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Effect of Pakkat Ethanol Extract (*Calamus L.* Blum) on Spermatogenesis and Testosterone Levels of Diabetes Mellitus Wistar Rats

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Abstract: Diabetes mellitus is a metabolic disorder marked by high blood glucose levels (hyperglycemia) that is caused by insulin deficiency. It also affects male infertility. Pakkat, young rattan, contains various phytochemicals, which can affect blood glucose levels, spermatogenesis, and testosterone production. Objective: To assess the effectiveness of Pakkat extract in regulating blood glucose levels, testosterone hormone, and spermatogenesis in alloxan-induced diabetic rats. This experimental study used 25 diabetic male Wistar rats and was grouped into five groups including negative control (distilled water), positive control (metformin), Treatment 1 (125 mg/KgBW Pakkat extract), 2 (250 mg/KgBW Pakkat extract), and 3 (500 mg/KgBW Pakkat extract) for 14 days. All data were analyzed by One-way ANOVA followed by a Post-Hoc Test. Pakkat extract at 125 mg/kgBW dose effectively reduced glucose levels (P-Value < 0.001) after 14 days. It also significantly increased spermatogenesis (P-Value < 0.001) and testosterone levels (P-Value < 0.001) in alloxan-induced diabetic rats. Thus, it can be concluded that any doses of Pakkat (Calamus L. Blume) extract significantly improve blood glucose levels after 14 days of administration. However, a higher dosage is required to increase spermatogenesis and testosterone hormone in diabetic conditions.

Keywords: Alloxan; Diabetesm pakkat; Spermatogenesis; Testosterone

Introduction

Diabetes mellitus (DM) is a metabolic disorder that is commonly found in Indonesian society, and many of them may not realize they have DM (Hestiana, 2017). People suffering from diabetes mellitus have an insulin resistance condition that is unable to use insulin, leading to dysregulation of insulin hormone. This condition is due to pancreatic β cell dysfunction and impaired glucose utilization in target cell responses such as tissues, muscles, and organs (Nugroho et al., 2017). The chief complaints of DM includes frequent urination at night, frequent thirst, frequent hunger, and weight loss (Rahmasari & Wahyuni, 2019). Diabetes mellitus is classified into insulin-dependent, non-insulin-dependent, gestational, and other types of diabetes mellitus (Awuchi et al., 2020; Cooke & Plotnick, 2008). Based on the World Health Organization (WHO) data, around 150 million people worldwide suffer from Diabetes Mellitus (Isnaini & Ratnasari, 2018). Furthermore, the WHO also reported that the prevalence of DM would reach 300 million people in 2025 (Condorelli et al., 2018). On the other hand, the IDF (International Diabetes Federation) 2019 also reported that Indonesia was the seventh country in Southeast Asia with the highest number of people suffering from

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diabetes mellitus, which was 10.7 million (Prihanto & Imbar, 2022; Nasution & Zara, 2025; Kitabichi et al., 2009). Riskesdas (Basic Health Research) reported that North Sumatra province had around 160 thousand people suffering from diabetes mellitus (Purwoningsih & Purnama, 2017; Jusup, 2016; Caspersen et al., 2012; Lubis et al., 2023).

Diabetes mellitus has some risk factors, including genetic/hereditary factors, obesity, age, lack of activity, mind/stress, and food (Rahmasari & Wahyuni, 2019). When these risk factors are not properly controlled, diabetes mellitus can cause some complications that affect either microvascular or macrovascular. One of these complications involves the spermatogenesis process in males and the secretion of testosterone hormone (Arundani et al., 2021; Bhavya & Sanjay, 2022). Furthermore, diabetes mellitus is also reported to cause sexual dysfunction, such as impotence, decreased libido, and infertility (Condorelli et al., 2018; Wang et al., 2017).

Indonesians have a high demand for Pakkat, especially in the Medan area, because of its good taste and ease of processing. Pakkat has various phytochemicals responsible for antidiabetic activity, including saponins, tannins, flavonoids, triterpenoids, alkaloids, and glycosides (Mayasari, 2022; Nasution et al., 2022; Rahmawati et al., 2021). Saponins and tannins can inhibit glucose absorption. Saponins also regenerate the damaged pancreas to increase the number of pancreatic beta cells and lead to improved insulin secretion (Kunu et al., 2020). Moreover, saponins can also inhibit α-glucosidase enzyme activity and lead to reduced blood glucose levels. On the other hand, flavonoids inhibit phosphodiesterase, which will cause an increase in cAMP in pancreatic beta cells and ultimately increase insulin secretion to reduce glucose levels. Tannins modulate insulin signaling by activating the insulin-mediated signaling pathway, which functions to increase glucose transport and reduce glucose absorption in the intestine (Aprillia & Safitri, 2020; Tjahjono et al., 2025; Nugroho et al., 2012; Hidayat & Wulandari, 2022), which will ultimately reduce glucose levels (Kunu et al., 2020). Finally, triterpenoid stimulates insulin secretion (GULT-4) and glucose uptake (Utomo et al., 2021; Premanath & Nanjaiah, 2015).

Some Indonesian people prefer to consume drugs from natural ingredients rather than chemical compounds because chemical-based drugs have a long-term effect on the body. Diabetic patients potentially receive antidiabetic long-term medicines, that is, chemical-based drugs. It becomes crucial to monitor blood glucose levels, clinical manifestations, and prevention of some complications (Utomo et al., 2021; Skovsa, 2014; Dwiannur et al., 2024). Hence, all authors were interested in evaluating the effect of Pakkat (*Calamus L. Blum*) ethanol extract on the quality of spermatogenesis and testosterone hormone levels in diabetic conditions.

Method

Study Design

This quantitative experimental study was conducted using male Wistar rats at the Pharmacology Laboratory of Universitas Prima Indonesia between March and May 2023. Ethical clearance was granted by the Health Research Ethics Committee of Universitas Prima Indonesia, under approval number 041/KEPK/UNPRI/II/2023.

Extraction Process

Pakkat was initially collected, dried in an oven at 30-50˚C, and then aerated. After that, the dried Pakkat (*Calamus L. Blume*) was ground into simplicial powder and then macerated using a 96% ethanol solution in a ratio of 1:7. After the maceration process, the filtrate was evaporated by a rotary evaporator to obtain concentrated Pakkat ethanol extract and stored in the refrigerator (Afifah, 2017; Suhartomi et al., 2020; Afita et al., 2022).

Treatment

This study used male Wistar rats as experimental animals weighing 175–200 g and aged about two months/years. All eligible male Wistar rats were acclimatized for a week. Afterwards, all rats were intraperitoneally injected to induce diabetic conditions with 150 mg/ kg BW of 10% alloxan monohydrate solution**.** Four days after induction, all rats were measured for blood glucose levels, and diabetes was defined as a blood glucose level higher than 200 mg/ dl. Then, all rats were grouped into five groups consisting of five rats. These five groups included negative control, positive control, Treatment 1, 2, and 3, which received distilled water, metformin, 125, 250, and 500 mg/kg BW, respectively. Each group received treatment once daily for two weeks. Blood was withdrawn from the lateral vein in the tail, and this blood was used to measure blood glucose level by a glucometer (Autocheck®) (Mutia & Suhartomi, 2022; Utomo et al., 2021).

Blood and Organ Harvest

All rats were sacrificed by ketamine injection followed by dissection after two weeks of treatment. After that, blood was withdrawn by intracardiac puncture to be stored in a red-colored blood tube, and then all reproductive organs (testes and cauda epididymis) were dissected, washed in normal saline, and fixed in 10% Buffered Formalin Solution (BFS)

(Chiuman et al., 2021; Utomo et al., 2021; Ongko et al., 2019; Rosa et al., 2022).

Serum Testosterone Measurement

Testosterone hormone was measured from blood serum by the ELFA (Enzyme Linked Fluorescent Immuno-Assay) method and expressed as ng/ml units. Blood serum was obtained from the centrifugation process. ELFA assay is more sensitive and reliable than ELISA (Enzyme-Linked Immunosorbent Assay) (Naully & Khairinisa, 2018).

Histology Study

The spermatogenesis process was evaluated by microscopic observation of testes and seminiferous tubule tissue. The spermatogenesis process was evaluated by the Johnsen scoring system, that was described in Table 1 (Berlina et al., 2019).

Table 1. Jhonsen Score (Thanh et al., 2020)

Score	Description
10	Complete spermatogenesis and many spermatozoa, the germinal epithelium is arranged regularly and leaves an open lumen.
9	Many spermatozoa, irregular epithelium characterized by peeling or elimination of the lumen
8	Few spermatozoa per tubule
7	No spermatozoa, many new spermatids
6	No spermatozoa and only a few spermatids are present
5	No spermatozoa or spermatids, many spermatocytes
4	No spermatozoa or spermatids, few spermatocytes
3	There are only spermatogonia.
2	No germ cells, only Sertoli cells
1	No seminiferous epithelium

Data Analysis

All data were analyzed by SPSS 27 and expressed as Mean ± Standard Deviation (Mean ± SD). Blood glucose levels and Johnsen scores were initially analyzed for data distribution and homogeneity. If data distribution was normal, it was analyzed by one-way ANOVA followed by Tukey HSD Post Hoc Test, instead of Kruskal–Wallis followed by Mann–Whitney (Santoso, 2014, 2019).

Result and Discussion

This study evaluated several parameters, including blood glucose levels, testosterone hormone levels, and the spermatogenesis process. The blood glucose level was analyzed, and the results were described in Table 2.

Table 2. Comparison of Glucose Levels of Rats in All Treatment Groups

Group	Glucose Level, mg/dL (Mean ± SD)			
	Before induction	After induction	7th Days	14th Days
Negative control	106.40±14.64	420.80±173.51	452.80±57.77	556.00±46.15[a]
Positive control	108.60±22.77	417.20±139.07	270.60±147.79	162.80±42.79[b]
Treatment-1	100.00±17.34	472.60±80.20	401.20±217.29	216.60±128.74[b]
Treatment-2	109.20±6.73	525.40±80.20	334.20±156.10	160.20±72.75[b]
Treatment-3	104.00±17.59	483.52±135.85	286.60±10.94	514.60±42.10[a]
P value	0.910	0.664	0.353	0.000

P-value was obtained from One-Way ANOVA; the Difference superscript in the same column indicated a significant difference.

Table 2 shows that there was no significant difference in blood glucose levels before induction, as indicated by a P-value of 0.910. Similarly, after induction, blood glucose levels remained statistically insignificant between groups (P-value = 0.664), both values being greater than 0.05. After seven days of treatment, no significant decrease in blood glucose levels was observed either (P-value = 0.353). However, after 14 days of treatment, a significant decrease in blood glucose levels was noted (P-value < 0.05). The negative control group exhibited the highest average blood glucose level (556.00 ± 46.15 mg/dL), followed by the treatment 3 group (514.60 ± 42.10 mg/dL), treatment 2 group (216.60 ± 128.74 mg/dL), and the standard group. The lowest blood glucose level was observed in the treatment 1 group (160.20 ± 72.75 mg/dL). Additionally, the Jhonsen Score was assessed as another parameter, with the results for each group expressed in Table 3.

Table 3. Comparison of Jhonsen Score System in Testes Tissue of All Group

Group	Jhonsen Score Mean	SD	P Value
Negative control	5.00	0.707	
Positive control	6.20	0.837	
Treatment-1	7.00	0.707	< 0.001
Treatment-2	6.80	1.304	
Treatment-3	8.20	0.837	

P-Value was obtained from One Way ANOVA; SD: Standard Deviation.

Table 3 shows that the Johnsen Score was significantly different in all groups. It can be seen from the P-value which is lower than 0.05. Treatment-3 (500 mg/kg BW of Pakkat extract) showed the highest Johnsen score, 8.20 ± 0.837, and the lowest was in the negative control group (5.00 ± 0.707). It clearly described that the highest dose of Pakkat extract (500 mg/kg BW) had the highest Johnsen score, indicating the best spermatogenesis process. In contrast to the Treatment-3 group, the negative control group showed the lowest Johnsen score, indicating the worst spermatogenesis process. Moreover, the spermatogenesis process in testes tissue of all groups was also described through a microscopic view in Figure 1. The last parameter, testosterone levels, was also analyzed, and the results were described in Table 4.

Table 4. Table Analysis of Anova Test of Testosterone Parameters in All Treatment Groups

Group	Testosterone Level, ng/ dl Mean	SD	P Value
Negative control	7.60	1.140	
Positive control	4.40	1.517	
Treatment-1	5.80	1.483	< 0.001
Treatment-2	5.60	1.140	
Treatment-3	15.20	3.271	

P-Value was obtained from One Way ANOVA; SD: Standard Deviation.

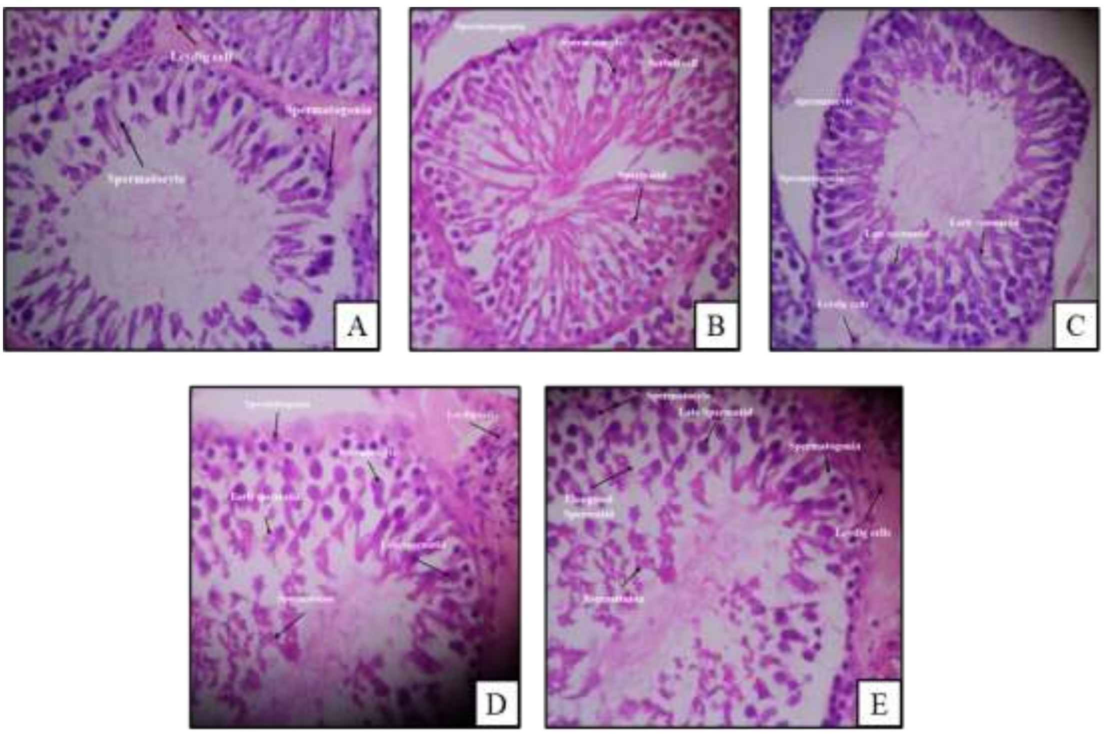

Figure 1. Testes tissue in all groups; A. Negative control (score 5); B. Positive control (score 6); C. Treatment-1 (125 mg/ kg BW of Pakkat extract) (score 7); D. Treatment-2 (250 mg/ kg BW of Pakkat extract) (score 8); E. Treatment-3 (500 mg/ kg BW of Pakkat extract) (score 9). Stain: Hematoxylin and Eosin. Magnification: 400x

Table 4 describes significant changes in testosterone levels in the five treatment groups. It can be seen from the P-value < 0.001. The highest testosterone level was found in Treatment-3 (500 mg/kg BW of Pakkat extract), which was 15.20 ± 3.271 ng/dL. In contrast, the lowest testosterone level was found in the positive control group (metformin), which was 5.80 ± 1.483 ng/dL. It may be due to the presence of flavonoids as the phytochemicals in Pakkat extract. Flavonoids have been reported to inhibit the aromatase enzyme, thereby increasing testosterone hormone levels.

Discussion

The results of this study clearly showed that Pakkat extract had antidiabetic activity and also improved the spermatogenesis process as well as increased testosterone levels. It can be seen from the P-value from blood glucose level, Johnsen score, and testosterone level, which were lower than 0.05.

Increased blood glucose levels on the fourth day were caused by decreased insulin secretion due to the destruction of pancreatic β cells, which was induced by alloxan administration. After fourteen days of extract administration, Pakkat extract significantly reduced blood glucose levels. This antidiabetic activity was caused by phytochemicals in Pakkat. Pakkat ethanol extract has been reported to contain some phytochemicals, including flavonoid, saponin, and tannin compounds, responsible for antidiabetic effects. Flavonoids reduce blood glucose levels by stimulating GLUT 2 in the intestines and stimulating insulin hormone secretion (Ayuni, 2020; Gulo et al., 2021; Kumalasari et al., 2020). Saponins can reduce glucose levels by inhibiting the alpha-glucosidase enzyme, which degrades complex glucose compounds into simple glucose compounds (Aprillia & Safitri, 2020). Tannins also reduce blood glucose levels by modulating insulin signaling through the P13K pathway (Haryoto & Devi, 2018).

This study also revealed that Pakkat extract significantly improved the spermatogenesis process in testes tissue by providing a good microenvironment. Some phytochemicals in Pakkat extract have been reported to improve spermatogenesis, including flavonoids, saponins, and triterpenoids. Flavonoids have antioxidant activity that can protect the spermatozoa from free radical damage by inhibiting free radical formation and neutralizing existing free radicals (Gulo et al., 2021; Utomo & Lubis, 2021). Saponins and flavonoids support Leydig cell growth, which is responsible for testosterone hormone secretion, and this testosterone hormone may regulate the spermatogenesis process (Paramita et al., 2023; Imelda et al., 2014). Triterpenoids have a structure like androgen hormones, stimulating testosterone hormone secretion and increasing spermatogenesis (Wattimena et al., 2023; Antari & Damayanti, 2025).

Furthermore, this study also showed that Pakkat ethanol extract increased testosterone levels, which was due to the presence of flavonoid and saponin in Pakkat extract. Flavonoids are also reported to suppress the anterior pituitary in secreting FSH (Follicle-Stimulating Hormone) and LH (Luteinizing Hormone) in spermatogenesis. FSH hormone increases the testosterone level, which affects the spermatogenesis process. Meanwhile, the LH hormone stimulates Leydig cells to secrete testosterone in the testes tissue. Finally, both saponins and flavonoids maintain the number of Leydig cells to preserve the testosterone level (Kunu et al., 2020; Paramita et al., 2023).

Conclusion

Overall, it can be concluded that a moderate dose (250 mg/kg BW of Pakkat extract) significantly reduced blood glucose levels after 14 days of treatment. A higher dose of Pakkat extract (500 mg/kg BW) was required to improve testosterone levels and the spermatogenesis process in testes tissue.

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Author Contributions
Conceptualization: Yolanda Eliza Putri Lubis, Anggi Sri Ananda Aipin, and Hanjaya; Methodology: Yolanda Eliza Putri Lubis, Anggi Sri Ananda Aipin, and Suhartomi; Investigation: Yolanda Eliza Putri Lubis, Anggi Sri Ananda Aipin, and Juliana Lina; Discussion of results: Yolanda Eliza Putri Lubis, Anggi Sri Ananda Aipin, and Hanjaya; Writing – Original Draft: Anggi Sri Ananda Aipin; Writing – Review and Editing: Yolanda Eliza Putri Lubis, and Hanjaya; Supervision: Yolanda Eliza Putri Lubis, and Hanjaya; Approval of the final text: Yolanda Eliza Putri Lubis, Juliana Lina, and Hanjaya.

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Conflicts of Interest
The author declares no conflict of interest in writing the article.

References

Afifah, U. N. (2017). *Uji Aktivitas Antidiabetes Ekstrak Etanol 96% Buah Pare (Momordica charantia L.) Terhadap Tikus Jantan Galur Wistar Yang Diinduksi Aloksan*. Universitas Muhammadiyah Surakarta.

Afita, M., Nurrahman, N. W. D., & Sudjarwo, G. W. (2022). Aktivitas Antidiabetes dari Berbagai *Genus Momodica* Secara In Vivo. *Journal of Pharmacy*

Science and Teacnology, 3(2), 55-63. Retrieved from https://farmasi-journal.hangtuah.ac.id/index.php/jurnal/article/download/43/29

Antari, N. W. S., & Damaanti, I. A. M. (2025). Activity of Zuriat Fruit Extract (*Hyphaene Thebaica*) on the DNA Fragmentation and Spermatozoa Quality of Male Mice (*Mus musculus*) Given Balinase Arak. *Jurnal Penelitian Pendidikan IPA, 11*(8). 711-719. https://doi.org/10.29303/jppipa.v11i8.11855

Aprillia, P., & Safitri, C. I. N. H. (2020). Uji Aktivitas Antidiabetes Kombinasi Ekstrak Herba Sambiloto dan Daun Sirih Hijau pada Mencit. *Seminar Nasional Pendidikan Biologi dan Saintek (SNPBS) ke-V*, 553–561. Retrieved from https://proceedings.ums.ac.id/snpbs/article/view/842/825

Arundani, P., I'tishom, R., & Purwanto, B. (2021). Pemberian Ekstrak Rumput Kebar (Biophytum petersianum Klotszch) Terhadap Viabilitas Spermatozoa Mencit (Mus musculus) Diabetes Melitus. *Oceana Biomedicina Journal*, *4*(1 SE-), 26–37. https://doi.org/10.30649/obj.v4i1.58

Awuchi, C. G., Echeta, C. K., & Igwe, V. S. (2020). Diabetes and the Nutrition and Diets for Its Prevention and Treatment: A Systematic Review and Dietetic Perspective. *Health Sciences Research*, *6*(1), 5–19. Retrieved from https://www.studocu.com/row/document/ladoke-akintola-university-of-technology/pure-and-applied-chemistry/diabetes-and-the-nutrition-and-diets-for/120966247

Ayuni, N. M. I. (2020). Efek Buah Naga Merah (Hylocereus Polyrhizus) Terhadap Penurunan Kadar Glukosa Darah pada Diabetes. *Jurnal Ilmiah Kesehatan Sandi Husada*, *9*(1), 554–559. https://doi.org/10.35816/jiskh.v10i2.350

Berlina, C. R., Eliyani, H., Sami, A., Widjiati, W., Mulyati, S., & Anwar, C. (2019). Pengaruh Pemberian Ekstrak Rumput Kebar (Biophytum petersianum Klotzsch) terhadap Jumlah Sel Sertoli Mencit (Mus musculus) yang Dipaparkan 2,3,7,8-Tetrachlorodibenzo-P-Dioxin. *Journal of Basic Medical Veterinary*, *8*(1), 45–52. https://doi.org/10.20473/.v8i1.19991

Bhavya, E., & Sanjay, G. (2022). Diabetes and the Importance of Insulin. International Journal of Health Sciences. 6(S1), 8479-8487. https://doi.org/10.53730/ijhs.v6nS1.6844

Caspersen, C. J., Thomas, G. D., Boseman, L. A., & Beckles, G. L. A. (2012). Aging, Diabetes, and the Public Health System in the United States. *American Journal of Public Health, 102*(8), 1482-1497. https://doi.org/10.2105/AJPH.2011.300616

Chiuman, L., Ginting, C. N., Yulizal, O., Suhartomi, & Chiuman, V. (2021). Improvement of Liver Function from Lemon Pepper Fruit Ethanol Extract in Streptozotocin-Induced Wistar Rats. *2021 IEEE International Conference on Health, Instrumentation & Measurement, and Natural Sciences (InHeNce)*. https://doi.org/10.1109/InHeNce52833.2021.9537284

Condorelli, R. A., Vignera, S. La, Mongioì, L. M., Alamo, A., & Calogero, A. E. (2018). Diabetes mellitus and infertility: Different pathophysiological effects in type 1 and type 2 on sperm function. *Frontiers in Endocrinology*, *9*(268), 1–9. https://doi.org/10.3389/fendo.2018.00268

Cooke, D. W., & Plotnick, L. P. (2008). Type 1 Diabetes Millitus in Pediatrics. *Pediatrics in Review*, *29*(11), 374-384. https://doi.org/10.1542/pir.29-11-374

Dwiannur, F. R., Peranginangin, J. M., Saptarini, O. (2024). Effect of Ethanol Extract and Fractions of Sauluang Balum Root Lavanga Sarmentosa (Blume) Kurz) on Aphrodisiac Activity and Spermatogenesis in Hyperglicemia Rats. *Jurnal Ilmiah Kesehatan*, *6*(2), 327-340. https://doi.org/10.36590/jika.v6i2.848

Gulo, K. N., Suhartomi, Saragih, A. D., Raif, M. A., & Ikhtiari, R. (2021). Antioxidant Activity of Flavonoid Compounds in Ethanol and Ethyl Acetate Extract from Citrus Sinensis. *AIMS 2021 - International Conference on Artificial Intelligence and Mechatronics Systems*, 1–6. https://doi.org/10.1109/AIMS52415.2021.9466078

Haryoto, & Devi, E. S. (2018). Efek Pemberian Ekstrak Etanol Daun Dan Batang Ubi Jalar Ungu (Ipomoea batatas L.) Terhadap Penurunan Kadar Glukosa Darah Pada Tikus Jantan Galur Wistar Yang Diinduksi Aloksan. *Talenta Conference Series: Tropical Medicine (TM)*, *1*(3), 139–143. https://doi.org/10.32734/tm.v1i3.279

Hestiana, D. W. (2017). Faktor-Faktor Yang Berhubungan Dengan Kepatuhan Dalam Pengelolaan Diet Pada Pasien Rawat Jalan Diabetes Mellitus Tipe 2 Di Kota Semarang. *Journal of Health Education*, *2*(2), 138–145. https://doi.org/10.15294/jhe.v2i2.14448

Hidayat, R., & Wulandari, P. (2022). Potential of Meniran (Phyllanthus niruri L.) and Sambiloto (Andrographis paniculata) as a Supplement to the Management of Coronavirus Disease 2019 (COVID-19). *Eureka Herba Indonesia*, *3*(2), 144-148. https://doi.org/10.37275/ehi.v3i2.58

Imelda, F., Faridah, D. N., & Kusumaningrum, H. D. (2014). Bacterial Inhibition and Cell Leakage by Extract of *Polygonum Minus* Hud. Leaves. *International Food Research Journal*, *21*(2), 553-560. Retrieved from https://www.cabidigitallibrary.org/doi/full/10.5555/20143367121

Isnaini, N., & Ratnasari, R. (2018). Faktor risiko mempengaruhi kejadian Diabetes mellitus tipe dua. *Jurnal Kebidanan dan Keperawatan Aisyiyah*, *14*(1), 59–68. https://doi.org/10.31101/jkk.550

Jusup, S. A. (2016). Antidiabetic and antioxidant activities of 70% ethanol-diluted extract of Piper crocatum leaves in stretozotocin induced diabetic rats. *Jurnal Kedokteran Brawijaya, 29*(1), 1-4. https://doi.org/10.21776/ub.jkb.2016.029.01.1

Kitabchi, A. E., Umpierrez, G. E., Miles, J. M., & Fisher, J. N. (2009). Hyperglycemic Crises in Adult Patients With Diabetes. *National Libry of Medicine: National Center for Biotechnology Impormation*, *32*(7), 1335-1343. https://doi.org/10.2337/dc09-9032

Kumalasari, E., Aina, A., ayu checaria, N., & Aisyah, N. (2020). Uji Aktivitas Antibakteri Ekstrak Etanol Daun Bawang Dayak (Eleutherine palmifolia (L.) Merr) terhadap Pertumbuhan Propionibacterium acne. *Jurnal Insan Farmasi Indonesia*, *3*(2), 261–270. https://doi.org/10.36387/jifi.v3i2.584

Kunu, M. B., Baszary, C. D. U., & Killay, A. (2020). Efek Pemberian Seduhan Kayu Ular (Strychnos lucida) Terhadap Penurunan Abnormalitas Spermatozoa Mencit (Mus musculus) Model Diabetes Melitus. *Rumphius Pattimura Biological Journal*, *2*(2), 037–042. https://doi.org/10.30598/rumphiusv2i2p037-042

Lubis, Y. E. P., Lister, N., Sihombing, B. (2023). Effect of Pakkat (*Calamus Caesius Blume*) Ethanol Extract on Testis Tissues Histology of Diabetic Rats. *Scientific Foundation SPIROSKI, Skopje, Republic of Macedonia*, *11*(1), 158-162. https://doi.org/10.3889/oamjms.2023.10994

Mayasari, U. (2022). Uji Aktivitas Antibakteri ekstrak Batang Muda Rotan Manau (Calamus manan) terhadap pertumbuhan bakteri Klebsiella pneumonia. *KLOROFIL: Jurnal Ilmu Biologi dan Terapan*, *6*(1), 9–12. https://doi.org/10.30821/kfl:jibt.v6i1.11762

Mutia, M. S., & Suhartomi. (2022). *Buku Monografi Model Hewan Coba Diabetes: Diet Tinggi Lemak dan Induksi Sterptozotosin*. Unpri Press.

Nasution, I. A., Sitanggang, K. D., Saragih, S. H. Y., & Dalimunthe, B. A. (2022). Karakterisasi Morfologi Tanaman Rotan di Labuhanbatu Sumatera Utara. *Jurnal Pertanian Agros*, *24*(2), 580–585. http://dx.doi.org/10.37159/jpa.v24i2.1950

Nasution, M. S. A., & Zara, N. (2025). Upaya Pendekatan Kedokteran Keluarga pada Perempuan Usia 52 Tahan dengan DM Tipe 2 di Kecamtan Nisam Kabupaten Aceh Utara. *Inovasi Kesehatan Global*, *2*(4), 94-101. https://doi.org/10.62383/ikg.v2i4.2353

Naully, P. G., & Khairinisa, G. (2018). *Panduan Analisis Laboratorium Imunoserologi untuk D3 Teknologi Laboratorium Medis*. Stikes Achmad Yani.

Nugroho, R. A., Tarno, T., & Prahutama, A. (2017). Klasifikasi Pasien Diabetes Mellitus Menggunakan Metode Smooth Support Vector Machine (SSVM). *Jurnal Gaussian*, *6*(3), 439–448. Retrieved from http://ejournal-s1.undip.ac.id/index.php/gaussian

Nugroho, A. E., Andrie, M., Warditiani, N. K., Siswanto, E., Pramono, S., & Lukitaningsih, E. (2012). Antidiabetic and Antihiperlipidemic Effect of Andrographis Paniculata (Burm. f.) Nees and Andrographolide in High-Fructose-Fat-Fed Rats. *Indian Journal of Pharmacology, 44*(3), 377-381. https://doi.org/10.4103/0253-7613.96343

Ongko, N. X., Chiuman, L., & Ginting, C. N. (2019) Effect of White Turmeric Rhizome Extract (*Curcuma zedoaria*) on Testis Histology of Male Wistar Rat. *Jurnal for Engineering, Technology, and Sciences,* 55(1), 69–74. Retrieved from https://asrjetsjournal.org/American_Scientific_Journal/article/view/4815

Paramita, C. A., Plumeriastuti, H., Madyawati, S. P., Arimbi, Mulyati, S., & Kurnijasanti, R. (2023). Protective Effect of Ethanol Extract of Kesum Leaves (Polygonum minus) on the Number of Leydig Cells in Mice Exposed to Cadmium Chloride. *Jurnal Medik Veteriner*, *6*(1), 43–50. https://doi.org/10.20473/jmv.vol6.iss1.2023.43-50

Premanath, R., & Nanjaiah, L. (2015). Antidiabetic and Antioxidant Potential of Andrographis Paniculata Nees. Leaf Ethanol Extract in Streptozotocin Induced Diabetic Rats. *Journal of Applied Pharmaceutical Science*, *5*(1), 069-076. https://doi.org/10.7324/JAPS.2015.50113

Prihanto, E. S. D., & Imbar, A. W. J. I. (2022). Edukasi Tentang Pengendalian Diabetes Mellitus pada Peserta Prolanis di Kota Ternate. *Jurnal Pengabdian Dharma Laksana Mengabdi Untuk Negeri*, *5*(1), 208–213. Retrieved from https://id.scribd.com/document/604786286/23458-54127-1-SM

Purwoningsih, E., & Purnama, M. (2017). Perbandingan Faktor Perilaku Suku Batak dan Melayu Terhadap Angka Kejadian Diabetes Melitus Tiper 2 di RSUD DR. Tengku Mansyur Tanjungbalai. *Ibnu Sina Biomedika*, *1*(2), 74–88. https://doi.org/10.31857/s013116462104007x

Rahmasari, I., & Wahyuni, E. S. (2019). Efektivitas Memordoca carantia (Pare) Terhadap Penurunan Kadar Glukosa Darah. *Infokes Jurnal Ilmiah Rekam Medis dan Informatika Kesehatan*, *9*(1), 57–64. https://doi.org/10.47701/infokes.v9i1.720

Rahmawati, N., Kusmiyati, D. K., & Afifah, D. N. (2021).

Antioxidant Total and HOMA-IR of Diabetic Rats Given Crocatum piper and Andrographis paniculata Leaf Extracts. *Journal of Biomedicine and Translational Research*, *7*(2), 56-61. https://doi.org/10.14710/jbtr.v7i2.11524

Rosa, D., Pranasti, E. A., & Halim, Y. (2022). Phytovhemical Characteritics of White Turmeric Rhizome (*Curcuma Zedoaria* (Berg.) Roscoe) Essential Oil From Lembang, West Java, Indonesia. *Interntional Journal of Agricultural Technology, 18*(4), 1797-1808. Retrieved from https://www.cabidigitallibrary.org/doi/pdf/10.5555/20220390026

Santoso, S. (2014). *Statistik NonParametrik Edisi Revisi Konsep dan Aplikasi dengan SPSS*. PT Elex Media Komputindo.

Santoso, S. (2019). *Statistik Parametrik Konsep dan Aplikasi dengan SPSS*. PT Elex Media Komputindo.

Skovsa, S. (2014). Modeling type 2 diabetes in rats using high fat diet and streptozotocin. *Journal of diabetes investigation*, *5*(4), 349-358. https://doi.org/10.1111/jdi.12235

Suhartomi, S., Gulo, K. N., Saragih, A. D., Martinus, A. R., & Ikhtiari, R. (2020). Antioxidant Properties of Sweet Orange Peels in Several Fractions of Methanolic Extract. *Proceedings of the International Conference on Health Informatics and Medical Application Technology*, 371–378. https://doi.org/10.5220/0009515503710378

Thanh, T. N., Van, P. D., Cong, T. D., Le Minh, T., & Vu, Q. H. N. (2020). Assessment of testis histopathological changes and spermatogenesis in male mice exposed to chronic scrotal heat stress. *Journal of Animal Behaviour and Biometeorology*, *8*, 174–180. https://doi.org/10.31893/JABB.20023

Tjahjono, K., Rahmawati, N., Afifah, D. N., & Kinasih, L. S. (2025). Combination of Red Betel (*Piper Crocatum*) Leaf and Sambiloto (*Andrographis Paniculata Ness*) Herb Extract on Reduction of Lipid Profile in Diabetic Rats. *Jurnal Ilmiah Biologi*, *13*(2), 950-957. https://doi.org/10.33394/bioscientist.v13i2.15828

Trisnawati, S. K., & Setyorogo, S. (2013). Faktor Risiko Kejadian Diabetes Militus Tipe II di Puskesmas Kecamatan Cengkareng Jakarta Barat Tahun 2012. *Jurnal Ilmuah Kesehatan, 5*(1), 6-11. Retrieved from https://fmipa.umri.ac.id/wp-content/uploads/2016/06/yuni-indri-faktor-resiko-dm.pdf

Utomo, W. W., Tiofanny, J., Agatha, Y. P., Lubis, M. A. R., Lubis, Y. E. P., & Mutia, M. S. (2021). Uji Efektivitas Ekstrak Etanol Pakkat (Calamus caesius Blume) terhadap Kualitas Sperma pada Tikus Wistar Jantan yang Diinduksi Aloksan. *Majalah Kedokteran Andalas*, *44*(6), 365–377. https://doi.org/10.25077/mka.v44.i6.p365-377.2021

Wattimena, M., Kakisina, P., & Unitly, A. J. A. (2023). Efek Terapi Ekstrak Etanol Sirih Cina (Peperomia pellucida L.) terhadap Peningkatan Konsentrasi dan Motilitas Spermatozoa Tikus (Rattus norvegicus) Terpapar Sopi. *Jurnal Biologi Edukasi*, *15*(1), 10–17. Retrieved from https://jurnal.usk.ac.id/JBE/article/view/32717/18228

Wang, C. P., Lorenzo, C., Habib, S. L., Jo, B., & Espinoza, S. E. (2017). Differential effects of metformin on age related comorbidities in older men with type 2 diabetes. *Journal of Diabetes and its Complications*, *31*(4), 679-686. https://doi.org/10.1016/j.jdiacomp.2017.01.013