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Original Article

The Activity of Pegagan Embun Extract (*Hydrocotyle sibthorpioides* Lam.) in Capsule Form to SGPT and SGOT Levels in Humans

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ABSTRACT

Purpose: The study aimed to determine the activity of administering *Hydrocotyle sibthorpioides* Lam. extract in capsule dosage on SGPT and SGOT levels in humans. **Methods:** The participants involved 20 healthy volunteers aged 20-25 years who were divided into 2 groups with placebo as a comparison. The treatment groups were given capsules containing *Hydrocotyle sibthorpioides* Lam. extract at a dose of 67 mg. The other group administered a placebo containing lactose for 3 days. SGPT and SGOT levels were measured before and after consuming the test capsules. The examination of SGPT and SGOT levels was carried out using a 5010 v5+ photometer. **Results:** SGPT levels before the capsules were 28.79 U/L for the placebo and 28.59 U/L for the test preparation group. After administration of *Hydrocotyle sibthorpioides* Lam. extract capsules were 24.26 U/L and for placebo 32.86 U/L. At the same time, the measurement results of SGOT levels before being given the capsule were 17.37 U/L for the placebo and 17.71 U/L for the test preparation group. After administration of *Hydrocotyle sibthorpioides* Lam. extract capsules, it was 14.56 U/L and 18.52 U/L for placebo. The study results show that *Hydrocotyle sibthorpioides* Lam. extract significantly decreases SGPT and SGOT levels in humans ($p<0.5$). **Conclusion:** This result indicates that Hydrocotyle sibthorpioides Lam extract is relatively non-toxic and safe for public use as an immunostimulant herbal medicine.

Keywords: Ethanol extract of pegagan embun, *Hydrocotyle sibthorpioides* Lam, SGPT, SGOT, Toxicant.

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INTRODUCTION

Traditional medicine as an alternative treatment has been practised long before formal health services with modern medicines were available. However, the efficacy and safety of traditional medicine in Indonesia have not been scientifically tested. The assumption that traditional medicine is safe and far from side effects cannot be entirely accepted. Some things that need to be considered regarding traditional medicine are the accuracy of dosage, time and method of use, and accuracy of information review[1].

Hydrocotyle sibthorpioides Lam. is a plant that plays a vital role in Chinese herbal medicine. Chinese people of the Hakka ethnic group use it to treat several diseases, including adenolymphitis, shingles, and cholecystitis[2]. *Hydrocotyle sibthorpioides* Lam has several uses in medicine, such as for fever, oedema, detoxification, and relieving throat pain[3]. *Hydrocotyle sibthorpioides* Lam. is an effective antidiuretic for skin tumours and enhances phagocytic activity and immune function when applied externally[4].

The *Hydrocotyle sibthorpioides* Lam. contains genistein, polyphenol, flavonoid, and flavonol compounds. Genistein in *Hydrocotyle sibthorpioides* Lam. provides preventive effects and repairs fibrotic liver cells through chronic alcohol administration[5]. Polyphenol compounds are essential in stabilising lipid oxidation and are associated with antioxidant activity. In addition, polyphenolic compounds have inhibitory effects on mutagenesis and carcinogenesis[6]. The ethanol extract of *Hydrocotyle sibthorpioides* Lam. has immunostimulant activity, where the results of the study show that ethanol extract of *Hydrocotyle sibthorpioides* Lam. can increase antibody titers at doses of 10, 50, and 200 mg/kg BW against male white mice[7]. Another study related to the extract of *Hydrocotyle sibthorpioides* Lam. has pharmacological activity to improve the immune system, with doses of 10, 50, and 200 mg/kg BW showing immunostimulant effects through increased macrophage activity and capacity, total leukocyte count, lymphocyte percentage, and significantly reduced TNF-α and total macrophage levels tested in male white mice[8]. The comprehensive utilisation of *Hydrocotyle sibthorpioides* Lam. in the field of pharmacology, significantly as an immunostimulant, can also increase the activity of NK cells and CD8 cells[9], increase the number of erythrocytes, the number of reticulocytes, hematocrit values, and haemoglobin levels[10].

Previous studies have also been conducted related to acute and sub-acute toxicity tests of *Hydrocotyle sibthorpioides* Lam. extract, where the results obtained from the doses given, namely 7, 35, and 150 mg/kg BW to test animals, did not show damage to the histology of the liver and kidneys of male white mice[11]. It also showed that the lethal dose (LD_{50}) value for ethanol extract of *Hydrocotyle sibthorpioides* Lam. amounted to 128.83 g/kg BW. From the LD_{50} category, the ethanol extract of *Hydrocotyle sibthorpioides* Lam. belongs to the practically non-toxic range (LD_{50} >15,000 mg/kg BW). Moreover, in previous studies, creatinine clearance and SGOT and SGPT levels after administration of *Hydrocotyle sibthorpioides* Lam. extract to test animals also had no toxic effects[12-13].

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The liver is often the target of toxicants because most toxicants enter the body through the gastrointestinal system and are absorbed, then carried to the liver by the portal vein. However, the liver has enzyme activity that can metabolise the toxicant to make it less toxic; if the toxicant level is too high, it can cause damage or death of liver cells[14]. Damage to liver cells due to toxicant levels that are too high can trigger an increase in Serum Glutamic Pyruvate Transaminase (SGPT) and Serum Glutamic Oxaloacetic Transaminase (SGOT) levels[15]. SGPT and SGOT will come out of liver cells if the liver cells are damaged, which will cause an increase in SGPT and SGOT levels in the blood serum[16]. The risk of causing liver damage is not only found in the use of chemical drugs[17] but also in the use of herbal drugs such as chaparral from the Larrea tridentate plant[18]. Since 1990, chaparral has been reported to the FDA in the United States for hepatotoxic incidents. A study observed that there was an association between repeated exposure and increasing doses of chaparral, leading to clinical signs of liver disease. Chaparral toxicity is caused by nordihydroguaiaretic acid, which inhibits cyclooxygenase and cytochrome P-450[18].

A Korean study revealed that 5.8% of hospitalisations per year were due to herbal medicine-induced liver injury[19]. Data from Iceland showed that the incidence of herbal medicine-induced liver injury was three cases per 100,000 people[20]. In addition, in Spain, there was an increase in the incidence of herbal medicine-induced liver injury from 2% in 1998 to 6% in 2016[21]. These events emphasise that toxicity and safety testing of herbal products and natural materials is important. Even the WHO states that the safety of traditional medicines is one of the crucial steps in the traditional medicine development strategy for the 2014-2023 period[22]. Based on that, the results of this study are expected to confirm the safety level of *Hydrocotyle sibthorpioides* Lam. extract and can be used as a basis for development into a phytopharmaceutical.

MATERIAL AND METHOD

Materials

Analytical balance (Ohaus), dropper, spatel, beaker glass (Pyrex), serum rack and tube, mortar and pestle, rotary evaporator (Buchi®), grinder, funnel, volumetric flask (Pyrex), Erlenmeyer (Pyrex), centrifuge, UV-Vis spectrophotometer (Thermo Scientific Genesys 10S UV-Vis), UV-lamp (Camag), measuring cup (Pyrex), thermo-shaker (BioSan), vortex (Ika Vortex Genius 3), volumetric flask (Pyrex), volume pipette (Pyrex), brown bottle, KLT vessel, oven, porcelain crucible (Pyrex), desiccator, test tube (Pyrex), tab density tester (Electrolab), disintegration tester (Lorderan), flow tester, photometer 5010 v5+ (Riele®).

Materials

Hydrocotyle sibthorpioides Lam., distilled water, 70% ethanol, ethanol P, rutin, silica gel 60 F254 (Sentana), phytochemical reagents (Mayer reagent, Dragendorff reagent, HCl, metal Mg, FeCl3, HgCl2, AlCl3, Sodium acetate), mobile phase (n-butanol and acetic acid), Whatman filter paper, aluminium foil, capsule shell, magnesium stearate, aerosol, Saccharum lactis, Manihot amylum, SGPT analysis reagent and SGOT analysis reagent.

Preparation of Ethanol Extract from *Hydrocotyle sibthorpioides* Lam.

The first process begins with the manufacture of *Hydrocotyle sibthorpioides* Lam. extract by collecting 5000 g of fresh *Hydrocotyle sibthorpioides* Lam. plants, then cleaned from dirt by washing using running water, then aerated to dry the simplicia. The dried simplicia was crushed using a blender and sieved using sieve no. 48. The sample that has been finely ground, then macerated by inserting 1 part of the powder and adding 10 parts of the solvent into a dark bottle as a maceration container, soaked with 70% ethanol for the first 6 hours while occasionally stirring, then let stand for 18 hours. Collect all the macerates and evaporate the solvent using a rotary evaporator until a thick extract is obtained. The thick extract is obtained, and then the yield is measured. The yield must reach at least the number specified in each extract monograph[17].

Capsule Formula

In a previous study, administering a standardised extract of *Hydrocotyle sibthorpioides* Lam. at 10 mg/kg BW can increase the antibody titer of male white mice exposed to H5N1 virus antigens. Based on the calculation and dose conversion, 67 mg of the ethanol extract of *Hydrocotyle sibthorpioides* Lam. was given to humans at the body weight of 50-60 kg. Capsule preparation started with weighing all the ingredients, where each capsule weighed 335 mg. Each ingredient for the composition of the test capsule consisted of *Hydrocotyle sibthorpioides* Lam. extract, aerosil, Manihot amylum, Mg stearate, and lactose, which were weighed. Put the extract of *Hydrocotyle sibthorpioides* Lam. into a mortar, then add some lactose little by little, grind until homogeneous, continue with the addition of Manihot amylum, grind again until homogeneous, then add aerosol and Mg stearate, grind again until homogeneous and added the remaining lactose little by little. After that, grind again until the powder is homogeneous, and then the powder formula of *Hydrocotyle sibthorpioides* Lam. extract and put into an empty capsule shell with a size of 0, which has a 300-500 mg capacity. The powdered formulation of Hydrocotyle sibthorpioides Lam. extract was filled into the capsule shell using a capsule board. It is shown in Table 1.

Standardisation of Condensed Extract *Hydrocotyle sibthorpioides* Lam.

The characterisation of ethanol extract of *Hydrocotyle sibthorpioides* Lam. was carried out by testing non-specific, specific parameters and testing the chemical content of the extract, which aims to ensure that the extract obtained is safe and guaranteed the quality met according to the standards. The non-specific characterisation was determined by drying shrinkage of 5.72%, total ash content of 2.25%, acid insoluble ash content of 0.07% and water content of 5.56%. Moreover, the specific characterisation was conducted by organoleptic tests, identity parameters, chemical content tests, thin layer chromatography, and determination of total flavonoid content.

Evaluation of Powder Contents of *Hydrocotyle sibthorpioides* Lam. Extract Capsules

The formulated powder must be evaluated before being put into capsules to ensure its effectiveness. The evaluation tests were the flow rate, compressibility, and angle of repose tests. It is shown in Table 2.

Table 1. Capsule Formula.

Composition	F1	F1
Hydrocotyle sibthorpioides Lam. Extract	-	67 mg
Aerosil	2%	2%
Amylum manihot	2%	2%
Magnesium stearate	1%	1%
Lactose	qs	Qs

Table 2. Evaluation of Powder-containing Capsule Extract.

Evaluation Type	Results	Condition
Flow rate	8.21 gram/s	4-10 gram/s
% compressibility	14.3%	11-15%
Angle of repose	32.31^0	$21\text{-}35^0$

Capsule Evaluation of *Hydrocotyle sibthorpioides* Lam. Extract

Finished capsules were evaluated to ensure their effectiveness by organoleptic test, weight uniformity, and destruction time. It shown in Table 3.

Clinical Trial Protocol

Twenty healthy volunteers were separated into two groups. Ten healthy volunteers were given the test preparation of *Hydrocotyle sibthorpioides* Lam. extract capsules; then, other ten healthy volunteers were given a placebo capsule preparation containing only lactose, which was consumed orally at a dose of one capsule per day after meals in the morning for three days.

Table 3. Capsule Evaluation Results.

Evaluation Type	Results	Observations
Organoleptic	Qualified	Dry, fine, dark green powder, slightly bitter, no particles attached to the capsule shell
weight diversity	Qualified	<10%
Disintegration time	2 min 41 second	<15 minutes

Table 4. Results of SGPT enzyme activity measurement of volunteers after ed *Hydrocotyle sibthorpioides* Lam. extract capsules and placebo.

Placebo group			*Hydrocotyle sibthorpioides Lam.* group		
Placebo samples	SGPT Levels (U/L)		*Hydrocotyle sibthorpioides* Lam. samples	SGPT Levels (U/L)	
	Pre	Post		Pre	Post
A1	28.90	33.10	A11	22.20	19.80
A2	27.20	36.20	A12	21.90	19.60
A3	27.30	29.90	A13	27.50	22.60
A4	24.90	36.90	A14	29.10	23.80
A5	25.20	36.90	A15	26.60	21.90
A6	25.60	29.20	A16	35.60	26.50
A7	28.90	24.40	A17	29.60	26.10
A8	34.40	28.20	A18	25.60	23.80
A9	29.90	36.90	A19	33.10	28.60
A10	35.60	37.90	A20	34.70	29.90
Average	28.79	32.96	Average	28.59	24.26
St. Deviation	3.682	4.725	St. Deviation	4.808	3.487

Table 5. Results of SGOT enzyme activity measurement of volunteers after consuming *Hydrocotyle sibthorpioides Lam.* extract capsules and placebo.

Placebo group			*Hydrocotyle sibthorpioides Lam.* group		
Placebo samples	SGOT Levels (U/L)		*Hydrocotyle sibthorpioides* Lam. samples	SGPT Levels (U/L)	
	Pre	Post		Pre	Post
A1	16.80	20.40	A11	13.80	12.40
A2	18.00	21.40	A12	16.60	13.60
A3	17.90	20.60	A13	13.80	11.20
A4	19.50	15.70	A14	15.20	13.40
A5	14.50	17.10	A15	20.40	17.10
A6	13.30	15.50	A16	21.40	15.70
A7	18.20	19.40	A17	15.90	12.70
A8	15.50	18.10	A18	21.60	16.60
A9	20.60	16.60	A19	21.60	19.40
A10	19.40	20.40	A20	16.80	13.50
Average	17.37	18.52	Average	17.71	14.56
St. Deviation	2.335	2.196	St. Deviation	3.220	2.542

Table 6. Paired T-test results of SGPT enzyme levels of healthy volunteers in the placebo and *Hydrocotyle sibthorpioides* Lam. groups.

Groups	t	df	Sig. (2-tailed)
Pre - Post Hydrocotyle sibthorpioides Lam. group	6.549	9	.000
Pre - Post Placebo group	-2.151	9	.060

Table 7. Paired T-test results of SGOT enzyme levels of healthy volunteers in the placebo and *Hydrocotyle sibthorpioides* Lam. groups.

Groups	t	df	Sig. (2-tailed)
Pre - Post *Hydrocotyle sibthorpioides* Lam. group	7.451	9	.000
Pre - Post Placebo group	-1.306	9	.224

Table 8. Independent T-test results of SGPT levels of healthy volunteers in placebo and *Hydrocotyle sibthorpioides* Lam. groups

Group	df	Sig. (2-tailed)
Equal variances assumed	18	.000
Equal variances not assumed	16.560	.000

Table 9. Independent T-test results of SGOT levels of healthy volunteers in placebo and *Hydrocotyle sibthorpioides* Lam. groups

Group	df	Sig. (2-tailed)
Equal variances assumed	18	.002
Equal variances not assumed	17.629	.002

Blood Specimen Collection and Testing

Health professionals help collect the blood specimens under the supervision of the doctor in charge of the study. It was taken after the volunteers had fasted for 6-12 hours. Blood was taken as much as 3 mL through the mediana cubital vein at the elbow fold of the hand, first cleaned above the stab site with 70% alcohol and allowed to dry. Moreover, a damming tie (tourniquet) was attached to the upper arm; the mediana cubital vein was stabbed at a 45-degree angle. The aspirated blood will flow into the syringe, then remove the tourniquet and pull the needle while still pressing the puncture hole with alcohol cotton and the former puncture is covered with plaster. The blood obtained was then tested for lymphocyte levels and centrifuged for 30 minutes at 3000 rpm. Then, the serum was used to test SGPT and SGOT levels using a 5010 v5+ photometer.

Data Analysis

The data was analysed statistically using the paired T-test analysis method between pre and post-data. Thus, the data was analysed with the Independent T-test. It was analysed using IBM SPSS 23 Version.

Ethical Approval

Ethical approval for this study was obtained from the Ethics Committee of the Faculty of Medicine, Universitas Andalas, with the contract number of the ethics letter: 1072/UN.16.2/KEP-FK/2022.

RESULTS

The SGPT enzyme activity measurement results of volunteers after consuming *Hydrocotyle sibthorpioides* Lam. extract capsules and placebo are shown in Table 4 and Figure 1.

The SGOT enzyme activity measurement results of volunteers after consuming *Hydrocotyle sibthorpioides* Lam. extract capsules and placebo are shown in Table 5 and Figure 2 below.

There was no significant difference between the mean levels of SGPT (Table 6) and SGOT (Table 7) before and after the administration of placebo capsules ($p>0.05$).

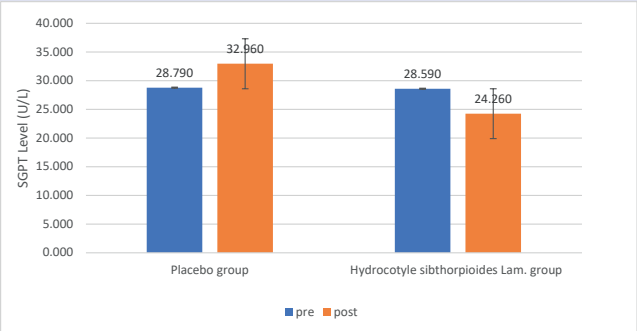

Figure 1. Volunteer's SGPT enzyme activity measurement after consuming *Hydrocotyle sibthorpioides* Lam. extract capsules and placebo.

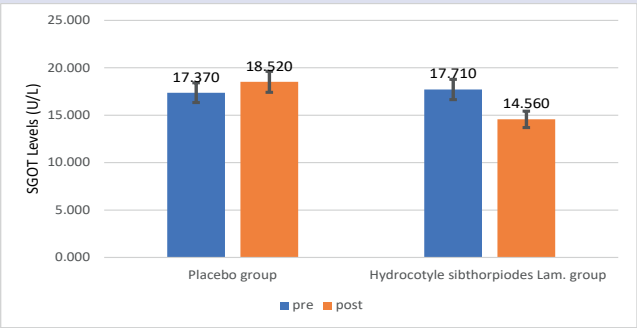

Figure 2. Volunter's SGOT enzyme activity after consuming *Hydrocotyle sibthorpioides* Lam. extract capsules and placebo.

Furthermore, the two test groups were compared using an independent T-test; there was a significant difference between the mean levels of SGPT (Table 8) and SGOT (Table 9) after healthy volunteers consumed *Hydrocotyle sibthorpioides* Lam. extract capsule preparation compared to placebo ($p>0.05$).

DISCUSSION

In this study, healthy volunteers were examined by the doctor and then divided into two test groups: ten healthy volunteers consumed *Hydrocotyle sibthorpioides* Lam. extract. Another ten healthy volunteers consumed a placebo (capsules containing lactose). The ethanol extract of *Hydrocotyle sibthorpioides* Lam. was given to healthy volunteers in capsules, and to adjust to the dose given, the capsules used in this study were size 0 capsules with a 300-500 mg capacity. Because this study employs a placebo as a comparison, the decision to use a capsule form was made to make it easier for the test subjects to consume the test preparation and to guarantee the researchers' impartiality when examining the test preparation's effectiveness. In this instance, capsules with the same size, shape, manner, and frequency of administration are filled with *Hydrocotyle sibthorpioides* Lam. extract and lactose as a placebo, but different codes are assigned to them.

Based on Table 4 and Table 5, healthy volunteers' average SGPT and SGOT enzymes were within the normal range in both the placebo and test groups. This result shows that *Hydrocotyle sibthorpioides* Lam. extract is relatively non-toxic. Previous preclinical studies on test animals have proven that *Hydrocotyle sibthorpioides* Lam. extract has immunomodulatory effects, as well as toxicity tests that have been conducted state that *Hydrocotyle sibthorpioides* Lam. extract is practically non-toxic[11].

The immunostimulatory activity of *Hydrocotyle sibthorpioides* Lam. is evident from the flavonoid chemical content in its ethanol extract[23]. *Hydrocotyle sibthorpioides* Lam. contains flavonoid chemicals that could boost the human body's defences. Once NK cells are activated, this plant produces interferon-γ. The primary MAC (Macrophage macrophage-activating cytokine) cytokine involved in non-specific cellular immunity is IFN-γ. Cytokine chemicals trigger IFN-γ, which increases macrophage phagocytic activity and makes them more effective and quicker at eliminating antigens[24].

The SGPT parameter was used because the SGPT enzyme is one of the enzymes produced in the liver and secreted into the blood, where its level is directly proportional to the state of the liver itself. The higher the level in the blood indicates, the more damaged the liver is. Meanwhile, the SGOT parameter was used because the SGOT enzyme is one of the enzymes produced in the liver and secreted into the blood in parallel with the SGPT enzyme. Increased levels of SGPT and SGOT, indicate damage to liver cells compared to other liver enzymes because these two enzymes increase before other enzymes in liver cells[25].

The results of this study indicate a significant difference between the average levels of SGPT and SGOT before and after the capsule preparation of *Hydrocotyle sibthorpioides* Lam. extract. However, for the placebo group, there is no significant difference. Based on the results of the paired T-test that has been carried out, it showed that there is a significant difference between the average SGPT enzyme with a value of $p<0.05$ (Table 6) and SGOT with a value of $p<0.05$ (Table 7) before and after consuming *Hydrocotyle sibthorpioides* Lam. extract capsules.

The decrease in SGPT and SGOT enzymes is thought to occur because flavonoid routin contained in *Hydrocotyle sibthorpioides* Lam. extract has antioxidant activity and potential as a hepatoprotector. Based on the research by Khan *et al.*[26] reported that flavonoid routine has significant protection to the liver of CCl4-induced Sprague-Dawley male white rats by suppressing the levels of SGPT, SGOT, ALP and γ-GT in serum.

CONCLUSION

Based on the results of the study to determine the safety of *Hydrocotyle sibthorpioides* Lam. extract (*Hydrocotyle sibthorpioides* Lam.) in capsule dosage form consumed by healthy humans, and it gives an effect in the form of a significant decrease in SGPT and SGOT enzyme levels.

CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest.

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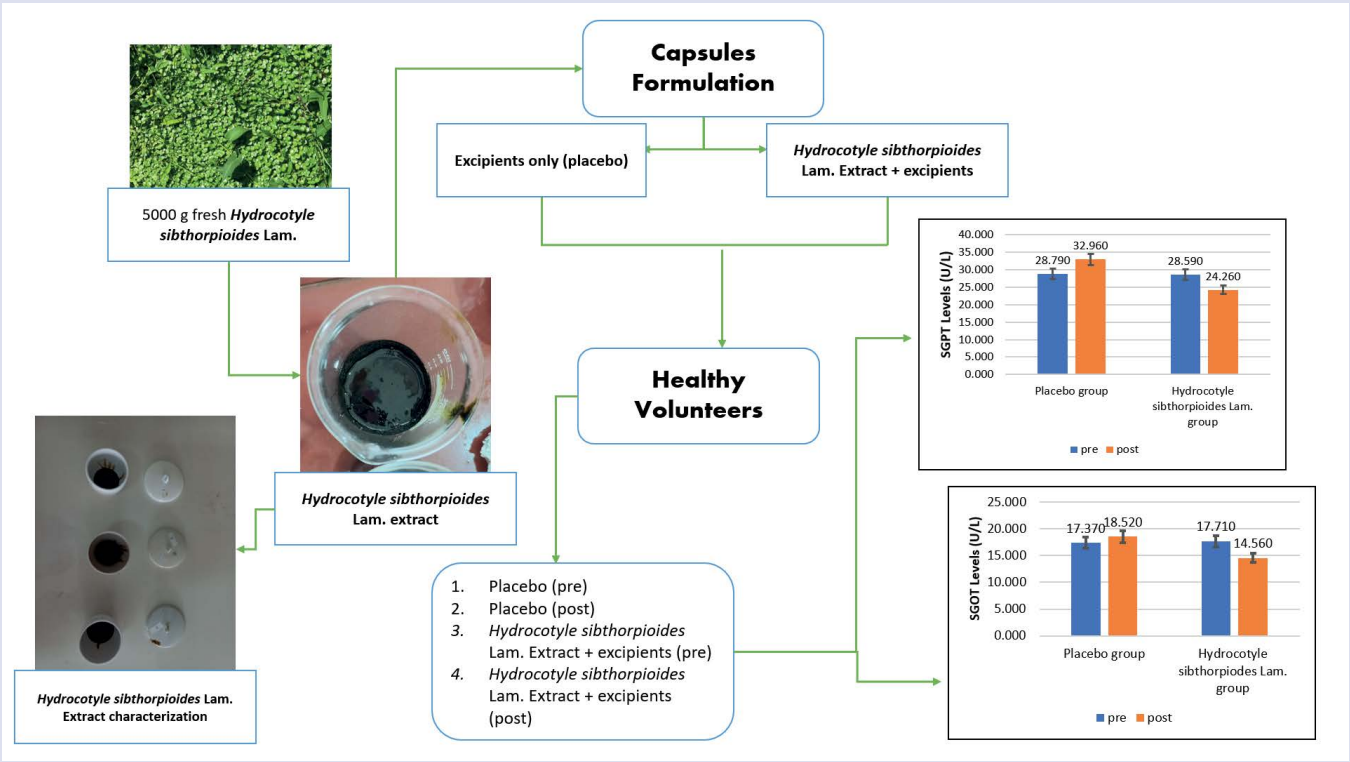
REFERENCES

1. Sari L.O.R.K. Pemanfaatan obat tradisional dengan pertimbangan manfaat dan keamanannya. Majalah ilmu kefarmasian. 2006 Apr;3(1):1-7.
2. Zhao L, Zhang N, Yang D, Yang M, Guo X, He J, Wu W, Ji B, Cheng Q, Zhou F. Protective effects of five structurally diverse flavonoid subgroups against chronic alcohol-induced hepatic damage in a mouse model. Nutrients. 2018 Nov 14;10(11):1754.
3. Afriwardi A, Aldi Y, Dillasamola D, Larakhansa YA, Badriyya E. Immunostimulatory activities of pegagan embun (*Hydrocotyle sibthorpioides* Lam.) in white male mice. Pharmacognosy Journal. 2021;13(2).
4. Husin F, Chan YY, Gan SH, Sulaiman SA, Shueb RH. The effect of Hydrocotyle sibthorpioides Lam. extracts on in vitro dengue replication. Evidence-Based Complementary and Alternative Medicine. 2015;2015(1):596109.

5. Huang Q, Huang R, Zhang S, Lin J, Wei L, He M, Zhuo L, Lin X. Protective effect of genistein isolated from Hydrocotyle sibthorpioides on hepatic injury and fibrosis induced by chronic alcohol in rats. Toxicology letters. 2013 Feb 27;217(2):102-10.
6. Supriningrum R, Fatimah N, Purwanti YE. Karakterisasi spesifik dan non spesifik ekstrak etanol daun putat (Planchonia valida). Al Ulum: Jurnal Sains Dan Teknologi. 2019 Nov 1;5(1):6-12.
7. Rahmadini R. Aktivitas Ekstrak Pegagan Embun (Hydricotyle sibthorpiodes Lam) Terhadap Titer Antibodi dan Jumlah Sel Leukosit Mencit Putih Jantan yang Terpapar Antigen H5N1, Bachelor Thesis Faculty of Pharmacy Universitas Andalas, 2021.
8. Umar S, Erman NP, Badriyya E, Aldi Y. The Activities of Pegagan Embun (Hydrocotyle sibthorpioides Lam.) on TNF-α, Macrophages and Leukocytes Male White Mice Exposed by H5N1 Virus Antigens. Pharmacognosy Journal. 2022;14(2).
9. Umar S, Gusriyani S, Afriwardi A, Aldi Y. Activities of Hydrocotyle sibthorpioides Lam. Extract in Capsule on Natural Killer and CD8 Cells in Human. Tropical Journal of Natural Product Research. 2023 Aug 1;7(8).
10. Husni E, Dillasamola D, Badriyya E, Angelia R, Aldi Y. Ethanol extract activity of pegagan embun (Hydrocotyle sibthorpioides l.) against hematopoietic on anemic male white mice. Pharmacognosy Journal. 2021;13(4).
11. Afriwardi A, Abdillah R, Husni E, Hardini H, Zuler KT, Alianta AA, Aldi Y. Subacute toxicity test of hydrocotyle sibthorpioides lam. extract on histopathological images of liver and kidney of white male mice. Pharmacognosy Journal. 2022;14(5).
12. Aldi Y, Afriwardi A, Badriyya E, Azukhruf WS, Alianta AA. Effects of Pegagan Embun (Hydrocotyle sibthorpioides Lam) Extract on Renal Function in Male Wistar Rats as Assessed by Creatinine Clearance. Tropical Journal of Natural Product Research. 2023 Mar 1;7(3).
13. Badriyya E, Latifah W, Aldi Y. Sub-acute Toxicity Study of Pegagan Embun (Hydrocotyle sibthorpioides Lam.) Extract on The SGPT and SGOT Level of Wistar White Male Rats. International Journal Applied Pharmaceutics. 2023 Feb 15(Special Issues 1), pp. 2547-2550.
14. Telles-Correia D, Barbosa A, Cortez-Pinto H, Campos C, Rocha NB, Machado S. Psychotropic drugs and liver disease: a critical review of pharmacokinetics and liver toxicity. World journal of gastrointestinal pharmacology and therapeutics. 2017 Feb 2;8(1):26.
15. Stickel F, Patsenker E, Schuppan D. Herbal hepatotoxicity. Journal of Hepatology. 2005 Nov 1;43(5):901-910.
16. Rumagit BI, Nahor E, Lalura CC. Identifikasi Senyawa Metabolit Sekunder Pada Ekstrak Etanol Kulit Buah Mangga Kweni (Mangifera odorata Griff.). In PROSIDING Seminar Nasional Tahun 2020 ISBN: 978-623-93457-1-6 2020 Dec 15 (pp. 14-19).
17. Hazarika I, Geetha KM, Sundari PS, Madhu D. Acute oral toxicity evaluation of extracts of Hydrocotyle sibthorpioides in wister albino rats as per OECD 425 TG. Toxicology reports. 2019 Jan 1;6:321-328.
18. Agarwal RA, Wang ZY, Bik DP, Mukhtar HA. Nordihydroguaiaretic acid, an inhibitor of lipoxygenase, also inhibits cytochrome P-450-mediated monooxygenase activity in rat epidermal and hepatic microsomes. Drug metabolism and disposition. 1991 May 1;19(3):620-624.
19. Cho JH, Oh DS, Hong SH, Ko H, Lee NH, Park SE, Han CW, Kim SM, Kim YC, Kim KS, Choi CW. A nationwide study of the incidence rate of herb-induced liver injury in Korea. Archives of toxicology. 2017 Dec;91:4009-4015.
20. Björnsson ES, Bergmann OM, Björnsson HK, Kvaran RB, Olafsson S. Incidence, presentation, and outcomes in patients with drug-induced liver injury in the general population of Iceland. Gastroenterology. 2013 Jun 1;144(7):1419-1425.
21. Medina-Caliz I, Garcia-Cortes M, Gonzalez-Jimenez A, Cabello MR, Robles-Diaz M, Sanabria-Cabrera J, Sanjuan-Jimenez R, Ortega-Alonso A, García-Muñoz B, Moreno I, Jimenez-Perez M. Herbal and dietary supplement-induced liver injuries in the Spanish DILI registry. Clinical Gastroenterology and Hepatology. 2018 Sep 1;16(9):1495-1502.
22. World Health Organization. WHO Traditional Medicine Strategy: 2014-2023. World Health Organization; 2013.
23. Badrunasar A. and Santoso H.B., Tumbuhan Liar Berkhasiat Obat, Bogor: Forda Press, 2016.
24. Bratawidjaja KG, Rengganis I. Imunologi Dasar Edisi 8. Fakultas Kedokteran Universitas Indonesia, Jakarta. XI. 2010.
25. Mitruka BM, Rawnsley HM. Clinical Biochemical and Hematological Reference Values in Normal Experimental Animals. 1977.
26. Khan RA, Khan MR, Sahreen S. CCl 4-induced hepatotoxicity: protective effect of rutin on p53, CYP2E1 and the antioxidative status in rat. BMC complementary and alternative medicine. 2012 Dec;12:1-6.

GRAPHICAL ABSTRACT



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