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Kimyada Hipokloröz Asit Kullanımı: Bilimsel Literatürün Bibliyometrik Analizi

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Anahtar Kelimeler
Hipokloröz asit
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Kullanım
Bibliyometrik analiz
Bibliyometri

ÖZ

Tarihsel olarak alkoller, aldehitler, klorlu bileşikler ve hipokloröz asit gibi kimyasallar enfeksiyon etkenlerini ortadan kaldırmak veya etkisiz hale getirmek için kullanılmıştır. Bilimsel literatürü analiz etmek için sağlam bir araç olarak bibliyometrinin potansiyelini kabul ederek, enfeksiyonlarda hipokloröz asit uygulamasıyla ilgili araştırmalar üzerine bibliyometrik bir çalışma yürüttük. Bu analiz, ortaya çıkan eğilimleri belirlemeyi, ortak kalıpları ortaya çıkarmayı, iş birliklerini ve ağları incelemeyi ve gelecekteki araştırma yönlerini tahmin etmeyi amaçlamıştır. Yöntemler: Scopus veri tabanını kullanarak, 1982 ile 2024 yılları arasında "hipokloröz asit", "enfeksiyon" ve "kullanım" anahtar kelimeleriyle yayınlanan belgeleri aradık. Veri analizi R-Studio 2024.09.0 Build 375'te, bibliometrix R paketi aracılığıyla makine öğrenimi tabanlı bir bibliyometrik yaklaşım kullanılarak gerçekleştirilmiştir. Yazar ilgisi, yayınların sayısı ve kesirli katkısı analiz edilerek değerlendirilirken, Lotka yasası yazar üretkenliğini değerlendirmiştir. Bradford yasası, konuyu kapsayan çekirdek dergileri belirlemek için kullanılmıştır. Tematik manzara niş temalar, yeni ortaya çıkan temalar, motor temalar ve çekirdek temalar olarak sınıflandırılmıştır. Sonuçlar: Toplam 574 belge tespit edilmiş ve bunların çoğunluğunu (%74) orijinal makaleler oluşturmuştur. Yayınların yıllık büyüme oranı %5.08 olarak hesaplanmıştır. Genel olarak, 424 dergi birden fazla belge yayınlamıştır. İlgili yazarların çoğu Amerika Birleşik Devletleri'nde çalışmaktadır. Nötrofiller, hayvanlar ve hidrojen peroksit yeni ortaya çıkan temalar iken, hipokloröz asit, insan ve makale temel temaları temsil etmektedir. Sonuçlar/Uygulama için Uygulamalar: Enfeksiyon uzmanlarının ilgi alanları zaman içinde çeşitlenmiş ve metabolizma, reaktif oksijen metabolitleri, anti-enfektif ajanlar eklenmiştir.

The Use of Hypochlorous Acid in Chemistry: Bibliometric Analysis of Scientific Literature

Review Article

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ABSTRACT

Historically, chemicals such as alcohols, aldehydes, chlorinated compounds and hypochlorous acid have been used to eliminate or inactivate infectious agents. Recognizing the potential of bibliometrics as a robust tool for analyzing scientific literature, we conducted a bibliometric study on research related to the application of hypochlorous acid in infections. This analysis aimed to identify emerging trends, reveal common patterns, examine collaborations and networks, and predict future research directions. Methods: Using the Scopus database, we searched for documents published between 1982 and 2024 with the keywords "hypochlorous acid," "infection," and "use." Data analysis was conducted in R-Studio 2024.09.0 Build 375, employing a machine learning-based bibliometric approach through the bibliometrix R package. Author relevance was assessed by analyzing the number and fractional contribution of publications, while Lotka's law evaluated author productivity. Bradford's law was used to pinpoint the core

journals covering the topic. The thematic landscape was classified into niche themes, emerging themes, engine themes, and core themes. Results: A total of 574 documents were identified, with original articles accounting for the majority (74%). The annual growth rate of publications was calculated at 5.08%. Overall, 424 journals published more than one document. Most of the corresponding authors work in the United States. Neutrophils, animals and hydrogen peroxide are emerging themes, while hypochlorous acid, human, and article represent the basic themes. Conclusions/Applications for Practice: The interests of infection specialists have diversified over time and metabolism, reactive oxygen metabolites, anti-infective agents have been added.

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Introduction

From past to present, human beings have had to struggle with countless infectious agents. Sterilization and disinfection processes have been used to eliminate or neutralize these infectious agents. Sterilization refers to the complete elimination of microbiological agents, including spores, from inanimate surfaces by physical or chemical methods, while disinfection refers only to the elimination of infectious agents. In disinfection processes, factors such as pre-cleaning of the application area, type and intensity of infection, pH, temperature, disinfectant concentration, application time, etc. are important factors that ensure the success of disinfection (Ateş, 2020). The destruction of pathogenic microorganisms in living tissues with chemicals is called antisepsis. While heat, radiation, filtration, gas vapor and chemicals can be used for sterilization; physical methods can be used for pasteurization. Alcohols, aldehydes, chlorinated compounds and oxidizers can be used for chemical disinfection. In addition to these, chemicals such as chlorine, hypochlorous acid and sodium dichloroisocyanurate (NaDCC) can also be used for disinfection (Külekçi, 2005). Regulation of environmental factors is not enough to protect against infections; strengthening the immune system, eating a balanced diet, paying attention to personal hygiene and taking precautions during travel are also effective protection methods (Ateş, 2020).

It is usual to prefer chemicals to be used in disinfection that do not cause corrosion on the surface they come into contact with, are non-toxic and low priced. Hypochlorous acid (HOCl) is widely used as an economical and effective disinfectant against pathogenic microorganisms in all mammals since it can be produced by electrolysis of water and NaCl. Neutrophils, eosinophils, B-lymphocytes produce HOCl in response to infections with nicotinamide adenine dinucleotide phosphate oxidase bound to the mitochondrial membrane (Kettle and Winterbourn, 1997). The resulting HOCl reaches maximum antimicrobial activity at pH=3-6 (Wang et al., 2007). In aqueous solutions, HOCl dissociates into H^+ and OCl^- ions, leading to the denaturation of proteins. HOCl neutralizes viruses by generating chloramine and nitrogen radicals, as well as disrupting double-stranded DNA (Winter et al., 2008). It can be stated that the destruction of infectious agents in humans and the ecosystem they live in through HOCl is a safe method. The

use of HOCl in the prevention of infections will enable national and international collaborations, networking capabilities and organizational activities to be carried out. In this study, a bibliometric review was conducted to analyze the literature, investigate trends, patterns in collaborative research, track collaboration networks and predict future research directions between 1982 and 2024 on the use of HOCl in infections.

Methods

Today, various databases such as Web of Science (WoS), Scopus, Google Scholar, Microsoft Academic, Crossref, Dimensions and CiteSeer can be used for bibliometric analysis. Google Scholar has been compared to other databases such as WoS and Scopus by a number of researchers because it is the bibliography database most preferred by researchers. These researchers found significant overlap in terms of content, number of articles, typology, number of conferences and proceedings (Bar-Ilan, 2010; García-Pérez, 2010; Jacsò, 2010; Li et al., 2010; Aguillo, 2012). There are several reports arguing that Scopus is a strong competitor of WoS in bibliometrics. Similarly, compared to WoS, Scopus is cited as having a broader coverage and possibly a larger research area, especially in the social sciences (Li et al., 2010; Mongeon and Paul-Hus, 2016). Bass J et al. stated that Scopus is an important source for curated, high quality, bibliometric data analysis in academic research (Baas et al., 2020). Therefore, in our study, the Scopus database was used for the analysis. A comprehensive search was conducted in the Scopus database between July 1982 and September 2024. Search fields included article title, abstract and keywords. The keywords “Hypochlorous Acid”, “Infection”, “Use” were used in the database searches. Bibliographic metadata were downloaded in BibTex format and exported in Excel format in the R environment (R-Studio 2024.09.0 Build 375 software). Bibliometric analysis of the excel file obtained from the Scopus database was performed through the R-Studio program.

A bibliographic data frame was constructed, encompassing various bibliographic attributes such as authors' names, affiliations, titles, keywords, journal details, publication year, volume, issue, page numbers, editors, and citation counts. The primary results were summarized using the summary function. The data collection process included basic metrics (annual scientific output, average annual citations), sources (most relevant and cited sources, source dynamics), authors (top contributing authors, collaboration networks, country affiliations, and production by country), and documents (most cited globally, frequently used keywords, and keyword trends). The annual growth rate was calculated to evaluate the progression of scientific output over time.

The most relevant authors were evaluated based on their publication count and

contributions in co-authorship. Lotka's law was utilized to analyze author productivity, while Bradford's law identified core journals concentrating on the subject. Multi-country production (MCP) was assessed by counting documents with at least one co-author affiliated with a country different from the first author. The frequency distribution of co-authorship links for each document was analyzed using semantic similarity to disambiguate link elements. Corresponding authors' countries were used to rank the most influential nations, while country-level scientific production referred to document counts based on authors' country affiliations. The institution of the first author determined the most productive country.

A correspondence analysis and clustering approach identified shared keywords and relationships among authors and institutions across research themes. A thematic map was generated by applying a clustering algorithm to the keyword network. The map categorized mainstream themes into niche themes, emerging themes, engine themes, and core themes. Each cluster was represented as a bubble, with bubble names derived from the highest-occurring keywords. Bubble size corresponded to cluster word frequency, and bubble position was determined by cluster centrality and density. The Biblioshiny ( ) function was used to visualize all results.

Results

Overview

We analyzed a total of 574 documents, predominantly consisting of original articles (n = 424; 74%) and review articles (n = 97; 16%). From 1982 to 2024, 2571 authors contributed to these publications, with an average of six co-authors per document. The annual growth rate of 5.08% reflects a steady increase in scientific output over this period. While only four documents were published in 1982, this number rose significantly to 574 by 2024. The average number of citations per year ranged from 2 to 3 citations. The highest average total citations per article occurred in 2017, with 11,24 citations per publication, whereas 1985 recorded the lowest average, at just 0.15 citations per article.

Sources

A total of 424 journals contributed to the publications analyzed, with 30 journals accounting for approximately 33% of all retrieved documents, as illustrated in Figure 1. The Journal of Hospital Infection led with 23 articles, followed by “Plos One” with 22 articles, “Infection and Immunity” with 21, and the “Journal of Wound Care” with 18 publications. Among the top five journals, the number of publications increased significantly during the period 2012–2024 compared to 1982–2012. The most cited journal in this field was “Nutrients”, which accumulated 1151 citations.

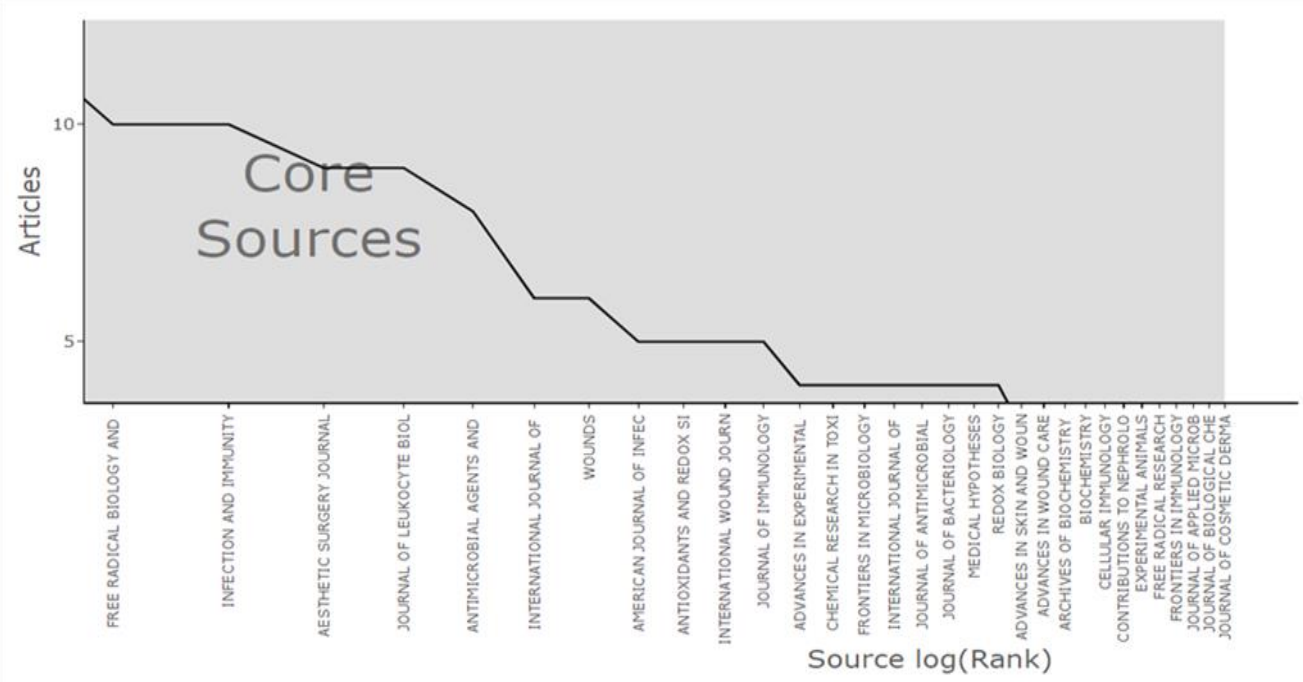
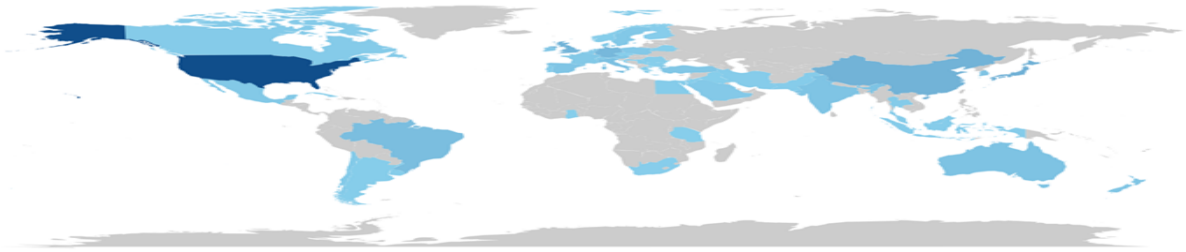


Figure 1. Source clustering through Bradford's Law

Authors, affiliations, countries

The most relevant authors were Kettle A.J., Beyenal H. and Patel R. with a fractional frequency of 16 (3.2), 13 (1.72) and 13 (1.72) documents, respectively. The frequency distribution of scientific productivity identified that there were several "core" authors (n = 287; 11.1%) who wrote at least two papers and "occasional" authors (n = 2284; 88.9%) who published only one paper. The countries of the top twenty authors are presented in Figure 2.



Country	Number of documents	Country	Number of documents
USA	542	SPAIN	35
JAPAN	111	NEW ZEALAND	33
CHINA	109	TURKEY	29
UK	98	IRELAND	28
GERMANY	87	AUSTRIA	25
BRAZIL	64	SWEDEN	25
ITALY	52	POLAND	24
AUSTRALIA	46	FRANCE	22
INDIA	41	MEXICO	22
SOUTH KOREA	39	SAUDI ARABIA	19

Figure 2. Country-specific production

Based on the Multi-Country Production (MCP) ratio, India, Turkey, and Ireland

demonstrate low levels of international collaboration, whereas the USA, New Zealand, and the United Kingdom exhibit the highest collaboration rates. As shown in Figure 2, the USA is the most prolific country, contributing 542 documents to the field. The most relevant institutions were Washington State University, University of Otago Christchurch, Louisiana State University Health Sciences Center.

Documents

The top ten most cited papers are listed in Table 1 (Schuller-Levis and Park, 2003; Barker et al., 2004; De Larco et al., 2004; El-Benna et al., 2008; Bar-Ilan, 2010; García-Pérez, 2010; Jacsò, 2010; Li et al., 2010; Aguillo, 2012; Boyce, 2016; Mongeon and Paul-Hus, 2016; Carr and Maggini, 2017; Baas et al., 2020). The most cited documents identified in the primary search strategy (keywords: "Hypochlorous Acid" and "Infection") remained prominent in the sensitivity analysis after adding the term "use." Among these, the majority were review articles. The top-ranked article, "Vitamin C and Immune Function" by Carr and Maggini (2017), received 1.151 global citations. Most of the highly cited articles (n = 10) were published between 2000 and 2017, while fewer recent articles (2018–2024) were noted, likely due to a shorter citation timeframe.

Table 1. Top ten most global cited documents

Paper	DOI	Total citation	TC per year	Normalized TC
Carr AC, 2017, NUTRIENTS	https://doi.org/10.3390/nu9111211	1151	143.875	12.802
EvanS P, 2001, BR J NUTR	https://doi.org/10.1079/bjn2000296	435	18.125	2.691
Knight JA, 2000, ANN CLIN LAB SCI		425	17.000	2.459
JaeschkE H, 2006, AM J PHYSIOL GASTROINTEST LIVER PHYSIOL	https://doi.org/10.1152/ajpgi.00568.2005	424	22.315	3.072
Schuller-Levis GB, 2003, FEMS MICROBIOL LETT	https://doi.org/10.1016/S0378-1097(03)00611-6	368	16,727	2.947
De Larco JE, 2004, CLIN CANCER RES	https://doi.org/10.1158/1078-0432.CCR-03-0760	359	17.095	3.247
Winterbourn CC, 2013, ANTIOXID REDOX SIGNAL	https://doi.org/10.1089/ars.2012.4827	355	29.583	6.145
Barker J, 2004, J HOSP INFECT	https://doi.org/10.1016/j.jhin.2004.04.021	325	15.476	2.939
E-Benna J, 2008, SEMINIMMUNOPATHOL	https://doi.org/10.1007/s00281-008-0118-3	293	17.235	4.060
Boyce JM, 2016, ANTIMICROB RESIST INFECT CONTROL	https://doi.org/10.1186/s13756-016-0111-x	292	3.444	5.620

*DOI: Digital object identifier; TC: total citations

When the terms "hypochlorous acid" and "infection" were excluded from the search strategy, keyword analysis revealed that "human," "article," and "humans" were the most frequently used terms, appearing 436, 335, and 324 times, respectively. A visualization of these keywords is presented in the word cloud shown in Figure 3.

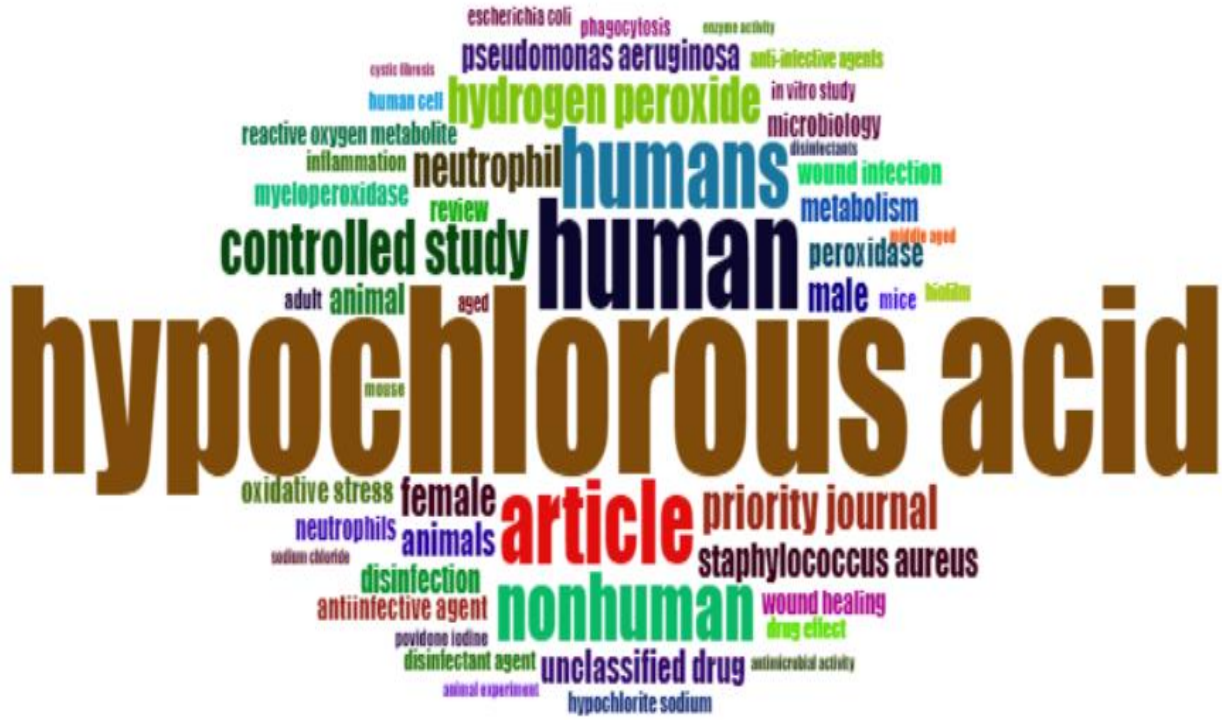


Figure 3. Word cloud

Conceptual structure

The main themes and trends are shown in Figure 4 and Figure 5. The thematic map (Figure 4) shows that neutrophils, animals and hydrogen peroxide are emerging themes, while hypochlorous acid, human, article represent the main themes. Figure 4 shows the evolution of the main thematic areas and their relationships over four different time periods: 1982-1994, 1995-2004, 2005-2014 and 2015-2024. Over time, the 'human' theme links have varied from hypochlorous acid, disinfection, microbiology, neutrophil, anti-infective agents. “Human” and “article” merged under “hypochlorous acid” in 1995-2004. The term “Taurine” initially appeared as a niche theme but began to merge with “hypochlorous acid” between 2005 and 2014. Similarly, “Anti-infective agent” emerged as a theme during 2005-2014 and continued to garner attention in the subsequent decade. The country collaboration network (Figure 6) illustrates international partnerships based on publications, with line thickness representing the strength of collaboration. The United States shows a strong connection with Japan and the United Kingdom, while European countries tend to collaborate predominantly with each other.

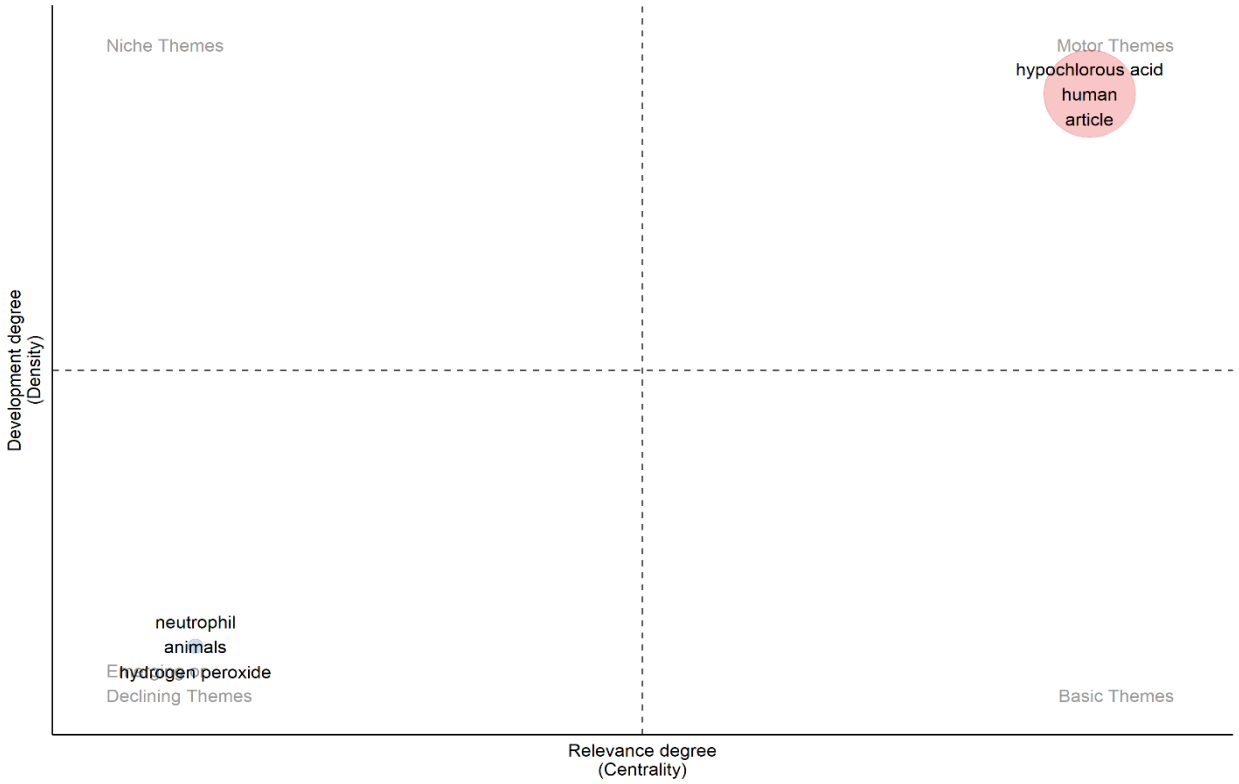


Figure 4. Thematic map

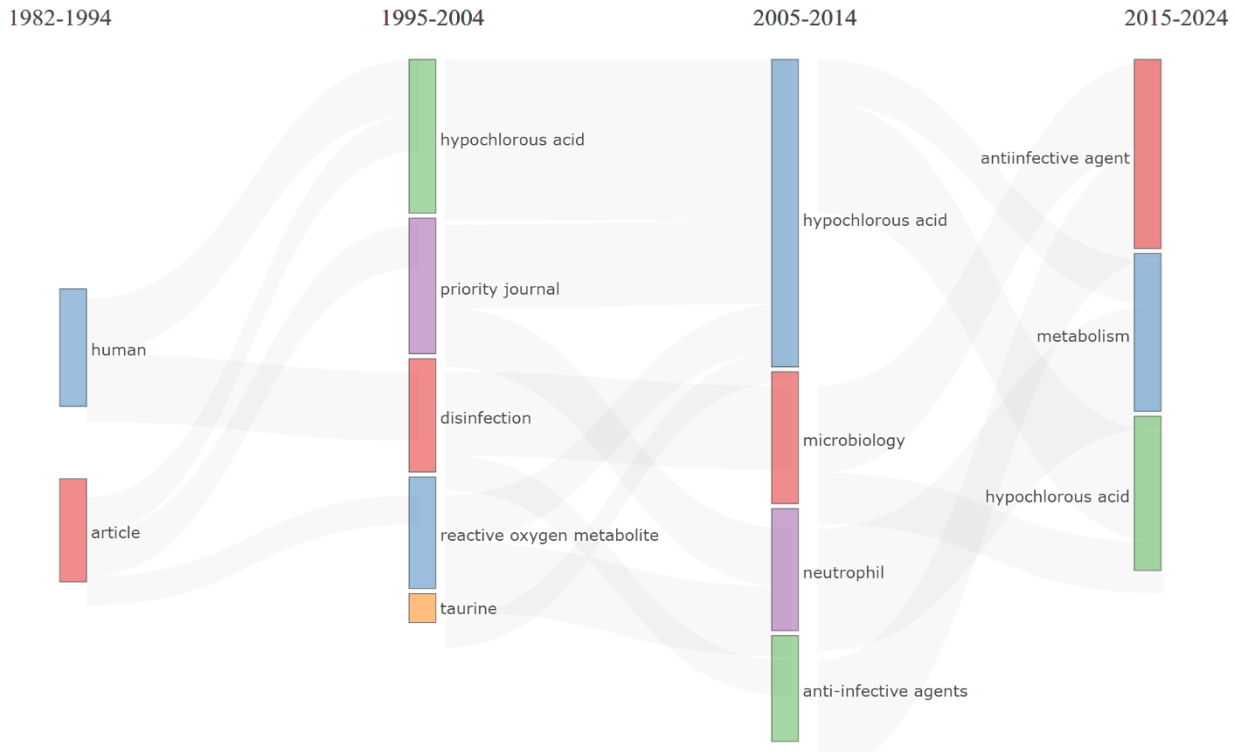


Figure 5. Thematic evolution

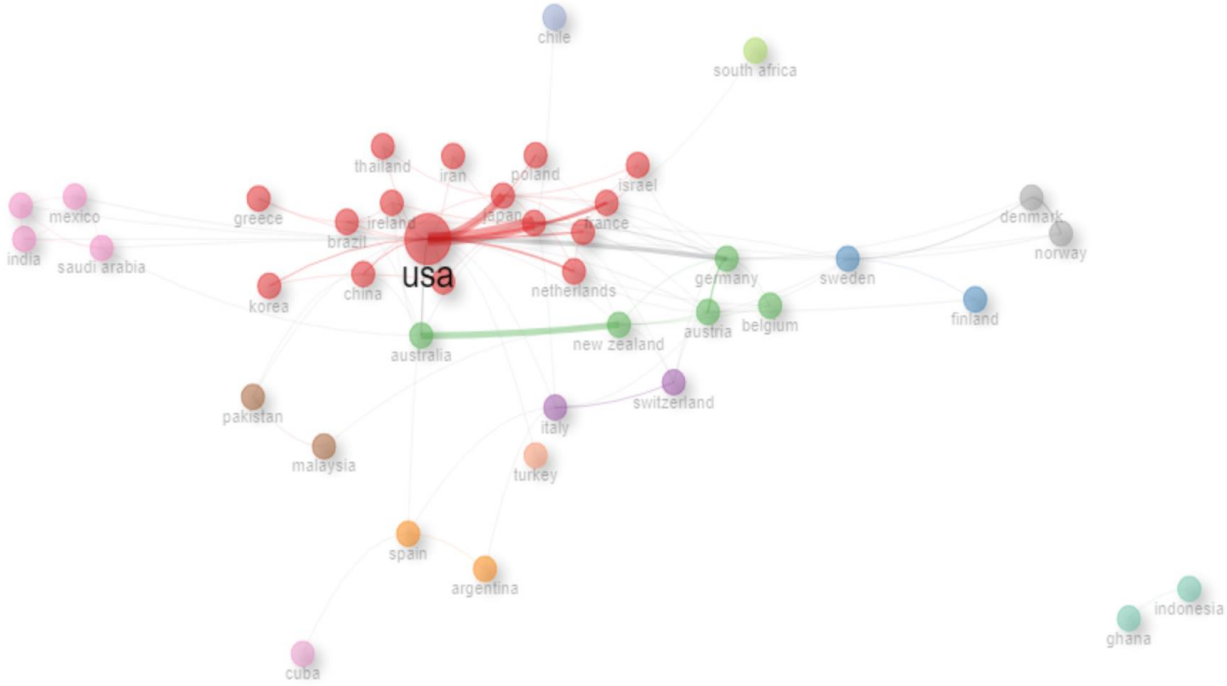


Figure 6. Collaboration network

Discussion and Conclusion

A bibliometric analysis of scientific literature on the use of HOCl in infections from 1982 to 2024 demonstrated an average annual increase in scientific production of approximately 6%, with 32 articles published up to October 2024. Among the 574 documents published during this period, 74% were original research articles, highlighting the novel contributions to this field of study. About one-fifth of all published documents come from a select group of highly ranked journals with an impact factor above 2, specializing in infection, microbiology, and immunology, as well as HOCl. Journals focused on infections saw a significant rise in the number of publications related to HOCl between 2012 and 2024, indicating growing scientific interest in neutrophils as part of a multidisciplinary approach to infection management.

The global distribution of scientific publications spans all continents, reflecting the widespread incidence of infections. Major hubs for scientific production include North America (USA, Canada, Mexico), Europe (Germany, Italy, UK, Spain), and Asia (China, India, South Korea). The USA, Canada, the UK, and China not only produce a large volume of scientific output but also maintain effective, focused collaborative networks. In contrast, continental European countries sustain high productivity and tend to foster collaboration at the European level. Scandinavian countries exhibit their own distinct collaborative networks. Other nations, such as Turkey, India, and South Korea, achieve high productivity through a more dispersed, national-level collaboration approach.

Notable academic institutions contributing to this body of research include those in North America (e.g., Washington State University, Louisiana State University Health Sciences Center, University of Iowa), Europe (e.g., Freie Universität Berlin, University of Copenhagen), and New Zealand (University of Otago Christchurch).

A limitation of this analysis is that collaboration is measured through a simple co-authorship proxy, which may not fully capture the dynamics of active scientific networks or the scientific impact of the published work. Additionally, the search strategy was designed to balance comprehensiveness and usability, which meant limiting the inclusion of broader keywords (such as "infection" or "use") to reduce potential background noise.

Some of the most cited publications between 2000 and 2024 are directly focused on infection. Articles by Carr, Evans, Knight et al (Vitamin C and Immune Function, Micronutrients: Oxidant/Antioxidant Status and Review: Free Radicals, Antioxidants, and the Immune System) addressed the use of hypochlorous acid in infections (Knight, 2000; Evans and Halliwell, 2001; Carr and Maggini, 2017). Similarly, Jaeschke 'Mechanisms of Liver Injury. II. Mechanisms of neutrophil-induced liver cell injury during hepatic ischemia-reperfusion and other acute inflammatory conditions' showed that it is possible to prevent infections by HOCl production in neutrophils (Jaeschke, 2005). Winterbourn & Kettle 'Redox Reactions and Microbial Killing in The Neutrophil Phagosome. Antioxidants & Redox Signaling' found, in line with previous researchers, that neutrophils rapidly kill most ingested microorganisms by a myeloproxidase-dependent mechanism that is almost certainly HOCl-dependent (Winterbourn and Kettle, 2013). In his study "Modern Technologies for Improving Cleaning and Disinfection of Environmental Surfaces in Hospitals," Boyce highlighted that hydrogen peroxide-based liquid disinfectants, as well as combination products containing peracetic acid and hydrogen peroxide, are effective alternatives to commonly used disinfectants. He also pointed out that electrolyzed water (hypochlorous acid) and cold atmospheric pressure plasma show promising potential for use in hospital settings (Boyce, 2016). HOCl is used in general cleaning and disinfection processes in the agricultural sector, food sector, medical sector (Park et al., 2007; Stroman et al., 2017). If HOCl is applied by fogging method, it is antibacterial and antiviral (Zhao et al., 2014). Due to the fact that HOCl is cheaper than other disinfectants and has a wide range of antimicrobial effects, different, especially medical uses have increased and diversified. One of the most important reasons for its widespread use is that HOCl can also be produced by the human defense system. Therefore, it can be said to be more natural when other cleaning and antimicrobial agents are considered (Ateş, 2020). The major limitation of the study is linked to its very nature. Bibliometric analysis provides quantitative

information with very high or low predictive potential. The quality of the data may be biased due to the lack of standardization of the elements investigated, such as their links. The use of only documents from the Scopus database is insufficient to present the current work on infection and all global research activities related to HOCl. Additionally, quantitative data, particularly citation counts, can be influenced by the number of years during which publications have had the opportunity to accumulate references. Furthermore, many studies may include updates and multiple publications, report different endpoints, or vary in their follow-up durations.

The research objectives surrounding the use of HOCl have evolved over time, reflecting the global progress in combating infections. Infection management today is based on a multidisciplinary approach that integrates various therapies, including systemic and targeted agents, as well as surgery. Over the years, the primary focus of infection specialists has shifted, incorporating factors such as safety, health-related quality of life, the sustainability of therapies, and their combination with systemic treatments, in addition to overall efficacy, effectiveness, and treatment outcomes. The data presented here offers a unique perspective on the diverse role of HOCl in infection prevention, emphasizing that technological advancements and clinical management must evolve together in a process of continuous growth and optimization.

Conflict of interest

The author declares no conflict of interest.

Author contributions

Authorsolely responsible for the entire work.

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