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Test of Ethanolextract Red Gedi Leaves (*Albelmoschus Manihot.*(L.) Medik) in White Rat (*Rattus Norvegicus)* Type 2 Diabetes Mellitus

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Abstract

The research aimed to examine the red gedi leaveethanol extrack on the blood glucose content, insulin, and HOMA-IR of diabetes mellitus type 2 the rats induced by a high cholesterol food and fructose. The research used an experimental method with the pretest- posttest randomized controlled group design and samles of 120 male white rats being devided into 6 groups in wich each group comprised 20 rats. I, II, and III were the control groups, IV, V, and VI were the experiment group.the group I; the healthy control was given Na.CMC 0,5%, group II; pain control was injected with high cholesterol food 15g and fructose given orally, group III; drugs control was given 9 mg/200gBW metformin. The exsperimen group was given the red gedi leave extract 0f 150, 300, and 450 mg/kgBW of rats. The research result indicates that:1.The Antioxidant of the Red Gedi leaf ethanol extrack give strong affect. 2. The red gedi leaf provision has influence on the decreases blood glucose content, increase insulin levels, and decreases HOMA-IR. 3.The efective dose to decrease blood glukosa level's, increase insulin level's and decrease HOMA-IR value is 150 mg/kgBW.

Keywords: extract red gedi leave; blood glucose; HOMA-IR.

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1. Introduction

Diabetes mellitus type 2 is a heterogeneous disease with many factors that influence it.The disease is characterized by metabolic disordersnamely disruption β cell function and insulin resistancein peripheral tissues such as skeletal muscle and fat tissue and insulin resistance in the liver.The state of chronic hyperglycemia of diabetes is associated with long-term damage, disfunction and failure of various organs,especially the eyes, kidneys, nerves, heart and blood vessels [1]. Diabetes Mellitus by*World Health Organization* is a chronic condition that occurs when blood glucose above normal due to the pancreas does not produce enough insulin or the body's ineffective use of insulin that is produced.according to *International Diabetes Federation* (IDF) [2], Diabetes is a chronic disease that occurs when the body is not enough to produce insulin or does not use insulin effectively within. Insulin resistance is a condition associated organ failure as normal target respond activity of the hormone insulin.Insulin resistance is associated with abnormalities in various organsincluding polycystic ovary syndrome, cancer, infection, obesity and type 2 diabetes mellitus [3]. Fasting insulin levels reflect insulin resistance, higher fasting insulin levels,the higher the degree of insulin resistance. According to Lee JM [4]. Insulin resistance is a condition associated with organ failure the target normal activities to respond to the hormone insulin are associated with abnormalities of various organs.This is one of the mechanisms underlying type 2 diabetes.In these circumstances there is a decrease in the activation*tyrosine kinase* which led to a decrease in phosphorylation of IRS-1(*insulin reseptor substrat-1*) the insulin receptor. The phosphorylation of IRS-1 is required on gene expression,lipid and protein metabolism as well as the activity of PI-3K(*phosphatidylinositol-3 kinase*) and MAPK (*mitogen activator protein kinase*). This will lead to a decrease in the ability of IRS-1to bind to*PI3 kinase* (MYMX ties with motifs in IRS-1), thus causing a decrease in the activity of PI3 kinase and also accelerated the degradation of protein IRS-1 [5]. The use of drugs of natural materials at this time that can control diabetes mellitus has many in the know.Stocks mostly been studied and shown to be effective as an alternative therapy,especially those containing antioxidant compounds. Plant red gedi (*Abelmochus manihot* (L.) Medik)is a tropical plant that originated in China known as Gedi [6]. In the town of Palu, the plant is known as one of the raw materials of vegetables.This plant is believed to have medicinal properties, among others, diabetes mellitus and renal failure [7]. This plant is rich in vitamins A, B1, B2: B3, C, E and calcium, potassium, copper, zinc and collagen as well as a variety of secondary compounds are like flavonoids, saponins and compounds that have activity fenolit antidote to free radicals and hydrogen peroxide [8]. Research conducted by V. Sabitha [10] stating the effects of hypoglycemia extract red gedi(*Abelmoschus esculentus* (L.) Moek) at a dose of 100 mg/kgBW and 200 mg/kgBW white rat(*Rattus norvegicus*) diabetes mellitus showed significant($p < 0,001$) the decrease in blood glucose levels and the use of up dose 2000 mg/kgBW does not show toxicity.This research generally aims to examine the effect of ethanol extract of leaves of red gedi (*Abelmoschus manihot.* (L.) Medik) on blood glucose levels, insulin sensitivity in male rats (*Rattus norvegicus*) models of type 2 diabetes mellitus.

2. Research Methods

The method used is the method of experimental designpretest postest randomized controlled group design, use white male rats(*Rattus norvegicus*) as many as 120 tails were divided into 6 groups,Each group consisted of 20 birds with details of group I, II, and IIIas the control group and the group IV, V, VIfor the experiment were

given the leaf extract of red gedi 150, 300 and 450 mg / kgBW of mice.to make the test animal models of type 2 diabetes diobesitaskan test animals during 50 days prior to the feed-induced high cholesterol and fructosethen continued feeding high cholesterol are: 15% duck egg yolk, 10% mutton fat, 1% synthetic cholesterol, and 74% P2 standard feed for 12 days and the high-cholesterol feed D12450B-LD10 *Low control Diets made in American* to improve the working *Sterol Regulatory Element Binding Protein* (STREBP) [10].

3. Materials and Methods

Tools: Stirring rod, Funnel glass(*Scott*), Photometer Autoanalyzer Modular P 800, Elisa (*Bio Rad Mode* 650), Beaker50 ml, 100 ml, 200 ml (*Pyrex*), Measuring cup10 ml, 100 ml, 250 ml (*Pyrex*), glucometer (One-Touch), Cage test animals,oral syringe10 ml (*Terumo*), Spektrofotometer UV-Vis (*Hewlett Packard*), an analytical balance(*Sartorius*), scales of test animals.

Materials: Distilled water, Streptozotocin, Alcohol 96%, Hydrochloric acid,Iron (III) chloride, Leaf red gedi(*Abelmoschus manihot* (L) Medik), Ethanol absolute, p.a, Dragendorf LP Liebermann-Burchard, NaCl, magnesium powder, p.a, Sodium CMC,and the high-cholesterol feed.

Population and Sample Research

The study population includes Rats(*Rattus nervegicus*) obtained from the Laboratory of the Faculty of Medicine, University of Airlanggaas many as 120 tails were divided into six treatment groupswhere each group consisted of 20 rats were taken randomlywhereas the leaves red gedi obtained from the city of Palu, Central Sulawesi Province.

Making Ethanol Extract Leaves Red Gedi

Gedi red leaf that has been powdered 5kgextracted with ethanol for 3 days was filtered and the residue obtained was concentrated using a rotary eveforator,the results are then evaporated on a water bath to be free of the solvent remaining in the extract.

Measurement of Blood Glucose

Mice were fasted for 5 hours in advance (fixed by drinking)before being measured blood glucose levels.Blood is then drawn through the blood dripped on the orbital eye and stick glucometer.Within 10 seconds the blood glucose levels automatically and the results can be read on a monitor glucometers.

Measurement of Insulin Levels

Insulin levels were measured using the methodELISA from*Boehringer-Mannheim kit.* Steps of insulin levels is as followsprepare a standard solution within 15 minutes before use.*Sentrifuge* on 10.000 x 9,8m/s^2 for 1 minute, add the standard solution with 1 ml*Reference Standard & Sample Diluent*, cover and let stand for 10 minutes.After dissolve completely, mencampu thoroughly with a pipette.This treatment resulted in a stock

solution of 200 ng/ml. Then make Serf dilution required.The recommended concentration is as follows200, 100, 50, 25, 12,5, 6,25, 3,13, 0 ng/ml. To create a standard solution with a concentration100 ng/ml ie take 0.5 ml standard solution at 200 ng / ml,add to the EP tube containing 0.5 ml*Reference standar & sample diluent*, and mix The procedure for preparing the concentration remains all the same.Pure standard serves as the highest standard (200ng / ml).*Reference Standard & Samplehari Diluent* serves as zero (ng / ml).(Anonim ELISA kit). Measurements of insulin levels performed 5 times that measured levels of insulin days 0, 42, 49, 56 and day 63.

Counting Insulin resistance

Insulin resistance was calculated by HOMA-IR*(homeostasis model assesment of insulin resistence).* This method is used in the calculation of insulin resistance in humans and experimental animals.Calculations using the formula is:fasting blood sugar(mmol/dL) multiplied by fasting insulin(n/mL) divided by 22.5. or

$$\frac{\boldsymbol{fasting\ blood\ sugar\ x\ fasting\ insulin}}{\mathbf{405}}, HOMA\ IR \geq 2{,}27$$

otherwise insulin resistance.

Data analysis

Primary data collected in the study include the measurement of glucose levels,Measurements of insulin levels and HOMA-IR value calculation before and after treatmentethanol extract of leaves of red gedi 150 mg/kg, 300 mg/kg, 450 mg/kgBW of rats and Metformin 9mg/200 gBW mice orally.Data analysis was performed with SPSS version 24.

4. Results

Research result

Table 1: Qualitative Test Results Ethanol Extract Leaves Red Gedi

No	parameter Test	reagent	result	**Metodhs**
1	Alkaloid	Dragendorff	+	KLT
2	Flavanoid	HClPekat	+	KLT
3	polyphenol	$FeCl_3$	+	KLT
4	Steroid	Liebermann-Buchard (LB)	-	KLT
5	Saponin	HCl 2N	+	KLT
6	Tannins	$FeCl_3$	+	KLT

Information :+ (positive) : No indication of bioactive compounds

- (negative) : there is no indication of bioactive compounds

Table 2: Quantitative Test Results Ethanol Extract Leaves Red Gedi

No	Chemical Ingredients	result	**Unit**	**Methods**
1	Equivalent Total Alkaloids Quinine	0,33	%b/b	UV-Vis spectrophotometry
2	Equivalent Total Flavonoid Quercetin	22,48 ± 0,215	%b/b	UV-Vis spectrophotometry
3	Total Phenol Acid Equivalent Gallat	3,37 ± 0,012	%b/b	UV-Vis spectrophotometry
4	Equivalent steroids Beta sitosterol	<68	mg/Kg	UV-Vis spectrophotometry
5	Tannin Total Equivalent Tannic Acid	1,34	%b/b	UV-Vis spectrophotometry
6	Saponins from Quillaja bark Quantitative	2,70	%b/b	UV-Vis spectrophotometry

Table 3: Results of testing Antioxidant Activity of Ethanol Extracts Red Leaf Gedi

No	parameter Test	**result**	**Unit**	**Methods**
1	Activities arrest free radicals DPPH (IC_{50})	91,53	mg/l (ppm)	UV-Vis spectrophotometry

Table 4: Average Average Weight Rats Before and After Treatment

Days to-	The mean ± SD Blood Glucose (mg/mL)					
	healthy controls	pain control	Positive controls (Metformin)	A dose of 150 mg/kgBW	A dose of 300 mg/kgBW	A dose of 450 mg/kgBW
0	87,75±7,41	91,00±4,32	89,00±2,58	88,00±7,96	88,25±5,85	91,25±5,32
42	94,75 ± 4,72	192,5±13,23	203±11,52	198,75±9,07	214,25±14,57	208,25±21,25
49	96,25±4,43	182,5±17,82	167,75±9,11	175,25±11,90	188,5±11,39	176,00±7,00
56	96,75 ±4,57	175,25±17,59	154,75±8,50	149,75±17,67	161,75±15,28	145,75±15,02
63	90,00±2,16	168,25±21,88	121,25±15,67	129,00±10,00	102,5±12,01	89,75±4,27

Table 5: The average of Blood Glucose Levels Before and After Treatment

Days to-	The mean ± SD Blood Glucose (mg/mL)					
	healthy controls	pain control	Positive controls (Metformin)	A dose of 150 mg/kgBW	A dose of 300 mg/kgBW	A dose of 450 mg/kgBW
0	87,75±7,41	91,00±4,32	89,00±2,58	88,00±7,96	88,25±5,85	91,25±5,32
42	94,7 ±4,72	192,5±13,23	203±11,52	198,75±9,07	214,25±14,57	208,25±21,25
49	96,25±4,43	182,5±17,82	167,75±9,11	175,25±11,90	188,5±11,39	176,00±7,00
56	96,75±4,57	175,25±17,59	154,75±8,50	149,75±17,67	161,75±15,28	145,75±15,02
63	90,00±2,16	168,25±21,88	121,25±15,67	129,00±10,00	102,5±12,01	89,75±4,27

Table 6: The average of Insulin Levels Before and After Treatment

Days to-	The mean ± SD Levels Insulin Levels (ng/mL)					
	healthy controls	pain control	Positive controls (Metformin)	A dose of 150 mg/kgBW	A dose of 300 mg/kgBW	A dose of 450 mg/kgBW
0	4,72±0,94	4,63±0,81	5,15±0,53	4,81±0,32	4,41±0,61	4,08±0,57
42	4,88±0,15	14,28±1,30	12,88±0,85	12,38±1,18	13,25±0,96	12,50±0,51
49	4,14±0,59	13,10±0,72	9,20±0,48	8,59±0,92	9,47±1,42	7,33±0,63
56	4,22±0,48	12,00±0,64	7,13±1,03	6,53±1,69	7,32±2,16	5,69±0,00
63	4,09±0,47	11,10±0,75	6,84±1,05	6,17±1,90	5,12±0,95	4,48±0,77

Table 7: Mean Value Calculation Results HOMA-IR

Days to-	Mean ± SD HOMA IR					
	healthy controls	pain control	Positive controls (Metformin)	A dose of 150 mg/kgBW	A dose of 300 mg/kgBW	A dose of 450 mg/kgBW
0	1,01±0,13	1,04±0,20	1,13±0,14	1,04±0,07	0,96±0,15	0,92±0,17
42	1,14±0,06	6,76±0,37	6,44±0,11	6,09±0,82	7,00±0,47	6,41±0,51
49	0,98±0,10	5,88±0,32	3,80±0,13	3,70±0,23	4,38±0,41	3,19±0,33
56	1,00±0,07	5,18±0,47	2,71±0,35	2,37±0,43	2,88±0,65	2,03±0,27
63	0,91±0,10	4,60±0,59	2,07±0,58	1,94±0,47	1,28±0,13	0,99±0,20

Profile Weight, Blood Glucose, Insulin Levels, and HOMA-IR Values Before and After Treatment

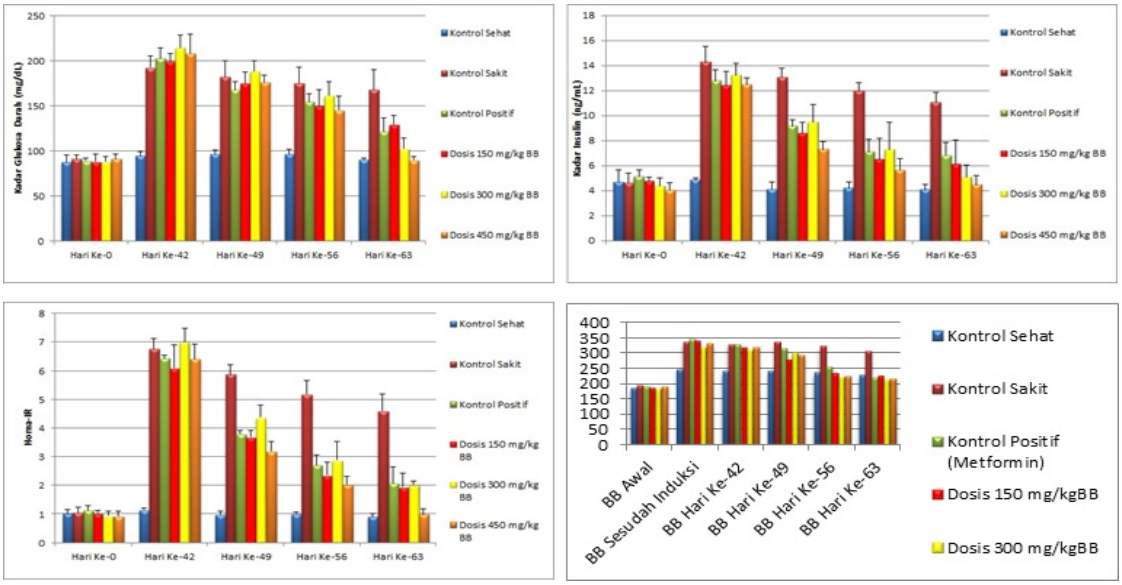

Figure 1: Profile Observations

5. Discussion

This study uses the White Rat (Rattusnorvegicus) obtained fromLaboratory of the Faculty of Medicine, University of Airlangga a total of 120 red tail and leaves gediobtained from the city of Palu, Central Sulawesi. Previously performed determination of plants in the Research Center for Biology LIPI Bogor to ascertain the type used gedi.The results show that gedi used in this study is completely species In this study measured body weight, glucose, insulin, and HOMA-IR value calculationon days 0, 42, 49, 56, and day 63.Determination of days counted from the provision of feed induced high cholesterol and fructose.On day 42 all treatment groups have shown elevated levels of glucose,decreased levels of insulin, HOMA-IR increased value,except in group I were used as healthy controls.Starting today all 42 group III were given metformin 9 mg/200gBW mice orally.Group IV by the ethanol extract of leaves of red gedi 150 mg/kgBW, group V by the ethanol extract of leaves of red gedi 300 mg/kgBW,and VI group were given ethanol extract of leaves of red gedi 450 mg/kgBW. The mean body weight, blood glucose levels, insulin levels and HOMA-IR values on days 0, 42, 49, 56,and day 63 of each group are shown in Table 4, 5, 6, and Table 7.In the table it appears that on the 42nd day average weight increased glucose levels begin to rise,insulin levels begin to decline and HOMA-IR values begin to increase when compared to before feeding high cholesterol diet and fructose.These results suggest that induction of high feed cholesterol and fructose effect on body weight,blood glucose levels and insulin sensitivity which is characterized by glucose levels that remain high,insulin levels remain low and HOMA-IR values in group II until the end of the observation. Induction of feed high in cholesterol and fructose causes the rats became obese (Table 4)resulting in metabolic disorders are disorders β cell function and insulin resistance in peripheral tissues such as muscle and fat tissue,as well as insulin resistance in liver cells causing hyperglycemia.Insulin resistance is one of the mechanisms that underlie the occurrence of type 2 diabetes.Insulin resistance is caused by the interference pre receptors, receptor and post receptor.The main area is the development of insulin resistance in post target cell receptors in skeletal muscle tissue and liver cells.Postreseptor damage this causes compensatory increase in insulin secretion by β cells resulting in hiperinsulinemi on fasting and postprandial state.

Hiperinsulinmia marked by decreased activity of the enzyme tyrosine kinase and increased activity of the enzyme tyrosine phosphatase.The enzyme tyrosine kinase and tyrosine phosphatase enzyme to function in regulating insulin signal where the enzyme tyrosine kinase responsible for the phosphorylation process, while the enzyme tyrosine phosphatase responsible for dephosphorylation and activation of the insulin receptor.A decrease in activity of the enzyme tyrosine kinase led to a decrease in phosphorylation of IRS-1 (Insulin Receptor subtrate-1) to the insulin receptor. The phosphorylation of IRS-1 is required on gene expression, and protein and lipid metabolism The activation PI-3K (*phosphatidylinositol-3 kinase*) and MAPK (*Mitogen Activator Protein Kinase*). This will lead to a decrease in the ability of IRS-1 binding to PI3 Kinase(Association with MYMX motif on IRS-1),thus causing a decrease in the activity of PI3 kinase and also accelerated the degradation of protein IRS-1 [5] The results showed that there was the influence of ethanol extract of leaves of red gedi to decreased glucose levels,insulin levels, and insulin sensitivity (HOMA-IR) in rats fed a high cholesteroland fructose characterized by ANOVA test with $p < 0.05$ in each treatment.After the treatment is on the 49, 56, and 63 mean glucose levels begin to decline, insulin levels begin to decline,and HOMA-IR values began to decline which can be seen in Figure 1.Decreased glucose levels, insulin levels increase occurred in the group duberi ethanol extract of leaves of red gedi and the group given metformin.The results showed that ethanol extracts of leaves of red gedi effect on glucose levels and insulin sensitivity in rats fed a high cholesterol and fructose. On the measurement of glucose levels result on day 0 there is a significant difference between the three dose variation with the positive control.Among the positive control to control pain is also not there is a significant difference thisdue to blood glucose levels rat model of diabetes on days 0 is almost the same because there is no treatment. On the 42 day there can be a significant difference between the three dose variation with the positive control. Between pain control with the third dose variation also there are no significant differences, but there aresignificant differences between the three variations of the dose and positive controls to control painit indicates that blood glucose levels rat model of diabetes have increased due to the induction of feeding high cholesterol diet and fructose than healthy controls were not induced. On the 49 day showed that between doses of 150 and 450 mg/kgBW there is not a significant difference to the positive controland significantly different to control pain while at a dose of 300 mg / kgBW showed a significant difference to the positive control this is due to the possible interference metabolic systemactive substance is not dissolved perfectly in the body of white rats that are not absorbed in the receptor maximum. On day 56 showed no significant difference between the three variations of doses of 150, 300, and 450 mg/kgBW withpositive control but differ significantly with pain control.This shows that on the 56 the three variations dose would give the same effect as a positive control by medformin.The effect occurs because the active substances contained in the ethanol extract of leaves of red gedi already absorbed perfectly within the receptor. On day 63 showed no significant difference between the doses of 150 and 300 mg/kgBW positive control but differ significantly with pain control,whereas at a dose of 450 mg/kgBW showed a significant difference to the positive controls and not significant with pain controlthis is because the saturation occurs dose or too concentrated, so by including a relatively long time has no effect because the active substances contained in the extract is not absorbed by the receptors. On the measurement of insulin levels result on day 0 showed no significant pebedaan between positive control dose third dose variation is 150.300, and 450 mg/kgBW.Among the positive control to control pain also showed no significant difference.This suggests that insulin levels of each group are still the same because there is no treatment. On day 42 showed no significant difference between pain control with the third dose variations ie

150.300 doses, and 450 mg/kgBW,but there is a significant difference to the healthy controls.This suggests that the increased insulin levels induced by feeding high cholesterol diet and fructose than healthy controls were not induced by feeding high cholesterol diet and fructose. On the 49th day showed a significant difference between the doses of 150 and 300 mg/kgBW positive control but differ significantly with pain control,whereas at a dose of 450 mg/kgBW showed a significant difference to the positive control, but different does not sugnifikan to control pain.This shows that at doses of 450 mg/kgBW occurred saturation or concentrated terlausehinnga not completely absorbed in sehinnga receptor had no effect. On day 56 showed no significant difference between the positive control with the third variation of doses that a dose of 150, 300, and 450 mg/kgBWthe positive control but differ significantly with pain control. This indicates that the active substances contained in the extract has been absorbed perfectly in sehinnga receptor gives the same effect as a positive control by medformin. On day 63 showed no significant difference between the positive control at a dose of 150 mg/kgBW,but differ significantly on pain control, whereas at doses of 300 and 450 mg/kgBW there is a significant difference to control pain but not significantly different to the positive control.This is because the saturation occurs dose or too concentrated sehinnga by including a relatively long time the active substances contained in the extract had no effect. In the calculation of the value of HOMA-IR results obtained on day 0 have not seen a decrease in HOMA-IR values are marked with $p > 0.05$ ($p = 0.586$).This is because there is no treatment of each group. On day 42 is starting to look a change in HOMA-IR values marked with $p < 0.05$ ($p = 0.017$).This is caused by the effect of feeding high cholesterol diet and fructose cause the value of HOMA-IR increased. On the 49, 56, and 63 effects of ethanol extract of the leaves of red gedi HOMA-IR values began to look marked with $p < 0.05$.P values are respectively 0.001, 0.002, and 0.001.It showed that the ethanol extract began to give effect in reducing insulin resistance sehinngga HOMA-IR value decreases. Based on one way ANOVA test with advanced test waller-duncan seen that: On day 0 indicates the value of $p < 0.05$ ($p = 0.463$), which means not happened insulin resistance rat model of diabetes because there is no treatment. On day 42 there is a significant difference between the positive control at a dose of 150, 300 and 450 mg/kgBW and significantly different rehadap healthy controls.Among the positive control to control pain there is also a difference insignificant.This suggests that insulin resistance (HOMA-IR value) increases induced by feeding high cholesterol diet and fructose. On the 49 day there is not a significant difference between the positive control at a dose of 150 mg/kgBW, but differ significantly on pain control.Between doses of 300 and 450 mg / kg with a positive control showed a significant difference, but not significantly different to control pain.This shows that at doses of 300 and 450 mg / kg body weight is too concentrated or experiencing burnout and therefore can not be absorbed in the receptor thereby giving the effect of lowering the value of HOMA-IR. On the 56 there is a significant difference between the positive control with the third dose variation (150,300,450 mg/kgBW) and significantly different to control pain.This shows that the three variations of doses (150, 300, 450 mg/kgBW) had effects comparable to positive control by medformin. On day 63 there is a significant difference between the positive control at a dose of 150 mg / kg, but differ significantly on pain control,whereas at a dose of 450 differ significantly from the positive control but not significantly different to the healthy controls.It showed that the ethanol extract of leaves of red gedi already gives the same effect as a positive control by medformin in reducing insulin resistance (HOMA-IR value). Based on the results of a further test LSD (Least Square Deferences) and waller-duncan obtained on days 49, 56, and 63 in each group showed that glucose levels, insulin levels, and the value of HOMA-IR between the groups was not significantly different

from that marked with a P value> 0.05.This shows that no differences in the effect of dosing stratified ethanol extract of leaves of red gedi to decreased glucose levels, insulin levels, and the value of HOMA-IR rats induced by feeding high cholesterol diet and fructose,while doses that are effective in lowering glucose levels, improve insulin level and HOMA-IR value is the dose of 150 mg / kg body weight because the dose is small doses, but has been able to lower,blood glucose levels, increasing insulin levels and lower HOMA-IR value equivalent to medformin. A decrease in blood glucose levels, decreased levels of insulin, HOMA IR impairment by the ethanol extract of leaves of red gedi caused bioactive compounds contained in extracts of leaves of red gedi such as alkaloids, flavonoids, saponins, tannins and polyphenols.Alkaloid contained in the ethanol extract of the leaves of red gedi works by stimulating the hypothalamus to increase the secretion of Growth Hormone Releasing Hormone (GHRH), so that the secretion of growth hormone (GH) on the pituitary increases.High levels of GH stimulates the liver to secrete*Insulin-like Growth Factor*-1(IGF-1). IGF-1 has the effect of inducing hypoglycemia and decrease gluconeogenesis that blood glucose levels and insulin demand decreases [11]. Flavonoids contained in red gedi leaf ethanol extract has antioxidant activity that can counteract free radicals by electron transfer and inhibition of peroxidation reaction so that the presence of flavonoids can reduce lipid peroxidation and were able to restore the sensitivity of insulin receptors on cells [5]. Saponins contained in able to lower blood glucose levels by inhibiting gastric emptying so that the absorption of the food will be longer, and blood glucose levels will have improved [8]. Tannins contained in the extract is able to stimulate the metabolism of glucose and lipids as well as serve as an astringent orchelating be pursed small intestine epithelium, thereby reducing the absorption of nutrients and consequently inhibit glucose intake and the rate of increase of blood glucose is not too high [12]. Polyphenols contained in the extract are known to reduce oxidative stress by preventing the conversion of superoxide to hydrogen chain superoxide by donating the hydrogen atoms of an aromatic hydroxyl (OH) polyphenols to scavenge free radicals and remove them from the body through the excretion system [13].

6. Conclusions

Based on the research results can be concluded that the ethanol extract of the leaves of red gedi*(Abelmoschus manihot* (L.) Medik) has strong antioxidant activity that ethanol extract of leaves of red gedi*(Abelmoschus manihot* (L.) effect on blood glucose levels, insulin sensitivity, decreased insulin resistance,however there was no difference in the effect of dosing stratified, Rats(*Rattus norvegicus*) Diabetes Mellitus Type 2. The dose is effective in lowering glucose levels, improve insulin levels, and lower the value of HOMA-IR is a dose of 150 mg/kgBW.

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