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The Oral Administration of Elastin Peptide Reduces Ultraviolet Light-Induced Photoaging in Hairless Mice

Zheng Yan[1,2,*], Shuang Liu[2], Ai-Qing Liu[2] and Hai-Yan Wang[2]

[1]*College of Bioengineering, Beijing Polytechnic, Beijing 100176, China*
[2]*Beijing Semnl Biotechnology Co., Ltd., Beijing 100062, China*

ABSTRACT

Ultraviolet (UV) radiation in sunlight is the main exogenous factor leading to skin aging. The prevention and repair of UV induced skin aging has become a significant research focus over recent years. To investigate the protective effects of the oral administration of elastin peptide on photoaged skin, BALB/C Nude mice were exposed to UVA+UVB for 16 weeks to establish the photoaging model. The concentrations of elastin peptide given to the low, medium, and high dose groups were 1.5, 5.0 and 10 mg/animal per day, respectively. Then, skin elasticity was measured using a cutimeter dual MPA 580. The concentraions of three type of collagens, hyaluronic acid and hydroxyproline in skin tissue were also determined. The results indicated that the oral administration of elastin peptide greatly improved the skin elasticity, accompanying with significantly upregulated expression of hyaluronic acid and hydroxyproline. In addition, the contents of collagen in animal skin were also significantly increased, especially Type III and IV collagen. However, the effects induced by elastin peptide did not show a dose-response relationship. In conclusion, the results implied that elastin peptide can significantly promote the recovery of collagen in photoaging skin to normal levels, and repair skin aging induced by UVA + UVB treatment.

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Key words
Photoaging, Skin health, Elastin-derived peptides, Collagen, Hydroxyproline, Hyaluronic acid.

INTRODUCTION

Ultraviolet (UV) irradiation is one of the major exogenous harmful agents to the skin. This irradiation not only has a cumulative effect on the photoaging of skin (Fisher *et al*., 1997); the ability of the human body to repair skin damage caused by photoaging will inevitably decrease with age (Silveira *et al*., 2014). Epidemiological studies have shown that 80-90% of facial aging is caused by chronic exposure to ultraviolet radiation (Hillebrand, 2010; Gonzaga, 2009). UV light consists of UVC (100-280 nm), UVB (280-320 nm), and UVA (320-400 nm), but only UVB and UVA reach the earth's surface (95% UVA and 5% UVB) (Fischer *et al*., 2011). UVA can penetrate deeper into the dermis and degrade collagen proteins and elastic fibers of the dermis via oxidative stress and the activation of MMPs (matrix metalloproteinases) (Natarajan *et al*., 2014; Wongrattanakamon *et al*., 2019). UVB penetrates the epidermis and the upper layer of the dermis. It promotes oxidative stress by inducing exacerbated reactive oxygen species (ROS) production, and further promotes protein, mitochondrial, and DNA alterations as well as lipid peroxidation (Duque *et al*., 2017). Although UVB representing the minor percentage of sunlight, it leads to greater skin damage than UVA at similar irradiation doses (Gęgotek *et al*., 2017; Yang *et al*., 2015). In the past few years, with the increase in environmental pollution and the depletion of the Earth's ozone layer, the level of UV irradiation, particularly UVA and UVB has increased seriously (Shah *et al*., 2013). Hence, the prevention and repair of problems associated with skin aging caused by UV light has become a significant research focus over recent years.

Oral supplementation with food ingredients, such as peptides and polyphenols, has demonstrated beneficial effects on skin health (Heinrich *et al*., 2006; Skovgaard *et al*., 2006). Elastin is a protein that has elastic and fibrous properties; this protein exists predominantly in elastic tissues, such as the cervical ligaments, blood vessels, the lungs, and the skin (Duca *et al*., 2004). As the hydrolysated form of elastin, elastin peptides can induce cell adhesion, migration, proliferation, differentiation, and apoptosis (Page *et al*., 2019; Sato *et al*., 2011). In a previous study, Liu *et al*. (2018) found that the administration of elastin peptide could significantly increase the content of hydroxyproline and water in skin, and significantly improve epidermal proliferation and the apoptosis of fibroblasts in photoaged skin. However, there is only limited information on whether elastin peptide intake reduces UV irradiation-induced loss of biomolecular constituents and skin

* Corresponding author: bioyanzheng@163.com
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elasticity in humans or animals. Therefore, the objective of the present study was to create a hairless mouse model of photoaging via the application of UVA + UVB irradiation. In addition, in order to explore the protective effects of the oral administration of elastin peptide on photoaged skin, and the specific mechanisms involved, we investigated the levels and distribution of collagen type I (Col~I), collagen type III (Col~III), collagen type IV (Col~IV), hyaluronic acid (HA), and hydroxyproline (Hyp) in samples of skin tissue.

MATERIALS AND METHODS

Establishment of the animal model

Fifty BALB/C nude mice were obtained from Laboratory Animal Center of Peking University Health Science Center (license No.: SCXK (Jing) 2016-0012). After 7 days of adaptive feeding, the mice were randomly divided into 5 groups as follows (n = 10/group): (i) blank control group, UV unexposed, and distilled water treated mice, (ii) model group, UVA+UVB exposed, and distilled water treated mice, (iii) low-dose group, UVA+UVB exposed, and elastin peptide treated mice (at 1.5 mg/animal per day), (iv) medium-dose group, UVA+UVB exposed, and elastin peptide (Beijing SEMNL Biotechnology Co. Ltd, Beijing, China) treated mice (at 5.0 mg/animal per day), (v) high-dose group, UVA+UVB exposed, and elastin peptide treated mice (at 10.0 mg/animal per day). The UV irradiator (UVA + UVB, UVA 340-80 W: wavelength range, 320-400 nm; wave crest, 340 nm; UVB 313-80 W: wavelength range, 300-320 nm; wave peak, 313 nm) was placed 30 cm above the ground. The minimum amount of erythema was 31 MJ/cm^2, measured by a UV irradiatometer (Photoelectric Instrument Factory of Beijing Normal University, Beijing, China). The initial irradiation dose was 20 min/d, increasing by 10 min to 30 min/d each week; this was maintained at 120 min/d for 16 weeks until the appearance of the skin showed typical signs of aging (*i.e.,* desquamation, erythema, and wrinkles); the presence of these signs demonstrated that the model of photoaging had been successfully created. Each group received an oral gavage 1 h before exposure to UV and irradiation was carried out 6 times each week.

Analysis of skin elasticity

One hour after the final exposure to UV, we measured skin elasticity using a cutimeter dual MPA 580 (Courage+Khazaka Electronic GmbH, Cologne, Germany). The testing principle was based on the principle of suction and stretching. The ratio of light emitted and received is directly proportional to the depth of the skin being inhaled; the elastic properties of the skin were then determined by MPA software analysis (Bonaparte *et al*., 2013). The main indices for elastic properties were R2 and Q1 (Kim *et al*., 2018). R2 (UA/UF) is the total elastic-plastic amount of the rebound component, while Q1 [(QE + QR) / Q0] is the total elastic-plastic area of the elastic-plastic portion of the spring-back component. The closer R2 and Q1 are to a value of 1, the better the elastic-plastic properties of the two processes.

The acquisition of skin tissue

All mice were culled at the end of the experiment. Samples of fresh skin tissue were removed from each mouse, along with the entire section of skin from the abdomen and back. Skin samples were washed 2-3 times in normal saline, dried on filter paper, placed into a microcentrifuge tube, and stored in liquid nitrogen to await analysis of relevant physiological and biochemical indices.

Determination of protein levels in skin tissue by the BCA (bicinchoninic acid) method

First, we created a homogenate of skin tissue for each mouse. The tissues were cut and weighed (0.1-0.2 g), and the samples were processed according to the proportion of tissue homogenate (10%). Tissue samples were then homogenized in PBS (pH 7.2-7.4, concentration 0.01) and centrifuged for 15 min at 5000 rpm; the supernatant was retained for analysis. The protein content of each sample was first adjusted and then measured using a BCA detection kit (ADS-W-DB005, Jiangsu Addison Biotechnology Co. Ltd., Jiangsu Province, China). Then, 2.626 mg/mL of the lowest protein content was selected as the reference, and other samples were appropriately diluted.

Analysis of Col~I, Col~III and Col~IV

The concentrations of Col~I, Col~III and Col~IV in skin tissue were determined according to the instructions of ELISA kits (MB-1582A Col~I ELISA Kit, MB-1621A Col~III ELISA Kit, MB-1837A Col~IV ELISA Kit, Jiangsu Kete Biotechnology Co. Ltd., China), and the results were normalized to ng/mL.

Analysis of hydroxyproline (Hyp)

Samples of skin tissue were hydrolyzed to produce free Hyp, which was then measured according to the instructions of a Hyp Detection Kit (ADS-DC-010, Jiangsu Addison Biotechnology Co. Ltd., China). The content of Hyp was calculated by measuring the absorbance of each sample (in 560 nm) and the results were normalized to μg/g. It was important to calculate the concentration of Hyp in each sample by also considering the amount of protein in the same sample.

Table I.- Effects of elastin peptide on body weight (Mean±SEM) of UV induced photoaged hairless mice (10 mice in each group).

Group	Dose (g/kg)	Body weight (g) on				
		Initial	4th week	8th week	12th week	16th week
Normal	-	17.40±0.47	19.38±0.71	20.77±0.78	21.37±0.49	22.13±0.61
UVA+UVB	-	16.99±0.34	18.32±0.53	19.40±0.52	20.78±0.63	21.44±0.72
Elastin peptide						
Low dose	1.5	17.19±0.56	19.02±0.61	20.17±0.80	20.88±0.56	21.61±0.48
Middle dose	5.0	17.02±0.27	18.37±0.32	20.00±0.69	21.07±0.84	21.79±0.94
High dose	10.0	17.34±0.43	18.71±0.63	19.82±0.81	20.78±0.81	21.56±0.84

Analysis of hyaluronic acid (HA)

HA was determined by the enzymatic hydrolysis of skin tissue samples and measured according to the instructions of a HA Detection Kit (ADS-DC-013, Jiangsu Addison Biotechnology Co. Ltd., China). The content of HA was then calculated by measuring the absorbance of each sample (in 480 nm) and the results were normalized to μg/g. The HA content of each skin sample also needed to be calculated by taking into account the protein concentration of each sample.

Morphological and histopathological examination of skin

Skin samples were removed from fixative and cut into small pieces (3 mm thickness) with a scalpel. These tissues were then embedded, sectioned, and stained with conventional hematoxylin and eosin. Sections were then observed by digital scanning imaging using an upright optical microscope (NIKON ECLIPSE TI-SR, Nikon, Japan). This allowed us to investigate pathological changes and to acquire representative images of typical lesions.

Statistical analysis

Data are expressed as mean ± standard error of the mean (SEM). Data were tested to ensure that variances were homogenous and that the data were normally distributed. Data that did not fit these were transformed using logarithms or square roots. Data were compared using the student's t-test and one-way analysis of variance (ANOVA test). These tests were performed in Statview statistical software (Brainpower, Calabasas, CA). Significant differences are denoted as follows: *P< 0.05, ** P< 0.01, and *** P< 0.001.

RESULTS

Clinical observations and body weight

There were no deaths during the experiment. No significant differences between any of the groups with regards to body weight and food consumption, details are provided in Table I.

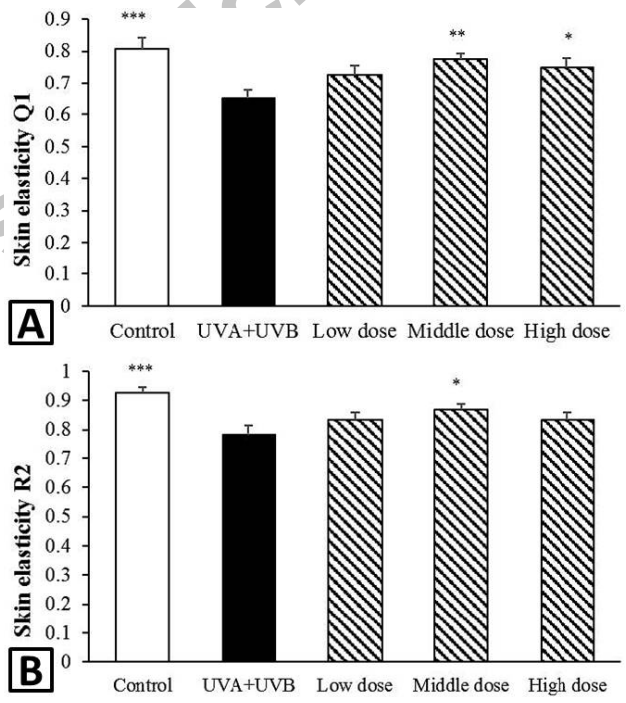

Fig. 1. Effect of elastin peptide on elasticity of skin of UV induced photoaged hairless mice. A, Q1 = total elastic – plastic area of the spring – back component; B, R2 = total elastic – plastic amount of the rebound component. For comparisons between UV-irradiated controls and experimental groups. *, P< 0.05; **, P< 0.01; ***, P<0.001.

Skin elasticity analysis

The appearance of mouse skin was observed visually and skin elasticity was analyzed *in vivo* (Fig. 1). After 16 weeks of UV irradiation, the skin of mice in the model group showed obvious erythema and wrinkling. The mice

in the blank group and the elastin peptide groups showed no evidence of erythema or other symptoms. Figure 1 showed that the Q1 and R2 values of the model group decreased significantly over time, thus indicating that we had successfully created a murine model of photoaging. The oral administration of elastin peptide improved both the Q1 and R2 values of photoaged skin, particularly in the medium-dose group.

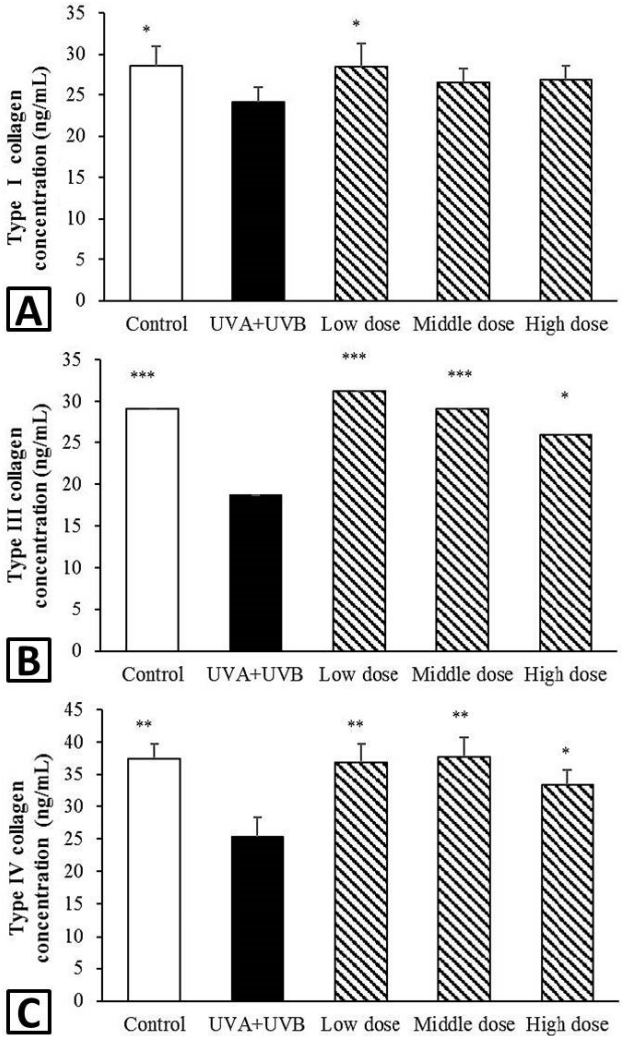

Fig. 2. Effect of elastin peptide on collagen content of skin of UV induced photoaging hairless mice. A, Col-I; B, Col-III; C, Col-IV. For comparisons between UV-irradiated controls and experimental groups. *, $P< 0.05$; **, $P< 0.01$; ***, $P<0.001$.

Furthermore, the elasticity of the skin was quantified by measuring the ability of the skin to return to its original state after deformation. Our data showed that low-, middle-, and high-dose elastin treatment improved the elasticity of photoaging skin. This indicated that elastin peptide could alleviate the reduction of skin elasticity and collagen content caused by chronic UV exposure.

Col~I, Col~III and Col~IV concentrations

It can be seen from Figure 2 that the concentrations of Col~I, Col~III, and Col~IV, in skin samples from the model group were significantly reduced after UV irradiation, and that the collagen content increased significantly following the oral administration of elastin peptide.

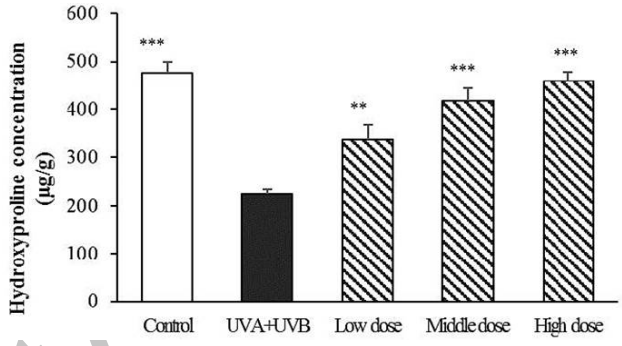

Fig. 3. Effect of elastin peptide on hydroxyproline (Hyp) content of skin of UV induced photoaging hairless mice. For comparisons between UV-irradiated controls and experimental groups. **, $P< 0.01$; ***, $P<0.001$.

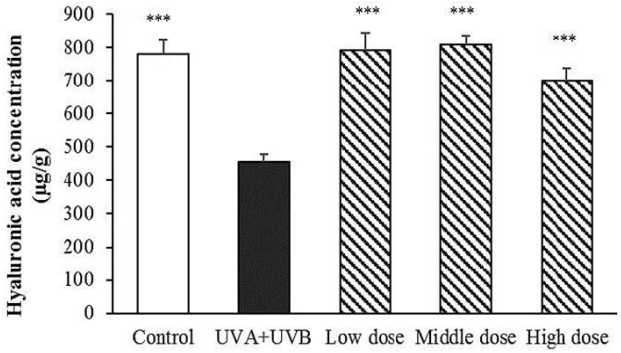

Fig. 4. Effect of elastin peptide on hyaluronic acid (HA) content of skin of UV induced photoaging hairless mice. For comparisons between UV-irradiated controls and experimental groups. ***, $P<0.001$.

Hyp and HA concentrations

The concentrations of Hyp and HA content are shown in Figures 3 and 4. The concentrations of Hyp and HA in skin samples from the model group were significantly decreased when exposed to UV light ($P < 0.001$) but increased significantly after the intragastric administration of elastin peptide. The increase of Hyp in the middle- and high-dose groups ($P < 0.001$) was more significant than

that in the low-dose group ($P < 0.01$), thus indicating the existence of a dose-dependent effect. The levels of HA in the low-, middle-, and high-dose elastin peptide groups all increased significantly ($P < 0.001$).

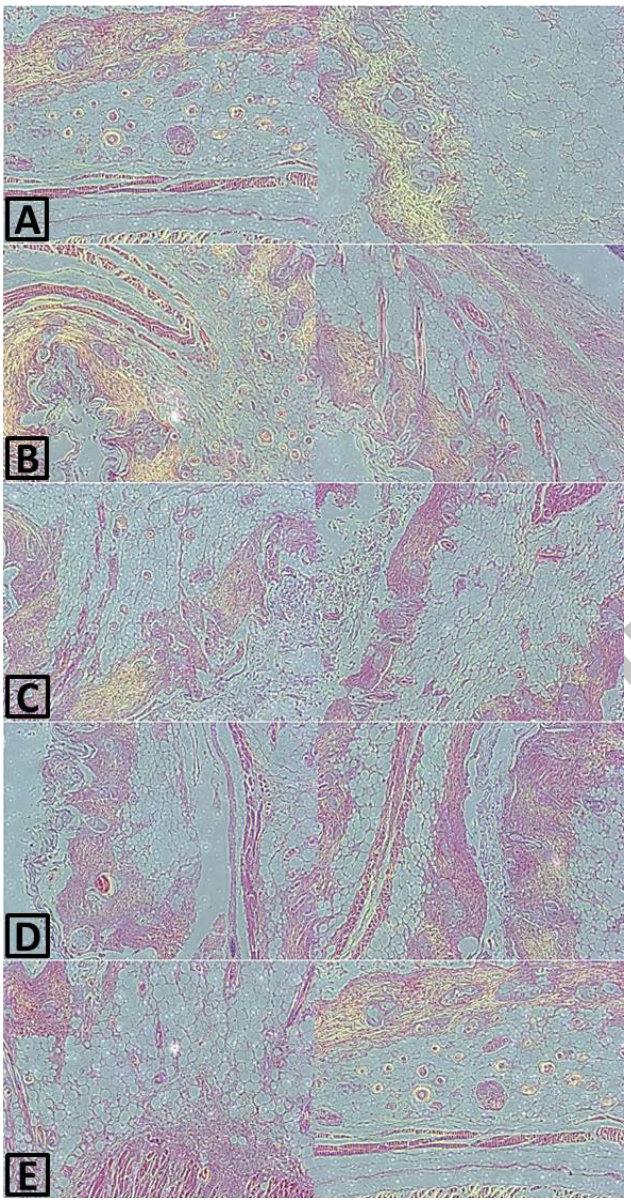

Fig. 5. Effect of elastin peptide on dorsal tissues of skin of UV induced photoaging hairless mice. A, normal group; B, UV induced group; C, low-dose group; D, middle-dose group; E, high-dose group. Staining, H&E; Magnification, ×400.

Histomorphometry

After sacrificing the mice, the mice dorsal tissues were collected. Then, H&E staining was performed. In the normal group (Fig. 5A), structure of the epidermis and dermis is clear, well-organized, and cell metabolism is balanced. But in the UV induced group (Fig. 5B), the result showed that irregular hyperplasia of the epidermis, atrophy of the dermis, damage of the basement membrane structure at the junction of epidermis and dermis, flattening of the papillary layer, and irregular hyperplasia of the sebaceous glands. The histomorphology of the skin was not significantly improved in the low-dose group (Fig. 5C). But the oral administration of elastin peptide significantly improved the histomorphology of photoaged skin, particularly in the middle-dose and high-dose group (Fig. 5D, E).

DISCUSSION

UVB is an important factor underlying the progression of skin aging and skin cancer (Oliveira *et al*., 2019). Causes of low energy level, UVA is considered to be weakly carcinogenic (Baier *et al*., 2007). But it has strong penetration ability and accounts for 95-98% of the total UV light reaching the Earth's surface. At the same time, UVA and UVB do not only cause skin photoaging, they also exhibit synergistic effects (Yin *et al*., 2020). In the past, researchers mainly focused on the skin aging damage caused by UVB, and often ignored the effect of UVA. During our modeling process, UVA and UVB were superimposed in order to be closer to the actual situation in nature. Our experimental results showed that after UVA + UVB irradiation, skin elasticity (Q1 and R2), and the concentrations of Col-I, Col-III, Col-IV, HA, and Hyp, were significantly lower than those of the blank control group. The expression levels of Col-1 and Col-III were consistent with previous results (Shi *et al*., 2011), thus indicating that a murine model of photoaging had been created successfully.

Long-term ultraviolet radiation can cause significant damage to the ECM of the dermis (Lu *et al*., 2011; Hynes, 2009). Collagen, elastin, and HA, are the most important and abundant structures in the ECM of the dermis (Oxlund *et al*., 1981). Collagen is the main protein in the extracellular matrix (ECM) of the skin and plays an important role in keeping the skin smooth, delicate, tight, and elastic. Type I collagen fibers play an important role in maintaining skin tension and bearing tension; it also provides the material basis for maintaining skin fullness (Lovwll *et al*., 1987). Type III collagen is a naive and slender collagen fiber and is the main component of reticular fibers (Kuivaniemi *et al*., 2019). Type IV collagen is the main component of the junction between the dermis and epidermis (Vázquez *et al*., 1996). Hyp is a non-essential amino acid that is unique to collagen. The concentrations of Hyp in collagen remains

relatively constant and accounts for 13% of total collagen. The concentration of Hyp can directly reflect changes of collagen fiber content in the dermis, and is, therefore, a sensitive index with which to determine the degree of skin aging. HA is one of the most important factors that are synthesized and secreted by fibroblasts. HA not only plays an important role in maintaining skin moisture and skin structure, but is also able to promote skin regeneration, enhance skin elasticity, and degrade free radicals in skin (Papakonstantinou *et al*., 2012). The results showed that the concentrations of Col-I, Col-III, Col-IV, and HA, increased significantly after the oral administration of elastin peptide, thus indicating that elastin peptide can significantly promote the recovery of collagen in photoaging skin to normal levels, while also improving elasticity. However, the effects induced by elastin peptide did not show a dose-response relationship; this may be due to the fact that elastin peptide acts in the form of a signal regulator.

Previous research showed that elastin peptide can inhibit the expression and activity of MMPs, reduce the phosphorylation level of key proteins in the mitogen activated protein kinase (MAPK) signaling pathway, significantly increase the expression of collagen and laminin in the dermis, and improve the structural characteristics of the dermal epidermal junction by stimulating cell basement membrane protein (Jeong *et al*., 2020). Sato *et al*. (2011) found that elastin peptide migrated into the blood in the form of a peptide when fed to healthy volunteers, thus indicating that elastin peptide should be transported to the dermal tissue in the form of peptide. This also makes it possible for elastin peptide to act as a signal factor and play a role in resisting photoaging. In a previous study, Tran *et al*. (2005) showed that elastin peptide could increase the concentration of Col-I by promoting the expression of MT1-MMP in endothelial cells, and could enhance the regeneration of type III collagen by promoting the expression of MMP-1 and MMP-3 in fibroblasts. Elastin receptors are expressed on the surface of keratinocytes, fibroblasts, melanocytes, tumor cell lines, smooth muscle cells, and chondrocytes. After binding with receptors on these cell surfaces, elastin peptide can induce cell adhesion, migration, proliferation, differentiation, apoptosis, and other biological behaviors (Duca *et al*., 2004). The administration of even a small amount of elastin peptide can repair the degradation of collagen and hyaluronic acid caused by UV irradiation, thus restoring skin elasticity. Further studies of elastin peptide are expected to reveal a wider range of functions for elastin peptide in the alleviation of photoaging.

As our understanding of the mechanisms underlying skin photoaging has improved, a variety of food products, drugs, cosmetics, and medical technologies, have been proposed as potential treatment options to repair skin photoaging. These methods provide us with a good range of preventative and control measures for photoaging in skin. These products aim to repair the elastic structure of aging skin cells and adjust the composition of the extracellular matrix through internal pathways. Researchers consider this to be a safe and effective approach. There has been significant interest in collagen peptides as one of the most effective active ingredients against photoaging in skin. For example, Proksch *et al*. (2014) showed that the oral administration of collagen peptide can significantly reduce the extent of wrinkling on the eyelids. Studies by Ma *et al*. (2017) further showed that soybean oligopeptides could effectively resist the degradation of Col-I and Col-III collagen in the photoaging skin of BALB/C mice when induced by UVB; these oligopeptides had a photoprotective effect on mouse skin.

Elastin is a large, complex, and hydrophobic protein (Debelle *et al*., 1999), that is generally relatively stable; consequently, it is difficult to supplement the daily diet with elastin. However, once hydrolyzed, the elastin peptide can be readily absorbed and utilized. In the present study, we showed that elastin peptide, as a signal factor, can significantly increase the concentrations of Col-1, Col-III, Col-IV, and HA, in photoaging skin. In turn, these effects reduce the damage caused by UV exposure, and help to alleviate disorders in the ECM caused by photoaging, thus restoring skin elasticity, promoting skin repair, and recovering skin elasticity. As a direct result of environmental pollution, the ozone layer in the atmosphere is becoming thinner and thinner. Consequently, the skin photoaging caused by exposure to UV radiation is becoming increasingly more serious. Damage incurred by UV radiation is also becoming increasingly serious and can lead to a variety of skin diseases.

CONCLUSION

Our present data indicated that the oral administration of elastin peptide greatly improved the skin elasticity, accompanying with significantly upregulated expression of hyaluronic acid and hydroxyproline. In addition, the intake of elastin peptide significantly increase the concentration of collagen protein in the skin, especially Type III and IV collagen. Even a small amount of elastin peptide can repair the degradation of collagen and hyaluronic acid caused by UV irradiation.

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Ethical compliance

All of the experimental procedures involving animals were conducted in accordance with the Institutional Animal Carge guidelines of Beijing Union University, China (SYXK (JING) 2012-0031) and approved by the Administration Committee of Experimental Animals, Beijing, China.

Statement of conflict of interest

SL, AL and HW are employees of Beijing Semnl Biotechnology Co., Ltd. ZY has no competing interest. The study was run and managed independently by Beijing Polytechnic, China. Beijing Polytechnic does not endorse any brand or product nor does it have any financial interests with any supplement manufacturer or distributor.

REFERENCES

Baier, J., Maisch, T., Maier, M., Landthaler, M. and Bäumler, W., 2007. Direct detection of singlet oxygen generated by UVA irradiation in human cells and skin. *J. Invest. Dermatol.,* **127**: 1498-1506. https://doi.org/10.1038/sj.jid.5700741

Bonaparte, J.P., Ellis, D. and Chung, J., 2013. The effect of probe to skin contact force on Cutometer MPA 580 measurements. *J. Med. Eng. Technol.,* **37**: 208-212. https://doi.org/10.3109/03091902.2013.779325

Debelle, L. and Tamburro, A.M., 1999. Elastin: Molecular description and function. *Int. J. Biochem. Cell B,* **31**: 261-272. https://doi.org/10.1016/S1357-2725(98)00098-3

Duca, L., Floquet, N., Alix, A.J.P., Haye, B. and Debelle, L., 2004. Elastin as a matrikine. *Crit Rev. Oncol. Hematol.,* **49**: 235-244. https://doi.org/10.1016/j.critrevonc.2003.09.007

Duque, L., Bravo, K. and Osorio, E., 2017. A holistic anti-aging approach applied in selected cultivated medicinal plants: A view of photoprotection of the skin by diffffferent mechanisms. *Ind. Crop. Prod.,* **97**: 431-439. https://doi.org/10.1016/j.indcrop.2016.12.059

Fischer, F., Zufferey, E., Bourgeois, J.M., Héritier, J. and Micaux, F., 2011. UV-ABC screens of luteolin derivatives compared to edelweiss extract. *J. Photoch. Photobiol. B,* **103**: 8-15. https://doi.org/10.1016/j.jphotobiol.2011.01.005

Fisher, G.J., Wang, Z., Datta, S.C., Varani, J., Kang, S. and Voorhees, J.J., 1997. Pathophysiology of premature skin aging induced by ultraviolet light. *New Engl. J. Med.,* **337**: 1419-1429. https://doi.org/10.1056/NEJM199711133372003

Gęgotek, A., Rybałtowska-Kawałko, P. and Skrzydlewska, E., 2017. Rutin as a mediator of lipid metabolism and cellular signaling pathways interactions in fifibroblasts altered by UVA and UVB radiation. *Oxid. Med. Cell. Longev*., **2017**: 4721352. https://doi.org/10.1155/2017/4721352

Gonzaga, E.R., 2009. Role of UV light in photodamage, skin aging, and skin cancer. *Am. J. clin. Dermatol.,* **10**: 19-24. https://doi.org/10.2165/0128071-200910001-00004

Heinrich, U., Neukam, K., Tronnier, H., Sies, H. and Stahl, W., 2006. Long-term ingestion of high flavanol cocoa provides photoprotection against UV-induced erythema and improves skin condition in women. *J. Nutr.,* 136: 1565-1569. https://doi.org/10.1093/jn/136.6.1565

Hillebrand, G., 2016. Facial wrinkling: the marquee clinical sign of aging skin. *In: Textbook of aging skin* (eds. M. Farage, K. Miller and H. Maibach). Springer, Berlin, Heidelberg. https://doi.org/10.1007/978-3-642-27814-3_86-2

Hynes, R.O., 2009. The extracellular matrix: Not just pretty fibrils. *Science,* **326**: 1216-1219. https://doi.org/10.1126/science.1176009

Jeong, S., Yoon, S., Kim, S., Jung, J., Kor, M., Shin, K., Lim, C., Han, H.S., Lee, H., Park, K.Y., Kim, J., Chung, H.J. and Kim, H.J., 2020. Anti-wrinkle benefits of peptides complex stimulating skin basement membrane proteins expression. *Int. J. mol. Sci.,* **21**: 73. https://doi.org/10.3390/ijms21010073

Kim, M.A., Kim, E.J. and Lee, H.K., 2018. Use of SkinFibrometer® to measure skin elasticity and its correlation with Cutometer® and DUB® Skinscanner. *Skin Res. Technol.,* **24**: 466-471. https://doi.org/10.1111/srt.12455

Kuivaniemi, H. and Tromp, G., 2019. Type III collagen (COL3A1): Gene and protein structure, tissue distribution, and associated diseases. *Gene,* **707**: 151-171. https://doi.org/10.1016/j.gene.2019.05.003

Liu, Y., Su, G., Zhou, F., Zhang, J., Zheng, L. and Zhao, M., 2018. Protective effect of bovine

elastin peptides against photoaging in mice and identification of novel antiphotoaging peptides. *J. Agric. Fd. Chem.,* **66**: 10760-10768. https://doi.org/10.1021/acs.jafc.8b04676

Lovwll, C.R., Smolenski, K.A., Duance, V.C., Light, N.D., Young, S. and Dyson, M., 1987. Type I and III collagen content and fibre distribution in normal human skin during ageing. *Br. J. Dermatol.,* **117**: 419-428. https://doi.org/10.1111/j.1365-2133.1987.tb04921.x

Lu, P., Takai, K., Weaver, V. and Werb, Z., 2011. Extracellular matrix degradation and remodeling in development and disease. *CSH Perspect. Biol.,* **3**: 1-24. https://doi.org/10.1101/cshperspect.a005058

Ma, L.W., Yin, Z., Zhuo, B.Z. and Luo, D., 2017. Effects of soybean oligopeptide on collagen type I and III in mice skin irradiated by UVB. *Chin. J. Dermatovener. Integr. Tradit. West. Med.,* **16**: 395-398.

Natarajan, V.T., Ganju, P., Ramkumar, A., Grover, R. and Gokhale, R.S., 2014. Multifaceted pathways protect human skin from UV radiation. *Nat. Chem. Biol.,* **10**: 542-551. https://doi.org/10.1038/nchembio.1548

Oliveira, M.M., Ratti, B.A., Daré, R.G., Silva, S.O., Truiti, C.T., Ueda-Nakamura, T., Auzély-Velty, R. and Nakamura, C.V., 2019. Dihydrocaffeic acid prevents UVB-induced oxidative stress leading to the inhibition of apoptosis and MMP-1 expression via p38 signaling pathway. *Oxid. Med. Cell Longev.,* **2019**: 2419096. https://doi.org/10.1155/2019/2419096

Oxlund, H. and Andreassen, T., 1981. The roles of hyaluronic acid, collagen and elastin in the mechanical properties of connective tissues. *J. Anat.,* **131**: 611-620.

Page, A.L., Khalil, A., Vermette, P., Frost, E.H., Larbi, A., Witkowski, J.M. and Fulop, T., 2019. The role of elastin-derived peptides in human physiology and diseases. *Matrix Biol.,* **84**: 81-96. https://doi.org/10.1016/j.matbio.2019.07.004

Papakonstantinou, E., Roth, M. and Karakiulakis, G., 2012. Hyaluronic acid: A key molecule in skin aging. *Dermato-Endocrinology,* **4**: 253-258. https://doi.org/10.4161/derm.21923

Proksch, E., Schunck, M., Zague, V., Segger, D., Degwert, J. and Oesser, S., 2014. Oral intake of specific bioactive collagen peptides reduces skin wrinkles and increases dermal matrix synthesis. *Skin Pharmacol. Phys.,* **27**: 113-119. https://doi.org/10.1159/000355523

Sato, M., Iwai, K., Onitsuka, E., Takahata ,Y., Morimatsu, F. and Sato, Y., 2011. Effect of long-term ingestion of porcine elastin peptide on human skin elasticity. *Nippon Shokuhin Kogyo Gakkaishi,* **58**: 159-163. https://doi.org/10.3136/nskkk.58.159

Shah, H., and Mahajan, S.R., 2013. Photoaging: New insights into its stimulators, complications, biochemical changes and therapeutic interventions. *Biomed. Aging Pathol.,* **3**: 161-169. https://doi.org/10.1016/j.biomag.2013.05.003

Shi, C.Y. and Yao, C.L., 2011. Changes in the expression of type I and type III collagen during skin photoaging treatment induced by ultraviolet. *Chin. J. Gerontol.,* **31**: 1831-1832.

Silveira, J.E.P.S. and Pedroso, D.M.M., 2014. UV light and skin aging. *Rev. environ. Hlth.,* **29**: 243-254. https://doi.org/10.1515/reveh-2014-0058

Skovgaard, G., Jensen, A. and Sigler, M., 2006. Effect of a novel dietary supplement on skin aging in post-menopausal women. *Eur. J. Clin. Nutr.,* **60**: 1201-1206. https://doi.org/10.1038/sj.ejcn.1602438

Tran, K.T., Lamb, P. and Deng, J.S., 2005. Matrikines and matricryptins: Implications for cutaneous cancers and skin repair. *J. Dermatol. Sci.,* **40**: 11-20. https://doi.org/10.1016/j.jdermsci.2005.05.001

Vázquez, F., Palacios, S., Alemañ, N. and Guerrero, F., 1996. Changes of the basement membrane and type IV collagen in human skin during aging. *Maturitas,* **25**: 209-215. https://doi.org/10.1016/S0378-5122(96)01066-3

Wongrattanakamon, P., Nimmanpipug, P., Sirithunyalug, B., Chaiyana, W. and Jiranusornkul, S., 2019. Investigation of the skin anti-photoaging potential of *Swertia chirayita* secoiridoids through the AP-1/Matrix metalloproteinase pathway by molecular modeling. *Int. J. Pept. Res. Ther.,* **25**: 517-533. https://doi.org/10.1007/s10989-018-9695-8

Yang, Y. and Li, S., 2015. Dandelion extracts protect human skin fifibroblasts from UVB damage and cellular senescence. *Oxid. Med. Cell Longev*., **2015**: 619560. https://doi.org/10.1155/2015/619560

Yin, S., Li, S.S., Bian, W.X., Yang, M.F., Liu, N.X., Hu, Y., Li, X.J., Wang, Y., Li, Z.L., Sun, J. and Yang, X.W., 2020. Antioxidant peptide AOP-P1 derived from odorous frog showed protective effects against UVB-induced skin damages. *Int. J. Pept. Res. Ther.,* **26**: 557-565. https://doi.org/10.1007/s10989-019-09862-y