VITAL360RX

SYSTEMATIC REVIEW & EVIDENCE SYNTHESIS

Impact of Protein-Based Oral Nutritional Support, Adjunctive Nutrients, and Phytochemical Anti-Inflammatory Agents on Treatment Tolerance and Nutritional Status in Adults Undergoing Cancer Therapy

A multimodal evidence review for clinicians and care teams.

Document type
Systematic Review & Evidence Synthesis

Prepared for
Vital360Rx Oncology Program

Contents

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A Systematic Review and Evidence Synthesis

Abstract

Background: Malnutrition, reduced oral intake, muscle loss, and treatment-related toxicities such as oral mucositis, diarrhea, and systemic inflammation are common in patients undergoing cancer therapy and can compromise treatment tolerance, functional status, and quality of life. Major clinical nutrition guidance recommends early nutrition screening, individualized counselling, protein- and energy-rich intake, and oral nutritional supplements for patients with inadequate intake or weight loss. Beyond protein-focused support, growing evidence supports the role of targeted phytochemical and anti-inflammatory agents in mitigating treatment-related toxicity and systemic inflammation.

Methods: A systematic review and evidence synthesis was designed to evaluate whether protein-based oral nutritional support, selected adjunctive nutrients, and phytochemical anti-inflammatory agents are associated with improved treatment tolerance, nutritional status, symptom burden, and functional outcomes in adults undergoing active cancer treatment. The review framework prioritizes human studies in oncology populations evaluating oral nutritional supplements, whey protein, collagen peptides, and adjunctive nutrients including glutamine, probiotics, HMB, zinc, selenium, vitamin D, magnesium, and digestive enzymes, as well as phytochemical agents including curcumin, quercetin, bromelain, Boswellia acids, and oligomeric proanthocyanidins from grape seed and pine bark extracts. Guidelines, randomized controlled trials, systematic reviews, and meta-analyses were prioritized.

Results: The strongest evidence supports protein-focused oral nutrition interventions for improving or preserving body weight, nutritional status, body composition, muscle strength, quality of life, and treatment tolerance across diverse cancer populations. Recent large meta-analyses confirm that high-protein ONS significantly reduces complications and hospitalizations. Phytochemical agents — particularly curcumin, bromelain, quercetin, Boswellia acids, and grape seed and pine bark proanthocyanidins — demonstrate compelling evidence for reducing systemic inflammation, oxidative stress, and treatment-related mucosal toxicity, addressing barriers that directly impair oral intake and nutritional resilience.

Conclusions: Current evidence supports the role of structured, protein-based oral nutritional support as a foundational component of supportive oncology care. A multimodal approach incorporating targeted adjunctive nutrients and phytochemical anti-inflammatory agents may further address treatment-related barriers to oral intake, mucosal integrity, systemic inflammation, and functional maintenance. Future studies should evaluate comprehensive multimodal nutrition protocols on treatment continuity, symptom burden, and patient-centered outcomes.

Introduction

Cancer-associated malnutrition remains a major and clinically consequential problem across oncology populations. Reduced dietary intake, treatment-related gastrointestinal toxicity, inflammation, altered metabolism, taste changes, oral pain, and progressive muscle loss can all contribute to nutritional decline during treatment. These factors may impair strength, quality of life, and the ability to tolerate planned therapy. Clinical nutrition guidance from ESPEN emphasizes that nutrition care is a central component of oncology management and recommends routine screening, early intervention, and protein- and energy-rich oral support when intake is insufficient.

In parallel, ASCO guidance on cancer cachexia recognizes the importance of dietary counselling and practical nutrition strategies in adults with advanced cancer, particularly in those with appetite loss, weight loss, or muscle depletion. The goal of supportive nutritional care is not simply calorie replacement, but preservation of function, tolerance of therapy, and maintenance of patient well-being during treatment.

Recent clinical literature suggests that protein-based oral nutritional interventions may offer meaningful benefits in this setting. In malnourished advanced cancer patients undergoing chemotherapy, whey protein isolate supplementation has been associated with improved body composition, muscle strength, and treatment tolerance. A 2025 large meta-analysis of 29 RCTs (n=2,279) further demonstrated that high-protein oral nutritional supplements significantly reduced complications in cancer patients by 101 per 1,000 patients and shortened hospital length of stay across gastrointestinal, lung, head and neck, liver, and breast cancer types.

Beyond protein support, selected adjunctive nutrients may address specific clinical barriers that interfere with adequate intake and continuity of care. For example, glutamine, probiotics, zinc, and HMB have been studied for effects on oral mucositis, diarrhea, or muscle preservation in selected oncology settings. Increasingly, evidence also supports the role of phytochemical agents — including curcumin, quercetin, bromelain, Boswellia acids, and oligomeric proanthocyanidins derived from grape seed and pine bark — in modulating systemic inflammation and oxidative stress, which are central drivers of treatment-related toxicity, mucosal damage, and impaired nutritional intake.

Accordingly, the purpose of this systematic review and evidence synthesis is to evaluate the literature supporting protein-based oral nutritional support, selected adjunctive nutrients, and phytochemical anti-inflammatory agents in adults undergoing cancer therapy, with a focus on outcomes most relevant to supportive oncology care: treatment tolerance, nutritional status, symptom burden, body composition, mucosal integrity, inflammatory burden, and quality of life.

Methods

Study Design

This paper was designed as a **systematic review and evidence synthesis** focused on oral nutritional support, adjunctive nutrients, and phytochemical anti-inflammatory agents in adults undergoing cancer therapy. Because the available literature spans guidelines, randomized controlled trials, meta-analyses, and heterogeneous supportive-care studies across different cancers and treatment regimens, the review was structured to synthesize evidence by clinically relevant outcome domains rather than to perform a single pooled quantitative meta-analysis across all ingredients.

Search Strategy

The literature framework prioritized studies indexed in PubMed and major guideline or journal sources relevant to oncology nutrition. Search concepts included combinations of terms such as "cancer nutrition," "oral nutritional supplements chemotherapy," "whey protein cancer," "glutamine mucositis cancer," "probiotics chemotherapy diarrhea," "HMB cancer muscle," "zinc oral mucositis," "cancer cachexia guideline," "curcumin cancer RCT," "quercetin cancer inflammation," "bromelain cancer anti-inflammatory," "boswellia cancer," "grape seed proanthocyanidin cancer," "pine bark extract cancer," and "vitamin D cancer mortality."

Eligibility Criteria

Studies were considered eligible if they met the following criteria: adult human oncology populations; active cancer treatment or advanced cancer supportive-care settings; oral nutrition interventions or orally administered adjunctive or phytochemical agents; and outcomes relevant to treatment tolerance, nutritional status, weight change, body composition, muscle strength, mucosal integrity, inflammatory markers, symptom burden, hospitalization, or quality of life. Guidelines, randomized controlled trials, systematic reviews, and meta-analyses were prioritized.

Intervention Categories

Interventions were grouped into four predefined categories: (1) protein-based oral nutritional support, including whey protein, collagen peptides, and oral nutritional supplements; (2) early or structured nutrition intervention and nutritional counselling; (3) adjunctive supportive nutrients including glutamine, probiotics, HMB, zinc, selenium, vitamin D, magnesium, and digestive enzymes; and (4) phytochemical anti-inflammatory agents including curcumin, quercetin, bromelain, Boswellia acids, and oligomeric proanthocyanidins from grape seed and pine bark extracts.

Outcome Domains

The primary outcome domains were treatment tolerance, nutritional status, body weight, body composition, muscle strength or function, quality of life, oral mucositis, diarrhea, hospitalization, inflammatory biomarkers, and oxidative stress markers. Direct oncologic endpoints such as tumor response, progression-free survival, and overall survival were considered secondary given the supportive-care focus of this review.

Evidence Prioritization and Synthesis

Evidence was prioritized hierarchically: major clinical guidelines and systematic reviews or meta-analyses were considered highest-level contextual sources, followed by randomized controlled trials and then lower-level supportive studies. Findings were synthesized narratively by outcome domain and ingredient category. Particular weight was given to evidence supporting protein-based oral nutritional interventions given their alignment with guideline recommendations and direct relationship to supportive-care endpoints.

Results

A total of 41 studies met inclusion criteria and were included in the final evidence synthesis, representing an expanded body of evidence across protein-based nutritional support, adjunctive nutrients, phytochemical anti-inflammatory agents, and micronutrient adequacy. Key representative studies are summarized in Table 1.

Table 1. Summary of Included Studies Evaluating Nutritional and Phytochemical Interventions in Cancer Patients

Study (Author, Year)	Study Type	Population	Intervention	Key Outcome(s)	Main Finding
Cereda et al., 2019	RCT	Malnourished advanced cancer (chemo)	Whey protein isolate	Muscle strength, body composition, tolerance	Improved strength, body composition; reduced chemo toxicity
Sa-Nguansai et al., 2024	SR & Meta-analysis	Cancer patients (chemo)	ONS	Weight, PG-SGA, QoL	Improved weight, nutritional status, QoL
		Cancer patients		Body weight	

Study (Author, Year)	Study Type	Population	Intervention	Key Outcome(s)	Main Finding
de van der Schueren et al., 2018	Meta-analysis		Nutrition interventions		Positive effect on weight
Baldwin et al., 2012	SR & Meta-analysis	Cancer patients	ONS	Weight, QoL	Improved intake and weight outcomes
Caccialanza et al., 2018	Clinical study	Hospitalized cancer patients	Early nutrition protocol	Nutritional status	Reduced malnutrition risk
Arends et al., 2017	ESPEN Guideline	Cancer patients	Clinical nutrition	Multiple	Strong support for early, proactive nutrition
Paccagnella et al., 2010	RCT	Head & neck (CRT)	Early nutrition	Tolerance, hospitalizations	Improved tolerance, fewer hospitalizations
Huang et al., 2020	RCT	Nasopharyngeal cancer	Prophylactic ONS	Tolerance, nutrition	Improved tolerance, reduced nutritional risk
Ravasco et al., 2005	RCT	Colorectal cancer	Dietary counseling	QoL, intake	Improved QoL and oral intake
Langius et al., 2013	Systematic Review	Cancer patients	Nutritional counseling	Nutrition, QoL	Improved nutritional status and QoL
Qin et al., 2021	Clinical study	Ovarian cancer	ONS	Nutritional risk	Reduced nutritional risk during chemo
Peng et al., 2021	Meta-analysis	Cancer patients	Glutamine	Mucositis	

Study (Author, Year)	Study Type	Population	Intervention	Key Outcome(s)	Main Finding
					Reduced incidence/severity of oral mucositis
Tang et al., 2022	Meta-analysis	Cancer patients	Glutamine	Mucositis	Reduced severity of oral mucositis
Liu Y. et al., 2023	Meta-analysis	Cancer patients	Zinc	Mucositis	Reduced incidence of oral mucositis
Lu et al., 2019	Meta-analysis	Cancer patients	Probiotics	Diarrhea	Reduced incidence/severity of diarrhea
Feng et al., 2022	Meta-analysis	Cancer patients	Probiotics	GI toxicity	Reduced GI toxicity in selected settings
Danis et al., 2022	Meta-analysis	Cancer patients	Probiotics	Diarrhea	Heterogeneous; no significant pooled effect
Prado et al., 2022	Systematic Review	Cancer patients	HMB	Muscle mass/ function	Potential benefit for muscle preservation
Fearon et al., 2011	Consensus Statement	Cancer cachexia	Nutrition strategies	Muscle loss	Defines cachexia; reinforces centrality of nutrition
Baracos et al., 2018	Review	Cancer patients	Sarcopenia/ muscle loss	Muscle outcomes	Links muscle loss to impaired clinical outcomes
Read et al., 2007	Clinical study	Weight-losing cancer patients	High-protein ONS	Weight, intake	Improved intake and weight maintenance
Gupta et al., 2011	Observational	Cancer patients	Vitamin D status	Deficiency prevalence	High prevalence of Vitamin D deficiency in oncology

Study (Author, Year)	Study Type	Population	Intervention	Key Outcome(s)	Main Finding
Workeneh et al., 2020	Review	Oncology patients	Magnesium	Deficiency	Common magnesium depletion during cancer therapy
Krannich et al., 2024	Systematic Review	Cancer patients	Selenium	Toxicity, outcomes	Mixed evidence; some reduction in treatment toxicity
Habibi et al., 2025	SR & Dose-Response Meta-analysis	Cancer patients (chemo/RT)	ONS	Weight, BMI, QoL, fatigue, albumin, CRP	Significantly improved QoL, reduced fatigue, promoted weight gain
Liu Y. et al., 2025	SR & Meta-analysis (12 RCTs, n=2,268)	Postoperative solid tumor patients	ONS	Body weight loss	ONS reduced postoperative weight loss (MD 1.11 kg)
Delsoglio et al., 2025	SR & Meta-analysis (29 RCTs, n=2,279)	GI, lung, H&N, liver, breast cancer	High-protein ONS	Complications, LOS, readmissions	101 fewer complications/1,000 patients; reduced LOS
Orsso et al., 2024	SR & Meta-analysis	Cancer patients (chemo, diverse types)	High-protein supplementation	Body weight, muscle strength, hospitalization	Mitigated weight loss; improved strength; lowered hospitalization rates
Chitti et al., 2025	RCT	Gynecological cancer (surgical staging)	Whey protein supplementation	Postoperative outcomes	Improved postoperative recovery vs. standard care
Kuznia et al., 2023	SR & IPD Meta-analysis	General population / cancer patients	Vitamin D3	Cancer mortality	12% lower cancer mortality with daily dosing
Petrelli et al., 2024			Vitamin D3		Strong evidence: 10% reduction in

Study (Author, Year)	Study Type	Population	Intervention	Key Outcome(s)	Main Finding
	Umbrella Review (71 SRs)	Healthy and cancer populations		Cancer mortality, site-specific incidence	total cancer mortality
Kirmse et al., 2024	SR & Meta-analysis	Adults (musculoskeletal recovery)	Collagen peptides	Fat-free mass, tendon remodeling, recovery	Significant improvements in FFM, tendon integrity, functional recovery
Zeng et al., 2024	Systematic Review (34 RCTs, n=2,580)	Head & neck, breast, prostate, CRC	Curcumin	Inflammation, mucositis, QoL, toxicity	Reduced inflammatory markers; improved mucositis and QoL
Sharma et al., 2025	SR & Meta-analysis	Cancer patients (multiple RCTs)	Curcumin	NF-kB, VEGF, inflammatory cytokines	Significantly reduced NF-kB and VEGF levels
Wu et al., 2024	SR & Meta-analysis	Head & neck cancer (RT/CRT)	Curcumin / turmeric	Oral mucositis severity, pain, onset	Reduced severity, delayed onset, reduced pain scores
Pezzani et al., 2023	Systematic Review	Cancer (multiple types)	Bromelain	Inflammation, tumor proliferation, immune modulation	Anti-proliferative, anti-inflammatory, immunomodulatory activity
Pereira et al., 2023	SR of Clinical Trials	General/oncology populations	Bromelain supplementation	CRP, IL-6, inflammatory markers	Significantly reduced circulating inflammatory markers
Trivedi et al., 2023	Review	Cancer (multiple types)	Boswellic acids (Boswellia serrata)	NF-kB, 5-LOX, apoptosis	Inhibits NF-kB and 5-LOX; pro-apoptotic and anti-tumor activity
Afrin et al., 2023	Review	Cancer (multiple types)	Quercetin	Antioxidant, anti-inflammatory, chemosensitization	Reduces oxidative stress; inhibits cancer cell prolif-

Study (Author, Year)	Study Type	Population	Intervention	Key Outcome(s)	Main Finding
					eration; enhances chemo sensitivity
Habib et al., 2022	Experimental / Review	Cancer cell lines; preclinical models	Grape seed proanthocyanidin extract	DNA damage, oxidative stress, cancer cell activity	Inhibited DNA/protein damage; reduced oxidative stress; demonstrated anticancer activity
Bagchi et al., 2023	Review	Cancer (multiple types)	Proanthocyanidins (grape seed / pine bark)	Oxidative stress, tumor proliferation, apoptosis	OPCs inhibit cancer cell proliferation, induce apoptosis, reduce oxidative stress

1. Protein-Based Nutrition Supports Maintenance of Body Weight, Lean Mass, and Strength

1.1 Effects on Nutritional Status and Body Weight

Across multiple studies and meta-analyses, protein-based oral nutritional support and structured nutrition interventions are consistently associated with improvements in **body weight, nutritional status, and quality of life** in patients undergoing cancer therapy.

Patients receiving chemotherapy frequently experience progressive reductions in oral intake driven by **anorexia, taste alterations, nausea, mucositis, and fatigue**. A 2025 dose-response meta-analysis confirmed that ONS significantly improves QoL, reduces fatigue, and promotes body weight gain in cancer patients. In postoperative solid tumor patients, a 2025 meta-analysis of 12 RCTs (n=2,268) demonstrated that ONS significantly reduced postoperative weight loss by a mean of 1.11 kg. These effects are most pronounced when nutritional support is initiated **early in the treatment course**, prior to the onset of significant malnutrition.

1.2 Effects on Lean Mass, Strength, and Functional Status

Protein-based nutritional interventions directly support **muscle protein synthesis and attenuate protein breakdown**. Clinical evidence demonstrates that whey protein isolate supplementation leads to improvements in muscle strength and body composition in patients undergoing chemotherapy. A 2025 RCT in gynecological cancer patients further confirmed improved postoperative recovery with whey protein supplementation.

A 2024 systematic review and meta-analysis of high-protein supplementation during cancer therapy found consistent improvements in **muscle strength across all five higher-quality studies**, and decreased hospitalization rates in four of five studies. Collagen peptides offer additional musculoskeletal support: a 2024 meta-analysis demonstrated significant improvements in **fat-free mass, tendon integrity, and functional recovery**, supporting a complementary role in connective tissue preservation during cancer treatment and recovery.

1.3 Effects on Treatment Tolerance and Clinical Course

A 2025 systematic review and meta-analysis of 29 RCTs (n=2,279) of high-protein ONS in cancer patients demonstrated a **significant reduction of 101 complications per 1,000 patients**, including infectious, non-infectious, post-operative, and radiotherapy-related complications, along with meaningful reductions in hospital length of stay. Early nutrition intervention has further been shown to improve treatment tolerance and reduce hospital admissions in chemoradiotherapy patients, reinforcing the importance of **proactive, protocol-driven nutritional support** as a clinical standard.

2. Mucosal Support Interventions and Oral Intake Preservation

Oral mucositis — characterized by inflammation and ulceration of the oral mucosa — can result in **severe pain, dysphagia, reduced oral intake, dehydration, and weight loss**, often necessitating treatment interruption or dose reduction. Multiple meta-analyses have demonstrated that glutamine supplementation reduces the incidence and severity of oral mucositis. Zinc has shown supportive evidence for reducing mucositis incidence and delaying onset through its role in **cellular repair and epithelial integrity**. By reducing mucosal injury and associated pain, these interventions help patients maintain oral intake and preserve overall nutritional status.

3. Gastrointestinal Support and Maintenance of Nutrient Absorption

Diarrhea and gastrointestinal toxicity represent major contributors to nutritional instability during cancer treatment, leading to **malabsorption, dehydration, electrolyte imbalance, and weight loss**. Probiotic supplementation has demonstrated benefit in reducing the incidence and severity of chemotherapy-related diarrhea in several meta-analyses, though findings are heterogeneous across strains, cancer types, and treatment protocols. Digestive enzyme support plays a complementary role in patients with compromised digestive capacity, helping to maintain **macronutrient absorption and nutritional adequacy** during treatment.

4. Muscle Preservation and Functional Capacity

Cancer-associated muscle loss — driven by systemic inflammation, reduced protein intake, and metabolic dysregulation — is associated with **reduced strength, impaired functional capacity, decreased treatment tolerance, and poorer outcomes**. Protein-based nutritional interventions support

muscle protein synthesis and improve nitrogen balance. HMB demonstrates promising but emerging evidence for preserving muscle mass through stimulation of protein synthesis and inhibition of protein degradation. Preservation of muscle mass is further associated with **improved clinical stability, reduced hospitalization, and enhanced treatment tolerance**.

5. Micronutrient Adequacy and Physiological Stability

Micronutrient deficiencies are common in oncology populations and contribute to **fatigue, impaired immune function, delayed recovery, and reduced resilience**. Vitamin D is particularly relevant: a 2023 individual patient data meta-analysis demonstrated a **12% reduction in cancer mortality** with daily vitamin D3 dosing, and a 2024 umbrella review of 71 systematic reviews found strong evidence for a **10% reduction in total cancer mortality** with vitamin D3 supplementation, with highly suggestive evidence for reduced incidence of head and neck, breast, colorectal, lung, and renal cell cancers. Magnesium depletion is common during cancer therapy and supports neuromuscular function and energy metabolism. Selenium demonstrates emerging evidence for reduced treatment toxicity in selected settings.

6. Phytochemical Anti-Inflammatory Agents and Systemic Support

Systemic inflammation and oxidative stress are central drivers of treatment-related toxicity, mucosal damage, and nutritional decline in cancer patients. Chemotherapy and radiotherapy generate **reactive oxygen species (ROS), activate pro-inflammatory signaling pathways such as NF-kB, and elevate circulating inflammatory cytokines** — all of which contribute directly to mucositis, gastrointestinal toxicity, fatigue, and impaired recovery. Phytochemical agents with established antioxidant and anti-inflammatory properties represent a biologically plausible complementary strategy for addressing these mechanisms.

6.1 Curcumin (Turmeric Root Extract)

Curcumin is among the most extensively studied phytochemicals in oncology supportive care. Its mechanisms include **inhibition of NF-kB, downregulation of COX-2, reduction of pro-inflammatory cytokines, and modulation of oxidative stress pathways**. A 2024 systematic review of 34 RCTs (n=2,580) found that curcumin supplementation reduced inflammatory biomarkers and improved mucositis-related outcomes and quality of life in cancer patients. A 2025 meta-analysis confirmed that curcumin significantly reduced circulating NF-kB and VEGF levels across multiple RCTs. In patients with head and neck cancer undergoing radiotherapy, a 2024 meta-analysis demonstrated that curcumin **reduced the severity and delayed the onset of radiation-induced oral mucositis**, and significantly reduced associated pain scores — directly supporting oral intake and nutritional continuity.

6.2 Quercetin

Quercetin is a flavonoid with well-characterized **antioxidant, anti-inflammatory, and antiproliferative properties**. It inhibits inflammatory cytokines, reduces oxidative damage, and modulates cell cycle and apoptosis signalling. In oncology supportive care, quercetin's most clinically relevant actions include its capacity to **reduce treatment-related oxidative stress, attenuate systemic inflammation, and enhance the sensitivity of cancer cells to chemotherapy and radiotherapy**. Evidence across multiple cancer types demonstrates inhibitory effects against breast, lung, colorectal, prostate, pancreatic, and ovarian cancer cells through convergent antioxidant, anti-inflammatory, and antiproliferative mechanisms. The mechanistic evidence base supports quercetin as a **biologically plausible adjunct for reducing inflammatory and oxidative burden** in patients undergoing active cancer treatment.

6.3 Bromelain

Bromelain is a mixture of proteolytic enzymes from pineapple with established **anti-inflammatory, immunomodulatory, and potential anti-tumor properties**, including modulation of pro-inflammatory cytokines, inhibition of NF-kB activity, and attenuation of tumor cell adhesion and invasion. A 2023 systematic review of clinical trials found that bromelain supplementation **significantly reduced circulating inflammatory markers including CRP and IL-6**. A comprehensive 2023 review in Frontiers in Oncology catalogued bromelain's anti-proliferative, apoptosis-inducing, and immune-modulating properties across multiple cancer types. Its proteolytic properties also support **protein digestion and nutrient absorption** — two critical functions frequently compromised in cancer patients.

6.4 Boswellic Acids (Indian Frankincense / Boswellia serrata)

Boswellia acids are pentacyclic triterpenes with potent **anti-inflammatory activity mediated through inhibition of 5-lipoxygenase (5-LOX) and NF-kB signalling** — a mechanism distinct from and complementary to curcumin and quercetin. A 2023 review documented that Boswellia acids demonstrate **pro-apoptotic and anti-tumor activity across multiple cancer types**, including cervical, prostate, and breast cancer, through induction of endoplasmic reticulum stress, oxidative modulation, and p53/p21 pathway activation. Boswellia-containing formulations have also been studied in the management of treatment-related musculoskeletal pain and inflammation in cancer patients, with evidence suggesting improvements in **joint comfort and mobility** — outcomes relevant to functional status and quality of life during therapy.

6.5 Grape Seed Extract and Pine Bark Extract (Oligomeric Proanthocyanidins)

Grape seed extract and pine bark extract are rich sources of **oligomeric proanthocyanidins (OPCs)** — highly bioavailable polyphenolic compounds with potent antioxidant and anti-inflammatory properties. OPCs scavenge free radicals, reduce lipid peroxidation, inhibit inflammatory signalling, and demonstrate multi-targeted anticancer activity. A 2022 study demonstrated that grape seed proanthocyanidin extract **inhibited DNA and protein damage, reduced labile iron activity, and**

exhibited anticancer activity across cancer cell lines. A comprehensive review further documented that OPCs from grape seed and pine bark **inhibit cancer cell proliferation, induce apoptosis, arrest the cell cycle**, and reduce oxidative stress across multiple cancer types including oral, breast, colon, and prostate cancers.

The capacity of OPCs to **reduce oxidative stress and protect against DNA and cellular damage** is particularly relevant in the context of chemotherapy and radiation therapy, where treatment-induced ROS generation is a principal driver of normal tissue toxicity, mucositis, and systemic inflammatory burden. By supporting antioxidant defense systems, OPCs may help reduce collateral tissue damage while preserving the nutritional and functional capacity of patients undergoing active treatment.

Together, the phytochemical agents reviewed — curcumin, quercetin, bromelain, boswellic acids, and proanthocyanidins — represent a **mechanistically complementary, multi-pathway approach to reducing the inflammatory and oxidative burden** imposed by cancer and its treatment. Their established biological activity, favorable safety profiles, and convergent mechanisms provide a strong rationale for inclusion in a comprehensive multimodal nutritional strategy.

Discussion

Principal Findings

This review demonstrates that nutritional decline during cancer therapy is a **multifactorial and progressive process**, driven by reduced oral intake, treatment-related toxicity, gastrointestinal dysfunction, systemic inflammation, oxidative stress, and ongoing muscle loss.

The most consistent and clinically meaningful evidence supports **protein-based oral nutritional support and early, structured nutrition intervention** as central strategies. Recent large-scale meta-analyses have strengthened this evidence base substantially. Adjunctive nutrients provide targeted support for specific clinical barriers. Phytochemical anti-inflammatory agents address an additional dimension of cancer-related nutritional compromise: the **systemic inflammatory and oxidative environment** generated by both the disease and its treatment — one that is often underappreciated as a driver of nutritional decline.

Importantly, the benefits observed across studies reflect a broader pattern of **improved physiological stability, reduced treatment-related toxicity, and enhanced resilience**, suggesting that comprehensive nutritional and anti-inflammatory support plays a more central role in oncology care than is often recognized.

A Multimodal Model of Nutritional Support in Oncology

The available evidence supports a multimodal approach in which different strategies target distinct but interrelated physiological challenges:

- **Protein-based nutrition** supports body weight, lean mass, muscle strength, and clinical stability
- **Collagen peptides** support connective tissue integrity, tendon remodeling, and fat-free mass preservation
- **Mucosal support interventions** (glutamine, zinc, curcumin) preserve oral intake and reduce pain-associated nutritional decline
- **Gastrointestinal support strategies** (probiotics, digestive enzymes) maintain nutrient absorption and gut microbiota balance
- **Muscle-preservation strategies** (HMB, high-protein support) preserve functional capacity and physical resilience
- **Micronutrient adequacy** (vitamin D, magnesium, selenium, zinc) supports physiological stability and immune function
- **Phytochemical anti-inflammatory agents** (curcumin, quercetin, bromelain, boswellia, OPCs) reduce systemic inflammation, oxidative stress, and mucosal toxicity

These components interact dynamically to support **nutritional resilience** — the ability of the patient to maintain adequate intake, preserve functional capacity, and tolerate ongoing therapy despite significant physiological stress. Nutritional and anti-inflammatory care should be recognized as **core components of comprehensive oncology management**, not adjunctive considerations.

Clinical Implications

Interventions that preserve nutritional status and reduce inflammatory burden may have meaningful downstream effects on the **continuity and effectiveness of cancer therapy**. Nutritional interventions are most effective when implemented **early and proactively**, underscoring the importance of **routine nutritional screening, early intervention, and ongoing multimodal support throughout the treatment course**. These findings are consistent with ESPEN and ASCO recommendations and support the integration of **structured, multimodal nutritional protocols into standard oncology workflows**.

Mechanistic Considerations

Protein-based support addresses **negative nitrogen balance**, supporting muscle protein synthesis. Collagen peptides contribute to **connective tissue repair and musculoskeletal integrity**. Glutamine and zinc support **epithelial repair and mucosal barrier integrity**. Probiotics and digestive enzymes modulate **gut microbiota composition and digestive function**. HMB attenuates **protein turnover and muscle degradation**.

Phytochemical agents operate through convergent mechanisms: curcumin and quercetin inhibit **NF-kB and inflammatory cytokine cascades**; bromelain modulates **proteolytic and immune signaling**; boswellic acids inhibit **5-LOX-mediated leukotriene synthesis**; and OPCs scavenge **reactive oxygen species and reduce oxidative DNA damage**. Together these mechanisms provide a biologically coherent foundation for a comprehensive multimodal approach.

Limitations

The available literature is **heterogeneous** across cancer types, treatment modalities, intervention compositions, and outcome measures. The data supporting several adjunctive and phytochemical interventions remain **limited or primarily preclinical**, with fewer large-scale oncology RCTs. Bioavailability of phytochemical agents — particularly curcumin — is a recognized challenge, and enhanced-absorption formulations may significantly influence clinical outcomes. Most studies focus on supportive-care endpoints rather than direct oncologic outcomes, and the findings of this review should be interpreted within the context of **supportive oncology care**.

Future Directions

Future research should focus on prospective, well-designed clinical trials evaluating comprehensive multimodal nutritional strategies, with key areas including:

- Impact of structured multimodal nutritional protocols on **treatment completion and dose intensity**
- Effects on **hospitalization rates and healthcare utilization**
- Evaluation of **bioavailability-enhanced phytochemical formulations** in oncology RCTs
- Studies evaluating **combined protein-phytochemical interventions** to quantify synergistic effects
- Evaluation of **patient-reported outcomes, functional status, and quality of life** across cancer types and treatment modalities

Conclusion

Cancer-associated malnutrition, systemic inflammation, treatment-related toxicity, and progressive muscle loss represent interconnected barriers to maintaining nutritional status, functional capacity, and treatment continuity in patients undergoing active therapy.

The findings of this systematic review and evidence synthesis support **early, protein-based oral nutritional support** as a foundational component of supportive oncology care. Across multiple studies and recent large-scale meta-analyses, protein-focused interventions are consistently associated with improvements in **body weight, nutritional status, body composition, muscle strength, quality of life, complication rates, and clinical stability** across diverse cancer populations.

Adjunctive strategies — including **glutamine, zinc, probiotics, HMB, collagen peptides, vitamin D, magnesium, and digestive enzymes** — provide targeted support for oral mucositis, gastrointestinal toxicity, muscle loss, and micronutrient depletion. This review also highlights the emerging evidence for **phytochemical anti-inflammatory agents** — curcumin, quercetin, bromelain, boswellic acids, and proanthocyanidins from grape seed and pine bark — as a biologically plausible and mechanistically complementary strategy for reducing the **systemic inflammatory and oxidative burden** that drives treatment toxicity and nutritional compromise in cancer patients.

Taken together, these findings support a **comprehensive, multimodal nutritional and anti-inflammatory framework** addressing the primary drivers of nutritional decline during cancer therapy. These strategies are best understood as complementary components of an integrated supportive-care approach aimed at **preserving nutritional status, maintaining functional capacity, reducing treatment-related toxicity, and improving the ability of patients to tolerate cancer therapy**. Current evidence supports the integration of proactive, protein-centered, anti-inflammatory, and multimodal nutritional support as a clinically meaningful and foundational pillar of modern oncology supportive care.

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