

## Photo-Aging: A Literature Review

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*The average age of people has been increasing over the years, triggering more awareness and more interest in the study of regenerative medicine, especially degeneration of the skin which is an organ that is crucial noticeably for appearance. Skin aging is the multifactorial process both internal and external factors, such as, age, sex, race, disease of internal organs and environmental exposure. However, the main causes of skin degeneration are heredity and sunlight. The latter induces the most skin degeneration. Due to strong sunlight all year round in the tropical zone, serious skin degeneration has an effect on Thai people, causing both anatomical change and microscopic change. Thus far, many studies have been conducted on pathogenesis and prevention of Photo-aging, as well as regeneration of damaged skin. The current article helps make further progress to these issues.*

**Keywords:** Photoaging, Ultraviolet light, Anti-aging, Aggravating factor

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Skin degeneration affects mental health of those who have it and their intimates<sup>(1)</sup>; hence, the significance of people's external look has been increased recently. In addition, the average, human age nowadays is rising, meaning the number of the elderly is higher<sup>(2)</sup>. As shown in the year of 2007, the number of the elderly is seven percent of the world population and it is more likely to go up to ten and sixteen percent in 2025 and 2050, respectively<sup>(2)</sup>. For Thailand, the National Statistics Office reveals that in 2008 there were seven percent of the elderly, and it tends to increase. The statistics indicate that the higher the average age, the more there are elderly, and consequently, the more skin degeneration trouble. The pathogenesis of skin degeneration includes natural and aggravating factors<sup>(3,4)</sup>. These factors are heredity which is internal and hard to control and environmental which is external<sup>(4-6)</sup>. Instances of the latter are cigarette smoke, water and air pollutions, and sunlight. Sunlight has the most influence on skin degeneration<sup>(6)</sup>; thus, those who reside in Thailand where there is strong sunlight all year round are more prone to have skin degeneration problems.

Sunlight is the sun's energy waves going through the atmosphere ozone to the Earth. It has

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several levels of wavelength/frequency, but the major wavelength is infrared light, visible light and invisible light called ultraviolet (UV). UV, the most powerful cause of skin degeneration, is divided into UV-A, UV-B and UV-C, with wavelengths of 315-400 nm, 280-315 nm, and 100-280 nm, respectively<sup>(6,7)</sup>. When the sunlight touches the skin, immediate effects occur<sup>(7)</sup>, for example, the beginning of skin damage, changes in skin immunization, and synchronizations of vitamin-D. Prolonged sunlight exposure even causes persistent changes, *i.e.* skin cancer and photo-aging.

Several theories have explained the process of photo-aging, but none is accepted in consensus. Nonetheless, most scientists believe that exposure to UV stimulates change in the immune system, resulting in mediator substances and matrix metalloproteinases (MMPs) which consist of several enzymes such as collagenases, gelatinases. These enzymes are closely related to both the generation and the degeneration of connective tissues. According to pathogenesis, photo-aging is connective tissue disorders in quality and quantity<sup>(3,4)</sup>, especially elastosis and proteoglycans. These disorders can be observed via diagnosis of anatomical changes<sup>(4,7,8)</sup>. The changes are in the forms of wrinkles, dehydration, less elasticity, uneven skin tone and pigmentation.

The skin problems mentioned above are of interest among beauty specialists and medical

professionals, who seek ways of degeneration prevention, skin care and regeneration, for instance, the external use of anti-wrinkle and depigmentation products and the massage therapy. Yet, there has been no detailed collection regarding skin degeneration. The present study was aimed extensively to present knowledge and understanding of skin degeneration, anatomical and microscopic skin changes, including prevention, treatment and regeneration of photo-aging skin, in the hope that dermatologists and skin care professionals, as well as academic experts can better understand the most current topics presented and apply this knowledge to do further research about them and develop higher technology to better solve the problems earlier mentioned.

### **Pathogenesis of skin degeneration**

Skin degeneration has been studied for many years and two major theories have been proposed in order to explain the degeneration process: the Programmatic Theory and the Stochastic Theory<sup>(3,4)</sup>, as described below.

The Programmatic Theory explains human genetic degeneration in different ethnic groups through telomere shortening. That is, in a normal state, chromosomes grow longer from the end in mitosis so as to substitute their shortening in cell division. In general, this degeneration occurs in patients with premature aging syndrome where telomere shortening and fibroblast disorders occur. Fibroblasts are cells that form collagen fibers, resulting in telomere shortening of over 30% of the normal length. Previous studies have shown that the collagen shortening rate in the elderly is close to that in these patients. In addition, cell senescence also induces chromosome shortening, cell division disorders, cell growth discontinuation and degenerated-cell devastation disorders. Incidentally, chromosome shortening can be used in cancer treatment.

Apart from the Programmatic Theory, the Stochastic Theory explains skin degeneration via inherited cell destruction and environmental damage, *e.g.*, cigarette smoke, water and air pollutions and sunlight. Sunlight causes the most damage to skin by the formation of reactive oxygen species-ROS, which demolish structures of certain normal biomolecules such as DNA and protein deterioration, as well as some proteins that are crucial for enzymes. Furthermore, hereditary diseases in relation to premature aging syndrome as found in the Programmatic Theory, *e.g.*, Cockayne syndrome and Ataxia Telangiectasia. The

destruction of DNA in patients of these diseases can be worsened by external factors. Moreover, the older the age, the more deteriorated the immune system<sup>(10)</sup>. As a consequence, B-lymphocytes and T-lymphocytes are less effective, causing higher risks to infection and cancer.

### **Skin changes**

Skin is gradually deteriorated by changes in skin<sup>(4)</sup>, *i.e.* wrinkles, uneven skin tone and skin disorders such as defects in skin barrier, chemical clearance, sensory perception, wound healing, thermoregulation, and sweat and oil production. Besides, there are also changes invisible to the naked eyes, *i.e.* microscopic changes<sup>(8)</sup> These changes mostly occur in the epidermis and the dermis<sup>(3)</sup>.

Changes in the epidermis are the most evident in the dermo-epidermal junction. The junction of people between the ages of 30-90 is 50% thinner. Also, at the ages between 40 and 60, women's dermo-epidermal junction is far thinner than men's. This is because women's dermo-epidermal junction declines the most at this period while men's worsens in a consistent rate during their adulthood. For changes in the dermis, the dermis in the elderly is 20% thinner, and it is much thinner around the area with exposure to a large amount of sunlight. In addition, degeneration also occurs in connective tissues in the dermis<sup>(3,4,7)</sup> such as collagen and elastin. It is found that the amount of collagen in adults decreases by approximately 1% every year, and the amount and the size of elastin go down in the early adulthood and elastin deteriorates in the old age<sup>(4)</sup>. The deterioration of connective tissues is referred to collagen fractures<sup>(9)</sup>, as shown via electron microscope. The changes in the epidermis and the dermis impede skin from its normal uses. The changes are drastic in skin with extended sunlight contact.

### **Photo-aging**

Once exposed to sunlight, skin is abruptly changed in the external layer, the immune system and the Vitamin D-synthesis. Prolonged sunlight exposure can induce chronic changes, *i.e.* skin cancer and photo-aging. The latter causes skin problems<sup>(4,7)</sup> such as wrinkles, aridness, roughness and discoloration. According to Glogau Photo-aging Classification-Wrinkle Scale<sup>(4,12)</sup>, there are 4 wrinkle levels that are compatible with photo-aging classification, based upon the external factor: exposure to sunlight. The wrinkle levels are described below.

Level 1: No wrinkle. The first stage of change is changes in skin tone and occurrences of minor wrinkles found in people at the age between 20 and 40. However, no skin thickness is seen.

Level 2: Wrinkle on motion. This occurs in people between 30-50 years of age, who have wrinkles during facial expressions or smiles, together with increasing pigmentation and invisible thicker skin owing to microscopic disorders.

Level 3: Wrinkle at rest. It is found in people above 50 years old, who possess wrinkles despite no muscle movement. Part of the facial skin is obviously thicker, and discoloration occurs.

Level 4: All wrinkle. People above 60 years of age are in this severe stage, possibly found together with malignant tumor.

Photo-aging stated above is more drastic than normal degeneration due to UVA<sup>(4,6)</sup>, causing reactive oxygen species-ROS that can destroy DNA. Besides, UVB<sup>(6,9)</sup> also induces changes in molecule complexity. That is to say, once UVB contacts human skin, it aggravates connective tissues and activated protein (AP)-1 and nuclear factor (NF)-kB to increase the higher number of enzymes, called extracellular matrix-degrading metalloproteinases, which consist of collagenase, stromelysin and gelatinase at the epidermis and the dermis. These enzymes also work harder to eliminate connective tissues, *i.e.* collagen and elastin. In addition, UV also makes the decrease of procollagen generation, therefore, procollagen 1 and 3 is reduced. Consequently, after extensive exposure to the sunlight, wrinkles occur<sup>(9)</sup>. As seen, the sunlight can cause changes of DNA qualitatively and quantitatively. Apart from wrinkles, another vital problem is discoloration<sup>(4,7,9)</sup>. There are two types of discoloration: 1) immediate darkening, which is the consequence of melanin distributions, and 2) pigmentation after prolonged contact with the sunlight, which is the result of the increasing number and work of melanocyte cells. This is in fact human's natural protection process. However, nowadays innovations of skin prevention, remedy and regeneration of photo-aging skin have been examined.

### **Protection of photo-aging skin**

Although the science of skin regeneration has been extensively developed, protection is still the most important key<sup>(3)</sup> because without appropriate prevention, any remedies can be less effective<sup>(11)</sup> and may make it worse. For example, the skin of patients under treatment with Hydroxy acid<sup>(11)</sup>, which rids the

upper layer of the skin and moisturizes the skin, can absorb 20 percent of UVB more than can normal skin. Therefore, it is necessary to prevent UVB contact. Four simple and basic ways of prevention are: 1) cover the skin with clothing, 2) wear a hat, 3) avoid being in the sunlight, and 4) use sunscreen cream<sup>(4,6)</sup>. For better effective protection, use a sufficient amount of sunscreen cream. Most people use less than half of the amount needed<sup>(11)</sup>. This prevention can help reduce appearances of wrinkles and discoloration, as well as risks of actinic keratoses and squamous cell carcinoma.

### **Treatments and regeneration of photo-aging skin**

Wrinkle and sagging skin is not an unavoidable result of aging, yet it is a healable disease<sup>(6)</sup>. Thus, people should try to keep their skin healthy as long as they can and in any possible effective ways. Statistic results of skin care studies show that other than surgery, skin specialists use injection of botulinum toxin which paralyzes muscles around the injected area<sup>(11)</sup>. This procedure was approved by the Food and Drug Association (FDA) of the United States in 2003. Another method of skin regeneration is microdermabrasion which peels off the epidermis<sup>(11)</sup> and stimulates formation of new skin cells. Also, soft tissue augmentation is widely used for deep wrinkles. Furthermore, chemical peelings and laser treatments utilize heat and power waves which aggravate the formation of collagen. As seen, between 1997 and 2002, advanced technology for beauty care mentioned above is being increasingly used, up to three and a half times as much as in the previous years<sup>(11)</sup>.

Apart from the skin regeneration methods stated earlier, consumption by eating or rubbing natural extracts in supplementary food that helps prevent free radicals<sup>(4,6)</sup>, *e.g.* E and C vitamins, co-enzyme Q10, as well as flavonoid extracted from several herbs<sup>(11)</sup>, *e.g.* green tea or Chinese tea. However, reports on benefits of supplementary food intake are still insufficient. vitamin-A acid treatment is approved by FDA that it helps delay skin aging by reducing roughness and pigmentation and giving hormone substitutes<sup>(4,11)</sup>.

It is believed that it can add collagen under the skin, help keep fluid under the skin, and reduce skin cancer risks<sup>(13,14)</sup>. Hence, skin specialists and patients should seriously consider options of regeneration methods before deciding to use any products or treatments, for increasing knowledge has been given continually. Sometimes, recent research shows that a certain regeneration methods, *e.g.*

hormone substitution, which is widely used, is now proven to be useless and even has bad side effects, more risk of breast cancer and ovary cancer<sup>(13,14)</sup>. As a consequence, the method is no longer approved to be used for skin regeneration.

## Discussion

As knowledge and technology relative to photo-aging have been dramatically advanced, physicians responsible for patients of photo-aging and academics interested in photo-aging should possess the most recent knowledge of its pathogenesis, anatomical and microscopic changes, prevention and treatment, as well as regeneration. Nonetheless, several issues on photo-aging are still in debate<sup>(3,11)</sup>, *e.g.*, benefits of products in use and the complicated pathogenesis of skin degeneration. Two major theories of pathogenesis of skin degeneration have been proposed, and the combination of both theories is currently applied<sup>(3,4)</sup>, *i.e.*, both heredity and environmental<sup>(4,6)</sup>, especially the sunlight<sup>(6)</sup> are key causes to skin degeneration. A good example for the pathogenesis based on heredity and the environment is the case of patients with premature aging syndrome<sup>(3)</sup>. Their skin degenerates rapidly at an early age, and it deteriorates swiftly with sunlight exposure.

Apart from the pathogenesis of skin degeneration, other possible factors that promote or impede photo-aging are investigated. For example, an observation of farmers working in the field with heat and humidity is attempted to find out whether, other than sunlight, heat and humidity accelerate skin degeneration. The hypothesis is worthy of studying Thai people in different regions of Thailand, which differ in atmosphere and geography, as well as ways of living such as consumptions of diverse nutrients. Besides, it is interesting to examine whether certain nutrients affect skin degeneration and whether people in each region or even province have dissimilar rates of skin degeneration, and if so, what causes the distinction. These hypotheses have not been studied in depth. Nevertheless, results from studies on these hypotheses should bring about advantages to the delay of skin degeneration due to housing developments that help control external factors causing skin degeneration. Furthermore, the results can be used to improve skin products for better control of the external factors.

One intriguing topic of skin product improvement is research on Thai herbs that can hinder skin degeneration. Successes of herbal skin product

development can fulfill the world's market high demand, which is around 4.4 quadrillion Baht yearly<sup>(15)</sup>, but Thailand exports herbs for only 1,560 million Baht worth per year. Even though Thailand produces 13,000 types of local herbs, only 5-6 types are exported<sup>(15)</sup>. Thus, promotion of local Thai herbal products for skin protection and regeneration is in need. This can also help increase incomes of cultivators and manufacturers. Besides Thai herbal promotion, ways to select skin treatment and products in all forms should be suggested due to on-going enhancement of knowledge and technology. Many products used in the past are now disapproved due to their side effects discovered lately<sup>(4,11)</sup>. The most essential and effective way for skin care is to prevent and avoid sunlight<sup>(3)</sup>.

## Conclusion

Hitherto, it is widely accepted that both internal and external factors are causes of skin degeneration<sup>(3,4)</sup>. Sunlight is the most crucial factor that affects skin degeneration<sup>(6)</sup>. Though the degeneration process due to sunlight is not evidently known<sup>(3,11)</sup>, it is generally believed that UV damages the skin the most<sup>(4,6)</sup>. UVA destroys DNA<sup>(4,6)</sup>, and UVB damages connective tissues of collagen and elastin<sup>(4,6,8,9)</sup>. UV also reduces procollagen distribution, causing the decrease of collagen amount. Although there is no clear explanation how skin degeneration occurs<sup>(4,6)</sup>, it is plausible that many factors are involved, including the decreased distribution and disorder of connective tissues due to DNA and connective tissues ruined by UV.

No matter what factor damages the skin anatomically and microscopically, the best way to protect the skin is to avoid sunlight exposure<sup>(3)</sup> by wearing clothes, which provide full coverage to the skin, and use suitable sunscreen cream<sup>(4,6)</sup>. There are other effective ways for skin treatment and regeneration, which yield different results. However, before making a final decision to choose a particular product or treatment, we should consider its description, advantages and disadvantages, as well as potential side effects. Moreover, the authors should keep up with more advanced knowledge and technology pertinent to skin degeneration by on-going research conduction.

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## การเสื่อมสภาพของผิวหนังจากแสงแดด

วิกันดา ลิ้มปိုင်คนันต์, วิชชุดา ลิ้มปိုင်คนันต์

ปัจจุบันอายุขัยโดยเฉลี่ยของประชากรเพิ่มขึ้นและมีแนวโน้มสูงขึ้นอีกในอนาคต ทำให้เกิดกระแสความตื่นตัวและสนใจในศาสตร์แห่งการชะลอวัยเพิ่มมากขึ้น โดยเฉพาะการศึกษาเกี่ยวกับการเสื่อมสภาพของผิวหนัง ซึ่งเป็นอวัยวะที่มีความสำคัญต่อรูปลักษณ์ภายนอก สาเหตุเกิดได้จากปัจจัยกระตุ้นทั้งจากภายในและภายนอก ปัจจัยภายใน อาทิเช่น อายุ เพศ เชื้อชาติ โรคภัยไข้เจ็บ แต่ที่มีส่วนสำคัญมากคือ พันธุกรรม ปัจจัยภายนอกที่สำคัญและก่อให้เกิดการเสื่อมสภาพมากที่สุด คือ แสงแดด โดยเฉพาะอย่างยิ่ง ผู้ที่อาศัยอยู่ในพื้นที่ที่มีแสงแดดมากตลอดทั้งปี เช่น ประเทศไทย การสัมผัสถูกแสงแดดปริมาณมาก และเป็นระยะเวลายาวนาน จะทำให้เกิดการเปลี่ยนแปลงสภาพของผิวหนังทั้งทางกายวิภาคและจุลกายวิภาค ปัจจุบันมีผู้สนใจศึกษากลไกการเกิดพยาธิกำเนิด การป้องกัน รักษา และฟื้นฟูการเสื่อมสภาพของผิวหนังจากแสงแดดเป็นจำนวนมาก ทำให้ความรู้ในเรื่องนี้ก้าวหน้าไปอย่างรวดเร็ว ดังที่ได้ปรากฏในบทความฉบับนี้