
Development of ASTALIFT Renewal Products

Eriko INUI*, Taichi MURAGUCHI*, Hiroyuki KITAOKA*, Mikinaga MORI*,
Toshihiko SAWADA**, Tadao SHIBAMOTO**, Atsushi ORIKASA***, and Kouzou NAGATA*

Abstract

The ASTALIFT series is a comprehensive anti-aging skincare brand, developed by applying Fujifilm's photo technology. After five years of success in the market, we renewed the ASTALIFT series having enhanced anti-aging capabilities realized by adding lycopene and an analog of resveratrol in appropriate form. We discovered novel benefits of lycopene, such as its ability to promote antioxidant production in human skin cells and boost astaxanthin's antioxidant capacity. We stabilized the lycopene in nano size, further enhancing the total antioxidant capacity. This nano lycopene is added to all products of this new series. Moreover, we also discovered that mesh collagen (type IV collagen) plays an important role in increasing the thickness of the epidermal layer; and thus, added high permeable resveratrol, which exerts a protective effect on mesh collagen, into one of the new series products, "ASTALIFT ESSENCE DESTINY".

1. Introduction

In September 2007, we released the "ASTALIFT" skincare range of cosmetics that impregnates skin with moisture to restore its freshness and resilience. It is the fruit of our experience in collagen research, anti-oxidization technology, nanotechnology, and photoreaction analysis/control technology cultivated in the photography domain. Containing a high antioxidant ingredient, astaxanthin, and a moisturizing ingredient, collagen, ASTALIFT has been promoted as an anti-aging functional cosmetic.

In September 2012, five years after its first launch onto the market, we updated the range by further enhancing its anti-aging functionality and released it as "Advanced cosmetics moving ahead". In the new range, nano-lycopene is included in all the items to increase their comprehensive antioxidant capacity. In addition, "ASTALIFT Essence Destiny" has joined the lineup as a feature item containing high-permeability resveratrol that we discovered while delving into our unique collagen research.

In this paper, we will report the details of the novel function of lycopene that we discovered in the research of anti-oxidization technology, nanotechnology, and the research of the usefulness of mesh collagen.

2. Advances in research on anti-oxidization

2.1 Research on lycopene's functionality

Lycopene is a kind of carotenoid and a red pigment present abundantly in tomatoes, watermelons and persimmons. It is known to have high antioxidant capacity among the antioxidant ingredients that eliminate active oxygen caused by UV-rays and environmental damage. In addition, it has been reported to have anticancer effects and to be able to relieve diabetes¹⁾. Focusing on these high capabilities of lycopene, we promoted research and discovered two new functions of lycopene: improving skin's self antioxidant capacity and improving astaxanthin's antioxidant capacity.

2.1.1 The effect of lycopene on improving skin's self antioxidant capacity

Human skin suffers oxidative damage by aging and being exposed to strong UV-rays, which is known to be the cause of wrinkles and blemishes. To protect skin from such oxidative damage, humans have a function to produce antioxidants *in vivo*. However, it has been reported that this function weakens with aging²⁾. To combat this, we put Nrf2 protein that controls the production of various *in vivo* antioxidants on the target. Normally, Nrf2 protein exists in the cytoplasm but, when damaged by oxidation,

Original paper (Received December 4, 2012)

* Pharmaceutical & Healthcare Research Laboratories
Research & Development Management Headquarters
FUJIFILM Corporation
Ushijima, Kaisei-machi, Ashigarakami-gun, Kanagawa
258-8577, Japan

** Analysis Technology Center
Research & Development Management Headquarters

FUJIFILM Corporation
Nakanuma, Minamiashigara, Kanagawa 250-0193,
Japan

*** Product Marketing Group
Life Science Products Division
FUJIFILM Corporation
Akasaka, Minato-ku, Tokyo 107-0052, Japan

it moves to the nucleus and induces the expression of a group of antioxidant genes. Thus, the production of various antioxidants is promoted there (Fig. 1-a).

We newly discovered that lycopene increases Nrf2 protein inside the nucleus of a human skin cell and induces the expression of the glutathione synthetase (GSS) gene as an *in vivo* antioxidant; and that it increases intracellular glutathione abundance (Figs. 1-b1, 1-b2 and 1-b3). It was also confirmed that the increase of intracellular glutathione abundance by lycopene inhibits cell injury by oxidative damage (Fig. 1-b4).

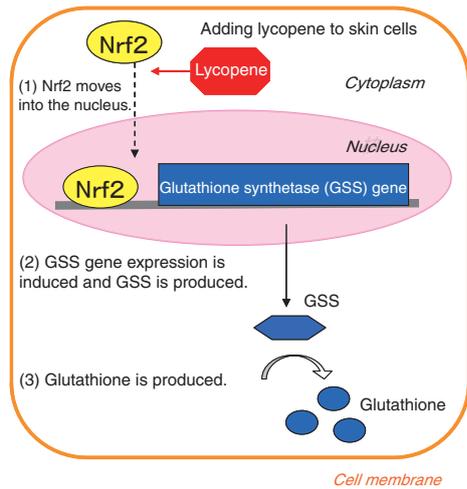


Fig. 1-a Glutathione synthesis mechanism.

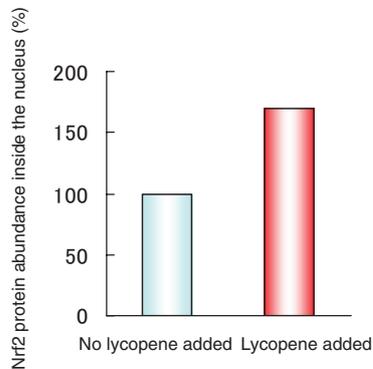


Fig. 1-b1 Effect of lycopene on Nrf2 protein in nucleus.

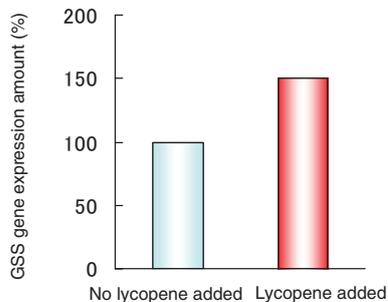


Fig. 1-b2 Effect of lycopene on gene expression of glutathione synthesis enzymes.

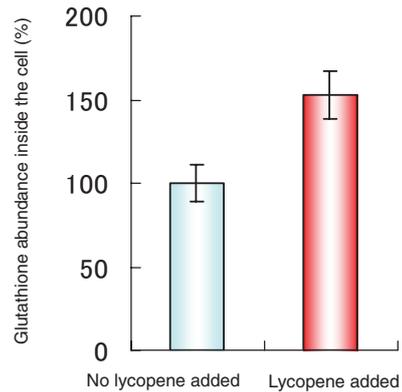


Fig. 1-b3 Effect of lycopene on intracellular glutathione production.

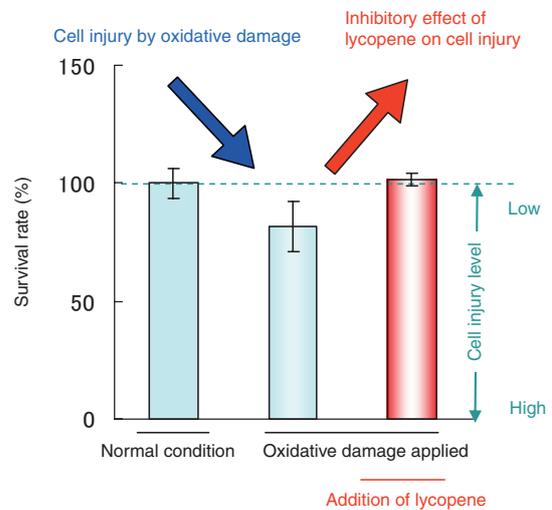


Fig. 1-b4 Effect of lycopene on inhibiting cell injury.

2.1.2 The effect of lycopene on improving astaxanthin's antioxidant capacity

Like lycopene, astaxanthin is known for its high antioxidant capacity. The addition of lycopene resulted in astaxanthin's antioxidant effects lasting to about three times their previous value (Fig. 2).

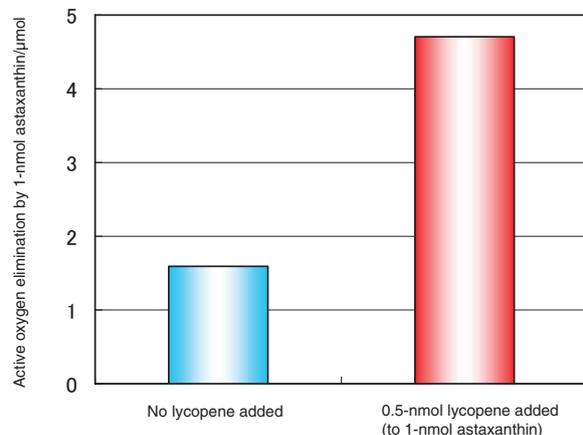


Fig. 2 Synergistic effect of astaxanthin and lycopene.

2.1.3 Mechanism of improving antioxidant capacity

One of the possible reasons for astaxanthin's antioxidant effects lasting longer with lycopene was the intermolecular one-electron transfer hypothesis. It was thought that lycopene provides its own π -electron to astaxanthin oxidants generated by astaxanthin's antioxidant reaction and is turned into lycopene oxidants. We verified this hypothesis by estimating the energy level relationship between astaxanthin and lycopene based on experiment and theoretical calculation and obtained results that support the hypothesis (Fig. 3).

2.2 Nanotechnology for lycopene

As described above, lycopene is expected to exhibit high functionality in cosmetics such as face lotion. For that purpose, it is preferable that lycopene be nanonized from the aspect of quality (transparency and stickiness), because of its oil-solubility. However, as it is an unstable substance that decomposes easily, with high crystallizability (Fig. 4), solid nanonization is difficult and had not been realized.

To solve those problems, we developed a new original technology to nanonize lycopene that is subject to crystallization to an extra small size (70 nm) and complexly increase its stability by combining several ingredients. With this technology, it has become possible to create optimal-size original nano-lycopene, transparent and expected to permeate the stratum corneum of skin without losing its usefulness such as high antioxidant capacity (Fig. 5). Thus, we succeeded in including nano-lycopene in all the items of the ASTALIFT range.

3. Deepening of research on collagen

3.1 Mesh collagen care

In conventional research, the cause of skin resilience being lost with aging was believed to be the change of the dermis as the skin base. However, we built a hypothesis that one of those causes might be the thinning of the skin (epidermis) with aging and conducted close functional observation, focusing on type-IV collagen, or mesh collagen, that has a unique mesh-like structure and exists in abundance in the basal lamina (Fig. 6).

To investigate the effect of mesh collagen on skin, we created a reconstructed skin model in collaboration with Professor Nishiyama of the Tokyo University of Agriculture and Technology. A histological analysis revealed that the reconstructed skin model with mesh collagen can have an epidermis at least twice as thick as the conventional one after

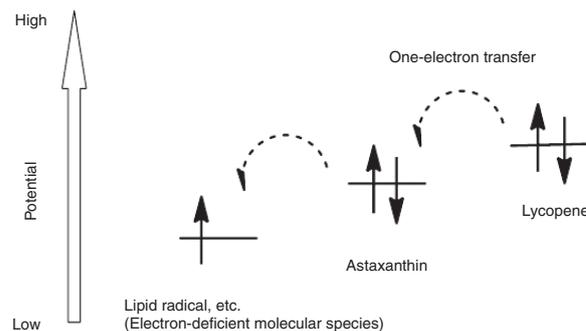


Fig. 3 Hypothesis of intermolecular electron transfer reaction.

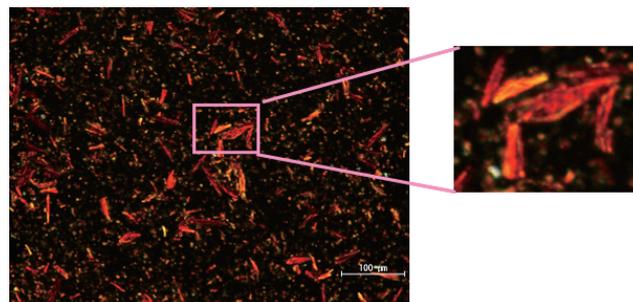


Fig. 4 Optical microscopic image of lycopene (at approx. 100x magnification).



Fig. 5 Transparency comparison between lycopene nano-sized by conventional technology (left) and nano-lycopene developed by Fujifilm (right).

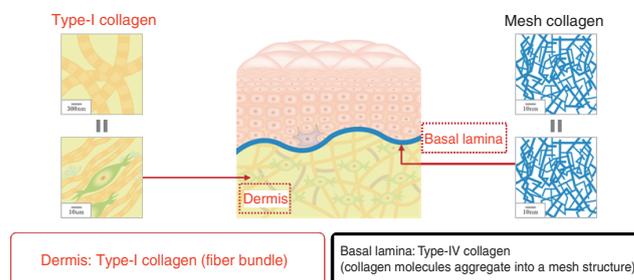


Fig. 6 Localization of Type I collagen and Type IV collagen (mesh collagen).

fourteen days of culture (Fig 7). This result suggests that *in vivo* mesh collagen of normal quality and quantity is a key element for the prevention of the thinning of the epidermis.

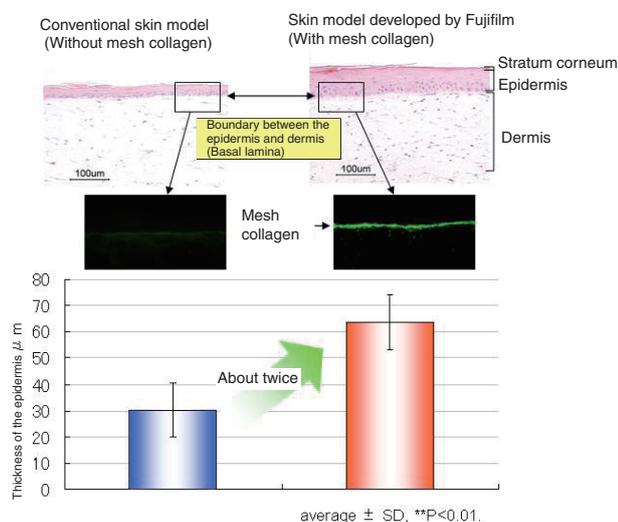


Fig. 7 Effect of mesh collagen on the thickness of the epidermis layer (Comparison of epidermis thickness after 14 days of culture).

3.2 High-permeability resveratrol that protects mesh collagen

Based on our above-described original findings, we started to search for compounds that can protect mesh collagen that is subject to decomposition by external factors such as aging and exposure to UV-rays. By screening of Fujifilm's compound library, we found a powerful type-IV collagen decomposition suppressant capability in a kind of polyphenol, resveratrol. However, resveratrol is weak in stability over time and in permeability. Therefore, we searched through its derivatives and discovered that a methoxy derivative, pterostilbene, has the same level of protective capability as resveratrol (Fig. 8). This compound is a natural ingredient contained in plants such as blueberries.

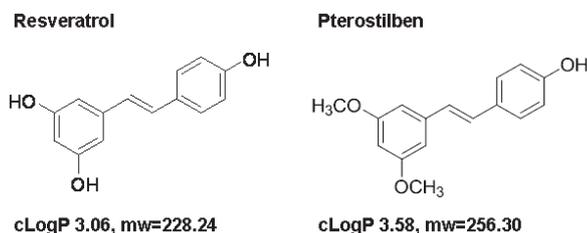


Fig. 8 The molecular structures of resveratrol and pterostilbene.

We then carried out an experiment to test pterostilbene's skin permeability with a 3D skin model and found that it had about thirty times larger permeability than ordinary resveratrol (Fig. 9). According to the calculation of the permeation speed, it can sufficiently permeate the stratum

corneum into the basal lamina where mesh collagen exists. Because its stability in water-based dosage forms is high, it is possible to include pterostilbene in cosmetics while maintaining all its benefits (Fig. 10).

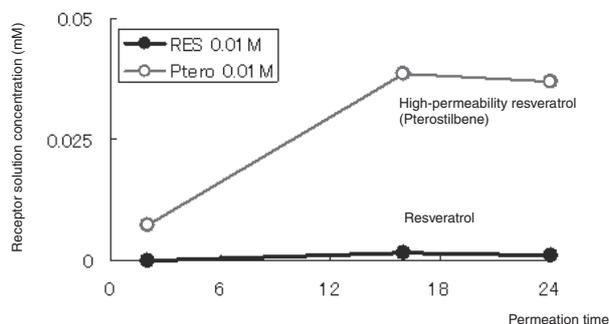


Fig. 9 Permeability of resveratrol in epidermis model.

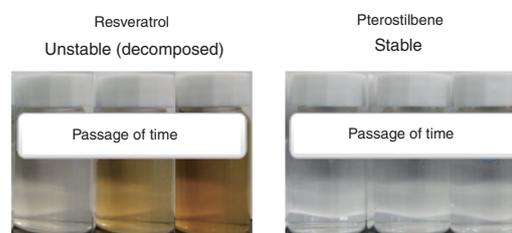


Fig. 10 The stability of resveratrol and pterostilbene under room temperature.

4. Conclusion

In the recent update of the ASTALIFT range, we have succeeded in improving its comprehensive antioxidant capacity by including nano-lycopene in all the items as the power-up ingredient. Moreover, ASTALIFT Essence Destiny, which employs high-permeability resveratrol newly found from the discovery of mesh collagen's involvement in the reproduction of the epidermis, has enabled the care of mesh collagen located deeper than the stratum corneum. It has been confirmed via experiments in accordance with the Guidelines for Evaluation of Anti-wrinkle Products that ASTALIFT Essence Destiny has the effect to make fine wrinkles caused by dryness less visible.

In this way, the ASTALIFT range can be regarded as a highly promising cosmetics brand that helps reproduce bright and resilient *photogenic skin*. Under the product concept of "Advanced cosmetics moving ahead", we will keep introducing valuable products to customers by leveraging our unique technologies.

References

- 1) Giovannucci, E. et al. J. Natl. Cancer Inst. **94** (5), 391-398 (2002).
- 2) Jung, Suh.H. et al. Proc. Natl. Acad. Sci. **101** (10), 3381-3386 (2004).

("ASTALIFT" and "Destiny" referred to in this paper are registered trademarks of FUJIFILM Corporation.)