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Antidiabetic Activity of Ethanolic Extract of Pandan Tikar (*Pandanus tectorius*) on Alloxan-Induced Diabetic White Male Rats

(Uji Aktivitas Antidiabetes Ekstrak Etanol Daun Pandan Tikar (Pandanus tectorius) Pada Tikus Putih Jantan Galur Wistar Yang Diinduksi Aloksan)

Magi Melia Tanggu Rame*, Yohana K.A. Mbulang

Jurusan Farmasi, Fakultas Kesehatan, Universitas Citra Bangsa, Kupang Indonesia.
**E-mail: magimelia93@gmail.com*

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Corresponding Author:
Magi Melia Tanggu Rame
Jurusan Farmasi
Fakultas Kesehatan
Universitas Citra Bangsa
Kupang
Indonesia
email: magimelia93@gmail.com

ABSTRACT

Background: Diabetes mellitus is a chronic disease caused by the body's incapacity to use insulin or the inability of the pancreas to produce insulin. Pandan tikar, belong to Pandanaceae plants, has been known for its benefits. Chemical compounds in pandan tikar leaves showed that it has a lot of medicinal activities, one of them is to lower glucose blood level in diabetes mellitus. **Objectives:** This study aimed to determine the activity of ethanolic extract of pandan tikar (*Pandanus tectorius)* leaves as antidiabetic agent in white male rats induced by alloxan. **Material and Methods:** This study used a pretest-posttest design, with 25 Wistar white male rats. The rats were divided into five groups, each consisting of 5 rats. Group I, a positive control, was given glibenclamide with a dosage of 0.45 mg/kg BW. For the negative control, Group II, Na-CMC 1% was used. The test groups were Group III, IV, and V, and each received an ethanolic extract of pandan tikar leaves with various dosages of 125, 250, and 375 mg/kg body weight (BW), respectively. The rats were conditioned in diabetic stage by using alloxan 150 mg/kg bw as an inducer, given intraperitoneally, then each rats treated accordingly to their own group for 14 days. The determination of blood glucose level was done enzymatically by using glucometer. **Result:** The result showed that ethanolic extract of pandan tikar leaves were able to lower the glucose blood level and not significantly different from glibenclamide. The most optimal dose of pandan tikar leaves ethanolic extract was 375 mg/kg bw, with the decreasing percentage was 56.72%. **Conclusions:** The ethanolic extract of pandan tikar leaves has antihyperglicemic ability on alloxan-induced diabetic white male rats.

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ABSTRAK

Latar Belakang: Diabetes melitus merupakan penyakit kronis yang disebabkan ketidakmampuan tubuh untuk meggunakan insulin yang dihasilkan pankreas atau ketidakmampuan pankreas dalam menghasilkan insulin. Daun pandan tikar termasuk dalam keluarga *pandanaceae* (pandan-pandanan) yang telah diketahui memiliki banyak manfaat. Kandungan kimia yang terkandung dalam daun pandan tikar menunjukkan bahwa daun pandan tikar memiliki aktivitas sebagai bahan obat. Salah satu efek terapi dari kandungan kimia tersebut yaitu menurunkan kadar glukosa darah pada penyakit metabolik diabetes melitus. **Tujuan**: Penelitian ini bertujuan untuk menguji aktivitas ekstrak etanol daun pandan tikar (*Pandanus tectorius*) sebagai antidiabetes pada tikus putih jantan yang diinduksi aloksan. **Bahan dan Metode**: *pre-test post-test only group design* menjadi metode yang digunakan dalam penelitian ini. Dua puluh lima ekor tikus putih jantan galur Wistar (*Rattus norvegicus*) dibagi dalam 5 kelompok dan setiap kelompok terdiri dari 5 ekor tikus. Kelompok I diberikan glibenklamid 0,45 mg/kg BB, kelompok II Na-CMC 1%, kelompok III ekstrak etanol daun pandan tikar dosis 125 mg/kg BB, kelompok IV esktrak etanol daun pandan tikar dosis 250 mg/kg BB dan kelompok V ekstrak etanol daun pandan tikar dosis 375 mg/kg BB. Hewan uji dikondisikan diabetes melitus dengan diinduksi aloksan 150 mg/kg BB secara intraperitoneal, kemudian diberi perlakukan sesuai kelompok uji dan pembanding selama 14 hari. Penetapan kadar glukosa darah dilakukan secara enzimatik menggunakan alat glukometer. **Hasil**: Pemberian ekstrak Etanol Daun Pandan Tikar mampu menurunkan kadar glukosa darah dan tidak berbeda signifikan dengan glibenklamid. Esktrak etanol daun pandan tikar dosis 375 mg/kg BB merupakan dosis yang optimal dalam mengurangi kadar glukosa darah dengan persentase penurunan 56,72%. Kesimpulan: Ekstrak Etanol Daun Pandan Tikar dapat menurukan kadar glukosa darah pada tikus putih jantan yang diinduksi aloksan.

Kata kunci: Pandan Tikar (*Pandanus tectorius*), Diabetes melitus, Hiperglikemia, Aloksan

INTRODUCTION

Generally, the level of public health can be seen from their daily pattern, including the food type and diet pattern. The increasingly advanced technology has led people to consume unhealthy foods, for example, fast foods, which leads to disorder of body metabolism because of the excessive amount of proteins, fats, and sugar, also fewer fibers in that type of foods. An example of a metabolism disorder that can arise is diabetes mellitus (Rahmi, 2014). Diabetes mellitus is a chronic disease caused by the body's incapacity to use insulin or the inability of the pancreas to produce insulin (WHO, 2016).

Diabetes management can be started with a healthy diet and exercise to reach the targeted glucose blood level. But if the target can not be reached yet, it can be helped by using medication to lower the glucose blood level (Atihuta F, 2018). The use of hypoglycemic medication is relatively expensive and can cause several adverse drug reactions. Hence, traditional medication is an alternative therapy. Based on the result of Riset Kesehatan Dasar 2018, the use of medicinal plants in Indonesia reached 24.6%, and 55.1% of people in Nusa Tenggara Timur Province used medicinal plants as alternative therapy (Riskesdas, 2018).

Pandan tikar is a member of the Pandanaceae family which is known for its benefits (Saifudin, 2014). Pandan tikar is different from other pandanaceae plants, such as Pandanus conoideus, pandanus julianeti, pandanus brosimos that are usually used as additional food materials and traditional medicine materials. Whereas in Indonesia, pandan tikar (*Pandanus tectorius*) leaves is still usually used as handicraft industry raw materials and roof materials of house. This Pandan tikar leaves is made for

handycraft such as plaited mats, hats, basket or other kinds handicraft by soaking, boiling or heating (Purwanto dan Munawaroh, 2010). Pandan tikar leaves are suspected to have lots of chemical compounds that can be useful as medicinal ingredients. From the pharmacognostic identification of pandan tikar leaves that had been done by Wulandari (2004), it is known that pandan tikar leaves contain flavonoids, saponins, and polyphenols. A study had been done by Sanjeeva *et al.,* (2011) proved that methanolic extract of pandan tikar contains alkaloids, carbohydrates, phenols, steroids, sterols, proteins, and glycosides. Another study done by Kumar *et al.,* (2017) showed that hydroalcoholic extract of pandan tikar leaves contains saponins, alkaloids, flavonoids, and carbohydrates.

Chemical compounds in pandan tikar leaves showed their potency to give medicinal benefits, one of them is the ability to lower the level of blood glucose in diabetes mellitus. But there are not enough studies to prove its direct effect to decrease the level of blood glucose. For that reason, this study focused on examining pandan tikar leaves extract for its hypoglycemic effect on alloxan-induced rats.

MATERIAL AND METHODS

Materials

Maceration container, beaker glass, reaction tubes, measuring cylinders, flannel fabrics, filter papers, 20 mesh sieve, aluminum foils, experimental animal models scales, analytical scales, oven, evaporator, glucometer, pandan tikar leaves, Glibenclamide (Indofarma), Alloxan monohydrate (Sigma Aldrich), distilled water (Jaya Mas Medika Industri), chloroform and ethanol 96% (Merck Chemical and Life Science), CMC Na 1%, $FeCl_3$, H_2SO4, chloroform, ethanol 96%, HCl 1%, NaOH 2%, Mayer reagent, and Wagner reagent (Smart Lab Indonesia).

Methods

Preparation of Pandan Tikar Leaves

Samples of Pandan tikar (*Pandanus tectorius*) leaves were obtained from Baun, West Kupang, Nusa Tenggara Timur. The chosen pandan tikar leaves were freshly picked, then washed and dried using the aeration drying method, by drying the plants in a place that not exposed by direct sunlight. This method is simple and easy, also this drying method does not need high temperature which can cause degradation of non-heat resistants chemical compounds (Azwanida, 2015). The drying process is aimed to reduce the water level in plant simplicia. The reduction of water level can stop the enzymatic reaction, which can inhibit the decrease and damage of simplicia (Utomo et al., 2009). Dried pandan tikar leaves were powdered using an electrical blender until obtained a fine powder, then sieved by using 20 mesh sieves. The process of this powdering process is to expand the surface area of pandan tikar leaves for easier contact with solvent to achieve a more effective result.

Extraction

About 800 grams of powdered pandan tikar leaves were dissolved in ethanol 96% with ratio 1:10 g/v, then put into maceration container, closed, and leave for 5 days protected from direct light while it was occasionally shaken. After 5 days, this mixture was filtered, and the filtrate was concentrated using a rotary evaporator at a maximal temperature of 50^{o}C.

Qualitative Identification of Ethanolic Extract

Chemical compounds identification of the extract was done to ensure that desired active ingredients are successfully obtained in the extraction process.

a. Alkaloid identification

About 0.5 g ethanolic extract of pandan tikar leaves was putted into a reaction tube, added with 2 mL of HCl 1% solution, then filtered it. The filtrate was divided into two parts, the first part was added by Mayer reagent and the second part was added by Wagner reaction. If yellowish-white precipitation formed with Mayer reagent and reddish-brown precipitation formed with Wagner reagent, then the ethanolic extract of pandan tikar leaves is positive for alkaloids (Yadav & Agarwala, 2011 ; Sopianti & Sary, 2018).

b. Flavonoid identification

About 0.5 g ethanolic extract of pandan tikar leaves was putted into a reaction tube, and added 2 mL of NaOH 2% solution. If the color is changed into deep yellow which vanished when diluted with adding HCl, then the ethanolic extract of pandan tikar leaves is positive for flavonoids (Yadav & Agarwala, 2011; Sopianti & Sary, 2018).

c. Tannin identification

About 0.5 g ethanolic extract of pandan tikar leaves was putted into a reaction tube, and dissolved with ethanol. Then added 3 drops of $FeCl_3$ 5%. If the color is changed into blackish-green or deep blue, then the ethanolic extract of pandan tikar leaves is positive for tannins (Fajriaty et al., 2018).

d. Saponin identification

About 0.5 g ethanolic extract of pandan tikar leaves was putted into a reaction tube, added 2 mL ethanol 96% then stirred. Next, added 20 ml of distilled water and shaken vigorously. If the foam is formed then the extract of pandan tikar leaves is positive for saponins (Sopianti & Sary, 2018)

e. Steroid identification

About 0.5 g ethanolic extract of pandan tikar leaves was putted into a reaction tube, and dissolved with ethanol, added 2 mL chloroform and 2 mL concentrated H_2SO_4 slowly through the inner side of the reaction tube. If a red ring is formed, then the extract of pandan tikar leaves is positive for steroids (Yadav & Agarwala, 2011; Sopianti & Sary, 2018).

Experimental Animal Treatment and Determination of Blood Glucose Level

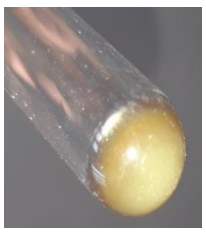
There were five experimental groups, each consisting of 5 rats, and the total is 25 wistar white male rats. Before any treatment, all rats were put into the adaptation process for 7 days, fed with standard animal feed and drink every day throughout the treatments. After adaptation, fasting blood glucose level was measured on day-1 as a baseline blood glucose level (T0). Next on the same day, the rats were injected intraperitonially by alloxan with a dose of 150 mg/kg BW. After three days (day-3), the rats were checked for their diabetic status which was marked by their hyperglycemic condition (plasma glucose level >110 mg/dL) (Ojiako et al., 2016), by measuring the blood glucose level again (T1). Then each group will be given treatments accordingly. The next blood glucose measurement will be done on the day-10 (T2) and day-17 (T3). The treatment groups were: Group I as negative control, was given CMC Na 1% suspension, Group II as positive control, was given glibenclamide 0,45 mg/kg BWof rats for peroral use, Group III, group IV and group V were orally given 125, 250 and 375 mg/kg bw ethanol extract of pandan tikar leaves, respectively.

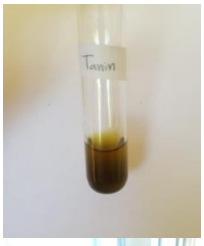
The determination of blood glucose level was enzymatically performed by using a glucometer. The blood sample was drawn by wounding the venous blood vessel in rat tails by using a scalpel. Blood drops from the tail were put into the glucometer strip and then the strip was put into the glucometer. The result of the blood glucose level will be seen on the glucometer screen.

RESULTS AND DISCUSSION

Chemical compound identification results

Table 1. The result of chemical compounds in Pandan Tikar (*Pandanus tectorius*) leaves ethanolic extract

Test	Reagent	Color/ precipitation	Picture	Result
Alkaloid	Wagner	Reddish brown precipitation		Positive
	Mayer	Yellowish white precipitation		Positive

Flavonoid	Alkaline Reagent Test (Extract + NaOH 2% solution)	Deep yellow		Positive
	Alkaline Reagent Test (Adding HCl)	Deep yellow which vanished when diluted by adding HCl		Positive
Tanin	$FeCl_3$ 5%	Blackish brown		Negative
Saponin	Ethanol 96% + Distilled water	Stabil foam		Positive
Steroid	(Salkowski test) Chloroform + concentrated H_2SO_4	Red ring		Positive

The result of chemical compound identification (Table 1), ethanol extract of pandan tikar leaves contains alkaloids, flavonoids, saponins and steroids but negative for tannins. This is in accordance with studies reported by Kido (2019) and Kumar *et al.,* (2017) about chemical compound identification in pandan tikar leaves.

The result of blood glucose level determination

Table 2. Averages of blood glucose level

Treatment Groups	Blood Glucose Level(mg/dL) ± SD			
	Day-0	Day-3	Day-10	Day-17
Positive Control	93 ± 11.66	135 ± 15.52	109.2 ± 6.4	92.2 ± 8.61
Negative Control	101.2 ± 8.32	180.2 ± 55.63	165 ± 36.16	161.4 ± 35.27

EPTL 125 mg/KgBW	85.2 ± 14.1	181.8 ± 44.73	138 ± 6.78	125 ± 5.43
EPTL 250 mg/KgBW	98 ± 18.79	217.2 ± 73.03	131.8 ± 6.4	115.2 ± 4.21
EPTL 375 mg/KgBW	104.4 ± 19.74	238 ± 85.26	121.2 ± 3.49	103 ± 7.00

EPTL = Ethanolic extract of Pandan Tikar Leaves
Positive Control = Glibenclamide 0,45 mg/kg BW
Negative Control = Na CMC 1%

Table 3. Percentages of blood glucose level reduction

Treatment Groups	Averages of blood glucose level reduction percentages	
	Day-10	Day-17
Positive Control	19.11	31.70[a]
Negative Control	8.44	10.43[b]
EDPT 125 mg/KgBW	24.09	31.24[a]
EDPT 250 mg/KgBW	39.32	46.96[a]
EDPT 375 mg/KgBW	49.08	56.72[a]

[a] Numbers followed by different alphabets in a the same line indicated significantly different test results ($p<0,05$).

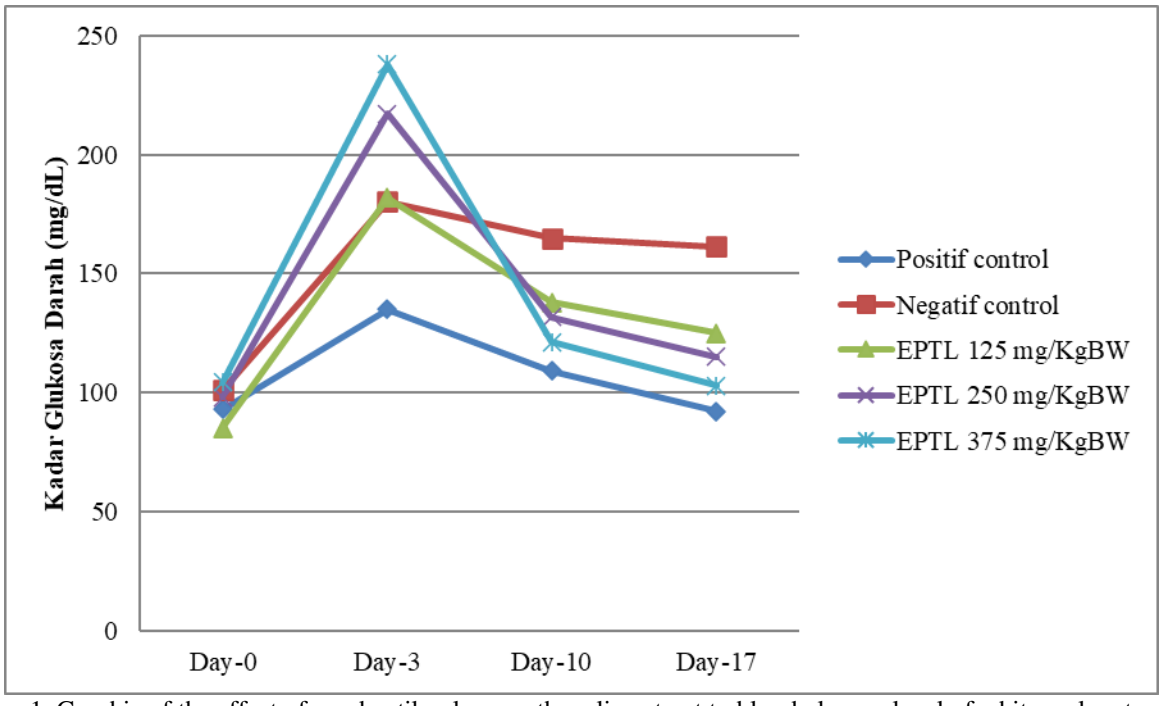


Figure 1. Graphic of the effect of pandan tikar leaves ethanolic extract to blood glucose level of white male rats in 14 days

Based on Table 2 and Figure 1 above, it can be seen that there is an increase in blood glucose level in rats after induced by alloxan. Single-dose of alloxan given intraperitoneally is one of the most common induction for a diabetic animal model. In several studies, the alloxan dose given was ranged from 90 mg/kg BW to 200 mg/kg BW and 150 mg/kg BW is the most frequently used dose (Ighodaro

et al., 2018). Alloxan was chosen because it has two pathological effects. This compound selectively inhibits insulin secretion by specifically inhibiting glucokinase or glucose sensors in pancreatic β-cell, causing the diabetic condition which depended on insulin through inducing ROS formation which causing necrosis of pancreatic β-cell (Lenzen, 2008). The positive control group has the least increase in blood glucose level compared to other groups. This can be caused by various factors, one of which is the different immunity or endurance to alloxan of each rat, which leads to a diverse increase of blood glucose levels (Suarsana et al., 2010).

After giving the test preparation, it can be seen that on day-10 (T2) the blood glucose level decrease started to show until day-17 (T3), except for the negative control group. The highest percentage of blood glucose level reduction on day-17 is the group which given 375 mg/kg BW pandan tikar leaves ethanolic extract, with a reduction percentage reached 56.72%, compared to positive control which is only reached 31.70%. This can be caused by the average increase of blood glucose level after alloxan induction in the positive control group was not as high as the increase in the 375 mg/kg BW treatment group. Based on the result of the statistic test, it is proved that administration of glibenclamide and pandan tikar leaves ethanolic extract to have a significant effect on the decrease of blood glucose level in rats ($p>0,05$). The effects of these three doses of ethanolic extract of pandan tikar leaves did not significantly differ from the positive control group, but significantly differ if compared to the negative control.

Glibenclamide is known as an effective antidiabetic oral which able to decrease the blood glucose level by stimulated pancreatic β-cell to release stored insulin and increasing glucose-induced insulin secretion (Soegondo, 2005). Based on the result of chemical compounds identification (Table I), ethanolic extract of pandan tikar leaves contains several chemical compounds: alkaloids, flavonoids, and saponins but negative for tannin. This is consistent with studies done by Kido (2019) and Kumar *et al.,* (2017) related to the identification of chemical compounds of pandan tikar leaves.

Secondary metabolites like alkaloids, saponins, flavonoids, and steroids, which are contained in pandan tikar leaves, are suspected to have anti-diabetic effects. According to Abba & Isaac (2017), these compounds have various action mechanisms to give antidiabetic effect, such as by increasing insulin secretion, decreasing gluconeogenesis in the liver, specific enzymes regulation which is involved in carbohydrate metabolism, like α-glucosidase inhibitor, hypolipidemic activity, antioxidant activity, disruption of several glycolytic enzymes activity, like phosphoenolpyruvate carboxykinase, glycolate hemoglobin repair, increased expression of glucose transporter, etc.

Flavonoid is a group of hydroxylated phenol compounds known as a strong antioxidant, that able to inhibit complications of diabetes mellitus. Flavonoids play a role in counteracting free radicals by donating their hydrogen atoms, activate antioxidant enzymes, bind metal ions, reduce α-tocopherol

radicals and dan inhibit oxidase (Sarian et al., 2017). Apart from as an antioxidant, flavonoids also able to inhibit aldose reductase, increase Ca^{2+} absorption, and regenerate pancreatic β-cell to increase insulin release, also play a part to restore the sensitivity of insulin receptor, these are the causes of the decrease in glucose levels in rats (Sandhar et al., 2011; Indrayani dan Resmi, 2020).

The result of this research approve that variety ethanolic extract of pandan tikar leaves with dosage 125mg/kg BW, 250kg/BW, and 375kg/BW have the antihyperglycemic activity. Based on the statistical analysis, these three variant doses were not significantly different from positive control namely glibenclamid. Based on the graphic, the decreasing of glucose blood degree which was best be shown by dosage of 375 mg/kg BW and it was followed by dosage of 250mg/kg BW and 125 mg/kg BW. This fact indicated that the more dosage of ethanolic extract of pandan tikar leaves, the bigger decreasing of glucose degree in blood. The decreasing was caused by the higher extract dosage that could be predicted that there were more content of active substance that covered in ethanolic extract of pandan tikar leaves.

CONCLUSION

Ethanolic extract of pandan tikar leaves with dosages of: 125 mg/kg BW, 250 mg/kg BW, and 375 mg/kg BW can effectively decrease the level of blood glucose in alloxan-induced rats. The most optimal dose is 375 mg/kg BW. This study still requires histopathological evaluation using hematoxylin and eosin staining (HE) also immunohistochemical staining with anti-insulin antibodies, to determine whether pancreatic β-cells regeneration in rats that have been induced by a diabetogenic agent.

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CONFLICT OF INTEREST

Authors declare no conflict of interest

REFERENCES

Aba, P.E., Isaac U.A., 2018, 'Mechanisms of actions of some bioactive anti-diabetic principles from phytochemicals of medicinal plants: A review', *Indian Journal of Natural Products and Resources*. 9, 85-96.

Atihuta., Frangki., 2018, 'Uji Aktivitas Ekstrak Kombinasi Batang Dan Daun Suruhan (Piperumia Pellucida L.H.B Kunth) Sebagai Anti Diabetes Pada Tikus Putih', *Jurnal Mitra Pendidikan (JMP Online)'*, 2, 205-216.

Azwanida NN., 2015, 'A Review on the Extraction Methods Use in Medicinal Plants, Principle, Strength and Limitation. *Medicinal & Aromatic Plants',* 4, 2167-0412.

Fajriaty, I., Hariyanto., Andres., Setyaningrum, R. 2018. Skrining Fitokimia dan Analisis Kromatografi Lapis Tipis dari Ekstrak Etanol Daun Bintangur (*Callophyllum soulattri* Burm. F). *Jurnal Pendidikan Informatika dan Sains*. 7, 54-67.

Ighodaro, O.M., Abiola M.A., Oluseyi, A.A. 2017, 'Alloxan-induced diabetes, a common model for evaluating the glycemic-control potential of therapeutic compounds and plants extracts in experimental studies', *Medicina*. 53, 365-374.

Indrayani, S., Resmi M. 2020, 'Review Artikel: Aktivitas Antidiabetes Beberapa Tanaman Di Indonesia', *Farmaka*. 18, 58-65.

Kido Rahelin, et al., 2019, 'Uji Aktivitas Analgesik Ekstrak Etanol Daun Pandan Tikar (*Pandanus tectorius*) Pada Mencit (Mus musculus) yang Diinduksi Asam Asetat. Fakultas Farmasi', *Skripsi*, Universitas Citra Bangsa.

Kumar, S., Seema, D., Pushpander, K., *et al*., 2017, 'Antifertility Effect of Hydroalcoholic Extract of Pandanus Odoratissimus L. Leaves'. Porto *Biomedical Journal*. 2,167-169. doi: 10.1016/j.pbj.2017.03.001

Lenzen, S., 2008. 'The mechanisms of alloxan- and streptozotocin-induced diabetes', *Diabetologia*. 51, 216-226. DOI 10.1007/s00125-007-0886-7

Ojiako, Okey A., Paul C. Chikezie., Agomuo C.Ogbuji., 2016, 'Blood glucose level and lipid profile of alloxan-induced hyperglycemic rats treated with single and combinatorial herbal formulations', *Journal of Traditional and Complementary Medicine*. 6, 184-192.

Purwanto, Y., Esti, M. 2010. Etnobotani Jenis-Jenis Pandanaceae Sebagai Bahan Pangan di Indonesia. *Pusat Penelitian Biologi-LIPI dan PKT Kebun Raya Bogor-LIPI*. Vol.5A:97-108

Rahmi, H., 2014, 'Aktivitas Ekstrak Daun Wungu (*Graptophyllum pictum* (L.) Griff) Dalam Menurunkan Kadar Glukosa Darah Tikus Hiperglikemia', *Thesis*, Pasca Sarjana Institute Pertanian Bogor

Riskesdas., 2018, 'Laporan Nasional Riskesdas 2018', Kementerian Kesehatan Republik Indonesia, Badan Penelitian dan Pengembangan Kesehatan.

Saifudin, A., 2014, *Senyawa Alam Metabolit Sekunder Teori, Konsep, dan Teknik Pemurnian*. Edisi 1. Cetakan 1. Deepublish: Yogyakarta.

Sanjeeva., Raveendra, K.N, Padmalaxmi, D., *et al*., 2011, 'Antioxidant Activity Of Methanol Extract Of Pandanus Fascicularis Lam', *Pharmacologyonline.* 1, 833-841.

Sandhar, H.K., Bimlesh, K., et al., 2011, 'A Review of Phytochemistry and Pharmacology of Flavonoids', *Internationale Pharmaceutica Sciencia.* 1, 25-41.

Sarian, M.N., Qamar U.A., et al., 2017, 'Research Article: Antioxidant and Antidiabetic Effects of Flavonoids: A Structure-Activity Relationship Based Study', *BioMed Research International.*

Soegondo, S., Soewondo, P, Subekti, I., 2009, *Penatalaksanaan Diabetes Melitus Terpadu*, Jakarta: Fakultas Kedokteran Universitas Indonesia.

Sopianti, D.S., Sary, D.W., 2018, 'Skrining Fitokimia dan Profil KLT Metabolit Sekunder dari Daun Ruku-ruku (*Ocimum tenulforum* L.) dan Daun Kemangi (*Ocimum sanctum* L.)', *Jurnal Farmasi dan Kesehatan.* 8, 44-52.

Suarsana, I.N., Iwan H. Utama., I Gusti Agung., Ayu Suartini., 2011, 'Pengaruh Hiperglikemia dan Vitamin E pada Kadar Malonaldehida dan Enzim Antioksidan Intrasel Jaringan Pankreas Tikus', Fakultas Kedokteran Hewan, Universitas Udayana.MKB 3

Utomo, A.D., Wiranti S.R., Binar, A.D., 2009, 'Pengaruh Beberapa Metode Pengeringan Terhadap Kadar Flavonoid Total Herba Sambiloto (*Andrographis Paniculata*)', *Fakultas Farmasi Universitas Muhammadiyah Purwokerto.* 6, 1693-3591.

WHO. 2016. *Global Report on Diabetes*. France: World Health Organization.

Wulandari D., 2004, 'Identifikasi Secara Farmakognostik Daun Pandan Duri (*Pandanus tectorius* Sol.)', *Skripsi*. Fakultas Farmasi, Universitas Sanata Dharma.

Yadav, R.N.S., Agarwala, M., 2011, '*Phytochemical Analysis of Some Medicinal Plants*', Journal of Phytology. 3, 10-14.