Advancement in skin aging: the future cosmeceuticals

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Abstract Aging is a multifactorial process defined as the accumulation of damage. The aging of the skin is characterized by specific clinical end points, the cause of which is not always thoroughly understood. The skin is exposed to environmental aggressions and the reactive oxygen species produced during cellular metabolism. Damage to the cellular and extracellular components of the skin can be avoided or removed by the appropriate topical application of active ingredients. Sunscreens are essential to avoid damage from the most important damaging environmental agent: solar radiation. Liposomes containing deoxyribonucleic acid repair enzymes and accelerate the endogenous removal of pyrimidine dimers after exposure to ultraviolet radiation. Specific antioxidants reduce the rate of formation of secondary ultraviolet-induced damages, particularly those induced by singlet oxygen. Anti-inflammatory agents, immunostimulants, and enhancers of molecular and cellular detoxification could enter the panoply of new cosmeceuticals to avoid age spots, dark circles, wrinkles, and other clinical aspects of skin aging. © 2008 Elsevier Inc. All rights reserved.

Introduction

One of the consequences of the technologic successes in the western world has been the prolongation of life. Gerontology schools discuss the possibility of extending human life to unexpected limits and search the way to achieve successful aging. Geriatrics has been at least partially successful in limiting the incidence of diseases associated with old age. As a societal corollary, the age at which one sees oneself as “old” has been postponed, and the trend to maintain a “young” aspect has emerged.

Aging has been defined as the accumulation of damages over time.1 Chemicals that help remove damages could be considered anti-aging pharmaceuticals. The question is, what is the meaning of removing damages? The layperson might understand that a hypothetic anti-aging chemical will be able to remove wrinkles or fix osteoporosis. It is not so simple. Damages can be actual molecular modifications (eg, the glycation of a protein or formation of a thymine dimer) or the disruption of a certain physiologic order (eg, the infiltration of fibroblasts in the liver). These damages are formed over time in different molecules in different organs of the body. Their accumulation is made possible by the slow turnover of the molecules where the damages are formed and by the lack of specific repair mechanisms. When these damages reach a certain “critical concentration,” they provoke a loss of the characteristics of youth (eg, wrinkles, age spots, unevenness of skin tone, and dark circles, which are characteristic of old skin, but also bone fragility, muscular atrophy, articular impairment, brain dysfunctions, loss of visual acuity, and loss of the ability to detect specific acoustic frequencies), and it is now too late to start a hypothetic “repair therapy.” Anti-aging treatments have to be performed while the individual is aging, not after the individual has become “visibly” old.

The first and foremost priority in the development of anti-aging pharmaceuticals and cosmeceuticals is an understanding of the aging process.

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Skin aging

Lines and wrinkles

Environmentally provoked damages to vital molecules (eg, deoxyribonucleic acid [DNA] or membrane lipids) within an epidermal or mesenchymal cell trigger the onset of inflammatory reactions that follow different pathways but share a common feature: the activation and infiltration of macrophages, monocytes, and other immune cells. The infiltrating immune cells release proteases and reactive oxygen species that damage the elastic fibers and perhaps the ground substance. These damages and the synthesis of new, disorganized elastic fibers that occur over time are believed to be the cause of the loss of elasticity that is observed in women at the onset of menopause. Indeed, the loss of capability to retain water, provoked by the lack of estrogen, adds to the disorderly structure of “old” elastic fibers in the skin to provoke the onset of visible signs of aging, such as dermal thinning, fine lines, and wrinkles.2

To accompany the process of aging, chemicals that can contribute to the repair of DNA after ultraviolet insult have been developed in recent years and are being used both as pharmacologic treatment of hereditary diseases (eg, Xeroderma pigmentosum) and as cosmeceutical care of healthy skin after exposure to solar radiation. Among these, T4 endonuclease V, when encapsulated in specific vesicles, can penetrate into the cells in the basal layers of the epidermis and promote the incision step to remove bulky DNA damage.3 There are also extracts from marine microorganisms containing DNA photolyase that, when encapsulated in specific vesicles, can penetrate into the cells of the basal layers of the epidermis, bind to pyrimidine dimers, and split them when exposed to blue light.4 By reducing the time necessary to achieve DNA repair, these chemicals reduce the time during which the cell releases proinflammatory signals, reduce the accumulation of inflammation-caused damages, and slow the rate of aging.

To accompany the process of skin aging while avoiding major damages to cell lipids, antioxidants have been studied as tools to prevent skin aging. A number of chemicals and plant extracts have been characterized for their capability to scavenge superoxide ions or hydroxyl radicals and to catalyze the breakdown of peroxides. Vitamins C and E, nordihydroguaiaretic acid, and eukaryon are a few select examples of the panoply of antioxidants currently used in anti-aging cosmetic products.

Singlet oxygen is a reactive oxygen species that is now receiving attention in connection with sun protection. Singlet oxygen may be the most abundant reactive oxygen species produced by solar radiation in the skin. Indeed, molecules able to absorb ultraviolet B and A, be they naturally encountered in skin (eg, tryptophane or riboflavin) or exogenously added to the skin (eg, some ultraviolet filters), possess the capability to transfer to oxygen the energy they acquire when absorbing an ultraviolet photon. By doing so, they generate a reactive chemical species called “singlet oxygen.”5 Singlet oxygen is able to react quickly with neighboring singlet oxygen. Human cells are equipped with catalase and superoxide dismutase to handle peroxides and superoxide, respectively, but there is no endogenous enzymatic defense against singlet oxygen.

Age spots

With age, the surface of the skin becomes irregularly covered with pigmented spots no larger than a few tenths of a square centimeter. The nature of the pigment is not fully determined, and the cause of these age spots is only partially understood. Exposure to solar radiation in a “youth” is recognized as a possible cause of the onset of age spots later in life, even though the individual might have avoided solar radiation for several decrenials between “youth” and “old age.” In some instances, the age spot is the consequence of an unusual invagination of the epidermis into the papillary dermis.6 In this case, the increased epidermal thickness and number of melanocytes per unit of surface are sufficient to provoke the apparent darkening of the surface. In other instances these dark spots seem to contain colored molecules other than melanins, and this might explain why antioxidants and tyrosinase inhibitors only meet partial success when used for “whitening.”

New cosmeceuticals to remove age spots and achieve whitening will be developed when the chemistry, biochemistry, and stereochemistry of colored molecules is understood. Indeed, we not only need to know the chemical species of these colored molecules to have a chance of altering their chromatic properties, but we also have to understand how cells remove unwanted bulky metabolites via ubiquitination and proteasomes to enable the cells making all of the cleaning. The stereochemistry of the clusters of colored molecules may be important because the organization of these molecules might have more of an effect on the absorption and scattering of light than the actual amount of the molecules themselves.7

Unevenness of tone

Another undesired effect of aging is scattered redness, perhaps associated to spider veins and the increased visibility of the capillary vessels, which is particularly noticeable in the sensitive skin of white persons or in skin subjected to extreme cold, as it is the case for the skin of the billion or so humans living in the upper northern hemisphere. Cosmeceuticals that can regulate the blood flow by stimulating the contraction of the smooth muscles when the skin is exposed to extreme temperatures may be helpful not only in
protecting the skin against the immediate damages of low
temperatures but also in delaying the onset of spider veins
and scattered redness.

Dark circles

Psychologic stress alters the physiologic characteristics of
stressed individuals. Immune depression and susceptibility
to strokes are the two main consequences of psychologic
stress. The first primarily affects those who think they cannot
cope with stress, and the second is mainly observed in
individuals who think they can cope with stress.8,9 By
affecting the immune and circulatory systems, psychologic
stress also affects the exterior aspect of the skin, which is in
turn characterized by an excess or a total lack of redness and
by generalized dark circles under the eyes.

Nervous endings release signaling molecules and tissue
plasminogen activator, which might have catastrophic
consequences on the structure of the capillary vessels.10
This change in structure may play a role in the physical
properties of blood vessel walls with visible effects on the
surface of the skin.

Understanding the effects of psychologic stress on the
immune system of the skin is a crucial step in understanding
the effects of stress on the health and appearance of the skin.
New cosmeceuticals are anticipated to be developed when
sufficient knowledge is gathered.

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