



Revista de Epidemiologia e Controle de Infecção

Review Article

Therapeutic potential of chalcones in combating dengue fever: bibliometric analysis

Potencial terapêutico das chalconas no combate à dengue: análise bibliométrica
Potencial terapéutico de las chalconas en la lucha contra el dengue: análisis bibliométrico

Site doi: <https://doi.org/10.17058/reci.v16i.20407>

Submitted: 05/13/2025

Accepted: 05/13/2026

Available online: 09/01/2026

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ABSTRACT

Background and Objectives: Dengue is a viral disease transmitted by the *Aedes aegypti* mosquito, characterized by rapid spread and global impact. In addition to dengue, this vector transmits Zika and Chikungunya viruses. Given the limited availability of antiviral therapies, the development of new treatments is critical. Chalcone compounds have demonstrated both larvicidal and antiviral potential, making them promising candidates in the fight against these diseases. This study aims to conduct a literature review on the therapeutic potential of chalcones in combating dengue, using bibliometric analysis. **Content:** The bibliometric analysis was performed using the Scopus database to identify both global and national publications. Data collection involved Boolean search strategies and specific filters, and the retrieved documents were analyzed using the Bibliometrix tool to assess key research trends, collaboration networks, and Brazil's contribution to the field. The analysis highlights the main research domains, author contributions, institutional affiliations, and publication trends by country. By examining publications from 2006 to 2024, the study identifies the most prominent research areas, leading authors, influential journals, and country-specific contributions. **Conclusion:** The findings reveal a growing body of scientific literature on chalcones and dengue, with pioneering studies underscoring their antiviral potential. The study also maps global collaboration networks, contributing to advances in antiviral discovery and vector control.

Keywords: *Bibliometric Study. Bibliometrix. Chalcone. Dengue. Aedes aegypti.*

RESUMO

Justificativa e Objetivos: A dengue é uma doença viral transmitida pelo mosquito *Aedes aegypti*, com rápida disseminação e impacto global. Além da dengue, esse vetor também transmite Zika e Chikungunya. Com poucas opções antivirais disponíveis, destaca-se a importância de novas terapias. Compostos de chalcona mostram potencial larvicida e antiviral, sendo promissores no combate à doença. O objetivo deste estudo é realizar uma revisão bibliográfica sobre o potencial terapêutico das chalconas no combate à dengue, utilizando análise bibliométrica. **Conteúdo:** A análise bibliométrica foi realizada utilizando a base de dados Scopus para identificar publicações globais e nacionais. A coleta de dados envolveu estratégias de busca booleana e filtros específicos, e os documentos recuperados foram analisados utilizando a ferramenta Bibliometrix para avaliar as principais tendências de pesquisa, as redes de colaboração e a contribuição do Brasil para a área. A análise destaca os principais domínios de pesquisa, as contribuições dos autores, as afiliações institucionais e as tendências de publicação específicas de cada país. Ao analisar publicações de 2006 a 2024, o estudo destaca as áreas de pesquisa mais proeminentes, os principais autores, os periódicos influentes e as contribuições por país. **Conclusão:** Os dados mostram um aumento na produção científica sobre chalconas e dengue, destacando estudos pioneiros que evidenciam seu potencial antiviral. O estudo também mapeia redes globais de colaboração, impulsionando avanços na descoberta de antivirais e no controle de vetores. **Descritores:** *Estudo Bibliométrico. Bibliometrix. Chalcona. Dengue. Aedes aegypti.*

RESUMEN

Justificación y Objetivos: El dengue es una enfermedad viral transmitida por el mosquito *Aedes aegypti*, caracterizada por su rápida propagación e impacto global. Además del dengue, este vector también es responsable de la transmisión de los virus del Zika y el Chikunguña. Dada la limitada disponibilidad de terapias antivirales, el desarrollo de nuevos tratamientos es crucial. Los compuestos de chalcona han demostrado potencial larvicida y antiviral, lo que los convierte en candidatos prometedores en la lucha contra estas enfermedades. Este estudio busca realizar una revisión bibliográfica sobre el potencial terapéutico de las chalconas en la lucha contra el dengue mediante análisis bibliométrico. **Contenido:** El análisis bibliométrico se realizó utilizando la base de datos Scopus para identificar publicaciones tanto globales como nacionales. La recopilación de datos incluyó estrategias de búsqueda booleana y filtros específicos, y los documentos recuperados se analizaron mediante la herramienta Bibliometrix para evaluar las principales tendencias de investigación, las redes de colaboración y la contribución de Brasil al campo. El análisis destaca los principales dominios de investigación, las contribuciones de los autores, las afiliaciones institucionales y las tendencias de publicación por país. Mediante el análisis de publicaciones de 2006 a 2024, el estudio identifica las áreas de investigación más destacadas, los autores principales, las revistas influyentes y las contribuciones específicas de cada país. **Conclusión:** Los hallazgos revelan una creciente producción científica sobre las chalconas y el dengue, con estudios pioneros que subrayan su potencial antiviral. El estudio también mapea las redes de colaboración global, contribuyendo a los avances en el descubrimiento de antivirales y el control de vectores. **Palabras Clave:** *Estudio Bibliométrico. Bibliometrix. Chalcona. Dengue. Aedes aegypti.*

INTRODUCTION

Dengue is a febrile illness that can range from asymptomatic infections to severe cases with multiple organ dysfunction. It is one of the most significant and rapidly growing mosquito-borne viral diseases worldwide, representing a major public health concern due to the potential risk of fatal outcomes in severe cases.¹ The primary vector of dengue is the *Aedes aegypti* mosquito, which is also responsible for transmitting other diseases, such as Chikungunya and Zika.² Dengue is caused by four distinct but closely related serotypes, designated as DENV-1, DENV-2, DENV-3, and DENV-4.³ Recently, a fifth serotype (DENV-5) was identified in Malaysia.⁴

The virus belongs to the genus *Flavivirus* within the family *Flaviviridae* and is characterized by its small, spherical structure and a single-stranded ribonucleic acid (RNA) genome of approximately 10,700 bases. Other known *Flavivirus* members include the Zika virus, West Nile virus, and encephalitis virus. Transmission occurs through the bite of the female *Aedes aegypti* mosquito. Tropical Asia and the Americas report the highest densities of dengue cases, with the disease considered hyperendemic in tropical and subtropical climates, particularly in urban and semi-urban areas.¹

In 2024, the Americas experienced the largest dengue epidemic ever recorded since surveillance began in 1980, with over 12.6 million cases, including 21,000 severe cases and 7,700 deaths, tripling the number reported in 2023.⁵ Globally, dengue affects approximately 400 million people annually, impacting around 5 billion individuals across more than 100 countries, including the United States and parts of Europe.⁴

The chalcone compound has demonstrated high efficacy against *Aedes aegypti* larvae, making it a promising foundation for future research on practical applications.² Chalcones are also notable for their remarkable anti-inflammatory properties and antiviral potential. In general, antiviral agents are used to treat a limited range of infectious diseases, to reduce viral virulence and minimize disease progression.⁶

Chalcones, which belong to the flavonoid class, serve as fundamental intermediates in the biosynthetic pathway of these metabolites, exhibit structural heterogeneity and act on various pharmacological targets. Members of the chalcone family have attracted significant scientific attention not only due to their potential for synthetic and biosynthetic production but also for their diverse biological activities.⁷

The chalcone fraction (trans-1,3-diaryl-2-propen-1-ones), which belongs to the α,β -unsaturated ketone group, consists of two aromatic rings and exhibits a wide range of antiviral, antibacterial, antifungal, and

antimalarial properties.⁸ Chalcone compounds also act as effective inhibitors involved in inflammatory processes, including cyclooxygenase (COX), lipoxygenase (LOX), interleukins (IL), and prostaglandins (PGs).⁹ Despite their various medicinal applications, their broad spectrum of bioactivity suggests a potentially promiscuous target profile. While promising, this characteristic also poses a challenge in clinical development, as it may hinder the identification of specific mechanisms of action.¹⁰

This study evaluates publication trends on chalcones, aminochalcones, dengue, and *Aedes aegypti* through a bibliometric analysis, aiming to identify and systematize relevant evidence on the therapeutic potential of chalcone molecules against the dengue vector. Using the Scopus database and the Bibliometrix R package (Biblioshiny tool), the research examines global and Brazilian scientific output, identifying growth patterns, key journals, publication hubs, and most-cited documents.

METHODS

To contextualize the topic under study, a search was conducted in the Scopus database to identify publications related to the subject, providing both a global and national perspective. The Scopus database comprises an extensive repository of abstracts and citations from the scientific literature, offering a comprehensive overview of research across various fields.

For this study, data collection was conducted using the Scopus database in October 2024, following the parameters specified below.¹¹ Different search strategies were employed, using the Boolean operator "AND" to combine all descriptors, such as ("*chalcone*" OR "*aminochalcones*") AND ("*dengue*" OR "*Aedes aegypti*"). Subsequently, after refining the search by selecting document types (articles or reviews), source type (Journal), and specific subject areas—Pharmacology, Toxicology, and Pharmaceutics (23), Biochemistry, Genetics, and Molecular Biology (12), Chemistry (6), Immunology and Microbiology (6), Medicine (5), and Multidisciplinary (2), a total of 33 documents were identified. These documents were analyzed using the Biblioshiny tool, which generated graphs and figures, enabling assessment of key aspects such as the most-cited documents, collaboration networks, leading research centers, and other relevant insights in the fields of chalcones, aminochalcones, dengue, and *Aedes aegypti*.

Considering the national context, a new search was conducted in the Scopus database, filtering only documents related to Brazil, that is, those containing at least one author affiliated with Brazilian institutions. This search yielded only five documents.

The bibliometric analysis was carried out using the Scopus database (query performed in October 2024), employing the search terms “chalcone” or “aminochalcones” in combination with “dengue” or “*Aedes aegypti*.” Filters were applied to include only scientific articles and journal reviews. In the global context, 33 documents were identified, while in the national context (Brazil), 5 documents were found.

The analysis of 33 documents published between 2006 and 2024 across 27 sources revealed an average of 9.35 years since publication and 24.79 citations per document. Among these, 22 were scientific articles, and 11 were reviews, with contributions from 208 authors, averaging 6.76 co-authors per document. This dataset, analyzed with the Bibliometrix tool in October 2024, highlights the topic's relative novelty and provides a basis for scientific mapping.

The extraction of scientific data for this study was conducted using the Scopus database in October 2024. Scopus is a widely accepted tool for data extraction and scientific research and was chosen as a reference due to its extensive collection of articles. The literature search included all available years and employed the advanced search options “title, abstract, and keywords.” Bibliometric analysis aids in understanding research traditions by employing citations, refinements, and

mapping clusters, thereby identifying research networks.

To compile and analyze the data, the Bibliometrix tool (<https://www.bibliometrix.org/>) was used. Bibliometrix is an open-source software written in the R programming language.¹²

The primary objective of this study is to provide a clear overview of the technical advancements in the field under investigation by analyzing the nature of the most frequently cited publications and highlighting Brazil's position in the global context.

RESULTS AND DISCUSSION

This bibliometric study, utilizing Scopus, was conducted in the third week of October 2024. The results of the bibliometric study were presented in the following sections, highlighting the most prominent research areas, keywords, affiliations, journals, authors and countries. Each section of the results was discussed to reveal research progress, trends, updates, and critical issues related to chalcones, aminochalcones, dengue, and *Aedes aegypti*. After applying filters, a total of 33 documents published since 2006 were identified (Figure 1). All selected works were journal articles.

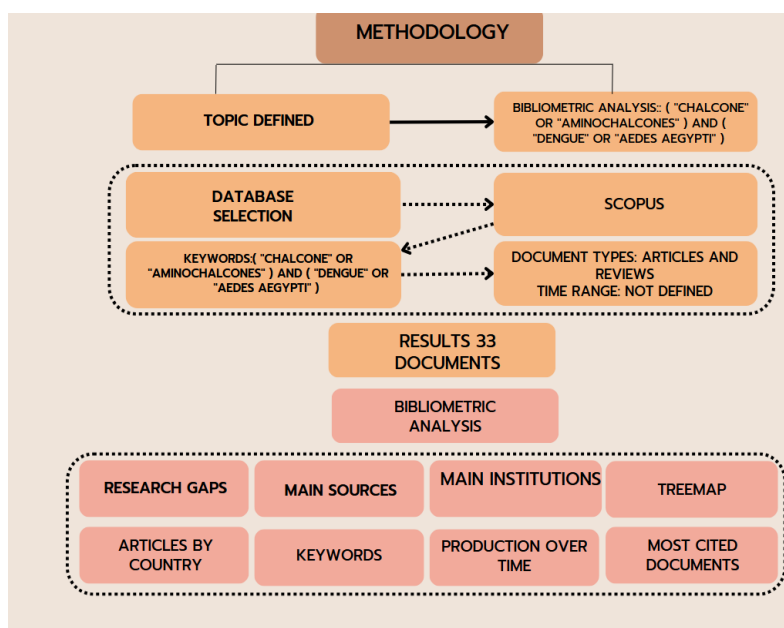


Figure 1. Search criteria and refinement conditions.

The number of citations within a field is crucial for categorizing and understanding current research trends, as well as for clearly indicating the impact of a journal or a specific publication. Thus, it is possible to provide transparent data on the most researched domains, along with current research trends.

Global context

The annual scientific production since 2006 shows a clear increase in publications in this area, particularly in recent years (Figure 2).

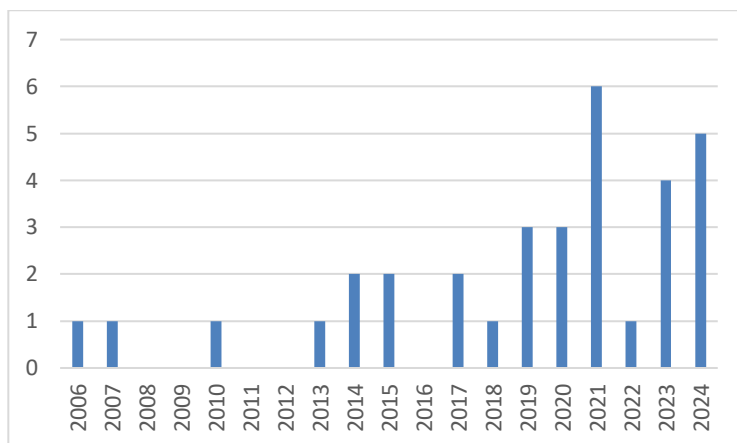


Figure 2. Annual scientific production since 2006.

The annual scientific output of India, Malaysia, the United States, and Brazil from 2006 to 2024 reveals distinct trends. India demonstrates consistent and increasing productivity, with notable acceleration from 2017 onward. Malaysia's contributions exhibit steady growth, peaking in 2019. The United States and Brazil show significant increases in output beginning around 2017 and 2019, respectively. These patterns underscore India's leading role in scientific production and reflect the expanding international collaborations involving Brazil and the United States in recent years.

The total number of publications has increased in recent years, indicating the topic's relevance and timeliness. This trend is also observed when analyzing the four countries individually.

The ten journals with the highest number of publications in the field, with *Phytotherapy Research* standing out as the leading journal, accounting for three documents.

Among the ten most relevant journals identified, *Phytotherapy Research* stood out with three articles accumulating 83 total citations since 2015 and an impact factor of 6.1. *Antiviral Research* and *Medicinal Chemistry* each contributed two articles, with 2 and 17 citations, respectively, and impact factors of 4.5 and 6.8. *Medicinal Chemistry Research* also had two articles with 28 citations since 2015, while *PLOS ONE* published two articles cited 43 times since 2019. Other notable journals with one article each included *Acta Tropica* (1 citation, 2023, impact factor 2.1), *Antibiotics* (55 citations, 2021, impact factor 4.3), *Biomed Research International* (6 citations, 2014), *Bioorganic and Medicinal Chemistry Letters* (250 citations, 2006, impact factor 2.5), and *Bioorganic Chemistry* (16 citations, 2022, impact factor 4.5). This information was obtained from the Scopus database using the Bibliometrix tool in October 2024.

There was an increase in scientific output across journals over time, with a significant rise beginning in 2014. *Antiviral Research* and *Phytotherapy Research* showed greater activity between 2016 and 2021, while *Plos One* experienced more recent growth beginning in

2020. These data indicate a growing interest from the scientific community, especially in recent years, reflecting the relevance of topics such as antivirals and bioactive compounds, possibly driven by the Covid-19 pandemic.

The analysis of the most productive authors reveals Noorsaadah Abd Rahman (Department of Chemistry, Faculty of Science, Universiti Malaya) and Rohana Yusof (UCSI University, Kuala Lumpur, Malaysia) as the two most prolific researchers in the field. Rahman N. A. and Yusof R. were the most prolific authors in the dataset, publishing 4 and 3 articles, respectively, since 2006, with high citation counts and notable h-indices. This analysis was conducted using the Scopus database and Bibliometrix tool in October 2024.

Among the key documents authored by Rahman N. A. and Yusof R., notable works include a 2006 study on cyclohexenyl chalcone derivatives published in *Bioorganic and Medicinal Chemistry Letters*, which received 250 citations; a 2013 article on dengue type 2 inhibitors in *Chemical Biology and Drug Design* with 44 citations; a 2010 synthesis study published in *Tetrahedron Letters* cited 41 times; and a 2019 work on thioguanine-based DENV-2 protease inhibitors in *PLOS ONE*, which accumulated 43 citations. This information was obtained from the Scopus database using the Bibliometrix tool in October 2024.

Regarding the collaboration network among authors, the mapping reveals distinct clusters of researchers, indicative of limited yet focused collaborative groups. The most prominent node, Rahman, N.A.A., leads a well-connected cluster, suggesting a central role in international or multidisciplinary partnerships. Smaller clusters centered around authors such as Patil, S.A., Ala, A., and Cosme, V.F., reflect more localized or institutional collaborations. The overall dispersed configuration of the clusters indicates that, although there is some cooperation among researchers, broader intergroup collaboration remains constrained. Strengthening connections across these clusters could facilitate greater knowledge exchange and amplify the impact of future research efforts.

Statistical information on research distributions across countries is beneficial as it provides insights into research productivity, influence, and collaborations. Researchers from various countries worldwide have contributed to the body of knowledge in the fields of chalcone, aminochalcones, dengue, and *Aedes aegypti*. The performance of the ten countries with the highest research output in this área.

India ranks first in terms of the number of published documents, contributing approximately 39% (13/33) of the total records in the dataset, followed by Malaysia 18,2% (6/33) and Brazil 15,2% (5/33).

The number of citations received by each country, indicating that although India has the highest number of publications, it does not hold the leading position in terms of citation count. Instead, it ranks second, preceded by Malaysia.

Chart 1. The 22 experimental articles considering the set of documents studied.

Regarding the countries with the highest citation counts in the analyzed field, Malaysia led with six articles and 378 total citations, followed by India with 13 articles and 147 citations. Romania, Italy, and Brazil contributed with fewer publications, one, one, and five articles, respectively, garnering 55, 41, and 32 citations each.

The relationship between selected experimental and review articles that address the topic in question. From these articles, the following information was extracted: (i) Name of the first author referenced in the article; (ii) Title of the article; (iii) Total number of citations per article; (iv) Journal in which the article was published; (v) Year of publication; and (vi) Country of the first author (Tables 1 and 2, respectively).

Rank	Citation	Article title	TC	Journal	Year	Country
1	Kiat et al., 2006 ¹⁶	Inhibitory activity of cyclohexenyl chalcone derivatives and flavonoids of fingerroot, Boesenbergia rotunda (L.), towards dengue-2 virus NS3 protease	250	Bioorganic & Medicinal Chemistry Letters	2006	Malaysia
2	Elkhalifa et al., 2021 ⁶	A comprehensive review on the antiviral activities of chalcones	75	Journal of Drug Targeting	2021	Qatar
3	Heh et al., 2013 ¹⁴	Rational Discovery of Dengue Type 2 Non-Competitive Inhibitors	44	Chemical Biology & Drug Design	2013	Malaysia
4	Hariono et al., 2019 ¹³	Thioguanine-based DENV-2 NS2B/NS3 protease inhibitors: Virtual screening, synthesis, biological evaluation and molecular modelling	43	Plos One	2019	Indonesia
5	Chee et al., 2010 ¹⁵	An efficient synthesis of (±)-panduratin A and (±)-isopanduratin A, inhibitors of dengue-2 viral activity	41	Tetrahedron Letters	2010	Malaysia
6	Md-Mustafa et al., 2014 ¹⁷	Transcriptome profiling shows gene regulation patterns in a flavonoid pathway in response to exogenous phenylalanine in Boesenbergia rotunda cell culture	26	BMC Genomics	2014	Malaysia
7	Kocyiğit-Kaymakçioğlu et al., 2015 ^{18b}	Discovery and structure activity relationships of 2-pyrazolines derived from chalcones from a pest management perspective	23	Medicinal Chemistry Research	2015	Turkey
8	Mottin et al., 2022 ¹⁹	Chalcones from Angelica keiskei (ashitaba) inhibit key Zika virus replication proteins	16	Bioorganic Chemistry	2022	Brazil
9	Jeon et al., 2015 ²⁰	Artocarpus altilis (Parkinson) Fosberg Extracts and Geranyl Dihydrochalcone Inhibit STAT3 Activity in Prostate Cancer DU145 Cells	13	Phytotherapy Research	2015	Republic of Korea
10	Patil et al., 2017 ²¹	Identification of Novel 5,6-Dimethoxyindan-1-one Derivatives as Antiviral Agents	10	Medicinal Chemistry	2017	India
11	Patil et al., 2019 ²²	Exploration of (hetero)aryl Derived Thierylchalcones for Antiviral and Anticancer Activities	7	Medicinal Chemistry	2019	India
12	Bharathi et al., 2014 ²³	In Vitro Larvicidal and Antioxidant Activity of Dihydrophenanthroline-3-carbonitriles	6	BioMed Research International	2014	India
13	Santos et al., 2018 ²⁴	Triazole-chalcones: Lack of antibacterial, anti-candida, and anti-dengue virus activities	6	Journal of Pharmaceutical Negative Results	2018	Brazil
14	Ganji et al., 2021 ²⁵	Design, synthesis, and evaluation of different scaffold derivatives against NS2B-NS3 protease of dengue virus	5	Medicinal Chemistry Research	2021	India
15	Parida et al., 2017 ²⁶	Novel Insights into the Molecular Interaction of a Panduratin A Derivative with the Non Structural Protein (NS3) of Dengue Serotypes: A Molecular Dynamics Study	5	Current Pharmaceutical Biotechnology	2017	India
16	Purohit et al., 2024 ²⁷	Evaluation of the inhibitory potency of anti-dengue phytocompounds against DENV-2 NS2B-NS3 protease: virtual screening, ADMET profiling and molecular dynamics simulation investigations	3	Journal of Biomolecular Structure and Dynamics	2024	India

continue

Rank	Citation	Article title	TC	Journal	Year	Country
17	Cao et al., 2023 ²⁸	A sulfonamide chalcone inhibited dengue virus with a potential target at the SAM-binding site of viral methyltransferase	2	Antiviral Research	2023	Thailand
18	Almeida e Sá et al., 2023 ²	A chalcone identified by in silico and in vitro assays possesses high larvicidal activity against <i>Aedes aegypti</i>	1	Acta Tropica	2023	Brazil
19	Lima et al., 2020 ²⁹	Antibacterial, antifungal, and antiviral activities of chalcone-bearing tetrahydropyranyl and 2, 4-dihydroxyl moieties	1	Revista Colombiana de Ciencias Químico-Farmacéuticas(Colombia)	2020	Brazil
20	Huq et al., 2024 ³⁰	Licochalcone A regulates viral IRES activity to inhibit enterovirus replication	0	Antiviral Research	2024	Taiwan
21	Musatat et al., 2024 ³¹	Harnessing high potential benzothiazole chalcones against dengue virus NS5 protein: A multi-faceted theoretical study through molecular docking, ADME, and DFT	0	Archives of Biochemistry and Biophysics	2024	Turkiye
22	Huq et al., 2024 ³⁰	Phenolic compounds of Theobroma cacao L. show potential against dengue RdRp protease enzyme inhibition by In-silico docking, DFT study, MD simulation and MMGBSA calculation	0	Plos One	2024	Bangladesh

Abbreviation: The country listed in this table corresponds to that of the first author of each article.

The 11 articles when considering the type of document to be analyzed as review Articles (Table 2).

Chart 2. The 11 articles in the review area.

Rank	Citation	Article title	TC	Journal	Year	Country
1	Ali et al., 2021 ³²	Medicinal plants: Treasure for antiviral drug discovery	57	Phytotherapy Research	2021	India
2	Marinescu, 2021 ³³	Synthesis of Antimicrobial Benzimidazole–Pyrazole Compounds and Their Biological Activities	55	Antibiotics	2021	Romania
3	Poonia et al., 2021 ³⁴	Recent Progress in 1H-1,2,3-triazoles as Potential Antifungal Agents	51	Generic placeholder image Current Topics in Medicinal Chemistry	2021	India
4	Melino & Paci, 2007 ³⁵	Progress for dengue virus diseases	41	The FEBS Journal	2007	Italy
5	Ali et al., 2021 ³⁶	A systematic review on phytochemicals for the treatment of dengue	13	Phytotherapy Research	2021	Botswana
6	Shawon et al., 2020 ³⁷	Current Landscape of Natural Products against Coronaviruses: Perspectives in Covid-19 Treatment and Antiviral Mechanism	11	Current Pharmaceutical Design	2020	Bangladesh
7	Pereira et al., 2023 ³⁸	Natural Products and Derivatives as Potential Zika virus Inhibitors: A Comprehensive Review	8	Viruses	2023	Brazil
8	Saha et al., 2024 ³⁹	Antiviral Flavonoids: A Natural Scaffold with Prospects as Phytomedicines against SARS-CoV2	2	Mini-Reviews in Medicinal Chemistry	2024	India
9	Sardari et al., 2020 ⁴⁰	Review of Phytochemical Compounds as Antiviral Agents Against Arboviruses from the Genera Flavivirus and Alphavirus	2	Current Drug Discovery Technologies	2020	Iran
10	Sobhia et al., 2019 ⁴¹	A Multi-Perspective Review on Dengue Research	1	Current Drug Targets	2019	India
11	Singh et al., 2023 ⁴²	Naturally Occurring Herbs and their Bioactive Metabolites: Potential Targets and Signaling Pathways of Antiviral Agents	0	Endocrine, Metabolic & Immune Disorders - Drug Targets	2023	India

Abbreviation: The country listed in this table corresponds to that of the first author of each article.

The analysis of the seven institutions with the highest number of related publications reveals the quantity of documents produced by each and their respective geographic locations. Universiti Malaya in Malaysia leads with five articles, followed by the Institute of Biological Sciences and the Federal University of São João del-Rei in Brazil, with three and two articles, respectively. Additionally, JAIN (Deemed-to-be

University) and the University of Hyderabad in India each contributed two publications, as did two institutions from the United States: Chicago Medical School and Rosalind Franklin University of Medicine and Science. (Source: Scopus Database, Bibliometrix tool, October 2024). The collaboration network between institutions is shown below (Figure 3).

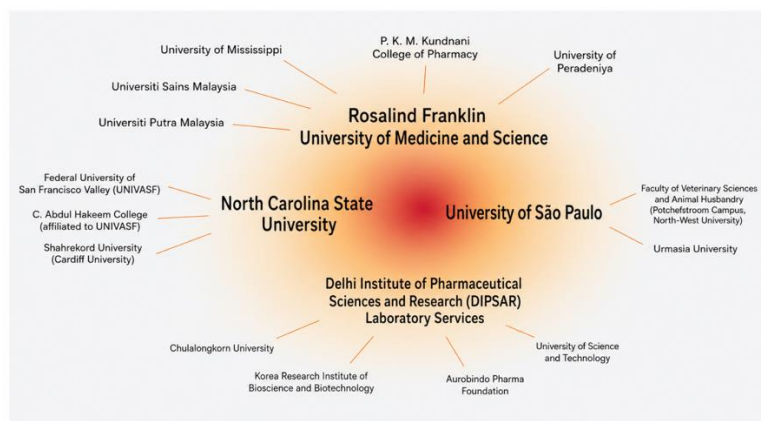


Figure 3. Collaboration between institutions.

Regarding the scientific collaboration network among countries, India stands out by occupying a central position and maintaining strong collaborations with the USA, Brazil, Malaysia, and Botswana. Regional groupings are also evident, including clusters formed by Asian, African, and European countries. The graph underscores India's central role in international research partnerships.

National Context

A focused search of the national context was conducted in the Scopus database by filtering for publications exclusively affiliated with Brazil, resulting in the identification of 5 documents. These publications not only represent local research initiatives but also demonstrate collaborations between Brazilian institutions and international partners, highlighting Brazil's increasing participation in global academic and technological networks. The identified works include studies on natural products as potential Zika virus inhibitors, larvicidal activity against *Aedes aegypti*, and antiviral, antibacterial, and antifungal activities of chalcone derivatives, involving institutions such as Universidade Federal de Minas Gerais, Federal University of San Francisco Valley, Universidade Federal de Goiás, Universidade de Brasília, and international collaborators from the United States.

This bibliometric analysis provides valuable insights into the research landscape surrounding chalcones, aminochalcones, dengue, and *Aedes aegypti*. The increasing volume of scientific output indicates a growing interest in exploring chalcones as potential antiviral agents and larvicides.

The study highlights significant contributions from India, Malaysia, and Brazil, underscoring their critical role in advancing research on mosquito-borne diseases. Additionally, the analysis identifies key collaborative networks and influential authors, emphasizing the importance of international partnerships in addressing these health challenges. In Brazil, enhanced cooperation among universities has been instrumental in strengthening national scientific progress and fostering therapeutic innovations. The use of *in silico* and *in vitro* methodologies has proven effective in identifying inhibitors of key proteins involved in viral replication, underscoring the importance of these approaches in the discovery of new therapeutic agents.

These findings contribute to a deeper understanding of research trends and offer valuable guidance for future studies and strategic investments in antiviral drug discovery and vector control initiatives.

This study conducted an analysis considering a global context, followed by a national context focusing on Brazil. Bibliometric analyses are scientific specialties and a significant aspect of research evaluation, particularly in both scientific and applied sectors.⁴³

This study presents the total number of publications per year throughout the entire period. In the years 2006, 2007, 2010, and 2013, only one publication was recorded annually. These include the study by Kiat et al., titled "*Inhibitory activity of cyclohexenyl chalcone derivatives and flavonoids of fingerroot, Boesenbergia rotunda (L.)*, towards dengue-2 virus NS3 protease", which has received 250 citations; the work by Melino & Paci, "*Progress for dengue virus diseases: Towards the NS2B-NS3pro inhibition for a therapeutic-based approach*", with 41 citations; the article by Chee et al.,

“An efficient synthesis of (±)-panduratin A and (±)-isopanduratin A, inhibitors of dengue-2 viral activity”, also with 41 citations; and the study by Heh et al., *“Rational discovery of dengue type 2 non-competitive inhibitors”*, which has received 44 citations (Figure 2).

Among the most recent publications from 2024, notable works include the study by Purohit et al.,²⁷ titled *“Evaluation of the inhibitory potency of anti-dengue phytocompounds against DENV-2 NS2B-NS3 protease: virtual screening, ADMET profiling and molecular dynamics simulation investigations”*, which has been cited three times; the publication by Saha et al.,³⁹ entitled *“Antiviral Flavonoids: A Natural Scaffold with Prospects as Phytomedicines against SARS-CoV2”*, which has received two citations; and the studies by Chuang et al.,⁴⁴ Huq et al.,³⁰ and Musat et al.,³¹ all of which have not yet been cited. Their respective titles are *“Licochalcone A regulates viral IRES activity to inhibit enterovirus replication”*, *“Phenolic compounds of Theobroma cacao L. show potential against dengue RdRp protease enzyme inhibition by in-silico docking, DFT study, MD simulation and MMGBSA calculation”*, and *“Harnessing high potential benzothiazole chalcones against dengue virus NS5 protein: A multi-faceted theoretical study through molecular docking, ADME, and DFT”*.

It is important to note that the journal with the highest impact factor is also the one with the highest number of publications. The journal that received the most citations was Bioorganic & Medicinal Chemistry Letters, with a single published document, while the first publication in this field appeared in Biomed Research International.

The documents published in Phytotherapy Research include the study by Jeon et al.,²⁰ titled *“Artocarpus altilis (Parkinson) Fosberg extracts and geranyl dihydrochalcone inhibit STAT3 activity in prostate cancer DU145 cells”*, which has received 13 citations. Another study, conducted by Ali et al.,³⁶ and titled *“A systematic review on phytochemicals for the treatment of dengue”*, has also accrued 13 citations. Additionally, the work of S. I. Ali et al.,³² titled *“Medicinal plants: Treasure for antiviral drug discovery”*, has received 57 citations to date.

The production trends of five journals over time, highlighting the cumulative number of publications indexed in Scopus. An overall increase in journal production is observed, particularly from 2015 onward. *Antiviral Research*, *Medicinal Chemistry Research*, and *Phytotherapy Research* show notable growth in publications between 2017 and 2023. *Phytotherapy Research* exhibits the most substantial rise beginning in 2020. *PLOS ONE* also shows an upward trend, beginning in 2021 and continuing to grow steadily. These results reflect heightened scientific interest and

expanding research output in the fields associated with chalcones and their derivatives in recent years.

The articles encompass a range of studies on chalcones and their derivatives, with a primary focus on their antiviral activities, including against dengue and Zika viruses. The investigations involve developing inhibitors targeting the NS3 and NS2B proteases of the dengue virus, highlighting compounds such as panduratin A, thioguanine, and sulfonamide chalcones. Additionally, other studies explore the larvicidal activity of chalcones against *Aedes aegypti* and the anticancer potential of certain chalcones. Research also includes the synthesis and evaluation of novel chalcone derivatives, their molecular interactions, and the assessment of their efficacy through in vitro and in silico assays. The scope further extends to the use of flavonoids and other natural compounds, with an emphasis on modulating key proteins involved in viral replication and immune responses. These studies, published between 2006 and 2024, reflect the ongoing efforts to investigate these compounds and their potential therapeutic applications.

Brazil is primarily connected to the United States, highlighting a significant research partnership. However, Brazil's interactions with other countries are limited, indicating restricted international collaboration beyond this axis. Regional collaboration is also evident among China, Bangladesh, and Indonesia. Some countries, such as Japan, Thailand, the United Kingdom, and Iran, appear isolated, suggesting a lower level of interaction with the main network.

Table 10 highlights documents authored by researchers from Brazilian institutions that investigated natural compounds with antiviral, antibacterial, and larvicidal activities. Among these studies is a 2023 review on natural products as inhibitors of the Zika virus, conducted by the Federal University of Minas Gerais. Also in 2023, a study on a chalcone compound with high larvicidal activity against *Aedes aegypti* was conducted by the Federal University of the São Francisco Valley and the Federal University of Cariri. In 2022, research on chalcones derived from *Angelica keiskei* was conducted by institutions including the Federal University of Goiás and the University of Brasília. Other studies, published between 2018 and 2020, explored the activity of chalcones against various pathogens, with contributions from institutions including the Federal University of São João del-Rei. These works reflect strong collaboration among several Brazilian universities and their contributions to internationally relevant research.

Limitations of the study

The results of this bibliometric study present some important limitations in terms of representativeness and generalizability. The relatively small number of

identified publications (33 articles over 18 years) restricts the ability to draw broad conclusions about global research trends on chalcones, aminochalcones, dengue, and *Aedes aegypti*. This limited volume of scientific output suggests that the topic, although growing, remains underexplored in the literature, potentially affecting the robustness and reliability of the observed trends.

The concentration of publications in a few countries, such as India, Malaysia, and Brazil, reveals a geographic imbalance in research production. This uneven distribution limits the global representativeness of the results, making it difficult to generalize the findings to other regions where research on the topic may exist but is not well indexed. Furthermore, the observed international collaboration networks were weak and restricted to a small number of countries, suggesting low levels of global cooperation in this research area.

Another relevant limitation of the results lies in the citation analysis. The most cited studies tend to be older, while more recent publications, particularly those from 2023 and 2024, have not yet had time to accumulate significant citations. This time-dependent factor affects the interpretation of research impact and visibility. Additionally, the dominance of a small group of authors and institutions in the publication output indicates a concentration of research efforts, which may not fully capture the diversity of scientific perspectives on the subject.

CONCLUSION

The bibliometric analysis showed growing scientific interest in the application of chalcones and their derivatives in the context of dengue fever and the control of *Aedes aegypti*, although the total number of publications was limited. In summary, the studies identified suggest that these molecules constitute a promising class of bioactive compounds, with potential for application both as antiviral agents targeting essential dengue viral proteins and as larvicides to control the transmission vector. The predominance of in silico and in vitro experimental approaches reinforces the relevance of these methodologies in the search for new therapeutic alternatives. However, the lack of preclinical and clinical trials limits the translational evidence for practical applications. There was also a geographical concentration of scientific production and limited international collaboration networks, indicating the need for greater integration between research groups to expand and accelerate the development of chalcone-based drugs. Therefore, the results of this review help clarify the current research landscape of chalcones and their derivatives as molecules eligible for future, more

robust prophylactic and treatments against dengue and related arboviruses.

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AUTHORS' CONTRIBUTIONS

Danúbio Andrade Bezerra Farias contributed to the literature review, drafting of the abstract, introduction, methodology, discussion, interpretation and description of results, preparation of tables, conclusions, and revision. **Luiz Francisco Wemmenson Gonçalves Moura** contributed to the methodology, discussion, interpretation and description of results, conclusions, and revision. **Natália do Vale Canabrava** contributed to the literature review and description of results. **Francisco Leandro Fernandes Sampaio** contributed to the literature review and description of results. **José Ítalo Magalhães de Sousa** contributed to the literature review and description of results. **Vânia Marilande Ceccatto** contributed to project administration, methodology, interpretation and description of results, conclusions, revision, and statistics. **Márcia Maria Mendes Marques** contributed to the methodology, interpretation and description of results, conclusions, and revision. **Maria Izabel Florindo Guedes** contributed to project administration, methodology, interpretation and description of results, conclusions, revision, and statistics.

All authors approved the final version to be published and are responsible for all aspects of the work, including ensuring its accuracy and integrity.

Please cite this article as: Farias DAB, Moura LFWG, Canabrava NV, Sampaio FLF, Sousa JIM, Ceccatto VM, Duque MMMM, Guedes MIF. Therapeutic potential of chalcones in combating dengue fever: bibliometric analysis. Rev Epidemiol Control Infect [Internet]. 2026 Sep. 1; 16. Available from: <https://seer.unisc.br/index.php/epidemiologia/article/view/20407>