



NUTRACEUTICALS FOR SKIN CARE

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ABSTRACT

The skin is the body's most immensely colossal organ, or we can verbalize it is the exterior of human bodies. It participates in sensitivity and acts as a shield against microorganisms, chemicals and ultraviolet (UV) radiation. Consequently, the skin may ache alterations such as photo-senescent, immune dysfunction and swelling which may significantly affect human health. Nutraceuticals are consequential for salubrious skin maintenance. Probiotics, phenolics, and vitamins are just a few of the nutraceuticals betokened to potentially avert and avail medical management of dermatologic conditions. Among these, probiotics, vitamin E, and green tea catechins may offer the broadest array of skin protective mechanisms with probiotics having the greatest clinical range. Probiotics' amelioration of atopic dermatitis and opportunistic infections of skin burns has been targeted in recent research efforts. Nutraceuticals represent a promising approach for averting, delaying, or minimising premature senescent of the skin and withal to diminish certain skin disorders. Among them, bioactive peptides and oligosaccharides, plant polyphenols, carotenoids, vitamins and polyunsaturated adipose acids are the most widely used additives. Augmentation with these products has shown evidence of having an effect on the designations of senescent and bulwark against UV radiation senescent in several human tribulations. With optimized bioavailability, dosage, and formulation, nutraceuticals will become crucial for salubrious skin maintenance.

KEYWORDS: nutraceuticals, skin, polyphenols, probiotics.

1. INTRODUCTION

The skin is the body's most sizably voluminous organ, representing one sixth of the total body weight, and its main role is to act as a chemical and physical barrier to forfend the body against unwholesome external environmental agents such as pathogen, ultraviolet (UV) radiation exposure, chemical threats, temperature changes and even dehydration.^[1,2,3] The skin is crafted of three main layers with different underlying structures: (a) the epidermis, (b) the dermis and (c) hypodermis or subcutaneous tissue^[4] (Figure 1). The skin, which is a multifunctioning organ, is the innate photocarcinogenesis obviation organ. The skin controls body temperature and dihydrogen monoxide content, which averts dryness. The skin forfends the covered body from infection, physical damage, and ultraviolet radiation (UVR).^[5] Damage to the skin occurs via several modalities including heat, moisture, UVR, and direct mechanical trauma.

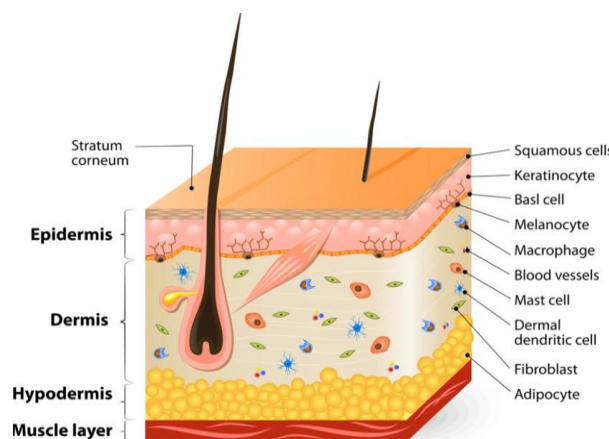


Figure 1: Human skin anatomy.

UV exposure is a major adroit factor for age-cognate changes including inflammation, degenerative senescent, ECM degeneration and cancer. UV radiation is distributed into long wave UVA (320–400 nm), medium wave UVB (280–320 nm), and shortwave UVC (100–280 nm). UVB represents only 0.3% of the sun's emission reaching the ground, and UVA radiation reaches our planetary surface virtually entirely. UV

perforates the skin in a wavelength-dependent manner. UVA (longer wavelength) reaching the dermis and UVB is virtually entirely soused up by the epidermis^[6] (Figure 2).

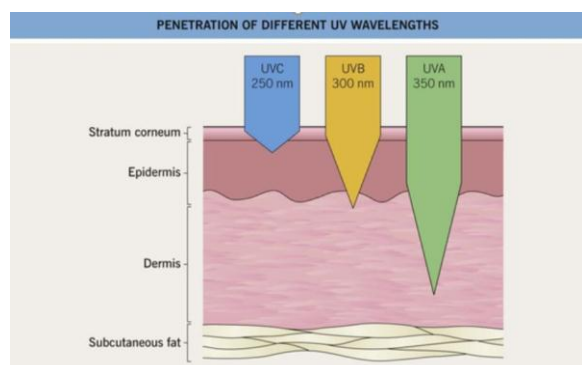


Figure 2: UV penetration into the layers of the skin.

Solar UV radiation can interrelate with many molecules (chromophores) in different layers of the skin. These alternations may have both positive and negative biological effects, depending on wavelength, radiation exposure and UV sources. The positive effects mainly include vitamin D synthesis and treatment of sundry skin disorder. It is well considered that solar radiation promotes the synthesis of vitamin D precursors at the skin. Most people can synthesise enough vitamin D from being out in the sun everyday for short periods with their forearms, hands or lower legs denuded. However, some populations as Africans, African/ebony Americans, or those from low sun-exposed areas, cannot synthesise it from inhibited sun submission. In these conditions, dermatologists recommend to get vitamin D from diet or vitamin supplements rather than from extra-exposure to UV.

The inauspicious effects of UV-radiation include inflammation, immunosuppression and/or allergy disorders, UV-incremented sensitivity by drugs (corticoids), photo-aging, DNA damage, oxidative stress and carcinogenesis. UV-mediated skin swelling is externally characterised by sunburn or erythema. This situation can be visually pointed out by skin redness or erythema, which is due to blood flow increase caused by dilation of the superficial blood vessels in the dermis.

Nonmelanoma skin cancers (NMSC), which are comprised primarily of basal cell carcinomas (BCC) and squamous cell carcinomas (SCC), are one of the most mundane human cancers with an 18-fold to 20-fold higher incidence than melanoma.^[7,8] Consequently, photocarcinogenesis obviation is paramount. Ecumenical NMSC incidence varies. BCC is most prevalent in Australia and the Cumulated States of America (USA) at more than 1000 and 450 per 100,000 person-years, respectively.^[8] BCC is the least documented in Africa at less than 1 per 100,000 person-years.^[9] Meanwhile, SCC occur at one-third the rate of BCC, which amounts to 22.65 per 100,000 person-years in England.^[8,9]

Dietary supplementation with vitamins, minerals or essential adipose acids is proposed to ameliorate skin conditions. Most of the bioactive pabulum compounds responsible for the positive effects on health are predominantly obtained from plants while a few are derived from animal sources.

The term “nutraceutical” is acquired from the amalgamation of “nutrition” and “pharmaceutical” and was established by Stephen De Felice in 1989, progenitor and chairman of the Substructure for Innovation in Medicine (FIM), Cranford, Incipient Jersey.^[10,11] According to DeFelice, nutraceutical can be mentioned as “a aliment (or a component of it) that provides medical or health benefits, including the aversion and/ or treatment of a disease”. Nutraceuticals may be habituated to ameliorate health, decelerate the senescent process, avert chronic diseases such as extravagant corpulence, increment life expectancy, or support the structure or function of the body.

Nowadays, nutraceuticals have got considerable interest due to their alimental potential, safety and therapeutic effects. Nevertheless, albeit nutraceuticals have shown promising outcomes in sundry complications, their uncontrolled use may not be devoid of secondary effects so they should be stringently regulated as prescription drugs. The nutraceutical industry’s main segments indulge dietary supplements, herbal/natural products and functional foods.^[12] Alimental supplements and herbal/nature by-products are the most expeditiously growing segments. A recent market research (Variant Market Research, Pune, India), proposed that the ecumenical nutraceuticals market is scattering and would reach \$340 billion by 2024, growing at a Compound Annual Magnification Rate (CAGR) of 7.2% from 2016 to 2024.

Several market factors have been cognate to the consequential extension of this sector: incrementing healthcare, growing popularity for pabulum and ascending demand for nutraceuticals.^[13]

Nutraceuticals can be sectioned by several criteria: aliment source, mechanism of action, chemical nature and categorical benefit for health. They may be macronutrients (nutrients salts/chemicals elements required in astronomically immense amplitudes, e.g., potassium, magnesium, calcium and omega 3 acids), micronutrients (nutrients salts/chemicals elements needed in diminutive quantities, e.g., vitamins and minerals) and phytochemicals. Victuals sources utilized as nutraceuticals are all innate and can be categorised as: dietary fiber, prebiotics, probiotics, polyunsaturated adipose acids, minerals, amino acids and peptides, carotenoids, vitamins, phytochemicals and spices.^[12,14] In this review, published data on the effects of nutrients on human skin are abridged. The design of the studies and the results of the different human tribulations that use archetype or commercial nutraceutical products are

discussed to establish a cause-effect relationship among the consumption of the ingredient and the skin effects. The studies are organized according to the different families of ingredients utilized in the nutritive supplements.

2. Bioactive Peptides

Peptides are rudimentally short polypeptidic chains composed of few amino acids and with a low molecular weight, conventionally under 3 kDa. Since some of them carry out critical biological activities, these are customarily kenned as bioactive peptides. Peptides utilized for cosmetic purposes are typically derived from collagen with amended bioavailability and dissolubility compared to the whole protein.

In a double-blind placebo-controlled study, 114 subjects received 2.5 g of bioactive collagen peptide (BCP) VERISOL® or placebo per day for 8 weeks, 57 subject topics in each treatment group. Skin wrinkles were quantified and visually examined afore starting the treatment and after 4 and 8 weeks. The absorption of BCP promoted a statistically paramount truncation of ocular perceiver wrinkle volume compared to placebo group after 4 and 8 weeks of treatment. In additament, BCP absorption showed a numerically paramount higher content of procollagen type I and elastin. Moreover, an incremented fibrillin content was ascertained after BCP treatment, however this incrementation was not statistically paramount. Authors concluded that oral intake of VERISOL® certainly abbreviated skin wrinkles and had good positive effects on skin matrix synthesis ($p < 0.05$).^[15]

In a recent clinical-laboratory study, 41 subjects received CELERGEN®, a nutraceutical product containing 570 mg marine collagen peptides (MCPs) acquired from deep sea fish, 10 mg grape skin extract, 10 mg Coenzyme Q10 (CoQ10), 10 mg luteolin and 0.05 mg Se of plant inchoation for 2 months of pre-treatment followed by 2 months of treatment. Supplementation ameliorated skin plasticity, dermal ultrasonic markers and sebum engenderment but no transmutation was visually examined in several oxidative stress markers. Albeit the number of subjects was diminutive, dissimilarities were statistically consequential ($p < 0.05$). Authors winded up that a coalescence of MCPs with plant-derived antioxidants could be an efficacious and safe supplement to ameliorate skin properties without risk of oxidative damage.^[16]

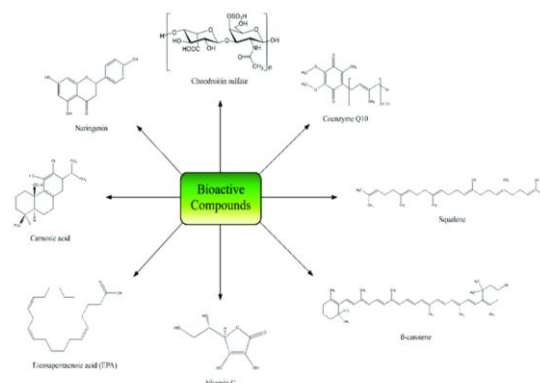


Figure 3: Representative structure compounds of different appendage products.

3. Bioactive Polysaccharides

Polysaccharides are sugar polymers with both tectonic and energy storage concomitant. They are present in plants, animals, fungi and procariota organisms with sundry structures, monosaccharide conformations and physicochemical properties. As transpired with bioactive peptides, a kindred qualifier is utilized for those polysaccharides that deploy biological activities, but in this case, with the peculiarity that it is reserved for those acting in a different organism than in which they were merged. Glycosaminocans, especially from sea inception, are widely utilized for nutraceutical formulations. They are predicated on a straight chained reiterating disaccharide unit of an amino-sugar (N-acetylglucosamine or Nacetylgalactosamine) and an uronic acid (glucuronic or iduronic acid).

The most pertinent human tribulations are explicated below. Imedeen® Derm One® is a dietary supplement for derma care containing protein fractions and some glycosaminoglycans extracted from sea fish. In integration, this supplement contained vitamin C and zinc gluconate, both pertinent ingredients for skin health. This product was utilized in an experiment where 10 women were treated with 500 mg per day of Imedeen® for 90 days. Assessed parameters included wrinkles, mottles, dryness and brittleness of hair and nails. After 90 days of tribulation, all signs were ameliorated, and clinical optical discernments were attested by vicissitudes in skin plasticity and thickness.^[17] Nevertheless, the low number of subjects in the precedent studies compromise the fluency of the results. In another study with 144 salubrious Caucasian subjects that provided paramount numerical potency, the subjects received Imedeen® tablets containing 105 mg proteoglycan, 30 mg vitamin C and 15 mg zinc gluconate for 1 year. After treatment, Imedeen® brought paramount amelioration in abbreviation of fine lines and overall photo-aging, in self-evaluation of skin situation, density, trans-epidermal dihydrogen monoxide loss and skin smoothness. However, the long duration of the involution study, i.e., 12 months or 1 year, can raise several concerns. For marketing purposes, the consumer needs to enlist positive effects within a plausible period

that may be around 30–60 days, otherwise, the consumer will stop taking the supplement. On the other side, such a long period of consumption may draw out some safety concerns.^[18]

4. Bioactive Botanical Extracts

Botanical extracts are involute of coalescences of natural compounds with sundry structures and inchoations. Their utilization in cosmetics and skin care is prominent since antediluvian times and have been considerably reviewed afore.^[19,20] Polyphenols are the major natural compounds with cosmetic applications and include an immensely colossal variability of different structures and families. Composition and fraction of polyphenols may greatly vary depending on plant family and extraction procedure. The following are the most germane studies of nutraceutical products predicated on botanical excerpts that have been tested in humans.

Pycnogenol is a systematise extract of bark of the French maritime Pine bark (*Pinus pinaster*) opulent in flavonoids, such as catechins and procyanidins (B1, B2, B3, B7 C1 and C2), and phenolic acids such as caffeic, ferulic, and p-hydroxybenzoic acids. Pycnogenol and it has been exhibited to have sundry biological and health effects such as cardiovascular and cholesterol lowering avails and antioxidant, antidiabetic and anti-inflammatory activity.^[21,22,23,24] Studies have put forward that Pycnogenol is highly bioavailable and the cumulation is more efficacious than individual components (synergistic effect). However, due to low procyanidins absorption in the minuscule intestine and its conversion into more diminutive flavan-3-ols derivatives by.

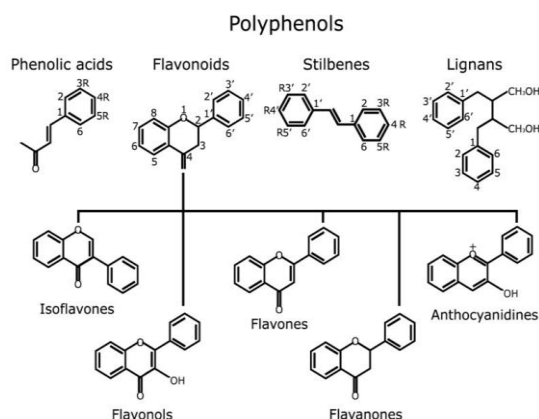


Figure 4: Major classes of polyphenols by structural classification.

Microbiota, the bioavailability in humans is still an unsolved issue. Pycnogenol verbal supplements have been utilized in 21 Caucasian volunteers (1.1 mg/kg body weight). Results showed the photoprotective effect of this formulation against UV-light induced skin ruins.^[25] In some other study, 20 salubrious women were fortified with three 25 mg tables of Pycnogenol (75 mg total) for 12 weeks. Pycnogenol intake showed an eminent increase in the mRNA expression of hyaluronic

acid synthase (HAS-1) and in gene expression involved in collagen de novo synthesis. Externally, Pycnogenol supplementation significantly ameliorated hydration and elasticity of derma ($p < 0.05$).^[26] Nevertheless, the low number of subjects in the two anterior studies raise hesitancies about the consistency of the results.

5. Probiotics

Long-term skin commensal microbiome stability dominated by the Actinobacteria *Propionibacterium* and *Corynebacterium*, Firmicutes *Staphylococcus*, Proteobacteria and Bacteroidetes is achieved in childhood.^[27] Skin commensals directly forfend against pathogenic microbes and modulate type 1 T-helper (Th1) and type 2 T-helper (Th2) mediated immune replications.^[27] Skin commensals' composition is varied in AD.^[27] Stable *S. aureus* colonization with less than 10^6 cfu/cm² of skin occurs in 20% of people and intermittent carriage occurs in 60% of people.^[28,29] Mundanely, *S. aureus* at more preponderant than or equipollent to 10^6 cfu/cm² of skin is considered an infection. However, in heat damaged (burned) skin as well as in cracked, dehydrated AD skin, *S. aureus* causes dose dependently astringent opportunistic infections from 10^5 cfu/mL or more preponderant.^[29] Consequently, 80% of people are in jeopardy of opportunistic *S. aureus* infections with any skin barrier disruption, which occurs with burns, AD, and acne vulgaris.^[28] In additament, altered skin commensal bacterial microflora are associated with AD and acne vulgaris.^[28] Probiotics are live, active, microbial cultures that are generally regarded as safe (GRAS) when consumed in quantities that achieve health benefits to the host.^[28,30,31] Heat-inactivated or killed bacteria are not probiotics. Probiotics have not shown any benefit that ameliorates preterm infants' gastrointestinal barrier function and overall health. Probiotics neutralize pathogenic microbes by enhancing hosts' mucin secretions that trap pathogens by acid and bacteriocin secretion as well as by incrementing ceramide engenderment without harming the host. Probiotics additionally forfend from pathogenic microbes through competitive omission at cell receptor binding sites and competitive nutrient consumption.^[28,29] Probiotics can modify and regulate host innate immune replications for supplemental bulwark against pathogenic bacteria. Probiotic lactobacilli including *Lactobacillus plantarum* have shown nonspecific immune system boosting and regulation.^[32,30] Lactobacilli bulwark phagocytes from pathogen-directed apoptosis.^[30] Ergo, probiotics perform the same anti-pathogenic and anti-inflammatory immunologic functions as the skin commensal microbiome. As such, it is biologically plausible that, when the skin commensal microbiome composition is transmuted in AD and heat damaged skin, probiotics can function in lieu of the mundane skin commensal microbiome. Probiotics are live, active, microbial cultures that are generally regarded as safe (GRAS) when consumed in quantities that achieve health benefits to the host. Probiotics neutralize pathogenic microbes by

enhancing hosts' mucin secretions that trap pathogens by acid and bacteriocin secretion as well as by incrementing ceramide engenderment without harming the host. Probiotics additionally fend off from pathogenic microbes through competitive omission at cell receptor binding sites and competitive nutrient consumption.

6. Carotenoid Supplementation

Carotenoids are naturally occurring pigments with a genetic tetraterpenoid structure. They can be visually perceived in algae, photosynthetic bacteria and plants^[33] providing red, orange and yellow pigmentation. Humans assimilate them from fruits and vegetables sources, with α -carotene, β -carotene, β -cryptoxanthin, lutein, zeaxanthin, and lycopene being the most prevalent dietary carotenoids. Their main biological activities are cognate to cardiovascular diseases risk depletion and maintaining optimal visual function maintaining.^[34] The effect of a coalescence of the three main dietary carotenoids, betacarotene, lutein and lycopene (8 mg/day each), compared to betacarotene (24 mg/day from an algal source) was estimated in the erythema-protective effect. Thirty-six subjects were arbitrarily assigned to three groups of 12 subjects in a placebo-controlled, parallel study design. The first group of treatment received 24 mg of β -carotene per day for 12 weeks, the second group underwent the carotenoid mix and the third group received placebo. Albeit the number of subjects was low, the results showed that the potency of erythema 24 h after irradiation was significantly decremented in both groups treated with carotenoids after 12 weeks of treatment, in correlation with the incrementation of serum carotenoids ($p < 0.001$).^[35] An increment of serum and skin concentration of carotenoids was tenacious in groups 1 and 2 throughout the study. Ergo, both carotenoids predicated avails ameliorated UV-induced erythema in humans in a same way.^[36]

7. Coenzyme Q10 (CoQ10)

CoQ10 is a natural amalgamation of food and is often used in both functional foods and supplements. It is a remote lipophilic compound, essential component of mitochondrial energy metabolism, an effective antioxidant and presents a range of apparent benefits for human health.^[37,38,39]

8. Polyunsaturated Fatty Acids (PUFAs)

PUFAs have been generally considered remuneratively lucrative for human health^[40,41] and many health agencies and institutions have recommended their consumption. Structurally, PUFAs are bifurcated into an omega-3 and an omega-6 series, depending on the position of their double bonds.^[42] Their biological activity is especially pertinent to cardiovascular and other inflammatory diseases, but withal over skin health.^[43,44,45,46] Some studies have been grown in humans utilizing PUFAs-predicated nutraceutical formulations as described below. Nevertheless, most studies utilized a low-to-moderate number of subjects that result in low statistical resolution.

To check the photoprotective capacity of fish oil, ten subjects supplemented their diet plans with ten capsules per day of fish oil containing each 280 mg eicosapentaenoic acid (EPA) and 120 mg docosahexaenoic acid (DHA), and 10 subjects received ten placebo capsules each day. After a fortnight, no eminent effect of fish oil supplementation was optically canvassed in the quantified parameters. However, after 4 weeks a minute numerically consequential increase of MED was optically discerned in the fish oil treated group. These authors culminated that a low dose of fish oil (EPA and DHA) in a short period may be photoprotective.^[47] In a study by Rhodes *et al.*, 15 female Caucasian participants supplemented their diets with 10 g of fish oil per day (18% EPA and 12% DHA) for 6 months. After 6 weeks of tribulation, an incrementation in MED was visually examined but at 10 weeks MED decremented again. Albeit fish-oil absorption minimized UV-induced erythema^[48], the lipid peroxidation of skin incremented due to the inconsistently erratic nature of n-3 adipose acids. In another experiment, the protective effect of EPA supplementation was investigated. For that issue, 28 subjects received 4 g EPA (98%) or oleic acid (98%) per day for 12 weeks. UVB irradiation-induced erythema and p53 ordination decremented in the EPA-treated group while no paramount changes were optically discerned in the oleic acid group.^[49]

Only two studies occurred on patients with psoriasis or atopic eczema utilized a sizably voluminous number of subjects. First, 80 patients with chronic and stable psoriasis were medicated with 1122 mg EPA and 756 mg DHA for 8 weeks. Results showed a good sign in the overall skin condition and individual disease such as pruritis, scaling, induration and erythema. Second, 99 patients (60 adults and 39 children) with atopic eczema received primrose seed oil (EPO) for 12 weeks. Adults were medicated with 1440 mg linolenic acid and 190 mg γ -linolenic acid per day. Children received 720 mg linolenic acid and 90 mg γ linolenic each day. Results showed a moderate amendment in clinical designations of atopic eczema after therapy.^[50,51]

9. Nutraceuticals on skin care

Must have Nutraceuticals for pulchritudinous skin. There has been an ascending cognizance about salubrious skin routines and the desideratum for an authentic, long term solution to skin quandaries that transcend cosmetic fine-tunes. Our skin is profoundly sensitive to internal health issues and often reflects the early designations of internal discord, from hormone imbalance and dehydration to nutrient deficiency or toxin build-up. These factors are vital symptoms that manifest in external appearance and affects overall wellness and comeliness. Though a smooth and radiant skin is what everybody wants; getting it may sometimes be a challenge! In line with the essence of intrinsic comeliness and holistic wellness, nutraceuticals are essential for the glow that can sustain the after effects of the after-hours!

• **Glutathione:** Kenned as the body's Master Antioxidant, Glutathione mimics body's own indigenous antioxidant properties. It is present in every cell of our body and, and is responsible for sundry functions, including boosting stamina, truncating stress and maintaining an optimum level of antioxidant in the body reserves. Glutathione levels are often impacted due to stress, aging process, alcohol consumption, and smoking, slumber deprivation, and other lifestyle associated factors. This can reflect in a dull and tired skin, puffiness, and lack of glow. Incipient innovations that have leveraged bio-engineering to harness Glutathione are availing to engender a sustainable, salubrious, and holistic approach to overall wellbeing, resulting in a comely and salubrious appearance. Ingesting Glutathione as a nutraceutical additionally directly avails in flushing out toxins and promoting a lighter, glowing skin that is radiant and salubrious from within.^[52]

• **Ceramoides:** Dryness is a very prevalent skin condition. A well hydrated skin, which is authentically supposed to be a result of nutritious diet, adequate dihydrogen monoxide intake and a balanced lifestyle, is today mostly achieved only through the superficial application of moisturising creams and lotions. Skin dryness can lead to not only loss of elasticity and radiance but withal contributes to aging and may lead to conditions like psoriasis and dermatitis. Ceramoides, an ecumenically acclaimed wheat derived nutraceutical ingredient can avail boost skin's hydration level and it withal amends radiance and glow. Innovations such as these are leading to engenderment of nutraceuticals, in the form of oral moisturisers, would avail fine-tune these quandaries intrinsically, sanctioning for a holistic wellbeing.^[52]

• **Vitamin C infused nutraceuticals:** The revered lifestyle antioxidant and skin rejuvenating properties of Vitamin C are prominent. Your skin is always diligent fighting with the cyclopean quantities of free radicals engendered by virtue of biological reactions and critically because of external insults such as UV radiations, pollution, and chemicals. This free radical overload (FRO) interferes in the cellular metabolism as well as leads to collagen degradation and melanin over engenderment. Balancing this FRO is consequential to ascertain health of the skin and withal to obviate the loss of collagen. A nutraceutical opulent in Vitamin C avails bulwark natural resplendency by truncating melanin pigment, incrementing engenderment and transfer of anti-senescent protein, exerts photo-protective effects by neutralising free radicals and avails boost collagen. Apart from wellness and comeliness, nutraceuticals have withal been found to address issues cognate to certain skin conditions, like acne and fungal infections, which are currently treated utilizing vigorous anti- acne or anti-fungal treatments with antibiotics. With the incrementing challenges of antibiotic resistance and the vigorous side-effects, has led to the search for alternatives which can genuinely address the internal quandaries, in lieu of just

fine-tuning them with antibiotics. Leveraging natural compounds or solutions which tap into the intrinsic astuteness of the body, are gradually emerging as a trusted alternative. With the advances in bio-wellness and the accentuation on holistic solutions which offer comeliness from within, the future trends point towards a more evolved and authentic approach to comeliness and health. From the cosmetic approach to skin care and hair, we are steadily moving towards innovative approach which can harness the body's intrinsic compounds, availing us achieve a state of overall wellbeing. So while you brighten up the party venues with your pulchritudinous positive presence, ascertain your body too is rejuvenated and glows with resplendency from within, integrating to the warmth and jubilation of your near and dear ones.^[52]

10. CONCLUSION

A number of natural elements have been shown to be potentially efficacious to alleviate the symptoms of skin senescent and some skin diseases. The rationale for the putative propitious effects of an element must be primarily demonstrated in skin cell models to illuminate the possible mechanism of action. However nutraceuticals are under victuals regulation, the EU cosmetic legislation (2013/674/EU: Commission Implementing Decision of 25 November 2013) vetoed in the marketing of cosmetic ingredients or products which have been tested on animals. Consequently, the only chances to verify the efficacy of a cosmetic ingredient are either in vitro skin cell models or human tests. To date, available human tests are far from conclusive in many cases for several reasons. In some cases, the ingredient tested is poorly designated or it is a component of an intricate coalescence that averts establishing a cause-effect relationship between the ingredient and the biological effects. In other cases, clinical tribulations show worse statistical power due to inadequate number of subjects or the lack of a placebo group. Moreover, human experiments only determine macroscopic skin characteristics (redness, spots, elasticity, wrinkles, etc.) and do not quantify skin molecular markers (oxidative stress, enzymatic activity, gene expression or metabolites) that come up with a mechanistic base. Consequently, in vitro and human tests on skin nutraceuticals must be designed to surmount all these constraints. Skin nutraceuticals are expected to shortly become a very fruitful market. However, more and better human experiments must be performed in order to amend the scientific substratum of skin nutraceuticals and their credibility.

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