Jurnal IJBPAS 2020 dg Entris

by Elis Susilawati

Submission date: 01-Sep-2021 07:33PM (UTC-0500)
Submission ID: 1639757596
File name: Jurnal_IJBPAS_2020_dgn_entris.pdf (710.47K)
Word count: 4293
Character count: 22250

IJBPAS, May, 2020, 9(5): 972-982

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

ANTIDIABETIC ACTIVITYOF ETHANOL EXTRACT OF KABAU SEEDS (*Archidendron bubalinum* (JACK.) I.C. NIELSEN) AS ANTI-DIABETIC

SUTRISNO E*, CAROLINA CP AND SUSILAWATI E

Department of Pharmacology, Faculty of Pharmacy, Bhakti Kencana University, Soekarno Hatta street 754 Bandung, Indonesia

***Corresponding Author: E Mail: elis.susilawati@bku.ac.id**

Received 28th Oct. 2019; Revised 20th Nov. 2019; Accepted 29th Dec. 2019; Available online 1st May 2020

https://doi.org/10.31032/IJBPAS/2020/9.5.5041

ABSTRACT

Empirically, Kabau seeds (*Archidendron bubalinum* (Jack.) I.C.Nielsen) are used by Sumatran people as antidiabetic drugs. This study aims to investigate the antidiabetic activity of ethanol extract of Kabau seeds. The methods used in this study were insulin resistance and insulin deficiency by using Swiss Webster mice, and α-glucosidase enzyme inhibition. The insulin resistance method was carried out preventively by inducing Lipofundin® 30 mL/Kg body weight (bw) and fructose 0.52g /Kg bw for 28 days. The insulin deficiency mice was induced by alloxan monohydrate at dose 55-60 mg / Kg bw and blood glucose levels were measured on days 0, 3, 6, 9, 12, and 15. The animals were divided into 6 groups: negative control, positive control, comparison group, Ethanol Extract of Kabau Seeds (EEKS) 95 mg/Kg bw, EEKS 190 mg/Kg bw, and EEKS 380 mg/Kg bw. Inhibition of the α-glucosidase enzyme was carried out at extract concentrations of 50, 100,150, 200, 250, 300, 350, 400, 450, and 500 ppm, and the absorbance was measured by using a micro-reader at a wavelength of 425 nm. In the insulin resistant method, the values of constant insulin tolerance test (CITT) for negative control, positive control, metformin 65 mg/Kg bw, EEKS 95 mg/Kg bw, EEKS 190 mg/Kg bw, and EEKS 380 mg/Kg bw obtained were 1.58, 0.45, 1.89, 1.75,1.82, and 1.62, respectively. In the insulin deficiency method, all doses could reduce blood glucose levels on the 6th day. In conclusion, the results of this study show that ethanol extract of Kabau seeds increases insulin sensitivity and insulin secretion at best dose of 190 mg/Kg bw.

Keywords: Kabau Seeds, *Archidendron bubalinum* (Jack.) I.C.Nielsen, diabetes mellitus

INTRODUCTION

Diabetes mellitus (DM) is a serious non-communicable chronic disease in which the pancreas does not produce enough insulin or a condition where the body cannot use insulin effectively. DM is one of diseases that has a high prevalence in the world. The number of people with diabetes in 2017 was 422 million where 1.5 million of them died. In 2014, there were 96 million adults with diabetes in 11 member countries in the Southeast Asia region **[1, 2]**, In 2018, there were 10.9% of Indonesians diagnosed with DM. Data showed that almost 90% of people with diabetes suffer from diabetes mellitus tipe 2 (T2DM). T2DM is characterized by insulin resistance and insulin deficiency.

During this time, metformin is the initial treatment for patients with T2DM. Metformin has the main effect of reducing liver glucose production (gluconeogenesis) and improving glucose uptake in peripheral tissues. Metformin has major side effects such as dyspepsia, diarrhea, and lactic acidosis **[3]**.

Apart from metformin, almost all classes of oral antidiabetic drugs have side effects so that many patients try to control their blood glucose levels by using natural remedies such as herbs. One of the plants that has been used as traditional medicine for diabetes mellitus treatment is Kabau seeds. Kabau (*Archidendron bubalinum* (Jack.) I.C.Nielsen) is a plant that can be found in Sumatera Untill now, Kabau plant is only used as vegetables or food complement **[4]**. Empirically, Kabau seeds are used by people in several areas as traditional antidiabetic drugs and herbal diuretics. Kabau seeds are used as herbal antidiabetic drugs by taking part of the seeds that are ripe and dried by roasting, then finely ground. Kabau seeds that have been mashed are then dissolved in water and taken twice a day, phytochemical tests showed that Kabau plant extracts (root bark, stem bark, fruit skin, seeds and leaves) with 96% ethanol solvent contained alkaloids, flavonoids, terpenoids, tannins and saponins **[4]**. The young Kabau seeds can be immediately eaten as ulap and traditionally used as a limited number of Diureutik in order not to cause problems with the kidneys **[5]**.

Based on previous study, Kabau seeds extract showed antibacterial and antioxidant activity **[6]**. While, the study of extract of Kabau seeds Total antioxidant activity and enzymatic inhibition against alpha-amylase, alpha-glucosidase and pancreatic lipase of irradiated **[7]**. Therefore, it is necessary to conduct further study on the benefits of Kabau seeds as an

alternative herbal treatment for diabetes mellitus.

MATERIALS AND METHODS

Animals

The animals used in this study were male Swiss Webster mice at an average bodyweight of 20-30 grams and 2-3 months of age which obtained from breeders in Lembang. All mice were adapted to the new environment for one week. The mices were randomly assigned into six groups: negative control, positive control, metformin 65 mg/Kg bw-treated diabetes mellitus group, EEKS 95 mg/Kg bw-treated diabetes mellitus group, 190 mg/Kg bw-treated diabetes mellitus group, and 380 mg/Kg bw-treated diabetes mellitus group. The protocol was approved by the Research Ethics Commission of Padjajaran University, Bandung (Permit Number: 334/UN6.KEP/EC/2019).

Determination of Kabau plant (*Archiendron bubalinum* (Jack.) I.C.Nielsen)

Kabau seeds were obtained from Lahat, South Sumatra. Then, determination of Kabau plants (*Archidendron bubalinum* (Jack.) I.C.Nielsen) was conducted in the School of Biological Science and Technology, Bandung Institute of Technology (Plant Identification Certificate, Number: 5974 / I1.CO2.2 / PL / 2018).

Characterization of simplicia

Characterization was carried out on Kabau seeds simplicia powder which included total ash content, acid insoluble ash content, water soluble extract content, ethanol soluble extract content and drying shrinkage.

Phytochemical screening

Phytochemical screening was carried out on ethanol extract of Kabau seed which included identification of alkaloids, flavonoids, saponins, tannins, and steroids/triterpenoids.

Ethanol Extract of Kabau seeds Preparation

A total of 800 grams of simplicia powder was macerated with 8 L of 96% ethanol. The liquid extract was then evaporated using a rotary evaporator until it became a thick extract.

In vivo Antidiabetic Activity Test:

Insulin Resistance: This method was conducted preventively. Insulin resistance animal model was developed by inducing lipid emulsion Lipofundin® 30 mL/Kg bw and fructose 2.52g/ Kg bw orally for 28 days. The parameters measured were blood glucose levels and values of constant insulin tolerance test (CITT) on the 0, 7th, 14th, 21st, and 28th day. The acclimated mice were fasted for 3 hours and then the initial blood glucose levels were measured. After that, mice were given treatment and

induction together for 28 days. After 28 days, mice were fasted for 3 hours and then their insulin tolerance was measured by administering insulin 0.0125 UI/Kg bw intraperitoneally, and then blood glucose levels were measured per 15 minutes for 60 minutes **[8]**.

Insulin Deficiency: In the insulin deficiency method, the animals was induction by using alloxan monohydrate 55-60 mg/Kg bw given intravenously through the tail of mice in all groups except negative controls. After 3 days of induction, fasting blood glucose levels were measured. The animals were considered diabetic if the fasting blood glucose level was ≥ 200 mg/dl (t0). The provision of therapy was given for 15 days orally. Fasting blood glucose levels were measured on the 3rd, 6th, 9th, 12th and 15th days **[9]**.

***In vitro* Antidiabetic Activity Test:**

Inhibition of α-glucosidase enzymes: Inhibition of α-glucosidase enzymes were performed under optimum conditions which include pH 6.8 and temperature 37 °C. The ethanol extract of Kabau seeds was made in several concentrations (50, 100,150, 200, 250, 300, 350, 400, 450 and 500) dissolved in 0.1 M phosphate (pH 6.8) by using acarbose as standard. The enzyme was weighed about 1.2 mg which was then dissolved with 0.1 M phosphate buffer (pH 6.8) resulting in an enzyme concentration of 27.84 U / mL. Then, the enzyme main solution was diluted until its concentration became 0.078 U/mL. A total of 60 µL of the test sample was added 50 µL of 0.1 M phosphate buffer (pH 6.8) and incubated in a 96 well microplate at 37°C for 20 minutes. The blanks was prepared by replacing 60 µL of the test sample with phosphate buffer. After pre-incubation, 50 µL p-nitrophenyl-α-D-glukopyranoside (PNPG) 5 mM was inserted into the micro plate, and then re-incubated at 37 ° C for 20 minutes. In the final stage, the reaction was stopped by adding 160 µL of 0.2 M Na_2CO_3 solution in the well and the absorbance was recorded using a micro-reader at a wavelength of 425 nm **[10]**.

Statistical Analysis

All data are expressed as mean – standard error of the mean. The quantitative were analyzed using the SPSS version 16 software (SPSS, Chicago, IL, USA). Data from experiments with more than two independent variables were analyzed using analysis of variance (ANOVA) followed by the Tukey–Kramer posthoc tests. Statistical differences were considered significant when $P < 0.05$ (two-tailed).

RESULTS AND DISCUSSION

In this study, *in vivo* antidiabetic activity of ethanol extract of Kabau seeds was carried out using insulin resistance and insulin

deficiency method, and *in vitro* study was carried out using inhibition of the α-glucosidase enzyme. The parameter observed in the insulin resistance method was a decrease in blood glucose levels on the 0, 7th, 14th, 21st, and 28th day and followed by measuring the values of constant insulin tolerance test (CITT). In the insulin deficiency method the parameters observed were a decrease in blood glucose levels on 0, 3rd, 6th, 9th, 12nd, and 15th day. Then in the α-glucosidase enzyme inhibition method, the absorbance was read using a *micro-reader* at a wavelength of 425 nm .

Characteristics of Kabau Seeds Simplisia

The simplicia characteristics were carried out on the simplicia ethanol of Kabau seeds (*Archidendron bubalinum* (Jack.) I.C.Nielsen) and the results were obtained as shown in **Table 1**.

Simplicia characteristics were carried out to determine the quality of the simplicia used for this study. The characteristics of Kabau seeds simplicia include drying shrinkage, total ash content, acid insoluble ash content, ethanol soluble extract content, and water soluble extract content **(Table 1)**.

Phytochemical Screening of Ethanol Extract of Kabau Seeds:

Phytochemical screening was carried out on simplicia and ethanol extract of Kabau seeds (*Archidendron bubalinum* (Jack.) I.C.Nielsen) and the results were obtained as shown in **Table 2**.

Phytochemical screening is carried out to determine the class of secondary metabolite compounds contained in the simplicia and ethanol extract of Kabau seeds to be used. Phytochemical analysis conducted in this study was only carried out qualitatively. Phytochemical screening included identification of alkaloids, flavonoids, saponins, quinones, tannins, and steroids/triterpenoids. **Table 2** shows that the simplicia and ethanol extract of Kabau seeds contain alkaloids, flavonoids, saponins, tannins, steroids/triterpenoids, but do not contain quinone compounds. These metabolite compounds such as alkaloids, flavonoids, saponins, tannins, and steroids/triterpenoids are potential as antidiabetic.

Decreased Blood Glucose Levels in Insulin Resistance Animals

Blood glucose levels obtained in this study are shown in **Table 3**.

Table 3 shows a decrease in the value of blood glucose levels that are quite varied. From the statistical results using the *One Way Anova* method then continued using Post-Hoc LSD obtained on negative controls day 14th to day 28th had a significant difference ($p < 0.05$) when compared with positive control. Whereas the positive control group was significantly

different ($p < 0.05$) with the negative control group and the metformin group 65 mg/Kg bw. This shows that the induction of lipid emulsion Lipofundin® and fructose succeeded in making insulin resistance mice model. Lipid emulsion Lipofundin® will be polyphilised to produce high fatty acids which are then released into the systemic circulation and flow to the liver, where they will stimulate the production of *Very Low Density Lipoprotein* (VLDL) in liver tissue that can damage insulin receptors so that insulin sensitivity is reduced **[11]**. While giving fructose can cause hepatic insulin resistance through 2 mechanisms, namely the formation of uric acid and *De Novo Lipogenesis* (DNL). In the body, fructose will form uric acid through phosphorylation by the help of the enzyme ketoheksokinase (KHK) and a number of ATP. Uric acid causes decreased levels of nitric oxide (NO) resulting in vasoconstriction and decreased glucose uptake in muscles. As a result of these two effects that cause insulin resistance. Another mechanism of fructose is by inducing DNL by providing carbon atoms (glycerol-3 phosphate and acyl-CoA) which are converted into monoacylglycerol and diacylglycerol (DAG). Furthermore, DAG will be converted into triglycerides and VLDL which cause insulin resistance **[12, 13]**. The high DAG can also activate Novel-PKC. Novel-PKC is a protein kinase C that can reduce phosphorylated tyrosine from IRS (Insulin Receptor Substrate) which causes a decrease in insulin sensitivity and an increase in blood glucose **[14]**.

In the metformin group showed significant differences with positive control on days 7 to 28. This showed an increase in insulin sensitivity in the metformin group dose of 65 mg/kg bw due to the mechanism of action of metformin by increasing insulin sensitivity. Whereas in the ethanol extract of Kabau seeds at a dose of 95 mg/Kg bw, 190 mg / Kg bw, 380 mg/Kg bw can significantly reduce blood glucose levels. At a dose of 190 mg/Kg bw a decrease in blood glucose levels began to be seen on the 7th day until the 28th day. Whereas at a dose of 95 mg/Kg bw and 380 mg/Kg bw a decrease in blood sugar levels began to be seen on the 14th day until the 28th day. Statistically, all doses of ethanol extract of Kabau seeds had a significant difference ($p < 0.05$) when compared to the positive control group. But statistically there were no significant differences in the three doses.

Constant Insulin Tolerance Test (CITT)

This test was carried out preventively on mice induced by lipid emulsion Lipofundin® 30 mL/Kg bw and fructose 2.52 g/Kg bw. Insulin sensitivity was

measured by calculating CITT which is the value of the gradients or the slope value of the linear logarithmic regression curve for blood glucose levels over time. The smaller the CITT value indicates the lower insulin sensitivity. The results of insulin tolerance tests are shown in **Table 4**.

Based on the results obtained in **Table 4**, it shows that the negative control group has a significantly different CITT value towards positive control. This shows a decrease in insulin sensitivity in the animals in the positive control group. In the metformin group and all test groups of ethanol extract of Kabau seeds showed significant differences in positive control ($p < 0.05$) and did not differ significantly in negative controls. This shows the effect of increasing insulin sensitivity by metformin and the ethanol extract of Kabau seeds material, where the metformin group and the EEKS groups had levels of insulin sensitivity that were almost the same as the level of insulin sensitivity possessed by the negative control group or healthy animal group. Whereas in the EEKS groups, based on the table above it can be seen that the EEKS groups did not have a significant difference to the metformin group used in this study as a comparison. This indicates that the EEKS material has the same effectiveness as metformin.

Decreased Blood Glucose Levels in Insulin Deficiency Animals

Antidiabetic activity was carried out curatively using insulin deficiency method, where the pancreas can not function properly in producing insulin because some of the pancreatic β cells are damaged. Here are the results of average blood glucose levels of mice on the 0, 3rd, 6th, 9th, 12nd, and 15th.

Table 1: Characteristics Of Kabau Seeds Simplicia

Parameters	% (percentage)
Drying Shrinkage	7.45
Total Ash Content	2.67
Acid Insoluble Ash Content	0.59
Ethanol Soluble Extract Content	9.0
Water Soluble Extract Content	24.0

Table 2: Phytochemical Screening Of Simplicia And Ethanol Extract Of Kabau Seeds (*Archidendron Bubalinum* (Jack.) I.C.Nielsen)

Compounds	RESULTS	
	Simplisia	Extract
Alkaloids	+	+
Flavonoids	+	+
Saponins	+	+
Steroids/ Triterpinoids	+	+
Tannins	+	+
Quinones	-	-

+: Contains secondary metabolite compounds; -: Does not contain secondary metabolite compounds

Table 3: Average Blood Glucose Levels In Insulin Resistance Animals

Groups	Blood Glucose Levels±SD				
	T0	T7	T14	T21	T28
Negative control	87.66±7.68	88.33±5.31	90.66±15.20*	87±13.03*	86.83±12.76*
Positive control	93.83±8.58	115.16±12.56@#	147.33±29.67@#	164.66±30.96@#	198.5±32.68@#
Metformin 65 mg/Kg bw	94.33±6.21	94.16±14.20*	89±13.05*	85.83±6.24*	79.16±7.67*
EEKS 95 mg/Kg bw	92.16±8.18	95.66±7.08	91.83±1.99*	87.8±13.80*	83.83±12.22*
EEKS 190 mg/Kg bw	91.5±6.05	94.5±11.94*	88.83±13.30*	84.5±12.88*	81.83±9.64*
EEKS 380 mg/Kg bw	93.16±7.52	95.16±11.72	92.83±15.34*	87±9.31*	86.33±7.03*

*: Significantly different compared to the positive control group ($p < 0.05$); @: Significantly different compared to the negative control group ($p < 0.05$); #: Significantly different compared to the metformin 65 mg/Kg bw group ($p < 0.05$)

Table 4: Average Constant Value Of Insulin Tolerance Test

Groups	CITT±SD
Negative Control	1.58±0.09*
Positive Control	0.45±0.09@#
Metformin 65 mg/Kg bw	1.89±0.28*
EEKS 95 mg/Kg bw	1.75±034*
EEKS 190 mg/Kg bw	1.82±0.29*
EEKS 380 mg/Kg bw	1.62±0.21*

*: Significantly different compared to the positive control group ($p < 0.05$); @: Significantly different compared to the negative control group ($p < 0.05$); #: Significantly different compared to the metformin group 65 mg /Kg bw ($p < 0.05$).

Table 5: Average Reduction Of Blood Glucose Levels In Insulin Deficiency Animals

Groups	Blood Glucose Levels±SD					
	T0	T3	T6	T9	T12	T15
Negative control	103.75±2.75*	96.75±2.21*	102±2.16*	102.75±1.5*	101±1.41*	98.75±2.5*
Positive control	206±2.44@	208.75±1.25@#	211.5±2.64@#	217.25±1.5@#	28.75±4.34@#	232±6.05@#
Metformin 65 mg/Kg bw	228±3.74	126.75±3.5*	120.5±1.91*	117.25±1.25*	112±2.16*	93.25±7.5*
EEKS 95 mg/Kg bw	218.75±11.14	179.25±52.89	149.25±28.5*	139±34.90*	21.75±19.15	98±10.98*
EEKS 190 mg/Kg bw	228.75±42.24	198.75±23.17	169.25±17.63*	144.5±18.69*	14.25±12.31	95.5±10.40*
EEKS 380 mg/Kg bw	237.5±31.21	213.75±28.05	182.20±20.78*	157.33±21.42*	33.25±30.42	109.25±20.46*

*: Significantly different compared to the positive control group ($p < 0.05$); @: Significantly different compared to the negative control group ($p < 0.05$); #: Significantly different compared to the Glibenclamid group 0.65 mg / Kg bw ($p < 0.05$)

In **Table 5**, the average reduction in blood glucose levels in mice is quite varied. Based on statistical results using the One Way Anova method and continued using Post-Hoc LSD obtained negative control has a significant difference ($p < 0.05$) on positive control on the third day after induction until the 15th day. This shows that alloxan induction was successful in creating a model of diabetes mice. Seeing from the mechanism of action of alloxan which can partially damage the pancreas so that the pancreas can still produce insulin. Selective alloxan inhibits glucose-induced insulin secretion by inhibiting specific glucokinase, a glucose sensor in beta cells that can cause insulin-dependent diabetes through its ability to induce the formation of reactive oxygen species (ROS), which results in selective necrosis of beta cells **[15]**. In the Glibenclamide group, there was a significant difference ($p < 0.05$) on positive control starting on day 3 to day 15. This shows a decrease in blood glucose in

the glibenclamide group 0.65 mg/Kg bw. The decrease in blood glucose levels in the glibenclamide group is due to the mechanism of action of glibenclamide, which stimulates insulin secretion in pancreatic β cells that can still function to produce insulin. At doses of 95 mg/Kg bw, 190 mg/Kg bw, and 380 mg/Kg bw statistically showed a significant difference ($p < 0.05$) to positive control on the 6th day to the 15th day. The decrease in blood glucose levels is thought to be an improvement in pancreatic β cells that can produce insulin in mice that have been given ethanol extract of Kabau seeds. So that the ethanol extract of Kabau seeds has antidiabetic activity. The antidiabetic activity of ethanol extract of Kabau seeds is due to the activity of secondary metabolite compounds contained in it. The mechanism for reducing blood glucose level depends on the mechanism of each compound. Flavonoid compound helps the regeneration of pancreatic β cells by counteracting free radicals, increasing insulin release, and stimulating the absorption of Ca^{2+} from cell tissue which is very effective in a condition of not having enough insulin. Alkaloid compounds have a tendency to release insulin from pancreatic β cells and have the ability to protect pancreatic β cells from pancreatic damage due to alloxan induction in the animals. Tannins are thought to induce phosphorylation of insulin receptors by forming glucose 4 transporters (GLUT-4) and tannins are known to be able to inhibit the loss of glucose transport that produces insulin. Saponin significantly improves clinical symptoms of diabetes including high blood glucose levels and mimics the action mechanism of the glucosidase enzyme inhibitor **[16]**. Saponin has an antioxidant effect that protects β cells and makes the amount of degranulation of insulin less than before. While steroid compounds have a mechanism to reduce blood glucose through its effect on the action of insulin at the cellular level, distal insulin receptors and reduce glucose production in the liver **[17]**.

CONCLUSION

Ethanol extract of Kabau seeds has an effect in increasing insulin sensitivity and insulin secretion.

ACKNOWLEDGEMENT

This research was fully funded by Centre of Research and Community Services of Bhakti Kencana University.

REFERENCES

[1] World Health Organization. Diabetes 2016. Available : https://www.who.int/news-room/fact-sheets/detail/diabetes.

[2] International Diabetes Federation: Diabetes Atlas, 8th edition

2017.Available: file:///C:/Users/X441NA/Downloads/english-6th%20.

[3] Young C, Dugan J, Kim Pfotenhauer, Jay H. Shubrook. Pharmacologic Management of Type 2 Diabetes Mellitus: Part 2. 2016; November 1.

[4] Hanafi, Irawan C, Rochaeni H, Sulistiawaty L, Roziafanto AN, Supriyono. Phytochemical Screening, LC-MS Studies and Antidiabetic. Pharmacognosy Journal. 2018; 6 (Suppl): 10.

[5] Lim TK. Edible Medicinal and Non-Medicinal Plants Fruits. Vol. 2. Springer. Dordrecht. 2012.

[6] Irawan C, Sulistiawaty L, Sukiman M. Volatile Compound Analysis using GC-MS, Phytochemical Screening and Antioxidant Activities of the Husk of "Julang-Jaling" (*Archidendron bubalinum* (Jack) IC Nielsen) from Lampung, Indonesia. Pharmacognosy Journal. 2018;10(1).

[7] Ja'afar NL *et al*. Total antioxidant activity and enzymatic inhibition against alpha-amylase, alpha-glucosidase and pancreatic lipase of irradiated (*Archidendron bubalinum*). Malaysian Journal of Medicine and Health Sciences 2019; 15(SP1): 120-128.

[8] Susilawati E, Sukmawati IK, Noranisa, Hayati NS,Aligita W. The Influence Of Ethanol Extracts of Rambutan Leaves (*Nephelium lappaceum* L.) Against Obesity And Insulin Resistance In Rats. International Journal of Pharmaceutical Sciences and Research 2019; 10(8): 3684-3690.

[9] Aligita W, Susilawati E, Sukmawati IK, Holidayanti L, Riswanti J. Antidiabetic Activities of *Muntingia calabura* L. Leaves Water Extract in Type 2 Diabetes Mellitus Animal Models. The Indonesian Biomedical Journal 2018; 10(2): 165-70.

[10] Zhang, J., Wang, G., Beta, T, and Dong, J. (2014): α-Glucosidase Inhibitory Activity of Polyphenols from the Burs of *Castanea mollissima* Blume. Molecules, 2014; 19: 8373-8386.

[11] Wannasiri S, Piyabhan P, Naowaboot J. Rhinacanthus nasutus leaf improves metabolic abnormalities in high-fat diet-induced obese mice. Asian Pacific Journal of Tropical Biomedicine 2016; 6(1): 1-7.

[12] Johnson RJ, Perez-Posa SE, Sautin YY, Manitius J, Lozada LG, Feig DI, et al. Hypothesis: Could

excessive fructose intake and uric acid cause type 2 diabetes? Endocr Rev. 2009; 30(1): 96-16.

[13] Basciano H, Federico L and Adeli K. Fructose, insulin resistance, and metabolic dyslipidemia. Nutr & Metab. 2005; 2(5):1-14.

[14] Copps K D, White MF. Regulation of insulin sensitivity by serine/ threonine phosphorylation of insulin receptor substrate proteins IRS1 and IRS2. Diabetologia, 2012; 55: 2565–2582.

[15] Ighodaro OM, Adeosun AM, Akinloye OA. Alloxan-induced diabetes, a common model for evaluating the glycemic-control potential of therapeutic compounds and plants extracts in experimental studies. Medicina 2017; 53(6): 365-374.

[16] Soares JMD, Leal AE, Silva JC, Almeida JR, Oliveira HP. Influence of Flavonoids on Mechanism of Modulation of Insulin Secretion. Pharmacogn. Mag., 2017; 13(52): 639-646.

[17] Wilcox Gisela. Insulin and Insulin Resistance. Clin Biochem Rev 2005; 26(2): 19-39.

Jurnal IJBPAS 2020 dg Entris

ORIGINALITY REPORT

17%	13%	14%	6%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

MATCH ALL SOURCES (ONLY SELECTED SOURCE PRINTED)

11%

★ W . Aligita, S . Muhsinin, E . Susilawati, Dahlia, D .S. Pratiwi, D . Aprilliani, A . Artarini, I .K. Adnyana. "ANTIDIABETIC ACTIVITY OF OKRA (Abelmoschus esculentus L.) FRUIT EXTRACT", Rasayan Journal of Chemistry, 2019

Publication

Exclude quotes	On	Exclude matches	< 1%
Exclude bibliography	On		

Jurnal IJBPAS 2020 dg Entris

GRADEMARK REPORT

FINAL GRADE

/123

GENERAL COMMENTS

Instructor

PAGE 1

PAGE 2

PAGE 3

PAGE 4

PAGE 5

PAGE 6

PAGE 7

PAGE 8

PAGE 9

PAGE 10

PAGE 11