© 2025 Journal of Pharmacy & Pharmacognosy Research, 13 (6), 1932-1946, 2025
ISSN 0719-4250
https://jppres.com

DOI: https://doi.org/10.56499/jppres25.2352_13.6.1932

Review

Unveiling the anticancer potential of mangroves: A 2005−2024 bibliometric analysis

[Descubriendo el potencial anticancerígeno de los manglares: un análisis bibliométrico 2005-2024]

Didi N. Illian[1,2], Lalu M. Irham[3], Fitri Deliana[4], Fiska M. Wardhani[5], Wirawan Adikusuma[6], Arini S. Al-Mustaqimah[7,8], Hayssam M. Ali[9], Refi Ikhtiari[10], Muhammad F. Lubis[11], Mohammad Basyuni[8,12*]

[1]Department of Pharmacy, Faculty of Mathematics and Natural Sciences, Universitas Syiah Kuala, Banda Aceh, Indonesia.
[2]Doctoral Program of Pharmaceutical Sciences, Faculty of Pharmacy, Universitas Gadjah Mada, Yogyakarta, Indonesia.
[3]Faculty of Pharmacy, Universitas Ahmad Dahlan, Yogyakarta, Indonesia.
[4]Department Pharmacy, School of Health and Clinical Sciences, University of Western Australia, Perth, WA, Australia.
[5]Faculty of Medicine, Universitas Pendidikan Indonesia, Bandung, Indonesia.
[6]Research Center for Vaccine and Drugs, National Research and Innovation Agency (BRIN), South Tangerang, Indonesia.
[7]Faculty of Public Health, Universitas Sumatera Utara, Medan, Indonesia.
[8]Center of Excellence for Mangrove, Universitas Sumatera Utara, Medan, Indonesia.
[9]Department of Botany and Microbiology, College of Science, King Saud University, Riyadh, Saudi Arabia.
[10] Department of Biomedical Sciences, Faculty of Medicine, Universitas Prima Indonesia, Medan, 20118, Indonesia.
[11]Department of Pharmaceutical Biology, Faculty of Pharmacy, Universitas Sumatera Utara, Medan, Indonesia.
[12]Department of Forestry, Faculty of Forestry, Universitas Sumatera Utara, Medan, Indonesia.
*E-mail: m.basyuni@usu.ac.id

Abstract

Context: Demographic forecasts suggest that new cancer cases may reach 35 million by 2050, underscoring the need for innovative, regionally tailored control strategies. Mangroves have yielded multiple potential anticancer compounds in recent years; however, no bibliometric investigation of their role has been conducted.

Aims: To provide a bibliometric overview of research on anticancer activity from mangroves.

Methods: Keywords related to anticancer activity and mangroves to search the Scopus database were used. VOSviewer and Biblioshiny were used for further analysis.

Results: Eighty-seven studies on cancer-associated mangroves were identified, with an annual growth rate of 9.89%. Publications have increased since 2005, reaching a peak in 2020. The top five countries and organizations in productivity were China, India, Indonesia, Malaysia, and Thailand. The top five affiliations were Guangdong Medical University, Shanghai Jiao Tong University, Sun Yat-Sen University, Wuhan University, and Guangdong University of Technology. Wu X, Liu J, Basyuni M, and Tang X were the most prolific authors. Five primary study themes emerged: antineoplastic activity, mangroves, apoptosis, cell proliferation, and protein expression.

Conclusions: Recent results indicate a growing interest in the anticancer potential of mangrove bioactive chemicals, which regulate multiple protein expression signaling pathways. This increase in study emphasizes the significance of mangrove bioactive compounds in cancer research.

Keywords: anticancer activity; bibliometrics; biblioshiny; mangrove; VOSviewer.

Resumen

Contexto: Las previsiones demográficas sugieren que los nuevos casos de cáncer podrían alcanzar los 35 millones para 2050, lo que subraya la necesidad de estrategias de control innovadoras y adaptadas a cada región. Los manglares han producido múltiples compuestos anticancerígenos potenciales en los últimos años; sin embargo, no se ha realizado ninguna investigación bibliométrica sobre su papel.

Objetivos: Proporcionar una visión general bibliométrica de la investigación sobre la actividad anticancerígena de los manglares.

Métodos: Se utilizaron palabras clave relacionadas con la actividad anticancerígena y los manglares para realizar búsquedas en la base de datos Scopus. Se utilizaron VOSviewer y Biblioshiny para un análisis más detallado.

Resultados: Se identificaron 87 estudios sobre manglares asociados al cáncer, con una tasa de crecimiento anual del 9,89 %. Las publicaciones han aumentado desde 2005, alcanzando su punto máximo en 2020. Los cinco países y organizaciones con mayor productividad fueron China, India, Indonesia, Malasia y Tailandia. Las cinco principales afiliaciones fueron la Universidad Médica de Guangdong, la Universidad Jiao Tong de Shanghái, la Universidad Sun Yat-Sen, la Universidad de Wuhan y la Universidad Tecnológica de Guangdong. Wu X, Liu J, Basyuni M y Tang X fueron los autores más prolíficos. Surgieron cinco temas de estudio principales: actividad antineoplásica, manglares, apoptosis, proliferación celular y expresión proteica.

Conclusiones: Resultados recientes indican un creciente interés en el potencial anticancerígeno de los compuestos bioactivos del manglar, que regulan múltiples vías de señalización de la expresión proteica. Este aumento en el estudio enfatiza la importancia de los compuestos bioactivos del manglar en la investigación del cáncer.

Palabras Clave: actividad anticancerígena; bibliometría; biblioshiny; manglar; VOSviewer.

ARTICLE INFO
Received: January 13, 2025.
Accepted: September 12, 2025.
Available Online: October 4, 2025.

AUTHOR INFO
ORCID: 0000-0003-3559-1106 (DNI) 0009-0001-5758-0689 (ASAM)
0000-0002-0091-4887 (LMI) 0000-0001-6801-4263 (HMA)
0009-0008-4098-766X (FD) 0000-0003-0824-6657 (RI)
0000-0003-3023-1574 (FMW) 0000-0001-9651-904X (MFL)
0000-0001-9165-690X (WA) 0000-0003-1120-8571 (MB)

Abbreviations: DE: Descriptor; ID: Index Keywords; NCDs: noncommunicable diseases.

INTRODUCTION

According to current global statistics, there will be nearly 20 million new cancer diagnoses and approximately 10 million cancer deaths in 2022. Based on demographic projections, the annual number of new cancer cases is expected to reach 35 million by 2050, representing a 77% increase from 2022 (Bray et al., 2024). Cancer constitutes a significant societal, public health, and economic challenge in the 21st century, accounting for about one in six mortalities (16.8%) and one in four deaths (22.8%) from noncommunicable diseases (NCDs) globally. The condition accounts for 30.3% of global premature deaths from NCDs in individuals aged 30 to 69 years, ranking among the top three causes of mortality in this demographic across 177 of 183 nations. Cancer not only impedes the enhancement of life expectancy but also incurs significant societal and macroeconomic expenses that differ by cancer type, geographic location, and gender (Bray et al., 2021; Chen et al., 2023).

A mangrove is a unique ecosystem distributed along the coastline of the tropical and subtropical regions globally, whose specific saline environment provides a distinctive ecosystem and fulfills numerous important biological and ecological functions (Liang et al., 2024; Prabhu and Guruvayoorappan, 2012). Anticipating the advancement of novel anticancer treatment methodologies and the identification of anticancer metabolites, this entails an investigation into essential resources regarding the research status of mangrove-derived natural products that warrant further development, highlighting the significant therapeutic advantages of mangrove-derived pharmaceuticals in the management of clinical cancers (Illian et al., 2021; 2022). Moreover, these strategies may provide significant insights and direction for developing targeted anticancer pharmaceuticals, which could be the focus of future research (Jia et al., 2020; Luo et al., 2022).

No bibliometric analysis has established the research trend for cancer therapies involving mangroves. Consequently, the present study provides context and a review of the diverse research on the medicinal potential of mangroves. The covered aspects encompassed keywords or co-occurrences, publication counts, geographical territories/countries, authors, institutions/organizations, and journals. A bibliometric study and visualization were performed to provide a detailed knowledge map of mangroves for medicinal applications. Moreover, the data were employed to pinpoint prospective areas for further investigations.

Bibliometric research is a powerful approach for examining qualitative and quantitative data from publications on a particular subject. This strategy is commonly used in the medical field and helps identify novel and emerging research areas. Notably, there is a lack of bibliometric studies that explicitly target the utilization of natural substituents in cancer treatment. This study aimed to analyze the scientific literature on the anticancer effectiveness of mangroves against cancer and identify research trends over the previous twenty years. The present study is the first to utilize VOSviewer to analyze articles on the impact of mangroves on cancer. Here, related authors, groups, nations, and journals were tracked using a systematic bibliometric analysis of the Scopus database, highlighting important subjects and areas of unmet research in this field. This study aims to provide a comprehensive overview of the findings and expectations regarding mangroves as potential anticancer agents. Accordingly, the present study was designed to map global research on mangrove-derived anticancer agents from 2005 to 2024, to identify influential contributors, thematic hotspots, and knowledge gaps.

MATERIAL AND METHODS

Source of documents

The Scopus database, accessed on October 21, 2024, was used to retrieve relevant publications in this study. It was chosen over other databases, such as PubMed and Google Scholar, due to its broader catalog coverage and significance (Falagas et al., 2008). It also offers features such as sorting by country, author, journal, and institution, as well as document citation counts, serving as a metric of scientific merit (Hirsch, 2005).

Indicators of bibliometric

The study examined several bibliometric indicators, including publication growth, commonly used author keywords, citation analysis (including highly cited articles), the top ten productive organizations, highly cited countries, and the top ten active journals. We sourced data on citations and country productivity from Scopus, a platform that tracks publication citations and annual paper output per country.

Keywords and search strategy

To find relevant articles, we searched articles published between 2005 and 2024 using the keywords ("mangrove" AND (cancer OR tumor)) within the article title, abstract, and keywords. We also conducted Scopus literature searches using an English search string.

Data extraction and bibliometric parameters

The study employed a range of bibliometric criteria to assess the quantity, distribution, and ranking of publications. These included the number of publications produced annually, the distribution of publications by subject area, and the ranking of contributing authors based on the number of publications they had produced. Furthermore, the research identifies frequently cited articles and displays the spread of publications by country and institutional affiliation. It also explores the types of documents, the main languages used, and the distribution of publications. All essential metadata from the publications, including titles, authors, affiliations, abstracts, keywords, journal names, publication years, and citation counts, were extracted during the data processing. The search and screening process was illustrated in Fig. 1.

Data management and data analysis

Data management and analysis were performed using VOSviewer version 1.6.16 (van Eck and Waltman, 2010) and the Biblioshiny R package (Aria and Cuccurullo, 2017), free software tools for creating and visualizing bibliometric maps. These methods enabled the creation of a comprehensive overview of the current research state, including the identification of co-authorship networks, keyword co-occurrence, and citation trends. VOSviewer was used to generate indicators, including a visualization of author distribution and a network visualization map of the most frequently used keywords among authors. The Biblioshiny R package was used to generate specific indicators, including annual scientific production on mangroves, the top ten contributing authors, the distribution of country-based publications, the distribution of affiliation-based publications, and a visualization of international collaboration among countries. This investigation was a secondary analysis based on the currently existing dataset and did not directly involve human participants or experimental animals. Therefore, ethics approval was not required in this paper. The annual growth rate (AGR) was calculated with the following formula [1].

The H-index, or Hirsch index, is a metric proposed by *Hirsch JE* in 2005 to quantify an individual's scientific research output. It is defined as the highest number *h* such that *h* papers have at least *h* citations each (Hirsch, 2005).

RESULTS

Types of documents and primary information

Eighty-seven documents, identified from 2005 to 2024 and involving approximately 421 authors globally, were extracted from the Scopus database. Analysis revealed that 76 (87.36%) were research articles and 7 (8.05%) were review papers. Other document types included errata (2, 2.30%), book chapters (1, 1.15%), and conference papers (1, 1.15%). Only English documents were chosen. Detailed data on the retrieved documents are presented in Table 1.

Analysis of global publication trends

Fig. 2 depicts the number of cancer-associated mangrove scientific publications that increased worldwide from 2005 to 2024. The number of publications increased annually, with the most significant increase occurring in 2014–2015 (150.00%), 2019–2020 (85.71%), and 2016–2017 (60.00%). This result suggests a growing global interest in cancer-associated mangrove research, particularly in health management.

Authors' country and authors' affiliation of publications

Many authors from China contributed to their affiliation with the Guangdong Medical University. According to Fig. 3, China has the highest number of citations (536 times), followed by India (421 times), Malaysia (195 times), United Kingdom (112 times), and Thailand (59 times). As shown in Fig. 4, the top five organizations with the most publications on cancer-associated mangrove research were Guangdong Medical University, with 43 publications, followed by Shanghai Jiao Tong University (23 publications) and Sun Yat-Sen University (22 publications). Furthermore, Wuhan University and Guangdong University of Technology have 20 and 19 publications, respectively.

Analysis of the core journal of cancer-associated mangrove research

The peer-reviewed journals that published the most articles on cancer-associated mangrove research during 2005–2024 are presented in Fig. 5. The top four were Marine Drugs (H index 159 and S.J.R 2023 0.88), Journal of Cancer (H index 81 and S.J.R 2023 0.9), Oncology Reports (H index 115 and S.J.R 2023 0.86), and Scientific Reports (H index 315 and S.J.R 2023 0.9). This evidence supported the position of these journals as leading scientific publications worldwide.

$$\text{AGR (\%)} = \frac{\text{Ending number of publications} - \text{Starting number of publications}}{\text{Starting number of publications}} \times 100 \quad [1]$$

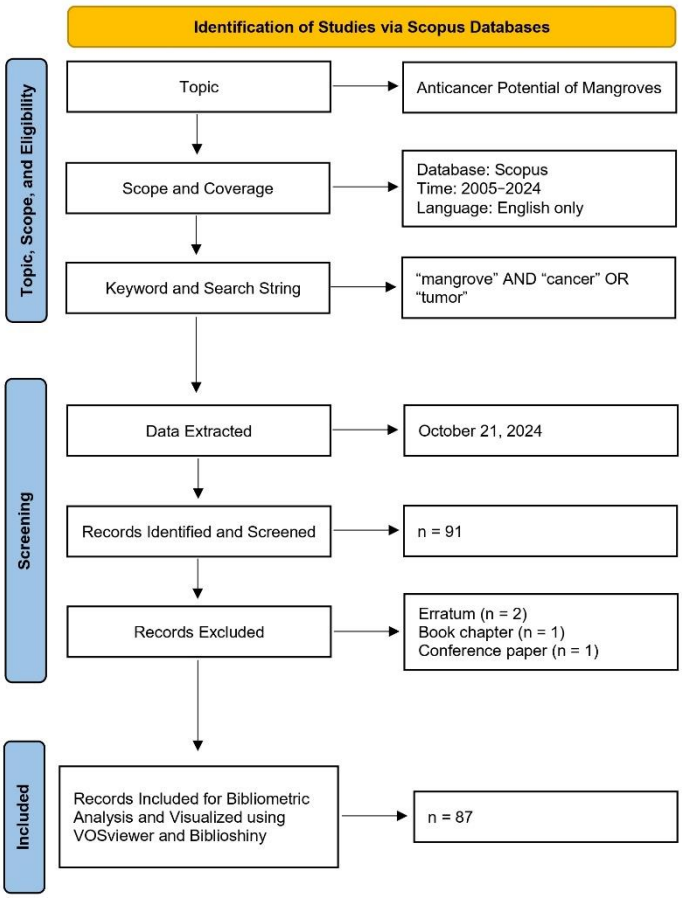

Figure 1. Flowchart diagram of the search process methodology.

Table 1. Main information of cancer-associated mangrove publications during 2005–2024.

Description	Results	Description	Results
Main information about data		**Authors collaboration**	
Timespan	2005-2024	Single-authored docs	1
Sources (Journals, Books)	67	Co-Authors per Doc	6.26
Documents	87	International co-authorships %	29.89
Annual Growth Rate %	9.89	**Document types**	
Document Average Age	5.56	Article	76
Average citations per doc	17.94	Review	7
References	3938	Erratum	2
Document contents		Book chapter	1
Keywords Plus (ID)	1441	Conference paper	1
Author's Keywords (DE)	293		
Authors			
Authors	421		
Authors of single-authored docs	1		

Note: DE (Descriptor) refers to the keywords provided directly by the authors, while ID (Index Keywords) represents the automatically generated keywords by the database to index the document's content.

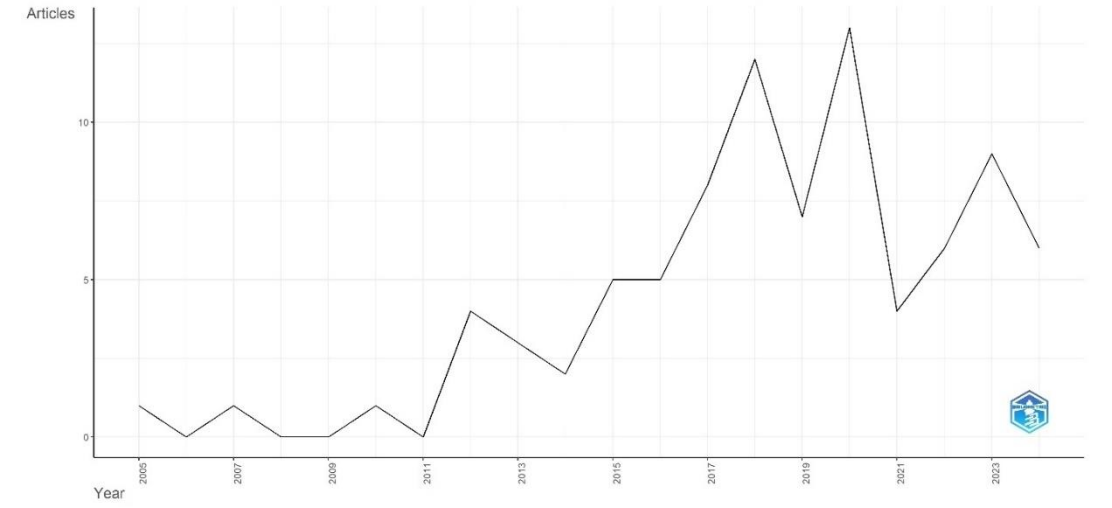

Figure 2. Annual scientific production of cancer-associated mangroves based on the number of publications (2005–2024).

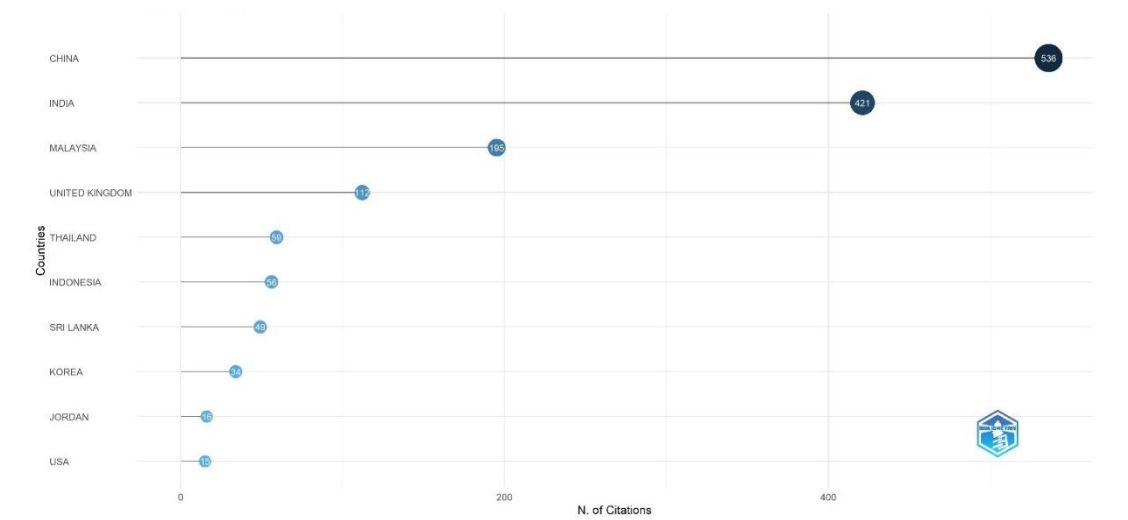

Figure 3. The most cited countries in cancer-associated mangrove research from 2005 to 2024.

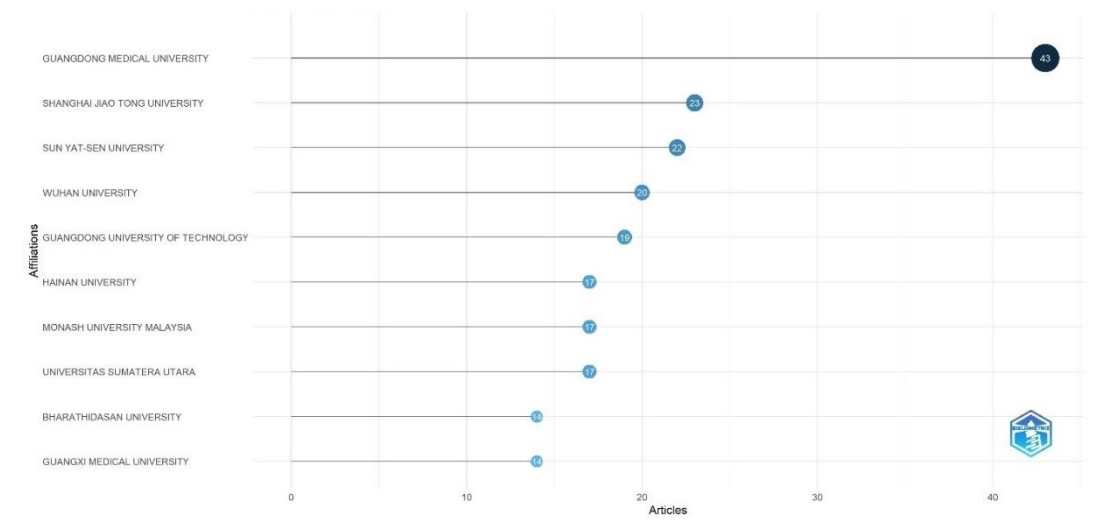

Figure 4. Distribution of organization-based publications on cancer-associated mangrove research during 2005–2024.

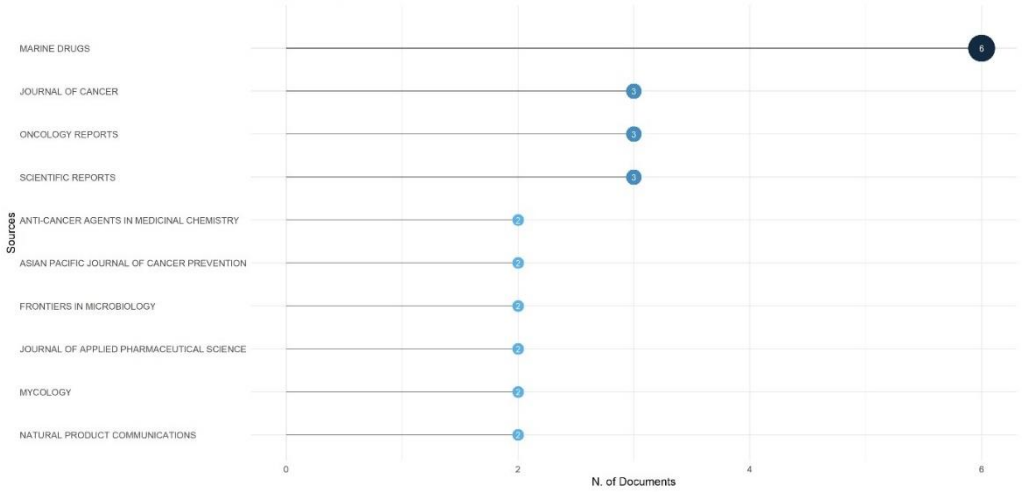

Figure 5. Top ten journals with the most publications on cancer-associated mangrove research during 2005–2024.

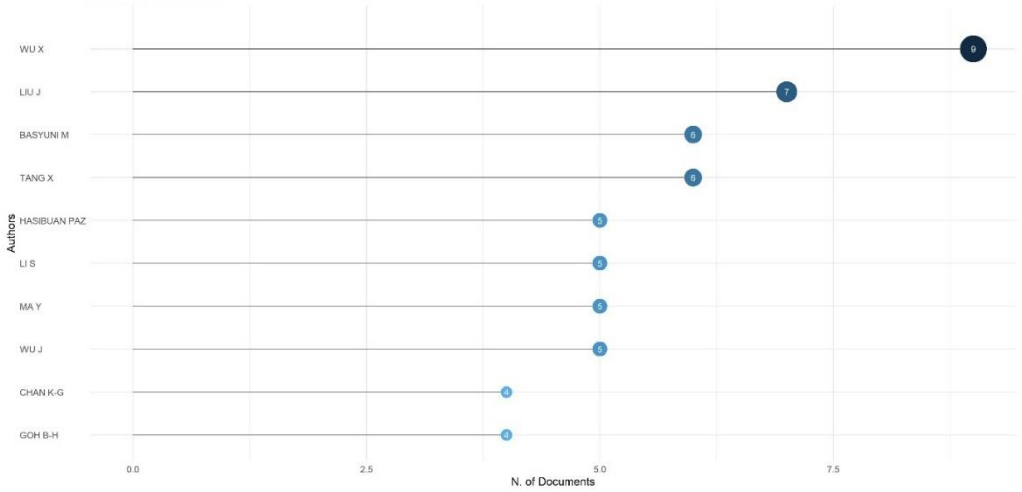

Figure 6. Distribution of the most productive authors on cancer-associated mangrove research during 2005–2024.

The most productive authors and citation analysis in the cancer-associated mangrove publication

The top ten contributors of articles published in Scopus journals regarding cancer-associated mangrove research were presented in Fig. 6. *Wu X* has published nine works, making this author the most prolific. *Liu J* authored seven publications, followed by *Basyuni M* and *Tang X* with six papers, respectively. Additionally, Hasibuan PAZ, Li S, Ma Y, and Wu J have each published five works, while *Chan KG* and *Goh BH* have published four additional articles.

All the authors have contributed a large number of cancer-associated mangrove works. Moreover, a summary of the ten most valuable publications by citation weight was displayed in Table 2.

Top countries of authors based on publication number of cancer-associated mangrove publications

Fig. 7A displays the top five countries based on the number of publications of cancer-associated mangrove research. China published the most articles concerning mangroves, with 255 publications (47.66%), followed by India with 92 (17.20%), Indonesia with 40 (7.48%), Malaysia with 26 (4.86%), and Thailand in fifth position with 17 publications (3.18%).

Biblioshiny's country collaboration map (Fig. 7B) reveals that China and India collaborated with the most countries (n = 16 and n = 11, respectively), confirming their status as the top two countries with the most collaborations. Moreover, India's collaboration with Saudi Arabia yielded the highest number of documents (n = 5 articles), followed by Malaysia's collaboration with Pakistan and Thailand, which each had three articles.

Table 2. Top ten most valuable publications of cancer-associated mangrove by citation weight.

Rank	Authors	Title	Year	Journal	Total citations
1	Uddin SJ, Nahar L, Shilpi JA, Shoeb M, Borkowski T, Gibbons S, Middleton M, Byres M, Sarker SD.	Gedunin, a limonoid from *Xylocarpus granatum*, inhibits the growth of the CaCo-2 colon cancer cell line in vitro.	2007	Phytotherapy Research	112
2	Ser HL, Palanisamy UD, Yin WF, Chan KG, Goh BH, Lee LH.	*Streptomyces malaysiense* sp. nov.: a novel Malaysian mangrove soil actinobacterium with antioxidative activity and cytotoxic potential against human cancer cell lines.	2016	Scientific Reports	78
3	Law JWF, Ser HL, Duangjai A, Saokaew S, Bukhari SI, Khan TM, Ab Mutalib NS, Chan KG, Goh BH, Lee LH.	*Streptomyces colonosanans* sp. nov. is a novel actinobacterium isolated from Malaysian mangrove soil exhibiting antioxidative activity and cytotoxic potential against human colon cancer cell lines.	2017	Frontiers in Microbiology	76
4	Cyril N, George JB, Joseph L, Raghavamenon AC, VP S.	Assessment of antioxidant, antibacterial, and anti-proliferative (lung cancer cell line A549) activities of green-synthesized silver nanoparticles from *Derris trifoliata*.	2019	Toxicology Research	69
5	Saeed AF, Su J, Ouyang S.	Marine-derived drugs: Recent advances in cancer therapy and immune signaling.	2021	Biomedicine & Pharmacotherapy	66
6	Tan LTH, Chan KG, Pusparajah P, Yin WF, Khan TM, Lee LH, Goh BH.	Mangrove-derived *Streptomyces* sp. MUM265 as a potential source of antioxidant and anti-colon cancer agents.	2019	BMC Microbiology	65
7	Jain S, Dwivedi J, Jain PK, Satpathy S, Patra A.	Medicinal plants for treatment of cancer: A brief review	2016	Pharmacognosy Journal	64
8	Tian S, Saravanan K, Mothana RA, Ramachandran G, Rajivgandhi G, Manoharan N.	Anticancer activity of biosynthesized silver nanoparticles using *Avicennia marina* against A549 lung cancer cells through ROS/mitochondrial damages.	2020	Saudi Journal of Biological Sciences	59
9	Prabhu VV, Guruvayoorappan C.	Anti-inflammatory and anti-tumor activity of the marine mangrove *Rhizophora apiculata*.	2012	Journal of Immunotoxicology	53
10	Yuan G, Hong K, Lin H, She Z, Li J.	New azalomycin F analogs from mangrove *Streptomyces* sp. 211726 with activity against microbes and cancer cells.	2013	Marine Drugs	45

Network visualization of co-occurrence

The VOSviewer tool was used to visualize the keywords from the 87 papers in the Scopus database about cancer-associated mangrove research themes. This endeavor helps identify the novelty of the research within this domain. The visualization, by default, depicted the keywords as circles (Fig. 8). The diameter of each circle represented the frequency and importance of a keyword. Colors were allocated to each circle according to its cluster to enhance clarity (van Eck and Waltman, 2010). A minimum occurrence threshold of five was established for keywords. The search yielded 1,628 terms, of which only 107 met the inclusion criteria. Following the analysis, five groupings were established as research trends on cancer-associated mangroves, each represented by distinct colors.

Fig. 8A presents the network visualization describing five clusters and their linkages among the examined areas. Each cluster consisted of numerous keywords with a high agreement in the map structure. For each cluster, specific high-frequency occurrences of keywords signified the research topic pursued in the past. The five clusters with the highest frequency of occurrence in their respective keywords were identified.

The first cluster included the following terms: human (55 occurrences), controlled study (41 occurrences), mangrove (39 occurrences), and human cell (38 occurrences). Besides, the second consisted of unclassified drugs (40 occurrences), non-human (37 occurrences), antineoplastic activity (36 occurrences), and antineoplastic agents (35 occurrences) as the most prominent common terms. The third cluster comprised apoptosis (30 occurrences), cell viability (22 occurrences), and cell line–tumor (19 occurrences). Meanwhile, the fourth cluster comprised humans (32 occurrences), chemistry (19 occurrences), and cell proliferation (17 occurrences).

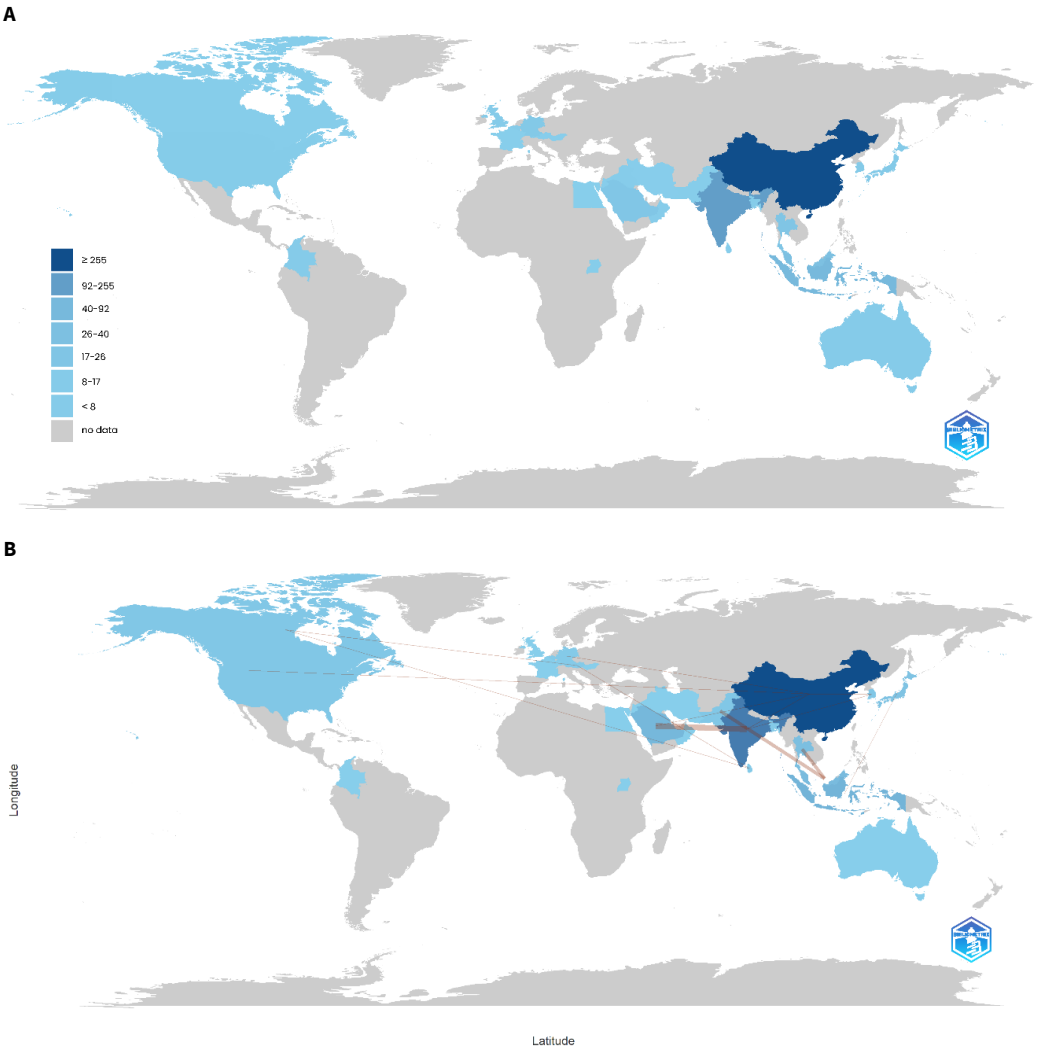

Figure 7. Distribution of country-based publications **(A)** and collaboration map **(B)** on cancer-associated mangrove research worldwide during 2005–2024.

Furthermore, the fifth cluster includes *in vitro* study (14 occurrences), protein expression (12 occurrences), and the A-549 cell line (9). Detailed information regarding the result of cluster analysis is documented in Table 3.

Moreover, the color gradient in Fig. 8B indicates brighter colors for terms with recent publications and darker colors for those with earlier publications. This data highlights that "antineoplastic activity," "mangrove," "colon cancer," "apoptosis," and "cell proliferation" were among the earlier terms in the publication trend. At the same time, "gene expression," "mtt assay," "*in vitro* study," "molecular docking," and "western blotting" were more recent terms.

We derived several key findings upon analyzing the specific connections among variables to elucidate the trends and novelty in cancer-associated mangrove research (Fig. 9). Fig. 10 illustrates the association between the terms "mangrove" (Fig. 9A), "apoptosis" (Fig. 9B), and "cell proliferation" (Fig. 9C) with other specific domains of anticancer downregulation mechanism-involved proteins, including "protein bcl-2," "protein bax," and "caspase 3."

DISCUSSION

Major findings

Several comprehensive studies have investigated the potential of natural compounds in cancer therapy. This review aims to be a pioneering effort to understand the research trends related to chemical compounds from mangroves between 2005 and 2024. One primary objective is to identify key contributors, including authors, institutions, countries, and academic journals, who have made significant advancements in this field. A bibliometric analysis uncovered prominent themes, subjects, and knowledge gaps in existing literature.

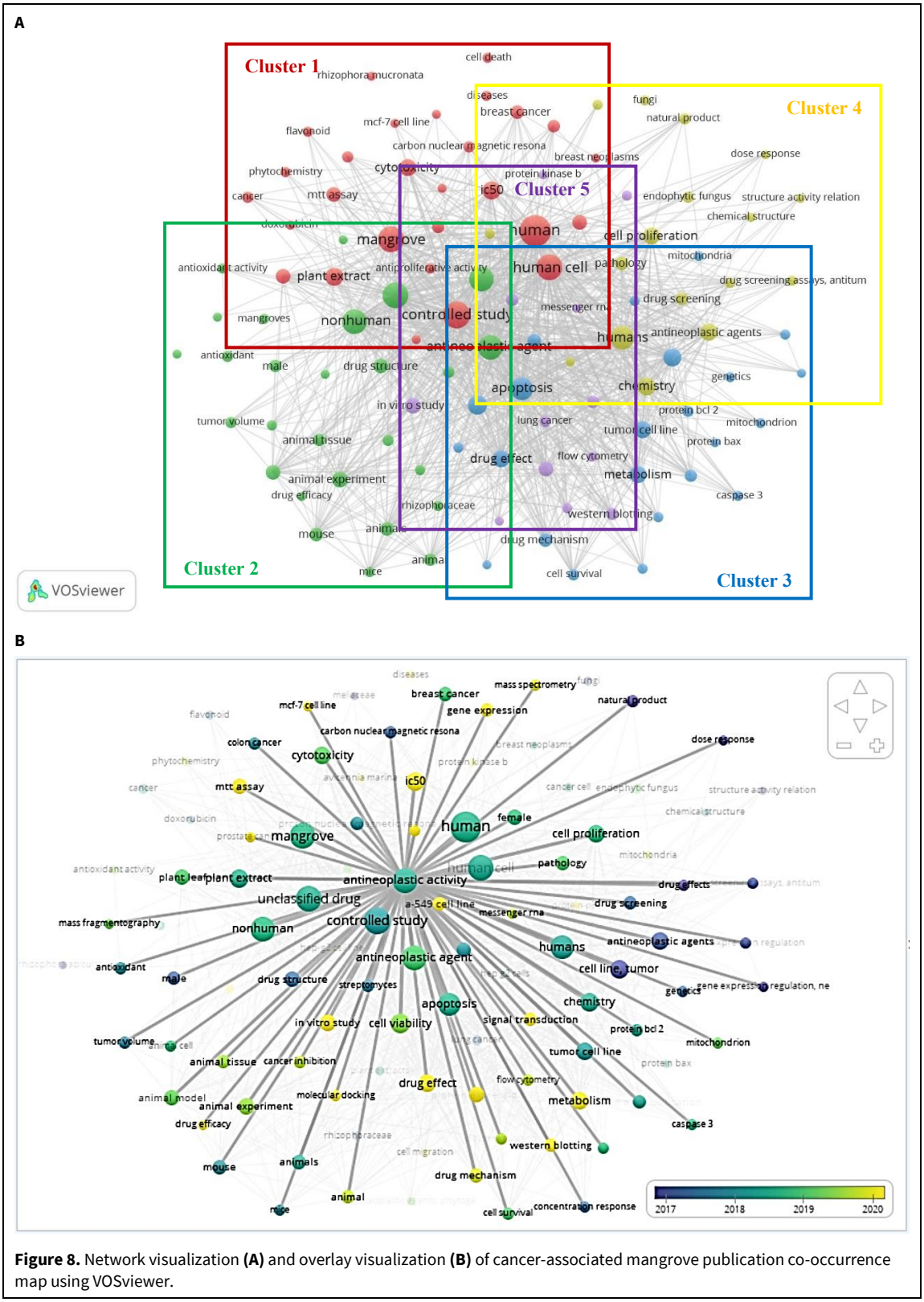

Figure 8. Network visualization **(A)** and overlay visualization **(B)** of cancer-associated mangrove publication co-occurrence map using VOSviewer.

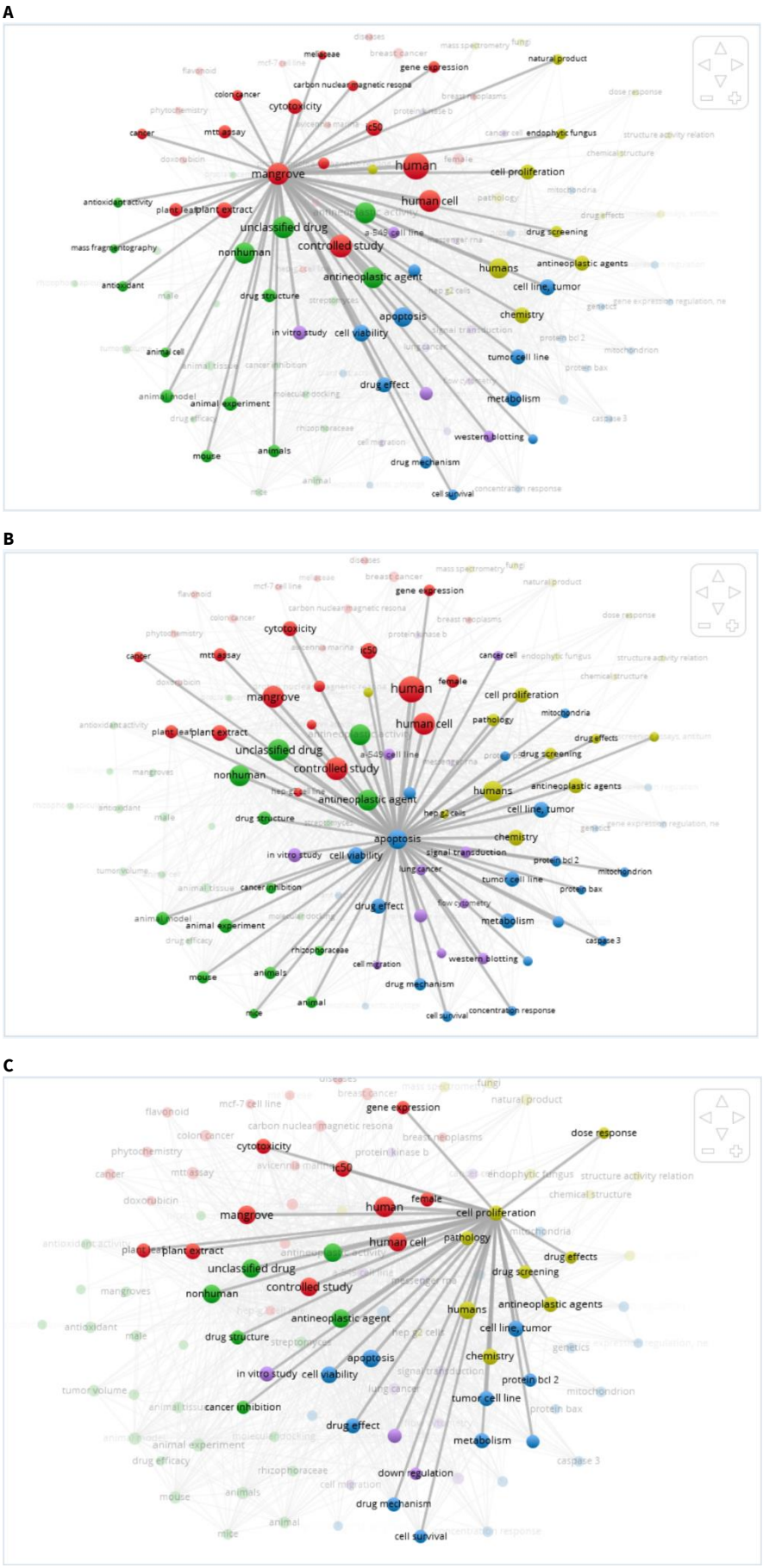

Figure 9. Illustration of the connection between mangrove **(A)**, apoptosis **(B)**, and cell proliferation **(C)** with other domains of protein involved in anticancer downregulation.

Table 3. Cluster analysis by the most occurring keywords.

Cluster	Most frequent keywords	Keywords
Red – 28 items	Human (55); controlled study (41); mangrove (39)	Human cell (38); ic50 (18); plant extract (18); cytotoxicity (17); female (13); MTT assay (12); plant leaf (12); breast cancer (11); gene expression (10); proton nuclear magnetic resonance (9); cancer (8); carbon nuclear magnetic resonance (8); colon cancer (8); antiproliferative activity (7); diseases (7); cell death (6); flavonoid (6); phytochemistry (6); avicennia marina (5); breast neoplasms (5); doxorubicin (5); hep-g2 cell line (5); mcf-7 cell line (5); meliaceae (5); rhizophora mucronata (5)
Green – 27 items	Unclassified drug (40); nonhuman (37); antineoplastic activity (36)	Antineoplastic agent (35); animal experiment (15); animal model (13); drug structure (12); animals (11); mouse (11); animal (9); animal tissue (9); male (9); antioxidant (8); cancer inhibition (8); streptomyces (8); tumor volume (8); animal cell (7); antioxidant activity (7); mice (7); molecular docking (7); rhizophoraceae (7); mangroves (6); drug efficacy (5); enzyme linked immunosorbent assay (5); mass fragmentography (5); prostate cancer (5); rhizophora apiculata (5)
Blue – 23 items	Apoptosis (30); cell viability (22); cell line – tumor (19)	Drug effect (17); metabolism (17); tumor cell line (16); drug cytotoxicity (11); drug mechanism (11); isolation and purification (10); cell survival (8); protein bcl 2 (8); mitochondrial membrane potential (7); protein p53 (7); caspase 3 (6); concentration response (6); gene expression regulation (6); genetics (6); mitochondria (6); mitochondrion (6); plant extracts (6); antineoplastic agents – phytogenic (5); gene expression regulation – neoplastic (5); protein bax (5)
Yellow – 17 items	Humans (32); Chemistry (19); Cell proliferation (17)	Antineoplastic agents (16); pathology (11); drug screening (10); endophytic fungus (8); natural product (8); drug effects (7); fungi (7); HeLa cell line (7); mass spectrometry (7); drug screening assays – antitumor (6); chemical structure (5); dose-response (5); hep g2 cells (5); structure-activity relation (5)
Purple – 12 items	*In vitro* study (14); protein expression (12); a-549 cell line (9)	Signal transduction (9); western blotting (9); lung cancer (8); downregulation (7); cancer cell (6); flow cytometry (6); cell migration (5); messenger RNA (5); protein kinase b (5)

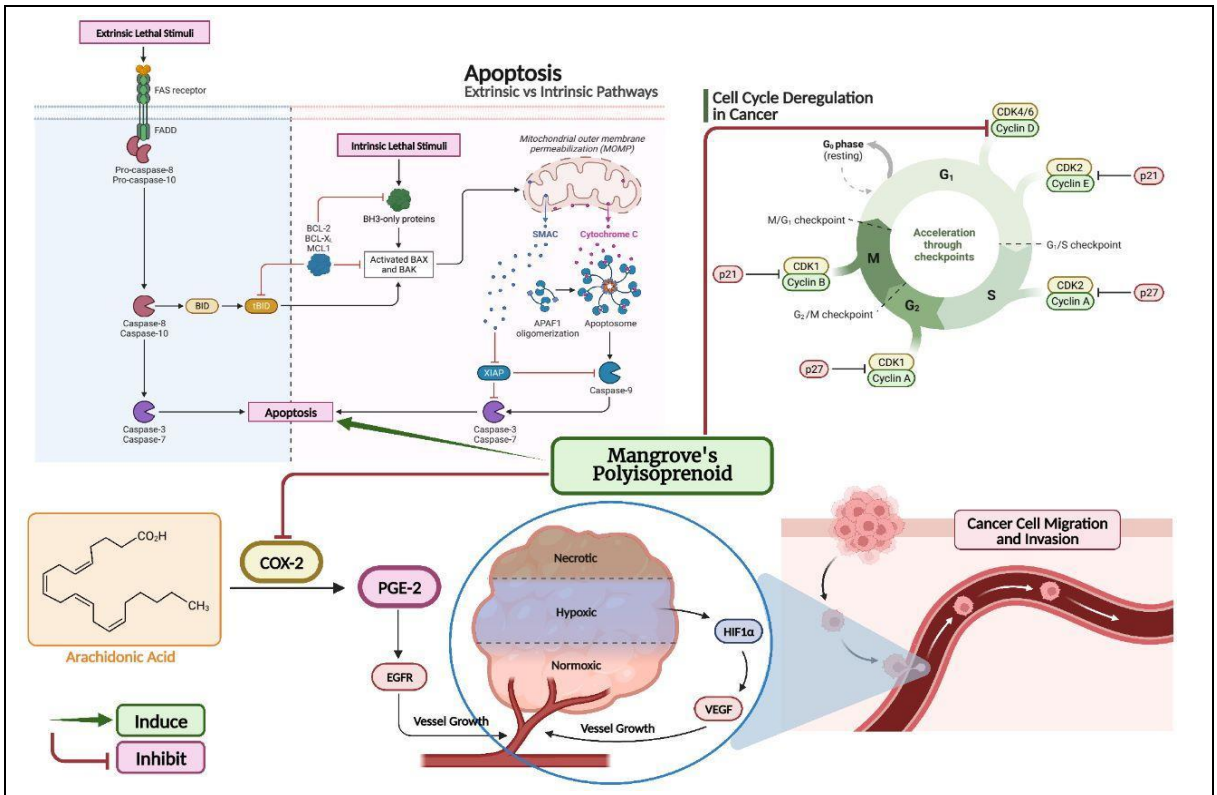

Figure 10. Illustration of several mechanisms involved in cancer progression, such as evading apoptosis, deregulating the cell cycle, and promoting tumor angiogenesis. The illustration also highlights the potential of mangrove's polyisoprenoid compounds to act as a therapeutic agent by inducing apoptosis, inhibiting cell cycle, and suppressing the COX-2-mediated pathway for vessel growth.

The analysis suggests an increasing number of publications on the anticancer properties of mangrove chemical compounds, with 2020 being a peak year.

A complete analysis was conducted to identify key individuals, countries, institutions, terms, and references relevant to this research topic. *Wu X* is a prominent individual in this group, acknowledged for his substantial achievements as a distinguished author. *Wu X* and his colleagues have published nine papers investigating critical subjects, specifically the impact of cytochalasin H (CyH), a compound isolated from the endophytic fungus Phomopsis liquidambar derived from mangrove, on the epithelial-mesenchymal transition (EMT) and cancer stemness in A549 and NCI-H460 non-small cell lung cancer (NSCLC) cells, along with the associated mechanisms, notably the involvement of the YAP/TAZ signaling pathway. Their research demonstrates that CyH markedly suppressed the invasive capacity and sphere formation of NSCLC cells. The expression of E-cadherin, an epithelial marker of epithelial-mesenchymal transition (EMT), was significantly up-regulated.

In contrast, the expression of Vimentin and N-cadherin, mesenchymal markers of EMT, was markedly down-regulated following CyH treatment in non-small cell lung cancer (NSCLC) cells. Furthermore, they illustrated that CyH markedly reduced the expression of YAP and TAZ. Their findings highlighted that CyH may serve as a prospective chemotherapeutic drug for NSCLC and elucidate a novel molecular mechanism for CyH's participation in the prevention and treatment of NSCLC (Xiu et al., 2021).

In addition, an examination of the primary country of origin and the most cited country of these publications revealed that China was the most prolific contributor, with impressive articles. China's academic output has shown a noticeable increase, with over 250 articles and 530 citations. Guangdong Medical University is a significant institutional hub, highlighting its pivotal position in this research field. The most often occurring author keywords were "human," "controlled study," "unclassified drug," "mangrove," "nonhuman," and "antineoplastic activity." The network visualization diagram highlights key themes, including "antineoplastic activity," "mangrove," "apoptosis," "cell proliferation," and "protein expression," across five distinct clusters. The increasing significance of China and India in international cooperation is reflected in the distribution of country-based publications and the collaboration map, highlighting their capabilities as collaborative partners in the research domain. Furthermore, Marine Drugs was the most productive journal in the research landscape.

The most often referenced work, published in 2007 and entitled "Gedunin, a limonoid from *Xylocarpus granatum*, inhibits the growth of the CaCo2 colon cancer cell line *in vitro*", was co-authored by Uddin and colleagues. *X. granatum* is a mangrove tree native to Bangladesh, widely distributed over several Southeast Asian countries, Australia, and East Africa, and has been utilized traditionally as a medicinal herb for numerous ailments. Gedunin has been extracted from the bark of *X. granatum*, and its cytotoxic efficacy has been assessed using the CaCo-2 colon cancer cell line (IC_{50} = 16.83 μm), indicating a targeted cytotoxic effect on neoplastic cell proliferation.

Action mechanism of mangrove's bioactive compounds toward cancer proliferation

Previous studies indicate the potency of bioactive compounds from mangrove plants as chemopreventive or anticancer by increasing cytotoxic activity against cancer cell lines (Darmadi et al., 2021; Illian et al., 2019; Sari et al., 2018). These mechanisms involve the induction of apoptosis, inhibition of the cell cycle, and suppression of COX-2 expression in cancer cell lines. Dolichols are the primary component in Okinawan mangrove roots and North Sumatran mangrove leaves and roots, while polyprenols are present in Okinawan mangrove leaves (Basyuni et al., 2018). Fig. 10 illustrates pathways that detail how chemical compounds from mangroves enhance cytotoxicity in cancer cells. They inhibit cancer cell proliferation by inducing cell cycle arrest in the G0-G1 phase through the downregulation of cyclin D (Illian et al., 2019; Sari et al., 2018), which leads to apoptosis by detecting damaged cells and continuing the apoptotic process (Weidner et al., 2016). Mangrove's chemical compounds induce apoptosis in cancer cells at the early apoptotic stage (Illian et al., 2019). Apoptosis dysregulation is associated with various diseases, including tumor growth and chemoresistance in malignant cells (Gorski and Marra, 2002). In mammals, apoptosis is initiated through two mechanisms. Extrinsic signals like tumor necrosis factor (TNF), Fas (CD95/APO1), and TNF-related apoptosis-inducing ligand receptors (TRAIL) can trigger apoptosis, while internal stimuli such as mitochondrial transduction can also induce apoptosis. Cysteine aspartyl proteases (caspases) activation leads to mitochondrial membrane permeabilization, chromatin condensation, and DNA fragmentation, ultimately causing cell death (Zörnig et al., 2001).

Furthermore, mangrove's chemical compounds suppress COX-2 enzyme expression (Illian et al., 2019), which is overexpressed in cancer cells (particularly in colorectal cancer cells), and aids in initiating angiogenesis for metastasis and tissue invasion (Abukhalaf et al., 2004; Leahy et al., 2000). Angiogenesis inhibition

leads to cancer cell death by depriving blood vessels of their nourishment and oxygen supply, thereby hindering metastasis (Fosslien, 2001; Muz et al., 2015; Saman et al., 2020). In addition, COX-2 inhibition reduces prostaglandin E synthesis (Wang and DuBois, 2004), diminishing Bcl-2 expression and promoting apoptosis in cancer cells (Han et al., 2017; Kassab, 2025; Pu et al., 2021; Sobolewski et al., 2010). Future research will explore the sensitivity of different cancer types to mangrove chemical compounds.

Strengths and limitations

To the best of our knowledge, this study is the first bibliometric analysis to focus on the anticancer activity and the role of bioactive compounds from mangroves. Given the significant health benefits of mangrove bioactive compounds, particularly in light of the high adverse effects of conventional cancer chemotherapeutics (Islam et al., 2022; Raju et al., 2022), Scopus was selected for its comprehensive coverage in MEDLINE. Moreover, Scopus indexes many journals (approximately 23,000) compared to PubMed and Google Scholar, enhancing the scope of the literature search. Scopus provides user-friendly features for citation analysis, tracking research collaborations, and exporting data to Excel for further analysis. Many previous bibliometric studies have utilized Scopus as a primary tool for data retrieval.

However, the bibliometric methodology employed in this study had limitations. Scopus, a scientific literature database focusing on English-language journals, may have missed publications on mangrove bioactive compounds from unindexed journals in Asia, Africa, the Middle East, and Eastern Europe. Due to these constraints, utilizing only one database was necessary, as combining and analyzing data from multiple databases, unlike in systematic reviews, was not feasible for document retrieval and analysis.

Countries with fewer publications in this field should prioritize research on the role of bioactive compounds in mangroves by offering sufficient funding and support. Enhancing research collaborations between developed and developing countries in this field is vital for advancing efforts to combat cancer.

CONCLUSION

Data indicate that natural chemical studies for cancer treatment have increased significantly in the last decade. Researchers have focused on the unique chemical composition and bioactive properties of mangroves, leading to increased studies on their potential anticancer effects. The Scopus database reveals that between 2005 and 2024, researchers conducted 87 investigations on the anticancer effects of mangrove chemical constituents. Wu X and Liu J were the authors with the most publications. China and India have emerged as leading countries and organizations in terms of productivity and international collaboration. Guangdong Medical University and Marine Drugs were the most productive affiliations and journals in the research landscape. Expanding collaboration between developed and developing countries in mangrove bioactive compound research is crucial for advancing efforts against cancer progression.

CONFLICT OF INTEREST

The research was conducted entirely free from any involvement in commercial, financial, or personal matters that might be perceived as a possible conflict of interest or that could have influenced the outcomes or interpretation of the study.

ACKNOWLEDGMENTS

The authors thank the Center of Excellence for Mangrove, Universitas Sumatera Utara, through Penelitian Kolaborasi Unggulan Universitas Sumatera Utara (PKUU) EQUITY 2023 [91/UN5.2.3.1/PPM/KPEP/2023] from the Indonesia Endowment Fund for Education and the Ministry of Education, Culture, Research and Technology, Republic of Indonesia covered the study. The authors sincerely thank the Ongoing Research Funding Program (ORF-2025-123), King Saud University, Riyadh, Saudi Arabia (H.M.A.). We are grateful to Dr. Severino Salmo III (University of the Philippines-Diliman) for providing Scopus access during the International Mobility Staff (M.B.) at UP-Diliman.

DATA AVAILABILITY

The authors state that the data supporting the findings of this study are available at doi: 10.6084/m9.figshare.29930492

GENERATIVE ARTIFICIAL INTELLIGENCE (AI)

The authors used Manus and Gemini (IA tools) to improve the language and readability of the manuscript. The authors reviewed and edited the content and take full responsibility for its accuracy. No images were generated or manipulated using AI tools.

REFERENCES

Abukhalaf IK, von Deutsch DA, Bayorh MA, Socci RR (2004) Nonsteroidal Antiinflammatory Drugs. Cyclooxygenase Inhibitors, Disease-Modifying Antirheumatic Agents, and Drugs Used in Gout. In: Mozayani A, Raymon LP (eds.), Handbook of Drug Interactions. Forensic Science and Medicine. Totowa, NJ: Humana Press, pp. 337–376. https://doi.org/10.1007/978-1-59259-654-6_10

Aria M, Cuccurullo C (2017) *Bibliometrix*: An R-tool for comprehensive science mapping analysis. J Informetr 11(4): 959–975. https://doi.org/10.1016/j.joi.2017.08.007

Basyuni M, Wati R, Sagami H, Sumardi S, Baba S, Oku H (2018) Diversity and Abundance of Polyisoprenoid Composition in Coastal Plant Species from North Sumatra, Indonesia.

Biodiversitas 19(1): 1–11. https://doi.org/10.13057/biodiv/d190101

Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, Jemal A (2024) Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 74(3): 229–263. https://doi.org/10.3322/caac.21834

Bray F, Laversanne M, Weiderpass E, Soerjomataram I (2021) The ever-increasing importance of cancer as a leading cause of premature death worldwide. Cancer 127(16): 3029–3030. https://doi.org/10.1002/cncr.33587

Chen S, Cao Z, Prettner K, Kuhn M, Yang J, Jiao L, Wang Z, Li W, Geldsetzer P, Bärnighausen T, Bloom DE, Wang C (2023) Estimates and projections of the global economic cost of 29 cancers in 204 countries and territories from 2020 to 2050. JAMA Oncol 9(4): 465–472. https://doi.org/10.1001/jamaoncol.2022.7826

Cyril N, George JB, Joseph L, Raghavamenon AC, Sylas VP (2019) Assessment of antioxidant, antibacterial and anti-proliferative (lung cancer cell line A549) activities of green synthesized silver nanoparticles from Derris trifoliata. Toxicol Res 8(2): 297–308. https://doi.org/10.1039/c8tx00323h

Darmadi J, Batubara RR, Himawan S, Azizah NN, Audah HK, Arsianti A, Kurniawaty E, Ismail IS, Batubara I, Audah KA (2021) Evaluation of Indonesian mangrove *Xylocarpus granatum* leaves ethyl acetate extract as potential anticancer drug. Sci Rep 11(1): 6080. https://doi.org/10.1038/s41598-021-85383-3

Falagas ME, Pitsouni EI, Malietzis GA, Pappas G (2008) Comparison of PubMed, Scopus, Web of Science, and Google Scholar: strengths and weaknesses. FASEB J 22(2): 338-342. https://doi.org/10.1096/fj.07-9492lsf

Fosslien E (2001) Molecular pathology of cyclooxygenase-2 in cancer-induced angiogenesis. Ann Clin Lab Sci 31(4): 325-348.

Gorski S, Marra M (2002) Programmed cell death takes flight: Genetic and genomic approaches to gene discovery in *Drosophila*. Physiological Genomics 9(2): 59–69. https://doi.org/10.1152/physiolgenomics.00114.2001

Han ZQ, Liao H, Shi F, Chen XP, Hu HC, Tian MQ, Wang LH, Ying S (2017) Inhibition of cyclooxygenase-2 sensitizes lung cancer cells to radiation-induced apoptosis. Oncol Lett 14(5): 5959–5965. https://doi.org/10.3892/ol.2017.6940

Hirsch JE (2005) An index to quantify an individual's scientific research output. Proc Natl Acad Sci 102(46): 16569–16572. https://doi.org/10.1073/pnas.0507655102

Illian DN, Hafiz I, Meila O, Utomo ARH, Nuryawan A, Siregar GA, Basyuni M (2021) Current status, distribution, and future directions of natural products against colorectal cancer in Indonesia: A systematic review. Molecules 26(16): 4984. https://doi.org/10.3390/molecules26164984

Illian DN, Hasibuan PAZ, Sumardi S, Nuryawan A, Wati R, Basyuni M (2019) Anticancer activity of polyisoprenoids from *Avicennia alba* Blume. in WiDr cells. Iran J Pharm Res 18(3): 1477–1487. https://doi.org/10.22037/ijpr.2019.1100719

Illian DN, Widiyana AP, Hasana AR, Maysarah H, Al Mustaniroh SS, Basyuni M (2022) *In silico* approach: Prediction of ADMET, molecular docking, and QSPR of secondary metabolites in Mangroves. J Appl Pharm Sci 12(11): 21–29. https://doi.org/10.7324/japs.2022.121103

Islam MR, Awal MA, Khames A, Abourehab MAS, Samad A, Hassan WMI, Alam R, Osman OI, Nur SM, Molla MHR, Abdulrahman AO, Rajia S, Ahammad F, Hasan MN, Qadri I, Kim B (2022) Computational identification of druggable bioactive compounds from *Catharanthus roseus* and *Avicennia marina* against colorectal cancer by targeting thymidylate synthase. Molecules 27(7): 2089. https://doi.org/10.3390/molecules27072089

Jain S, Dwivedi J, Jain PK, Satpathy S, Patra A (2016) Medicinal plants for treatment of cancer: A brief review. Pharmacogn J 8(2): 87–102. https://doi.org/10.5530/pj.2016.2.1

Jia SL, Chi Z, Liu GL, Hu Z, Chi ZM (2020) Fungi in mangrove ecosystems and their potential applications. Crit Rev Biotechnol 40(6): 852–864. https://doi.org/10.1080/07388551.2020.1789063

Kassab AE (2025) Recent advances in targeting COX-2 for cancer therapy: A review. RSC Med Chem 16(7): 2974–3002. https://doi.org/10.1039/D5MD00196J

Law JWF, Ser HL, Duangjai A, Saokaew S, Bukhari SI, Khan TM, Ab Mutalib NS, Chan KG, Goh BH, Lee LH (2017) *Streptomyces colonosanans* sp. nov., a novel actinobacterium isolated from Malaysia mangrove soil exhibiting antioxidative activity and cytotoxic potential against human colon cancer cell lines. Front Microbiol 8: 877. https://doi.org/10.3389/fmicb.2017.00877

Leahy KM, Koki AT, Masferrer JL (2000) Role of cyclooxygenases in angiogenesis. Curr Med Chem 7(11): 1163–1170. https://doi.org/10.2174/0929867003374336

Liang Y, Ban Y, Liu L, Li Y (2024) Inhibitory effects of the polyphenols from the root of *Rhizophora apiculata* Blume on fatty acid synthase activity and human colon cancer cells. Molecules 29(5): 1180. https://doi.org/10.3390/molecules29051180

Luo Y, Luo X, Zhang T, Li S, Liu S, Ma Y, Wang Z, Jin X, Liu J, Wang X (2022) Anti-tumor secondary metabolites originating from fungi in the south China sea's mangrove ecosystem. Bioengineering 9(12): 776. https://doi.org/10.3390/bioengineering9120776

Muz B, de la Puente P, Azab F, Azab AK (2015) The role of hypoxia in cancer progression, angiogenesis, metastasis, and resistance to therapy. Hypoxia 3: 83–92. https://doi.org/10.2147/hp.s93413

Prabhu VV, Guruvayoorappan C (2012) Anti-inflammatory and anti-tumor activity of the marine mangrove Rhizophora apiculata. J Immunotoxicol 9(4): 341–352. https://doi.org/10.3109/1547691x.2012.660997

Pu D, Yin L, Huang L, Qin C, Zhou Y, Wu Q, Li Y, Zhou Q, Li L (2021) Cyclooxygenase-2 inhibitor: A potential combination strategy with immunotherapy in cancer. Front Oncol 11: 637504. https://doi.org/10.3389/fonc.2021.637504

Raju SK, Sekar P, Kumar S, Murugesan M, Karthikeyan M, Elampulakkadu A (2022) Plant secondary metabolites for the prevention and treatment of colorectal cancer: A review. J Pharmacogn Phytochem 11(2): 229–246. https://doi.org/10.22271/phyto.2022.v11.i2c.14390

Saeed AF, Su J, Ouyang S (2021) Marine-derived drugs: Recent advances in cancer therapy and immune signaling. Biomed Pharmacother 134: 111091. https://doi.org/10.1016/j.biopha.2020.111091

Saman H, Raza SS, Uddin S, Rasul K (2020) Inducing angiogenesis, a key step in cancer vascularization, and treatment approaches. Cancers 12(5): 1172. https://doi.org/10.3390/cancers12051172

Sari DP, Basyuni M, Hasibuan PAZ, Sumardi S, Nuryawan A, Wati R (2018) Cytotoxic and antiproliferative activity of polyisoprenoids in seventeen mangroves species against WiDr colon cancer cells. Asian Pac J Cancer Prev 19(12): 3393–3400. https://doi.org/10.31557/apjcp.2018.19.12.3393

Ser HL, Palanisamy UD, Yin WF, Chan KG, Goh BH, Lee LH (2016) *Streptomyces malaysiense* sp. nov.: A novel Malaysian mangrove soil actinobacterium with antioxidative activity and cytotoxic potential against human cancer cell lines. Sci Rep 6(1): 24247. https://doi.org/10.1038/srep24247

Sobolewski C, Cerella C, Dicato M, Ghibelli L, Diederich M (2010) The role of cyclooxygenase-2 in cell proliferation and cell death in human malignancies. Int J Cell Biol 2010: 215158. https://doi.org/10.1155/2010/215158

Tan LTH, Chan KG, Pusparajah P, Yin WF, Khan TM, Lee LH, Goh BH (2019) Mangrove derived *Streptomyces* sp. MUM265 as a potential source of antioxidant and anticolon-cancer agents. BMC Microbiol 19: 38. https://doi.org/10.1186/s12866-019-1409-7

Tian S, Saravanan K, Mothana RA, Ramachandran G, Rajivgandhi G, Manoharan N (2020) Anticancer activity of biosynthesized silver nanoparticles using *Avicennia marina* against A549 lung cancer cells through ROS/mitochondrial damages. Saudi J Biol Sci 27(11): 3018–3024. https://doi.org/10.1016/j.sjbs.2020.08.029

Uddin SJ, Nahar L, Shilpi JA, Shoeb M, Borkowski T, Gibbons S, Middleton M, Byres M, Sarker SD (2007) Gedunin, a limonoid from *Xylocarpus granatum*, inhibits the growth of CaCo-2 colon cancer cell line *in vitro*. Phytother Res 21(8): 757–761. https://doi.org/10.1002/ptr.2159

van Eck N, Waltman L (2010) Software survey: VOSviewer, a computer program for bibliometric mapping. Scientometrics 84(2): 523–538. https://doi.org/10.1007/s11192-009-0146-3

Wang D, DuBois RN (2004) Cyclooxygenase 2-derived prostaglandin E2 regulates the angiogenic switch. Proc Natl Acad Sci 101(2): 415–416. https://doi.org/10.1073/pnas.0307640100

Weidner C, Rousseau M, Micikas RJ, Fischer C, Plauth A, Wowro SJ, Siems K, Hetterling G, Kliem M, Schroeder FC, Sauer S (2016) Amorfrutin C induces apoptosis and inhibits proliferation in colon cancer cells through targeting mitochondria. J Nat Prod 79(1): 2–12. https://doi.org/10.1021/acs.jnatprod.5b00072

Xiu Z, Liu J, Wu X, Li X, Li S, Wu X, Lv X, Ye H, Tang X (2021) Cytochalasin H isolated from mangrove-derived endophytic fungus inhibits epithelial-mesenchymal transition and cancer stemness via YAP/TAZ signaling pathway in non-small cell lung cancer cells. J Cancer 12(4): 1169–1178. https://doi.org/10.7150/jca.50512

Yuan G, Hong K, Lin H, She Z, Li J (2013) New azalomycin F analogs from mangrove *Streptomyces* sp. 211726 with activity against microbes and cancer cells. Mar Drugs 11(3): 817–829. https://doi.org/10.3390/md11030817

Zörnig M, Hueber AO, Baum W, Evan G (2001) Apoptosis regulators and their role in tumorigenesis. Biochim Biophys Acta Rev Cancer 1551(2): F1–F37. https://doi.org/10.1016/s0304-419x(01)00031-2

AUTHOR CONTRIBUTION:

Contribution	Illian DN	Irham LM	Deliana F	Wardhani FM	Adikusuma W	Al-Mustaqimah AS	Ali HM	Ikhtiari R	Lubis MF	Basyuni M
Concepts or ideas	x	x								x
Design	x	x	x	x	x	x	x	x	x	x
Definition of intellectual content	x						x			x
Literature search	x	x	x	x	x	x	x	x	x	x
Experimental studies	x	x	x	x	x	x	x	x	x	x
Data acquisition	x	x				x				x
Data analysis	x	x	x	x	x	x	x	x	x	x
Statistical analysis	x	x	x	x	x	x	x	x	x	x
Manuscript preparation	x	x	x	x	x	x	x	x	x	x
Manuscript editing	x	x	x	x	x	x	x	x	x	x
Manuscript review	x	x	x	x	x	x	x	x	x	x

Citation Format: Illian DN, Irham LM, Deliana F, Wardhani FM, Adikusuma W, Al-Mustaqimah AS, Ali HM, Ikhtiari R, Lubis MF, Basyuni M (2025) Unveiling the anticancer potential of mangroves: A 2005−2024 bibliometric analysis. J Pharm Pharmacogn Res 13(6): 1932–1946. https://doi.org/10.56499/jppres25.2352_13.6.1932

Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Open Access: This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (http://creativecommons.org/ licenses/by/4.0/), which permits use, duplication, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license and indicate if changes were made.