

Therapeutic Implementation for Hyperpigmentation and Anti-aging: A Cosmeceutical Approach

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ABSTRACT

Nowadays the most preferred substance to glow skin surface by cosmeceutical products for the aged population and hyperpigmentation cases. These type of skin queries are seen in different environmental conditions including pollution, and radiation. The skin care industries are developing cosmetic products by using natural and synthetic ingredients which is biodegradable and compatible with the skin layer. Cosmetic products currently show drug-like profits because it contain vitamins, antioxidants, essential oils, phytochemical constituents, and enzymes. Cosmo-pharmaceutical products were developing rapidly to avoid skin aging or hypo/hyperpigmentation. The melanocyte or melanin is the main reason for this factor. Selecting natural extracts or resources helps to increase the therapeutic effect and reduces toxicity. The reviewer and researcher found that the term cosmeceutical, skin glowing agent, or hyperpigmentation is widely used in various treatments of melasma, and post-inflammatory hyperpigmentation. The cosmeceutical carefully preclinical and clinical evaluation studies were carried out for safety, and efficacy and no other adverse reactions were shown. Therefore the dermatologist can only provide accurate information to the patient. For the fastest growing area of research and development for a novel formulation of micro-emulsion, nano-emulsion, liposomes, niosomes, solid lipid nanoparticles and nanospheres. These nanocarriers help to incorporate into the formulation and enhance the skin permeation, high stability, and customized release properties with targeting and higher efficacy. The quality of cosmetics and cosmeceuticals is based on evidence of *in-vivo* and *in-vitro* efficacy and therapeutic effect.

Keywords: Cosmeceuticals, Skin hyperpigmentation, Anti-aging, Formulation, Treatment

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INTRODUCTION

Cosmeceuticals

Initially, the name cosmeceutical was started by Dr. Albert Kligman. By their idea of research, it means cosmeceutical is the combined form of cosmetics and pharmaceuticals.¹ So It can be either 'a drug' or 'a cosmetic' or a mixture of both which gives medicinal benefits. This is a skin ailment that arises due to the exudation of melanin, which is secreted inside the human body. The secretion of melanin causes dermatological disorders, for example, inflammations, dermatitis, irritation, and photosensitivity on the exterior part of the skin.² These illnesses are difficult to treat therefore, the developed agents were needed for the lightening of skin with cosmeceuticals. These semisolid preparations helped to affect hyperplastic melanocytes and inhibit major controlling of melanin synthesis.³ Many ingredients are there in cosmeceuticals which are chemically synthesized or obtained from plants or animals.

Cosmeceuticals are part of cosmetics that can be used topically to do their functions as protective, tanning, anti-wrinkling, anti-aging, anti-hyperpigmentation, cleansing, and hair care. It does not show any harmful impact on the structure and role of the skin.⁴ In so current scenario cosmetic products were developed with biologically potent ingredients. Which are based on their structures, sources, mechanism of the skin, safety and efficacy of the targeted site of the skin.⁵ Alike cosmetics, cosmeceuticals deliver nutrients for healthful skin that can influence biological functions. It comprises various potent ingredients vitamins, phytochemicals, essential oils, enzymes, and antioxidants that can be applied as a cream, ointment, lotion, etc.⁶

In recent days (Figure 1), cosmetic and cosmeceutical products are the fastest-developing sectors of the personal care industry. It's having expensive items which make the consumer feel better such as skin care products.⁷ Cosmeceutical products are mainly examined across *In-vitro* studies using

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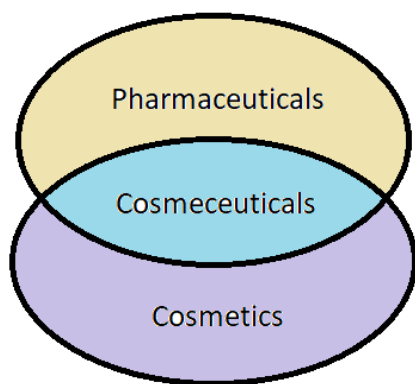


Figure 1: The comparison of cosmetics, cosmeceuticals, and Pharmaceuticals

silicone replicas of skin and open-label studies carried out by industries themselves.⁸ The preparation of cosmeceutical and pharmaceuticals is not mandatory. Patients sometimes often did not get actual information and efficacy of the product through social media or the internet. Dermatologists need to understand the theoretical knowledge and mechanism of action (MoA) of cosmeceuticals. The real information will provide dermatologists be well-trained to help patients.⁹ By the dermatologist, the patient should be aware of use/application, adverse effects, duration of time, which portion of skin to be applied, etc., currently skincare formulations were needed as per the demand of users and for marketing purposes.¹⁰ (Figure 2) shows the data of the cosmeceutical market increasing day by day from 2020 to 2028.

Hyperpigmentation

Human skin is the soft and sensitive part of the organ. This is revealed by various environmental factors like humidity, microbes, and dust.¹¹ Because of the day-by-day change in environmental conditions, based on exposure to UV light affects skin structure of acute or delayed pigmentation.¹² The overcoming of skin pigmentation appearance has been the main focus of numerous medicinal and remedial grounded diligence.¹³ The causes of hyperpigmentation are numerous including acne vulgaris, Inflammation of the skin, overexposure to UV radiation that produces reactive oxygen species (ROS), hormonal imbalance, vitamin B₁₂, etc.¹³ The main enzymes were responsible for the production of melanin (tyrosinase and dopachrome tautomerase). Melanocytes generate a technical lysosomal organelle named melanosome.¹⁴ The skin membrane also has several hormonal receptors e.g; estrogen, androgens, progesterone, etc. Androgens are situated in keratinocytes of nuclei in the gland or hair follicles. Progesterone receptors are widely present in melanocyte cells. The tyrosinase enzyme has the main role in melanin synthesis.¹⁵ The melanosome hormone synthesizes melanin which gives hair and skin color. For the changes of L-tyrosine to L-DOPA (3, 4-dihydroxyphenylalanine) enzyme, its performance as a compound for more oxidation into L-Dopaquinone. The modification of dopaquinone leads to the formation of eumelanin and pheomelanin. The cysteine/

glutathione was found out due to the occurrence of amino acids including the sulpho group. The absence of cysteine and glutathione marks the oxidation of dopaquinone afterward it results in the formation of eumelanin.¹⁶ The synthesis of melanin is mentioned in below Figure 3.

Anti-aging

Skin aging is a biological, physiological change in the human being that follows several body parts, various tissues, and cells along with time. Aging means changes in human skin, face, and eyes starting from childhood. Anti-aging is a complicated organic procedure that is affected by the blend of two factors endogenous, and intrinsic factors (this factor having several processes like metabolic, genetical, cellular metabolism, and secretion), and the second factor is exogenous or extrinsic factors (environmental factors like various types of pollution, radiation, chemicals, and toxins).¹⁷ Above above-discussed reasons lead to increasing structural and physiological variations in the skin layer. Especially variations in skin look, and sun-exposed skin areas. As related symptoms, wrinkled and dry skin, premature skin and various skin rashes usually show a congealed stratum, spotted discoloration, laxity, dullness, wrinkles, and roughness.¹⁸ The epidermis layer is a frequent barrier to the passage of transcutaneously damaging substances. The skin barrier primarily resides in the outermost layer known as the stratum corneum.¹⁹ It is composed of corneocytes, surrounded by intercellular lipid lamellae, and connected by corneo desmosomes. Tight junctions, situated in the upper part of the stratum granulosum, link to the lateral walls of keratinocytes. Components such as intercellular lipids, cholesterol, ceramides, and free fatty acids work together to impede the loss of fluid through the skin.²⁰ The epidermis controls and regulates body temperature and fluid balance, as well as guarding against external elements. Skin plays a main role in sensing stimuli, vitamin D synthesis, and immune surveillance. Skin is having unique personality so many researchers are searching for remedies against anti-aging.²¹ The challenge of finding an anti-aging product for treatments for dermatological research. The skincare products require development and extensive knowledge. The skincare products concerned with biodegradable materials, mainly increase environmental concern and ecological impact. The aging process disturbs the intricate equilibrium of enzymes responsible for overseeing, restructuring, and rejuvenating the dermal matrix. It also leads to a decline in collagen synthesis and other connective tissues. Cellular senescence, which occurs in both extracellular and intracellular stress, is one of the major dangers.²² Other variables connected with aging include growth factors, interleukins, and chemokines. The extracellular matrix is the main component of skin and it is made from proteins, carbohydrates, collagen fiber, elastin, laminin, and hyaluronic acid. Hyaluronic acid is important in retaining skin hydrated by filling empty spaces with water molecules.²³ In human beings, the factors of both intrinsic and extrinsic (natural, and environmental) cause a decrease in the skin elements which are prone to damage wrinkles and

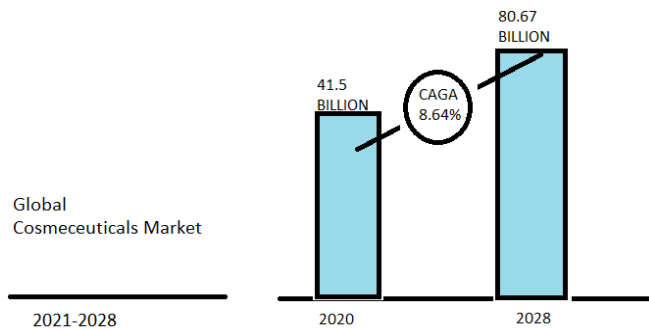


Figure 2: The graphical data showing of cosmeceutical market from 2020 to 2028

sagging. Wrinkles are caused by a decrease in collagen and fibrillin. A specific loss of fibrillin structure adds to wrinkles in aged skin by decreasing the link between the derma and stratum. Scleroprotein causes uneven skin structure.²⁴ The original dermal skin matrix glycosaminoglycans are water-binding components. Aging is concerned with health and the reduction of indications of aging on the skin, face, and body.²⁵ Any anti-aging treatment can help you get healthy, smooth, semitransparent, robust skin. The anti-aging benefits remain longer because many various variables are involved, such as immunological, genetic, emotional, and health-related factors, which prevent the production of wrinkles by degrading primary ingredients such as scleroprotein, elastin, and others.²⁶

Prevention and Therapy of Skin

Topical treatment of hyperpigmentation

Antagonists, melanocytes, tyrosinase, melanosome inhibitors transmission, and degraders to generate melanin which serves as targets for depigmentation and hyperpigmentation monitor agents. For this condition, semisolid dosage forms (creams, gels) are widely used for site-specific skin hyperpigmentation.²⁷ Hydroquinone is a standard for hyperpigmentation treatment, a derivative of hydroquinone is arbutin. Its hyperpigmentation activity is due to tyrosinase and melanosome inhibition activity. Glycolic acid and kojic acid, retinoid, and azelaic acid all are mechanisms that include tyrosinase inhibition. The melanin production route is a complicated process in which numerous topical treatments are utilized in tandem, resulting in a synergistic impact.²⁸

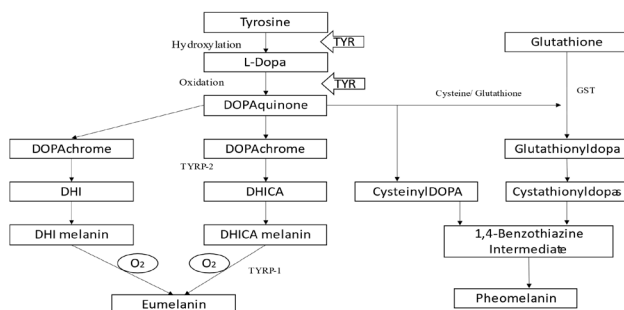


Figure 3: The melanosome hormone synthesizes melanin

Topical treatment of anti-aging skincare

How to breach the barrier against the protector, primarily dehydration, irritants, allergens, contamination of many bacteria, radiation, and reactive oxygen species, for healthy skin (ROS). Thus, everyday skin care is crucial for improving skin regeneration, suppleness, and smoothness, and preventing wrinkle development.²⁹ The lipid layer produces a thicker layer, which serves as the greatest defensive mechanism against harmful elements. The skin's strength gives softness and a smooth texture, making the skin appear healthier as well as hydrated. Another strategy is to use topical or systemic anti-oxidants to prevent wrinkles and inflammation.³⁰

Topical and systemic anti-oxidants

Extrinsic factors include skin aging (photoaging).

In chronic photodamage of the skin, key occurrences include DNA photodamage and the presence of reactive oxygen species (ROS) generated by UV exposure. These factors contribute to issues like wrinkles and hyperpigmentation, characteristic manifestations of photoaging on the skin. The main focus on preventing photo-aging includes sunlight protection by using sunscreen care products to protect skin from UV rays and retinoids by inhibiting collagenase synthesis and an antioxidant combination of both will reduce and neutralize free radicals. The potential for providing nutritional supplements to proactively deter skin aging and enhance skin conditions.³¹ Free radicals directly neutralize the free radicals

- Reduces the peroxide concentration and repairs oxidized membranes
- Decreasing ROS levels by quenching the iron
- Reactive oxygen species are neutralized through lipid metabolism, with fatty acids and cholesteryl esters playing a key role in this process.

Endogenous antioxidant responses are both enzymatic and non-enzymatic. Nutrition is the major source of antioxidants. Vitamin C, E, carotenoids, copper and selenium, are the most well-known systemic antioxidants.³²

Chemical peels

These are scrapes that cause chemical excision of certain skin layers to trigger skin regeneration mechanisms once inflammation occurs. These are divided into three types: superficial peels,¹⁹ trichloroacetic acid peels, and deep husks (TCA > 50%, phenol). Peels are a popular topical treatment for hyperpigmentation. The purpose of a chemical peel is to remove the uppermost stratum corneum layer. When used with other topical therapies, the peels improve penetration. Jessner's chemical peel solution preparation contains 14% lactic acid, 14% salicylic acid, and 14% resorcinol in an alcohol solution. Primarily it is utilized as a safe and effective de-keratinizing agent, as well as a penetration booster. Tretinoin, glycolic acid, salicylic acid, and trichloroacetic acid peels are all excellent depigmenting peels.²⁴

Precaution for age-related skin changes

Factors related to skin mild-stress, dehydration, alcohol, exercise, food restriction, heavy metals, hypergravity,

improving angiogenesis, wound healing, and other cell activities linked to reducing collagen synthesis are due to acute exposures to UV rays. The role of chronic sun exposure increases the UV radiation which increases both melanoma and non-melanoma skin cancer.³³ Premature aging and photoaging are intimately related to pigmentary changes caused by DNA damage, including wrinkling and pigmentation. Avoiding sun exposure is the most effective way to avoid photoaging. Wearing UV-blocking clothes, a cap, and sunglasses, as well as using anti oxidants and retinoids to enhance collagen formation and synthesis, are all methods of prevention.³⁴

Healthy and balanced diet

It is dependent on cell proliferation, which is a key physiological process underpinning aging that causes cellular senescence and changes the biosynthetic activity of skin-related components. It displays external aspects such as muscle action, lifestyle, nutrition chart, sleep patterns, and so on. A healthy, balanced diet and a healthy lifestyle promote skin improvement. A balanced diet entails avoiding skin damage, avoiding foods with a high glycemic index, avoiding alcohol, and taking antioxidants, vitamin C, E, and other supplements.³⁵

Age-related pigmentation and collagen synthesis

The pigmentation is caused by UV rays from sunshine. Sunlight provides vitamin D and is responsible for melanin hormone release. Pigmentation is caused by the oversecretion of melanin. Photoaging, pigmentation, and wrinkles are all caused by DNA damage. The uppermost layer of skin is tough enough to prevent the absorption of numerous agents/ingredients into the circulation.³⁶ The marketed care products are unable to enter the bottom layer of the skin or the bloodstream. This can boost collagen synthesis to cure wrinkles, anti-aging, and stretch marks. Vitamin C and retinoids can only stimulate collagen synthesis. So both are responsible for hyperpigmentation and anti-aging.³⁷

Natural anti-aging constituents

Natural products have been chosen for cosmeceuticals because it promises to provide nutrition and has little medicinal effect or no side effect. Natural anti-aging products are usually hormesis with beneficial effects. The various ingredients are antioxidants, vitamins, moisturizing agents, skin-lightening agents, sun-block agents, barrier repair agents, and anti-inflammatory agents.³⁸ As we all know, antioxidants play a critical part in the skin barrier effect, which protects against free radical damage. There are several antioxidants classified as water-soluble (vitamin C, green tea, glutathione, and coffeeberry) or oil-soluble (vitamin A, E, and coenzymes). Vitamins contribute to the effectiveness of skincare products. Vitamins are natural substances that promote excellent health and a young appearance. Vitamins A, E, and C are commonly present in skin care products and assist the body build collagen to tighten up, wrinkles, scars, fine lines, and so on. Vitamin E is great at neutralizing free radicals and softening skin. Vitamin A is essential for the creation of healthy skin cells and stimulates collagen synthesis, which reduces skin-related issues such

as wrinkles, scars, natural aging, skin burns, stretch marks, and so on. Moisturizing agents are classified into three types: occlusives, humectants, and emollients.³⁹ Occlusives provide an excellent physical barrier to prevent water loss from the epidermal layer. The occlusive characteristics of coconut oil, olive oil, jojoba oil, different waxes, beeswax, and candelilla waxes are among the substances. Emollients soften and smooth the skin while also reducing roughness and flakiness. Almond oil, sunflower oil, fruit oil, cocoa butter, mango butter, murumuru butter, chia seed oil, and other oils can be fluid or thick. Humectants attract water towards the stratum corneum while also binding water from the atmosphere. Examples include glycerine, sorbitol, and honey. Naturally, the oils include fatty acids, which play an important function in preserving the skin barrier by providing anti-inflammatory and anti-irritancy properties. Omega3s (linseed, walnut, and chia seed oil) and Omega6s are the two most significant fatty acids (grapeseed, sunflower, safflower, blackcurrant seed, borage, and primrose oil). These are the components of healthy cell membranes. Ceramide and cholesterol are two major components that help to strengthen the skin barrier.⁴⁰ It gives the skin the appearance of being firm and full. Skin-lightening agents are substances that aid in the reduction or elimination of melanin production. Tyrosinase enzymes are essential for melanin biosynthesis. Other whitening agents either inhibit the tyrosinase enzyme or transport melanocytes to the surrounding keratinocytes for depigmentation through skin tone preparation. It is used in melasma, hyperpigmentation, dullness, and dark age spots. Many more natural ingredients are both safe and efficient for skin whitening. Licorice extract, citrus extract, hydroquinone, kojic acids, vitamin B3, and C are among examples. In this case, inflammation refers to swelling and redness on the skin. The researchers evaluated various plant species. Turmeric, calendula, lavender, licorice root, yarrow, and other herbs are commonly used. Tree nuts have the ability to suppress inflammation-causing molecules as well as free radicals, boost the enzymes and antioxidants, and inhibit mitochondrial malfunction. UV radiation from the sun causes skin burns, discoloration, black patches, skin reddening, wrinkles, and skin cancer. Sunscreen protection refers to UV light protection. Several sunscreen lotions comprise titanium dioxide and zinc oxide powdered minerals that are applied to the skin to prevent and absorb damaging rays. Several natural and organic substances have a minor influence on the photoprotective characteristics of skin care products.⁴⁰ Aloe vera, caffeic acid, tocopherol, green tea, ginger, coconut oil, and other plant extracts.

CONCLUSION

Here the article represents how to overcome the photoaging/skin aging or anti-hyperpigmentation effect on topical skin. The researcher and scientist focus on the development of cosmeceutical products like creams, pastes, emulsions, solutions, and topical agents from natural sources and extracts. The formulation has a moisturizing effect smoothens skin texture and prevents wrinkles, dark spots, skin aging, and

hypo/hyperpigmentation. The application of cosmeceutical products gives us low toxicity and affordable cost. It's easy to apply over the skin and safer and more effective for the skin.

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