Original Article

Thymoquinone and cancer treatment: A scientometric analysis

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ABSTRACT

Background

Thymoquinone (TQ), a bioactive compound derived from Nigella sativa, has gained attention for its multifaceted therapeutic potential, particularly its significant anticancer properties.

Objective

This study aimed to conduct a comprehensive bibliometric analysis to evaluate the global research landscape on TQ's impact on neoplasms.

Methods

A bibliometric analysis was performed using data from the Web of Science Core Collection and Scopus databases, covering the years 1997–2024. A total of 896 studies authored by 3695 researchers and published across 485 sources were included in the analysis. The study assessed publication trends, key contributors, institutional productivity, and thematic areas of focus.

Results

The scholarly output on TQ and cancer exhibited an annual growth rate of 14.53%, peaking in 2021. The journal Molecules was the most prolific in terms of publication count, whereas Cancer Research garnered the highest local citations. Leading institutions such as the Egyptian Knowledge Bank and King Abdulaziz University were identified as major contributors. Collaborative research comprised nearly 20% of the total output. Mechanistically, TQ was shown to exert anticancer effects by inhibiting cell proliferation, inducing apoptosis, and disrupting key processes such as migration, invasion, and epigenetic modifications. Importantly, TQ demonstrated a non-toxic profile in normal cells, underscoring its potential for combination therapies.

Conclusion

This bibliometric analysis provides valuable insights into global collaboration networks, influential researchers and institutions, and evolving thematic trends in TQ-related cancer research. The findings establish a foundation for future studies aimed at optimizing and expanding the therapeutic applications of TQ in oncology.

Keywords

Thymoquinone; Neoplasms; Cancer; Cancer Treatment; Bibliography Analysis

INTRODUCTION

Cancer, a collective term for a variety of diseases characterized by uncontrolled cellular proliferation, is recognized as the second most common cause of mortality [1]. Despite considerable advancements in therapeutic strategies and enhancement of detection techniques, the global incidence and mortality rates of cancer continue to escalate. It is projected that in 2020, the global burden of this disease will encompass approximately 19 million new diagnoses and close to 10 million fatalities [2]. The traditional modalities employed in the treatment of cancer encompass surgical intervention, radiotherapy, and chemotherapy, supplemented by targeted and hormonal therapies. These conventional approaches, however, have not been able to halt the relentless growth of this global health challenge [3,4]. Predominantly, dietary compounds are plant-derived and commonly referred to

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as phytochemicals. Recent scientific explorations, employing both ex-vivo cell line methodologies and in vivo animal models, have substantiated the dual role of these phytochemicals in cancer prevention and eradication. This highlights the promising potential of these botanical compounds in the field of oncology [5,6].

Thymoquinone (TQ) is recognized as a bioactive compound present in *Nigella sativa*, also known as black seed or Alhabba Al-Sauda [7]. This bioactive compound has been utilized for its antineoplastic effects in vitro and in vivo [8]. Moreover, other biological activities such as antioxidant, analgesic, and anti-inflammatory properties have also been shown from TQ, either [9]. For instance, Nigella sativa seed oil has been explored in herbal analgesic creams, demonstrating its potential in topical therapeutic applications [10]. Additionally, the growing interest in traditional medicine, including the use of Nigella sativa, is evident among healthcare professionals, as seen in studies evaluating knowledge and practices in pharmacy education [11]. The efficacy of TQ has been demonstrated in the mitigation of various ailments, including hepatic diseases and neurological disorders, notably Parkinson's and Alzheimer's diseases [12-14]. Regarding TQs effect on cancer cells, it has been shown that TQ exhibits a range of anticancer activities, including the suppression of cell proliferation, the initiation of apoptosis, and the disruption of other cancer-promoting processes such as cell migration, invasion, and the alteration of epigenetic events in cancerous cells [15,16]. However, the appeal of TQ as a therapeutic agent is significantly enhanced by its benign profile. It has been demonstrated to exhibit non-toxicity to a variety of normal human and non-human cells [17-19].

As previous studies have demonstrated based on in vitro and in vivo evidences [8,20], the potent anticancer attributes of TQ have positioned it as a compelling candidate for combined therapy with conventional therapeutic agents or other natural products, with the aim of enhancing the effectiveness and safety of cancer treatment [20]. It is significant to note that a substantial period has passed since the initial publication reporting the anticancer effects of TQ; it is crucial to recognize the transformative influence that TQ has exerted on cancer treatments [24]. Moreover, an in-depth exploration of the existing literature is vital for comprehending the worldwide and regional adaptations in the utilization of natural products for cancer treatment. While a multitude of review articles have broached the subject of cancer treatment with TQ procured from *N. sativa* [20-22], none have specifically probed into the global research contributions and evolving trends in this sphere. Bibliometric analysis stands as a robust technique for the quantitative scrutiny of scholarly articles, equipping researchers to track the advancement of specific academic fields; it is a noteworthy tool that applies mathematical and statistical methodologies to gauge the growth, productivity, and overarching patterns of publications related to a distinct topic [29,30]. In the medical sciences, such evaluations are pivotal in mapping out research trends and breakthroughs, spurring researchers to identify leading countries and institutions, as well as pinpoint areas in need of augmentation. This study is positioned to act as a reference point for future comparative studies and assessments. It strives to detect patterns and advancements in this area of research and highlight potential areas that could benefit from further focus and refinement.

MATERIALS AND METHODS

In the scorching month of April 2024, data were harvested from the Web of Science Core Collection (WOS-CC) and Scopus to conduct a comprehensive analysis of research on impact of TQ on neoplasms. The search strategy employed was akin to casting a wide net over a blazing landscape, aiming to be inclusive and cover various aspects of the topic (Table S1).

To ensure the accuracy of the data, specific inclusion criteria were applied. These criteria were: (1) articles published in the heat of the years between 1997 and 2024, (2) articles written in the universally understood language of English, and (3) exclusion of review articles, proceeding papers, book chapters and editorial material. The data extracted from two databases were merged (Table S2, Supplementary Excel File), rechecked, and duplicated data was deleted. To provide a visual representation of this data extraction process, akin to a road map, a flowchart outlining the selection process is presented in Figure 1.

2.1. Performance Analysis

The performance analysis and science mapping were executed using RStudio v.2024.04.0 software, in conjunction with the bibliometrix R-package (4.2.0), was harnessed for these incandescent analyses [65]. Biblioshiny, an open-source package, was harnessed for data analysis. This software possesses the capability to operate with a singular database exclusively. WOS

and Scopus were selected due to their provision of comprehensive and detailed citation information, akin to a detailed heat map. This feature is particularly invaluable for conducting exhaustive bibliometric analysis and assessing the impact of research outputs. The trends in local publications and the average total citations per article were assessed annually.

2.2. Identification of Leading Institutions, Sources, Authors, and Collaborating Countries

The most productive institutions and authors, ranked in the top 10, were determined based on the proportion of papers they authored. The interplay between institutions and authors was graphically represented to decipher their patterns of collaboration. For the analysis at the country level, the proportion of articles from each country was used to determine the most productive country, and the proportion of multi-country production was calculated for the top 10 countries. The network of collaboration among countries was charted based on the quantity of publications each country contributed.

2.3. Keywords Frequencies Analysis

An analysis over time was carried out with amplified precision to track the periodic appearance of specific keywords throughout the years. A TreeMap was meticulously constructed to demonstrate the spread and prominence of the top 10 most recurring keywords. An intensified thematic analysis was conducted to spotlight the dominant trends and themes within the selected articles.

RESULTS

3.1. Overview of the Studies

This study conducted a thorough investigation into the impact of TQ on neoplasms, analyzing articles published between 1997 and 2024. A total of 896 relevant studies were meticulously reviewed, originating from 485 distinct sources. The analysis involved contributions from 3695 authors, resulting in an impressive average of 30.75 citations per document over the past decade. The most significant discoveries regarding the impact of TQ on different neoplasms are outlined, drawing from the most frequently cited research articles of the past decade (Table 1). Furthermore, the Annual Growth Rate for this field of research was computed to be 14.53%, signifying a consistent rise in scholarly publications over the study duration. The substantial volume of research output is further underscored by the inclusion of 19,910 references and 2076 unique author keywords. Collaborative studies involving the authors accounted for 19.98% of the research endeavors.

3.2. Publication and Citation Trends

The number of publications (N) varied annually, with the highest number of articles published in 2021 (N = 111) and the lowest in 2002 (N = 0). Figure 2A visually depicts the publication trend across the years. Additionally, the data indicate variations in the average total citations per article across different years (Figures 2B). Notably, in 2004, there was a substantial surge in the mean total citations per year, reaching 9.2. Conversely, 2000 witnessed the lowest value, with an average of 0.2 citations per year.

Our analysis of publication data from top 10 journals revealed that the journal “Molecules” emerged as the most prolific, contributing a noteworthy 20 articles—approximately 2.2% of the total articles within the study period. Additionally, we delved into the local citations received by these core journals from other articles within our dataset. Remarkably, “Cancer Research” stood out with the highest number of local citations, amassing an impressive total of 530 citations (Table S2).

3.3. Top Contributing Authors, Institutions, Countries and Their Interconnected Network

In the scorching landscape of academic productivity, certain institutions have blazed a trail (Figure 3A). The Egyptian Knowledge Bank (N=170, 38.2%, EKB, Egypt), King Abdulaziz University (N=60, 13.48%, Jeddah, Saudi Arabia Kingdom), King Saud University (N=48, 10.79%, Riyadh Saudi, Arabia), Cairo University (N=28, 6.28%, Giza, Egypt), and Mashhad University Medical Sciences (N=26, 5.84%, Mashhad, Iran) have emerged as the most incandescent, contributing the highest number of articles (Figure 3A). Among the authors, Gali-Muhtasib H. has been a veritable pioneer, with the highest number of articles (20, 2.78%), followed closely by Khan M., who has been a burning beacon with 18 articles (Figure 3B). The Three-Fields Plot is a radiant illustration of the intricate web of connections among cited references, authors, and author keywords. It provides invaluable insights into the complex landscape of TQ effects on various neoplasms, much like a thermal image revealing the hotspots of activity during the decade spanning from 1997 to 2024 (Figure S1).

In the blazing arena of scientific production over a

decade, Saudi Arabia and China were the torchbearers among countries, illuminating the field with 329 and 310 publications respectively. They were followed by Egypt, which contributed 288 publications, Iran with 205, and the USA with 197 (Table S4). In terms of publication patterns, Iran blazed a solitary trail, with a scorching 96.25% of its publications being single-country productions. South Korea also demonstrated a similar pattern, with a high rate of 94.11% single-country publications, akin to a lone bonfire in the dark. In stark contrast, China preferred the warmth of collaborative research, with a significant 75% of Chinese authors' publications being co-authored with researchers from other countries, like sparks flying from a shared flame. The strength of this collaboration was primarily fueled by the United States, Bangladesh and India (Figure 4).

3.4. Convergence, Heat Maps, and Rising Keywords

The most frequently encountered author keywords were scrutinized using Biblioshiny, much like examining the hotspots in a thermal image. The analysis spanned the heated landscape of commonly encountered TQ, apoptosis, antineoplastic activity, and terms related to cancer. Keywords related to TQ ("thymoquinone") and apoptosis ("apoptosis") both showed a rising temperature trend, with 420 and 318 occurrences in 2024, respectively, like a heatwave sweeping across the field. Research on *N. sativa* showed a significant spike, with 114 occurrences in 2024, indicating a growing focus on this species of black seed, much like a sudden flare-up in a fire. Keywords related to antineoplastic activity demonstrated a steady research interest over the years, with 92 occurrences in 2024, reflecting the continued efforts to address this biological effect of TQ, like the persistent glow of embers in a fire (Figure 5).

The timeline analysis of crucial keywords is akin to a heat map, revealing that "thymoquinone" hit a scorching peak in citations in 2016, followed closely by "apoptosis" remained a hot topic during this year. Other subjects such as oxidative stress (9.9%), *N. sativa* (5.4%), and inflammation (5.2%) also radiated considerable frequencies, showcasing the enduring interest in understanding the effects of TQ on physiology of cells and suppressing cancer and inflammation (Figure S2).

Taken together, this study served as a blazing torch, illuminating the global research output on TQ among cancer studies over the past fiery decade. It identified the top journals that shone the brightest, the articles that made the most impact, and the collaborations between institutions, authors, and countries that burned the hottest, as well as the important and emerging keywords that sparked interest. The findings shed warm light on the research landscape, highlighting potential areas that are heating up for future studies.

DISCUSSION

In the current academic era, there has been a marked acceleration in the fields of bibliometric analysis and scientific mapping, largely attributed to the burgeoning interest within the scientific community towards the insights derived from various bibliometric studies [23]. Bibliometric analysis provides a platform for delving into the impact of diverse research areas, the clout of individual researchers, and the relevance of specific scholarly articles. It also assists in identifying particularly influential papers, thereby augmenting our understanding of the comprehensive intellectual terrain within specific research fields [24].

Cancer continues to be a significant global health concern, with its burden, mortality, and effects on human life being extensively studied over time. A previous study provides a summary of the global burden of cancer based on population-based cancer data and registries [25]. Statistics show that 1 in 5 men and 1 in 6 women worldwide will develop cancer during their lifetime, and 1 in 8 men and 1 in 11 women will die from cancer globally [25]. The GLOBOCAN data shows an estimated 18.1 million new cancer cases and 9.6 million cancer deaths in 2018 [25]. Demographics-based predictions indicated that the annual number of new cases of cancer will reach 35 million by 2050, which is a 77% increase from the number in 2022 [25]. These studies collectively highlight the significant burden of cancer globally and the ongoing efforts to understand and mitigate its impact. However, more comprehensive and long-term evaluations are needed to fully understand the trends and devise effective strategies for cancer prevention and treatment. Among all treatments of cancer disease, the use of natural products in cancer treatment has been a significant area of research over the years [26].

The derived outcomes suggest that TQ, a naturally derived product from *N. sativa*, has garnered considerable interest from the international scientific community. The substantial volume of research conducted in this area underscores its importance and relevance in the field [27]

. Previous studies have demonstrated that TQ is a potent bioactive compound with anticancer, anti-inflammatory, antioxidant, and cell protective properties against chemotherapy [9,28] . TQ demonstrates a selective suppressive impact on the growth of cancer cells across a range of types, encompassing leukemia, breast, lung, larynx, colon, and osteosarcoma. Notably, it exhibits no detrimental effect on healthy cells [28,29] . It has been shown that TQ has effects on a diverse array of anticancer actions, encompassing the suppression of cell proliferation, the initiation of apoptosis, and the disruption of other tumorigenic processes. These processes include cell migration, invasion, and the modification of epigenetic events within cancer cells. [15,16] . TQ also showcases antitumor attributes by influencing various targets, such as nuclear factor kappa B (NF-Kb), peroxisome proliferator-activated receptor-γ (PPARγ), and c-Myc [1], which culminates in the activation of caspases proteins [17]. Additionally, it triggers the re-expression of tumor suppressor genes (TSG), including p53 and phosphatase and tensin homolog (PTEN) in lung cancer [18]. All of these pieces of literature and the pathways they encompass demonstrate that TQ is a valuable compound for anticancer research. A long-term assessment of TQ studies could prove to be beneficial.

TQ has been the subject of extensive research due to its potential anticancer properties. The research trends and advancements in this area have been significant and continue to evolve. Homayoonfal et al. in 2022 highlighted the potential anticancer properties and mechanisms of TQ in osteosarcoma and bone metastasis [21] . The study emphasized that TQ exerts its anticancer features by inducing cytotoxic effects against cancerous cells without having any detrimental impact on normal cell macromolecules such as DNA and enzymes [21] . It also combats the oncogenic signaling axis activated in tumor cells [21] . In another study, Farooqi et al. in 2022 discussed the anticancer and anti-metastatic role of TQ, focusing on the regulation of oncogenic signaling cascades [30] . The study underscored the importance of natural products in cancer prevention and inhibition and highlighted the multifunctionalities of TQ in cancer chemoprevention [30] . Research has also explored the redox cycling and anticancer activity of TQ [31] . This line of research has gradually gained momentum due to the extraordinary cancer chemo-preventive multifunctionalities of TQ [30] . An interesting study reported that while TQ is a potent apoptosis inducer in cancer cells, it exerts an antiapoptotic effect through attenuating oxidative stress in other types of cells injury [15] . These studies collectively indicate that TQ has attracted significant attention in cancer research due to its distinctive properties, including apoptosis induction, cell cycle arrest, angiogenesis and metastasis inhibition, and reactive oxygen species (ROS) generation [21] . The research trends suggest a growing interest in the potential of TQ as a natural compound for cancer treatment. However, more long-term evaluations and clinical trials are needed to fully understand and harness the anticancer potential of TQ.

CONCLUSIONS

To the best of our knowledge, this represents the inaugural study to evaluate TQ within the context of cancer treatments using a bibliometric approach. Certainly, it is important to acknowledge the inherent limitations of this study, which stem from the reliance on a single publication database. While WOS provides comprehensive coverage of many publications, it may not encompass all publications available in databases such as Scopus and PubMed. Our approach to bibliometric analysis was grounded in empirical data from original articles, with an emphasis on metadata rather than content, extracting information about authors, institutions, and countries for the assessment of productivity, collaboration, and impact. The analysis did not extend to textual content. Additionally, the scope of the analysis was limited to full-text articles published in English. As such, publications that only had English abstracts were not included in the study. This could potentially result in the exclusion of certain articles from journals published in other languages.

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Informed Consent Statement

Not applicable.

Patient and Public Involvement Statement

Patients or the public WERE NOT involved in the design, or conduct, or reporting, or dissemination plans of our research

Data Availability Statement

The original contributions presented in the study are

included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

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Conflict of interest

Authors Alireza Afshar and Amin Tamadon were employed by PerciaVista R&D Co. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author Contributions

Conceptualization, Amin Tamadon; Data curation, Nadiar M. Mussin and Madina A. Kurmanalina; Formal analysis, Alireza Afshar, Madina A. Kurmanalina and Amin Tamadon; Investigation, Alireza Afshar, Madina A. Kurmanalina and Amin Tamadon; Methodology, Alireza Afshar and Nadiar M. Mussin; Resources, and Amin Tamadon; Software, and Alireza Afshar; Supervision, Ramazon Safarzoda Sharoffidin, and Amin Tamadon; Validation, Ramazon Safarzoda Sharoffidin; Visualization, Nadiar M. Mussin; Writing – original draft, Alireza Afshar and Amin Tamadon; Writing – review & editing, Ramazon Safarzoda Sharoffidin, Nadiar M. Mussin, and Madina A. Kurmanalina.

Table 1. The ten most referenced documents on the thymoquinone biological effects on neoplasms (1997–2024).

Rank	Study ID [References]	Title of the Document	Journal Name	Total Citations	DOI/PMID
1	Gullett Np, 2010 [32]	Cancer prevention with natural compounds	Seminars in Oncology	416	10.1053/j.seminoncol.2010.06.014
2	Woo Cc, 2012 [33]	Thymoquinone: potential cure for inflammatory disorders and cancer	Biochemical Pharmacology	377	10.1016/j.bcp.2011.09.029
3	Worthen Dr, 1998 [34]	The in vitro anti-tumor activity of some crude and purified components of blackseed, *Nigella sativa* L.	Anticancer Research	346	9673365
4	Gali-Muhtasib H, 2006 [35]	Thymoquinone: a promising anti-cancer drug from natural sources	The International Journal of Biochemistry & Cell Biology	304	10.1016/j.biocel.2005.10.009
5	Yi Tf, 2008 [36]	Thymoquinone inhibits tumor angiogenesis and tumor growth through suppressing AKT and extracellular signal-regulated kinase signaling pathways	Molecular Cancer Therapeutics	274	10.1158/1535-7163.MCT-08-0124
6	Sethi G, 2008 [37]	Targeting nuclear factor-κB activation pathway by thymoquinone: role in suppression of antiapoptotic gene products and enhancement of apoptosis	Molecular Cancer Research	252	10.1158/1541-7786.MCR-07-2088
7	Shoieb Am, 2003 [38]	In vitro inhibition of growth and induction of apoptosis in cancer cell lines by thymoquinone	International Journal of Oncology	216	10.3892/ijo.22.1.107
8	Badary Oa, 1997 [39]	Thymoquinone ameliorates the nephrotoxicity induced by cisplatin in rodents and potentiates its antitumor activity	Canadian Journal of Physiology and Pharmacology	210	10.1139/y97-169
9	AL-ALI A, 2008 [40]	Oral and intraperitoneal LD50 of thymoquinone, an active principle of *Nigella sativa*, in mice and rats	Journal of Ayub Medical College Abbottabad	208	19385451
10	EL-NAJJAR N, 2010 [18]	Reactive oxygen species mediate thymoquinone-induced apoptosis and activate ERK and JNK signaling	Apoptosis	203	10.1007/s10495-009-0421-z

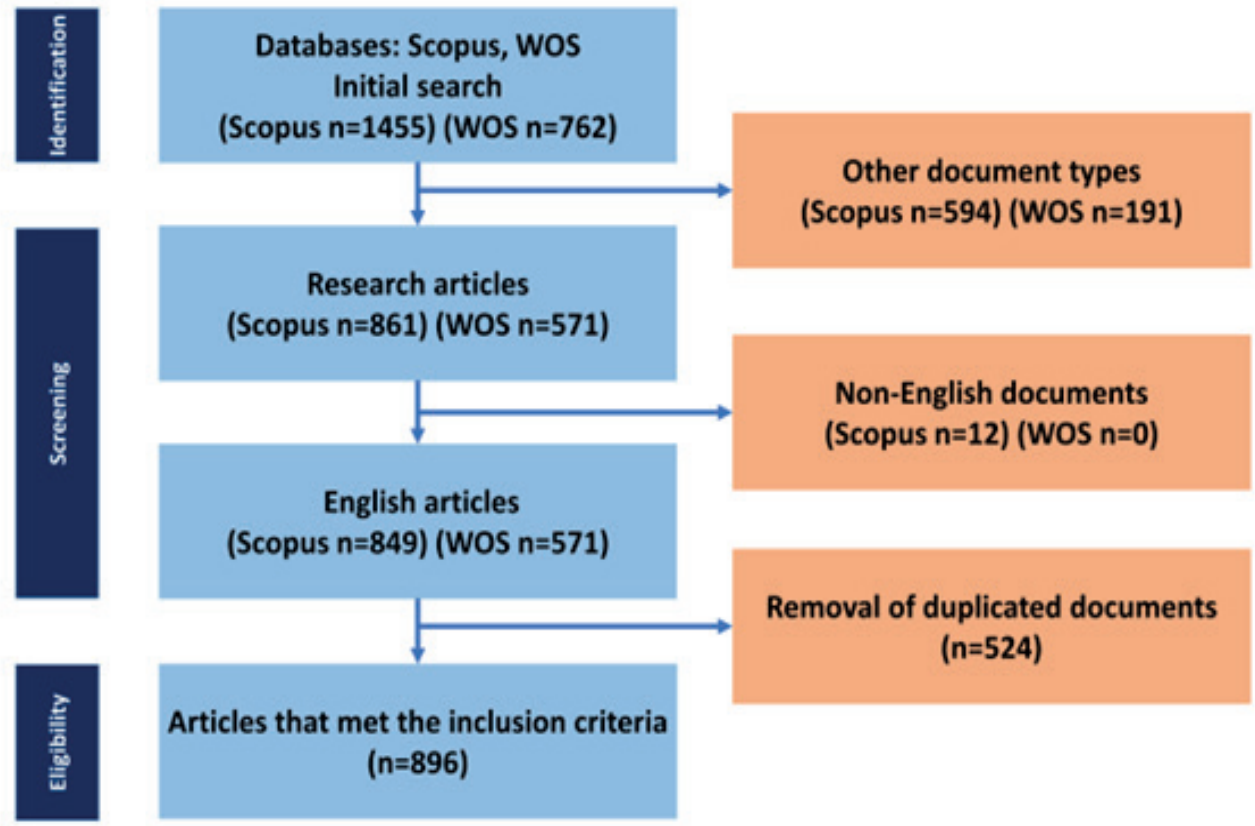

Figure 1. Screening process of articles from Scopus and Web of Science (WOS) databases.

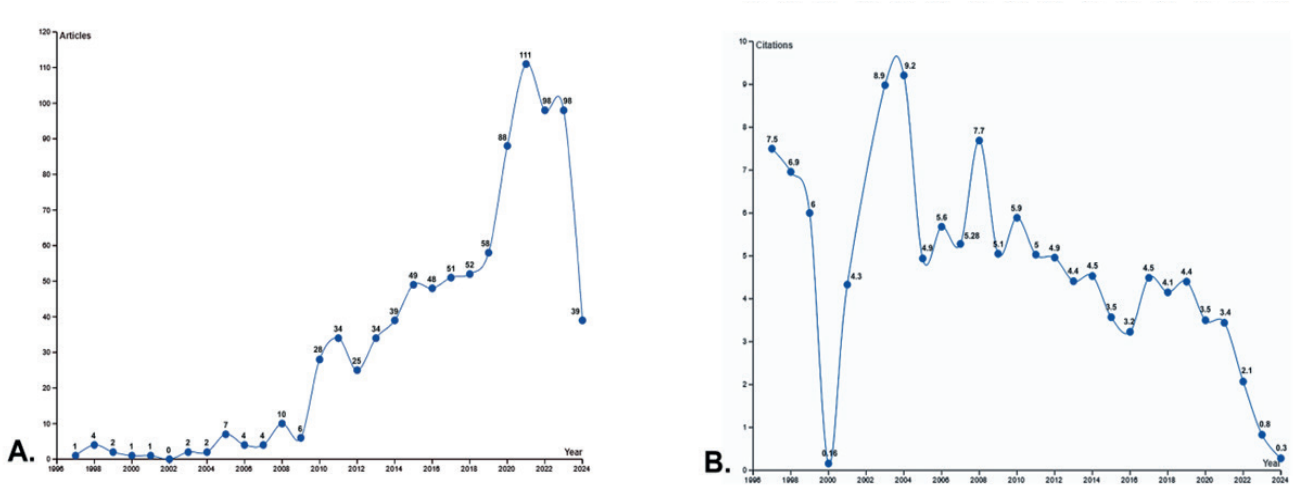

Figure 2. The global annual pattern of (A) publication and (B) citation concerning the impact of thymoquinone on neoplasms (1997–2024).

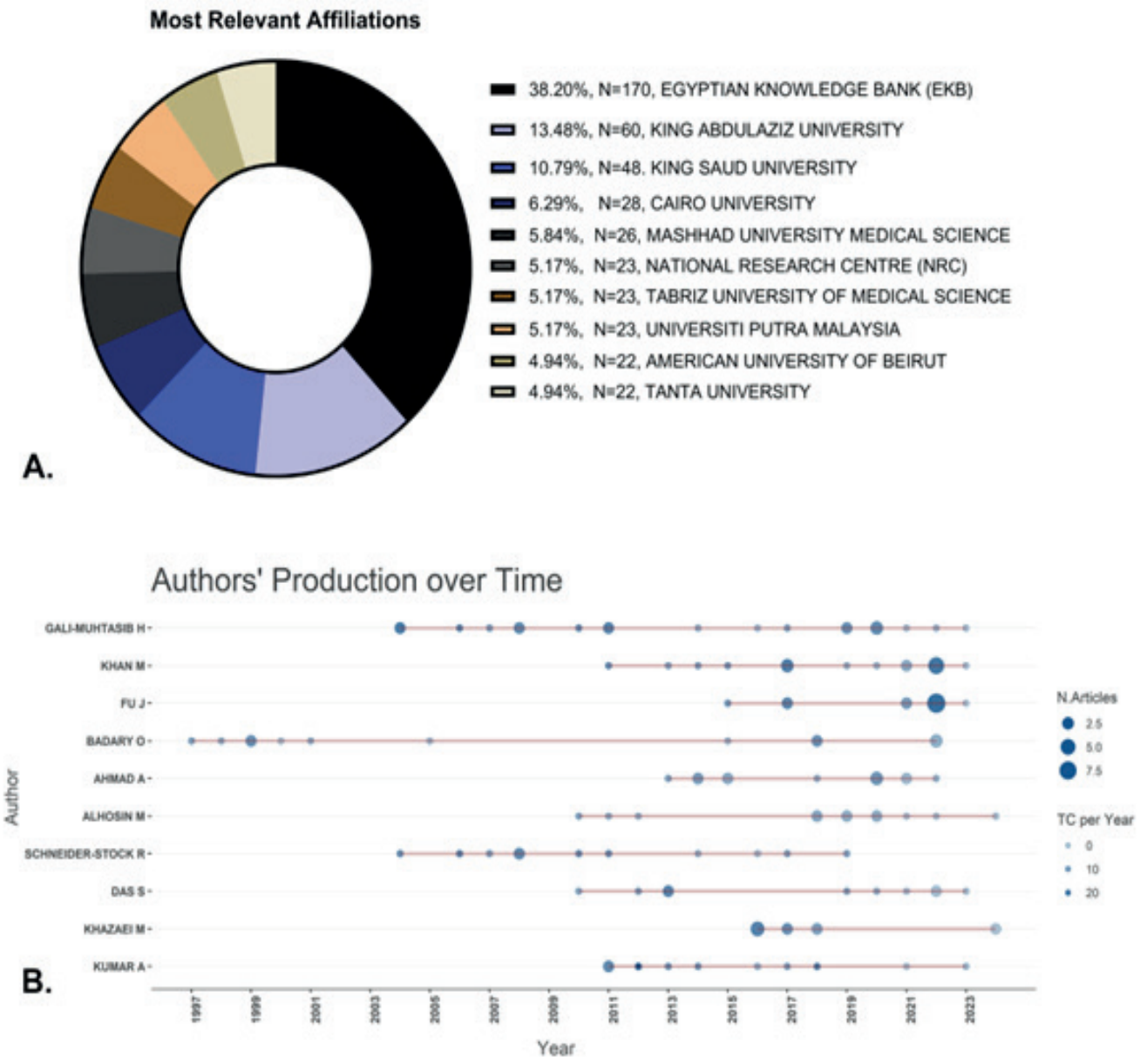

Figure 3. Presents the most productive authors, institutions, countries, and their network of collaboration (A). It also shows the ten authors who have contributed the most to the field and their production over time on the topic of the thymoquinone effects on neoplasms (1997–2024) (B).

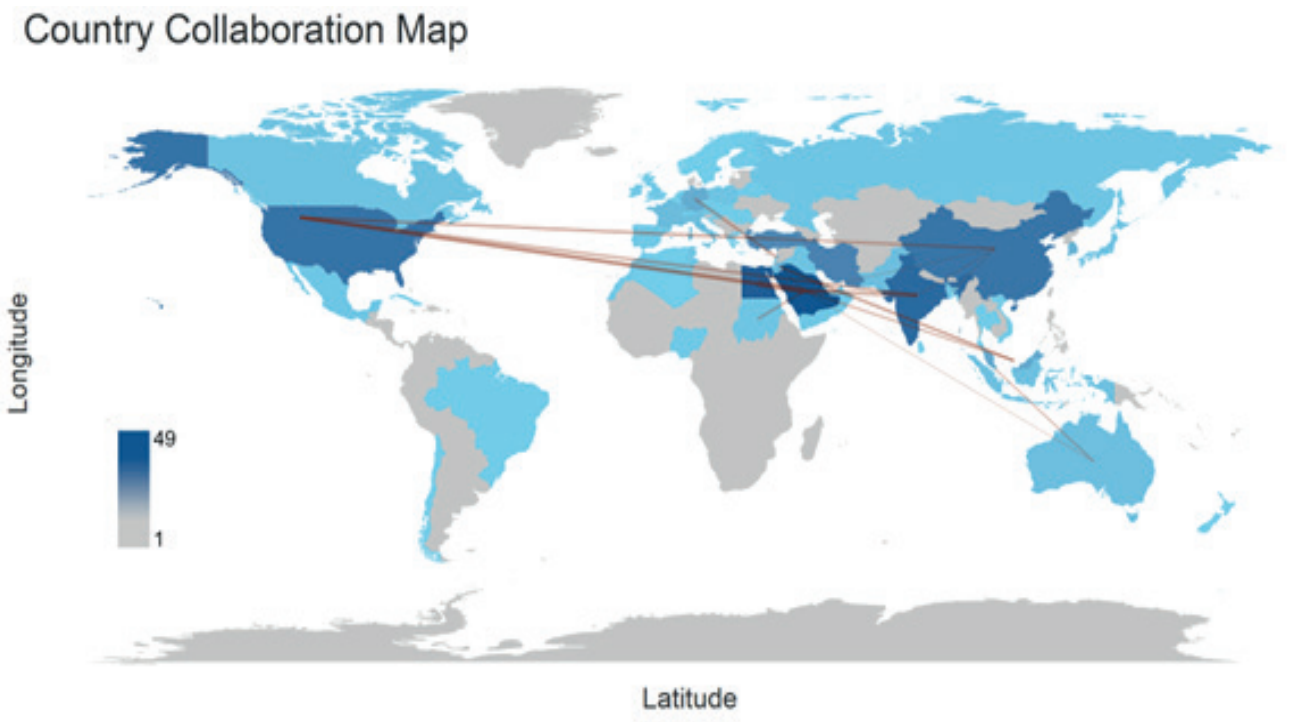

Figure 4. This word map is a global collaboration map on the subject of the thymoquinone effects on neoplasms (1997–2024). The depth of color saturation corresponds to the increasing number of articles within each country. The collaboration between countries is represented by the thickness of the connecting arrows.

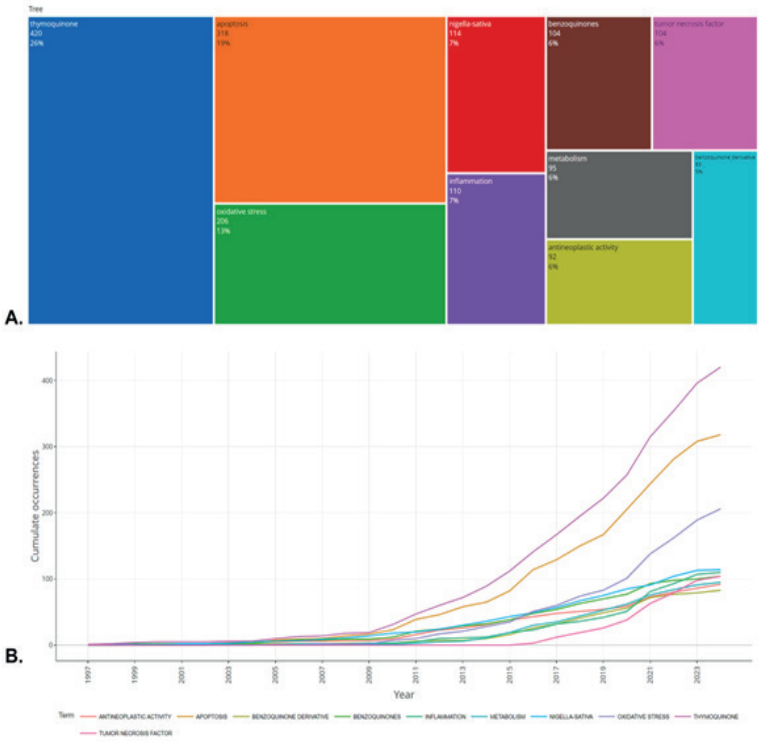

Figure 5. Includes a TreeMap (A) and a scatter plot (B) that represent the top ten author's keywords in the research on the thymoquinone effects on neoplasms (1997–2024).

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