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REVIEW

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A bibliometric analysis of ginger's anticancer potential: bioactive compound, cancer type, and mechanism of action

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Abstract: This study explores the anticancer properties of ginger (*Zingiber officinale*) through comprehensive bibliometric analysis of literature published from 2015 to 2024. Using PRISMA methodology, 49 relevant articles were identified from PubMed and analyzed through Biblioshiny and VOSviewer software. The *International Journal of Molecular Sciences* emerged as the leading publication source. Network visualization identified three major research clusters: antioxidant mechanisms, cancer biology, and phytochemical applications. Triple-negative breast cancer and colorectal cancer represent the most extensively studied malignancies. Mechanistically, ginger compounds (particularly gingerols and shogaols) demonstrate anticancer effects through multiple pathways including apoptosis induction, cell cycle arrest, anti-metastatic activity, oxidative stress modulation, and angiogenesis inhibition. While in vitro and preclinical evidence is robust, clinical translation remains limited. This analysis provides a comprehensive overview of ginger's anticancer research landscape, highlighting established mechanisms, identifying knowledge gaps, and suggesting future directions. The findings support ginger's potential as a complementary therapeutic agent and source of lead compounds for anticancer drug development, while emphasizing the need for advanced clinical investigations.

Keywords: gingerol, apoptosis, cancer, phytochemicals, bibliometric analysis

Introduction

Cancer is one of the most prevalent chronic diseases and remains a leading cause of death worldwide. Each year, approximately 10 million people succumb to cancer, with this figure expected to rise due to lifestyle changes and the aging global population [1] . Cancer is characterized by uncontrolled cell proliferation, which invades surrounding healthy tissues and can metastasize to other body parts. Consequently, developing effective prevention, early detection, and treatment strategies poses a critical challenge in global cancer management.

One promising area of cancer research involves the exploration of natural material-based therapies. Bioactive compounds derived from plants have demonstrated significant potential in cancer prevention and treatment, often presenting fewer side effects than conventional therapies like chemotherapy and radiation. Among these natural ingredients, ginger (*Zingiber officinale*) has garnered increasing attention from researchers [2]. Traditionally used in systems of medicine such as Ayurveda, Unani, and traditional Chinese medicine, ginger is valued for its anti-inflammatory and antimicrobial properties.

The main phytochemical compounds in ginger—gingerol, shogaol, paradol, zingerone, and essential oils—are known for their therapeutic properties. Notably, gingerol exhibits antiproliferative effects, inhibiting cancer cell growth, while shogaol stimulates apoptosis in cancer cells [3]one of the most ancient known spices, contains bioactive compounds with several health benefits. [6]-Gingerol constitutes the most pharmacologically active among such compounds. The aim of the present work was to review the literature pertaining to the use of ginger extract and [6]-gingerol against tumorigenic and oxidative and inflammatory processes associated with cancer, along with the underlying mechanisms of action involved in signaling pathways. This will shed some light on the protective or therapeutic role of ginger derivatives in oxidative and inflammatory regulations during metabolic disturbance and on the antiproliferative and anticancer properties. Data collected from experimental (in vitro or in vivo. Among these, 6-gingerol has been

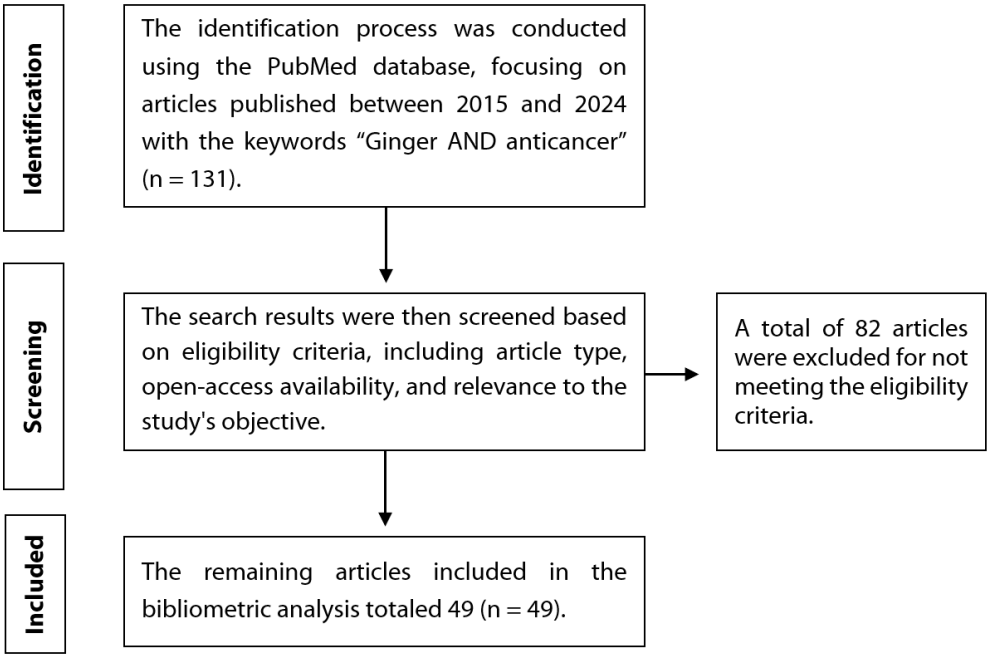

Figure 1. Prisma method

identified as particularly effective in combating cancer [4], outperforming other derivatives such as 8-gingerol, 10-gingerol, and 6-shogaol. These compounds position ginger as a promising candidate for preventive and rehabilitative cancer therapy.

Research on ginger's anticancer properties has expanded across a range of experimental models, including in vitro cell culture studies, animal models, and a limited number of clinical investigations. This expanding literature necessitates systematic analysis to identify trends, evaluate the strength of evidence, and highlight areas requiring further investigation. Bibliometric analysis represents a valuable approach for quantitatively assessing the research landscape, enabling the identification of key contributors, prevalent research themes, and evolving trends in the field [5].

This study aims to conduct a bibliometric analysis of research on ginger's anticancer properties published between 2015 and 2024. By examining publication patterns, keyword frequencies, and thematic clusters, we seek to provide a holistic overview of the current state of knowledge regarding ginger's anticancer potential. Additionally, through in-depth analysis of mechanisms of action, bioactive compounds, and cancer-specific effects, this study aims to synthesize existing evidence and identify promising directions for future research. The findings from this analysis will serve as a valuable resource for researchers, clinicians, and pharmaceutical developers interested in harnessing ginger's anticancer properties for therapeutic applications.

Methods

This study employed the PRISMA method (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) to systematically identify and analyze relevant publications, as illustrated in Figure 1. The process was conducted in three stages: identification, screening, and inclusion. In the identification stage, the PubMed database was searched using the keywords "ginger AND anticancer" for articles published between 2015 and 2024. This search yielded 131 open-access publications related to the keywords.

During the screening stage, these articles were reviewed to identify those most relevant to the study's objective: exploring the potential of ginger as an anticancer agent for enhancing cancer medical treatment. Articles that were not aligned with this focus were excluded. In the inclusion stage, 82 articles were excluded due to irrelevance, leaving 49 articles for further analysis. These selected articles were then analyzed using bibliometric methods to assess trends, contributors, and key themes in ginger-related anticancer research.

Publication patterns and sources

The bibliometric analysis of data retrieved from the PubMed database reveals a general increase in

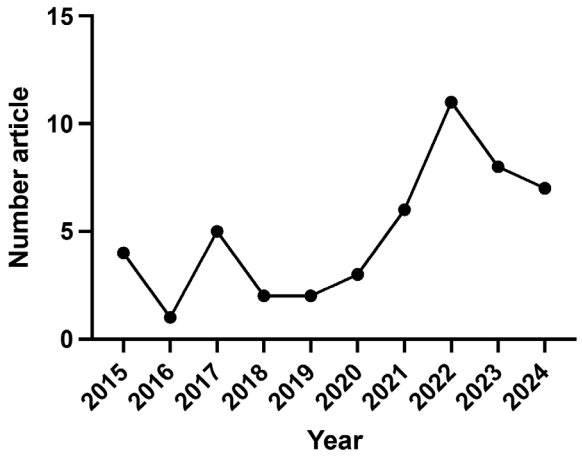

Figure 2. Annual publication trends of articles on ginger (2015–2024)

the number of publications on ginger as a potential anticancer agent from 2015 to 2024 (Figure 2). While the yearly publication trend has shown fluctuations, the notable surge in 2022 reflects researchers' sustained interest from in ginger's anticancer properties.

The analysis of the most relevant reference sources shows that the *International Journal of Molecular Sciences* has made the most significant contribution to this research area, with four articles published during the studied period. This indicates the journal's dominant role in disseminating relevant literature, likely due to its thematic alignment with molecular studies on ginger compounds.

Other journals have also made substantial contributions to the field. *Molecules*, *Nutrients*, and *Scientific Reports* have each published three articles on ginger's anticancer properties during the study period. This distribution pattern indicates that research on ginger's anticancer potential spans multiple disciplines, including molecular biology, nutrition science, and general scientific discovery. The multidisciplinary nature of these publications reflects the complex and varied mechanisms through which ginger compounds may exert their anticancer effects.

Keyword analysis

The examination of keyword frequency and distribution provides crucial insights into the conceptual focus and thematic trends within ginger anticancer research. Through bibliometric mapping of keywords from the selected literature, clear patterns emerge regarding both the methodological approaches and biological mechanisms under investigation.

Figure 3B illustrates the most frequently occurring keywords in this research area, offering a quantitative perspective on the dominant themes. The keyword "humans" appears with the highest frequency (23 occurrences), indicating a significant focus on studies with direct relevance to human applications. This emphasis suggests that research on ginger's anticancer properties is largely oriented toward translational outcomes rather than remaining purely exploratory.

Following this, "tumor cell lines" (9 occurrences) represents the second most common keyword, highlighting the methodological reliance on in vitro cancer models. This prevalence reflects the importance of controlled experimental systems in establishing mechanistic understanding before advancing to more complex models or clinical studies.

The terms "cell proliferation/drug effects" and "Zingiber officinale/chemistry" each appear with 6 occurrences, underscoring two parallel research interests: the functional outcomes of ginger treatment on cancer cell growth, and the phytochemical characterization of ginger's bioactive compounds. This dual focus demonstrates how research in this field bridges traditional pharmacognosy with modern cancer biology.

"Apoptosis" (4 occurrences) emerges as another significant keyword, reflecting the central importance of programmed cell death as a mechanism through which ginger compounds exert their anticancer effects. This finding aligns with the mechanistic studies detailed in the literature, where various ginger compounds have been shown to activate both intrinsic and extrinsic apoptotic pathways across different cancer types.

Network visualization of keyword relationships

Additional analysis using VOSviewer software visualized keyword relationships within the literature (Figure 3C), revealing complex interconnections between research themes. The network visualization demonstrates significant overlaps between molecular mechanisms and clinical applications. Key terms like "humans" and "Zingiber officinale" appear as central nodes connecting preclinical and clinical studies, underscoring the translational aspect of ginger research.

The network reveals three distinct but interconnected clusters representing the primary research directions: antioxidant mechanisms, cancer biology, and phytochemicals/nutraceuticals. In the antioxidant mechanism cluster, keywords such as "ginger,"

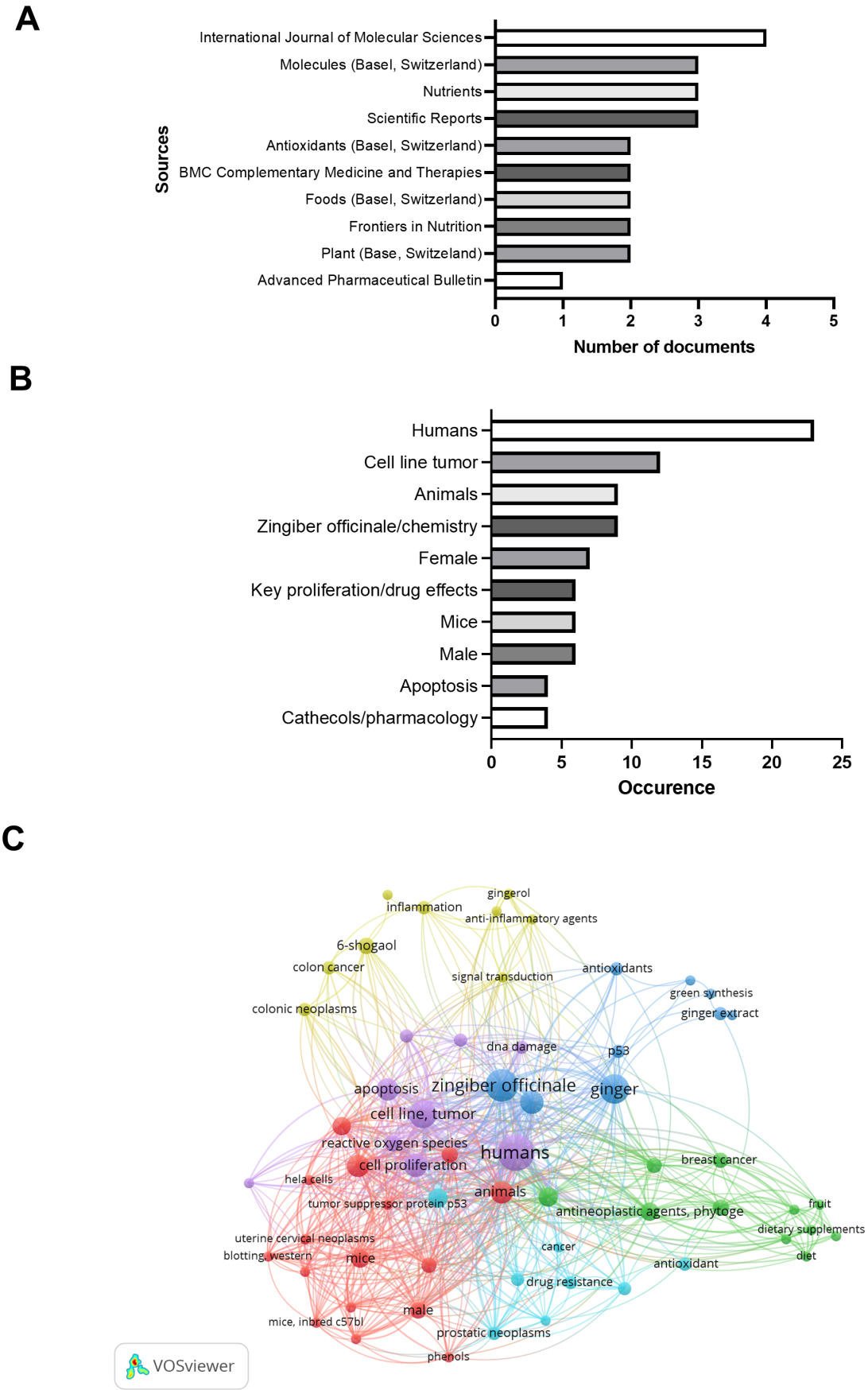

Figure 3. Analysis of journal source, keyword, and keyword analysis**.** (A) Relevant sources ranked by the number of published articles, (B) Frequency graph of the most relevant keywords in the study, (C) Network visualization of keyword relationships

"antioxidants," "ginger extract," "p53," and "DNA damage" demonstrate a focus on ginger's antioxidant effects. This cluster highlights research on how bioactive compounds like gingerol and shogaol protect cells from DNA damage caused by reactive oxygen species (ROS). The prominence of "p53" within this cluster indicates significant research on ginger's role in modulating tumor suppressor genes involved in apoptosis and DNA repair.

The cancer biology cluster features keywords such as "apoptosis," "cell proliferation," "tumor suppressor protein p53," "reactive oxygen species," and "tumor," highlighting ginger's role in inducing apoptosis and modulating ROS in cancer cells. The phytochemicals and nutraceuticals cluster focuses on ginger as a phytochemical-based anticancer agent, such as gingerol and 6-shogaol.

Ginger's anticancer effects across cancer types

The bibliometric analysis reveals that ginger's anticancer properties have been extensively investigated across various cancer types, with particular focus on certain malignancies. Breast cancer emerges as the most thoroughly studied cancer type, with significant attention given to triple-negative breast cancer (TNBC) models (Figure 4A). Research has demonstrated that 10-gingerol effectively inhibits metastatic dissemination in TNBC in vivo [6], while 6-shogaol targets cancer stem cells by inhibiting mammosphere formation and downregulating stemness markers [7]. Additionally, multiple studies have confirmed that ginger-derived compounds target lipid raft-associated PI3K/Akt signaling in radio-resistant TNBC cells [8], and revert the malignant phenotype in 3D culture models [9].

Colorectal cancer represents another extensively investigated malignancy, with research spanning from molecular mechanisms to in vivo models. Studies have shown that 8-gingerol regulates colorectal cancer cell proliferation through the EGFR/STAT/ERK pathway [10], while 6-shogaol inhibits cell migration through suppression of epithelial-mesenchymal transition via the IKKβ/NF-κB/Snail pathway [11]. Furthermore, in animal models, ginger extract delivered via PEGylated nanoliposomes has demonstrated significant anti-tumor effects [12], and 6-gingerol has shown promise in delaying tumorigenesis in chemically-induced colorectal cancer models [13].

Hepatocellular carcinoma has also been the subject of substantial research, with ginger extract demonstrating significant hepatoprotective and anticancer effects. Standardized ginger extract has been shown to ameliorate liver cancer by reducing proliferation and inducing apoptosis through inhibition of oxidative stress and inflammatory pathways [14]. Additionally, ginger polysaccharides induce cell cycle arrest and apoptosis in HepG2 cells through modulation of the Bax/Bcl-2 ratio and activation of caspase pathways [15].

In the context of cervical cancer, research has focused on mechanistic pathways involving p53 and proteasome inhibition. 6-Gingerol has been shown to reactivate p53 through proteasome inhibition, leading to enhanced apoptosis in cervical cancer cells [16]. Similarly, 6-shogaol serves as a novel thioredoxin reductase inhibitor, inducing oxidative stress-mediated apoptosis in HeLa cells [17].

Head and neck cancers, including oral cancers, have been examined through various models. 6-Shogaol induces apoptosis and cell cycle arrest in these malignancies [18], while 6-gingerol promotes autophagy and apoptosis via AMPK activation and AKT/mTOR inhibition [19]. Recent research also indicates that ginger compounds can act as radiosensitizers in head and neck squamous cell carcinoma [20].

Lung cancer studies demonstrate that ginger extract promotes telomere shortening and cellular senescence [21], while 6-gingerol downregulates iron transport and PD-L1 expression, inducing apoptosis in non-small cell lung cancer cells [22]. Furthermore, 6-gingerol has been shown to enhance autophagy-dependent ferroptosis through USP14 inhibition in lung cancer models [23].

Research on gastric cancer indicates that 6-gingerol enhances the radiosensitivity of gastric cancer cells through G2/M phase arrest and apoptosis induction [24]. Additional studies have explored the palliative role of aqueous ginger extract in chemically-induced gastric cancer models [25].

Less extensively studied cancers include prostate cancer, where ginger extract shows anti-drug resistance effects on malignant cells [26]; and glioblastoma, where paradol induces cell cycle arrest and apoptosis [27]. These diverse findings across multiple cancer types highlight the broad spectrum of ginger's anticancer potential and suggest that certain bioactive compounds may have targeted efficacy against specific malignancies based on their unique molecular mechanisms.

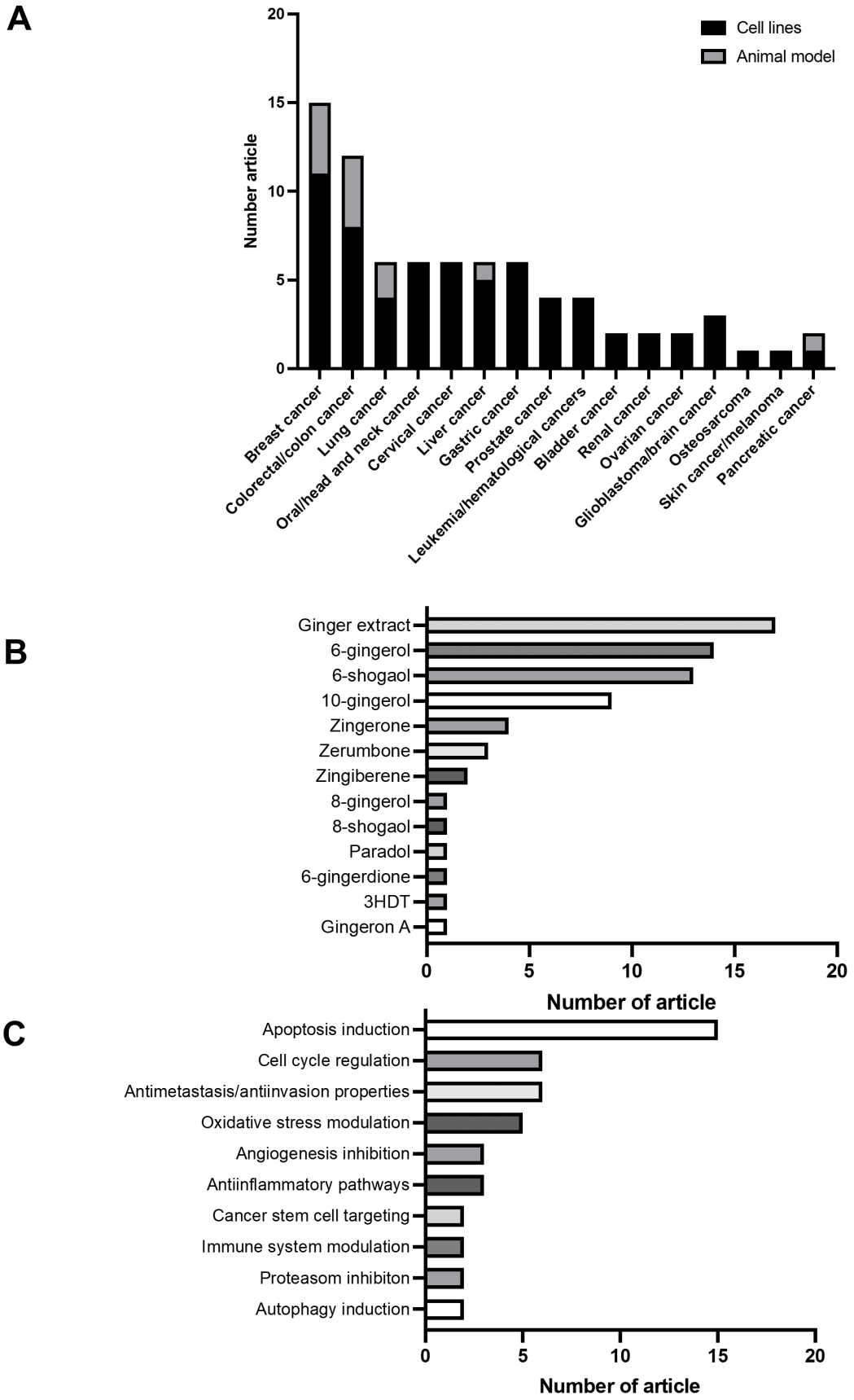

Figure 4. Expanding the bibliometric analysis. (A) Ginger's anticancer effects across cancer types, (B) Bioactive compounds and extracts of ginger, (C) Ginger's anticancer mechanisms of action

Bioactive compounds and extracts of ginger

The bibliometric analysis reveals that research on ginger's anticancer properties has extensively investigated both whole extracts and specific bioactive compounds, with certain molecules emerging as particularly promising therapeutic agents (Figure 4B). 6-Gingerol stands out as the most thoroughly studied compound, demonstrating remarkable versatility in its anticancer mechanisms across multiple cancer types (Figure 4A). Studies have shown that 6-gingerol effectively induces caspase-dependent apoptosis in bladder cancer cells through MAPK and ROS signaling pathways [28], reactivates p53 through proteasome inhibition in cervical cancer cells [16], and promotes autophagy and apoptosis via AMPK activation and AKT/mTOR inhibition in oral cancer cells [19]. Additionally, 6-gingerol demonstrates cell cycle regulatory effects by inducing G1-phase arrest via the AKT-GSK3β-cyclin D1 pathway in renal cell carcinoma [29], and inhibits iron transport and PD-L1 expression in non-small cell lung cancer cells [22].

10-Gingerol has shown particular promise in breast cancer research, with studies demonstrating its ability to inhibit metastatic dissemination of triple-negative breast cancer in vivo [6], target lipid raft-associated PI3K/Akt signaling in radio-resistant cancer cells [8], and revert the malignant phenotype of breast cancer cells in 3D culture [9]. The compound also effectively inhibits proliferation and invasion of MDA-MB-231 breast cancer cells through suppression of Akt and p38MAPK activity [30]. Research on 8-gingerol, though less extensive, has shown that it regulates colorectal cancer cell proliferation and migration through the EGFR/STAT/ERK pathway [10].

6-Shogaol emerges as another significant compound with potent anticancer properties. It has been shown to inhibit cell migration in colon cancer by suppressing the epithelial-mesenchymal transition process through the IKKβ/NF-κB/Snail pathway [11], induce apoptosis and cell cycle arrest in head and neck squamous cell carcinoma [18], and serve as a novel thioredoxin reductase inhibitor inducing oxidative stress-mediated apoptosis in HeLa cells [17]. Notably, 6-shogaol also demonstrates particular efficacy against cancer stem cells in breast cancer models [7] and can overcome TRAIL resistance in colon cancer cells via inhibition of survivin [31].

Less studied compounds showing anticancer potential include zerumbone, which reduces motility and proliferation of oral cancer cells [32]; zingerone, which suppresses tumor development through decreasing cyclin D1 expression and inducing mitotic arrest [33]; and paradol, which induces cell cycle arrest and apoptosis in glioblastoma cells [27]. Emerging research has also identified novel compounds such as gingerenone A, which induces ferroptosis in colorectal cancer via targeting suppression of SLC7A11 signaling pathway [34].

Whole ginger extracts have demonstrated significant anticancer effects in various formulations. Standardized extract of ginger has been shown to ameliorate liver cancer by reducing proliferation and inducing apoptosis through inhibition of oxidative stress and inflammatory pathways [14], while aqueous ginger extract has demonstrated a palliative role in chemically-induced gastric cancer [25]. Advanced delivery systems have also been investigated, with PEGylated nanoliposomes containing ginger extract showing significant anti-tumor effects in colorectal cancer-bearing mice [12], and ginger exosome-like nanoparticles inducing apoptosis and cell cycle arrest in triple-negative breast cancer cells [35]. These diverse findings across multiple compounds and extract formulations highlight the chemical complexity of ginger's anticancer properties and suggest that different constituents may have targeted efficacy against specific cancer types through distinct molecular mechanisms.

Ginger's anticancer mechanisms of action

The bibliometric analysis reveals a comprehensive landscape of research exploring ginger's anticancer properties through multiple mechanistic pathways (Figure 4C). Apoptosis induction emerges as the predominant mechanism, with numerous studies demonstrating that bioactive compounds from ginger, particularly 6-gingerol, 6-shogaol, and 10-gingerol, trigger both intrinsic and extrinsic apoptotic pathways across diverse cancer types. These compounds consistently activate caspase cascades, modulate Bcl-2 family proteins, and regulate mitochondrial membrane potential [16]. For instance, 6-gingerol reactivates p53 in cervical cancer through proteasome inhibition, while 6-shogaol exhibits potent apoptotic effects in head and neck squamous cell carcinoma by targeting the AKT signaling pathway [18]. Investigation of 10-gingerol in triple-negative breast cancer revealed its ability to induce apoptosis through modulating the expression of Bax and Bcl-2 [36].

Cell cycle regulation represents another significant mechanism, with ginger compounds demonstrating the ability to induce cell cycle arrest at different phases. Notably, 6-gingerol frequently induces G2/M and G1 phase arrest through modulation of cyclins and cyclin-dependent kinases, as observed in renal cell carcinoma via the AKT-GSK3β-cyclin D1 pathway [29]. In gastric cancer cells, 6-gingerol enhances radiosensitivity through G2/M phase arrest and apoptosis induction [24]. Zingerone has been shown to suppress tumor development through decreasing cyclin D1 expression and inducing mitotic arrest in neuroblastoma models [33].

The anti-metastatic properties of ginger compounds, particularly 10-gingerol and 6-shogaol, constitute another critical mechanism. These compounds suppress epithelial-mesenchymal transition (EMT) by regulating key proteins like E-cadherin, N-cadherin, and vimentin. In colon cancer, 6-shogaol specifically inhibits cell migration through the IKKβ/NF-κB/Snail pathway [11], while 10-gingerol demonstrates potent anti-metastatic effects in triple-negative breast cancer models both in vitro and in vivo [6]. Zerumbone has been shown to target the CXCR4-RhoA signaling axis to reduce motility of oral cancer cells [32].

Oxidative stress modulation emerges as an increasingly recognized mechanism through which ginger compounds exert anticancer effects. Multiple studies reveal that ginger bioactives like 6-gingerol and zingerone can generate reactive oxygen species (ROS) in cancer cells while paradoxically exhibiting antioxidant properties in normal cells [22]. This dual effect creates a therapeutic window where cancer cells undergo oxidative stress-induced death pathways, including novel mechanisms like ferroptosis, as demonstrated with gingerone A in colorectal cancer [34]. 6-Shogaol serves as a novel thioredoxin reductase inhibitor, inducing oxidative stress-mediated apoptosis in HeLa cells [17].

The anti-inflammatory activity of ginger compounds provides another important anticancer mechanism, with research showing inhibition of pro-inflammatory cytokines and signaling pathways, particularly NF-κB and STAT3. Zingerone demonstrates immune-enhancing properties in breast cancer models [37], while 6-shogaol significantly inhibit inflammatory pathways in prostate cancers [27]. Standardized ginger extract ameliorates liver cancer by reducing proliferation and inducing apoptosis through inhibition of oxidative stress and inflammatory pathways [14].

Emerging evidence also points to ginger's ability to inhibit angiogenesis, with zerumbone and 6-gingerol showing particular promise in this area. 6-Gingerol's stabilization of the p-VEGFR2/VE-cadherin/β-catenin/actin complex promotes microvessel normalization and suppresses tumor progression, representing a sophisticated mechanism for controlling tumor growth [11]. Zerumbone specifically inhibits tumor angiogenesis via suppression of NF-κB activity in gastric cancer [38].

Novel mechanisms continue to emerge, including effects on cancer stem cells, as demonstrated by 6-shogaol and pterostilbene in breast cancer [7], and the induction of non-apoptotic cell death pathways like paraptosis and autophagy. 6-Shogaol induces caspase-independent paraptosis through proteasomal inhibition [39], while 6-gingerol enhances autophagy-dependent ferroptosis in lung cancer by inhibiting USP14 [23]. Recent research has also identified the potential of ginger compounds to modulate the tumor microenvironment, with ginger extract promoting anti-tumor immunity through mitochondrial biogenesis in CD8+ T cells [40].

Conclusion

This bibliometric analysis of ginger's anticancer properties provides an overview of research trends, mechanistic insights, and therapeutic potential. The mechanistic analysis reveals that ginger compounds exert anticancer effects through multiple pathways, with apoptosis induction, cell cycle regulation, and anti-metastatic activities emerging as the most documented mechanisms.

The cancer-specific analysis demonstrates that breast cancer, particularly triple-negative breast cancer, and colorectal cancer have received the most research attention, with promising results in both in vitro and animal models. However, research on other cancer types remains relatively limited, presenting opportunities for expanded investigation.

Despite the robust preclinical evidence, a significant gap exists in translating these findings to clinical applications. Future research should prioritize clinical trials, bioavailability studies, and novel delivery systems to overcome the pharmacokinetic limitations of ginger compounds. Additionally, combination therapies with conventional treatments warrant further exploration to potentially enhance efficacy and reduce side effects.

This bibliometric analysis synthesizes the current state of knowledge regarding ginger's anticancer potential but also identifies promising avenues for future research. The diverse mechanisms and broad-spectrum activity of ginger compounds against various cancer types suggest significant potential for therapeutic applications, either as complementary treatments or as lead compounds for drug development. As research continues to advance, ginger may emerge as a valuable addition to the anticancer therapeutic arsenal, offering natural, potentially safer alternatives or adjuncts to conventional treatments.

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Author contribution

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Declaration of interest

The authors declare there are not competing interests.

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