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Potential of Glycine max-Based Cream in Restoring Skin Structure Through PDGF and Collagen Modulation After UVB Exposure

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ABSTRACT

Premature aging is caused by excessive activity in the sun, causing oxidative stress and inflammatory reactions, which include changes in skin structure such as shortening and thickening of collagen fibers, damage to elastic fibers, and changes in the proportion of collagen types in the dermis. The purpose of this study was to determine the effect of administering soy extract cream (Glycine max (L.) Merr) on PDGF concentration and collagen density in BALB/c mice exposed to UVB rays. The experimental study used a Post Test Only Control Group Design with 30 BALB/c mice divided into five treatment groups: a group of healthy mice (K1), a negative group without exposure to UVB rays (K2), a positive group exposed to UVB rays and smeared with vitamin E cream (K3), and a treatment group with a dose of soy extract cream (KEKD) 10% (K4) and 20% (K5). Data analysis used the One Way Anova statistical test. The results of the study showed significant differences in the average PDGF levels in each group: (K1) 149.5±7.1 ng/mL, (K2) 40.4±4.4 ng/mL, (K3) 88.6±41.7 ng/mL, (K4) 323.2±86.1 ng/mL, and (K5) 330.2±34.3 ng/mL, with the One Way Anova test obtaining a p value = 0.001 ($p<0.05$). The average collagen density of group (K1) was 50.10±12.33%, (K2) 32.75±6.6%, (K3) 33.07±7.48%, (K4) 41.07±10.8%, and (K5) 41.9±13.4%, with One Way Anova test showing p=0.088 ($p>0.05$), which means there is no significant difference in collagen density between groups. Administration of soy extract cream (KEKD) affected PDGF levels, but did not show a significant difference in collagen density in BALB/c mice exposed to UVB light.

Keywords: Soy extract cream, PDGF, Collagen density, UVB

INTRODUCTION

Premature aging is caused by excessive sun exposure which produces free radicals, resulting in oxidative stress and inflammatory reactions that contribute to changes in skin structure, such as shortening and thickening of collagen fibers, damage to elastic fibers, and changes in the proportion of collagen types in the dermis. (Salminen et al., 2022a) (Leite et al., 2023). UVB rays are known to be the main factor causing photoaging, characterized by wrinkles, loss of skin firmness, and inflammatory effects (Zasada & Budzisz, 2019). In addition, UVB exposure can induce DNA damage, cause skin inflammation, and contribute to immunosuppression (Petruk et al., 2018).

To overcome these negative impacts, topical therapies based on natural ingredients are increasingly popular because they are safer than synthetic ingredients that can cause skin irritation (Kong et al., 2016)(Tanveer et al., 2023). One of the natural ingredients that has the potential to prevent premature aging is soybeans. Soybean extract contains isoflavones, soyasaponins, phytosterols, lignans, and phytic acid which have antioxidant, anti-inflammatory effects, and increase collagen synthesis (Kuhns, 2023). Previous studies have shown that soy extract-based creams can increase collagen-I levels in human fibroblasts and skin (Leite et al., 2023).

Platelet-Derived Growth Factor (PDGF) plays a role in tissue repair by increasing cell migration and proliferation and inducing collagen synthesis through stimulation of Transforming Growth Factor-β (TGF-β).(Moon et al., 2020) UVB radiation is known to inhibit PDGF release by increasing ROS (Reactive Oxygen Species) production, which leads to decreased collagen synthesis and accelerated skin aging. (Costa et al., 2022; Salminen et al., 2022b)Therefore, the use of soy extract cream is expected to increase PDGF expression and improve collagen density in skin that has aged due to UVB.

Although several studies have proven the benefits of soy extract in increasing collagen levels, studies on its effects on PDGF expression and collagen density due to UVB exposure are still limited. Based on this, this study

aims to evaluate the potential of soy extract cream in increasing PDGF expression and collagen density in BALB/c mice exposed to UVB light.

METHODS

The experimental research used is the Post Test Only Control Group method which will be implemented in June 2024 at the SCCR Semarang Research Laboratory. The research subjects were mice aged 6-8 weeks with a body weight ranging from 18-35 grams which were adapted for 7 days. A total of 30 mice, The back hair of the mice was shaved clean before treatment. For five consecutive days, the mice were exposed to UV light with a peak wavelength of 302 nm for 8 minutes per day at a dose of 160 mJ/cm² (1 MED).

After the UV exposure period was over, the mice were divided into 5 groups, namely the healthy group (K1) were mice without treatment that were given standard feed, the negative group (K2) were mice exposed to UV-B rays and given a cream base, the positive group (K3) were mice exposed to UV-B rays and smeared with vitamin E cream, Treatment group 1 (K4) were mice exposed to UV-B rays and smeared with 10% soybean extract cream, and treatment group 2 (K5) were mice exposed to UV-B rays and smeared with 20% soybean extract cream, the treatment was carried out for 14 days, on the 15th day, samples of mouse skin tissue were taken to analyze PDGF levels using the ELISA method and collagen density with Masson Trichrome staining where measurements of collagen fiber density were carried out by observing histological preparations at 400x magnification. Measurements were made in 3 different fields of view using a camera attached to a microscope. Measurements were made using the ImageJ application. The results of the study were then analyzed using the One Way Anova test.

RESULTS AND DISCUSSION

This study was conducted at the Semarang SCCR Laboratory, to evaluate the effect of soybean extract cream (KEKD) on PDGF levels and collagen density in 30 female Balb/c mice. The mice were exposed to UVB light at a dose of 1 MED for 8 minutes, 5 times a week before the application of the cream. Visual observations showed that wrinkles were more pronounced in UVB-exposed mice, and anatomical analysis showed a decrease in elastin expression after exposure, as seen in Figure 1.

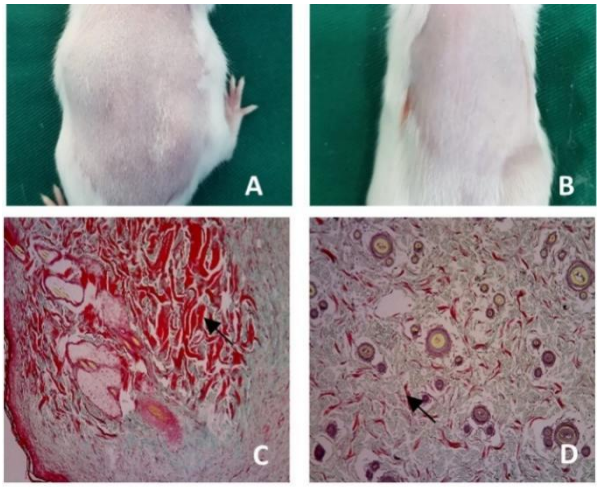

Figure 1. Macroscopically, there were no wrinkles in mice that were not exposed to UVB (A) compared to those exposed to UVB (B). The density of elastin, seen as red (black arrow), was higher in the group without UVB (C) exposure compared to the group with UVB (D) exposure.

The group of mice that had been validated to experience a decrease in elastin after UVB exposure was divided into five treatment groups as follows: healthy mice without UVB exposure were used as a healthy control group (K1); the Negative Control group (K2) is given UVB light and given a cream base; the Positive Control group (K3) was given UVB light and given Vitamin E cream; Treatment groups 1 and 2 (K4 and K5) were given UVB light and given KEK with doses of 10% and 20%, respectively. The treatment was carried out every day for 14 days and tissue sampling was carried out on the 15th day. The tissue was then homogenized using RIPA buffer with the addition of protease inhibitors. After the tissue formed the suspension, centrifugation was carried out and supernatants were collected for analysis of PDGF levels and collagen density using the ELISA method.

The results of the PDGF level analysis shown in Table 1 showed that the Healthy group (K2) had the lowest PDGF level (40.4 ± 4.4 pg/mL), followed by K3 (88.6 ± 41.7 pg/mL), K1 (149.5 ± 7.1 pg/mL), and K4 (323.3 ± 86.05 pg/mL), while the K5 group had the highest PDGF level (330.2 ± 34.3 pg/mL). The Shapiro-Wilk test was used to evaluate the normality of the distribution of PDGF level data and showed that all groups met the assumption of normality (P>0.05). However, the variance homogeneity test with the Levene test showed that the data were non-homogeneous (P<0.05).

Table 1
PDGF level data analysis.

Variable	Group					
	K1	**K2**	**K3**	**K4**	**K5**	***p value***
PDGF	149.5	40.4	88.6	323.2	330.2	
Std. Dev	7.1	4.4	41.7	86.1	34.3	
Saphiro Wilk	0.49	0.68	0.82	0.88	0.25	
Levene's Test						0.001
One Way Anova						0.001

Information:
*Uji *Saphiro Wilk* (p > 0,05 = normal); **Levene's Test* (p > 0,05 = homogen); **One Way Anova* (p <0,05 = signifikan)

The five groups were tested for parametric statistics. The test used is *One Way ANOVA*, which shows a P<0.05 result, as seen in table 1. These results show that there is a significant difference in PDGF levels. Identifying differences between groups, a *post-hoc Tamhane* follow-up test was carried out, see Table 2.

Table 2
Average difference in PDGF levels between the two groups with the post hoc Tamhane test.
Group

Group	K1	K2	K3	K4	K5
K1	-	0.001*	0.261	0.100	0.002*
K2	0.001*	-	0.465	0.018*	0.001*
K3	0.261	0.465	-	0.017*	0.001*
K4	0.100	0.018*	0.017*	-	1.000
K5	0.002*	0.001*	0.001*	1.000	-

Description: * Means p<0.05

The results showed that collagen density in the healthy group (K1) was significantly different compared to the negative (K2) and positive (K3) groups (p < 0.05), but not significantly different compared to the treatment groups given soy extract cream (K4 and K5) (p > 0.05). In addition, there was no significant difference between K2, K3, K4, and K5 (p > 0.05), as well as between K4 and K5, indicating that increasing the dose of soy extract did not have a significant effect on collagen density. However, the pattern of change showed a dose-dependent trend, where the highest dose resulted in a more significant decrease in collagen density. On the other hand, PDGF levels showed a significant increase with the application of soy extract cream. The groups treated with soy extract (K4 and K5) had significantly higher PDGF levels compared to the other groups, with K5 showing the highest levels. This indicates that soy extract cream can significantly increase PDGF expression.

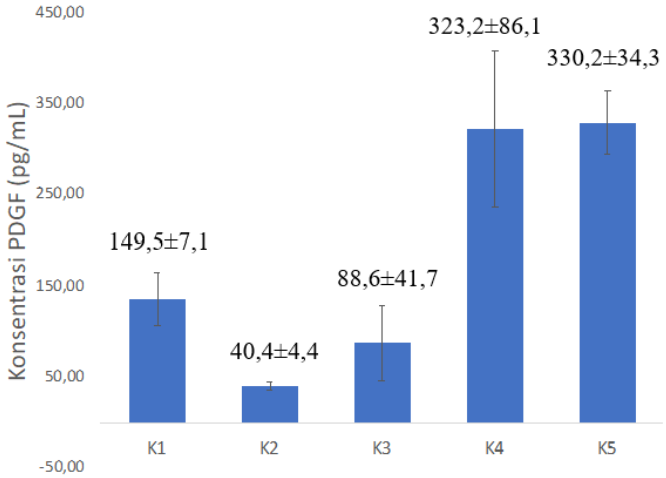

Figure 2. Graph of average PDGF levels after administration of soybean extract cream (KEKD) in mice exposed to UVB.

The collagen density analysis data shown in Table 3 shows that K2 and K3 have the lowest collagen density, namely 32.75 ± 6.6% and 33.07 ± 7.48%, while the K4 and K5 groups have higher densities, namely 41.07 ± 10.8% and 41.9 ±13.4%. while the K1 group is 50.10 ± 12.33%. The results of *the Shapiro-Wilk* and *Levene tests* showed that the P value for the five groups was greater than 0.05, indicating that the distribution of collagen density data in the five groups was normal and homogeneous.

Table 3
Data from collagen density analysis.
Group

Variable	K1	K2	K3	K4	K5	*p value*
Collagen Density	50.10	32.75	33.07	41.07	41.9	

Std. Dev						
Saphiro Wilk	12.33	6.6	7.48	10.8	13.4	
Levene's Test	0.94	0.87	0.92	0.54	0.98	
One Way Anova						0.619
						0.088

Information:
*Uji *Saphiro Wilk* (p > 0,05 = normal)
**Levene's Test* (p > 0,05 = homogen)
**One Way Anova* (p <0,05 = signifikan)

Based on normal and homogeneous data, the *One Way Anova parametric test* was used to determine the average difference in collagen density between the five groups. Based on the results of *the One Way Anova* test which produced a P of 0.088, it showed that there was no significant difference in collagen density in each group. *The Post hoc LSD* test was performed to show the difference in collagen density between the two groups and the results are shown in Table 4.

Table 4
Difference in average collagen density between the two groups with the post hoc LSD test.
Group

Group	K1	K2	K3	K4	K5
K1	-	0.016*	0.018*	0.188	0.230
K2	0.016*	-	0.962	0.223	0.182
K3	0.018*	0.962	-	0.241	0.198
K4	0.188	0.223	0.241	-	0.903
K5	0.230	0.182	0.198	0.903	-

Description: * Means p<0.05

From the results of *the LSD post hoc test* on collagen density, it was found that the value of K1 was significant compared to K2 and K3 ($p < 0.05$), but not significantly compared to K4 and K5 ($p > 0.05$). In addition, K2 and K3 were not significant compared to K4 and K5 ($p > 0.05$). The administration of KEKD cream to K4 and K5 also did not give a noticeable difference in results ($p > 0.05$), see Figure 3.

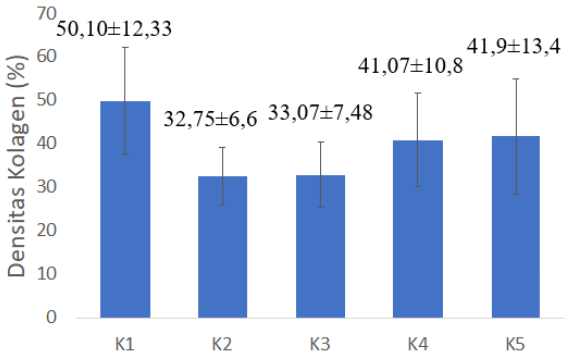

Figure 3. The decrease pattern shown is a dose-dependent manner where the highest dose results in a significant decrease in collagen density.

Interestingly, although PDGF levels increased, collagen density did not show significant differences between treatment groups. This suggests that increased PDGF was not necessarily followed by increased collagen synthesis during the study period. Several factors that may influence these results include the duration of the study, which may not have been long enough to detect differences in collagen density or the presence of other factors such as MMP (Matrix Metalloproteinases) enzyme activity that can degrade collagen even though PDGF increased. In addition, the results of the normality test showed that the PDGF level data were normally distributed ($p>0.05$, Shapiro-Wilk test), but the homogeneity of variance test with Levene's test showed that the data were not homogeneous ($p<0.05$). This could be a potential bias in statistical analysis that needs to be considered in interpreting the results. Further research with a longer treatment period and additional analysis of other factors that play a role in collagen regulation, such as TGF-β and MMP, is needed to better understand the relationship between PDGF and collagen density in UVB-exposed skin.

Discussion

The results showed that soybean extract cream (KEKD) doses of 10% and 20%, were effective in influencing PDGF levels, higher than Vitamin E cream.

Exposure to UV rays on the skin can cause a complex set of changes in response to such exposure that can cause skin damage, including wrinkles. This exposure can result in damage to DNA, leading to activation of cytokylem C by mitochondria leading to apoptosis. Apoptosis will then lead to the formation of DAMP which triggers inflammation and also has an impact on increasing the production of pro-inflammatory cytokines such as TNF-alpha and IL-1b in the skin. The production of these inflammatory cytokines will continue to occur as long as free radicals are still occurring in the skin of mice, causing

the non-production of growth factors such as PDGF (Saw et al., 2011) (Guo et al., 2020).

UVB exposure to the skin can cause significant skin damage, including inflammation, free radical formation, and collagen degradation that causes premature aging. KEKD administration can reduce damage by increasing PDGF in skin exposed to UVB rays. PDGF is a growth factor that plays an important role in the wound healing process and tissue regeneration, while collagen is the main structural component that provides strength and elasticity to the skin. (Juhl et al., 2020; Madsen et al., 2023).

The increase in PDGF due to the administration of soybean extract cream (SEC) on the skin of mice exposed to UVB rays is likely due to the content of isoflavones, such as genistein and daidzein. Isoflavones have strong antioxidant activity, which can reduce oxidative stress and inflammation caused by UVB rays. Reducing oxidative stress allows skin cells to produce PDGF more effectively, which stimulates fibroblasts to increase collagen synthesis (Luthfi et al., 2023; Nirwana et al., 2017).

Isoflavones can activate cellular signaling pathways, especially PI3K/Akt and MAPK/ERK, which play a role in fibroblast proliferation and collagen synthesis. Activation of these pathways increases PDGF expression and supports the regeneration of skin damaged by UVB exposure (Triswara et al., 2020).

Administration of KEKD to the skin of mice exposed to UVB light increases PDGF expression and collagen density through antioxidant mechanisms and molecular regulation. However, this study has limitations, such as not evaluating other proteins that play a role in collagen production and potential bias in the PDGF measurement method using ELISA. The possibility of cross-reactivity with other proteins in the sample or variability in the sensitivity of the method may affect the accuracy of the results obtained. Therefore, additional validation, such as using other confirmation methods (eg Western Blot or immunohistochemistry), is needed in future studies to ensure the accuracy of the results obtained.

CONCLUSION

There was a difference in PDGF levels in the K4 and K5 groups who were given soybean extract cream (KEKD) doses of 10% and 20% compared to the control group.

There was a difference in the amount of collagen density in the K4 and K5 groups who were given soybean extract cream at doses of 10 and 20% compared to the control group.

SUGGESTION

The study found that KEKD doses of 10 and 20% were more effective in increasing PDGF and collagen density because they exceeded standard therapy, so this study suggested the use of KEKD at a dose of 10% to reduce collagen loss. This study did not analyze the protein substances involved in the production pathway so that it could not explain in detail the pathway that PDGF influences in increasing collagen density.

REFERENCES

Costa, E. F., Magalhães, W. V., & Di Stasi, L. C. (2022). Recent Advances in Herbal-Derived Products with Skin Anti-Aging Properties and Cosmetic Applications. In *Molecules* (Vol. 27, Issue 21). MDPI. [Crossref], [Publisher]

Guo, S., Wang, T., Zhang, S., Chen, P., Cao, Z., Lian, W., Guo, J., & Kang, Y. (2020). Adipose-derived stem cell-conditioned medium protects fibroblasts at different senescent degrees from UVB irradiation damages. *Molecular and Cellular Biochemistry*, *463*, 67–78. [Crossref], [Publisher]

Juhl, P., Bondesen, S., Hawkins, C. L., Karsdal, M. A., Bay-Jensen, A.-C., Davies, M. J., & Siebuhr, A. S. (2020). Dermal fibroblasts have different extracellular matrix profiles induced by TGF-β, PDGF and IL-6 in a model for skin fibrosis. *Scientific Reports*, *10*(1), 17300. [Crossref], [Publisher]

Kong, R., Cui, Y., Fisher, G. J., Wang, X., Chen, Y., Schneider, L. M., & Majmudar, G. (2016). A comparative study of the effects of retinol and retinoic acid on histological, molecular, and clinical properties of human skin. *Journal of Cosmetic Dermatology*, *15*(1), 49–57. [Crossref], [Publisher]

Kuhns, L. (2023). Soy-Based Products Have Useful Dermatologic Applications. *Medical Bag*, NA-NA. [Crossref], [Publisher]

Leite, B. A., Bezerra, P. H. A., Stocco, B., Abichabki, N., Andrade, L. N., Fonseca, M. J. V, & Torqueti, M. R. (2023). Biotransformed soybean cream as a new nutraceutical for skin care: collagen stimulation in vitro and ex vivo. *Brazilian Journal of Medical and Biological Research*, *56*, e12781. [Crossref], [Publisher]

Luthfi, M., Rachmawati, A. E., & Razak, F. B. A. (2023). Platelet derived growth factor expression after administration of okra fruit extract on diabetic wistar rats. *Research Journal of Pharmacy and Technology*, *16*(11), 5329–5333. [Crossref], [Publisher]

Madsen, S. F., Sand, J. M. B., Juhl, P., Karsdal, M., Thudium, C. S., Siebuhr, A. S., & Bay-Jensen, A.-C. (2023). Fibroblasts are not just fibroblasts: clear differences between dermal and pulmonary fibroblasts' response to fibrotic growth factors. *Scientific Reports*, *13*(1), 9411. [Crossref], [Publisher]

Moon, H. R., Jung, J. M., Kim, S. Y., Song, Y., & Chang, S. E. (2020). TGF-β3 suppresses melanogenesis in human melanocytes cocultured with UV-irradiated neighboring cells and human skin. In *Journal of Dermatological Science* (Vol. 99, Issue 2, pp. 100–108). [Crossref], [Publisher]

Nirwana, I., Rachmadi, P., & Rianti, D. (2017). Potential of pomegranate fruit extract (Punica granatum Linn.) to

increase vascular endothelial growth factor and platelet-derived growth factor expressions on the post-tooth extraction wound of Cavia cobaya. *Veterinary World*, *10*(8), 999. [Crossref], [Publisher]

Petruk, G., Del Giudice, R., Rigano, M. M., & Monti, D. M. (2018). Antioxidants from plants protect against skin photoaging. *Oxidative Medicine and Cellular Longevity*, *2018*(1), 1454936. [Crossref], [Publisher]

Salminen, A., Kaarniranta, K., & Kauppinen, A. (2022a). Photoaging: UV radiation-induced inflammation and immunosuppression accelerate the aging process in the skin. *Inflammation Research*, *71*(7), 817–831. [Crossref], [Publisher]

Salminen, A., Kaarniranta, K., & Kauppinen, A. (2022b). Photoaging: UV radiation-induced inflammation and immunosuppression accelerate the aging process in the skin. In *Inflammation Research* (Vol. 71, Issues 7–8, pp. 817–831). Springer Science and Business Media Deutschland GmbH. [Crossref], [Publisher]

Saw, C. L., Huang, M., Liu, Y., Khor, T. O., Conney, A. H., & Kong, A. (2011). Impact of Nrf2 on UVB-induced skin inflammation/photoprotection and photoprotective effect of sulforaphane. *Molecular Carcinogenesis*, *50*(6), 479–486. [Crossref], [Publisher]

Tanveer, M. A., Rashid, H., & Tasduq, S. A. (2023). Molecular basis of skin photoaging and therapeutic interventions by plant-derived natural product ingredients: A comprehensive review. *Heliyon*, *9*(3). [Crossref], [Publisher]

Triswara, R., Farishal, A., & Siregar, B. A. (2020). Potensi Isoflavon Genistein Sebagai Terapi Suportif Imunonutrisi Pada Pasien Kanker Payudara. *Medical Profession Journal of Lampung*, *9*(4), 736–741. [Crossref], [Publisher]

Zasada, M., & Budzisz, E. (2019). Retinoids: active molecules influencing skin structure formation in cosmetic and dermatological treatments. *Advances in Dermatology and Allergology/Postępy Dermatologii i Alergologii*, *36*(4), 392–397. [Crossref], [Publisher]