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HEPATOTOXIC TEST OF BURDOCK ROOTS (*Arctium lappa L*) ON HISTOPATHOLOGY HEPAR OF MALE WHITE RATS (*Rattus norvegicus*)

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Abstract

Burdock (*Arctium lappa L*) is a homologous medical plant that is considered having with many advantages as a traditional medicine. Burdock root contains several substances such as inulin, essential oils, tannins, quercetin,iron, and arctigenin. This study was conducted to determine investigates effect of burdock root extract on the hepar histopathology of male white rats. This study used an experimental method with 20 rats and was divided into 4 groups. The positive control group was given gentamicin induction intramuscularly. The negative control group was given distilled water. The 150 mg/kgBW dose group and the 450 mg/kgBW dose group were given burdock root extract with treatment for 14 days and surgery was performed oin the 15th day to take hepatic organs to make histopathology preparations. The results of the this study were are interpreted by scoring and tabulated, the analysis was is done carried out descriptively with the results, in positive control group found mild damage, the negative group found no damage, in the extract dose group 150mg/kgBW found necrosis, bleeding and vacuolization, and in the extract dose group 450mg/kgBW found degeneration, necrosis, bleeding and vacuolization. The conclusion of this study is the hepatoprotective potential of burdock root extract *(Arctium lappa L.)* and its related effects on liver tissue in an experimental model. On the other hand, parasitic worms *Taenia taeniaeformis* were found in the liver which interfered with the interpretation of the results.

Keywords: *Burdock Root Extract (Arctium Lappa L); Hepar; Histopathology; Toxic.*

1. Introduction

Almost every country in the world has accepted the use of herbal medicine. The use of herbal medicine is quite popular widespread, one of which is in Indonesia, where Indonesia is one of the countries that has abundant natural resources in the form of plants that can be utilized as herbal medicines where herbal medicine enthusiasts in Indonesia are still high. One of the plants that are widely spread in Indonesia and considered to have potential as herbal medicine is the burdock plant (*Arctium lappa L*). The plant with the scientific name *Arctium lappa L* or commonly referred to as mainly called burdock, is a family of *Asteraceae* plants that grow abundantly, especially Asia. Burdock plants are popular around the world is famous worldwide because it can be utilized in all its parts. of the burdock plant can be utilized. Burdock roots have several chemical compounds such as inulin, essential oils, tannins, resins, sugars, iron, calcium, quercetin, arctigenin, and vitamin C. Burdock root has traditionally has been used for treating infectious diseases much as sore throats, boils, rashes and various other skin disorders for human (Gurunanselage Don & Yap, 2019). Chemical compound analysis was conducted through phytochemical tests, revealing that burdock roots contain saponins, flavonoids, alkaloids, and tannins, which exhibit antibacterial, antipyretic, anti-inflammatory, and antioxidant properties (Anindita, 22 C.E.) Furthermore, burdock root is known to contain arctin, lignan, and chlorogenic acid molecules, which play a role in increasing transferrin levels in cases of anemia (Jiang et al., 2019; Ogun & Adeyinka, 2022).

The utilization of burdock roots (*Arctium*

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lappa L.) is focused on the roots which have various ingredients that can be antioxidants that function as free radicals and have potential as hepatoprotectors. Burdock roots are made into extracts and then induced in the appropriate treatment group of rats to determine the activity against hepatotoxicity with histopathological examination as an indicator, (Fauziah, 2021). This study uses experimental animals to avoid undesirable things when tested on humans and ensure that the compounds contained and used in this study are entirely safe for humans. According to previous research conducted by (Ahangarpour et al., 2017) that burdock root has hypoglycemic properties and antioxidant effects, and has been is used for the in traditional medicines to treatment of diabetes. in traditional medicines. The study showed that the *Arctium lappa L* root extract, has anti-diabetic effects through hypolipidemic and insulinotropic in a dose-specific manner, properties in a dose-specific manner, has anti-diabetic effects through hypolipidemic and insulinotropic properties. Therefore, this plant extract may be beneficial for the treatment of diabetes. Therefore, this plant extract may be useful helpful in the treatment of diabetes. Burdock plants that are likely to be used as traditional medicine have the potential to be consumed in the short or long term, this it will definitely cause side effects on the organs in the human body if consumed in the ong term with improper dosage, and one of these organs is the hepar hepar. Hepar in the human body functions to neutralize toxins. The causes of damage to hepatic cells include drugs, viruses, and several other compounds that are hepatotoxic compounds (Fitriani et al., 2021).

The hepar damage caused by toxic substances is influenced by a few factors, such as the dose given, the type of chemical substance, the length of exposure to the substance such as acute subchronic or chronic, and the higher the concentration/dose of the compound given, an even more toxic response.

One hepatotoxic or hepar-damaging agent caused by reactions from the accumulation of harmful substances in the hepar system is gentamicin. Gentamicin is the prototypical antibiotic of the aminoglycoside class, a bactericidal drug, this aminoglycoside gentamicin is often used and is known to be toxic to the kidneys and hepar. One such hepatotoxic agent or hepatic damaging agent caused by causing a reaction due to the accumulation of toxic substances in the hepatic system is gentamicin. Gentamicin is a prototype of the aminoglycoside class which is a bactericidal drug and gentamicin is an aminoglycoside that is often used and is known to be toxic to the kidneys (Muda et al., 2020). The study of burdock root is lackingneeds to be improved, therefore this study was conducted to find concrete evidence to determine the potential of burdock root extract against hepatotoxicity with supporting examination of hepatic histopathology in male white rat test animals.

2. Method

Methods used in this research are quasy experimental with etchical no 114/KEPK/PE/VIII/2023. Using 20 male white rats divided into 4 groups with each group totaling 5 rats, and given gentamicin antibiotics 100mg by intramuscular injection for the positive control group, given aquadest for the negative control group and given burdock root extract preparations orally for the 150 mg/ kgBW dose group and the 450 mg / kgBW dose group, and for 14 days then performed surgery, observed hepar histopathology. Data analysis was derived from examination data that had been tabulated and subjected to obtained from tabulated examination data and analyzed descriptively qualitative. The study was conducted for 6 months from December 2023 to May 2024. The research was conducted in the laboratory of the faculty of pharmacy, science and technology, Al-Irsyad University, Cilacap, from making extracts to dissecting experimental animals, and making preparations at BLUD RSUD R. A Kartini Jepara The research started with the preparation of burdock root extract by maceration method for 3 days. Then the determination of the dose of the drug medicament is divided into 2 groups, namely the dose of 150mg / kgBW and 450mg / kgBW which will be given for 14 days in the form of as a suspension solution using a 0.9% CMC-Na mixture orally. The next stage is the preparation of test animals, group division is carried out with Federer's calculation, divided into 4 groups with information: Group 1 (positive control): given gentamicin 100mg induction, Group 2 (negative control): given aquadest, Group 3 (low dose): was given a dose of 150 mg/kg BW extract Group 4 (high dose): given an extract dose of 450 mg / kg BW extract. Make sure the test animals weigh 200-350gr and are 2-3 months old. with acclimatization for 7 days before being given treatment. During the 14-day treatment, rats were fed 2 times a day adlibitum, and drank adlibitum. Rat cages were cleaned every 2 days. After 14 days, the rats were dissected on the 22nd day from the time of 7 days of acclimatization and 14 days of treatment. Before being dissected, the experimental animals were first killed by cervical dislocation (neck dislocation), accompanied by a veterinarian. The surgery was accompanied by a veterinarian and the test animals were euthanized (killed) by cervical dislocation (neck

dislocation), if it was felt that the test animals were lifeless, the test animals were immediately dissected and the hepatic organs were taken and the hepatic organs were inserted into the urine cup containing 10% NBF solution to make histopathological preparations.

Histopathology preparations were examined under a microscope each at 8 microscopic field of view. Examination with a microscope was carried out with 100x magnification then continued with 400x magnification (Swarayana et al., 2012). The changes observed were the presence of fatty degeneration, vacuolization, necrosis, and inflammatory cell infiltration. Histopathology preparations were observed and scored to obtain quantitative data.

The scoring system employed for evaluating histopathological damage is as follows: a score of 0 indicates no histopathological damage, a score of 1 corresponds to focal damage categorized as mild, a score of 2 represents multifocal damage classified as moderate, and a score of 3 reflects diffuse damage, indicating severe pathology. This scoring method is adapted from the criteria established by Darmayanti et al. (2020).

3. Result and Discussion

Table 1. Characteristics of experimental animals before and after treatment

Sample characteristics	Before treatment			
	Positive Control	Negative Control	Dose 150mg/kg BW/day	Dose 450mg/kg BW/day
Rat species and strain	*Rattus Norve-Gicus*	*Rattus Norve-Gicus*	*Rattus Norve-gicus*	*Rattus Norve-Gicus*
Sex	Males	Males	Males	Males
Quantity of rats	5	5	5	5
Color	White	White	White	White
General condition	Move actively, healthy	Move actively, healthy	Move actively, healthy	Move actively, healthy
Sample character-istics	After treatment			
	Positive Control	Negative Control	Dose 150mg/kg BW/day	Dose 450mg/kg BW/day
Rat species and strain	*Rattus Norve-gicus*	*Rattus Norve-gicus*	*Rattus Norve-gicus*	*Rattus Norve-Gicus*
Sex	Males	Males	Males	Males
Quantity	2	3	4	3
Color	White brownish	White brownish	White brownish	White brownish
General condition	Move actively	Move actively	Move actively	Move actively

Active movement = Animals are always movinginquisitively

Healthy = The fur is clean, smooth and shiny, there are no fleas, the eyeballs look pink and clear, the mouth does not salivate continuously, the consistency of the feces is normal and solid, not liquid (Solihah & Haris, 2019).

Table 2. Interpretation of Hepar Organ Damage on Hematoxilin Eosin (HE) Staining Results

Group	observed parameter score					
	Degeneration (microsteatosis)	Necrosis	Blockage of blood vessels	Hemorrhage	Vacuolization	Desc.
Positive control	0	1.5	0	0	1.5	Worms found In hepar
Negative control	0	0	0	0	0	Worms found In hepar
Dose 150mg/ kgBW /day	0	1.80	0	2.4	3.00	Worms found In hepar
Dose 450mg/ kgBW /day	3,00	3.00	0	2.25	2.25	Worms found In hepar

Score description:
0= no damage
1= mild
2= moderate
3= severe

In Table 2. in positive control group found signs of necrosis and vacuolization with a damage score of 1.5 from the damage score obtained it can be said that the positive control group suffered minor damage because the score of 1.5 entered into score 1. mild damage was found in other damage parameters such as degeneration, blockage of blood vessels or bleeding no change or damage occurred. While in the negative control no changes or damage to hepatic cells were found as seen from the score obtained in all parameters of damage is 0. Changes in hepatic cells occurred at a dose of 150mg / kgBW / day did not occur cell changes such as degeneration and blockage of blood vessels, but in this dose group there were changes in hepatic cells in the form of necrosis with a score of 1.80 where the score is still included in the score 1 which means the damage is mild. As for the bleeding damage that occurs in the 150mg/kgBW/day dose group with the damage score is 2.4, the value included in moderate damage and the severest damage in this group is that the hepatic cells experience vacuolization with a damage score of 3.00 which means the level of damage is severe. After being observed in Table 2, the higher the dose given, the greater the damage score obtained, this can be seen in the 450mg/kgBW/day dose group where the damage parameters occur degeneration and necrosis with a score of 3 which means that the damage is severe, and the bleeding and vacuolization damage obtained a score of 2.25 which means that the damage is included in the moderate group. However, in the four groups all get results in the form of the discovery of worms in the hepatic organ and it affects the results obtained.

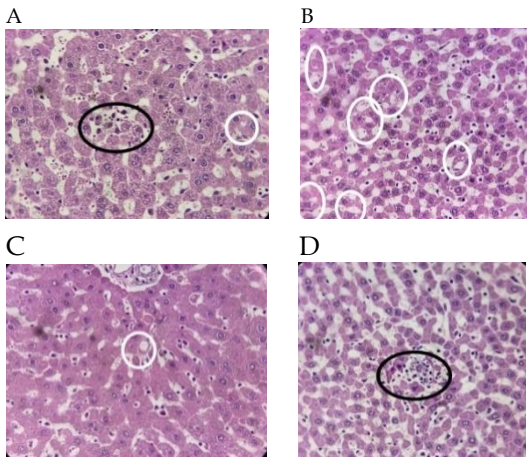

Figure 1. *Results of Microscopic Examination of HE Painting Group 1 Positive Control (Gentamicin), magnification 400x focal necrosis (black circle), degeneration (white circles)*

In the results of Figure 1. microscopic examination of hepatic tissue with Hematoxilin Eosin (HE) painting of the positive control group induced by gentamicin, it was found that there was focal necrosis marked with black circles in figures A and D. There was also degeneration marked in white circles in figures A, B, and C.

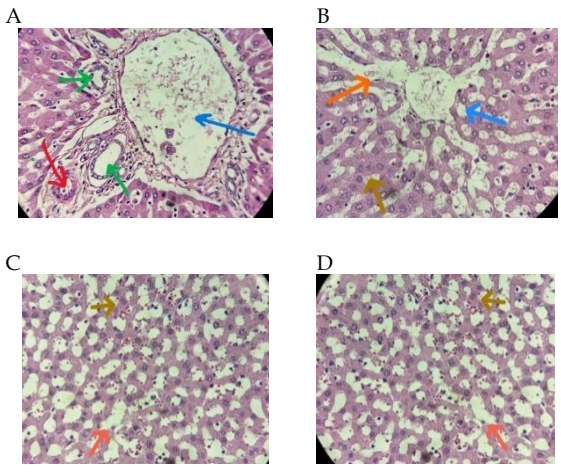

Figure 2. *Results of Microscopic Examination of HE Painting Group 2 Negative Control, magnification 400x The portal segment consists of the portal vein (blue arrow), ductus biliaris (green arrow) and artery hepatica (red arrow). Vena centralis (blue arrow), sinusoids (orange arrow) that separate hepatic cell plates (brown arrow).*

In the results of microscopic examination of hepatic tissue with Hematoxilin-Eosin (HE) painting of the negative control group which was only given distilled water.aquadest alone found in this group what was seen is Segita portal consisting of portal vein (blue arrow),mductus biliaris (green arrow) and artery hepatica red arrow in Figure A. Vena centralis (blue arrow), sinusoid (orange arrow) which separates the hepatic cell plate (brown arrow) in Figure B. Sinusoid (orange arrow), hepatic cells (brown arrow) in Figure C and D. In this group, no damage was found in the experimental animals, where this group was a negative control group so that during the study period they were not given gentamicin antibiotics or burdock root extract.

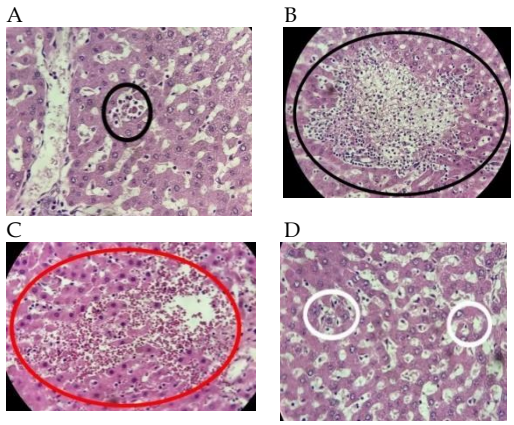

Figure 3. *Results of Microscopic Examination of HE Painting Group 3 Dose 150mg/kgBW/day, magnification 400x focal necrosis (black circles) degeneration (white circles) and hemorrhage (red circles)*

In the results of microscopic examination of hepatic tissue with Hematoxilin-Eosin (HE) painting of the 150mg / kgBW dose group found focal necrosis marked with black circles in Figure A and B, found degeneration marked with white circles in Figure D and the presence of bleeding marked with red circles in Figure C.

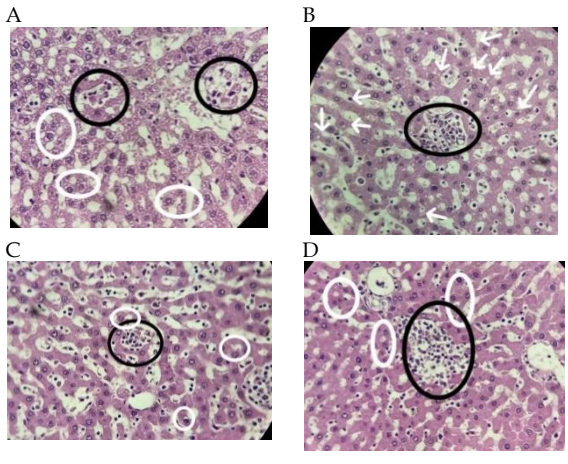

Figure 4. *Results of Microscopic Examination of HE Painting Group 4 Dose 450mg/kgBW/day , magnification 400x focal necrosis (black circle), degeneration (white circles)*

In the results of microscopic examination of hepatic tissue with Hematoxilin-Eosin (HE) painting of the 450mg/kgBW/day extract dose group found focal necrosis marked with black circles in pictures A, B, C and D. There was also d Degeneration marked in white circles in figures A, B, C and D and there was extensive degeneration in figure B marked with white arrows. The damage that occurred in this group was the same as the positive control group, that is focal necrosis and degeneration, extensive

degeneration marked with white arrows and no hemorrhage was found as in the 150mg / kgBB dose group, but the damage value that occurred in this group was greater than the 150mg / kgBB group.

The results of microscopic observation of hepatic histopathology of male white rats from the positive control group, negative control, 150mg / kgBW dose, and 450mg / kgBW dose showed some hepatic tissue damage. This is not only related to toxic substances and important for human survival, but also where toxic substances are metabolized and concentrated. The damage seen with the difference in mean interpretation can be seen in Table 2.

Basically every chemical substance must have toxic properties and every poisoning is determined by the dose and method of administration if given continuously or given in excessive doses, the chemical substance will be toxic. Many factors can be used to determine whether the substance is toxic, but the dose is the most important factor, to determine the substance is toxic. The toxic effect is due to the biochemical interaction between the toxicant in the extract and the cells in the organ (Nofrian & Wijayahadi, 2017). Cell damage that occurs is also likely to be caused by the environmental conditions of rats both from cages, food given to test animals that experience stress levels, and other internal factors that are thought to be a factor in the occurrence of hepatic cell damage in experimental animals (Melisa et al., 2022).

From these microscopic observations we know the histopathological picture and changes that occur in the hepatic organs of experimental animals using 400x magnification which can be seen in figures 1, 2, 3, and 4. And in the scoring results in table 2 and the microscopic picture it can be concluded that the greater the dose given, the greater the hepatic damage that occurs in experimental animals. From these microscopic observations we know the histopathological picture and changes that occur in the hepatic organs of experimental animals using 400x magnification which can be seen in figures 1, 2, 3, and 4. And in the scoring results in table 2 and the microscopic picture it can be concluded that the greater the dose given, the greater the hepatic damage that occurs in experimental animals. Burdock root *(Arctium lappa L.)* is known to have a variety of active compounds, including arctigenin, inulin, flavonoids, and polyphenols, which exhibit antioxidant and anti-inflammatory activity. This study is relevant to evaluate the hepatoprotective potential of burdock root against hepar damage induced by gentamicin, an antibiotic that can cause oxidative stress and inflammation in the hepar (Faizal, Puspodewi, et al., 2024). Burdock's Potential Mechanism Eliminates Gentamycin which is known to trigger the accumulation of reactive oxygen species (ROS), lower glutathione levels (GSH), and increase the activity of inflammatory enzymes such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Compounds in burdock root, such as arctigenin, are able to reduce Oxidative Stress: The antioxidant activity of flavonoids and polyphenols increases GSH levels and superoxide dismutase (SOD) activity, as well as lowers lipid peroxidation in hepar tissue, Suppresses Inflammation: Burdock can lower inflammatory mediators such as tumor necrosis factor-alpha (TNF-α) and interleukin-1β (IL-1β), as well as reduce cellular damage due to ROS. Research shows burdock is able to restore damaged histological structures of the hepar, including hepatocyte regeneration and microvascular repair (Dwi Saputri et al., 2023; Faizal, Irmansa, et al., 2024).

In this study, parasites were also found in the form of worms, suspected to be *T. taeniaeformis.* In this study also found parasites in the form of *T. taeniaeformis* worms. The *T. taeniaeformis* worm is a type of cestode worm that can live in the hepar of rats at the larval stage and *T. taeniaeformis* forms cysticerci inside or on the surface of the hepar (Lovitasari et al., 2021a). Some of the factors that cause this to happen are, Contamination of food, shelter, and water can cause pathogenic infections in laboratory animals, especially rats. Liver damage can be caused by toxic substances in burdock root doses and other factors such as the parasitic worm *Taenia taeniaeformis (T. taeniaeformis)* (Lovitasari et al., 2021b) This cestode worm lives in the liver at the larval stage, forming cysticerci. In this study, *T. taeniaeformis* worms were found in the all groups. Pathogen contamination through food, housing, and water can cause infections in laboratory animals, especially mice, transmitted via cat feces containing *T. taeniaeformis* eggs. Effective animal quarantine, health surveillance programs, and transportation safety measures are essential to control *T. taeniaeformis* infections during laboratory experiments (Wardani et al., 2021).

To control *T. Taeniaeformis* infection, animal quarantine programs for laboratory experiments, animal health surveillance programs, and transportation safety considerations are necessary (Chairunnisa et al., 2019). The biggest cause is the experimental animal managers did not have the facilities, equipment, skills, and good sanitation management, infection also spread. sanitation management, infections also spread. the study period.

4. Conclusion and Suggestion

The conclusion of this study is the hepatoprotective potential of burdock root extract *(Arctium lappa L.)* and its related effects on liver tissue in an experimental model. On the other hand, parasitic worms *Taenia taeniaeformis* were found in the liver which interfered with the interpretation of the results. There are several suggestions, such as explore dose variations to determine the optimal and safe dosage, ensure careful extraction processes and monitor the condition of test animals, use biochemical parameters to evaluate the therapeutic effects of burdock root, and conduct long-term studies to confirm the safety of consumption over time.

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6. References

Ahangarpour, A., Heidari, H., Oroojan, A. A., Mirzavandi, F., Nasr Esfehani, K., & Dehghan Mohammadi, Z. (2017). Antidiabetic, hypolipidemic and hepatoprotective effects of Arctium lappa root's hydro-alcoholic extract on nicotinamide-streptozotocin induced type 2 model of diabetes in male mice. *Avicenna Journal of Phytomedicine*, *7*(2), 169–179.

Anindita, B. (22 C.E.). *Potensi Nanoemulsi Ekstrak Akar Burdock (Arctium lappa L.) Sebagai Antibakteri Staphylococcus Aureus.* Universitas Al-Irsyad Cilacap.

Chairunnisa, S., Wartini, N. M., & Suhendra, L. (2019). Pengaruh Suhu dan Waktu Maserasi terhadap Karakteristik Ekstrak Daun Bidara (Ziziphus mauritiana L.) sebagai Sumber Saponin. *Jurnal Rekayasa Dan Manajemen Agroindustri*, *7*(4), 551. https://doi.org/10.24843/jrma.2019.v07.i04.p07

Darmayanti, M. D., Samsuri, S., Setiasih, N. L. E., & Berata, I. K. (2020). Kidney Histopathological Alteration of White Rats After 21 Days Consumed Tape Yeast. *Indonesia Medicus Veterinus*, *9*(6), 889–899. https://doi.org/10.19087/imv.2020.9.6.889

Dwi Saputri, R., Faizal, I. A., & Puspodewi, D. (2023). Hubungan Kadar Aspartate Aminotransferase (Ast) Dan Alanine Aminotransferase (Alt) Pada Penderita Demam Berdarah Dengue (Dbd) Di Rumah Sakit Islam Fatimah Cilacap. *Jurnal Pharmaqueous*, *6*(2), 122–127.

Faizal, I. A., Irmansa, J., Pangesti, I., Oktaviany, F., Avivah, A. avivah L., Oktafiani, D. P., & Yuniasari, S. D. (2024). Assessing the Therapeutic Potential of Arctium lappa L. (Burdock Root) Ethanol Extract in Wound Healing on Male Rattus norvegicus. *Jurnal Teknologi Laboratorium*, *13*(2), 8395. https://doi.org/10.29238/teknolabjournal.v13i2.417

Faizal, I. A., Puspodewi, D., & Aji, A. P. (2024). Uji Toksisitas Subkronik Nanoemulsi Akar Burdock (Arctium Lappa L.) Berdasarkan Histopatologi pada Tikus Albino Rattus noverticus (strain Wistar). *Indonesian Journal of Innovation Multidisipliner Research*, *2*, 331–342.

Fauziah. (2021). Uji Aktivitas Ekstrak Daun Samarinda (Carissa Carandas L.) Terhadap Histopatologi Ginjal Tikus Putih (Rattus Norvegicus L.) Hiperkolesterolemia. *NBER Working Papers*, 89.

Fitriani, N., Rif'ah, M., Aulia, R., & Hidayat, S. (2021). Studi Literatur Pengaruh Pemberian Beberapa Zat Terhadap Perubahan Struktur Hepar Tikus Putih (Rattus norvegicus) Dan Mencit (Mus musculus). *BIO EDUCATIO : (The Journal of Science and Biology Education)*, *6*(1), 25–29. https://doi.org/10.31949/be.v6i1.2629

Gurunanselage Don, R. A. S., & Yap, M. K. K. (2019). Arctium lappa L. root extract induces cell death via mitochondrial-mediated caspase-dependent apoptosis in Jurkat human leukemic T cells. *Biomedicine and Pharmacotherapy*, *110*(September 2018), 918–929. https://doi.org/10.1016/j.biopha.2018.12.023

Jiang, Y. yuan, Yu, J., Li, Y. bo, Wang, L., Hu, L., Zhang, L., & Zhou, Y. hong. (2019). Extraction and antioxidant activities of polysaccharides from roots of Arctium lappa L. *International Journal of Biological Macromolecules*, *123*, 531–538. https://doi.org/10.1016/j.ijbiomac.2018.11.087

Lovitasari, Mulyanto, A., & Ritma Dhanti, K. (2021a). The Effect Of Stratified Doses Of High Sugar Instant

Coffee On The Hepar Histologicalprofileof Wistar Rats Rattusnorvegicus. *Bioma : Jurnal Biologi Makassar*, *06*(02), 21–30.

Lovitasari, Mulyanto, A., & Ritma Dhanti, K. (2021b). The Effect Of Stratified Doses Of High Sugar Instant Coffee On The Hepar Histologicalprofileof Wistar Rats Rattusnorvegicus. *Bioma : Jurnal Biologi Makassar*, *06*(02), 21–30. http://journal.unhas.ac.id/index.php/bioma

Melisa, E., Muhaimin, Yuliawati, & K, F. S. (2022). Uji Toksistas Akut Ekstrak Etanol Daun Sungkai (Peronema cenescens Jack) Terhadap Fungsi Ginjal. *Majalah Farmasi Dan Farmakologi*, *26*(April), 32–37. https://doi.org/10.20956/mff.v26i1.19447

Muda, G. J., Arjana, A. A. G., Berata, I. K., & Merdana, I. M. (2020). Perubahan Histopatologi Hati Tikus Putih yang diberikan Ekstrak Etanol Sarang Semut dan Gentamisin. *Buletin Veteriner Udayana*, *9*(3), 7. https://doi.org/10.24843/bulvet.2020.v12.i01.p02

Nofrian, R. A., & Wijayahadi, N. (2017). Uji Toksisitas Akut Ramuan Ekstrak Produk X. *Jurnal Kedokteran Diponegoro*, *6*(2), 1134–1142.

Ogun, A. S., & Adeyinka, A. (2022). Biochemistry, Transferrin. In *National Library of Medicine* (Vol. 06, pp. 4–7). The National Center for Biotechnology Information. https://www.ncbi.nlm.nih.gov/books/NBK532928/#:~:text=The

Swarayana, I. M. I., Sudira, I. W., & Berata, I. K. (2012). Perubahan Histopatologi Hati Mencit (Mus musculus) yang Diberikan Ekstrak Daun Ashitaba (Angelica keiskei). *Buletin Veteriner Udayana*, *4*(2), 119–125.

Wardani, D. P. K., Dhanti, K. R., Mulyanto, A., & Sudarsono, T. A. (2021). Deteksi Endoparasit Cacing pada Hepar Tikus Laboratorium (Rattus norvegicus) dari Sentra Peternak di Kabupaten Banyumas dan Kabupaten Purbalingga. *Balaba: Jurnal Litbang Pengendalian Penyakit Bersumber Binatang Banjarnegara*, 119–126. https://doi.org/10.22435/blb.v17i2.4713