RESEARCH

MMP expression alteration and MMP-1 production control by syringic acid via AP-1 mechanism

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Abstract

Background: Syringic acid is a phenolic compound that can be produced through selective hydrolysis of eudesmic acid containing 20% sulfuric acid. The acid is obtained by breaking down components, such as anthocyanin and lignin acid, present in the oils of acai berries and other fruits. Recently, the anti-inflammatory, selective toxicity, anticancer, and antioxidant effects of syringic acid have been studied, but few studies on the effects of syringic acid on human keratinocytes (HaCaT) cells have been published. The present study investigated the antioxidant effects of syringic acid, as a potential cosmetic ingredient, on matrix metalloproteinase (MMP) expression alteration and MMP production control through the activator protein-1 (AP-1) mechanism in HaCaT cells exposed to ultraviolet B radiation.

Methods: A reactive oxygen species (ROS)-scavenging assay using a luciferase reporter that utilizes the AP-1 response element, an enzyme-linked immunosorbent assay (ELISA), and quantitative reverse transcription polymerase chain reaction (qRT-PCR) were used. To confirm if ROS in HaCaT cells damaged by ultraviolet B are eliminated by syringic acid, 2′-7′-dichlorofluorescein diacetate was used to measure the ROS quantity. qRT-PCR analysis was used to measure the expressions of *SOD1* mRNA, *GPx1* mRNA, and catalase (*CAT*) mRNA, which are related to oxidation inhibition. To measure the anti-aging effects of syringic acid, qRT-PCR was used to measure the expression levels of *MMP* mRNA, *c-Jun*, and *c-Fos*.

Results: ROS were eliminated by syringic acid, and cell aging due to ultraviolet B was suppressed. Results of qRT-PCR analysis confirmed that syringic acid suppressed oxidation in HaCaT cells damaged by ultraviolet B. Further, syringic acid was found to suppress the expression of *MMP* mRNA, *c-Jun*, and *c-Fos* in a concentration-dependent manner. ELISA showed that MMP-1 production decreased in a concentration-dependent manner. The luciferase reporter analysis revealed a concentration-dependent decrease in the transcriptional activity of AP-1 promoter caused by syringic acid.

Conclusions: Syringic acid was shown to be involved in altering MMP expression and controlling MMP-1 production through the AP-1 mechanism. Thus, the antioxidant and anti-aging effects of syringic acid increased the survival rate of HaCaT cells damaged by ultraviolet B, suggesting that it can be used as a natural phytochemical in cosmetic products.

Keywords: Syringic acid, HaCaT , Ultraviolet B, ROS, Antioxidant, MMPs, Procollagen type I

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Background

External stimuli, including the sun's rays as well as direct and continuous exposure of keratinocytes to the external environment, lead to oxidative stress and skin aging. When the skin is in a continuous oxidative state with slow recovery, it becomes rough and dull, which causes skin aging characterized by loss of elasticity and wrinkles (Agarwal et al. 1988; Wong et al. 2007). Therefore, improving the body's antioxidant system is important for protecting keratinocytes and delaying cellular aging (Applegate et al. 1995).

Skin aging can be divided into two classes: intrinsic aging caused by natural genetics and extrinsic aging caused by exposure to the external environment (Naylor et al. 2011). Short-wavelength ultraviolet light (UVB) induces the production of matrix metalloproteinases (MMPs), which harm the skin (Pygmalion et al. 2010). The primary function of MMPs is to break down proteins and enzymes in the extra cellular matrix (ECM) (Egeblad and Werb 2002). Thus, MMPs have a destructive effect on the ECM and cause a decrease in fibrous collagen (Scharffetter-Kochanek et al. 2000). UCB passes through the skin keratin, causes DNA damage, and interacts with photosensitizers and chromatophores to induce oxidative stress (Ma et al. 2001). Consequently, UVB promotes the production of activator protein-1 (AP-1) and vitalization of nuclear factor kappa-light-chain-enhancer of activated B cells and induces the production of reactive oxygen species (ROS) on cell surface receptors, such as mitogen-activated kinases (MAPK) (Xu and Fisher 2005; Jiang et al. 2006). As such, UV is a major cause of skin aging. To delay aging, continuous research and development have been conducted in a variety of fields to normalize the signal systems within skin cells and prevent harm caused by UV and external stimuli.

Syringic acid, a type of phenolic compound, can be obtained through the selective hydrolysis of eudesmic acid containing 20% sulfuric acid (Bogert and Ehrlich 1919). It is contained in large amounts in oils of acai berries and other fruits (Pacheco-Palencia et al. 2008). Syringic acid is isolated from medicinal plants and biosynthesized through the shikimic acid pathway (Andrade et al. 2001; De Heredia et al. 2001; Dawidar et al. 2000). Studies on the selective effects of syringic acid (Shim et al. 1995; Goldberg et al. 1999; Ferguson 2001), such as strong anticancer and anti-inflammatory effects (Lü et al. 1998; Sun et al. 2002; Rekha et al. 2014), antioxidant effects (Srinivasn et al. 2014), and DPPH radical-scavenging activity, have been conducted. Compared with traditional chemical agents, natural ingredients extracted from plants are known to be less toxic to normal cells but are selectively toxic to cancer cells. Accordingly, there has been a growing interest in

the mechanisms and extracted components of natural active compounds (Shim et al. 1995).

The present study investigated the antioxidant effects of syringic acid on MMP expression alteration and MMP production control through the AP-1 mechanism in human keratinocytes exposed to UVB radiation and confirmed the protective effects of syringic acid against cell damage and its potential as a cosmetic component.

Methods

Cell culture and sample treatment

Cell culture

A human keratinocyte (HaCaT) cell line was obtained from American Type Culture Collection (USA) and cultured Dulbecco's modified Eagle's medium (Hyclone, USA) containing HaCaT cells in 10% fetal bovine serum (Hyclone) and 1% penicillin/streptomycin (penicillin 100 IU/mL, streptomycin 100 μg/mL; Invitrogen, USA) and incubated at 37 °C in 5% CO_2.

Syringic acid treatment

Syringic acid was purchased from Sigma-Aldrich (USA) in refined powder form and was dissolved in dimethyl sulfoxide (Sigma-Aldrich) for the experiment. After culturing HaCaT cells (1×10^6 cells/well) in culture dishes for 24 h, syringic acid was added to the medium, and the culture was incubated for 6 h. The cells were then irradiated with a UVB lamp (UVP, USA). UVB wavelengths were measured using a USB 2000 fiberoptic spectrometer system (Ocean Optics, USA). To investigate the effects of UVB on HaCaT cells, the medium was removed from the culture plate and washed with phosphate-buffered saline (PBS; pH 7.4). To prevent the cells from drying, 1-mL PBS was added to the washed HaCaT cells, which were then irradiated with UVB with the lid open. After UBS irradiation, PBS was removed, fresh medium was added, and the cells were further cultured for 24 h.

Measurement of cell viability

The cell viability was measured using the principles of the water-soluble tetrazolium salts (WST)-1 assay, which measures the absorbance of formazan, a chromogenic material obtained by the reaction of mitochondrial dehydrogenase and soluble tetrazolium salts. The cells were inoculated into 96-well plates at a concentration of 3×10^3 cells/well in 100-μL amounts and incubated for 24 h. The cells were then treated with syringic acid at concentrations of 1, 2, 5, and 10 μM and incubated for another 24 h after exposure to UVB. Subsequently, 10-μL aliquots of EZ-Cytox cell viability assay kit reagent (ItsBio, Korea) was added to the cell culture plates. After 1-h incubation, a microplate reader (Bio-Rad, USA) was

used to measure the absorbance at 490 nm to determine the cell viability; this process was repeated thrice to derive the mean and standard deviation of cell viability.

RNA extraction and cDNA production

After extracting RNA for a quantitative analysis of the changes in gene expression pattern in HaCaT cells due to syringic acid, cDNA was synthesized, and the expression level of the desired gene was determined through quantitative real-time polymerase chain reaction (qRT-PCR). After dissolving the incubated cells in TRIzol reagent (Invitrogen, USA), 0.2-mL chloroform (Biopure, Canada) was added, and the cells were kept at room temperature before centrifuging at 12000 rpm at 4 °C for 20 min. Subsequently, the supernatant fluid, including mRNA from the infranatant liquid with protein, was separated, and 0.5-mL isopropanol was added to it. The cells were kept at room temperature for 10 min and then centrifuged at 12000 rpm at 4 °C. After precipitating the RNA, it was washed with 75% ethanol, ethanol was removed, and the RNA was dried in room temperature. The dried mRNA was dissolved in diethylpyrocarbonate (DEPC; Biopure) water for use in the experiment, and only the extracted RNA that exceeded the purity level of 260/280 nm (1.8 ratio), as determined using nanodrop (Maestrogen, USA), was used in the experiment. After obtaining 10 μL of 1-μg RNA, 0.5-ng oligo dT18 with DEPC water was added in a PCR tube and kept at 70 °C for 10 min. After inducing RNA denaturation, RNA was incubated with M-MLV reverse transcriptase (Enzynomics, Korea) at 37 °C for 1 h to synthesize cDNA.

Measurement of gene expression

qRT-PCR is used to measure the amount of amplification products by measuring the real-time fluorescence of fluorescent material, such as double-strand DNA SYBR green, bound by PCR products. The threshold at which fluorescence can be detected was set to the threshold cycle (ct), and after measuring the number of cycles that were needed to reach the ct, the difference in expression levels was determined. If the expression level is high, ct is reached quickly. As the number of cycles decreases, expression decreases. Therefore, the difference in one cycle results in twice the expression.

qRT-PCR was performed using Linegene K (BioER, China) and mixing 0.2 μM of primers with 50 mM KCl, 20 mM Tris/HCl (pH 8.4), 0.8 mM dNTP, 0.5 U Extaq DNA polymerase, 3 mM MgCl, and 1× SYBR green (Invitrogen) in a PCR tube. The validity of PCR was verified by performing a melting curve analysis. The expression of each gene was normalized to β-actin expression in a comparative analysis. The primers used in the experiments were as follows (Table 1).

Measurement of AP-1 promoter activity

AP-1 promoter luciferase assay was used to determine the effects of syringic acid on the transcriptional activity of AP-1 promoter. In this experiment, expression was confirmed after transfection using a vector (BPS Bioscience, CA, USA) in which AP-1-responsive elements were located in front of the luciferase gene. The cells were placed in 96-well culture dishes at a concentration of 3×10^4 cells/well and incubated for 24 h. After stabilizing the cells, 1 μL of the reporter gene was mixed with 15 μL of the cell culture medium. Subsequently, after adding 0.35-μL lipofectamine 2000 to 15-μL cell culture medium, diluent DNA and lipofectamine 2000 diluent were mixed and reacted at room temperature for 25 min. After the mixture was added to the cell plates in 30-μL amounts, it was incubated for 24 h and treated with reagents and stimuli. After an additional 24 h of incubation, the transcriptional activity of AP-1 promoter was measured.

Production of MMP-1 and procollagen type I

The enzyme-linked immunosorbent assay (ELISA) is an enzyme-substrate binding assay that uses antigen-specific reactivity to detect an antigen. This method was used to measure the production of MMP-1 and procollagen type I. After seeding, the cells were incubated for 24 h. After stimulating the cells with the

Table 1 List of primers used in this study

Gene	Forward primer	Reverse primer
SOD1	GGGAGATGGCCCAACTACTG	CCAGTTGACATGCAACCGTT
GPx1	TTCCCGTGCAACCAGTTTG	GGACGTACTTGAGGGAATTCAGA
CAT	ATGGTCCATGCTCTCAAACC	CAGGTCATCCAATAGGAAGG
MMP1	TCTGACGTTGATCCCAGAGAGCAG	CAGGGTGACACCAGTGACTGCAC
MMP2	GGAATGCCATCCCCGATAAC	CAGCCTAGCCAGCCAGTCGGATTT
MMP9	GGGCTTAGATCATTCCTCAGTGCC	GAAGATGTTCACGTTGCAGGCATC
c-Fos	CGAAGGGAACGGAATAAGATG	GCTGCCAAAATAAACTCCAG
c-Jun	TCCTATGACGATGCCCTCAAC	GTGTTCTGGCTGTGCAGTTC

sample, the cells were cultured for another 24 h, and the cell culture medium was then separated. ELISA of MMP-1 and procollagen were performed using the MMP-1 ELISA kit (QIA55; Merck & Co., Inc., USA) and the procollagen type I C-peptide enzyme immunoassay kit (MK 101; Takara, Japan). A 100-μL aliquot of cell culture medium was added to the surface of each plastic cell culture dish well fixated with MMP-1 monoclonal antibody and incubated at room temperature for 2 h. The cells were washed five times with 1× washing buffer, 100-μL horseradish peroxidase-conjugated anti-MMP-1 antibody was added, and the cells were incubated at room temperature for 1 h. Subsequently, 100-μL of 3,3′,5,5′-tetramethylbenzidine (TMB) substrate was added and incubated in a dark room at room temperature for 30 min. The absorbance was measured at 450 nm.

Subsequently, 100 μL of the culture medium was dispensed into the anti-procollagen type I C-peptide (PIP) monoclonal antibody-coated plate and kept at room temperature for 2 h. The medium was washed five times with 1× washing buffer and procollagen type-IC-peptide (anti-PIP) monoclonal antibody, which was labeled with peroxidase, and hydrogen peroxide used to catalyze the dehydrogenation of substrates was added and reacted for 3 h. After adding 100-μL TMB substrate and incubating at room temperature for 15 min, the absorbance was measured at 450 nm.

Statistical analysis

All experiments were independently repeated ≥three times under the same conditions to obtain the experimental results. The results of each experiment were analyzed using the non-paired Student's *t* test. The *p* value was calculated, and any value < 0.05 was considered to indicate statistical significance.

Results

To examine the cytotoxicity of syringic acid and cytoprotective effects against UVB, HaCaT cells were treated with syringic acid at concentrations of 1, 2, 5, 10, and 20 μM and incubated for 25 h before WST-1 assay. We found that 1 μM of syringic acid resulted in a 105% cell survival rate, 2 μM resulted in a 108% cell survival rate, 5 μM resulted in a 104% cell survival rate, 10 μM resulted in a 96% cell survival rate, and 20 μM resulted in an 88% cell survival rate (Fig. 1). To investigate the cytoprotective effects of syringic acid against cell damage caused by UVB, the HaCaT cells were treated with syringic acid at concentrations of 1, 2, 5, and 10 μM and irradiated with 15 mJ/cm^2 UVB. Compared with the cell survival rate of 72% for the control group irradiated with UVB, that of cells treated with 1 μM of syringic acid increased to 78%, that of cells treated with 2 μM of syringic acid increased to 88%, that of the cells treated with 5 μM of syringic acid increased to 92%, and that of cells treated with 10 μM of syringic acid increased to 102% (Fig. 2).

In addition, we confirmed that ROS in HaCaT cells harmed by UVB were eliminated by syringic acid. After ROS produced by UVB were fluorescently stained with DCF-DA, flow cytometry (BD Biosciences, USA) was used to measure the change in values. It revealed that 15 mJ/cm^2 UVB caused a 2.6-fold increase in ROS, but after treatment with syringic acid at concentrations of 2, 5, and 10 μM, the ROS levels in the UVB-exposed HaCaT cells decreased by 2.1-, 1.5-, and 1.2-fold, respectively. In particular, 10 μM of syringic acid was more effective in eliminating ROS than the same concentration of *N*-acetyl-L-cysteine (NAC; Calbiochem, USA), which acts as a ROS scavenger (Fig. 3). We used qRT-PCR to verify that *SOD1* mRNA, which decreased in response to UVB, had an antioxidant effect of superoxide anion radical elimination due to UVB and found that exposure to 15-mJ/cm^2 UVB caused the expression
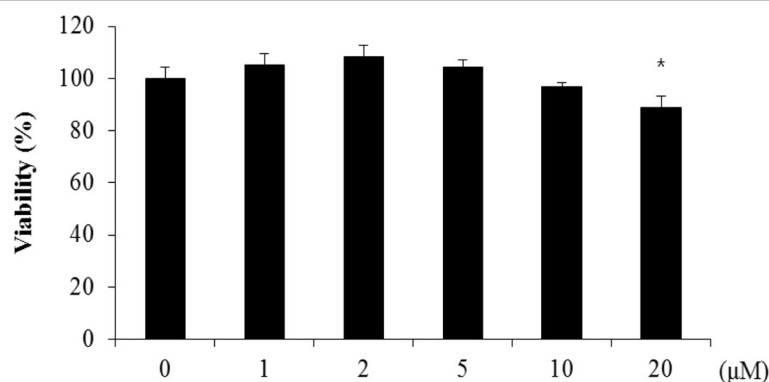
Fig. 1 Cellular toxicity of syringic acid in HaCaTs. Effect of syringic acid on HaCaT cell viability at the indicated concentrations. Results are expressed as the mean ± SD in triplicate; *p* < 0.05 vs the non-treated group
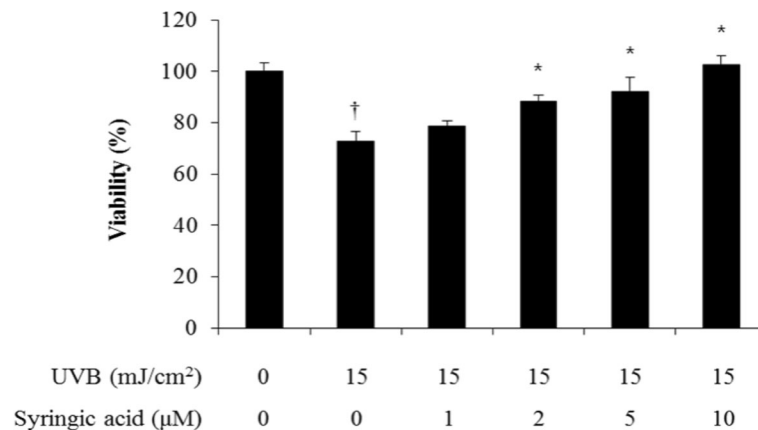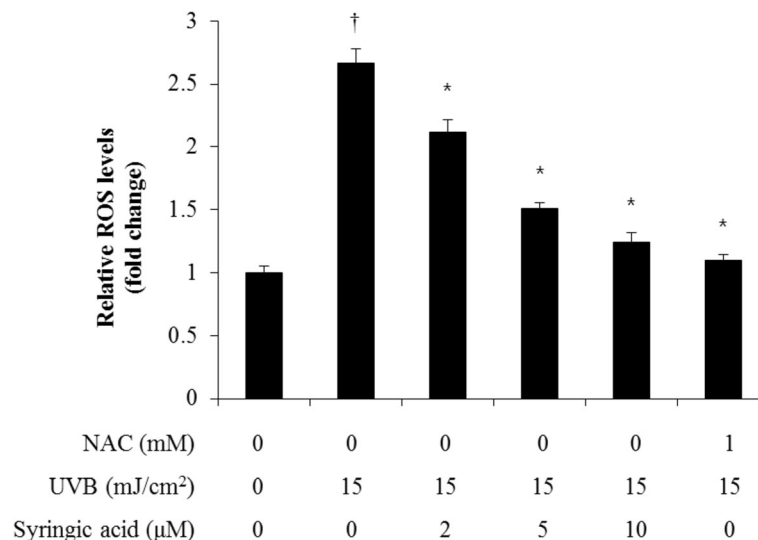
Fig. 2 Effect of syringic acid on the viability of UVB-irradiated HaCaTs. Data are expressed as the mean ± SD in triplicate; †$p < 0.05$ vs the non-treated group, *$p < 0.05$ vs the UVB-treated group without syringic acid

level of *SOD1* to decrease 0.7-fold, but after treatment with 2, 5, and 10 μM of syringic acid, the *SOD1* mRNA expression after exposure to 15 mJ/cm^2 UVB increased 0.9-, 1.1-, and 1.2-fold, respectively (Fig. 4). We also used qRT-PCR to verify that *GPX1* mRNA, which decreased in response to UVB, had an antioxidant effect of superoxide anion radical elimination caused by UVB and found that 15-mJ/cm^2 UVB caused the expression level of *GPX1* to decrease 0.2-fold, but after treatment with 2, 5, and 10 μM of syringic acid, the *SOD1* mRNA expression after exposure to 15 mJ/cm^2 UVB increased 0.8-, 1.4-, and 2.2-fold, respectively (Fig. 5). In this experiment, qRT-PCR was used to determine whether catalase (*CAT*) mRNA, which decreased in response to UVB, could be recovered to some extent by syringic acid and

found that 15-mJ/cm^2 UVB caused the expression level of *CAT* mRNA to decrease 0.2-fold, but after treatment with 2, 5, and 10 μM of syringic acid, *CAT* mRNA expression after exposure to 15 mJ/cm^2 UVB increased 0.4-, 0.7-, and 0.9-fold, respectively (Fig. 6).

To examine the changes in MMP expression and MMP-1 production caused by syringic acid through the AP-1 mechanism, qRT-PCR was used to determine the degree of reduction in *c-Jun and c-Fos* mRNA expression due to syringic acid after their increase in response to UVB. Our results revealed that 15-mJ/cm^2 UVB caused a 2.1-fold increase in the expression level of *c-Jun* mRNA, but after treatment with 2, 5, and 10 μM of syringic acid, *c-Jun* mRNA expression decreased 1.9-, 1.3-, and 1.1-fold, respectively. Exposure

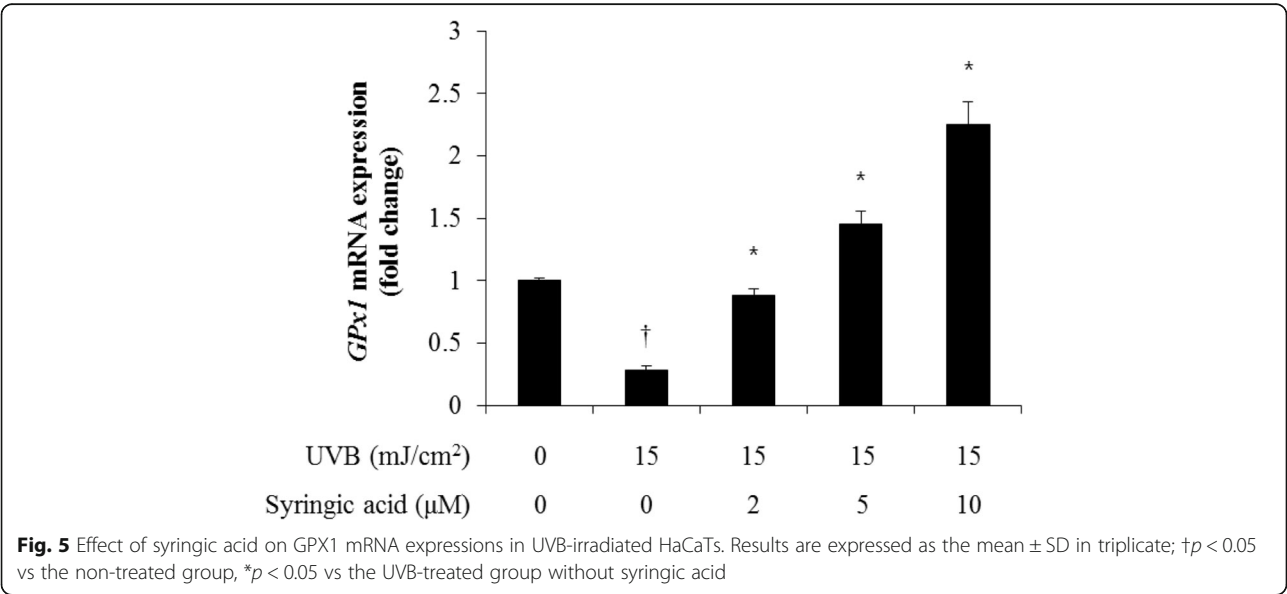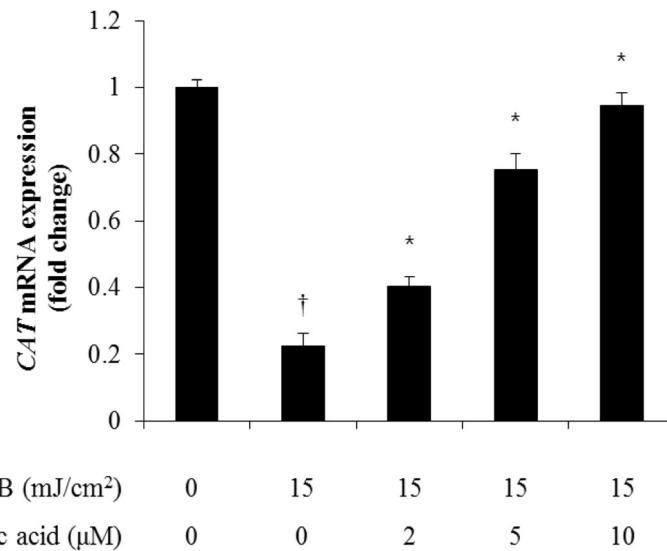**Fig. 3** ROS scavenging effect of syringic acid in UVB-irradiated HaCaTs. Results are expressed as the mean ± SD in triplicate; †$p < 0.05$ vs the non-treated group, *$p < 0.05$ vs the UVB-treated group without syringic acid

Fig. 4 Effect of syringic acid on the SOD1 mRNA expressions in UVB-irradiated HaCaTs. Data are represented as the mean ± SD in triplicate; †$p <$ 0.05 vs the non-treated group, *$p < 0.05$ vs the UVB-treated group without syringic acid
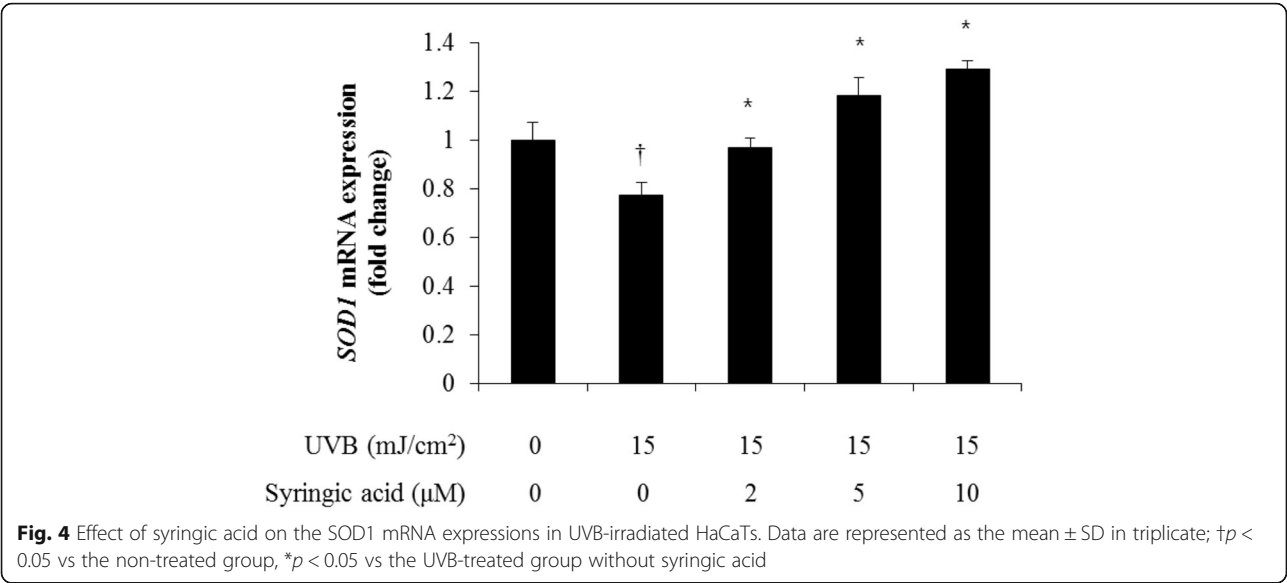
to 15-mJ/cm^2 UVB caused a 1.2-fold increase in the expression level of *c-Fos* mRNA, but after treatment with 2, 5, and 10 μM of syringic acid, *c-Fos* mRNA expression after exposure to 15 mJ/cm^2 UVB decreased 1.1-, 1.0-, and 0.9-fold, respectively (Fig. 7). In this experiment, AP-1 luciferase reporter vector (BPS Bioscience, CA, USA) with AP-1-responsive elements located in front of luciferase in the promoter region was used for transfection before luciferase gene expression was measured via luciferin luminescence measurement. The results confirmed the transcriptional activity of the transcription factor AP-1

promoter, which affects skin aging via inflammation, immune response, cell proliferation, and collagen degradation. The luminescence of luciferin increased twofold due to 15-mJ/cm^2 UVB, but after syringic acid treatment at concentrations of 2, 5, and 10 μM, it decreased 1.5-, 1.2-, and 1.0-fold, respectively, after exposure to 15 mJ/cm^2 UVB. We confirmed that the decrease in the luminescence of luciferin due to syringic acid was concentration-dependent. This finding confirmed that syringic acid inhibited the transcription activity of the transcription factor AP-1 promoter, which affects skin aging via skin inflammation,
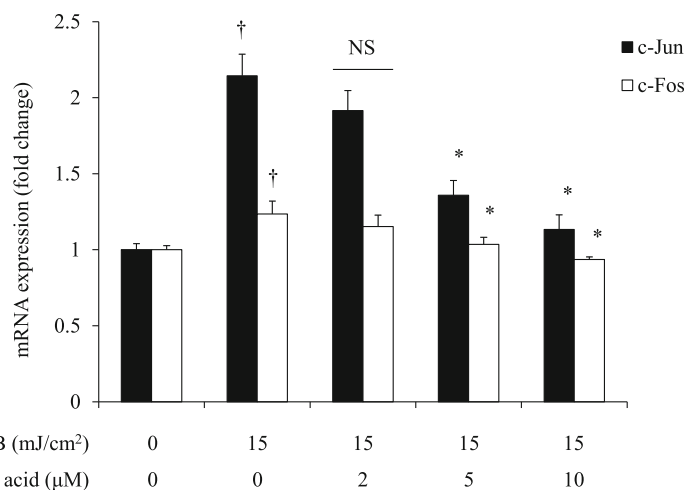

Fig. 5 Effect of syringic acid on GPX1 mRNA expressions in UVB-irradiated HaCaTs. Results are expressed as the mean ± SD in triplicate; †$p < 0.05$ vs the non-treated group, *$p < 0.05$ vs the UVB-treated group without syringic acid

Fig. 6 Effect of syringic acid on CAT mRNA expressions in UVB-irradiated HaCaTs. Data are expressed as the mean ± SD in triplicate; †$p < 0.05$ vs the non-treated group, *$p < 0.05$ vs the UVB-treated group without syringic acid

immune response, cell proliferation, and collagen degradation (Fig. 8).

Change in *MMP* mRNA expression

The effect of syringic acid on *MMP-1*, *MMP-2*, and *MMP-9* expressions was confirmed by qRT-PCR. It demonstrated that after exposure to 15-mJ/cm^2 UVB, the expression levels of *MMP-1*, *MMP-2*, and *MMP-9* increased 2.5, 4.3, and 1.8-fold, respectively, but after treatment with 2, 5, and 10 μM of syringic acid, the *MMP-1* mRNA expression after exposure to 15-mJ/cm^2 UVB decreased 1.9-, 1.4-, and 1.06-fold, respectively. Because of syringic acid treatments at concentrations of 2, 5, and 10 μM, *MMP-2* mRNA expression after

exposure to 15-mJ/cm^2 UVB decreased 3.4-, 2.1-, and 0.9-fold, respectively, in a concentration-dependent manner, and *MMP-9* mRNA expression decreased to 1.0-, 0.9-, and 0.8-fold, respectively, in a concentration-dependent manner (Fig. 9). ELISA was used to determine the effects of syringic acid on the production of MMP-1, which is a collagen inhibitor that increases in response to UVB. It demonstrated that exposure to 15-mJ/cm^2 UVB caused a 1- to 1.9-fold increase in MMP-1 production, but after treatment with 2, 5, and 10 μM of syringic acid, MMP-1 production after exposure to 15-mJ/cm^2 UVB decreased 1.8-, 1.5-, and 1.3-fold, respectively (Fig. 10). Therefore, it seems that syringic acid has anti-aging effects in HaCaT cells.

Fig. 7 Effect of syringic acid on c-Jun and c-Fos mRNA expressions in UVB-irradiated HaCaTs. Results are expressed as the mean ± SD in triplicate; †$p < 0.05$ vs the non-treated group, *$p < 0.05$ vs the UVB-treated group without syringic acid. NS means not significance
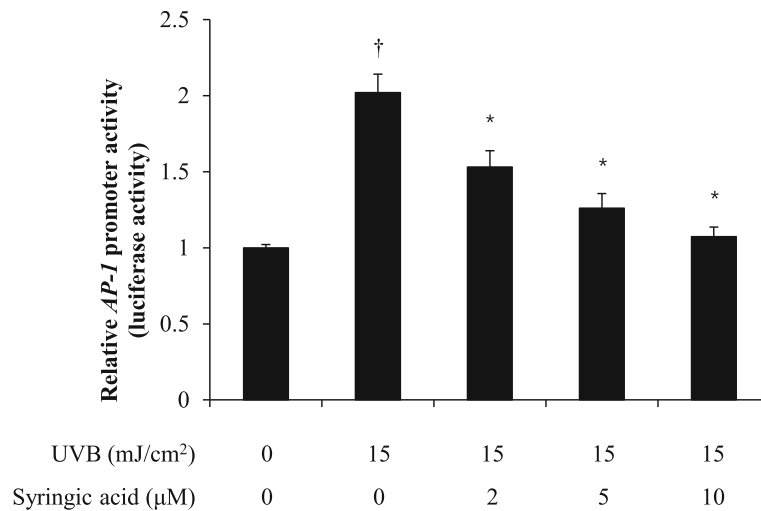
Fig. 8 Effect of syringic acid on AP-1 promoter activity in UVB-irradiated HaCaTs. Data are expressed as the mean ± SD in triplicate; $†p < 0.05$ vs the non-treated group, $*p < 0.05$ vs the UVB-treated group without syringic acid

Discussion

This study demonstrated that 10 μM was the highest concentration of syringic acid used in the UVB cytoprotective experiments. We found that the cytoprotective effects of syringic acid and the cell survival rates in HaCaT harmed by UVB were concentration-dependent.

The oxidation inhibition effects of syringic acid on HaCaT cells harmed by UVB were examined. ROS decreased in HaCaT after pretreatment with syringic acid and also confirmed that syringic acid increased the expression of *SOD1* mRNA, an antioxidant gene, in a concentration-dependent manner. And found that syringic acid increased *GPX1* expression in a concentration-dependent manner, which reduced

oxygen-free radicals and suppressed cellular aging. This experiment confirmed the antioxidative effects of *GPX1*, where syringic acid increased the concentration of *CAT* mRNA, an antioxidant gene, in a concentration-dependent manner.

In this study, *c-Jun and c-Fos* mRNA, which are involved in the expression of proteins, such as MMP, increased in response to UVB but decreased in response to syringic acid in a concentration-dependent manner. Therefore, syringic acid is considered to have anti-aging effects in human keratinocytes, confirming the transcriptional activity of the transcription factor, AP-1 promoter, which affects skin aging due to inflammation, immune response, cell proliferation, and
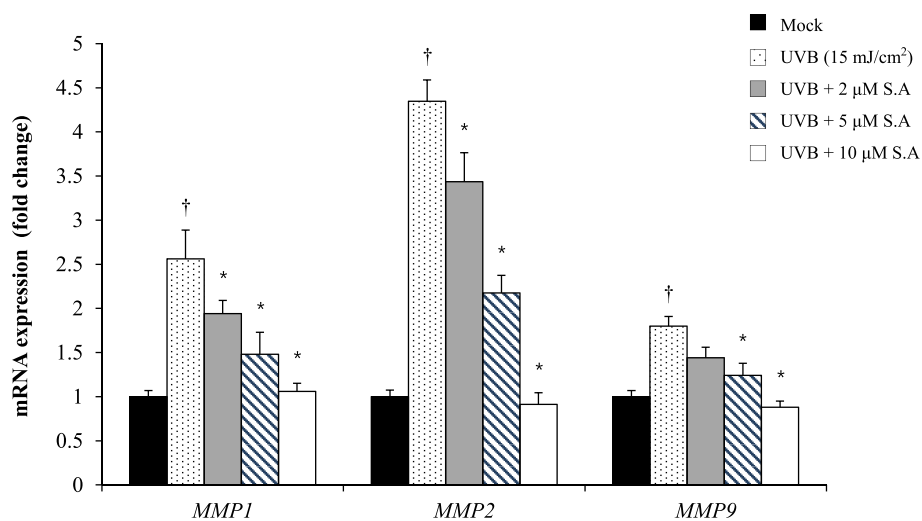
Fig. 9 Effect of syringic acid on MMPs mRNA expressions in UVB-irradiated HaCaTs. Results are expressed as the mean ± SD in triplicate; $†p < 0.05$ vs the non-treated group, $*p < 0.05$ vs the UVB-treated group without syringic acid
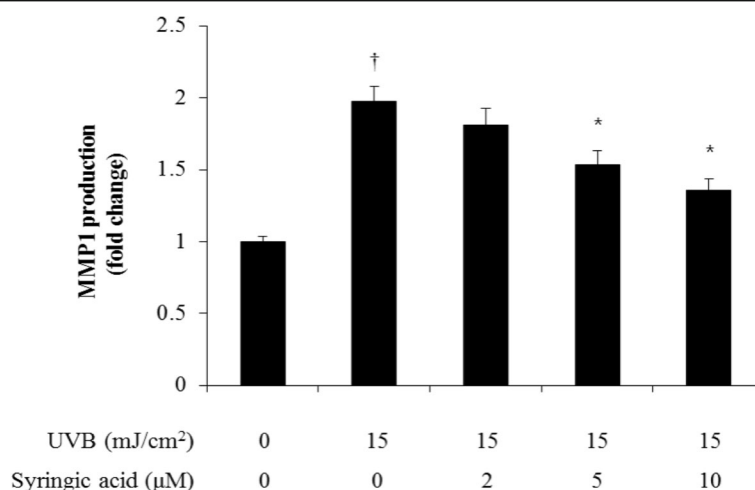
Fig. 10 Effect of syringic acid on MMP-1 production in UVB-irradiated HaCaTs. Data are represented as the mean ± SD in triplicate; †$p < 0.05$ vs the non-treated group, *$p < 0.05$ vs the UVB-treated group without syringic acid

collagen degradation. Therefore, syringic acid appeared to be an effective anti-aging agent in human keratinocytes.

Proteinases, such as MMP-1, play a crucial role in skin aging by abnormally suppressing collagen in dermal tissues (Chen et al. 2008). In the present study, we confirmed that syringic acid decreased the production of collagen-inhibiting enzyme MMP-1 in a concentration-dependent manner. Thus, syringic acid has an anti-aging effect in the human keratinocyte cell line HaCaT.

Therefore syringic acid was shown to be involved in altering MMP expression and controlling MMP-1 production through the AP-1 mechanism. Thus, the antioxidant and anti-aging effects of syringic acid increased the survival rate of HaCaT cells damaged by ultraviolet B, suggesting that it can be used as a natural phytochemical in cosmetic products.

Conclusion

Most studies related to syringic acid have focused on its antioxidant and anti-inflammatory roles in the fields of food, medicine, pharmacy, and life sciences. No study has been conducted on its role in anticancer treatments or cosmetics. In particular, no research on the effects of syringic acid in human keratinocytes has been published. The present study investigated the effects of syringic acid, which has been shown to protect against cell damage via anti-inflammatory, antioxidant, and anticancer effects. It examined antioxidative effects of syringic acid in HaCaT cells exposed to UVB and the effect on *MMP* expression alteration and MMP production control through AP-1 regulation. Syringic acid was tested for its cytoprotective effect and its potential as a cosmetic ingredient. Syringic acid was shown to be involved in

MMP gene expression and MMP production control through AP-1 regulation, thereby protecting human keratinocytes from damage and restoring the survival rate of the cells harmed by UVB. Syringic acid was shown to have antioxidant and anti-aging effects; therefore, it can potentially be used as a natural phytochemical ingredient in cosmetic products.

Publisher's Note

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