BIODIDAKTIKA: Jurnal Biologi dan Pembelajarannya, Vol.19, No.2, 2024, pp. 55-67
e-ISSN 2527-4562. DOI. 10.30870/biodidaktika.v19i2.24806

Anti-Diabetes Activity of Ethanolic Extract of Cassia Alata Leaves on Hyperglycemia Model Mice

Submitted 02 April 2024 Revised 28 May 2024 Accepted 18 June 2024

Sasmita Sasmita[1], Noor Hujjatusnaini[2*], Ridha Nirmalasari[3]

[1,2,3]Department of Biology Education, Faculty of Tarbiya and Teaching Sciences, IAIN Palangkaraya, Indonesia

Corresponding Email: noor.hujjatusnaini@iain-palangkaraya.ac.id

Abstract

Indonesia has a geographically rich region with medicinal plants, including Cassia alata. The utilization of this medicinal plant still needs to be improved, including documentation of its use as medicine. Information about the extract of Cassia alata leaves as an anti-diabetes therapy can be conveyed to future generations. This research aims to prove the potential of Cassia alata leaf extract as a hyperglycemia therapy material through a mouse model. The research design uses a pretest-posttest group design. The antidiabetic activity of Cassia alata leaf extract in vivo is determined by the indicator of reducing blood sugar levels in mice with hyperglycemia, supported by quantitative testing of secondary metabolite compounds. The experimental animals used 24 male Balb/c mice induced with 0.75 mg/kgBb alloxan. Measure blood sugar levels in mice with hyperglycemia after treatment with Cassia alata leaf extract at concentrations of 25%, 50%, 75%, and 100%, and a positive control using metformin—data analysis using one-way ANOVA correlation analysis. Cassia alata leaf extract is proven to contain alkaloids, flavonoids, tannins, triterpenoids, and saponins. The antidiabetic activity is evidenced by an effective reduction in blood sugar levels at a concentration of 50%, where the average data for the reduction in blood sugar levels in hyperglycemic mice is 93 mg/dL. The 50% concentration is proven to have the best antidiabetic effect, supported by a more significant reduction in blood sugar levels than the positive control. The findings of this research are expected to serve as the basis for further development of innovative hyperglycemia therapy products.

Keywords: *Cassia alata*, Mice, Hyperglikemia.

INTRODUCTION

Hyperglycemia is an increase in blood sugar levels beyond the normal range caused by a decrease in the insulin produced by the pancreas. Diabetes mellitus is a lifelong disease (Lestari *et al*., 2021). Elevated blood sugar levels indicate pancreatic disease that disrupts metabolism. If a patient's blood sugar level is higher than usual or if there is glucose in the urine, normal blood sugar levels range between 70 and 110 mg/dL. Diabetes mellitus can lead to cardiovascular disorders, a severe condition that needs prompt treatment to prevent hypertension and heart attacks (Dewi *et al*., 2023). The International Diabetes Federation reported that Indonesia had 19.8 million diabetes patients in 2021, an increase from 28.6 million in 2005 (Soelistijo, 2021). The use of herbal plants is one of the alternatives for the community to treat diabetes mellitus (Agustina *et al*., 2023)

Traditional treatments are usually affordable and easily accessible due to natural raw materials readily available in the surroundings, such as Cassia alata leaves, which people in rural

areas often practice. Traditional treatment of diabetes mellitus with natural ingredients has proven to have the same medical benefits as synthetic drugs (Adhitia, 2016). Additionally, traditional treatments generally do not have side effects on health if consumed (Sumayyah & Salsabila, 2017). Therefore, based on scientific research findings on traditional treatment, various methods have been developed using natural ingredients as therapy materials. Cassia alata, in particular, has many medical benefits, including treating scabies, tinea corporis, tinea versicolor, acne, cholesterol, and gout, in addition to diabetes mellitus treatment (Intannia *et al*., 2015); Nugraha & Anwar, 2015; Pimpel (Fitriani & Nuryanti, 2023); cholesterol (Chitania *et al*., 2020); and gout in addition to diabetes (Syaifudin *et al.,* 2021*).*

Given the above background, further natural research exploring the utilization of Cassia alata leaves is essential. Therefore, this study aims to determine the analgesic effect of Cassia alata leaves on reducing blood sugar levels in male Balb/c mice. This serves as the basis for exploring the potential of Cassia alata leaves in this research. Cassia alata leaves contain anti-hyperglycemic properties that help reduce pancreatic damage (Oktaviona *et al*., 2023). Previous research states that Cassia alata contains substances that can lower blood glucose levels, such as flavonoids, tannins, and saponins (Hujjatusnaini, 2007). Saponins improve pancreatic cells and increase glycogen in the liver, while flavonoids increase insulin secretion, and tannins slow down carbohydrate digestion (Barky & Hussein, 2018). Other studies report that Cassia alata leaves can reduce insulin resistance and blood sugar levels (Fattaheian *et al*., 2021).

An alternative solution through exploring the use of Cassia alata leaves needs careful consideration as one of the alternative therapies for lowering blood sugar levels. The development of natural therapeutic materials is crucial. The hope is that, by the end of this research, an adequate formulation of Cassia alata leaf compounds will be found in vivo as a therapeutic material for lowering blood sugar levels, serving as the basis for further development of innovative health products.

METHOD

This research is an experimental study conducted in the greenhouse laboratory of IAIN Palangka Raya. The study used male Balb/c mice as experimental animals. The Faculty of Medicine, Palangka Raya University, with No. 153/UN24.9/LL/2023, has declared this research ethically acceptable.

The research began with sorting Cassia alata leaves, which were then used to produce the simplicia. Subsequently, the simplicia was macerated for 5 days using 96% ethanol solvent with a solvent ratio 1:7:5 until a semi-solid extract gel was obtained. According to the research design, this gel was then used as an antidiabetic therapy material in vivo. The research design included 6 treatments: 25%, 50%, 75%, 100%, and positive control with metformin 1 ml/kgBW. Using that concentration range validates previous research findings that assert the 50% concentration as the most effective concentration in addressing hyperglycemia in vivo. Determining dosage range and treatment of the extract refers to several relevant studies, as does the IC50 testing method for the antioxidant potential in Cassia alata leaf extract (Tallarida, 2001; Sebaugh, 2011).

$$y = \frac{A}{1 + \left(\frac{z}{C}\right)^{B} + D}$$

Where Y is response (percentage inhibition), z is drug concentration, A is upper asymptote or maximum response, B is slope parameter (Hill slope), which indicates the steepness of the curve, C is IC50 value (the concentration of drug that produces 50% of the maximum response), and D is lower asymptote or minimum response (often assumed to be zero in some cases).

Preparation of male Balb/c mice as experimental animals with hyperglycemia involved administering 0.75 mg/kg BW alloxan with sweetened condensed milk with high sugar content. This treatment was given after the mice underwent a one-week adaptation period, and initial blood sugar levels were measured before conditioning the experimental animals as hyperglycemia patients. Alloxan supplementation and stimuli to increase mouse blood sugar levels were continued until physical symptoms of hyperglycemia appeared, such as red eyes, swollen feet, and hair loss.

Subsequently, blood sugar levels were measured in male Balb/c mice. If the mouse's blood sugar level exceeded the normal range or was already considered high, the mouse was fasted for 12 hours, and then blood sugar levels were rechecked. Normal blood sugar levels (before treatment) and abnormal/hyperglycemic mouse blood sugar levels (during fasting) were compared. This served as the basis for analysis, indicating that any reduction in mouse blood sugar levels would be influenced only by the treatment given, namely the administration of *Cassia alata* leaf extract as a therapeutic material. The therapy was administered for one week, followed by a final blood sugar level measurement for hyperglycemic Balb/c mice. After the

treatment, the data obtained in this study were statistically analyzed using one-way ANOVA correlation analysis to determine the effective formulation for this research.

RESULTS AND DISCUSSION

The data from the secondary metabolites test of *Cassia alata* leaves used in the laboratory experimental study were quantitatively measured, and they are presented in Table 1.

Table 1. Phytochemical Testing Results Data of Cassia alata Leaves

Compound Identification							
Flavonoid	Alkaloid			Terpenoid			
	Meyer	Dragendrof	Bouchardat	Tanin / Feno	Steroid	Triterpenoid	Saponin
+	+	-	+	+	-	+	+

Description:
(+) : Detected to contain the tested chemical compound
(-) : Not detected to contain the tested chemical compound

Phytochemical testing was conducted on Cassia alata leaves. This research aimed to identify the secondary metabolite compounds in Cassia alata leaves, including flavonoids, alkaloids, tannins, saponins, and terpenoids. The results of the phytochemical testing on Cassia alata leaves in Table 1 above indicate a positive presence of flavonoids, alkaloids, tannins, triterpenoids, and saponins. In contrast, the testing for steroid and Dragendorff content yielded negative results. The research data is related to observational results, such as examining blood sugar levels in mice. This data forms the basis for understanding the in vivo testing mechanism of Cassia alata leaf extract in reducing blood sugar levels in mice.

Table 2. Antioxidant Testing Results in Data of Cassia alata Leaves

Sample Concentration (ppm)	Sample Absorbance	Inhibition	% Inhibition
125,0000	0,2189	0,6533	65,3255
62,5000	0,3933	0,3770	37,7000
31,2500	0,4628	0,2669	26,6910
15,6250	0,5062	0,1982	19,8163
7,812 5	0,5450	0,1367	13,6702

Table 2 displays color changes and absorbance values, with larger values indicating higher antioxidant test results along with an increase in the tested concentration. An

absorbance value of 0.2189 was found at a concentration of 125,0000 ppm. Figure 1 below shows the concentration inhibition values (IC50) of Cassia alata leaf extract.

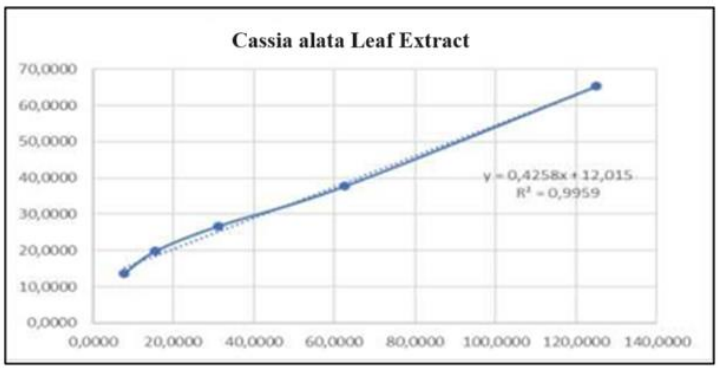

Figure 1. Analysis Results of IC50 Values of Cassia alata Leaf Extract

Analysis of the IC50 value for antioxidant activity in Cassia alata leaf extract was quantitatively calculated, resulting in an IC50 value = (50 - B) = 89.2085 ppm. Based on Figure 1, the value of y= 0.4258 x 12.015 was obtained from the Cassia alata leaf extract solution, which can be elaborated as follows:

Y = 0,4258 + 12,015

50 = 0,4258 x 12,015

$$x = \frac{50-12,01\%}{0,4254} = 89,2085$$

Figure 1 indicates that the higher DPPH absorbance value (IC50) is associated with the sample concentration, with a confidence level of 95%, namely 89.2085 ppm. In this study, a decrease in blood sugar levels in mice occurred. Data before and after the use of Cassia alata leaf extract are presented in the recapitulation table as seen in Table 3 below:

Table 3. Recapitulation of Data After and Before Administration of Cassia alata Leaf Extract Treatment

Treatment	Mean Normal Blood Sugar Level (mg/dL)	Mean Fasting Blood Sugar Level (mg/dL)	Mean Increase in Blood Sugar Before Therapy (mg/dL)	Mean Before Therapy (mg/dL)	Mean After Therapy (mg/dL)	Decrease (mg/dL)
P1 (-)	136,5	87	18	154,5	84,25	70,25
P2 (+)	125,75	82,75	58,25	184	77,5	106,5
P3 (25%)	137,25	83,75	7,5	144,75	81,75	63
P4 (50%)	144	93,75	73	217	89	128
P5 (75%)	120,5	76,75	49	169,5	76,5	93
P6(100%)	136	88	37,5	173,5	82,5	91

Table 3 compares blood sugar levels between diabetic mice and mice after Cassia alata leaf extract treatment according to the research design. There appears to be a significant decrease in blood sugar levels across all treatment groups. Based on the average, the highest decrease in blood sugar levels was observed in the P4 group with a concentration of 50%, reaching 128 mg/dL, while the lowest decrease occurred in the P3 group with a concentration of 25%, 63 mg/dL.

Furthermore, Table 3's data on the decrease in blood sugar levels in diabetic mice after treatment were tested for normality and homogeneity as prerequisites for advanced ANOVA statistical analysis. This statistical analysis aims to determine whether the research data follows a normal distribution. Differences in significance values greater than 0.01% and vice versa were used to assess the data's normality. Table 4 shows the results of the data normality test.

Table 4. Statistical Analysis of Blood Sugar Levels in Mice Post-Therapy

Cassia alata Leaf Extract		**Shapiro-Wilk**		
		Statistic	**df**	**Sig**
Normaliti test	Aquades	941	4	659
	Metformin	948	4	218
	25%	895	4	403
	50%	833	4	331
	75%	953	4	734
	100%	630	4	001
Homogeneity test	Based on Mean			
	Levene Statistic	13.796		
	df1	3		
	df2	18		
	Sig of homogeneity			0.00
One Way Anava	Sum of Homogeneity			11289.2082
	df			5

Cassia alata Leaf Extract	Shapiro-Wilk		
	Statistic	df	Sig
Mean Square			2257.842
f			11.863
Sig			.000

After completing the normality test for blood sugar levels, the data were entered into treatments as indicated in Table 4. Significance values based on Shapiro-Wilk above 0.05 indicate that the data is usually distributed. Significance values below 0.05 indicate that the data is not considered Y data. Table 4 shows the homogeneity test results.

The analysis results in Table 4 indicate a significance value of 0.000 < p-value α (α = 0.05), suggesting that the obtained data is not homogeneous. The Levene Statistic value of 15.796 supports this conclusion, indicating that more homogenous data has smaller values. Therefore, homogeneous data can be used for further analysis. The next objective is to determine the significance of each variable involved in the study. This is done using the ANOVA statistical test. The results show that F was computed with a p-value = 0.000 and p-value < α (α = 0.05) or at a significance level of 1%. Based on these results, it can be inferred that treating Cassia alata leaf extract with the specified formulation has a significant effect. The Duncan, 1% test is used in Table 5 to determine the significance differences at each treatment level in the study.

Table 5. Results of Duncan 1% Test for Blood Sugar Levels in Mice Post-Therapy

Cassia alata Leaf Extract		N	Subset for alpha= 0.05	Notation		
				1	2	3
Blood Sugar Levels	P3(25%)	4		63.00		
	P1(-)	4		70.27		
	P6 (100%)	4			91.00	
	P5 (75%)	4			93.00	
	P2(+)	4			106.5	
	P4 (50%)	4				0 128.00
	Sig.			467	149	1.000

Based on the results of the Duncan test analysis in Table 5 with a significance level of 5%, it is indicated that the treatment of Cassia alata leaf extract concentrations differs significantly from the negative control, except for P3 (25%) which has the same significance as the negative control. Therefore, this concentration does not have a statistically significant difference. Compared to the negative control in mice with hyperglycemia, the 25% concentration could not suppress blood sugar levels more effectively. The data analysis results

in Table 5 suggest that the 50% concentration is the most effective analgesic concentration compared to the others in mice with diabetes in vivo.

The body's metabolism obtains energy from glucose as the final product of carbohydrate metabolism, where the insulin hormone controls its utilization (Hikmah et al., 2022). Insulin hormone is produced by the pancreas, which regulates the glucose transport system into cells, thus playing a crucial role in membrane permeability. The recommended serum or plasma blood sugar levels are 70–110 mg/dL; postprandial blood sugar after two hours should not exceed 140 mg/dL/hour, and fasting blood sugar levels should not exceed 110 mg/dL (Siregar et al., 2020). This study indicates that Cassia alata leaf extract can reduce blood sugar levels in mice with high blood sugar or hyperglycemia. According to the phytochemical test results shown in Table 1, the phytochemical test results on Cassia alata leaves reveal that the extract contains secondary metabolites such as flavonoids, alkaloids, tannins, saponins, and terpenoids. Saponins are known to regenerate the pancreas or have a hypoglycemic effect. This increased insulin secretion will assist in the decrease in blood sugar levels. Additionally, tannin compounds also act as triggers in lowering blood sugar levels by reducing oxidative stress, thereby controlling blood sugar levels (Novalinda et al., 2021).

The tannin content in Cassia alata leaf extract also acts as an anti-hyperglycemic by increasing glycogenesis (Ma'shum, 2020). Furthermore, tannins have an astringent property that can contract the epithelial membrane of the small intestine, blocking blood sugar absorption. This prevents blood sugar absorption, resulting in decreased blood sugar levels (Syarifudin et al., 2021).

The analysis of the antioxidant activity of Cassia alata leaf extract, quantified through IC50 values as shown in Table 2, indicates that the DPPH absorbance values (IC50) increase with the sample concentration, and the IC50 value is 89.2085 ppm at a 95% confidence level. This data suggests that Cassia alata leaves cumulatively demonstrate potent antioxidant potential. The above research proves that Cassia alata leaves contain various active compounds, including flavonoids, tannins, and saponins, which have potential as antioxidant compounds (Safitri et al., 2020). The potential mechanism of action of active compounds in Cassia alata leaves to provide antioxidant effects includes preventing oxidative stress, free radical scavenging, regeneration of other antioxidants, inhibition of prooxidative enzymes, and protection against molecular damage (Raharjo et al., 2022).

Antioxidant compounds in Cassia alata leaves can play a role in preventing oxidative stress (Ramadhayanti, 2021). Antioxidant compounds can stop the chain reaction of free radicals by providing additional electrons, stopping harmful effects on cells and tissues (Rusiani et al., 2019). Examples of such compounds include vitamins C and E.

Antioxidant compounds in Cassia alata leaves, including flavonoids and tannins, can provide this cumulative effect to help maintain redox balance in cells and prevent oxidative stress. The three groups of compounds, flavonoids, tannins, and saponins, can play a role in free radical scavenging and provide antioxidant effects (Nurjanah, 2017). Each group of compounds has different antioxidant mechanisms; often, the best effects are achieved when these compounds work together. Flavonoids are known for their potent antioxidant properties (Susila Ningsih et al., 2023). Flavonoids can also interact with endogenous antioxidant enzymes, enhancing the body's capacity to face free radicals (Nisa et al., 2022). Tannins also have antioxidant properties and can act as free radical scavengers (Suryanto & Frenly, 2019). Saponins, besides having surfactant properties, can contribute to antioxidant effects (Schreiner et al., 2022). Some saponins perform direct antioxidant functions, protecting cells from oxidative damage (Wang et al., 2023). Moreover, saponins can modulate inflammatory signaling pathways and reduce the production of free radicals associated with inflammation (Khotimah, 2016) Therefore, the consumption.

CONCLUSION

This study indicates that Cassia alata leaf extract contains secondary metabolites such as alkaloids, flavonoids, tannins, saponins, and triterpenoids, capable of reducing blood sugar levels in hyperglycemic mice. The concentration that effectively lowers blood sugar levels is observed in group P4 with a concentration of 50%, as evidenced by the average decrease after administering Cassia alata extract amounting to 128mg/dL. Meanwhile, there is no significant difference in the average decrease in group P3 (25%) compared to the P1 (-) control group in vivo. Therefore, Cassia alata extract has the potential to be a natural alternative treatment for lowering blood sugar levels, as revealed in this study.

ACKNOWLEDGEMENT

A heartfelt thank you for the immense support and facilities provided by the Microbiology Laboratory of the State Islamic Institute of Palangka Raya, enabling the completion of this research.

REFERENCES

Adhitia. (2016). Efek Perseptif Penggunaan Antidiabetes Herbal Bersamaan Dengan Penggunaan Obat Antidiabetes Oral Pada Pasien Diabetes Melitus Tipe 2 Di Puskesmas Kotamadya Depok Skripsi Adhitia 0706264412 Fakultas Matematika Dan Ilmu Pengetahuan Alam Program Studi Farmas. *Universitas Indonesia*.

Agustina, L., Permatasari, D. W., Fatimah, E., Jannah, M., & Julia, M. (2023). *Penanaman*

Tanaman Obat Keluarga (Toga) Sebagai Salah Satu Usaha Pemberdayaan Siswa Dalam Menumbuhkan Kepedulian Kesehatan Keluarga. The Implementation Of Family Medicinal Plant (Toga) Cultivation To Promote Students ' Engagement In Promoting Family Hea. *20*, 126–131.

Barky, A. El, & Hussein, S. A. (2018). *Saponins And Their Potential Role In Diabetes Mellitus*. *January 2017*.

Chitania, N., Alawiyah, T., Listiawati Ayu Dwi, M., & Yustian Adhany, A. (2020). Potensi Ekstrak Daun Ketepeng Cina (Cassia Alata L.) Terhadap Penurunan Kolesterol Darah Mencit Jantan Hiperlipidemia'. *Journal Of Pharmaceutical Care And Science*, *1*(1), 36–44.

Dewi, R., Budhiana, J., Fatmala, S. D., Yulianti, M., & Arsyi, D. N. (2023). Pengaruh Senam Diabetes Terhadap Penurunan Kadar Gula Darah, Stres, dan Kecemasan Pengaruh Senam Diabetes Terhadap Penurunan Kadar Gula Darah, Stres, dan Kecemasan Pada Penderita Diabetes Melitus Tipe Ii. *Jurnal Media Karya Kesehatan*, *6*(2), 300–318.

Fattaheian-Dehkordi, S., Hojjatifard, R., Saeedi, M., & Khanavi, M. (2021). A Review On Antidiabetic Activity Of Centaurea spp.: A New Approach For Developing Herbal Remedies. *Evidence-Based Complementary And Alternative Medicine*, *2021*. Https://Doi.Org/10.1155/2021/5587938

Hikmah, A. M., Luthfianto, D., Silitonga, M., Vertygo, S., Rita, R. S., Gultom, E. S., Ulfah, M., & Tika, I. N. (2022). *Buku Ajar Biokimia Teori Dan Aplikasi* (Vol. 1).

Hujjatusnaini, N. (N.D.). *Uji Potensi Ekstrak Daun Ketepeng Cina (Cassia Alata L .) Terhadap Penghambatan Pertumbuhan Trichophyton Sp*. 1–17.

Intannia, D., Amelia, R., Handayani, L., & Santoso, H. B. (2015). Pengaruh Pemberian Ekstrak Etanol Dan Ekstrak N -Heksan Daun Ketepeng Cina (Cassia Alata . L) Terhadap Waktu Kematian Cacing Pita Ayam (Raillietina Sp .) Secara In Vitro. *Jurnal Pharmascience*, *2*(2), 24–30.

Khotimah, S. N. (2016). Riview Artikel: Beberapa Tumbuhan Yang Mengandung Senyawa Aktif Antiinflamasi. *Farmaka,Fakultas Farmasi, Universitas Padjadjaran, 14*(2), 28–40.

Lestari, Zulkarnain, & Sijid, S. A. (2021). Diabetes Melitus: Review Etiologi, Patofisiologi, Gejala, Penyebab, Cara Pemeriksaan, Cara Pengobatan Dan Cara Pencegahan. *Uin Alauddin Makassar*, *November*, 237–241. Http://Journal.Uin-Alauddin.Ac.Id/Index.Php/Psb

Ma'shum, A. J. (2020). Pengaruh Ekstrak Etanol Bekatul Terfermentasi Rhizopus Oryzae Terhadap Histologi Limpa Mencit (Mus Musculus) Diabetes. *Skripsi*, 1–143.

Nisa, A. M. U., Si, S., Si, M., Nisa, A. M. U., Si, S., Si, M., Tanaman, P., & Peranannya, D. A. N. (2022). *Dr. A. Mu'nisa, S.Si., M.Si.*

Novalinda, N., Priastomo, M., & Rijai, L. (2021). Literature Review: Bahan Alam Yang Berpotensi Sebagai Antidiabetes. *Proceeding Of Mulawarman Pharmaceuticals Conferences*, *14*, 389–397. Https://Doi.Org/10.25026/Mpc.V14i1.595

Nurjanah, S. (2017). *Aktivitas Antioksidan Ekstrak Etanol Korteks Batang Salam (Syzygium Polyanthum)*. 128.

Oktaviona, E. E. P., Qomariyah, N., & Khaleyla, F. (2023). Aktivitas Hepatoprotektif Ekstrak Daun Phyllanthus Acidus L . Pada Mencit Diabetes Mellitus Tipe 2. *Jurnal Lenterabio: Berkah Ilmiah Biologi*, *12*(3), 381–388.

Raharjo, D., Hidayah, N., & Siwi Artini, K. (2022). Antioxidant Activity Of Ethanol Extracts And Fractions Ketepeng Cina Leaves(Cassia Alata) With Abts Assay. *Proceeding Of International Conference On Science, Health, And Technology*, 435–442. Https://Doi.Org/10.47701/Icohetech.V3i1.2187

Ramadhayanti, A. A. (2021). *2021_S1_Skripsi_2016210231_Fulltext_Compressed*.

Reski Fitriani, I., & Nuryanti, S. (2023). Aktivitas Antibakteri Ekstrak Etanol Daun Ketepeng Cina (Cassia Alata L.) Terhadap Beberapa Bakteri Penyebab Infeksi Kulit. *Makassar Natural Product Journal*, *1*(4), 22. Https://Journal.Farmasi.Umi.Ac.Id/Index.Php/Mnpj

Rusiani, E., Rusiani, E., Junaidi, S., Subiyono, H. S., & Sumartiningsih, S. (2019). Suplementasi Vitamin C Dan E Untuk Menurunkan Stres Oksidatif Setelah Melakukan Aktivitas Fisik Maksimal. *Media Ilmu Keolahragaan Indonesia*, *9*(2), 32–37.

Sebaugh, J.L. (2011). Guidelines for accurate EC50/IC50 Estimation. *Pharmaceutical Statistics*, 10(2), 128–134.

Safitri, E. R., Rohama, & Vidiasari, P. (2020). Skrining Fitokimia Serta Uji Aktivitas Antioksidan Ekstrak Bunga Ketepeng Cina (Senna Alata (L.) Roxb.) Dengan Metode Dpph. *Journal Of Pharmaceutical Care And Science*, *1*(1), 10–18.

Schreiner, T. B., Dias, M. M., Barreiro, M. F., & Pinho, S. P. (2022). Saponins As Natural Emulsifiers For Nanoemulsions. *Journal Of Agricultural And Food Chemistry*, *70*(22), 6573–6590. Https://Doi.Org/10.1021/Acs.Jafc.1c07893

Siregar, R. A., Amahorseja, A. R., Adriani, A., & Andriana, J. (2020). Pemeriksaan Kadar Glukosa Darah Sewaktu, Kadar Asam Urat Dankadar Cholesterol Pada Masyarakat Di Desa Eretan Wetan Kabupatenindramayu Periode Februari 2020. *Jurnal Comunitã Servizio : Jurnal Terkait Kegiatan Pengabdian Kepada Masyarakat, Terkhusus Bidang Teknologi, Kewirausahaan Dan Sosial Kemasyarakatan*, *2*(1), 291–300. Https://Doi.Org/10.33541/Cs.V2i1.1511

Soelistijo, S. (2021). Pedoman Pengelolaan Dan Pencegahan Diabetes Melitus Tipe 2 Dewasa Di Indonesia 2021. *Global Initiative For Asthma*, 46. Www.Ginasthma.Org.

Sumayyah, S., & Salsabila, N. (2017). Obat Tradisional : Antara Khasiat Dan Efek Sampingnya. *Farmasetika.Com (Online)*, *2*(5), 1. Https://Doi.Org/10.24198/Farmasetika.V2i5.16780

Suryanto, E., & Frenly, W. (2019). Aktivitas Penangkap Radikal Bebas Dari Ekstrak Fenolik Daun Sukun (Artocarpus Altilis F.). *Chem. Prog.*, *2*(1), 1–7.

Susila Ningsih, I., Chatri, M., & Advinda, L. (2023). Flavonoid Active Compounds Found In Plants Senyawa Aktif Flavonoid Yang Terdapat Pada Tumbuhan. *Serambi Biologi*, *8*(2),

126–132.

Syarifuddin, A., & Amalia, R. (2021). Studi Etnomedisin Pada Masyarakat 5 Desa Kecamatan Secang Kabupaten Magelang. In *Jurnal Ilmiah Ibnu Sina (Jiis): Ilmu Farmasi Dan Kesehatan* (Vol. 6, Issue 2). Https://Doi.Org/10.36387/Jiis.V6i2.747

Tallarida, R.J. (2001). Drug Synergism and Dose-Effect Data Analysis. CRC Press

Wang (2023). Flavonoids And Saponins: What Have We Got Or Missed? *Phytomedicine, 109*, 154580. Https://Doi.Org/10.1016/J.Phymed.2022.154580