Continuing Medical Education Article—Skin Care

Review Article

The Truth About Over-the-Counter Topical Anti-Aging Products: A Comprehensive Review

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Learning Objectives:

The reader is presumed to have knowledge of the basic concepts of skin aging. After studying this article, the participant should be able to:

1. Summarize the causes of skin aging.
2. Discuss the commonly used anti-aging compounds
3. Distinguish which products have been proven through double-blinded placebo-controlled studies to have anti-aging effects.

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One of the main objectives for an aesthetic surgery patient seeking consultation is a desire to look younger and reverse the appearance of aging. Most of these patients also use topical creams in addition to undergoing surgical procedures. Over-the-counter (OTC) anti-aging products are a billion-dollar industry to which even young patients who wish to prevent the aging process contribute.

Many OTC products advertise dramatic results, but there have been relatively little scientific data to support these claims. We reviewed the literature on ingredients commonly found in OTC anti-aging creams. We conclude that although many different compounds are marketed as anti-aging products, studies proving their efficacy are limited. Vitamin C and alpha-hydroxy acids have been the most extensively researched products, and their anti-aging capabilities have been demonstrated in the literature. There have also been some promising studies on vitamin A and vitamin B derivatives. Moisturizers have been shown to increase skin hydration and improve the overall appearance of skin. Studies also indicate that pentapeptides can be effective in decreasing facial wrinkles and roughness. However, botanicals, which have become popular over the last few years, require significantly more research to formulate any positive conclusions for their topical application. As aesthetic surgeons, it behooves us to educate ourselves on the most common ingredients found in topical anti-aging products and their efficacy. (Aesthetic Surg J 2007; 27:402–412)

A common reason for patient consultation in a plastic surgery office is aging of the skin. There are two processes that lead to aging: the intrinsic chronologic aging of the skin, which is largely genetic, and environmentally induced aging.[1] Environmental exposure to ultraviolet (UV) radiation, smoking, wind, and chemical exposure result in roughness, fine lines, sagging, irregular pigmentation, and decreased skin elasticity.[1] Cumulative exposure to UV irradiation is one of leading causes of these skin changes. On a cellular level, UV degrades collagen and alters skin connective tissue.

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Many of these alterations in the extracellular matrix are mediated by matrix metalloproteinases that degrade fibrillar collagen (type I and III).[2,3] However, the primary mechanism by which UV irradiation damages skin cells is by the photochemical generation of reactive oxygen species (ROS)—superoxide anion, peroxide, and singlet oxygen—that damage nucleic acids, lipids, and proteins, including collagen.[3,4] This cumulative collagen damage disrupts the structural integrity of skin and contributes to wrinkle formation.

The skin protects itself with naturally occurring antioxidants, such as vitamins A, C, and E, squalene, and coenzyme Q-10, which donate electrons and neutralize the ROS.[5,6] These natural antioxidants become depleted with age and UV exposure.[7] UV radiation also forms thymine dimers—an inappropriate bond between two thymine bases in the DNA. These nucleic acid errors are excised and repaired, but if cumulative damage allows for the replication of a dimer, carcinogenesis results.

In 2000, according to *Time* magazine, Americans spent more than $2 billion on OTC anti-aging products.[8,9] Many OTC products boast dramatic results using various combinations of ingredients to produce the desired youthful effects. To participate in a patient's quest for slowing down the visible signs of aging, it behooves the plastic surgeon to educate him- or herself about the most common ingredients found in OTC cosmetics and their efficacy.

Vitamins

Vitamin A/retinols

Vitamin A is a naturally occurring antioxidant in the skin. The biologically active form of vitamin A is all-trans retinoic acid or tretinoin (Retin-A). Retinoic acid aids in epidermal proliferation, keratinization, and peeling. It also modifies keratin synthesis, fibroblastic proliferation, and collagen metabolism.[10] Topical application of retinoic acid has been widely proven to improve global appearance, fine and coarse wrinkling, roughness, pigmentation, and sallowness in many studies.[11,12] However, retinoic acid is a prescription formulation that can be irritating to the skin and is not used in OTC cosmetics. Only less potent forms of vitamin A are available for nonprescription use: retinol, retinaldehyde, and retinyl palmitate, which is the ester of retinol combined with palmitic acid. All vitamin A derivatives are converted to their biologically active form, retinoic acid, in the skin.[13]

A few experimental studies have investigated OTC vitamin A derivatives as anti-aging alternatives. In 2000, Varani et al[14] found that retinol was effective in improving the extracellular matrix of aging skin. They applied 1% retinol for 7 days on volunteers over 80 years of age. Histologic study of skin samples revealed increased fibroblast growth and collagen synthesis with decreased matrix-degrading matrix metalloproteinases as compared with untreated individuals.

Some studies on retinyl esters have been promising. In 1998, Creidi et al[15] applied 0.5% retinaldehyde to the skin of volunteers for 18 weeks. They used optical profilometry to determine quantitative calculations of skin texture, wrinkling, roughness, and other surface irregularities. With these measurements, they found a significant reduction of wrinkles and surface roughness of the crow's feet area. Vitamin A esters also appear to be protective against the carcinogenic effect of UV radiation. In 2003, Antille et al[16] reported that application of retinyl palmitate on the buttocks of young adult men exposed to UVB rays inhibited the formation of thymine dimers equivalent to that of SPF 20. However, retinyl palmitate has not yet been proven to be an effective anti-aging agent. The studies on vitamin A derivatives are promising, but there have been few large-scale double-blinded placebo-controlled trials investigating the clinical benefits of any of the OTC vitamin A products.

Vitamin B

There has been minimal investigation of the B vitamins as anti-aging ingredients, but a few studies have been encouraging. In a study in which a group of middle-aged women applied topical niacinamide B_3 daily to one side of their face and compared it to the other side as a control for 12 weeks, there were significant improvements in fine lines and wrinkles, hyperpigmented spots, red blotchiness, and skin yellowing. There was also quantitative improvement in elasticity.[17] Nicotinamide, another vitamin B analog, has been shown in in-vitro culture to increase the synthesis of ceramide, a compound that decreases with aging.[18] However, the clinical relevance of this analog has not been established.

A new vitamin B choline analog, called 2-dimethylaminoethanol (DMAE), has recently been investigated. In 2005, a randomized clinical study by Grossman[19] found that application of 3% DMAE facial gel for 16 weeks resulted in improvement of coarse wrinkles, under-eye dark circles, nasolabial folds, sagging neck skin, and neck firmness. These effects did not regress during a 2-week cessation of application. Studies measuring cutaneous tensile strength by subjecting treated

and untreated skin to suction distension have found that DMAE-treated skin has increased firmness.[20]

Vitamin C

Vitamin C is a water-soluble antioxidant and the most plentiful antioxidant in the skin.[6,21] Its biologically active form, L-ascorbic acid, an alpha-hydroxy acid, is a cofactor for collagen synthesis and is naturally found in fruits, vegetables, and tea.[22-24] Vitamin C is one of the most well-studied vitamins in anti-aging and has been proven effective in multiple studies. Reports comparing the clinical appearance of mild to moderately photodamaged facial skin after a 3-month application of 10% topical vitamin C (Cellex-C; Cellex-C International, Toronto, Ontario, Canada) to the hemi-face found statistically significant improvement compared with the untreated hemi-face with respect to surface texture, fine wrinkling, tactile roughness, coarse rhytids, skin laxity, and sallowness.[25]

Many groups have used optical profilometry to demonstrate significant improvements in skin texture, wrinkling, and roughness with vitamin C treatment.[25,26] Histologic proof that vitamin C improves skin has also been published. In 2002, Fitzpatrick and Rostan[27] applied 10% vitamin C to the cheek of volunteers and compared it with the opposite untreated cheek. At 12 weeks, biopsy specimens revealed an increase in the Grenz zone collagen (the connective tissue immediately beneath the epidermis) and increased gene expression of type I collagen in the skin. There have even been significant changes noted with lower concentrations of vitamin C. In another randomized double-blinded placebo-controlled study, 5% vitamin C applied to one forearm of volunteers and placebo to the other forearm for 6 months resulted in increased expression of collagen I, collagen III, and tissue inhibitor of matrix metalloproteinase on the treated side I.[28] Similar studies with 5% vitamin C also found an increase in elastic fibers and more uniform distribution of type I collagen bundles.[29] In 2004, Sauermann et al[30] investigated the epidermal-dermal junction and depth of dermal papilla in volunteers of all ages and found that as people age, the papillae and its nutritive capillary decrease in density. They then applied topical 3% vitamin C on the forearm of volunteers and saw that there was an increase in the dermal papillae with new vessel formation after 1 month of treatment, compared with the opposite forearm where placebo was applied. These studies suggest that vitamin C increases the integrity of the extracellular matrix in the skin. On the basis of the large body of evidence supporting its anti-aging effects, topical vitamin C has proven to be an effective ingredient in OTC formulations.

Vitamin E

Vitamin E is a lipophilic antioxidant that occurs naturally in the skin. Vitamin E scavenges free radicals, preventing their ability to damage the lipid cell membrane. Forms of vitamin E that may be seen on cosmetic labels are tocopherols and tocotrienols. There have been no clinically applicable human studies demonstrating an anti-aging benefit of topical vitamin E. In in-vitro cultures, some antioxidant effects have been noted. In 2002, Chung et al[31] found that human dermal fibroblasts treated with vitamin E show decreased expression of human macrophage metalloelastase in response to UVB radiation. In 1999, Jones et al[32] reported that a vitamin E analog suppressed UVR-induced oxidative stress in human skin fibroblasts in vitro.[32]

The combination of antioxidant vitamins appears to be synergistic. On a molecular level, vitamin C helps regenerate vitamin E from its oxidized form, thus enhancing its antioxidant capacity.[6,33] Application of topical 1% vitamin E and 15% vitamin C for 4 days before irradiation with a solar simulator was shown to decrease thymine dimer and sunburn cell formation in pigs.[34,35] Sunburn cells are keratinocytes undergoing apoptosis—a protective mechanism controlled by tumor suppressor gene p53 to eliminate cells at risk of malignant transformation—and an indicator of UV cellular damage.[36] Although vitamin E appears to be protective, more clinical studies need to be performed on humans before any conclusions can be made about vitamin E as an anti-aging compound.

Antioxidants

Other lipophilic antioxidants found in the skin are coenzyme Q-10 and squalene. These antioxidants have been found to decrease with age and irradiation and have therefore been investigated as anti-aging products.[37-39] Both ubiquinone and idebenone, a synthetic derivative of coenzyme Q-10, have been used as an antioxidant replacement, but studies have shown that topical application does not increase their concentrations in the skin.[38] There have also been no human clinical studies studying the efficacy of coenzyme Q-10 or squalene as a photoprotective anti-aging agent, and a porcine skin study showed that 1% ubiquinone and 1% idebenone applied topically to pig skin daily for 4 days had no photoprotective effect.[35]

Alpha lipoic acid (ALA) is an antioxidant that is not naturally found in the skin but has been used as an additive in cosmetic creams.[40-42] ALA is a potent reactive oxygen scavenger and has been found to repair oxidative damage in vitro.[43] In an animal study, 0.5% ALA was applied to the skin of rats and found to increase collagen synthesis in the dermis and epidermis.[44] In a randomized, placebo-controlled double-blind study performed by Beitner[45] in 2003, 5% alpha-lipoic acid was applied twice daily to the cheek of volunteers for 12 weeks. Laser profilometry showed 50% decreased skin roughness compared with 40% on the placebo, which had carrier cream of 0.3% coenzyme Q-10 and .03% acetyl-L-carnitine. Although this difference was not statistically significant, clinical self-assessment by patients reported subjective improvement with the ALA-containing cream.

Alpha-Hydroxyl Acids

Alpha-hydroxyl acids (AHAs) may be seen on cosmetic product labels as glycolic acid, lactic acid, malic acid, citric acid, alpha-hydroxyethanoic acid, alpha-hydroxyoctanoic acid, alpha-hydroxycaprylic acid, hydroxycaprylic acid, and hydroxyl fruit acids. Many alpha-hydroxyl acids occur naturally in foods. Glycolic acid is present in sugar cane, lactic acid is present in sour milk and tomato juice, malic acid is found in apples, tartaric acid is found in grapes and wine, citric acid occurs in citrus fruits, and ascorbic acid, as mentioned above, is widely found in fruits, vegetables, berries, and tea.[22] The most commonly used alpha-hydroxyl acids in cosmetics are glycolic acid and lactic acid. The Food and Drug Administration limits OTC AHAs to less than 10% concentration. Mild peels of 10% to 40% can be used in salons by trained professionals. Peels with more than 40% AHA concentration can be used only by medical doctors.

Alpha hydroxyl acids thin the stratum corneum by reducing corneocyte (the dead layer of surface skin cells) cohesion and speeding up the normal process of skin cell regeneration and exfoliation.[46-48] At higher concentrations of 25%, AHAs can cause increased epidermal or papillary dermis thickness, increased acid mucopolysaccharides, improved quality of elastic fibers, and increased collagen density.[49] They also can promote increased gene expression of collagen and hyaluronic acid in the dermis and epidermis.[50,51] These findings have been reproduced in many studies and in different species of animals.[52-55]

The degree of exfoliation is directly proportional to the duration of application, and higher concentrations of acids have more potent anti-aging effects.[22] A study comparing 5% versus 12% lactic acid found that application of 12% lactic acid twice daily for 3 months resulted in increased epidermal and dermal firmness and thickness with clinically improved skin smoothness and appearance of lines and wrinkles. With 5% lactic acid, there were similar clinical and epidermal changes but no modulation of the dermis.

However, the clinical changes induced by lower concentrations of alpha-hydroxyl acids still significantly improve the appearance of photodamaged skin without causing as much irritation. In 1996, Stiller et al[56] performed a double-blind vehicle-controlled randomized clinical trial in which 8% glycolic acid or 8% L-lactic acid creams were applied twice daily to the face and outer forearms for 22 weeks. A significant percentage of patients had at least one grade of facial improvement (scale 0 to 9) in photodamage compared with placebo. On the forearms, treatment with glycolic acid cream or L-lactic acid cream ameliorated the overall severity of photodamage, as demonstrated by decreasing sallowness, mottled hyperpigmentation, and roughness. Extensive clinical studies have proven alpha hydroxyl acids to be an effective anti-aging compound.

Botanicals

Plant polyphenols are responsible for the intrinsic antioxidant properties found in botanicals. Polyphenols can be divided into several classes of chemicals: anthocyanins, bioflavonoids, proanthocyanidins, catechins, hydroxycinnamic acids, and hydroxybenzoic acids.[57] Various plants used in anti-aging creams contain these compounds. Anthocyanins are found in red wine and berries; bioflavonoids are found in citrus fruits, soybeans, red wine, *Ginkgo biloba*, and many other vegetables; proanthocyanidins are found in coca, red wine, grape seed extract, green tea, and black tea; catechins are found in tea, chocolate, apples, pears, grapes, and red wine; hydroxycinnamic acids are found in coffee and red wine; and hydroxybenzoic acids are found in fruits, nuts, tea, and red wine.[57]

Bioflavonoids are antioxidant, anticancer, and antiinflammatory.[58-60] Bioflavonoids also inhibit UV-induced matrix metalloproteinases, which cause connective tissue damage to the skin.[2,61] Anthocyanins, a group of flavonoids present in many common vegetables, have been shown to decrease UVB-induced DNA fragmentation and reactive oxygen species in human keratinocytes, thereby decreasing cancer formation.[62,63] Proanthocyanidins are believed to inhibit production of free radicals and inflammatory pathways, such as histamine, serine protease, prostaglandins, and leukotrienes.[64] There have

been many in-vitro cell culture and animal experiments investigating the photoprotective potential of commonly used botanicals, but relatively few randomized placebo-controlled human clinical studies have been conducted. Several representative findings are summarized in the Table. Given the limited data, it is not yet possible to formulate any conclusions on the efficacy of botanicals.

Moisturizers

Skin hydration is important for the overall appearance of the skin. Dryness can cause the skin to appear discolored, flaky, and rough. The stratum corneum (SC) contains corneocytes held together by a lipid bilayer. Lipid membranes in the stratum corneum comprised of cholesterol, free fatty acids (the most abundant being linoleic acid), and ceramides restrict transepidermal water loss (TEWL) and maintain the skin barrier.[96] Corneocytes contain water-soluble molecules called *natural moisturizing factors* that allow the skin to bind water.[97] It is the combined action of binding water and preventing water loss that maintains skin hydration and allows the stratum corneum to be soft and flexible.

Moisturizers contain occlusives, humectants, and emolients.[98,99] Occlusives prevent transepidermal water loss and are comprised of oils or fats such as petroleum, lanolin, mineral oil, vegetable oil, or waxes.[96,100] Humectants are low-molecular-weight substances that attract water. Natural moisturizing factors are naturally occurring humectants. Common humectants used in moisturizers are glycerin, propylene glycol, and urea.[96] Emollients have no hydrating properties, but they are often used in moisturizers to act as a filler between desquamating corneocytes to allow for a smoother skin surface.

There have been only a limited number of studies on moisturizers published in the literature. Petrolatum—the most commonly used occlusive substance—is able to decrease water loss from the skin by about 50% but does not produce any increase in hydration.[101,102] In the epidermis of aged individuals, there is about a 30% decrease in stratum corneum lipid content and significantly delayed barrier recovery.[103] Therefore many of the investigations of moisturizers have involved topical application and replacement of stratum corneum lipids. In a mouse model, all three lipid components (fatty acids, cholesterol, and ceramide) were necessary for normal barrier repair.[104] Betz et al[105] investigated the hydrating power of liposomes—vesicles with a phospholipid bilayer membrane identical to natural cell membranes—in 2005. They found that a liposome made from egg phospholipids applied to the forearm increased skin water content 1.5-fold after 30 minutes and that daily application maintained this level of hydration.

Glycerin (glycerol) and propylene glycol are commonly used humectants. However, there have been few clinical studies demonstrating their hydrating effects. The best clinical study investigating the hydrating and protective effects by glycerol was performed by Gloor and Gehring[106] in 2001. Topical application of 85% glycerol emulsion for 3 weeks in volunteers with normal skin resulted in significant reduction in TEWL measured by three different machines. All other studies in the literature on humectants involved experiments on individuals with atopic dermatitis or looked at barrier repair with skin injury. In a study in which glycerol was applied for 3 days to tape-stripped and sodium lauryl sulphate–damaged skin, faster barrier repair and greater stratum corneum hydration was seen in glycerol-treated sites.[107] However, the results in the literature are inconsistent. In a study looking at topical application of 20% glycerin to the skin of patients with atopic dermatitis, there was no difference in TEWL compared with placebo.[108] Unfortunately, most of the research on humectants involves subjects with preexisting dry skin conditions with altered stratum corneum, and the findings may not be applicable to the hydration of normal skin.

An anti-aging compound that has recently been investigated for its hydrating properties is the vitamin B analog nicotinamide, which was discussed previously. In 2005, Soma et al[109] compared topical application of 2% nicotinamide cream with white petrolatum to patients with atopic dermatitis for 4 weeks. They found that both substances increased stratum corneum hydration, but nicotinamide application was significantly more effective and resulted in a higher desquamation index and decreased transepidermal water loss. On a molecular level, human keratinocytes incubated with nicotinamide showed increased biosynthesis of ceramide, glucosylceramide and sphingomyelin, all stratum corneum lipids crucial to the skin water barrier.[110]

Pentapeptides

In 1993, Katayama et al[111] found that a subfragment pentapeptide of type I collagen lysine-threonine-threonine-lysine-serine significantly increased production of type I collagen, type III collagen, and fibronectin in human lung and dermal fibroblasts in a dose and time dependent manner. To make this peptide more lipophilic and increase its ability to penetrate skin, Lintner[112] linked it to palmitic acid and patented the pentapeptide known as palmitoyl-lysine-threonine-threonine-lysine-

Table. Photoprotective potential of commonly used botanicals

Compound	Findings
Grape seed extract	
Rat	Grape seed extract injected subcutaneously decreased inflammation (dec IL-TFNα, PGE2) in injured ears and paws.[65]
Human beings	Grape seed extract accelerated human healing.[65,66]
Human keratinocytes	Keratinocytes cultured in grape seed proanthocyanidins showed dose-dependent decrease in UVB-induced oxidative stress pathways.[67]
Tree bark	
Hairless mice	Pycnogenol (*Pinus puinaster*) bark extract applied after solar-simulated UV radiation to dorsal skin decreased tumor formation, erythema, and edema.[68]
Human keratinocytes	Keratinocytes cultured with pycnogenol showed downregulation of antiinflammatory genes.[69,70]
Human beings	Witch hazel (*Hamamelis virginiana*) bark extract applied to irradiated skin for 3 days resulted in decrease in erythema.[71]
Soy extract	
Hairless mice	Topical application of genistein (soy extract) 60 minutes before UVB resulted in complete blockage of UVB-induced acute skin burns, dose-dependent inhibition of skin carcinogenesis >90%, and inhibition of photodamage (epidermal hyperplasia and reactive acanthuses) after UVB exposure twice weekly for 4 weeks.[72] Ten percent bifidobacterium-fermented soy extract (BE) applied topically for 6 weeks increased hyaluronic acid content, hydration.[73]
Human fibroblasts	Fibroblasts treated in vitro with soy extract showed increased expression of collagen and hyaluronan.[74]
Human beings	Genistein applied to dorsal skin 60 min before UVB radiation blocked erythema and discomfort.[72] Soy extract emulsion applied topically for 2 weeks showed increased dermal papillae density.[74]
Milk thistle	
Hairless mice	Silbinin (milk thistle extract) applied topically 30 minutes before or immediately after UV exposure decreased number of apoptotic sunburn cells, thymine formation, and compounds responsible for oxidative stress.[74-77] Silbinin applied topically 30 minutes before or immediately after UV exposure decreased tumor formation and markers of cell proliferation and apoptosis.[78]
Green tea	
Mouse	Topical application of EGCG (-)-epigallocatechin-3-gallate (green tea polyphenol) for 10 days before UVB decreased depletion of antioxidant enzymes[79] Topical application of EGCG resulted in reduced UVA-induced skin roughness and sagging, as well as increased collagen secretion.[80]
Rat keratinocytes	Keratinocytes cultured in tea decreased lipid peroxidation production and decreased apoptosis.[81]
Human dermal fibroblasts	Topical application of EGCG has decreased UVA- and UVB-induced collagenase synthesis in dermal fibroblasts.[80]
Human beings	Topical application decreased UVB-induced inflammation and myeloperoxidase activity in skin and decreased pyrimidine fibers.[82] Topical application decreased UVA-induced erythema, sunburn cells, and injury to epidermal Langerhan cells.[83]
Ginkgo biloba	
Mouse	*G biloba* extract applied topically to dorsal skin inhibited croton oil-induced edema (down-regulation of COX-2) induction.[84] *G biloba* extract applied topically to mouse skin increased antioxideant activity (superoxide dismutase & zinc) after UV irradiation.[85]

Table. Photoprotective potential of commonly used botanicals—continued

Compound	Findings
Algae/seaweed extract	
Human keratinocytes	Keratinocytes cultured with algae (*Phaeodactylum tricornutum*) extract showed decreased oxidative protein damage when exposed to UVA and UVB.[86]
Human stratum corneum cells	Cells cultured with algae (*P tricornutum*) extract showed decreased oxidative protein damage when exposed to UV skin cell cultures.[87]
Human skin fibroblasts	Fibroblasts cultured with algal extract showed decreased UVA-induced superoxide dismutase activity.[88]
Aloe vera	
Rat	Topical application to dermal rat wounds showed increased biosynthesis and turnover of collagen, and accumulation of glycosaminoglycans resulting in scars of greater tensile strength.[89-91]
	Aloe vera applied to second-degree burns showed decreased inflammation measured by capillary permeability and leukocyte adhesion.[92]
Rat keratinocytes	Keratinocytes irradiated and cultured in aloe extract and the supernatant injected into rats showed decreased IL-10 and suppressed, delayed hypersensitivity, suggesting an antiinflammatory effect.[93]
Kinetin (N-6 furfuryladenine)	
Hairless dogs	Topical application for 50 days showed normalization of hyperpigmentation and dermal connective tissue organization.[94]
Pig skin	Topical application had no effect on erythema or apoptotic sunburn cell formation with UV irradiation.[35]
Human fibroblasts	Fibroblasts cultured in kinetin passaged multiple times had decreased morphologic alterations.[95]

serine (pal-KTTS). This is the compound that is currently used in OTC pentapeptide-based creams.

The compound received a significant amount of attention after effective anti-aging results were presented at the 20th World Congress of Dermatology in Paris, France in 2002. In vivo studies of cultured explanted human skin incubated with pal-KTTS showed a dose-dependent increase in collagen IV and glycosaminoglycan synthesis.[112] In a double-blind, placebo-controlled study in which .005% (50-ppm) pal-KTTS was applied to the right eye area of female volunteers twice a day for 28 days, optic profilometry revealed a quantitative decrease in wrinkle depth, wrinkle density, and skin rugosity by 18%, 37%, and 21% respectively.[112] Another study in which 25 volunteers were treated with twice-daily applications of 3% Matrixyl (Sederma, Paris, France) (a commercial product containing 100-ppm pal-KTTS) to the half-face for 6 months also revealed significant decreases in wrinkle depth, roughness, wrinkle volume, and main lines density by 21.6%, 16.4%, 24.4%, and 46.8% compared with placebo.[113] Similar results were confirmed in 2005 by Robinson et al,[114] who used the same concentration of pal-KTTS (3 ppm) to treat 93 women in a 12-week, double-blind, placebo-controlled, split-face randomized clinical study.

When compared with a commercially available cream containing 5% vitamin C in 10 volunteers who applied either cream on a half-face twice daily for 6 months, wrinkle depth, roughness, wrinkle volume, and main lines density decreased significantly more on the half-face treated with Matrixyl as compared with the half-face treated with vitamin C.[113] When compared with 0.07% retinol applied twice daily, at 2 months there appeared to be a slightly greater decrease in main wrinkle depth and volume with Matrixyl, but at 4 months, retinol was more effective in all categories. None of these differences were statistically significant.[113] Nevertheless, there appears to be an overwhelming body of evidence that pal-KTTS is effective in decreasing facial wrinkles and roughness.

Conclusion

Although many different compounds are marketed as anti-aging products, there are few studies proving their efficacy. Vitamin C, alpha-hydroxyl acids, and pentapep-

tides have been the most extensively researched compounds, and their anti-aging capabilities have been replicated in the literature. There have also been some promising studies on vitamin A and vitamin B derivatives. Other newer botanicals require more research to formulate conclusions that can be extended to their topical application. Moisturizers have been shown to increase skin hydration and improve the overall appearance of skin.

Despite the limited body of evidence, patients continue to use a variety of OTC products. However, for many patients, OTC remedies alone may not be sufficient to produce the desired effects, and prescription-strength medications or surgical procedures may be necessary. ■

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