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Activity Test of Ginger (Zingiber Officinale) Extract Nanoemulsion on Decreasing Sgpt, Sgot Levels, Assessment of Necrosis, Fibrosis and Liver Lobules in Male Rats Induced by Streptozotocin and Histopathological of the Liver

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ABSTRACT
This study aims to test the activity of ginger (Zingiber officinale) extract nanoemulsion on reducing SGPT and SGOT levels, as well as assessing the level of necrosis, fibrosis, and liver lobule condition in streptozotocin-induced male rats. Rats were divided into control and treatment groups, where the treatment group received ginger extract nanoemulsion preparation. The results showed that treatment with nanoemulsion significantly reduced SGPT and SGOT levels, as well as reduced the level of necrosis and fibrosis in liver tissue compared to the control group. Phytochemical screening results on ginger (Zingiber officinale) extract revealed the presence of flavonoids, tannins, saponins, alkaloids, and polyphenols. These compounds act as natural antioxidants that support antidiabetic effects in test animals. Treatment group 3 with a nanoemulsion of ginger extract (zingiber officinale) at a dose of 200 mg/kgBW experienced a significant decrease in SGOT and SGPT levels compared to the other treatment groups, approaching the control group. The ANOVA test showed a significant difference between groups ($p < 0.05$), which was confirmed by the results of the LSD test. Microscopic image of the liver of mice in treatment group 3 showed improvement. structure histology heart However Still There is degeneration hydropic , so that Still enter in category Score 1. The percentage of necrosis decreased to 5% . Histopathological findings showed improvements in the structure of the liver lobules. This study concluded that ginger extract nanoemulsion preparations can function as an effective therapy in protecting the liver from diabetes-induced damage.

Keywords: *Nanoemulsi ginger, SGPT, SGOT, Liver.*

INTRODUCTION
Diabetes mellitus is a metabolic condition characterized by hyperglycemia due to impaired insulin secretion, insulin action, or both (Ministry of Health of the Republic of Indonesia, 2018). Diabetes can trigger various complications, including organ damage, which most often occurs in the liver. Elevated levels of SGPT (ALT) and SGOT (AST) indicate liver cell damage. These enzymes are released into the bloodstream when hepatocytes are damaged. Diabetes can cause liver cell necrosis due to oxidative stress and inflammation. This process can progress to fibrosis, where scar tissue forms in response to chronic damage.
The use of a streptozotocin (STZ)-induced animal model allows for in-depth studies of diabetic liver histopathological changes, including disorganization of liver lobules and inflammatory cell infiltration. Diabetes causes increased production of free radicals, which

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come from various sources, including inefficient glucose metabolism and the activity of immune cells. Free radicals damage lipids in hepatocyte cell membranes, a process known as lipid peroxidation. This damage disrupts membrane integrity, causing leakage of enzymes and cellular components. Oxidative stress can damage mitochondria, which serve as the cell's energy source. This damage disrupts ATP production, reducing the cell's ability to survive and function properly. Oxidative stress triggers the activation of inflammatory pathways, releasing pro-inflammatory cytokines that attract immune cells to the damaged area. This can exacerbate tissue damage and contribute to necrosis (Jauhar Firdaus, 2022). Increased oxidative stress ultimately leads to hepatocyte cell death through necrosis, which is characterized by cell swelling, structural damage, and the release of cell contents into the circulation. Repeated damage to liver cells can trigger fibrogenesis, which results in the formation of scar tissue. This alters the structure of the liver lobules and impairs hepatocyte function.

The liver is a vital organ responsible for the metabolism of toxic substances in the body (Salasam PYL, 2015). In this regard, the liver is often targeted by toxins because toxic substances enter the body through the gastrointestinal tract and are then absorbed and transported to the liver through the portal vein (Huda MN, 2017). This process can easily cause changes in the structure or dysfunction of liver cells. Therefore, the liver The liver plays a vital role in the body as an organ involved in digestion and metabolism. Maintaining liver health is crucial for those with type 2 diabetes. Complications of nonalcoholic fatty liver disease (NAFLD) are more likely in people with diabetes. Keep in mind that type 2 diabetes or obesity are common causes of liver disease (WebMD, 2020). Having type 2 diabetes increases the risk of developing a more severe liver disease called nonalcoholic steatohepatitis. In this case, liver fat causes dangerous inflammation that leads to scarring. This disease can lead to cirrhosis and end-stage liver disease.

The liver is responsible for the body's overall health. It performs many functions, including breaking down toxins in the blood and producing proteins, which aid in digestion. The purpose of this liver function test is to assess the overall condition of the liver and any potential problems. existence disease heart. SGOT And SGPT is two type enzyme Produced by liver cells, it is used to assess liver function. Normal SGOT levels are 3-45 µ/L (micrograms per liter), while normal SGPT levels are 0-35 µ/L. Elevated SGOT and SGPT levels can be caused by hepatitis, fatty liver disease, gallbladder obstruction, and other diseases (Mochamad Rizal, 2022).

Pharmacotherapy or oral hyperglycemic agents are the most common treatments for diabetes mellitus used by patients with diabetes. Because can functioning control level sugar in blood (Natalia, 2024)However, clinically, excessive use of chemicals can have negative effects on the body. Furthermore, consuming medications and undergoing medical procedures to lower blood sugar levels, according to Several studies on the properties of plants that can reduce glucose levels in the blood, such as ginger (*Zingiber Officinale)*.

Ginger is a biopharmaceutical plant used as a herbal medicine. Ginger is commonly used to treat bloating, warm the body, cure irritation, treat headaches, colds, and increase appetite (stimulant). Ginger contains gingerol and shogaol which function as immunomodulators, anti-inflammatories, and antioxidants that can relieve symptoms of lung inflammation caused by the Corona virus (Reddy, 2020). Oleoresin, as another processed form of ginger, is used in the food, agricultural, pharmaceutical, and cosmetic industries in the form of emulsions. However, emulsions have the disadvantage of being unstable. Emulsions are easily affected by environmental factors such as temperature, heat, and light (Jayanudin, 2017). Emulsions are also hydrophobic, meaning they are difficult to dissolve in water, difficult to disperse, have low speed, low absorption, and reduce their ability as flavor agents (Hosseini, 2021). One alternative to overcome the weaknesses of ginger oleoresin emulsion is to process the oleoresin in the form of nanoemulsion ((Çinar, 2017). Nanoemulsion is a mixture of oil, water and surfactant phases that have particle sizes of 1-1000 nm (Jonassen, 2014). Nanoemulsion is able to increase the solubility, bioavailability of active ingredients,

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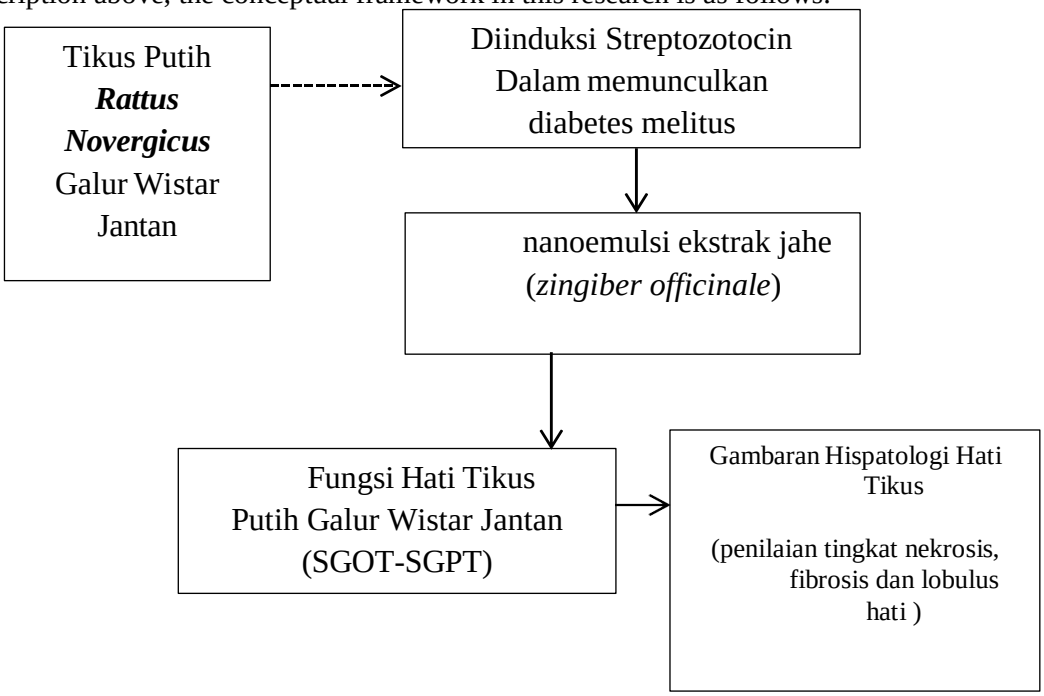
absorption and improve sensory properties so that it is more stable (Hosseini, 2021). Nanoemulsion is a lipid-based drug delivery system that is thermodynamically stable, clear, does not damage normal human and animal cells. Nanoemulsion consists of oil, surfactant, cosurfactant, and water that has a droplet size in the nanometer. Nanoemulsion has been reported to have desired characteristics such as high drug solubility, significant protection, and thermodynamic stability (Aprilya, 2021). Nanoemulsion preparations are made by stirring using a homogenizer and ultraturrax, namely by mixing the oil phase and the water phase with the help of surfactants and cosurfactants to reduce surface tension. Tween 80 is a surfactant that is widely used in the manufacture of nanoemulsions. Tween 80 Stable against electrolytes, weak acids, and bases. The use of Tween 80 alone is not sufficient to reduce surface tension to form a nanoemulsion formulation. Therefore, in the manufacture of nanoemulsions, surfactants are often combined with cosurfactants. In this study, sorbitol was used as a cosurfactant. Sorbitol has been widely used as an excipient in pharmaceutical, cosmetic, and food product formulations.

Based on description on researchers interested make title study activity test of ginger (*zingiber officinale*) extract nanoemulsion on decreasing sgpt, sgot levels, assessment of necrosis, fibrosis and liver lobules in streptozotocin-induced male rats and liver histopathology.

Objective in study This that is To know the process of making ginger extract (*zingiber officinale*) in nanoemulsion preparation , To know the content of active substances in ginger extract (*zingiber officinale*) , To know the effect of administering ginger extract nanoemulsion preparation (*zingiber officinale*) with doses of 90mg/kgBW, 140mg/kgBW and 190mg/kgBW on reducing SGPT and SGOT levels in male rats induced by streptozotocin) And Analyze the histopathological features of the liver after the treatment period and liver tissue will be taken for histopathological examination using hematoxylin-eosin (HE) staining for assessment of necrosis, fibrosis, and liver lobules. From the description above, the conceptual framework in this research is as follows:



Picture 1 Framework Conceptual

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METHODS

This research uses an experimental quantitative research type, namely by using a true experiment or laboratory experimental design where this research was conducted. to examine the effectiveness of administering ginger (zingiber officinale) extract nanoemulsion on reducing sgpt, sgot levels, assessing the level of necrosis, fibrosis and liver lobules in male rats induced by streptozotocin and histopathological features of the liver. The research design uses a post-test with control group design or controls the sample based on the treatment group. post test done For see success extract in reducing SGOT-SGPT levels in mice that had diabetes mellitus, which were then histopathologically observed in the livers of mice in each treatment group . The research location was the Laboratory of the Department of Pharmacology and Therapeutics Faculty Medical University Sumatra North on Month June- August 2025. Ethical Clearance is still in the process of submitting the Health Research Ethics Commission (KPEK) of Prima Indonesia University.

Based on the calculations above, the minimum number of test animals per group was 6. In this study, the researchers used 24 Wistar rats were used in each experimental group. The test animals were randomly divided into four groups: the control group, treatment group 1, treatment group 2, and treatment group 3. The test animals that had passed the acclimation period and consumed a high-fat and cholesterol diet were then randomly divided into 4 groups, each group consisting of 6 mice. The researchers adapted the previous study and modified the dosage as follows: Control group (P-0): only given standard mouse pellet feed + distilled water/day/head for 14 days , Treatment group I (P-1): Induction Streptozotocin + ginger extract nanoemulsion (zingiber officinale) at a dose of 90mg/kgBW orally via gastric tube And given feed pellets/ distilled water/day/tail during 14 day , Treatment group II (P-2): Induction Streptozotocin + ginger extract nanoemulsion (zingiber officinale) at a dose of 140mg/kgBW orally via gastric tube And given feed pellet /aquades/day/tail during 14 day and Treatment Group III (P-3) Induction Streptozotocin + ginger extract nanoemulsion (zingiber officinale) with a dose of 190mg/kgBW orally via gastric tube and given pellet feed/distilled water/day/tail for 14 days.

After the entire sample of mice developed diabetes mellitus, the next step was to examine liver function. Liver function can be measured by examining serum enzyme activity, one of which is serum aminotransferase or transaminase. Aminotransferase is a good indicator of liver damage. The main indicator Which observed against liver function disorders, namely the activity of the enzymes AST (Aspartate Aminotransferase)/ SGOT (Serum Glutamic Oxaloacetic Transaminase) and ALT (Alanine Aminotransferase)/ SGPT (Serum Glutamic Oxaloacetic Transaminase) Pyruvic Transaminase). transaminase enzyme is intracellular enzymes, Which where if If there is damage to liver cells, such as disruption of the permeability of liver cell walls, then their activity will increase (Rahayu, 2018). Toxic symptoms observed include SGOT-SGPT examination. Normal SGOT levels are 3-45. µ/l (micro per liter) while SGPT: 0-35 µ/l (micro per liter) if there is an increase then liver function damage is detected (Mochamad Rizal, 2022).

From the results of liver function (SGOT -SGPT enzymes) then histopathological observations were made on the rat liver and scoring was carried out from the image. Data from results study tabulated And analyzed with help SPSS (Statistical Package for Social Science) 25.0. for windows. Data normality was analyzed using the Kolmogorov-Smirnov test ($p > 0.05$). To test the significance between test groups, a one-way analysis of variance (ANOVA) was used at a 95% confidence level ($p < 0.05$). Further analysis or testing was performed using a Post Hoc Test with the LSD technique.

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RESULTS

Phytochemical Test Results

Table 1 Test Phytochemicals

Secondary Metabolites	Color	Results
Flavonoid	Pink	+
Saponin	Yellow and foamy	+
Tannin	turquoise	+
Alkaloid	Yellow sediment	+
Steroids/Triterpenoids	Green	+

Information: (+) = Contain group compound Which tested
(-) = Does not contain the tested compound

Based on the results of the phytochemical tests carried out, it can be concluded that ginger extract (*zingiber officinale*) contains secondary metabolites in the form of flavonoids, saponins, tannin, alkaloids, And triterpenoids.

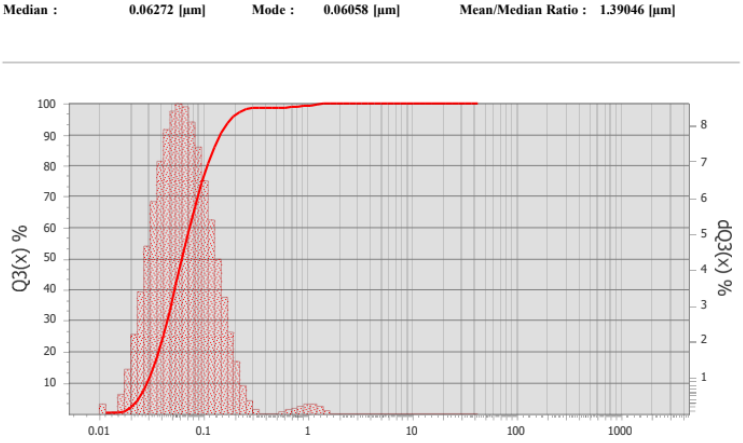

Table 2 Figure Measurement PSA Nanoemulsion Ginger Extract (Zingiber Officinale)

The results of the description of the PSA measurement analysis of ginger extract nanoemulsion (*zingiber officinale*) are The average particle size is very small, which is around 60–63 nm , which indicates that this system is already in the ideal nanoemulsion category . The size distribution is narrow and uniform , because the mode ≈ median and the histogram shape is symmetrical. A Mean/Median Ratio higher than 1 indicates that there are still a small number of larger particles (possibly agglomerates), but not significant. Ginger nanoemulsion in this formulation shows very good particle distribution **,** with a dominant size below 100 nm. It is very suitable for pharmaceutical, cosmetic, or food applications because small particle size can increase physical stability, bioavailability and absorption by the body.

Results Observation SGPT and SGOT levels

Liver function can be measured by examining serum enzyme activity, one of which is serum aminotransferase or transaminase. Aminotransferase is a good indicator of liver damage. If both are elevated, liver damage has occurred. The two aminotransferases are aspartate aminotransferase (AST), formerly known as with Serum Glutamic Oxaloacetic Transaminase (SGOT), and Alanine Aminotransferase (ALT) or formerly known as Serum Glutamic Pyruvic Transaminase (SGPT). ALT and AST are markers of liver functional status because they can indicate liver parenchymal damage. Treatment was given for 14 days

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after H7, it was stated that the P1, P2, and P3 rat groups had diabetes. And the P0 group was the reference group. After that, the rats were then terminated under anesthesia and a laparotomy was performed to remove the liver organs to then measure the SGOT and SPGT levels. The following are the average results of SGOT and SGPT liver function before being given soursop leaf extract treatment (Annona Muricata L.) and after being given treatment according to the dose of each group:

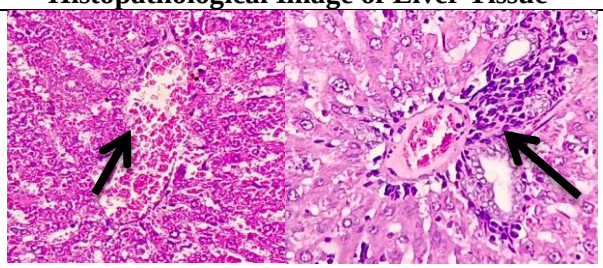
Table 2 Average SGOT And SGPT

H14 Group	SGOT (U/L)	SGPT (U/L)	H28 SGOT (U/L)	H28 SGPT (U/L)
P0	73±8.48	24±3.34	73.16±7.27	25.4±2.75
P1	203.57±26.8	118.8±41.8	90.66±15.06	30.65±4.8
P2	203.6±15.7	106.18±9.62	80.66±8.9	24±3.46
P3	187±15.37	105.3±10.09	51.5±5.9	20±2.68

Range mark normal SGPT on mouse is 17.5-30.2 (IU/L), while the normal SGOT value in mice is 45.7-80.8 (IU/L). Group P0 is the reference group because this group was not given streptozotocin and was only given standard feed. From the table above, it can be seen that the groups of mice P1, P2, and P3 induced by streptozotocin showed an increase above the normal value on D14 with the highest average SGOT value in group P2, namely 203.6±15.7 and the SGPT value of 106.18±9.62.

From the table above, it can also be seen that after 14 days and treatment (H28) was given to the P0 group, the SGOT results were 73.16±7.27 and the SGPT results of 25.4±2.75 were the reference group because they were not induced by alloxan. Meanwhile, groups P1, P2, and P3, which were given ginger extract (zingiber officinale) at doses of 90 mg/kg/BW, 140 mg/kg/BW, and 190 mg/kg/BW, showed results normal is on group P2 with mark SGOT 80.66±8.9 and SGPT 24±3.46. Then on P3 group with SGOT values of 51.5±5.9 and SGPT 20±2.68. Meanwhile, group P3 received The best value among the other treatment groups. Meanwhile, group P1, despite experiencing a decrease, still did not achieve normal liver function results, with SGOT values of 90.66±15.06 and SGPT values of 30.67±4.8. Thus, ginger extract (zingiber officinale) given to male Wistar rats (Rattus norvegicus) for 14 days of treatment produced significant results in restoring liver function to normal after the rats experienced diabetes mellitus.

Table 3 Histopathological Description of Liver Tissue

No	Group	Histopathological Image of Liver Tissue
1	Control (Aquades)	 Because there is no change in the histological structure of the liver (normal), it falls into score category 1.

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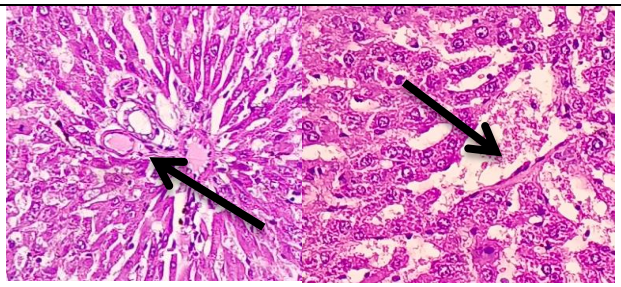
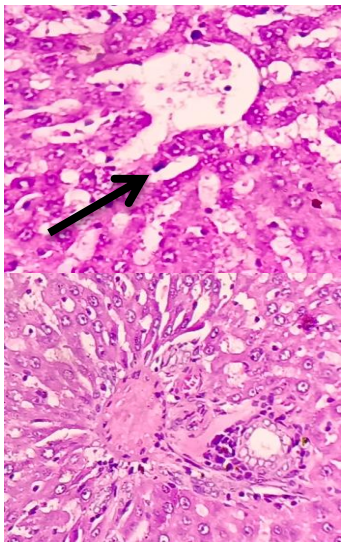
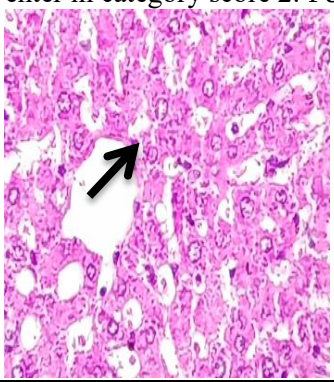
2	Treatment 1	 The microscopic image of the liver of mice in treatment group 1 shows that the liver still experiences changes in the form of parenchymatous degeneration or bleeding, there is necrosis in the liver cells but it appears to have disappeared, so it is included in the score category 3 (necrosis appears). The percentage of necrosis is around 15% .
3	Treatment 2	 Microscopic image of the liver of mice in treatment group 2 showed improvement. structure histology heart However Still There is degeneration hydropic , so that enter in category score 2. Percentage of necrosis 10% .
4	Treatment 3	

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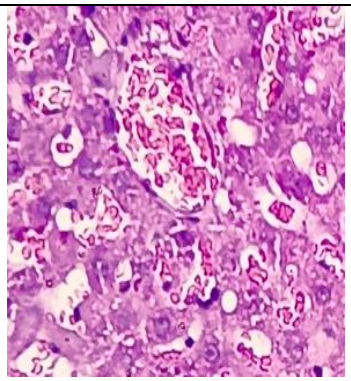

Microscopic image of the liver of mice in treatment group 3 showed improvement. structure histology heart However Still There is degeneration hydropic , so that Still enter in category score 1. The percentage of necrosis decreased to 5%

Histopathological observations using a light microscope at 400x magnification showed a significant reduction in inflammation and bleeding in the group given ginger extract nanoemulsion, demonstrating the treatment's effectiveness in protecting the liver from damage.

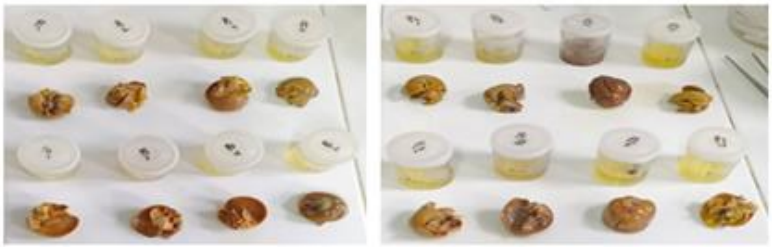

Figure 3. Image of the rat liver after surgery in each group.

DISCUSSION

This research uses an experimental quantitative research type, namely by using a true experiment or laboratory experimental design where this research was conducted. to examine the effectiveness of administering nano emulsion of ginger extract (zingiber officinale) on reducing sgpt, sgot levels, assessing the level of necrosis, fibrosis and liver lobules in male rats induced by streptozotocin and histopathological features of the liver.

The research design uses a post-test with control group design or controls the sample based on the treatment group. post test done For see success extract in reduce SGOT-SGPT levels in mice that have diabetes mellitus, then histopathological observations were carried out on the livers of mice in each treatment group.

High blood sugar levels are a sign of a chronic disease known as diabetes mellitus (DM). This disease is caused by the ineffective use of the body's insulin production or the body's inability to produce the hormone. In the article (Drg. Widyawati, 2021), diabetes is disease term long Which most often appear At the moment And is one of the ten most common causes of death in the world.

The liver is a vital organ responsible for metabolizing toxic substances in the body (Salasam, et al., 2023). In this regard, the liver is often targeted by toxins because toxic substances enter the body through the gastrointestinal tract and are then absorbed and transported to the liver via the portal vein (Huda MN, Holidah D, 2021). Having diabetes mellitus can cause impaired liver function. Approximately three out of four people with type 2 diabetes or prediabetes have excess fat in the liver. Liver fat triggers dangerous inflammation that can

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lead to cirrhosis. One way to detect liver damage is by perform histopathological examination of the specimen. This allows for viewing the morphology And histological structure changed as well as level the damage that occurs in the liver (Gibson, 2022)

This study used rats (Rattus norvegicus) male Wistar strain weighing 160-250 grams and aged 2-3 months. The research sample size was 24 male rats which will be divided into 4 groups, each group consisting of 6 rats. mark normal SGPT on mouse is 17.5-30.2 (IU/L), while the normal SGOT value in mice is 45.7-80.8 (IU/L). Group P0 is the reference group because this group was not given streptozotocin and was only given standard feed. From the table above, it can be seen that the groups of mice P1, P2, and P3 induced by streptozotocin showed an increase above the normal value on D14 with the highest average SGOT value in group P2, namely 203.6±15.7 and the SGPT value of 106.18±9.62.

From the table above, it can also be seen that after 14 days and treatment (H28) was given to the P0 group, the SGOT results were 73.16±7.27 and the SGPT results of 25.4±2.75 were the reference group because they were not induced by alloxan. Meanwhile, groups P1, P2, and P3, which were given ginger extract (zingiber officinale) at doses of 90 mg/kg/BW, 140 mg/kg/BW, and 190 mg/kg/BW, showed results normal is on group P2 with mark SGOT 80.66±8.9 and SGPT 24±3.46. Then on P3 group with SGOT values of 51.5±5.9 and SGPT 20±2.68. Meanwhile, group P3 received The best value among the other treatment groups. Meanwhile, group P1, despite experiencing a decrease, still did not achieve normal liver function results, with SGOT values of 90.66±15.06 and SGPT values of 30.67±4.8. Thus, ginger extract (zingiber officinale) given to male Wistar rats (Rattus norvegicus) and these data can be proven by the results of the histopathological images of the rat livers which show that in the P1 treatment group at a dose of 100 mg/kgBW ginger extract, there are still quite a lot of fatty degeneration livers which are quite widespread, parenchymatous degeneration or bleeding in the liver cells. inflammatory cell infiltration scoring in this group is 3 namely there are change in the form of degeneration hydropic. On group treatment P2 At a dose of 140 mg/kgBW ginger extract, the liver showed signs of fatty degeneration, congestion, and inflammatory cell infiltration. The scoring for this group was 2. And in the P3 treatment group at a dose of 200 mg/kgBW ginger extract, the liver looked normal, no inflammation was seen, cells began to improve, no necrosis or fatty deposits were seen, and the same scoring was given as the P0 group, namely 1, which was in the normal category.

In this way, ginger extract has been proven not only to lower blood sugar levels in mice, this extract can also improving liver function in mice that have been diagnosed with diabetes mellitus and is most effective at a dose of 200 mg/kgBW, and this is in line with research (Elis, 2015) regarding the benefits and content of ginger in reducing blood sugar levels in mice.

CONCLUSION

1. Phytochemical screening results on ginger (*Zingiber officinale*) extract revealed the presence of flavonoids, tannins, saponins, alkaloids, and polyphenols. These compounds act as natural antioxidants that support antidiabetic effects in test animals.
2. Treatment group 3 with a nanoemulsion of ginger extract (*zingiber officinale*) at a dose of 200 mg/kgBW experienced a significant decrease in SGOT and SGPT levels compared to the other treatment groups, approaching the control group. The ANOVA test showed a significant difference between groups ($p < 0.05$), which was confirmed by the results of the LSD test.
3. Microscopic image of the liver of mice in treatment group 3 showed improvement. structure histology heart However Still There is degeneration hydropic , so that Still enter in category score 1. The percentage of necrosis decreased to 5%

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