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Paeonia lactiflora Pallas Root Extract Protects Against Blue Light-Induced Mitochondrial Damage

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The skin is under constant stress from external factors such as ultraviolet (UV) and dryness. In addition, photoaging, such as darkness, spots, and wrinkles, caused by blue light (BL), a visible light source, was recently reported. Therefore, protecting the skin not only from UV but also from damage caused by BL is important. The roots of *Paeonia lactiflora* Pallas and their constituents, paeoniflorin and albiflorin, have blood circulation–promoting and anti-inflammatory effects; however, few studies have reported their effects on BL–induced skin damage. In the present study, we examined the effects of *P. lactiflora* Pallas root extract (PE) on BL–induced skin damage. BL caused dose-dependent human dermal fibroblast damage. BL irradiation increased mitochondrial singlet oxygen levels and decreased cell viability, mitochondrial content, and mitochondrial membrane potential. In contrast, PE, paeoniflorin, and albiflorin ameliorated BL damage in BL–irradiated cells. Furthermore, BL induced damage in the skin model at the same irradiation intensity as that in the monolayer condition, while PE improved adenosine triphosphate (ATP) production and mitochondrial content by reducing BL–induced mitochondrial singlet oxygen levels. Collectively, these findings suggest that PE aids in the prevention of skin aging by downregulating mitochondrial singlet oxygen levels, which are increased by BL, and by improving mitochondrial content, mitochondrial membrane potential, and ATP production.

Key words: blue light, *Paeonia lactiflora*, paeoniflorin, albiflorin, human skin, fibroblasts, mitochondria, damage, singlet oxygen, mitochondrial membrane potential, ATP

1. Introduction

Aging of the human skin is caused by both intrinsic damage associated with chronological aging and extrinsic damage resulting from dryness, sunlight exposure, smoking, and environmental pollution.[1,2] The effect of ultraviolet (UV) irradiation on extrinsic damage, generally referred to as photoaging, is well documented. In recent years, the effects of photoaging, such as darkness, spots, and wrinkles, have been reported to be accelerated by blue light (BL) irradiation.[3,4] Several studies have demonstrated the harmful effects of BL on human health. Visible light is the part of the spectrum that can be perceived by the human eye at wavelengths of 400–700 nm. BL represents high-energy visible light with wavelengths of 400–500 nm.

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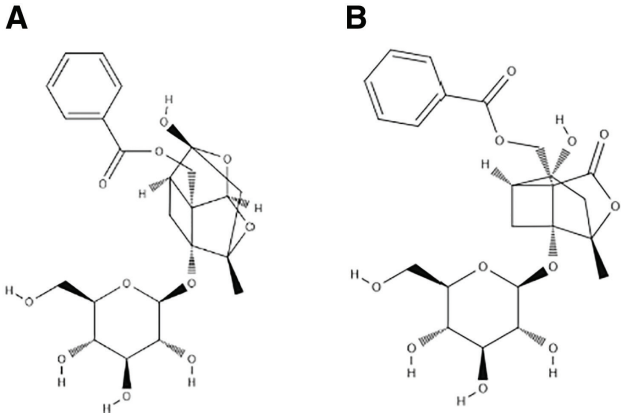

Fig. 1 Chemical structures of paeoniflorin (A) and albiflorin (B).

According to some theories, BL induces the overproduction of reactive oxygen species (ROS) such as singlet oxygen, superoxide anion, hydrogen peroxide, and hydroxyl radicals,[5–8] and BL may lower mitochondrial membrane potential and affect mitochondrial activity or cell functionality.[5,9] In particular, mitochondrial singlet oxygen damages the components of the intermembrane space, including the mitochondrial electron transport chain, and subsequently produces superoxide and hydrogen peroxide within the mitochondria, which then lead to mitochondrial fragmentation and DNA damage. Therefore, we focused on singlet oxygen production by BL because we thought it was important to suppress singlet oxygen production in mitochondria.

Paeonia lactiflora Pallas is frequently used in traditional Japanese medicinal formulas.[2,10] Paeoniflorin and albiflorin are the major bioactive components of *P. lactiflora* Pallas and exert anti-inflammatory, antioxidative, and blood circulation–promoting effects.[11–14] In addition, *P. lactiflora* Pallas roots and paeoniflorin suppress skin damage caused by UV radiation.[12,15] However, few studies have reported the effects of *P. lactiflora* Pallas roots, paeoniflorin, and albiflorin on skin damage caused by BL–induced photoaging. In this study, we examined the effects of P. lactiflora roots and their constituents on BL–induced skin damage by singlet oxygen.

2. Materials and Methods

2.1. Reagents

Paeoniflorin and albiflorin were procured from FUJIFILM Wako Pure Chemical (Osaka, Japan; Fig. 1). D-α-Tocopherol (α-Toc) and 2,5-diphenyl-3,4-benzofuran (DPBF) were also procured from FUJIFILM Wako Pure Chemical. Hoechst 33342 stain was obtained from Dojindo Laboratories (Kumamoto, Japan), while 3-(1,4-epidioxy-4-methyl-1,4-dihydro-1-naphthyl) propionic acid (EP) was obtained from Wakenyaku (Kyoto, Japan). Phosphate-buffered saline (PBS) without Ca^{2+} and Mg^{2+} and Hanks' balanced salt solution (HBSS) without Ca^{2+} and Mg^{2+} were procured from FUJIFILM Wako Pure Chemical. All of the other chemicals were purchased from FUJIFILM Wako Pure Chemical.

2.2. Plant material and extract preparation

P. lactiflora Pallas roots were dried, cut into small pieces, and extracted using a 1:1 solution of 1,3-butylene glycol and water at 50°C for 5 h. The *P. lactiflora* Pallas root extract (PE) was then stored at 4°C for 3 days, filtered using a 5-μm filter, and used for the assays.

2.3. Cell and skin model culture

Neonatal normal human dermal fibroblasts (NHDF; Kurabo, Osaka, Japan) were cultured in Dulbecco's modified Eagle's medium supplemented with 10% fetal bovine serum, 100 U/mL penicillin, and 100 μg/mL streptomycin. Cells were seeded in culture plates and grown to sub-confluency in an incubator at 37°C and 5% CO_2. EpiDermFT full-thickness reconstituted skin tissue (skin model; MatTek, Ashland, MA, USA) was pre-cultured in a 5% CO_2 incubator at 37°C using the attached assay medium and used in the assays.

2.4. BL exposure

NHDF (1×10^4 cells/well) were cultured in 96-well plates for 24 h. Thereafter, the medium was replaced with medium only or medium containing PE, and the cells were further incubated for 24 h. The skin surface was then treated with PE or PBS for 24 h. The medium in the NHDF and skin models was replaced with HBSS prior to BL exposure, and the cells were exposed to BL using a sunlight irradiation system (SERIC, Tokyo, Japan) with a 400–500-nm transmission filter.

The radiation intensity of the BL was measured using a UVR-300 instrument equipped with a UV400 detector (TOPCON, Tokyo, Japan). The sham BL–irradiated NHDF and skin models were shielded from the lamp during the BL exposure.

2.5. Cell viability assessment

To investigate cellular proliferation, NHDF and the skin model were cultured, and viability assays were performed using a Cell Counting Kit-8 (Dojindo Laboratories), according to the manufacturer's instructions.

2.6. Ultra-performance liquid chromatography analysis

Paeoniflorin and albiflorin were quantified via ultra-performance liquid chromatography (UPLC) using an ACQUITY H-class PLUS system (Waters, Milford, MA, USA) coupled with tunable UV and photodiode array detectors (Waters). The analysis was performed using an ACQUITY UPLC BEH C18 (1.7 μm, 2.1 × 50 mm; Waters). For the quantification of paeoniflorin and albiflorin, a mobile phase consisting of 85% (v/v) acetonitrile and 0.1% phosphoric acid was used at a flow rate of 1 mL/min and a column temperature of 20°C. UV detection was performed at a wavelength of 232 nm. The concentrations of paeoniflorin and albiflorin were calculated from the standard curves.

2.7. Measurement of mitochondrial singlet oxygen in NHDF

NHDF was incubated with HBSS containing Si-DMA (Dojindo Laboratories) for 1 h at 37°C. The cells were then exposed to 1–70 J/cm^2 BL. Immediately after the BL exposure, mitochondrial singlet oxygen was measured using a microplate reader at excitation and emission wavelengths of 640 and 665 nm, respectively.

2.8. Measurement of mitochondrial content and mitochondrial membrane potential of NHDF

Immediately after BL exposure, the mitochondrial content and mitochondrial membrane potential were measured by staining with MitoBright LT dye (Dojindo Laboratories) and an MT-1 MitoMP Detection Kit (Dojindo Laboratories) for 1 h, respectively, according to the manufacturer's instructions. The nuclei were stained with Hoechst 33342. The nuclei, mitochondrial content, and mitochondrial membrane potential fluoresced blue, green, and red, respectively, under an IX70 microscope coupled with a DP80 digital camera (Olympus, Tokyo, Japan). The images were analyzed using WinROOF2015 (Mitani, Fukui, Japan), and the average luminance value was calculated by dividing the luminance value by the number of cells.

2.9. Singlet oxygen absorption capacity measurement

The singlet oxygen absorption capacity (SOAC) values of samples were measured according to the method described by Takahashi et al.[16] The capacity of the extract to scavenge the singlet oxygen was determined using EP as a singlet oxygen generator and DPBF as a UV–Vis absorption probe. α-Toc (1.5 mM) was used as a standard compound in the SOAC assay. Briefly, 0.19 mM DPBF and 1.2 mM EP were added on ice, followed by the addition of the sample or 1.5 mM α-Toc. SOAC values were determined by monitoring the change in absorption of DPBF at 413 nm due to its chemical reaction with singlet oxygen in the absence and presence of the sample. The absorbance of each well was measured by using a microplate reader at 413 nm every 30 s for 120 min at 35°C. The SOAC values were calculated using the analysis template and are expressed as 1.5 mM α-Toc equivalents.

2.10. Staining of mitochondria in the skin model

Immediately after BL exposure, the mitochondrial content was stained using the MitoBright IM red (Dojindo Laboratories) for 1 h, according to the manufacturer's instructions. The skin model tissue was cryoembedded, and the epidermal layer of the specimen was cut using a cryostat (CM1860, Leica, Werzlar, Germany). The epidermis and dermis were then separated, and 10-μm-thick frozen sections of dermis were obtained using the film-transfer (Kawamoto) method. The mitochondrial content fluoresced red under an IX70 microscope coupled with a DP80 digital camera. The images were analyzed using WinROOF2015, and the average luminance value was calculated by dividing the luminance value by the number of cells.

2.11. ATP assay

The skin model tissue was cryoembedded 1 h after irradiation. The epidermal layer of the specimen was cut using a cryostat, and the epidermis and dermis were separated. In addition, the cryo-dermal tissue was cut into small pieces and immersed in adenosine triphosphate (ATP) extraction solution to measure the ATP level, which is mainly present in the dermal layer.

The ATP levels, which are primarily present in the dermis of the skin model, were determined using a Cell ATP Assay Reagent Ver. 2 kit (TOYO B-Net, Tokyo, Japan), according to the manufacturer's instructions. Luminescence levels were measured using a GLOMAX multidetection system (Promega, Madison, WI, USA).

2.12. Statistical analysis

The statistical significance of the experimental data was evaluated using Dunnett's multiple comparison test. Values of $p < 0.05$ were considered statistically significant. The data are expressed as mean ± standard deviation.

3. Results

3.1. BL–induced damage to NHDF

Since BL penetrates the dermis and causes skin damage, we investigated the effects of BL irradiation on dermal fibroblasts. BL increased the mitochondrial singlet oxygen levels in the NHDF in a dose-dependent manner. The maximum irradiation dose used was 30 J/cm^2 (Table 1). The effects of BL irradiation on cell viability were evaluated 1 h after irradiation. NHDF viability was >70% after 1–10 J/cm^2 BL irradiation. Additionally, sham BL–irradiated cells showed neither an increase in singlet oxygen nor a decrease in survival rate. In contrast, the viability of NHDF irradiated with 30–70 J/cm^2 BL was extremely low (<50%). We evaluated mitochondrial activity at 10 J/cm^2 BL because irradiation of NHDF at this dose increased the singlet oxygen levels but did not cause an extreme decrease in viability or change in cell state.

3.2. Effect of PE on BL damage

BL increased mitochondrial singlet oxygen levels in NHDF and decreased cell viability. Therefore, we next examined the effect of PE on the induction of photoaging by BL and investigated the effects of PE on 10 J/cm^2 BL irradiation. BL treatment increased singlet oxygen levels in the mitochondria of fibroblasts (Fig. 2A). The addition of 7 μg/mL PE did not suppress singlet oxygen production, whereas the addition of 35 and 70 μg/mL PE decreased singlet oxygen production caused by BL damage in a concentration-dependent manner (Fig. 2A). Furthermore, we investigated the effect of 10 J/cm^2 BL irradiation on mitochondria. BL decreased the mitochondrial content and mitochondrial membrane potential of NHDF (Fig. 2B –2D). The addition of 7 μg/mL PE did not improve mitochondrial content, whereas the addition of 35 and 70 μg/mL PE significantly improved mitochondrial content in a concentration-dependent manner.

3.3. Quantification of PE components

To identify the active components of PE that protect against BL damage, we quantified them using UPLC. The peaks were characterized by comparison of their retention times and UV spectra with those of the standards. The retention times of paeoniflorin (Fig. 3A) and albiflorin (Fig. 3B) were 2.8 and 2.5 min, respectively.

The retention times of the compounds in 70 μg/mL PE were also 2.8 and 2.5 min, respectively (Fig. 3C), while the paeoniflorin and albiflorin concentrations in 70 μg/mL PE were 2.7 ± 0.2 and 0.4 ± 0.1 μM, respectively (Fig. 3C). However, several peaks other than paeoniflorin and albiflorin were also observed.

3.4. Effect of PE and components on SOAC

On evaluating the SOAC of PE, paeoniflorin, and albiflorin, PE showed a dose-dependent effect, with concentrations of 12.1 ± 1.2, 5.1 ± 1.8, and 0.8 ± 0.6 μM α-Toc/g at 70, 35, and 7 μg/mL, respectively (Table 2). Furthermore, paeoniflorin showed a dose-dependent effect, with concentrations of 27, 2.7, and 0.27 μg/mL resulting in 8.1 ± 1.5, 6.6 ± 0.6, and 4.0 ± 0.3 μM α-Toc/g, respectively. In addition, albiflorin showed a dose-dependent effect at 4, 0.4, and 0.04 μg/mL, yielding 8.0 ± 2.0, 4.9 ± 1.4, and 0.2 ± 0.1 μM α-Toc/g, respectively.

PE was speculated to show a SOAC effect due to the presence of paeoniflorin and albiflorin, because 70 μg/mL PE contained 2.7 μM paeoniflorin and 0.4 μM albiflorin, comparable to the total SOAC values of the 2 compounds.

3.5. Effect of BL exposure on mitochondrial content and ATP levels in the skin model

To evaluate whether BL causes mitochondrial damage under conditions similar to those of human skin, an evaluation was performed using a skin model in which the epidermis was removed after BL exposure. First, we investigated the effect of 10 J/cm^2 BL irradiation on cell viability 1 h after irradiation. BL decreased the cell viability of the skin model (Table 3). On the other hand, the pre-addition of 35 or 70 μg/mL PE, 2.7 μM paeoniflorin, and 0.4 μM albiflorin improved cell viability (Table 3). In addition, because mitochondrial membrane potential is involved in ATP synthesis, we evaluated the effects of BL exposure on mitochondrial content and ATP levels. The BL–irradiated dermis of the skin model had decreased mitochondrial content compared to the sham BL–irradiated skin model (Fig. 4A). Similarly, ATP levels, which are primarily present in the dermis, were reduced (Fig. 4B). On the other hand, the pre-addition of 35 or 70 μg/mL PE, 2.7 μM paeoniflorin, and 0.4 μM albiflorin improved the mitochondrial content and ATP levels (Fig. 4). Moreover, the prior addition of a mixture of 2.7 μM paeoniflorin and 0.4 μM albiflorin, or 1.4 μM paeoniflorin and 0.2 μM albiflorin, improved the cell viability, mitochondrial content, and ATP levels in the skin model (Table 3 and Fig. 4).

4. Discussion

In recent years, it has been reported that the effects of photoaging, such as darkness, spots, and wrinkles, are accelerated by BL irradiation.[2,6] In addition, BL induces the production of ROS in mitochondria. In particular, mitochondrial singlet oxygen damages the components of the intermembrane space, including the mitochondrial electron transport chain, and

Table 1 Mitochondrial singlet oxygen production and cell viability.

	Fluorescence intensity of singlet oxygen (A.U.)		Cell viability (%)	
	Sham BL	BL	Sham BL	BL
BL irradiation (J/cm^2)				
0	160.4 ± 7.7	—	100 ± 0.0	—
1	163.8 ± 7.0	194.5 ± 19.5*	101 ± 3.0	79.8 ± 2.2*
2	157.5 ± 6.5	228.5 ± 18.7*	97.4 ± 5.0	75.1 ± 2.7*
5	166.7 ± 7.2	253.6 ± 14.4*	100.0 ± 1.1	71.5 ± 0.3*
10	168.4 ± 6.8	290.4 ± 12.3*	99.0 ± 2.2	70.4 ± 3.6*
30	164.9 ± 7.5	320.5 ± 10.3*	96.8 ± 1.4	47.0 ± 2.3*
60	160.4 ± 7.7	305.9 ± 18.5*	96.5 ± 2.1	42.2 ± 7.8*
70	137.3 ± 5.8	234.9 ± 19.5*	97.3 ± 5.2	36.8 ± 2.6*

Changes in fluorescence intensity of mitochondrial singlet oxygen and cell viability in normal human dermal fibroblasts. Data are presented as mean ± standard deviation (n = 3).

*$p < 0.05$ versus sham BL using Dunnett's multiple comparisons test.

A.U., arbitrary unit; BL, blue light

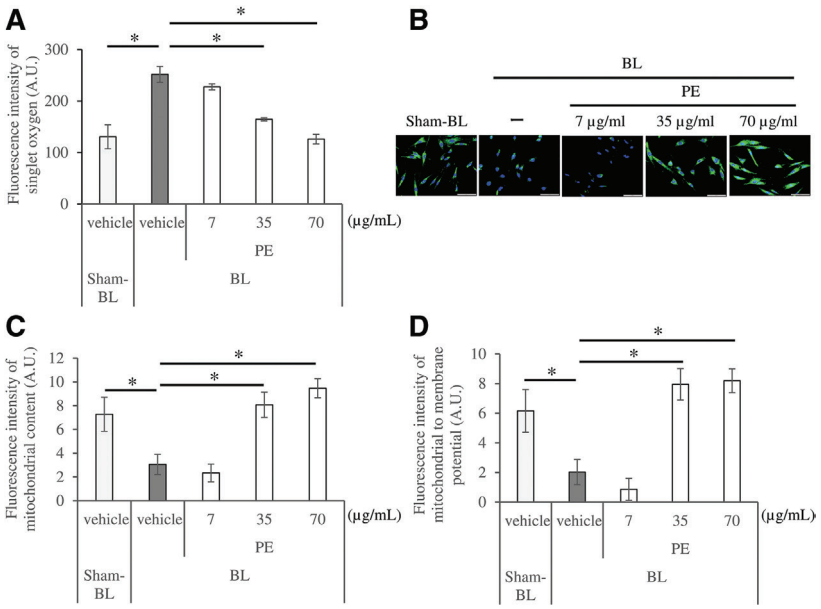

Fig. 2 Effects of BL exposure on mitochondria in normal human dermal fibroblasts. (A) Changes in fluorescence intensity of singlet oxygen. (B) Representative merged images of mitochondrial expression (green) and cell nuclei (blue). Scale bar, 100 μm. (C, D) Changes in fluorescence intensity of mitochondrial content and mitochondrial membrane potential. Data are presented as the mean ± standard deviation (n = 3). *$p < 0.05$ versus sham BL, vehicle BL, or PE and were compared by Dunnett's multiple comparison test. A.U., arbitrary unit; BL, blue light; PE, *Paeonia lactiflora* Pallas root extract.

subsequently produces superoxide and hydrogen peroxide within the mitochondria, which then leads to mitochondrial fragmentation and DNA damage.[5,6,9] Therefore, we focused on singlet oxygen production by BL because we considered it important to suppress singlet oxygen production in mitochondria. However, few studies have reported that cosmetic ingredients improve BL–induced skin damage. In this study, we examined the effects of PE and its constituents on BL–induced skin damage. First, we investigated the effects of BL irradiation on NHDF and confirmed that BL increased mitochondrial singlet oxygen levels in a dose-dependent manner (Table 1). We measured the intensity of natural sunlight irradiation in Nara and found that it reached 10 J/cm^2 in approximately 6 min on sunny days in September (data not shown). This suggests that 10 J/cm^2 BL is routinely applied to the skin and that repeated BL exposure may lead to skin photoaging.

Preventing BL–induced skin damage is necessary because photoaging can occur in human skin owing to damage caused by BL as well as exposure to UV light. Here, we investigated the effect of PE on 10 J/cm^2 BL irradiation. BL treatment increased mitochondrial singlet oxygen levels and decreased mitochondrial content and mitochondrial membrane potential in NHDF (Fig. 2). In addition, the BL–irradiated skin model showed a decreased mitochondrial content

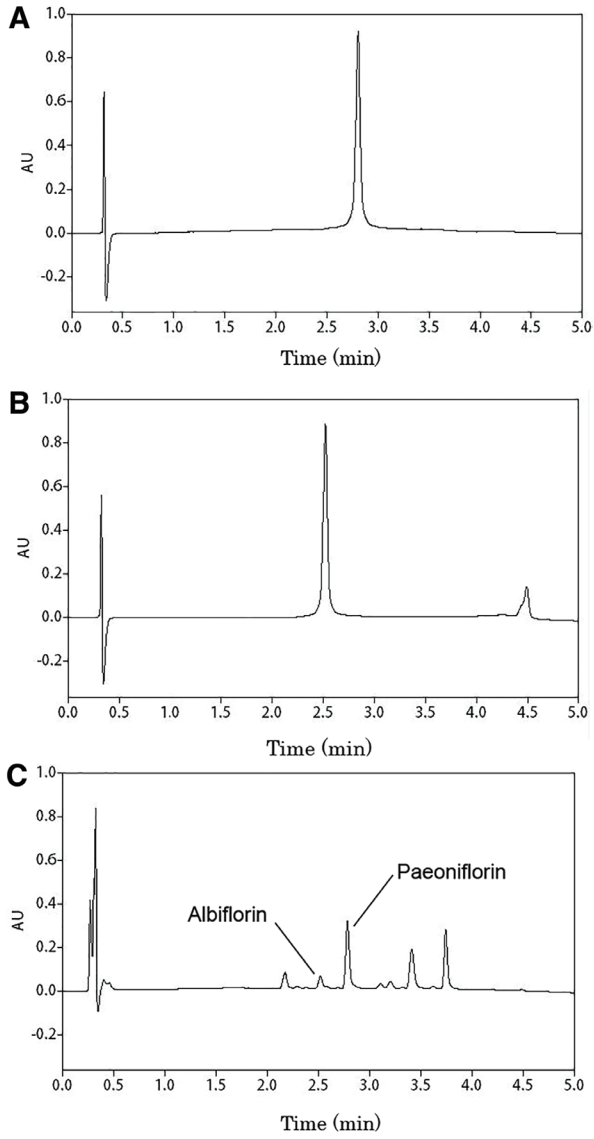

Fig. 3 Quantification of paeoniflorin and albiflorin. Chromatograms of paeoniflorin, albiflorin, and PE. The peaks of paeoniflorin (A), albiflorin (B), and PE (C) were characterized based on their retention times and UV spectra. A.U., arbitrary unit; PE, *Paeonia lactiflora* Pallas root extract.

Table 2 Effects of PE and its components on SOAC.

	SOAC (μM α-Toc/g)
PE	
7 μg/mL	0.8 ± 0.6
35 μg/mL	5.1 ± 1.8
70 μg/mL	12.1 ± 1.2
Paeoniflorin	
0.27 μM	4.0 ± 0.3
2.7 μM	6.6 ± 0.6
27 μM	8.1 ± 1.5
Albiflorin	
0.04 μM	0.2 ± 0.1
0.4 μM	4.9 ± 1.4
4 μM	8.0 ± 2.0

α-Toc, D-α-Tocopherol; PE, *Paeonia lactiflora* Pallas root extract; SOAC, singlet oxygen absorption capacity

Table 3 Effect of BL exposure on cell viability in the skin model.

			Cell viability (%)
Sham BL	Vehicle		100 ± 0.0
10 J/cm² BL irradiation	Vehicle		72.5 ± 2.0*
	PE	7 μg/mL	73.8 ± 4.2
		35 μg/mL	94.5 ± 2.7†
		70 μg/mL	97.7 ± 2.4†
	Paeoniflorin	0.27 μM	75.5 ± 4.3
		2.7 μM	73.2 ± 5.4
		27 μM	105.5 ± 4.8†
	Albiflorin	0.04 μM	71.5 ± 1.5
		0.4 μM	74.2 ± 5.9
		4 μM	104.3 ± 5.6†
	Mixture of paeoniflorin and albiflorin	1.4 μM + 0.2 μM	97.1 ± 2.1†
		2.7 μM + 0.4 μM	104.3 ± 5.6†

Changes in cell viability in the skin model. Data are presented as mean ± standard deviation (n = 3). *$p < 0.05$ versus sham BL of vehicle. †$p < 0.05$ versus BL of vehicle. Values were compared using Dunnett's multiple comparisons test.

BL, blue light; PE, *Paeonia lactiflora* Pallas root extract

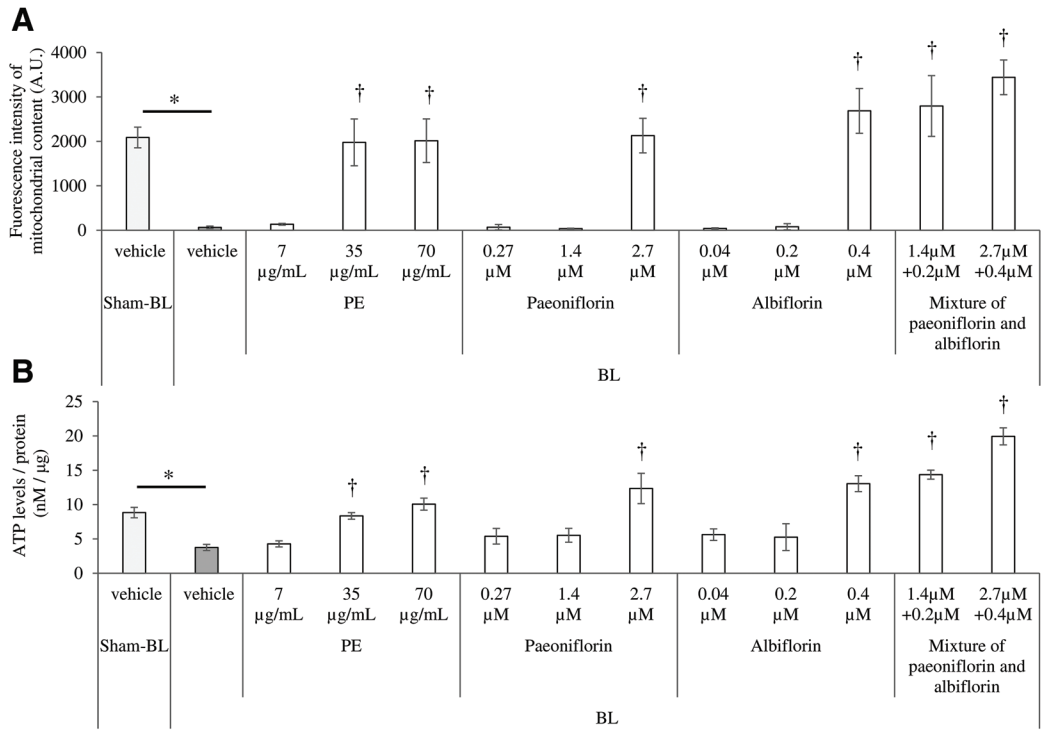

Fig. 4 Effects of BL exposure on mitochondria in the skin model. Changes in fluorescence intensity of mitochondrial content (A) and ATP levels primarily present in the dermis (B). Data are presented as mean ± standard deviation (n = 3). *$p < 0.05$ versus sham BL of vehicle. †$p < 0.05$ versus BL of vehicle. Values were compared using Dunnett's multiple comparisons test.

A.U., arbitrary unit; BL, blue light; PE, *Paeonia lactiflora* Pallas root extract

compared to the sham BL–irradiated human skin model (Fig. 4A). PE reversed the BL–induced damage (Figs. 2 and 4). Interestingly, BL–induced damage in both the skin model and NHDF was observed at the same irradiation intensity. This suggests that BL may reach the dermis and induce photoaging in human skin; thus, we consider it necessary to reduce BL–induced damage in the skin model.

Mitochondria maintain their function through repeated fission and fusion[17] and produce ATP by maintaining the mitochondrial membrane potential. In contrast, mitochondria undergo cell damage due to increased ROS production following UV exposure.[18] Mitochondrial damage caused by UV radiation is reflected by a decreased mitochondrial membrane potential due to a decrease in mitochondrial fusion proteins.[19] Furthermore, a decreased mitochondrial membrane potential is thought to reduce ATP production, leading to cell dysfunction. Based on these findings, we hypothesized that PE inhibits mitochondrial damage by suppressing the BL–induced increase in mitochondrial singlet oxygen levels, probably because of the presence of components that scavenge mitochondrial singlet oxygen.

To identify the active components of PE that protect against BL damage, we examined the paeoniflorin and albiflorin concentrations. The SOAC evaluation showed that PE, paeoniflorin, and albiflorin had singlet oxygen absorption capacities (Table 2). These results suggest that PE scavenges intramitochondrial singlet oxygen due to the presence of paeoniflorin and albiflorin. Singlet oxygen in the mitochondria is thought to oxidize lipids in the mitochondrial membranes, causing the mitochondria to cease biosynthesis, such as ATP production, leading to cellular and skin dysfunction. In addition, fibroblasts produce the extracellular matrix, but ATP is consumed for extracellular matrix production.[20] It has been suggested that a decrease in ATP leads to a decrease in the extracellular matrix, which is a factor in wrinkle formation.

Therefore, we evaluated the effects of BL exposure on mitochondrial ATP levels using a skin model. The BL–irradiated skin model showed decreased ATP levels compared to sham BL–irradiated human skin (Fig. 4B). PE, paeoniflorin, and albiflorin improved ATP levels in the skin model. In addition, paeoniflorin and albiflorin tended to further increase the mitochondrial content and ATP levels corrected for proteins than did PE. Paeoniflorin has been reported to have effects different from those of PE, such as altered mRNA expression and cell cycle regulation.[21] These results suggest that paeoniflorin and albiflorin increased mitochondrial content and ATP levels compared to PE because their effects on intracellular activity and mitochondrial function were greater than those of PE.

On the other hand, the cell viability of paeoniflorin and albiflorin exposed to BL was comparable to that of PE and the sham BL vehicle. It has been reported that paeoniflorin produces more ATP than PE, but is not involved in cell proliferation.[21] Furthermore, it has been reported that the proliferation and division of cells and mitochondria are essential for proteins specific to the phases of proliferation and division.[22] These findings suggest that paeoniflorin and albiflorin regulated factors involved in cell proliferation and promoted factors involved in mitochondrial division more than PE, which may have decreased the ATP levels consumed by cell proliferation and increased the ATP levels more than PE or sham BL.

Interestingly, 1.4 μM paeoniflorin and 0.2 μM albiflorin showed no effect individually; however, combining the 2 components exhibited synergy (Fig. 4). Thus, we conclude that it is more meaningful to use whole PE rather than a single isolated component (paeoniflorin or albiflorin) to assess BL damage.

5. Conclusion

In conclusion, PE is a promising cosmetic ingredient that prevents skin aging because it not only has excellent antioxidant activity but also improves mitochondrial function by suppressing BL–induced damage.

Conflict of Interest: There are no conflicts of interest to declare.

Abbreviations: α-Toc, D-α-tocopherol; ATP, adenosine triphosphate; BL, blue light; DPBF, 2,5-diphenyl-3,4-benzofuran; EP, 3-(1,4-epidioxy-4-methyl-1,4-dihydro-1-naphthyl) propionic acid; HBSS, Hanks' balanced salt solution; NHDF, normal human dermal fibroblasts; PBS, phosphate-buffered saline; PE, *Paeonia lactiflora* Pallas root extract; ROS, reactive oxygen species; SOAC, single oxygen absorption capacity; UPLC, ultra-performance liquid chromatography; UV, ultraviolet

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