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ANTICANCER AND CHEMOPREVENTIVE EFFECTS OF ISOTHIOCYANATES DERIVED FROM CRUCIFEROUS VEGETABLES ON ONCOLOGICAL DISORDERS: A SYSTEMATIC REVIEW

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ABSTRACT

Background: Cancer is a major global health concern, and increasing research suggests that dietary bioactive substances can affect carcinogenesis and tumour progression. Isothiocyanates (ITCs) are naturally occurring phytochemicals derived from glucosinolates found in cruciferous vegetables like garden cress, broccoli, cabbage, cauliflower and watercress. Sulforaphane (SFN), benzyl isothiocyanate (BITC) and phenethyl isothiocyanate (PEITC) have shown potential anticancer activity by modulating several cellular and molecular pathways. **AIM** This systematic review aimed to review the proposed biological mechanisms of these isothiocyanates and to assess the experimental evidence for their anticancer effects. **Methods**: A systematic literature search was carried out using PubMed, Google Scholar, ScienceDirect, ResearchGate, and pertinent oncology and pharmacology publications. Studies published between 2009 and 2026 were reviewed. **Result**: a total of 415 records were identified. Seven Studies were designated for inclusion in the review. **Conclusion:** The existing experimental evidence indicates that isothiocyanates generated from cruciferous vegetables, particularly sulforaphane, benzyl isothiocyanate, and phenethyl isothiocyanate, have promising anticancer effects

KEYWORDS: Isothiocyanates; Benzyl isothiocyanate; Phenethyl isothiocyanate; Cruciferous vegetables; Cancer.

INTRODUCTION

Cancer is a major global public health concern and comprises a broad group of diseases characterized by uncontrolled cellular proliferation, abnormal tissue growth, invasion, and, in some cases, metastasis. The burden of cancer extends beyond mortality because the disease is also associated with long-term disability, reduced quality of life, substantial treatment expenditure, and socioeconomic consequences for individuals and health system. The global distribution of cancer is influenced by demographic changes, population ageing, environmental exposures, lifestyle-related factors, infectious agents, and inequalities in access to prevention, early detection, and treatment services. Consequently, cancer prevention has become an important component of public health strategies, alongside improvements in diagnosis and therapeutic care [1] . The relationship between diet and cancer has been investigated extensively because dietary exposures are potentially modifiable and may influence several stages of carcinogenesis. Dietary patterns can affect metabolic processes, inflammation, oxidative balance, hormonal regulation, and the availability of bioactive compounds [2] . Although dietary factors cannot be considered independent causes or preventive agents for every cancer type, evidence from nutritional epidemiology and experimental research suggests that food components mamjy modify biological pathways involved in cancer development. Therefore, identifying naturally occurring dietary compounds with plausible chemopreventive properties remains an important area of cancer research.

Cruciferous vegetables, belonging primarily to the family Brassicaceae, include commonly consumed foods such as broccoli, cabbage, cauliflower, Brussels sprouts, radish, mustard, and other Brassica species. These vegetables contain a range of nutrients and phytochemicals, including glucosinolates, phenolic compounds, flavonoids, vitamins, and minerals. Glucosinolates are particularly important because their enzymatic breakdown can produce biologically active compounds, including isothiocyanates and indole-related products [3]. The composition and concentration of these compounds vary according to plant species, cultivar, growing conditions, maturity, storage, and food-processing practices. Glucosinolates are sulfur- and nitrogen-containing secondary metabolites characteristic of cruciferous

vegetables. Following plant tissue disruption during cutting, crushing, chewing, food preparation, or digestion, glucosinolates may undergo enzymatic hydrolysis, primarily through the activity of myrosinase[4]. This process can generate different hydrolysis products, including isothiocyanates, nitriles, and other compounds, depending on the glucosinolate precursor, plant matrix, enzyme activity, processing conditions, and gastrointestinal environment. These variables are important because they may influence the quantity, stability, bioavailability, and biological activity of the compounds ultimately available to tissues. Glucosinolates are sulfur- and nitrogen-containing secondary metabolites characteristic of cruciferous vegetables. Following plant tissue disruption during cutting, crushing, chewing, food preparation, or digestion, glucosinolates may undergo enzymatic hydrolysis, primarily through the activity of myrosinase.

Dietary interventions and nutritional strategies have also been considered in the context of cancer prevention and treatment support. Plant-based dietary patterns may provide fibre, micronutrients, and a wide range of phytochemicals, while potentially reducing exposure to some dietary factors associated with adverse health outcomes[5]. Nevertheless, the effects of dietary patterns are complex and may be influenced by total energy intake, body composition, physical activity, socioeconomic circumstances, adherence, and other lifestyle characteristics.

The presence of a potentially beneficial food component does not mean that consumption of a particular food or supplement can replace established cancer prevention, screening, or treatment approaches. Certain vegetable components only have Interest in cruciferous vegetables has increased because epidemiological and experimental studies have investigated their possible association with cancer-related outcomes .[6]. The proposed biological relevance of these vegetables is not attributed to a single constituent but to a combination of phytochemicals that may act through overlapping or complementary pathways. However, epidemiological findings can vary according to the cancer site, dietary assessment method, population characteristics, cooking practices, and overall dietary pattern. Associations between cruciferous vegetable consumption and cancer risk should be interpreted carefully and should not be equated automatically with proof of a direct preventive effect . Studies of plant-based dietary patterns have also explored their relationship with site-specific cancers, including prostate cancer. However, differences in study design, dietary exposure measurement, confounding factors, and the population under investigation may contribute to inconsistent findings.

Among the bioactive constituents of cruciferous vegetables, isothiocyanates have received particular attention because of their potential effects on cellular and molecular processes associated with carcinogenesis. Isothiocyanates are formed from specific glucosinolate precursors through enzymatic hydrolysis. The most frequently investigated compounds include sulforaphane (SFN), benzyl isothiocyanate (BITC), and phenethyl isothiocyanate (PEITC) [9]. Other related compounds may also be studied, but the biological properties of individual isothiocyanates can differ because of variations in chemical structure, lipophilicity, cellular uptake, metabolic transformation, and interaction with intracellular targets.

The biological effects of isothiocyanates have been investigated in relation to cellular proliferation, apoptosis, oxidative stress, cell-cycle regulation, detoxification pathways, and carcinogen metabolism. Some studies have examined the induction of phase II detoxification enzymes and the modulation of enzymes involved in the activation or inactivation of carcinogenic compounds. Other investigations have focused on the regulation of signaling pathways related to cellular survival, inflammation, stress responses, and abnormal growth. These mechanisms provide a biological rationale for studying isothiocyanates as potential chemopreventive agents, although the presence of a plausible mechanism does not independently establish clinical effectiveness.

Experimental investigations have reported different effects of isothiocyanates across cancer models. Some studies have focused on inhibition of cancer-cell proliferation and viability, whereas others have evaluated apoptosis, oxidative stress, cell-cycle arrest, autophagy, migration, angiogenesis, molecular signalling, or carcinogen-metabolizing enzymes[11]. The reported findings may vary according to the compound studied, cancer type, concentration, exposure duration, control condition, and experimental system. In particular, results obtained from in vitro studies may depend on concentrations that are not necessarily achievable in human tissues. Therefore, findings from one experimental model should not be generalized automatically to all cancer types or to all isothiocyanates.

A systematic review can help organize these findings, identify areas of agreement and uncertainty, and clarify the limitations that should be considered before translating preclinical observations into clinical applications. Previous nutritional research has examined the relationship between diet quality, fruit and vegetable intake, and cancer risk in different populations. The potential influence of diet may involve multiple mechanisms, including regulation of oxidative stress, inflammation, insulin-related pathways, hormone metabolism, and cellular responses to environmental carcinogens.

Accordingly, the present systematic review was undertaken to examine the reported anticancer and chemopreventive effects of isothiocyanates derived from cruciferous vegetables, with particular attention to compounds such as sulforaphane, benzyl isothiocyanate, and phenethyl isothiocyanate. The review aims to synthesise the available experimental evidence concerning their effects on cancer-related biological outcomes, identify the mechanisms investigated across studies, and describe the influence of cancer type, experimental model, concentration, and

exposure conditions on the reported findings. By consolidating the available evidence, this review seeks to identify research gaps and provide a balanced basis for understanding the potential and limitations of isothiocyanates in cancer-related research

MATERIAL AND METHODS

Review design and reporting guideline

This systematic review was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement**.**

Review question and PICOS framework

Component	Definition
Population/Models	Experimental cancer models, including cancer-cell lines, primary cancer cells, animal cancer models, and mechanistic systems directly relevant to carcinogenesis or carcinogen metabolism.
Intervention/Exposure	Isothiocyanates derived from cruciferous vegetables, particularly SFN, BITC, and PEITC.
Comparator	Untreated, vehicle, control, normal/non-cancerous cells, or another experimental comparator where applicable.
Outcomes	Cancer-cell viability/proliferation, apoptosis, cell-cycle effects, migration, angiogenesis, autophagy, molecular signalling, and carcinogenmetabolism/chemo preventive mechanisms.
Study designs	Original experimental laboratory, animal, and mechanistic studies meeting the eligibility criteria.

INFORMATION SOURCES

A comprehensive literature search was carried out to identify studies evaluating the anticancer effects of isothiocyanates derived from cruciferous vegetables. The following electronic databases and search engines were used:

- PubMed
- Google Scholar
- ScienceDirect
- ResearchGate
- Frontiers in Pharmacology / Frontiers in Oncology / Frontiers in Nutrition
- Cancer Research (AACR)

SEARCH STRATEGY

A systematic search was conducted across the databases listed above, using a combination of keywords and MeSH terms including "isothiocyanates," "sulforaphane," "phenethyl isothiocyanate," "benzyl isothiocyanate," "allyl isothiocyanate," "cruciferous vegetables," "Brassica," "cancer," "carcinoma," "apoptosis," "cell cycle arrest," "chemoprevention," and "anticancer activity." The terms were combined with the Boolean operators “AND” and “OR” to maximize the sensitivity and specificity of the search . The search was limited to articles published from 2009 to 2026.

STUDY SELECTION

- Titles and abstracts were initially screened against predefined inclusion and exclusion criteria .
- Independent full-text review of shortlisted articles was conducted.
- Data extraction from the final set of eligible articles was carried out in a standardized data extraction format.

ELIGIBILITY CRITERIA

Inclusion criteria

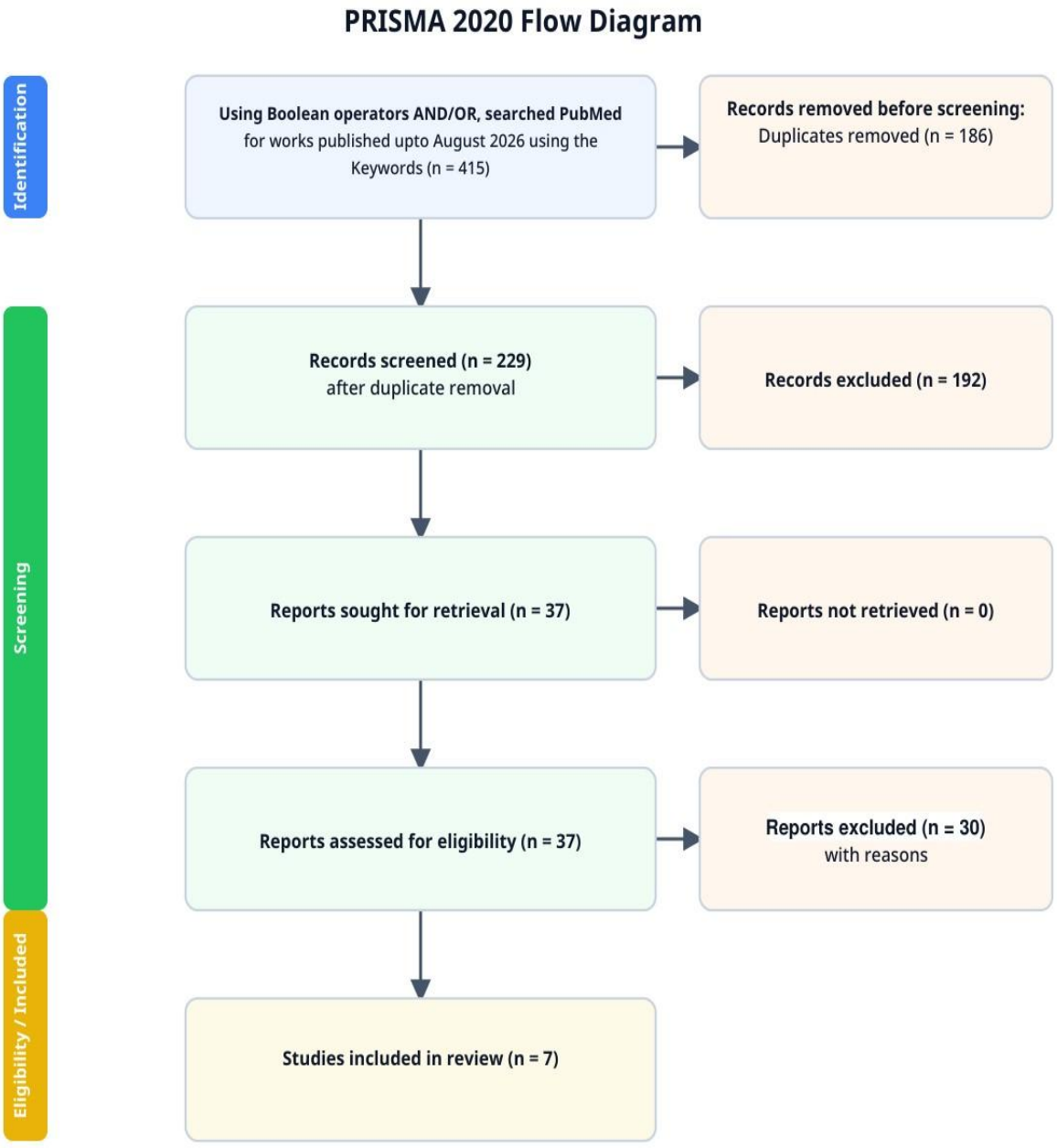
- Original experimental studies evaluating isothiocyanates derived from cruciferous vegetables.

- Studies addressing anticancer, chemo preventive, cellular, molecular, or relevant carcinogenmetabolism outcomes.
- Full-text English language articles within the prespecified publication period.
- Experimental models relevant to the review question such as cancer cell studies and other preclinical or mechanistic systems only when explicitly justified by the review protocol.

Exclusion criteria

- Articles in languages other than English.
- Studies for which only abstracts were available, but no full text could be accessed.
- Review articles, editorials, letters and conference abstracts.
- Articles that are not related to isothiocyanates, cruciferous vegetables or oncological outcomes.

RESULTS



The revised search produced 415 records. Predefined eligibility criteria were used to screen the records and full writings of potentially relevant reports were assessed. A total of 7 studies were identified for inclusion in the final review

CHARACTERISTICS OF THE INCLUDED STUDIES:

Seven studies met the final inclusion criteria. They investigated SFN, BITC, and PEITC in different experimental systems, including bladder cancer, acute myeloid leukaemia, breast cancer, multiple myeloma, prostate cancer, breast epithelial models, and CYP2E1-mediated carcinogen metabolism

Table 1:**Characteristics and the experimental model included from the In Vitro studies**

No.	Study	Isothiocyanate	Experimental model	Study design
1	**Xie et al., 2022[16]**	Sulforaphane (SFN)	RT4, RT112, T24 and TCCSUP human bladder cancer cell lines, including cisplatin- and gemcitabine-resistant variants	**In vitro**
2	**Bertova et al., 2024[**17]	Sulforaphane (SFN) and benzyl isothiocyanate (BITC)	SKM-1 human AML cells and multidrug-resistant SKM/VCR cells	**In vitro**
3	**Renaud Warin et al., 2010[19]**	Benzyl isothiocyanate (BITC)	MDA-MB-231 human breast cancer cells and subcutaneous xenograft model in female nude mice	**In vitro and in vivo**
4	**Jakubikova et al., 2011[18]**	Sulforaphane (SFN) and phenethyl isothiocyanate (PEITC)	Multiple myeloma cell lines, primary myeloma cells, HS-5 stromal cells and mouse xenograft model	**In vitro and in vivo**
5	**Yoshigae et al., 2013[13]**	Phenethyl isothiocyanate (PEITC)	Recombinant human CYP2E1 and human liver microsomal preparations	**Mechanistic experimental study**
6	**Jane In den Birken et al., 2025[14]**	Sulforaphane (SFN)	PC-3 and LNCaP prostate cancer cells, PNT2 prostate epithelial cells and engineered heart tissue generated from hiPSC-derived cardiomyocytes	**In vitro**
7	**Telang et al., 2009[15]**	Phenethyl isothiocyanate (PEITC) and sulforaphane (SFN)	MCF-7 estrogen-dependent breast cancer cells and normal human mammary epithelial (HME) cells	**In vitro**

SFN, sulforaphane; BITC, benzyl isothiocyanate; PEITC, phenethyl isothiocyanate; AML, acute myeloid leukemia

Table 1 summarizes the authors name, year of the study ,type of study and isothiocyanate compounds and experimental models.

Table 2. Characteristics of Methods, Results and Outcomes of the Included Studies

S.NO	AUTHOR	METHODS	RESULTS	OUTCOME

1.	**Xie et al 2022[16]**	In-vitro study using RT4, RT112, T24 and TCCSUP human bladder cancer cell lines and cisplatin/gemcitabine-resistant variants. Cells were treated with different concentrations of sulforaphane (SFN) to evaluate antiproliferative effects.	SFN showed antiproliferative effects against bladder cancer cells, including chemotherapyresistant variants.	SFN demonstrated potential as an antiproliferative agent against bladder cancer, including drug-resistant cells.
2.	**Bertova et al 2024[**17]	In-vitro study using SKM-1 human AML cells and multidrugresistant SKM/VCR cells. SFN and BITC were evaluated for effects on cell viability, proliferation, cell cycle, autophagy and apoptosis.	SFN and BITC exhibited anticancer effects in AML cells, including multidrugresistant cells, with alterations in proliferation, cell cycle, autophagy and apoptosis.	SFN and BITC demonstrated potential against AML and multidrug-resistant leukaemia cells.
3.	**Warin et al,2010[19]**	In-vitro and in-vivo study using MDAMB-231 human breast cancer cells and subcutaneous MDA-MB-231 xenografts in female nude mice. BITC was evaluated for effects on tumour growth, proliferation, migration and angiogenesis.	BITC inhibited parameters associated with breast cancer progression, including tumour growth, proliferation, migration and angiogenesis.	BITC demonstrated antitumor and antimetastatic potential in breast cancer models.
4.	**Jakubikova, et al,2011[15]**	SFN and PEITC were evaluated in multiple human myeloma cell lines, primary CD138+ myeloma cells and a mouse xenograft model. Cytotoxicity, apoptosis and cellcycle effects were investigated xenograft model. Cytotoxicity, apoptosis and	SFN and PEITC produced cytotoxic and pro-apoptotic effects and induced cellcycle changes in myeloma cells.	SFN and PEITC demonstrated potential anti-myeloma activity and possible therapeutic value.

		cellcycle effects were investigated		

5.	**Yasushi Yoshigae et al ,2013[13]**	Mechanistic study using recombinant human CYP2E1 and human liver microsomal preparations to investigate the effects of PEITC on CYP2E1 and oxidative carcinogen bioactivation.	PEITC modulated CYP2E1mediated carcinogen metabolism and oxidative bioactivation.	PEITC may contribute to cancer chemoprevention through modulation of carcinogen metabolism.
6.	**Jane In den Birken, et al,2025[14]**	In-vitro study using PC-3 and LNCaP prostate cancer cells, with PNT2 normal prostate epithelial cells as comparison. SFN effects were also evaluated in engineered heart tissue derived from human iPSC cardiomyocytes.	SFN was evaluated for anticancer activity in prostate cancer cells and for potential cardiotoxic effects in cardiac tissue.	SFN showed potential as an experimental prostate cancer agent, while its safety and cardiotoxicity require consideration.
7.	**Telang et al ,2009[15]**	In-vitro study using MCF-7 estrogendependent breast cancer cells and normal human mammary epithelial cells. SFN and PEITC were tested at 0.3 and 3.0 μM, with geneexpression effects evaluated.	SFN and PEITC altered gene-expression pathways related to estrogen-receptor signalling, apoptosis and cell-cycle regulation.	SFN and PEITC demonstrated potential chemopreventive activity through modulation of molecular pathways involved in breast cancer.

SFN, sulforaphane; BITC, benzyl isothiocyanate; PEITC, phenethyl isothiocyanate; AML, acute myeloid leukemia; CYP2E1, cytochrome P450 2E1.

Table 2 *Summarize the methods, findings, and outcomes including inhibition of cancer-cell proliferation and viability, induction of apoptosis, cell-cycle modulation, alteration of autophagy, inhibition of migration and angiogenesis, and modulation of carcinogen metabolism*

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TABLE 3 : The Risk of bias was assessed across the included studies using study selection, outcome measurement and reporting bias

SciRAP Version 2.1 tool used In Vivo Reliability Assessment of Animal-Specific Components The assessment is limited to the animal/xenograft components of Warin et al. (2010) and Jakubikova et al. (2011).

Study	Test compound controls	Test system / animals	Administration / exposure	Data Collection & analysis	Funding& competing interests
Warin et al., 2010[19]	**F**	**F**	**F**	**F**	**F**
Jakubikova et al., 2011[18]	**PF**	**F**	**F**	**F**	**F**

Legend: Green = Fulfilled (F); Yellow = Partially fulfilled (PF); Red = Not fulfilled (NF); Grey = Not determined (ND).

Source basis: the supplied systematic-review document identifies Warin et al. (2010) as using subcutaneous MDA-MB-231 xenografts in female nude mice and Jakubikova et al. (2011) as including a mouse xenograft model. The uploaded SciRAP in-vivo checklist was used as the requested framework.

SciRAP In Vitro Tool (Version 2.1)[38]
Reliability Assessment of the Five Included In Vitro Studies
Assessment basis: SciRAP evaluates reliability through Reporting Quality (RQ) and Methodological Quality (MQ), separately.

STUDY	RQ: TEST COMPOUND &CONTROLS	RQ: TEST SYSTEM	RQ: ADMINISTRATION	RQ: DATA COLLECTION & ANALYSIS	RQ: FUNDING/COI
Xie et al., 2022[16]	PF	F	F	F	F
Bertova et al., 2024[17]	PF	F	F	F	F
Yoshigae et al., 2013[13]	PF	F	F	F	F
Jane In den Birken et al., 2025[14]	PF	F	F	F	F

Telang et al., 2009[15]	PF	PF	F	F	F

STUDY	MQ: TEST SYSTEM	MQ: ADMINISTRATION	MQ: DATA COLLECTION &ANALYSIS	MQ: OTHER
Xie et al., 2022[16]	F	F	F	F
Bertova et al., 2024[17]	F	F	F	F
Yoshigae et al., 2013[13]	F	F	F	PF
jane in den Birken et al., 2025[10]	F	F	F	F
Telang et al., 2009[15]	PF	F	F	PF

Colour Coding: F (GREEN)= Fulfilled ; PF (YELLOW)Partially fulfilled ; NF(RED) = Not fulfilled ; ND = Not determined

DISCUSSION:

The present systematic review examined the anticancer and potential chemopreventive effects of isothiocyanates derived from cruciferous vegetables, with particular emphasis on sulforaphane (SFN), benzyl isothiocyanate (BITC), and phenethyl isothiocyanate (PEITC). The evidence identified in the manuscript includes experimental studies involving bladder cancer, acute myeloid leukemias, breast cancer, multiple myeloma, prostate cancer, breast epithelial models, melanoma, cervical cancer, glioblastoma, gastric cancer, colon cancer, and mechanistic systems related to carcinogen metabolism. The findings collectively suggest that isothiocyanates can influence several processes involved in cancer biology, but the magnitude and direction of the effects vary according to the compound, cancer model, concentration, exposure duration, and biological endpoint. Reported that BITC induced reactive oxygen species accumulation, DNA damage, and apoptosis in canine lymphoma and leukemias cells evidence in the study of Henklewska et al.. These findings support the possibility that oxidative imbalance contributes to BITC-associated cytotoxicity. However, the use of canine malignant cells limits direct extrapolation to human cancers. Species-specific differences in cellular metabolism, antioxidant defense, and drug sensitivity may influence the response. The study is therefore useful as mechanistic support but cannot independently establish the effectiveness of BITC in human oncology.

According to Shoaib et al. reported that PEITC induced apoptosis in cervical cancer cells through reactive oxygen species generation and caspase-3 activation, with an enhanced response when PEITC was combined with cisplatin. This observation is relevant because combination approaches may permit lower exposure to an individual compound

or may affect complementary cellular pathways. Nevertheless, combination effects observed in vitro should not be interpreted as proof of clinical synergy. Future studies must establish whether the interaction is reproducible, whether it is dependent on dose and sequence of administration, and whether the combination increases toxicity in normal tissues.

The study of Greco et al. expanded the discussion of SFN-associated cell death by reporting ferroptosis in U-937 leukaemia cells. The study suggested that the type of cell death may vary with concentration and cellular conditions, with changes involving glutathione, GPX4, and lipid peroxidation. This is important because it indicates that SFN may influence more than one cell-death pathway. However, the presence of ferroptosis-related markers should be interpreted together with functional evidence and appropriate rescue experiments, because oxidative stress and lipid peroxidation can occur in several overlapping forms of cellular injury.

Evaluated PEITC, BITC, and SFN in colon cancer cells under heparin-stimulated experimental conditions in the study of Zhang et al. The reported reduction in proliferation and changes in ErbB-related growth signaling, Bax, and Bcl-2 suggest that isothiocyanates may affect both proliferative signalling and apoptotic regulation. The use of more than one isothiocyanate is useful for identifying shared responses; however, it does not establish that the compounds have equal potency or identical mechanisms. Differences in molecular structure and intracellular metabolism may produce different biological effects even when the same pathway is investigated.

Examined BITC-induced cytotoxicity in human gastric adenocarcinoma AGS cells and reported concentration- and time-dependent reductions in viability, together with changes in autophagy-related proteins and lysosomal function in the study of Po et al. These findings are relevant because autophagy may function as a protective response that enables cancer cells to tolerate stress. Inhibition of protective autophagy may therefore increase cellular vulnerability to BITC. However, the interpretation of autophagy requires attention to both autophagosome formation and lysosomal degradation, because an apparent increase in autophagy markers may reflect either increased autophagic activity or impaired autophagic flux.

He et al. reported that the inhibitory effect of SFN on bladder cancer cells was related to Nrf2 translocation and glutathione depletion, with a concentration-dependent response. This provides a mechanistic explanation for the role of cellular antioxidant systems in SFN-associated growth inhibition. The findings can be compared with Xie et al., who examined SFN in several bladder cancer cell lines, including drug-resistant variants. The two studies may differ because of concentration, exposure duration, cell-line characteristics, and the molecular endpoints assessed. Therefore, the results support a context-dependent mechanism rather than a single universal response to SFN.

According to the Rutz et al. examined allyl-, butyl-, and phenethyl-isothiocyanate in cisplatin- and gemcitabine-resistant bladder cancer cell lines and reported modulation of Akt-mTOR and cyclin-CDK signalling with associated G2/M cell-cycle arrest. This work is relevant to the present review because it connects isothiocyanate exposure with signalling pathways involved in treatment resistance and cell-cycle progression. Nevertheless, the findings also demonstrate why individual isothiocyanates should not be treated as interchangeable. The study involved compounds other than SFN and BITC and used resistant cell lines, so the results should be used as supporting evidence rather than directly merged with every SFN study.

Hsu et al. investigated PEITC in glioblastoma cells and reported suppression of pro-inflammatory cytokines through modulation of the PI3K/Akt/NF-κB signalling pathway. This suggests that the biological effects of isothiocyanates may extend beyond direct cytotoxicity to include regulation of inflammatory signalling. Inflammation is relevant to tumour development and progression, but the effect of cytokine modulation in a cell culture system cannot be equated with an anti-inflammatory or antitumour effect in patients. The tumour microenvironment contains immune cells, stromal cells, blood vessels, and extracellular signals that are not fully represented in a single-cell model.

Mitsiogianni et al. examined major isothiocyanates in non-metastatic and metastatic melanoma cells and reported changes in reactive oxygen species, glutathione status, cell-cycle progression, and cell death. The use of different melanoma contexts is important because cellular sensitivity may vary with metastatic phenotype, antioxidant capacity, and baseline signalling activity. These findings support the view that the response to an isothiocyanate depends not only on the compound itself but also on the biological characteristics of the target cells. The results should therefore be interpreted without assuming that one concentration or response pattern will apply to all melanoma subtypes or other cancers.

Kyriakou et al. investigated PEITC and its N-acetylcysteine-conjugated form in malignant melanoma and highlighted the possible contribution of ITC metabolism to biological activity. This is particularly relevant to translational research because the parent compound and its metabolites may differ in stability, cellular uptake, target interaction, and toxicity. A compound's biological effect cannot be understood fully by measuring only the administered parent molecule.

Future research should therefore evaluate metabolite formation and activity, especially when considering dietary exposure or oral administration.

The experimental evidence from the included studies supports the relevance of isothiocyanates across several cancer models. Xie et al. reported antiproliferative effects of SFN in drug-sensitive and drug-resistant bladder cancer cell lines. Bertova et al. reported effects of SFN and BITC on proliferation, cell-cycle progression, autophagy, and apoptosis in acute myeloid leukemias models, Warin et al investigated BITC in breast cancer cells and xenografts, including tumour growth, migration-related outcomes, and angiogenic parameters. Jakubikova et al. evaluated SFN and PEITC in multiple myeloma models, including primary cells and a xenograft system. These studies support the biological plausibility of anticancer activity, but their different models and outcomes prevent the results from being treated as one uniform effect.

Examined PEITC-mediated modulation of CYP2E1 and oxidative carcinogen bioactivation in Yoshigae et al. This study is conceptually different from studies measuring cancer-cell viability or tumour growth. It provides mechanistic evidence relevant to chemoprevention rather than direct treatment of an established tumor. The distinction is essential because inhibition of carcinogen metabolism may theoretically reduce carcinogenic exposure, whereas apoptosis or growth inhibition addresses the response of existing malignant cells.

Investigated SFN in prostate cancer models and engineered heart tissue generated from human induced pluripotent stem cell-derived cardiomyocytes in the study of In den Birken et al . The inclusion of a safety-related model is important because anticancer activity must be considered together with potential toxicity. The study also demonstrates the value of using models that examine normal tissue responses. However, engineered tissue cannot fully reproduce the physiological complexity of a human organ, and further pharmacokinetic and in vivo safety investigations are needed.

The study of Telang et al. compared SFN and PEITC in breast cancer cells and normal human mammary epithelial cells and reported changes in gene-expression pathways related to estrogen-receptor signalling, apoptosis, and cell-cycle regulation. Such comparisons may help identify differences between malignant and non-malignant cellular responses. However, gene-expression changes should be interpreted as mechanistic evidence and should be supported by functional assays, protein-level confirmation, and reproducibility in additional models.

Royston and Tollefsbol reviewed the epigenetic impact of cruciferous vegetables, particularly SFN and indole-3-carbinol, with emphasis on mechanisms such as histone deacetylase inhibition, DNA methyltransferase regulation, and microRNA-related effects. 33 Atwell et al. focused more specifically on SFN and epigenetic regulation in breast and prostate cancer, while emphasizing the need to establish appropriate human doses, bioavailability, and tissue distribution before clinical translation. These reviews provide mechanistic context for the present findings, but they include broader phytochemical and epigenetic literature beyond the specific experimental evidence synthesized in this systematic review.
Beaver et al. reported cell-type- and time-dependent transcriptional responses to SFN in normal and prostate cancer cells and identified suppression of Sp1 as a possible contributor to chemopreventive activity. This study is relevant because it illustrates how the same compound may produce different transcriptional responses according to cellular status and exposure duration. It also reinforces the importance of not interpreting one molecular target as the only mechanism responsible for SFN activity. Transcriptional changes require functional validation before their clinical relevance can be established.

Wei et al. reported an association between pre-diagnosis consumption of cruciferous vegetables and dietary isothiocyanates and survival among Chinese patients with epithelial ovarian cancer. This finding provides human observational context for the experimental literature. However, the study examined dietary intake and survival in a patient cohort, whereas most studies in the present review evaluated in vitro, in vivo, or mechanistic outcomes. The designs answer different questions: observational research may identify associations between exposure and outcomes, while experimental research may clarify biological mechanisms. The findings are complementary but should not be interpreted as proof that dietary isothiocyanates caused improved survival.

Cruciferous vegetable intake, dietary glucosinolate exposure, and breast cancer risk in large prospective studies of Romanos-Nanclares et al. Such epidemiological research is relevant because it addresses dietary exposure in human populations. Nevertheless, dietary assessment is subject to measurement error, and associations may be influenced by overall dietary pattern, lifestyle, body composition, and other confounding factors. In addition, the amount of an isothiocyanate generated from a food depends on plant composition, preparation, myrosinase activity, digestion, and

metabolism. Therefore, dietary findings should not be directly equated with the effects of purified compounds used in laboratory experiments.

Mitra et al. reviewed bioactive compounds from cruciferous vegetables and their relationship with the p53 family and gastrointestinal cancers. Their work supports the biological importance of cruciferous-derived compounds in DNA-damage responses and tumour-suppressive pathways such as p21 regulation. However, the review covered several bioactive compounds and gastrointestinal malignancies, whereas the present systematic review focuses specifically on SFN, BITC, and PEITC across multiple experimental cancer models. Differences between the findings may therefore reflect the phytochemical studied, cancer type, model, and molecular endpoint.

Addition of bio-compatible products makes it even more effective P Priyadarshini et al . Thus, the anticancer effect produced was due to both caspase-dependent and mitochondrial apoptotic pathways. In support to the therapeutic potential of GA modified SeNPs@DOX was demonstrated through in vivo xenograft model where the mice treated showed tumor growth suppression with minimal systemic toxicity. There was no significant damage to major organs like liver, kidney, heart, spleen and lungs when examined histopathological. Immunohistochemical studies reveled decreased Ki67 expression and increased TUNEL and caspase-3 positivity which shows enhanced apoptosis and poor proliferation of tumor cells. Thus, the biologically derived GA SeNPs act as a promising nanocarrier for targeted chemotherapy in hepatocellular carcinoma with reduced adverse effects in comparison to conventional chemotherapy.

Evidence from the study of Al-Haidari et al investigated aqueous broccoli extract in prostate cancer cells and reported dose-dependent cytotoxicity. This finding may support the broader concept that cruciferous vegetables contain biologically active constituents. However, the study evaluated a whole aqueous extract rather than an isolated isothiocyanate. The observed effect could therefore reflect multiple compounds, differences in extraction, and interactions between constituents. Whole-plant extracts and purified SFN should be discussed as related but distinct interventions.

Overall, the available evidence suggests that SFN,BITC and PEITC have anticancer related effects through multiple mechanisms, Including apoptosis,cell cycle regulation ,oxidative stress,autophage and carcinogen mechanism. More representative models incorporating tumour heterogeneity, immune components, and the tumour microenvironment may improve translational relevance. Human studies will be required to determine whether experimental effects translate into meaningful prevention or treatment outcomes, and these studies should distinguish dietary vegetable intake from purified or concentrated isothiocyanate administration. Further research should also examine the activity of metabolites, the interaction of isothiocyanates with standard anticancer drugs, and the effects on normal tissues.

CONCLUSION

The studies included in this systematic review provide preclinical evidence that isothiocyanates derived from cruciferous vegetables, particularly SFN, BITC, and PEITC, exhibit anticancer effects across different experimental models. The reported effects include inhibition of cancer-cell growth and viability, induction of apoptosis, alteration of cell-cycle progression, and modulation of processes such as migration, angiogenesis, and carcinogen metabolism. However, the available evidence is predominantly laboratory-based and heterogeneous, and therefore does not establish their efficacy for cancer prevention or treatment in humans. Further well-designed animal and clinical studies are required to clarify their effective dose, bioavailability, safety, mechanisms of action, and potential role alongside established cancer therapies.

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