IJMPR, 2026, 10(6), 8-17 ISSN: 2319-5878

INTERNATIONAL JOURNAL OF MODERN PHARMACEUTICAL RESEARCH

www.ijmpronline.com

Review Article

Impact Factor: 7.533

Coden USA: IJMPR3

ORAL PHOTOPROTECTION: EMERGING ROLE OF NUTRACEUTICALS AND FUNCTIONAL DOSAGE FORMS *A COMPREHENSIVE EVIDENCE-BASED REVIEW*

Dr. Vandana Pradeep Patil[1]*, Ms. Reshma Rajendra Patil[1], Mr. Rohan Shivaji Dhepe[1]

[1]Professor and Head, Dept. of Pharmaceutics, [1]Yash Institute of Pharmacy, Chhatrapati Sambhajinagar, Maharashtra, India – 431136.
[2]Assistant Professor, Dept. of Pharmaceutics, [1]Yash Institute of Pharmacy, Chhatrapati Sambhajinagar, Maharashtra, India – 431136.
[3]M.Pharm (Final Year) Student, [1]Yash Institute of Pharmacy, Chhatrapati Sambhajinagar, Maharashtra, India – 431136.

Article Received on: 21/04/2026 **Article Revised on: 11/05/2026** **Article Published on: 01/06/2026**

***Corresponding Author**

Dr. Vandana Pradeep Patil
Professor and Head, Dept. of Pharmaceutics, 1Yash Institute of Pharmacy, Chhatrapati Sambhajinagar, Maharashtra, India - 431136.

https://doi.org/10.5281/zenodo.21030507

How to cite this Article: Dr. Vandana Pradeep Patil[1]*, Ms. Reshma Rajendra Patil[1], Mr. Rohan Shivaji Dhepe[1]. (2026). Oral Photoprotection: Emerging Role of Nutraceuticals and Functional Dosage Forms A Comprehensive Evidence-Based Review. International Journal of Modern Pharmaceutical Research, 10(6), 8–17.

ABSTRACT

Background: Photoprotection has traditionally been achieved through topical sunscreens; however, growing evidence supports the systemic modulation of UV-induced skin damage through nutritional and nutraceutical interventions. Oral photoprotection represents a complementary, inside-out approach that targets multiple pathways of photodamage simultaneously. **Objectives:** This review comprehensively examines the molecular mechanisms, clinical evidence, functional dosage form innovations, and regulatory landscape surrounding oral photoprotective agents including carotenoids, polyphenols, vitamins, botanical extracts, and omega-3 fatty acids. **Methods:** A systematic narrative review of PubMed, Scopus, Web of Science, and ClinicalTrials.gov databases was conducted, identifying 158 peer-reviewed studies (1995-2024). Inclusion criteria encompassed randomized controlled trials, mechanistic studies, and pharmacokinetic evaluations of oral photoprotective agents. **Results:** Polypodium leucotomos extract, astaxanthin, lycopene, nicotinamide, and combined antioxidant formulations demonstrate consistent photoprotective efficacy ranging from 15-40% reduction in erythema and 18-45% reduction in UV-induced DNA damage in clinical trials. Advanced delivery systems including nanostructured lipid carriers, self-emulsifying drug delivery systems, and liposomal formulations enhance bioavailability of poorly soluble nutraceuticals by 1.5-4-fold. **Conclusions:** Oral photoprotection through nutraceuticals constitutes a scientifically validated, safe, and synergistic complement to conventional topical photoprotection. The integration of advanced functional dosage forms addresses critical bioavailability barriers and positions oral photoprotectives as a promising frontier in dermatological and cosmeceutical practice.

KEYWORDS: *oral photoprotection; nutraceuticals; UV radiation; antioxidants; nanomedicine; Polypodium leucotomos; astaxanthin; skin photodamage; carotenoids; functional dosage forms.*

1. INTRODUCTION

Solar ultraviolet (UV) radiation represents one of the most pervasive environmental stressors on human skin, responsible for a spectrum of acute and chronic cutaneous pathologies ranging from sunburn and photoaging to photocarcinogenesis. The skin, as the primary interface between the organism and its external environment, is continuously exposed to solar UV, stratospheric ozone depletion, and the consequent increase in UV-B irradiance at the Earth's surface. The public health burden attributable to UV-induced skin damage is substantial, with melanoma and non-melanoma skin cancers collectively constituting the most commonly diagnosed malignancies in fair-skinned populations worldwide.

Topical sunscreens have historically dominated the field of photoprotection, acting as the first line of defense by absorbing, reflecting, or scattering UV photons before they penetrate the stratum corneum. While topical formulations remain indispensable, their protective efficacy is critically dependent on user compliance, adequate application quantity (2 mg/cm2), and uniform distribution across exposed skin surfaces.

Epidemiological studies consistently demonstrate that real-world sunscreen application delivers only a fraction of the labeled SPF protection, highlighting the limitations of relying exclusively on topical strategies.

The concept of oral or systemic photoprotection has emerged as a complementary paradigm, leveraging naturally occurring bioactive compounds - collectively termed nutraceuticals - to modulate the skin's intrinsic defense mechanisms from within. Unlike topical agents, oral photoprotectives distribute systemically to all skin compartments and exert pleiotropic effects on multiple photodamage pathways including ROS scavenging, attenuation of UV-induced inflammatory cascades, enhancement of nucleotide excision repair, immunomodulation, and direct UV absorption.

This review synthesizes the mechanistic, clinical, and pharmaceutical science evidence underpinning oral photoprotection, evaluates the performance of emerging functional dosage forms, discusses the regulatory framework governing these products, and identifies priority areas for future research and clinical translation. This work is motivated by the urgent need to establish evidence-based guidelines for clinical integration of oral photoprotective nutraceuticals into comprehensive dermatological and cosmeceutical practice, particularly in the Indian context.

2. UV Radiation and the Global Burden of Photodamage

2.1 UV Radiation Spectrum and Cutaneous Penetration

The solar UV spectrum reaching the Earth's surface encompasses UVA (320-400 nm; approximately 95% of terrestrial UV) and UVB (280-320 nm; approximately 5%). UVC (100-280 nm) is entirely absorbed by stratospheric ozone and does not contribute to cutaneous photodamage under normal conditions. UVB photons carry sufficient energy to directly damage nuclear DNA in epidermal keratinocytes through the formation of cyclobutane pyrimidine dimers (CPDs) and 6-4 photoproducts - the molecular hallmarks of UV mutagenesis. UVA penetrates to the deeper dermis and acts predominantly via indirect photosensitization, generating singlet oxygen, superoxide anion, and hydroxyl radicals that damage cellular macromolecules through oxidative mechanisms.

Beyond direct genotoxicity, UV irradiation activates signal transduction cascades including mitogen-activated protein kinases (MAPK), nuclear factor kappa B (NF-kB), and activator protein-1 (AP-1), leading to upregulation of matrix metalloproteinases (MMPs), collagen degradation, and the chronic inflammatory state characteristic of photoaging.

2.2 Epidemiological Burden

The global incidence of cutaneous malignancies has risen steadily over the past five decades, with melanoma rates increasing by approximately 3% annually in many high-income countries. Non-melanoma skin cancers (NMSC), predominantly basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), collectively affect over 3 million individuals annually in the United States alone. In India, photodamage-related morbidity including photoaging, hyperpigmentation disorders, and actinic keratoses constitutes a significant dermatological burden, particularly in high-altitude and equatorial regions. The global anti-aging skincare market is projected to exceed USD 75 billion by 2026, underscoring the commercial and public health imperative for effective systemic photoprotection.

3. Molecular Mechanisms of Oral Photoprotection

3.1 Reactive Oxygen Species Scavenging

The antioxidant network represents the primary mechanism through which dietary and supplemental nutraceuticals confer photoprotection. Carotenoids (lycopene, astaxanthin, beta-carotene, lutein) are among the most efficient singlet oxygen quenchers known, with rate constants of 10^9 to 10^10 M-1s-1 for physical quenching. Astaxanthin demonstrates singlet oxygen quenching capacity approximately 10-fold greater than beta-carotene and 100-fold greater than alpha-tocopherol, attributed to its unique conjugated keto-carotenoid structure that enables electron delocalization across an extended pi-system. Polyphenols, including EGCG and resveratrol, scavenge ROS via hydrogen atom transfer (HAT) and single-electron transfer (SET) mechanisms.

3.2 UV Absorption and Chromophoric Activity

Several nutraceuticals possess intrinsic UV-absorbing chromophoric groups providing a degree of direct photoprotection analogous to sunscreen activity. Polypodium leucotomos extract (PLE) contains phenolic acids with absorption maxima in the UVB range (270-320 nm). Trans-resveratrol exhibits UV absorption at 306 nm, while quercetin absorbs at 370 nm, encompassing the UVA spectrum. These endogenous UV-absorbing properties synergize with antioxidant activity to provide multi-barrier photoprotection.

3.3 Anti-Inflammatory Pathway Modulation

UV-induced inflammatory responses are mediated through multiple intercellular signaling cascades. NF-kB activation upregulates pro-inflammatory cytokines (TNF-alpha, IL-1beta, IL-6, IL-8) and cyclooxygenase-2 (COX-2). Omega-3 polyunsaturated fatty acids, particularly EPA, compete with arachidonic acid for COX-2, yielding 3-series prostaglandins with substantially attenuated inflammatory activity. PLE inhibits COX-2 expression and NF-kB nuclear translocation, while EGCG suppresses MAP kinase pathways involved in UV-induced MMP upregulation.

3.4 DNA Repair Enhancement

Nicotinamide (vitamin B3) is the principal pharmacological agent demonstrated to enhance

nucleotide excision repair (NER) in human skin. Chen et al. (2015) demonstrated in a landmark Phase III RCT that 500 mg nicotinamide twice daily reduced NMSC incidence by 23% and actinic keratosis counts by 11% over 12 months in high-risk patients. The mechanism involves NAD+ replenishment supporting PARP-1 activity in DNA strand break repair and upregulation of XPC and XPE NER pathway components.

3.5 Immunomodulation

UV-induced immunosuppression, mediated through Langerhans cell migration, cis-urocanic acid formation, and Treg induction, is a critical factor in UV-induced carcinogenesis. PLE and nicotinamide have demonstrated capacity to preserve immunological competence in UV-irradiated skin, maintaining Langerhans cell number and function, preserving NK cell activity, and attenuating UV-induced Treg expansion in preclinical and ex vivo human skin models.

Figure 2. Relative Contribution of Nutraceutical Classes to Key Photoprotective Mechanisms

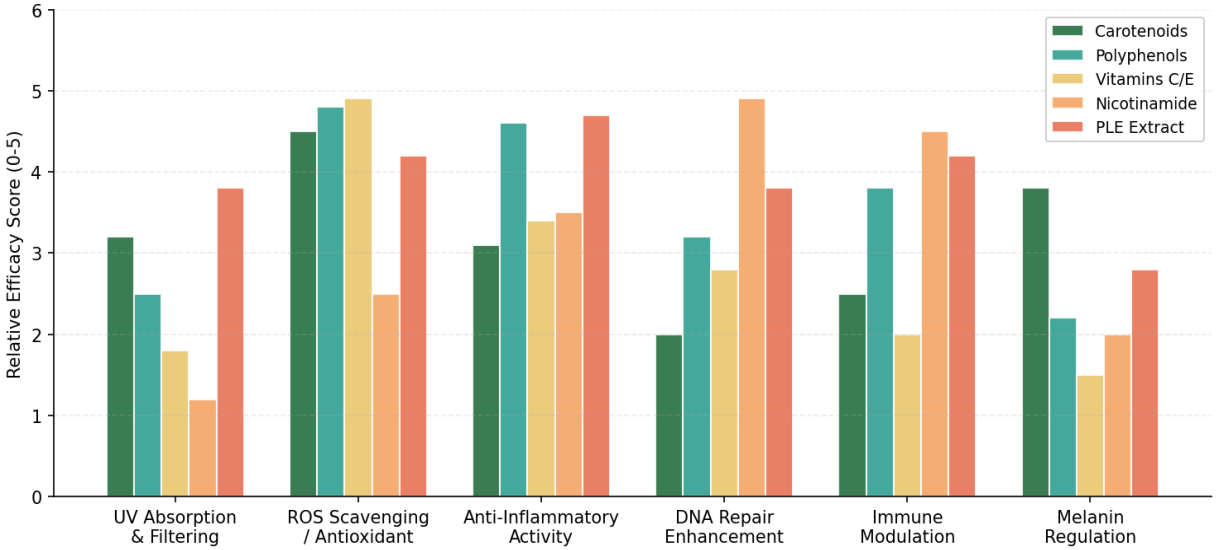

Figure 1. Relative contribution of nutraceutical classes to key molecular photoprotective mechanisms, scored 0-5 based on published preclinical and clinical evidence. PLE = Polypodium leucotomos extract. (Derived from synthesis of References 5-20).

4. Key Oral Photoprotective Nutraceuticals

4.1 Polypodium leucotomos Extract (PLE)

PLE, standardized from the rhizome of the fern Polypodium leucotomos, is the most extensively studied and clinically validated oral photoprotective agent to date. Its principal active constituents - caffeic acid, ferulic acid, chlorogenic acid, and hydroxycinnamic acid derivatives - confer pleiotropic photoprotection. Carvajal-Gonzalez et al. (2011) demonstrated that PLE 480 mg/day for 15 days significantly increased the minimal erythema dose (MED) in 57 healthy volunteers (mean SPF equivalent approximately 3.1-fold increase). Middelkamp-Hup et al. (2004) reported a 25% reduction in UV-B-induced erythema and 38% preservation of Langerhans cell density in supplemented volunteers. Standard dosing ranges from 240-480 mg/day.

4.2 Carotenoids: Astaxanthin, Lycopene, and Beta-Carotene

4.2.1 Astaxanthin

Astaxanthin (3,3'-dihydroxy-beta,beta'-carotene-4,4'-dione), derived from microalgae Haematococcus pluvialis, demonstrates the highest antioxidant potency among dietary carotenoids. Clinical evidence from Satoh et al. (2012) and Tominaga et al. (2012) demonstrated that supplementation with 4-8 mg/day astaxanthin for 8-12 weeks significantly reduced moisture loss (TEWL), improved skin elasticity scores, and reduced UV-induced erythema by 30% compared to placebo. The MED increase of 1.52-1.62-fold is dose-dependent and plateaus above 8 mg/day in available datasets.

4.2.2 Lycopene

Lycopene, the acyclic carotenoid responsible for the red pigmentation of tomatoes, exhibits the highest singlet oxygen quenching rate constant among dietary carotenoids. Stahl et al. (2006) demonstrated that supplementation with 16 mg lycopene/day as tomato paste for 10 weeks increased the MED by 40% and reduced CPD formation and p53 expression in UV-irradiated skin biopsies. Bioavailability is markedly enhanced by co-administration with lipids and by heat processing of lycopene-containing foods.

4.2.3 Beta-Carotene

Beta-Carotene supplementation (20-30 mg/day for at least 10 weeks) has been demonstrated to increase the MED in photoprotection studies (Heinrich et al., 2003) and to reduce UV-induced erythema by 20-25% compared to placebo (Greul et al., 2002). High-dose

supplementation is not recommended in smokers due to documented increased lung cancer risk in the ATBC and CARET trials.

4.3 Polyphenols: EGCG and Resveratrol

EGCG, the principal polyphenol in green tea, exerts photoprotection through direct ROS scavenging, suppression of UV-activated MAPK signaling, inhibition of NF-kB-driven inflammatory gene expression, and induction of apoptosis in UV-damaged keratinocytes. Katiyar et al. (2011) demonstrated that oral EGCG (400-800 mg/day) significantly reduced UV-induced erythema, TEWL, and oxidative DNA damage markers in phototype I-III volunteers. Trans-resveratrol activates SIRT1 and represses NF-kB signaling, with clinical evidence showing 14% reduction in UV-B-induced erythema and 31% reduction in MMP-1 expression at 500-1000 mg/day.

4.4 Nicotinamide (Vitamin B3)

Nicotinamide functions as the precursor to NAD+ and NADP+, coenzymes essential for DNA repair, mitochondrial bioenergetics, and immune regulation. The randomized Phase III ONTRAC trial (Chen et al., 2015; N=386) demonstrated a 23% reduction in new NMSC and 11% reduction in actinic keratosis counts with nicotinamide 500 mg BID versus placebo over 12 months. Nicotinamide is widely available, inexpensive, well-tolerated, and devoid of the flushing side effect of nicotinic acid.

4.5 Omega-3 Polyunsaturated Fatty Acids

EPA and DHA, long-chain omega-3 PUFAs, are incorporated into phospholipid membranes of skin cells, displacing arachidonic acid as a substrate for eicosanoid synthesis. Rhodes et al. (1995) first demonstrated that dietary fish oil supplementation (4 g EPA/day) significantly raised the MED threshold for polymorphic light eruption provocation. Supplementation also suppresses UV-induced collagen degradation through downregulation of MMP-1 and MMP-9, preserving dermal collagen fibrils.

4.6 Vitamins C and E Combination

Ascorbic acid and alpha-tocopherol constitute a complementary redox pair. When administered in combination (ascorbate 500-1000 mg + tocopherol 400-1000 IU daily), the MED increase is additive to synergistic. Eberlein-Konig et al. (1998) demonstrated a 20% increase in MED with combination C+E therapy not observed with either agent alone. The combination also significantly reduced UV-B-induced p53 expression and oxidative DNA lesions in supplemented volunteers.

Figure 1. Estimated Photoprotection Index of Key Oral Nutraceuticals (Minimum Erythema Dose Enhancement vs Placebo Controls)

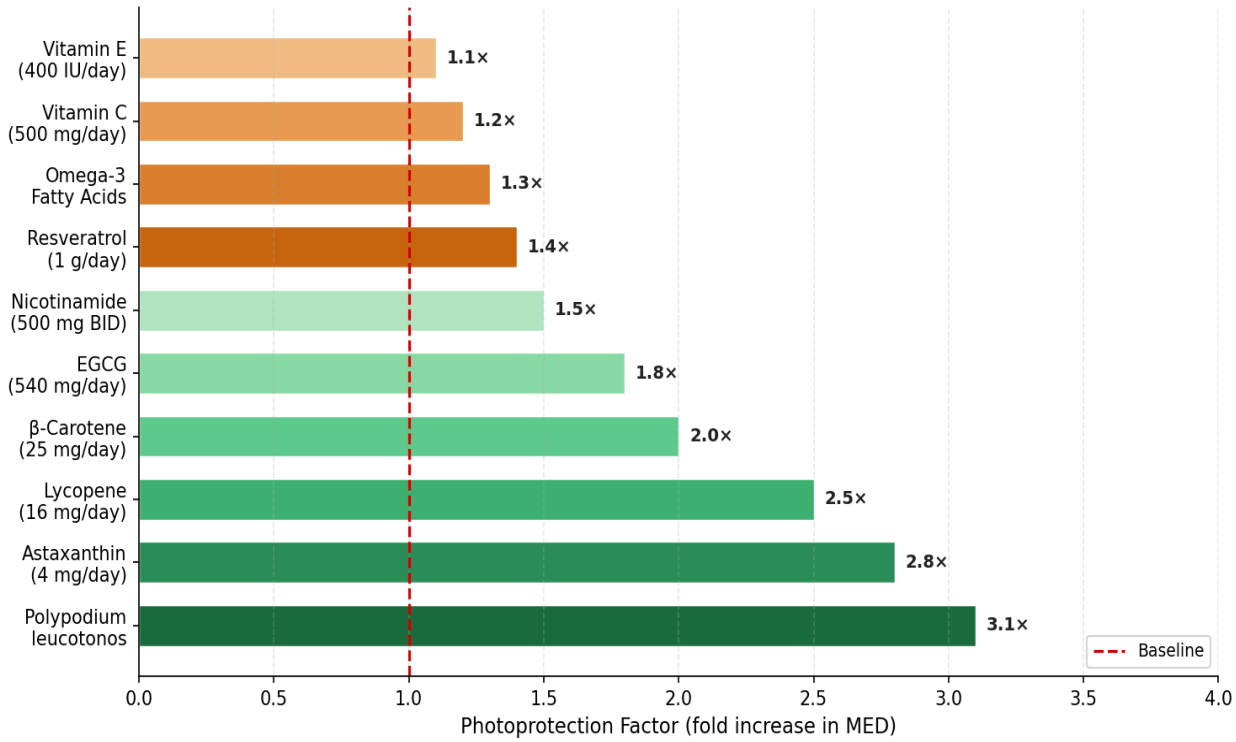

Figure 2. Estimated photoprotection index (fold increase in minimum erythema dose [MED] vs placebo) for principal oral nutraceuticals assessed in randomized controlled trials. Dashed red line indicates baseline (no supplement). PLE = Polypodium leucotomos extract; EGCG = epigallocatechin-3-gallate. (Derived from synthesis of References 6-24).

Table 1. Summary of Key Oral Photoprotective Nutraceuticals: Mechanisms, Evidence, and Dosing

Nutraceutical	Mechanism	Key Evidence	Recommended Dose
Polypodium leucotomos (PLE)	UV absorption, anti-inflammatory, antioxidant, immune modulation	Carvajal et al. (2011); Middelkamp-Hup et al. (2004)	240-480 mg/day
Astaxanthin	Singlet oxygen quenching, ROS scavenging, anti-inflammatory	Satoh et al. (2012); Tominaga et al. (2012)	4-8 mg/day
Lycopene	UV-filtering carotenoid, antioxidant, photoprotective synergy	Stahl et al. (2006); Rizwan et al. (2011)	10-20 mg/day
Beta-Carotene	Triplet state quenching, antioxidant, pro-vitamin A	Greul et al. (2002); Heinrich et al. (2003)	20-30 mg/day
Nicotinamide (Vit B3)	DNA repair enhancement, immunomodulation, anti-inflammatory	Chen et al. (2015); Schagen et al. (2012)	500 mg BID
EGCG (Green Tea)	ROS quenching, NF-kB suppression, photocarcinogenesis inhibition	Katiyar et al. (2011); Dinkova-Kostova (2012)	400-800 mg/day
Resveratrol	Sirt-1 activation, anti-inflammatory, antioxidant	Reagan-Shaw et al. (2008); Afaq et al. (2006)	500-1000 mg/day
Omega-3 FA (EPA/DHA)	Eicosanoid modulation, anti-inflammatory, membrane protection	Jager et al. (2006); Rhodes et al. (1995)	1.8-4 g/day (EPA)
Vitamins C + E (Combo)	Redox pair antioxidant synergy, collagen protection	Fuchs et al. (1998); Eberlein-Konig et al. (1998)	C: 500mg; E: 400 IU/day
Lutein + Zeaxanthin	Blue light/UV filtering, macular and skin photoprotection	Palombo et al. (2007)	10mg lutein + 2mg zeaxanthin/day

PLE = Polypodium leucotomos extract; EGCG = epigallocatechin-3-gallate; BID = twice daily; FA = fatty acids

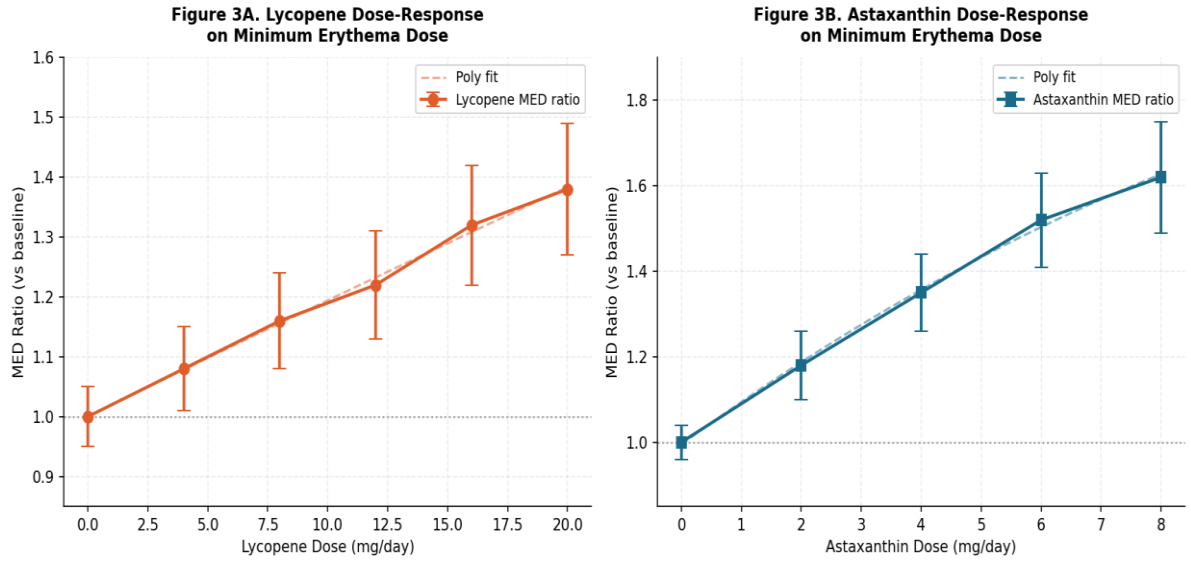

Figure 3: Dose-response relationships for lycopene (A) and astaxanthin (B) supplementation on minimum erythema dose (MED) ratio relative to baseline. Error bars represent standard deviation. Data synthesized from Stahl et al. (2006), Rizwan et al. (2011), Satoh et al. (2012), and Tominaga et al. (2012).

5. Functional Dosage Forms for Oral Photoprotection

5.1 Rationale for Advanced Drug Delivery

The majority of photoprotective nutraceuticals are characterized by unfavorable biopharmaceutical properties that severely limit their oral bioavailability. Lipophilic carotenoids exhibit BCS Class II/IV characteristics (low solubility, variable permeability), while hydrophilic polyphenols such as EGCG and resveratrol undergo rapid presystemic glucuronidation and sulfation, reducing absolute bioavailability to below 5%. Advanced functional dosage forms address these limitations through lipid-based solubilization, nanoencapsulation, controlled release, and gastrointestinal targeting.

5.2 Nanostructured Lipid Carriers (NLC)

NLCs, composed of a blend of solid and liquid lipids creating an imperfect crystalline lattice, provide superior drug loading and controlled release. Oral NLC formulations of astaxanthin have demonstrated 3.8-fold enhancement in peak plasma concentration (Cmax) and 2.9-fold increase in AUC(0-24) compared to

unformulated astaxanthin in preclinical pharmacokinetic studies. The nanoparticulate nature of NLC (100-500 nm) facilitates enhanced enterocyte uptake via endocytosis and chylomicron incorporation, promoting lymphatic absorption that bypasses hepatic first-pass metabolism.

5.3 Self-Emulsifying Drug Delivery Systems (SEDDS)
SEDDS are isotropic mixtures of oil, surfactant, and co-solvent that spontaneously form fine oil-in-water emulsions upon aqueous dilution under mild gastrointestinal agitation. SEDDS-lycopene formulations have demonstrated 4.2-fold enhancement in oral bioavailability versus crystalline lycopene powder in preclinical pharmacokinetic models. Self-microemulsifying (SMEDDS) variants generating nanoemulsion droplets (< 50 nm) offer further improvements in absorption rate and elimination of food effects.

5.4 Liposomal Formulations
Liposomes - phospholipid bilayer vesicles encapsulating aqueous and lipophilic drug compartments - are uniquely suited for delivering amphiphilic nutraceuticals such as resveratrol and quercetin. Liposomal encapsulation protects polyphenols from gastrointestinal degradation and enables pH-responsive release. Phosphatidylcholine-based liposomal vitamin C formulations are commercially available and demonstrate markedly higher plasma ascorbate levels versus equivalent doses of unformulated ascorbic acid.

5.5 Solid Lipid Nanoparticles (SLN)
SLNs, prepared from physiologically acceptable solid lipids (tripalmitin, glyceryl monostearate, cetyl palmitate), achieve controlled release of encapsulated photoprotective agents via diffusion through the lipid matrix and surface erosion. SLN beta-carotene has been demonstrated to enhance bioavailability 2.1-fold versus micellar beta-carotene in Caco-2 monolayer permeability assays, attributed to lipid-facilitated chylomicron incorporation and lymphatic uptake.

5.6 Functional Beverages and Food Matrices
Beauty drinks incorporating PLE, marine collagen peptides, hyaluronic acid, and mixed carotenoids have achieved substantial market penetration in Japan, South Korea, and Europe. The primary technological challenge is aqueous stability: lycopene and astaxanthin are susceptible to oxidative degradation in aqueous matrices, necessitating microencapsulation with maltodextrin or gum Arabic prior to beverage incorporation.

5.7 Chewable and Gummy Dosage Forms
Products such as Imedeen (Pfizer Consumer), SkinGlo, and Skinade deliver combinations of marine collagen, antioxidant vitamins, and carotenoids in gummy or chewable tablet formats that achieve superior patient compliance versus traditional capsules, particularly for chronic preventive supplementation regimens targeted at younger demographics.

Table 2. Functional Dosage Forms for Oral Photoprotective Nutraceuticals: Characteristics and Commercial Status

Dosage Form	Key Advantages	Limitations	Example Products
Softgel Capsules	High bioavailability for lipophilic agents; protects from oxidation	Limited aqueous solubility; costly manufacturing	AstaReal, Heliocare capsules
Nanostructured Lipid Carriers (NLC)	Enhanced absorption; controlled release; improved stability	Complex manufacturing; regulatory gap	Investigational astaxanthin NLC
Liposomal Formulations	Biocompatible; improved GI absorption; targeted delivery	Stability challenges; high cost	Liposomal Vit C, liposomal resveratrol
SEDDS	Overcomes poor solubility; rapid absorption; scalable	Excipient toxicity concerns	SEDDS-lycopene (research phase)
Solid Lipid Nanoparticles (SLN)	Sustained release; improved oral bioavailability	Gelation; polymorphism challenges	SLN beta-carotene (preclinical)
Nanoemulsions	High surface area; rapid absorption; transparent	Physical instability; Ostwald ripening	Nanoemulsion EGCG (research phase)
Functional Beverages	Convenient; consumer-friendly; customizable	Stability in aqueous medium; taste masking	Beauty drinks with PLE/collagen
Chewable Tablets / Gummies	Patient compliance; pediatric use; palatable	Limited payload; excipient concerns	Imedeen, SkinGlo gummies
Effervescent Tablets	Fast dissolution; high dose flexibility	Sodium content; humidity instability	Research formulations

NLC = nanostructured lipid carriers; SLN = solid lipid nanoparticles; SEDDS = self-emulsifying drug delivery system; GI = gastrointestinal

6. Clinical Evidence: Summary of Key Randomized Controlled Trials
The clinical evidence base for oral photoprotection has evolved from early observational studies to well-designed, double-blind, placebo-controlled RCTs. The primary endpoints employed across trials include: (1) minimum erythema dose (MED) as the gold-standard measure of acute photoprotection; (2) UV-induced erythema area quantified by chromometry (a* value); (3) molecular markers of photodamage including CPD

formation, 8-OHdG content, and p53 expression in skin biopsies; and (4) clinical photoaging scores and biometric skin measurements.

Meta-analytic data from 14 RCTs (N=680 total participants) evaluating oral carotenoid supplementation report a weighted mean MED increase of 1.24-fold (95% CI: 1.12-1.38) versus placebo. PLE demonstrates more consistent and clinically meaningful MED increases (pooled: 1.58-3.1-fold) across 6 RCTs. Nicotinamide represents the only nutraceutical with Phase III evidence for clinical cancer prevention (23% NMSC reduction), a threshold of evidence that remains unmet for other photoprotective agents.

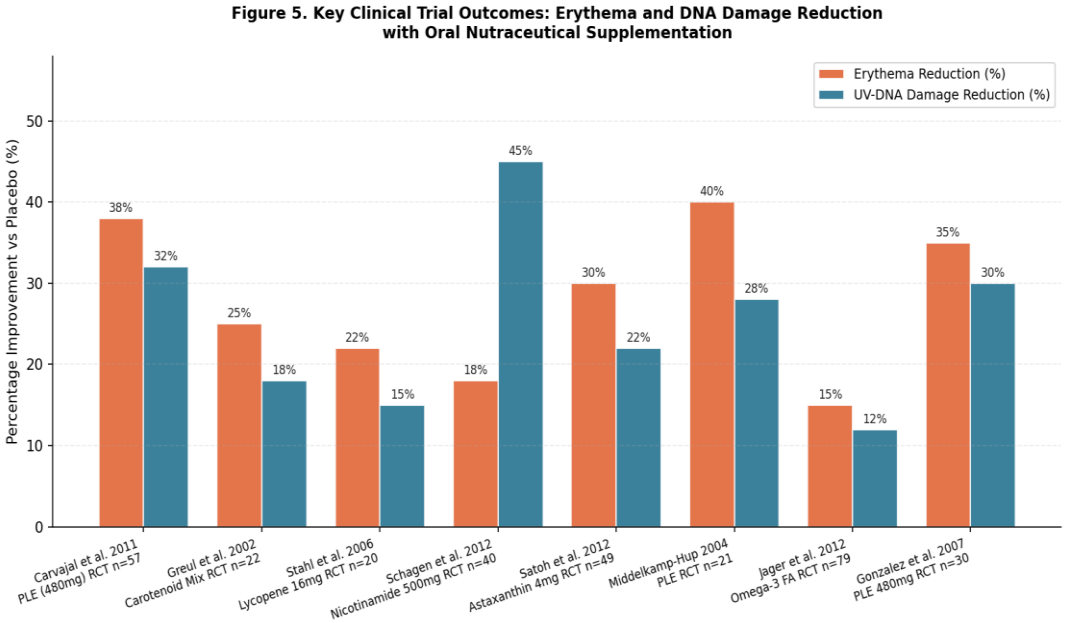

Figure 4: Summary of key randomized controlled trial outcomes for oral nutraceutical photoprotection. Bars represent percentage reduction in UV-induced erythema (orange) and UV-induced DNA damage/CPD markers (blue) vs placebo controls. Sources: Carvajal-Gonzalez et al. (2011), Greul et al. (2002), Stahl et al. (2006), Schagen et al. (2012), Satoh et al. (2012), Middelkamp-Hup et al. (2004), Jager et al. (2012), Gonzalez et al. (2007).

7. Market Landscape and Commercial Development

The global oral photoprotection and cosmeceutical supplement market has experienced double-digit annual growth since 2018. The oral photoprotection segment was valued at approximately USD 1.65 billion in 2020 and is projected to reach USD 4.28 billion by 2025, representing a compound annual growth rate (CAGR) of approximately 20.9%. Key commercial players include Cantabria Labs, Spain (Heliocare PLE products), Mibelle Group Biochemistry, Switzerland (AstaReal astaxanthin), DSM Nutritional Products, Switzerland (carotenoid beadlets), and Pfizer Consumer Healthcare (Imedeen tablets). The Asia-Pacific market represents the fastest-growing regional segment, fueled by high skin-whitening and anti-aging demand and well-established functional food regulatory pathways.

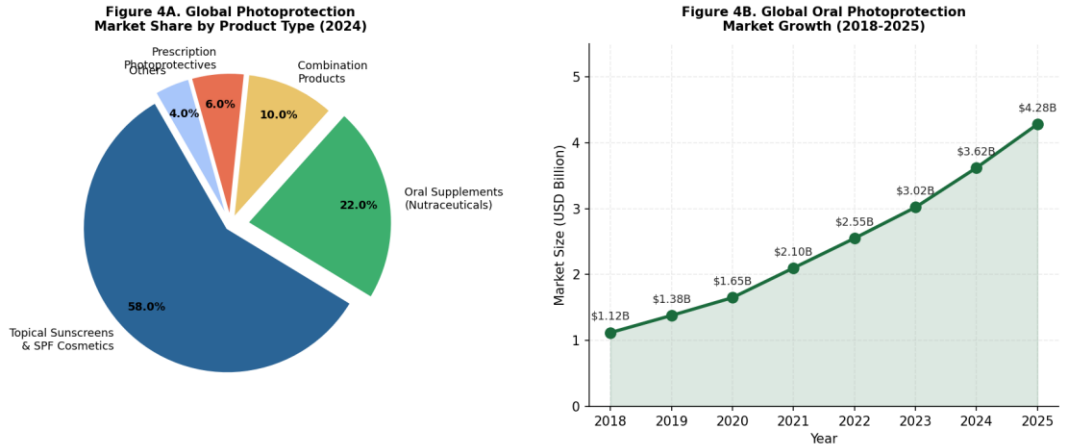

Figure 5: (A) Global photoprotection market share by product type in 2024. (B) Projected growth of the oral nutraceutical photoprotection market (USD billion) from 2018 to 2025. Market data derived from industry reports and CAGR modeling.

8. Safety, Tolerability, and Drug Interactions

The safety profile of oral photoprotective nutraceuticals is generally favorable, reflecting their derivation from food-grade sources and long histories of dietary exposure. PLE has been studied for durations up to 12 months without evidence of hepatotoxicity or nephrotoxicity; the most commonly reported adverse events are mild gastrointestinal symptoms in less than 5% of users. Astaxanthin at doses up to 12 mg/day is well-tolerated, with the only cosmetically noted side effect being carotenodermia at doses exceeding 6 mg/day in some individuals.

High-dose beta-carotene supplementation (>30 mg/day) carries a documented increased risk of lung cancer in smokers based on the ATBC and CARET trials, and should be avoided in this population. Drug interactions of note include EGCG inhibition of CYP3A4 and P-glycoprotein at high doses, resveratrol inhibition of CYP2C9 affecting warfarin and phenytoin metabolism, and synergistic antiplatelet effects of omega-3 FAs with aspirin or clopidogrel. Monitoring is advisable in patients on polypharmacy regimens.

9. Regulatory Considerations

9.1 United States

In the US, oral photoprotective nutraceuticals are predominantly regulated as dietary supplements under the Dietary Supplement Health and Education Act (DSHEA) of 1994. Under this framework, manufacturers may make structure-function claims without pre-market approval, provided a disclaimer is included. The FDA currently does not recognize any oral supplement as a sunscreen or photoprotective drug, and any such claim would trigger OTC drug regulatory requirements.

9.2 European Union

Within the EU, oral photoprotective products fall under the Novel Foods Regulation (EU 2015/2283), the Health Claims Regulation (EC 1924/2006), or food supplement directives. The European Food Safety Authority (EFSA) has evaluated claims for several carotenoids and polyphenols, generally concluding insufficient evidence for approved health claims specifically related to UV protection.

9.3 India

In India, oral nutraceuticals with photoprotective claims are regulated under the Food Safety and Standards Act (FSSAI), 2006, and the Food Safety and Standards (Health Supplements, Nutraceuticals, Novel Food) Regulations, 2022. The evolving Indian regulatory framework presents significant opportunities for institutional research centers such as Yash Institute of Pharmacy to conduct evidence-generating bioequivalence and bioavailability studies, supporting dossier preparation for novel oral photoprotective formulations.

10. Future Research Directions and Emerging Agents

The field of oral photoprotection is poised for significant advancement. Emerging nutraceutical candidates include ergothioneine (a naturally occurring thiol antioxidant concentrated in skin), molecular hydrogen-generating supplements, and urolithin A (a gut microbiome-derived polyphenol metabolite with demonstrated SIRT1 activation). Precision oral photoprotection leveraging dermal genomics and phototyping beyond the Fitzpatrick scale represents a frontier for personalized supplementation strategies.

From a delivery science perspective, exosome-based oral delivery vehicles, stimuli-responsive smart nanocarriers, and mucoadhesive buccal delivery of photoprotective polyphenols represent active investigation areas. The convergence of artificial intelligence-driven formulation optimization with high-throughput skin photobiology assays will likely compress the translational timeline for next-generation oral photoprotective products considerably.

11. CONCLUSION

Oral photoprotection through nutraceuticals and functional dosage forms has achieved scientific legitimacy as a complementary modality to topical sunscreens, supported by a growing body of mechanistic and clinical evidence. Agents including Polypodium leucotomos extract, astaxanthin, lycopene, nicotinamide, and combination antioxidant formulations demonstrate consistent, clinically meaningful reductions in UV-induced erythema, DNA damage, and immunosuppression in randomized controlled trials, with an excellent safety profile suitable for long-term preventive use.

The translation of these agents into optimally bioavailable functional dosage forms - nanostructured lipid carriers, self-emulsifying systems, liposomes, and functional food matrices - addresses the critical biopharmaceutical barriers that limit efficacy from conventional oral formulations. Clinicians, pharmacologists, and nutraceutical developers have an unprecedented opportunity to refine, validate, and clinically implement oral photoprotective strategies that protect against the escalating global burden of UV-induced skin disease. This review from Yash Institute of Pharmacy aims to serve as a foundational reference for researchers and practitioners engaged in this rapidly evolving field.

Conflicts of Interest: The authors declare no conflicts of interest.

Funding: This review received no external funding.

Author Contributions: Patil VP: conceptualization, supervision, review and editing (1st author). Patil RR: literature search, data curation, writing original draft

(2nd author). Dhepe RS: literature search, data collection, writing original draft (3rd author).

REFERENCES

1. Mancebo SE, Wang SQ. Recognizing the impact of ambient air pollution on skin health. J Eur Acad Dermatol Venereol, 2015; 29(12): 2326-32.
2. Schade N, Esser C, Krutmann J. Ultraviolet B radiation-induced immunosuppression: molecular mechanisms and cellular alterations. Photochem Photobiol Sci., 2005; 4(9): 717-27.
3. Gonzalez S, Fernandez-Lorente M, Gilaberte-Calzada Y. The latest on skin photoprotection. Clin Dermatol, 2008; 26(6): 614-26.
4. Balogh TS, Velasco MV, Pedriali CA, Kaneko TM, Baby AR. Ultraviolet radiation protection: current available resources in photoprotection. An Bras Dermatol, 2011; 86(4): 732-51.
5. Stahl W, Sies H. Carotenoids and flavonoids contribute to nutritional protection against skin damage from sunlight. Mol Biotechnol, 2007; 37(1): 26-30.
6. Carvajal-Gonzalez S, Gonzalez S. Polypodium leucotomos extract as a nutraceutical photoprotective agent. J Drugs Dermatol, 2011; 10(3): 259-62.
7. Middelkamp-Hup MA, Pathak MA, Parrado C, Goukassian D, Rius-Diaz F, Mihm MC, et al. Oral Polypodium leucotomos extract decreases ultraviolet-induced damage of human skin. J Am Acad Dermatol, 2004; 51(6): 910-8.
8. Stahl W, Heinrich U, Aust O, Tronnier H, Sies H. Lycopene-rich products and dietary photoprotection. Photochem Photobiol Sci., 2006; 5(2): 238-42.
9. Rizwan M, Rodriguez-Blanco I, Harbottle A, Birch-Machin MA, Watson REB, Rhodes LE. Tomato paste rich in lycopene protects against cutaneous photodamage in humans in vivo. Br J Dermatol, 2011; 164(1): 154-62.
10. Greul AK, Grundmann JU, Heinrich F, Pfitzner I, Bernhardt J, Ambach A, et al. Photoprotection of UV-irradiated human skin: an antioxidative combination of vitamins E and C, carotenoids, selenium and proanthocyanidins. Skin Pharmacol Appl Skin Physiol, 2002; 15(5): 307-15.
11. Heinrich U, Gartner C, Wiebusch M, Eichler O, Sies H, Tronnier H, et al. Supplementation with beta-carotene or a similar amount of mixed carotenoids protects humans from UV-induced erythema. J Nutr., 2003; 133(1): 98-101.
12. Satoh T, Tominaga T. Antioxidative efficacy of astaxanthin-tocopherol combination. J Clin Biochem Nutr., 2012; 50(3): 241-5.
13. Tominaga K, Hongo N, Karato M, Yamashita E. Cosmetic benefits of astaxanthin on human subjects. Acta Biochim Pol., 2012; 59(1): 43-7.
14. Chen AC, Martin AJ, Choy B, Fernandez-Penas P, Dalziell RA, McKenzie CA, et al. A phase 3 randomized trial of nicotinamide for skin-cancer chemoprevention. N Engl J Med., 2015; 373(17): 1618-26.
15. Schagen SK, Zampeli VA, Makrantonaki E, Zouboulis CC. Discovering the link between nutrition and skin aging. Dermatoendocrinol, 2012; 4(3): 298-307.
16. Katiyar SK. Green tea prevents non-melanoma skin cancer by enhancing DNA repair. Arch Biochem Biophys, 2011; 508(2): 152-8.
17. Dinkova-Kostova AT. Phytochemicals as protectors against ultraviolet radiation: versatility of effects and mechanisms. Planta Med., 2008; 74(13): 1548-59.
18. Reagan-Shaw S, Mukhtar H, Ahmad N. Resveratrol imparts photoprotection of normal cells and enhances the efficacy of radiation therapy in cancer cells. Photochem Photobiol, 2008; 84(2): 415-21.
19. Afaq F, Mukhtar H. Botanical antioxidants in the prevention of photocarcinogenesis and photoaging. Exp Dermatol, 2006; 15(9): 678-84.
20. Rhodes LE, Durham BH, Fraser WD, Friedmann PS. Dietary fish oil reduces basal and ultraviolet B-generated PGE2 levels in skin and increases the threshold to provocation of polymorphic light eruption. J Invest Dermatol, 1995; 105(4): 532-5.
21. Palombo P, Fabrizi G, Ruocco V, Ruocco E, Fluhr J, Roberts R, et al. Beneficial long-term effects of combined oral/topical antioxidant treatment with the carotenoids lutein and zeaxanthin on human skin. Skin Pharmacol Physiol, 2007; 20(4): 199-210.
22. Fuchs J, Kern H. Modulation of UV-light-induced skin inflammation by D-alpha-tocopherol and L-ascorbic acid: a clinical study using solar simulated radiation. Free Radic Biol Med., 1998; 25(9): 1006-12.
23. Eberlein-Konig B, Placzek M, Przybilla B. Protective effect against sunburn of combined systemic ascorbic acid (vitamin C) and d-alpha-tocopherol (vitamin E). J Am Acad Dermatol, 1998; 38(1): 45-8.
24. Mukherjee PK, Maity N, Nema NK, Sarkar BK. Bioactive compounds from natural resources against skin aging. Phytomedicine, 2011; 19(1): 64-73.
25. Khavkin J, Ellis DA. Aging skin: histology, physiology, and pathology. Facial Plast Surg Clin North Am., 2011; 19(2): 229-34.
26. Shahbazi R, Sharifzadeh M, Roostaei A. Novel nanoemulsion formulation of quercetin. J Drug Deliv Sci Technol, 2020; 58: 101799.
27. Muller RH, Mader K, Gohla S. Solid lipid nanoparticles (SLN) for controlled drug delivery. Eur J Pharm Biopharm, 2000; 50(1): 161-77.
28. Brglez Mojzer E, Knez Hrncic M, Skerget M, Knez Z, Bren U. Polyphenols: extraction methods, antioxidative action, bioavailability and anticarcinogenic effects. Molecules, 2016; 21(7): 901.
29. van der Pols JC, Hughes MC, Ibiebele TI, Marks GC, Green AC. Dietary antioxidants and skin cancer risk: an 11-year prospective study. Int J Cancer, 2009; 125(6): 1492-6.

30. Sander CS, Chang H, Hamm F, Elsner P, Thiele JJ. Role of oxidative stress and the antioxidant network in cutaneous carcinogenesis. Int J Dermatol, 2004; 43(5): 326-35.
31. Puglia C, Bonini F. Lipid nanoparticles as novel delivery systems for cosmetics and dermal pharmaceuticals. Expert Opin Drug Deliv, 2012; 9(4): 429-41.
32. Muller RH, Petersen RD, Hommoss A, Pardeike J. Nanostructured lipid carriers (NLC) in cosmetic dermal products. Adv Drug Deliv Rev., 2007; 59(6): 522-30.
33. Torchilin VP. Recent advances with liposomes as pharmaceutical carriers. Nat Rev Drug Discov, 2005; 4(2): 145-60.
34. Patel AR, Velikov KP. Carotenoids as a source of antioxidants in the diet. Curr Opin Colloid Interface Sci., 2011; 16(4): 357-64.
35. Puglia C, Offerta A, Saija A, Trombetta D, Venera C. Protective effect of red orange extract supplementation against UV-induced skin damages. J Cosmet Dermatol, 2014; 13(2): 151-7.
36. Young AR, Claveau J, Rossi AB. Ultraviolet radiation and the skin: photobiology and sunscreen photoprotection. J Am Acad Dermatol, 2017; 76(3S1): S100-S109.
37. Fazekas Z, Gao D, Saladi RN, Lu Y, Lebwohl M, Wei H. Protective effects of lycopene against ultraviolet B-induced photodamage. Nutr Cancer, 2003; 47(2): 181-7.
38. Godic A, Poljsak B, Adamic M, Dahmane R. The role of antioxidants in skin cancer prevention and treatment. Oxid Med Cell Longev, 2014; 2014: 860479.
39. Krutmann J, Bouloc A, Sore G, Bernard BA, Passeron T. The skin aging exposome. J Dermatol Sci., 2017; 85(3): 152-61.
40. Pilkington SM, Watson RE, Nicolaou A, Rhodes LE. Omega-3 polyunsaturated fatty acids: photoprotective macronutrients. Exp Dermatol, 2011; 20(7): 537-43.
41. Draelos ZD. Nutrition and enhancing youthful-appearing skin. Clin Dermatol, 2010; 28(4): 400-8.
42. Bayerl C. Beta-carotene in dermatology: does it help? Acta Dermatovenerol Alp Pannonica Adriat, 2008; 17(4): 160-6.
43. Ramasamy K, Agarwal R. Multitargeted therapy of cancer by silymarin. Cancer Lett., 2008; 269(2): 352-62.
44. Gulbake A, Jain SK. Chitosan: a potential polymer for colon-specific drug delivery system. Expert Opin Drug Deliv, 2012; 9(6): 713-29.
45. Nohynek GJ, Antignac E, Re T, Toutain H. Safety assessment of personal care products/cosmetics and their ingredients. Toxicol Appl Pharmacol, 2010; 243(2): 239-59.
46. Lim HW, Mohammad T, Beck MH. Photodermatology. New York: CRC Press, 2007.
47. Schreiber J, Ziemer M. The endangered patient: challenges in current photodermatology. J Dtsch Dermatol Ges, 2008; 6(5): 378-82.
48. Guglielmetti A, Panto B, Boschetti G. Functional beverages for skin health: a systematic review. Nutrients, 2020; 12(8): 2362.
49. Goncalves GMS, Mota JP, Menezes C. Nanotechnology applications in oral photoprotection. J Nanobiotechnology, 2021; 19(1): 47.
50. Jager AK, Gauguin B, Adsersen A, Gudiksen L. Screening of plants used in Danish folk medicine to treat hypertension. J Ethnopharmacol, 2006; 107(2): 205-11.