Antihyperglycemic Effect and Glucose Tolerance of Ethanol Extract the Rind of Jengkol (*Pithecollobium jiringa Jack*) in Diabetic Rats

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Abstract: In traditional medicine, the rind of jengkol or skin of jengkol fruit (Pithecellobium jiringa Jack) has been used by some people to reduce blood glucose levels in some districts of Indonesia. This study aims to determine the antihyperglycemic effect and glucose tolerance of ethanol extract of the rind of jengkol (Pithecollobium jiringa Jack) in diabetic rats. Jengkol fruit was bought from Kebonjeruk market, West Jakarta and determination of jengkol rind was done at the Biology Research Center, Indonesian Institute of Sciences, Bogor.Indonesia. Jengkol rind was separated from the fruit seeds. Preparation of jengkol rind extract was done by cold maceration extraction technique using ethanol 70%. The male albino rats that qualify for the experiment were made into diabetics using the alloxan method. The rats were divided into 7 groups, each group consisted of 5 rats. as positive control for anti-diabetic was used glibenclamide and for glucose tolerance test was used acarbose, as normal control just given aquadest and for negative control wass given a solution for suspending the test preparation (1% CMC Na). For extract of jengkol rind was given low dose (24,5 mg/200 gr bw), medium dose (49 mg/200 gr bw) and high dose (196 mg/200 gr bw) and glucometer tool was used to measure blood sugar levels. Statistical results with ANOVA test and Kruskal-wallis test showed that small and medium doses of jengkol rind extract had the same antidiabetic effect and glucose tolerance with positive control and were significantly different to negative controls. ($P \leq 0.05$). and high dose was not significantly different to negative controls ($P \geq 0.05$).

1 INTRODUCTION

According to the World Health Organization, In 2017, there are about 150 million people have diabetes mellitus worldwide, this number may well double by the year 2025. Majority of this increase will occur in developing countries and will be due to population growth, ageing, unhealthy diets, obesity and sedentary lifestyles. It is estimated in 2025, most people with diabetes in developed countries will be aged 65 years or more and in developing countries most will be in the 45-64 year. Around 1.6 million people worldwide died due to diabetes in 2017. It is estimated about 500 million people are living with diabetes all over the world. By 2045, Therefore, in recent years, diabetes has become one of the leading causes of deaths worldwide (WHO, 2017)

There are 2 forms of diabetes that are most common, i.e. Diabetes (type 1), This is known as insulin-dependent, in which the pancreas fails to produce the insulin. Majority of this form develops in children and adolescents, but is being increasingly noted later in life. Diabetes (type 2) This is known as non-insulin-dependent which results from the body's inability to respond properly to the action of insulin produced by the pancreas. Type 2 diabetes is around 90% of all diabetes cases worldwide. It occurs most frequently in adults, there are about 40% of diabetes sufferers require oral agents for their blood glucose control, and also there are about 40% need insulin injections. (WHO, 2017)

Insulin is unaffordable in many poor countries. On the other hand, the use of synthetic drugs for diabetes has many side effects. Moreover, oral diabetes medications rarely work double as a decrease in blood glucose levels and work as a glucose tolerance inhibitor (WHO, 2017).

Double work as a decrease in blood glucose levels and works as a glucose tolerance inhibitor, only possible on drugs that are sourced from natural products. Because natural products are usually chemical compounds that work as diabetes drugs not

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only one chemical compound, but can be more than one chemical compound, namely the form of synergy of several chemical compounds. Therefore the discovery of diabetes drugs from natural products is very necessary (WHO, 2017; Muslim and Majid, 2010; Zurhana et al., 2018)

Pithecellobium jiringa (Jack) or called as Jengkol in Indonesia, jering in Malayasia, krakos in Combodia and niang-yai in Thailand (Muslim N, 2010). The seeds or beans of jengkol fruit is delicious to make curry or fried with chili. and many people are addicted to eating jengkol because of its delicious taste. Generally, the rind of jengkol fruit seeds or the skin of jengkol fruit is not eat, usually not used for anything, and just thrown away as organic waste. (Muslim and Majid, 2010; Zurhana et al., 2018; Bunawan et al., 2013)

In traditional medicine, usually jengkol used, to treat toothache, gum pains, chest pains and skin ailments in the old Indonesia and Malaysian folk. Raw eaten jengkol fruit seeds are believed to help to purify the blood and to serve as anti-diabetic agent and to induce urination. (Bunawan et al., 2013).

As the research was conducted by Ruzilawati et al (2012) and Zurhana et al (2017), that jengkol fruit also works as antimicrobial and anti-jamur, including the bacteria Trychophyton mentagrophytes, S. aureus, S. epidermidis and M. gypsum (Zurhana et al., 2018; Ruzilawati et al., 2012; Charungchitraka et al., 2011)

Jengkol was reported containing chemical compounds among others : five flavan-3-ol derivatives which include new flavan-3-ol gallatesgallocatechin 3‘- and 4‘-O-gallates as well as gallocatechin 7,3‘- and 7,4‘-di-O-gallates , procyanidinds B-3 and B-4 and prodelphinidin B-1, as well as flavan-3-ols. The metabolites identified were generally found to be fatty acids, terpenoids, ally sulphur, vitamin E, Djenkolic acid and alkaloid. (Bunawan et al., 2013)

The specific and stinging smell of jengkol is sourced from djenkolic acid which is contained by jengkol fruit (figure 2). Because the taste of jengkol is very delicious, many people consume jengkol excessively and cause poisoning known as Djengkolism, In other words, djenkolism is an uncommon but important cause of acute kidney injury. It sporadically occurs after an ingestion of the jengkol bean (Zurhana et al., 2018; Bunawan et al., 2013).

1a 1b

Figure 1a. the Jengkol rind and 1b. Jengkol seed

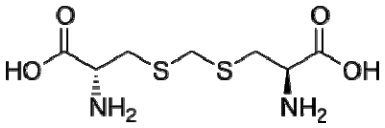

Figure 2: Djenkolid Acid

2 METHODS

Jengkol fruit was purchased in the Kebon Jeruk market, West Jakarta and the taxonomy determination of plants was carried out at the Biology Research Center, Indonesian Institute of Sciences, Bogor, Indonesia.

The making of simplicia was done as follow; A total of 700 g of jengkol rind powder was extracted by repeated maceration method by using 70% ethanol solvent and stirred occasionally until the solution obtained was clear. The obtained filtrate was evaporated by using a vacuum evaporator. The extract obtained was dried in an oven at 70 °C.

Screening of chemical compound groups of jengkol rind extract were done based on Harbone methods, in this cases, analysis of chemical compound groups were done for groups of alkaloid, flavonoid, saponin, steroid, triterpenoid, tannin, quinone and essential oil (Harborne, 1998).

The male white rats, strain of Sprague-Dawley with 3-4 months old (weight 190-250 g) were acclimatized for two weeks. The rats qualified for the experiment were divided into 7 groups. each group consists of 5 rats, before the experiment begins, the rats was fasted for 10 hours.

The animals were fed with standard pellet diet and water was given ad libitum. This study was carried out in the animal house of State Islamic University, Syarif Hidayatullah Jakarta and this study was approved by the Institutional Ethical Committee. The grouping of rats for experiment as shown in table 1.

The dose of acarbose and glibenclamid given to rats were calculated based on effective doses for humans (50-200 mg / kg bw for acarbose and 5 - 10 mg/ kg bw for glibenclamid) and converted based on the conversion of Paget and Barnes ie the dose for every 200 g of rat equivalent to 0.018 x human dose (Watts, 1984)

Table 1: The grouping of rats for experiment

Group	Treatment
1	Normal control, given aquadest 3ml/200 g bw
2	Negative control was made diabetes, given (50 % glucose, 1%, CMC Na, aquadest) each 1ml/200 g bw
3	Positive control was made diabetes, given (acarbose 1,8 mg in1%, CMC Na, 50% glucose, aquadest) each 1ml/200 g bw
4	Positive control was made diabetes, given (glibenklamid 0,09 mg in1%, CMC Na, 50% glucose, aquadest) each 1ml/200 g bw
5	Low dose was made diabetes, given (jengkol rind extract 24,5 mg in 1% CMC Na, 50% glukose , aquadest) each 1ml/200 g bw
6	Medium dose was made diabetes given given (jengkol rind extract 49 mg in 1% CMC Na, 50% glukose , aquadest) each 1ml/200 g bw
7	High dose was made diabetes, given (jengkol rind extract 98 mg in 1% CMC Na, 50% glukose , aquadest) each 1ml/200 g bw

To make rats become diabetic was given alloxan through intravenous injection. Rat blood measurements were carried out before giving alloxan. Alloxan dosage was calculated based on the effective dose to make the rats become diabetic, i.e.13 mg / 200 g bw of rat. On the days 7th until 14th usually the blood sugar levels of rats became stable with diabetes. (Kurniati, 2007). The method for administering test animals and animal grouping in more detail is shown in Table 1.

The rats blood were taken through intravenous and their blood sugar levels were measured by using a glucometer tool. Furthermore, rat blood was taken at 30, 60, 90, 120, 150 and 180 minutes. Data of blood glucose level obtained was calculated by using statistical with methods of Levena, ANOVA and Kruskal Walis.

3 RESULT AND DISCUSSION

The result of the taxonomic determination of the plants that was carried out in Biological Research Center, Indonesian Institute of Sciences showed that plant was used in this research was *Pithecollobium jiringa Jack*

The results of phytochemical screening of methanol extract of jengkol rind showed that the group of chemical compounds contained in this plant Was as shown in Table 2.

Table 2: The content of groups of chemical compounds of jengkol rind extract

Chemical group	Results
Alkaloids	+
Flavonoids	+
Saponin	+
Tannin	+
Quinone	+
Steroids & Triterpenoids	+
Essential oil	+
Qoumarine	-

Results of measurement of blood glucose levels of test animals before treatment and after treatment was shown in Table 3 and Figure 1.

Table 3: Results of measurements of average blood glucose levels for oral glucose tolerance in experimental rats

minutes	Average of blood glucose level (mg / dl)					
	NC	C(+)	C(-)	LD	MD	HD
0	114	110.75	118.5	149	134.5	199.75
30	106.75	107	161.75	115.5	135.5	219.75
60	123	105	280.75	120.75	114.5	206.25
90	105	118.75	285.25	122.25	119.25	192
120	111	100.25	244.5	139.75	119.75	185.25
150	134.25	114.75	237	137.25	128.5	182
180	143.5	139.25	228	168.25	131.75	194

Notes :

NC : Normal Control LD: Low Dose
C(+) : Positive Control MD: Medium Dose
C(-) : Negative Control HD: High Dose

As shown in Table 3 and Figure 1. On the negative control of rats group, due to glucose administration in diabetic rats, in observation every 30 minutes, there was a gradual increase in glucose levels compared to 0 minutes (118.5 mg / dL) with an increase value for 30, 60, 90 minutes were 161.75; 280.75; 285.25 mg / dL, respectively. Based on Statistical test was significantly different. Then it starts to decrease bit by bit at 120, 150, 180 minutes with a value of 244.5; 237; 228mg / dL, respectively($P \leq 0.05$).

In normal group rats, or rats that did not have diabetes, due to glucose administration there were no increase in glucose levels. The results of measurement of glucose levels every 30 minutes to 180 minutes, only fluctuated and based on statistical tests did not differ significantly (P≥0.05)

In the group of positive control, the rats with diabetes were given drugs that acted as glucose tolerance, due to glucose administration in diabetic rats, no increase in glucose levels. The results of measurement of glucose levels every 30 minutes to 180 minutes, only fluctuated and based on statistical tests did not differ significantly (P≥0.05)

On the low dose of jengkol rind extract, the rats with diabetes, due to administration of jengkol rind extract, showed decrease in glucose levels compared to the 0 minute (149 mg / dL) with decrease value for 30, 60, 90, 120, 150 minutes were 115.5; 120.75; 122.25; 139.75; 137.25 mg / dL, respectively and increased at 180 minutes with a value of 168.25 mg / dL.

While, on the middle dose of jengkol rind extract, the rats with diabetes, showed decrease in glucose levels compared to the 0 minute (134.5 mg / dL) with decrease value for 60, 90, 120, 150 and 180 minutes were 114.5; 119.25; 119.75; 128.5; 131.75; mg / dL, respectively, work effect of this middle dose was same with work effect of positive control (acarbose), only different on 180 minutes, where positive control at 24 days was still high i.e. 139.25 mg/dL or higher than 0 minutes (110.75 mg/dL).

On the high dose of jengkol rind extract, the rats with diabetes, showed decrease in glucose levels compared to the 0 minute (199.75mg / dL) with inrease value for 30, 60, minutes were 219.75; 206.25 mg / dL, respectively and decreased at 90, 120, 150 and 180 minutes with a value of 192; 185.25; 182 and 194mg / dL, respectively. As shown in Table 3 and Figure 1.

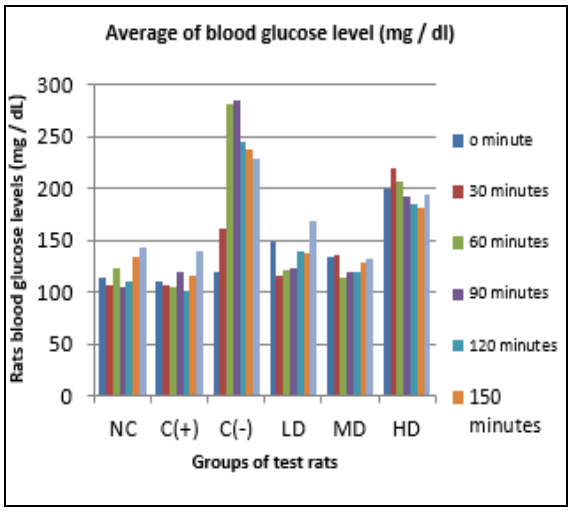

Figure 1. Results of measurements of average blood glucose levels for oral glucose tolerance in experimental rats.

Notes :

NC	: Normal Control	LD: Low Dose
C(+)	: Positive Control	MD: Medium Dose
C(-)	: Negative Control	HD: High Dose

Table 4: Results of measurements of average blood glucose levels in experimental rats

Days	Average blood glucose level (mg / dl)					
	NC	C(+)	C(-)	LD	MD	HD
0	84.75	85.5	83.75	84.75	86.25	82.75
14	88.5	172.25	106.25	149	134.5	199.75
17	121.5	72.5	130.25	124	117.75	128.75
22	104.25	77	158.25	99	114.5	135.5
28	90.5	78.5	152	84	94.75	111.5

The Results of measurements of average blood glucose levels in experimental rats, as shown in Table 4 and Figure 2. On the negative control of rats group, due to glucose administration in diabetic rats, on measurement at 14, 17, 22 and 28 days, there were a gradual increase in glucose levels compared to 0 day (83.75 mg / dL) with an increase value for 30, 60, 90 minutes were 106.25; 130.25; 158.25 and 152mg / dL, respectively. Based on Statistical test was significantly different (P≤0.05).

In normal group rats, or rats that did not have diabetes, due to glucose administration there was no increase in glucose levels. The results of measurement of glucose levels at 14, 17, 22 and 28 days, only fluctuated and based on statistical tests did not differ significantly (P≥0.05)

In the group of positive control, the rats with diabetes were given glibenclamid that acted to decrease glucose, due to glibenclamid administration in diabetic rats, no increase in glucose levels. The

results of measurement of glucose levels at 14, 17, 22 and 28 days, only fluctuated and based on statistical tests did not differ significantly (P≥0.05)

On the low dose of jengkol rind extract, the rats with diabetes, due to administration of jengkol rind extract, showed increase in glucose levels compared to the 0 day (84.75 mg / dL) with increase value for 14 and 21, days were 149 and 124 mg / dL, respectively and decreased at 22 and 28 days with value of 99 and 84 mg / dL. and so for the middle dose of jengkol rind extract. Work effect of low dose and middle dose of jengkol rind extract were same wit work effect of positive control (glibenclamid) in decrease glucose.

While, on the high dose of jengkol rind extract, the rats with diabetes, showed glucose levels on days compared to the 0 day (86.25 mg / dL) with decrease value for at 14, 17 and 22 days with the value 199.75; 128.75 and 135.5 mg/dL, respectively, then a little decrease at 22 days, i.e 111.5 mg/dL. As shown in Table 4 and Figure 2.

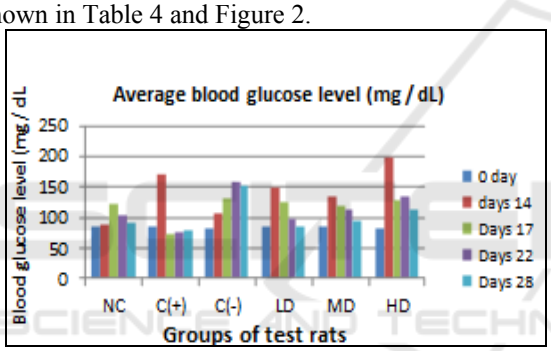

Figure 2: Results of measurements of average blood glucose levels in experimental rats

If this study (Jengkol Rind as an antidibetic) was compared with the research of Rahanah et al (2011) by using jengkol seeds as antidiabetic, then jenkol rind is stronger than jengkol seeds as an antidibetic.

Because jengkol rind extract with a low dose (24.5 mg / 200 g bw) could reduce blood glucose levels within 28 days, while in the results of research of Rahanah et al (2011) Jengkol beans extract could reduce glucose levels on day 84 or 12 weeks. Whereas for the effect of glucose tolerance of jengkol rind extract can also inhibit glucose tolerance in 48 hours or in 2 days after administration of jengkol rind extract for moderate dose or 49 mg / 200 g bw.

On the test for hypoglycemia effect on oral glucose tolerance ethanol extract of jengkol rind could reduce blood glucose levels, as shown wit not significantly differet at low doses of 24.5 mg / 200 g bw and 49 mg/200 g bw with normal and positive controls (P≥0.05) and significantly different between the test dose with negative control (P≤0.05) in the 60th and 90th minutes. At high doses it had no effect because there was no difference significant between high doses with negative controls in the 60th, 90th, 120th, 150th and 180th minutes.

On the hypoglycemia effect test, on diabetic rats, the ethanol extract of jengkol rind was proven to reduce blood glucose levels, this was shown, with there was no significantly different at low doses of 24.5 mg / 200 g bw of rats and middle doses of 49 mg / 200 g bw of rats with normal and positive control (P≥0.05), and there were significantly different between the test dose with negative control (P≤0.05) on the 22nd and 28th days. And at high doses did not have an effect because it was not there were significantly different between high doses and negative controls on days 17 and 22.

If this study (Jengkol Rind as an antidibetic) was compared with the research of Rahanah et al. (2011) by using jengkol seeds as antidiabetic, then the jengkol rind is stronger than jengkol seeds as antidabetic.

Because jengkol extract with a low dose (24.5 mg / 200 g bw) could reduce blood glucose levels within 28 days, while in the results of research of Rahanah et al (2011) Jengkol beans extract could reduce glucose levels on day 84 or 12 weeks. Whereas for the effect of glucose tolerance, jengkol rind can also inhibit glucose tolerance in hours or 2 days after administration of jengkol rind extract for moderate dose (49 mg / 200 g bw). In research of Rahanah et al., Studied for glucose tolerance testing were not conducted

Based on research of Yanti et al 2017, Jengkol protein could reduce interleukin-6 and leptin as compound for trigger obesity, as we know obesity is one of trigger diabetes disease. (Yanti et al, 2017)

4 CONCLUSION

Ethanol extract of jengkol (*Pithecellobium jiringa Jack*) rind Pram was potential to reduce blood glucose levels, both with oral glucose tolerance test and alloxan diabetes test.

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