paper_sholihatil

by Jurnal Galenika

Submission date: 12-Feb-2021 03:53AM (UTC-0500)
Submission ID: 1507798129
File name: 15429-Research_Materials-49599-2-2-20210110_sholihati.doc (136K)
Word count: 2099
Character count: 11559

Antidiabetic Activity Of *Peperomia pellucida* In Streptozotocin-Induced Diabetic Mice

ABSTRACT

Background: Diabetes mellitus is a heterogeneous group of diseases in the form of disorders in the body's metabolism clinically. *Peperomia pellucida* herbs have phytochemical containing which is antidiabetic potential development. **Objectives:** This study was conducted to compare the antidiabetic activity of ethanol extract and n-hexane fraction of *Peperomia pellucida*. **Material and Methods:** This research was conducted by make diabetic mice with 50 mg/kg.bw of streptozotocin induction, which was then treated with ethanol extract and n-hexane fraction of *Peperomia pellucida* with doses 250 mg/kgbw for 7 days. **Results:** The results showed that the ethanol extract and n-hexane fraction of *Peperomia pellucida* reduced blood glucose levels in diabetic mice due to streptozotocin induction. The n-hexane fraction of *Peperomia pellucida* can lower blood glucose levels as much 244.00 ± 18.99 mg/dL better than the ethanol extract, which is 99.50 ± 28.17 mg/dL. **Conclusions:** *Peperomia pellucida* herb has the potential to be developed as an antidiabetic agent.

Keyword: Antidiabetic, *Peperomia Pellucida*, Ethanol Extract, n-hexane Fraction

INTRODUCTION

Diabetes mellitus is a heterogeneous group of diseases in the form of disorders in the body's metabolism clinically (Dianaly *et al*., 2017). A report from the International Diabetes Federation (2017) states that around 425 million adults in the world with an age range of 20th to 79th have diabetes mellitus desease, it is estimated that in 2045 there are 629 million sufferers (IDF, 2017).

Chronic hyperglycemia in diabetes is associated with long-term damage, dysfunction or failure of several organs, especially the eyes (diabetic retinopathy), nerves (diabetic neuropathy), heart (cardiovascular), and kidneys (diabetic nephropathy) (Lim, 2014). Treatment of diabetes mellitus and its complications is chronic and lifelong treatment. Management of diabetes is currently carried out with lifestyle modifications or the use of antidiabetic agents such as metformin, sulfonylurea or thiazolidinediones. However, the use of these antidiabetic agents has not been able to achieve good glycemic control and has not been able to restore insulin sensitivity and prevent the degeneration of pancreatic beta cells as the only insulin-producing cells. In addition, long-term use of antidiabetic agents has been shown to cause side effects and tolerance (Rotenstein *et al*., 2012). Therefore, exploration in obtaining alternative diabetes treatment is very important to do (Patel *et al*., 2014).

The identification of chemicals from medicinal plants provides an opportunity in the development of new drugs, one of which is an antidiabetic agent. One of the plants that has the potential to be developed as an antidiabetic agent is the messenger plant *Peperomia pellucida*. The herbs contains phytochemical groups such as alkaloids, flavonoids, saponins, terpenoids, steroids and glycosides (Raghavendra and Kekuda, 2018).

Based on literature studies, the active compound and the mechanism of action of the antidiabetic of *Peperomia pellucida* are not yet known with certainty. Ethanol is a solvent used to attract polar and non-polar active compounds. Therefore, the researcher wanted to do a comparative study of the antidiabetic effect between ethanol extract and the n-hexane fraction of ordered plants in diabetes model mice.

MATERIALS AND METHODS

Materials

Materials used in this study incuded Glucose test and test-strips, animal husbandry tools, surgical instruments, scales, digital analytical balances, beaker glass, measuring cups, watch glasses, stirring rods, syringes, syringes, sonde. The chemicals used in this study were plant plants taken from the area around Jember, streptozotocin (obtained from Bioworld), aquades, CMC Na, 0.9% NaCl solution, 5% dextrose).

Methods

Sample preparation

A total of 1 kg of herbs powder *Peperomia pellucida* was macerated using 10 L of 80% ethanol for 5 days, then filtered using a vacuum filter. The residue was macerated again using 2 L of 80% ethanol for 24 hours. The obtained maserate was concentrated until thick using a vacuum rotary evaporator at a temperature of 60°C.

10 grams of ethanol extract ordered divided into 10 tubes added with distilled water and dissolved in 5 ml of n-hexane solvent with a ratio (2: 1: 2), then vortexed and centrifuged until 2 phases were obtained, namely the supernatant phase as the soluble hexane fraction and the precipitate phase as n-hexane insoluble fraction. The supernatant which is the n-hexane fraction is separated from the precipitate and placed in a separate container. The sediment phase is added with n-hexane, vortexed and centrifuged again until it is clear and the green color of the supernatant is gone.

Diabetic-induced in mice

Male mice aged 6-8 weeks were placed in groups in cages at room temperature 25 ± 1ºC. During the study, the need for food and drink was maintained in excess. Before testing the mice were checked for normal blood glucose levels. On day 0, mice were induced with streptozotocin at a dose of 50 mg/kg.bw intra-peritoneally. On the day 10 the development of hyperglycemia mice was examined. Blood samples were taken through the tail by injuring the tail of the mice. Blood glucose levels were measured by means of the Glucose Test. If after 10 days the blood glucose levels is> 200 mg/dL, the mice have become diabetic.

Treatment of experimental animals

A total of 20 mice were used and divided into 4 groups with 5 mice per group.

1. Group I (normal control, a healthy mice).
2. Group II (diabetic control, were diabetic mice treated with CMC Na 0.5%).
3. Group III (the treatment group was given ethanol extract ordered at a dose of 250 mg/kg.bw),
4. Group IV (the treatment group was given the hexane fraction ordered at a dose of 250 mg/kg.bw.

The treatment was carried out orally for 7 days. On day 8, all mice were fasted and their blood sugar levels were measured.

Data analysis

To describe or identify the meaningful differences from the data set obtained in this study by blood glucose level data after induction were statistically analyzed using paired t-test. Blood glucose level data after treatment were statistically analyzed using the One Way-Anova test

RESULT AND DISCUSSION

Results of Observation of Experimental Animal Blood Glucose Levels

Diabetes mellitus is a chronic disease due to disorders of the metabolism of carbohydrates, proteins and fats which is a health problem for most people around the world. This disease is caused by decreased insulin secretion, decreased insulin sensitivity or both (Dipiro *et al*., 2016). Antidiabetic drugs currently in use can lower blood glucose levels. This has been proven by experimental and clinical data so that the drug is used as a diabetes mellitus therapy, but not all of these drugs have a direct effect on pancreatic beta cells (Nakatsuma *et al*., 2015).

In this study, ethanol extract and n-hexane fraction were used as an antidiabetic given to mice after streptozotocin induction. Making the experimental animal model for diabetes was used 20 male Babl/C strain rate aged 6-8 weeks and divided into 4 groups. Before being used for research, an adaptation was carried out for 1 week first. Mice that have met the requirements were given streptozotocin at a dose of 50 mg/kg.bw by intraperitoneally (i.p). on day 0. 15 mice were fasted for 4 hours and then given intraperitoneal injection of streptozotocin at a dose of 50 mg/kg in a freshly prepared citrate buffer to induce diabetes. Blood glucose levels were measured on day 10, diabetic mice were indicated by blood glucose levels> 200 mg/dL (Hajiaghaalipour *et al*., 2015). Blood glucose data before and after induction can be seen in table 1.

Table 1. Blood glucose levels before and after diabetes induction

Groups	Number of mice	Blood Glucose Levels (mg/dL) (X±SE)	
		Day-0	Day-10
Normal	5	108,50±13,21	70,50±17,69
Diabetic	15	79,27±5,97	324,45±50,17 *

Day-0, all groups were homogeneous (p>0,05)

*) Day-10 of blood glucose levels data differed significantly on the day-0 (p<0,05)

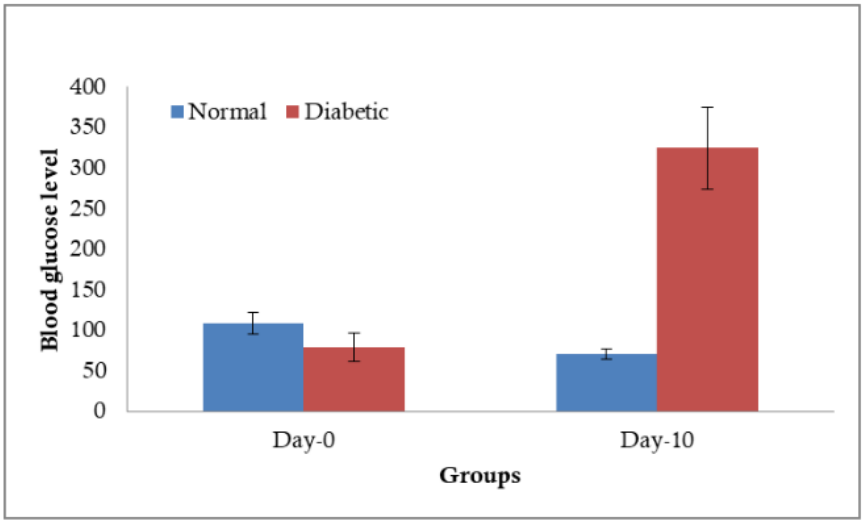

Figure 1. Diagram of pre-induction and post-induction blood glucose levels

The levels of blood glucose induced by mice on the day-10 increased significantly from 79.27 ± 5.97 mg / dL to 324.45 ± 50.17 mg/dL. After the statistical test was carried out, it was obtained p <0.05, which means that the injection of streptozotocin was able to significantly increase blood glucose levels compared to the normal group on the day-10.

Results of Blood Glucose Levels on Pre-Treatments and Post-Treatments in Mice

The treatment was carried out for 7 days, blood glucose levels were measured on the day 8. The pre-treatmet blood glucose levels in each treatment group can be seen in table 2.

Table 2. Pre-treatment and post-treatment blood glucose levels

Groups	Pre-treatment blood glucose levels (mg/dL)	Post-treatment blood glucose levels (mg/dL)
Normal control	101,25±1,38	98,00±8,95*
Diabetic control	200,25±19,80	462,00±24,09
Diabetic + ethanol extract	353,00±85,12	253,50±58,54*
Diabetes + n-hexane fraction	475,50±46,49	231,50±41,91*

*) Different meaning with the diabetic group (p<0,05)

Based on table 2.The blood glucose levels of mice before treatment showed that the healthy group was 101.25 ± 1.34 mg/dL and the diabetes treatment group was> 200 mg/dL. Blood glucose levels of diabetic mice treated with ethanol extract ordered at a dose of 250 mg/kg.bw for 7 days were different from the diabetes group. This shows that the administration of ethanol extract and n-hexane fraction ordered at a dose of 250 mg/kg.bw shows a significant improvement in blood sugar levels.

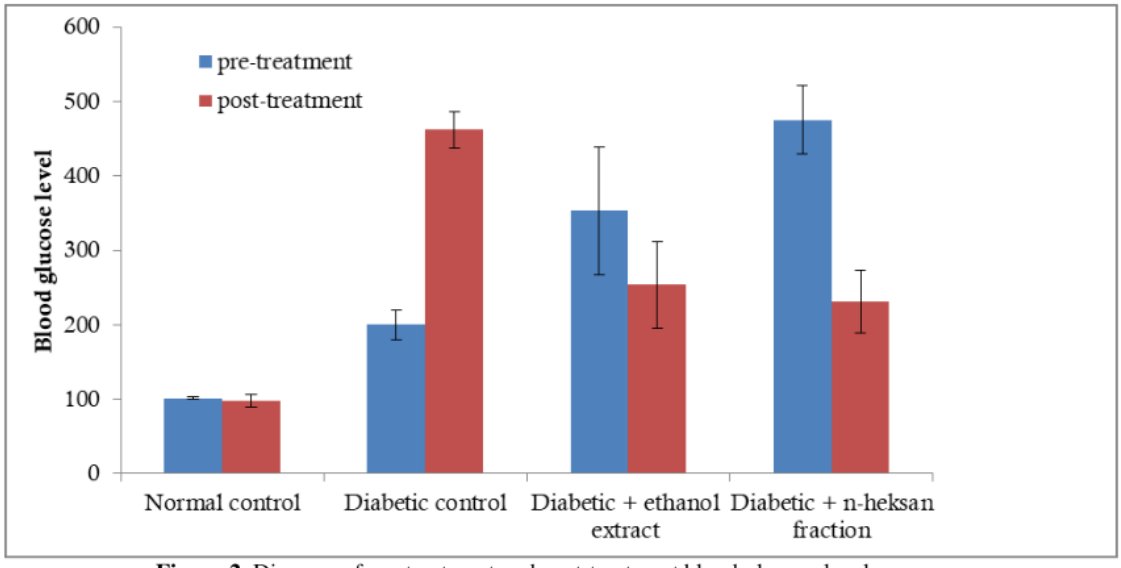

Figure 2. Diagram of pre-treatment and post-treatment blood glucose levels

Observation Results of Decreasing Blood Glucose Levels of Experimental Animals

The decrease in blood glucose levels in each treatment group can be seen in table 3. The results of the decrease in blood glucose levels are shown in Table 3. where from the data it can be seen that the administration of CMC Na (diabetic control) for 7 days caused glucose levels to increase, while the ethanol extract and n-hexane fraction at a dose of 250 mg/kg.bw decreased blood glucose levels. The largest decrease in blood glucose levels was 244.00 ± 18.99 mg/dL, namely by giving n-hexane treatment a dose of 250 mg/kg.bw.

Table 3. Post-treatment reduction in blood glucose levels

Groups		Decrease in post-treatment blood glucose levels (mg/dL)
Normal control	-	3,25±4,71
Diabetic control	+	261,75±43,89
Diabetic + ethanol extract	-	99,50±28,17
Diabetes + n-hexane fraction	-	244,00±18,99

Peperomia pellucida is a plant originating from tropical America. Empirically, herbal herbal plants used for the treatment of diabetes and gout by drinking boiled water all parts of the plant, as fresh vegetables or by grinding all parts of the plant and then affixed to the sick for headaches, fever and colic (Kinho *et al*., 2011).

Several studies related to antidiabetic activity have been carried out. Ordered ethanol extract at a dose of 40 mg/kg.bw had a better antidiabetic effect than hexane extract in diabetic mice with sucrose administration (Togubua *et al*., 2013). Administration of the 40 mg/kg.bw dose of the extract gave an effective reduction in blood sugar levels compared to the 20 mg/kg.bw and 80 mg/kg.bw doses (Salma *et al*., 2013). In addition, ethanol extract of the order can also reduce blood sugar levels in mice by induction of alloxan (Purwati, 2019).

Peperomia pellucida contain alkaloid compounds, tannins, saponins, flavonoids, calcium oxalate, fats, glycosides, carbohydrates, phenolics, steroids, triterpenoids, proteins, amino acids and essential oils (Patel *et al*., 2014). Saponins are chemical compounds from plants that are classified as triterpenoids and have been widely reported to have antidiabetic activity. The antidiabetic activity of triterpenoids is thought to increase insulin expression. The use of phytotherapy such as flavonoids in the management of diabetes is thought to be related to the effect of antioxidants and modulation of glucose

transporter through increased GLUT-2 expression in pancreatic beta cells and increased expression and promotion of GLUT-4 translocation through PI-3K / Akt, CAP / Cb1 / TC10 and AMPK pathway (Hajiaghaalipour *et al*., 2015). On the other research stated that the alkaloid fraction rich in isokuinolin significantly decreased gluconeogenesis in mouse hepatocytes as with insulin use and increased insulin secretion in RINm5F cells equivalent to that of tolbutamide (Patel and Mishra, 2011). Alkaloids also have an antidiabetic effect by increasing GLUT 4, glucokinase activity and PPARγ peroxisome [Aba and Asuzu, 2018).

The n-hexane fraction of *Peperomia pellucida* showed a decrease in blood glucose levels better than the ethanol extract (Table 3.). In preliminary research, it was found that the n-hexane fraction of *Peperomia pellucida* contained more alkaloids. The alkaloid compounds that may dissolve in n-hexane solvent, namely piperine (Mgbeahuruik *et al.*, 2018). Antidiabetic studies of piperine showed that 9 out of 10 piperine derivatives had higher antidiabetic activity compared to standard rosiglitazone. This inherited antidiabetic mechanism is thought to be related to PPARγ agonists (Kharbanda *et al*., 2016).

CONCLUSION

The ethanol extract and the n-hexane fraction were able to reduce blood glucose levels in diabetic mice with streptozotocin induction. The decrease in blood glucose levels in diabetic mice with n-hexane was greater than the ethanol extract administered.

paper_sholihatil

ORIGINALITY REPORT

17%	6%	13%	3%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	talenta.usu.ac.id Internet Source	1%
2	Salehi, Ata, V. Anil Kumar, Sharopov et al. "Antidiabetic Potential of Medicinal Plants and Their Active Components", Biomolecules, 2019 Publication	1%
3	Cheng-chin Hsu, Hui-ting Yang, Jing-jing Ho, Mei-chin Yin, Jen-ying Hsu. "Houttuynia cordata aqueous extract attenuated glycative and oxidative stress in heart and kidney of diabetic mice", European Journal of Nutrition, 2015 Publication	1%
4	Wilnoska Wilnellia D'silva, Prakash Rajshekhar Biradar, Ashwini Patil. "Luffa cylindrica: a promising herbal treatment in progesterone induced obesity in mice", Journal of Diabetes & Metabolic Disorders, 2021 Publication	1%
5	"Abstracts 2007", Diabetologia, 2007 Publication	1%

6	innovareacademics.in Internet Source	1%
7	repositorio.unifesp.br Internet Source	1%
8	"Bioactive Natural Products for Pharmaceutical Applications", Springer Science and Business Media LLC, 2021 Publication	1%
9	Hayat M. Mukhtar, S.H. Ansari, Z.A. Bhat, T. Naved. " Antihyperglycemic Activity of . Beans on Blood Glucose Levels in Alloxan-Induced Diabetic Rats ", Pharmaceutical Biology, 2008 Publication	1%
10	Submitted to Institut Teknologi Sumatera Student Paper	1%
11	www.memoireonline.com Internet Source	1%
12	Sunil Kumar, Vipin Kumar, Om Prakash. " Antidiabetic, Hypolipidemic, and Antioxidant Activities of Leaves Extract ", Journal of Herbs, Spices & Medicinal Plants, 2011 Publication	1%
13	Manisha Rastogi, Rudra P. Ojha, G. V. Rajamanickam, Aruna Agrawal, Abha Aggarwal, G. P. Dubey. "Curcuminoids modulates	1%

oxidative damage and mitochondrial dysfunction in diabetic rat brain", Free Radical Research, 2009
Publication

14	Submitted to Glasgow Caledonian University Student Paper	1%
15	V. Madhavan, Richa Joshi, Anita Murali, S.N. Yoganarasimhan. " Antidiabetic Activity of . Root Tuber ", Pharmaceutical Biology, 2008 Publication	1%
16	Submitted to Sriwijaya University Student Paper	<1%
17	Kazumasa Miyawaki, Yuichiro Yamada, Nobuhiro Ban, Yu Ihara et al. "Inhibition of gastric inhibitory polypeptide signaling prevents obesity", Nature Medicine, 2002 Publication	<1%
18	Xiaojiao Zheng, Tianlu Chen, Runqiu Jiang, Aihua Zhao et al. "Hyocholic acid species and the risk of type 2 diabetes", Cold Spring Harbor Laboratory, 2018 Publication	<1%
19	"42nd EASD Annual Meeting of the European Association for the Study of Diabetes", Diabetologia, 2006 Publication	<1%

20	Yu Na Lee, Hye-Jin Yi, Eun Hye Seo, Jooyun Oh, Song Lee, Sarah Ferber, Teruo Okano, Inkyong Shim, Song Cheol Kim. "Improvement of therapeutic capacity of insulin-producing cells trans-differentiated from human liver cells using engineered cell sheet", Research Square, 2020 Publication	<1%
21	123dok.com Internet Source	<1%
22	B. A. Magnuson, G. A. Burdock, J. Doull, R. M. Kroes et al. "Aspartame: A Safety Evaluation Based on Current Use Levels, Regulations, and Toxicological and Epidemiological Studies", Critical Reviews in Toxicology, 2008 Publication	<1%
23	Evelin Fabjan, Etje Hulzebos, W. Mennes, A. H. Piersma. "A Category Approach for Reproductive Effects of Phthalates", Critical Reviews in Toxicology, 2008 Publication	<1%
24	Toshinari Takamura, Hitoshi Ando, Yukihiro Nagai, Haruhisa Yamashita, Erika Nohara, Ken-ichi Kobayashi. "Pioglitazone prevents mice from multiple low-dose streptozotocin-induced insulitis and diabetes", Diabetes Research and Clinical Practice, 1999 Publication	<1%

25	Qi Ge, Liang Chen, Min Tang, Shu Zhang, Lanlan Liu, Lu Gao, Shangshang Ma, Ming Kong, Qin Yao, Fan Feng, Keping Chen. "Analysis of mulberry leaf components in the treatment of diabetes using network pharmacology", European Journal of Pharmacology, 2018 Publication	<1%
26	Yong-Yu Liu, Kadaba Rajkumar, Liam J Murphy. "Hepatic regeneration in insulin-like growth factor binding protein-1 transgenic mice", Journal of Hepatology, 1999 Publication	<1%

Exclude quotes	On	Exclude matches	Off
Exclude bibliography	On		

paper_sholihatil

PAGE 1

PAGE 2

PAGE 3

PAGE 4

PAGE 5