

Natural Compounds in Cancer Chemoprevention: Mechanisms, Challenges, and Future Prospects

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ABSTRACT

Cancer remains a significant global health challenge, with increasing incidence rates despite advancements in treatment modalities. Chemoprevention, utilising natural or synthetic agents to hinder, delay, or reverse carcinogenesis, has emerged as a promising approach to reduce cancer risk alongside conventional therapies. This review explores the roles of various natural compounds, including plant-derived phytochemicals such as curcumin, resveratrol, Epigallocatechin Gallate (EGCG), and sulforaphane, which exhibit potent anticancer effects through mechanisms of apoptosis induction, cell cycle arrest, and inhibition of angiogenesis. These compounds demonstrate powerful antioxidant properties, modulating oxidative stress and inflammatory responses, critical factors in cancer progression. By interacting with key molecular targets like NF- κ B, Nrf2, and the PI3K/AKT pathway, these bioactive substances suppress oncogenic signalling and promote tumour-suppressing mechanisms. Additionally, the review addresses challenges in employing natural compounds for chemoprevention, such as issues related to bioavailability and optimal dosing, as well as strategies for enhancing their efficacy, including nanotechnology-based delivery systems and synergistic combinations with standard therapies. Comprehensive analysis of current preclinical and clinical studies underscores the potential of natural compounds in cancer prevention. Ultimately, this article aims to provide insights and a roadmap for advancing the development of natural compound-based chemoprevention strategies, highlighting their significance in improving patient outcomes and reducing cancer burden globally.

Keywords: Cancer, Chemoprevention, Natural Compounds, Phytochemicals, Antioxidant Properties.

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INTRODUCTION

Cancer persists as a leading cause of mortality globally, with incidence rates continuing to rise despite therapeutic advances.¹ Chemoprevention, a strategic methodology to obstruct, defer, or turn around carcinogenesis using natural or synthetic agents, has garnered considerable focus as a complementary technique to standard care.² Chemopreventive medicines target numerous phases of cancer progression, such as inception, promotion, and advancement, by modulating oxidative stress, inflammation, and

signalling pathways.³ Given the restrictions of chemotherapy, such as toxicity and medication resistance, chemoprevention presents a promising alternative to decrease cancer risk and improve patient outcomes. Organic compounds derived from plants, fungi, and oceanic sources have revealed powerful chemopreventive qualities with minimal side effects.⁴ Phytochemicals such as curcumin, resveratrol, Epigallocatechin Gallate (EGCG), and sulforaphane exhibit anticancer impacts through mechanisms involving apoptosis induction, cell cycle arrest, and restraint of angiogenesis.^{5,6} Epidemiological research suggests diets abundant in fruits, vegetables, and spices are related to reduced cancer risk, highlighting the role of bioactive compounds in prevention.⁷ Moreover, natural products modulate epigenetic changes, immune responses, and gut microbiota, further enhancing their chemopreventive potential.⁸ This review comprehensively examines the mechanisms by which natural substances exert chemopreventive effects, with a focus on their interactions with



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molecular targets like NF- κ B, Nrf2, and PI3K/AKT pathways. We also discuss the challenges associated with bioavailability, optimising dosages, and clinical translation of these substances. Furthermore, we explore prospects, including delivery systems employing nanotechnology and synergistic combinations with standard therapies. By consolidating recent preclinical and clinical evidence, this article aims to provide a roadmap for advancing natural compound-based chemoprevention strategies.

Mechanisms of Action

Antioxidant Properties

Reactive oxygen species and unrestrained free radicals can impose considerable harm within our bodies, triggering DNA mutations, lipid destruction, and protein disarray—all drivers of tumour initiation and progression. Compounds native to nature display mighty antioxidant properties, playing a pivotal role in thwarting carcinogenesis by tempering oxidative damage, a key contributor. Antioxidants from organic sources counterbalance these effects through diverse avenues.

Role in Free Radical Neutralisation

Plants bountiful in polyphenols like curcumin, resveratrol, and quercetin, alongside flavonoids, directly scavenge ROS such as superoxide anions, hydroxyl radicals, and hydrogen peroxide. These gifts from nature donate electrons to stabilise wayward radicals, sparing cells from harm's way.⁹ For instance, Curcumin exhibits a dual antioxidant mechanism: it directly neutralizes ROS through electron donation and, more significantly, induces the expression and activity of phase II antioxidant enzymes such as Superoxide Dismutase (SOD) and Glutathione Peroxidase (GPx), primarily via the activation of the Nrf2-Keap1 pathway. Meanwhile, green tea's epigallocatechin gallate quenches free radicals fiercely and binds pro-oxidant metals, including iron.¹⁰

Impact on Oxidative Tension

Beyond direct neutralisation, nature's compounds modulate oxidative stress by enhancing cellular protection systems. Sulforaphane's cruciferous gifts and lycopene's tomato treasures trigger the Nrf2 pathway, inducing antioxidant genes to new performance peaks.¹¹ Additionally, resveratrol enhances mitochondrial functions, reducing ROS production via activation of SIRT1.¹² Collectively, these mechanisms help lower oxidative stress, DNA damage, and inflammation, thereby decreasing the threat of cancer.

Modulation of Cell Signalling Pathways

Natural compounds can manipulate key molecular pathways involved in cancer development and progression. They can inhibit cancer-promoting routes while energising tumour-suppressing mechanisms, thereby reestablishing standard cellular balance.

Suppression of Oncogenic Pathways

Numerous natural compounds in plants have demonstrated an ability to suppress hyperactive oncogenic signalling in cancer cells that is often disrupted. For example, curcumin from turmeric inhibits the PI3K/Akt pathway, leading to decreased proliferation of breast and colorectal cancer cells and more apoptosis.¹³ Resveratrol, found in grapes and berries, similarly suppresses the MAPK/ERK pathway, hindering tumour growth and spread.¹⁴ Epigallocatechin-3-gallate, a key component of green tea, also reduces Akt phosphorylation, enhancing its effects against prostate cancer cell growth.¹⁵ Acting as natural kinase inhibitors inside cancer cells, these bioactive substances from nature show potential as a therapeutic approach targeting abnormal oncogenic signalling in tumours (Table 1).

Activation of Tumour Suppressor Pathways

Cancer preventive compounds found in nature have the remarkable ability not only to hinder tumorigenic signalling cascades but also to reawaken dormant safeguard mechanisms integral to defending against malignant transformation. For example, sulforaphane—an isothiocyanate concentrated in cruciferous vegetables—upregulates both the antioxidant transcription factor Nrf2 and the cellular sentinel p53, enhancing defensive enzymes and promoting programmed cell death in carcinogenic cells.¹⁶ Likewise, berberine derived from goldenseal root activates the cellular energy sensor AMPK, resulting in mTOR pathway inhibition and suppression of proliferative signals in tumour cells.¹⁷ Genistein, the predominant isoflavone in soy, has also been shown to replenish expression of the tumour suppressor PTEN, counterbalancing the hyperstimulation of the pro-growth PI3K/Akt pathway prevalent in breast malignancies.¹⁸ By reactivating these disrupted caretaker networks, phytochemicals help restore critical cellular checkpoints, preventing uncontrolled augmentation and bolstering strategies to avert cancer development.

Induction Of Apoptosis And Cell Cycle Arrest

Natural compounds have demonstrated significant potential in inducing apoptosis and cell cycle arrest in cancer cells, thereby suppressing tumour progression. These mechanisms are crucial for eliminating malignant cells and preventing uncontrolled proliferation.

Mechanisms of Apoptosis in Cancer Cells Apoptosis, or programmed cell death, is a highly regulated process that selectively removes compromised or aberrant cells from an organism. Naturally occurring compounds have shown promise in inducing apoptosis in malignant cells through diverse molecular routes. A key mechanism involves directly targeting the intrinsic apoptotic pathway, wherein phytochemicals such as curcumin promote mitochondrial outer membrane permeabilisation, releasing cytochrome c and activating caspase-9 and caspase-3

cascades. Curcumin also tweaks the balance of Bcl-2 family proteins, elevating pro-apoptotic Bax and Bak while suppressing anti-apoptotic Bcl-2 and Bcl-xL, thereby tilting the scales toward demise.^{19,20} As an alternative, the extrinsic apoptotic pathway can be triggered by substances like resveratrol, which stimulates Fas and TRAIL receptors, leading to a caspase-8-mediated fate.²¹ Furthermore, natural agents, including epigallocatechin gallate, induce endoplasmic reticulum stress, upregulating C/EBP homologous protein and caspase-12 to initiate apoptosis. Compounds such as genistein and sulforaphane also reestablish p53 tumour suppressor functions, promoting cell cycle arrest and apoptosis in cancer cells.²² Collectively, these data highlight the multifaceted aptitude of natural compounds to provoke apoptosis through diverse routes, presenting possible therapeutic options for cancer treatment.

Examples of Natural Compounds

Numerous plant compounds exhibit potent abilities to induce programmed cell death and suppress abnormal cell proliferation, effectively restoring cellular homeostasis. Curcumin, for one, modulates pivotal pathways such as NF- κ B and Akt, prompting apoptosis in diverse cancer types through pleiotropic molecular mechanisms.²³ Similarly, resveratrol exerts its impacts by activating the longevity-associated protein SIRT1 while inhibiting survivin, thereby allowing p53 to initiate cell demise.²⁴ Quercetin disturbs the cell cycle by obstructing cyclin-dependent kinases, arresting progression at critical checkpoints, and fostering oxidative stress to eliminate damaged cells.²⁵ Additionally, sulforaphane regulates inhibitor proteins such as p21 and p27, provoking apoptosis through the mitochondrial route and upregulating pro-apoptotic Bax.²⁶ These compounds epitomise nature's capacity to rebalance the intricate networks governing growth, division, and endurance by targeting key effectors.

ANTI-INFLAMMATORY EFFECTS

Role of Inflammation in Cancer Progression

Chronic inflammation is certainly a well-documented facilitator in cancer initiation, promotion, and progression within the body. An array of provocative mediators, including cytokines like TNF- α and IL-6, along with chemokines, as well as prostaglandins, generates a welcoming environment for tumours to thrive by inciting oxidative stress, DNA damage, and cellular overproliferation. Significant pathways such as NF- κ B, STAT3, and COX-2, which govern pro-inflammatory signalling and encourage malignant survival, angiogenesis, and metastasis, are core to this process. However, recent research has also highlighted the role of microRNAs in inflaming and altering the tumour microenvironment. Certain microRNAs, such as miR-21, have been shown to activate NF- κ B and STAT3 signalling and augment cancer-related inflammation. Conversely, other microRNAs like let-7 suppress IL-6 expression and thereby reduce inflammation-driven growth and metastasis of tumours.^{27,28}

Natural Compounds with Anti-Inflammatory Properties

Several plant-derived molecules display powerful anti-inflammatory characteristics, positioning them as promising agents for cancer avoidance. Gingerol, a key component in ginger, decreases swelling by repressing the NF- κ B and COX-2 routes, thereby lowering the production of pro-inflammatory cytokines.²⁹ Quercetin, plentiful in apples and onions, restricts TNF- α , IL-6, and NF- κ B activation, interrupting inflammation-related carcinogenesis.³⁰ Curcumin, the active ingredient in turmeric, manifests both anti-inflammatory and antitumor properties by downregulating NF- κ B, STAT3, and COX-2 signalling.³¹ Similarly, resveratrol, situated in grapes and berries, alleviates inflammation by obstructing NF- κ B and AP-1 pathways.³² Considering chronic swelling is a well-established driver of cancer, these natural compounds may help mitigate cancer risk and progression by targeting inflammatory mechanisms. Gingerol suppresses pathways to lower cytokine production, quercetin interrupts inflammatory activation to disrupt carcinogenesis, and curcumin downregulates key signaling pathways, thereby demonstrating its anti-inflammatory properties. Resveratrol likewise alleviates inflammation by blocking these pathways; therefore, natural anti-inflammatories may help prevent cancer by targeting these mechanisms.

RECENT NOVELTY IN NATURAL COMPOUNDS

Advances in Formulations and Delivery Systems

Natural compounds often have low bioavailability and solubility, hindering their use in cancer prevention. Recently, though, advances in nanotechnology and combination therapies have demonstrated promise in overcoming these obstacles.

Nanoemulsions and Liposomes for Enhanced Bioavailability

Liposomes and nanoemulsions have been extensively studied for their ability to enhance solubility, stability, and targeted delivery of natural bioactive compounds. For example, curcumin—a polyphenol derived from turmeric known for its low water solubility and rapid metabolic process—exhibits enhanced bioavailability and accumulation in tumours when packaged in phosphatidylcholine-based liposomes or nanoemulsions, as demonstrated by Anand *et al.*, in 2010.³³ Similarly, resveratrol formulated in nanoemulsions displays greater permanence and sustained release, thereby enhancing its chemoprotective impacts in colorectal cancer models, according to a study by Sessa *et al.*, in 2014.³⁴ What's more, green tea polyphenols such as EGCG show amplified cellular intake and reduced gastrointestinal disintegration when conveyed through liposomal carriers, as Singh *et al.*, found in 2016.³⁵ Emerging analysis proposes that sophisticated multifunctional nanotransporters, integrating nanotechnology with complementary tactics, could further

optimise the delivery of natural substances. Such advances may help bridge the gap between their promising preclinical benefits and genuinely practical clinical application in cancer avoidance and therapy.

Combination Therapies with Natural Compounds and Conventional Drugs

The strategic combination of organic bioactive ingredients and standard chemotherapeutic medications presents a promising approach to enhance healing outcomes while reducing toxicity hazards. For example, when co-delivered with the taxane medication paclitaxel through nanotransporters, curcumin has been shown to enhance apoptosis in breast cancer cells significantly and overcome multidrug resistance, addressing key limitations of paclitaxel alone therapy.³⁶ Correspondingly, the flavonoid quercetin has manifested the capacity to amplify cisplatin's antitumor impacts while markedly decreasing its nephrotoxic side effects in preclinical prototypes.³⁷ Another compelling model is sulforaphane, which boosts the cytotoxicity of 5-fluorouracil in colon cancer by regulating oxidative stress pathways, highlighting its probable clinical importance.³⁸ While challenges remain in optimising dosage schedules, improving pharmacokinetics, and scaling up manufacturing, these integrated methodologies underscore the potential of multi-targeted cures to advance cancer therapy outcomes. By exploiting the complementary systems of natural extracts and chemotherapeutic medications, scientists may unlock more effective and targeted treatment strategies for people living with cancer.

PERSONALISED NUTRITION AND DIETARY PATTERNS

While individual genetics, epigenetics, microbiome components, and metabolic idiosyncrasies determine responses to nutritious substances and their preventive capacities, personalised nourishment also acknowledges how one's distinctive constitution impacts the transformation and operation of natural elements. Should sustenance alterations be personalised according to a person's inherent cancer predispositions, the chemoprotective impacts could be exponentially intensified. Moving ahead, matching interventions to the specific traits of individual persons further bolsters the probable effect of sustenance for decreasing the chances of cancer.

Impact of Individual Genetic Variations on Response to Natural Compounds

Genetic variations in biosynthetic pathways and metabolic enzymes can significantly impact how the body responds to cancer-preventing elements in foods. For example, the anticancer effects of sulforaphane, found abundantly in broccoli and other cruciferous plants, have been shown to

fluctuate significantly due to changes in GSTM1 and GSTT1, genes controlling detoxification.³⁹ Prasad and colleagues also demonstrated that genetic diversity in UGT1A1 influences how curcumin, with its anti-proliferative qualities, is metabolised in the body.⁴⁰ Additional research by Berman *et al* revealed that COMT polymorphisms are capable of modulating resveratrol's absorption and influence over hormone-sensitive cancers through alterations in estrogen regulation.⁴¹ Findings like these emphasise the value of nutrigenomic profiling in identifying the most suitable natural compounds for each person based on their unique genetic makeup, thereby enabling individually tailored dietary approaches for cancer inhibition.

Dietary Interventions Tailored to Cancer Risk Profiles

Emerging studies support specially tailored nutrition strategies aligning eating habits with an individual's cancer vulnerabilities. High-risk carriers of BRCA mutations could greatly benefit from ramped intake of flavonoids like quercetin and genistein, fighting DNA harm.⁴² Those prone to colorectal cancer due to APC aberrations may potentially gain more from fibre-rich diets and butyrate-generating foods protecting intestinal integrity.⁴³ Lynch syndrome patients could profit from omega-3 fatty acids and green tea polyphenols, decreasing microsatellite disarray.⁴⁴ Challenges include the intricate nature of gene-diet interplay and large-scale clinical trials required to validate individualised dietary directives. The complex manner in which our genetics interact with food is poorly understood, necessitating further exploration into customising eating plans according to one's predispositions.

CHALLENGES IN IMPLEMENTATION

Bioavailability and Pharmacokinetics

Despite the promising anticancer properties inherent to natural compounds, their clinical applications are often hampered by inadequate bioavailability and unfavourable pharmacokinetics. Several key factors influence absorption and metabolism. Some phytochemicals exhibit exceedingly poor solubility in water, constraining their absorption within the gastrointestinal tract.³³ Compounds such as flavonoids and polyphenols undergo extensive preliminary metabolism, thereby diminishing their systemic availability.⁴⁵ Additionally, specific natural products serve as substrates for efflux transporters localised to cell membranes, further decreasing intracellular concentrations.⁴⁶ Interactions between gut microbiota and plant-derived molecules can also modify compound structures and activities, impacting efficacy.⁴⁷ The intricate interplay between an agent's inherent properties and biological processing influences whether promising experimental data manifests as clinical potential. Overcoming such hurdles demands innovative strategies to optimise natural therapies (Table 2).

Strategies to Enhance Bioavailability

Nanotechnology presents promising techniques to improve the solubility and stability of bioactive substances through sophisticated delivery vehicles such as liposomes, nanoparticles, and micelles. For example, nano-curcumin shows a significantly enhanced pharmacokinetic profile relative to conventional curcumin.⁴⁸ Moreover, chemical changes-such as prodrugs and designed analogues-can strengthen metabolic persistence, as seen with esterified resveratrol demonstrating prolonged presence in the body.⁴⁵ Naturally derived boosters like piperine, the signature component of black pepper, can further optimise bioavailability by inhibiting drug-metabolising enzymes in the digestive tract and liver, leading to higher systemic concentrations of compounds like curcumin.⁴⁹ In addition, phospholipid-based phytosomes-such as silymarin complexes-supply a novel strategy to enhancing the absorption of poorly soluble phytochemicals, though their accurate mechanisms remain under investigation.⁵⁰ Collectively, these approaches highlight the latent capacity of creative formulations and chemical optimisations to defeat bioavailability challenges in natural therapies.

Standardisation And Quality Control

The use of natural compounds in cancer chemoprevention faces significant challenges related to standardisation and quality control. These hurdles stem from the inherent complexity of plant-derived extracts and the lack of uniform regulatory frameworks.

Variability in Natural Extracts

Natural remedies frequently demonstrate heterogeneity between collections owing to facets including the plant type, geographical source, cultivation situations, extraction techniques, and storage conditions.⁵¹ For illustration, the density of bioactive parts such as curcumin in turmeric root or resveratrol in berries can diverge significantly, influencing effectiveness and replicability in preclinical and medical investigations.⁵² This variability complicates determining an appropriate dose and undermines the dependability of clinical conclusions. Furthermore, lengthy

clinical studies on certain supplements have yielded results that are difficult to confirm or compare due to production variations between study groups. Whereas standardised extracts offer better quality control, the unique benefits of diverse herbal formulations deserve considered research to support or refute claims of tailored healing.

Importance of Rigorous Testing Methodologies

To ensure safety and efficacy, standardised protocols for extraction, purification, and characterisation are essential. Advanced analytical techniques, such as High-Performance Liquid Chromatography (HPLC), Mass Spectrometry (MS), and nuclear magnetic resonance (NMR), are critical for quantifying active compounds.⁵³ Additionally, adherence to Good Manufacturing Practices (GMP) and pharmacopoeial standards can mitigate quality issues.⁵⁴ However, the high cost and technical expertise required for these methodologies remain barriers to widespread implementation.

Regulatory Hurdles And Clinical Trial Design

The translation of natural compounds from preclinical studies to clinical applications faces significant regulatory and methodological challenges. Despite their potential in cancer chemoprevention, natural products often encounter obstacles in gaining regulatory approval and require rigorous clinical trial designs to establish efficacy and safety.

Challenges in Obtaining Approval for Natural Products

Natural compounds face unique regulatory challenges due to their complex compositions, variability in sourcing, and lack of patentability. Regulatory agencies such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) require stringent evidence of safety, efficacy, and standardisation before approval. However, many natural products are classified as dietary supplements rather than drugs, which limits their clinical validation.⁵⁵ Additionally, issues such as batch-to-batch variability, bioavailability, and potential

Table 1: Key Natural Compounds and Their Mechanisms of Action in Cancer Chemoprevention.

Natural Compound	Source	Mechanism of Action	References
Curcumin	Turmeric	Inhibits NF- κ B, PI3K/Akt; induces apoptosis via Bax/Bcl-2 modulation	Aggarwal <i>et al.</i> , (2006); Gupta <i>et al.</i> , (2013)
Resveratrol	Grapes, Berries	Activates SIRT1, suppresses MAPK/ERK, induces apoptosis via p53	Kundu & Surh (2008); Baur & Sinclair (2006)
EGCG	Green Tea	Downregulates Akt, induces Endoplasmic Reticulum stress (CHOP/caspase-12)	Khan & Mukhtar (2010); Hsu <i>et al.</i> , (2003)
Sulforaphane	Cruciferous Veggies	Activates Nrf2/p53, upregulates Bax, induces cell cycle arrest	Zhang <i>et al.</i> , (2014); Wu <i>et al.</i> , (2013)
Quercetin	Apples, Onions	Blocks cyclin-dependent kinases, increases ROS-mediated apoptosis	Gibellini <i>et al.</i> , (2011); Murakami <i>et al.</i> , (2008)

Table 2: Challenges and Solutions in the Clinical Application of Natural Compounds.

Challenge	Example	Potential Solutions	References
Poor Bioavailability	Curcumin, Resveratrol	Nanoemulsions, liposomes, piperine as bioenhancer	Anand <i>et al.</i> , (2010); Shoba <i>et al.</i> , (1998)
Batch-to-Batch Variability	Plant extracts (e.g., curcumin)	Standardized HPLC/MS testing, GMP compliance	Heinrich <i>et al.</i> , (2012); Barnes <i>et al.</i> , (2016)
Regulatory Hurdles	Lack of RCTs for natural products	Biomarker-driven trials, public-private partnerships for funding	Surh (2011); Kelloff <i>et al.</i> , (2006)
Herb-Drug Interactions	Green tea polyphenols + drugs	Pharmacokinetic studies, personalized dosing	Yang <i>et al.</i> , (2009); Bode & Dong (2015)
Low Solubility	Flavonoids, Polyphenols	Phospholipid complexes (Phytosomes), prodrug formulations	Semalty <i>et al.</i> , (2010); Walle <i>et al.</i> , (2004)

herb-drug interactions complicate the approval process.⁵⁶ For example, curcumin, despite its well-documented anticancer properties, has poor bioavailability, necessitating advanced formulations to meet regulatory standards.³³

Need for Well-Designed Randomised Controlled Trials

Natural remedies often lack rigorous scientific backing due to inadequate large-scale, controlled experimental validation, which is viewed as the gold standard approach. Numerous existing studies suffer from constraints like small participant pools, brief timelines, and inconsistent outcome measures, complicating efforts to form definitive deductions.⁴ Complicating matters further, chemoprevention trials involving natural solutions encounter additional difficulties stemming from the placebo effect and patient diversity. For example, while observational research proposes potential advantages from green tea polyphenols, controlled experiments have generated inconsistent conclusions, probably attributable to variances in dosage amounts, forms, and participant adherence.⁵⁷ To enhance the reliability of future work, experiments should prioritise standardised dosing and forms, incorporate long-term monitoring to assess sustained impact, and adopt biomarker-guided approaches to examine mechanism effects.⁵⁸ Overcoming these methodological and regulatory barriers is fundamental for the successful integration of natural remedies into evidence-based cancer prevention strategies supported by research findings.

Future Prospects

The growing body of research on natural compounds in cancer chemoprevention highlights their potential as adjunctive or alternative strategies alongside conventional therapies. However, several challenges-such as bioavailability, standardisation, and clinical validation-must be addressed to harness their benefits fully. Future directions should focus on the following key areas:

Integration of Natural Compounds in Cancer Prevention Strategies

Natural remedies such as turmeric, resveratrol, and green tea have shown promising cancer prevention potential in animal studies. Still, their use in patients faces limitations of uptake in the body, varying impacts on individuals, and insufficient proof that it works in people.⁵⁹ To help with this, future analysis should target three key methods. First, customised medication strategies could optimise outcomes by discovering markers that forecast how people react to these substances.⁴ Second, exploring combined therapies-like sulforaphane with cisplatin-could increase beneficial effects while reducing harm by synchronised actions.⁶⁰ Finally, advancements in methods of supply, containing Nanocarriers and lipid carriers, could significantly enhance the uptake and stability of these normal substances.⁶¹ By addressing these locations, researchers may unlock the full capability of natural cancer prevention agents in clinical practice.

Role of Research Collaborations in Drug Development

Multidisciplinary collaborations among researchers from various fields, including pharmacology, oncology, and nutrition science, play a pivotal role in expediting the drug development process by integrating diverse expertise. Partnerships between public institutions and private organisations, such as the NIH's Natural Product Clinical Trials Network, provide vital funding for clinical tests exploring biologically active compounds, thereby fostering novelty in therapeutic discovery. Additionally, global digital repositories like NAPRALERT and PubChem function as standardised databases detailing the mechanisms of phytochemicals and enhancing investigational efficiency.⁶³ By uniting resources, knowledge, and technological advances, these initiatives bridge gaps between specialisations, ultimately propelling the evolution of novel cures. Diverse viewpoints combined with shared goals accelerate progress towards helping patients, as researchers build upon each other's efforts across organisations and disciplines.

Potential for Public Health Interventions and Dietary Recommendations

Epidemiological research highlights the promising role of dietary polyphenols, such as various flavonoids and lignans, in lowering cancer risk.⁶⁴ These studies indicate that harnessing the benefits of polyphenol-rich foods requires a dual-pronged strategy. First, authoritative health organisations, including the WHO and FDA, must develop evidence-based dietary guidelines that spotlight functional foods containing potent cancer-fighting properties. Guidelines should emphasise antioxidant-dense options like turmeric and cruciferous vegetables known to inhibit carcinogenesis.⁶⁴ Second, community-level nutrition initiatives must promote cuisine rich in phytochemicals, for example, Mediterranean and Asian-style meals. A wealth of data supports the protective impacts of such dietary patterns against cancer development and progression.⁶⁵ By merging these tactics, public health efforts can better champion cancer prevention via achievable modifications to dietary behaviours.

Future Areas of Research

Emerging fields are unveiling groundbreaking insights into the mechanisms of natural substances, revealing their potential for disease prevention and therapy. A key area is gut microbiome modulation: short-chain fatty acids produced through dietary fibre metabolism influence cancer risk by regulating immunity and inflammation, as shown by Zitvogel *et al.*, in 2018.⁶⁵ Epigenetic regulation also promises significantly: bioactive compounds like soy's genistein and cruciferous vegetables' sulforaphane can modify DNA methylation and histone acetylation, potentially reversing aberrant gene expression linked to diseases, as described by Vanden Berghe in 2020.⁶⁶ Furthermore, AI-driven drug discovery is revolutionising bioactive compound identification: machine learning models can now forecast molecular interactions and optimise therapeutic candidates, according to Gupta *et al.*, (2022).⁶⁷ Collectively, these emerging disciplines are expanding our understanding of natural compounds and inaugurating new precision medicine avenues.

CONCLUSION

In conclusion, natural compounds, especially curcumin, resveratrol and sulforaphane provide strong possibilities for cancer chemoprevention via modulating oxidative stress, inflammation; apoptosis; oncogenic signaling pathways. This is true despite the fact that obstacles related to bioavailability and clinical validation are still present, however the use of nanotechnology, personalized medicine and combination therapies demonstrate a sign of promise. Nevertheless, as with probiotics and prebiotics, large randomized controlled trials are still needed to provide unequivocal recommendations of the said substances for prevention or cure of the aforementioned diseases in lieu of understanding the systems biology of health

and disease, particularly potential interactions identified through microbiome and epigenetic research. These natural agents should be combined with evidence-based prevention strategies and public health efforts to bring us closer to the day when cancer risk can be reduced through safe, accessible, scientifically sound methods.

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ABBREVIATIONS

Nrf2: Nuclear factor erythroid 2-related factor, **PI3K:** Phosphoinositide 3-kinase, **AKT:** Protein kinase B, **ROS:** Reactive oxygen species, **SIRT1:** Sirtuin 1, **EGCG:** Epigallocatechin gallate, **MAPK:** Mitogen-activated protein kinase, **ERK:** Extracellular signal-regulated kinase, **NF-κB:** Nuclear factor kappa-light-chain-enhancer of activated B cells, **SOD:** Superoxide dismutase, **AMPK:** Adenosine 5'-monophosphate (AMP)-activated protein kinase.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

SUMMARY

This review highlights the role of natural compounds in cancer chemoprevention, a strategy aimed at obstructing, delaying, or reversing the carcinogenic process. With rising cancer incidence rates despite advancements in treatment, chemoprevention offers a complementary approach using agents derived from natural sources like plants and fungi. Key phytochemicals, such as curcumin, resveratrol, epigallocatechin gallate (EGCG), and sulforaphane, exhibit powerful anticancer properties by inducing apoptosis, causing cell cycle arrest, and inhibiting angiogenesis.

The mechanisms of action include potent antioxidant effects that mitigate oxidative stress and inflammation, both of which are critical in cancer progression. Natural compounds interact with molecular pathways like NF-κB, Nrf2, and the PI3K/AKT pathway, effectively suppressing oncogenic signalling while enhancing tumour-suppressing mechanisms.

Challenges such as bioavailability, optimal dosing, and the clinical translation of these compounds are addressed, along with potential strategies, including nanotechnology for delivery and the use of synergistic combinations with standard therapies. Overall, the review compiles recent preclinical and clinical evidence to provide insights into the development of natural compound-based chemoprevention strategies, emphasising their potential to improve patient outcomes and lower the global cancer burden.

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