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MSC-Exosomes Hypoxia (EH-MSCs) in modulating Apaf-1 and Survivin in UVB-induced skin aging

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Abstract: Skin aging is marked by decreased elasticity and increased wrinkle formation, often associated with altered expression of key genes such as *APAF-1* and *Survivin*. Exposure to UVB radiation, particularly in tropical regions, accelerates collagen degradation, thereby heightening the risk of premature aging. Mesenchymal stem cell-derived hypoxic exosomes (MSCs-Exosome Hipoksia) have shown potential in suppressing *APAF-1* expression and enhancing *Survivin* levels, although their effects on UVB-induced skin damage have not been fully explored. This study investigated the impact of MSCs-Exosome Hipoksia on *APAF-1* and *Survivin* gene expression in UVB-exposed rat skin. Rats with reduced collagen levels due to UVB exposure were randomly assigned into four groups: normal control (KN; UVB + 0.9% sodium chloride 300 µL), positive control (KP; UVB + hyaluronic acid 200 µL), treatment group 1 (T1; UVB + MSCs-Exosome Hipoksia 200 µL), and treatment group 2 (T2; UVB + MSCs-Exosome Hipoksia 300 µL). The T2 group demonstrated the lowest *APAF-1* expression (1.03 ± 0.33 pg/mL) and the highest *Survivin* expression (4.35 ± 0.73 pg/mL). Both treatment groups (T1 and T2) showed statistically significant reductions in *APAF-1* and increases in *Survivin* expression compared to control groups ($p < 0.05$). These findings indicate that MSCs-Exosome Hipoksia, particularly at a dose of 300 µL, may effectively modulate molecular markers associated with skin aging and hold therapeutic potential in mitigating UVB-induced dermal damage.

Keywords: MSCs-Exosome; Collagen Loss; Apaf-1; Survivin.

INTRODUCTION

Skin aging is a major concern in both health and aesthetic fields due to its visible impact and underlying biological complexity. As individuals age, the skin undergoes structural and functional changes, including reduced elasticity, moisture loss, and increased wrinkle formation[1]. One of the molecular mechanisms implicated in skin aging involves the dysregulation of apoptotic and proliferative signaling pathways, particularly through the expression of *Apoptotic Protease Activating Factor-1* (*APAF-1*) and *Survivin*. Elevated *APAF-1* expression and diminished *Survivin* levels have been associated with increased apoptosis and collagen degradation, contributing to visible signs of aging[2].

The prevalence of collagen degradation is particularly pronounced in tropical regions, where chronic exposure to ultraviolet (UV) radiation, especially UVB, accelerates skin aging. This environmental stressor leads to increased oxidative stress and breakdown of dermal collagen, resulting in wrinkles, loss of skin elasticity, and hyperpigmentation[3]. Moreover, factors such as high humidity, air pollution, and diets deficient in collagen-supporting nutrients—such as vitamin C, antioxidants, and proteins—further exacerbate this condition[3]. Studies show that

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individuals living in tropical climates face a higher risk of collagen loss and degenerative skin changes compared to those in temperate regions.

Physiologically, humans lose approximately 1% of collagen annually. By the age of 30, collagen levels decline by 15–20%, and by age 40, collagen production significantly diminishes, resulting in a cumulative loss of up to 40%[2]. A 2015 study reported that 4.2% of subjects showed significant collagen reduction after three exposures to UVB at the minimal erythema dose (MED)[2]. Additionally, the incidence of wrinkles and pigmentation-related skin conditions has risen, with an estimated 100 to 350 new cases recorded in 2020[4].

Apoptosis plays a critical role in maintaining skin homeostasis, and *Survivin* and *APAF-1* are two key regulators of this process[2]. *Survivin* is an anti-apoptotic protein that promotes cell survival by inhibiting caspase activation[5] and plays a role in cell cycle regulation, ensuring proper mitosis. Conversely, *APAF-1* is a pro-apoptotic protein that responds to cellular stress signals such as oxidative damage and DNA injury[6]. Upon mitochondrial release of cytochrome c, *APAF-1* forms the apoptosome complex, triggering caspase-9 activation and initiating the intrinsic apoptosis cascade[3,6]. The balance between these two proteins is essential in regulating keratinocyte survival and preventing premature aging[8,9].

Recent research has highlighted the potential of hypoxia-induced mesenchymal stem cell-derived exosomes (MSCs-Exosome Hypoxia) as modulators of skin regeneration. These exosomes carry various molecular cargoes, including regulatory microRNAs (miRNAs) and proteins involved in apoptosis modulation[3,4]. MiRNAs such as miR-23a, miR-21, and miR-125b have been shown to suppress *APAF-1* expression[9]. For instance, miR-23a can directly inhibit *APAF-1*, while miR-21 is associated with downregulation of apoptotic pathways. Moreover, proteins within MSC-derived exosomes can modulate intracellular signaling, including pathways involving Bcl-2, Bax**,** and caspases, thereby influencing *Survivin* expression[7].

Regulation of *APAF-1* and *Survivin* expression plays a pivotal role in keratinocyte apoptosis and overall skin aging[8,9]. Despite their potential, the use of MSCs-Exosome Hypoxia (EH-MSCs) in photoaging therapy remains underexplored, particularly regarding their dose-dependent impact on apoptotic pathways. This study uniquely investigates the molecular effects of EH-MSCs on *APAF-1* and *Survivin* as mechanistic markers of regeneration, positioning EH-MSCs as a potential next-generation therapy for UVB-induced skin aging.

Conventional therapies, such as topical sunscreens and hyaluronic acid (HA), are widely used to protect the skin from UVB damage and reduce wrinkles[10]. However, these approaches often focus only on surface hydration and do not address the deeper molecular mechanisms of skin aging. HA, for example, lacks significant anti-inflammatory or antioxidant activity, and its benefits are often short-lived[11]. Current treatments fail to modulate the apoptotic pathways that drive collagen loss and keratinocyte death. Therefore, this study aims to evaluate the potential of MSCs-Exosome Hypoxia in modulating *APAF-1* and *Survivin* expression in UVB-induced skin aging models. By exploring their molecular regulatory effects, this research may contribute to the development of targeted regenerative strategies for managing photoaging and improving dermal resilience.

MATERIAL AND METHOD

This study is a *posttest only control group* with a complete random design method with five repetitions per treatment. The object of the study was male rats of the Wistar strain with a body weight of 200-250 grams.

This study used equipment in the form of cell culture equipment consisting of *a Biosafety Cabinet* (BSC), micropipette, CO2 incubator, dissecting kit, and 25T flask. Oxygen-meters are used to measure oxygen levels in *hypoxic chambers*. In addition, this study also used equipment in the form of UVB light (broadband with

peak emission at 302 nm) with an energy of 160 mJ /cm2 which was given 5 times for one week to 2 weeks to induce rats until collagen density was reduced and was carried out on the back of the rats, sterile swabs to sterilize the area to be injected. The tools used for data collection were vacutainers, hematocrit tubes, 6 mm *biopsy punch*, centrifuges, micropipettes, 1000 µL micropipette tips, and razors, exposure cages, maintenance cages, drinking water containers for rats. The tool used for the analysis of APAF-1 and Survivin gene expression is qRT-PCR (Ilumina). Tools used for data analysis include microplate readers, microscopes, staining jars, coated desk glass, cover glass, and laptops. The materials of this study consisted of culture materials composed of *umbilical cord,* NaCl 0.9%, PBS, DMEM, FBS, fungizone, and penstrep. Meanwhile, the ingredients used for the treatment process are 70% alcohol, PBS, ketamine, and xylasine. The materials used for PCR analysis are APAF-1 and Survivin primers.

The entire process is carried out in a class 2 biosafety cabinet, using sterile equipment and done with high sterility techniques. *Umbilical cords* are collected in a transport medium. Using tweezers, *the umbilical cord* is placed onto the petri dish, the *umbilical cord* is washed thoroughly using PBS. *The umbilical cord* is cut and the blood vessel is removed. *The umbilical cord* is finely chopped and placed on the 25T flask evenly, let it sit for 3 minutes until the tissue is attached to the surface of the flask. A complete medium consisting of DMEM, fungizone, penstrep, and FBS) is added slowly until it covers the tissue. The explant is incubated in an incubator at a temperature of 37ºC and 5% CO2. Cells will emerge after approximately 14 days from the beginning of the culture process. Replacement of the medium is carried out every 3 days by removing half of the medium and replacing it with a new complete medium. Cell maintenance is carried out until the cell reaches 80% confulness. Then the cells are harvested (*passage*) for propagation, passage 1 of the confluent is then subcultured until passage 4, condition medium is collected after the cells reach 70% confluence or more.

The condition medium that has been collected from passage 4, then in a centrifuge of 300xg for 5 minutes to remove the cells, then in a centrifuge of 200xg for 30 minutes to remove debris. *Supernatant* that has been centrifuged is then filtered by the TFF (*Tangential Flow Filtration*) method using *sterile hollow fiber polyether-sulfone membrane* 10, 50, 100, 500 kD, validation was performed via flow cytometry for markers CD63, CD81, and CD9, confirming their identity as MSC-derived exosomes. MSC that has reached 80% confluence is added complete medium up to 10 mL. The flask that has contained the MSC is then placed in the *hypoxic chamber.* Nitrogen gas is delivered through an inlet valve and an oxygen meter is placed in the sensor hole to measure the oxygen concentration in the chamber. Nitrogen is added until the indicator needle shows a concentration of 5% oxygen. *The chamber* that has been filled with flasks is incubated for 24 hours at a temperature of 37°C. After 24 hours, the culture medium was taken and filtered using TFT with 100-500 kDa to obtain EH-MSC which was then in accordance with the T1 and T2 doses. Wash 2 times with *stain buffer* (PBS) and resuspension with 300-500µL *stain buffer* (PBS) or 1 wash *buffer* (FBS). Read in *flow cytometry* use tubes 1-5 as controls for setting up *cytometry* (as compensation). Validation of EH-MSC content using flowcytometry with surface markers in the form of CD63+, CD81+, CD9+. The validated results containing EH-MSCs were stored in 2.5 ml tubes and stored at 2-8 °C.

Rats that had been adapted for 7 days were anesthetized with a mixture of ketamine (60mg/kgbb) and xylasine (20mg/kgbb). The hair on the rat's back is cut clean. The back of the mice was exposed to UV light (broadband with *peak emission* of 302 nm) with a minimum *erythema dose* (MED). UVB exposure (160 mJ/cm² for five sessions over two weeks) was standardized to induce collagen degradation, validated through macroscopic wrinkle observations and microscopic Masson Trichrome staining. Treatment 1 and Treatment 2

mice were then treated using MSCs-Exosome injection with doses of 200µL and 300µL administered once on day 15. The doses of 200 µL and 300 µL were selected based on preliminary studies demonstrating their effectiveness in modulating inflammatory responses without inducing adverse effects.[12]

Tissue sampling was carried out on day 29 after the first day of treatment. All mice are first killed by means of cervical dislocation before tissue is taken. Tissue was taken using a 6 mm punch biopsy on the part of the skin exposed to UVB and taken at 50 mg for RT-PCR analysis. The tissue samples were divided into two for fixation in 10% formalin for 24 h and in RNA later. The tissue is inserted into formalin for 24 hours and then stored in a tube containing 70% alcohol and stored at room temperature until the process of making paraffin preparation. The sample is put into RNA later and then put in the freezer until the data analysis process.

The normality and homogeneity of data were tested using Shapiro-Wilk and Levene's tests, respectively. Data with normal distribution were analyzed using One-Way ANOVA followed by Post Hoc LSD, while non-normal data were evaluated using Kruskal-Wallis and Mann-Whitney tests. Data analysis processing was carried out using SPSS 22.0 *for Windows*.

RESULTS AND DISCUSSION

Isolation of MSCs was carried out at the *Stem Cell and Cancer Research* Laboratory (SCCR), Semarang, using *umbilical cord* of 21-day-old pregnant rats. The results of the isolation were then cultured in a culture flask with a special medium. The results of MSCs culture after the 4th pasage were obtained with a picture of cells attached to the base of the flask with *spindle-like cell* morphology in microscopic observation (Figure 1A).

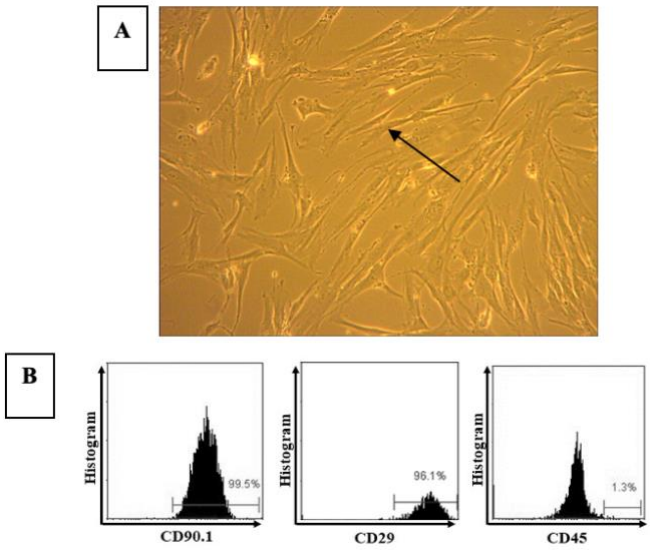

Figure 1. (A) Isolation of MSC with 80% confluence obtained a spindle-like cell image (indicated by an arrow) at 100x magnification. (B) Flow cytometry *analysis* of CD90, CD29, and CD45 expression.

This study examined how the injection of MSCs-Exosome Hypoxia subcutaneous affected the expression of Apaf-1 and Survivin in 30 male rats of the Wistar strain who experienced *collagen loss* due to UVB exposure. The creation of collagen loss model mice was carried out by UVB irradiation. The mice were exposed to UVB light at a distance of 20 cm with the intensity used was 1 MED (160mJ/cm2) for 8 minutes, carried out 10 times in 14 days to make the mice model *collagen loss.* Validation of the formation of a collagen loss model

in mice was carried out macroscopic by looking at wrinkles in mice exposed to UVB compared to mice not exposed to UVB. Based on the results of macroscopic observations, it was seen that there were more pronounced wrinkles in mice exposed to UVB than in mice not exposed as seen in (Figure 2A). In addition to being carried out macroscopicly, validation was also carried out microscopically using *Masson Trichrome* painting to see the density of collagen in mice exposed to UVB. Based on the results of the painting, it was found that there was a decrease in collagen density after UVB exposure as seen in (Figure 2B).

Mice without UVB exposure were used as a healthy control group (sham). Rats that experienced a decrease in collagen density after UVB exposure were grouped as mice that experienced collagen loss and then divided into 4 treatments, including, K- (mice exposed to UVB and 0.9% *sodium chloride* (NaCl) injection treatment with a dose of 300uL subcutaneously), K+ (mice exposed to UVB rays and *Hyaluronic Acid* injection treatment(HA) with a dose of 200uL subcutaneously), T1 and T2 (mice exposed to UVB rays and MSCs-Exosome Hypoxia injection treatment at doses of 200uL and 300uL, respectively).

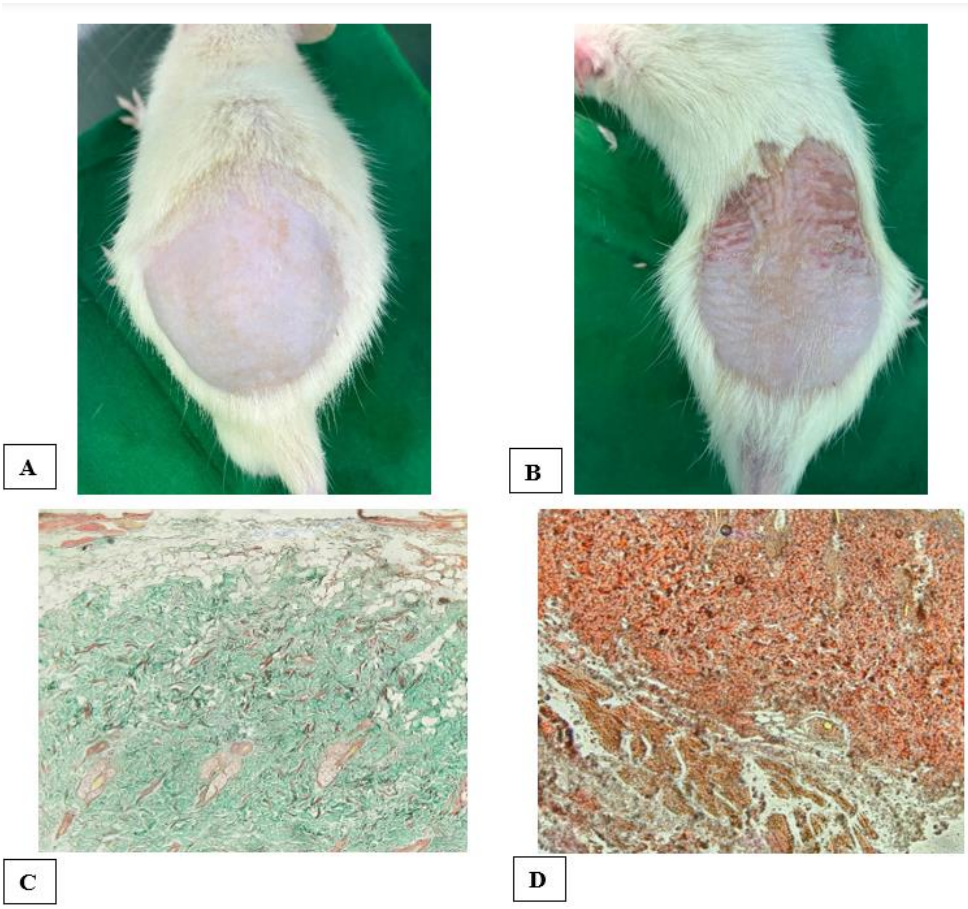

Figure 2. Collagen Loss *Validation*. Wrinkles were more pronounced in mice exposed to UVB (B) compared to those not exposed (A). Collagen shown in blue (black arrow) was less visible in the group exposed to UVB (D), compared to the group without UVB exposure (C)

MSCs-Exosome Hypoxia injection was done once and tissue sampling was carried out on day 15 after MSCs-Exosome Hypoxia injection. The tissue is then stored in RNA later for RNA extraction using Trizol. After the tissue formed the suspension, then centrifuge and supernatants were collected for the analysis of Apaf-1 and Survivin expression using the qRT-PCR method.[13,14]

Table 1. Data from Apaf-1 and Survivin Expression Analysis

Variable	Group					
	Sham (pg/mL)	C- (pg/mL)	C+ (pg/mL)	T1 (pg/mL)	T2 (pg/mL)	P
Apaf-1	1.17	3.45	2.59	1.53	1.03	
Std. deviasi	0.14	0.65	0.96	0.69	0.33	
Shapiro Wilk						0.05
Lavene test						0.056
One Way Anova						0.001
Survivin	1.25	2.35	3.21	2.64	4.35	
Std. deviasi	0.55	0.35	1.48	0.77	0.73	
Shapiro Wilk						0.05
Lavene test						0.012
Kruskal-Wallis						0.000

Based on the results of the Apaf-1 normality and homogeneity test, it was followed by *the One Way Anova test* to determine the distribution of data that showed a value of p<0.05 and *Post Hoc LSD* to find out the group that showed a significance value of p<0.05. As a result, the negative control (C-) compared to the injection treatment of MSCs-Exosome Hypoxia at doses of 200uL (T1) and 300uL (T2) produced a value of <0.001 meaning p<0.05. The significant reduction in Apaf-1 expression in the T1(200uL EH-MSC) group T2 group (300 µL EH-MSC) compared to the control groups suggests effective inhibition of pro-apoptotic pathways. This aligns with miRNA-mediated downregulation of Apaf-1, particularly by miR-21 and miR-23a.

Survivin expression was based on the normality test because the data distribution was abnormal, so it was followed by *the Kruskall Wallis* and *Mann Whitney post hoc* tests to determine the distribution of data per treatment group. The result was that negative control (C-) compared to T1 produced no difference or non-significant value (P>0.05), while compared to T2 produced significant (p<0.05). The dose-dependent increase in Survivin expression in the T2 group indicates enhanced cell survival and reduced apoptosis, mediated by miRNAs such as miR-126 and miR-125b, which regulate anti-apoptotic pathways.

The Apaf-1 group based on the *shapiro wilk test* was normally distributed with *a p-value* of >0.05 and the homogeneity test using the *lavene test* the results were homogeneous with *a p-value* of 0.056 (p >0.05) on Apaf-1, so the data analysis used the One *Way Anova* parametric test. *The One Way Anova* parametric test was used to identify whether there was a significant difference in the mean expression of Apaf-1 between the five groups compared. Based on the results of *the One Way Anova* test, there was a significant difference (p<0.05) in the Apaf-1 expression data between these groups, indicating that there was a significant difference in at least two groups. Furthermore, to evaluate the relationship between groups, a *Post* Hoc *LSD* test was carried out. The test result data is shown in Table 2.

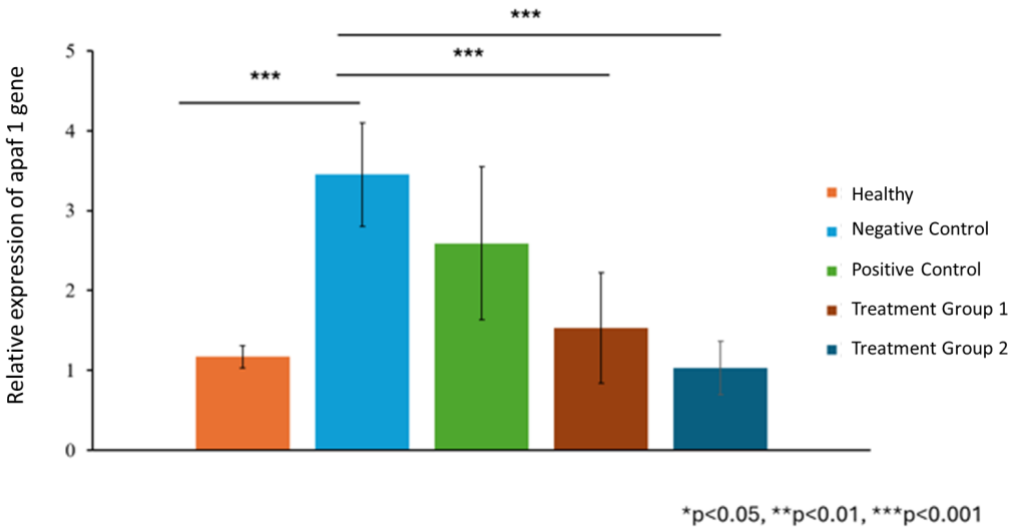

Figure 3. Graph of Apaf-1 Expression after MSCs-Exosome Hypoxia Injection in UVB-Exposed Rats

Table 2. Mean difference in Apaf-1 expression between the two groups with the Post Hoc LSD Test

Group	Comparison Group	Significance
Sham	C-	0.001
	K+	0.001
	T1	0.324
	T2	0.712
C-	C+	0.025
	T1	0.001
	T2	0.001
C+	T1	0.007
	T2	0.001
T1	T2	0.180

The results of *the post-hoc LSD* test of Apaf-1 expression data showed that the healthy group had a $p<0.05$ value when compared to the negative control group. The data revealed that there was a significant difference between the T1 and T2 groups when compared to the positive control group ($p<0.05$). The analysis also showed a significant difference between the T1 and T2 groups on the injection of MSCs-Exosome Hypoxia when compared to the negative control group ($p<0.05$). This shows that the expression of Apaf-1 with MSCs-Exosome Hypoxia injection treatment at doses of 200uL and 300uL is significantly different from the treatment of sodium *chloride* 0.9% injection and *hyaluronic acid*. The data also showed that there was no difference between the T1 and T2 groups ($p>0.05$) indicating that the 200uL dose of MSCs-Exosome Hypoxia did not confer a difference in Apaf-1 expression compared to the 300uL dose.

On the other hand, Survivin expression data that had been verified abnormal and heterogeneous data distribution was used in a *Kruskal-Wallis non-parametric* analysis to evaluate the variation in the mean Survivin expression among the five treatment groups. The *Kruskal-Wallis* results showed significance with a value of $p<0.001$ indicating a significant difference in Survivin expression between at least two treatment groups. To detail these differences, the *Mann Whitney* test was

conducted to analyze the comparison between the two groups, with the results documented as in Table 3.

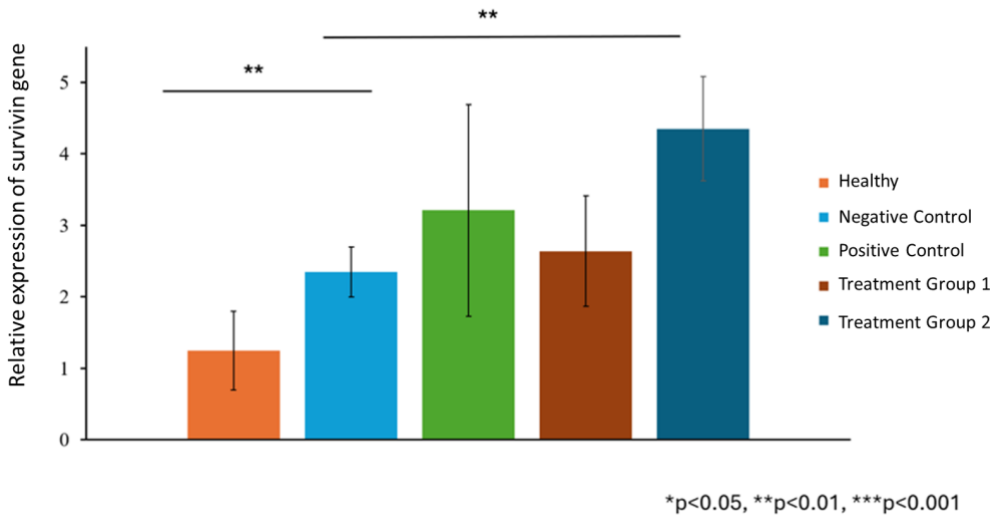

Figure 4. Survivin Expression Graph. The decrease pattern shown was *a dose-dependent manner* where the highest dose resulted in a significant increase in Survivin expression

Table 3. Differences in the average expression of Survivin between the two groups with *the Mann Whitney Test*

Group	Comparisson Group	Significance
Sham	C-	0.003
	C+	0.003
	T1	0.003
	T2	0.003
C-	C+	0.337
	T1	0.423
	T2	0.004
C+	T1	0.631
	T2	0.078
T1	T2	0.006

The results *of the Mann Whitney* test Survivin expression obtained a value of ($p<0.05$) for several comparison groups. The healthy group had a significant difference from the negative control group with a significance value of 0.003 ($p<0.05$). The negative control group had a significant difference to treatment 2 with a value of 0.04 ($p<0.05$), and treatment 1 had a significant difference from treatment 2 with a significance value of 0.006 ($p<0.05$). The increase pattern shown was a *dose-dependent manner* where the highest dose resulted in an increase in Survivin expression and produced a significant statistical value ($p<0.05$).

This study aims to evaluate the impact of injection of MSCs-Exosome Hypoxia with different levels (200uL and 300uL) on male Wistar rats who are repeatedly exposed to UVB light for 2 weeks. The findings of the study showed that both doses of MSCs-Exosome Hypoxia injection were subcutaneously successful in decreasing the expression of Apaf-1. In addition, injections with a dose of 300uL also showed the ability to increase Survivin expression. This indicates the potential for injection of MSCs-Exosome Hypoxia subcutaneously as

an effective anti-inflammatory, anti-apoptosis, and anti-angiogenesis agent on skin exposed to UVB rays. The photoaging process involves the skin's complex response to UV light, which causes significant structural and molecular changes.[15] UVB exposure triggers skin DNA damage, increases ROS production, causes oxidative stress, and stimulates collagen loss, leading to premature skin aging.[16] UVB exposure causes oxidative stress in the skin, activating the NF-κB signaling pathway that leads to the production of pro-apoptotic cytokines, including Apaf-1.[17]

Based on the research conducted, it was found that the group that was exposed to UVB and 0.9% NaCl injection subcutaneously had the highest expression among other groups. This can indicate that there is still a prolonged inflammatory process in the skin area after exposure to UVB.[18] The study also found that injections of MSCs-Exosome Hypoxia at doses of 200uL and 300uL were able to significantly decrease the expression of Apaf-1. This shows that the injection of MSCs-Exosome Hypoxia has subcutaneous anti-apoptic activity. MSCs-Exosomes Hypoxia contain various types of miRNAs and cytokines that play an important role in relieving inflammation.[19,20] miR23a, miR125b, and miR-21 were identified as key regulators in controlling inflammatory responses, particularly those related to apoptosis.[19,20] miR23a and miR21 have a role in suppressing Apaf-1 expression and regulating the NF-kB pathway, while miR-21 is involved in reducing oxidative stress.[21] This is important because the activation of Apaf-1 is related to the production of cytochrome c which will form the apoptosome and activate the early pathway of apoptosis i.e. caspase 9, which contributes to the process of cell death.

Recent research has found that Apaf-1 expression can suppress Survivin activity, so that inflammation that occurs continuously due to UVB exposure will decrease Survivin expression so that ROS levels will increase and cause oxidative stress that gets worse.[22,23] The reduction in Apaf-1 expression aligns with miRNA-mediated inhibition of intrinsic apoptotic pathways. Specifically, miR-23a and miR-21 suppress Apaf-1 expression by interfering with cytochrome c release, preventing apoptosome formation and caspase-9 activation. However, miR-21 contained in MSCs-Exosome Hypoxia can re-increase Survivin expression, thereby neutralizing ROS and reducing oxidative stress.[24] By regulating the NF-kB pathway, MSCs-Exosome Hypoxia can decrease Apaf-1 expression and increase Survivin expression in inflammatory responses caused by UVB light exposure.

In addition, these findings align with prior studies showing the role of miRNA-enriched exosomes in suppressing apoptosis and inflammation. Zhu et al., (2018) demonstrated the efficacy of MSC-derived exosomes in reducing oxidative stress markers in myocardial models, which parallels the observed effects in skin tissue.[25] For example, miR-23a is involved in the regulation of responses to oxidative stress and may modulate the expression of genes associated with anti-apoptotic activity, including Survivin.[26] In addition, miR-21 plays a role in various cellular processes such as proliferation, apoptosis, and response to oxidative stress, and may affect the expression of antioxidant enzymes. miR-126 also has an important role in angiogenesis and tissue regeneration, as well as in the regulation of antioxidant defence mechanisms.[27] Meanwhile, miR-125b is known to reduce oxidative stress and inflammation, which impacts enzymes such as caspase. Finally, miR-200c, which is involved in the regulation of oxidative stress, has a modulating effect on the expression of antioxidant enzymes. Nonetheless, the exact mechanism by which these miRNAs affect Survivin still requires further research for a more in-depth understanding.[28,29] The observed increase in Survivin expression is likely due to miR-126, which enhances anti-apoptotic signaling and promotes cellular repair by stabilizing mitochondrial function and reducing oxidative stress.

Previous studies have reported that the overall secretome secreted by MSCs is able to suppress inflammation seen from the decrease in Apaf-1. In addition, MSCs are also known to be able to stimulate the production of Survivin which can ward off free radicals.[30] This is in accordance with this study which found a

decrease in Apaf-1 expression and an increase in Survivin expression after administration of MSCs-Exosome Hypoxia on skin exposed to UVB. Based on the study, MSCs-Exosome Hypoxia injection is able to subcutaneously decrease the expression of Apaf-1 and increase the expression of Survivin through the regulation of the NF-kB and caspase pathways. However, this study only focused on the effect of injection of MSCs-Exosome Hypoxia on Apaf-1 and Survivin without examining the *pathways* that regulate both such as NF-κB and caspase. This study did not evaluate upstream regulators of Apaf-1 or Survivin, such as NF-kB or downstream caspase markers, limiting the understanding of the complete signalling cascade. Future research should investigate these pathways and characterize the exosome miRNA profile. These limitations should be the basis for further research.

CONCLUSION

This study demonstrates the dose-dependent efficacy of EH-MSCs in modulating Apaf-1 and Survivin expression in UVB-induced skin aging. These findings highlight the potential of EH-MSCs as a novel, cell-free therapeutic strategy targeting apoptotic and inflammatory pathways, paving the way for advanced regenerative treatments in dermatology.

AUTHORS' CONTRIBUTIONS

Citra Megawati Agustina: Supervision, Conceptualization, Data curation, Reviewing.: Eko Setiawan: Data curation, Investigation, Writing- Original draft preparation.: Agung Putra: Supervision, Methodology, Validation.

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DATA AVAILABILITY STATEMENT

The utilized data to contribute to this investigation are available from the corresponding author on reasonable request

DISCLOSURE STATEMENT

There is no conflict of interest.

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