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EVALUATION OF THE EFFECTS OF FRESH GEDI LEAF (*ABELMOSCHUS MANIHOT* (L.) MEDIK.) DECOCTION ON LIVER AND KIDNEY FUNCTION IN FEMALE WHITE RATS (*RATTUS NORVEGICUS)*

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ABSTRACT

Gedi leaf (*Abelmoschus manihot* (L.) Medik.) is widely utilized as a functional food and traditional medicinal plant in Indonesia. However, scientific data regarding its safety, particularly its effects on liver and kidney function, remain limited. This study aimed to evaluate the effects of fresh Gedi leaf decoction on liver and kidney function in female white rats (*Rattus norvegicus*) based on serum Serum Glutamic Oxaloacetic Transaminase (SGOT) and creatinine levels. A laboratory experimental study using a post-test-only control group design was conducted. Fourteen female Wistar rats were randomly divided into two groups: a control group receiving distilled water and a treatment group receiving fresh Gedi leaf decoction ad libitum for 40 days. Serum SGOT and creatinine levels were measured using a semi-automatic analyzer, and the data were analyzed using an independent samples t-test at a 95% confidence level. The results showed that SGOT levels in the control and treatment groups were 199.86 ± 59.62 U/L and

159.00 ± 26.06 U/L, respectively (p = 0.120). Serum creatinine levels were 0.74 ± 0.05 mg/dL and 0.79 ± 0.07 mg/dL, respectively (p = 0.220). All SGOT and creatinine values remained within the normal physiological range for experimental rats, and no significant differences were observed between the two groups. These findings indicate that administration of fresh Gedi leaf decoction for 40 days did not produce significant changes in liver or kidney function parameters in female white rats. Under the conditions of this study, fresh Gedi leaf decoction showed no evidence of hepatotoxic or nephrotoxic effects based on serum SGOT and creatinine parameters.

KEYWORDS: *Abelmoschus manihot*, Gedi leaf, SGOT, creatinine, liver function, kidney function, female white rats.

INTRODUCTION

The use of medicinal plants as part of healthcare practices has been carried out for centuries across various cultures worldwide (World Health Organization, 2013; Heinrich et al., 2018). Along with the increasing public interest in natural products, the utilization of medicinal plants has expanded beyond traditional medicine and has developed into an important component of functional foods with potential health benefits (Hasler, 2002; Bigliardi & Galati, 2013). Nevertheless, the continued use of herbal materials requires scientific evidence that encompasses not only their efficacy but also their safety (Bruschi, 2012). Safety evaluation is essential because bioactive compounds present in plants undergo metabolism and excretion processes that may affect the function of major organs, particularly the liver and kidneys (Klaassen & Watkins, 2015). The liver is the primary organ responsible for the metabolism, biotransformation, and detoxification of various foreign compounds entering the body (Hall, 2021; Gu & Manautou, 2012). Most bioactive constituents of medicinal plants are metabolized in the liver before being distributed throughout or eliminated from the body (Stockham & Scott, 2008). Consequently, the liver is among the organs most susceptible to adverse effects resulting from long-term exposure to bioactive substances (Gu & Manautou, 2012). One of the most widely used biomarkers for assessing liver function is Serum Glutamic Oxaloacetic Transaminase (SGOT), also known as Aspartate Aminotransferase (AST) (Hall, 2021). Elevated serum SGOT activity is commonly associated with hepatocellular injury caused by disruption of hepatocyte membrane integrity (Giannini et al., 2005). In addition to the liver, the kidneys play a crucial role in maintaining body homeostasis through blood filtration and the excretion of metabolic waste products (Guyton

& Hall, 2021; Stockham & Scott, 2008). Impaired kidney function can hinder the elimination of waste substances and xenobiotics from the body (Schnellmann, 2008). Serum creatinine is a commonly used indicator of renal filtration function because it is produced at a relatively constant rate from muscle metabolism and excreted primarily through glomerular filtration (Perrone et al., 1992). Elevated serum creatinine levels generally indicate a reduction in glomerular filtration capacity and are frequently used as an early marker of renal dysfunction (Levey et al., 2009).

One medicinal plant widely utilized as both a food source and traditional remedy in Indonesia is Gedi leaf *(Abelmoschus manihot* (L.) Medik.) (Lunga, 2016). This plant grows extensively in eastern Indonesia, particularly in North Sulawesi, and has long been consumed as a vegetable and herbal beverage by local communities (Heyne, 1987; Pandiangan, 2020). Traditionally, Gedi leaves are frequently consumed by women during pregnancy and the postpartum period because they are believed to promote recovery and support breast milk production (Lunga, 2016).

Previous studies have demonstrated that *Abelmoschus manihot* contains flavonoids, phenolic compounds, polysaccharides, and other secondary metabolites with antioxidant and anti-inflammatory properties (Kumar & Pandey, 2013; Panche et al., 2016). These biological activities may provide protective effects against tissue damage through the inhibition of oxidative stress and inflammatory processes (Li et al., 2019). Several studies have also reported the beneficial effects of *A. manihot* in various pathological conditions, including metabolic disorders and tissue injuries associated with oxidative stress (Zhang et al., 2020). However, most of these investigations have focused on extracts or purified fractions derived from dried leaves (Pandiangan et al., 2025; Pasaribu et al., 2023; Pandiangan et al., 2026), and information regarding the safety of fresh Gedi leaf decoction, particularly its effects on liver and kidney function, remains limited. Research on *Abelmoschus manihot* has predominantly emphasized its pharmacological activities and therapeutic potential rather than the safety evaluation of target organs following repeated consumption (Klaassen & Watkins, 2015).

Furthermore, most studies have employed organic solvent extracts or flavonoid-rich fractions that do not fully represent the form in which the plant is commonly consumed by the public (Pandiangan, 2020). To date, studies evaluating hepatic and renal responses to fresh Gedi leaf decoction based on SGOT and creatinine biomarkers are still scarce (Gu & Manautou, 2012).

This knowledge gap highlights the need for further investigation into the safety profile of Gedi leaf when consumed in its traditional preparation form (WHO, 2013).

The novelty of the present study lies in its specific evaluation of liver and kidney responses to fresh Gedi leaf decoction prepared using a traditional decoction method (Bruschi, 2012). Furthermore, the study employs SGOT as a biomarker of liver function and serum creatinine as an indicator of kidney function, providing a more specific assessment of the effects of consumption on the major organs involved in metabolism and excretion (Hall, 2021; Levey et al., 2009). Therefore, this study aimed to evaluate the effects of fresh Gedi leaf decoction (*Abelmoschus manihot* (L.) Medik.) on liver and kidney function in female white rats (*Rattus norvegicus*) through the measurement of serum SGOT and creatinine levels (Stockham & Scott, 2008; Guyton & Hall, 2021). The findings are expected to provide scientific evidence regarding the safety of Gedi leaf consumption and contribute to the toxicological data necessary to support its use as a traditional herbal remedy and functional food (Heinrich et al., 2018; Zhang et al., 2020).

MATERIALS AND METHODS

Study Period and Location

The study was conducted from October to November 2025 at the Biovina Laboratory, Sea Mitra, Pineleng District, Minahasa Regency, North Sulawesi, Indonesia. All experimental procedures, including animal maintenance, treatment administration, sample collection, and observation, were carried out under controlled laboratory conditions to ensure environmental consistency throughout the study (Suckow et al., 2019; National Research Council, 2011). Serum SGOT and creatinine analyses were performed using a Biosystems BTS-350 Semi-Automatic Analyzer (BioSystems S.A., Spain) following standard clinical laboratory procedures (Tietz et al., 2018).

Study Design

This study was a laboratory-based experimental investigation employing a quantitative approach to evaluate the effects of fresh Gedi leaf decoction (*Abelmoschus manihot* (L.) Medik.) on liver and kidney function in female rats (*Rattus norvegicus*) (Friedman et al., 2015; Montgomery, 2017). A post-test-only control group design was used, as it is commonly applied in preclinical toxicological studies to minimize baseline measurement bias and improve the validity of experimental outcomes (Festing, 2006). Randomization was

performed to ensure a homogeneous distribution of animals between experimental groups (Vogel & Vogel, 2013).

Experimental Animals

Fourteen healthy, non-pregnant female Wistar rats aged 8–10 weeks and weighing 160–280 g were used in this study. Prior to treatment, the animals were acclimatized for seven days to stabilize their physiological conditions (National Research Council, 2011). During the experimental period, rats were housed individually under controlled environmental conditions and provided with standard laboratory feed and drinking water ad libitum in accordance with laboratory animal welfare guidelines (Suckow et al., 2019). Following acclimatization, the animals were randomly assigned into two groups consisting of seven rats each. The control group received distilled water, whereas the treatment group received fresh Gedi leaf decoction as the primary source of drinking fluid throughout the study period (Bruschi, 2012; Pandiangan, 2020).

Preparation of Fresh Gedi Leaf Decoction

Fresh Gedi leaves (*Abelmoschus manihot* (L.) Medik.) were harvested from the fourth to eighth leaves below the shoot apex. The leaves were washed thoroughly under running water to remove dirt and contaminants, air-dried, and cut into approximately 1-cm pieces (WHO, 2007). The decoction was prepared using a traditional decoction method with a plant material-to-solvent ratio of 1:10 (w/v), following procedures commonly employed in herbal and phytochemical studies (Heinrich et al., 2018). The mixture was boiled for 30 minutes to facilitate optimal extraction of bioactive compounds. The resulting liquid was filtered and allowed to cool before administration to the experimental animals (Bruschi, 2012).

Treatment Administration

The control group received distilled water, while the treatment group received fresh Gedi leaf decoction (*Abelmoschus manihot* (L.) Medik.) as the sole source of drinking fluid ad libitum for 40 consecutive days (Bruschi, 2012; WHO, 2013). Continuous access to fluids was provided without volume restriction to maintain normal physiological conditions throughout the exposure period, consistent with standard preclinical toxicological protocols (Klaassen & Watkins, 2015; Suckow et al., 2019). Daily observations were conducted to monitor the general clinical condition of the animals as an initial screening for potential systemic effects during treatment (Suckow et al., 2019). Parameters observed included spontaneous activity, behavioral responses, physical appearance (including fur condition), and patterns of feed and

fluid consumption as non-invasive indicators of animal health status (Klaassen & Watkins, 2015). All animal husbandry procedures were performed under controlled environmental conditions to minimize external variability and ensure experimental consistency (National Research Council, 2011; Suckow et al., 2019).

Serum Creatinine Analysis (Kidney Function)

Serum creatinine concentration was measured as an indicator of kidney function. The normal reference range for serum creatinine in healthy rats is 0.2–0.8 mg/dL (Pandiangan et al., 2022). At the end of the treatment period, animals were anesthetized, and blood samples were collected via venipuncture using sterile syringes according to standard laboratory animal procedures. Blood samples were transferred into plain tubes without anticoagulants and allowed to clot at room temperature. After coagulation, the samples were centrifuged using a Hettich EBA 200 centrifuge to separate serum from cellular components. The obtained serum was subsequently analyzed for creatinine concentration using a Biosystems BTS-350 Semi-Automatic Analyzer (BioSystems S.A., Spain) following standard clinical laboratory procedures (Tietz et al., 2018).

Serum SGOT Analysis (Liver Function)

Serum Glutamic Oxaloacetic Transaminase (SGOT/AST) was measured as an indicator of liver function. The normal reference range for SGOT in healthy rats is 50–200 U/L (Pandiangan et al., 2022). Following anesthesia, blood samples were collected from the tail vein using sterile syringes according to standard laboratory animal procedures. The collected blood was transferred into plain tubes and allowed to clot at room temperature. Samples were then centrifuged using a Hettich EBA 200 centrifuge to obtain serum. Serum SGOT (AST) levels were subsequently measured using a Biosystems BTS-350 Semi-Automatic Analyzer (BioSystems S.A., Spain) according to standard clinical laboratory procedures (Tietz et al., 2018).

Statistical Analysis

Data were expressed as mean ± standard deviation (SD). Data normality was assessed using the Shapiro–Wilk test (Razali & Wah, 2011). Comparisons between groups were performed using an Independent Samples t-test with a 95% confidence level (Field, 2013). All statistical analyses were conducted using IBM SPSS Statistics software.

Ethical Approval

This study was approved by the Health Research Ethics Committee of the Manado Health Polytechnic, Ministry of Health, Indonesia (Approval No. DP.04.03/FXXX.28/568/2025). All procedures involving experimental animals were reviewed and approved by the ethics committee and conducted in accordance with laboratory animal welfare principles, the 3Rs principles (Replacement, Reduction, and Refinement), and applicable ethical guidelines for animal research. All experimental procedures complied with institutional guidelines for the care and use of laboratory animals and were designed to minimize discomfort and stress to the animals throughout the study.

RESULTS AND DISCUSSION

Kidney Function (Serum Creatinine) of Female Rats Following Administration of Fresh Gedi Leaf Decoction

Serum creatinine levels were measured in 14 female rats divided into two groups: a control group receiving distilled water and a treatment group receiving fresh Gedi (*Abelmoschus manihot* (L.) Medik.) leaf decoction, with seven animals in each group. Measurements were performed at the end of the 40-day treatment period. The control group exhibited a mean serum creatinine level of 0.74 ± 0.05 mg/dL, while the treatment group showed a mean value of 0.79 ± 0.07 mg/dL. Both values remained within the normal reference range for rats (0.20–0.80 mg/dL). Although the treatment group demonstrated a 6.76% increase in serum creatinine compared with the control group, statistical analysis indicated that the difference was not significant ($p = 0.220$). As presented in Figure 1, rats receiving fresh Gedi leaf decoction exhibited slightly higher serum creatinine levels than the control group. However, all measured values remained within the normal physiological range, indicating that glomerular filtration and overall renal function were maintained throughout the experimental period. The absence of a significant increase in serum creatinine suggests that administration of fresh Gedi leaf decoction for 40 days did not adversely affect kidney function in female rats.

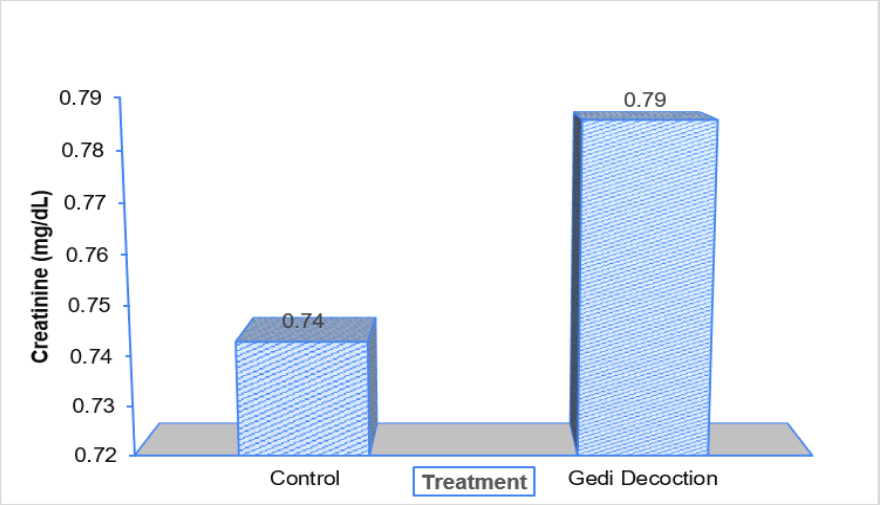


Figure 1: Comparison of serum creatinine levels (mg/dL) in female rats administered fresh Gedi leaf (*Abelmoschus manihot* (L.) Medik.) decoction and the control group.

Table 1: Distribution of Serum Creatinine Levels (mg/dL) in Female Rats from the Control and Treatment Groups Following Administration of Fresh Gedi Leaf Decoction for 40 Days.

Group	n	Creatinine (mg/dL) Mean ± SD	Normal Range (mg/dL)	p-value	% Change	T Test Statistic
Control	7	0.74 ± 0.05	0.20–0.80	0.220	Reference	Normal
Treatment (fresh Gedi decoction)	7	0.79 ± 0.07	0.20–0.80	–	+6.76%	Not Significant

Effect of Gedi Leaf Decoction on Kidney Function

Kidney function was evaluated using serum creatinine levels as an indicator of glomerular filtration rate (GFR). Creatinine is a commonly used parameter for assessing renal function because it reflects the kidney's ability to excrete metabolic waste products derived from muscle metabolism (Perrone et al., 1992; Levey et al., 2009).

Based on the study results (Figure 1), the mean serum creatinine level in the treatment group receiving Gedi leaf decoction was 0.79 ± 0.07 mg/dL, slightly higher than that of the control group (0.74 ± 0.05 mg/dL). Although an increase of 6.76% was observed, the difference was not statistically significant ($p = 0.220$). Furthermore, all measured values remained within the normal physiological range for rats (0.20–0.80 mg/dL), indicating that renal filtration function was maintained under normal conditions.

Physiologically, elevated serum creatinine levels are generally associated with reduced glomerular filtration resulting from structural or functional impairment of nephrons (Guyton & Hall, 2021). However, no evidence of such impairment was observed in the present study. Therefore, the findings suggest that administration of Gedi leaf decoction did not induce detectable nephrotoxic effects based on biochemical assessment.

The stability of serum creatinine levels in the treatment group may be associated with the bioactive compounds present in Gedi leaves, particularly flavonoids and polyphenols, which possess potent antioxidant properties. These compounds are known to reduce oxidative stress and maintain redox homeostasis, thereby protecting renal tissue from oxidative damage (Panche et al., 2016; Li et al., 2019). In addition, the anti-inflammatory activity of *Abelmoschus manihot* may provide further renal protection through suppression of inflammatory mediators that contribute to kidney tissue injury (Zhang et al., 2020).

The absence of a significant increase in serum creatinine levels following 40 days of treatment suggests that fresh Gedi leaf decoction did not adversely affect renal function in female rats. These findings support the safety of traditional Gedi leaf consumption and indicate that the decoction preparation used in this study does not impair kidney filtration capacity under the tested conditions. Liver Function (SGOT) in Female White Rats Following Administration of Gedi Leaf Decoction Serum SGOT (AST) levels were measured in fourteen female white rats equally divided into control and treatment groups. The assessment was conducted after 40 days of treatment administration.

The control group exhibited a mean serum SGOT level of 199.86 ± 59.62 U/L, whereas the treatment group showed a mean value of 159.00 ± 26.06 U/L. Although the treatment group demonstrated a 20.44% reduction in SGOT levels compared with the control group, the difference was not statistically significant ($p = 0.120$). All measured values remained within the normal reference range for rats (50–250 U/L).

As presented in Figure 2, rats receiving fresh Gedi (*Abelmoschus manihot* (L.) Medik.) leaf decoction tended to exhibit lower SGOT levels than those in the control group. However, the absence of a statistically significant difference and the maintenance of SGOT values within the normal physiological range indicate that liver function was not adversely affected by the treatment. These findings suggest that administration of fresh Gedi leaf decoction for 40 days did not induce hepatocellular damage in female rats.

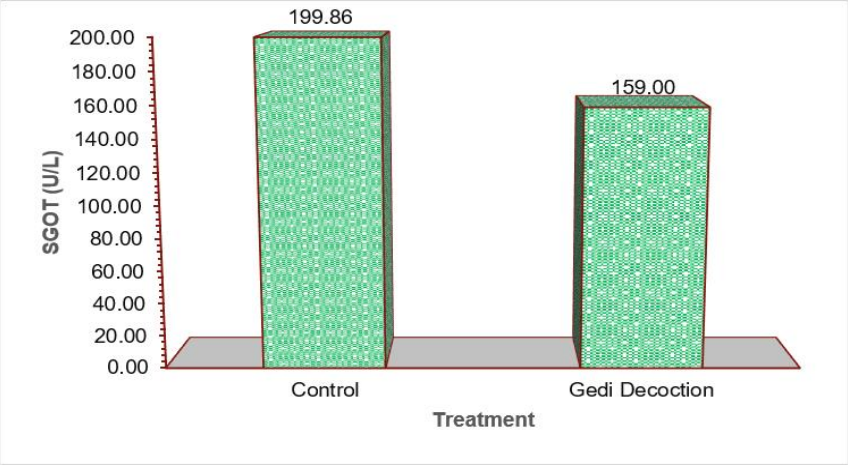


Figure 2: Comparison of serum SGOT (AST) concentrations (U/L) between female white rats receiving fresh Gedi (*Abelmoschus manihot* (L.) Medik.) leaf decoction and the control group after 40 days of treatment.

Table 2: Distribution of Serum SGOT (AST) Levels in Female White Rats of the Control and Treatment Groups After 40 Days of Gedi Leaf Decoction Administration (Median, IQR, Value Range, Normal Range, and Percentage Change Analysis).

Group	n	SGOT (U/L) Mean ± SD	Normal Range (U/L)	p-value	% Change	T-Test Statistic
Control	7	199.86 ± 59.62	50–250	0.120	Reference	Normal
Treatment (fresh Gedi decoction)	7	159.00 ± 26.06	50–250	–	−20.44%	Not Significant

Effect of Gedi Leaf Decoction on Liver Function

Liver function in this study was evaluated through serum SGOT (AST) levels as an indicator of hepatocellular integrity. SGOT is a transaminase enzyme that increases in circulation when hepatocyte membrane damage occurs and is therefore widely used as a biomarker of liver injury (Giannini et al., 2005; Klaassen & Watkins, 2015).

Based on the study results (Figure 2), the mean serum SGOT level in the treatment group was 159.00 ± 26.06 U/L, which was lower than that observed in the control group (199.86 ± 59.62 U/L). Although a 20.44% reduction in SGOT levels was observed in the treatment group, the difference was not statistically significant ($p = 0.120$). Furthermore, all measured values remained within the normal physiological range for rats (50–250 U/L), indicating that administration of Gedi leaf decoction did not impair liver function as assessed by SGOT measurement.

Consistent with these findings, no marked increase in SGOT levels was observed in Figure 2, suggesting the absence of significant hepatocyte membrane disruption. From a toxicological perspective, this finding indicates that exposure to Gedi leaf decoction did not induce meaningful hepatocellular injury.

In studies involving xenobiotic exposure, elevated SGOT levels generally reflect hepatocellular damage associated with oxidative stress and inflammatory responses (Klaassen & Watkins, 2015; Gu & Manautou, 2012). Conversely, the lower SGOT levels observed in the treatment group may be associated with the flavonoids and other bioactive compounds present in Abelmoschus manihot, which possess antioxidant properties. These compounds are known to inhibit lipid peroxidation and maintain hepatocyte membrane stability (Panche et al., 2016; Kumar & Pandey, 2013).

Furthermore, the anti-inflammatory properties of *Abelmoschus manihot* have been reported to modulate inflammatory mediators, thereby potentially exerting hepatoprotective effects and supporting the maintenance of liver tissue integrity (Zhang et al., 2020; Li et al., 2019). The maintenance of SGOT concentrations within the normal physiological range further supports the absence of hepatotoxic effects following 40 days of fresh Gedi leaf decoction administration.

Safety Implications of Gedi Leaf Decoction Consumption

Overall, the results of this study demonstrated that administration of fresh Gedi leaf decoction for 40 days did not cause significant alterations in either liver or kidney function. Both SGOT and serum creatinine levels remained within their normal physiological ranges, indicating the absence of systemic toxicity (Suckow et al., 2019; Klaassen & Watkins, 2015). The use of a decoction preparation in this study reflects the traditional mode of consumption practiced by local communities, thereby enhancing the practical relevance of the findings (Heinrich et al., 2018). In the context of herbal standardization, evaluating preparations that closely resemble real-world consumption patterns is important for generating biologically relevant safety data (Pandiangan et al., 2022). Therefore, under the conditions of the present study, consumption of fresh Gedi leaf decoction appeared to be relatively safe with respect to liver and kidney function in female white rats. Nevertheless, a limitation of this study is the absence of histopathological examination. Consequently, microscopic tissue alterations could not be fully assessed, despite the normal SGOT and creatinine values observed (Klaassen & Watkins, 2015; Suckow et al., 2019).

CONCLUCION

Administration of Gedi leaf (*Abelmoschus manihot* (L.) Medik.) decoction for 40 days did not produce significant changes in serum glutamic oxaloacetic transaminase (SGOT) or serum creatinine levels in female white rats (*Rattus norvegicus*) compared with the control group ($p > 0.05$). Furthermore, all SGOT and creatinine values remained within normal physiological ranges, indicating no evidence of liver or kidney dysfunction following treatment. These findings suggest that consumption of fresh Gedi leaf decoction is safe for liver and kidney function in female rats under the conditions of this study.

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REFERENCES

1. Bigliardi, B., & Galati, F. (2013). Innovation trends in the food industry: The case of functional foods. *Trends in Food Science & Technology, 31*(2): 118–129.
2. Bruschi, M. L. (2012). *Strategies to develop herbal medicines: Standardization, formulation, and pharmacological approaches*. Springer.
3. Bruschi, P. (Ed.). (2012). *Plants as a source of medicinal compounds*. Bentham Science Publishers.
4. Ekor, M. (2014). The growing use of herbal medicines: Issues relating to adverse reactions and challenges in monitoring safety. *Frontiers in Pharmacology, 4*: 177.
5. Festing, M. F. W. (2006). Guidelines for the design and statistical analysis of experiments using laboratory animals. *ILAR Journal, 43*(4): 244–258. https://doi.org/10.1093/ilar.43.4.244
6. Field, A. (2013). *Discovering statistics using IBM SPSS Statistics* (4th ed.). Sage Publications.
7. Friedman, L. M., Furberg, C. D., DeMets, D. L., Reboussin, D. M., & Granger, C. B. (2015). *Fundamentals of clinical trials* (5th ed.). Springer.

8. Giannini, E. G., Testa, R., & Savarino, V. (2005). Liver enzyme alteration: A guide for clinicians. *Canadian Medical Association Journal, 172*(3): 367–379. https://doi.org/10.1503/cmaj.1040752
9. Gu, X., & Manautou, J. E. (2012). Molecular mechanisms underlying chemical liver injury. *Expert Reviews in Molecular Medicine, 14:* e4. https://doi.org/10.1017/erm.2012.2
10. Guyton, A. C., & Hall, J. E. (2021). *Textbook of medical physiology* (14th ed.). Elsevier.
11. Hall, J. E. (2021). *Guyton and Hall textbook of medical physiology* (14th ed.). Elsevier.
12. Hasler, C. M. (2002). Functional foods: Benefits, concerns and challenges. *The Journal of Nutrition, 132*(12): 3772S–3781S. https://doi.org/10.1093/jn/132.12.3772S
13. Heinrich, M., Barnes, J., Gibbons, S., & Williamson, E. M. (2018). *Fundamentals of pharmacognosy and phytotherapy*. Elsevier.
14. Heyne, K. (1987). *Tumbuhan berguna Indonesia* (Vol. 1–3). Yayasan Sarana Wana Jaya.
15. Klaassen, C. D., & Watkins, J. B. (2015). *Casarett & Doull's essentials of toxicology* (3rd ed.). McGraw-Hill Education.
16. Kumar, S., & Pandey, A. K. (2013). Chemistry and biological activities of flavonoids: An overview. *The Scientific World Journal, 2013;* 162750. https://doi.org/10.1155/2013/162750
17. Levey, A. S., Stevens, L. A., Schmid, C. H., Zhang, Y. L., Castro, A. F., Feldman, H. I., … & Coresh, J. (2009). A new equation to estimate glomerular filtration rate. *Annals of Internal Medicine, 150*(9): 604–612. https://doi.org/10.7326/0003-4819-150-9-200905050-00006
18. Li, S., Yuan, W., Deng, G., et al. (2019). Anti-inflammatory and antioxidant effects of flavonoids. *Food Chemistry, 277:* 1–12.
19. Lunga, P. K. (2016). Antimicrobial steroidal saponin and oleanane-type triterpenoid saponins from *Abelmoschus manihot*. *Phytochemistry Letters, 16*: 39–43. https://doi.org/10.1016/j.phytol.2016.02.001
20. Montgomery, D. C. (2017). *Design and analysis of experiments* (9th ed.). Wiley.
21. National Research Council. (2011). *Guide for the care and use of laboratory animals* (8th ed.). National Academies Press. https://doi.org/10.17226/12910
22. Panche, A. N., Diwan, A. D., & Chandra, S. R. (2016). Flavonoids: An overview. *Journal of Nutritional Science, 5:* e47. https://doi.org/10.1017/jns.2016.41
23. Pandiangan, D. (2020). Antioxidant and quality test of 'Pasote' leaf tea products in tea bag packaging to be used as functional drinks. *Patent S00201909051*.

24. Pandiangan, D., & Nainggolan, N. (2021). PKM for women's empowerment in Biovina herbal MSMEs for improvement of drying of BPOM standard herbal raw materials. *JPAI: Jurnal Perempuan dan Anak Indonesia, 3*(1): 22. https://doi.org/10.35801/jpai.3.1.2021.36745
25. Pandiangan, D., Nainggolan, N., & Kandou, F. (2018). Effectiveness of Sambote extract on decreasing blood glucose levels of male white rats (*Rattus norvegicus*) induced with sucrose. *International Journal of Scientific Research*.
26. Pandiangan, D., Nusa, A., Maramis, R. T. D., Nainggolan, N., Maabuat, P. V., Tumbol, M. V. L. 2025. Total serum immunoglobulin G levels in female Wistar rats administered Abelmoschus manihot. World Journal of Pharmacy and Pharmaceutical Sciences, 14(8): 495–507. https://doi.org/10.20959/wjpps20258-30411.
27. Pandiangan, D., Kaeng, M. M. J., Lamba'Pareken, D., Katili, D., Nainggolan, N., Tumbol, M. V. L., & Pongoh, J. (2026). *Safety evaluation of dried gedi (Abelmoschus manihot L.) leaf brewed water based on urinalysis parameters in postpartum female Rattus norvegicus*. International Journal for Multidisciplinary Research, 8(3): https://doi.org/10.36948/ijfmr.2026.v08i03.80357
28. Pandiangan, D., Nainggolan, N., & Nainggolan, I. (2022). Standardization of Raw Materials for Traditional Medicinal Plants: Preclinical Tests Based on BPOM Regulations. CV. Patra Media Grafindo, Manado, 203.
29. Perrone, R. D., Madias, N. E., & Levey, A. S. (1992). Serum creatinine as an index of renal function. *Clinical Chemistry, 38*(10): 1933–1953.
30. Razali, N. M., & Wah, Y. B. (2011). Power comparisons of Shapiro–Wilk, Kolmogorov–Smirnov, Lilliefors and Anderson–Darling tests. *Journal of Statistical Modeling and Analytics, 2*(1): 21–33.
31. Schnellmann, R. G. (2008). Toxic responses of the kidney. In C. D. Klaassen (Ed.), *Casarett & Doull's toxicology* (7th ed.). McGraw-Hill.
32. Stockham, S. L., & Scott, M. A. (2008). *Fundamentals of veterinary clinical pathology* (2nd ed.). Blackwell Publishing.
33. Suckow, M. A., Hankenson, F. C., Wilson, R. P., & Foley, P. L. (2019). *The laboratory rat* (3rd ed.). Academic Press.
34. Tietz, N. W., Rifai, N., & Horvath, A. R. (2018). *Tietz fundamentals of clinical chemistry and molecular diagnostics* (8th ed.). Elsevier.
35. Vogel, H. G., & Vogel, W. H. (2013). *Drug discovery and evaluation: Pharmacological assays* (3rd ed.). Springer.

36. World Health Organization. (2007). *WHO guidelines for assessing quality of herbal medicines with reference to contaminants and residues*. WHO.
37. World Health Organization. (2013). *WHO traditional medicine strategy 2014–2023*. WHO Press.
38. Zhang, H., et al. (2020). Pharmacological activities of *Abelmoschus manihot*: A review. *Phytomedicine, 76*: 153–xxx.