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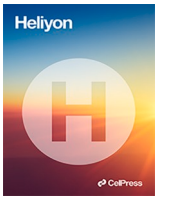

Review article

# Plant natural compounds in the cancer treatment: A systematic bibliometric analysis

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ABSTRACT

Plant-derived natural compounds are significant resources for the discovery of potential anticancer drugs. While research in the plant-based anticancer field has surged in recent years, systematic bibliometric analyses covering a longer period and containing up-to-date publications remain scarce. Here, we conducted a bibliometric analysis of literature on the anticancer properties of plant natural compounds over the past three decades, leveraging the bibliometric framework and open-access platform, KNIME. Our findings showed that the number of plant anticancer-related publications underwent an accelerating growth from 1992 to 2023. The country and institution analyses revealed that countries with traditional medical systems contributed a large portion of publications in the plant anticancer field, such as India, China, and South Korea. This study also highlighted the top ten eminent researchers and publications, assisting researchers in identifying pivotal literature. The primary publications were domains of chemistry and biology-related fields, such as Pharmacology & Pharmacy, Plant Sciences, and Biochemistry & Molecular Biology. Additionally, we noted that flavonoids have been focal plant compounds in anticancer, with strong anticancer potential. Our study provides new insights into the progress and trends in the plant anticancer field and will assist researchers in grasping the future research direction.

## 1. Introduction

Cancer remains a paramount threat to human health [1]. Forecasts from the International Agency for Research on Cancer (IARC), predict 30.2 million new cancer cases globally by 2040, leading to 16.3 million fatalities. Such projections hinder the realization of Sustainable Development Goal 3 (SDG3) which aspires to ensure healthy lives and promote well-being for all at all ages. At its core, cancer is a malignant tumor caused by the uncontrolled proliferation and development of body cells [2]. The metastasis behavior of these uncontrolled cells resulted in multiple organ dysfunction, ultimately causing death [3]. Generally, cancer is the result of multiple factors, including hereditary and environmental factors (radiation, chemicals, and viruses) [4–7].

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While cancer mainly affects middle-aged and elderly individuals (40–80 years old), it has a trend towards younger people because of deterioration of the external environment and transformation of diet and lifestyle. For instance, rectal cancer incidence among individuals aged 30–39 has been increasing in recent years [8]. Traditional cancer treatments, including surgical excision, chemotherapy, and radiotherapy, usually have great side effects on patients [9,10]. However, the advent of precision medicine, such as targeted therapy and immunotherapy, has revolutionized cancer care by enhancing treatment efficacy and minimizing adverse effects [11]. Nevertheless, despite these advancements, cancer cure rates remain less than ideal. Thus, there is an urgent need for more effective and less toxic anticancer treatments and drugs.

As significant sources of new drug development, plant natural compounds played an important role in primary medicine and health [12]. Remarkably, over half of cancer prescription drugs trace their origins to plant-derived natural products [13]. Previous studies have illustrated that these compounds could mitigate chemotherapy side effects and increase host immunity, thereby reducing the chances of cancer recurrence and metastasis [11,14]. However, the intricate chemical compositions of natural products make the exploration of anticancer drugs a formidable challenge. For example, out of 35,000 species screened by the National Cancer Institute (NCI) for bioactivity both in vitro and in vivo, only two drug structures - paclitaxel and camptothecin - were identified [15]. To explore effective anticancer compounds among numerous natural products, increasing research focused on target plant search, bioactive compound isolation, and molecular pathway clarification, combined with multidisciplinary approaches. Until now, a plethora of phytochemicals have been confirmed anticancer-related compounds, e.g., tanshinones, vinblastine, paclitaxel, podophyllotoxin, camptothecin, curcumin, cannabinoids, greatly promoting the progress of cancer treatments [16–22]. Consequently, anticancer phytochemicals have emerged as a topic of widespread concern in biology and the medical domain and have led to an important accumulation of valuable scientific findings.

The growing research on plant-anticancer compounds has placed significant stress on the systematic literature review. Previous studies usually focused on specific anticancer plants or plant-derived compounds, offering insights into their anticancer mechanisms, drug development processes, and clinical applications [19–21]. Recently, the emergence of bibliometrics greatly increased the comprehensiveness and systematicness of literature review in a hot area [23]. Bibliometrics provided an informative analysis framework to analyze research trends, hotspots, expectations, as well as limitations within a particular field, which reduced the significant time of scholars to read and comprehend extensive literature [24].

KNIME (Konstanz Information Miner) stands out as a trailblazing open-source data processing platform dedicated to data processing. It facilitates the rapid construction of data-driven workflows [25,26]. Boasting an intuitive visual interface, KNIME streamlines processes like data cleansing, statistical analysis, and visualization. Its multi-language support amplifies its versatility, positioning it as an indispensable tool for efficient literature analysis. Merging bibliometric techniques with the capabilities of KNIME allows for simultaneous analysis of vast swathes of publications. Yet, surprisingly, the synergy of these tools remains underexplored in numerous disciplines, the field of plant-derived anticancer compounds being a prime example.

In this study, to provide a comprehensive insight into the research developments and future trends of plant-anticancer compounds, we applied the KNIME platform to analyze 16,119 publications in the field over the past three decades based on the bibliometric framework. We aimed to reveal the following objectives: (1) characterize the spatiotemporal distribution of publication outputs in the plant anticancer field. (2) reveal the research hotspots and potential trends in the field of plant anticancer. (3) summarize the key questions and limitations, promoting the field development.

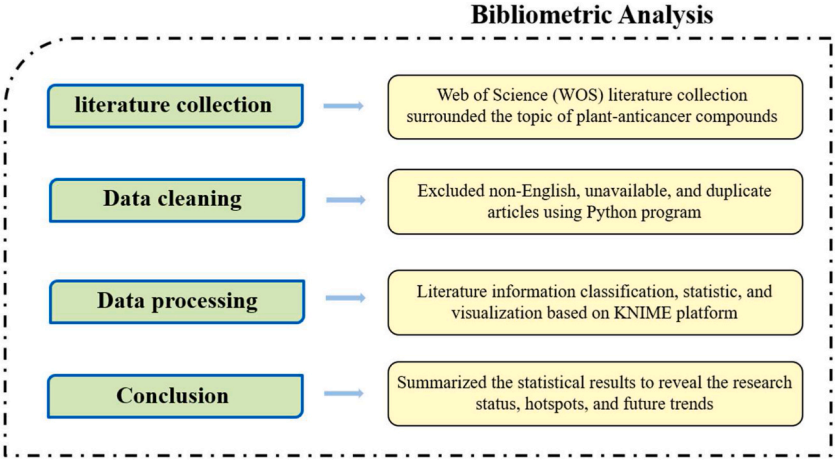


**Fig. 1.** Flowchart of the bibliometric analysis methodology.

## 2. Methods

### 2.1. Literature search strategy

Web of Science (WOS), an authoritative and international database offering comprehensive information on each publication, was selected as the bibliometric database to obtain the literature search results. The search formula we used in this study was: TS = plant AND (cancer or anticancer or anti-cancer) AND (natural compounds or natural compound or natural products or natural product or metabolism products or metabolism product or metabolites or metabolite or phytochemicals or phytochemical or extracts or extract). The collection of literature records was through the WOS API and the JSON file format was applied to sort the full information of each record for data cleaning and processing. We obtained 21,637 row records up to December 2023. There were 16,408 articles after excluding review publications. We further filtered non-English, unavailable, and duplicate articles, and a total of 16,199 records were used for bibliometric analysis. Among these records, anticancer mechanism related studies accounted for approximately 20 % using the search formula (TS = mechanism or mechanisms).

### 2.2. Bibliometric analysis

In this study, we used classic bibliometric methods that were divided into four steps as shown in Fig. 1. The first step is literature collection. We searched related literature around the topic of plant-anticancer compounds using the strategy mentioned before. For the data cleaning step, we excluded non-English, unavailable, and duplicate articles based on an automated Python script. During the data processing step, we classify the information of all literature, e.g., abstract, keywords, year of publication, journal, countries, affiliation, co-cited literature, etc. The classified information was performed for statistical analysis and visualization. A workflow we established on the KNIME platform based on Python was applied to support this step. In the last step, we summarized the statistical results to reveal the research status, hotspots, and future trends.

## 3. Results

### 3.1. Global publication outputs and trends

There were approximately 16,119 related articles published in the plant-anticancer field from 1992 to 2023 globally. The number of publications in this field displayed a rapidly increasing trend during the past 30 years (Fig. 2). Seventeen paper numbers were published as early as 1992. After a development of nearly ten years, the annual number of publications exceeded one hundred in 2002. Up to 2012, the number of one-year publications was increased to 631 which is approximately six times as many as a decade ago. In the last ten years, the number of publications about plant-anticancer has increased significantly benefiting from the advance of biological and medical technologies, such as mass-spectrometric analysis, genomic sequencing, and targeted therapy. The publications were more than 1000 annually in 2016 and the accumulation of publications exceeded 10,000 up to 2019. The exponential increases in global publication outputs showed the rapid growth of the plant-anticancer field and the enormous potential of plant-derived compounds in anticancer in the future.

### 3.2. Contributed countries/territories and institutions

A total of 117 countries/territories contributed more than one publication output in the plant-anticancer field. According to the gross publications from 1992 to 2023, the top ten countries included India, Peoples R China, USA, Saudi Arabia, South Korea, Iran, Brazil, Egypt, Germany, and Italy, which contributed 10,235 publications in plant-anticancer reaches accounting for 2/3 of total publications (Fig. 3, Table S1). Among them, the number of publication outputs of India, Peoples R China, and USA were 1,946, 1,848,

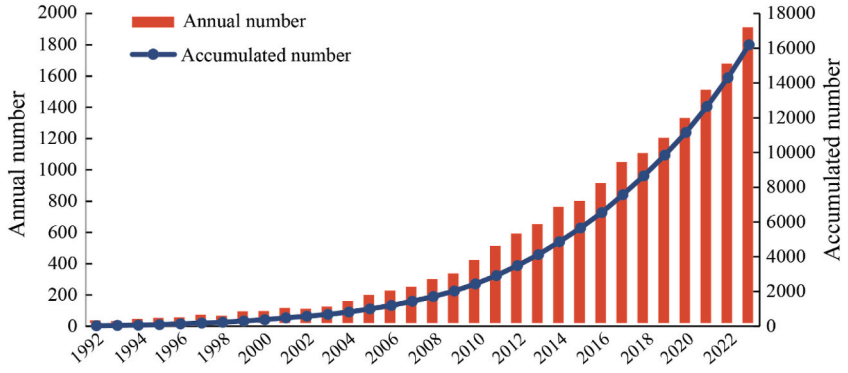


**Fig. 2.** Annual number and the accumulated number of publications in the plant anticancer field from 1992 to 2023.

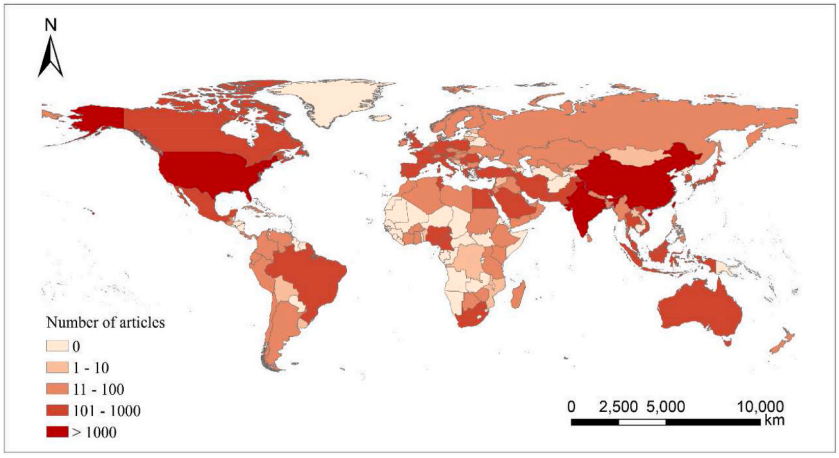


**Fig. 3.** Number of publications among different countries/territories from 1992 to 2023. The color shades represent the variation of publication numbers. Countries with darker colors contributed more publications in the plant anticancer field.

and 1645 respectively, contributing more than 1/2 in the top ten. Mechanism related publications had a positive relationship with the total number of publications in each country, except India, Saudi Arabia, Egypt, and Germany (Table S1). Research and development expenditures of each country were a general factor in publication production. The research spending of Peoples R China, USA, South Korea, Germany, India, and Brazil was among the top 10 in the world (Table S1). In addition, countries with traditional medicine that contained rich accumulation in the application of herbals in disease treatment promoted the development of plant-anticancer studies. For example, as the most productive country, India has an ancient and well-established traditional medicine system known as Ayurveda similar to traditional Chinese medicine, which provides an abundant bank of medicinal plants available for anticancer drug screening and efficacy tests.

To measure the cooperation situation among different countries/territories, we established the country network map as shown in Fig. 4. It revealed extensive cooperation between these countries in plant-anticancer reaches, which is particularly evident in

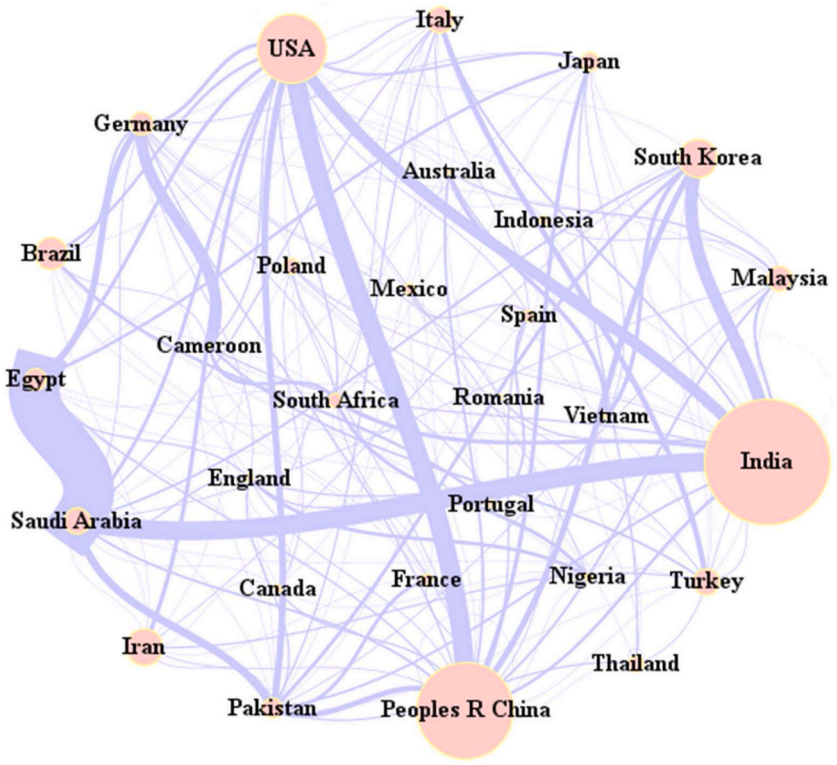


**Fig. 4.** Global academic cooperation network map. The thicker the wire, the higher the number of cooperation between any two countries.

productive countries, e.g., India, Peoples R China, USA, and Saudi Arabia. The strength of cooperation between different countries was inconsistent. For instance, Chinese scholars cooperated more frequently with American scholars, while Indian researchers preferred to collaborate with scholars from Saudi Arabia. Besides, Egypt had a strong cooperation with Saudi Arabia benefiting from their proximity. Although publication output numbers of Iran, Brazil, Germany, and Italy were also in the top ten, there is no obvious bias in their cooperation with other countries.

We also explored the contribution of different institutions in plant-anticancer research in terms of publication numbers (Fig. 5). More than 3000 institutions over the world outputted related papers, ranging from 1 to 418. However, only 522 institutions contributed more than ten publications. Among them, the top ten productive institutions were Egyptian Knowledge Bank (Egypt), Council of Scientific & Industrial Research (India), King Saud University (Saudi Arabia), Chinese Academy of Sciences (China), Universiti Putra Malaysia (Malaysia), National Research Centre (Egypt), Islamic Azad University (Iran), Universiti Sains Malaysia (Malaysia), Universiti Malaya (Malaysia), University of Illinois System (USA). In some countries, the output of articles in plant-anticancer research was concentrated in a few institutions, such as Egypt. The institution of the Egyptian Knowledge Bank contributed more than two-thirds of the total of related publications in Egypt. Notably, there were three institutions from Malaysia among the top ten, and their contribution accounted for approximately 54 % of the gross publications about plant-anticancer in Malaysia.

### 3.3. Contribution of authors

In order to identify the contribution of authors in the plant-anticancer field, we counted the number of publications that each author outputted from 1992 to 2023 and listed the top 10 most productive authors (Table 1). During the past 30 years, the cumulative number of publications per author was more than 20, which made remarkable contributions to the rapid development of plant-anticancer research. As the most active author, Thomas Efferth of Johannes Gutenberg-Universität Mainz in Germany published 78 papers about plant-anticancer in his academic studies. Notably, two authors (Victor Kuete and Armelle T Mbaveng) both from Université de Dschang in Cameroon contributed 86 publications which was more than half of all publications of the country in the plant-anticancer field. Besides, Mohamad Fawzi Mahomoodally affiliated with the University of Mauritius also made great contributions in the field for Mauritius, outputting 31/50 related publications. However, most institutions that they served did not appear in the top 10 in terms of publication numbers except for the University of Illinois.

### 3.4. Analyses of influential publications

In this section, we screened the top 10 influential representative publications in the plant-anticancer field during the past three decades (Table 2). These highly cited publications were usually published at the early stage (1997–2010) and cited more than 600 times. The results showed that the publication titled “Antioxidant activity and phenolic compounds of 112 traditional Chinese medicinal plants associated with anticancer” published in collaboration with three Chinese authors and one three and an Israeli scholar was the most influential representative publication cited by 1778 times. This paper focused on the efficacy of traditional Chinese medicines in cancer prevention and treatment and explored the antioxidant activity of natural compounds from 112 traditional Chinese medicinal plants. It revealed the major types of herbs-derived compounds with strong antioxidant activity, such as flavonoids, tannins, and curcuminoids, and compared with common vegetables and fruits, the medicinal herbs exhibited high levels of antioxidant activity. These important findings increased attention to traditional medicinal plants in the anticancer field. In fact, other articles among the top ten were also mainly focused on the phenolic content of plants and their antioxidant activity that was closely related to cancer precaution. Besides, the article titled “Plants as a source of anti-cancer agents” reviewed the application of some plant natural compounds in cancer drug exploitation, such as etoposide derived from epipodophyllotoxin. Moreover, Balunas et al. also mentioned anticancer drug discovery from medicinal plants in the publication named “Drug discovery from medicinal plants”.

To further excavate influential representative publications at different stages, we also calculated the highly cited articles every five

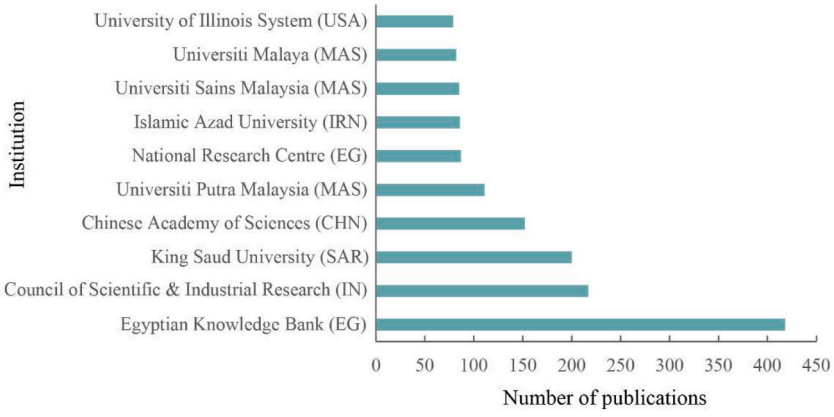


**Fig. 5.** Contribution of institutions in the plant anticancer field from 1992 to 2023. In parentheses is the abbreviation of the country of institutions.

**Table 1**
The top ten most productive authors from 1992 to 2023.

| Name | Number of publications | Institution | Country | Department |
|---|---|---|---|---|
| Thomas Efferth | 78 | Johannes Gutenberg-Universität Mainz | Germany | Pharmaceutical Biology |
| Gokhan Zengin | 57 | Selcuk University | Turkey | Biology |
| Victor Kuete | 56 | Université de Dschang | Cameroon | Biochemistry |
| John M. Pezzuto | 34 | University of Illinois | USA | Medicinal Chemistry and Pharmacognosy |
| A. Douglas Kinghorn | 31 | The Ohio State University | USA | Pharmacognosy |
| Mohamad Fawzi Mahomoodally | 31 | University of Mauritius | Mauritius | Health Sciences |
| Armelle T. Mbaveng | 30 | Université de Dschang | Cameroon | Biochemistry |
| J.N. Govil | 28 | Indian Agricultural Research Institute | India | Biology |
| V.K. Singh | 26 | Pondicherry University | India | Biology |
| Christophe Hano | 24 | Eure et Loir Campus | France | Phytochemistry |

**Table 2**
The top ten most influential publications from 1992 to 2023.

| Rank | Year | Publication title | Journal | IF (2022) | Total citations |
|---|---|---|---|---|---|
| 1 | 2004 | Antioxidant activity and phenolic compounds of 112 traditional Chinese medicinal plants associated with anticancer (Cai et al.) | Life Sciences (vol. 74, 17) | 6.1 | 1778 |
| 2 | 2005 | Plants as a source of anti-cancer agents (Cragg et al.) | Journal of Ethnopharmacology (vol. 100, 1) | 5.4 | 1259 |
| 3 | 2003 | Engineering a mevalonate pathway in Escherichia coli for production of terpenoids (Martin et al.) | Nature Biotechnology (vol. 21,7) | 46.9 | 1200 |
| 4 | 2003 | Antioxidant activity of apple peels (Wolfe et al.) | Journal of Agricultural and Food Chemistry (vol. 51,3) | 6.1 | 1052 |
| 5 | 2003 | Total antioxidant capacity of plant foods, beverages and oils consumed in Italy assessed by three different in vitro assays (Pellegrini et al.) | Nutrient Requirements (vol. 133,9) | 5.9 | 1039 |
| 6 | 1997 | Broccoli sprouts: An exceptionally rich source of inducers of enzymes that protect against chemical carcinogens (Fahey et al.) | Proceedings of the National Academy of Sciences of the United States of America (vol. 94,19) | 11.1 | 1011 |
| 7 | 2005 | Drug discovery from medicinal plants (Balunas et al.) | Life Sciences (vol.78,5) | 6.1 | 969 |
| 8 | 1998 | Phytoestrogens: the biochemistry, physiology, and implications for human health of soy isoflavones (Setchell) | American Journal of Clinical Nutrition (vol. 68,6) | 0.0 | 872 |
| 9 | 2010 | Phenol-Explorer: an online comprehensive database on polyphenol contents in foods (Neveu et al.) | Database (vol. 2010) | 4.5 | 804 |
| 10 | 2002 | Anti-oxidant activity and total phenolic content of some Asian vegetables (Kaur et al.) | International Journal of Food Science and Technology (vol. 37,2) | 3.6 | 685 |

years (Table S2). In the last five years (2018–2022), the top ten influential representative papers have been cited 145–228 times, mainly focused on the anticancer activity of plant-derived extractions and potential therapeutic agent explorations from plant compounds for different types of cancer. From 2013 to 2017, the top ten high-cited articles with more than 222 citations and their subject generally related to medicinal plants, drugs, antioxidants, and apoptosis. Among them, four review articles summarized medicine plants and natural compounds in cancer prevention and treatment, providing abundant information about research achievements in the plant-cancer field during this stage. From 2008 to 2012, the citations ranged from 252 to 804 times among the top ten influential representative papers, and these publications focused on polyphenol contents and antioxidant activity. The citations of the top ten influential publications in 2003–2007, 1998–2002, and 1993–1997 ranged from 404 to 1,778, 321 to 685, and 48 to 398, respectively.

### *3.5. Analyses of historical and current research fields*

As an important branch in anticancer, the research of plant anticancer spanned multiple subjects. To explore hot research fields in plant anticancer, we listed the top ten subdivision fields, including Pharmacology & Pharmacy, Plant Sciences, Biochemistry & Molecular Biology, Integrative & Complementary Medicine, Food Science & Technology, Chemistry, Chemistry Medicinal, Oncology, Biotechnology & Applied Microbiology, Chemistry Multidisciplinary (Fig. 6a).

We also calculated the number of annual publications in these hot research fields over the past three decades to reveal the trends of the historical and current research fields. As shown in Fig. 6b, the number of articles in each research field displayed an increasing trend during the past 30 years. In the first decade (1992–2000), publications in plant anticancer research were mainly from Biochemistry & Molecular Biology, Oncology, Pharmacology & Pharmacy, and Plant Sciences. From 2001 to 2010, publication numbers from Pharmacology & Pharmacy field increased significantly, which laid the foundation for it to be the hottest field in plant anticancer research. However, the accumulation of articles from Biotechnology & Applied Microbiology and Chemistry Multidisciplinary field was still low during this stage. In 2011–2023, scholars paid increasing attention to Chemistry, Food Science & Technology, and Integrative & Complementary Medicine besides Biochemistry & Molecular Biology and Pharmacology & Pharmacy, yet the growth rate of publication numbers from Oncology was small or even negative.


**Fig. 6.** Research fields of publications from 1992 to 2023. (a) the number of publications of the top ten most productive fields. (b) the historical variation of publication outputs from the top ten fields. The size of the circles represents the number of articles.

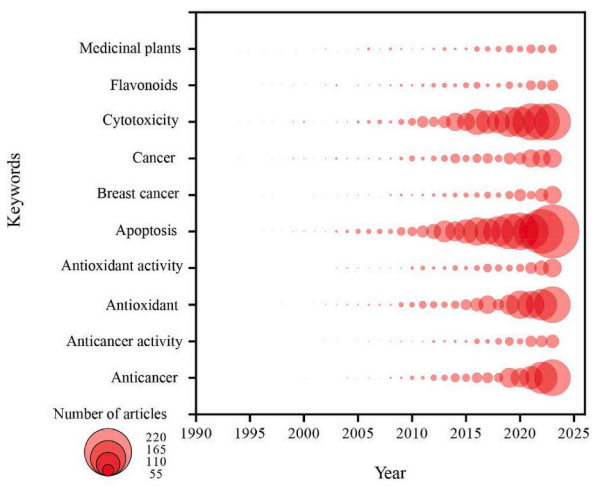


**Fig. 7.** The historical variation of research hotspots from 1992 to 2023. The size of the circles represents the number of articles.

### 3.6. Research hotspots and trends

Keywords are important for scholars to understand the subject and content of an article rapidly and trace hotspots in different fields. Here, we calculated the number of times the keyword appears in the publications and selected the top 10 keywords to show the research hotspots in the plant anticancer field (Table S3). As the most frequent keyword, apoptosis appears in 1755 publications, which indicated that apoptosis analyses were a hot technology to observe the intervention effect of natural compounds on cancer. Besides, many scholars also focused on cytotoxicity and antioxidant analyses. The former analysis was to measure the destruction of plant compounds to cells for low-toxic anticancer drug selection, and the antioxidant analysis was mainly to detect the antioxidant activity of the compounds for cancer prevention. In addition, breast cancer got the most attention of all cancers, with 417 publications. For plant-derived compounds, the flavonoids were the most concerned in the plant anticancer field.

Moreover, we selected the top ten keywords to analyze their frequency presented in publications from 1992 to 2023, exploring the trend of research hotspots. There are some differences in the research hotspots in different periods (Fig. 7). At the initial stage (1992–2000), the research hotspots included apoptosis, cancer, cytotoxicity, flavonoids, and medicinal plants. From 2001 to 2010, apoptosis and cytotoxicity were still research hotspots. Additionally, anticancer and antioxidant grew rapidly during the last five years (2006–2010). Between 2011 and 2023, the research about anticancer, antioxidant, apoptosis, and cytotoxicity attracted a lot of attention from scholars and became hotspots during this stage. Antioxidants as potential anticancer agents are recognized for bio-macromolecule protecting at a minimum concentration. Moreover, apoptosis and cytotoxicity are two significant indexes for screening potential anticancer agents. Therefore, antioxidants, apoptosis, and cytotoxicity are continuous hotspots in the plant anticancer field.

## 4. Discussion

### 4.1. Traditional medicine played an important role in the plant anticancer field

For millennia, traditional medicine has harnessed various plant species for treating a myriad of ailments, as evidenced by practices such as Ayurveda, Egyptian, and Chinese medicinal systems, such as Ayurveda, Egyptian, and Chinese traditional medicinal systems [27,28]. These systems accumulated rich resources of medicinal plants. Out of the roughly 70,000 plant species believed to possess medicinal properties, more than 3000 demonstrate anticancer activities, creating an expansive pool for the exploration, screening, and application of anticancer drugs [12,29]. Moreover, more new plant species in the same taxonomic group of these documented anti-cancer plants could further explore their natural compounds with anticancer activities because of closely related plant species usually with some similar phytochemicals [30]. A prime example is podophyllotoxin and its semisynthetic derivatives, etoposide and teniposide, which were identified in different species of the Podophyllodidae family [31,32]. Furthermore, traditional medicine is a historical inheritance of many countries and is widely accepted by the people [33,34]. Since thousands of years, the Chinese traditional medicinal system and Indian Ayurveda system have accumulated numerous clinical experiences, with strong influence over the world [35,36]. Such profound accumulation made anticancer drugs developed based on these traditional medicinal plants safer and easier to accept and promote. Therefore, traditional medicine is significant to the exploration of plant natural compounds in the anticancer field.

Our finding revealed that the publication contribution in the plant anticancer field was closely related to the development of traditional medicine in corresponding countries. Conventionally, a country's research publication output aligns with its research and development (R&D) expenditures. For instance, the United States often leads in publication counts across multiple fields due to its substantial investment in R&D [24,37]. However, in this study, the top ten most productive countries in the plant anticancer field included 40 percent of countries with relatively low research expenditures. This deviation is particularly striking in India. While India's R&D expenditure ranked seventh globally in 2018, its publication counts in the plant anticancer domain surpassed that of the United States, which leads in global research spending. Ayurveda, Siddha, and Unani systems of India prompted the development of the plant anticancer field [38–40]. In addition, mechanism publications usually could reveal the complex regulatory process of drugs in vivo at the molecular level, providing theoretical support for anticancer medicine exploration. Thus, these studies were also important for the output evaluation of each country. Here, China had the highest proportion of mechanism research, followed by South Korea and the United States. As two countries with traditional medicine history, China and South Korea contributed high quantity and quality publications in the plant anticancer field. Furthermore, analysis of contributed institutions also supported that traditional medicine played an important role in the plant anticancer field. Institutions from countries with traditional medicine foundations accounted for 90 % of the top ten productive institutions, such as the Egyptian Knowledge Bank, Council of Scientific & Industrial Research, and King Saud University.

Nevertheless, it is still a challenge to fully develop the advantages of traditional medicine in cancer treatment limited by the existing technology. Traditional medicines often contain complex plant metabolites in cancer therapy, and the synergy of these metabolites helps traditional medicines achieve a significant therapeutic effect. At present, in the plant anticancer field, researchers generally focus on individual plant compounds purified from mixtures for mechanism analyses and drug developments. The study of the synergistic effect between complex metabolites of plants is still a challenge to be overcome in future research.

### 4.2. Flavonoids: focal plant compounds in anticancer

As a family of polyphenolic compounds, the natural occurring flavonoids wildly exist in plants, especially in some medicinal plants [41]. Flavonoids displayed strong antioxidant activity, which possessed a vast array of anticancer effects, such as cell cycle arrest,

apoptosis inducing, and invasiveness inhibition [42–44]. Therefore, flavonoids have attracted the interest of many scholars, and their molecular mechanisms and related drugs have been investigated for cancer therapy in recent years. In this study, research hotspot analyses revealed that flavonoids, one of the top ten research hotspots, are the most concerned natural products in the field of plant anticancer, accumulating numerous related publications. The research is mainly about two subjects: the detection of the content and antioxidant activity of flavonoids in plants, and the anticancer activity and molecular mechanisms of purified and identified flavonoids. The study of Chung et al. [45] reported flavonoid constituents of *Chorizanthe diffusa*, which exhibited significant antioxidant activity. In addition, Li et al. [46] discovered an unusual biflavonoid in the hairy root of Glycyrrhiza glabra. About 14 flavonoids were identified from the flowers of 48 Zhongyuan tree penoy cultivars, including anthocyanins, flavone glycosides, and flavonol glycosides, and the antioxidant activity differed among different penoy cultivars [47]. There were several flavonoidal constituents found in Leucaena leucocephala, such as Caffeic acid, Chrysoeriol, and Luteolin-7-glucoside, and these flavonoids showed high antioxidant activity [48]. With the advance of molecular techniques, the potential mechanisms of different types of flavonoids were further explored in the anticancer field. Many flavonoids have been certified strong activities in oxidative stress, e.g., Flavanone hesperetin could activate the mitochondrial apoptotic pathway to induce ROS-dependent apoptosis of multiple cancer cells [49–52]. Moreover, some flavonoids also had immunomodulatory and anti-inflammatory effects. Previous studies revealed that genistein was related to inflammatory gene expressions in breast cancer cell lines [53]. Besides, flavonoids displayed other anticancer functions in cells, such as influencing mitochondrial functions and suppressing gut microbiota [54–57]. In cancer prevention, eating vegetables and fruits rich in flavonoids can effectively reduce the incidence of different types of cancer [58]. We believed that flavonoids had strong potential in the anticancer field and that more flavonoid-related drugs could be explored and applied in cancer therapy.

### *4.3. Limitations*

Although our study offers a systematic analysis of the publications of the plant anticancer field in the past 30 years, including publication outputs, contribution countries/institutions/authors, influential publications, trends of research fields, and hotspots, it still has limitations that need to be considered. First, due to language restrictions in analyses, we only accessed the publication in English, resulting in some non-English but valuable publications being excluded. Additionally, our study did not analyze the specific methodology, findings, and conclusions of each publication to provide deeper insight into the plant anticancer field. This was because the massive publications (more than 10,000 publications) were included in analyses and it is still a challenge to process these huge volumes of information manually. In the future, the plant anticancer field can be subdivided into several specific subjects for further research. Moreover, the number of related publications will be dramatically reduced after narrowing down, which makes it possible to summarize and classify the contents of each publication. Finally, we encourage future researchers with different language backgrounds to extend our study to cover more publications other than English.

## 5. Conclusion

Plant-derived natural compounds play a pivotal role in the quest for high-efficiency and low-toxicity drugs. Given the surge in related global research, we conducted a comprehensive bibliometric analysis of literature in the plant anticancer domain spanning 1992 to 2023. Our findings underscored the burgeoning interest in plant anticancer studies, with over 15,000 publications recorded. Distinctly, countries and institutions with deep roots in traditional medicine emerged as significant contributors to the literature. We also analyzed the contributions of different countries and institutions in the field and revealed that traditional medicine promoted the outputs of plant anticancer related publications. In addition, the most influential authors and publications were explored for tracking related research. Furthermore, the analyses of historical and current research fields showed accelerating growth in Pharmacology & Pharmacy field and Biochemistry & Molecular Biology field. Finally, in plant anticancer research, breast cancer and flavonoids attracted more attention from scholars than other cancer and plant compounds.

## Ethics approval and consent to participate

Not applicable.

## Data availability statement

All data used in the study are available in the article and Supplementary Material. Further inquiries can contact the corresponding authors.

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## CRediT authorship contribution statement

**Mengting Wang:** Writing – review & editing, Writing – original draft, Visualization, Methodology, Funding acquisition, Formal analysis, Data curation. **Yinshuai Li:** Writing – review & editing, Visualization, Conceptualization. **Tiejun Pan:** Writing – review & editing, Funding acquisition, Conceptualization. **Nan Jia:** Writing – review & editing, Visualization, Validation, Supervision, Software.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Appendix A. Supplementary data

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