The Effect of Modern Lifestyle on Cardiovascular Health

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Abstract. Polyethylene terephthalate (PET) is one of the most widely used microplastics in food packaging and various industrial applications. PET has been detected in the cardiovascular system and shown to adversely affect endothelial cells, however, the underlying mechanisms remain poorly understood. Sirtuin 1 (SIRT1), a protein high secreted during exercise, maintains vascular health by regulating the crucial balance between reactive oxygen species (ROS) and endothelial nitric oxide synthase (eNOS) in endothelial cells. However, the potential of SIRT1 to mitigate PET-induced endothelial impairment has yet been investigated. This study aimed to assess the impact of polyethylene terephthalate (PET) on endothelial cell survival and function, and to investigate the role of SIRT1 in mediating these effects. HUVECs were cultured and treated with PET at 0, 1, 10, 50, 100, 200, 500, 1000 μg/ml for 24-72 hours to assess viability and apoptosis. SIRT1 level was modulated by plasmid overexpression or siRNA knockdown, and the efficacy was confirmed via qPCR and Western blot. ROS levels, eNOS expression, cell viability, and apoptosis were analyzed following PET treatment and SIRT1 modulation. As a result, PET significantly reduced HUVECs viability and increased apoptosis in a dose dependent manner. SIRT1 overexpression protects against PET-induced reduction in cell viability and increase in apoptosis, whereas SIRT1 knockdown exacerbated PET-induced impairments. In addition, PET reduced HUVECs eNOS levels and increased ROS levels. SIRT1 overexpression restored eNOS and ROS levels to those comparable to untreated controls, whereas SIRT1 knockdown further worsened these parameters. Our findings indicate PET impairs endothelial cell survival and eNOs/ROS balance and highlight the protective role of SIRT1 in PET-treated endothelial cells, providing foundation for future therapeutic strategies targeting PET-induced cardiovascular diseases.

Keywords: Polyethylene terephthalate (PET), Sirtuin 1 (SIRT1), Endothelial cells, Endothelial nitric oxide synthase (eNOS), Reactive oxygen species (ROS).

1. Introduction

Microplastic pollution has emerged as a critical environmental issue, with polyethylene terephthalate (PET) comprising a significant proportion of microplastic waste. PET contains terephthalic acid (TPA) and ethylene glycol (EG) subunits which makes it a durable and versatile material. Due to its thermostability, high strength, and resistance to moistures and chemicals feature, PET is the most found type of microplastic on Earth, which is up to 6% of global plastic production. PET is widely used in food packaging, textiles, and industrial applications; however, PET is increasingly found in terrestrial, aquatic, and even human systems. PET has been found to be present in our livers, throat, and eyes, and its average concentration of plastic particles found in the human serum is 1.6 μg/ml. Common health concerns of PET includes birth problems, cancer, hormone changes, liver dysfunction, etc.

Recent studies have highlighted the potential health implications of microplastic exposure, raising concerns about their effects on cellular function and systemic health. Of particular interest is the vascular endothelium, a monolayer of cells lining blood vessels that plays a pivotal role in maintaining vascular integrity, regulating blood flow, and controlling inflammatory responses. Endothelial dysfunction, often characterized by reduced nitric oxide (NO) bioavailability, increased oxidative stress, and heightened inflammation, is a precursor to numerous cardiovascular diseases, including atherosclerosis and hypertension. The cellular mechanisms underlying PET-induced endothelial dysfunction remain poorly understood, but emerging evidence suggests that oxidative stress and inflammatory pathways may play a central role.

On the other hand, lifestyle interventions such as exercise have been shown to improve endothelial function through SIRT1 activation. Sirtuin 1 (SIRT1), a NAD+-dependent deacetylase, is a well-recognized regulator of endothelial function. By modulating key transcription factors such as NF-KB and promoting NO production via eNOS activation, SIRT1 exerts protective effects against oxidative damage. Dysregulation of SIRT1 activity has been implicated in the progression of endothelial dysfunction and cardiovascular disease, making it a potential mediator in the vascular effects of PET microplastic exposure. Exercise enhances vascular health by promoting NO bioavailability, reducing oxidative stress, and improving endothelial barrier function. The role of SIRT1 as a mediator of exercise-induced vascular benefits is well-established, but whether it can counteract the detrimental effects of PET microplastics on endothelial cells remains unexplored.

This study aims to address critical gaps in understanding how PET microplastics, and SIRT1 intersect to influence endothelial cell function. Specifically, we investigate (1) the impact of PET microplastic exposure on endothelial cell survival and function, (2) whether exercise-mimicking interventions that enhance SIRT1 activity can mitigate the adverse effects of PET on endothelial cells. This research provides novel insights into the molecular mechanism affected by environmental microplastics and highlights potential therapeutic strategies to protect vascular health under microplastic over-exposure.

2. Material & Methods

2.1. Cell culture

Human Umbilical Veins Endothelial Cells (HUVECs) were used with MEC culture medium (ScIenCell™, 1001) for cell culture. Cells were cultured in 5% CO2 and 37˚ Celsius environment with controlled humidity. Cells were passaged and expanded when reaching 90% cell density. Up to passage 10 were used for evaluation.

2.2. PET treatment

Stock PET solution (20mg/ml, ~100nm in size, Zhong ke ke you) was serial diluted in sterile water containing 0.05% BSA. The following concentrations were prepared: 0, 1, 10, 50, 100, 200, 500, 1000 μg/ml. HUVECs were treated with PET at 24 hours, 48 hours, and 72 hours, respectively.

2.3. SIRT1 overexpression

Gain of SIRT-1 was achieved by transiently transfecting SIRT-1 expression plasmid using Lipofectamine (Invitrogen Life Technologies, L3000001), according to the manufacturer's instructions. Empty plasmid was served as additional control group. Briefly, HUVECs were plated in T25 flasks and transfection was initiated when reaching 70-80% confluency. 1.8μL of plasmid was mixed with 9μL of Lipofectamine prior adding to cell culture plate. SIRT1 overexpression was evaluated by qPCR and Western Blot 48 hours post transfection.

2.4. SIRT1 siRNA knockdown

SIRT1 knockdown was achieved by transiently transfecting SIRT1 siRNA with Lipofectamine (Invitrogen Life Technologies, L3000001), according to the manufacturer's instructions. siRNA-NC was used as control group. Briefly, HUVECs were plated in T25 flasks and transfection was initiated when reaching 70-80% confluency. 15μL of siRNA was mixed with 9μL of Lipofectamine prior adding to cell culture plate. After 48 hours, total RNA and protein were extracted for evaluating SIRT1 knockdown efficiency by qPCR and Western Blot.

2.5. RT-qPCR

Cells were lysed by washing with PBS and adding RNA extraction solution (1mL) to 6-wells plate and 0.5mL to 12-wells plate. Then, 100 uL of chloroform substrate (Shan Dong Shuang Shuang Hua

Gong, GB/T682-2002) was added per each mL of RNA extraction solution. After centrifuged in 4 degrees for 15 min, 500 uL of isopropanol (Tian Jin Zhi Yuan, 1010) was added. Then, the solution was centrifuged for 10 min in 4 degrees and 75% ethanol was added to solution. 20-50 uL DEPC water were added for RNA extraction.

The reverse transcription was conducted using a commercial reverse transcription kit (Novoprotein E047-01B) according to manufacturer's instructions. Briefly, 1μg of total RNA was used with reaction mix. Subsequently, samples were incubated at 50℃ for 15min, then 75℃ for 5min.

The cDNA product was subjected to qPCR using a commercial kit (Novoprotein E096-01A) according to manufacturer's instructions. Briefly, 1μL of total cDNA was used with reaction mix, the primer sequences are listed in Table X. Subsequently, samples were incubated at 95℃ for 5min, 1 cycle, then 95℃ for 10 seconds, 60℃ for 10 seconds, and 72℃ for 10seconds, 40 cycles. Data was plotted and analyzed using the 2-ΔΔct method.

Table 1. The forward and reverse primer sequences are listed below

GAPDH-Forward	ATTCCACCCATGGCAAATTCC
GAPDH-Reverse	GACTCCACGACGTACTCAGC
SIRT1-Forward	GTAGGCGGCTTGATGGTAATC
SIRT1-Reverse	TACCTCAGCGCCATGGAAAA

2.6. Western blot analysis

HUVECs were lysed in 6-wells plate with 100μL RIPA lysing solution with 10μL protease inhibitor (100mM) and 10μL PMSF (100mM). The cells were washed once with PBS after removing culture medium, followed by adding precooled lysis solution. Then, the lysates were centrifuged for 10 minutes at 4°C, 12000 rpm. Protein concentration was measured by BCA assay kit according to manufacturer's recommendation. Samples were subjected to 12.5% SDS-PAGE analysis and electrophoresed at 80V, 15min, and 120V, 60min. Membranes were transferred at 150mA for 90 min, followed by treating with primary antibody (concentration: 1:1000, GADPH concentration 1:10000) and secondary antibody (HRP labeled goat anti-rabbit IgG dilution ratio 1: 10000).

2.7. Cell Viability Assay

Cell Viability was measured by CCK-8 (SuperKine™ Abbkine, BMU106-CN) according to manufacturer's recommendations. Briefly, after treatment, 10 μL of CCK-8 working solution was added into each well and incubated for 2 hours. Absorbance was measured at 450nm by TECAN SPARK plate reader. Cell viability was calculated by subtracting the absorbance of blank wells containing only the medium and normalizing the resulting values to the untreated control group.

2.8. Cell Apoptosis Assay

Cell apoptosis was evaluated by Caspase-Glo® 3/7 Assay (Promega, G8091) accordingly to manufacture's recommendations. Briefly, after treatment, Caspase-Glo® 3/7 solution was added to HUVECs' culture medium in 1:1 ratio. After 1 hour of incubation, luminescence was tested with microplate reader (TECAN SPARK). The cell apoptosis was calculated by subtracting the absorbance of blank wells containing only the medium.

2.9. eNOs measurement by ELISA

eNOs level was measured with eNOs ELISA Kit (Cloud-Clone Corp, SEA868Hu) according to manufacturer's instructions. Briefly, HUVECs were placed in 96-well plate (100 μL/well, 4,000 cells/well) and pre-cultured for 24 hours. After transfecting with si-SIRT1 3 for 6 hours, cells were treated with PET microplastics at 1000 μg/ml for 72 hours. HUVECs cell lysate was collected by trypsin and eNOs concentration was measured by ELISA kit. The results were read at 450nm by TECAN SPARK plate reader.

2.10. ROS Measurement

ROS was measured with ROS Assay Kit (Elabscience E-BC-K138-F) according to manufacturer's instructions. HUVECs were placed into a 6-well plate and pre-cultured for 24 hours. After being transfected with si-SIRT1 3 or vector control for 6 hours, cells were treated with PET microplastics at 1000 μg/ml and incubated for 72 hours. Cells were then washed with serum free medium, and a 10 μM solution was used. This incubation happened in a dark environment at 37c. Last, ROS levels were read at 500nm and 525nm with flow cytometry.

3. Results

3.1. PET reduced cell viability in HUVECs

The impact of PET on endothelial cell viability was evaluated in HUVECs treated with increasing concentrations of PET (0, 1, 10, 50, 100, 200, 500, and 1000 μg/mL) for up to 72 hours. As a result, PET reduced cell viability in a dose-dependent (P<0.001) and time course dependent manner. (P<0.001).

Notably, at 100 μg/mL, cell viability decreased to 93.51% at 24 hours (P<0.01, Figure 1A) and 84.52% at 72 hours (P<0.01, Figure 1C). At the highest concentration treated (1000 μg/mL), cell viability was reduced to 78.50% at 24 hours (P<0.01, Figure 1A), 75.42% at 48 hours (P<0.01, Figure 1B), and 55.96% at 72 hours (P<0.01, Figure 1C). These results indicate a significant time- and concentration-dependent cytotoxic effect of PET on HUVECs. (Figure 1)

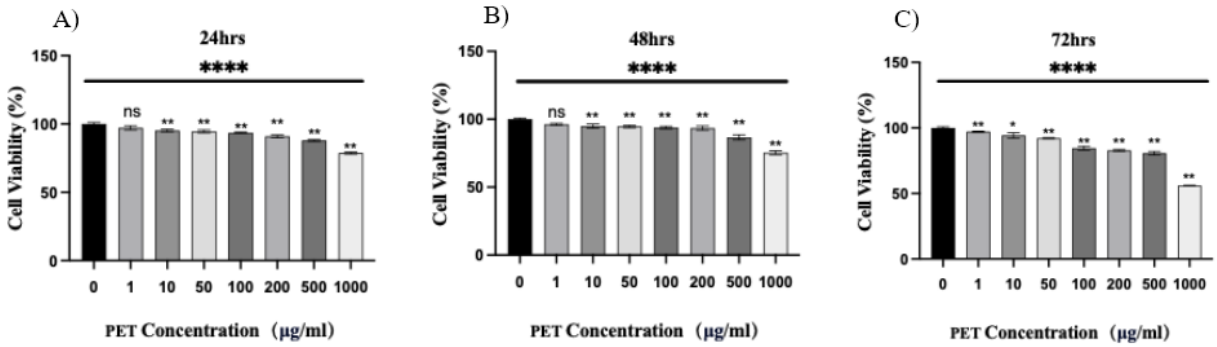

Figure 1. HUVECs viability (normalized to untreated control) post PET treatment (A) HUVECs cell viability under 0, 1, 10, 50, 100, 200, 500, 1000 μg/ml after 24 hours. (B) HUVECs cell viability under 0, 1, 10, 50, 100, 200, 500, 1000 μg/ml after 48 hours (C) HUVECs cell viability under 0, 1, 10, 50, 100, 200, 500, 1000 μg/ml after 72 hours. Data represented as Mean± SD. n=3, NS: none significant. * P<0.05, **P<0.01 versus control, ****P<0.0001 by one-way Anova and unpaired T-test

3.2. PET increased cell apoptosis in HUVECs

The effect of PET on endothelial cell caspase 3/7 activity and apoptosis was assessed in HUVECs treated with PET at concentrations of 0, 1, 10, 50, 100, 200, 500, and 1000 μg/mL. Compared to the untreated control group, PET treatment resulted in a significant increase in apoptosis up to 124% (P<0.0001, control vs 500 μg/ml, 48 hours). At the highest concentration tested (1000 μg/mL), caspase-3/7 activity was elevated by 68%, 95%, and 124% after 24, 48, and 72 hours, respectively, relative to the corresponding control (P<0.001, P<0.0001, P<0.01).

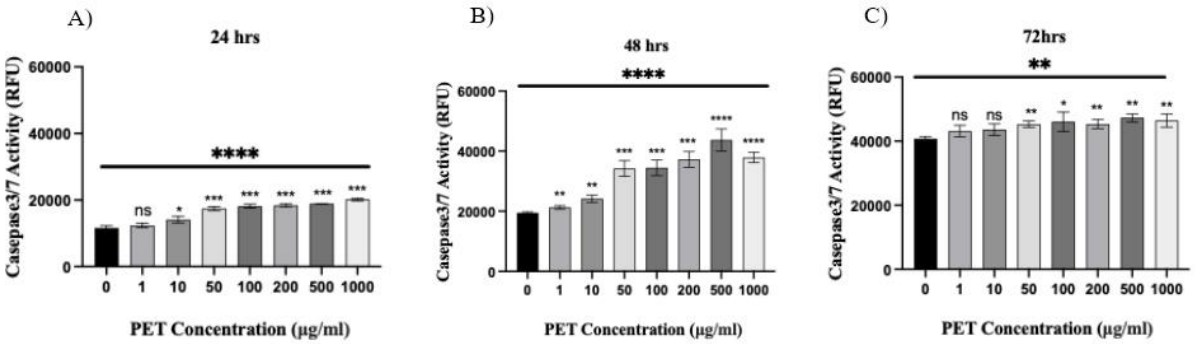

Figure 2. Caspase 3/7 activity in HUVECs post PET treatment. (A) Caspase 3/7 activity post 0, 1, 10, 50, 100, 200, 500, 1000 μg/ml of PET after 24 hours. (B) Caspase 3/7 activity post 0, 1, 10, 50, 100, 200, 500, 1000 μg/ml of PET after 48 hours. (C) Caspase 3/7 activity post 0, 1, 10, 50, 100, 200, 500, 1000 μg/ml of PET after 72 hours. Data represented as Mean± SD. n=3, NS: none significant. * P<0.05, **P<0.01, ****P<0.0001 versus control by one-way Anova and unpaired T-test

3.3. SIRT1 knockdown

To determine how SIRT1 affects PET-induced changes in endothelial cells. SIRT1 was knockdown. Three SIRT1 siRNA with different sequences were used to for knockdown optimization. Compared to the control group, si-SIRT1 1 reduced SIRT1 gene expression by 9.24% (P=0.77; si-SIRT1 2 reduced SIRT1 gene expression by 30.26% (P<0.01*);* si-SIRT1 3 reduced SIRT1 gene expression by 56.47% (P<0.01). Together these data indicate si-SIRT1 3 was most effective at decreasing SIRT1 level, therefore was selected for further protein evaluation in HUVECs, as a result, si-SIRT 3 reduced SIRT1 protein level by 66.72% (P<0.01), further confirming the knockdown efficiency at protein level.

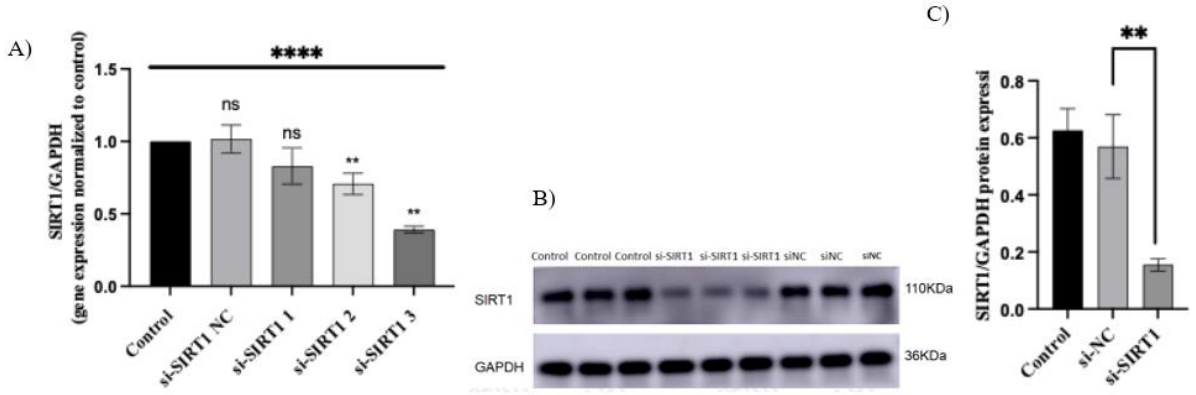

Figure 3. SIRT1 knockdown. (A) SIRT1 gene expression was significantly down regulated with si-SIRT1 2 and si-SIRT1 3 after 48 hours post transfection. (B) Representative images of Western Blot showing SIRT1 protein expression after 48 hours post transfection. (C) Quantification data showing SIRT1 protein expression was significantly reduced with si-SIRT1 3 after 48 hours post transfection. Data represented as Mean± SD. n=3, NS: none significant. * P<0.05, **P<0.01, ****P<0.0001 versus control or si-NC by one-way Anova and unpaired T-test

3.4. SIRT1 overexpression

To further determine whether gain of SIRT1 protects against PET-induced damage in endothelial cells. SIRT1 was overexpressed by transfection. As a result, compare to control group with empty vector, SIRT1 transfected HUVECs increased SIRT1 gene expression by 23294.1% (P<0.01), and increased SIRT protein level by 136.642% (P<0.01), confirming SIRT1 overexpression at both gene and protein level.

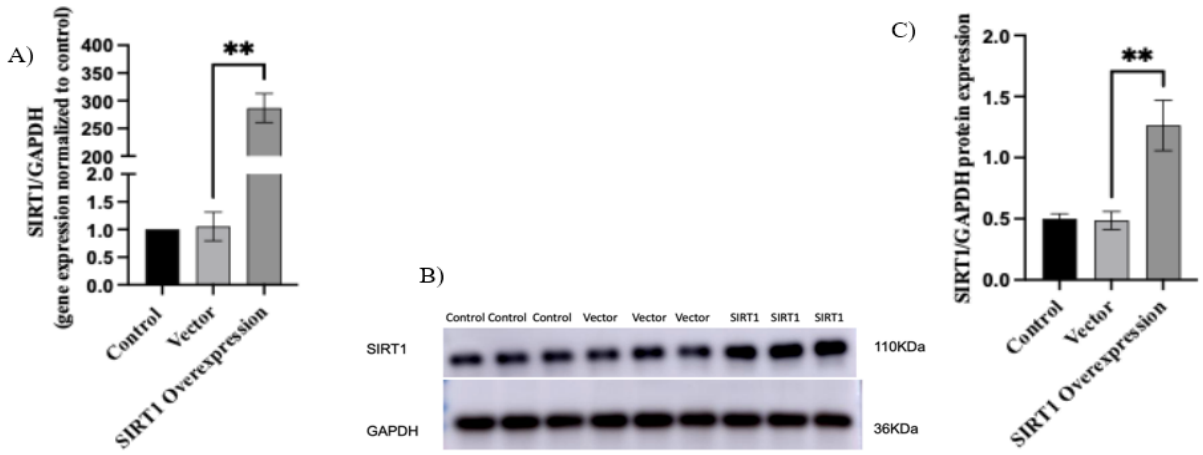

Figure 4. SIRT1 overexpression. (A)SIRT1 gene expression was significantly up regulated with SIRT1 overexpression after 48 hours post transient transfection. (B) Representative images of Western Blot showing SIRT1 protein expression after 48 hours post transfection. (C) Quantification data showing SIRT1 protein expression was significantly increased with SIRT1 overexpression after 48 hours post transfection. Data represented as Mean± SD. n=3, NS: none significant. * P<0.05, **P<0.01, ****P<0.0001 versus control by one-way Anova and unpaired T-test

3.5. SIRT1 protected against PET-induced reduction of cell viability.

To measure the effect of SIRT1 on PET-induced reduction of cell viability, HUVECs were treated with PET, with or without SIRT1 knockdown or overexpression. As a result, we observed that compare to untreated control group, PET treated HUVECs significantly reduced cell viability. (ctrl: 100%, PET: 61.53%, *P*<0.0001). SIRT1 siRNA knockdown further reduced cell viability. (SIRT1 siRNA: 45.38%%, *P*<0.0001), whereas SIRT1 overexpression restored cell viability (95.08% *P*<0.0001). Si-NC, empty vector did not show statistic difference compared to untreated control. (*P*=0.24)

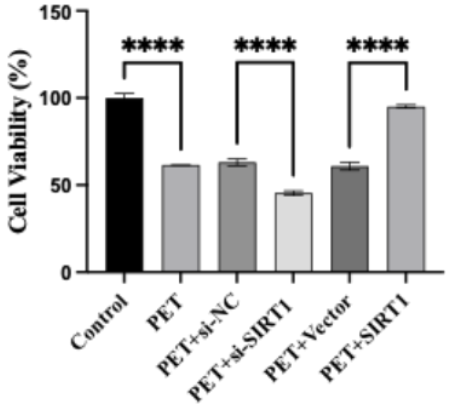

Figure 5. HUVECs cell viability (normalized to control) under PET treatment and SIRT1 knockdown or overexpression. Data represented as Mean± SD. n=3, NS: none significant. * P<0.05, **P<0.01, ****P<0.0001 versus control by unpaired T-test

3.6. SIRT1 protected against PET-induced increase of cell apoptosis.

To measure the effect of SIRT1 on PET-induced reduction of cell apoptosis, HUVECs were treated with PET, with or without SIRT1 knockdown or overexpression. As a result, we observed that compare to untreated control group, PET treated HUVECs significantly increased cell apoptosis by 32% (*P*<0.01). PET treated HUVECs with SIRT1 siRNA knockdown further increased cell apoptosis by 9.6% compared to PET treated group (*P*<0.05), PET treated HUVECs with SIRT1 overexpression greatly reduced cell apoptosis by 38.9% compared to PET treated group (*P*<0.0001). PET treated

with Si-NC, empty vector did not show statistic difference compared to PET treated control, respectively. Together these data indicates that SIRT1 protect against PET-induced cell apoptosis.

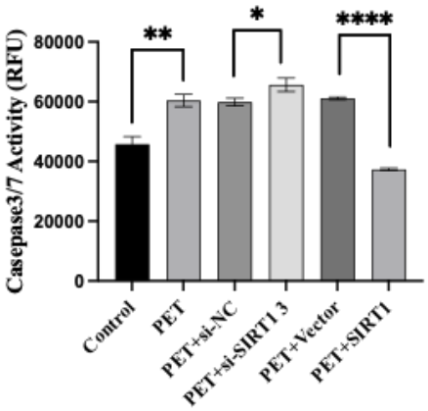

Figure 6. HUVECs cell apoptosis under PET treatments and SIRT1 knockdown or overexpression. Data represented as Mean± SD. n=3, NS: none significant. * P<0.05, **P<0.01, ****P<0.0001 versus control by unpaired T-test

3.7. PET reduced eNOs and SIRT1 rescued eNOs concentration

HUVECs were treated with PET, with or without SIRT1 knockdown or overexpression. As a result, we observed that compare to untreated control group, PET treated HUVECs had a significantly decreased eNOs level (ctrl: 0.27, PET: 0.19, P<0.0001). PET treated HUVECs with SIRT1 siRNA knockdown further decreased eNOS levels in cell (SIRT1 siRNA: 0.06, P<0.0001), whereas PET treated HUVECs with SIRT1 overexpression greatly increased eNOS level (0.25, P<0.0001). PET+Si-NC, PET+empty vector did not show statistic difference compared to PET treated group, respectively. Together these data indicates that PET reduces eNOs concentration and SIRT1 rescues eNOs concentration in endothelial cells.

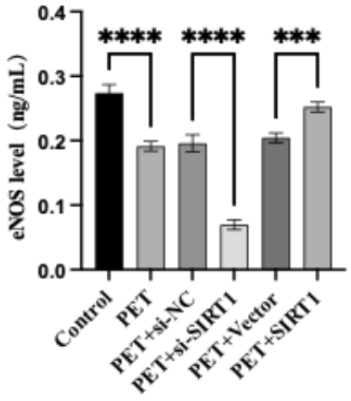

Figure 7. HUVECs eNOS level under PET treatment and SIRT1 knockdown or overexpression. Data represented as Mean± SD. n=3, NS: none significant. ****P<0.0001 versus control by unpaired T-test

3.8. PET increased ROS and SIRT1 reduced PET-induced ROS

HUVECs were treated with PET with or without SIRT1 knockdown or overexpression and tested for their ROS levels. As a result, we observed that compare to untreated control group, PET treated HUVCEs had an increase in ROS level (ctrl: 292640, PET: 383180, P<0.0001). PET treated HUVECs with SIRT1 siRNA knockdown further increased ROS levels (SIRT1 siRNA: 785000, P<0.0001), PET treated HUVECs with SIRT1 overexpression significantly reduced ROS level (310113, P<0.0001) to similar levels in untreated control group. PET+Si-NC, PET + empty vector did not show statistic difference compared to PET treated group, respectively. Together these data suggests that PET increases ROS level in endothelial cells whereas SIRT1 protects against PET-induced ROS.

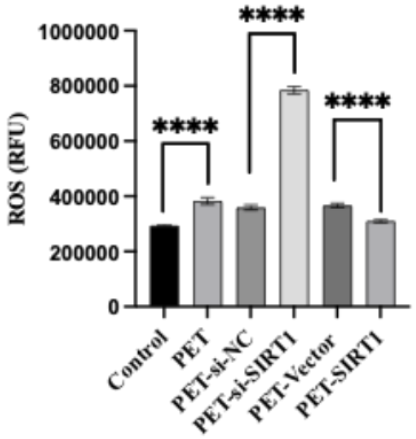

Figure 8. HUVECs ROS level under PET treatment and SIRT1 knockdown or overexpression. Data represented as Mean± SD. n=3, NS: none significant. ****P<0.0001 versus control by unpaired T-test

4. Discussion

This study demonstrates for the first time that PET impaired endothelial cells by significantly reduced endothelial cell viability, increased apoptosis, reduced eNOS levels and increased ROS concentrations, whereas SIRT1 protect against PET-induced impairments in these parameters. Together these findings demonstrated the toxic effects of polyethylene terephthalate (PET) nanoplastic particles on human umbilical vein endothelial cells (HUVECs) and the protective role of SIRT1 in mitigating these adverse outcomes. This research contributes to the growing understanding of the biological effects of nanoplastics, a ubiquitous and concerning environmental pollutant.

The toxicological profile of PET nanoplastics is especially concerning given the widespread environmental and human exposure to these particles. PET is commonly found in consumer goods and is a known contaminant in food and water sources, as evidenced by its detection in human stool samples [1] and blood [2]. The ingestion of PET particles, primarily through polluted water or food, exposes the gastrointestinal system and, as shown in this study, the vascular system to their toxic effects.

PET particles are not merely inert contaminants; their additives and breakdown products, such as antimony, are known to have endocrine-disrupting and potentially carcinogenic properties [3]. Chronic exposure to PET and its associated chemicals may exacerbate conditions such as inflammation, oxidative stress, and endothelial dysfunction, contributing to broader health risks such as cardiovascular disease and metabolic disorders.

Our results show that PET exposure significantly reduced HUVEC viability and increased apoptosis, indicating that PET particles directly impair endothelial cell survival. These findings align with earlier studies reporting that exposure to PET suppresses cell proliferation and migration while producing toxic effects on endothelial and mesenchymal cells [4]. Such toxicity may contribute to the broader adverse health impacts associated with microplastics, including potential risks to the vascular system and other critical biological functions.

Our study also demonstrated that PET nanoplastics significantly reduced eNOS levels and increased ROS production in endothelial cells, highlighting their detrimental effects on vascular health. eNOS is a critical enzyme for vascular homeostasis, producing nitric oxide (NO), which regulates vasodilation and reduces oxidative stress. A decrease in eNOS compromises these protective mechanisms, while elevated ROS levels promote oxidative stress and endothelial damage, potentially leading to vascular dysfunction.

Interestingly, oxidative stress and ROS signaling have dual roles in cellular stress responses. Low ROS levels can activate protective pathways, such as mitohormesis, which induce mitochondrial adaptation to stressors. However, excessive ROS production, as observed in PET exposure,

overwhelms these mechanisms and leads to cellular damage. PET's impact on ROS highlights the need for further investigation into its dose-dependent effects on oxidative stress and mitochondrial adaptation pathways.

The impact of PET on endothelial cells is particularly concerning given recent evidence of MNPs, including PET, in human cardiovascular tissues. PET has been detected in thrombi, atherosclerotic plaques, and other vascular lesions, with concentrations up to 469 μm and most particles smaller than 50 μm [5]. These findings suggest that PET particles are bioavailable and capable of accumulating in the vascular system, exacerbating endothelial dysfunction through mechanisms such as eNOS reduction and ROS elevation.

Given the detection of plastic concentrations as low as 1.62 μg/ml in human blood [6], further research is warranted to determine whether these levels are sufficient to induce the vascular toxicity observed in this study. Future studies should explore the chronic effects of lower PET doses and investigate the potential for adaptation or recovery mechanisms, such as mitohormesis, in endothelial cells exposed to nanoplastics.

Moreover, the interplay between PET particle properties (e.g., size, shape, surface charge) and their biological effects remains to be fully elucidated. Smaller particles, which penetrate deeper into tissues, may exacerbate ROS production and other harmful pathways. Investigating these variables will provide a more comprehensive understanding of the toxicological profile of PET nanoplastics and inform strategies to mitigate their impact on human health.

On the other hand, our study highlights the significant protective effects of SIRT1 against PET-induced impairments in endothelial cells (ECs). The ability of SIRT1 to counteract PET-induced apoptosis and reduction in cell viability suggests its involvement in promoting cell survival through anti-apoptotic pathways. By restoring a balance between pro-survival and pro-apoptotic signals, SIRT1 effectively maintains endothelial homeostasis in the presence of PET-induced stressors. Additionally, SIRT1 restored eNOS levels, a crucial factor for vascular health, by promoting nitric oxide (NO) production and counteracting oxidative stress. SIRT1 also reduced ROS levels, limiting oxidative damage and preserving cellular integrity. These effects align with SIRT1's known functions as a regulator of endothelial function and a modulator of oxidative stress pathways.

5. Conclusion

In conclusion, we found that PET significantly reduced cell viability; increased cell apoptosis; decreased cell eNOS level; and increased cell ROS level. On the other hand, the experimental group which treated with SIRT1 overexpression showed that SIRT1 was able to mediate those negative effects. In general, this study demonstrates the toxic effects of PET nano-plastics on endothelial cells and highlights the potential of SIRT1 as a protective factor. These findings, combined with evidence of widespread human exposure to microplastics, emphasize the urgent need for further research to elucidate their long-term health impacts. Exercising, or treatment with SIRT1 can revert and protect against the harmful effects of PET microplastics. As microplastics are a ubiquitous environmental pollutant, understanding their biological effects and developing mitigation strategies are critical for safeguarding public health and environmental sustainability.

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