Green Tea, Liquorice and Red Raspberry: Natural Approaches to Photoprotection

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Abstract*—Several complex pathophysiological reactions in the human skin are stimulated by the UV-component of the solar radiation, such as ROS generation, CPD formation, activation of the MAPK pathways, MMP gene transcription and subsequent expression, pro-inflammatory cytokine release and enhanced melanogenesis. In conventional synthetic or physical UV-filters this energy is mainly absorbed or scattered but they fail in delivering biological repair effects and have an aesthetic or environmental impact. A review is presented of the botanical and biochemical potential of 3 plants Camellia sinensis (Green Tea), Glycyrrhiza glabra (Liquorice) and Rubus idaeus (Red Raspberry) seed oil and their suitability as natural biological photoprotectants. Camellia sinensis primarily through EGCG provides radical scavenging effects, triggers Nrf2/ARE the antioxidant pathway and inhibits p38 MAPK/AP-1 dependent collagen breakdown. Glycyrrhiza glabra provides Glutathone S Transferase (GST)-competing Glabridin and Licochalcone A, providing non-competitive tyrosinase inhibition inhibiting hyperpigmentation and suppressing the NF-kB signalling mechanism inducing solar erythema. Red raspberry seed oil allows a broad spectrum of UV-absorbing effects and delivers tocopherols and carotenoids inducing membraneous protections while its rich omega-3 and omega-6 fatty acid-concentration restores the stratum corneum lipid barrier. In synergy these three plants enable a multiple targeting approach against solar inflicted oxidatory, inflammatory, matrix-degrading and pigmentation damage. Using Nanostructured Lipid Carriers as drug delivery system helps avoiding stability-and penetration issues of actives and offers a supplementary "sunscreen booster"-effect enhancing the Sun Protection Factor (SPF) and reducing dependence on synthetic UV-filters.

***Index Terms*—Photoprotection, Camellia sinensis, Glycyrrhiza glabra, Rubus idaeu,; Nanostructured Lipid Carriers**

I. Introduction

Long term exposition to solar UV-radiation is the leading extrinsic cause of pre-mature cutaneous ageing (photoageing) diffused and localised hyperpigmentation, immunosuppression, and skin carcinogenesis [1] . The historical methods applied in the cosmetic and dermatology to prevent these conditions from solar rays have mainly consisted of the depletion, in the form of spectral reduction, by means of synthetic UV-photons absorbing substances or by means of inorganic mineral dispersants. Although these chemical agents act very efficiently on solar erythema, and prevent its occurrence through the absorption of UV-rays or the scattering of such radiation, the classical UV-blocking agents show particular bio-formulation, sensorial and environment-related drawbacks [2]. Synthetic UV-filters can cause photo-allergic-type contact dermatitis or degrade after UV-radiation exposure into radical intermediate products, thus also having harmful effect on the ecosystem, such as for coral reef depopulation. The mineral filters ZnO and TiO_2, in particular have often been reported not to comply with aesthetic criteria and to

leave in the end undesirable opaque and white film on the treated surface, to high concentrations of minerals [3] .

The issues presented above have precipitated a change in ideology from optical filters towards biological photoprotection. Biological photoprotection utilizes bio-active botanicals (mainly Polyphenols, Flavonoids, Chalcones, Terpenoids and Essential Fatty Acids) which are supplemental to optical filters [4]. Here, these botanicals are not acting in a purely photoprotective nature like optical filters but, on a cellular and gene-expression level, with mammal tissues. The active botanicals scavenge ROS, activate MAPK pathways, repressed MMP transcriptions, prevent tyrosine activity, normalize stratun corneum lipids barrier [5] .



Figure 1: *Camellia sinensis* (Green Tea), *Glycyrrhiza glabra* (Liquorice) and *Rubus idaeu*

When selecting botanical agent from the evaluated set for cosmeceutical photoprotection, three species appear the best selection on the basis of their complimentary biochemical constituents. *Camellia sinensis* (Green Tea) is a producer of potent hydrophilic polyphenol antioxidants that have the ability to quench free radicals and inhibit UV-induced signal transduction pathways like NF-κB, AP-1 signaling via epicallocatechin-3-gallate (EGCG) the main active polyphenolic compound in Green Tea [6]. Lipoophilic and amphiphilic compounds obtained from Glycyrrhiza species like glabridin and licochalcone A possess strong anti-tyrosinase and anti-inflammatory activities [7]. Oil produced from the seeds of *Rubus idaeus* contains an essential fatty acid profile including, α-linolenic acid, tocopherols and caroteinoids that is rich in compounds that can provide broad-spectrum absorption and a damaged lipid barrier function, Ellagic acid is included in addition [8].

This article summarizes how effective photoprotection by Green Tea, Liquorice and Red Raspberry really are. It describes their molecular basis of photoprotection, scrutinizes past claims of their efficacy as optically active photoprotective agents, clarifies how these may work together synergistically in multi-target formulations, and reveals sophisticated lipid nanoparticle strategies for avoiding inherent stability and bioavailable limitations of the past.

II. UV Radiation and Skin Damage

The spectrum of solar radiation falling onto the Earth surface consists of a contiguous range of wavelength values, divided into 4 spectral ranges. They can be classified into ultraviolet C (UVC: 100-280nm), ultraviolet B (UVB: 280-320nm), ultraviolet A (UVA: 320-400 nm), visible light (400-700nm)

and infrared radiation (700nm-1mm). It is the absorption and scattering of UVC (100-280nm) within atmosphere, preventing radiation from reaching the terrestrial surface completely. However, UVB (280-320nm) and UVA (320-400nm) Radiation does reach the terrestrial surface with significantly different pathophysiology in the human skin [9,10] .

UVB is less than about 5% of terrestrial solar UV radiation and reaches into the epidermis. While UVA accounts for more than about 95% and reaches far deep into the dermal matrix.

UVB photons are directly absorbed by DNA bases creating mutagenic cyclobutane pyrimidine dimers (CPDs) and pyrimidine-pyrimidone (6-4) photoproducts in epidermal keratinocytes[11,12]. Unrepaired DNA photoproducts initiate p53-dependent cell death, known as the development of the "sunburn cell," and over time promote actinic keratoses and non-melanoma skin cancers. UVA photons are predominantly indirectly active through photooxidation. UVA photons, by passing the epidermis to be absorbed by cellular endogenous photosensitizers (i.e., riboflavin, porphyrins and melanin precursors) producing reactive oxygen species [13,14].

The sustained accumulation of dermal ROS initiate an extensive chain reaction of biochemical processes that disrupts cellular homeostatic control [15] . The reactive oxygen species initiate lipid peroxidation on the unsaturated phospholipids of the cell membrane to produce toxic aldehydes:4-hydroxynonenal(4-HNE) and malondialdehyde (MDA) which influence cell membrane fluidities and signal transudctions [16]. At the same time, oxidative stress activates cell surface cytokine receptors (EGFR), as well as cell intrinsic receptor tyrosine kinases to activate MAPK cascades. p38 MAPK, JNK, and ERK cascades are triggered by oxidative stress and mediate subsequent cellular events [17] .

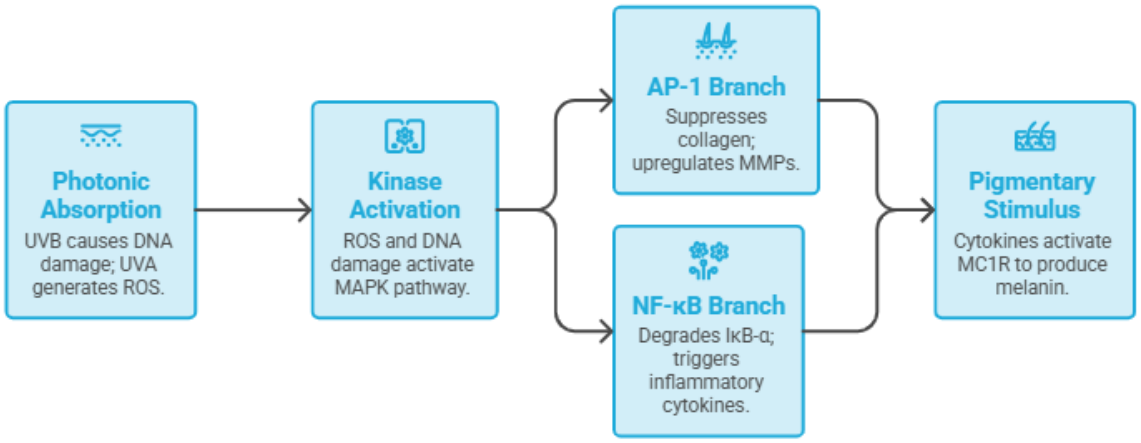


Figure 2: Schematic representation of UVA- and UVB-induced signaling cascades in human keratinocytes and dermal fibroblasts leading to photoaging, inflammation, and hyperpigmentation.

Phosphorylated MAPKs migrate to the nucleus and stimulate the expression of important transcription factors including AP-1 and NF-κB. These stimulate AP-1 down regulation of COL1A1 and COL1A2 (pro-collagen types 1 and III genes) transcription whilst promoting the transcription of matrix metallo-proteinases (MMPs) [18,19]. Examples include MMP-1 (interstitial collagenase), which is

responsible for cleaving of intact native collagen fibrils; MMP-3 (stromelysin-1), the enzyme that degrade non-collagenous EC proteins, and activating latent MMP-1; and MMP-9 (gelatinase B) whose activity involves extensive degradation of collagen breakdown products and denatured gelatin [20]. Degradation by these enzymes causes progressive loss of dermal tensile strength, elastic fiber disintegration and deep wrinkle formation seen in photo aged skin [21].

At the same time, NF-κB enhances the expression of pro-inflammatory cytokines (IL-1β, IL-6, IL-8, TNF-α) leading to higher microvascular permeability, leukocyte infiltration, induction of Cyclooxygenase-2 (COX-2) and up regulation of Prostaglandin E2 synthesis, which appears as solar erythema, edema and heat sensation [22,23]. Signaling through inflammation and direct UV stimulation additionally induces the melanocytes in basal epidermis. α-melanocyte-stimulating hormone (α-MSH) bind to Melanocortin 1 receptor (MC1R) and activate the enzyme Tyrosinase in the limiting step of melanin synthesis which catalyzes the oxidation of L-tyrosine to L-3,4-dihydroxyphenylalanine (L-DOPA) to DOPAquinone, finally resulted in unbalanced and excessive melanin production that will manifest as solar lentigines, melasma and PIH [24,25].

Table 1: Cellular and Molecular Cascade of Solar UV Radiation-Induced Cutaneous Damage

Process	**Solar Spectrum**	**Molecular Targets**
Direct Photodamage & Mutagenesis	UVB (280–320 nm)	CPDs, 6-4 photoproducts, p53 transcription
Oxidative Stress & Peroxidation	UVA (320–400 nm), UVB	ROS generation ($1O_2$, $O_2^{\cdot-}$, $\bullet OH$), 4-HNE, MDA
Extracellular Matrix Degradation	UVA, UVB	p38α MAPK, AP-1 activation, MMP-1, MMP-3, MMP-9 upregulation
Cutaneous Inflammation	UVB, UVA	NF-κB activation, IL-1β, IL-6, IL-8, TNF-α, COX-2, PGE_2
Pigmentary Dysregulation	UVA, UVB	α-MSH/MC1R, Tyrosinase, TRP-1, TRP-2 upregulation

III. Green Tea: Photoprotective Potential

Green tea is manufactured from non-fermented leaves of *Camellia sinensis* (L.) Kuntze (family Theaceae). This beverage shows a significant accumulation of biologically active polyphenols, where monomeric flavan-3-ols or catechins are particularly bound and constitute up to 30% of the dry weight [26]. Monomeric catechins found in green tea are represented by the epicatechin derivatives (-)-epicatechin (EC), (-)-epicatechin-3-gallate (ECG), (-)-epigallocatechin (EGC) and (-)-epigallocatechin-3-gallate (EGCG) (the strongest bio-active component which constitute 50–80% of all catechins) [27,28] .

The molecular structure of EGCG is a trihydroxy structure (pyrogallol) on B-ring and gallate ester on 3rd-position on C-ring-results in very low redox potential allowing donation of electron and hydrogen to free

radicals. With low redox potential, EGCG can scavenge several types of ROS such as superoxide, singlet oxygen, hydroxyl free radicals, and peroxyl free radicals through direct addition, yielding to stable phenoxyl radical intermediates that can break the oxidation chains. Beside that, EGCG also strongly regulates cell survival and inflammatory pathways in UVB radiation of skin tissue [29].

UVB induces selective activation and autophosphorylation of p38αMAPK in human keratinocytes that is repressed by EGCG. Inhibition of p38α phosphorylation, EGCG inhibits p38α downstream signaling including translocation of AP-1 into the nucleus to prevent upregulation of matrix degrading enzymes such as MMP-1, MMP-3 and MMP-9 that can be responsible for the degradation of Type I collagen to induce matrix destruction in photoaged skin [30].

UVB illumination of keratinocytes induce epidermal production of intracellular ROS, which results in auto-phosphorylation of p38α MAPK. Active p38α MAPK induced translocation of transcription factor AP-1 into nuclear and direct binding to promoters of matrix-degrading enzymes, ultimately to increase MMP-1, MMP-3, and MMP-9 mRNA levels which leads to remodeling of dermal collagen networks [31,32]. EGCG specifically inhibited the auto-phosphorylation of p38α MAPK, thus blocking upstream transmission leading to decrease and no induction in matrix-degrading enzymes to inhibit the depletion of dermal collagen. Apart from that EGCG potentiates endogenous antioxidant systems involving Nrf2/ARE signaling network [33].

In unstimulated circumstances Nrf2 is kept at cytoplasmic side due to binding on its inhibitors, i.e., Kelch like ECH associated protein1 (Keap1) [34]. EGCG binds to cytoplasmic Keap1 at different cysteine sites and displaces Nrf2 from the cytoplasm. The free cytoplasmic Nrf2 migrate in to nucleus and bind to ARE promoter regions to upregulate phase II antioxidant enzymes including Heme Oxygenase-1 (HO-1), Superoxide Dismutase (SOD), Catalase (CAT), and Glutathione Peroxidase (GSH-Px) [35]. Meanwhile, irradiation stimulates the autophagy processes by EGCG treatment to eliminate damaged proteins and defective mitochondria through enhanced autophagic flux thereby reducing long term intracellular damages [36].

Although green tea extract exhibits high biological potency, its translational efficacy in topical products is limited due to its poor physicochemical stability. EGCG is a hydrophilic polyphenol (log P~1.1), particularly sensitive to heat and light. In neutral or alkaline aqueous solutions it quickly oxidizes itself and epimerizes to the less active gallocatechin gallate (GCG). Also, as it is hydrophilic it shows difficulty diffusing across the lipophilic stratum corneum to be effectively delivered into the viable epidermis and dermis. By means of advanced lipid nano-encapsulation systems (NLC's and Phytosomes), the stability of EGCG in the vehicle and, significantly, the retention of the compound in the skin can be optimized [37].

IV. Liquorice: Photoprotective Potential

The liquorice extract is produced from the dried roots and rhizomes of the plants of the genus Glycyrrhiza, such as *Glycyrrhiza glabra* L., *Glycyrrhiza uralensis* Fisch. and *Glycyrrhiza inflata* Batalin.

(family: Fabaceae). Liquorice is used in traditional medicine as well as the most modern cosmeceuticals because of its demulcent, anti-inflammatory, anti-oxidant and skin- lightening activities. The main secondary metabolites with photoprotective potential are isoflavonoids (mainly Glabridin) and chalcones (Licochalcone A, B and D), triterpenoid saponins (Glycyrrhizin and Glycyrrhizic acid) and flavones (Liquiritin) [38].

Concentrated at *G. glabra*, prenylated isoflavan, Glabridin is the most potented natural depigmenting agent discovered so far at botanical medicine. Based upon mechanisms on solar-induced hyperpigmentation, Glabridin acts as the reversible competitive inhibitor on Tyrosinase which is the rate limiting enzyme for melanogenesis synthesis. It is revealed by in vitro enzymatic test that Glabridin inhibits both the monophenolase (tyrosinase hydroxylase) activity of tyrosinase and diphenolase (dopa oxidase) activity of tyrosinase on concentration of sub-micro molar ranges more potently than synthetic references [39] e.g. Hydroquinone and Kojic Acid. By inhibiting the binding action on binuclear copper of Tyrosinase active site of L-tyrosine and L-DOPA, it suppressed melanogenesis without introducing cytotoxity of human melanocytes and resulted permanent deprivation of pigmentation that human is afraid of, which is the main disadvantages of Hydroquinone.

In melanogenesis sequence, enzymatic steps include L-Tyrosine hydroxylation to L-DOPA, L-DOPA oxidation to DOPAquinone and polymerisation to black melanin pigment [40]. Glabridin inhibits both enzyme steps by binding to binuclear copper centre in Tyrosinase. This competitive block prevents substrate turnover, block DOPAquinone formation and hyperpigmentation without damaging basal melanocytes. Unlike, Glabridin which performs anti-tyrosinase function, Licochalcone A, a retrochalcone that comes from *G. inflata* and *G. uralensis*, is effective in reducing UV-induced inflammatory pathway. Solar UV irradiation causes an inflammatory signal pathway, activation of NF-κB and subsequently, up-regulation of pro-inflammatory cytokines and inducible nitric oxide synthase (iNOS), and COX-2 in epidermal cells [41,42]. Licochalcone A reduces the NF-κB pathway by inhibiting the phosphorylation and degradation of inhibitor Iκ-α) and blocking p65 unit nuclear translocation to nucleus and this transcriptional suppression significantly attenuates expression of pro-inflammatory cytokines (IL-1β, IL-6, IL-8, and TNF-α), further reduces post transcriptional PGE2 production. Clinically, topically applied liquorice extract that contains Licochalcone A has been demonstrated to obviously suppress UV induced erythema, vascular edema and microvascular flush [43].

Within Liquorice extracts, Glycyrrhizin (glycyrrhizic acid)-a triterpenoid saponin-serves as an epithelial demulcent and soothe agent. Within the epithelial cell membrane, Glycyrrhizin acts to reduce cellular swelling and in doing so blunt pain sensation and irritation evoked by acute thermal and UV radiation. Glycyrrhizin also serves to inhibit 11β-hydroxysteroid dehydrogenase type 2, thereby locally increasing endogenous cortisol levels within the irradiated dermis and to ensure a maximal anti-inflammatory response. Challenges with topic delivery of hydrophobic liquorice bioactives-primarily Glabridin- arise from their low

water solubility and ineffective transit over the barrier layer of the stratum corneum. Innovative delivery strategies have been employed including tetrahedral framework nucleic acid nanocarriers, nanostructured lipid carriers and ethosomes to effectively formulate and deliver Glabridin, increase its transdermal flux and focus its effects on basal level melanocytes, thus achieving maximum depigmentation and photoprotection capacity [44].

V. Red Raspberry: Photoprotective Potential

Red Raspberry Seed Oil (RSO), cold pressed from *Rubus idaeus* L. (family Rosaceae) seed, is an oil extracted from waste from the fruit processing industry. The composition of lipid and phytochemicals distinguishes RSO from other commonly used conventional vegetable carriers. Overall the PUFA content is approximately 80 - 85% with both linoleic acid ($C_{18:2\,n-6}$, ~54.5%) and α-linolenic acid ($C_{18:3\,n-3}$, ~29.1–32.0%) very high in concentration (with 12.0% oleic acid, $C_{18:1\,n-9}$, ~12.0%). RSO is characterized by having the highest amount of alpha-linolenic acid relative to other fruit seed oils [45,46].

With the lipid content RSO also displays a high density of lipophilic/amphiphilic unsaponifiable bioactive compounds. The concentrations of total tocopherols in the oil are 295–302 mg/100 g (equivalent of total V E ~97 mg/100 g) which is primarily composed of γ-tocopherol (272 mg/100 g), α-tocopherol (71 mg/100 g) followed by δ-tocopherol (17.4 mg/100 g). Carotenoids (in which the concentration found includes lutein, β -carotene, zeaxanthin in this oil concentration value) amount to 23 mg/100 g, 5.38 mg/g of phytosterols (with high values found mostly in β-sitosterol and campesterol) and polyphenolic phenols, where Ellagic Acid was mostly present [47].

Table 2: Physicochemical composition, key bioactive constituent ranges, and targeted cellular photoprotective mechanisms of cold-pressed Red Raspberry (Rubus idaeus) seed oil.

Physicochemical Parameter	**Range**	**Significance**
Polyunsaturated Fatty Acid (PUFA) Ratio	Linoleic: 54.0–55.0%; α -Linolenic: 29.0–32.0%	Stratum corneum lipid barrier restoration; reduces TEWL
Total Tocopherol Content (Vitamin E)	295.0–302.0 mg/100 g (γ-tocopherol dominant)	Quenches singlet oxygen; terminates lipid peroxidation
Carotenoid Content	~23.0 mg/100 g	Absorbs blue/violet spectra; quenches excited states
Phytosterol Content	5.38 mg/g (β -sitosterol, campesterol)	Repairs damaged barrier membranes; anti-inflammatory
Polyphenol Marker	Ellagic Acid	Inhibits UVB-induced MMP expression; protects collagen

The photoprotection claims for Red Raspberry Seed Oil continue to be a hot topic in research and historical discussion over optical transmission versus true in-vivo. Optical absorption extinction values are within the range of many commercial TiO_2 products [48]. The authors derive hypothetical extinction-derived protection indices equal to UVB SPF 28-50 and UVA SPF 6.5-7.5. Follow-on studies performed in the cosmetic science arena shed further light on this historical data. An in vitro Spectrophotometric optical absorption of diluted oil dissolved in organic solvent (e.g. Dissolved in ethanol or octane) can never directly substitute for a standard in vivo human clinical SPF test (ISO 24444 or FD C protocols), which quantifies the MED on skin covered with a precisely $2\,mg/cm^2$ film. Straight unformulated CP RSO on the skin gives an SPF between 0.4 and 2.6 in vivo. This disparity is due to the absence of the same type of polymers to form a cohesive film, uniformity of application, and same higher optical refractive index needed to sustain a continuous film on the skin [49].

VI. Combined Potential for Herbal Photoprotection

Although each single botanical extract possessed valuable biological activity, a single-ingredient formula cannot completely combat against multiple aspects of UV skin damage cascades. Thus, integration of Camellia sinensis, species of Glycyrrhiza, and *Rubus idaeus* seed oil generates a multi-targeted system that acts at multiple scales (cellular and physical) of solar UV damage. Multi-level defense starts in outermost corneum with topical Red Raspberry Oil creating a physical lipid barrier. The liphophilic chromophores and carotenoids of the oil absorb incidental UV photo radiation, and tocopherols are able to scavenge peroxyl radicals within the bilayer itself. Deeper still in the living epidermis, Glabridin from Liquorice intervenes at the melanocyte level in the stratum basale by reversibly inhibiting Tyrosinase to prevent UV-triggered excess melanin production. Deepest, the synergistic effect of Green Tea EGCG, Liquorice Licochalcone A, and Red Raspberry Ellagic Acid occurs at the dermal and nuclear level [50] .
EGCG and Ellagic Acid block p38α MAPK auto-phosphorylation, stopping downstream AP-1 activation of the MMP-1, 3, & 9 collagenase producing enzymes; at the same time Licochalcone A and EGCG block NF-κB p65 nuclear translocation, stopping the synthesis of IL-1β, IL-6, TNF-α, and COX-2; then, Nrf2 is activated by EGCG to stimulate our body's own antioxidant defenses (HO-1, SOD, GSH-Px) and red Raspberry essential fatty acids fill any holes in the broken lamella in the epidermis thus sealing the skin barrier to prevent water loss[51] . The synergistic interaction among these three botanicals operates across six coordinated defense mechanisms:

- **Broad-Spectrum Optical and Photonic Attenuation:** By absorbing influx of UVA and UVB and UVC wavelengths at the skin surface with their respective lipophilic pigments and phenolic chromophores, Red Raspberry seed oil prevents the photon from entering into and acting on viable layers of the skin surface.

- Dual-Phase Free Radical Quenching: The hydrophilic polyphenols of Green Tea (ECG and EGCG) quench intracellular free radical species within aqueous cell interiors whereas lipophilic tocopherols (γ-, α -tocopherol), fatty acids and carotenoids present within the Red Raspberry seed oil quench free radical species within the cellular lipid bilayer membrane, thereby averting a free radical cascade on the lipid peroxide chain reaction [52].
- **Transcriptional Repression of Extracellular Matrix Degradation:** Blocking of p38 MAPK phoshorylation and AP-1 activation by Green Tea EGCG and Red Raspberry Ellagic Acid combination blocks the up-regulation of transcription of MMP-1, MMP-3 and MMP-9 which inhibit and prevent the degradation of the collagen lattice.
- **Anti-inflammatory cascade suppression:** Liquoric Licochalcone A and Glycyrrhizin cooperate with Green Tea EGCG in the inhibition of NF-κB activation. The result of this coordinated action is the suppression of the downstream synthesis of inflammatory cytokines (IL-1β, IL-6, IL-8, TNF-α) and of inflammatory enzymes (COX-2, iNOS), which ultimately leads to the inhibition of solar erythema and microvascular dilation [53].

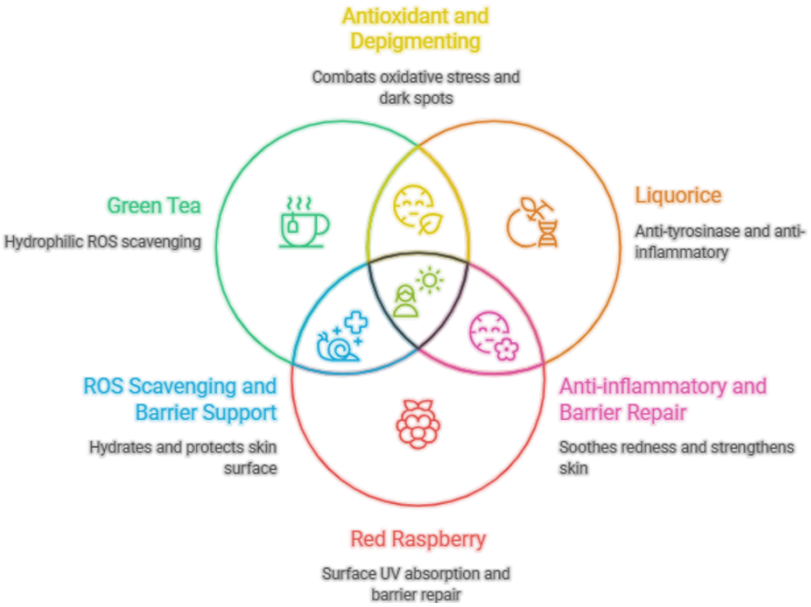


Figure 3: Multi-Target Biological Synergy and Formulation Delivery Roles of Green Tea, Liquorice, and Red Raspberry Actives

- **Targeted melanogenesis control:** Liquorice Glabridin regulates, by competitive inhibition of Tyrosinase activity on basal melanocytes, UV-stimulated melanin production without the direct phototoxicity of melanocytes, thus limiting the formation of solar lentigines and of post-inflammatory hyperpigmentation.
- **Stratum corneum lipid barrier repair:** Red Raspberry Seed Oil provides essential Ω-3 (α -linolenic) and Ω-6 (linoleic) fatty acids in synergy with phytosterols at a precise ratio.

These natural lipids integrate seamlessly into the disrupted lamellae of stratum corneum lipids. The barrier is thus restored:trans-epidermal water loss (TEWL) is controlled,and dry, irritated skin is soothed [54] .

VII. Herbal Sunscreen Formulations and Future Perspectives

Translating botanicals formulation to perform high-functioning cosmeceutical sunscreens is a very difficult task and involves sophisticated formulation design methods. Conventional vehicles of topical product application (simple emulsions, ointments, creams and gels) usually provide the formulation which have problems with low dermatropism, poor chemical stability of actives compound, oxidation of actives and low dermatropism of actives compound [55].

These are overcomes by use of modern nanostructured lipid delivery vehicles - Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs). NLCs are a second generation nano carrier which is obtained from precise mixing of solid lipids (e.g.: cetyl palmitate, glyceryl monostearate, Precirol ATO 5) with liquid lipids (oil) at a certain proportion of each to obtain spatially distorted non-ordered crystalline structure [56]. The difference of first generation SLNs from second generation NLCs is based upon ability to accommodate drug and their stability. SLNs contain pure solid lipids and solid lipid melt solidify to highly organized, perfectly ordered crystalline lattice, but on prolonged storage at room temperature, there is possibility of polymorphic rearrangement to less stable 3 form which leads to ejection of the entrapped drug (product failure) [57] .

Whereas, in NLCs addition of liquid oil into the solid lipid matrix introduces lattice defects and imperfection which accommodates high quantity of drugs. It also permits polymorphism free state so it avoids ejection of drugs. In an combined botanical photoprotection formulation, Red Raspberry Seed Oil may be blended into the NLC matrices directly as the liquid lipid component where its function will not only be structural-disrupting the formation of solid lipid crystalline structures in a co-structured carrier system- but its characteristic EFAs, tocopherols and ellagic acid may also be imparted into the formulations, simultaneously[58]. Hydrophobic Glabridin and hydrophilic Green Tea EGCG may then be simultaneously co-encapsulated into the NLC-in-emulgel core. Formulation studies report that high EE ($>$ 98% for lipophiles, $>$ 90% for polyphenols), sustained release from 24-48 hours and doubled dermal tissue retentivity compared to non-encapsulated botanicals occur within NLC nanostructures. In addition, a tight particulate layer is created by the lipid nanoparticles on the stratum corneum.

A particulate film which will create an optical scattering effect-decreasing path length as well as increasing incidents UV photons trajectory, thus enhancing total formulation SPF.

This ability makes the "Sunscreen Booster Effect" possible. This means you can add plant based NLCs with rich levels of polyphenols into an organic or inorganic (ZnO and/or TiO_2) sunscreen and boost SPF to such high levels (e.g. 30-50+); that levels of synthetic filters may be reduced by 30-50% in some formulations. Reducing the amount of mineral and chemical filter should minimize the aesthetic problem of white cast,

significantly reduce the cost and skin irritation, and minimize the aquatic ecotoxicology risk from ingredients released into the environment [59].

Future research and commercial development must address three major regulatory and technical challenges:

- **Standardization of raw materials:** The composition of botanicals used in the extraction varies with plant variety, conditions of growth, method of harvesting, and extraction technique (e.g. Hexane extraction vs Suprercitical CO_2 extraction vs Cold pressed).

Thus, to achieve uniform photoprotective effect it is necessary to standardize commercial raw materials using techniques such as High Performance Liquid Chromatography (HPLC) of the major marker constituents (e.g., ≥90% EGCG, ≥40% Glabridin, ≥1% Ellagic Acid) [60].

- **Analytical and Regulatory SPF Testing Protocol:** Spectrophotometric (in-vitro) and in-vivo photoprotective studies are easily confused. Therefore a clear distinction must be made at both analytical levels and on regulatory standards using guidelines as the ISO 24444 / FDA recommendations. All SPF values related to natural oils need to be confirmed by standardized human clinical studies to avoid misleading the consumer about the level of protection obtained [61].
- **Stability Long term chemical and physical stability:** Polyunsaturated vegetable oils (RSO) in form of the formulation are expected to undergo auto-oxidation on prolonged storage. Natural antioxidant stabilizers (mixed tocopherols and rosemary extract) must be added, also appropriate opaque, airless package systems have to be developed, to avoid generation of toxic lipid peroxides [62].

VIII. Conclusion

Sun protection has developed from simple physical photon interception to multi-target biologically-mediated photoprotection. Sun exposure induce damage to the skin by complex cascade mechanisms related to ROS formation, induction of the intracellular signaling pathway (p38 MAPK, AP-1, NF-κB), degradation of the extracellular matrix by matrix metalloproteinases, hyperpigmentation by tyrosinase and breakdown of stratum corneum barrier.

The blend of three botanical extracts from *Camellia sinensis* (Green Tea), *Glycyrrhiza* species (Liquorice) and *Rubus idaeus* (Red Raspberry) seed oil generates a wide-spectrum, naturally occurring solution to solar radiation damage. Green Tea catechins (EGCG) contribute to the hydrophilic antioxidant support, inhibitory action of AP-1 and MMP transcriptions, and reinforcement of natural endogenous protective cell responses via Nrf2/ARE signal transduction pathways. The Liquorice compounds (Glabridin and Licochalcone A) deliver strong competitive depigmentary effects via anti-tyrosinase activity and downregulating erythema and cytokine amplification at the molecular level mediated via NF-kB pathways. Red Raspberry Seed Oil provides robust, full-spectrum UVA/UVB UV filtering capabilities and contributes lipid peroxidation defense while Tocopherols/carotenoids help restore lipid barriers in the stratum corneum by supplying essential fatty acids (Linoleic/alpha-linolenic acid).

Today, overcoming prior physical limitations regarding chemical stability and dermal delivery has been approached by a variety of advanced nanostructured lipid carrier (NLC) technologies. Serving as structural matrices and protective photoadjuvants, lipid nanocarriers enhance stability, longevity of release, and follicular/stratum corneum cutaneous retention of active materials. By forming these standardized botanic complex components, it is possible to incorporate them into sunscreen formulations to create high-end, multi-action ecologically responsible cosmecutical products for the cosmetic industry that repair, regenerate, and defend.

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