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Acute Toxicity Test of Tamarillo Fruit Ethanol Extract (*Solanum betaceum Cav.*) on the Levels of Liver Transaminase Enzymes in Male Wistar Rats

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ABSTRACT

Indonesians traditionally utilize tamarillo for its various health benefits. However, the lipophilic compounds it contains have the potential to cause hepatotoxicity and increase transaminase enzymes, namely SGPT and SGOT enzymes. The study aimed to test the toxicity of tamarillo ethanol extract acutely on SGPT and SGOT levels in male Wistar white rats. The study used a post-test only experimental design with a control group design. Fifteen rats were randomly divided into five treatment groups. Group K1 as a control was given distilled water, group K2 was given paracetamol 2.5 g/kgBW, while groups K3, K4, and K5 were each given tamarillo ethanol extract in single doses of 200, 400, and 600 mg/kgBW. After 24 hours, rat blood serum samples were taken through the orbital sinus to measure SGPT and SGOT levels using the UV test method. The results showed that the average SGPT levels increased in the K2 group by 295.34±13.31 U/L and K5 by 93.67±19.03 U/L. Meanwhile, the average SGOT levels increased in the K2 group by 874±25.06 U/L, K4 by 164.67±7.57 U/L and K5 by 213.34±13.50 U/L. The One-Way ANOVA test showed a significance value of p=0.000 in the K2 and K5 groups for SGPT, while SGOT in the K2, K4 and K5 groups. Administration of tamarillo ethanol extract can cause liver damage at doses of 400 mg/kgBW and 600 mg/kgBW.

1. INTRODUCTION

The tamarillo (*Solanum betaceum Cav.*) is a plant from the Solanaceae family widely cultivated in tropical and subtropical highlands (Nurmaisah & Murdianto, 2019). Traditionally, this fruit is consumed fresh or processed and is believed to have various health benefits. Tamarillo contains vitamins (A, B complex, C, and E), carotenoids, flavonoids, and fiber, which act as natural antioxidants (Satopa *et al.*, 2019). Phytochemical screening showed that the ethanol extract of tamarillo fruit contains flavonoids, triterpenoids, saponins, alkaloids, and tannins (Dewi *et al.*, 2021).

Despite its pharmacological potential, the use of tamarillo in extract form requires adequate safety assessment. The extraction process with ethanol solvents is known to increase the concentration of bioactive compounds, potentially increasing therapeutic effects while also increasing the risk of toxicity, especially with high doses or long-term use (OECD, 2015; Ballotin *et al.*, 2021). Therefore, evaluating the safety of tamarillo ethanol extract is crucial for its further development as a health product or traditional medicine.

The potential toxicity of tamarillo has been reported in several studies, both in vitro and in vivo. In vitro studies using tamarillo peel and fruit extracts were tested against RAW 264.7 macrophage cells (an immune cell model) using the MTS cell assay method, showing that cell viability dropped below 80% at a concentration of 100 µg/mL and could cause cell stress or cytotoxicity before counteracting inflammation (Li & Li, 2021). Another study by Valor-Llácer *et*

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al. (2025) showed that tamarillo fruit protein can act as an antigen in sensitized individuals, triggering severe allergic reactions or systemic anaphylaxis, with evidence of increased tryptase enzyme levels confirming mast cell activity and a positive prick test.

In vivo toxicology studies using zebrafish embryo models showed that acute administration of tamarillo leaf and fruit extracts had teratogenic effects on fish embryo development and increased embryonic mortality (Borges *et al.*, 2025). Another study by Kustantina (2020) reported that administering tamarillo fruit extract to male mice (Mus musculus) exposed to lead acetate (75 mg/kgBW) significantly reduced testosterone levels in all treatment groups at various doses (100 mg/kgBW, 200 mg/kgBW, and 400 mg/kgBW). These studies indicate that even for short periods, high concentrations of tamarillo ethanol extract have toxic potential because they can alter cellular function and damage target organs.

Toxicity testing aims to assess the potential adverse effects of a substance on living organisms before clinical use in humans and to select the appropriate dose for both acute and chronic exposure. The initial step in identifying the toxic potential of herbal extracts on an organ, as well as determining the LD_{50} (Lethal Dose 50) value after single or repeated exposure over a short period of time, is an acute toxicity test (BPOM RI, 2022). One of the organs primarily targeted for damage during acute toxicity due to herbal extracts is the liver, as it plays a role in the metabolism and detoxification of xenobiotics entering the body (Teschke & Frenzel, 2015; Jabbar *et al.*, 2020; Ballotin *et al.*, 2021).

Hepatotoxicity is a state of liver dysfunction or damage caused by toxic exogenous compounds (Abidin, 2017). Exogenous compounds contained in tamarillo, such as flavonoids, alkaloids, saponins, and tannins, are known to have dualistic potential, providing a protective effect at low doses but potentially toxic at high doses (Arjadi *et al.*, 2017; Li *et al.*, 2015). Flavonoids have the potential to cause excessive free radical production, as well as damage DNA, membrane lipids, and hepatocyte cell proteins. Alkaloids can cause acute hepatocellular necrosis through oxidative mechanisms. Tannins can form strong bonds with cytoplasmic proteins, causing protein precipitation and impacting enzyme function and damaging cell membrane structures. Saponins can bind to lipid membranes and disrupt hepatocyte membrane integrity. As a result, hepatocyte membrane permeability increases, causing leakage of transaminase enzymes and other cell structures (Ujowundu *et al.*, 2022; Gajender *et al.*, 2023; Qadri *et al.*, 2025).

These compounds undergo metabolism in the liver through two main phases. In phase I, lipophilic compounds undergo oxidation, reduction, or hydrolysis mediated by cytochrome P450 enzymes (especially CYP3A4/5), potentially producing reactive metabolites. These metabolites can contribute to oxidative stress and hepatocellular damage if not adequately neutralized in the conjugation reaction with glucuronic acid in phase II (Ganiswarna *et al.*, 2011; Arjadi *et al.*, 2017), which can then cause damage to liver cell membranes and increase the levels of transaminase enzymes released into the bloodstream (Arjadi *et al.*, 2017; Li *et al.*, 2015). Transaminase enzymes, namely Serum Glutamic Pyruvic Transaminase or Alanine Aminotransferase (SGPT/ALT) and Serum Glutamic-Oxaloacetic Transaminase or Aspartate Aminotransferase (SGOT/AST), are early and sensitive indicators of liver cell damage, so they are often used as the main biochemical parameters in the evaluation of hepatic toxicity (Rosida, 2016; Ballotin *et al.*, 2021).

To date, scientific data regarding the acute toxicity test of tamarillo ethanol extract on liver function, particularly as assessed by SGPT and SGOT levels, is still very limited. This limited data indicates a research gap that needs to be filled to support the safety aspects of the use of tamarillo ethanol extract as a herbal or nutraceutical ingredient. Therefore, this study aims to evaluate the acute toxicity of tamarillo ethanol extract (*Solanum betaceum Cav.*) on liver function in male white rats of the Wistar strain by measuring transaminase enzyme levels (SGPT and SGOT). The results of this study are expected to provide scientific contributions in the form of initial safety data on tamarillo ethanol extract as a basis for further development in the pharmaceutical and health fields.

2. METHOD

The method used is a true experimental design with a post-test only design with a control group on experimental animals. The research design used a completely randomized design (CRD). The experimental animal samples used were male white rats (*Rattus norvegicus*) of the Wistar strain. Ethanol extract of tamarillo (*Solanum betaceum Cav.*) fruit as the independent variable and transaminase enzyme levels (SGPT and SGOT levels) as the dependent variable. The study was conducted from May to July at the Pharmacognosy, Chemistry, and Pharmacology Laboratory of Ibnu Sina Ajibarang Health College.

Materials and Equipment

The tools used in this study included a rat cage, a rat food container, a rat drinking container, a digital gram scale, a magnetic stirrer, an oven, a water bath, a gastric tube, an Eppendorf tube, a centrifugator, a micropipette, a water bath, a stir bar, a rotary evaporator, a UV-vis spectrophotometer, a hematocrit pipette, a syringe, and a non-EDTA vacutainer tube.

The materials used for phytochemical screening included 2N HCl, 2M HCl, Mayer's reagent, Dragendorf's reagent, Mg powder, concentrated HCl, 10% FeCl3, anhydrous acetic acid, and concentrated sulfuric acid. Other materials needed are tamarillo fruit, male Wistar white rats (*Rattus norvegicus*), 96% ethanol, Diasys® reagent kit, filter paper, distilled water, AQUA® mineral water, distilled water, rat feed (HI-PRO-VITE A594K) and chloroform.

Data Collection

Plant identification is necessary to confirm the taxonomy of the plants used. The tamarillo (*Solanum betaceum Cav.*) plants were obtained from the highlands of Muktisari Hamlet, Legoksayem Village, Wanayasa District, Banjarnegara Regency, Central Java Province. The tamarillo fruit used was ripe and can be stored at room temperature for up to 10 days. The fruit is egg-shaped, measuring between 5-6 cm long and over 5 cm wide. The skin of ripe tamarillo fruit is dark purple, blood red, or brownish red. The thick, yellowish flesh is wrapped in a thin, easily peeled membrane. The ripe fruit has a tomato-like flavor and a plum-like texture (Solihat *et al.*, 2017; Nara, 2019).

Tamarillo was extracted using the maceration method. Five kilograms of tamarillo were cleaned of dirt and washed thoroughly under running water, then cut into pieces. The cut fruit was dried in a drying cabinet at 30-40°C. The dried fruit was ground into a powder, then sieved using a 40-mesh sieve. 500 grams of the resulting powder was extracted by maceration and placed in a dark glass container. 2500 ml of 96% ethanol was added, then allowed to stand for 24 hours (stirring every 12 hours for 5 minutes during the maceration process). The resulting maceration product was then filtered to obtain the first maceration product (Adilla, 2018).

The second maceration was carried out on the first filter dregs added with 2500 ml of 96% ethanol, then stirred and left for 24 hours, then filtered to produce the second maceration result. The mixture of the first and second maceration results was then evaporated using a rotary evaporator and thickened with a water bath which aims to evaporate the ethanol content to obtain a pure extract of tamarillo fruit. Next, the yield of the simplicia and ethanol extract of the tamarillo fruit was also calculated.

Extract characterization consists of two processes, specific and nonspecific parameters. Specific parameters for the tamarillo ethanol extract in this study included determining the extract identity, organoleptic characteristics, and identification of the extract's chemical constituents. Nonspecific parameters included determining the drying loss, water content, and specific gravity (Dewi *et al.*, 2021).

The study samples were male Wistar rats (Rattus norvegicus) obtained from a Wistar rat breeder in Karangklesem Village, South Purwokerto District, Banyumas Regency. The samples were randomly assigned and divided into five groups: a negative control group given distilled water (K1), a positive control group given paracetamol at a dose of 2.5 g/kgBW (K2), a treatment group given tamarillo ethanol extract at a dose of 200 mg/kgBW (K3), a treatment group given a dose of 400 mg/kgBW (K4), and a treatment group given a dose of 600 mg/kgBW (K5). In accordance with the acute toxicity test guidelines based on the Organization for Economic Co-

operation and Development (OECD), 3 rats are required for each group, so the total experimental animals used consisted of 15 white rats aged 8-12 weeks with a body weight between 150-200 grams. The rats were acclimatized for 7 days and treatment was given on the 8th day or the first day after acclimatization was completed. After 24 hours of treatment for each group, blood samples were taken and the rats were euthanized (Arjadi *et al.*, 2017).

Blood was drawn from all experimental animals (groups K1, K2, K3, K4, and K5) via the orbital sinus. The collected blood was then placed in a non-EDTA tube and centrifuged at 4,000 rpm for 10 minutes to produce serum. The resulting serum was separated from the blood cell sediment and collected using a micropipette, then transferred to an Eppendorf tube for SGPT and SGOT levels to be measured.

Data Analysis

Univariate analysis was used to determine the mean and standard deviation of SGPT and SGOT data. The research data were tested for normality using the Shapiro-Wilk test and then for homogeneity using the Levene test. Bivariate analysis used One-Way Analysis of Variance (ANOVA) as a parametric test. Significant bivariate tests were followed by a Post Hoc test to determine the group with the most significant results. Data analysis in the study was conducted with a 95% confidence level (Arjadi *et al.*, 2017).

3. RESULT AND DISCUSSION

Result

a. Plant Determination

The results of plant determination conducted at the Environmental Laboratory, Faculty of Biology, Jenderal Soedirman University, Purwokerto by Dra. Wiwik Herawati, M.Sc., showed that the plant used was the *Solanum betaceum Cav.* species with certificate number B/294/UN23.6.10/TA.00.01/2023. Plant determination is the initial step taken before research, which aims to ensure that the plants used for this research originate from the desired plant (Nursofia, 2021).

Figure 1. Tamarillo (*Solanum betaceum Cav.*)

b. Extract Yield

The yield results of tamarillo fruit, both simple and extract, can be seen in the following table:

Table 1. Results of tamarillo fruit yield

Type	Initial weight	Simplisia weight	Yield
Simplisia	5 kg	552,40 gr	11,048%
Extract	500 gr	159,95 gr	31,99 %

c. Extract Standardization

1) Spesific Parameters

Specific parameters tested included identity, organoleptic, and phytochemical screening of the extract. The identification and organoleptic parameters are as follows:

Table 2. Results of determining identity and organoleptic parameters for tamarillo ethanol extract

Parameters	Results
Extract Identity:	
Extract Name	Tamarillo fruit extract
Latin Name	*Solanum betaceum Cav.*
Plant Part	Whole fruit
Extract Organoleptic:	
Shape	Thick extract
Color	Dark red brown
Taste	Bitter
Smell	Distinctive smell

Phytochemical screening of ethanol extract of tamarillo fruit obtained the following results:

Table 3. Results of phytochemical screening of ethanol extract of tamarillo fruit

Testing	Reagents	Results
Alkaloids	2N HCl + Aquadest + Mayer + Dragendorff	+
Flavonoids	Aquadest + Mg + Concentrated HCl	+
Saponins	Aquadest + 2N HCl	+
Tannin	$FeCl_3$ 10%	+
Triterpenoids / Steroids	Chloroform + Anhydrous Acetic Acid + Concentrated H2SO4	+
Anthocyanin	2M HCl + 2M NaOH	+

2) Non-Spesific Parameters

The non-specific parameters of the ethanol extract of tamarillo fruit can be seen in the following table:

Table 4. Results of determining non-specific parameters of ethanol extract of tamarillo fruit

Parameters	Results
Drying Loss	45%
Water Content	55%
Specific Gravity	1,63 g/ml

d. Measurement of Transaminase Enzyme Levels

1) Average SGPT and SGOT Levels

Table 5. Results of measurements of serum transaminase enzyme levels in mice

Group	SGPT Levels (U/L)			SGOT Levels (U/L)		
	Min.	Max.	Mean ± SD	Min.	Max.	Mean ± SD
K1	26	59	44,67 ± 16,92	84	108	99 ± 13,07
K2	284	310	295,34 ± 13,31	850	900	874 ± 25,05
K3	53	61	56,34 ± 4,16	122	127	124,34 ± 2,51
K4	62	71	67 ± 4,58	156	170	164,67 ± 7,57
K5	74	112	93,67 ± 19,03	200	227	213,34 ± 13,50

Description: K1 = Negative control group with distilled water; K2 = Positive control group with paracetamol dose of 2.5 g/kgBW; K3 = Treatment group with ethanol extract of tamarillo fruit dose of 200 mg/kgBW); K4 = Treatment group with ethanol extract of tamarillo fruit dose of 400 mg/kgBW); K5 = Treatment group with ethanol extract of tamarillo fruit dose of 600 mg/kgBW. Mean = average level. SD = standard deviation.

According to the Laboratorium Penelitian dan Pengujian Terpadu (LPPT) of Gadjah Mada University, normal SGPT levels in rats range from 44.5 to 74.9 U/L, and normal SGOT levels in rats range from 72.9 to 127.9 U/L (Nurkhasanah *et al.*, 2016; Arjadi *et al.*, 2017). Table 5 shows an increase in mean SGPT levels in groups K2 (295.34 ± 13.31 U/L) and K5 (93.67 ± 19.03 U/L). The increase in mean SGOT levels was found in groups K2 (874 ± 25.05 U/L), K4 (164.67 ± 7.57 U/L), and K5 (213.34 ± 13.50 U/L).

The standard deviation is used to determine the distribution of data within a sample, as well as how close individual data points are to the mean or average value of several sample data points. A standard deviation smaller than the mean indicates low data deviation. A standard deviation higher than the mean indicates high data deviation. This indicates heterogeneity in the data and reflects very high data deviation (Swarjana, 2022). All standard deviation values in each group, both SGPT and SGOT, were lower than the mean, indicating low data deviation and homogeneity. Increased levels of transaminase enzymes in the study showed liver damage in mice due to acute exposure to drugs (K2 = paracetamol dose 2.5 g / kgBW) and ethanol extract of tamarillo (K4 = dose 400 mg / kgBW and K5 = dose 600 mg / kgBW). Liver dysfunction occurs as a result of reduced enzyme biosynthesis and decreased membrane permeability so that enzymes can be released into the blood. Liver damage can occur due to direct exposure to toxic substances during the detoxification process of metabolite products and xenobiotic compounds (Gu & Manautou, 2012).

2) Analysis of SGPT and SGOT Levels

The normality test (Shapiro-Wilk) and homogeneity of variance test (Levene test) were performed on the SGPT level data, resulting in a p value > 0.05 for each group, indicating that the data were normally distributed and homogeneous. Bivariate analysis using One-Way ANOVA yielded a p value = 0.000 (p < 0.05). These results indicate that there is a significant difference in the mean values of the SGPT data, indicating that there are at least two groups of SGPT data that have significant mean differences, as shown in the following table:

Table 6. Results of the LSD Post Hoc test of SGPT levels

Group	K1	K2	K3	K4	K5
K1	-	0,000*	0,303	0,064	0,001*
K2	0,000*	-	0,000*	0,000*	0,000*
K3	0,303	0,000*	-	0,344	0,006*
K4	0,064	0,000*	0,344	-	0,032*
K5	0,001*	0,000*	0,006*	0,032*	-

Description: * = significantly different (p<0.05)

The normality test (Shapiro-Wilk) and homogeneity of variance test (Levene statistic) were performed on the SGOT level data, resulting in a p value > 0.05 for each group, indicating that the data were normally distributed and homogeneous. Bivariate analysis using One-Way ANOVA yielded a p value = 0.000 (p < 0.05). These results indicate that there is a significant difference in the mean values of the SGOT data, indicating that there are at least two groups of SGOT data that have significant mean differences, as shown in the following table:

Table 7. Results of the LSD Post Hoc test on SGOT levels

Group	K1	K2	K3	K4	K5
K1	-	0,000*	0,057	0,000*	0,000*
K2	0,000*	-	0,000*	0,000*	0,000*
K3	0,057	0,000*	-	0,007*	0,000*
K4	0,000*	0,000*	0,007*	-	0,002*
K5	0,000*	0,000*	0,000*	0,002*	-

Description: * = significantly different (p<0.05)

Discussion

The tamarillo fruit (*Solanum betaceum Cav.*) used in this study was obtained from Legok Sayeim Village, Wanayasa District, Banjarnegara Regency. Legoksayem Village where the tamarillo was collected has an altitude of more than 1000 meters above sea level with an average temperature of 16-25°C, where tamarillo fruit can survive at an altitude of 1000 meters above sea level, and can still survive above 2000 meters above sea level if the average monthly temperature remains above 10°C. The fruit was picked in the morning because at this time the fruit weight is in an optimal state due to the accumulation of nutrients during the night and the fruit has not been exposed to sunlight so that the fruit has not undergone the evaporation process, and the harvested

fruit is ripe fruit with characteristics of brownish red fruit (Situmorang, 2012; Saparinto & Susiana, 2024).

Harvested tamarillos are cleaned and then dried in a drying cabinet at 30-40°C for 3-4 days, resulting in dried herbal preparations. Drying reduces the water content in the sample, thus preventing contamination by microorganisms that could damage the sample (Jabbar *et al.*, 2020). The process of grinding the herbal preparations into powder optimizes the extraction of the active compounds contained in the herbal preparations by increasing the surface area of the herbal preparations in contact with the solvent (Manarisip *et al.*, 2019).

The ready-to-use herbal preparations are then macerated using 96% ethanol as a solvent. Maceration involves soaking the sample in an organic solvent at room temperature. This maceration method was chosen for extraction due to its simplicity, allowing the solvent to penetrate the cell walls and enter the cell cavities containing the active ingredients. Soaking the sample in an organic solvent at room temperature and the maceration method can prevent damage to thermolabile compounds such as phenolics and their derivatives (Putri *et al.*, 2024). The 96% ethanol solvent is semipolar, allowing both polar and non-polar compounds present in the drug to be attracted and evaporate easily with a boiling point of 78°C, thus leaving a high residue. Furthermore, 96% ethanol is the solvent with the highest extraction power for all low-weight substances and molecules such as alkaloids, saponins, and flavonoids, and is selective and non-toxic (Jabbar *et al.*, 2020).

Ethanol extract from the simple fruit of tamarillo (*Solanum betaceum Cav.*) produced the yield shown in Table 1. Yield is the ratio of the weight of the resulting extract to the amount of the extracted herbal material. Yield determination is carried out to measure the amount of active compounds successfully extracted from the material. Determining the yield also aims to determine the estimated amount of herbal material needed to produce a specific amount of thick extract (Handayani *et al.*, 2019; Rifkia & Prabowo, 2020; Lupitasari & Azzahra, 2025). The yield of a plant extract can be influenced by several factors, including temperature, maceration time, and the interaction between treatments. The higher the temperature and the longer the maceration time, the higher the yield obtained until the optimum temperature and time are reached. Longer extraction times result in prolonged heating and prolonged contact between the solid and the solvent, which will increase the number of cell ruptures and the dissolution of active ingredients (Nursofia, 2021).

The extract yield was 31.99% (Table 1). A yield is considered good if the value is greater than 10%. The higher the yield, the more active compounds are extracted from the extract (Marpaung & Septiyani, 2020). Therefore, the extract yield obtained is considered good, indicating that the extract meets the requirements according to the Farmakope Herbal Indonesia (2017), which is not less than 10% (Badriyah & Farihah, 2022).

Organoleptic analysis of extracts is performed as an indicator of the physical and visual quality of the extract (Table 2). Extract quality can be assessed through its color, aroma, and characteristic consistency. Furthermore, it is used to avoid contamination or undesirable variations due to changes in sensory properties beyond the standard (Gannasin *et al.*, 2012). Thick extracts exhibit high viscosity, often caused by high solids content, such as polyphenols, pigments, sugars, or natural hydrocolloids from the fruit. The reddish-brown color corresponds to the pigment profile, such as carotenoids, betacyanins, or phenolic components, in ripe *Solanum betaceum Cav.* fruit (Asih *et al.*, 2021; Al-Hakim *et al.*, 2024).

Factors affecting organoleptic properties include temperature, extraction method, phytochemical compound stability, solvent content, and post-extraction stabilization. Extraction processes at high temperatures or exposure to oxygen can darken the natural pigments (browning) or cause a change in texture, becoming more liquid or thickened. Polyphenols or carotenoid pigments can oxidize, affecting the color (e.g., becoming browner) and texture of the extract. The amount of remaining solvent, such as ethanol in this study, can affect viscosity; the greater the residual solids, the thicker the consistency. Storage conditions (temperature, light) and the use of antioxidants or preservatives can maintain the stability of the extract's color and consistency over a period of time (Silva *et al.*, 2020; Asih *et al.*, 2021; Isla *et al.,* 2022; Al-Hakim *et al.*, 2024).

Tamarillo fruit extract contains alkaloids, flavonoids, saponins, tannins, triterpenoids/steroids, and anthocyanins, indicating a broad biochemical spectrum (Table 3). This supports the potential for multiple pharmacological activities such as antioxidant, hepatoprotective, antimicrobial, anticancer, and immunomodulatory activities. This phytochemical combination is consistent with findings that *Solanum betaceum Cav.* fruit contains various bioactive compounds (Asih *et al.*, 2021; Dewi *et al.*, 2021).

The purpose of determining drying loss is to provide a maximum limit (range) for the amount of compound lost during the drying process. The drying loss parameter is essentially a measurement of the remaining substance after drying at a temperature of 105°C to a constant weight, expressed as a percentage. The drying loss value obtained from the ethanol extract of tamarillo (*Solanum betaceum Cav.*) fruit is 45% (Table 4). The mass that can be lost due to this heating includes water molecules, essential oils, and ethanol solvents. The drying loss limit set by the Indonesian Ministry of Health in 2017 is 10%, thus the ethanol extract of tamarillo (*Solanum betaceum Cav.*) fruit exceeds the drying loss standard. If the evaporated material is assumed to be water, then it can be interpreted that the water content of the extract is ≥30% and exceeds the permitted standard. This can occur if the extract is not stored in an appropriate place because the extract can absorb water from the air. Drying loss and water content are important to avoid microbial growth and degradation of active compounds due to high humidity. Therefore, the extract must be re-dried before being used for pharmacological activity testing or preparation (Nursofia, 2021; Nurzahra *et al.*, 2022).

Specific gravity testing is performed using a pycnometer. Before use, the pycnometer must be cleaned and dried until no water droplets remain. This is to determine the empty weight of the instrument. Any remaining water droplets will affect the results. The pycnometer to be used is first calibrated with distilled water at 25°C. The extract used is then diluted to 5% using distilled water as the solvent. This test yielded a specific gravity of 1.63 g/ml (Table 4). A specific gravity value approaching 1 or greater than 1 indicates that the extract is increasingly miscible with water, and vice versa. A specific gravity value greater than 1 indicates that it is miscible with water (Nurzahra *et al.*, 2022).

Toxicity testing is a test used to detect toxic effects on biological systems, using dose and response data typical of a test preparation of a substance. Toxicity testing on a test preparation using test animals as models aims to observe biochemical, physiological, and pathological reactions in humans. Although the results cannot be used to definitively prove the safety of a material/preparation in humans, the presence of relative toxicity can provide clues to identifying toxic effects in the event of human exposure. The purpose of acute oral toxicity testing is to detect the intrinsic toxicity of a particular substance, determine target organ and species sensitivity, obtain hazard information after acute exposure to a particular substance, obtain preliminary information that can be used to determine dosage levels, design further toxicity tests, determine the LD50 value of a material/preparation, and determine the classification and labeling of the material/preparation (Klaassen, 2019; BPOM RI, 2022).

The experimental animals used in this study were male white rats (*Rattus norvegicus*) of the Wistar strain. White rats are a species commonly used as experimental animals in toxicology research. The sex of the mice used was male, because male mice are relatively less affected by hormones. Meanwhile, the Wistar strain has advantages, including better endurance compared to other strains. The mice used were healthy, naive, and aggressive with normal behavior during the acclimatization period. Acclimatization was carried out so that the mice could become accustomed to their surroundings and were fed a standard diet (Arjadi *et al.*, 2017). During the study, no experimental animals died, so the LD50 level of the ethanol extract of tamarillo fruit could not be determined in this study (BPOM RI, 2022).

SGPT is released when hepatocyte damage occurs and is a more specific parameter for liver damage. Acute hepatocyte damage will cause an increase in liver transaminase enzymes (SGPT), because SGPT is found in the cytoplasm of hepatocytes (Arjadi *et al.*, 2017). SGOT is found in heart cells, liver, skeletal muscle, kidneys, brain, pancreas, spleen, and lungs. The highest levels are found in heart cells. 30% of SGOT is found in the cytoplasm of liver cells and 70% is found in the mitochondria of liver cells. High SGOT levels are directly related to the amount of cell damage.

Cell damage will be followed by an increase in SGOT levels within 12 hours and persist in the blood for 5 days. Increased SGPT or SGOT is caused by changes in permeability or damage to the liver cell wall and is therefore used as a marker of impaired liver cell integrity (hepatocellular) (Nursofia, 2021).

An increase in SGPT and SGOT enzymes up to 300 U/L is not specific for liver disorders alone. An increase of more than 1000 U/L can be found in viral liver disease, liver ischemia caused by prolonged hypotension or acute heart failure, and liver damage caused by drugs or toxins. In inflammation and initial (acute) hepatocellular damage, cell membrane leakage occurs so that cytoplasmic contents leak out, causing SGPT to increase higher than SGOT, indicating mild damage. In chronic or severe inflammation and damage, liver cell damage reaches the mitochondria, causing an increase in SGOT levels higher than SGPT, indicating severe or chronic liver damage (Nursofia, 2021).

Post Hoc LSD data analysis of SGPT levels in groups K3 (p=0.303) and K4 (p=0.064) did not show any significant differences (Table 6), so they were considered the same as the aquadeist negative control (K1). This indicates that treatment in groups K3 and K4 did not have the potential to cause liver damage. Meanwhile, data analysis for group K5 showed a significant difference with group K1, namely p=0.000. This indicates that group K5 has a toxic effect on the liver, but the increase in SGPT levels in group K5 was not higher than the positive control group paracetamol (K2). The mechanism of the increase in SGPT enzyme levels in liver cell damage occurs due to damage to the liver cell, especially the liver membrane. This causes the SGPT enzyme found in the liver cell to come out and flow into the blood (Nursofia, 2021).

The average SGOT levels increased above normal levels as the dose of ethanol extract of tamarillo fruit increased. However, based on Post Hoc LSD data analysis, the SGOT level in group K3 (p = 0.057) did not show a significant difference (Table 7), so it was considered the same as the negative control group (K1). The results of data analysis of groups K4 and K5 showed a significant difference with group K1, each with a p value of 0.000, which indicated that groups K4 and K5 had a toxic effect on the liver, but the increase in SGOT levels in groups K4 and K5 was not higher than the positive control group paracetamol (K2). This indicates that tamarillo ethanol extract can cause liver damage in both groups.

The active compounds in herbal plants have the potential to be hepatoprotective at effective exposure, but at excessive doses or long exposure times, these compounds can also be potentially toxic to the liver because they turn into prooxidants (Arjadi *et al.*, 2017; Indarto, 2013). Lipophilic compounds such as flavonoids, anthocyanins, alkaloids, and saponins can cause damage to hepatocytes. This damage occurs because these compounds bind more readily to cell membranes, disrupting membrane permeability. Furthermore, these compounds can increase the duration of drug metabolism and excretion in the body (Corcoran *et al.*, 2012; Matsuura & Fett-Neto, 2015; Bugel *et al.*, 2016).

Flavonoids have an inhibitory effect on the activity of cytochrome P450 (CYP450) enzymes, which inhibits the metabolism and elimination of various compounds, which can accumulate and trigger hepatitis or obstruction. Flavonoids, with their prooxidant phenoxyl radicals, can also damage the mitochondrial cell membranes of hepatocytes (Ujowundu *et al.*, 2022; Gajender *et al.*, 2023; Qadri *et al.*, 2025). Saponin, steroid and triterpenoid metabolites can cause hemolysis and reduce the surface pressure of cell membranes, which can result in damage to the permeability of hepatocyte cell membranes (Purwita *et al.*, 2013; Amalia, 2022).

The toxic effects of drugs and herbs are often seen in the liver because the liver plays a crucial role in detoxifying compounds entering the body. Hepatotoxicity can occur due to the accumulation of xenobiotics in the liver, excreted through bile, which can damage liver cells and increase SGPT and SGOT enzyme levels in test animals. Increased SGPT and SGOT enzyme activity is a strong and sensitive indicator of abnormalities in liver cells. Furthermore, differences in extract concentrations administered at different doses can also affect liver morphology (Nursofia, 2021).

Other factors that can increase transaminase enzyme levels, particularly SGOT levels, include damage to organs other than the liver, such as muscles, heart, brain, and kidneys. Furthermore, the condition of the herbal extract, sampling method, blood serum levels, and the

condition and age of the experimental animals can increase cellular susceptibility to oxidative stress caused by reactive oxygen species (ROS), leading to increased transaminase enzyme levels (Teschke, 2019; Santiago *et al.,* 2021). These factors were not measured in more detail in this study.

Measuring SGPT and SGOT in mice before treatment can be performed to obtain better research results in the future. Furthermore, measuring transaminase enzymes using methods other than UV-Vis spectrophotometry can be used for comparison. Other biochemical parameters should also be examined to assess overall liver function. Toxicity tests on other organs, such as the kidneys or brain, can be continued to determine the effects of tamarillo fruit extract on these organs. Non-specific parameters of the extract need to be well standardized to produce better results.

4. CONCLUSION

Administration of tamarillo (*Solanum betaceum Cav.*) ethanol extract can cause liver damage characterized by an increase in serum SGPT in male Wistar white rats at a dose of 600 mg/kgBW (K5), as well as an increase in SGOT at a dose of 400 mg/kgBW (K4) and a dose of 600 mg/kgBW (K5). However, the increase in SGPT and SGOT levels in these treatment groups was not as large as the increase in SGPT and SGOT levels in the treatment group given paracetamol at a dose of 2.5 g/kgBW.

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