Eduvest – Journal of Universal Studies
Volume 6 Number 5, May, 2026
p- ISSN 2775-3735- e-ISSN 2775-3727

The Effect of Bajakah Wood Extract on Collagenase Activity of Glycated Proteins in Rats and its Review from an Islamic Perspective

Ainuzzahra[1]*, Harliansyah[2], Nenden Lilis Setiasih[3], Luh Ade Lela Arika[4], Puput Putuh Anisa[5]
Universitas YARSI, Indonesia[1,2,3,5]
Universitas Medika Suherman, Indonesia[4]
Email: ainuzzahra01@gmail.com*, drharlians@gmail.com, nenden.sobarna@gmail.com, kimeka.la97@gmail.com, puputpanisa96@gmail.com

Keywords
red fertilizer wood; collagenase; D-galactose; skin aging; antioxidants.

ABSTRACT
Skin aging is a biological process that is influenced by oxidative stress and the accumulation of advanced glycation end products (AGEs) that can increase the activity of the collagenase enzyme so that it causes collagen degradation. Red logan wood (Spatholobus littoralis Hassk.) is known to have antioxidant content that has the potential to inhibit this process. This study aimed to determine the effect of administration of ethanol extract of red logs on collagenase activity in male white rats of the Sprague-Dawley strain induced by D-galactose. This study is a laboratory experimental research with a post-test only control group design. A total of 36 rats were divided into six groups, namely the blank group, negative control, positive control, and three treatment groups given red bajakah wood ethanol extract with doses of 25 mg/kgBB, 50 mg/kgBB, and 100 mg/kgBB. Induction of aging was carried out using D-galactose, then serum collagenase activity was measured using the ELISA method. Data were analyzed using a one-way ANOVA test followed by an LSD test with a significance level of $p < 0.05$. The results showed that the administration of ethanol extract of red logs was able to significantly reduce collagenase activity compared to the negative control group ($p < 0.05$). Doses of 100 mg/kgBB showed the greatest decreasing effect and were close to positive control groups. This suggests that red logwood extract has the potential to be a natural anti-aging agent through a mechanism of inhibition of collagen activity.

INTRODUCTION

Collagen is the main structural protein that plays a role in maintaining the strength and elasticity of tissues, especially in the skin (Chen et al., 2023; Emam, 2025; Shenoy et al., 2022; Singh et al., 2023; Zhang et al., 2023). Thin, wrinkled skin is a typical sign of normal aging due to reduced collagen levels (Liu et al., 2024).

Collagen is the main component of the extracellular matrix (ECM) and can be divided into fibrillar families, including collagen types I, II, III, and V, and non-fibrillar collagens such as types IV, VI, VII, VIII, and XIV, which do not form classical fibrils. In human skin, type I collagen comprises 80 to 90% of the total collagen, while type III comprises 8 to 12%, and type V comprises less than 5%. In the dermis, collagen is produced by fibroblasts in the form of procollagen, which is then processed into collagen fibers that maintain the strength and firmness of the skin. During the aging process, there is a significant loss of collagen fibers in the dermis, leading to the formation of wrinkles and sagging, as well as a loss of skin viscoelasticity. The degradation of collagen fibers is initiated by matrix metalloproteinases (MMPs), particularly MMP-1. Once cleaved, collagen fibers can be further degraded by MMP-

3 and MMP-9. In addition, the loss of collagen fibers in aging skin is associated with an imbalance between collagen synthesis and degradation, particularly due to increased MMP-1 activity (Bar & Valiukevičienė, 2025; Lai et al., 2026; Loo et al., 2023). This suggests that enhancing collagen synthesis in dermal fibroblasts and inhibiting MMP activity are effective approaches to prevent and/or improve symptoms of skin aging (Costa et al., 2022).

Under hyperglycemic conditions, such as in diabetes mellitus, there is an increase in non-enzymatic glycation processes in proteins, leading to the formation of advanced glycation end products (AGEs). AGEs can cause structural damage to collagen, making tissues stiff and more susceptible to damage (Reddy et al., 2022). One of the enzymes involved in collagen degradation is collagenase, which normally aids in the tissue repair process; however, under certain conditions, excessive collagenase activity can exacerbate damage in already glycated tissues (Zgutka et al., 2023).

Research on natural compounds that can reduce the negative effects of protein glycation and normalize collagenase activity is important, especially as a complementary approach in the management of diabetes and age-related diseases. One plant with potential anti-aging properties is Bajakah Tampala (Spatholobus littoralis Hassk.), which is traditionally used by the Dayak people in Kalimantan as a natural remedy. Several studies report that bajakah wood extract exhibits cytotoxic, anti-inflammatory, antiviral, immunostimulatory, antioxidant, central nervous system-related, vascular, hypotensive, mutagenic, and antibacterial activities, which may contribute to the inhibition of protein glycation as well as the regulation of collagenase activity in tissues (Maulina et al., 2021).

Bajakah wood extract is known to contain active compounds such as flavonoids, tannins, and saponins, which act as antioxidants and antimicrobials. However, there are still limited studies that specifically examine the effect of bajakah wood extract on collagenase activity in animal models with glycated proteins. Therefore, this study aims to determine the effect of bajakah wood extract on collagenase activity in mice with glycated protein conditions, in order to assess its therapeutic potential in reducing tissue damage caused by glycation (Maulidie et al., 2018).

The novelty of this research is fivefold. First, it is the first study to evaluate the effect of bajakah wood extract on collagenase activity (not limited to antioxidant capacity or MMP-1 expression) in a D-galactose-induced aging model. Second, it provides dose–response data at three concentrations (25, 50, and 100 mg/kg body weight), enabling identification of the most effective dose. Third, it employs a post-test-only control group design to minimize bias. Fourth, it quantitatively measures collagenase levels using ELISA rather than qualitative or semi-quantitative methods. Fifth, it integrates an Islamic perspective on the use of natural remedies, viewing the pursuit of healing as an act of worship and gratitude for Allah's creation.

This study was conducted to determine the effect of administering bajakah wood extract on collagenase enzyme activity in mice experiencing protein glycation and to assess whether there is a significant difference between treated and untreated groups. The general objective of this study is to analyze the therapeutic potential of bajakah wood extract in reducing collagenase activity under glycated protein conditions. The specific objectives include analyzing the effects of different extract concentrations and determining the most effective dose. This research is expected to benefit students by enhancing their experience and understanding of scientific research, support YARSI University in improving academic quality

and biomedical research contributions, assist researchers in developing methodological and laboratory analysis skills, and contribute to the recognition of bajakah wood as part of the local wisdom of the Dayak community in traditional medicine.

METHOD

This study is a laboratory experimental research with a post-test only control group design approach. The research was conducted at the Integrated Research Laboratory of YARSI University, the Pharmacology Laboratory, and the Biochemistry Laboratory of the Faculty of Medicine, YARSI University. This design was chosen because it was able to objectively evaluate the effect of treatment on the research subject without being influenced by the initial conditions before the treatment was given.

This study aims to determine the effect of ethanol administration of red logwood ethanol extract (Spatholobus littoralis Hassk.) on collagenase activity in male white rats of the Sprague-Dawley strain that experience protein glycation due to D-galactose induction. The study subjects were divided into blank groups, negative controls, positive controls, and treatment groups with different doses of extracts. All groupings were randomized to minimize bias and increase the validity of the research results.

The population in this study was male white rats of the Sprague-Dawley strain that met the established inclusion and exclusion criteria. The inclusion criteria included male rats weighing 170–200 grams and 2–3 months old, while the exclusion criteria were mice that had health problems that could affect the results of the study.

The study sample consisted of 36 mice, which were determined using Federer's formula, then randomly divided into six groups, namely the blank group, the negative control group, the positive control group, and three treatment groups that received red logwood extract at a dose of 25 mg/kgBB, 50 mg/kgBB, and 100 mg/kgBB, respectively. Each group consisted of 6 mice. Random sample selection is done to avoid selection bias as well as ensure that the samples represent the characteristics of the study population biologically and physiologically.

Data collection was carried out through a controlled experimental procedure. The test animals were first acclimatized for 7 days under standard maintenance conditions. Furthermore, rats in the control and treatment group were induced with D-galactose at a dose of 500 mg/kgBB subcutaneously from day 8 to day 56. On the 29th to the 56th day, each group received treatment according to the research design, namely the administration of saline, vitamin C, or red log wood ethanol extract according to the predetermined dose.

On the 57th day, blood was taken through the heart after the rats were anesthetized using ketamine and xylazin. Blood serum is then examined to determine collagenase activity using the ELISA (Enzyme-Linked Immunosorbent Assay) method according to standard factory procedures. The measurement results were in the form of optical density values which were then converted into collagenase concentration or activity as the main data of the study.

The data obtained was analyzed using IBM SPSS Statistics software version 30. Before the analysis is carried out, the data is first tested for normality. If the data is distributed normally, analysis is carried out using a one-way ANOVA test to determine the difference in the average collagenase activity between groups. If the results of the ANOVA test show a significant difference, then the analysis is continued with the Least Significant Difference (LSD) test to find out which group is significantly different.

If the data is not distributed normally, then the data transformation is carried out first. If after the data transformation becomes normal, then the one-way ANOVA test and the LSD follow-up test are still used. The results of the analysis are considered statistically significant if the probability value of $p < 0.05$.

RESULT AND DISCUSSION

This study used test animals in the form of male Sparague Dawley strain white rats with an age range of 2-3 months and a body weight between 175-200 grams. The rats used were healthy rats characterized by normal movement activity and good eating and drinking ability. The study was conducted using six treatment groups, each consisting of six mice. The entire series of studies lasted for eight weeks, beginning with an adaptation period of seven days before the treatment. During the study, the weight measurements of the mice were carried out routinely every week. Throughout the study, all the mice that received the treatment remained alive and no dead test animals were found.

This study is an experimental study with different treatments given to each group of test animals. A total of 6 groups of mice were used in the study. The first group was given 0.9% saline from week 2 to week 8. The second to sixth groups were given 500 mg/kgBB of D-galactose by subcutaneous injection.

In weeks 5 to 8, each group received additional treatment. The second group as a negative control was given 0.9% saline. The third group as a positive control was given Vitamin C 50 mg/kgBB through subcutaneous injection. The fourth, fifth, and sixth groups were given red logbait ethanol extract with doses of 25 mg/kgBB, 50 mg/kgBB, and 100 mg/kgBB respectively as treatment groups I, II, and III.

After the entire series of treatments is completed, blood samples are then taken to be analyzed in the laboratory. Blood samples were examined using the Enzyme-Linked Immunosorbent Assay (ELISA) method. This examination aims to measure collagenase levels as a marker of skin aging. The use of the ELISA method was chosen because it has high sensitivity and specificity in detecting collagenase concentrations.

A. Collagenase Concentration Test

The results of the test results of the effect of bajakah wood extract on collagenase concentration using Rat Collagen Type I ELISA kit Bioenzy 96 wells with catalog number BZ-08188000-EB. The results of statistical testing showed that the research data met the criteria of normal distribution and homogeneity of variance. Therefore, the data analysis was then carried out using a parametric statistical test in the form of One-Way Analysis of Variance (One-Way ANOVA) to determine the average difference between treatment groups. These results show that a decrease in collagenase levels shows good anti-aging activity, because collagenase is an enzyme that plays a role in the degradation of collagen in skin tissue. In the aging process, collagenase activity is known to increase causing damage to the extracellular matrix, decreased elasticity, and thinning of skin structure. Therefore, the inhibition or decrease in collagenase activity reflects the maintenance of the integrity of dermal collagen, which contributes to maintaining the structure and function of the skin and slowing down the aging process (Maulina and Kesehatan Hermina, 2021)

The results of the test of the effect of log wood extract on the concentration of glycated collagen protein were obtained with the One-Way Anova test. The results are shown in Table 1.

Table 1. Collagenase Concentration Analysis

Groups	n	Average	SD	Kel.1	Kel.2	Kel.3	Kel.4	Kel.5	Kel.6
Kel.1	4	144,451	0,0279	–	0,141	0,216	**0,033***	**0,040***	0,204
Kel.2	4	132,153	0,0297		–		0,314	0,365	0,280
Kel.3	4	122,214	0,0194			–		0,916	**0,046***
Kel.4	4	123,240	0,0272				–		0,056
Kel.5	4	142,840	0,0260					–	0,265
Kel.6	4	131,785	0,0227						–

Remarks: * = there is a significant difference with the p< value of 0.05

The lowest concentration value of Collagenase was found in group 3, namely the group that received an induction of D-galactose of 500 mg/kgBB and received a Vitamin C treatment of 50 mg/kgBB through subcutaneous injection, with an average dilution concentration of 5x of 122.214 ng/mL. This value was lower than the negative control group that received an induction of D-galactose of 500 mg/kgBB and 0.9% saline with an average of 132.153 ng/mL, while the blank group that was only given 0.9% saline by subcutaneous injection showed the highest average concentration of Collagenase at 144.451 ng/mL. The results of Anova's One-Way showed no significant difference with the result p = 0.141 (p < 0.05). The results of the Post Hoc test using the LSD method showed that the positive control group had a significant difference compared to the blank group (group 1). In addition, the group given bajakah wood extract at a dose of 25 mg/kgBB (group 4) showed significant differences in the blank group (group 1). Furthermore, the group given bajakah wood extract at a dose of 50 mg/kgBB (group 5) showed a significant difference compared to the positive control group (group 3), with a significance value (p < 0.05).

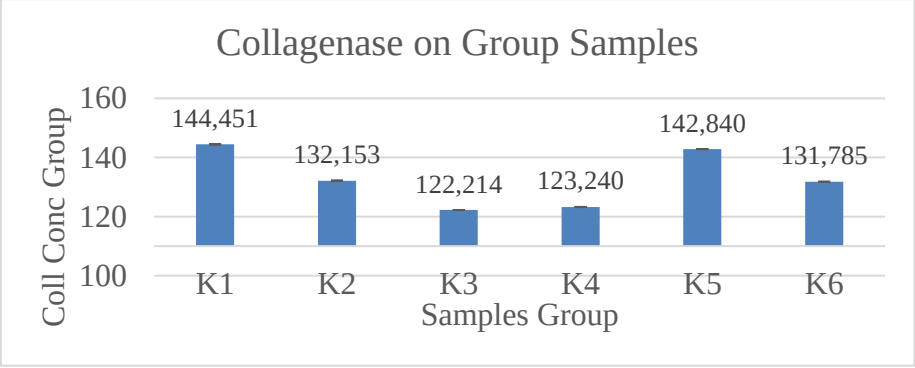

Figure 1. Average Collagenase Results In Each Group

B. Data Analysis with Normality Test

Normality tests are performed to see if the levels of the collagenase enzyme are normally distributed or not. In this study, the normality test carried out was the Shapiro – Wilk method because the data obtained was less than 30. The basis for making this test decision is that if the significance value of p > 0.05, then the data is distributed normally. However, if the significance value of p < 0.05, then the data is not normally distributed.

Table 2. Normality Test Results

Treatment Groups	Kolmogorov–Smirnov Statistic	df	Sig.	Shapiro–Wilk Statistic	df	Say.
K1 (Blanko)	0,258	4	.	0,954	4	0,738
K2 (Negative Control)	0,238	4	.	0,970	4	0,845
K3 (Positive Control)	0,339	4	.	0,871	4	0,302
K4 (Bajakah 25 mg/KgBB)	0,237	4	.	0,927	4	0,579
K5 (Bajakah 50 mg/KgBB)	0,273	4	.	0,885	4	0,358
K6 (Bajakah 100 mg/KgBB)	0,396	4	.	0,759	4	0,047

Based on the results of the normality test in Table 6. Group 1 (Blanko) had a significance value of 0.738 ($p > 0.05$) which showed that the data was distributed normally. Furthermore, Group 2 (Negative Control) had a significance value of 0.845 ($p > 0.05$) which showed that the data was distributed normally. In group 3 (Positive Control), a significance value of 0.302 ($p > 0.05$) showed so that the data could be declared to be normally distributed. Then, in Group 4 (Bajakah 25 mg/kgBB) obtained a significance value of 0.579 ($p > 0.05$) which indicates that the data is normally distributed. Group 5 (Bajakah 50 mg/kgBB) had a significance value of 0.358 ($p > 0.05$) which showed that the data was normally distributed. As for group 6 (Bajakah 100 mg/kgBB) showed a significance value of 0.047 which corresponded to ($p > 0.05$) so that the data could be stated that the data was distributed normally.

Based on the results of the normality test in table 4.xx, the significance value of the Kolmogorov–Smirnov test in each treatment group is not shown in the form of numbers, but is indicated by the symbol ".". This is due to the small number of samples in each group, which is only 4 mice per group. Statistically, the Kolmogorov-Smirnov test is more suitable for use on large sample sizes, generally more than 50 subjects, so that at a very small sample size SPSS cannot calculate the significance value of the test. Therefore, significance values are not displayed and only points appear on the SPSS output.

Considering the limitations of the sample, the normality test in this study is more appropriate using the Shapiro-Wilk test, with a sample number of less than 50. The results of the Shapiro-Wilk test showed a significance value ($p > 0.05$) in all treatment groups, so it can be concluded that virgins met the normality test.

C. Data Analysis with Homogeneity Test

The homogeneity test is one of the stages of statistical analysis that aims to determine the uniformity between treatment groups. This test is important because it is a prerequisite before proceeding to the ANOVA analysis, so that the results of the comparison between groups can be validly interpreted. In this study, the homogeneity test was carried out using the Levene method, which is commonly used to test for similarity of variance between groups.

The basis for decision-making in the homogeneity test is determined based on the significance value (p – value) produced. If the significance value ($p > 0.05$), then it can be concluded that the data is homogeneous or uniform. On the other hand, if the significance value ($p < 0.05$) then the data is declared inhomogeneous, so the homogeneity assumption is not met.

Table 3. Homogeneity Test Results

Method	Levene Statistic	df1	df2	Sig.
Based on Mean	0,834	5	18	0,543
Based on Median	0,751	5	18	0,596
Based on Median and with Adjusted df	0,751	5	15,518	0,598

Method	Levene Statistic	df1	df2	Sig.
Based on Trimmed Mean	0,828	5	18	0,546

Based on Table 7, the results of the homogeneity test show that the significance value based on the average is obtained as 0.543 which corresponds to ($p > 0.05$), then it can be stated that the data is homogeneous. In addition, the test based on the median yielded a significance value of 0.596 according to ($p > 0.05$), so it can be said that the data between groups remained homogeneous.

Tests based on the median with adjusted degrees of freedom showed a significance value of 0.598 according to ($p > 0.05$), so the data was declared homogeneous. Similarly, the test results based on the adjusted average obtained a significance value of 0.546 according to ($p > 0.05$), which shows that the data can be said to be homogeneous.

Based on the results of the homogeneity test using the Levene Test, significance values were obtained in all tests, both based on the mean, median, median with adjusted degrees of freedom, and the adjusted average, all of which showed a p value of $p > 0.05$. These results indicate that the data between treatment groups is homogeneous. Thus, it can be concluded that the homogeneity of variance has been met, so that the research data meets the requirements to conduct statistical analysis using the One - Way ANOVA test validly.

This study is an in vivo study that aims to evaluate the effect of administering bajakah wood extract (Spatholobus littoralis Hassk), in D-galactose-induced aging model mice at a dose of 500 mg/kgBB. The parameter analyzed was the glycated collagen content of proteins. Giving D-galactose in high doses is known to trigger oxidative stress thereby accelerating the aging process.

D. Effect of Logan Wood Extract on Collagenase Enzyme Concentration

The results of the study on the effect of bajakah wood extract on the collagenase concentration of rats, significant results were obtained ($p < 0.05$), it can be concluded that bajakah wood extract can potentially inhibit the occurrence of aging which is characterized by decreasing the concentration of collagenase.

Collagenase is a proteolytic enzyme that plays an important role in the degradation of collagen, which is the main structural protein that makes up the extracellular matrix (ECM), especially in skin tissue. Collagen has a vital function in maintaining the strength, elasticity, and structural integrity of the skin. As we age, collagenase activity, especially the metalloproteinase-1 matrix (MMP-1), tends to increase, leading to collagen and elastin damage that contribute to the skin aging process, such as the appearance of wrinkles, sagging skin, and decreased elasticity (Ranneh et al., 2021).

Physiologically, collagenase activity is necessary in the process of wound healing and tissue remodeling, but uncontrolled increased activity can accelerate skin aging. Collagenase regulation is naturally controlled by Tissue Inhibitors of Metalloproteinases (TIMPs) to maintain the balance of the extracellular matrix (Verzijl et al., 2019). In aging skin, exposure to UV radiation and oxidative stress increases MMP production, while the process of glycation and the formation of advanced glycation end products (AGEs) causes collagen to become stiffer and less elastic. The combination of increased collagen degradation and biochemical changes contributes to decreased elasticity and uneven pigmentation (Puspita Sari et al., 2023)

In this study, in general, no significant reduction in collagenase levels was found in all treatment groups ($p > 0.05$). However, the results of the comparative analysis between groups showed a significant difference between group 5 given logwood extract at a dose of 50 mg/kgBB and group 3 as a positive control, with a significance value of $p = 0.046$ ($p < 0.05$). In addition, based on the analysis of the average value, it can be seen that there is a fairly clear tendency to decrease collagenase levels in groups 3 and 4, which can be seen from the decrease in the graph although not all of them reach statistical significance.

Previous research has shown that bajakah wood extract (Spatholobus littoralis Hassk.) has significant potential as an anti-aging agent through antioxidant mechanisms and inhibition of collagen degradation. Bajakah wood extract contains secondary metabolite compounds such as flavonoids, tannins, saponins, alkaloids, and phenolic compounds that act as antioxidants. These antioxidant activities have been shown to be able to reduce oxidative stress by capturing free radicals, which are known to play an important role in the activation of the enzyme Matrix Metalloproteinase (MMP), especially MMP-1 as the main collagenase enzyme in the skin. This decrease in oxidative stress contributes to the inhibition of collagen degradation, thus helping to maintain skin structure and elasticity (Hidayati Salsabilla et al., 2023).

In line with this, another study reported that the administration of bajakah wood ethanol extract to experimental animals induced aging or exposed to ultraviolet radiation showed a decrease in MMP-1 expression as well as an increase in collagen and elastin density in skin tissue. This decrease in collagenase activity indicates that bajakah wood extract plays a role in maintaining the integrity of the extracellular matrix and slowing down the aging process of the skin characterized by thinning of the dermis and the formation of wrinkles. This effect is thought to be related to the ability of flavonoids and phenolic compounds to inhibit the activity of collagenase enzymes through metal ion binding on the active side of the enzyme, thereby reducing the enzyme's ability to break down collagen fibers (Luh Ade Lela Arika et al., 2025)

The results of the study support the findings in this study, where the group given bajakah wood extract showed significant differences compared to the control group. This suggests that bajakah wood extract provides a real biological effect in suppressing the aging mechanism, which is most likely to occur through a combination of antioxidant activity and inhibition of the enzyme collagenase. Thus, overall previous research and the results of this study corroborate each other that bajakah wood extract has the potential to be developed as a natural anti-aging ingredient that works through modulation of oxidative stress and protection of skin collagen

E. Weaknesses of the research

1. The use of test animals, namely mice, with a relatively long research time, has the potential to increase the risk of animal death during the research process.
2. The implementation of the research requires large resources, both in terms of funding and time, and the variables used do not fully reflect all the complex factors that play a role in the aging mechanism.
3. This research was only conducted at the in vivo level. In vivo research has the advantage of being able to describe the biological response in a complete way in living organisms, including interactions between systems, metabolism, and the physiological effects of the test compounds. However, this study also has limitations in the form of relatively greater time and cost, ethical considerations of the use of experimental animals, biological

variation between individuals, and limitations in generalizing results directly to humans, so that the results obtained cannot be used as a basis for safety assessments if developed into products that will be widely marketed.

CONCLUSION

Based on the results of the research that has been conducted, it can be concluded that the administration of ethanol extract of red bajakah wood (Spatholobus littoralis Hassk.) has an effect on reducing collagenase activity in male white rats of the Sprague-Dawley strain that are induced by D-galactose. Decreased collagenase activity shows the potential of red bajakah wood extract in inhibiting collagen degradation which plays an important role in the skin aging process. In addition, there is a dose-response relationship, where a dose of 100 mg/kgBB provides the most optimal effect of reducing collagenase activity compared to doses of 25 mg/kgBB and 50 mg/kgBB. Thus, red logwood extract has the potential to be developed as a natural anti-aging ingredient, although further research is still needed to examine the molecular mechanism of action as well as clinical trials in humans.

REFERENCES

Bar, O., & Valiukevičienė, S. (2025). Skin aging and type I collagen: A systematic review of interventions with potential collagen-related effects. *Cosmetics, 12*(4), 129.

Chen, Q., Pei, Y., Tang, K., & Albu-Kaya, M. G. (2023). Structure, extraction, processing, and applications of collagen as an ideal component for biomaterials: A review. *Collagen and Leather, 5*(1), 20.

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. *Molecules*. https://doi.org/10.3390/molecules27217518

Emam, A. N. (2025). Collagen and collagen-derived materials: Synthesis, structure, classification, fundamental properties and biomedical applications. *Discover Applied Sciences, 7*(10), 1114.

Hidayati Salsabilla, Rizki Febriyanti, & Wilda Amananti. (2023). Penentuan aktivitas antioksidan infudasi akar bajakah tampala (*Spatholobus littoralis* Hassk) dan kalalawit (*Uncaria gambir* Roxb) dengan metode DPPH. *Jurnal Crystal: Publikasi Penelitian Kimia dan Terapannya, 5*.

Lai, C.-F., Esam, G., Lin, Y.-C., & Chung, R.-J. (2026). From destruction to protection: Rethinking MMP-1 in skin aging and anti-aging strategies. *Archives of Dermatological Research, 318*(1), 56.

Lee, M. W., & Katz, P. O. (2021). Nonsteroidal anti-inflammatory drugs, anticoagulation, and upper gastrointestinal bleeding. *Clinics in Geriatric Medicine, 37*(1), 31–42. https://doi.org/10.1016/j.cger.2020.08.004

Liu, X., Yuen, M., Yuen, T., Yuen, H., Wang, M., & Peng, Q. (2024). Anti-skin aging effect of sea buckthorn proanthocyanidins in D-galactose-induced aging mice. *Food Science & Nutrition, 12*, 1082–1094. https://doi.org/10.1002/fsn3.3823

Loo, Y. C., Hu, H.-C., Yu, S.-Y., Tsai, Y.-H., Korinek, M., Wu, Y.-C., Chang, F.-R., & Chen, Y.-J. (2023). Development of potential skin anti-aging agents of *Cosmos caudatus* Kunth via inhibition of collagenase, MMP-1, and MMP-3 activities. *Phytomedicine, 110*, 154643.

Luh Ade Lela Arika, Puput Putuh Anisa, Harliansyah, & Nenden Lilis Setiasih. (2025). Effect of *Spatholobus littoralis* Hassk extract on matrix metalloproteinase-1 and elastin fiber morphology in D-galactose-induced aging model rats, *31*.

Maulidie, M., Saputera, A., & Ayuchecaria, N. (n.d.). Uji efektivitas ekstrak etanolik batang bajakah tampala (*Spatholobus littoralis* Hassk.) terhadap waktu penyembuhan luka. *Jurnal Ilmiah Ibnu Sina*.

Maulina, D. (2021). Peran mangiferin sebagai inhibitor enzim kolagenase dan elastase. *Indonesian Journal of Health Science*.

Maulina, S., Ryn Pratiwi, D., & Harliansyah. (2021). Skrining fitokimia dan bioaktivitas ekstrak akar *Uncaria nervosa* Elmer (bajakah).

Puspita Sari, W., Meligasari Gaya, L., Galih Irianto, M., & Karima, N. (2023). Manajemen topikal anti-aging pada kulit.

Ranneh, Y., Abu Bakar, M. F., Ismail, N. A., Kormin, F., Mohamed, M., Md Akim, A., & Isha, A. (2021). Anti-aging and antioxidant of four traditional Malaysian plants using simplex centroid mixture design approach. *Saudi Journal of Biological Sciences, 28*, 6711–6720. https://doi.org/10.1016/j.sjbs.2021.07.048

Reddy, V. P., Aryal, P., & Darkwah, E. K. (2022). Advanced glycation end products in health and disease. *Microorganisms*. https://doi.org/10.3390/microorganisms10091848

Sari, I. P., Ichwan, M., & Siregar, Y. (2020). Pengaruh pemberian D-galaktosa terhadap perubahan berat badan mencit jantan. *Jurnal Keperawatan dan Fisioterapi (JKF), 2*, 113–116. https://doi.org/10.35451/jkf.v2i2.336

Shenoy, M., Abdul, N. S., Qamar, Z., Al Bahri, B. M., Al Ghalayini, K. Z. K., Kakti, A., Murad, M., Fadul, M., Alamri, M. A. M., & Alqarni, M. A. (2022). Collagen structure, synthesis, and its applications: A systematic review. *Cureus, 14*(5).

Singh, D., Rai, V., & Agrawal, D. K. (2023). Regulation of collagen I and collagen III in tissue injury and regeneration. *Cardiology and Cardiovascular Medicine, 7*(1), 5.

Verzijl, N., Degroot, J., Oldehinkel, E., Bank, R. A., Thorpe, S. R., Baynes, J. W., Bayliss, M. T., Bijlsma, J. W. J., Lafeber, F. P. J. G., & Tekoppele, J. M. (2019). Age-related accumulation of Maillard reaction products in human articular cartilage collagen. *Biochemical Journal*.

Zgutka, K., Tkacz, M., Tomasiak, P., & Tarnowski, M. (2023). A role for advanced glycation end products in molecular ageing. *International Journal of Molecular Sciences*. https://doi.org/10.3390/ijms24129881

Zhang, Y., Wang, Y., Li, Y., Yang, Y., Jin, M., Lin, X., Zhuang, Z., Guo, K., Zhang, T., & Tan, W. (2023). Application of collagen-based hydrogel in skin wound healing. *Gels, 9*(3), 185.