

Article Effect of Coriander (*Coriandrum sativum* Lour) Seed-Ethanol Extract on Spermatozoa Quality in Alloxan-Induced Male Rats

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Abstract. Coriander fruit (Coriandrum sativum Lour) has long been used and utilized by humans as a medicine to lower blood sugar levels. This study aimed to test the ethanol extract of coriander (Coriandrum sativum Lour) against alloxan-induced reduction in blood sugar levels in white rats. This study used 30 male white rats induced with 120 mg/kgBW of alloxan solution. The treatment was carried out after 72 hours of alloxan induction and measurement of blood sugar levels that had previously been fasted for 12 hours. The maximum effective dose of alloxan in diabetic rats was 800 mg/kgBW. Coriander seed extract showed the most effective effectiveness in improving sperm quality. Coriander seed extract at the highest dose of 800 mg/kgBW showed the highest motility among all groups of rats receiving coriander seed extract, which was $67.37 \pm 0.57\%$; the highest viability was 88.76(87.76-89.67)%; the highest density was 12.40 (10.20-12.60) x106/ml. Increasing the dose of coriander seed extract significantly improved sperm quality both through the density, mobility, and sperm viability of alloxan-induced diabetic rats (P < 0.05 for each) of alloxan-induced diabetic rat sperm cells

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1. Introduction

High blood glucose, known as hyperglycemia, is a characteristic of diabetes mellitus (DM) and can be caused by a number of factors, including decreased synthesis. Things that are often found in diabetes mellitus such as hyperglycemia, enzyme deficiency, increased basal metabolic rate, lipoprotein abnormalities, and increased oxidative stress. Type 1 diabetes mellitus is triggered by excess glucose in the blood, which causes beta cell death in the pancreas, and is one of two forms of the disease. Insulin resistance and constantly increasing blood glucose levels are the hallmarks of type 2 diabetes, the incidence of which is increasing [1-3].

Based on several studies, it is stated that diabetes mellitus in men can cause erectile dysfunction due to a decrease in the bioavailability of nitric oxide (NO) which is a neurotransmitter in penile erection. Other studies mention ejaculation disorders that occur in diabetics caused by peripheral neuropathy so that it can reduce the sensitivity of the nerves that regulate ejaculation [4-5]. Changes in the structure of mitochondrial DNA fragmentation and sperm nuclei, decreased sperm motility, and decreased binding of the zona pellucida in men with diabetes mellitus were found due to increased stress oxidative stress caused by an increase in free radicals [5].

The hyperglycemic state will cause tissue damage through the mechanism of Reactive Oxygen Species (ROS) accelerated by activating protein kinase C (PKC), having more hexosamines, more glycation end products (AGE), and more polyol pathways. To prevent the increase in the production of free radicals, it is necessary to provide antioxidants [6-7].

High glucose levels in diabetics result in increased free radicals that can cause oxidative stress resulting in a decrease in head mass, corpus, caudal mass in the testes and a reduced number of spermatozoa in the testicular tubules. Diabetes mellitus is the cause of sexual dysfunction so that it can cause infertility because there has been damage to nuclear DNA and mitochondrial DNA in sperm [8-9].

Research on the effect of binahong leaf decoction at a dose of 114 mg can improve the quality of spermatoza in diabetic men by increasing the number and motility of sperm while reducing the morphology of aberrant spermatoza. Several studies using extracts in which there are compounds such as flavonoids, terpenoids, alkaloids, thiamine, riboflavin, lysine and zinc the quality, quantity, and mobility of sperm can all be improved by expanding the size of the seminiferous tubules and stimulating spermatogenesis [10-11].

Based on the background description, it is important to find traditional and effective medicines at affordable prices with local resources with relatively safe side effects, one of which is coriander seeds (*Coriandrum sativum* Lour) which contain many phytochemical compounds such as flavonoids, which These compounds act as antioxidants that can improve oxidative stress in the body. Several previous studies have been conducted to determine the pharmacological effects of this plant such as the effect of inhibiting pancreatic damage, decreasing blood sugar levels, lowering blood sugar levels, and reducing blood sugar levels [12-13].

Glomerular hypertrophy, lowers cholesterol levels. Coriander seeds (*Coriandrum sativum* Lour) have been used for centuries, but their potential to improve sperm quality has never been studied. As a result, scientists were curious whether coriander seed extract could restore normal sperm quality in male rats whose fertility was compromised by alloxan [14-16].

2. Methode

Conducted a study using post test only control group design to assess differences in the quality of spermatozoa in each group of rats [17].

2.1 Test Animal Preparation

Thirty male Wistar rats, measuring 180–200 grams and 2-3 months old, were initially habituated in cages with ordinary food and water for 7.

2.2 Alloxan Induction

Induction in male wistar rats using alloxan monohydrate. A total of 120 mg/kgBW of alloxan monohydrate was dissolved in a single dose of 0.9% NaCl intraperitoneally [18]. After 72 hours, alloxan was induced to measure blood sugar levels which had previously been fasted for 12 hours. Alloxan is induced to check blood sugar levels. When blood glucose levels remain continuously above 200 mg/dL, a diagnosis of diabetes is made.

2.3 Blood Sugar Level Check

Glucose was measured using a glucometer from samples collected from the tail vein of rats after being trimmed with sterile scissors to a distance of 0.2 cm from the roots [19-20].

2.4 Test Animal Surgery

Vas deferens were removed from surgically anesthetized mice. The vas deferens was then placed in a cup with 1 ml (0.9% NaCl) warm (37°C) to make the stock solution. Furthermore, a homogeneous suspension of spermatozoa was formed by cutting the vas deferens with scissors until smooth. This suspension was then examined for its morphology, motility, viability, and the total number of spermatozoa [21-23].

3. Results and Discussion

In the investigation, coriander seeds obtained from one of the traditional markets in Medan were extracted by maceration method and the properties of coriander seed extract were used in this analysis [24].

Table 1. Characteristics of coriander seed extract			
Characteristics	Score		
Fresh Simplicia Weight (gr)	500		
Dry Simplicia Powder Weight (gr)	451		
Solvent Volume (ml)	5		
Extract Weight (gr)	229		
Yield (%)	50.78		

The data in the table above shows that from 500 grams of fresh coriander samples, 451 grams of dried coriander simplicia powder were found. Then, the simplicia powder was macerated into 5,000 ml of ethanol solution and after being evaporated with a rotary evaporator, 229 grams of coriander seed extract was found. So the yield of coriander seed extract is 50.78%. The coriander seed extract was then examined for its phytochemical content using a phytochemical screen, the results of which are presented here [25-26].

Phytochemicals	Reactor	Result
Alkaloid	Bouchardart	+
	Maeyer	+
	Dragendroff	+
	Wagner	+
Steroid dan Triterpenoid	Salkowsky	-
	Lieberman-Burchad	-
Saponin	Aquadesr + Alkohol 96%	+
Flavonoid	FeCl ₃ 5%	+
	Mg(s) + HCl(p)	-
	NaOH 10%	-
	$H_2SO_4(p)$	+
Tanin	FeCl ₃ 1%	+
Glikosida	Mollish	-

Table 2 Result	ofnh	wtochemical	screening	of	coriander	seed	extract
Table 2. Result	s or ph	lytochenneal	scieening	01	Contailuer	seeu	EXILACI

Phytochemicals such as alkaloids, saponins, flavonoids, and tannins have been identified in coriander seed extract, as shown in the data table above [27]. Then, this coriander seed extract was used for the In Vivo test and before the in vivo test, all experimental animals were measured their initial body weight and the initial body weight ratio of the mice was analyzed depending on what was studied.

Table 3. Results of analysis of initial body weight data distribution based on the shapirowilk test

Parameter	Treatment Group	P value	Data Distribution
Weight	Negative Control	0.490	Normal
Beginning	Positive Control	0.826	Normal
	Coriander Seed Extract 200 mg/kgBB	0.928	Normal
	Coriander Seed Extract 400 mg/ kgBB	0.086	Normal
	Coriander Seed Extract 800 mg/ kgBB	0.490	Normal

The attached data table shows the typical dispersion of the data on the initial body weight of the mice. The fact that the P value in each treatment group is more than 0.05 is proof. Thus, the table below shows the results of a study comparing the initial weight of mice in each group [28-29].

Table 4. Initial differences in body mass of rats in each treatment group			
Treatment Group	Initial Body Weight (grams)	P value	
Negative Control	174.20 ± 12.15		
Positive Control	175.20 ± 12.44		
Coriander Seed Extract 200 mg/ kgBB	175.80 ± 13.31	0.998	
Coriander Seed Extract 400 mg/ kgBB	176.20 ± 13.33		
Coriander Seed Extract 800 mg/ kgBB	177.00 ± 13.55		

According to the previous data table, the mean baseline body weight across groups of mice did not vary significantly which was used in the investigation (P value > 0.05) (P value: 0.998). The area where mice usually weigh between 174.30 and 177.00 grams. Research factors, such as blood sugar, from in vivo studies were also analyzed in depth using data mining [30-31]. Analysis of the distribution of blood sugar levels of rats before comparison is shown

Parameter	Treatment Group	P value	Data Distribution
Blood Sugar	Negative Control	0.470	Normal
Levels Before	Positive Control	0.587	Normal
Induction	Coriander Seed Extract 200 mg/kgBB	0.945	Normal
	Coriander Seed Extract 400 mg/ kgBB	0.739	Normal
	Coriander Seed Extract 800 mg/ kgBB	0.893	Normal
Blood Sugar	Negative Control	0.309	Normal
Level After	Positive Control	0.738	Normal
Induction	Coriander Seed Extract 200 mg/kgBB	0.919	Normal
	Coriander Seed Extract 400 mg/ kgBB	0.358	Normal
	Coriander Seed Extract 800 mg/ kgBB	0.441	Normal
Weekly Blood	Negative Control	0.438	Normal
Sugar Level	Positive Control	0.829	Normal
	Coriander Seed Extract 200 mg/kgBB	0.511	Normal
After	Coriander Seed Extract 400 mg/ kgBB	0.539	Normal
Treatment	Coriander Seed Extract 800 mg/ kgBB	0.528	Normal
	Negative Control	0.780	Normal
	Positive Control	0.039*	Abnormal
	Coriander Seed Extract 200 mg/kgBB	0.329	Normal
	Coriander Seed Extract 400 mg/ kgBB	0.289	Normal
	Coriander Seed Extract 800 mg/ kgBB	0.995	Normal

Table 5. Data analysis of distributed blood sugar levels based on the shapiro-wilk test

The data table above shows that the blood sugar levels of mice were normally distributed before, during, and after the induction and therapy phases. If P > 0.05, most likely so. But blood sugar levels in the treated mice that had been tightly controlled were abnormal. This is the post-treatment blood glucose data group, where P is less than 0.05. To this end, a one-way analysis of variance was used to compare baseline glucose levels with those during induction and again at one week post-treatment (ANOVA) [30-31]. Post-treatment blood sugar levels were analyzed using the Kruskal-Wallis test.

Treatment Groun	Before	Blood Sugar Level (mg/dl)			
freatment Group	Induction	After Induction	Week After	After	
	mauction	After induction	Treatment	Treatment	
Negative Control	103.40 ± 5.41	357.80 ± 115.89	388.40 ± 73.77	420	
-				(291-500)	
Positive Control	102.20 ± 6.83	302.20 ± 116.64	234.40 ± 103.95	127	
				(100-279)	
Seed Extract	99.80 ± 3.96	371.40 ± 168.64	341.20 ± 136.97	299	
				(186-561)	
Coriander 200	99.40 ± 10.88	416.00 ± 135.82	338.40 ± 99.96	274	
mg/kgBB				(207-552)	
Coriander Seed	97.00 ± 5.79	346.40 ± 124.33	310.20 ± 131.99	229	
Extract 800				(109-369)	
mg/kgBB					
P value	0.636	0.753	0.308	0.024	

Table 6. Rats from several treatment groups comparing blood sugar levels

As can be seen in the table, there was a significant difference in the blood sugar levels of the treated and untreated mice (P value 0.05). There appears to be some consistency of induction effect on blood sugar levels in mice. The average blood sugar level of the mice did rise, but only slightly, there was still a lot of variation after 1 week. P 0.05 indicates that after 2 weeks of therapy (P value: 0.024). Blood sugar trends were compared across groups after the two treatments, and the findings are shown in the table below [30-31].

Table 7. Assessment of	post-treatment de	ecrease in	blood sugar l	levels betw	veen treatment	groups
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Treatment Group	Comparison	P value
Negative Control	Positive Control	0.008*
	Coriander Seed Extract 200 mg/kgBB	0.310
	Coriander Seed Extract 400 mg/ kgBB	0.310
	Coriander Seed Extract 800 mg/ kgBB	0.032*
Positive Control	Coriander Seed Extract 200 mg/kgBB	0.032*
	Coriander Seed Extract 400 mg/ kgBB	0.056
	Coriander Seed Extract 800 mg/ kgBB	0.151
Coriander Seed Extract 200 mg/ kgBB	Coriander Seed Extract 400 mg/ kgBB	1.000
	Coriander Seed Extract 800 mg/ kgBB	0.421
Coriander Seed Extract 400 mg/ kgBB	Coriander Seed Extract 800 mg/ kgBB	0.421

Only the control group (P = 0.008) and coriander seed extract 800 mg/kgBW (P = 0.032) showed a significant difference between the two treatment groups (P < 0.05). However, when

comparing the extract group with the control group, blood sugar levels were not much lower whether the extract dose was 200 or the dose based on weight.400 milligrams per kilogram. Coriander seed extract at 800 milligrams per kilogram of body weight significantly improved yield compared to kel. positive control. Coriander seed extract, 800 mg/kg body weight was equivalent to metformin in reducing blood sugar levels in rats, the standard for this experiment [32-33].

Based on the data in table 2, the avarage diameter of inhibitory zones of Andalas JDT 1B extraction on *S. Aureus* shows different result for each different treatment. At 6,25% concentration, the avarage of inhibition zone produced has the smallest value of 1,157 cm. The increasing of the concentration is followed by the increasing value of avarage diameter of inhibitory zone. Based of further test of DMRT, extracts of Andalas fermentation product JDT 1B using 70% of ethanol concentration has best treatment at 6,25% concentration. Because it is able to inhibit the growth of *S. Aureus* approaching to positive control of anti-biotic *ampicilin*.

Not only rat sperm and blood sugar levels were monitored, but also the density, motility, viability, and morphology parameters of rat sperm after. 2 weeks of treatment. The table below presents the study analysis findings on the distribution of data from sperm testing parameters [34-35].

Parameter	Treatment Group	P value	Data Distribution
Density	Negative Control	0.303	Normal
	Positive Control	0.037*	Abnormal
	Coriander Seed Extract 200 mg/ kgBB	0.783	Normal
	Coriander Seed Extract 400 mg/ kgBB	0.490	Normal
	Coriander Seed Extract 800 mg/ kgBB	0.036*	Abnormal
Motility	Negative Control	0.441	Normal
	Positive Control	0.156	Normal
	Coriander Seed Extract 200 mg/ kgBB	0.501	Normal
	Coriander Seed Extract 400 mg/ kgBB	0.999	Normal
	Coriander Seed Extract 800 mg/ kgBB	0.569	Normal
Viability	Negative Control	0.040*	Abnormal
	Positive Control	0.983	Normal
	Coriander Seed Extract 200 mg/ kgBB	0.763	Normal
	Coriander Seed Extract 400 mg/ kgBB	0.622	Normal
	Coriander Seed Extract 800 mg/ kgBB	0.970	Normal

 Table 8. Results of analysis of data distribution of sperm examination results based on the shapirowilk test

The density and viability parameters show the atypical distribution in the data table above is not normal. Meanwhile, the sperm motility parameter, the data distribution is normal. Therefore, the data on the density and viability of sperm cells were analyzed by the Kruskal-Wallis test. On the other hand, one-way test analysis ANOVA was used to test the dynamics of the data. The following table compares the results of rat sperm testing in all treatment groups [36-37].

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Table 9. Comparison of mice sperm examination results in all treatment groups				
_	Sperm C	heck Parameters		
Treatment Group	Densitas (x10 ⁶ /ml)	Motilitas (%)	Viabilitas (%)	
Negative Control	4.90 (4.20-5.20)	14.59 ± 0.19	48.80 (48.75-49.60)	
Positive Control	15.60(12.40-16.00)	72.94 ± 1.70	91.40 (89.90-93.30)	
Coriander Seed Extract	10.60 (10.00-11.00)	51.40 ± 1.29	59.95 (58.67-61.50)	
200 mg/kgBB	12.10(11.80-12.20)	61.49±1.11	76.50 (75.00-77.20)	
Coriander Seed Extract	12.40(10.20-12.60)	67.37 ± 0.57	88.76 (87.76-89.67)	
P value	< 0.05	< 0.05	< 0.05	

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The table shows there were substantial changes in sperm density, motility, and viability among the various treatment groups. As indicated by the fact that all sperm testing parameters had a P value of less than 0.05 [38-40].

4. Conclusion

The conclusion of the research (1) coriander seed extract showed the most effective effectiveness in improving sperm quality. The maximum effective dose of alloxan in diabetic rats was 800 mg/kgBW; (2) coriander seed extract at the highest dose of 800 mg/kgBW showed the highest motility among all groups of rats receiving coriander seed extract, which was $67.37 \pm 0.57\%$; (3) coriander seed extract at the highest base of 800 mg/kgBW showed the highest dose of rats receiving coriander seed extract, which was $67.37 \pm 0.57\%$; (3) coriander seed extract at the highest dose of 800 mg/kgBW showed the highest viability among all groups of rats receiving coriander seed extract, which was 88.76 (87.76-89.67)%; (4) coriander seed extract at the highest dose of 800 mg/kgBW showed the highest density among all groups of rats receiving coriander seed extract, which was $12.40 (10.20-12.60) \times 106/ml$; (5) Increasing the dose of coriander seed extract significantly improved sperm quality both through the density, mobility, and sperm viability of alloxan-induced diabetic rats (P < 0.05 for each) of alloxan-induced diabetic rat sperm cells. Meanwhile, all rat treatment groups showed sperm cell morphology which was still within normal limits in all groups of coriander seed extract doses.

References

- [1] Adelita, M., Arto, K. S., & Deliana, M. (2020). *Kontrol Metabolik pada Diabetes Melitus Tipe-1*. 47(3), 227–232.
- [2] Aftab, A., Haider, M., Ali, Q., & Malik, A. (2021). Genetic Evaluation for Morphological Traits of Coriandrum Sativum Grown Under Salt Stress. *Biological and Clinical Sciences Research Journal*, 2021(1), 1–7.
- [3] Al, A., Akil, S., Yassin, E., Maraghi, A. Al, Aliyev, E., Malki, K. Al, & Fakhro, K. A. (2021). Diagnosis and treatment of type 1 diabetes at the dawn of the personalized medicine era. *Journal of Translational Medicine*, 1–19.
- [4] Alejandro, E. U., Mamerto, T. P., Chung, G., Villavieja, A., Gaus, N. L., Morgan, E., & Pineda-Cortel, M. R. B. (2020). Gestational diabetes mellitus: a harbinger of the vicious cycle of diabetes. *International journal of molecular sciences*, 21(14), 5003.
- [5] Anggraini, D., Sutyarso, S., Kanedi, M., & Busman, H. (2019). Pengaruh Pemberian Ekstrak Etanol Jahe Merah (Zingiber Officinale Roxb var Rubrum) Terhadap Kuantitas dan Kualitas Spermatozoa Mencit Jantan (Mus musculus L.) Yang Diinduksi Paraquat Diklorida. Jurnal Ilmiah Biologi Eksperimen Dan Keanekaragaman Hayati, 5(2), 47–54.

- [6] Bajaj, S., & Khan, A. (2012). Antioxidants and diabetes. *Indian journal of endocrinology and metabolism*, *16*(Suppl 2), S267.
- [7] Josten, S., Mutmainnah, & Hardjoeno. (2006). Profil Lipid Penderita Diabetes Mellitus Tipe 2. *Indonesian Journal*, *13*(1), 20–22.
- [8] Barkabi-zanjani, S., Ghorbanzadeh, V., & Aslani, M. (2020). Diabetes & Metabolic Syndrome : Clinical Research & Reviews Diabetes mellitus and the impairment of male reproductive function : Possible signaling pathways. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, 14(5), 1307–1314.
- [9] Bulqis, A. R., Ermayanti, N. G. A. M., & Wirasiti, N. (2020). Perbedaan kualitas sperma pada pasien penderita diabetes mellitus tipe 1 dan 2 di rsud. Lamadukelleng, sengkang, sulawesi selatan. *SIMBIOSIS*, *8*(1), 17-27.
- [10] Chen, L., Shi, G. rui, Huang, D. dan, Li, Y., Ma, C. chao, Shi, M., Su, B. xiao, & Shi, G. jiang. (2019). Male sexual dysfunction: A review of literature on its pathological mechanisms, potential risk factors, and herbal drug intervention. *Biomedicine and Pharmacotherapy*, 112.
- [11] Cho, N. H., Shaw, J. E., Karuranga, S., Huang, Y., da Rocha Fernandes, J. D., Ohlrogge, A. W., & Malanda, B. (2018). IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. *Diabetes Research and Clinical Practice*, 138, 271–281.
- [12] Nazira, S., Thadeus, M. S., & Hardini, N. (2020). Uji Efektivitas Ekstrak Biji Ketumbar (Coriandrum Sativum L.) Terhadap Gambaran Histopatologi Ginjal Tikus Hiperkolesterolemia Diabetes. Jurnal Muara Sains, Teknologi, Kedokteran Dan Ilmu Kesehatan, 4(2), 357.
- [13] Susanti, N. M. P., Budiman, I. N. ., & Warditiani, N. K. (2015). Skrining Fitokimia Ektrak Etanol 90 % Daun Katuk (Sauropus androgynus (L.). *Repository Universitas Udayana*, 83–86.
- [14] Dennedy, M. C., Rizza, R. A., & Dinneen, S. F. (2015). Classification and Diagnosis of Diabetes Mellitus. *Endocrinology: Adult and Pediatric, 1– 2*(January), 662-671.e2.
- [15] Nasution, F., Andilala, & Siregar, A. A. (2021). Faktor Risiko Kejadian Diabetes Mellitus. *Jurnal Ilmu Kesehatan*, 9(2), 94–102.
- [16] Dersing, K., Rusmini, H., & Triwahyuni, T. (2020). Efektivitas Ekstrak Ketumbar (Coriandrum sativum L.) Terhadap Penurunan Kadar Gula Darah Tikus Putih Jantan (Rattus norvegicus L.) Galur Wistar yang Diinduksi Aloksan. *Journal Kedokteran Raflesia*, 6(1), 36–44.
- [17] Kumar, D., & Chauhan, P. (2018). Coriandrum Sativum : A Multipurpose Medicinal Plant-A Review. 7(15),322–327.
- [18] Melita, D., Dasrul, D., & Adam, M. (2014). The Effect of Bull Age and Ejaculation Frequency on Quality of Aceh Bull Spermatozoa. *Jurnal Medika Veterinaria*, *8*(1), 15–19.
- [19] Fitriani, N., & Erlyn, P. (2019). Aktivitas Antidiabetik Kombinasi Ekstrak Etanol Daun Ciplukan (Physalis angulata) dan Daun Gaharu (Aquilaria malaccensis) pada Tikus Diabetes. Syifa' MEDIKA: Jurnal Kedokteran Dan Kesehatan, 9(2), 70.
- [20] Guariguata, L., Whiting, D. R., Hambleton, I., & Beagley, J. (2013). Global estimates of diabetes prevalence for 2013 and projections for 2035. *Diabetes Research and Clinical Practice*, 103(2), 137–149.
- [21] Muntafiah, A., Pratama, T. S., & Ati, V. R. B. (2019). Evaluasi Potensi Antidiabetes Sari Buah Markisa Ungu (Passiflora edulis var edulis) pada Tikus Model Diabetes Melitus yang Diinduksi Aloksan. Jurnal Kedokteran Brawijaya, 30(3), 191.
- [22] Nangoy, B. N., De Queljoe, E., & Yudistira, A. (2019). Uji Aktivitas Antidiabetes Dari Ekstrak Daun Sesewanua (Clerodendron squamatum Vahl.) Terhadap Tikus Putih Jantan Galur Wistar (Rattus norvegicus L.). *Pharmacon*, 8(4), 774.
- [23] Fatimah, P. S., & Siregar, P. A. (2019). Pola Konsumsi Buah Dan Sayur Dengan Kejadian Diabetes Mellitus Pada Masyarakat Pesisir. *Bali Health Published Journal*, 2(1), 26–36.

- [24] Laia, J. (2020). Hubungan Tingkat Kepatuhan Diet Makan Dengan Tingkat Kadar Gula Darah Pasien Diabetes Melitus. *Jurnal Ilmiah Wijaya*, *12*(September), 92–97.
- [25] Lende, M., & Rijhsinghani, A. (2020). Gestational Diabetes : Overview with Emphasis on Medical Management.
- [26] Fatimah, R. N. (2015). Diabetes Melitus Tipe 2. 4, 93–101.
- [27] Maiorino, M. I., Bellastella, G., & Esposito, K. (2014). Diabetes and sexual dysfunction: Current perspectives. *Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy*, 7, 95– 105.
- [28] Muthmainnah. (2017). Skrinning Fitokimia Senyawa Metabolit Sekunder Dari Ekstrak Etanol Buah Delima (Punica granatum L.) Dengan Metode Uji Warna. *Medis Farmasi Poltekkes Makassar*, 13.
- [29] Firman, R. C., & Simmons, L. W. (2010). Sperm midpiece length predicts sperm swimming velocity in house mice. *Biology Letters*, 6(4), 513–516.
- [30] Meliyana, Y., & Nugroho, R. A. (2016). Pengaruh Rebusan Daun Binahong (Anredera cordifolia) Terhadap Kualitas Spermatozoa Mencit (Mus musculus L.) Diabetes. *Bioprospek*, 11(2), 32–41.
- [31] Maleki, S. J., Crespo, J. F., & Cabanillas, B. (2019). Anti-inflammatory effects of flavonoids. *Food Chemistry*, 299 (July), 125124.
- [32] Hamel, D. V, Sambou, C., Karauwan, F. A., & Ginting, M. (2021). Uji Efektivitas Infusa Biji Ketumbar Coriandrum sativum L. Sebagai Antikolesterol Pada Tikus Putih Rattus norvegicus. *Jurnal Biofarmasetikal Tropis*, 4(1), 45–52.
- [33] Haryoto, H., & Nur'aini, A. R. (2018). Antidiabetes Melitus Ekstrak Etanol Batang dan Daun Ubi Jalar Kuning (Ipomoea batatas Linn.) Terhadap Kadar Glukosa Pada Tikus Jantan. Jurnal Farmasi Sains Dan Praktis, 4(2), 1–8.
- [34] Irza Haicha Pratama, Ermi Girsang, & Tan Suyono. (2022). Coriander Seed Extract (Coriandum Sativum L) as an antioxidant. *International Journal of Health and Pharmaceutical (IJHP)*, 2(1), 65–69.
- [35] Jangra, S. S., Madan, V. K., & Singh, I. (2017). Coriander (Coriandrum sativum L.) An important medicinal plant for antioxidant activity: A review. Open Access Journal of Medicinal and Aromatic Plants, 8(2), 9–25.
- [36] Hasanah, N., & Dori, R. S. (2019). Daya Hambat Ekstrak Biji Ketumbar (Coriandrum Sativum L) Terhadap Pertumbuhan Bakteri Shigella Dysenteriae Metode Cakram. *Edu Masda Journal*, 3(2), 115.
- [37] Hasnita, AZ, R., & Astuti, A. (2019). Hubungan Durasi Penyakit dan Kadar Gula Darah Dengan Keluhan Subyektif Pada Penderita Diabetes Mellitus Tipe II di Puskesmas Putri Ayu Kota Jambi. 5 (293).
- [38] HE, Z., YIN, G., LI, Q. Q., ZENG, Q., & DUAN, J. (2021). Diabetes mellitus causes male reproductive dysfunction: A review of the evidence and mechanisms. *In Vivo*, 35(5), 2503–2511.
- [39] Saputra, N. T., Suartha, I. N., & Dharmayudha, A. A. G. O. (2018). Agen Diabetagonik Streptozotocin untuk Membuat Tikus Putih Jantan Diabetes Mellitus. *Buletin Veteriner Udayana*, 10(2), 116.
- [40] Saxena, S. N., & Agarwal, D. (2019). Pharmacognosy and phytochemistry of coriander (Coriandrum sativum L.). *International Journal of Seed Spices*, 9(1), 1–13.