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## Mini Review on Cosmeceuticals

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### ABSTRACT

Cosmeceutical is now commonly used to describe a cosmetic product that exerts a pharmaceutical therapeutic benefit but not necessarily a biologic therapeutic benefit. Cosmetics are products that are used to cleanse and beautify the skin (Millikan, 2001). The aim of this review is to summarize cosmeceutical properties of the various botanicals, vitamins, alpha lipoic acid (ALA), Coenzyme Q-10 (CoQ-10), idebenone, polyphenols, and kinetin.

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## INTRODUCTION

The term cosmeceutical is attributed to Dr. Albert Kligman, who identified a hybrid category of products lying on the spectrum between drugs and cosmetics. The difference between a drug and a cosmeceutical is that the former is defined by having a biological effect on living tissue. [1]

The first recorded use of cosmetics is attributed to Egyptian since 4000 B.C [2]. Pharmaceuticals are essentially drug products and are defined as products that prevent, mitigate, treat or cure disease and /or affect the structure or function of the body [3]. Cosmeceuticals is a deliberate portmanteau of these two terms and is intended to connote drug like benefits from an otherwise cosmetic product. Kligman may be described as the father of Cosmeceuticals, a term he popularized [4], but they first appeared in the world market in 1996 [5].

Cosmeceuticals are not regulated by the U.S. Food and Drug Administration (FDA) and, thus, are not subject to premarket requirements for proof of safety or efficacy. Cosmeceutical products often are tested through in vitro studies using silicone replicas of skin and, at best, clinical trials are small, open-label studies usually supported by the cosmetic companies themselves.

Cosmeceuticals are generally presented as lotions or creams and are mostly targeted at dermatological issues [6]. Recently, orally delivered products of similar claims as cosmeceuticals have been labeled as either oral cosmeceuticals or as nutricosmetics or nutraceuticals. Commonly, all these are simply called cosmeceuticals. Recently an alarming term called physician dispensed cosmeceuticals has been used in the United States [7].

The main product lines of human cosmeceuticals are anti-aging while very few are anti acne or moisturizers.

Almost all are the products of research and development (R and D) from basic sciences [6]. As at 2005, the global market was estimated at \$53 billion. Anti-aging Cosmeceuticals control over 95% of these and has a double digit growth in most global markets [8]. Anti-aging cosmeceuticals have been formulated on sound biological grounds but with unsubstantiated clinical claims. Aging may be intrinsic or extrinsic. Restated, the score of the aging process at any time depends on the outcome of dynamic interactions between biological (intrinsic), psychological (intrinsic and extrinsic) and environmental factors [9]. The final pathway to all the mechanism of aging is apparently the same and involves disruption of the network of collagen and elastin [12]. Antiaging cosmeceuticals are therefore designed to repair and/or maintain the body's maintenance and repair systems-so called MRSs.

These formed the grounds for products like cosmeceutical peptides which may contain neurotransmitters, signal peptides or carrier proteins. Up to 500 peptides have been characterized [9] and are theorized to increase growth factor (Rattan, 2007).



Botanical cosmeceuticals contain botanical ingredients with traditional or folk medicine usage. These often include grape seed extracts, Aloe Vera, mushrooms, olive oil, green tea, licorice, coffee Arabica and coffee berry extracts [10]. Antioxidants play a large role in the MRSs. This may explain incorporation of Vitamins C and E into cosmeceuticals sometimes called better cosmeceuticals [11]. Better cosmeceuticals may also contain niacinamide and kinetin [12].

### **Herbal Extracts For Cosmetics:**

Herbals extracts are processed for curing several remedies and serve other health prospective.

Following are the gigantic variety of herbal extracts,

Andrographis Paniculata (Kalmegh), Asparagus Racemosus (Shatawari), Boswellia Serrata (Salai Guggal), Asphalt (Shilajit), Azadirachta Indica (Neem), Bacopa Monnieri

(Brahmi), Camellia Sinensis (Green tea), Centella Asiatica (Mandukparni), Cassia Angustifolia (Sena), Chlorophytum Borivilianum (Safed Musli) and Pudina are some of the prime herbal extracts used in our daily lives. [13]

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Herbal extracts in liquid and other forms have proved to be panacea in the diseases like cardiac problems, digestive disorders and in mental fatigues. In some cases, herbal extracts accuracy was detected more than English medicines which are usually comprised of complex chemicals. Herbal extracts have very less chances of side effects than any other medicines. [14]

Cosmetics made up of herbal extracts for antimarks, fairness, cleansing and hair-care are very popular for their reliability.

### **Polyphenols**

Polyphenols are plant-derived antioxidants that have anti-inflammatory, photo protective, and anticarcinogenic properties. Flavonoids are a subgroup of polyphenols that are popular ingredients in many cosmeceuticals. They include grape seed extract, green tea extracts, and soy isoflavones. Grape seed extract can induce vascular endothelial growth factor expression on keratinocytes to enhance dermal wound healing. [15] Green tea extracts such as epigallocatechin 3-allate have been shown to decrease levels of UVB damage, DNA damage, sunburn, and erythema.

Soy isoflavones include genistein and daidzein. These are antioxidants with anti-inflammatory and anticarcinogenic properties. Isoflavones function as phytoestrogens, which increase skin thickness through an estrogenic effect [16]. Fresh soy milk contains 2 serine protease inhibitors: soybean trypsin inhibitor (STI) and Bowman-Birk inhibitor (BBI). STI inhibits melanosome transfer to keratinocytes, which can lighten the skin. BBI inhibits hair growth presumably as an inhibitor of ornithine decarboxylase.

#### **Botanicals for anti-inflammatory activity:**

Licochalcone A, from the licorice plant *Glycyrrhiza inflata*, has anti-inflammatory properties. The mechanism of action is thought to be dual inhibition of cyclo-oxygenase and lipoxygenase, thereby reducing proinflammatory cytokines and UVB-induced prostaglandin E2 release by keratinocytes [17].

Pycnogenol is an extract of the French maritime pine bark tree, *Pinus pinaster*. It has multiple biological effects, including antimicrobial [18], anti-inflammatory, antioxidant, and anticarcinogenic properties [19]. Pycnogenol may accelerate wound healing and reduce scar formation [20], as well as stabilize elastin fibers [21]. It decreases erythema after UV radiation [22] and improves UV-induced pigmentation [23]. In addition, it reduces the vitamin C radical which, in turn, regenerates vitamin E, thus recycling the endogenous antioxidant enzyme system.

Silymarin is found in the milk thistle plant, *Silbum marianum*, and is touted to decrease the erythema of rosacea. It is a polyphenolic flavonoid that inhibits UVB-induced sunburn, apoptotic cell formation, and edema [24]. Its anti-inflammatory effect is caused by the inhibition of COX-2 and IL-1. Silymarin also has anticarcinogenic effects and has been shown to reduce pyrimidine dimer formation in murine models [25].

Quercetin is a flavonoid found in many common fruits and vegetables that is thought to have antioxidant, anti-inflammatory [26] and anticarcinogenic effects [27]. It counters inflammation by inhibiting lipoxygenase and COX-2. In addition, quercetin is an antihistamine that inhibits histamine release from basophils and mast cells.

Allantoin is derived from the comfrey root and is now commercially manufactured by the alkaline oxidation of uric acid in a cold environment [28]. This botanical has a number of touted effects on the skin. It is an antioxidant, anti-inflammatory agent, and a soothing keratolytic. Allantoin also induces cell proliferation, promotes repair of photo damage, and reduces UV-induced inflammation [29].

Chamomile and aloe vera are botanicals that inhibit cyclooxygenase and lipoxygenase and are soothing anti-inflammatory agents.

Aloe vera is purported to reduce inflammation and enhance wound healing [28]. It also has antibacterial, antifungal, and viricidal properties [29]. Feverfew, a botanical folk remedy for

fevers and inflammation, is an antioxidant/anti-inflammatory booster that inhibits nuclear factor- $\kappa$ B-dependent gene transcription in a manner similar to that of corticosteroids.

Curcumin is derived from the herb turmeric (*Curcuma domestica*), which is used to flavor and color curry in foods. It has antioxidant, anticarcinogenic, antimicrobial, and antiinflammatory effects. Studies show that curcumin's anti-inflammatory effects are mediated through the inhibition of lipoxygenase and cyclo-oxygenase, prostaglandins, and various proinflammatory cytokines. Curcumin can also inhibit collagenase, elastase, and hylauronidase. Whether application of topical curcumin may improve the signs of photo aging is yet to be determined in clinical studies [29].

### **Antioxidants**

Oxidative stressors create inflammatory molecules that lead to the formation of free radicals species. These free radicals are highly reactive molecules with unpaired electrons, and they can cause cellular damage to cell membranes, lipids, proteins, and DNA. Damage to DNA eventually results in collagen breakdown. Free radicals also play a role in 3 additional detrimental processes: inflammation, photo damage, and carcinogenesis. Antioxidants neutralize damaging free radicals by quenching reactive molecules and, thus, protecting cells from both endogenous stress (byproducts of cellular energy) and exogenous stressors (ultraviolet [UV] light, pollution, cigarette smoke).

Antioxidants comprised a group of diverse molecules including, but not limited to, vitamins (A, B, C, E), alpha lipoic acid (ALA), Coenzyme Q-10 (CoQ-10), idebenone, polyphenols, and kinetin. They vary in their abilities to protect against inflammation, photo damage, and carcinogenesis [30].

### **Retinol**

Vitamin A, or retinol, is an antioxidant member of the retinoid family, which includes tretinoin. It has been studied extensively for treatment of photo damage and acne. Available by prescription, tretinoin improves fine wrinkles by increasing collagen production. Retinol is a cosmeceutical with less biological activity than tretinoin that is also less potentially irritating.

#### **Mechanism**

1. Retinol can increase epidermal water content, epidermal hyperplasia, and cell renewal while enhancing collagen synthesis [31].

2. Retinol also interferes with melanogenesis and inhibits matrix metalloproteinases (MMPs), which are involved in collagen breakdown. The clinical benefits include a reduction in the appearance of fine lines and wrinkles and lightening of lentigines.

3. Retinol can be less irritating than the prescription retinoids so for patients who might not tolerated prescription retinoid, they might be able to tolerate an over-the-counter retinol. The over-the-counter retinol will be better tolerated for those who might be sensitive and will still be helpful but not as efficacious as a prescription.

### **The vitamin B complex**

The vitamin B complex includes niacinamide (Vitamin B3) and panthenol (provitamin B5). Topical B vitamins have been studied for treatment of acne, wounds, and bullous pemphigoid and for preventing photo carcinogenesis.

The mechanisms of action for these vitamins have not been completely elucidated. Niacinamide improves the lipid barrier component of the epidermis by increasing ceramide and free fatty acids, as well as the epidermal barrier proteins such as keratin, filaggrin, and involucrin. This results in a decrease in transepidermal water loss. Like Vitamin A, niacinamide is thought to stimulate collagen synthesis by fibroblasts. It can inhibit melanosome transfer from melanocytes to keratinocytes and subsequently reduce melanin content in the skin. Another benefit is the reduction of skin yellowing or sallowness by preventing oxidative glycation of proteins. The use of niacinimide results in improvements in skin tone and texture, decreases of fine lines and wrinkles, and diminished hyperpigmentation. Topical niacinamide is well tolerated and typically does not induce skin irritation responses [32].

### **Vitamin C**

Vitamin C (ascorbic acid) is a water-soluble antioxidant that is essential for collagen biosynthesis. It confers both photo protective and antioxidant effects. Various clinical studies have investigated its use to improve the signs of photo damage.

### **Mechanism**

1. Skin biopsies showed an increase in grenz zone collagen and increased mRNA for type I collagen.
2. The necessary role of vitamin C in collagen biosynthesis makes it important for wound healing.
3. Vitamin C may inhibit elastin biosynthesis by fibroblasts, which may reduce solar elastosis of photo aged skin [33].
4. Vitamin C also has anti-inflammatory properties. It inhibits tyrosinase and decreases melanogenesis, which may contribute to clinical lightening of melasma and lentigines [34].

### **Vitamin E**

Vitamin E ( $\alpha$ -tocopherol) is lipid soluble and, when taken orally, it protects membrane lipids from peroxidation. In the skin, it has been shown to decrease sunburn cells after UV exposure, neutralize free radicals, and also act as a humectant. There is substantial evidence

that combining topical Vitamins C and E enhances their individual antioxidant as well as photo protective effects [16].

### **Alpha lipoic acid**

Alpha lipoic acid (ALA) is a lipoamide synthesized in the mitochondria of plants and animals. It is a scavenger of reactive oxygen species and a metal chelator. ALA regenerates endogenous antioxidants.

ALA is both water and lipid soluble, allowing it to penetrate lipophilic cell membranes and enter the aqueous intracellular matrix. The molecule prevents lipid peroxidation, has anti-inflammatory properties, and acts as an exfoliant. In a split face study, topical 5% ALA applied twice daily for 12 weeks decreased skin roughness, lentigines, and fine wrinkles.<sup>11</sup> Notably, ALA does not protect against UV-induced erythema or reduce the number of sunburn cells [35].

### **Ubiquinone**

CoQ-10, or ubiquinone, is a fat-soluble antioxidant located in the inner mitochondrial membrane of nearly all living cells that is necessary for steps in adenosine triphosphate (ATP) production for cellular energy. It acts by down regulating MMPs. CoQ-10 also inhibits lipid peroxidation in plasma cell membranes [36]. There is good in vitro evidence that CoQ-10 can decrease periorbital wrinkles [37]. Idebenone is a more potent synthetic analog of CoQ-10 that is a powerful antioxidant.

### **Panthenol**

Panthenol is a water-soluble cosmeceutical that easily penetrates the stratum corneum and is a humectant. It is a precursor to pantothenic acid, a cofactor in lipid biosynthesis, and it promotes lipid synthesis to improve the barrier function of the skin .

Panthenol also promotes fibroblast proliferation and epidermal re-epithelialization to promote wound healing. Finally, it has anti-inflammatory and antipruritic effects [38].

### **Growth Factors**

Growth factors comprise a large group of regulatory proteins that attach to cell surface receptors to mediate inter- and intracellular signaling pathways. Wound healing relies on a complex interaction of various cytokines and growth factors.

Growth factors relevant to wound healing may induce new collagen, elastin, and glycosaminoglycan formation and mediate angiogenesis.

One human growth factor presently used in cosmeceuticals is transforming growth factor- $\alpha$ , which is derived from cultured fibroblasts harvested from neonatal foreskin.

Advances in biotechnology have lead to further products such as processed skin cell proteins (PSPTM) harvested from fetal cell lines [39]. Other growth factors include placental extract, recombinant epidermal growth factor, and platelet- derived growth factor.

## Peptides

Peptides maybe used to stabilize and deliver copper into cells. For example, the tripeptideglycyl-L-histidyl-L-lysine-copper complex is used as a copper vehicle. As a cosmeceutical, copper peptide is thought to improve skin firmness and texture, fine lines, and hyper pigmentation [40].

Amino peptides are produced during wound healing. Pal-KTTKS is a procollagen pentapeptide fragment that stimulates collagens I and III and fibronectin production by fibroblastsin vitro [41]. Conjugation of palmitic acid to pal-KTTKS (Palmitoyl-Pal-KTTKS) imparts lipophilic properties that facilitates tratum corneum penetration.

Acetyl hexapeptide-3 (argireline) is a synthetic peptide that inhibits SNARE complex formation, which is involved insynaptic vesicle exocytosis in vitro [42].

## Polysaccharides

Polysaccharides include the family of hydroxy acids: alphahydroxy acids (AHA), beta hydroxyl acids (BHA), and polyhydroxy acids (PHA). The AHAs include glycolic acid(grapes), lactic acid (milk), malic acid (apples), and citric acid(citrus fruits) among others. They are considered to be keratolytics because they diminish corneocyte adhesion in the lower levels of the stratum corneum, allowing exfoliation and improvement in skin dullness. They also function as humectants, possibly by increasing dermal glycosaminoglycans [43], as well as improve stratum corneum barrier function [44]. The exact mechanism of action of AHAs is not known.

BHAs, such as beta-lipohydroxy acid and tropic acid, are exfoliants appropriate for acne prone and oily skin. Salicylic acid was once thought to be a BHA, but it is structurally aphenolic aromatic acid. Its lipophilic structure allows it topenetrate into the sebaceous follicles, thus making it useful for patients with oily skin. Salicylic acid is available in a wide range of concentrations.

PHAs can hydrate, moisturize, as well as exfoliate the skin. They include gluconolactone, which may protect against UV-radiation in vitro [45], and lactobionic acid, which is both an antioxidant and a humectant. Because of their large size, PHAs do not penetrate the skin as easily and are therefore less irritating to sensitive skin [46].

## Pigment Lightening

The most commonly used pigment lightening agent is hydroquinone, which works by inhibiting tyrosinase activity. Tyrosinase is the rate-limiting, essential enzyme in the biosynthesis of melanin. It is available both in over-the-counter and in prescription strengths, and it is often combined with other agents such as retinol, AHAs, vitamin C, and topical steroids [47]. Side effects include an irritant contact dermatitis and, more rarely, exogenous ochronosis.

Glabridin is the main active ingredient in licorice extract and can inhibit tyrosinase activity [47]. In addition, glabridin has anti-inflammatory properties attributed to cyclooxygenase inhibition [48].

Ellagic acid is a polyphenol widely found in plants such as pomegranates, which inhibits tyrosinase by chelating copper at the active center of this enzyme. It may selectively inhibit melanin synthesis only in UV-activated melanocytes. Fatty acids such as linoleic acid act by tyrosinase degradation without toxic effects on melanocytes [49].

Many of the cosmeceuticals already described also have pigment-lightening effects. Vitamins C and E decrease tyrosinase activity. Pycnogenol decreases UV-induced pigmentation.

Niacinamide (B3) inhibits transfer of melanosomes to epidermal keratinocytes. Finally, the 2 serine protease inhibitors found in soy, BBI and STI, can reduce melanin transfer.

## THE TOXICITY OF COSMECEUTICALS

The term 'natural' is frequently used for most components of cosmeceuticals and willingly or unwillingly connotes safety. This is far from the truth. Vitamin E has been shown to cause a significant increase in contact dermatitis [11] while the anti-oxidant P-hydroxyanisole increases skin pigmentation [6]. Some component peptides have also been shown to be carcinogenic [11]. Perhaps the greatest danger is from deliberate adulterations and incorporation of harmful products like steroids and retinoid. These can lead to devastating skin and systemic changes [50]. Microbial contaminants have been reported with unfavorable consequences [6].

The broad categories of cosmeceuticals are antioxidants, growth factors, peptides, anti-inflammatories/botanicals, polysaccharides, and pigment lightening agents.

## CONCLUSION

The great demand of cosmeceuticals has led to development of products to counteract the signs of aging skin, to decrease erythema, and to even out tone and pigmentation. These cosmeceuticals can help protect the skin from photo damage and in some ways repair it through stimulation of new collagen production.

Using them in conjunction with sunscreens and prescription retinoids may enhance results when used as an adjunct to rejuvenating procedures. They can also help to increase tolerability of retinoids by improving the epidermal barrier. With different cosmeceuticals being publicized to impart different effects, an upcoming trend will be the multi-functional cosmetic [51]. The further research in wound healing and biotechnology will serve to expand this field.

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