



Antioxidant Activity and Phenolics of Kabau (*Archidendron bubalinum*) Pod Peel Extract from East Lampung on Blood Cell Male Mice Induced by Cadmium

Elisa Nurma Riana^{1*}, Muhammad Eka Prastya², Gian Primahana², Faniza Aini Subhi¹, Berkat Afni Maruli¹, Hida Arliani Nur Anisa¹, Iffa Afia Khairani¹, Lisana Husna Imaniar¹

(Received August 2024/Accepted January 2025)

ABSTRACT

Cadmium (Cd) increases oxidative stress, which increases the likelihood of health problems. To protect the body from oxidative stress, natural antioxidants obtained from plants are required. The kabau plant (*Archidendron bubalinum*) is thought to have antioxidant phytochemicals. The purpose of this study was to assess the antioxidant activity and total phenolic component content of kabau pod peels, as well as their effect on the quantity of erythrocytes and leukocytes in male mice exposed to cadmium. This study used a completely randomized design, with 24 mice divided into six groups: three control groups and three treatment groups. The findings of assessing the antioxidant activity of peel extract revealed that the IC₅₀ was 93.6 ppm, which is considered strong. The phenolic content of peel extract was 72.26 mg GAE/g. Giving pod peel extract to mice increased the number of erythrocytes and leukocytes, however the impact was not significant ($p = 0.028$ and $P = 0.239$). Mice with 380 mg/kg BW produced better outcomes.

Keywords: antioxidant, *Archidendron*, blood cell, kabau, phenolics

INTRODUCTION

Anthropogenic activities can pollute the ecosystem, causing health problems and other negative consequences. Heavy metals are one of the most harmful contaminants. Cadmium (Cd) is one of the heavy metals responsible for damage. Cadmium will build in the liver and kidneys. Cadmium exposure increases ROS (reactive oxygen species), which leads to oxidative stress (Deakandi *et al.* 2017). Low and moderate CdCl₂ exposure causes oxidative stress, DNA damage, and elevated apoptotic markers in rat liver (Bayram 2022). According to Andjelkovic *et al.* (2019), exposure to CdCl₂ 15 mg/kg BW can produce a rise in renal malondialdehyde (MDA), reducing the number of leukocytes and erythrocytes in mice.

Antioxidants are required to protect the organism from excessive ROS. Kabau (*Archidendron bubalinum* (Jack.)) is an antioxidant-rich herb. According to Riasari *et al.* (2019), kabau pod peels and seeds contain phytochemical substances such as alkaloids, flavonoids, phenols, tannins, terpenoids, saponins, quinones, and mono/sesquiterpenes. *A. jiringoides* exhibits high antioxidant activity, with an IC₅₀ of 32.01

ppm (Riana *et al.* 2024). The chemicals found in the pod peel extract have antidiabetic effect, reducing blood sugar levels in aloxan-induced male mice (Wahidah 2018). In addition, the kabau pod peel extract can increase the concentration of lead-induced male mouse spermatozoa (Riana 2024). Apa nama latin yang benar? *A. bubalinum* atau *A. jiringoides*?

Phenolic compounds are natural antioxidants with hydroxy groups, making them easily oxidized by giving hydrogen atoms to free radicals (Dhurhania and Novianto 2018). Erjon *et al.* (2022) found that ethanol extracts of *jengkol* (*A. jiringa* (Jack) I.C Nielsen) leaves increased phagocytosis capacity and leukocyte count. Based on the foregoing, this study was undertaken to investigate the antioxidant activity and total phenolic components of kabau (*A. bubalinum*) pod peel extract on the number of erythrocytes and leukocytes in male mice exposed to the heavy metal cadmium (Cd).

METHODS

Preparing the Materials and Extracting Pod Peels

Kabau samples were collected from East Lampung Regency. The pod peels were chopped into small pieces, dried, and aired at room temperature ($\pm 25\text{--}30^\circ\text{C}$). The dried material was pulverized in a blender until it forms a powder. The powder was macerated with 96% ethanol solvent in a 1:5 ratio (200 g material: 1 L of solvent) until it is immersed. It was

¹ Biology Study Program, Faculty of Science, Sumatra Institute of Technology, Lampung 35365, Indonesia

² Research Center for Pharmaceutical Ingredients and Traditional Medicine, National Research, and Innovation Agency (BRIN), Tangerang 15311 Indonesia

* Corresponding Author: Email: elisa.riana@bi.itera.ac.id

then extracted using the maceration process for 3 days, filtered with filter paper, and concentrated the filtrate using a rotary evaporator at 50°C.

Antioxidant Activity Determination

The antioxidant activity of the extract was determined using the DPPH (2,2-diphenyl-1-picrylhydrazyl) method, and the percentage inhibition was derived using the following formula:

$$\text{Inhibition (\%)} = (A_{\text{control}} - A_{\text{sample}}) / A_{\text{control}} \times 100\%$$

The IC₅₀ was calculated using a linear regression formula based on the relationship between the percentage of inhibition and sample concentration. The IC₅₀ was determined using the following equation:

$$y = a(x) + b$$

where

y = % inhibition

x = Sample concentration

Total Phenolics Determination

A standard gallic acid solution was used for the total phenolics determination, prepared from a 1000 ppm parent solution. Concentrations of 5, 10, 15, 20, and 30 µg/mL were set. To create the gallic acid calibration curve, 50 µL of each concentration was pipetted into a microplate, added 100 µL of Folin-Ciocalteu 10% reagent, and put it on a shaker for 3 min to ensure homogeneity. After 5 min at room temperature, a 100 µL solution of 6% sodium carbonate was prepared and left at room temperature for 90 min. A microplate reader was also used to evaluate absorption at 725 nm in the standard gallic acid solution.

The sample solution was prepared by dissolving 50 mg in 5 mL of methanol and mixing well. The 1000 ppm concentration sample solution was pipetted to 500 µL and 5 mL of methanol was added. To the 50 µL of extract, 100 µL of Folin-Ciocalteu 10% reagent was added. The mixture was agitated for 3 min until homogenous, then let to stand for 5 min at room temperature. Next, 100 µL of 6% sodium carbonate solution was added and let it sit at room temperature for 90 min. The extract solution was then tested for

absorbance at 725 nm. The absorbances were used to compute the total phenol concentration in the extract using a linear equation derived from the calibration curve. The total phenolics were reported as gallic acid equivalent (GAE) in mg/g.

$$\text{Total phenolics} = \frac{\left(\text{mg} \frac{\text{GAE}}{\text{g}} \text{ Ekstrak} \right)}{\frac{\text{Concentration of standard solution from calibration curve}}{\text{Concentration of test sample used}}} =$$

Acclimatization and Treatment of Test Animals

Test animals were acclimatized over a seven-day period. The test animals were 24 healthy male mice, separated into six treatment groups (Table 1).

Erythrocytes and Leukocytes Determinations

To count erythrocytes, 0.5 µL of blood was taken and diluted with 100.5 µL of Hayem solution. To calculate leukocytes, 0.5 µL of blood was taken and diluted with 10.5 µL of Turk solution. The hemocytometer was used to measure up to ±10 µL of blood suspension, which was then covered with glass. Cell counting began in the upper left corner and progressed to the right before descending from right to left. Cells that violate one of the plane lines are tallied, followed by cells that violate both the upper and left boundary lines (Syarifah *et al.* 2020). The number of cells observed can be estimated using the formula:

$$\text{Number of cell/mm}^3 = \frac{N}{V} \times P$$

where:

N = The number of blood cells in the counter box

V = Counter box volume

Leukocyte counter box volume: $0.1 \times 4 \text{ mm}^3 = 0.4 \text{ mm}^3$

Erythrocyte counter box volume: $0.1 \times (5 \times 0.04 \text{ mm}^2)$

$= 0.02 \text{ mm}^3$ (Syarifah *et al.* 2020)

P = Dilution ratio

Data were analyzed using the One-Way ANOVA statistical test. This test was performed to determine the significance of test parameters and the effect of administering kabau pod peel extract on the amount of blood cells in mice. If the results differ, a follow-up test using an LSD test was performed.

Table 1 Test animal treatment group

	Group	Information
Control	Control treatment (KP)	Distilled water for 14 days.
	Positive control (K+)	Given CdCl ₂ at a dose of 3.15 mg/kg BW for 7 days and vitamin C of 0.036 mg/kg BW on days 8 to 14.
	Negative control (K-)	Given CdCl ₂ at a dose of 3.15 mg/kg BW for 7 days.
Treatment	Treatment 1 (P1)	Given a CdCl ₂ of 3.15 mg/kg BW for 7 days and a dose of 95 mg/kg of extract on the 8th to 14th day.
	Treatment 2 (P2)	Given a CdCl ₂ of 3.15 mg/kg BW for 7 days and a dose of extract at a dose of 190 mg/kg BW on the 8th to 14th day.
	Treatment 3 (P3)	Given a CdCl ₂ of 3.15 mg/kg BW for 7 days and a dose of 380 mg/kg of extract on the 8th to 14th day.

RESULTS AND DISCUSSION

Antioxidant Activity

The antioxidant activity test showed that the IC₅₀ of the kabau pod peel extract was 93.6 ppm (Table 2), indicating substantial antioxidant activity, meaning that the extract may absorb 50% of free radicals. The lower the IC₅₀ value, the greater the capacity to protect against free radicals. Secondary metabolites found in plants, such as flavonoid molecules, tannins, saponins, and terpenoids, are known to have antioxidant properties. The IC₅₀ in this study employing 96% ethanol solvent is in the strong category, ranging from 50 to 100 ppm. This study differs from Rahmawati *et al.* (2020) findings, which state that kabau pod peel extract exhibits very strong antioxidant activity with an IC₅₀ of 26.77 ppm. Riasari *et al.* (2019) discovered that extract of the same species from South Sumatra has 44.7 ppm, indicating very strong antioxidant activity. Antioxidants are substances that can be utilized to prevent oxidative stress by transferring electrons to free radicals, therefore preventing damage to the body's cells and tissues (Dewi *et al.* 2018). The discrepancy in IC₅₀ values is most likely due to geographical location and regional altitude.

Total Phenolics

The total phenolics were measured to estimate the phenols compounds present in the extract. According to the test results, the extract has a total phenol content of 72.26 mg GAE/g. This study's total phenolic levels differ from those found in previous research. Table 3 shows the difference in total phenolics between this study and other investigations. Kabau pod peel extract has been shown to include secondary metabolite components such as flavonoids, tannins, saponins, terpenoids, and phenols (Okta *et al.* 2019). The total phenolics in this study was 72.26 mg GAE/g. Riasari *et al.* (2019) discovered that the total phenolics of the same species from Lampung was 11.75 g GAE/100 g

and from South Sumatra was 5.89 g GAE/100 g, whereas the total phenol content of kabau pod peel extract from Lampung was 6.11 g GAE/100 g and from South Sumatra was 5.42 g GAE/100 g. This variation could be due to the method utilized in the extraction procedure.

The extraction process chosen has a significant impact on the metabolite chemicals extracted from the extract (Verawati *et al.* 2020). According to Sirumapea *et al.* (2021), the maceration process attracts more phenolics than the Soxhlet method, which is associated with a higher total phenol concentration. Riasari *et al.* (2019) found that the maceration approach yielded higher total phenolics than the Soxhlet method.

The geographical conditions in which the kabau plant grow can also influence the phytochemicals in the plant. According to Riasari *et al.* (2019), environmental factors such as temperature, light, and humidity pressure might influence the formation of the secondary metabolites by plants. Environmental stress can cause plants to create more phytochemicals. The sample for this study was collected from Way Jepara, a lowland area in East Lampung with an elevation of 25 m above sea level, according to the Lampung Province Central Statistics Agency.

Effects of Kabau Pod Peel Extract on Erythrocytes and Leukocytes

The One-Way ANOVA statistical test revealed that the average number of erythrocytes in mice had a significant level of *p*-value 0.078 (*p*>0.05). This demonstrates that the average quantity of erythrocytes in mice did not differ significantly across treatment groups. Based on the average number of erythrocytes in mice, the K-treatment with cadmium chloride (CdCl₂) resulted in erythrocytes that was lower than normal, at 4.3 million cells/mm³. In contrast to the outcomes of the KP and K+ treatments, as well as the treatment given by kabau pod peel extracts, namely P1, P2, and P3, the average number of erythrocytes remained within

Table 2 Antioxidant activity of kabau (*Archidendron bubalinum*) pod peel extract

Sample	IC ₅₀ (ppm)	Antioxidant category
Kabau pod peel extract	93.60 ± 11.90	Strong
Ascorbic acid	6.31 ± 0.36	Very strong

Table 3 Total phenolics of kabau (*Archidendron bubalinum*) pod peel

Origin of <i>A. bubalinum</i>	Extraction method	Total phenolics g GAE/g	Source	Year
East Lampung	Maceration with 96% ethanol	72.26	This study	2024
Lampung	Maceration with ethanol	11.75	Riasari <i>et al.</i>	2019
Lampung	Soxhlet with ethanol	6.11	Riasari <i>et al.</i>	2019
South Sumatra	Maceration with ethanol	5.89	Riasari <i>et al.</i>	2019
South Sumatra	Soxhlet with ethanol	5.42	Riasari <i>et al.</i>	2019
West Sumatra	Maceration with ethanol	9.507	Okta <i>et al.</i>	2019

normal limits. The normal erythrocyte counts in mice, according to Suckow *et al.* (2001), is between 5.0 and 9.5 million cells/mm³. This study found that administering kabau pod peel extract might sustain the quantity of erythrocytes in mice exposed to cadmium chloride (Table 4).

The One-Way ANOVA statistical test with a significance level of 5% on the average number of leukocytes in male mice gave a value of 0.239 ($p > 0.05$). This demonstrates that the average number of leukocytes is not significantly different across the treatment groups. According to the average data, the number of leukocytes in mice in each treatment remains within the normal range. However, the K-treatment with CdCl₂ had a lower number of leukocytes than the other treatments, with 4.6 thousand cells per mm³. The results of the K- treatment revealed that the CdCl₂ dose was insufficient to reduce the number of leukocytes above the normal range. According to Suckow *et al.* (2001), the average number of normal leukocytes in mice ranged from 3.0 to 14.3 thousand cells per mm³. This study revealed that administering kabau pod peel extract could keep the number of leukocytes within normal ranges (Table 5).

According to this study on mouse blood cells, exposure to CdCl₂ reduces the quantity of erythrocytes. CdCl₂ induces oxidative stress in erythrocytes, which might exacerbate lipid peroxidation produced by free radicals. Cadmium in the blood is bound by erythrocytes and blood plasma. Cadmium can increase zinc protoporphyrin, resulting in a decrease in the number of erythrocytes and iron deficiency anemia (Lubis *et al.* 2013). Zinc protoporphyrin is a chemical present in red blood cells that results from interference with heme production. Cadmium can disrupt heme production by inhibiting the activation of enzymes δ -

aminolevulinic acid dehydratase (δ -ALAD) and ferrochelatase, which produce zinc protoporphyrin (ZPP). An increase in ZPP concentration in the blood indicates a reduction in iron levels and heme production (Mwangi *et al.* 2014). Cadmium can also inhibit the synthesis of erythropoietin, a red blood cell formation hormone (Nazima *et al.* 2015). Erythropoietin is a hormone that interacts to certain red blood cell progenitor receptors, signaling proliferation and differentiation (Suryanty *et al.* 2005). Erythropoietin causes the bone marrow to create red blood cells (Sanjaya *et al.* 2019). The peritubular interstitial (endothelial) kidneys manufacture erythropoietin. Cadmium accumulation in the kidneys causes kidney damage, preventing the kidneys from producing erythropoietin and leading the bone marrow to create fewer red blood cells, resulting in anemia (Sanjaya *et al.* 2019).

Cadmium element in erythrocytes inhibits the glucose-6-phosphate dehydrogenase (G6PD) enzyme, which creates glutathione and protects hemoglobin from oxidative stress. G6PD is an enzyme that catalyzes the pentose phosphate pathway and gives a reducing impact to all cells in the form of NADPH. NADPH molecules can help cells withstand oxidative stress by generating glutathione while decreasing oxidized glutathione. Glutathione will diminish hydrogen peroxide, a potent oxidant that reduces antigens. Exposure to CdCl₂ lowered the quantity of erythrocytes and leukocytes in mice.

The average number of leukocytes in mice obtained with the K- treatment was lower than that of other treatments, even though the number of leukocytes remained within the normal range. Cadmium can disrupt the hematopoiesis system by preventing the development of blood cells, including leukocyte

Table 4 Average number of erythrocytes in each treatment group

Treatment	N	Average number of erythrocytes (million cells/mm ³) \pm St. dev
KP	4	5.66 \pm 1.17
K+	4	6.01 \pm 0.79
K-	4	4.35 \pm 1.56
P1	4	6.33 \pm 0.91
P2	4	6.82 \pm 1.69
P3	4	7.24 \pm 1.45

Remarks: KP = Control treatment (distilled water); K+ = Positive control: vitamin C of 0,036 g/kg BW and CdCl₂ 3.15 mg/kg BW; K- = Negative control: CdCl₂ 3.15 mg/kg BW; P1 = Pod peel extract 95 mg/kg BW; P2 = Pod peel extract 190 mg/kg BW; and P3 = Pod peel extract 380 mg/kg BW.

Table 5 Average number of leukocytes in each treatment group

Treatment	N	Average number of leukocytes (thousand cells/mm ³) \pm St. dev
KP	4	6.96 \pm 2.1
K+	4	7.80 \pm 3.5
K-	4	4.64 \pm 1.2
P1	4	7.94 \pm 0.4
P2	4	7.94 \pm 2.1
P3	4	8.90 \pm 2.5

Remarks: KP = Control treatment (distilled water); K+ = Positive control: vitamin C of 0,036 g/kg BW and CdCl₂ 3.15 mg/kg BW; K- = Negative control: CdCl₂ 3.15 mg/kg BW; P1 = Pod peel extract 95 mg/kg BW; P2 = Pod peel extract 190 mg/kg BW; and P3 = Pod peel extract 380 mg/kg BW.

differentiation in the bone marrow (Scharf *et al.* 2020). This study also found that the peel extract of kabau pod peel given to P1, P2, and P3 treated mice produced normal erythrocytes and leukocytes. The results revealed that administering the extract had a protective effect on erythrocytes and leukocytes in mice because it could preserve the quantity of erythrocytes and leukocytes in mice exposed to CdCl₂ due to phenolics in it. Muliarsari *et al.* (2023) also said that phenolic compounds exhibit antioxidant properties due to the presence of hydroxyl groups, which give hydrogen atoms during interactions with free radicals via an electron transfer mechanism, thereby limiting the oxidation process. Antioxidant chemicals also serve to maintain and reinforce the red blood cell wall against free radicals, as well as aid in red blood cell regeneration, oxidative stress protection, lipid peroxidation prevention, and SOD (superoxide dismutase) activity reduction.

CONCLUSION

The study results showed that kabau pod peel extract had a moderately high antioxidant activity, with an IC₅₀ of 93.6 ppm. The total phenolic components found in the extract were 72.26 g GAE/g. The phenolics concentration was higher than in previous research due to differences in extraction procedures and the geographical location of the plant. The treatment of kabau pod peel extract increased the number of erythrocytes and leukocytes, although the increase was not statistically significant (*p* values of 0.028 and 0.239, respectively).

ACKNOWLEDGEMENT

This research is supported by the BOPTN Young Lecturer Research Scheme of the Directorate of Research, Technology, and Community Service (DRTPM), Directorate General of Higher Education, Research, and Technology of the Ministry of Education, Culture, Research, and Technology of the Republic of Indonesia for the 2024 Fiscal Year. with contract number 039/E5/PG.02.00.PL/2024, dated 11 June 2024. Ethical clearance was obtained from the Faculty of Medicine, University of Lampung with the number 196F/UN26.18/PP.05.02.00/2024.

REFERENCES

Andjelkovic M, Djordjevic AB, Antonijevic E, Antonijevic B, Stanic M, Kotur-Stevuljevic J, Spasojevic-Kalimanovska V, Jovanovic M, Boricic N, Wallace

D, Bulat Z. 2019. Toxic effect of acute cadmium and lead exposure in rat blood, liver, and kidney. *International Journal of Environmental Research and Public Health*. 16(1): 274. <https://doi.org/10.3390/ijerph16020274>

Bayram EN, Al-Shmgani HS, Al-Bakri NA. 2022. Comprehension of the zinc chloride's ameliorative apoptotic and genotoxic effects on mice with cadmium-induced hepatotoxicity. *Journal of Animal Behaviour and Biometeorology* 10(2232): 1–8 <https://doi.org/10.31893/jabb.22035>

Deakandi WY, Risandiansyah R, Yahya A. 2017. Pengaruh dekokta eceng gondok (*Eichhornia crassipes*) terhadap Kadar malondialdehida (MDA) dan nekrosis sel tubulus proksimal ginjal tikus Wistar jantan dengan induksi oral kadmium klorida (CdCl₂) subkronis dosis rendah. *Journal of Islamic Medicine Research*. 1: 65–76.

Dewi SR, Argo BD, Ulya N. 2018. Kandungan flavonoid dan aktivitas antioksidan ekstrak *Pleurotus ostreatus*. *Rona Teknik Pertanian*. 11: 1–10. <https://doi.org/10.17969/rtp.v11i1.9571>

Dhurhanian CE, Novianto A. 2019. Uji kandungan fenolik total dan pengaruhnya terhadap aktivitas antioksidan dari berbagai bentuk sediaan sarang semut (*Myrmecodia pendens*). *Jurnal Farmasi dan Ilmu Kefarmasian Indonesian*. 5: 62. <https://doi.org/10.20473/jfiki.v5i22018.62-68>

Erjon E. 2022. Efek imunostimulan ekstrak etanol daun jengkol (*Archidendron jiringa* (Jack) I.C. Nielsen) pada mencit putih jantan. *Jurnal Ilmiah Farmasi Farmasyifa*. 5: 62–70. <https://doi.org/10.29313/jiff.v5i1.7704>

Kiran, Bharti R, Sharma R. 2021. Effect of heavy metals: An overview. *Materials Today: Proceedings*. 51: 880–885. <https://doi.org/10.1016/j.matpr.2021.06.278>

Lubis B, Rosdiana N, Nafi S, Rasyianti O, Panjaitan FM. 2013. Hubungan keracunan timbal dengan anemia defisiensi besi pada anak. 40: 17–21.

Mahardika RG, Roanisca O. 2018. Aktivitas antioksidan dan fitokimia dari ekstrak etil asetat pucuk idat (*Cratoxylum glaucum*) Antioxidant Activity and Phytochemical of Extract Ethyl Acetat Pucuk Idat (*Cratoxylum glaucum*). *Indonesian Journal of Chemical Research*. 5: 69–74. <https://doi.org/10.30598/ijcr.2018.5-rob>

Muliarsari H, Sopiah B, Yuanita E, Ningsih BNS. 2023. Free-radical scavenging activity and total phenolic compounds of red and green Poinsettia leaves (*Euphorbia pulcherrima* Willd.) from Lombok Island. *Makara Journal of Science*. 27: 273–278.

- <https://doi.org/10.7454/mss.v27i4.1349>
- Mwangi MN, Maskey S, Andang'o PEA, Shinali NK, Roth JM, Trijsburg L, Mwangi AM, Zuilhof H, Lagen B, Savelkoul HFJ, Demir AY, Verhoef H. 2014. Diagnostic utility of zinc protoporphyrin to detect iron deficiency in Kenyan pregnant women. *BMC Medicine: Medicine for Global Health*. 12: 1–13. <https://doi.org/10.1186/s12916-014-0229-8>
- Nazima B, Manoharan V, Miltonprabu S. 2016. Oxidative stress induced by cadmium in the plasma, erythrocytes and lymphocytes of rats: Attenuation by grape seed proanthocyanidins. *Humuan and Experimental Toxicology*. 35: 428–447. <https://doi.org/10.1177/0960327115591376>
- Okta FN, Sukrasno S, Anggadiredja K. 2022. Immunostimulatory activity test of extract and isolation of the secondary metabolites of kabau (*Archidendron bubalinum*) fruit peel. *Biointerface Research in Applied Chemistry*. 12: 2691–2700. <https://doi.org/10.33263/BRIAC122.26912700>
- Rahmawati F, Kurniaty L, Bintang M. 2019. Skrining golongan senyawa aktif dan analisis toksisitas ekstraks biji kabau (*Archidendron bubalinum*) 1. *Jurnal Ilmiah Widya Kesehatan dan Lingkungan*. 1(2): 153–158.
- Riana EN, Aulia S, Azizah N, Khairani IA, Ariyanti Y, Imaniar LH, Setiawan T. 2024. Phytochemical screening and antioxidant activity of kabau seed pod extract from South Lampung. *BIO Web of Conference*. 101(03003): 1–8. <https://doi.org/10.1051/bioconf/202410103003>
- Riasari H, Fitriansyah SN, Hartati R, Anggadiredja K, Sukrasno. 2019. Comparison of extraction methods, antioxidant activities, total phenol in seeds and seed shells of Kabau (*Archidendron bubalinum* (Jack) IC Nielsen) from Lampung and South Sumatra. *Pharmacognosy Journal*. 11: 1278–1284. <https://doi.org/10.5530/pj.2019.11.198>
- Sanjaya AGB, Santhi DGDD, Lestari AAW. 2019. Gambaran anemia pada pasien penyakit ginjal kronik di RSUP Sanglah Pada Tahun 2016. *Jurnal Medika Udayana* 8: 1–6.
- Scharf P, Broering MF, da Rocha GHO, Farsky SHP. 2020. Cellular and molecular mechanisms of environmental pollutants on hematopoiesis. *International Journal of Molecular Sciences*. 21: 1–30. <https://doi.org/10.3390/ijms21196996>
- Sirumapea L, Indryasari S, Darwis D,. 2021. Perbandingan total fenolik ekstrak etanol hasil metode maserasi dan sokletasi dari daun pedada (*Sonneratia alba* Smith.) menggunakan spektrofotometri Uv-Vis. *Molluca Journal of Chemistry Education*. 11: 74–80. <https://doi.org/10.30598/mjocevol11iss2pp74-80>
- Suckow MA, Danneman P, Brayton C. 2001. The Laboratory Mouse. The Laboratory Mouse. London (UK): CRC Press. <https://doi.org/10.1201/9780849376276>
- Suryanty R, Rosdiana N, Lubis B. 2005. Peran eritropoietin pada anemia akibat keganasan pada anak. *Sari Pediatri*. 7: 34. <https://doi.org/10.14238/sp7.1.2005.34-8>
- Syarifah SST, Prasetyaswati MKMDB, Martati MS, Utami N, 2020. Hematologi Dasar. Jakarta Selatan: Cipta Gadhing Artha.
- Verawati V, Sari TM, Savera H. 2020. Pengaruh perbedaan metode ekstraksi terhadap aktivitas antioksidan dan kadar fenolat total dalam ekstrak daun kelor (*Moringa oleifera* Lam.). *Pharmacy: Jurnal Farmasi Indonesia*. 17: 90. <https://doi.org/10.30595/pharmacy.v17i1.6013>