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Coenzyme Q_{10} enhances dermal elastin expression, inhibits IL-1α production and melanin synthesis *in vitro*

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Synopsis

Coenzyme Q_{10} (CoQ_{10}) is a well-known antioxidant and has been used in many skincare products for anti-ageing purpose. However, the molecular mechanisms of CoQ_{10} function in skin cells are not fully understood. In this paper, we compared the effects of CoQ_{10} on primary human dermal fibroblasts from three individuals, including adult. We demonstrated that CoQ_{10} treatment promoted proliferation of fibroblasts, increased type IV collagen expression and reduced UVR-induced matrix metalloproteinases-1 (MMP-1) level in embryonic and adult cells. In addition, CoQ_{10} treatment increased elastin gene expression in cultured fibroblasts and significantly decreased UVR-induced IL-1α production in HaCat cells. Taken together, CoQ_{10} presented anti-ageing benefits against intrinsic ageing as well as photo damage. Interestingly, CoQ_{10} was able to inhibit tyrosinase activity, resulting in reduced melanin content in B16 cells. Thus, CoQ_{10} may have potential depigmentation effects for skincare.

Introduction

Cutaneous ageing results from two distinct processes, the intrinsic ageing and actinic damage/photo-ageing superimposed on the intrinsic ageing in sun-exposed areas of skin [1–4]. Skin ages chronologically as other parts of the body. The ageing process is revealed by reduced cell turnover rate in both epidermis and dermis, resulting in skin atrophy [5]. Aged skin shows thin epidermis with flattening of the dermal–epidermal junction (DEJ) and reduced dermal papillae and epidermal redge pegs [4]. Progressive shortening of the telomeres is currently believed to be a critical mechanism during intrinsic ageing process [6]. In addition, deteriorated cellular functions, such as lower collagen and elastin biosynthesis, can lead to less supportive fibres in the dermis that provides the skin tensile strength and resilience [4].

External factors such as smoking, alcohol, environmental pollution, poor nutrition and particularly UV exposure cause additional damage to skin [1, 4]. Massive accumulation of solar elastosis in papillary dermis is a striking feature of sun-damaged skins [7, 8]. Significant loss of dermal collagen fibres has been observed in sun-damaged skins, due to degradation by various matrix metalloproteinases (MMPs) and other types of proteases induced by UVA and/or UVB radiation [9]. Activation of AP-1 and inhibition of TGF-beta signalling are the major underlying mechanisms for UV-induced collagen damage [10]. Formation of reactive oxygen species (ROS) is believed to be another major contributor to UV damage [4, 10]. UV irradiation also induces significant increase in IL-1α expression in keratinocytes, which subsequently elicits a cascade of pro-inflammatory cytokine production, such as IL-6, IL-8 and TNF-α. These cytokines contribute to the skin damage following UV exposure [11–13].

Deregulated pigmentation is another clinical presentation of photo-aged skin. Skin melanin is synthesized by melanocytes at the basal layer of epidermis and gets transferred to stratified keratinocytes through melanosomes. UV exposure enhanced melanin production and usually resulted in undesirable darkness and age-spots among Asian populations [14, 15]. It is widely accepted that the rate-limiting enzyme of melanin synthesis is tyrosinase [16], and extensive effort has been devoted to developing tyrosinase inhibitors for skin-whitening products [17].

Coenzyme Q_{10} (CoQ_{10}) has been widely used in cosmetic products for antioxidative and anti-ageing purposes. However, some of the underlying mechanisms are yet to be elucidated. CoQ_{10} plays important roles in cellular and molecular functions within a cell. As an electron carrier in mitochondrial respiratory chain, CoQ_{10} is critical in the functions of mitochondrial complex I and III [18, 19]. CoQ_{10} is found to effectively reduce UVA-mediated oxidative stress in human keratinocytes by thiol depletion, activation of specific phosphotyrosine kinases and prevention of oxidative DNA damage [20]. As the level of intracellular CoQ_{10} decreases with age, the supplementation of dietary or topical CoQ_{10} has been proposed to decelerate the ageing process of skin. A body of literature demonstrates that CoQ_{10} has anti-ageing effects in skin [21–23]. Studies have shown that CoQ_{10} reduced the area of facial wrinkles by inhibiting the expression of MMPs in fibroblasts [21]; CoQ_{10} also promoted the proliferation of human neonatal fibroblasts, enhanced gene expression of type IV and VII collagens and decreased wrinkle depth around the eyes after 6 months of topical application [22]. Additionally, one report suggested that CoQ_{10} can suppress the UVR- or IL-1α-mediated inflammatory response in human dermal fibroblasts by inhibiting production of pro-inflammatory factors PGE-2 and IL-6 [23].

In this study, we set to understand the molecular mechanisms of CoQ_{10}'s anti-ageing effects. We demonstrated CoQ_{10} treatment led to increased collagen IV and elastin expression and cell proliferation in adult fibroblasts. CoQ_{10} was able to protect cells from UVR

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by inhibiting MMP-1 and IL-1α expression. Additionally, CoQ_{10} reduced melanin synthesis by inhibiting tyrosinase activities in B16 cells. These data pointed to a novel mechanism of CoQ_{10}'s anti-ageing function and demonstrated CoQ_{10}'s potential depigmentation effects for skincare products.

Materials and methods

Cell culture

Human embryonic skin fibroblasts (ESF), HaCat cells and B16 were purchased from Cell Resource Center, IBMS, CAMS/PUMC (Beijing, China). Primary skin fibroblasts were isolated from human foreskins of 8-year-old (8-year old-F) and 20-year-old donors (20-year old-F) with informed consents. Human foreskins were disinfected at room temperature for 20 min in DMEM (Invitrogen Corp., Carlstries, CA, U.S.A.) with Pen/Strep and amphotericin B (Gibco). Fat and other subcutaneous tissues were trimmed off, and the remaining skin was cut into pieces (approximately 1×2 mm^2) before plating in DMEM (Gibco) containing 10% FBS (Hyclone, Thermo Scientific, Victoria, Australia) and cultured at 37°C with 5% CO_2 for about 4 weeks. Fibroblasts and keratinocytes were harvested with 0.25% trypsin solution (Gibco), based on the difference in time required for each cell to detach from the culture plate. All above cells were maintained in DMEM (Gibco) containing 10% FBS (Hyclone) at 37°C with 5% CO_2.

Cell proliferation assay

Coenzyme Q_{10} (Sigma-Aldrich Corp., St Louis, MO, U.S.A.) was dissolved in ethanol at stock concentration of 2 mM and added to cultured media based on the concentrations previously reported [22]. ESF, 8-year old-F, 20-year old-F, HaCat and B16 cells were seeded in 24-well plates ($2–4 \times 10^4$ per well) and cultured in DMEM containing 10% FBS for 24 h. Culture medium was then changed to DMEM with 1% FBS containing CoQ_{10} for another 72 h. Cell viability in each well was determined by cell counting kit-8 [(CCK-8); Dojindo Laboratorise, Japan], a colorimetric assay based on the formation of water-soluble yellow formazan by mitochondrial dehydrogenase in active mitochondria.

RNA extraction and QPCR

Embryonic skin fibroblasts and primary skin fibroblasts were cultured in 6-well plates (2×10^5 per well) in DMEM containing 10% FBS for 24 h and then treated with CoQ_{10} at a final concentration of 0.5, 1 or 2 μM, respectively, for another 24 h. Total RNAs were extracted using RNeasy Mini Kit (Qiagen, Valencia, CA, U.S.A.) and reverse transcribed using SuperScript® III First-Strand Synthesis System (Invitrogen Corp., Carlstries, CA, U.S.A.). Real-time QPCRs were performed on 7500 Sequence Detector (ABI, U.S.A.) using Power SRBR® Green PCR Master Mix reagents (ABI) following manufacture's instruction. Primers for real-time PCR are as follows: elastin, sense primer, GGTATCCCATC AAGGCCCC; anti-sense primer, TTTCCCTGTGGTGTAGGGCA; type IV collagen alpha 1, sense primer, CGCTTACAGCTTTTG GCTCG; anti-sense primer, GACGGCGTAGGCTTCTTGAA. GAPDH, sense primer, ATCTCTGCCCCCTCTGCTG; and anti-sense primer, ATGGTTCACACCCATGACGA. These primers were synthesized by Sangon Biotech Co. Ltd (Shanghai, China).

CoQ_{10} emulsion

Owing to limited solubility of CoQ_{10} in ethanol, an oil-in-water nano-emulsion containing 23 mM CoQ_{10} was produced in our laboratory. A vehicle of CoQ_{10}-free emulsion was used as control.

UV irradiation

Embryonic skin fibroblasts, primary human fibroblasts and HaCat cells were seeded in 12-well plates (1×10^5 per well) with DMEM containing 10% FBS for 24 h and then treated with CoQ_{10} (1, 5 or 10 μM) for another 24 h. The choice of above CoQ_{10} concentration was based on previous report [24]. CoQ_{10}-treated cells were washed with1 × phosphate-buffered saline (PBS; Invitrogen Corp., Carlstries, CA, U.S.A.) and then subjected to UVA (in PBS) or UVB (without PBS) irradiation. The doses of UVA were 15 J cm^{-2} for ESF and fibroblasts and 14 J cm^{-2} for HaCat. The doses of UVB were 60 mJ cm^{-2} for ESF and fibroblasts and 20 mJ cm^{-2} for HaCat. After UV irradiation, cells were washed with PBS and cultured with media containing CoQ_{10} for another 24 h. Intracellular ROS, MMP-1 and IL-1α in cultured media were then measured. UV irradiations were carried out with UVA or UVB light source (wave length: UVA: 320–400 nm, wave peak 365 nm, UVB: 280–320 nm, wave peak 312 nm, Spectroline Corp., Westbury, NY, U.S.A.).

Intracellular ROS assay

Embryonic skin fibroblasts, primary human fibroblasts and HaCat cells were collected after UV irradiation, and the intracellular ROS levels were measured using ROS Assay Kit (Beyotime Institute of Biotechnology, Haimen, Jiangsu, China) with fluorescent probe 2′,7′-Dichlorofluorescin diacetate (DCFH-DA). Fluorescent signal was detected by Fluoroskan Ascent (Thermo Fisher Scientific, Shanghai, China) at excitation wavelength of 485 nm and emission wavelength of 538 nm. Results were normalized by total protein of each well, measured with Enhanced BCA Protein Assay Kit (Beyotime Institute of Biotechnology, Haimen, Jiangsu, China).

Enzyme Linked Immunosorbent Assay (ELISA)

Matrix metalloproteinases-1 contents in culture media of ESF, 8-year old-F and 20-year old-F fibroblasts after UV irradiation, were determined by human total MMP-1 DuoSet ELISA kit (R&D Systems, Inc. Minneapolis, MN, U.S.A.) according to the manufacturer's instructions. Results were normalized by total proteins measured with Enhanced BCA Protein Assay Kit (Beyotime Institute of Biotechnology).

For IL-1α ELISA assay, HaCat cells were treated with UV irradiation, and cell culture media were collected for IL-1α detection by human IL-1α/IL-1F1 DuoSet ELISA kit (R&D Systems, Inc.) according to the manufacturer's instructions. Results were normalized by total proteins measured with Enhanced BCA Protein Assay Kit (Beyotime Institute of Biotechnology, Haimen, Jiangsu, China)

Melanin assay, tyrosinase activity measurement and DOPA staining

B16 mouse melanoma cells were seeded in 24-well plate (4×10^4 per well) in DMEM containing 1% FBS for 24 h, followed by culturing in DMEM containing 1% FBS plus CoQ_{10} for another 72 h. Melanin contents and tyrosinase activities were then measured, in these cells.

B16 cells in 24-well plates were washed twice with PBS, followed by addition of 300 μL trypsin in each well. After cells were detached, 300 μL medium with 10% FBS was added to each well, and cells were fully suspended. Of 500 μL of cell suspension was transferred to 1.5-mL microtube and centrifuged at 13 800× g for 10 min. The majority of the supernatant was removed, and remaining supernatant residue was subsequently air-dried. Of 200 μL 1 N NaOH (Sigma-Aldrich Corp., St Louis, MO, U.S.A.) was added to each tube and incubated for 15 min at 85°C. After cooling to room temperature, the melanin solution was transferred to a 96-well plate, and OD was read at 405 nm.

B16 cells in 24-well plates were washed with PBS and lysed with 250 μL PBS (pH 6.8) containing 1% Triton X-100 (Sigma-Aldrich Corp., St Louis, MO, U.S.A.) for 20 min. Of 100 μL of cell extract was added to each well of a 96-well plate, together with 100 μL PBS containing 0.1% L-DOPA (Sigma), then incubated at RT for 1 h. Dopachrome formation was monitored by measuring absorbance at 490 nm.

B16 cells in 24-well plates were washed three times with 500 μL PBS for 10 min on an orbital shaker, then fixed in 500 μL 10% buffered formalin for 10 min. Thereafter, cells were washed with 1 mL PBS for three times. Then, 500 μL PBS with 0.1% L-DOPA was added to each well, followed by incubation at 37°C for 4–5 h. Pictures were taken using inverted microscope (Olympus, Japan).

Statistical analysis

All statistical data were analysed with independent sample t-test. Data were represented as the mean ± SD. All p values were considered significant when $P < 0.05$.

Results

CoQ_{10} has anti-ageing effects against multiple ageing processes

It was reported previously that CoQ_{10} increased cell proliferation of neonatal fibroblast [22]. To examine whether CoQ_{10} has similar effect in adult fibroblast, we measured the proliferation of CoQ_{10}-treated cells with CCK-8 assays. HaCat, ESF and two lines of primary human dermal fibroblasts, isolated from 8 to 20-year old individuals, respectively, were treated with increasing concentrations of CoQ_{10}. As shown in Fig. 1A, CoQ_{10} treatment was able to increase cell numbers in a dose-dependent manner in all three fibroblast lines. Consistent with previous report, the proliferation effect was not observed in HaCat cells with similar CoQ_{10} concentrations [22]. Flattening of the DEJ is a typical feature of aged skin, which is associated with reduced expression of protein components of the basement membrane, such as collagen IV and VII [4]. Our results reproduced previous reports that CoQ_{10} enhanced collagen IV gene expression. As shown in Fig. 1B, CoQ_{10} treatment significantly increased type IV collagen expression in both adult and embryonic cells. These results suggest that CoQ_{10} can promote proliferation and increase type IV collagen gene expression in adult fibroblasts as well as in embryonic cells.

Loss of elastic fibres is mostly responsible for the wrinkled and sagging appearance of aged skin [3]. To examine whether CoQ_{10} has any effect on elastin gene expression, RNAs were isolated from fibroblasts treated with CoQ_{10} or vehicle control, and elastin expression level was determined by quantitative RT-PCR. As shown in Fig. 1C, treatment of CoQ_{10} was able to enhance elastin gene expression in a dose-dependent manner, in both adult and embryonic fibroblasts, highlighting a novel mechanism of CoQ10's anti-ageing function.

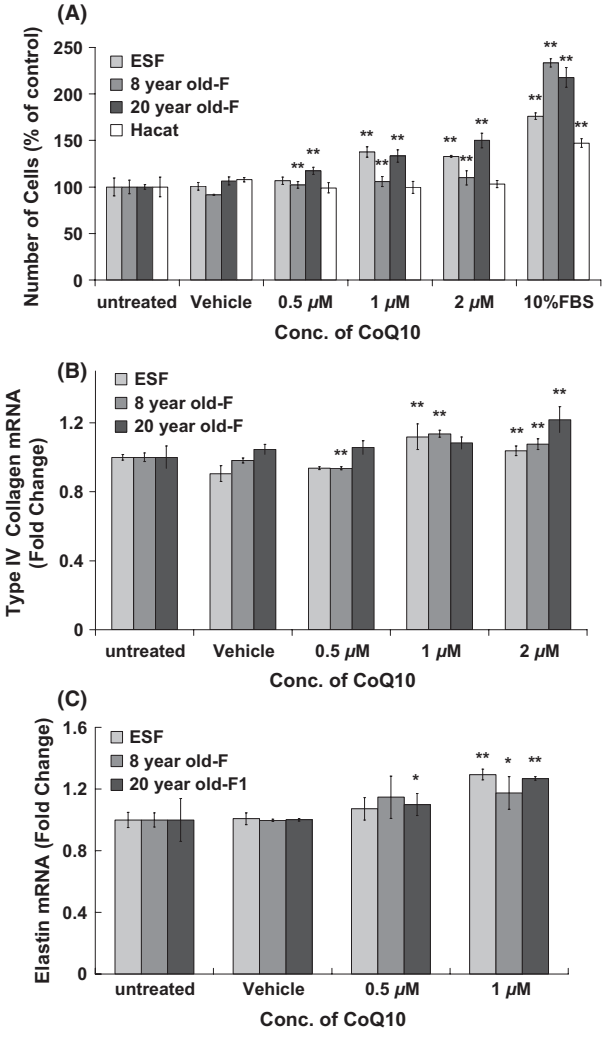

Figure 1 Effects of Coenzyme Q_{10} (CoQ_{10}) treatment on fibroblasts proliferation, collagen IV and elastin gene expressions. (A) HaCat cells and human dermal fibroblasts were treated with CoQ_{10}, vehicle or 10% FBS for 72 h. Cell proliferation was examined by cell counting kit-8 assay. Results were presented as per cent of cells in treatment groups compared with untreated. (B,C) Quantitative RT-PCR analysis of RNA isolated from human dermal fibroblasts treated with CoQ_{10} or vehicle for 24 h. Type IV collagen (B) and elastin (C) gene expressions were normalized to GAPDH. Fold change was calculated as ratio of treated groups to untreated. Each bar represented mean ± SD of three independent experiments. (*$P < 0.05$, **$P < 0.01$ compared with vehicle).

CoQ_{10} protects cells from UV irradiation induced damage

Ultraviolet Radiation (UVR)-induced damage is believed to be partially owing to the formation and activity of ROS [4]. To study whether CoQ_{10} has any effect on ROS production, HaCat, ESF and primary human fibroblasts were irradiated with UVA or UVB, and

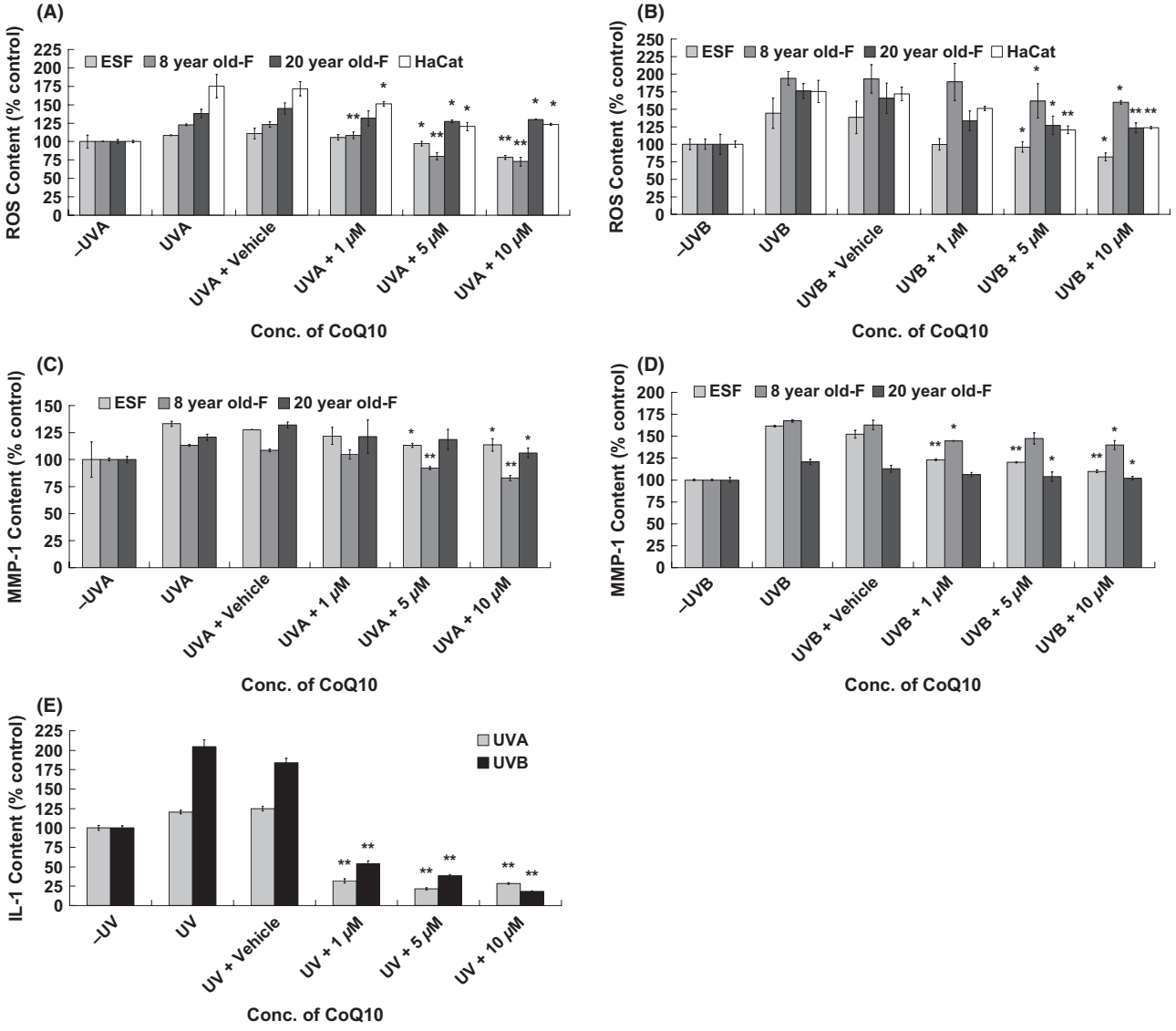

Figure 2 Effects of Coenzyme Q_{10} (CoQ_{10})on reactive oxygen species (ROS), matrix metalloproteinases-1 and IL-1α in UVA- or UVB-irradiated fibroblasts and HaCat cells. Cells were treated with CoQ_{10} or vehicle for 24 h before and after UV irradiation. Cellular ROS levels following UVA (A) and UVB (B) irradiation were measured by spectrophotometer (Bio-Rad Laboratories, Inc., Tokyo, Japan) and normalized to total protein levels. ELISA analysis of matrix metalloproteinases-1 level in cultured medium after UVA (C) or UVB irradiation (D) was performed. IL-1α level was determined by ELISA in the medium of UVA- or UVB-irradiated HaCat cells (E). The values of matrix metalloproteinases-1 and IL-1α were normalized to total protein levels. Results were presented as percentage of treated cells compared with untreated. Each bar represented mean ± SD of three independent experiments, ($^*P < 0.05$, $^{**}P < 0.01$ compared with UV(A/B) + vehicle).

intracellular ROS levels were measured. As shown in Fig. 2A,B, UVA and UVB irradiation increased ROS levels in HaCat cells, and treatment with CoQ_{10} resulted in dose-dependent decrease in ROS levels in these cells. ESF and primary fibroblasts responded to UVB irradiation by increasing cellular ROS levels, and CoQ_{10} treatment could reduce the ROS levels as shown in Fig. 2B. These data suggest a general protection effect of CoQ_{10} against UVR-induced oxidative stress. UVR-induced MMP-1 expression is mostly responsible for degradation of extracellular matrix during photo-ageing [9]. ELISA analysis revealed that CoQ_{10} treatment reduced MMP-1 protein level in cultured media of all three lines of fibroblasts in a dose-dependent manner (Fig. 2C,D). These data suggest that CoQ_{10} can protect adult fibroblasts from UVR-induced ROS and MMP-1 damage.

Pro-inflammatory cytokine IL-1α was reported to be induced in UVR-treated HaCat cells and responsible for initiation of a cascade of pro-inflammatory responses following UV irradiation [12, 13]. To evaluate whether CoQ_{10} has protective effect against UVR-induced inflammation, we measured IL-1α level in cultured medium of UV-irradiated HaCat cells treated with increasing

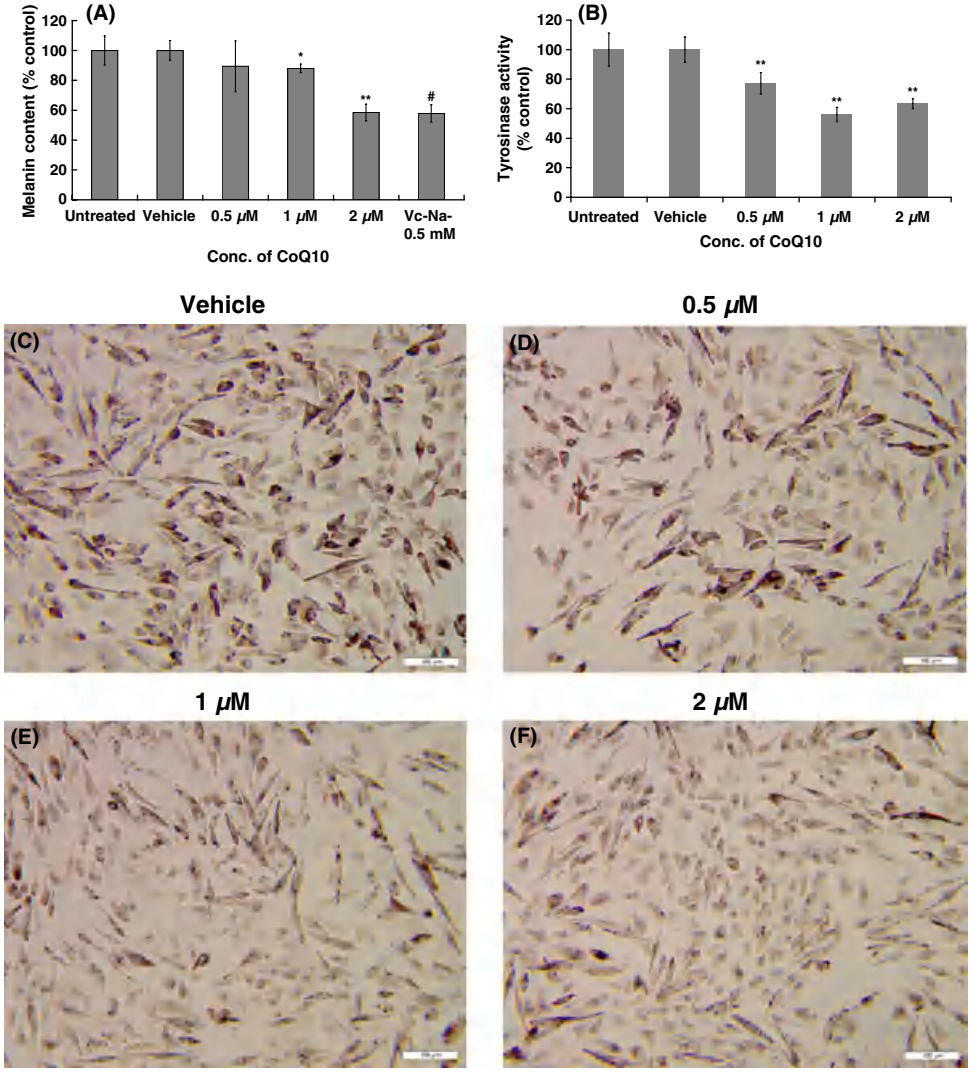

Figure 3 Effects of Coenzyme Q_{10} (CoQ_{10}) on melanin synthesis and tyrosinase activity in B16 melanoma cells. B16 cells were treated with CoQ_{10} (0.5, 1, 2 μM) or sodium ascorbate (Vc-Na) (0.5 mM) for 72 h. (A) Melanin content was determined by spectrophotometer and normalized to the value of cell counting kit-8 measurement. (B) Cell lysates were incubated with DOPA, and tyrosinase activity was evaluated by spectrophotometer and normalized to total protein level. Results were presented as percentage of treated cells compared with untreated. Each bar represented mean ± SD of three independent experiments. (C–F) DOPA staining was visualized by phase-contrast microscopy in vehicle treated (C), 0.5 μM (D), 1 μM (E) and 2 μM (F) CoQ_{10}-treated groups. Scale bar: 100 μm. (*$P < 0.05$, **$P < 0.01$ compared with vehicle, #$P < 0.01$ compared with untreated).

concentrations of CoQ_{10}. As shown in Fig. 2E, both UVA and UVB induced IL-1α secretion from HaCat cells, with UVB having a more dramatic effect. CoQ_{10} significantly decreased IL-1α production induced by UVA and UVB, to a level much lower than the basal level, suggesting an effective anti-inflammatory function of CoQ_{10}.

CoQ_{10} reduces melanin synthesis

Photo-ageing also leads to deregulated pigmentation. Although CoQ_{10} has been applied as an anti-ageing agent in skincare products, its effect on pigmentation has not been reported. To evaluate whether CoQ_{10} affects melanin synthesis, B16 melanoma cells were treated with CoQ_{10} or vehicle, and melanin content was measured after 72 h. CoQ_{10} treatment resulted in decreased melanin levels in a dose-dependent manner (Fig. 3A). CoQ_{10} at a concentration of 2 μM showed similar effects as that of 5 mM ascorbic acid. As tyrosinase is the key enzyme for melanin synthesis, tyrosinase activities were measured in CoQ_{10}-treated B16 melanoma cells. CoQ_{10} treatment significantly inhibited tyrosinase activity in these cells (Fig. 3B). Furthermore, DOPA staining, as a morphological indicator of tyrosinase activity [25], confirmed the decreased tyrosinase activity following CoQ_{10} treatment (Fig. 3C). These results suggested that CoQ_{10} could be used as an alternative skin-lightening agent.

Discussion

Coenzyme Q_{10} is a critical component of respiratory complex and plays pivotal role in mitochondrial activity and ATP production. Skin cells depend on mitochondria activity to produce enough energy for cell proliferation, DNA replication, protein synthesis and other cellular activities to repair the damages resulted from environmental insults. Mitochondrial function and ATP contents in fibroblasts are reduced following repeated UV exposure [26]. Other studies have indicated cellular level of CoQ_{10} declines in skin with age [20]. Therefore, skin would potentially benefit from topical supplementation of CoQ_{10}.

A number of studies have uncovered the molecular mechanisms of the anti-ageing effect of CoQ_{10} on human skin cells, such as increased proliferation of fibroblasts, enhanced-type IV collagen expression and inhibition of UVR-induced ROS and MMP-1 production [20–22]. However, most of these studies were carried out in neonatal cells. In this study, we evaluated the effect of CoQ_{10} on fibroblasts isolated from adolescent and adult human dermis and demonstrated that adolescent and adult cells were equally responsive to CoQ_{10} treatment as embryonic cells. These results confirmed the effectiveness of CoQ_{10} in skincare products.

Elastic fibres are assembled from elastin protein and other microfibrillar components, which in aggregate create a network that can stretch and relax [27, 28]. The synthesis of elastin in skin is most active in early childhood and adolescence, and declines thereafter. Meanwhile, the release of human neutrophil and macrophage elastases increases with age, causing further degradation of mature elastic fibers [29–31]. It is well established that elastin gene expression is regulated at transcriptional and post-transcriptional level [32], and transforming growth factor (TGF-β) is the most potent modulator of elastin production through transactivation of elastin promoter, and perhaps more significantly stabilization of elastin mRNA [33, 34]. Although the loss of skin elastic fibres is the single most important cause of age-related wrinkles and sagging, strategies aiming at enhancing the elastic fibre network are limited [4]. Recently, natural extracts of dill [35] and non-denatured soybean [36] as well as retinol [37] were suggested for enhancing skin elasticity. Our study demonstrated that the expression of elastin was significantly increased by CoQ_{10}, although the exact mechanism remained to be investigated. It will be insightful to study whether CoQ_{10} has any effect on regulation of elastin promoter activity and mRNA stability and whether it is mediated through TGF-β signalling pathway.

Ultraviolet irradiation activates transcription factor NF-κB that stimulates the production of pro-inflammatory cytokines in skin cells. These cytokines can subsequently activate AP-1 and NF-κB through paracrine/autocrine mechanisms to further amplify the UV responses [38]. Our study showed that UVR-induced IL-1α, a main switch in the initiation of inflammation [7], was significantly decreased by CoQ_{10} treatment. The mechanism of CoQ_{10} inhibition of IL-1α production requires further investigation. It has been reported that CoQ_{10} inhibits NF-κB activation in dopaminergic neurons suggesting neuroprotective potential of CoQ_{10} [39]. It will be interesting to investigate the regulation of NF-κB signalling pathway in UV-irradiated skin cells following CoQ_{10} treatment. Additional mechanisms maybe involved considering the observation that CoQ_{10} treatment was able to decrease UV-induced IL-1α production in skin cells to a level significantly below the basal level. UV irradiation is the most profound factor causing photo-ageing in sun-exposed skin. Previous report also indicated that CoQ_{10} was able to suppress IL-1α-induced PGE-2 and IL-6 production [21, 23]. It is evident that CoQ_{10} played an important role in anti-inflammatory response following UV irradiation and thus protect the cells from UV damage.

In the present study, melanin production was significantly decreased by CoQ_{10} through inhibition of tyrosinase activity. CoQ_{10} at a concentration of 2 μM showed similar inhibitory effect on melanin synthesis as that of 0.5 mM ascorbic acid. However, the mode of action for tyrosinase inhibition remains to be elucidated. In this experiment, the CoQ_{10} applied to cells was in the oxidized form, thus it is unlikely to act through reducing dopaquinone as ascorbic acid. Whether it directly interacts with the active site of tyrosinase or some cofactors needs to be further investigated.

In summary, using human fibroblast isolated from individuals of different age, we demonstrated that CoQ_{10} was able to induce proliferation of adult skin fibroblast, enhance gene expression of type IV collagen and elastin and decrease production of UVR-induced ROS and MMP-1. CoQ_{10} also decreased UVR-induced IL-1α expression in HaCat cells. Additionally, CoQ_{10} treatment resulted in reduced melanin synthesis primarily through inhibiting tyrosinase activity. Thus, CoQ_{10}, as a natural factor could serve as an effective agent for anti-skin ageing, anti-inflammation as well as skin-whitening purposes.

Acknowledgements

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