligence to predict resistance, leveraging computational tools to uncover new applications, embracing green chemistry to minimize environmental impact, and advancing precision medicine through genetic biomarkers.

Keywords: Metronidazole, Bibliometric Analysis, VOS viewer, Scopus, Cite Space

INTRODUCTION

Metronidazole is a 5-nitroimidazole antimicrobial included on the World Health Organization's (WHO) list of essential medicines because it is effective against anaerobic infections. First synthesized in 1959 to treat Trichomonas vaginalis, the parasite that causes Trichomoniasis, metronidazole changed how this genital tract disease is managed. Today, it is still widely used to treat various parasitic and bacterial anaerobic infections[1]. Metronidazole was once thought to come from the natural compound 2-nitroimidazole Azomycin. It was first sold as Flagyl® and showed strong effectiveness against Trichomonas vaginalis[2], [3]. Metronidazole is now also used to treat Giardia lamblia, Entamoeba histolytica, and anaerobic bacteria such as Clostridium spp., Fusobacterium fusiforme, Bacteroides fragilis, and Helicobacter pylori. Because it works against many microaerophilic and anaerobic pathogens, it is still an important antimicrobial for treating infections worldwide[4], and is considered a key part of anti-infective therapy[1].

Metronidazole is also used to treat bacterial vaginosis in women. It is still the first-line treatment for both bacterial vaginosis (BV) and trichomoniasis, and is considered the drug of choice for these conditions[5][6]. Reviewing the available works published by scholars on metronidazole is crucial for understanding the global and regional advancements made by researchers over time[7]–[16]. Previous literature review covers qualitative and quantitative analysis of metronidazole [17], and others scholars covers the area of contextualizes the history and current use of metronidazole, rates of metronidazole resistance including metronidazole MDR as well as the biosynthesis of azomycin, the natural precursor of metronidazole [18], and other bibliometric analysis have focused of drug resistance in Trichomonas vaginalis where scholars were research activities were mainly focused on resistance mechanisms, prevalence, and in vitro activity[19].

Bibliometrics is a field that has emerged to offer quantitative research possibilities for vast amounts of bibliographic information. One of the primary functions of bibliometric analysis is to examine and classify scholarly publications published over time, thereby constructing systematic overviews of existing research. Such methodology is consistently used to quantify and analyse academic journals[20]–[22], and any other subject[23]–[26]Many researchers have used the concept of bibliometrics in many fields[23], [27]–[29]. The use of both the Web of Science and Scopus for quantitative analysis, identifying research hotspots, and forecasting emerging trends has been comprehensively reported in many research fields. However, no bibliometric on metronidazole research that integrates multiple disciplines, bridges existing knowledge gaps, and maps its interdisciplinary applications across diverse fields.

This study systematically analyzes existing research on Metronidazole indexed in the Scopus database to address current knowledge gaps. The primary objective is to provide a comprehensive thematic evaluation that offers scholars a clear and informed overview of Metronidazole literature and its interdisciplinary applications.

The study seeks to answer the following research questions regarding Metronidazole research:

1. What are the annual trends of Metronidazole publication according to the literature?
2. Who are the influential authors in this field, according to the literature?
3. What founds bodies, research area and countries contributed in the Metronidazole field?
4. How do the Metronidazole research themes evolve over time?

MATERIALS AND METHODS

Include The study utilized the Scopus database (https://www.scopus.com/).Scopus is a large, multidisciplinary database of peer-reviewed literature that offers several advantages, including the ability to collect publications from diverse disciplines, track citations and references, and index web pages and patents. It claims to include over 167 million relevant web pages and allows researchers to search both forward and backward in time[30]. The search strategy involved generating search formulas with relevant keywords restricted to article titles. TITLE (metronidazole*) AND (LIMIT-TO (LANGUAGE, "English")). Finally, both articles & reviews published in English between 1960 and 2024. Further details of the search methodology can be found in **Figure 1.**

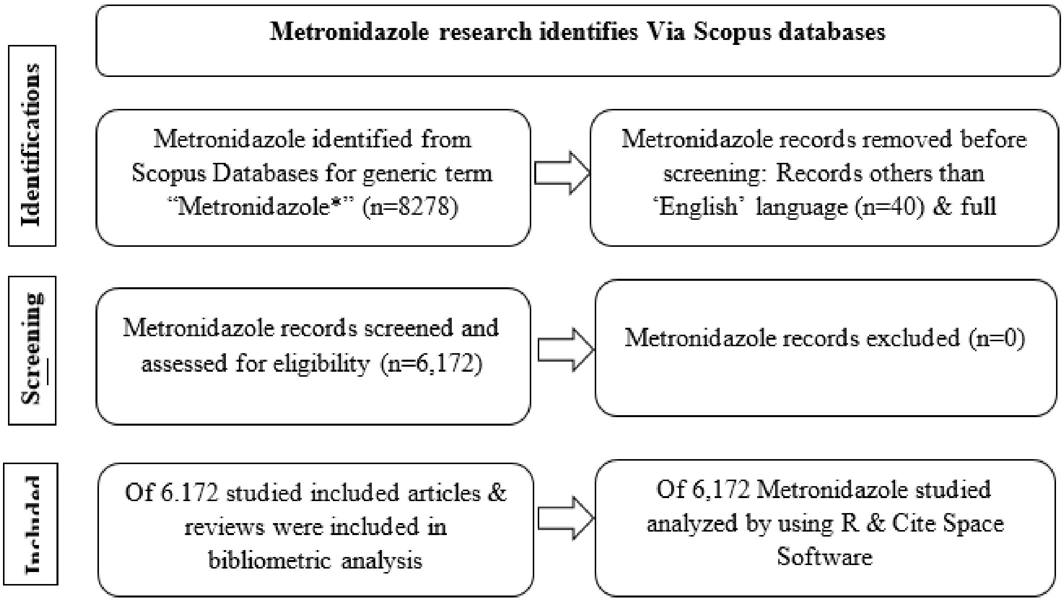

Figure 1: Metronidazole Meta data collection workflow

Inclusion and Exclusion

Inclusion criteria for the literature were as follows overall publications on Metronidazole in English where others language includes (Spanish, French, Portuguese, German, Turkish, polish, Dutch, Czech, and Chinese) were excluded, and documents type limited to articles or reviews, and Metronidazole publication published during the timespan January 1960 to December 2024. Finally, all data were extracted in a single day (7th August 2024) to ensure consistency and avoid discrepancies due to database updates.

Data Analysis

Data processing was carried out using the Bibliometrix R package (Ver 4.1.3), and its R-Biblioshiny web interface was used for analyzing bibliographic data and Thematic Evolution of reported Keyword Plus [31]. Cite Space Ver 6.4.R2 was employed for temporal and burst analysis [32]. Additionally, VOS viewer Ver 1.6.20 was use to generate a collaboration network between authors and co-occurrence patterns among countries [33]. The association between study variables and citation counts was assessed using Spearman's rank correlation coefficient. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Overview of the Metronidazole Meta Data

A total of 6172 Metronidazole articles and reviews were published between 1960 and 2024. In 1960. There was a significant negative correlation between number of articles published and the total citations per year (r=0.1802, P=0.147) **(Figure 2).**

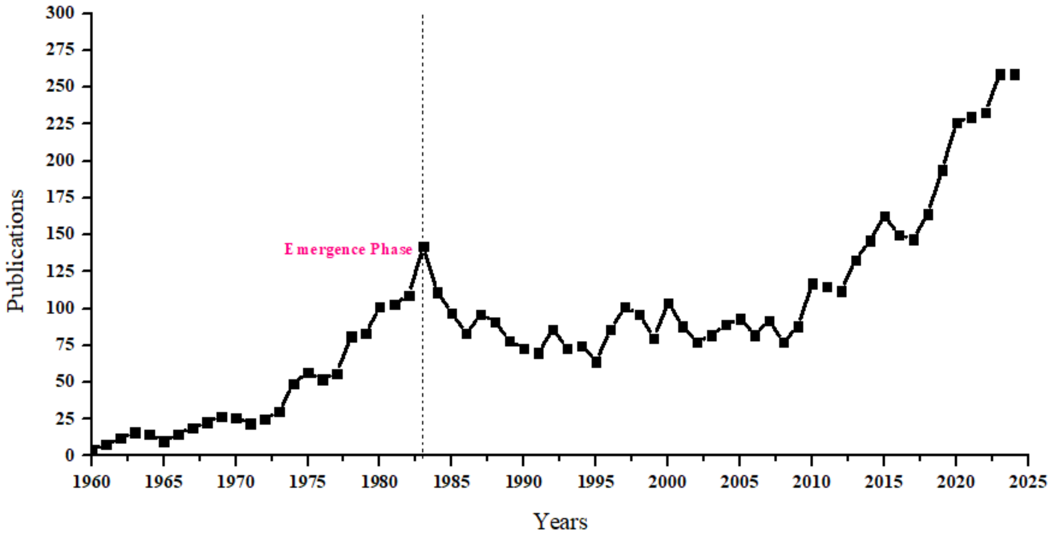

Figure 2: The annual trend of Metronidazole from 1960 to 2024.

The document's average was 26.08, with an Annual Growth Rate of 6.26% per document. The peak of research was an annually increase in 2024, with over 259 articles published. Authors' Collaboration highlighted that a total of 445 single-authored docs were reported, with 13.55 % of international co-authorships **(Table 1).**

Table 1: Summary statistics for Metronidazole metadata from 1960 to 2024.

Description	**Results**
Timespan	1960 to 2024
Sources (Journals, Books, etc.)	2009
Documents	6172
Annual Growth Rate %	6.26
Document Average Age	21.7
Average citations per doc	26.08
Document Contents	
Keywords Plus (ID)	19486
Author's Keywords (DE)	7492
Authors	
Authors	20907
Authors of single-authored docs	363
Authors Collaboration	
Single-authored docs	445
Co-Authors per Doc	4.67

International co-authorships %	13.55
Document Types	
article	6003
Review article	169

Most Influence Publication in Metronidazole

Metronidazole papers with high citation counts show their importance and usefulness in research. **Table 2** lists the most influential metronidazole papers, each with at least 446 citations. Most of these are studies.[7]–[16] that published during and after the emergence phase' of metronidazole as reported in Figure 2.

These works have played a pivotal role in defining the scope of the field. The most top cited article was published by Zar F.A. et al. (2007) on C.difficile treatment (1,126 citations) highlights metronidazole's role vs. vancomycin in severe disease[10]. On others hands articles published during the years1980s–1995s[9], [11], [14], [15] provide a historical impact of the metronidazole research with reflecting foundational of research over past periods.

In more recent year Löfmark S.(2010) [7] emphasized that metronidazole has been used to treat infections for over 45 years and remains a first-line therapy for trichomoniasis, amoebiasis, giardiasis, and anaerobic infections[7].

Table 2: Top 10 most cited documents on Metronidazole

Serial no.	Title	Authors	Total Citations
1	A comparison of vancomycin and metronidazole for the treatment of Clostridium difficile-associated diarrhea, stratified by disease severity	Zar F.A., et al, 2007	1126
2	Effect of Ranitidine and Amoxicillin plus Metronidazole on the Eradication of Helicobacter pylori and the Recurrence of Duodenal Ulcer	Hentschel E. et al,. 1993	768
3	Controlled trial of metronidazole treatment for prevention of crohn's recurrence after ileal resection	Rutgeerts P. et al, 1995	761
4	High recurrence rates of bacterial vaginosis over the course of 12 months after oral metronidazole therapy and factors associated with recurrence	Bradshaw C.S. et al, 2006	593
5	Prospective Randomised Trial of Metronidazole Versus Vancomycin For Clostridium-Difficile-Associated Diarrhoea And Colitis	Teasley David G. et al, 1983	591

6	Metronidazole to prevent preterm delivery in pregnant women with asymptomatic bacterial vaginosis	Carey J.C. et al,.2000	583
7	Reduced incidence of preterm delivery with metronidazole and erythromycin in women with bacterial vaginosis	Hauth J.C. et al, 1995	568
8	Metronidazole is still the drug of choice for treatment of anaerobic infections	Löfmark S. et al, 2010	498
9	Double blind, placebo-controlled trial of metronidazole in Crohn's disease	Sutherland L. et al,. 1991	493
10	Metronidazole Therapy for Perineal Crohn's Disease: A Follow-Up Study	Brandt L.J. et al, 1982	446

Authorship Analysis

Table 3 lists the top authors who have contributed most to Metronidazole research in Scopus databases. Of 20,907 authors in our dataset from 1960 to 2024, the table highlights those with at least twenty publications.

Most leading authors are from Chinese institutions such as Sichuan University, Harbin Institute of Technology, Kunming University of Science and Technology, the Ministry of Education of the People's Republic of China, Henan Institute of Science and Technology, Shihezi University, Guizhou Minzu University, and Beijing Normal University. Chinese researchers have played a major role in Metronidazole research since 1984 and continue to do so. Among these, WANG J from Sichuan University stands out as an influential author. Li Y from Harbin Institute of Technology and WANG X from Kunming University of Science and Technology are also leading contributors. From the United States, Graham DY and from Hong Kong, Zhang Y of The Hong Kong Polytechnic University have made significant contributions to global Metronidazole research. The figure shows the trend of collaborations among these authors. There is a significant positive correlation between the number of articles and the number of citations (r = 0.3858, 95% CI: 0.373-0.398; P < 0.0001).

Table 3: Descriptive analysis: Most prolific authors published articles on Metronidazole based on authors' level metrics in Scopus databases.

Author name	Affiliations	Country	TNP	TNC	*h_index*	PY_start
WANG J	Sichuan University, Chengdu, China	China	36	489	13	1996
LI Y	Harbin Institute of Technology, China	China	32	1531	19	2008
WANG X	Kunming University of Science and Technology, China	China	31	993	18	2007
GRAHAM DY	Department of Medicine,	United	28	2055	22	1993

	Michael E DeBakey Veterans Affairs Medical Center, Baylor College of Medicine, Houston United States	State				
WANG Y	Ministry of Education of the People's Republic of China, Beijing, China	China	27	952	16	1984
LI X	Henan Institute of Science and Technology, China	China	27	476	13	2014
LIU Y	Shihezi University, The institution will open in a new tab, Shihezi, China	China	27	715	13	1987
ZHANG Y	The Hong Kong Polytechnic University, Hong Kong	Hong Kong	27	458	13	2000
LI J	Guizhou Minzu University, China	China	25	689	13	2009
ZHANG J	Beijing Normal University, Beijing, China	China	23	399	9	2010

H-index = Hirsh-index (number of papers (h) with a citation number ≥ h), TNC = Total Number of Citations, TNP = Total Number of Publications, PY-start = Publication year start date.

Top 10 Corresponding Author's Analysis

Table 4 lists the countries with the highest numbers of Metronidazole publications and citations.

Table 4: Top 10 Corresponding Author's Countries

Country (n=91)	Corresponding Author's Countries					Most Cited Countries	
	Articles	Articles %	SCP	MCP	MCP %	Country	TNC
CHINA	477	7.7	406	71	14.9	USA	17504
USA	380	6.2	307	73	19.2	CHINA	13202
INDIA	324	5.2	278	46	14.2	IRAN	8185
IRAN	302	4.9	253	49	16.2	INDIA	5229
BRAZIL	135	2.2	103	32	23.7	BRAZIL	3151
JAPAN	105	1.7	89	16	15.2	UK	3113
UK	97	1.6	67	30	30.9	GERMANY	2620
EGYPT	90	1.5	75	15	16.7	AUSTRALIA	2575
TURKEY	80	1.3	72	8	10.0	FRANCE	2472
ITALY	67	1.1	53	14	20.9	CANADA	2317

UK: United Kingdom; TNC = Total Number of Citations, SCP: Single Country Publications; MCP: Multiple Country Publications.

This is based on the corresponding authors' affiliations. Researchers from 91 countries contributed to 20,907 author entries worldwide. Of these, 13.55% involved international co-authorship (see Tables S2 and S3).

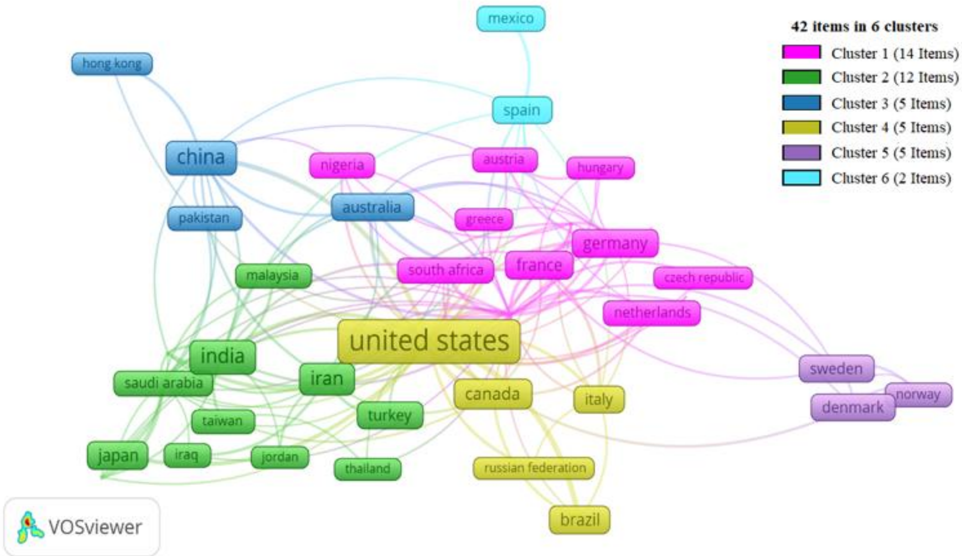

Figure 3: Co-authorship analysis by Units of country where only 46 countries were identified and display in 6 cluster with at least 25 documents reported by each country

China led in publication count, with 477 papers that represent 7.7% of the global total. The USA, India, and Iran produced similar numbers of publications. However, articles from the USA received the most citations. Figure 3 shows international collaboration and highlights six main cooperation clusters globally.

Table 5: Top 10 most relevant sources

SN.	Source (n=2009)	TNC	TNP	PY_start
1	Journal of antimicrobial chemotherapy	6103	164	1975
2	Antimicrobial agents and chemotherapy	7094	139	1969
3	Journal of clinical periodontology	4534	75	1979
4	Alimentary pharmacology and therapeutics	3131	63	1989
5	International journal of pharmaceutics	1715	49	1982
6	Journal of periodontology	2231	45	1982
7	Helicobacter	1691	43	1996
8	Scandinavian journal of infectious diseases	628	40	1971
9	American journal of obstetrics and gynecology	2210	37	1962
10	International journal of antimicrobial agents	1281	33	1992

TNP = Total Number of Publications, TNC = Total Number of Citations, PY-start = Publication year start date.

Top 10 Journals Analysis

Out of 2,009 journals indexed in the Scopus database, the Journal of Antimicrobial Chemotherapy leads with 164 publications, followed by Antimicrobial Agents and Chemotherapy with 163 publications. Together, these two journals contributed 301 articles, making up 4.88% of all metronidazole research. The high citation counts of these journals highlight the continued importance of metronidazole in chemotherapy. Additionally, the presence of specialty journals in Table S4 shows that metronidazole is used in a wide range of therapeutic areas (Table 5).

Top 10 Research Area on Metronidazole

Figure 4 shows the top 10 research areas. Over 50 % of documents were published in the field of Medicine. About 24.1% of studies were published in pharmacology, toxicology, and pharmaceutics.

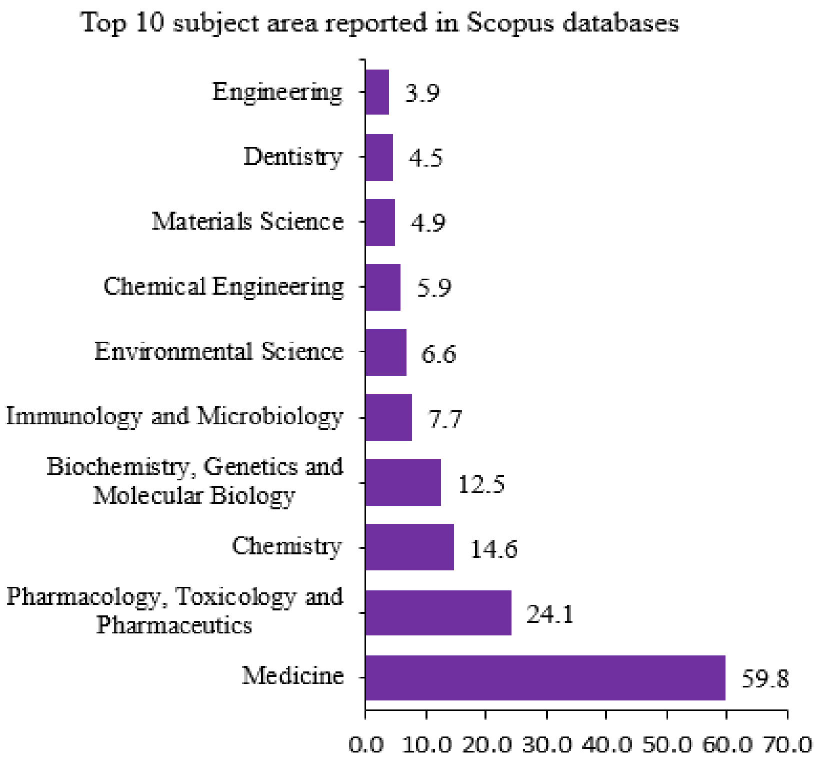

Figure 4: Top 10 Research area on Metronidazole (n=26)

Co-word Network Based on Authors' Keywords

Figure 5 displays nine keyword clusters. Cluster 1 includes seven keywords related to periodontal disease management: Amoxicillin, Antibiotics, Chronic periodontitis, periodontal disease, Periodontitis, Scaling and root planning, and Treatment. Cluster 2 also contains seven keywords and focuses on antibiotic resistance in Helicobacter pylori infections. The keywords are Antibiotic resistance, antimicrobial resistance, Clarithromycin, Eradication, H. pylori, Helicobacter pylori, and Resistance. This cluster highlights the development of resistance and the challenges in treating H. pylori, particularly with clarithromycin. Cluster 3 has six terms: Adsorption, Antibiotic, Degradation, Kinetics, Metronidazole, and Photocatalysis. Cluster 5 includes four terms, such as bacterial vaginosis, High-Performance Liquid Chromatography (HPLC), Pharmacokinetics, and Tinidazole. Cluster 6 features three keywords: Chitosan, Ciprofloxacin, and Drug delivery. These clusters highlight advancements in antibiotic delivery systems. Chitosan-based carriers may improve ciprofloxacin efficacy. Cluster 7 includes two keywords: Clostridium difficile and Vancomycin. Cluster 8 contains only Tetracycline, while Cluster 9 includes only the electrochemical sensor. These clusters suggest emerging methods for detecting antibiotics in environmental or clinical samples (Figure 5).

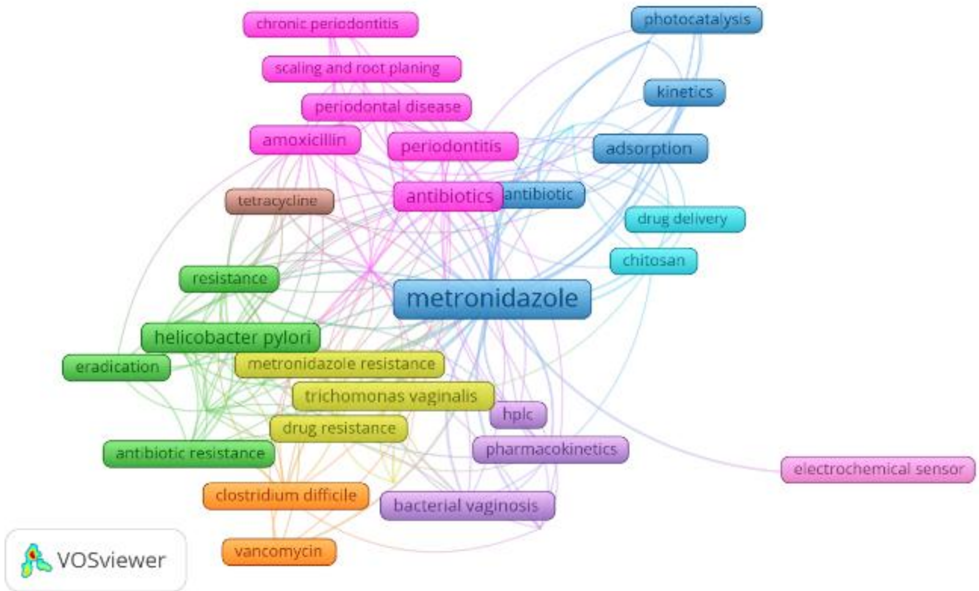

Figure 5: Co-word network based on authors' keywords.

Hot Research Subject

The figure 6 shows the hot subject index from the Scopus database divided into eight clusters. Core research focuses on Helicobacter pylori as the main pathogenic agent and antibiotic resistance as the main challenge in treatment. Other research explores chitosan as a key biomaterial for building the sensor's biocompatible matrix and electrochemical sensors as platforms for rapid, sensitive, and specific pathogen detection.

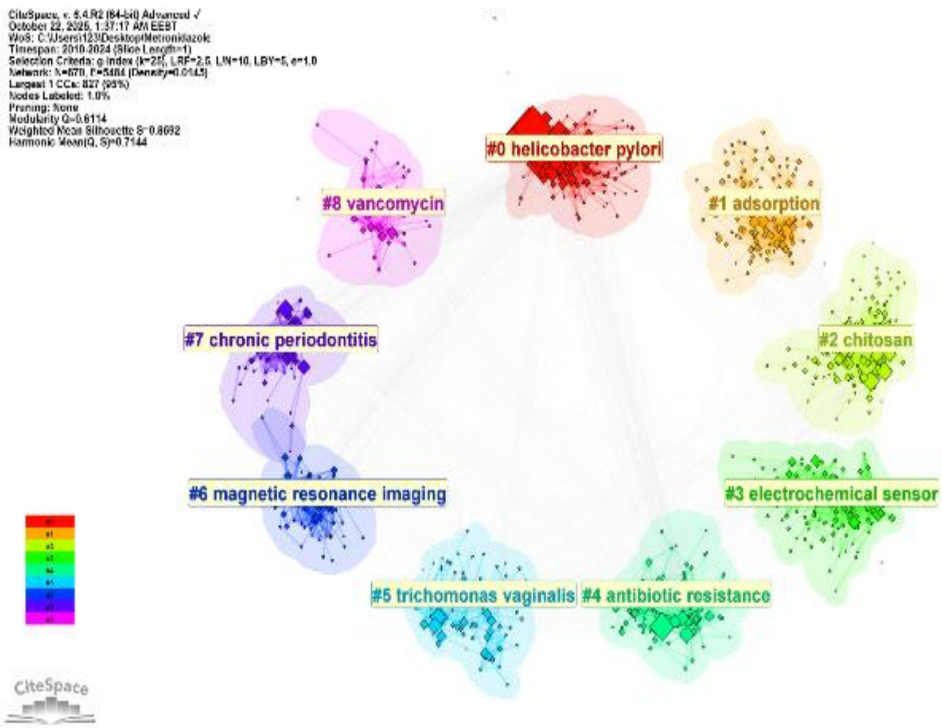

Figure 6: Analysis of the hot research subject

Other clusters examine therapeutic challenges and agents like vancomycin, as well as conditions such as chronic periodontitis. The analysis indicates that metronidazole research centers on creating chitosan-based electrochemical biosensors to detect Helicobacter pylori and its antibiotic resistance, with MRI providing possible signal amplification. The close connection between biomaterials and antimicrobials points to promising directions for future research and broader applications in infectious disease detection.

Keywords with the Strongest Citation

The figure highlights the main keywords with the strongest citation bursts. Between 2010 and 2019, most Metronidazole research focused on the clinical and biological effects of drugs, marking the early stage of pharmaceutical development and testing. In later years, Metronidazole research shifted to materials science, synthesis, and environmental uses, showing a move from basic efficacy studies to advanced material design and sustainability **(Figure 7).**

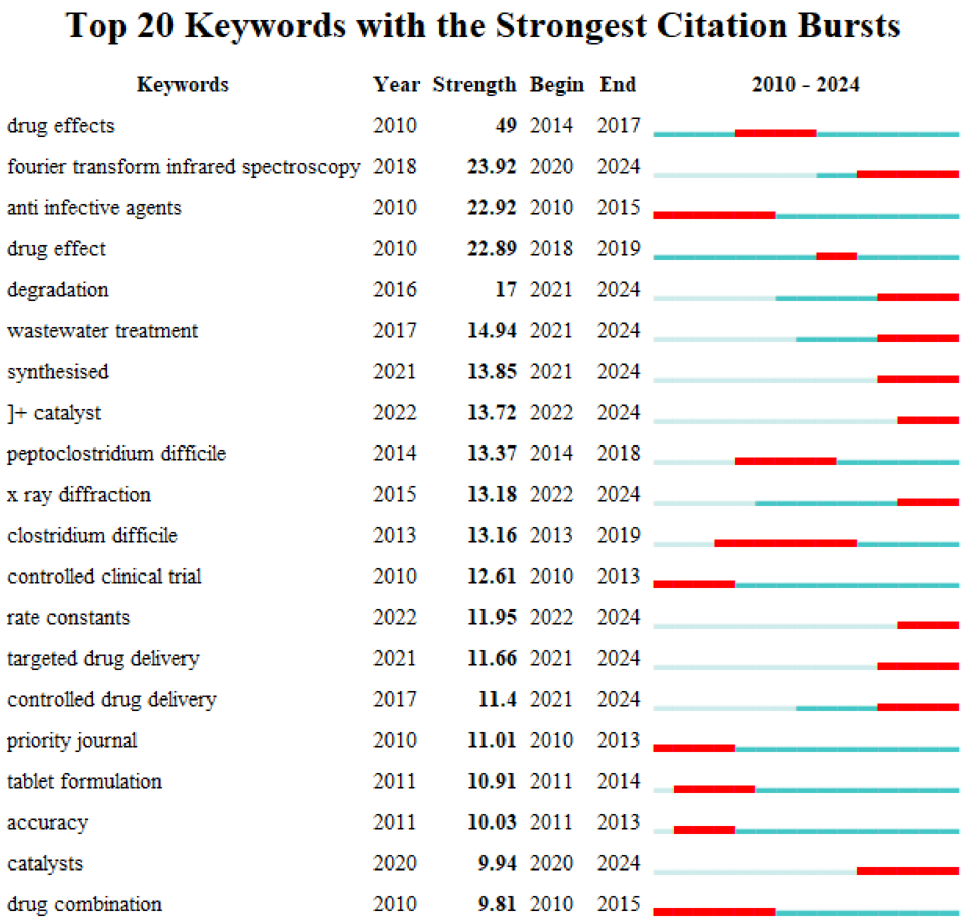

Figure 7: Top 20 Keywords with the strongest Citation Burst using CiteSpace

Evolution of Metronidazole Research

The analysis identifies nine primary scientific clusters, each with a specific focus. Cluster #0 covers adsorption in chemistry and materials science. Cluster #1 explores the role of Helicobacter pylori in serious diseases. Cluster #3 focuses on chitosan, noted for its biocompatibility and sustainability. Cluster #4 reviews the use of live animal models in medicine, pharmacology, and microbiology. Cluster #5 addresses antibiotic resistance, its causes, and new treatments for multidrug-resistant bacteria. Cluster #6 highlights vancomycin's importance in treating resistant infections. Cluster #7 examines chronic periodontitis, the oral microbiome, key pathogens, and targeted antibiotic therapies. Cluster #8 reviews advances in magnetic resonance imaging, including new contrast agents and improved diagnostics for infection and inflammation. Cluster #9 investigates bacterial vaginosis, the vaginal microbiome, etiological factors, and innovative diagnostic methods (Figure 8).

Analysis of the Top 10 Funding Organizations on Metronidazole

A total of top 10 organizations display in Table 6. China is the leading contributor, with the National Natural Science Foundation of China (NSFC) providing 40% of all project funding **(Table S5).**

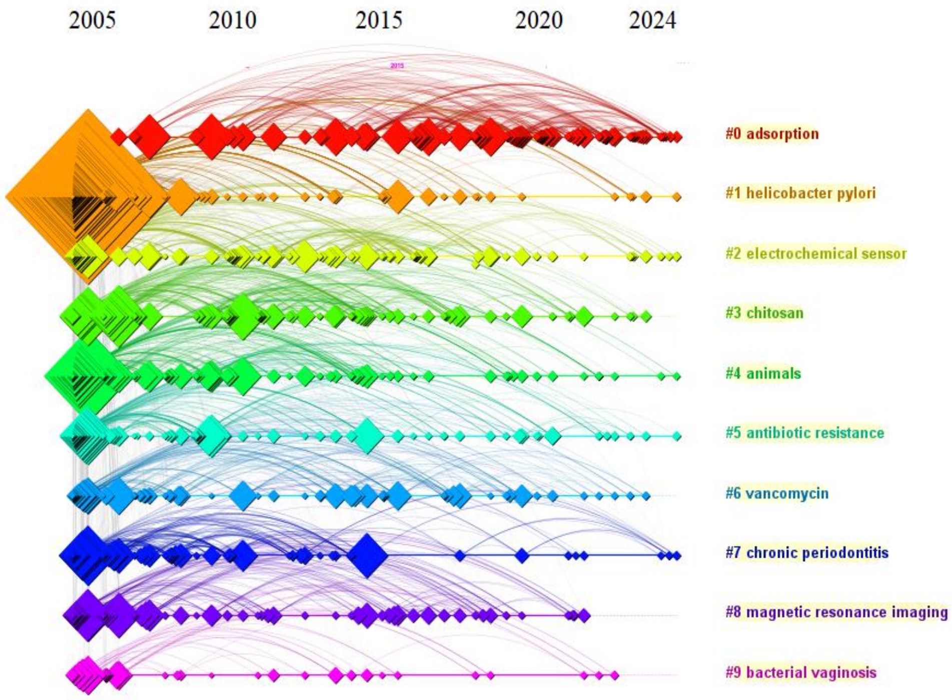

Figure 8: Thematic evolution of hot subject in Metronidazole

DISCUSSION

Since Metronidazole was first introduced, most research has used quantitative methods to study its use, with fewer studies taking a qualitative approaches. This review brings together over sixty years of research on Metronidazole, showing its continued importance as an antimicrobial agent since 1959. It covers scientific publications, highlighted new research trends and topics, examines research collaborations, and points out leading research groups. The review also looks at studies from various scientific fields. Citation analysis is used to identify the most influential articles and their impact in the academic community. Between 1960 and 2024, these articles averaged 26.08 citations each, and 13.55% included international co-authors[10]. The study determined that metronidazole and vancomycin are equally well for effective for treating mild Clostridioides difficile-associated diarrhea (CDAD), but vancomycin is superior for severe cases. Hentschel E. et al. (1993) published a prominent article with 768 citations investigating the effects of ranitidine and amoxicillin plus metronidazole on H. pylori eradication and duodenal ulcer eradicating H. pylori using a regimen that does not directly target the mucosa significantly reduces ulcer recurrence. These findings support a direct link between H. pylori infection and recurrent duodenal ulcers[11].

Most publications on metronidazole comes from China, the USA, India, and Iran [34]–[37]. China leads with 477 publications, making up 7.7%, of the total, while the USA, India, and Iran contribute similar numbers. Authors, institutions, and funding for Scopus indexing studies are mainly based in Asia and North America.

Research from these countries also tends to receive more citations, which boots research impact and journal rankings. In contrast, many African regions are underrepresented in metronidazole research need more support to increase scientific output, especially where resources are limit.

Encouraging collaboration and building partnership between organizations could help strengthen research in these areas.

The top 10 journals were selected according to their cumulative publication history. The Journal of Antimicrobial Chemotherapy, published by British Society for Antimicrobial Chemotherapy, was identified as one of the leading sources for metronidazole research. Chemotherapy published 164 articles, followed by Antimicrobial Agents and Chemotherapy of American Society for Microbiology. Collectively, these two journals contributed 301 publications, representing 4.8% of all Metronidazole researches.

The approximately half of the metronidazole research appeared in medical journals, underscoring the field's substantial global research output. These findings emphasize the significant influence of leading journals in advancing metronidazole research and highlight the widespread scientific interest in this topic.

The steady increase in publications highlights ongoing reliance on metronidazole in clinical practice and expanding research into its mechanisms, resistance, and new applications.

Our results confirm metronidazole's serves both as well-established "gold standard" treatment for anaerobic and protozoal infections [38], [39], and as a topic of ongoing scientific research. The rise in publications matches the overall increases in global antimicrobial research, as seen in bibliometric analyses of antibiotics [40], antifungals, and vaccine development [16]. Our findings also agree with those of Leitsch and Dingsdag & Hunter[6], who highlighted metronidazole's continued effectiveness despite concerns about the resistance. Inclusion on World Health Organization (WHO) essential medicines list shows its importance in clinical practice[17].

The analysis shows that China leads in research volume, producing more publications than either the United States or Europe. This trend is consistent with earlier studies in pharmaceutical sciences. China's leading role in research productivity highlights differences in both the amount and visibility of research. These results are similar to recent bibliometric studies on antimicrobial resistance and parasitology [19], further supporting the global scope of metronidazole research.

Metronidazole remains essential for the management of Clostridium difficile infection, bacterial vaginosis, and Helicobacter pylori eradication. Landmark studies comparing metronidazole with vancomycin in C. difficile infections continue to inform clinical guidelines. Recent research has identified increasing recurrence rates of bacterial vaginosis following metronidazole treatment. In H. pylori therapy, combination regimens containing metronidazole remain effective, although resistance is increasingly reported 16. Current research explores advanced applications beyond infectious diseases, including oncology [17], nanoformulation strategies for improved drug delivery [18], and use in sustainable agriculture [19]. Chemometric and spectroscopic techniques have also been employed to ensure the quality of metronidazole formulations, enhancing their relevance in pharmaceutical technology.

The thematic analysis looked at drug resistance, pharmacokinetics, and new formulations. The results show a move toward interdisciplinary research and the use of advanced. These tools [20]. These tools now facilitate drug design and assist in predicting resistance, which may extend the clinical applications of metronidazole. The thematic evolution illustrates the progression of metronidazole research over time. Research has transitioned from initial studies on adsorption and microbial susceptibility to more advanced topics. Recent research has moved into specialized and multidisciplinary areas. The evolution of interconnections demonstrates how metronidazole research has progressed and become more integrated. The map highlights a transition from early studies on adsorption and microbial susceptibility to more advanced, multidisciplinary research. The largest and most sustained research cluster focused on adsorption, which dominated the early years of metronidazole studies. This cluster reflects extensive work on adsorption mechanisms for removing metronidazole, developing formulations, and environmental remediation. As the field advanced, research expanded into clinical and biomedical areas. Key topics now include Helicobacter pylori and antibiotic resistance. These themes highlight Metronidazole's ongoing role in treating H. pylori infections demonstrates the growing concern over resistance, which is central to antimicrobial stewardship. In recent years, research has included more technological advances. Clusters such as electrochemical sensors and chitosan show how nanotechnology and polymer science are used to improve drug delivery, biosensing, and treatment results. The vancomycin and chronic periodontitis clusters also show that metronidazole is studied in combination therapies and for treating oral and periodontal diseases. Following this trend, the most recent clusters include words such as magnetic resonance imaging and bacterial vaginosis, showing new directions in research. Metronidazole research has grown steadily, starting with basic chemistry and microbiology and now involving many different areas of study.

The connections between clusters show that the field adapts to new therapies and addresses antimicrobial resistance [38][39], and a dynamic subject of ongoing scientific inquiry. The increase in publications after 2000 parallels a general rise in global antimicrobial research, consistent with bibliometric analyses in related fields such as antibiotics [40], antifungals , and vaccine development.

Our findings are consistent with those of Leitsch and Dingsdag & Hunter [6], who highlighted metronidazole's resilience even with concerns about resistance. Its place on the World Health Organization (WHO) essential medicines list shows its importance in clinical practice [17].

The analysis indicates that China leads in research volume, exceeding both the United States and Europe. This trend aligns with previous findings in pharmaceutical sciences, which show that China consistently produces more publications than either region.

China demonstrates higher research productivity than the United States. These results highlight differences in both the quantity and visibility of research. Similar patterns have been observed in recent bibliometric studies on antimicrobial resistance [18] and parasitology [19], further strengthening the global landscape of metronidazole research.

Metronidazole remains essential for the management of Clostridium difficile infection, bacterial vaginosis, and Helicobacter pylori eradication. Landmark studies comparing metronidazole with vancomycin in C. difficile infections continue to inform clinical guidelines. Recent research has identified increasing recurrence rates of bacterial vaginosis following metronidazole therapy.

In Helicobacter pylori therapy, combination regimens that include metronidazole remain effective; however, resistance is increasingly reported. Recent research highlights advanced applications beyond infectious diseases and oncology [17] , including nano-formulation strategies for enhanced drug delivery [18]and applications in sustainable agriculture [19].

Chemometric and spectroscopic methods have been utilized for quality control of metronidazole formulations, thereby expanding the drug's significance within pharmaceutical technology. The thematic analysis addressed drug resistance, pharmacokinetics, and novel formulations. Findings indicate a shift toward interdisciplinary research and the adoption of advanced analytical tools [20]. These tools facilitate drug design and resistance prediction, potentially extending the clinical utility of metronidazole.

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Thematic evolution demonstrates that metronidazole research has progressed from early studies on adsorption and microbial susceptibility to more specialized, multidisciplinary areas.

Thematic evolution highlights advancements and connections in metronidazole research, reflecting a transition from basic studies on adsorption and microbial susceptibility to more specialized, multidisciplinary Keywords such as formulation development and environmental remediation underscores metronidazole's continued relevance and the need for responsible antibiotic use. Advances in electrochemical sensors and chitosan demonstrate the application of nanotechnology and polymer science to enhance drug delivery, biosensing, and treatment outcomes. Research clusters on vancomycin and chronic periodontitis emphasize metronidazole's role in combination therapies and oral disease management. Emerging research areas include magnetic resonance imaging and bacterial vaginosis. Overall, metronidazole research has evolved from basic chemistry and microbiology to a multidisciplinary field, reflecting adaptability to new therapeutic approaches. Metronidazole remains significant in clinical practice and research, highlighting its medical value and the persistent challenge of resistance. Future research should prioritize resistance monitoring, improved nitroimidazole drug design, and the integration of artificial intelligence. Developing safer manufacturing processes is also essential to minimize environmental impact. Although this review is comprehensive, reliance on Scopus alone may have excluded studies from other databases. Incorporating additional databases in future research will ensure broader coverage and more robust conclusions. Scopus data supported the creation of evidence and gap maps for metronidazole research, illustrating trends, author contributions, and thematic evolution through visual analysis.

This study looks at how countries and researchers work together on metronidazole research, both internationally and nationally. The field covers clinical treatments, drug development, and diagnostic methods. New tools like FTIR spectroscopy and computer-aided drug design have helped move research forward. Other important topics include drug degradation and antibiotics. The findings show that using genetic and microbiome-based strategies is important for predicting resistance and improving treatment results. There is growing interest in creating new nitroimidazoles that work better and have fewer side effects. Future research should pay attention to tracking resistance, using artificial intelligence in drug design, and supporting environmental sustainability to increase the global impact of metronidazole research.

CONCLUSION

This bibliometric review documents over 60 years of metronidazole research, confirming its enduring role as a clinical cornerstone for infections like H. pylori and C. diff. Researchers have evolved the field into a dynamic, interdisciplinary domain. The analysis provides evidence that a significant geographic imbalance: China, the USA, India, and Iran lead research output, while African regions remain critically underrepresented. Thematic mapping traces a clear progression from foundational studies on microbiology and adsorption to today's advanced, multidisciplinary investigations in nanotechnology, drug delivery systems, and environmental remediation.

FUTURE RESEARCH

Future research should focus on a few key areas to o build and keep sustainable research capacity and foster equitable international collaborations. To address global inequities, researchers need to form partnerships that build research capacity in regions with fewer resources. Work should also aim to fight resistance by using AI to new or novel nitroimidazoles, improving resistance tracking with genomic and microbiome data, and creating sustainable ways to make and break down these drugs. Closing these scientific and geographic gaps will help ensure metronidazole stays effective and important for global health and it is remains a strong and responsibly used tool in the global medical resource.

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