

Original article

Effect of *Spatholobus littoralis* hassk extract on matrix metalloproteinase-1 and elastin fiber morphology in d-galactose-induced aging model ratsLuh Ade Lela Arika¹, Puput Putih Anisa¹, Harliansyah^{2*}, Nenden Lilis Setiasih³¹Magister of Biomedic Sciences, Sekolah Pascasarjana, Universitas YARSI, Jakarta, Indonesia²Department of Magister of Biomedic Science, Telomere Longevity and Oxidative Stress Research Center, Universitas YARSI, Indonesia³Department of Dermatology and Venereology, Faculty of Medicine, Universitas YARSI, Jakarta, Indonesia**Abstract**

This study investigates the effects of ethanol extract of bajakah wood (*Spatholobus littoralis* Hassk) on skin aging with D-galactose-induced Sprague-Dawley rats, focusing on Matrix Metalloproteinase-1 (MMP-1) concentration and elastin fiber morphology. A total of 36 male rats were divided into six groups; CG1, CG2, CG3, TG1, TG2 and TG3, receiving varying doses of the extract. MMP-1 levels were measured using an ELISA kit, while elastin fibers were assessed through Verhoeff Van Gieson staining. The results show that the extract significantly inhibit MMP-1 activity, with group CG2 exhibiting the highest concentration (35.78 ng/ml) compared to other groups ($p = 0.039$). Furthermore, the extract notably increased elastin fiber content, particularly in group TG6 (100 mg/kgBB), which showed a mean percentage of 7.10% compared to 2.22% in the control group ($p < 0.001$). Qualitative analysis revealed a more intense and evenly distributed brown coloration in higher-dose treatment groups, indicating enhanced elastin density. These findings suggest that bajakah wood extract possesses antioxidant and anti-inflammatory properties, making it a promising candidate for therapeutic interventions aimed at improving skin quality and combating age-related changes. By modulating MMP-1 activity and promoting elastin synthesis, the extract could serve as a valuable addition to skincare formulations. Future research should explore the specific mechanisms through which bajakah wood extract exerts its effects, as well as its long-term efficacy and safety in human applications, to fully realize its therapeutic potential.

Keywords: Antioxidant, bajakah wood, elastin fibers, Matrix Metalloproteinase-1 (MMP-1), skin aging

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Introduction

Skin aging is a multifaceted biological phenomenon characterized by a gradual decline in physiological functions and increased susceptibility to various diseases, influenced by both intrinsic and extrinsic factors that lead to tissue damage and diminished body function (Agrawal et al., 2023; Guo et al., 2022; Karimi, 2023). Intrinsic aging, driven by genetic and biological factors, manifests as a loss of skin elasticity, decreased collagen levels, and the emergence of wrinkles and dryness (Chalise, 2019; Shin et al., 2023). Conversely, extrinsic aging, exacerbated by environmental influences such as ultraviolet light exposure, pollution, and unhealthy lifestyle choices, accelerates the aging process through mechanisms like non-enzymatic glycation. Glycation involves the reaction between simple sugars, such as glucose and galactose, with proteins, resulting in the formation of Advanced Glycation End-products (AGEs). The accumulation of AGEs in skin tissue can lead to significant damage to structural components like collagen and elastin, while also increasing oxidative stress, which activates Matrix Metalloproteinase-1 (MMP-1). This enzyme plays a crucial role in the degradation of extracellular matrix components, further contributing to skin aging by promoting the breakdown of elastin and

collagen, ultimately resulting in wrinkles and loss of skin firmness (Bo-Htay et al., 2018; Gao et al., 2022; Rosmarwati et al., 2023; Xiao et al., 2021; Zheng et al., 2022).

D-galactose, a naturally occurring sugar, has been widely employed in experimental models to induce accelerated aging in rodents, effectively mimicking age-related physiological changes observed in humans. This model is particularly valuable for elucidating the underlying mechanisms of aging and evaluating potential therapeutic interventions aimed at mitigating age-related decline (Liu et al., 2019; Umbayev et al., 2020; Yamamoto et al., 2023). Recent studies have highlighted the role of oxidative stress and inflammation as pivotal factors in cellular damage and tissue integrity deterioration during aging. In this context, the ethanol extract of bajakah wood (EEB) (*Spatholobus littoralis* Hassk) has garnered attention for its potential health benefits, particularly its antioxidant and anti-inflammatory properties. Rich in bioactive compounds such as flavonoids, phenolics, tannins, and saponins, bajakah wood extract may counteract oxidative stress and inflammation, both critical contributors to the aging process (Adhityasmara & Ramonah, 2022; Nursyafitri et al., 2021). This study aims to investigate the effects of ethanol extract of bajakah wood on MMP-1 concentration and the morphological description of elastin fibers in D-galactose-induced rat skin, potentially paving the way for novel therapeutic strategies to combat age-related skin changes (Hong et al., 2024; Lan et al., 2023).

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Methods

Subjects and Objects of Research

This study used 36 male Sprague-Dawley rats (*Rattus norvegicus*). The object of the study included measurement of Matrix Metalloproteinase-1 (MMP-1), and morphological description of elastin fibers.

Population and Sample

The study population consisted of Sprague-Dawley rats selected based on inclusion and exclusion criteria. Inclusion criteria included male white rats aged 8-9 weeks with body weight between 160-200 grams, which were in good health without signs of disease. Exclusion criteria included rats that did not meet these criteria. Sample size determination was done using Federers formula (Robson et al., 1967), which resulted in a minimum of 24 rats, but in anticipation of possible losses, the sample size was increased to 36 rats, with 6 rats per group.

Research Variables

The independent variable in this study was the administration of bajakah wood extract (EEB) (*Spatholobus littoralis* Hassk), while the dependent variables included MMP-1 concentration and morphological description of elastin fibers. Controlled fixed variables include rat type, body weight, age, temperature, feed, and cage conditions.

Type and Method of Data Collection

This study was experimental and conducted at the Integrated Laboratory of the Research Institute of YARSI University. The rats used were injected with D-galactose at a dose of 500 mg/kgBB and treated with ethanol extract of bajakah wood. The research subjects were divided into six groups: blank group (CG1), negative control (CG2), positive control (CG3), and three treatment groups (TG1, TG2, TG3). Measurement of MMP-1 concentration was carried out using the Enzyme-Linked Immunosorbent Assay (ELISA) method, while the morphological description of elastin fibers was obtained through Verhoeff Van Gieson staining. This research is planned to take place from August to December 2024 at the Integrated Laboratory of the Research Institute of YARSI University and iRATco Laboratory in Bogor Regency, Indonesia.

Instrument and Materials

The tools used in this study include ELISA Reader, light microscope, and various other laboratory equipment. Materials used include Sprague-Dawley male rats, NaCl 0.9%, ketamine, xylazine, buffered neutral formalin (BNF) 10%, and ethanol extract of bajakah wood.

Working Protocol

Before treatment, rats were acclimatized for seven days to reduce stress. After that, D-galactose injection was done in the second and eighth week. At the beginning of the 9th week, blood was taken from the heart and skin samples for MMP-1 analysis and elastin fiber morphology. Bajakah wood extract was prepared through maceration process with 96% ethanol, and the dose given was determined based on the body weight of the rats.

Sampling and Data Analysis

Blood sampling was conducted after anesthetizing the rats with ketamine and xylazine, and serum was used to measure MMP-1 concentration via ELISA. Skin samples were fixed in 10% BNF and stained with Verhoeff Van Gieson for histopathological analysis. Observations assessed elastin fiber thickness. Data were analyzed using IBM SPSS Statistics Version 30, with normality tests guiding the use of *One-way* ANOVA or Kruskal-Wallis tests. A p-value <0.05 was considered significant, indicating differences between groups.

Results

Matrix Metalloproteinase-1 (MMP-1) Concentration

This study aims to evaluate the effect of ethanol extract of bajakah wood on the concentration of MMP-1 in the serum of *Rattus norvegicus* Sprague-Dawley (SD) rats in the aging model, using the Rat Matrix Metalloproteinase-1 ELISA Kit 96 wells BZ-08182130-EB Bioenzy. Measurements were made by determining the absorbance value (OD) at a wavelength of 450 nm using a microplate reader, and the results were analyzed with the Shapiro-Wilk Test and Lavene Test for normality and homogeneity of data, it can seen in Table 1.

Table 1. Results of MMP-1 Concentration Examination and Comparison of P-Value in Treatment Groups

Treatment Group	n	Mean MMP-1 (ng/ml)	SD	One-Way ANOVA (p-value)*	Post Hoc LSD (p-value)*				
					CG2	CG3	TG4	TG5	TG6
CG1	4	31,44	2,88	0,039*	0,084	0,348	0,353	0,557	0,179
CG2	4	35,78	4,37			0,012*	0,393	0,026*	0,005*
CG3	4	29,16	2,31				0,071	0,719	0,670
TG4	4	33,71	3,04					0,138	0,030*
TG5	4	30,02	0,72						0,435
TG6	4	28,13	5,01						

Normality test results showed that MMP-1 concentration data were normally distributed ($p > 0.05$), and Levene's Test homogeneity test indicated homogeneous variants between groups ($p = 0.342$). The *One-way* ANOVA test resulted in a p-value of 0.039,

indicating a significant difference in mean MMP-1 concentration among the six treatment groups. Post Hoc LSD analysis revealed that group CG2 had the highest MMP-1 concentration (35.78 ng/ml) compared to groups

5 (30.02 ng/ml) and TG3 (28.13 ng/ml), as illustrated in Figure 1.

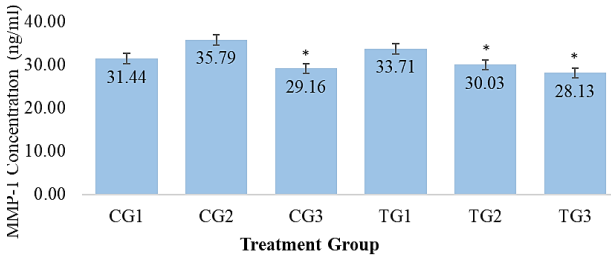


Figure 1. Average MMP-1 Concentration in Treatment Groups. Notes: * p < 0.05, compared with the negative control group (CG2).

Morphological Description of Rat Skin

This study analyzed the effect of ethanol extract of bajakah wood on the morphology of elastin fibers, as well

as the thickness of epidermis and dermis in D-galactose-induced rats as a model of aging. Observations were made with the Verhoeff Van Gieson (VVG) staining method using a light microscope. Quantitative analysis was performed with ImageJ software to ensure data accuracy and consistency, thus providing a clear picture of the changes that occur due to the treatment of bajakah wood extract.

Elastin Fibers

The test results showed the effect of ethanol extract of bajakah wood on the percentage of elastin fibers in each treatment group. Complete data regarding the percentage of elastin fibers measured in each group can be seen in Table 2, which illustrates significant differences due to the treatment given.

Table 2. Elastin Fiber Content and Comparison of P-Value in Treatment Groups

Treatment Group	Mean Elastin (%)	SD	One-Way ANOVA (p-value)*	Post Hoc LSD (p-value)*				
				CG2	CG3	TG4	TG5	TG6
CG1	4,24	1,38	<0,001*	0,016*	0,722	0,334	0,762	0,002*
CG2	2,22	0,86			0,008*	0,099	0,009*	<0,001*
CG3	4,50	1,13				0,196	0,957	0,004*
TG4	3,51	0,69					0,231	<0,001*
TG5	4,47	0,20						0,003*
TG6	7,10	0,51						

The administration of ethanol extract of bajakah wood significantly affected elastin fiber percentage in skin tissue. One-Way ANOVA analysis yielded a p-value <0.001, indicating significant differences among treatment groups. The Post Hoc LSD test revealed that group TG3, receiving 100 mg/kgBB, had a mean elastin percentage of 7.10%, significantly higher than group CG2 2.22%. This finding suggests that the ethanol extract of bajakah wood at 100 mg/kgBB is notably effective in enhancing elastin fiber content in skin tissue. Consequently, this extract shows potential as a therapeutic agent for improving skin quality and addressing age-related decreases in skin elasticity, as illustrated in Figure 2.

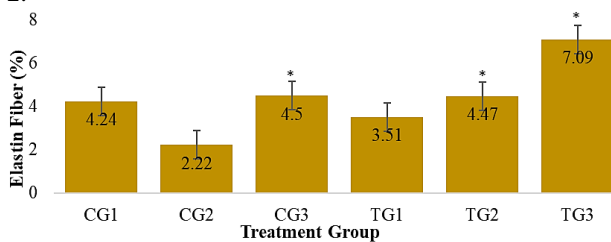


Figure 2. Average Percentage of Elastin Fiber Density in Each Treatment Group. Notes: * p < 0.05, compared with the negative control group (CG2).

Assessment of elastin fiber density using Verhoeff Van Gieson (VVG) staining involved observing the intensity of brown coloration, indicating elastin fibers, while pink indicated collagen fibers. Results shown in Figure 3 demonstrate that the treatment group receiving higher doses of bajakah wood extract exhibited a more intense and evenly distributed brown color, suggesting that increased extract dosage enhances elastin fiber

density in skin tissue, potentially improving skin elasticity.

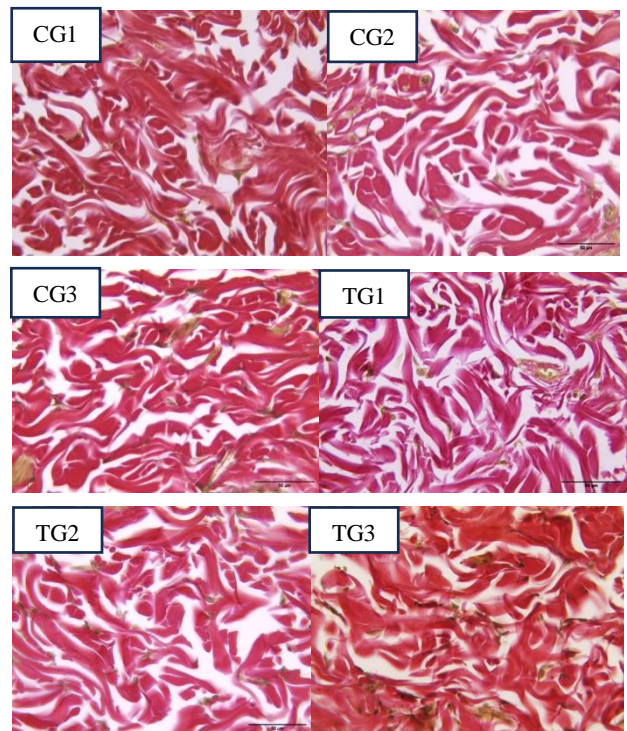


Figure 3. Morphology of Elastin Fibers (Verhoeff Van Gieson). **Description:** CG1 (blank), CG2 (negative control), CG3 (positive control), TG1 (treatment 1, dose of ethanol extract of bajakah wood 25 mg/kgBB), TG2 (treatment 2, dose of 50 mg/kgBB), TG3 (treatment 3, dose of 100 mg/kgBB). Black arrows indicate elastin fibers (blackish brown color), and pink color indicates collagen fibers. The percentage of elastin fiber density to the total elastin area in three fields of view was analyzed using ImageJ software at 400x microscope magnification with a measurement scale of 50 μm.

Discussion

This study reveals that ethanol extract of bajakah wood (EEB) plays a crucial role in reducing Matrix Metalloproteinase-1 (MMP-1) levels and protecting elastin fibers in D-galactose-induced Sprague-Dawley rats. MMP-1 is a proteolytic enzyme that degrades type I and III collagen, damaging the extracellular matrix (ECM). High MMP-1 activity can decrease skin elasticity, accelerate wrinkle formation, and worsen skin aging (Bo-Htay et al., 2018). MMPs are essential for tissue homeostasis and are involved in key physiological processes such as bone remodeling, angiogenesis, immune responses, and wound healing. MMP activity is regulated at various levels, including transcriptional regulation, proteolytic activity, and inhibition by tissue inhibitors of MMPs (TIMPs). Dysregulated MMP activity can contribute to pathological conditions like inflammation, arthritis, and cancer, making MMP inhibition a key target in drug development (Cabal-Pacheco et al., 2020).

The induction of 500 mg/kgBW D-galactose in Control Group 2 (CG2) significantly increased MMP-1 levels and reduced elastin fiber density. This indicates the formation of Advanced Glycation End Products (AGEs), activation of NF- κ B and AP-1 signaling pathways, leading to increased MMP-1 expression and accelerated ECM degradation (Shin et al., 2023). These findings align with (Bo-Htay et al., 2018) who demonstrated that AGEs accumulation increases reactive oxygen species (ROS) production, activates pro-inflammatory signaling pathways, and accelerates skin aging damage.

In the positive control group (CG3), which received 50 mg/kgBW vitamin C, MMP-1 levels decreased and elastin fiber density improved, confirming the antioxidant effects of vitamin C. However, the results showed that Treatment Group 6 (TG6), which received 100 mg/kgBW of EEB, exhibited a greater decrease in MMP-1 levels (28.13 ng/ml, $p = 0.005$) and a higher increase in elastin fiber density (7.10%) compared to CG3. This suggests that EEB provides stronger anti-aging effects, likely due to its rich bioactive compounds, such as flavonoids and phenols, which inhibit MMP-1 activity and protect ECM integrity (Sari et al., 2023). This suggests that EEB not only exerts antioxidant effects but may also inhibit MMP-1 activity more directly through phenolic compounds binding to the catalytic domain of MMP-1 (Schmelzer & Duca, 2022). Flavonoids and tannins in EEB may offer additional protection by disrupting free radical cascades and preventing glycation-induced ECM damage, complementing the antioxidant action of vitamin C (Speisky et al., 2022; Zahra et al., 2024).

Further analysis of elastin fiber morphology reinforces the protective effect of bajakah wood extract. Treatment Group 6 (TG6) showed elastin fiber content of 7.10%, significantly higher than CG2 (2.22%) and surpassing CG3, indicating that EEB might stimulate fibroblast activity or inhibit elastase, mechanisms not typically attributed to vitamin C alone. This aligns with (Heinz, 2021), who found that certain anti-glycation compounds can directly bind to elastin, reducing fragmentation and stiffness. The safety of bajakah wood extract was also confirmed through toxicological studies, which showed that doses up to 5,000

mg/kgBW did not trigger acute toxic effects in experimental animals (Andriani et al., 2023). This strengthens the potential of bajakah as a therapeutic agent that can be developed into oral supplements or topical formulations to slow skin aging.

Our study provides new insights into the potential of bajakah wood as a natural anti-aging agent that works through MMP-1 inhibition, elastin fiber protection, and modulation of oxidative stress and glycation-related signaling pathways. Future research should explore the key active compounds responsible for these effects, investigate the precise molecular interactions with MMP-1, and assess the long-term effects of EEB in clinical settings. In addition, studies using human skin cell cultures or 3D skin models could provide more accurate insights into the cellular mechanisms of EEB in humans. Clinical trials with diverse populations, varying dosages, and long-term follow-ups are essential to determine the extracts efficacy, safety, and optimal administration route. Exploring the synergistic effects of EEB combined with established anti-aging agents, such as retinoids or peptides, could further enhance its therapeutic potential.

Conclusion

This study reveals that ethanol extract of bajakah wood (EEB) (*Spatholobus littoralis* Hassk) significantly influences Matrix Metalloproteinase-1 (MMP-1) concentration and elastin fiber morphology in D-galactose-induced aging in Sprague-Dawley rats. EEB demonstrated stronger effects than vitamin C in reducing MMP-1 levels and increasing elastin fiber density, highlighting its potential as a therapeutic agent for improving skin quality and combating aging. With its antioxidant, anti-inflammatory, and anti-glycation properties, EEB shows promise for development into supplements or topical formulations for anti-aging therapy. Further research is needed to explore its detailed molecular mechanisms, identify key active compounds, and evaluate its long-term efficacy in clinical studies.

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