

DENTINO
JURNAL KEDOKTERAN GIGI
Vol X. No 1. MARCH 2025

**TOXICITY TEST OF KELAKAI LEAF EXTRACT (*Stenochlaena palustris*)
TOWARD WISTAR RATS LIVER (*Rattus norvegicus*)**

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ABSTRACT

Background: Kelakai leaf extract can be used as an alternative wound healing medicine because it contains flavonoid and phenolic compounds that act as antioxidants. Before use, herbal plants must ensure the level of safety that can be obtained from toxicity tests, one of which is *in vivo* which can be seen from their effect on the liver of Wistar rats based on SGOT and SGPT levels. **Purpose:** Proving there is no toxic effect from the administration of kelakai leaf extract doses of 2,000, 2,500, and 3,000 mg/kgBW on the liver of Wistar rats based on SGOT and SGPT levels. **Method:** Pure laboratory experimental research with posttest-only design with control group design, consisting of 16 wistar rats divided into 4 groups with 1 negative control group given distilled water and 3 treatment groups given doses of kelakai leaf extract 2,000, 2,500 and 3,000 mg/kgBW twice a day every morning and evening for 28 days. **Results:** SGOT and SGPT levels after 28 days were still in the normal range. SGOT levels in treatment groups 1, 2, and 3 were 61.244 U/L, 58.953 U/L, and 53.536 U/L. SGPT levels in treatment groups 1, 2 and 3 were 25.137 U/L, 23.331 U/L, and 21.179 U/L. Based on statistical tests, there were significant differences in all treatment groups. **Conclusion:** There is no toxic effect from the administration of kelakai leaf extract doses of 2,000, 2,500, 3,000 mg/kgBW orally for 28 days on the liver of Wistar rats based on SGOT and SGPT levels.

Keywords: Kelakai leaf extract, Liver, SGOT, SGPT, Toxicity

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INTRODUCTION

South Kalimantan is a province in Indonesia that has great biodiversity, one of which is the kelakai plant.¹ Dayak and Banjar ethnic communities often use kelakai plants as their favorite food and traditional medicinal contents. Kelakai leaves are the part of the kelakai plant that is often used. This part is believed to be beneficial as a youth medicine, blood enhancer supplement, lowers high blood pressure, lowers fever, increases maternal milk, itching and allergy medicine.² Based on the results of phytochemical tests, secondary metabolite substances contained in kelakai leaves include flavonoids, phenolics, alkaloids, tannins, steroids, and terpenoids.³

Flavonoids and phenolics are contents in kelakai that act as antioxidant agents. The leaves of kelakai have a flavonoid content of 503.56 mg QE/g and phenolics of 252.32 mg GAE/g.⁴ Flavonoids are secondary metabolite substances with a variety of biological activities, such as inhibiting the formation of free radical substances. While phenolics are efficient natural antioxidants, so they play an important role in the prevention of many diseases, such as cardiovascular disease, aging, and effective cleaning of reactive oxygen species (ROS).^{2,3,5} Antioxidants play a role in reducing ROS levels so that it will increase the ability of tissues to regenerate, so that wound healing will be induced.⁶ According to regulations from the Food and Drug Administration, for the development of drugs, besides having evidence of their effectiveness, preclinical trials are also required.⁷

Preclinical tests are used to examine materials from nature that may have potential as drugs. Toxicity test is one form of preclinical testing. Toxicity tests can be conducted in vitro and in vivo.⁸ In vivo toxicity tests can be conducted on experimental animals that are useful to determine physiological, biochemical and pathological reactions before their use in humans.^{7,9} In vivo toxicity tests are divided into acute, subchronic and chronic. Subchronic toxicity tests can be conducted to test the degree of toxicity of an herbal product given in repeated doses with several dose levels for 28 days.¹⁰ The purpose of this test is to determine the dose that has no toxic effects or No Observed Adverse Effect Level (NOAEL), to see the toxic effects of an ingredient after repeated exposure, and to study the cumulative effects and reversibility. One of the excretory organs that can be tested for toxicity is the liver.¹¹

The liver is an important organ in the body's metabolic process. The metabolized compounds by the liver are fats, proteins, iron, drugs and other substances. Compounds that get into the body will be detoxed by the liver. However, the liver also has the risk of being damaged/hepatotoxic.¹² One indicator that can be used to determine the existence of damage to the liver is by measuring the levels of transaminase enzymes, such as *Serum Glutamic Oxaloacetic Transaminase* (SGOT) and *Serum Glutamic Pyruvic Transaminase* (SGPT).¹³ The increase in transaminase enzyme levels is caused by liver cells that have been damaged or necrotized so that this enzyme will move from liver cells to the blood circulation. The levels of SGOT and SGPT enzymes in normal blood are low because these enzymes are located in liver cells. If liver cell damage has occurred, it will increase the levels of SGOT and SGPT in the blood above normal.^{12,14}

The study on toxicity tests on kelakai leaf extract has previously been conducted in an in vitro test on BHK-21 fibroblast cells by Farida (2021). The results of this study show that kelakai leaf extract at concentration of 40%, 50%, 60%, 70%, 80%, and 90% have no toxic effect on BHK-21 fibroblast cells.¹⁵ Based on this, it is important to conduct in vivo research about the toxicity test of kelakai leaf extract on the liver of Wistar rats based on SGOT and SGPT levels with doses of 2,000 mg/kgBW, 2,500 mg/kgBW, and 3,000 mg/kgBW to see how toxic effects through blood biochemical tests for 28 days.

METHODS

This toxicity test research has received a license from the Ethics Committee of the Faculty of Dentistry, Lambung Mangkurat University with the number 093/KEPKG-FKGULM/EC/VIII/2023. The preparation of kelakai leaf extract, treatment of wistar rats, and toxicity tests were located at the Biochemistry Laboratory, Faculty of Medicine, Lambung Mangkurat University and the determination test of kelakai plants at the Basic Laboratory, Faculty of Mathematics and Natural Sciences, Lambung Mangkurat University.

The method used is pure experimental (true experimental design) using posttest-only with control group design to test the toxic effects of the giving of kelakai leaf extract doses of 2,000, 2,500, and 3,000 mg/kgBW on the liver of Wistar rats based on SGOT and SGPT levels given orally for 28 days. The number of samples for each group of wistar rats was taken using the analytical comparative numerical unpaired formula so that 4 rats were obtained in each group.

Table 1. Table of Test Animal Groups

Group	Treatment	Samples
K	Aquades	4
P1	Kelakai leaf extract doses of 2.000 mg/kgBW	4
P2	Kelakai leaf extract doses of 2.500 mg/kgBW	4
P3	Kelakai leaf extract doses of 3.000 mg/kgBW	4
Total		16

Materials and Tools for Research

The materials used are mature leaves of dark green kelakai which have a rigid texture with a length of about 5-7 cm and a width of 1-2 cm, 96% ethanol, distilled water, potassium dichromate ($K_2Cr_2O_7$), male wistar rats (*Rattus norvegicus*) aged 8-12 weeks with a weight of 200-250 grams, ketamine-xylazine for anesthesia and euthanasia in wistar rats, 70% alcohol for preparation of tools, reagent measuring kit Human brand for blood biochemical analysis of SGOT and SGPT, cotton swabs, injection syringes, eppendorf, vacutainer, BR2 standard wistar rat food material, rat drink in the form of distilled water, and husk for cage mats.

The tools used are extractor, WH40 filter paper, analytical balance (Precisa), erlenmeyer flask (Iwaki), blender (Phillips), shaker, oven, rotary vacuum evaporator (Heidolp), waterbath (SMIC), Genesys 20 UV-Vis spectrophotometer, test tube, centrifuge, vortex, gastric probe and 3 ml syringe.

Preparation of Kelakai Leaf Extract with Maceration Method

Kelakai leaf extract is made using the maceration method. A total of 20 kg of kelakai leaves were cleaned and then dried for 4 hours in the oven at 40°C, then blender until smooth. After that, the powder was sieved and dry sorted to get simplisia powder. This process produced as much as 8 kg of simplisia powder. Then the simplisia powder was diluted in 96% ethanol solvent as much as 25 liters. The dissolution was carried out for 3x24 hours and the ethanol solvent was replaced for each day. During the immersion, shaking was carried out using a shaker. After that, the ethanol solvent was evaporated using a vacuum rotary evaporator for 4-6 hours at a temperature of 50-60°C, after which it was placed on a waterbath until a viscous extract was produced. The results of this process produced 250 grams of viscous extract of kelakai leaves. Ethanol-free test using potassium dichromate ($K_2Cr_2O_7$) on 3 ml of viscous extract of kelakai leaves.

Preparation and Acclimatization of Test Animals

Test animals are weighed first to determine their body weight. Before acclimatization, test animals were grouped using the simple random sampling method. Each rat was given a number to be chosen, then the rats were put into 4 groups, each group contained 4 rats. A population of 16 wistar rats were adapted to the laboratory situation for 1 week. The rat cage size was 60 x 40 x 35 cm made of plastic with a wire netting cover, so it was easy to remove and clean. The cage floor was covered with chaff and replaced every 2 days. Rats were given BR2 feed as much as 20% of the rat's body weight or about 40 grams (for rats with a body weight of 200 grams) and drinking water was given in a 500 ml bottle with a small pipe and filled with distilled water. This treatment was the same for all groups of test animals.

Animal Treatments and Toxicity Tests

Before treatment, rats were fasted for approximately 6 hours with the purpose of minimizing the effect of food consumed by the test animals on the absorption of the extract to be given. Rats were taken randomly and given kelakai leaf extract at doses of 2,000, 2,500, and 3,000 mg/kgBW orally twice in the morning and evening for 28 days each giving 1 ml. After that, the test animals were sacrificed on the 29th day for intracardial blood collection. Then the levels of SGOT and SGPT enzymes were measured by the kinetic-IFCC method using a spectrophotometer. The data obtained were then subjected to statistical analysis using SPSS.

RESULTS

The data of SGOT and SGPT levels that have been obtained were tested for normality (Shapiro-Wilk) and homogeneity test (Levene's Test), then One Way Anova test and Bonferroni post hoc to determine significant differences between all groups. All data were statistically analyzed using SPSS.

Table 2. Average Results of SGOT and SGPT Levels of Wistar Rats with Standard Deviation.

Group	Mean $\pm$ Std. Deviation (U/L)	
	SGOT	SGPT
K	63,883 $\pm$ 0,277	36,552 $\pm$ 0,377
P1	61,244 $\pm$ 0,661	25,137 $\pm$ 0,532
P2	58,953 $\pm$ 1,386	23,331 $\pm$ 0,456
P3	53,536 $\pm$ 0,616	21,179 $\pm$ 0,616

The results of the normality test (Shapiro-Wilk) on SGOT and SGPT data show the significance value of all groups has a p value more than equal to 0.05 ($p \geq 0.05$) which means the data is normally distributed. The results of the homogeneity test (Levene's Test) of SGOT and SGPT levels show a significance value of p more than 0.05 ($p > 0.05$) so the data is homogeneous. Based on this, SGOT and SGPT data can be continued with the One-Way Anova test. One-Way Anova test of SGOT and SGPT levels showed a significance value of 0.000 ($p < 0.05$) which means there is a significant difference at minimum in one treatment group so it is required to continue the Bonferroni post hoc test.

Table 3. Bonferroni Post Hoc Test SGOT Levels

	K	P1	P2	P3
K		0,005*	0,000*	0,000*
P1	0,005*		0,013*	0,000*
P2	0,000*	0,013*		0,000*
P3	0,000*	0,000*	0,000*	

Description:

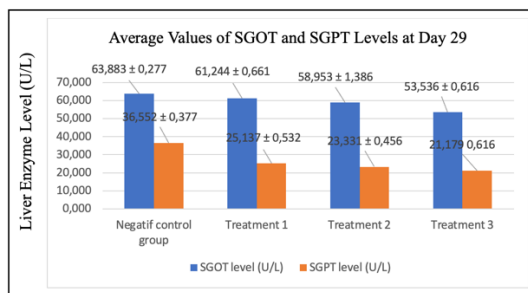
Sign * : There is a significant difference ($p < 0.05$)**Table 4.** Bonferroni Post Hoc Test SGPT Levels

	K	P1	P2	P3
K		0,000*	0,000*	0,000*
P1	0,000*		0,002*	0,000*
P2	0,000*	0,002*		0,000*
P3	0,000*	0,000*	0,000*	

Description:

Sign * : There is a significant difference ($p < 0.05$)

Based on tables 3 and 4, the Bonferroni post hoc test shows that the significance value of all groups is ($p < 0.05$), which mean that there are significant differences between all groups in SGOT and SGPT data.

**Figure 1.** Diagram of Average SGOT and SGPT Levels of Wistar Rats at day 29

Based on Figure 1, the highest value of SGOT levels is found in the negative control group (63.883 U/L) compared to the treatment group given kelakai leaf extract (P1 = 61.244 U/L; P2 = 58.953 U/L; P3 = 53.536 U/L). SGOT levels decreased as the dose of kelakai leaf extract given increased. The highest value of SGPT levels was also found in the negative control group (36.552 U/L) compared to the treatment group given kelakai leaf extract (P1 = 25.137 U/L; P2 = 23.331 U/L; P3 = 21.179 U/L). Similar to SGOT, SGPT levels decreased as the dose of kelakai leaf extract given increased.

DISCUSSION

The results of this study showed that the average SGOT value in the negative control group was 63.883 U/L; the treatment group giving kelakai leaf extract was 61.244 U/L for treatment 1; 58.953 U/L for treatment 2; and 53.536 U/L for treatment 3. Based on this, the SGOT value decreased significantly with increasing doses of kelakai leaf extract and was significantly different from the control group. This value is still in the normal range of SGOT which is 50-150 U/L so it can be assumed that it does not indicate a toxic effect.¹⁶

The average SGPT value in the control group was 36.552 U/L; the treatment group giving kelakai leaf extract was 25.137 U/L for treatment 1; 23.331 U/L for treatment 2; and 21.179 U/L for treatment 3. Similar to the SGOT value, the SGPT value decreased significantly with increasing doses of kelakai leaf extract and was significantly different from the control group. This value is still in the normal range of SGPT which is 10-40 U/L so it can also be assumed that it does not indicate a toxic effect.¹⁶

Based on these results, it shows that the doses of kelakai leaf extract 2,000 mg/kgBW, 2,500 mg/kgBW, and 3,000 mg/kgBW do not have a toxic effect on the liver and even with increasing doses of kelakai leaf extract can decrease SGOT and SGPT levels. SGOT and SGPT levels are used as measurements because the quantities are proportional to the condition of the liver, the higher their quantity in the blood circulation, it is certain that there has been severe damage in the liver. The results of this in vivo study are in line with previous toxicity test research, which is in vitro kelakai leaf extract against Baby Hamster Kidney fibroblast

cells (BHK-21) conducted by Farida (2021) that at concentrations of 40%, 50%, 60%, 70%, 80%, and 90% showed no toxic effects.^{14,15}

Decrease in SGOT and SGPT levels in the treatment group along with the addition of doses of kelakai leaf extract is due to the availability of secondary metabolites, namely flavonoids and phenolics which have the greatest antioxidant activity. Based on the results of the phytochemical test, kelakai leaves contain flavonoids of 503.56 mg QE/g and phenolics of 252.32 mg GAE/g.⁴ This is supported by research by Ilyas (2017) which states that ethanol extract of galing leaves (*Cayratia trifolia* L. Domin) is able to reduce SGOT and SGPT levels in white rats along with the increase in the concentration of galing leaf extract. The largest antioxidant activity shown by the ethanol extract of galing leaves is in the form of flavonoid compounds.¹⁷ Wahyuni's research (2018) also proved that *Moringa oleifera* leaf extract was able to decrease SGOT levels in white rats along with the addition of the dose given. The greatest antioxidant activity in moringa leaf extract is indicated by the availability of flavonoids and phenolic compounds.¹⁸ The activity of compounds that can play a part in decreasing SGOT and SGPT levels to provide protection to the liver from damage is known as the hepatoprotector effect.¹⁹

The hepatoprotector effect in this study is directly proportional to the dose of treatment, which can be characterized by the higher the dose of kelakai leaf extract given, the higher the inhibition of damage to the liver so that there is a decrease in SGOT and SGPT levels. The hepatoprotector activity shown is due to the presence of antioxidant activity in form flavonoids and phenolic compounds, where the higher the levels, the higher the antioxidant ability.¹⁹

The increase in SGOT and SGPT enzyme levels is caused by the presence of toxic substances that enter the body and are metabolized in the liver into free radical substances by cytochrome P450 enzymes. These free radicals bind to liver cells and change the permeability of cell membranes, causing damage or can even cause necrosis of liver cells.²⁰ This condition causes an increase in the transfer of SGOT and SGPT enzymes from liver cells to the bloodstream, so that their levels will increase above normal limits.²¹ The mechanism of action of antioxidants is to stop the reaction of free radicals by transferring their electrons, thus preventing chain reactions of fat and protein peroxidation. Flavonoids and phenolic compounds are known to have antioxidant activity through their mechanisms as free radical scavengers, reducers, absorbers of singlet oxygen formation as well as electron donors and metal ion chelators. Therefore, both flavonoids and phenolics play an important role in reducing Reactive Oxygen Species (ROS) through their activity as antioxidants.²²

Flavonoids are able to protect liver cell membrane lipids from damage due to oxidation processes by various mechanisms, such as suppressing the formation of ROS by binding to elements involved in the process of free radical formation, free radical capture (scavenging), and maintaining the defense of antioxidants.^{23,24} The antioxidant mechanism of flavonoid compounds is to inhibit lipid peroxidation caused by radical substances such as R•, RO•, and ROO•. Another antioxidant mechanism of flavonoids is by reducing ROS or radical compounds such as •OH, •O₂⁻, ¹O₂ through hydrogen atom transfer or electron donation. Flavonoids inhibit lipid peroxidation by free radicals, thus preventing changes in cell membrane structure. Sustained lipid peroxidation can also destroy DNA, proteins, and cell enzyme activity, leading to cell death.²³

Phenolics have many hydroxyl groups and aromatic rings that function as peroxy radical catchers. The activity of phenolic structures depends on the many -OH groups that will neutralize free radicals. Phenolic (ArOH) can stop the initiation reaction of free radicals through the transfer of hydrogen atoms to form phenoxyl radical cations (Ar•OH⁺). Phenoxyl radical (Ar•OH⁺) will release its proton and immediately form phenoxyl radical (ArO•). Then the phenoxyl radical will capture the peroxy radical (ROO•) which is radical and form a more stable compound.²³

Flavonoids and phenolics can also work by increasing the activity of endogenous antioxidant enzymes such as *Superoxide dismutase* (SOD), *Glutathione peroxide* (GPx), and *Catalase* (CAT).²⁵ Both activate *Nuclear factor erythroid 2-related factor 2* (Nrf2) in the cell cytoplasm which binds to *Kelch ECH associating protein 1* (Keap 1). Nrf2 can release its bond with Keap 1 when there is an overload of oxidative stress. Activated Nrf2 will go to the cell nucleus and bind to *Antioxidant Responsive Element* (ARE), thus inducing the formation of the endogenous antioxidant enzyme. SOD plays a role in catalyzing superoxide anion (O₂⁻) into stable oxygen (O₂) and hydrogen peroxide (H₂O₂). Then, CAT and GPx enzymes together catalyze H₂O₂ into O₂ and H₂O.^{23,25}

The residual H₂O₂ compounds that have not been catalyzed can also potentially bind to transition metals such as Fe²⁺ and Cu⁺ so that they will form more reactive hydroxyl radicals (OH•). Flavonoids and phenolics also play an important role by transferring hydrogen ions (H⁺) to hydroxyl radicals so that H⁺ turns into H₂O which will cause a decrease in ROS.²³ The decrease in ROS will not cause liver cell damage

and SGOT and SGPT enzymes also do not migrate excessively so that their levels will be low in the blood circulation.^{20,21}

Based on this, this study can show that there is no toxic effect from the administration of kelakai leaf extract (*Stenochlaena palustris*) doses of 2,000 mg/kgBW, 2,500 mg/kgBW, and 3,000 mg/kgBW on the liver of Wistar rats (*Rattus norvegicus*) based on SGOT and SGPT levels given orally for 28 days. Kelakai leaf extract with these concentrations can also act as a hepatoprotector by reducing SGOT and SGPT levels along with the increase in the dose of kelakai leaf extract given.

REFERENCES

1. Mahdiyah D, Sari A, Palimbo A, Vidia Sari P, Al Kahfi R, Nurdin F. Pemanfaatan Kekayaan Hayati Lokal: Teh Fermentasi dari Kelakai (*Stenochalena palustris*) Sebagai Produk Kewirausahaan. *Jurnal Pengabdian Al-Ikhlas*. 2021;7(1):124–30.
2. Siswanto Syamsul E, Yunita Hakim Y, Nurhasnawati H. Penetapan Kadar Flavonoid Ekstrak Daun Kelakai (*Stenochlaena palustris* (Burm.F.) Bedd.) dengan Metode Spektrofotometri UV-Vis. *Jurnal Riset Kefarmasian Indonesia*. 2019;1(1):11–20.
3. Ndanusa H, Cicuzza D, Siddique MM. Analysis of The Phytochemical Contents and Anti-oxidative Properties of *Stenochlaena palustris*. *International Food Research Journal*. 2020;27(5):798–804.
4. Chear NJY, Khaw KY, Murugaiyah V, Lai CS. Cholinesterase inhibitory activity and chemical constituents of *Stenochlaena palustris* fronds at two different stages of maturity. *Journal of Food and Drug Analysis*. 2016;24(2):358–66.
5. Yanti MN, Rahmawati I, Herdwiani W. Uji Aktivitas Sitotoksik Herba Kelakai (*Stenochlaena palustris* (Burm.F.) Bedd.) Terhadap Sel Kanker Hati HEPG2. *Jurnal Bioteknologi dan Biosains Indonesia*. 2021;8(2):255–66.
6. Ardiana T, Kusuma ARP, Firdausy MD. Efektivitas Pemberian Gel Binahong (*Anredera cordifolia*) 5% Terhadap Jumlah Sel Fibroblast pada Soket Pasca Pencabutan Gigi Marmut (*Cavia cobaya*). *Odonto Dental Journal*. 2015;2(1):64–70.
7. Nida' HK, Sjakoeer NAA, Mubarakati NJ. Uji Toksisitas Subkronik 28 Hari Ekstrak Metanolik kombinasi Daun Benalu Teh dan Benalu Mangga terhadap fungsi Hepar Pada Tikus (*Rattus norvegicus*) Betina. *Jurnal Biosaintropis (Bioscience-Tropic)*. 2022;7(2):15–26.
8. Tarukbua Y, Queljoe E De, Bodhi W. Skrining Fitokimia dan Uji Toksisitas Ekstrak Etanol Daun Brotowali (*Tinospora crispa* (L.) Hook F. & T) dengan Metode *Brine Shrimp Lethality Test* (BSLT). *Jurnal Ilmiah Farmasi Pharmacoon*. 2018;7(3):330–7.
9. Nurviana V, Purwandi Sukmawan Y, Fauzan Roeswanto G. Toksisitas Sub Kronik Fraksi Etil Asetat Biji Limus (*Mangifera foetida lour.*) Terhadap Hepar dan Ginjal pada Tikus Putih Galur Wistar. *Journal of Pharmacopolium*. 2022;5(2):199–204.
10. BPOM RI. *Pedoman Uji Toksisitas Praktikum In Vivo*. Jakarta: BPOM. 2022;8–12.
11. Rachmawati E, Ulfa EU. Uji Toksisitas Subkronik Ekstrak Kayu Kuning (*Arcangelisia flava Merr*) terhadap Hepar dan Ginjal. *Jurnal Global Medical and Health Communication*. 2018;6(1):1–6.
12. Nurfatwa M. Uji Toksisitas Akut Ekstrak Buah Okra (*Abelmoschus esculatus L.Moench*) terhadap Parameter Kadar SGOT dan SGPT serta Histopatologi Hepar Tikus Galur Wistar. *Journal of Pharmacopolium*. 2018;1(2):88–93.
13. Yuneldi RF, Saraswati TR, Yuniwati EYW. Profile of SGPT and SGOT on Male Rats (*Rattus norvegicus*) Hyperglycemic After Giving Insulin Leaf Extract (*Tithonia diversifolia*). *Journal of Biology & Biology Education*. 2018;10(3):519–25.
14. Kresnadipayana D, Herawati Subianto R, Faradilla R. Efek Subkronik Pemberian Ekstrak Etanol Kunyit (*Curcuma domestica* Val) Terhadap Hati Tikus Galur Wistar dengan Pemeriksaan SGOT dan SGPT. *Jurnal Biotek Medisiana Indonesia*. 2019;8(1):77–85.
15. Farida, Firdaus IWAK, Apriasari ML. Toxicity Test of Kelakai Leaves Extract (*Stenochlaena palustris* (Burm) Bedd) to BHK-21 Fibroblast Cells In Vitro. *Malaysian Journal of Medicine and Health Sciences (Proceedings of the 3rd International Conference Brawijaya Dentistry on October 8th-10th 2021)*. 2021;17(1).
16. Hasan KMM, Tamanna N, Haque MA. Biochemical and Histopathological Profiling of Wistar Rat Treated with *Brassica napus* as a Supplementary Feed. *Food Science and Human Wellness*. 2018;7(1):77–82.
17. Ilyas M, Muthmainnah A, Parawansah P. Efek Hepatoprotektor Ekstrak Etanol Daun Galing (*Cayratia trifolia* L.Domin) pada Tikus Putih (*Rattus norvegicus*). *Jurnal Warta Farmasi*. 2017;6(1):19–27.
18. Wahyuni DW, Widiyanti NLPM, Ristiati NP. Analisis Ektrak Daun Kelor (*Moringa oleifera* L.) sebagai Pengawet Alami Ikan Cakalang Terhadap Kadar Serum *Glutamic Oxaloacetic Transaminase* (SGOT) Tikus Putih (*Rattus norvegicus*) Galur Wistar Jantan. *Jurnal Pendidikan Biologi Undiksha*. 2018;5(2):100–12.
19. Yusuf MI, Tee SA, Karmila K, Jabbar A. Efek Hepatoprotektor Ekstrak Terpurifikasi Batang Galing (*Cayratia trifolia* L.Domin) Pada Tikus Putih Wistar Jantan (*Rattus norvegicus*). *Jurnal Mandala Pharmacon Indonesia*. 2018;4(1):13–9.
20. Wahyudi A, Bahar Y, Septianawati P. Pengaruh Ekstrak Etanol Daun Kemangi (*Ocimum basilicum* L folium) Terhadap Kadar SGOT dan SGPT Tikus Putih (*Rattus norvegicus* strain wistar) yang Diinduksi MSG. *Herb-Medicine Journal*. 2018;1(1):30–9.

21. Dinana A, Latipudin D, Darwis D, Mushawwir A. Profil Enzim Transaminase Ayam Ras Petelur yang Diberi Kitosan Iradiasi. *Jurnal Nutrisi Ternal Tropis dan Ilmu Pakan*. 2019;1(1):6–11.
22. Nur S, Sami FJ, Awaluddin A, Afsari MIA. Korelasi Antara Kadar Total Flavonoid dan Fenolik dari Ekstrak dan Fraksi Daun Jati Putih (*Gmelina Arborea Roxb.*) Terhadap Aktivitas Antioksidan. *Jurnal Farmasi Galenika (Galenika Journal of Pharmacy) (e-Journal)*. 2019;5(1):33–42.
23. Salwa IN, Firdaus IWAK, Azizah A. Uji Toksisitas Ekstrak Kulit Batang Ulin (*Eusideroxylon zwageri*) Terhadap Sel Fibroblas BHK-21 Secara *In Vitro*. *Jurnal Kedokteran Gigi Dentin*. 2021;5(3):148–53.
24. Arum BG, Firdaus IWAK, Oktiani BW. Toxicity Test of Ironwood Bark Extract (*Eusideroxylon zwageri*) Toward Wistar Rats Kidney (*Rattus norvegicus*). *Dentino Jurnal Kedokteran Gigi*. 2023;8(1):47–52.
25. Apriasari ML, Sari TIP, Firdaus IWAK. Toxicity test of *Stenochlaena palustris* extract based on kidney histopathology examination. *Dental Journal Majalah Kedokteran Gigi*. 2023;56(3):178–83.