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THE NUTRITIONAL POTENTIAL OF CHOCOLATE IN CANCER PREVENTION: A SIGNIFICANT LITERATURE REVIEW

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Abstract:

Chocolate, rich in bioactive compounds such as flavonoids and polyphenols, has attracted growing interest for its potential role in cancer prevention. This Systematic Literature Review (SLR), guided by the PRISMA protocol, evaluates the nutritional potential of chocolate in cancer prevention. Comprehensive searches in Scopus and ScienceDirect identified 33 primary studies that met inclusion criteria. Thematic analysis revealed three key research domains: (1) the role of chocolate and cocoa in functional foods and health promotion, focusing on antioxidant, anti-inflammatory, and chemopreventive properties; (2) agricultural and biotechnological aspects affecting cocoa phytochemical profiles; and (3) dietary behaviors and public health perspectives on chocolate consumption. Findings suggest a strong association between moderate chocolate intake and reduced oxidative stress, inflammation, and cancer risk. However, inconsistencies in processing methods and dosage limit generalizability. This review highlights the need for standardized clinical trials and integrative nutritional frameworks to better utilize chocolate's chemopreventive potential in public health and oncology.

Keywords:

Chocolate, Functional Food, Nutritious, Cancer, PRISMA

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Introduction

Chocolate, once regarded primarily as a confectionery indulgence, has undergone a significant paradigm shift in nutritional science. It is now increasingly recognized for its rich profile of bioactive compounds, especially polyphenols such as flavonoids, catechins, and procyanidins (Kongor et al. 2024). These compounds are predominantly found in cocoa, the principal ingredient in dark chocolate, and have been associated with a wide range of physiological benefits, including antioxidant, anti-inflammatory, and cardioprotective effects (Ramiro-Puig and Castell 2009). Among the emerging areas of interest is the potential role of chocolate in cancer prevention, a hypothesis supported by mechanistic studies demonstrating the ability of cocoa polyphenols to modulate cellular processes related to carcinogenesis. This includes oxidative stress, inflammation, apoptosis, and angiogenesis (Allgrove and Davison 2018; Martín and Ramos 2016). This topic is of growing relevance considering the global cancer burden and the urgent need for complementary dietary strategies to support conventional therapies or serve as preventive measures. As nutrition science intersects with oncology, exploring natural food sources with functional properties has become a critical research frontier.

Current evidence from in vitro, in vivo, and limited human studies provides promising but inconclusive support for the anticancer potential of chocolate and its constituent compounds. Key studies have demonstrated that cocoa flavonoids can inhibit tumor cell proliferation and induce apoptosis in various cancer cell lines, including colon, breast, prostate, and pancreas (Taniguchi et al. 2013). In particular, animal models further corroborate these effects, with cocoa-supplemented diets leading to suppressed tumor growth and reduced inflammatory biomarkers. However, findings from human epidemiological and clinical studies remain inconsistent, with factors such as chocolate type, dosage, bioavailability, individual metabolic responses, and dietary context contributing to the variability. Moreover, commercial chocolates often contain high levels of sugar and fat, which may counteract or obscure the potential health benefits of cocoa (Markey, Lovegrove, and Methven 2015). These complexities highlight unresolved questions about optimal intake levels, the role of chocolate matrix components, and potential interactions with other dietary or lifestyle factors. Thus, this article seeks to address these gaps by critically examining the nutritional composition of chocolate in relation to its mechanistic and clinical evidence for cancer prevention. The central hypothesis is that chocolate can serve as a functional food with tangible chemopreventive properties when formulated and consumed appropriately. By synthesizing findings from molecular, preclinical, and population-level studies, this review aims to clarify the current scientific understanding and propose future directions for research. Ultimately, the article contributes to advancing knowledge in functional nutrition and integrative oncology by evaluating whether chocolate can transcend its traditional role as a treat and emerge as a tool in cancer prevention strategies.

Literature Review

The scientific community has increasingly recognized dark chocolate as more than just a decadent treat, with mounting evidence highlighting its potential role in cancer prevention due to its rich bioactive composition. Central to this potential are flavonoids like catechins and procyanidins, which exhibit robust antioxidative and anti-inflammatory properties capable of mitigating oxidative stress, a key driver of carcinogenesis (Sundararaj et al. 2024). These compounds are not static, as their concentration can vary significantly based on factors like cocoa origin. Madagascar-sourced cocoa hulls demonstrate particularly high polyphenol levels linked to superior antioxidant activity (Bruna et al. 2009). Technological advancements have

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further expanded chocolate's functional potential, as observed in studies enriching chocolate with synergistic ingredients such as yellow tea extract. It amplifies antiradical effects (Gramza-Michałowska et al. 2021), or inulin, a prebiotic demonstrated to support gut health and reduce colon cancer risk (Norhayati, Suzielawanis, and Khan 2013). Even sensory challenges, like the bitterness of polyphenol-rich formulations, are being addressed through innovations that balance palatability and bioactivity, as evidenced by the consumer acceptance of prebiotic-fortified milk chocolate (Norhayati and Ayob 2014). However, while in vitro and short-term clinical studies, such as those documenting improved nutritional status in palliative cancer patients consuming 55% cocoa chocolate (Vettori et al. 2022), are promising, critical gaps remain. Furthermore, the lack of long-term human trials, inconsistent polyphenol stability during storage (Gramza-Michałowska et al. 2021), and insufficient mechanistic data on how chocolate-derived compounds interact with cancer pathways (Ferrari 2004) underscore the need for more rigorous, translational research to validate chocolate's chemopreventive claims.

Despite these limitations, the convergence of biochemical, technological, and clinical insights positions chocolate as a compelling candidate for functional food development in oncology. The integration of botanicals like nettle extract, which enhances cytotoxic effects against colon cancer cells while maintaining shelf stability (Belščak-Cvitanović et al. 2015), exemplifies the innovative approaches explored to amplify chocolate's therapeutic properties. Such efforts align with broader trends in personalized nutrition, where genetic factors like bitter taste perception (Gorovic et al. 2011) may influence individual responses to high-polyphenol chocolate formulations. Nevertheless, the field must overcome significant hurdles, including standardized profiling of cocoa sources (Bruna et al. 2009), optimization of bioactive delivery systems, and demonstration of efficacy in diverse populations through longitudinal studies. Current research, while fragmented, lays a foundation for multidisciplinary collaboration, uniting food scientists, clinicians, and epidemiologists to transform chocolate from a culturally entrenched indulgence into a validated, accessible tool for cancer prevention. Hence, future directions should prioritize clinical trials with robust biomarkers, stability-enhanced formulations, and consumer-centric designs to bridge the gap between laboratory potential and real-world health benefits.

Research Question

Research Questions (RQs) are crucial in a Systematic Literature Review (SLR) since they provide the foundation and direction for the entire review process. They guide the scope and focus of the SLR, helping to determine which studies to include or exclude, ensuring that the review remains relevant and specific to the topic of interest. Note that a well-defined RQ ensures that the literature search is exhaustive and systematic, covering all relevant studies that address key aspects of the topic. This minimizes the risk of bias and ensures a complete overview of the existing evidence. Additionally, RQs facilitate the categorization and organization of data from included studies, providing a framework for analyzing findings and synthesizing results to draw meaningful conclusions. They also enhance clarity and focus, avoiding ambiguity and keeping the review concentrated on specific issues, making the findings more actionable and relevant. Furthermore, well-formulated RQs contribute to the transparency and reproducibility of the review, allowing other researchers to follow the same process to verify findings or extend the review to related areas. Ultimately, RQs ensure that the review aligns with the overall objectives of the study, whether it is to identify gaps in the literature, evaluate the effectiveness of interventions, or explore trends in a specific field, making them the backbone of a rigorous, focused, and relevant SLR.

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Specifying the RQs is the most crucial activity at the planning stage and the most fundamental part of any SLR, as it drives the entire review methodology (Kitchenham 2007). Our SLR aims to explore and understand the current state of research in this area. The PICo framework is a mnemonic style used to formulate RQs, particularly in qualitative research, proposed by Lockwood, Munn, and Porritt (2015), and was applied in this study. PICo stands for Population, Interest, and Context. Here is what each component means:

1. Population (P): This refers to the group or participants of interest in the study. It specifies who the research is focused on, such as a specific demographic, patient group, or community.

2. Interest (I): This represents the main focus or phenomenon of interest in the study. It could be a particular experience, behavior, intervention, or issue that the research aims to explore or understand.

3. Context (Co): This defines the setting, environment, or specific context in which the population and interest are situated. It might refer to geographical location, cultural or social settings, or any other relevant backdrop for the research.

Using the PICo framework helps structure RQs clearly and systematically by breaking down the key elements of the study into these three components. This approach ensures that the research is focused and the questions are well-defined, making searching for relevant literature or designing a study easier. This study achieved three RQ as follows:

1. How does the regular consumption of cocoa-rich functional foods influence biomarkers related to cancer prevention among adults at risk of chronic diseases?
2. What are the effects of biotechnological interventions on disease resistance and nutritional quality in genetically improved cacao cultivars used for functional food production?
3. How does the inclusion of chocolate in dietary patterns influence nutritional behavior and cancer prevention awareness among adolescents in a public health setting?

Materials and Methods

For conducting SLRs, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) approach is a widely accepted standard that guarantees transparency, completeness, and consistency throughout the procedure (Page et al. 2021). Researchers can improve the accuracy and rigor of their analysis by adhering to PRISMA guidelines, which guide how to systematically identify, screen, and include studies in their review. The method also highlights the significance of randomized studies, acknowledging their ability to lessen bias and provide strong evidence for the review. Two notable databases, Scopus and ScienceDirect, were used in this analysis due to their wide coverage and robustness. The PRISMA approach is organized into four key stages: identification, screening, eligibility, and data abstraction. In the identification phase, databases are searched to locate all relevant studies. The screening phase then evaluates these studies against predefined criteria to eliminate irrelevant or low-quality research. The remaining studies are thoroughly assessed during the eligibility phase to confirm they meet the inclusion criteria. Finally, data abstraction focuses on extracting and synthesizing data from the included studies, essential for deriving meaningful and reliable conclusions. This structured method ensures that the systematic review

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is conducted with rigor, leading to trustworthy results that can guide future research and practice.

Identification

The identification phase is the critical first step in the SLR process, where researchers aim to collect a comprehensive pool of potentially relevant studies. For this review, the focus was on investigating the functional properties of chocolate, particularly its nutritional value and potential role in cancer prevention. To ensure wide coverage of existing literature, two reputable databases, Scopus and ScienceDirect, were utilized. The search strategy involved using the keywords “chocolate,” “nutritious,” and “cancer” to capture studies aligned with the research objectives, as summarized in Table 1. This initial search resulted in a total of 1133 records, with 939 articles identified through Scopus and 194 through ScienceDirect. These records represent the total number of documents retrieved before any screening or filtering procedures were applied. At this stage, the goal is to maximize the sensitivity of the search to avoid missing any potentially valuable studies. The results include all types of publications regardless of language, document type, or direct relevance, acknowledging the possibility of duplicates and non-eligible records. This broad and inclusive approach provides a solid foundation for the following SLR stages: screening, eligibility assessment, and final inclusion, where the relevance and quality of each study will be critically appraised to refine the final selection.

Table 1: The search string

Database	Search String
Scopus	TITLE-ABS-KEY ((chocolate) AND (healthy OR wholesome OR nutritious OR beneficial) AND (cancer OR disease OR disorder OR sickness)) **Date of Access: May 2025**
ScienceDirect	(chocolate OR cocoa OR cacao OR “theobroma cacao” OR “dark chocolate” OR “chocolate extract” OR “chocolate product”) AND (nutritious OR nutritional OR “nutrient-rich” OR healthy OR healthful OR dietary OR “functional food”) AND (cancer OR tumor OR tumour OR malignancy OR carcinoma OR neoplasm OR oncology) **Date of Access: May 2025**

Screening

The screening phase is the second critical step in the SLR process, where the initial pool of identified records undergoes a rigorous filtering based on predefined inclusion and exclusion criteria. From the initial 1,133 records retrieved during the identification stage, a total of 988 records were excluded after applying several exclusion parameters, as presented in Table 2. These criteria included the removal of non-English language publications, studies published before 2020, and document types such as conference papers, book chapters, reviews, and in-press articles. Furthermore, records that did not fall within the relevant subject areas, specifically Agricultural and Biological Sciences; Medicine; Nursing; Biochemistry, Genetics and Molecular Biology; Chemistry; Immunology and Microbiology; Pharmacology, Toxicology and Pharmaceutics; Neuroscience; Health Professions; and Engineering, were also excluded. After this screening process, 132 studies from Scopus and 13 from ScienceDirect were retained, resulting in a total of 145 records for further evaluation. Following the screening, a duplicate check was conducted to eliminate overlapping articles across the databases. This

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led to the removal of six duplicate records, refining the total to 139 unique studies. Consequently, these remaining records were subjected to full-text screening to assess their relevance and quality more thoroughly. During this step, several studies were excluded for multiple reasons: some were outside the scope of the research field, others had titles that lacked relevance, or their abstracts did not align with the core objectives of the study, which focused on chocolate's nutritional properties and its potential role in cancer prevention. Additionally, a few articles were excluded due to a lack of full-text access, making it impossible to evaluate their in-depth content. This rigorous multi-step process ensured that only the most relevant, high-quality studies were included in the final review.

Table 2: The selection criterion is searching

Criterion	Inclusion	Exclusion
Language	English	Non-English
Time line	2020 – 2025	< 2020
Literature type	Journal (Article)	Conference, Book, Review
Publication Stage	Final	In Press
Subject Area	Agricultural and Biological Sciences, Medicine, Nursing, Biochemistry, Genetics and Molecular Biology, Chemistry, Immunology and Microbiology, Pharmacology, Toxicology and Pharmaceutics, Neuroscience, Health Professions, Engineering	Besides Agricultural and Biological Sciences, Medicine, Nursing, Biochemistry, Genetics and Molecular Biology, Chemistry, Immunology and Microbiology, Pharmacology, Toxicology and Pharmaceutics, Neuroscience, Health Professions, Engineering

Eligibility

The eligibility phase represents a crucial step in the SLR process, where the remaining articles undergo a more detailed and critical assessment to determine their suitability for inclusion in the final analysis. At this stage, a total of 139 articles, refined from the earlier screening and duplicate removal steps, were carefully examined in full text. Each study was evaluated against the core objectives of the review, which focused on the role of chocolate as a functional food in the context of cancer prevention and health promotion. Articles were excluded based on several key factors, including being outside the field of interest, having a title that lacked relevance, containing an abstract unrelated to the research focus, or lacking full-text access. This stringent assessment ensures that only studies with strong methodological rigor and clear relevance to the research topic are considered for the final synthesis.

As a result of this detailed eligibility evaluation, 106 articles were excluded, leaving 33 high-quality studies that met all inclusion criteria. These selected studies formed the basis of the qualitative analysis, offering valuable insights into the potential health-promoting and anticancer properties of chocolate, particularly through its nutritional and bioactive components. The thoroughness of the eligibility phase is essential to maintaining the integrity and credibility of the SLR, as it filters out irrelevant or low-quality literature and focuses the review on evidence that can meaningfully contribute to scientific understanding and practical applications in nutrition and health sciences.

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Data Abstraction and Analysis

An integrative analysis was employed in this study as a key assessment strategy to examine and synthesize diverse research designs, primarily focusing on quantitative methods. The primary objective was to identify and organize relevant topics and subtopics related to the nutritional potential of chocolate in cancer prevention. The thematic development began with a comprehensive data collection process. As illustrated in Figure 2, the authors systematically reviewed 33 selected publications to extract relevant claims and information aligned with the study's focus. Each study's methodology and findings were carefully analyzed to assess their contribution to the research context. Collaborative discussions among the authors were conducted to refine and finalize the thematic structure, ensuring consistency and relevance. A log was maintained throughout the analysis to document interpretations, emerging insights, challenges, and analytical reflections. To ensure the reliability of the thematic framework, the authors cross-checked findings for discrepancies and resolved disagreements through group discussions.

Table 3: Number and details of Primary Studies Database

No	Authors	Year	Journal	Scopus	ScienceDirect
1	(Jabeen et al. 2024)	2024	Foods	/	
2	(Osorio-Guarín et al. 2020)	2020	G3: Genes, Genomes, Genetics	/	
3	(Soares and Del Ciampo 2024)	2024	International Journal of Nutrology	/	
4	(Auger et al. 2020)	2020	Movement Disorders Clinical Practice	/	
5	(Feraco et al. 2024)	2024	Frontiers in Nutrition	/	
6	(Kent et al. 2024)	2024	International Journal of Behavioral Nutrition and Physical Activity	/	
7	(Mayra et al. 2024)	2024	AIMS Agriculture and Food	/	
8	(Kim and Jeon 2021)	2021	Nutrition Research and Practice	/	
9	(Shin et al. 2022)	2022	Journal of Nutritional Biochemistry	/	
10	(Senda et al. 2024)	2024	Nutrients	/	
11	(Espinoza et al. 2023)	2023	Revista Chilena de Nutricion	/	
12	(Bolenz and Glöde 2021)	2021	European Food Research and Technology	/	
13	(Pepito and Ross 2024)	2024	Journal of Food Science	/	
14	(Weikart et al. 2022)	2022	Journal of Nutritional Biochemistry	/	
15	(González-Barrio et al. 2020)	2020	Foods	/	

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16	(Oro et al. 2020)	2020	International Journal of Biological and Chemical Sciences	/	
17	(Ashfaq et al. 2024)	2024	Pakistan Journal of Agricultural Research	/	
18	(Küçükyilmaz, Okburan, and Gezer 2024)	2024	Revista de Nutricao	/	
19	(Gammone and D'Orazio 2021)	2021	Current Research in Nutrition and Food Science	/	
20	(Chu et al. 2024)	2024	Frontiers in Public Health	/	
21	(Latif, Richardson, and Marshall 2024)	2024	Nutrients	/	
22	(Głąbska, Guzek, and Lech 2023)	2023	Nutrients	/	
23	(Milewska-Wróbel and Lis-Święty 2022)	2022	Explore	/	
24	(Lasala et al. 2022)	2022	Nutrients	/	
25	(Pedrinolla et al. 2023)	2023	BMJ Open	/	
26	(Kozarski et al. 2020)	2020	Food and Feed Research	/	
27	(Mohatar-Barba et al. 2025)	2025	Nutrients	/	
28	(Iaia et al. 2020)	2020	Archives of Biochemistry and Biophysics	/	
29	(Arini et al. 2021)	2021	Indian Journal of Agricultural Research	/	
30	(Christen et al. 2020)	2020	Cardiovascular Digital Health Journal	/	/
31	(Martín and Ramos 2016)	2021	Food and Chemical Toxicology	/	
32	(Astrup et al. 2020)	2020	Journal of the American College of Cardiology	/	
33	(Samanta et al. 2022)	2022	Current Research in Food Science	/	

Quality of Appraisal

Following the guidelines established by Kitchenham and Charters (Kitchenham 2007), once the primary studies were selected, it was necessary to assess the quality of the research and perform a quantitative comparison. For this SLR, the Quality Assessment (QA) framework proposed by Abouzahra, Sabraoui, and Afdel (2020) was adopted, which includes six specific QA criteria. Each criterion was evaluated using a three-point scoring system: a score of 1 ("Yes") was assigned if the criterion was fully met, 0.5 ("Partly") if the criterion was partially fulfilled but presented some limitations, and 0 ("No") if the criterion was not met at all.

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• QA1. Is the purpose of the study clearly stated?
• QA2. Is the interest and the usefulness of the work clearly presented?
• QA3. Is the study methodology clearly established?
• QA4. Are the concepts of the approach clearly defined?
• QA5. Is the work compared and measured with other similar work?
• QA6. Are the limitations of the work clearly mentioned?

The table presents a QA process for evaluating each study based on defined criteria. Three experts independently reviewed and rated the studies using a standardized scoring system: “Yes” (Y), “Partly” (P), or “No” (N). Below is a detailed description of each criterion:

1. **Is the purpose of the study clearly stated?**
   - This criterion assesses whether the study clearly defines its objectives. A well-articulated purpose provides direction and establishes the research scope.
2. **Is the interest and usefulness of the work clearly presented?**
   - This evaluates the clarity with which the study conveys its relevance and potential value. It reflects the extent to which the research contributes meaningfully to its field.
3. **Is the study methodology clearly established?**
   - This criterion examines whether the research methods are well-described and appropriate for meeting the stated objectives. A transparent methodology ensures the reliability and reproducibility of findings.
4. **Are the concepts of the approach clearly defined?**
   - This focuses on the clarity of the theoretical framework and key terms used in the study. Clearly defined concepts are vital for understanding and interpreting the research approach.
5. **Is the work compared and measured with other similar work?**
   - This evaluates whether the study situates its findings in relation to existing literature. Comparative analysis helps contextualize the work and underscores its unique contributions.
6. **Are the limitations of the work clearly mentioned?**
   - This assesses whether the study openly discusses its limitations. Acknowledging limitations demonstrates critical reflection and transparency in the research process.

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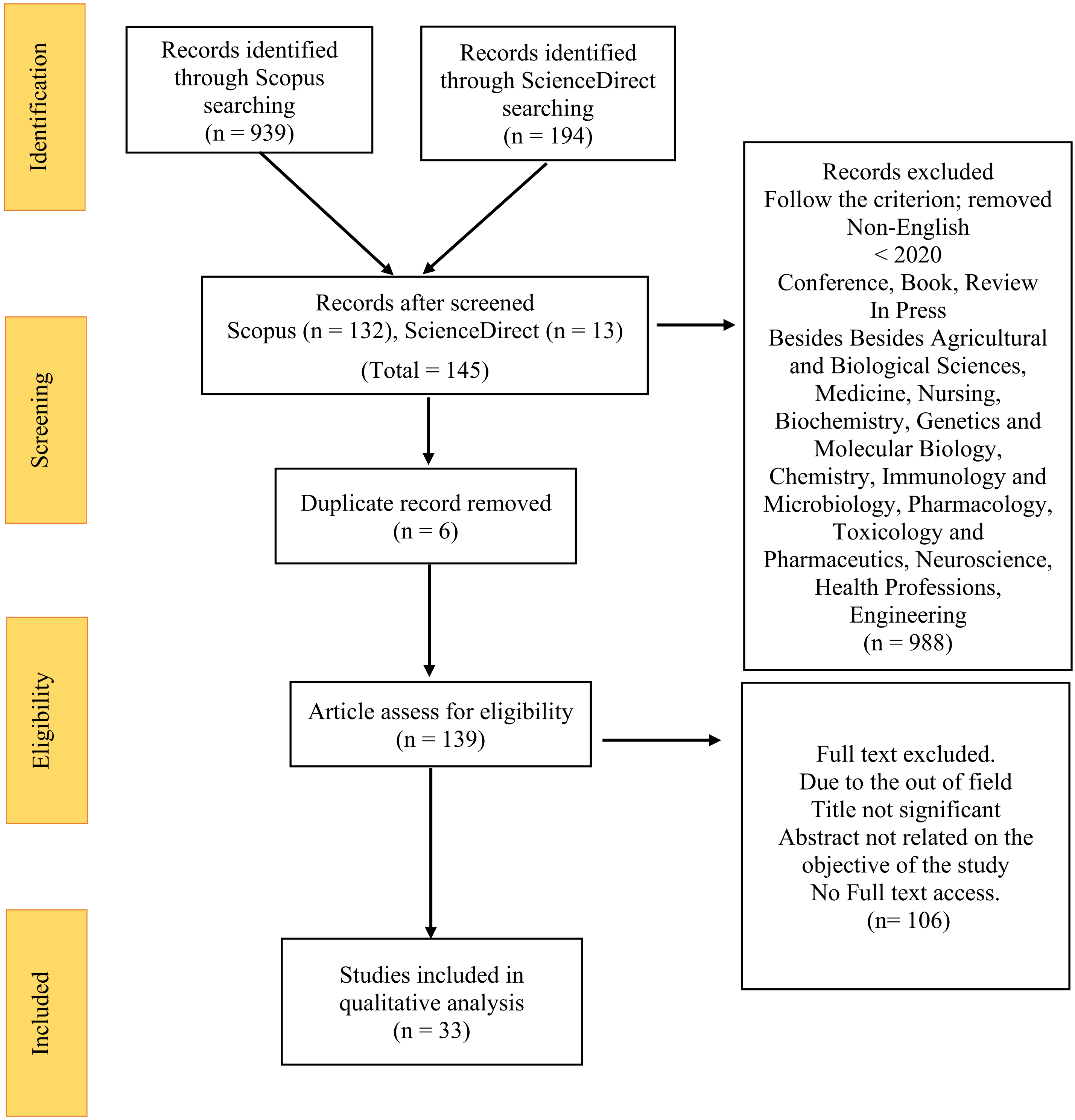

Figure 2. Flow Diagram Of The Proposed Searching Study

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Result and Finding

Based on QA, Table 4 summarizes the result of the assessment performance for selected primary studies. The QA of 33 primary studies indicates a generally high standard across the reviewed literature. Every study clearly stated its purpose, usefulness, methodology, and conceptual framework, as reflected by consistent "Yes" (Y) ratings for QA1 through QA4. This demonstrates strong foundational clarity and relevance in the selected research. Out of the 33 studies, 13 (approximately 39.4%) achieved a score of 91.7%, while the remaining 20 (approximately 60.6%) scored 83.3%. This suggests that all studies met a solid threshold of methodological rigor.

However, a recurring limitation across the dataset is the partial treatment of QA5 and QA6, which assess comparative analysis with similar works and discuss study limitations. These areas were frequently marked as "Partial" (P), indicating that while the studies were methodologically sound, many lacked thorough benchmarking or critical reflection on their limitations. Correspondingly, addressing these gaps in future research or within a comprehensive literature review can enhance the findings' contextual depth and critical engagement.

Table 4: Performance Quality Assessment Table For The Selected Papers

Primary Study	QA1	QA2	QA3	QA4	QA5	QA6	Total Mark	Percentage (%)
(Jabeen et al. 2024)	Y	Y	Y	Y	P	P	5	83.3
(Osorio-Guarín et al. 2020)	Y	Y	Y	Y	Y	P	5.5	91.7
(Soares and Del Ciampo 2024)	Y	Y	Y	Y	P	P	5	83.3
(Auger et al. 2020)	Y	Y	Y	Y	Y	P	5.5	91.7
(Feraco et al. 2024)	Y	Y	Y	Y	Y	P	5.5	91.7
(Kent et al. 2024)	Y	Y	Y	Y	Y	P	5.5	91.7
(Mayra et al. 2024)	Y	Y	Y	Y	Y	P	5.5	91.7
(Kim and Jeon 2021)	Y	Y	Y	Y	Y	P	5.5	91.7
(Shin et al. 2022)	Y	Y	Y	Y	Y	P	5.5	91.7
(Senda et al. 2024)	Y	Y	Y	Y	P	P	5	83.3
(Espinoza et al. 2023)	Y	Y	Y	Y	P	P	5	83.3
(Bolenz and Glöde 2021)	Y	Y	Y	Y	Y	P	5.5	91.7
(Pepito and Ross 2024)	Y	Y	Y	Y	P	P	5	83.3
(Weikart et al. 2022)	Y	Y	Y	Y	Y	P	5.5	91.7
(González-Barrio et al. 2020)	Y	Y	Y	Y	Y	P	5.5	91.7
(Oro et al. 2020)	Y	Y	Y	Y	P	P	5	83.3
(Ashfaq et al. 2024)	Y	Y	Y	Y	P	P	5	83.3
(Küçükyilmaz, Okburan, and Gezer 2024)	Y	Y	Y	Y	P	P	5	83.3
(Gammone and D'Orazio 2021)	Y	Y	Y	Y	P	P	5	83.3

(Chu et al. 2024)	Y	Y	Y	Y	P	P	5	83.3
(Latif, Richardson, and Marshall 2024)	Y	Y	Y	Y	P	P	5	83.3
(Głąbska, Guzek, and Lech 2023)	Y	Y	Y	Y	P	P	5	83.3
(Milewska-Wróbel and Lis-Święty 2022)	Y	Y	Y	Y	P	P	5	83.3
(Lasala et al. 2022)	Y	Y	Y	Y	P	P	5	83.3
(Pedrinolla et al. 2023)	Y	Y	Y	Y	P	P	5	83.3
(Kozarski et al. 2020)	Y	Y	Y	Y	P	P	5	83.3
(Mohatar-Barba et al. 2025)	Y	Y	Y	Y	P	P	5	83.3
(Iaia et al. 2020)	Y	Y	Y	Y	P	P	5	83.3
(Arini et al. 2021)	Y	Y	Y	Y	P	P	5	83.3
(Christen et al. 2020)	Y	Y	Y	Y	P	P	5	83.3
(Martín and Ramos 2016)	Y	Y	Y	Y	Y	P	5.5	91.7
(Astrup et al. 2020)	Y	Y	Y	Y	Y	P	5.5	91.7
(Samanta et al. 2022)	Y	Y	Y	Y	Y	P	5.5	91.7

Chocolate and Cocoa in Functional Foods and Health Promotion

The nutritional potential of chocolate, particularly its polyphenolic compounds, has been extensively studied for its role in cancer prevention. Research indicates that cocoa flavonoids, such as flavanols, procyanidins, and catechins, exhibit antioxidant and anti-inflammatory properties, which may mitigate oxidative stress, a key contributor to carcinogenesis (Jabeen et al. 2024; Ashfaq et al. 2024). For instance, dark chocolate with high cocoa content (≥ 70%) has been proven to reduce inflammatory markers, such as interleukin-6 (IL-6) and C-Reactive Protein (CRP), which are linked to chronic inflammation and cancer progression (Shin et al. 2022; Weikart et al. 2022). Additionally, cocoa polyphenols modulate cellular signaling pathways, including those involved in apoptosis and cell proliferation, suggesting a protective effect against tumor development (González-Barrio et al. 2020; Iaia et al. 2020). However, the extent of these benefits varies depending on processing methods, as fermentation and roasting can alter polyphenol bioavailability (Weikart et al. 2022).

Clinical and observational studies further support the association between chocolate consumption and reduced cancer risk. For example, a cross-sectional analysis of Korean adults revealed that chocolate consumers had healthier metabolic profiles, including lower obesity and dyslipidemia rates, risk factors for certain cancers (Kim and Jeon 2021). Similarly, enriched dark chocolate with elevated flavanol content demonstrated enhanced antioxidant capacity, potentially counteracting Deoxyribonucleic acid (DNA) damage implicated in oncogenesis (González-Barrio et al. 2020). Nevertheless, inconsistencies persist, as some trials, such as the COCOA-BP study, reported no significant impact of short-term chocolate intake on biomarkers like blood pressure, highlighting the need for longer-term interventions (Christen et al. 2020). Moreover, while cocoa’s prebiotic effects, such as promoting gut microbial diversity, may indirectly reduce cancer risk by improving immune function, the optimal dosage and formulation for maximal efficacy remain unclear (Shin et al. 2022; Pedrinolla et al. 2023).

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Cocoa and Cacao in Agriculture, Biotechnology, and Disease Resistance

Recent research highlights the critical role of genetic and biotechnological approaches in enhancing cocoa productivity and disease resistance. A genome-wide association study identified key genes linked to resistance against *Moniliophthora* spp., which cause frosty pod rot and witches' broom disease, significantly impacting cacao yields (Osorio-Guarín et al. 2020). The study revealed two genes associated with productivity and seven with disease resistance, providing valuable insights for marker-assisted breeding programs. Similarly, antifungal strategies, such as the combined application of biostimulants and fertilizers, have proven effective in reducing cocoa black pod rot caused by *Phytophthora* spp., with four consecutive treatments exhibiting the highest efficacy in maintaining healthy cherelles (Oro et al. 2020). Additionally, endophytic bacteria isolated from cocoa plants demonstrated promising suppression of *Phytophthora palmivora*, with certain strains exhibiting disease control indices exceeding 70%, attributed to antibiotic biosynthesis genes like phenazine-1-carboxylic acid and pyrrolnitrin (Arini et al. 2021). Collectively, these findings underscore the potential of integrated genetic and microbial interventions in sustainable cocoa cultivation.

The fermentation process in cocoa post-harvesting significantly influences its biochemical quality, particularly polyphenol content, which correlates with flavor and health benefits. Studies on Ecuadorian cocoa varieties demonstrated that fermentation duration critically affects antioxidant capacity and total polyphenol levels, with the CCN-51 clone retaining higher polyphenol concentrations than the Nacional variety (Mayra et al. 2024). These polyphenols define cocoa's sensory profile and contribute to its potential protective effects against chronic diseases, including cancer and diabetes. However, excessive polyphenol retention may lead to undesirable bitterness, necessitating optimized fermentation protocols. The interplay between genetic resistance, microbial biocontrol, and post-harvest processing underscores the multifaceted approach required to improve cocoa quality and resilience against biotic stresses, ensuring economic viability and nutritional value.

Dietary Behavior, Food Consumption, and Nutritional Public Health

Emerging research paints a concerning picture of modern dietary habits and their consequences for public health, especially among younger populations. A recent study examining Brazilian preschoolers uncovered startling rates of excess weight, with 35% classified as overweight or obese. At the same time, nearly two-thirds regularly consumed powdered chocolate and over half frequently ate sugary foods (Soares and Del Ciampo 2024). Parallel findings from Spanish universities revealed that vending machines predominantly stocked unhealthy options, where chocolates and snack bars accounted for most offerings, nearly all containing excessive fat and sugar content (Lasala et al. 2022). The situation appears exacerbated by digital marketing, as analysis indicates that influencers primarily advertise nutritionally poor foods to children, including chocolate products and fast food, with fewer than 20% of promoted items meeting basic health standards (Kent et al. 2024). These converging findings highlight a critical need for comprehensive policy reforms and educational initiatives to address the growing epidemic of poor nutrition among youth.

Gender and cultural factors also play a critical role in shaping dietary preferences and consumption patterns. A study of Italian adults noted that women exhibited healthier food choices, including higher consumption of vegetables and dark chocolate, while men preferred red meat and processed foods (Feraco et al. 2024). Religious influences further modulate dietary behaviors, as Muslim schoolchildren in Spain consumed significantly more ultra-

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processed foods, such as chocolates and industrial pastries, compared to their Christian peers (Mohatar-Barba et al. 2025). Additionally, family functioning emerged as a protective factor during the COVID-19 pandemic, with higher cohesion associated with reduced consumption of processed foods like chocolates and sugar-sweetened beverages (Espinoza et al. 2023). These findings emphasize the importance of tailored nutritional education and policy measures that account for socio-cultural and familial contexts to address disparities in dietary quality and mitigate long-term health risks.

Discussion

The SLR presents a comprehensive analysis of chocolate's dual role in cancer prevention and public health, synthesizing evidence across three interconnected themes: cocoa polyphenols' bioactive properties, agricultural and biotechnological advancements, and dietary behavior trends. Cocoa polyphenols, particularly flavanols and procyanidins, exhibit significant antioxidant, anti-inflammatory, and anti-carcinogenic effects, modulating pathways linked to oxidative stress, apoptosis, and tumor proliferation. Clinical studies associate high-cocoa dark chocolate ($\geq$ 70%) with reduced inflammatory biomarkers like IL-6 and CRP, underscoring its potential as a functional food. However, the translation of these molecular benefits into real-world health outcomes is complicated by variability in human trials due to differences in chocolate types, dosages, and individual metabolic responses. Meanwhile, agricultural innovations, such as genome-wide association studies and microbial biocontrol, aim to enhance cacao disease resistance and polyphenol retention, addressing challenges like climate change and fungal infections that threaten sustainable cocoa production. Simultaneously, optimized fermentation and drying protocols further improve polyphenol stability, yet these advancements have not bridged the gap between high-quality cocoa supply and consumer access, as sugar-laden commercial chocolates dominate markets. Furthermore, dietary analyses reveal alarming trends, particularly among children and adolescents, whose high consumption of ultra-processed chocolates is driven by targeted marketing and socio-cultural influences. This duality positions chocolate as both a chemopreventive agent and a public health concern, highlighting the need for interdisciplinary collaboration to align scientific, agricultural, and behavioral insights.

The review emphasizes the necessity of standardized formulations to maximize polyphenol bioavailability, stricter regulations on marketing unhealthy products, and educational campaigns promoting dark chocolate as part of balanced diets. For the food industry, reformulating chocolates to reduce sugar and fat while preserving bioactive compounds, through innovations like prebiotic fortification or synergistic botanical extracts, could enhance functional value without compromising taste. In addition, public health policymakers must address systemic issues, such as the ubiquity of ultra-processed chocolates in vending machines and digital platforms, perpetuating dietary disparities. Agriculturally, integrating disease-resistant cacao cultivars with sustainable farming practices is critical for ensuring a stable supply of nutrient-rich cocoa, particularly in low-resource regions reliant on cacao economies. Clinically, incorporating polyphenol-rich chocolate into dietary guidelines for high-risk populations warrants exploration, though longitudinal human trials are needed to establish causal relationships between consumption and cancer risk reduction. Hence, future research must adopt a translational approach, employing omics technologies to elucidate molecular interactions and expanding methodologies to include non-English studies and gray literature, reducing publication bias. Moreover, socio-behavioral research should investigate culturally tailored interventions to mitigate unhealthy dietary habits, while economic studies could assess the feasibility of scaling biotechnological innovations in vulnerable cacao-producing areas. Nevertheless, limitations of the review, such as its exclusion of pre-2020 studies and reliance on observational data, underscore the need for randomized controlled trials and diverse participant demographics to generalize findings across ethnicities and lifestyles. Ultimately, advancing chocolate's role in cancer prevention requires reconciling its cultural status as an indulgence with its scientific potential, leveraging Artificial Intelligent (AI)-driven meta-analyses and predictive modeling to create a cohesive roadmap from farm to clinic. Note that by addressing these gaps, stakeholders can transform cocoa from a global commodity into a validated tool for improving public health outcomes.

Conclusion

This systematic literature review examined the nutritional potential of chocolate in cancer prevention, focusing on cocoa-derived bioactive compounds, agricultural advancements, and dietary influences. Evidence indicates that cocoa polyphenols, particularly flavanols and procyanidins, exhibit antioxidant and anti-inflammatory properties capable of modulating cancer-related pathways, including oxidative stress and tumor proliferation. However, their efficacy is highly dependent on processing techniques, with traditional methods like fermentation and roasting potentially diminishing bioactive content. Innovations such as prebiotic fortification and botanical enhancements show promise in improving functional benefits. Agricultural research highlights biotechnological progress in disease-resistant cacao cultivation and microbial biocontrol, which may enhance polyphenol retention while addressing challenges like frosty pod rot. Despite these advances, scaling such innovations for global supply chains remains a hurdle. Dietary analyses reveal conflicting trends, with excessive consumption of sugar-laden chocolates—particularly among youth—posing public health risks, while nutrient-dense dark chocolate variants demonstrate potential as part of a cancer-preventive diet.

The findings underscore the need for a multidisciplinary approach to maximize chocolate's health benefits. Standardizing processing methods to preserve bioactive compounds, regulating marketing of unhealthy products, and promoting nutrient-rich chocolate formulations are critical steps. Practical applications include reformulating commercial chocolates to reduce additives without compromising taste, integrating disease-resistant cacao into sustainable farming, and launching education campaigns to foster mindful consumption. However, limitations such as reliance on observational data and demographic gaps highlight the necessity for longitudinal clinical trials and broader population studies. Future research should prioritize translational studies combining omics technologies to elucidate molecular mechanisms, culturally tailored behavioral interventions, and economic analyses of biotech adoption in cacao-producing regions. By addressing these gaps, chocolate could transition from a cultural indulgence to a scientifically validated component of cancer prevention strategies, fostering cross-sector collaboration to unlock its full public health potential.

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Conflicts of Interest

The authors declare that they have no conflicts of interest to report regarding the present study.

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