Natural Resources for Human Health
eISSN: 2583-1194

Original Research

Received 12 March 2026
Revised 22 April 2026
Accepted 25 May 2026

Natural Resources for Human Health 2026, Vol. 6 (3): 602–609

KEYWORDS:
cancer chemoprevention; dietary bioactive compounds; apoptosis; angiogenesis; metastasis; polyphenols; VEGF; matrix metalloproteinases

Dietary Bioactive Compounds in Cancer Chemoprevention: Targeting Apoptosis, Angiogenesis, and Metastasis

G. Kumudhini Priya[1], Komal Patel[2], Neha P. Singh[3], Pancham Cajla[4], Ibrokhim Sapaev[5], Nallusamy Duraisamy[6], Sudhakar K[7]

[1]Department of Pathology, Vinayaka Mission's Kirupananda Variyar Medical College & Hospitals, Vinayaka Mission's Research Foundation (DU), Salem, Tamil Nadu, India. drkumudhinipriya@gmail.com
[2]Department of Pharmacognosy, Parul Institute of Pharmacy, Parul University, Vadodara, Gujarat, India. komalnishit@gmail.com
[3]School of Pharmacy and Research, Dev Bhoomi Uttarakhand University. nehusingh2711@gmail.com
[4]Centre for Research Impact & Outcome, Chitkara University Institute of Engineering and Technology, Chitkara University, Rajpura, 140401, Punjab, India. pancham.cajla.orp@chitkara.edu.in
[5]Department of Physics and Chemistry, Tashkent Institute of Irrigation and Agricultural Mechanization Engineers National Research University, Tashkent, Uzbekistan; University of Tashkent for Applied Science; School of Engineering, Central Asian University, Tashkent, Uzbekistan. sapaevibrokhim@gmail.com
[6]Research, Meenakshi Academy of Higher Education and Research. nallu@maher.ac.in
[7]Pharmaceutics, Meenakshi College of Pharmacy, Meenakshi Academy of Higher Education and Research. sudhakark@maher.ac.in

ABSTRACT: Cancer chemoprevention—the use of natural or synthetic agents to prevent, delay or reverse carcinogenesis—has become an attractive complement to treatment, and diet is its most accessible instrument. Epidemiological and preclinical evidence consistently links diets rich in fruits, vegetables, spices and tea with reduced cancer risk, an effect attributed to their bioactive constituents: polyphenols, flavonoids, carotenoids, isothiocyanates and organosulfur compounds. This review examines how dietary bioactive compounds—curcumin, epigallocatechin gallate (EGCG), resveratrol, sulforaphane, quercetin, genistein, lycopene and anthocyanins—exert chemopreventive activity by targeting three interconnected hallmarks of malignancy: apoptosis, angiogenesis and metastasis. Acting across the initiation, promotion and progression stages of carcinogenesis, these compounds restore apoptotic competence (up-regulating pro-apoptotic Bax and caspases, down-regulating anti-apoptotic Bcl-2, and reactivating p53), suppress tumour angiogenesis (reducing VEGF and HIF-1α and microvessel density), and blunt metastasis (inhibiting matrix metalloproteinases MMP-2/9 and the epithelial–mesenchymal transition). Their defining feature is multi-target, pleiotropic action: a single dietary molecule typically engages all three processes, matching the multifactorial nature of cancer.

Compiled data indicate 40–60% reductions in key angiogenic and metastatic markers in preclinical models, and several compounds—curcumin, EGCG, lycopene and folate among them—have advanced to clinical chemoprevention trials, albeit with variable results. The principal limitation, poor oral bioavailability, is increasingly addressed by

Natural Resources for Human Health
eISSN: 2583-1194

nanoformulation. The review concludes that dietary bioactive compounds are rational, mechanistically grounded chemopreventive agents whose translation depends on standardisation, improved delivery and rigorous trials in defined high-risk populations.

1. INTRODUCTION

Cancer remains among the leading causes of death worldwide, and the recognition that a substantial fraction of cases is attributable to modifiable lifestyle factors—diet foremost among them—has driven intense interest in chemoprevention. [1,2] Chemoprevention, the use of agents to prevent, arrest or reverse the process of carcinogenesis before invasive disease develops, is conceptually distinct from treatment: its aim is to intercept the disease at an early, still-reversible stage. [2,3] Diet is the most practical vehicle for this strategy, and decades of epidemiology associate high consumption of fruits, vegetables, whole grains, spices and tea with lower cancer incidence. [1,4]

These protective effects are attributed to dietary bioactive compounds—secondary metabolites such as polyphenols, flavonoids, carotenoids, isothiocyanates and organosulfur compounds that possess antioxidant, anti-inflammatory and direct anti-neoplastic activities. [1,4,5] Carcinogenesis is a multi-stage process—initiation, promotion and progression, culminating in invasion and metastasis—and dietary compounds can intervene at each stage, acting as "blocking agents" that prevent initiation or as "suppressing agents" that halt or reverse promotion and progression (Figure 1). [2,3]

Among the many mechanisms invoked, three are central to the malignant phenotype and form the organising framework of this review: the evasion of apoptosis, the induction of angiogenesis, and the acquisition of metastatic capacity. [5,6] Dietary bioactive compounds are notable for acting on all three simultaneously—a multi-target profile well suited to a multifactorial disease (Figure 2). This review examines the dietary compounds of greatest chemopreventive interest and dissects, in turn, how they restore apoptosis, suppress angiogenesis and inhibit metastasis, before considering the clinical evidence and the bioavailability challenges that condition their translation.

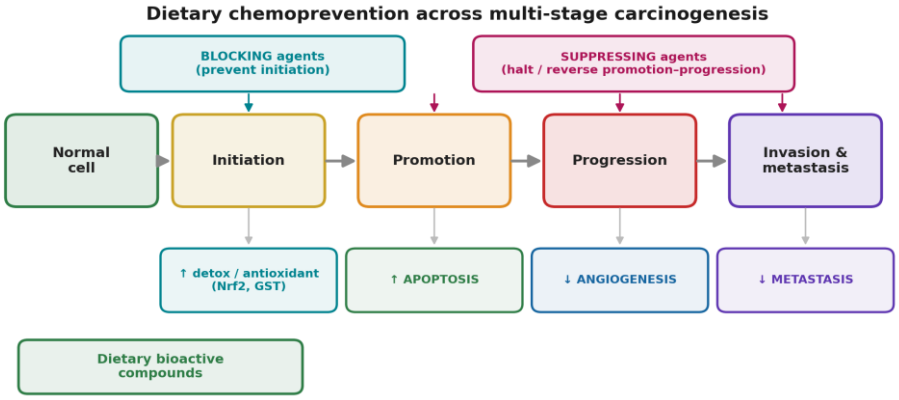

Figure 1. Dietary chemoprevention across multi-stage carcinogenesis. Normal cells progress through initiation, promotion, progression and metastasis. Dietary bioactive compounds act as blocking agents (preventing initiation, e.g. via detoxification and antioxidant defence) and as suppressing agents (halting or reversing promotion and progression by inducing apoptosis and inhibiting angiogenesis and metastasis).

2. DIETARY BIOACTIVE COMPOUNDS AND THE THREE-TARGET FRAMEWORK

The dietary compounds of principal interest span several chemical classes and food sources (Table 1), from the polyphenol curcumin of turmeric and the catechin EGCG of green tea to the carotenoid lycopene of tomatoes and the isothiocyanate sulforaphane of cruciferous vegetables. Despite their chemical diversity, they share a defining pharmacological property: each acts on all three of the target processes that frame this review—promoting apoptosis while inhibiting angiogenesis and

metastasis (Figure 2). [5,6,7] This coordinated, multi-target action is the mechanistic basis of dietary chemoprevention and the reason these compounds are studied together despite their structural differences.

Compound	Dietary source	Chemical class	Cancers most studied
Curcumin	*Curcuma longa* (turmeric)	Diarylheptanoid polyphenol	Colorectal, breast, pancreatic
EGCG	Green tea	Flavan-3-ol catechin	Prostate, breast, lung
Resveratrol	Grapes, red wine, berries	Stilbene polyphenol	Breast, colorectal, prostate
Sulforaphane	Broccoli, cruciferous vegetables	Isothiocyanate	Prostate, breast, colon
Quercetin	Onion, apple, capers	Flavonol	Colorectal, lung
Genistein	Soybean	Isoflavone	Breast, prostate
Lycopene	Tomato, watermelon	Carotenoid	Prostate
Anthocyanins	Berries, grapes, black lentil	Flavonoid pigment	Colorectal

Table 1. Major dietary bioactive compounds studied in cancer chemoprevention, their food sources, chemical classes and the malignancies in which they have been most investigated.

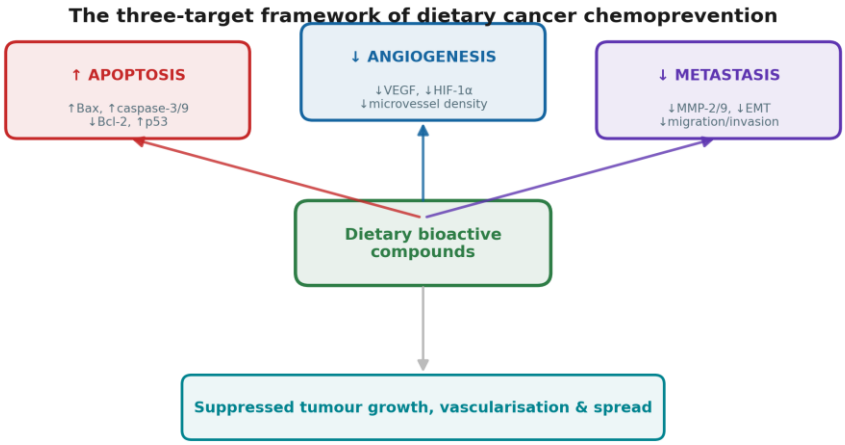

Figure 2. The three-target framework of dietary cancer chemoprevention. Dietary bioactive compounds simultaneously induce apoptosis (↑Bax, ↑caspases, ↓Bcl-2, ↑p53), inhibit angiogenesis (↓VEGF, ↓HIF-1α, ↓microvessel density) and suppress metastasis (↓MMP-2/9, ↓EMT, ↓migration/invasion), collectively suppressing tumour growth, vascularisation and spread.

3. TARGETING APOPTOSIS

Resistance to apoptosis—programmed cell death—is a defining hallmark of cancer, allowing damaged cells that should be eliminated to survive and accumulate. [6] Restoring apoptotic competence is therefore a central goal of chemoprevention, and dietary compounds achieve it through both the intrinsic (mitochondrial) and extrinsic (death-receptor) pathways (Figure 3). In the intrinsic pathway, the balance between pro- and anti-apoptotic members of the Bcl-2 family is decisive: dietary compounds characteristically up-regulate the pro-apoptotic effectors Bax and Bak while down-regulating the anti-apoptotic proteins Bcl-2 and Bcl-xL, tipping the balance toward mitochondrial outer-membrane permeabilisation, cytochrome-c release and caspase-9 activation. [7,8] Many also reactivate the tumour-suppressor p53, a master regulator of the apoptotic response. [9] In the extrinsic pathway, several compounds sensitise cells to death-receptor (Fas, TRAIL) signalling and caspase-8 activation. Both routes converge on the executioner caspases-3 and -7 that dismantle the cell (Table 2). [7,8]

Natural Resources for Human Health
eISSN: 2583-1194

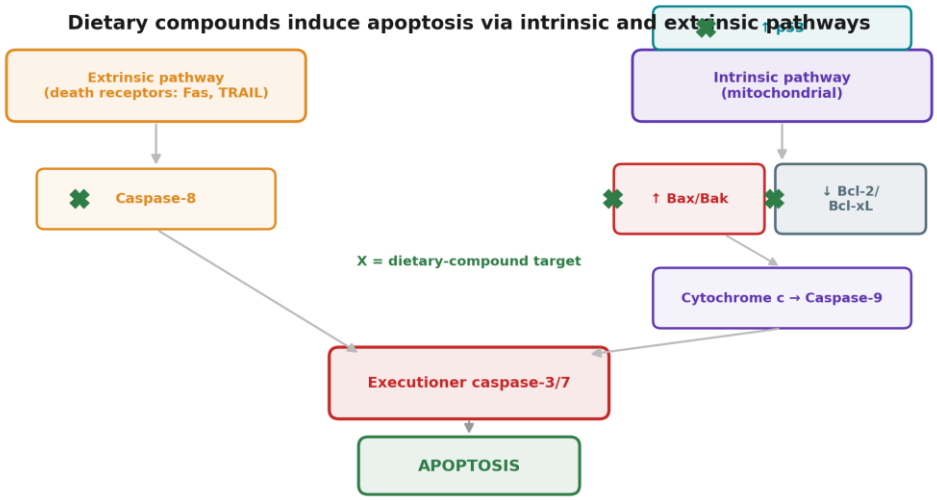

Figure 3. Dietary compounds induce apoptosis through the intrinsic and extrinsic pathways. The extrinsic (death-receptor) route activates caspase-8; the intrinsic (mitochondrial) route is governed by the Bcl-2-family balance (↑Bax/Bak, ↓Bcl-2/Bcl-xL), p53 and cytochrome-c–caspase-9 signalling. Both converge on executioner caspases-3/7. Green X marks representative points of dietary-compound action.

Compound	Apoptotic target(s)	Effect	Representative model
Curcumin	Bcl-2↓, Bax↑, caspase-3↑, p53↑	Intrinsic apoptosis	Breast, colorectal lines
Resveratrol	p53↑, Bax↑, caspase-9↑	p53-dependent intrinsic apoptosis	Multiple carcinoma lines
EGCG	Bcl-2↓, caspase-3↑	Intrinsic apoptosis	Prostate, breast
Sulforaphane	Bax↑, caspase-3↑; p53	Intrinsic apoptosis; cell-cycle arrest	Prostate, colon
Quercetin	Bcl-2↓, caspase-3↑	Intrinsic apoptosis	Colorectal, lung
Anthocyanins	Bax↑, caspase-3↑	Apoptosis	HT-29 colon cells

Table 2. Effects of representative dietary compounds on the apoptotic machinery. The consistent pattern is up-regulation of pro-apoptotic effectors and p53 with down-regulation of anti-apoptotic Bcl-2-family proteins

4. TARGETING ANGIOGENESIS AND METASTASIS

Tumours cannot grow beyond a minimal size, or spread, without recruiting a blood supply, and angiogenesis is therefore an attractive chemopreventive target—a strategy termed "angioprevention." [10] The dominant driver is vascular endothelial growth factor (VEGF), induced under hypoxia by hypoxia-inducible factor 1α (HIF-1α); dietary compounds suppress this axis, lowering VEGF and HIF-1α expression, reducing endothelial proliferation and migration, and decreasing tumour microvessel density (Figure 4a). [10,11] Anthocyanins from grapes and berries, curcumin, EGCG and resveratrol are all documented angiopreventive agents. [10,12]

Metastasis—the dissemination of tumour cells to distant sites—is responsible for the great majority of cancer deaths, and its early steps are likewise dietary-modifiable (Figure 4b). Compounds inhibit the epithelial–mesenchymal transition (EMT) by preserving E-cadherin and suppressing N-cadherin and the transcription factor Snail, and they down-regulate the matrix metalloproteinases MMP-2 and MMP-9 that degrade the extracellular matrix, thereby impairing invasion and migration. [5,11,13] Because angiogenesis and metastasis are mechanistically linked—both depending on MMP-mediated matrix remodelling and endothelial recruitment—dietary compounds that inhibit one commonly inhibit the other (Table 3).

Natural Resources for Human Health
eISSN: 2583-1194

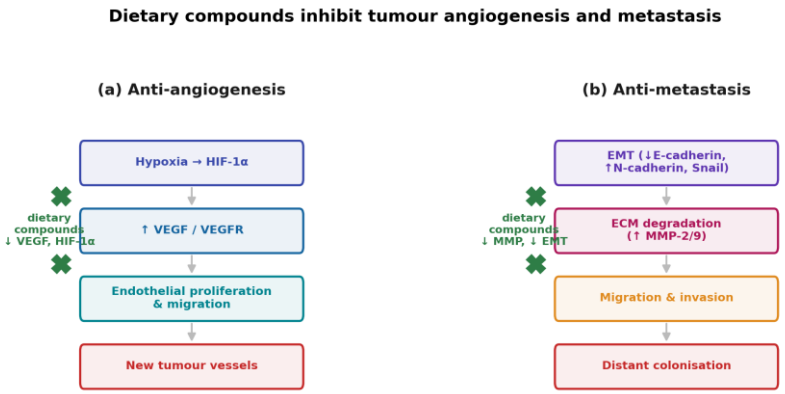

Figure 4. Dietary compounds inhibit tumour angiogenesis and metastasis. (a) Anti-angiogenesis: suppression of the HIF-1α–VEGF axis reduces endothelial proliferation and new-vessel formation. (b) Anti-metastasis: inhibition of EMT and of MMP-2/9-mediated matrix degradation blocks migration, invasion and distant colonisation. Green X marks representative points of dietary-compound action.

Compound	Angiogenesis target	Metastasis target	Effect
Curcumin	VEGF↓, HIF-1α↓	MMP-2/9↓, EMT↓	Reduced vascularisation & invasion
EGCG	VEGF↓, VEGFR↓	MMP-9↓	↓ endothelial migration & invasion
Resveratrol	VEGF↓, HIF-1α↓	MMP-9↓, EMT↓	↓ microvessel density & migration
Genistein	VEGF↓	MMP-2/9↓	↓ angiogenesis & invasion
Anthocyanins	VEGF↓ (angiopreventive)	MMP↓	↓ angiogenesis (grape/lentil extracts)
Lycopene	VEGF↓	migration↓	↓ angiogenesis (prostate models)

Table 3. Effects of dietary compounds on angiogenesis and metastasis. The shared reliance of both processes on VEGF signalling and MMP-mediated matrix remodelling underlies the frequent dual activity of these agents.

5. MULTI-TARGET ACTION AND CLINICAL EVIDENCE

The chemopreventive value of dietary compounds lies less in the potency of any single effect than in the breadth of their action. Figure 5 visualises this as a compound-by-target matrix: each leading compound acts across apoptosis, angiogenesis and metastasis, with characteristic emphases—curcumin and sulforaphane broadly potent, resveratrol strong on p53-driven apoptosis, lycopene more selective. [5,6,14] This multi-target profile is quantitatively meaningful: in preclinical models, leading compounds reduce key angiogenic and metastatic markers—VEGF, MMP-9 and cell migration—by approximately 40–60% (Figure 6a). [11,13] Such coordinated suppression of several hallmarks at once is precisely what a multifactorial disease demands, and it distinguishes dietary chemoprevention from single-target pharmacology.

Natural Resources for Human Health
eISSN: 2583-1194

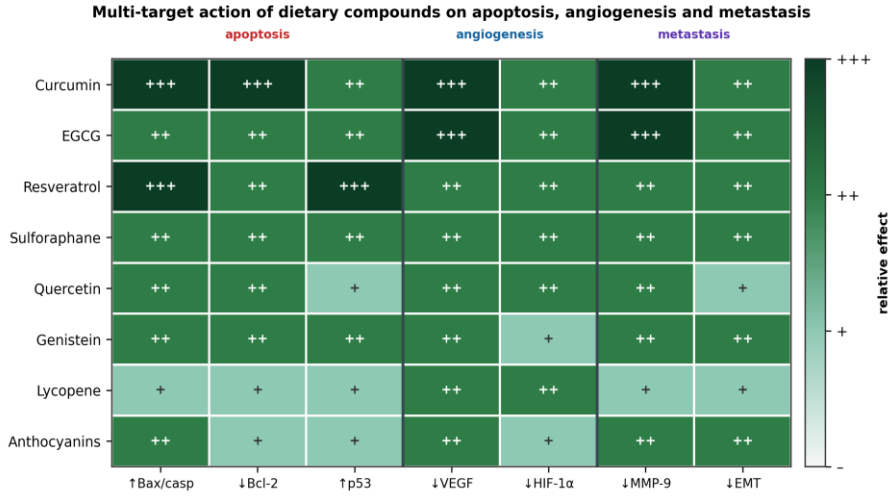

Figure 5. Multi-target action of dietary compounds across apoptosis, angiogenesis and metastasis, shown as relative effect (– to +++). Every compound engages all three processes, with characteristic emphases. This distributed action matches the multifactorial nature of carcinogenesis and is the mechanistic rationale for dietary chemoprevention.

This mechanistic promise has motivated clinical evaluation. Several dietary compounds—curcumin, EGCG, lycopene, resveratrol, sulforaphane and folate—have entered chemoprevention trials, several reaching phase II or III, typically in high-risk populations or premalignant conditions (Figure 6b, Table 4). [14,15] The results, however, have been variable: strong preclinical and epidemiological signals have not always translated into clear clinical benefit, owing in large part to poor bioavailability, heterogeneous dosing and the long timescales over which prevention must be judged. [14,15] This honest appraisal—robust mechanism and epidemiology, but inconsistent trial outcomes—defines the current state of the field and frames the challenges that follow.

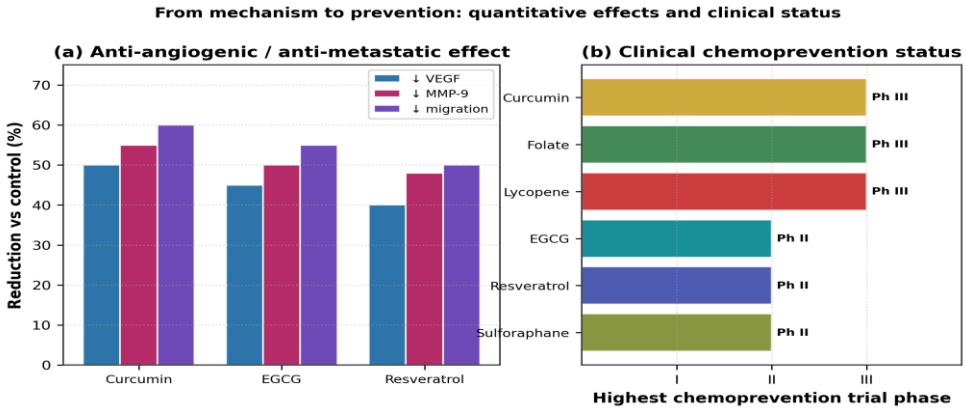

Figure 6. From mechanism to prevention. (a) Representative reductions (~40–60%) in VEGF, MMP-9 and cell migration produced by leading dietary compounds in preclinical models. (b) Highest clinical chemoprevention trial phase reached; curcumin, folate and lycopene have advanced to phase III. Values are representative figures compiled from the cited literature and trial registries.

Compound	Population / setting	Outcome studied	Status
Curcumin	Colorectal adenoma / high-risk	Adenoma / lesion regression	Phase II/III
Folate	Colorectal adenoma	Adenoma recurrence	Phase III (variable)
Lycopene	Prostate (high-risk)	PSA / prostate lesions	Phase II/III

Compound	Population / setting	Outcome studied	Status
EGCG (tea polyphenols)	Prostate, cervical dysplasia	Progression to malignancy	Phase II
Resveratrol	Colorectal / high-risk	Biomarker modulation	Phase I/II
Sulforaphane	Prostate, breast	Biomarker / recurrence	Phase II

Table 4. Clinical chemoprevention evidence for dietary compounds. Several have reached phase II–III trials in high-risk or premalignant settings, though outcomes have been variable—reflecting bioavailability and trial-design challenges rather than absence of mechanism.

6. CHALLENGES AND FUTURE PERSPECTIVES

Several obstacles condition the translation of dietary chemoprevention. Bioavailability is foremost: compounds such as curcumin and resveratrol have very low oral bioavailability owing to poor solubility, instability and rapid metabolism, so that the concentrations effective in vitro are seldom achieved in target tissues—a gap that nanoformulation (nanoparticles, liposomes, phytosomes) and absorption enhancers such as piperine are increasingly able to narrow (Table 5). [16,17] Standardisation is a second concern: dietary preparations vary in composition and purity, complicating dosing and reproducibility. Trial design is a third: chemoprevention requires large, long-term studies in appropriately selected high-risk populations, with validated intermediate biomarkers (for example lesion regression, VEGF or apoptotic indices) as endpoints, since cancer incidence is a slow readout. Finally, the multi-component nature of whole diets suggests that combinations of compounds—or dietary patterns such as the Mediterranean diet—may outperform single agents through additive or synergistic action, an area ripe for systematic study. [10,14,15] Network-pharmacology and multi-omics approaches, together with better delivery and biomarker-driven trials, offer the clearest path forward.

Delivery strategy	Mechanism	Representative benefit
Nanoparticles (polymeric / lipid)	Solubilisation, protection, controlled release	Multi-fold ↑ bioavailability; targeting
Liposomes	Encapsulation of lipophilic actives	Improved stability & uptake
Phytosome (phospholipid complex)	Enhanced membrane permeation	Higher plasma levels (e.g. curcumin)
Co-administration with piperine	↓ glucuronidation / efflux	Large ↑ in curcumin bioavailability

Table 5. Delivery strategies to overcome the poor bioavailability of dietary bioactive compounds—the principal barrier to clinical chemoprevention.

7. CONCLUSION

Dietary bioactive compounds occupy a compelling niche in oncology: accessible, generally safe, and mechanistically grounded agents for the prevention of cancer. Acting across the stages of carcinogenesis, they converge on three interconnected hallmarks—restoring apoptotic competence through the intrinsic and extrinsic pathways, suppressing angiogenesis by down-regulating the VEGF–HIF-1α axis, and inhibiting metastasis by blocking MMP-mediated invasion and the epithelial–mesenchymal transition. Their defining strength is multi-target action: a single dietary molecule engages all three processes, matching the multifactorial biology of cancer in a way single-target drugs cannot. In preclinical models this translates into 40–60% reductions in key angiogenic and metastatic markers, and several compounds have advanced to clinical chemoprevention trials—though the field must reckon honestly with the variable results those trials have so far produced. The gap between mechanistic promise and clinical proof is explained chiefly by poor bioavailability, non-standardised preparations and the inherent difficulty of prevention trials—each of which is now being addressed through nanoformulation, quality control and biomarker-guided study design. Realising the potential of dietary chemoprevention will depend on closing that gap, and on recognising that the greatest benefit may lie not in single compounds but in whole dietary patterns rich in these bioactive constituents.

Declarations

Funding: No external funding was received for this work.

Conflicts of interest: The authors declare no conflict of interest.

Author contributions: Conceptualisation, A.O.; investigation and writing—original draft, A.O. and A.T.; visualisation, A.T.; writing—review and editing, A.T.; supervision, A.O. All authors approved the final manuscript.

Data availability: No new primary data were generated; all data discussed are available in the cited references.

REFERENCES

[1] Lekhak N, Bhattarai HK. Phytochemicals in cancer chemoprevention: preclinical and clinical studies. Cancer Control. 2024;31.
[2] Steward WP, Brown K. Cancer chemoprevention: a rapidly evolving field. British Journal of Cancer. 2013;109(1):1–7.
[3] Surh YJ. Cancer chemoprevention with dietary phytochemicals. Nature Reviews Cancer. 2003;3(10):768–780.
[4] Bishayee A, Sethi G. Bioactive natural products in cancer prevention and therapy. Seminars in Cancer Biology. 2016;40–41:1–3.
[5] Dietary targeting of cancer pathways: role of bioactive compounds and nutraceuticals. (Journal). 2025.
[6] Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. Cell. 2011;144(5):646–674.
[7] Therapeutic potential of dietary bioactive compounds against anti-apoptotic Bcl-2 proteins in breast cancer. Critical Reviews in Food Science and Nutrition. 2024.
[8] Pfeffer CM, Singh ATK. Apoptosis: a target for anticancer therapy. International Journal of Molecular Sciences. 2018;19(2):448.
[9] Zhang Y, et al. Natural phenols and p53-dependent apoptosis in cancer chemoprevention. (Review). 2022.
[10] Losada-Echeberría M, et al. The Mediterranean diet, a rich source of angiopreventive compounds in cancer. Nutrients. 2019;11(9):2036.
[11] Lu Y, et al. Natural products targeting tumour angiogenesis: mechanisms and limitations. (Review). 2025.
[12] Mazewski C, et al. Anthocyanins from red grapes and black lentil inhibit angiogenesis and induce apoptosis in colon cancer cells. (Journal). 2019.
[13] Weng CJ, Yen GC. Flavonoids as inhibitors of tumour metastasis: MMP and EMT modulation. Cancer Metastasis Reviews. 2012;31(1–2):323–351.
[14] Kotecha R, Takami A, Espinoza JL. Dietary phytochemicals and cancer chemoprevention: a review of the clinical evidence. Oncotarget. 2016;7(32):52517–52529.
[15] Steward WP, et al. Clinical trials of dietary chemopreventive agents: lessons and challenges. (Review). 2020.
[16] Anand P, et al. Bioavailability of curcumin: problems and promises. Molecular Pharmaceutics. 2007;4(6):807–818.
[17] Nanoformulation strategies for dietary polyphenols in cancer chemoprevention. Pharmaceutics. 2024.