The Rationale of Anti-Aging Cosmetic Ingredients

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ABSTRACT

Anti-aging cosmetics are a mainstay in the skin care regimen irrespective of gender or human ethnics. Skin aging involves functional slowdown combined with environmental induced alterations. This paper focuses on cosmetic ingredients that aim at alleviating the signs of skin aging, with proven/controlled results of efficacy. Anti-aging skin care widely benefits from new ingredients and modern evaluation methods that can substantiate the effects of innovative products in a perceivable and sensitive manner. Our approach in controlling skin aging consists of following steps: 1) Developing novel testing methods; 2) Preventing photo-aging by sunscreens that protect from UV damage; 3) Protecting and restoring skin from damage induced by environmental exposure through active ingredients; 4) Boosting the cell metabolism and cell renewal to restore skin mechanical properties and improved appearance.

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INTRODUCTION

Skin aging is a multifactorial process resulting from both intrinsic and external factors. Intrinsic functional alterations resulting from metabolic slowdown that cumulates with age is a major factor resulting in skin aging. External environmental factors include: exposures to solar rays, pollutants such as ozone, smog or particulate matter or lifestyle factors (smoking, alcohol consumption etc). A combination of all these factors leads to a premature skin aging leading to the perception (self-perceived or perceived by others) of an older look than the true chronological age of the skin

The major extrinsic factor of skin aging is UV rays, as evidenced by the clearly altered condition of naturally uncovered skin areas such as the face and dorsum of hands. Extensive studies have demonstrated the damaging effects of acute and chronic solar UVB rays[1] on epidermal cells including DNA damage, mainly on Caucasian skin. However, the last two decades have emphasized the insidious effects of the far more abundant and common (no zenithal hours) UVA rays that penetrate much deeper into skin and that, unlike UVB, are not associated with warning signs such as erythema/sunburn. UVA's are indeed strong inducers of oxidative stress through generating reactive oxygen species (ROS) and of early signs of skin aging through dermal damage[2] and pigmentation disorders. Facial wrinkles, mottled uneven pigmentation, pigmented spots, laxity, and sagging are usual UV-related photo-aging signs.[1] Recently, specific signs of skin aging according to skin color have been identified.[3]

Other extrinsic factors are tobacco and pollutants, as highlighted by recent studies. Tobacco smoking reduces elastin and collagen I-III synthesis resulting in older skin appearance and dull complexion.[4] The skin of subjects who live in highly polluted cities presents higher oxidative stress, higher lactic acid content, and a lower hydration level, as compared to those living in less polluted areas.[5-8]

Developed or fast emerging societies express an overall growing concern for a younger look. Accordingly, there is a strong demand for rejuvenating cosmetic products, treatments, and techniques to reduce wrinkle appearance, restore skin texture, smoothness, radiance, even pigmentation, and to lighten aging spots, etc. This article focuses on cosmetic ingredients that aim at alleviating the signs of both chronological and environmental skin aging, with proven/controlled results of efficacy.

1. Development of Novel Testing Methods

The first requirement for developing a skin anti-aging cosmetic ingredient lies in developing reliable instruments for objective measurements of changes occurring in aged condition and appearance of skin. Visual grading methods for affording quantitative support to clinical evaluation or self-appraisal of subjects are now available together with instrumental/objective methods of skin properties, or imaging the skin surface relief or the ultra-structure of skin at various depths as well as determining the location and amount of various biological molecules of interest, such as melanin, collagen, and elastin.[9]

Photographic charts for grading signs of aging in Caucasian, Asian, dark-skinned subjects have been published.[3] Evaluation scores can be determined by trained individuals at baseline and different time-points of product application or follow up post treatment or sessions.

The palette of techniques[9] used for assessing age-related skin properties and effect of treatment, which include high-frequency ultrasound, laser confocal microscopy, optical coherence

FIGURE 1. Skin aging induced by pollution: clinical signs and biological mechanisms.

Dryness	↓	Desquamation
Increased visibility of pores	↓	Hydration
Uneven skin texture	↑	SC Lipids and proteins peroxidation, decreased barrier function
Increased sebum flow		Aryl carbon receptors activation
Increased lentigines	↑	Inflammation

tomography (epidermis and dermis thickness), fringe projection (wrinkles), colorimetry (skin color, pigmentation evenness), devices for measuring visco-elastic properties, surface texture, and hydration (SkinChip™), have been published.[10-12]

2. Prevention from UV Damage

First line of defense against UV induced skin damage is daily application of photo-stable sunscreens with high UVA protection index. Even short term exposures over long periods of time can add to cumulative damage to the dermal and epidermal structures and functions. The harmful effects of skin exposure to sun (and simulated solar UVA's) including sub-erythemal doses and the efficient prevention of damage afforded by broad spectrum sunscreens have been thoroughly documented albeit mainly on subjects with light skins of phototypes I-III, ie, the most concerned people. Interestingly, a recent study on an ethnically diverse subject cohort treated for 8 weeks with either a SPF 30/UVA PF 20 or SPF 60/UVA PF 20 product showed a significant decrease in lightening of pre-existing face and hand pigmentary abnormalities and the overall lightening of facial skin in subjects with skin of color.[13] No difference was found between the two sunscreens, suggesting the relevance of high UVA protection to prevent hyperpigmentation disorders of sun exposed skin areas, a sign of perceived age in dark-skinned subjects.

Prevention of skin aging can also be obtained by using highly photo-protective products that combine effective UVB and UVA sunscreens, in all skin color phenotypes. The efficiency of combinations of antioxidants (Vit C, Vit E) in alleviating the signs of skin aging has also been extensively studied.

3. Protection and Restoring Skin

Topical antioxidants are among the most adequate complementary products to sunscreens as they protect cells from oxidative stress and UVA-induced ROS that are highly involved in skin photo-aging process. Hydrophilic vitamin C (Vit C) and lipophilic vitamin E (Vit E) are the gold standards for this purpose. Topically applied Vit C enhances the mRNA levels of collagen I and III and epidermal turnover, which improves skin surface condition.[14] Combining vitamins C and E provides an interactive, synergistic pair of antioxidants in tissues, Vit C regenerating and Vit E involved in neutralization of ROS.[14] Stabilized by the plant antioxidant ferulic acid, the combination turned out to efficiently supplement the protection against UV-induced cell damage.[15]

Many reported studies show that extrinsic aging is at least partially reversible and may be retarded or corrected by some cosmetic ingredients. One of the most investigated ingredient has been vitamin A (Retinol), and its derivatives, where a number of clinical trials have proven its benefits. Collagen

FIGURE 2. Quantification and evaluation methods for skin aging.

FIGURE 3. Skin aging in different skin color types.

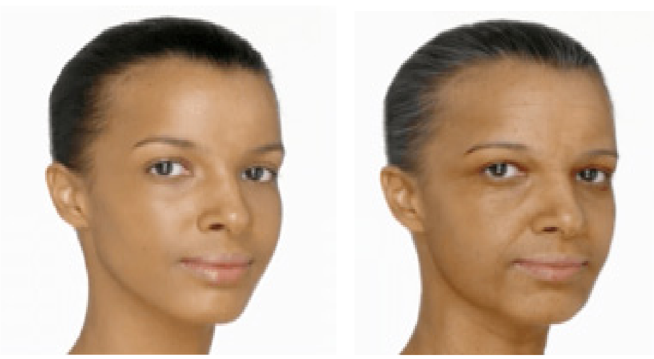
Caucasian

Aging: Fine wrinkles, deep wrinkles in men too.

Asian

Aging: Long lasting pigmented spots UV induced.

African-American



Aging: Long lasting pigmented spots UV induced.

synthesis becomes stimulated, together with an enhanced regulation of epidermal cell proliferation and differentiation. Among others, two 6-month clinical studies on a retinol lotion vs vehicle[16] and on a retinol-sunscreen combination[17] in elderly and 45-60-year-old cohorts led to a significant reduction of wrinkles, as compared to their respective vehicles.

Another successful anti-aging agent is dehydrojasmonic acid, a derivative of a plant stress hormone that possesses various activities. It favors a gentle desquamation of the upper layers of the stratum corneum (SC) thus restoring a "younger" rate of epidermal renewal. It also induces a significant deposit of fibrillin-rich microfibrils in the papillary dermis of photo-aged volunteers[18] and reverses steroid-induced atrophy.[19] Twice daily application for 3 months resulted in significant improvement of crow's feet wrinkles, skin texture, and reduction in facial skin pores. Other restoring approaches are illustrated by the results of studies on a new C-xylopyranoside derivative and fragmented hyaluronic acid that respectively show improved morphogenesis of the whole dermal epidermal junction and clues to the remodeling of the dermal architecture network.

4. "Boosting" or Stimulating Cell Metabolism

The daily use of mild exfoliating agents such as alpha hydroxyacids (AHA's) has been widely recommended to help remove the outermost layers of SC and improve epidermal renewal. In this respect, a close member of this family (β-hydroxyacids), n-capryloyl salicylic acid (LHA), has been demonstrated to have unique properties. Being lipophilic, with slow penetration into the SC layers, LHA acts on loose interfaces, closely mimicking the normal physiological process of desquamation through a controlled thinning of SC leading to epidermal cell renewal similar to that of younger skin. It thus reduces age-related changes including hyper pigmentation, fine lines, and wrinkles.[20]

An interesting boosting approach is by modulating the glucosaminoglycan (GAG) and proteoglycan (PEG) content of the skin. GAG and PEG are major players in inter-cellular communications, cell migration, and tissue modeling. Significant changes in GAG's and PEG's have been identified in aged skin. Hyaluronic acid (HA) is a unique non-sulfated GAG the role of which appears essential in re-epithelialization process, control of proliferation, and migration of keratinocytes from the epidermal basal layer. The high molecular weight (MW) of HA (around 10^6 Da) makes it a surface protective film that cannot penetrate when applied as a lotion onto skin but maintains hydration by trapping water. A fragmented HA, with low MW fragments, that can penetrate and contribute to remodel the architecture of the collagen network has been tested successfully in reconstructed skin models.[21]

Skin aging entails dramatic changes in the extracellular matrix (ECM), particularly in the superficial dermis and dermal epidermal junction (DEJ), the outline of which loses papillary structure and anchor fibers, thus flattening with age. These alterations gather pace with exposure to extrinsic factors. A C-xylopyranoside derivative (C-xyloside) was shown to stimulate the expression and deposit of GAG and key ECM proteins in the superficial dermis, thereby improving the morphogenesis of the whole functional DEJ.[22-25]

The clinical efficacy of C-xyloside combined with blueberry extract was shown on diabetic subjects older than 50 yrs where fine lines were found significantly decreased.[26] In a multicenter blinded study, C-xyloside was also found significantly effective in alleviating skin aging signs in menopausal women.[27, 28]

CONCLUSION

Advances in methods for quantitative and reproducible evaluation of aging signs by clinicians, trained individuals, and panelists have resulted from outstanding progress in imaging techniques with high resolution level and software for observing, recording, and collecting data up to the ultrastructural level. Skin aging status and appearance can thus be objectively assessed to provide optimal answers to huge demand for skin anti-aging options for all skin types. New strategies using prevention, protection and boosting skin metabolism have been devised to test new evidence-based ingredients for skin antiaging benefits. Sun and associated oxidative stress are clearly causative factors in premature altering of the facial appearance and exposed areas. These obviously make sun avoidance and protection by broad spectrum sunscreens with strong absorption in the UVA range a primary daily care, especially when coupled with antioxidants. Mild exfoliative products that smooth coarse or rough skin can prompt a faster epidermal turnover. A large range of carefully composed combinations of evidence-based ingredients can now be used for preventing or reversing troublesome concerns about the deterioration of the facial look and its related aged skin appearance.

DISCLOSURES

Dr. Verschoore and Dr. Nielsen are full-time employees of L'Oréal Research & Innovation.

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