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Passion fruit seed extract protects hydrogen peroxide-induced cell damage in human retinal pigment epithelium ARPE-19 cells

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Age-related macular degeneration (AMD) is a major cause of vision loss among adults. We investigated the protective effects of passion fruit seed extract (PFSE) and its rich polyphenol piceatannol in an AMD cell model in which human retinal pigment epithelial ARPE-19 cells were exposed to hydrogen peroxide (H_2O_2). Using a cell viability WST-8 assay, we revealed that PFSE and piceatannol increased the cellular viability of ARPE-19 cells by 130% and 133%, respectively. Moreover, PFSE and piceatannol recovered the cell viability of ARPE-19 cells, which had decreased to 60% owing to H_2O_2-induced damage, to approximately 84% and 89%, respectively. In addition, we found that the treatment of ARPE-19 cells with H_2O_2 decreased the mitochondrial and glycolytic ATP production rate to approximately 54% that of healthy control ARPE-19 cells using a Seahorse extracellular flux analyzer. Furthermore, pretreatment with PFSE and piceatannol restored the oxidative stress-induced decrease in the mitochondrial and glycolytic ATP production rate to approximately 97% and 82%, respectively. These results indicated the cytoprotective effects of PFSE and piceatannol against oxidative stress in human ARPE-19 cells by resolving the dysfunction of mitochondrial and glycolytic energy metabolism.

Keywords Age-related macular degeneration, ARPE-19 cells, Functional food, Hydrogen peroxide, Mitochondrial function, Oxidative stress, Passion fruit seed extract, Piceatannol

Oxidative damage is associated with the pathogenesis of visual dysfunctions such as age-related macular degeneration (AMD)[1,2]. AMD is a complex multifactorial disease and is one of the major causes of severe visual loss in the elderly population[1,2]. Retinal pigment epithelial (RPE) cells, which are located in the outermost retinal layer, are crucial for the normal functioning and health of retinal photoreceptors and play an important role in the visual process; moreover, their oxidative damage contributes to macular degeneration[2]. AMD is categorized into wet and dry types[1,2]. Photodynamic therapy, laser photocoagulation, and antivascular endothelial growth factor (anti-VEGF) therapy are used to treat wet AMD[2]. In particular, anti-VEGF therapy is the current standard treatment for suppressing pathological neovascularization in wet AMD[2]. In contrast, dry AMD has no established treatment. Currently, the only Food and Drug Administration–approved treatment is pegcetacoplan, an anticomplement therapy with targeted C3 inhibition[2]. However, it has limited therapeutic effects[2,3]. Therefore, effective prevention and further treatment strategies for dry AMD need to be established.

Antioxidants have been proposed as potential preventive or curative options for dry AMD because oxidative stress is a major contributor to RPE cell degeneration[2]. Indeed, clinical studies have revealed that antioxidants and zinc-containing supplements could substantially reduce AMD progression rate[2]. Increasing the consumption of fruits and vegetables that contain antioxidant nutrients and phytochemicals may provide some protection against AMD[2]. Previous study shows that AMD protection and treatment should be focused on rescuing RPE cells from oxidative damage[2]. Some antioxidants, including vitamin C (ascorbic acid), vitamin E (α-tocopherol), curcumin, resveratrol, and catechin, have been investigated as antiaging agents[2,4]. Among them, resveratrol has been extensively examined for its antioxidant and free radical scavenging properties[2,5,6].

Piceatannol (3,3′,4′,5-*trans*-tetrahydroxy-stilbene) is a natural stilbene derivative and a structurally similar polyphenol analog of resveratrol (3,4′,5-*trans*-trihydroxy-stilbene)[7,8]. Several studies have revealed that piceatannol has antioxidative[8–14], anti-inflammatory[8,15–18], and neuroprotective properties[19–22]. Kang et al.

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reported that resveratrol and piceatannol protect ARPE-19 cells from N-retinylidene-N-retinylethanolamine (A2E)- and blue light–induced photodamage[23]. Additionally, Hao et al. reported the preventive function of piceatannol in hydrogen peroxide (H_2O_2)-induced ARPE-19 cell damage and apoptosis through the PI3K/Akt signaling pathway[24].

Passion fruit (*Passiflora edulis* Sims) is a tropical plant, whose seeds contain various nutrients and functional components[25,26]. Passion fruit seed extract (PFSE) is rich in piceatannol, a polyphenol, and is gaining attention as a functional food[25–27]. Previous studies have reported that piceatannol and/or piceatannol-rich PFSE demonstrated various biological activities such as skin protection[11,27], vasodilatation[28], chronic disease prevention[29], metabolic improvement[30–32], and anticancer effect[33]. In addition, as per the results of our recent study, piceatannol-rich PFSE protects beta-amyloid-induced neuronal cell death in the differentiated human neuroblastoma SH-SY5Y cell model[22].

The present study aimed to investigate the metabolic profile of piceatannol and piceatannol-rich PFSE and their protective effect on H_2O_2-induced RPE cell ARPE-19 damage.

Results

PFSE and piceatannol promote cell viability and mitochondrial energy metabolism

In this study, we examined the cytoprotective effects of piceatannol-rich PFSE and piceatannol and analyzed their effects on H_2O_2-induced RPE cell damage and energy metabolism in an AMD cell model using H_2O_2-treated ARPE-19 cells.

First, we investigated the cellular effects of PFSE and piceatannol on cell proliferation/activation and cell viability in ARPE-19 cells. Previously, several studies focused on RPE cell protective effects of the bioactivity of piceatannol in the 5–60 μM concentration range[23,24]. Additionally, we have recently reported that PFSE at 0.0023 mg/mL and piceatannol at 1 μM protect beta-amyloid-induced neuronal cell death in an Alzheimer's disease cell model[22]. We treated ARPE-19 cells with PFSE (0.023 mg/mL or 0.0023 mg/mL, i.e., piceatannol equivalent of 10 μM and 1 μM, respectively) and piceatannol (10 μM or 1 μM) for 25 h (Fig. 1A). PFSE and

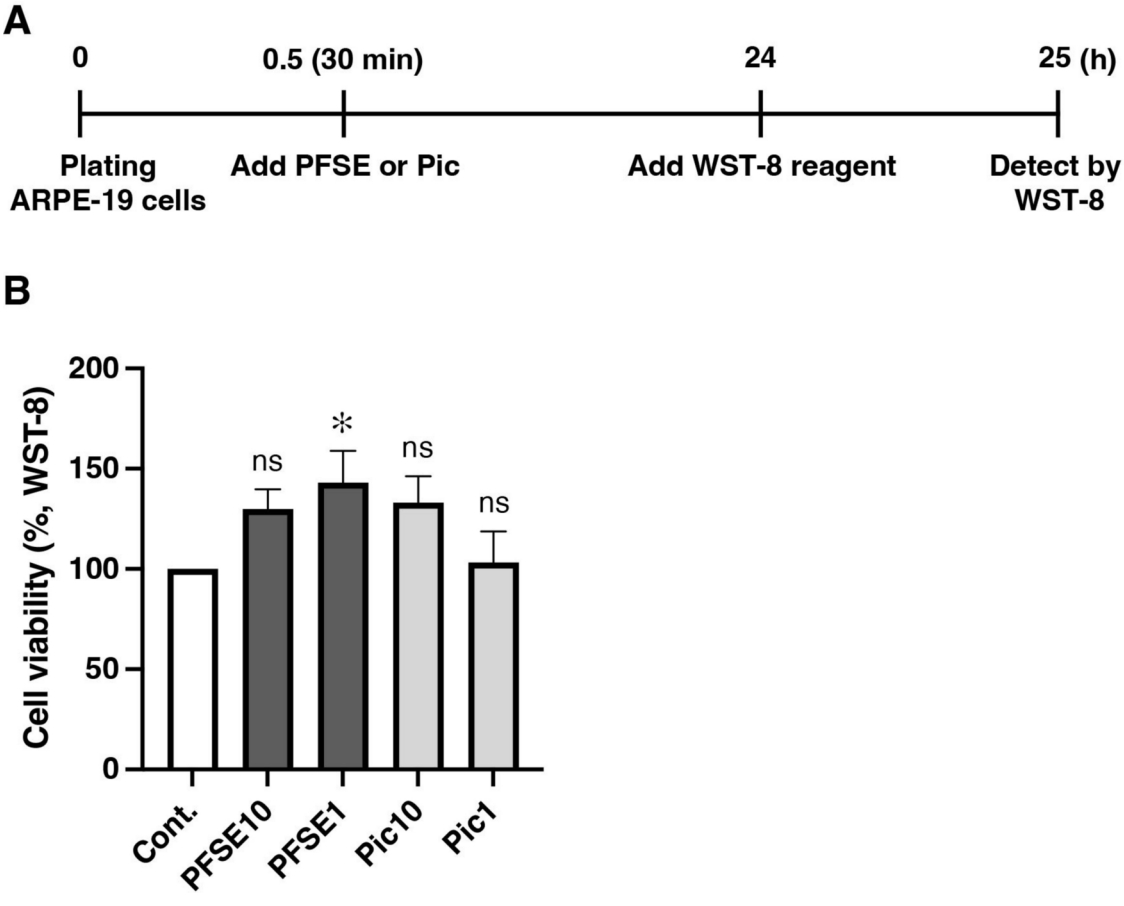


Fig. 1. Physiological effect of PFSE and piceatannol on cell viability in human RPE cells ARPE-19. (**A**) Experimental timeline. Cells were treated with the indicated PFSE or Pic concentrations for 24 h. After incubation for 1 h, cell viability was assessed by WST-8 assay. (**B**) Cell viabilities (%) are the means of three independent experiments, with error bars showing ± standard error of the mean (SEM). Cont., control (solvent alone); PFSE10, 0.023-mg/mL PFSE (Pic equivalent of 10 μM); PFSE1, 0.0023-mg/mL PFSE (Pic equivalent of 1 μM); Pic10, 10-μM Pic; Pic1, 1-μM Pic.

piceatannol were administered 30 min after cell seeding when the cells had adhered to the culture plate. The groups treated with 0.023-mg/mL PFSE, 0.0023-mg/mL PFSE, and 10-μM piceatannol showed an increased cellular viability compared with that of the control (solvent alone) group in ARPE-19 cells (Fig. 1B). In particular, PFSE administration at 0.0023 mg/mL in ARPE-19 cells significantly increased cellular viability to 143% compared with that of the control stage (Fig. 1B). Additionally, 0.023-mg/mL PFSE and 10-μM piceatannol increased cellular viability to 130% and 133%, respectively, compared with that of the control stage (Fig. 1B). We found that both PFSE and piceatannol enhanced cellular viability in ARPE-19 cells.

Second, we examined the relationship between energy metabolism and cellular activation by using an extracellular flux analyzer XFe24 to analyze the ECAR and OCR of ARPE-19 cells with PFSE or piceatannol. The ECAR and OCR are important indicators of glycolysis and mitochondrial respiration[34]. Figure 2 shows the timeline of the experiment. PFSE or piceatannol treatment of ARPE-19 cells resulted in higher baseline OCR and ECAR than those in the control stages (Fig. 2B, C). Cells treated with PFSE or piceatannol had an increased mitochondrial ATP production rate compared to control cells (Table 1, Fig. 2D, E). On the other hand, the glycolysis ATP production rate was comparable between control cells and cells treated with PFSE or Piceatannol (Table 1, Fig. 2D, E). In contrast, intracellular and extracellular ATP levels were similar in all experimental groups (Table 1, Fig. 2F, G. Thus, PFSE and piceatannol enhance the cellular activity of ARPE-19 cells and increase the rate of mitochondrial ATP production in the cellular energy metabolism. This finding indicates that PFSE and piceatannol may be able to prevent H_2O_2-induced RPE cell damage in the AMD mimic cell model.

PFSE and piceatannol suppress H_2O_2-induced RPE cell damage

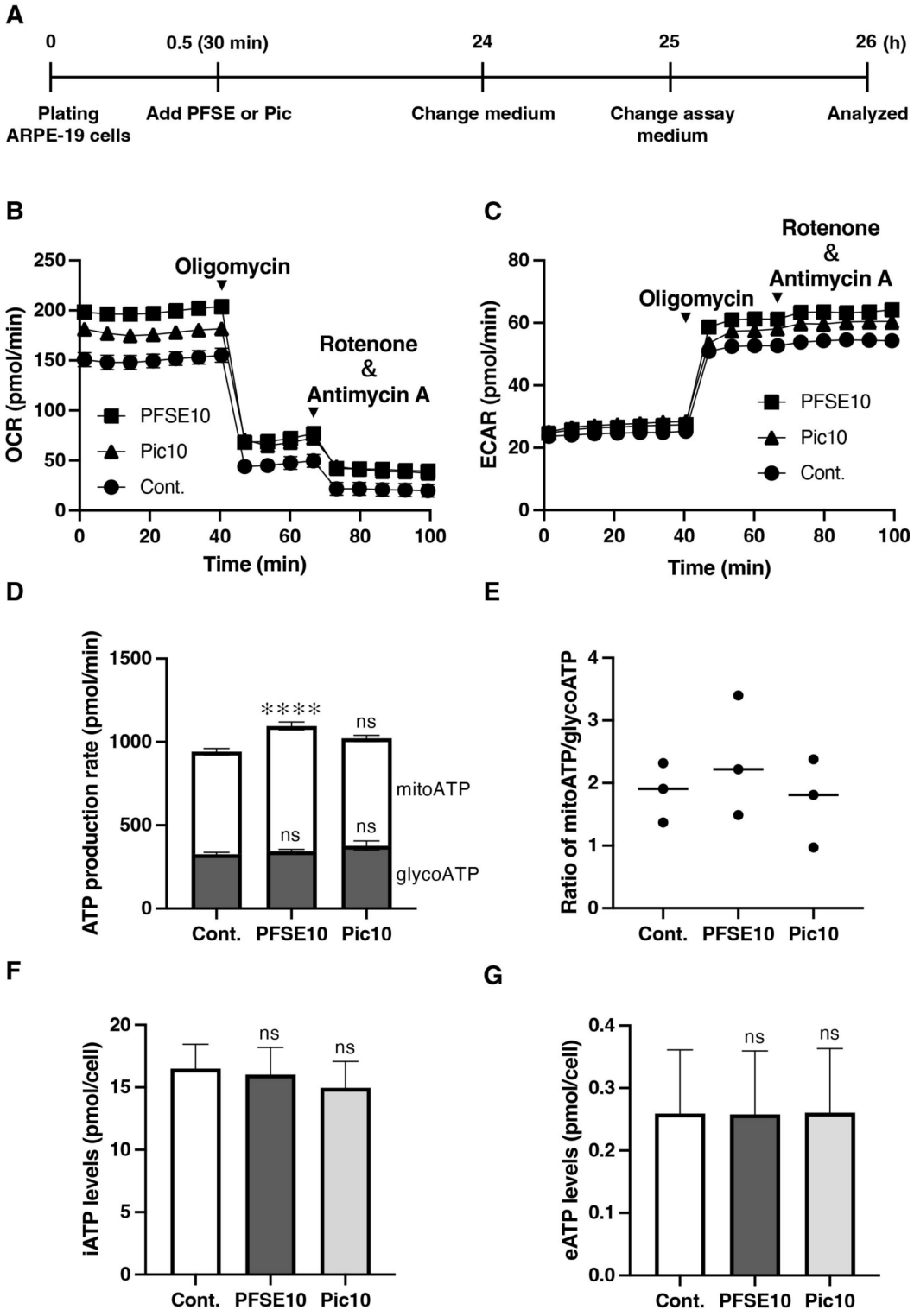
Next, we investigated the protective effects of PFSE and piceatannol on cellular damage in an AMD cell model. The AMD cell model was prepared as shown in Fig. 3A. We treated the cells with H_2O_2 for 1 h and replaced the culture medium with fresh medium for another hour. The cell viability was reduced to 60% in this AMD cell model (Fig. 3B). Cell viability in the AMD cell model increased with PFSE and piceatannol pretreatment (Fig. 3B). Cell viability in the cell model was increased to approximately 84% and 89% after the pretreatment of PFSE at 0.023 mg/mL and 0.0023 mg/mL, respectively (Fig. 3B). Similarly, cell viability in the cell model increased to approximately 94% and 80% after the pretreatment of piceatannol at 10 μM and 1 μM, respectively (Fig. 3B). Interestingly, the AMD model cells demonstrated reduced cell damage by PFSE and piceatannol pretreatment (Fig. 3B). Furthermore, morphological observations revealed that PFSE and piceatannol treatments at 24 h do not negatively affect ARPE-19 cells (Fig. 3C). Interestingly, we also observed that PFSE and piceatannol reduces H_2O_2-induced ARPE-19 cell damage at similar levels (Fig. 3C). These results indicated that both PFSE and piceatannol can suppress H_2O_2-induced RPE cell damage in the AMD cell model.

PFSE and piceatannol restore the reduction of ATP production rate in H_2O_2-damaged RPE cells

We analyzed the ECAR and OCR with and without PFSE or piceatannol in H_2O_2-induced AMD cell models using an extracellular flux analyzer to elucidate the association of energy metabolism and cytoprotective effects of PFSE or piceatannol on H_2O_2-induced RPE cell damage. Figure 4A shows the experimental timeline for metabolic analysis. The baseline OCR and ECAR from 0 to 40 min in the AMD cell model are significantly lower than those in the control stage, as shown in Fig. 4B, C. Conversely, PFSE or piceatannol pretreatment of ARPE-19 cells resulted in higher baseline OCR and ECAR than those in the control stages (Fig. 4B, C). The mitochondrial ATP production rate in the AMD cell model was significantly reduced to approximately 34% compared with that of the control stage (Table 2 and Fig. 4D). In contrast, the ATP production rate of glycolysis in the AMD cell model was 84% slightly lower than that in the control stage (Table 2 and Fig. 4D). Interestingly, PFSE or piceatannol pretreatment of ARPE-19 cells significantly reduced H_2O_2-induced declines in mitochondrial and glycolysis ATP production rates compared with AMD model cells (Table 2, Fig. 4D, E). Notably, pretreatment with PFSE and piceatannol restored the mitochondrial ATP production rate, which had reduced to 36% owing to oxidative stress, to approximately 71% and 63%, respectively. Moreover, pretreatment with PFSE and piceatannol restored and upregulated the glycolysis ATP production rate, which had decreased to 87% owing to oxidative stress, to approximately 145% and 117%, respectively. Furthermore, we investigated intracellular and extracellular ATP levels in the H_2O_2-induced AMD cell model with PFSE or piceatannol pretreatment. Intercellular ATP level in the AMD cell model was considerably lower than that in the control stage (Table 2 and Fig. 4F). In addition, intracellular ATP levels were lower in ARPE-19 cells pretreated with PFSE and piceatannol followed by H_2O_2 than in ARPE-19 cells treated with H_2O_2 alone (Table 2 and Fig. 4F). Therefore, PFSE or piceatannol pretreatment of ARPE-19 cells potentiated ATP level reduction due to H_2O_2 treatment. By contrast, extracellular ATP levels were similar in all experimental groups (Fig. 4G). These findings indicate that PFSE or piceatannol increases ATP consumption after H_2O_2-induced cell damage in ARPE-19 cells.

Discussion

AMD is associated with several environmental and genetic risk factors that are connected to increased oxidative stress[35]. Among them, age is the major risk factor[35]. Oxidized nucleic acid, protein, and lipid accumulation in aged cells and tissues are the evidence for an overall increase in oxidative stress with aging[35]. Damage to the RPE due to oxidative stress is considered to be an important factor in AMD pathology[35]. RPE cells are constantly exposed to oxidative stress, which may result in the accumulation of damaged nucleic acids, proteins, lipids, and organelles, including mitochondria[35]. Oxidative stress ultimately involves excessive reactive oxygen species (ROS) production mainly in mitochondria[35]. ROS then cause mitochondrial damage and cell death. Mitochondrial dysfunction generally occurs in patients with AMD[35]. Previously, two different research groups have revealed reduced mitochondrial function and ATP production in RPE cells from patients with AMD



compared with those from healthy controls[35–37]. These results indicate the involvement of mitochondrial damage and dysfunction in AMD pathology.

This study provides evidence that dependent changes in energy metabolism, i.e., enhanced glycolysis, mitochondrial citric acid cycle, and oxidative phosphorylation, may explain the cytoprotective effect of PFSE and piceatannol against H_2O_2-induced cell damage in ARPE-19 cells. Numerous studies have revealed piceatannol as a potent antioxidant[8]. Additionally, several previous studies have reported the cytoprotective effect of piceatannol against H_2O_2-, A2E-, and blue light–induced cell damage in ARPE-19 cells[23,24]. Our findings indicate that PFSE and piceatannol not only act as antioxidants but also increase the metabolic dependence of mitochondrial oxidative phosphorylation in cellular energy metabolism, i.e., enhance mitochondrial function. Notably, PFSE and piceatannol did not recover H_2O_2-induced ATP reduction. This phenomenon raised the possibility that intercellular ATP is consumed to repair H_2O_2-induced cell damage. Future studies need to

◀**Fig. 2**. Effect of PFSE and piceatannol on energy metabolism in human RPE cells ARPE-19. (**A**) Experimental timeline. Cells were seeded in an Agilent Seahorse XFe24 cell culture microplate. After incubation for 30 min, cells were treated with 0.23 mg/ml PFSE (i.e., piceatannol equivalent 10 μM) or 10 μM piceatannol for 24 h. Then, the culture medium was replaced with fresh medium. After incubation for 1 h, the culture medium was replaced with the analysis medium, and the OCR and ECAR were analyzed using an Agilent Seahorse XFe24 analyzer. (**B**) OCR. (**C**) ECAR. The OCR (pmol/min) and ECAR (mpH/min) represent the average of three independent experiments, with error bars showing ± SE. Black circle, control; black square, PFSE; black triangle, Pic. Oligomycin (final concentration: 0.5 μM); Rotenone and antimycin A (final concentration: 0.5 μM each). (**D**) Rate of ATP production (pmol/min) represents the average of three independent experiments, with error bars showing ± SE. Gray bar, glycoATP. White bar, mitoATP. One-way ANOVA followed by Dunnett's multiple comparisons test. ns, not significance; ****, $p < 0.0001$, compared to the control group. (**E**) The ratio of mitoATP to glycoATP represents the average of three independent experiments. mitoATP, ATP production from mitochondria; glycoATP, ATP production from glycolysis. (**F**) Levels of intracellular ATP. (**G**) Levels of extracellular ATP. The iATP and eATP (pmol/cell) represents the average of three independent experiments, with error bars showing ± SE. One-way ANOVA followed by Dunnett's multiple comparisons test. iATP, intracellular ATP. eATP, extracellular ATP. ns, not significance, compared to the control group.

	Control	PFSE10	Pic10
Total ATP production rate (pmol/min)	1267.6	1439.8	1398.3
ATP production rate (pmol/min) mitoATP rate/glycoATP rate	941.3/326.3	1096.0/343.8	1021.3/377.0
Intracellular ATP level (pmol/cell)	16.5	16.0	15.0

Table 1. Summary of PFSE and piceatannol on energy metabolism dependency, glycolysis, and mitochondrial respiration in ARPE-19 cells.

investigate whether PFSE and piceatannol directly enhance glycolysis, mitochondrial biogenesis, mitochondrial activity, or functional regulation by removing mitochondrial oxidative stresses.

Overall, our findings indicate that PFSE and piceatannol exhibit cytoprotective effects by maintaining glycolysis, mitochondrial function and suppressing H_2O_2-induced mitochondrial dysfunction in ARPE-19 cells. This effect may be exerted by PFSE and piceatannol by modulating cellular dependence on glycolysis and mitochondrial respiration, i.e., tricarboxylic acid cycle and oxidative phosphorylation, in energy metabolism (Fig. 5).

In conclusion, piceatannol-rich PFSE can be a promising functional food in maintaining glycolysis and mitochondrial function in RPE cells as well as in preventing and treating AMD pathology.

Methods

Reagents

We prepared piceatannol-rich PFSE as previously described[33]. Piceatannol was obtained from Tokyo Chemical Industry (Tokyo, Japan). We stored PFSE as 100-mg/mL stocks in dimethyl sulfoxide (DMSO, Sigma-Aldrich; Merck KGaA, Darmstadt, Germany) at − 20 °C. Piceatannol was stored as 100-mM stocks in DMSO at − 20 °C. H_2O_2 was purchased from FUJIFILM Wako Pure Chemical (Osaka, Japan).

Cell culture

The human retinal pigment epithelium cell line ARPE-19 was obtained from the American Type Culture Collection. We cultured ARPE-19 cells in DMEM/Ham's F-12 medium (FUJIFILM Wako Pure Chemical) containing 10% heat-inactivated fetal bovine serum, 100 units/mL of penicillin, and 100 μg/mL of streptomycin in an incubator at 37 °C in an atmosphere with 5% CO_2 and 100% relative humidity.

Cell viability by WST-8 assay

Cell viability assays were performed as previously described[38]. We determined cell viability using the WST-8 (Cell Counting Kit-8) cell proliferation assay (Dojindo, Tokyo, Japan). Briefly, we seeded the cells into 96-well plates (4,000 cells per well) in triplicate and incubated for 30 min; further, we treated them with PFSE or piceatannol and solvent (DMSO, as a negative control; final concentration of 0.2%) for 24 h. We administered PFSE at 0.023 mg/mL (piceatannol equivalent of 10 μM) or 0.0023 mg/mL (piceatannol equivalent of 1 μM) and piceatannol at 10 μM or 1 μM concentrations. Subsequently, the culture medium was replaced with a fresh medium. Additionally, we treated the cells with 400 μM of H_2O_2 and water (negative control). We transferred the culture media to fresh media 1 h after the H_2O_2 treatment. After an incubation for 1 h, we added WST-8 reagent to each well and placed the plate in a 5% CO_2 incubator at 37 °C for an additional 1 h. We measured the absorbance at 450 nm on a Tecan microplate reader (Mannedorf, Switzerland).

Cellular respiration analysis

We performed cellular respiration analysis as previously described[38]. The cells were dissociated using Accutase® and suspended in DMEM/Ham's F-12 medium. The cells were then seeded in an Agilent Seahorse XF24 cell culture microplate (Agilent Technologies, Santa Clara, CA) (4×10^4 cells per well). After incubation for

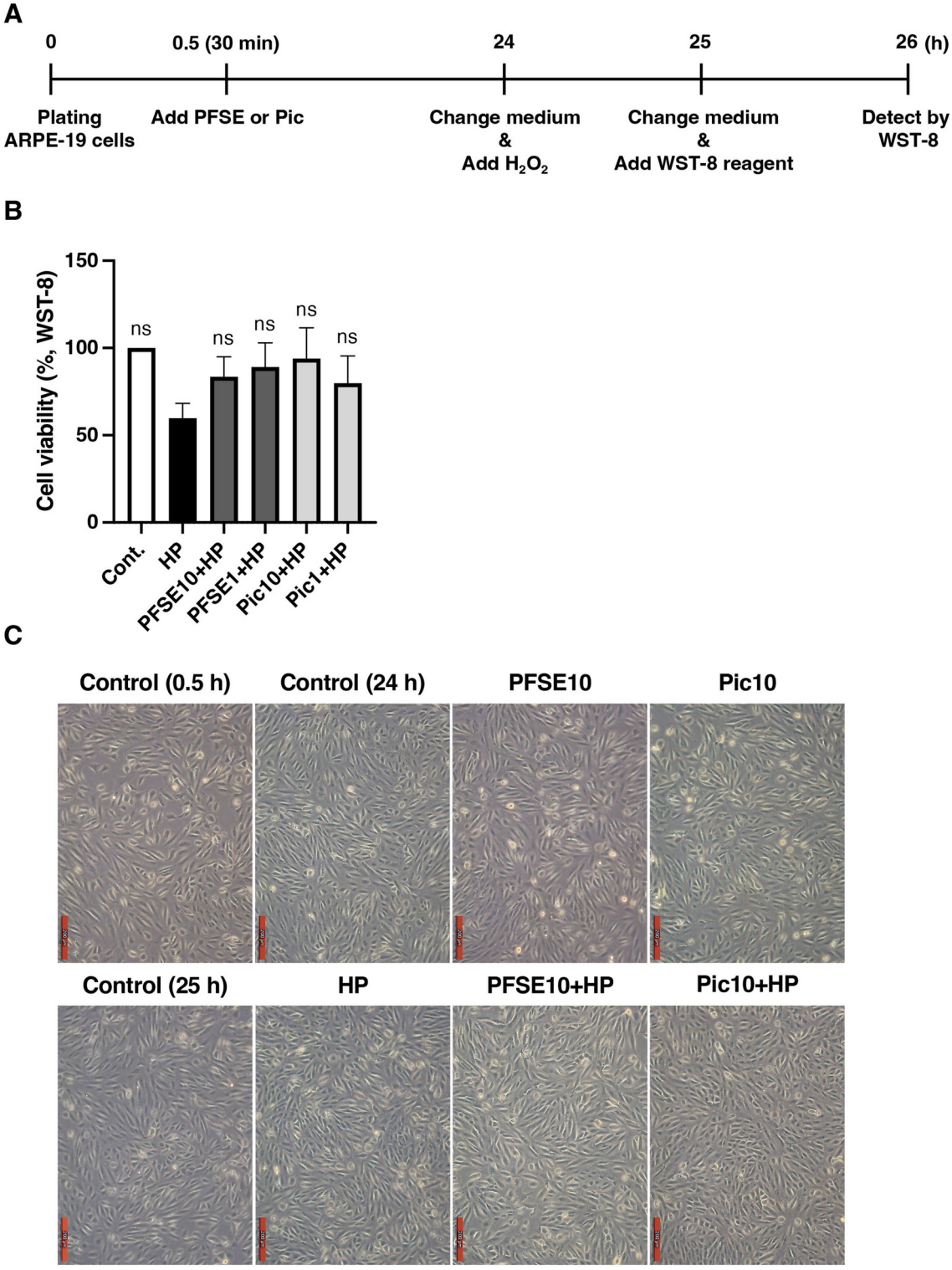


Fig. 3. Protective effect of PFSE or piceatannol on H_2O_2-induced human RPE cell damage. (**A**) Experimental timeline. Human RPE cell line ARPE-19 cells were seeded in a 96-well plate and incubated for 30 min. Cells were treated with PFSE or Pic for 24 h at indicated concentrations. After PFSE and Pic administration, the culture media was transferred to fresh media. Additionally, cells were treated with 400-μM H_2O_2 for 1 h. The culture medium was then replaced with fresh media. After incubation for 1 h, cell viability was detected by WST-8 assay. PFSE, passion fruit seed extract; Pic, piceatannol. (**C**) The protective effect of PFSE and Pic on H_2O_2-induced RPE cell damage. Cell viabilities (%) are averages of three independent experiments, with error bars showing ± SEM. Cont., control; HP, 400-μM H_2O_2. One-way ANOVA followed by Dunnett's multiple comparisons test was conducted for testing significant differences. ns, not significant; *, $p < 0.05$, compared with the control group. (**D**) Morphological features were analyzed using a Leica DMi1 microscope with LAS V4.12 at 100 × magnification. The scale bar indicates 200 μm.

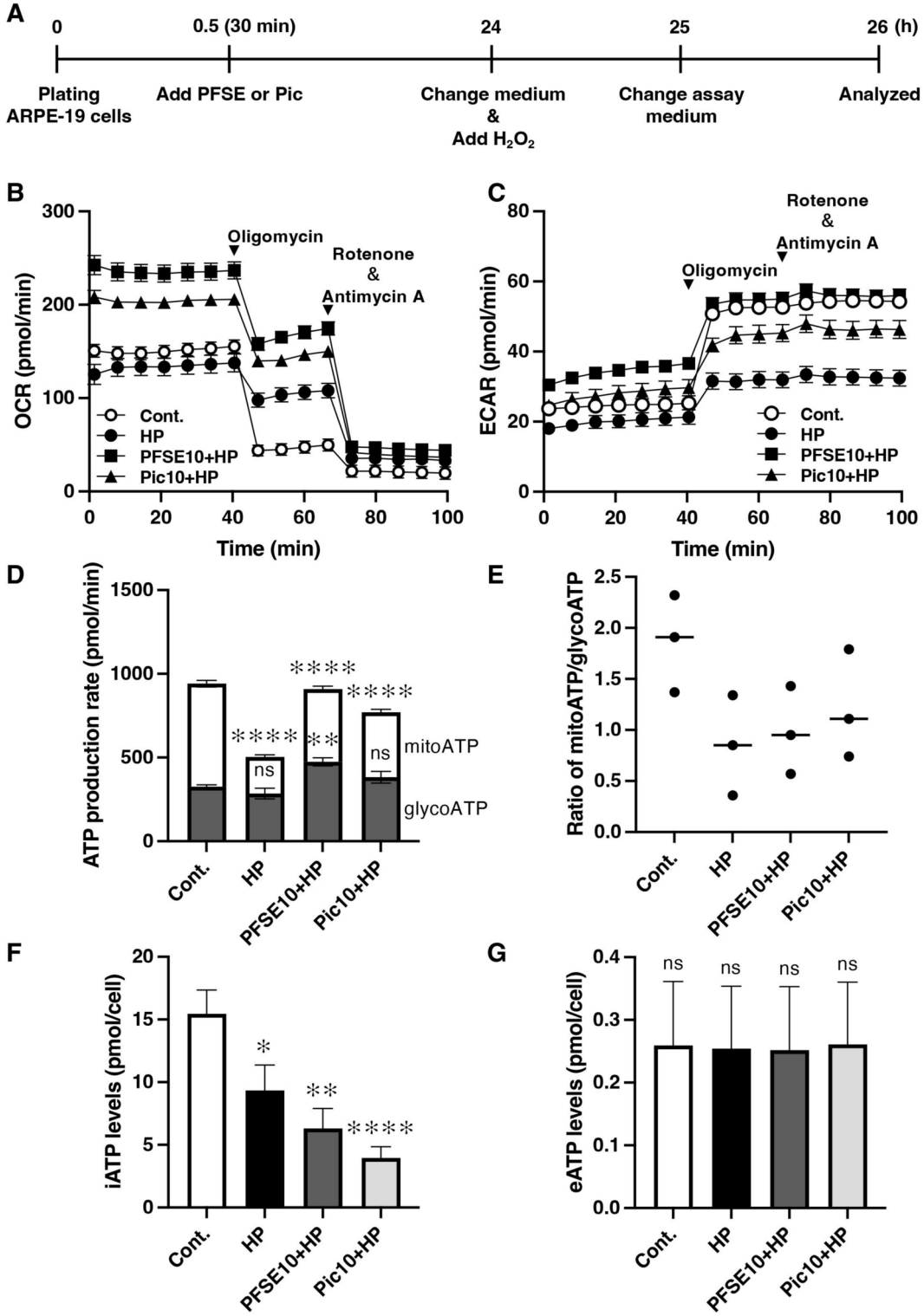
30 min, cells were treated with 0.023-mg/mL PFSE (i.e., piceatannol equivalent 10 μM) or 10-μM piceatannol for 24 h. Further, the culture medium was replaced with fresh DMEM/Ham's F-12 medium. After incubation for 1 h, the culture medium was replaced with XF DMEM medium (Cat#103,575–100, Agilent Technologies), and the oxygen consumption rate (OCR) and extracellular acidification rate (ECAR) were analyzed using an Agilent Seahorse XFe24 analyzer (Agilent Technologies). The analysis medium contained 2-mM Seahorse XF glutamine solution (Agilent Technologies), 1-mM Seahorse XF pyruvate solution (Agilent Technologies), and 25-mM glucose. Additionally, we used a Seahorse XF Real-Time ATP Rate Assay Kit (Cat# 103,592–100, Agilent Technologies) to analyze the ATP production rate, following the manufacturer's protocol.

Measurement of intracellular/extracellular ATP levels

We measured the intracellular and extracellular ATP levels using the CellTiter-Glo® 2.0 Cell Viability Assay (Promega, WI). Briefly, the cells were seeded into 96-well plates (2,500 cells per well) in triplicate and incubated for 30 min. They were treated with 0.023-mg/mL PFSE (piceatannol equivalent of 10 μM) or 10-μM piceatannol and solvent (DMSO, as a negative control; final concentration of 0.2%) for 23 h. After treatment with supplements, we replaced the culture medium with a fresh medium. In addition, the cells were treated with 400-μM H_2O_2 and water (negative control) for incubation at 1 h. Luminescence was measured using a Tecan microplate luminometer (Mannedorf, Switzerland).

Statistical analysis

We used GraphPad Prism 9 software for statistical analyses. We determined the significance of differences among groups using Student's *t*-test and one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison test. *P*-values < 0.05 were considered significant.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0
0.5 (30 min)
24
25
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Plating ARPE-19 cells
Add PFSE or Pic
Change medium & Add H2O2
Change assay medium
Analyzed
B
OCR (pmol/min)
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Cont.
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PFSE10+HP
Pic10+HP
Time (min)
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Fig. 4. Cellular respiration property and protective effect of PFSE and piceatannol in H_2O_2-induced human RPE cell damage. (**A**) Experimental timeline. Cells were seeded in an Agilent Seahorse XFe24 cell culture microplate. After incubation for 30 min, cells were treated with 0.023-mg/mL PFSE (i.e., Pic equivalent of 10 μM) or 10-μM Pic for 24 h. The culture medium was then replaced with a fresh medium. Additionally, cells were treated with 400-μM H_2O_2 for 1 h. After incubation for 1 h, the culture medium was replaced with the analysis medium, and the OCR and ECAR were analyzed using an Agilent Seahorse XFe24 analyzer. (**B**) OCR. (**C**) ECAR. The OCR (pmol/min) and ECAR (mpH/min) represent the average of three independent experiments, with error bars showing ± SEM. Open circle, control; solid circle, HP alone; solid square, PFSE plus HP; solid triangle, Pic plus HP. Oligomycin (final concentration: 0.5 μM); Rotenone and antimycin A (final concentration: 0.5 μM each). OCR, oxygen consumption rate; ECAR, extracellular acidification rate. (**D**). The rate of ATP production (pmol/min) represents the average of three independent experiments, with error bars showing ± SEM. Gray bar, glycoATP. White bar, mitoATP. (**E**) The ratio of mitoATP to glycoATP represents the average of three independent experiments. mitoATP, ATP production from mitochondria; glycoATP, ATP production from glycolysis. (**F**) Levels of intracellular ATP. The iATP (pmol/cell) represents the average of three independent experiments, with error bars showing ± SEM. (**G**) Levels of extracellular ATP. The eATP (pmol/cell) represents the average of three independent experiments, with error bars showing ± SEM. One-way ANOVA followed by Dunnett's multiple comparisons test was conducted for testing significant differences. ns, not significant; *, $p < 0.05$; **, $p < 0.01$; ****, $p < 0.0001$, compared with the control group. iATP, intracellular ATP; eATP, extracellular ATP.

	Control	HP	PFSE10 + HP	Pic10 + HP
Total ATP production rate (pmol/min)	941.2	504.0	908.8	770.8
ATP production rate (pmol/min) mitoATP rate/glycoATP rate	614.9/326.3	218.9/285.1	434.1/474.7	388.4/382.4
Intracellular ATP level (pmol/cell)	15.5	9.3	6.3	4.0

Table 2. Summary of PFSE and piceatannol on energy metabolism dependency, glycolysis, and mitochondrial respiration in H_2O_2-damaged ARPE-19 cells. Note. HP, Hydrogen peroxide (H_2O_2).

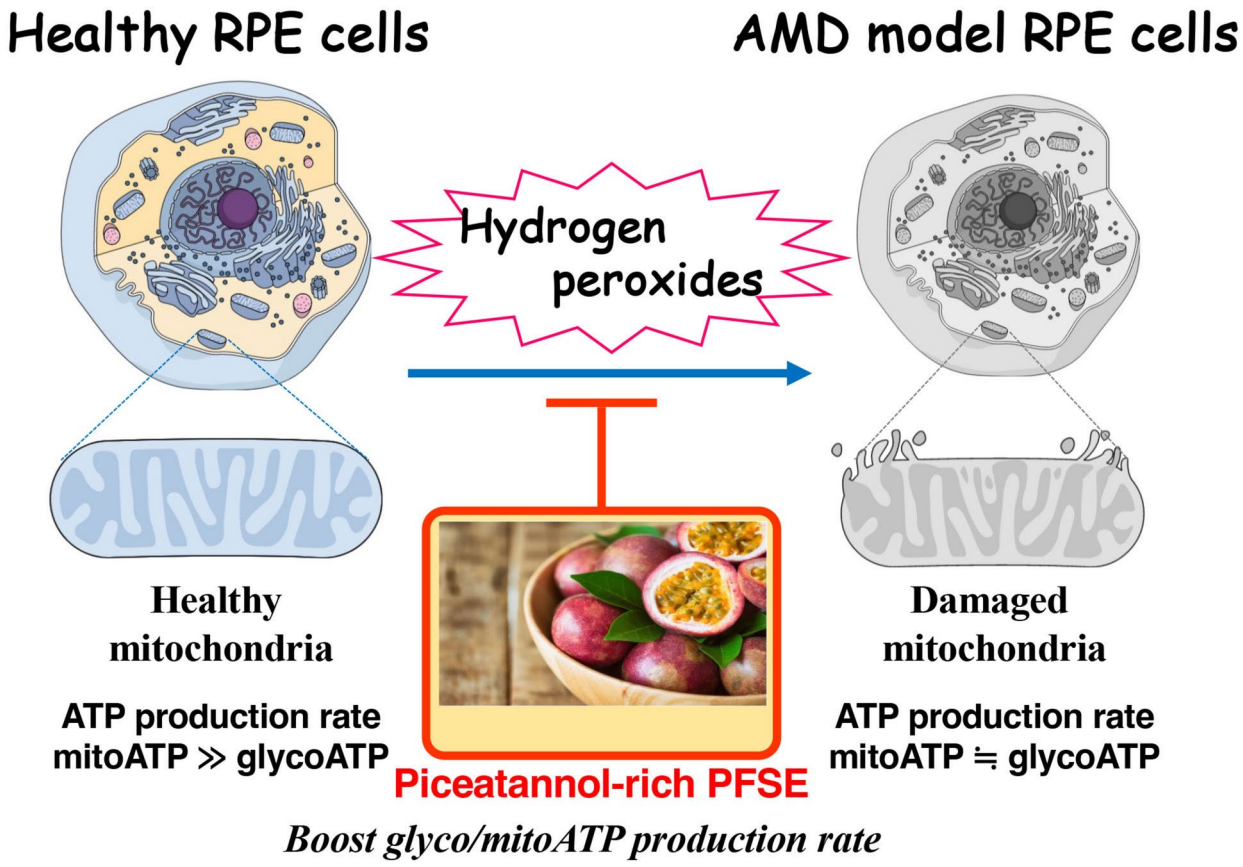

Fig. 5. Overview of the cytoprotective effects of piceatannol-rich PFSE in H_2O_2-induced AMD model ARPE-19 cells.

Data availability

All data generated or analysed during this study are included in this published article.

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Author contributions
A.S. conceived and designed the research. H.U. and A.S. performed the research and acquired the data. H.U., S.K., Y.M., S.M., and A.S. analyzed and interpreted the data. A.S. wrote the main manuscript text. H.U. and A.S. prepared Figs. 1–5. All authors reviewed the manuscript.

Declarations

Competing interests
Akira Sato received a research grant from Morinaga & Co., Ltd. All other authors declare that they do not have any competing interest.

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