

Role of Topical Flavonoids as Antioxidants to Preserve Healthy Skin – A Review

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Abstract

As a result of the negative effect of some of the horny extract's associated proteins, the skin is continuously exposed to numerous environmental factors, particularly pollution as well as ultraviolet radiation (UV). As a result, the horny isolate can be adversely affected by the toxic influence of many of its associated proteins. The immediate absorption of UV light through the use of epithelial chromophores, the creation of excited states as well as the subsequent chemical changes, or even photosensitization processes, wherein UV light is absorbed by excited photosensitizer and their responses encourage the production of reactive oxygen species, are all processes that are involved in the environmental pollutants advanced by UV light. Polluting chemicals' actions are not completely understood, but evidence suggests that one of the key processes involved is oxidative stress caused by lipid peroxidation, which has the potential to cause harm to sebum content, stratum corneum integrity, and skin ageing. Numerous studies have indicated the effectiveness of natural antioxidants, with a focus on natural substances, in promoting the preservation of the skin's physiological equilibrium.

Key words: Antioxidants, cosmetics, epidermis, flavonoids, quercetin, skin

INTRODUCTION

Skin and mucous membranes are constantly acting as a connection and defensive shield from physicochemical, biological, and hostile actions.^[1] The skin is subjected to a variety of adverse environmental conditions of various sorts and strengths, so there is a paucity of research linking air pollution to cutaneous illnesses. In summary, the scant clinical evidence imply that pollution worsens atopic dermatitis, with the theory that microparticles aggravate the inflammatory reaction, harming the skin's surface or deeper layers, and therefore causing dermatological illnesses.^[2,3] With pollution's detrimental effects, it's critical that the skin, especially the innermost layer, stays unchanged so that it may perform its protection from external role. The barrier function tries to protect from exogenous pollutants and environmental pollutants, preventing absorption and toxic and damaging consequences.^[4,5]

Skin consistency is necessary for ensuring an effective protective barrier; nevertheless, various variables, such as geography, anatomy, aging, skin moisture, and physicochemical features of the pollutants, may aid the systemic absorption process. As a consequence of the greater absorption of pollutants,

youngsters and the aged are more vulnerable to vulnerable attack.^[6,7] As a result, the combination of modern way of life, air quality progressively polluted by smoke byproducts (from automobiles, industry, and cigarettes), and reassurance of participation in outdoor recreational activities without adequate safeguards can result in serious health consequences, particularly for the skin and many of its connections. The negative effects of sunshine and contamination on the skin may be exceedingly detrimental, encouraging epidermal and systemically immunosuppressive, inflammatory disorders, oxidative stress, including metabolic deficits, as well as endothelial dysfunction to genetic information, and favoring the development of skin cancer.^[8-10]

The combination of polluting substances including such fine particulates that may encompass polyaromatic hydrocarbons as well as primary pollutants including carbon dioxide, carbon monoxide, sulfur dioxide, nitrogen dioxide, or other oxides of nitrogen and also the total combined activity

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of ultraviolet (UV) light on the skin without safeguard causes the development of contaminant and physical responses, including such reactive oxygen species (ROS), histopathological alterations of various severity, skin bulking, and corrective action.^[8-10]

UV light may be absorbed by the a broad range of skin components; nevertheless, reception can cause biochemical reactions in the molecules, since deoxyribonucleic acid (DNA) has become one of the substances that really can absorb the most UV rays other, as a result, suffer oncogenic alterations and changes. Another damaging effect of UV radiation is its propensity to stimulate body's immune elements in the skin, causing an inflammatory reaction through a variety of methods. UV light may harm various areas of the body as well, including the eyes, producing eye problems, photoconjunctivitis, and cataracts.^[11] Although the processes behind the dermatological impacts of contaminants and UV rays are unknown, it is anticipated that exposure might alter the content of sebaceous and the integrity of the stratum corneum, as well as exacerbate the indications of skin ageing, such as the production of blotches and wrinkles. Knowledge of the mechanisms implicated is critical for minimizing skin problems.

The research describes a number of *in vitro* and *ex vivo* research. Production of free radicals is also one of the essential mechanisms involved in the harm caused to the skin by contamination and UV light; sentient culturing proved responsiveness to the poisonous impact of pollution concentrations in the air; one of the essential mechanisms involved in the harm caused to the skin by pollution and UV light is peroxidation. Over the past few decades, there has been an increase in the number of research on antioxidants. These compounds might help to enhance skin problems by protecting it from pollutants and UV rays. As a result, certain courses should become more popular in the future years.^[12,13]

ANTIOXIDANTS

Antioxidants are substances that have the ability to oxidize itself before or instead of other compounds. They are chemicals or complexes that really can engage with free radicals and halt a domino effect from causing harm to critical components.^[14] Food, cosmetics, drinks, and medications, as well as the feed business employ antioxidants. They can be utilized as herbal remedies, active substances, and stabilizers, among other things.^[15] Antioxidants are available in both inorganic and organic forms, and both are utilized in cosmetics.^[16] Since they are comparatively inexpensive, synthetic antioxidants (e.g., butylatedhydroxyanisole [BHA], butylatedhydroxytoluene [BHT], and propyl gallate) are generally implemented.^[17] Extreme use of synthetic antioxidants, meanwhile, may be harmful to one's health, according to the study. Regardless of the fact that synthetic antioxidants control the industry, natural antioxidant consumption has increased over the past

decade and is likely to grow in the future.^[18] A rising consumer demand for natural and organic goods, which include fewer chemicals and could have less adverse effects than synthetic substances, might explain this phenomenon.

COSMETICS WITH NATURAL ANTIOXIDANTS

Natural antioxidants are chemicals and compounds obtained from a large number of plants, cereals, and fruits that can reduce oxidative stress on the epidermis or preserve goods from oxidative deterioration.^[19] Reactive oxygen moieties (ROM) are one of the main sources of oxidative stress, which promotes skin ageing.^[20] Exogenous ageing is linked with exogenous factors that alter the ageing process, while intrinsically ageing is related with the inherent process of ageing (e.g., UV radiation, air pollution, and pathogenic microorganisms). The fundamental source of ROS generation is most probably photoaging.^[21-25] Figure 1 illustrates the variables that impact the ageing process of the skin. Numerous possible skin substrates that associate to ROM have been identified (e.g., fats and DNA, as well as peptides).^[26] Antioxidant compounds can be proteins or low-molecular-mass antioxidants that transfer an electron to radical intermediates, stopping the radical chain reaction from becoming reactive oxidants, or function as metal chelating agents and oxidative enzyme blockers, as well as enzyme cofactors.^[27] Antioxidants could also be employed as stabilizers to keep lipids from becoming rotten. Lipid oxidation happens in the human body as well as in cosmetics.^[28] Antioxidants may, therefore, perform several purposes whenever included in an item. During the starting step of lipid oxidation, the quantity of radicals rises. During in the exponential growth phase, hydroperoxide compounds are generated when O₂ or lipids radicals interact. Hydroperoxides are fragile and they can breakdown into radicals, speeding up the diffusion process. Radical processes predominate the ending phase. By interacting using phospholipid and peroxy

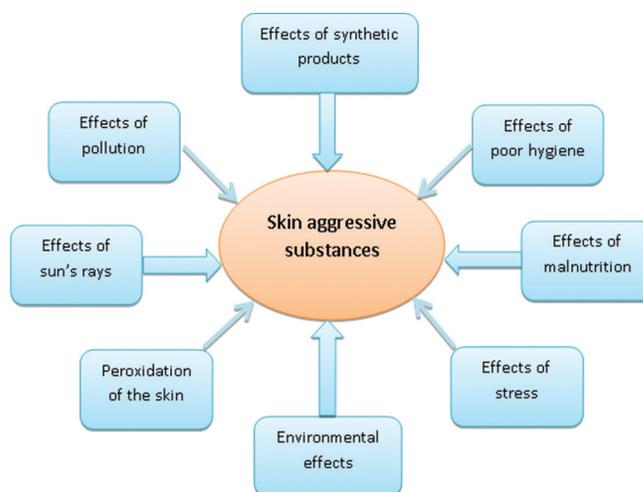


Figure 1: Skin aggressive substances

electrons and transforming these to much more stable, non-radical molecules and antioxidants can reduce lipid oxidation.^[29-32] Antioxidants can also diminish molecular oxygen, neutralize singlet oxygen, remove peroxidative metallic ions, transform hydrogen into the other antioxidants, and scatter UV radiation.^[33] Antioxidants can be mainly used to treat carcinoma since the formation of ROS is changed during carcinogenesis and they have anti-inflammatory and antibacterial properties. Natural antioxidant molecules produced by plants have been shown to lower the number of oxidative stress induced by sunshine and oxygen.^[34]

Phytoconstituents may be found in a wide range of patented and professional cosmetics. Plant extracts such as green tea, grape seed, rosemary, basil grape, tomato, blueberry, pine bark, acerola seed, and milk thistle are prevalent in esthetic compositions. Natural antioxidants present in plant components (particularly carotenoids and essential oils) include flavonoids, polyphenols, stilbenes, flavanols, and terpenes.^[35] Thus, according to their activity, antioxidants are classed as main or organic antioxidants as well as auxiliary or artificial antioxidants. Main antioxidants include minerals (including such selenium, zinc, copper, iron, and manganese), vitamins (C and E), and phytoantioxidants. Mineral antioxidants are often cofactors for enzymatic antioxidants.^[36-40] Auxiliary antioxidants, also known as artificial antioxidants, catch free radicals as well as halt the domino effect. Additional antioxidants include BHA, BHT, propyl gallate, metal chelating agents, tertiary butylhydroquinone, and nordihydroguaiaretic acid.^[41,42] Phytoantioxidants are becoming more popular, and they may someday supplant artificial antioxidants. Such antioxidants are frequently utilized in esthetic goods and can be a single

pure compound/isolate, a mixture of substances, or derived from plants. Natural antioxidants typically utilized in esthetic formulations are summarized in the Table 1. Oxygen free radical scavengers (singlet and triplet), ROM, peroxide detritivores, and enzyme blocker are all functions of innate antioxidants.^[42-44] The most frequent natural antioxidants comprise polyphenols and terpenes, which are distinguished by its molecular mass and polarity, as well as absorption. Benzene circles containing -OH groups are connected to polyphenols. Antioxidant properties are determined by the quantity and location of -OH members on the aromatic rings. Phenolic radicals prevent lipid peroxidation, which influences peptide phosphorylation. Flavonoids and stilbenes seem to be the most prevalent polyphenols, while carotenoids, which operate as superoxide anion quenchers, are the most prevalent terpenes.^[45]

NATURAL ANTIOXIDANTS' DISADVANTAGES IN COSMETICS

Dermal antioxidants, which are usually found in cosmetic formulations, have been broadly applied and are considered safe. Nevertheless, since there is a shortage of clinical data and indeed the evidence that is accessible is of limited importance, the practical applicability of the impacts stated here will be demonstrated clearly. In addition, the published data and articles usually do not specify which galenic idea the formulations were founded on or if the epidermal absorption of antioxidants in the intended region was evaluated. Nevertheless, the findings raise some fascinating concerns for dermatologists to think about when it comes to topical treatment. Vitamins and other

Table 1: Antioxidant chemicals and related molecular compositions, primary active components, significant effect, and assessment methodologies

Name	Compound types	Main effects	Method	Reference
Ascorbic acid	Aqueous soluble phenolic	UVB and UVA rays cause erythema	Solar simulator that is used in real life	[46]
Vitamin E (α -tocopherol)	Lipophilic phenolic	Blocked UVB light	Solar simulator that is used in real life	[46]
Lycopene	Carotenoid	The use of a microemulsion improved the penetration of lycopene and its antioxidant effect	Porcine ear skin, <i>ex-vivo</i>	[47]
<i>Vitis vinifera</i> L	Phenolic	Improved sun protection factor and a broader range of protection	2,2-diphenyl-1-picrylhydrazyl, diffuse reflectance spectrophotometry <i>in vitro</i>	[48]
Bamboo extracts from Brazilian species	Phenolic	UV sunscreens have improved efficacy and photostability	2,2-diphenyl-1-picrylhydrazyl, diffuse reflectance spectrophotometry <i>in vitro</i>	[49]
Caffeine	Phenolic	<i>In vivo</i> , there is a $\pm 25\%$ boost in anti-UVB resistance	Global sun protection factor test method <i>in-vivo</i> (Cosmetics Europe, 2006). Reflectance spectrophotometers with <i>in-vitro</i> diffuse	[50]

UVB: Ultraviolet B, UVA: Ultraviolet A

bioactive molecules used topically can induce skin irritation, erythema multiforme, and xanthomatous responses in certain people. Many plant extracts, nevertheless, have yet to be explored for their constituents leading to a shortage of separation procedures. Although natural antioxidants are free from hazardous antioxidants, naturally antioxidant-containing cosmetics are much more costly than artificial antioxidant-containing cosmetics. Moreover, even if initial study suggests promising findings, clinical confirmation is required. Natural antioxidants breakdown quickly and have a low bioavailability due to poor absorption. Herbal polyphenols have a poor stability and their susceptibility to light from the sun prevents them from being used in cosmetics. When plant extracts in cosmetics come into touch with the skin, they trigger allergic responses. Furthermore, antioxidants can cause an including acute toxicity, variety of side effects, skin and skin sensitization, eye irritation, and photosensitization.^[51]

FLAVONOIDS

Flavonoids include secondary plant metabolites that are mostly made up of a benzopyrone ring with phenolic or polyphenolic compounds at various locations.^[52] Fruits, stems, herbs, grains, flowers, nuts, vegetables, and seeds seem to be the most prevalent sources.^[53] The therapeutic efficacy and biological activity of such various plant components are due to the presence of bioactive phytochemical substances.^[54] There have been approximately 10,000 flavonoid molecules recovered and characterized so far. The majority of flavonoids have been approved as medicinal agents. These are produced naturally through the phenylpropanoid pathway and their therapeutic efficacy is determined by their absorption route and bioavailability.^[55]

Herbal colors, cosmetics, and beauty products, including anti-wrinkle skin treatments, have all employed flavonoids. Those polyphenols, on the other hand, have the most prominent uses in medicine. Anticancer, antiviral, antibacterial, antiangiogenic, antioxidant, antimalarial, antitumor, neuroprotective, and anti-proliferative drugs have all been extensively employed with flavonoids. *In vitro*, flavonoid-rich apple peel extract suppresses acetylcholinesterase and is an efficient antihypertensive drug. It also protects against cardiometabolic diseases and improves learning and memory as people age.^[56]

They are divided into several categories that depend on the chemical architecture, amount of unsaturation, including carbon rings oxidation. The various subgroups of flavonoids are anthoxanthins (flavanol and flavanone), flavanones, flavans, flavanols, anthocyanidins, chalcones, and isoflavonoids. All of these flavonoids may be found in abundance in environment [Figure 1]. There are several health implications of eating more flavonoid-rich meals. Because these natural substances have beneficial impacts on human health, there is a growing push to separate them

from diverse plants. *Citrus* fruits, for example, are high in flavonoids. Oranges, grapes, lemons, and Indian gooseberries (Amla) contain two flavonoids called hesperetin and naringenin. Mulberry contains flavonoids such as quercetin and anthocyanins glycosides.^[57]

COSMETICS WITH NATURAL FLAVONOIDS

Bioflavonoids, commonly known as flavonoids, are a wide group of plant compounds that provide health benefits. These are polyphenolic that means they have a phenol circle in their chemical composition. Their greatest advantage to our health is their high antioxidant potential. Many herbs and teas include bioflavonoids, which may be found in a range of foods.

Flavonoids enable blood vessels dilate, which is good for their health. They also aid the endothelium or vasculature lining, in maintaining its viability. Both aid in the reduction of blood pressure and the prevention of stroke.^[58]

However, the advantage to skin that is what we are most concerned in. Antioxidants are necessary for reversing the indications of ageing and repairing UV-induced skin problems. Flavonoids have the ability to both prevent and cure damage to the skin caused by UV exposure. Plants, in fact, employ flavonoids to shield themselves from the sun. UVB radiation induces the formation of flavonoids in plants, which then concentrate in the plant's outer tissues.

Flavonoids have been shown to offer skin advantages in several researches. Apigenin, a kind of flavonoid, was studied in one research. Apigenin, when applied as a cream, increased the thickness and suppleness of the dermis, reduced wrinkle length, improved skin tone, and increased skin water content. Rutin, a flavonoid, was the subject of another investigation. Rutin was capable of improving skin suppleness and reduce wrinkle size and quantity.

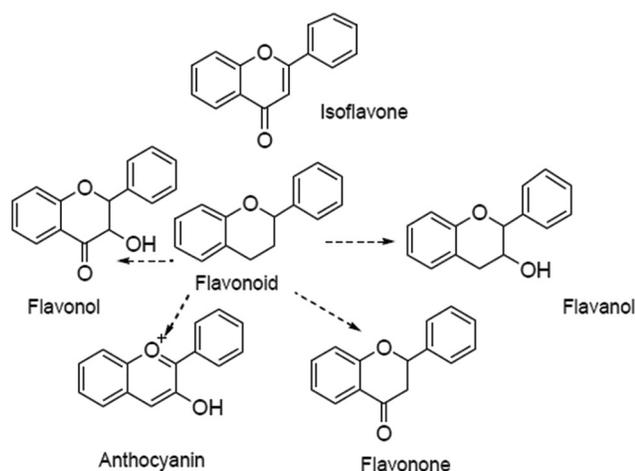
Quercetin, hesperidin, and rutin are three of the most widely studied flavonoids that show anti-ageing benefits for skin. Some bioflavonoids have estrogenic activity such as those in soy which have additional skin benefits with collagen production and skin thickness.

Bioflavonoids have long been known to boost Vitamin C and delay its decomposition. Vitamin C increases collagen formation and evens out skin tone, making it a crucial vitamin for skin. Bioflavonoids are divided into six subclasses based on minor changes in their molecular compounds. Flavonols, flavones, flavan-3-ols, flavones, flavones, and anthocyanidins are the subcategories [Figure 2]. There are about 4000 distinct bioflavonoids known, providing researchers' lots to research.

The following are also some of the botanicals and bioflavonoids included in colorado aromatics beauty products [Table 2]:

Table 2: Flavonoids that exhibit antioxidant properties and related molecular compositions, primary active components, significant effect, and assessment methodologies

Name	Compound types	Main effects	Method	Reference
<i>Helichrysum odoratissimum</i> (L.) Sweet	Flavonoid, chalcones	Increases SPF and reduces UV-induced erythema	<i>In vivo</i> -SANS 1557:2013 and ISO 24444:2010	[60,61]
Genistein	Isoflavone	Agents against UV-induced photodamage	<i>In vitro</i> Human skin grown in 3D	[62]
Buckwheat extract	Flavonoids, flavones, phytosterols	Lipid protection	<i>In-vivo</i>	[63]
Rutin	Polyphenol, flavonoid	Prevent UV irradiation-induced oxidative stress	<i>In-vivo</i>	[64]
Apigenin	Flavones	human dermal fibroblasts	<i>In vitro</i>	[58]
Baicalin	Flavonoid	UVB-induced skin ageing	<i>In vitro</i>	[65]

**Figure 2:** Flavonoids' chemical structure and distinct kinds

Quercetin, calendoflavoside, isorhamnetin, and rutin are all found in calendula. Springtide alpine breeze palm, skin cream, and body lotion as well as elbow balm are just a few of the products that include calendula. Apigenin, quercetin, luteolin, and kaempferol are all found in parsley. Our parsley eye serum contains parsley.^[59]

CONCLUSION

Clients are gradually opting for ecological alternatives to synthetic ingredients in cosmetics and cosmetic goods. Because of the underlying economic opportunities in the resource extraction in environments, plant extracts may be employed in aesthetic science to improve and preserve the physiological equilibrium of human skin. They are also biodegradable and also have a lesser toxicity level than manufactured cosmetic components. However, some by because of plant-processing businesses (such as the food manufacturing) constitute a serious disposal issue. Most of these by-products, on the other hand, appear to be interesting sources of chemicals with biological features that may be

used topically. Natural plant extracts produced from both naturally produced and industrially produced botanicals can therefore be used to make natural external antioxidants, color correctors, and stabilizers, extending the usefulness of items that are now neglected or abandoned. Vitamins and antioxidants are incredibly common as major elements in cosmetics. The advantages of other more biological cosmetic for customers are extensively documented in both scientific and anecdotal research. A component must be consistent in manufacture, storage, and usage, harmless to consumers, and effective at the target location once administered to be helpful.^[66,67] To increase the absorption of these biological cosmetics into the epidermis, more investigation is necessary. Instrumentation, such as iontophoresis, may be required to enhance skin delivery. Antioxidant and vitamin compositions are obviously famous and widespread loved, according to the market-driven economics. Vitamins, on the other hand, are limited in their application due to their volatility and hydrophilic nature. Delivery of drugs systems has been introduced in recent times and many seem to address these restrictions using encapsulation and controlled distribution. In addition, the study has resulted in an improved comprehension of these compounds, resulting in the production of more durable analogues with various chemical features. Vitamins can help with hyperpigmentation, keratinocyte differentiation, skin photo damage prevention, and dermal-epidermal connection cohesiveness when applied topically. Flavonoids, which are present in a variety of cosmetics, are largely utilized for their antioxidant and calming effects. Flavonoids are underused notwithstanding their multifunctional characteristics. The objectives of this paper were to talk about how flavonoids may be used as the major active component in cosmeceuticals. We spoke about some of the most important plant-based antioxidants that might be employed in cosmetics. Although the usage of antioxidants appears to be beneficial, there are few human clinical trials assessing its effect in reducing skin ageing. As a result, more experimental data may be investigated in the prospective, and synergistic effects are suggested for improved efficacy when used together.

DECLARATIONS

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Ethics approval

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

The datasets of research were collected from experiments and analysis of variables during current study. These datasets are available from the corresponding author on reasonable request.

Authors' contributions

SJ designed and optimizes the study and developed the methodology. SJ performed the survey, collection, and interpretation data. SJ wrote the manuscript. NS contributed to manuscript revision and provided supervision. All authors read and approved the final manuscript.

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