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Antidiabetic Activity of Mangosteen (Garcinia Mangostana L.) Peel Extract Nanoemulsion on Reducing Glucose Levels, Liver Function (SGOT-SGPT) and Liver Histopathology in Male Rats

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ABSTRACT

If not properly controlled, diabetes can lead to serious complications, including hypertension, diabetic neuropathy, kidney disease, heart disease, stroke, and liver disorders. SGOT and SGPT are two types of enzymes produced by liver cells, used to examine liver function. This study was conducted to determine the antidiabetic activity of mangosteen (Garcinia mangostana L.) rind extract nanoemulsion on reducing glucose levels and liver function (SGOT-SGPT) and liver histopathology in male rats.The sample of mice used was 24 in 4 groups (control, treatment 1, 2 and 3) where the extract preparation in the treatment was in the form ofnanoemulsion of skin extractmangosteen peel extract (Garcinia Mangostana L)onconcentrations of F1 (1%), F2 (2%), and F3 (3%).OnThe average examination of the levels of KGD, SGOT-SGPT in rats that had diabetes mellitus and were given mangosteen peel extract at a concentration of 1% KGD was 124.3 mg/dL, SGOT 93.1 U/L and SGPT 26.5 U/L. At a concentration of 2% KGD was 94.5 mg/dL, SGOT 75.8 U/L and SGPT 21.1 U/L. At a concentration of 3% KGD was 80.1 mg/Dl, SGOT 52.8 U/L and SGPT 18.5 U/L. In liver histopathologyThe best result group was in treatment group 3 (P3) which was given a 3% concentration of mangosteen peel extract nanoemulsion.

Keywords: Mangosteen Peel, Nanoemulsion,SGOT-SGPT, Liver, Glucose

INTRODUCTION

To prevent diabetes, one should avoid sugary foods and processed drinks, and replace white bread and pasta with whole grains. White flour and white bread, white rice and pasta, sweetened drinks or soda, candy, and sugary breakfast cereals are some examples. These foods and drinks should be limited. In diabetes mellitus, the body's cells cannot absorb and process glucose into energy because the pancreas is unable to produce insulin or the body cannot use insulin effectively. Glucose that is not properly absorbed by the body's cells then accumulates in the blood over time, causing various health problems.(Dudi Hardianto, 2020)Diabetes can also cause various complications if not managed properly. If not properly controlled, this condition can lead to serious complications, including hypertension, diabetic neuropathy, kidney disease, heart disease, stroke, and liver damage.

Insulin resistance can cause chronic liver damage such as cirrhosis and liver failure.(Pouwels et al., 2022)Hepatocyte damage is a serious problem for people with type 2 diabetes mellitus. Insulin resistance, which increases oxidative stress and activates inflammatory signals, can lead to liver damage. The liver is a vital organ in the body that plays a role in the metabolism of toxic substances. It maintains overall body health by performing various tasks, including

Nomor ISSN: 3124-1115

destroying toxins in the blood, producing proteins, and aiding in digestion.(Polyzos SA, 2019). The examination can be carried out using the SGOT and SGPT enzymes. These enzymes are enzymes produced by cells in the liver.(Mochamad Rizal, 2022).

SGOT and SGPT are two types of enzymes produced by liver cells, used to examine liver function.(Emy Oktaviani, Lusi Indriani, 2022)Elevated SGOT and SGPT levels can be caused by hepatitis, fatty liver disease, gallbladder obstruction, and other diseases. Having diabetes mellitus can lead to 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 lead to cirrhosis.(Mochamad Rizal, 2022).

Medications used to treat diabetes mellitus are known as antidiabetics. Regular use of diabetes medication can stabilize blood sugar levels and reduce the risk of diabetes complications such as diabetic ulcers, vision problems, or stroke. Several classes of medications are known as antidiabetics. Each group works differently to lower high blood sugar levels in people with diabetes.(T, 2024)However, several studies have shown that excessive medication use can negatively impact the health of organs such as the kidneys and liver. Therefore, the use of herbal remedies has become an alternative for diabetes sufferers. Mangosteen peel is one type of plant used as an alternative medicine in the treatment of diabetes mellitus. According to a health website written by(Nurin, 2022)Mangosteen peel has several benefits for those with diabetes. These benefits are due to the xanthone content in the rind. Mangosteen extract is formulated as a nanoemulsion because the flavonoid particles are smaller, thus potentially having higher antidiabetic activity. This preparation can increase the effectiveness of drug therapy and minimize side effects and toxic reactions.(Lina, NWM, Maharani, T., Sutharini, MR, Wijayanti & Astuti, 2017).

Based on this background, the author is interested in conducting research on "the antidiabetic activity of mangosteen peel extract nanoemulsion (Garcinia mangostana L.) on reducing glucose levels and liver function (SGOT-SGPT) and liver histopathology in male rats".

LITERATURE REVIEW

The liver maintains the overall health of the body by performing various tasks, including breaking down toxins in the blood, producing proteins, and aiding in the digestive process.(Polyzos SA, 2019). However, other functions of the liver include: destroying red blood cells, cleaning the blood, producing proteins, metabolizing proteins,nutrient storage,producing cholesterol and hormones, etc.The liver is also a major site of metabolism for endogenous and exogenous substances (e.g., drugs and toxins). This process, known as biotransformation, converts lipophilic substances into hydrophilic ones for subsequent elimination (Yip et al., 2021).SGOT and SGPT are two enzymes produced by liver cells and 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).

In the article(Drg. Widyawati, 2021)Diabetes is the most common long-term disease today and is one of the ten most common causes of death worldwide. The liver does many things, including breaking down toxins in the blood and making proteins, which aid in digestion.(Deora & Venkatraman, 2022).

Mangosteen not only tastes delicious, but is also known to be high in antioxidants, such as xanthones, which are thought to have numerous health benefits, such as fighting free radicals, reducing inflammation, and supporting the immune system. Mangosteen also

Nomor ISSN: 3124-1115

contains vitamin C, minerals, and fiber, all of which are essential for good health. In this article, we will discuss the history of mangosteen, its characteristics, classification, growing conditions, and how to grow it.(Agricultural Equipment, 2025).

METHODS

This study uses a quantitative experimental research type, namely by using a true experiment or laboratory experimental design where this study was conducted to test the antidiabetic activity of mangosteen peel extract nanoemulsion (Garcinia mangostana L.) on reducing glucose levels, liver function (SGOT-SGPT) and liver histopathology through assessment of the level of necrosis and parenchymatous degeneration in male rats.The research design uses a post-test with control group design or controls the sample based on the treatment group.*post test*was carried out to see the success of the extract in reducing glucose levels, liver function (SGOT-SGPT)in mice that had experienced diabetes mellitus after being inducedalloxan which was then observedLiver histopathology through assessment of the level of necrosis and parenchymatous degeneration in male rats.

The research samples were male Wistar rats (Rattus norvegicus) weighing 160-250 grams and aged 2-3 months. Six rats were used per group. In this study, researchers used 24 Wistar rats for each experimental group. The animals were acclimatized for 7 days in the laboratory of the Department of Pharmacology and Therapeutics, Faculty of Medicine, University of North Sumatra.Nanoemulsion of Mangosteen Peel Extract (Garcinia Mangostana L)with the methodextraction process using the maceration methodand made in nanoemulsion preparations with adjusted particles where the size of the nanoemulsion particles is carried out using a Particle Size Analyzer (Horiba Scientific, Nanoparticle Analyzer SZ-100) and the results will be given to rat samples once a day for 14 days. Treatment was given to treatment groups 1, 2 and 3 using the concentration of the nanoemulsion extract preparation.mangosteen peel with concentrations of F1 (1%), F2 (2%), and F3 (3%). Liver function is seen from the levels of SGOT and SGPT in the liver as seen from the results of blood sample tests on mice that have been induced by alloxan. For histopathological description of the mouse liver using liver observation and seeing the level of necrosis score in the mouse liver using a 400x magnification myxopsis. Diabetes mellitus mouse model with alloxan induction within 14 days of induction. Then the data from the research results were tabulated and analyzed using SPSS (Statistics of Package for Social Science).

RESULT

In phytochemical testing of mangosteen peel extract, it contains xanthones, flavonoids, alkaloids, terpenoids, tannins, saponins, and steroids. The phytochemical properties of mangosteen peel extract with ethanol solvent show that the extract is rich in bioactive compounds that can have various pharmacological effects, such as antioxidant, antimicrobial, and anti-inflammatory activities..

In the characterization test of mangosteen peel extract nanoemulsion, the average particle size is around 150 nm, Polydispersity Index (PDI) is 0.2 which indicates a homogeneous and physically stable particle size distribution, physical stability during observation for several weeks at room temperature, without phase separation or significant color changes, pH 5.2 indicates that it is suitable for topical application and safe for the skin.

The results of the study tested the antidiabetic activity of mangosteen peel extract nanoemulsion (Garcinia mangostana L.) on reducing glucose levels, liver function (SGOT-SGPT) and liver histopathology through assessment of necrosis and parenchymatous

Nomor ISSN: 3124-1115

degeneration levels in male rats. This study used male wistar rats (Rattus norvegicus) weighing 160-250 grams and aged 2-3 months with a total of 24 wistar rats for each experimental group. The grouping of test animals was carried out randomly into 4 test groups with 6 rats each, namely the control group, treatment group 1, treatment 2 and treatment 3.

On day 0, the mice's blood glucose levels were measured as the initial sugar levels before alloxan induction. All groups of mice were induced with alloxan at a dose of 55 mg/kgBW by intraperitoneal injection three times a week, and their blood sugar levels were calculated, which were listed in the table for day 14. The results were as follows:

Table 1. Body Weight Graph (gr) in Mice

Group	Beginning Day 0	Induction Day 14	Extraction Day 28
P0	206.7	215	212.8
P1	208.3	180.8	203.8
P2	208.3	183.3	202.3
P3	207.5	183.3	204.1

From the table above, it can be seen that on day 0 (beginning) all groups of mice had an average according to the inclusion criteria, namely 160-250 gr. After being given alloxan induction, which was seen on day 14, it was seen that groups P1, P2 and P3 experienced a decrease in body weight with an average result of 180.8 gr, 183.3 gr, and 183.3 gr. Meanwhile, in this study, group P0 was not induced so that the body weight of the mice did not experience a decrease. After being given alloxan induction ...The nanoemulsion preparation of mangosteen peel extract (Garcinia mangostana L.) showed an increase again in group P1 to 203.8g, P2 to 202.3g and P3 to 204.1g so that the administration of the extract was effective in increasing the body weight of mice with diabetes mellitus. Furthermore, monitoring of blood glucose levels (KGD) was as follows:

Table 2. Average Blood Glucose (KGD)mg/dL

Group	Day - 0	Day - 14	Day- 28
P0	93.3	96.3	97.5
P1	95.3	328.5	124.3
P2	92	333.3	94.5
P3	92.6	329.3	80.1

The table above shows the average blood glucose levels (BG) in mice in groups P1, P2, and P3. The results show that the mice experienced an increase after being induced by alloxan, with an average BG of > 300 mg/dL, indicating that this group had diabetes mellitus. The P0 group, which was not induced, served as the reference group for its blood sugar levels.. After being givennanoemulsion of mangosteen peel extract (Garcinia mangostana L.) visible groupP1, P2, and P3 experienced a decrease in blood sugar levels and showed that they did not have diabetes mellitus with an average result of124.3mg/dL,94.5mg/dL and80.1mg/dL. For the lowest and best results in reducing KGD in the P3 group with an average result80.1 mg/DL and the results are below the P0 group as a reference. So the results of the mice's

Nomor ISSN: 3124-1115

glucose levels returned to normal andNanoemulsion of mangosteen peel extract (Garcinia mangostana L.) is effective in reducing blood glucose in rats with diabetes mellitus.
Liver function can be measured by examining serum enzyme activity, one of which is serum aminotransferase or transaminase. The normal range for SGPT in rats is 17.5-30.2 IU/L, while the normal range for SGOT in mice is 45.7-80.8 IU/L. Observations were made on day 14, the day after diabetes induction, and day 28 after lime peel extract treatment. Afterward, liver histopathology was observed and data analyzed.

Reporting Research Results

Observations were made on the 14th day, which is the day after diabetes induction was carried out, and the 28th day after lime peel extract treatment was given. The following are the results of observations of the liver function of mice:

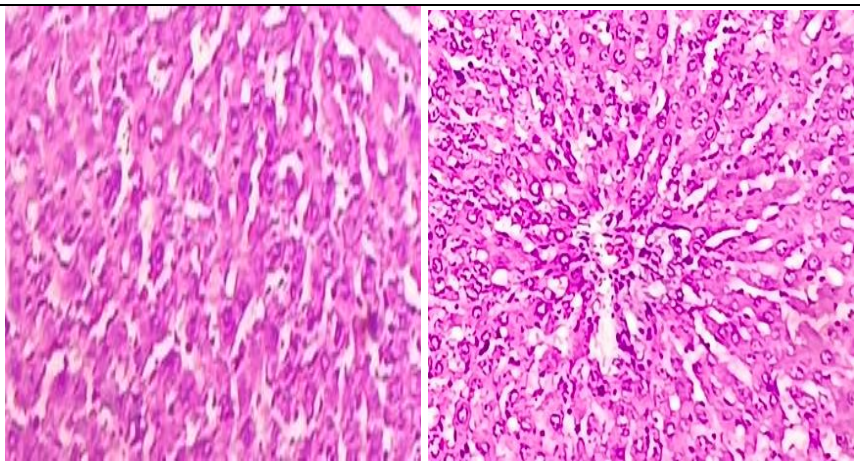
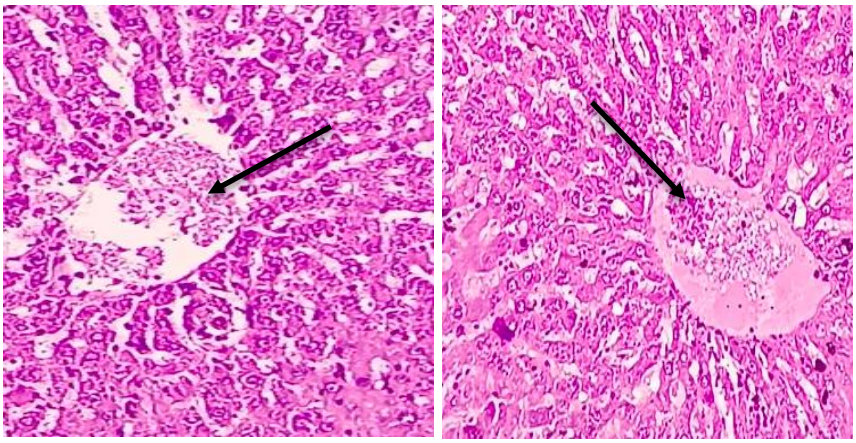
Table 3. Average SGOT(U/L)and SGPT(U/L)

	Induction - Day 14		Extraction - Day 28	
Group	**SGOT**	**SGPT**	**SGOT**	**SGPT**
P0	64.8±5.5	23.1±1.6	66.8±5.6	24.8±1.16
P1	199.5±2.5	104.5±5.7	93.1±3.3	26.5±1.8
P2	211.1±35.5	104.5±5.05	75.8±6.01	21.1±1.32
P3	191.6±11.2	105.6±9.8	52.8±7.8	18.5±1.37

From the table above it can also be seen after 14 days of administrationnanoemulsion of mangosteen peel extract (Garcinia mangostana L.) given and monitored the results on the 28th day are visiblein group P1 showed the average SGOT results93.1±3.3and the SGPT results are26.5±1.8 and the SGOT results have not reached normal values but there has been a good decrease from before while the SGPT levels have reached normal serum levels.. For group P2, the average SGOT results were shown, namely 75.8±6.01and the SGPT results are21.1±1.32, so that if we look at the results in this group, it has reached the normal limit value. In group P3shows the average SGOT results, namely 52.8±7.8and the SGPT results are18.5±1.37 so that if we look at the results in this group, it has also reached the normal limit value.
Based on the data that has been studied, researchers then looked at liver function and described it through histopathological images of liver function to determine the impact of liver function that has experienced diabetes mellitus.

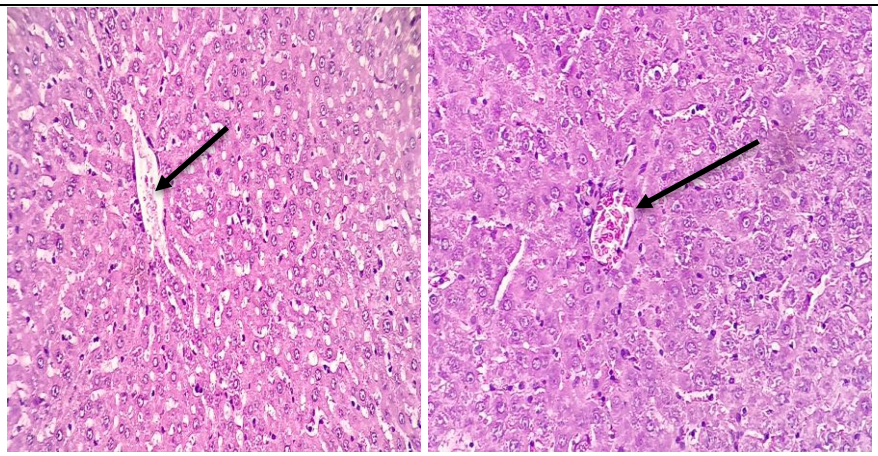
Nomor ISSN: 3124-1115

Table 4. Histopathology Results of Rat Liver

Group	Histopathological Image Results of Rat Liver Function
Control (P0)	 This group was fed standard rat pellets + distilled water/day/head for 14 days. Microscopic images of the livers of Wistar rats in the Control group (P0) showed no changes in liver histology, no fatty liver, and no liver necrosis, so the score for this group was 1, which is normal.
Treatment (P1)	 This group was induced by alloxan + nanoemulsion of mangosteen peel extract at a concentration of 1% and given pellet feed/distilled water/day/head for 14 days. Microscopic images of the liver of mice in treatment group 1 (P1) in this group showed a fairly large and widespread fatty degeneration liver, parenchymatous degeneration or bleeding in liver cells, inflammatory cell infiltration, the scoring in this group was 3, namely there were changes in the form of hydropic degeneration.

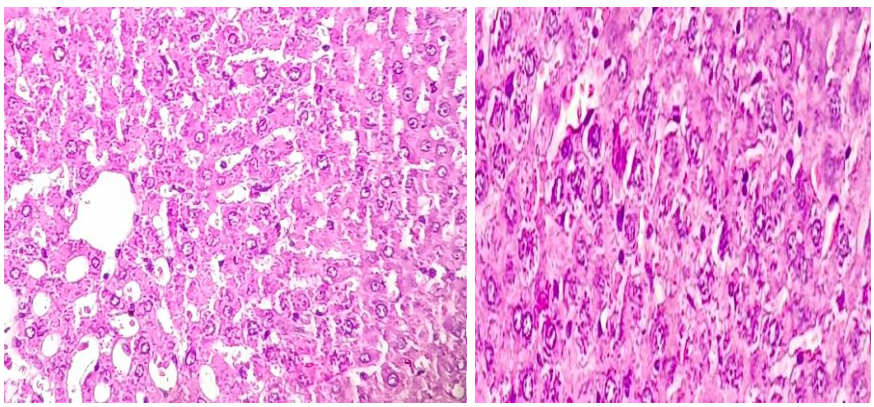
Nomor ISSN: 3124-1115

Treatment (P2)



This group was induced by alloxan + nanoemulsion of mangosteen peel extract at a concentration of 2% and given pellet feed/distilled water/day/head for 14 days. Microscopic image of the liver of mice in Treatment Group 2 (P2). The liver showed fatty degeneration, congestion, and inflammatory cell infiltration, with a score of 2 for this group.

Treatment (P3)



This group was induced with alloxan + mangosteen peel extract nanoemulsion at a concentration of 3% and fed pellets/distilled water/day/head for 14 days. Microscopic images of the livers of mice in treatment group 3 (P3) appeared normal, with no visible inflammation, cells were beginning to recover, and no necrosis or fatty deposits were observed. The score for this image was 1, meaning normal.

For data analysis on the results of the data normality test in this study, it can be seen in the following table:

Table 5. Shapiro Wilk Normality Test

Group		df	Sig
SGOT	P0	6	.235
	P1	6	.090
	P2	6	.605
	P3	6	.611
SGPT	P0	6	.421
	P1	6	.080
	P2	6	.514

Nomor ISSN: 3124-1115

	P3	6	.178

So from the table above, the significance results of the SGOT and SGPT examinations for all groups (P0, P1, P2, P3) are > 0.05, so the data is normally distributed.To test whether there is a statistically significant difference between two averages from the same group, before and after treatment, use the Paired Sample t-Test with the following results:

Table 6. Test*Paired Sample t-Test*

	Mean	t	df	Sig. (2-tailed)
SGOT (Induction – Extraction)	94.62	7,704	23	.000
SGPT (induction – extraction)	61.70	7,975	23	.000

From the test results above, the significance value at a 95% confidence level ($p < 0.05$) is 0.00 for SGOT and SGPT liver function, so there is a significant difference in each average value between sample groups. The conclusion obtained is that there is a significant difference in the average (mean) percentage of liver function of the three groups.

DISCUSSION

Due to their potential as antioxidants and anticancer agents, xanthones found in ethanol extracts of mangosteen peel have been the subject of much research. This is evident from phytochemical tests conducted on mangosteen peel extracts using ethanol as a solvent, indicating that the extract is rich in bioactive compounds that can have various pharmacological effects, such as antioxidant, antimicrobial, and anti-inflammatory activity. because it contains compounds xanthones, flavonoids, alkaloids, terpenoids, tannins, saponins and steroids.

On day 0 (beginning) all groups of mice had an average according to the inclusion criteria, namely 160-250 gr and the average blood glucose level (KGD) in mice in groups P1, P2 and P3 resulted in mice experiencing an increase after being induced by alloxan with an average KGD result of > 300 mg/dL and the group had experienced diabetes mellitus.examination of blood glucose levels in mice that had diabetes mellitus, for the lowest and best results in reducing KGD in group P3 with average results80.1 mg/DL and the results are below the P0 group as a reference. So the results of the mice's glucose levels returned to normal andNanoemulsion of mangosteen peel extract (Garcinia mangostana L.) is effective in reducing blood glucose in rats with diabetes mellitus.

From the examination of SGOT and SGPT levels, it can be concluded thatnanoemulsion of mangosteen peel extract (Garcinia mangostana L.)given toMale Wistar strain rats (Rattus norvegicus) were given significant results for 14 days of treatment to restore liver function to normal after the rats experienced diabetes mellitus, with the effectiveness of administration at concentrations of 3% and 2% being more effective than 1%. BecauseP3 groupshows the average SGOT results, namely 52.8±7.8and the SGPT results are18.5±1.37. WhereOnThe average examination of the levels of KGD, SGOT-SGPT in rats that had diabetes mellitus and were given mangosteen peel extract at a concentration of 1% KGD was 124.3 mg/dL, SGOT 93.1 U/L and SGPT 26.5 U/L. At a concentration of 2% KGD was 94.5 mg/dL, SGOT 75.8 U/L and SGPT 21.1 U/L. At a concentration of 3% KGD was 80.1 mg/Dl, SGOT 52.8 U/L and SGPT 18.5 U/L. Sothe effectiveness of administration at concentrations of 3% and 2% is more effective than 1%.

Nomor ISSN: 3124-1115

These results are also in line with liver histopathology.The liver was examined histopathologically for congestion, degeneration, necrosis, and inflammatory cell infiltration. It was then scored using the Manja Roenigk scoring method.(Sukmaningbayu AJ, 2016) where the results showControl group (P0) there was no change in the histological structure of the liver, no fatty liver and necrosis so that the score in this group was 1 which is normal, treatment group 1 (P1) showed a picture of the liver with fatty degeneration which was quite extensive and widespread, parenchymatous degeneration or bleeding in liver cells, inflammatory cell infiltration, the scoring in this group was 3 which was a change in the form of hydropic degeneration, Treatment group 2 (P2) showed a picture of the liver experiencing fatty degeneration, congestion, inflammatory cell infiltration, the scoring for this group was 2. And treatment group 3 (P3) looked normal, no inflammation was seen, cells began to improve, no necrosis and fatty liver were seen. And the scoring for this picture was 1 which was normal.

Phenolic and flavonoid compounds in medicinal plants are compounds that can lower blood sugar levels and thus have an anti-diabetic effect.(Linda Wati, Linda Chiuman, Ali Napiah Nasution, 2021).So this is in line with the research results (Lina, NWM, 2017)Xanthones found in mangosteen peel have antioxidant, antidiabetic, anticancer, anti-inflammatory, hepatoprotective, immunomodulatory, aromatase inhibitor, antibacterial and other functional properties.

CONCLUSION

1. The compounds found in mangosteen peel extract (Garcinia mangostana.L) through phytochemical screening are:xanthones, flavonoids, alkaloids, terpenoids, tannins, saponins and steroids.
2. OnThe average examination of the levels of KGD, SGOT-SGPT in rats that had diabetes mellitus and were given mangosteen peel extract at a concentration of 1% KGD was 124.3 mg/dL, SGOT 93.1 U/L and SGPT 26.5 U/L. At a concentration of 2% KGD was 94.5 mg/dL, SGOT 75.8 U/L and SGPT 21.1 U/L. At a concentration of 3% KGD was 80.1 mg/Dl, SGOT 52.8 U/L and SGPT 18.5 U/L. Sothe effectiveness of administration at concentrations of 3% and 2% is more effective than 1%.
3. In liver histopathologyThe best results were obtained in treatment group 3 (P3), which was given a 3% concentration of mangosteen peel nanoemulsion. The liver appeared normal, with no visible inflammation, cells starting to improve, and no necrosis or fatty deposits. The score for this image was 1, meaning normal.

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