

DAFTAR PUSTAKA

- Afrianto, R., Tien, T., Indriyani, N., Sudiro, T. Y., Syarifin, A. N. K., & Haryati, H. (2022). Pengaruh Extra Virgin Olive Oil (EVOO) Terhadap Kadar Lipid dan Indeks Massa Tubuh Wanita Obesitas Usia Produktif. *Poltekita: Jurnal Ilmu Kesehatan*, 16(2), 184-190.
- Aprilasani, Z., & Adiwarna, A. (2014). Pengaruh Lama Waktu Pengadukan dengan Variasi Penambahan Asam Asetat dalam Pembuatan Virgin Coconut Oil (VCO) dari Buah Kelapa. *Jurnal Konversi*, 3(1).
- Baradero, M., Dayrit, M.W., Siswadi, Y., 2008. *Klien Gangguan Hati: Seri Asuhan Keperawatan*. Jakarta:EGC.
- Behera, S., Babu, S. M., Ramani, Y. R., & Choudhury, P. K., Panigrahi, R., (2012). Protective Effect Of Pongamia Pinnata On Isoproterenol-Induced Hepatotoxicity In Rats Life Sciences Feed Vol. 1. *Life Sciences Feed*. 1. 8-15.
- Bhattacharjee, S., Elancheran, R., Dutta, K., Deb, P. K., & Devi, R. (2022). Cardioprotective potential of the antioxidant-rich bioactive fraction of *Garcinia pedunculata* Roxb. ex Buch.-Ham. against isoproterenol-induced myocardial infarction in Wistar rats. *Frontiers in pharmacology*, 4049.
- Bryant, B., Knights, K., Darroch, S., Rowland, A., 2014. *Pharmacology for Health Professionals ebook*. Elsevier Health Sciences
- Corbett, J.V., Banks, A.D. (2013). *Laboratory Tests and Diagnostic Procedures with Nursing Diagnoses*. 8th ed. Upper Saddle River, N.J. : Pearson.
- Dias, R. J., Bhise, S. B., & Dias, F. J. (2009). Assessment of hepatic function: a review. *International Journal of Pharmaceutical Research and Development*, 10, 1-16
- Ermanita, O. V., Handayani, R. A., Muharamah, E., & Purbayanti, D. (2020). Gambaran Aktivitas Enzim Alkaline Phosphatase (ALP) pada Pemain Game Online di Kecamatan Jekan Raya Kota Palangka Raya: Profile of Alkaline Phosphatase (ALP) Activity in Online Game Players in District of Jekan Raya. *Borneo Journal of Medical Laboratory Technology*, 3(1), 183-188.

- Fajrian, F. M. (2020). Enzim Transferase dengan Bilirubin Total Penderita Ikterus Obstruktif. *Jurnal Ilmiah Kesehatan Sandi Husada*, 9(1), 176-182.
- Fitrianingsih, A. (2022). *Morfologi, Taksonomi dan Filosofi Tumbuhan*. Penerbit P4I.
- Ghanbari R, Anwar F, Alkharfy KM, Gilani AH, Saari N. Valuable Nutrients and Functional Bioactives in Different Parts of Olive (*Olea europaea* L.)-A review. *Int J Mol Sci* 2012;13(3):3291– 3340. 01-406
- Goodman & Gilmans. 2018. *The Pharmacological Basis of Therapeutics*. 13th edition. New York: The McGraw-Hill Companies.
- Gumay, B. S., & Mustofa, S. (2020). Penggunaan Klinis Aktivitas Enzim Gamma-Glutamyl Transferase (GGT) Plasma dan Potensinya sebagai Biomarker untuk Berbagai Penyakit. *MAJORITY*, 9(1), 167-173.
- Gunardi, S., & Setiyono, S. (2018). Extra Virgin Olive Oil Dapat Menurunkan Kolesterol Total Pada Lansia Anggota Posbindu Kenanga. *Jurnal Ilmiah Ilmu Keperawatan Indonesia*, 8(02), 401-406.
- Guyton, A. C., Hall, J. E., 2014. *Buku Ajar Fisiologi Kedokteran*. Edisi 12. Jakarta : EGC,
- Harrison, M. F. (2018). The misunderstood coagulopathy of liver disease: a review for the acute setting. *Western Journal of Emergency Medicine*, 19(5), 863.
- Hasanzadeh-Moghadam, M., Khadem-Ansari, M. H., Farjah, G. H., & Rasmi, Y. (2018). Hepatoprotective effects of betaine on liver damages followed by myocardial infarction. *In Veterinary Research Forum* (Vol. 9, No. 2, p. 129). Faculty of Veterinary Medicine, Urmia University, Urmia, Iran.
- Hasibuan, C. F., Rahmiati, R., & Nasution, J. (2018). Pembuatan virgin coconut oil (vco) dengan menggunakan cara tradisional. Martabe: *Jurnal Pengabdian Kepada Masyarakat*, 1(3), 128-132.
- Hussain, S. Z., Naseer, B., Qadri, T., Fatima, T., & Bhat, T. A. (2021). Olive (*Olea europaea* L.)—Morphology, Taxonomy, Composition and Health Benefits. In *Fruits Grown in Highland Regions of the Himalayas: Nutritional and Health Benefits* (pp. 117-129). Cham: Springer International Publishing.

- Ibrahim, M. A. B., Wani, F. A., & Rahiman, S. (2017). Hepatoprotective effect of olive oil and camel milk on acetaminophen-induced liver toxicity in mice. *International Journal of Medical Science and Public Health*, 6(1), 186-194.
- Jimenez-Lopez, C., Carpena, M., Lourenço-Lopes, C., Gallardo-Gomez, M., Lorenzo, J. M., Barba, F. J., ... & Simal-Gandara, J. (2020). Bioactive compounds and quality of extra virgin olive oil. *Foods*, 9(8), 1014.
- Jiménez-Sánchez, A., Martínez-Ortega, A. J., Remón-Ruiz, P. J., Piñar-Gutiérrez, A., Pereira-Cunill, J. L., & García-Luna, P. P. (2022). Therapeutic properties and use of extra virgin olive oil in clinical nutrition: a narrative review and literature update. *Nutrients*, 14(7), 1440.
- Juárez-Hernández, E., Chávez-Tapia, N. C., Uribe, M., & Barbero-Becerra, V. J. (2015). Role of bioactive fatty acids in nonalcoholic fatty liver disease. *Nutrition journal*, 15, 1-10.
- Juliarta, I. G., Mulyantari, N. K., & Yasa, I. W. P. S. (2018). Gambaran Hepatotoksisitas (ALT/AST) Penggu-naan Obat Antituberkulosis Lini Pertama dalam Pengobatan Pasien Tuberkulosis Paru Rawat Inap di RSUP Sanglah Denpasar Tahun 2014. *E-Jurnal Medika*, 7(10), 1-10.
- Kamariah, L., Azmi, A., Rosmawati, A., Ching, M. W., Azlina, M. D., Sivapragasam, A., Tan, C.P., & Lai, O. M. (2008). Physico-chemical and quality characteristics of virgin coconut oil—A Malaysian survey. *J. Trop. Agric. and Fd. Sc*, 36(2), 000-000.
- Katzung, B.G., 2012, Farmakologi Dasar dan Klinik , Edisi 12. Jakarta: Penerbit Buku Kedokteran EGC.
- Kendran, A. A. S., Arjana, A. A. G., & Pradnyantari, A. A. S. I. (2017). Aktivitas Enzim Alanine-Aminotransferase dan Aspartate Aminotransferase pada Tikus Putih Jantan yang Diberi Ekstrak Buah Pinang. *Buletin Veteriner Udayana*, 132-138.
- Kurniawan, L. B. (2012). Hubungan Kadar Transaminase terhadap Mortalitas dan Lama Perawatan Pasien Infark Miokard. *Jurnal Kedokteran YARSI*, 20(1), 29-35.
- Lobo, R. O., & Shenoy, C. K. (2015). Myocardial potency of bio-tea against isoproterenol induced myocardial damage in rats. *Journal of food science and technology*, 52(7), 4491-4498.

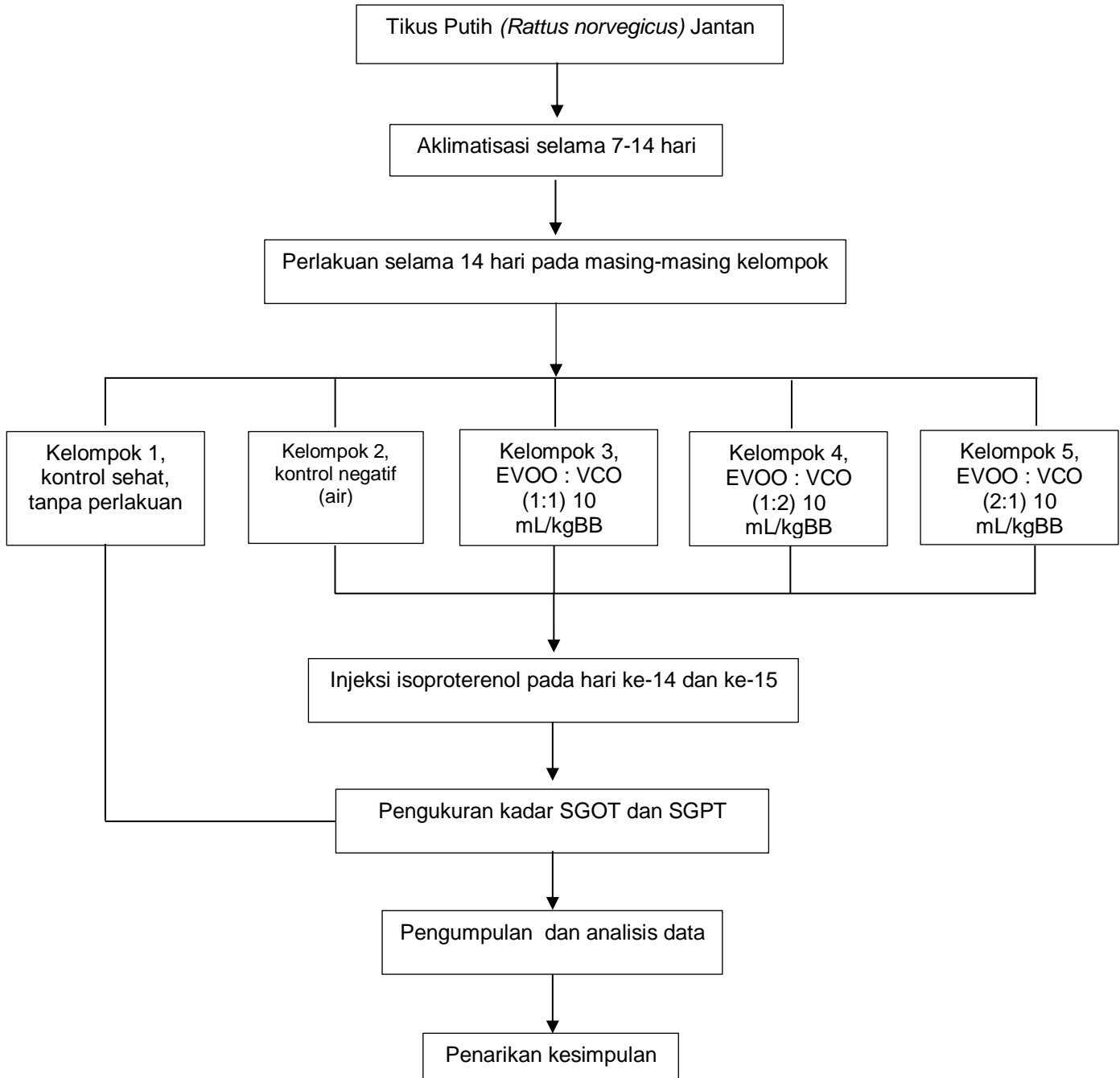
- Nuhamara, I. M. (2022). *Buku Ajar Teknologi Lemak/Minyak (Virgin Coconut Oil)*. Penerbit Lakeisha.
- Mappa, N., Rumallang, A., (2022). *Agribisnis Syariah*. CV. Azka Pustaka
- Margata, L., Silalahi, J., Harahap, U., & Satria, D., (2018). The effect of hydrolyzed virgin coconut oil on lipid profile and liver enzymes in dyslipidemic rats. *Asian J. Pharm. Clin. Res*, 11(2), 406-409.
- Marlina, M., Wijayanti, D., Yudiastari, I. P., & Safitri, L. (2018). Pembuatan Virgin Coconut Oil dari Kelapa Hibrida Menggunakan Metode Penggaraman dengan NaCl dan Garam Dapur. *Jurnal Chemurgy*, 1(2), 7-12.
- Moghimian, M., Abtahi-Eivary, S. H., Nematollahi, M., Ebadi, A., Bahri, N., Alami, A.(2019). The effects of omega-3 on liver damage after acute myocardial infarction: a randomized controlled clinical trial. *International Cardiovascular Research Journal*, 13(1).
- Ndrepepa, G. (2021). Aspartate aminotransferase and cardiovascular disease—a narrative review. *J. Lab. Precis. Med*, 6(6).
- Obeidat, H. M., Althunibat, O. Y., Alfwuaires, M. A., Aladaileh, S. H., Algefare, A. I., Almuqati, A. F., & Abukhalil, M. H. (2022). Cardioprotective Effect of Taxifolin against Isoproterenol-Induced Cardiac Injury through Decreasing Oxidative Stress, Inflammation, and Cell Death, and Activating Nrf2/HO-1 in Mice. *Biomolecules*, 12(11), 1546.
- Panda, S., Kar, A., & Biswas, S. (2017). Preventive effect of agnucastaside C against isoproterenol-induced myocardial injury. *Scientific reports*, 7(1), 1-14.
- Paniagua, A. C., & Amariles, P. (2017). Hepatotoxicity by drugs. *Pharmacokinetics and Adverse Effects of Drugs-Mechanisms and Risks Factors*.
- Perdani, C. G., Pulungan, M. H., & Karimah, S. (2019). Pembuatan Virgin Coconut Oil (VCO) Kajian Suhu Inkubasi dan Konsentrasi Enzim Papain Kasar. *Industria: Jurnal Teknologi dan Manajemen Agroindustri*, 8(3), 238-246.
- Rathod, S., Agrawal, Y., Sherikar, A., Nakhate, K. T., Patil, C. R., Nagoor Meeran, M. F., & Goyal, S. N. (2022). Thymoquinone Produces Cardioprotective Effect in β -Receptor Stimulated Myocardial Infarcted

- Rats via Subsiding Oxidative Stress and Inflammation. *Nutrients*, 14(13), 2742.
- Rosida, A. (2016). Pemeriksaan Laboratorium Penyakit Hati. *Berkala Kedokteran*, 12(1), 123-131.
- Saragih, G. G., Waleleng, B. J., & Haroen, H. (2016). Gambaran Gangguan Hemostasis Pada Penderita Sirosis Hati yang Dirawat Di RSUP Prof. Dr. Rd Kandou Periode Agustus 2013 - Agustus 2015. *e-CliniC*, 4(1).
- Sharma, P., Verma, P. K., Raina, R., Sood, S., Prawez, S., & Manhas, L. (2020). Isoprenaline Induced Hepatic Alterations and Modulation by Hydroalcoholic Extract of Juglans Regia Hull in Wistar Rats. *Toxicology International*, 58-69..
- Siddiqui, M. A., Ahmad, U., Khan, A. A., Ahmad, M., Badruddeen, K. M., & Akhtar, J. (2016). Isoprenaline: a tool for inducing myocardial infarction in experimental animals. *Int J Pharm*, 6(2), 138-44
- Silalahi, J. (2020). Nutritional values and health protective properties of coconut oil. *Indonesian Journal of Pharmaceutical and Clinical Research*, 3(2), 1-12.
- Sinaga, F. A., Harahap, U., Silalahi, J., & Sipahutar, H. (2020). Antioxidant and hepatoprotective effects of virgin coconut oil at maximum physical activity. In Progress in social science, humanities and education research symposium (pp. 171-178). *Redwhite Press*.
- Sivakrishnan, S., & Pharm, M. (2019). Liver disease overview. *World Journal of Pharmacy and Pharmaceutical Sciences*, 8(1), 1385-1395.
- Sultang, A. A. (2022). Uji heptoprotetif Virgin Coconut Oil (VCO) dan Extra Virgin Olive Oil (EVOO) serta Kombinasinya pada Tikus Putih (*Rattus norvegicus*) Jantan yang Diinduksi Doksoribisin. Universitas Hasanuddin.
- Trajkovska Petkoska, A., & Trajkovska-Broach, A. (2022). Health Benefits of Extra Virgin Olive Oil. *Olive Oil - New Perspectives and Applications*. doi: 10.5772/intechopen.96570
- Utari, A. U., Djibir, Y. Y., & Palinggi, B. P. (2022). A combination of virgin coconut oil and extra virgin olive oil elicits superior protection against doxorubicin cardiotoxicity in rats. *Turkish Journal of Pharmaceutical Sciences*, 19(2), 138.

- WHO. Cardiovascular diseases (CVDs) [Internet]. 2021 [cited 2023 Apr 6]. Available from: [https://www.who.int/en/news-room/fact-sheets/detail/cardiovascular-diseases-\(cvds\)](https://www.who.int/en/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds))
- Widiyaningsih, W., Sugiyanto, S., Widyarini, S., & Pramono, S. (2017). Isoproterenol Sebagai Model Infark Miokardial Akut Pada Tikus Wistar. *Jurnal Ilmu Farmasi dan Farmasi Klinik*, 20-27.
- Yang, J., Peng, T., Huang, J., Zhang, G., Xia, J., Ma, M., Danwen, D., Gong, D., & Zeng, Z. (2020). Effects of medium-and long-chain fatty acids on acetaminophen-or rifampicin-induced hepatocellular injury. *Food Science & Nutrition*, 8(7), 3590-3601.

LAMPIRAN

Lampiran 1. Skema Kerja



Lampiran 2. Hasil Pengukuran Biomarker

Tabel 2. Data hasil pengukuran biomarker SGOT

Normal	Isoproterenol	EVOO:VCO (1:1)	EVOO:VCO (1:2)	EVOO:VCO (2:1)	
101	126	75.1	104	107	
108	269	157	91.5	143	
99.6	205	114	89.6	81.7	
112	273	185	100	96	
Minimum	99.60	126.0	75.10	89.60	81.70
Maximum	112.0	273.0	185.0	104.0	143.0
Range	12.40	147.0	109.9	14.40	61.30
Mean	105.2	218.3	132.8	96.28	106.9
Std. Deviation	5.861	68.94	48.28	6.853	26.19
Std. Error of Mean	2.931	34.47	24.14	3.427	13.09

Tabel 3. Data hasil pengukuran biomarker SGPT

Normal	Isoproterenol	EVOO:VCO (1:1)	EVOO:VCO (1:2)	EVOO:VCO (2:1)	
52.8	57.7	53	50.4	55.7	
58.5	61.6	75.4	44.7	44.7	
73.7	78.8	64	40.5	37.5	
53.2	171	74.9	57.6	58.3	
Minimum	52.80	57.70	53.00	40.50	37.50
Maximum	73.70	171.0	75.40	57.60	58.30
Range	20.90	113.3	22.40	17.10	20.80
Mean	59.55	92.28	66.83	48.30	49.05
Std. Deviation	9.785	53.28	10.61	7.409	9.697
Std. Error of Mean	4.892	26.64	5.306	3.705	4.849

Lampiran 3. Analisis Statistika

3.1 Analisis biomarker SGOT

1. Analisis menggunakan *Shapiro-Wilk*

Shapiro-Wilk test					
W	0.9103	0.8746	0.9776	0.9079	0.9394
P value	0.4841	0.3162	0.8877	0.4712	0.6506
Passed normality test (alpha=0.05)?	Yes	Yes	Yes	Yes	Yes
P value summary	ns	ns	ns	ns	ns

2. Analisis menggunakan *one-way ANOVA*

ANOVA summary					
F	6.410				
P value	0.0032				
P value summary	**				
Significant diff. among means (P < 0.05)?	Yes				
R squared	0.6309				
ANOVA table					
	SS	DF	MS	F (DFn, DFd)	P value
Treatment (between columns)	40262	4	10066	F (4, 15) = 6.410	P=0.0032
Residual (within columns)	23553	15	1570		
Total	63815	19			

3. Analisis menggunakan *Tukey HSD*

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value	
normal vs. isoproterenol	-113.1	-199.6 to -26.58	Yes	**	0.0081	A-B
normal vs. EVOO:VCO (1:1)	-27.63	-114.1 to 58.90	No	ns	0.8575	A-C
normal vs. EVOO:VCO (1:2)	8.875	-77.65 to 95.40	No	ns	0.9976	A-D

normal vs. EVOO:VCO (2:1)	-1.775	-88.30 to 84.75	No	ns	>0.9999	A-E
isoproterenol vs. EVOO:VCO (1:1)	85.48	-1.048 to 172.0	No	ns	0.0536	B-C
isoproterenol vs. EVOO:VCO (1:2)	122.0	35.45 to 208.5	Yes	**	0.0044	B-D
isoproterenol vs. EVOO:VCO (2:1)	111.3	24.80 to 197.8	Yes	**	0.0092	B-E
EVOO:VCO (1:1) vs. EVOO:VCO (1:2)	36.50	-50.02 to 123.0	No	ns	0.6937	C-D
EVOO:VCO (1:1) vs. EVOO:VCO (2:1)	25.85	-60.67 to 112.4	No	ns	0.8838	C-E
EVOO:VCO (1:2) vs. EVOO:VCO (2:1)	-10.65	-97.17 to 75.87	No	ns	0.9951	D-E

3.2 Analisis biomarker SGPT

1. Analisis menggunakan *Shapiro-Wilk*

Shapiro-Wilk test					
W	0.8092	0.7653	0.8765	0.9793	0.9217
P value	0.1199	0.0532	0.3237	0.8982	0.5463
Passed normality test (alpha=0.05)?	Yes	Yes	Yes	Yes	Yes
P value summary	ns	ns	ns	ns	ns

2. Analisis menggunakan *one way ANOVA*

ANOVA summary						
F	2.025					
P value	0.1425					
P value summary	ns					
Significant diff. among means (P < 0.05)?	No					
R squared	0.3506					
ANOVA table	SS	DF	MS	F (DFn, DFd)	P value	
Treatment (between columns)	5176	4	1294	F (4, 15) = 2.025	P=0.1425	
Residual (within columns)	9587	15	639.2			
Total	14764	19				

3. Analisis menggunakan *Tukey HSD*

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value	
normal vs. isoproterenol	-32.73	-87.93 to 22.48	No	ns	0.3931	A-B
normal vs. EVOO:VCO (1:1)	-7.275	-62.48 to 47.93	No	ns	0.9936	A-C
normal vs. EVOO:VCO (1:2)	11.25	-43.95 to 66.45	No	ns	0.9679	A-D
normal vs. EVOO:VCO (2:1)	10.50	-44.70 to 65.70	No	ns	0.9749	A-E
isoproterenol vs. EVOO:VCO (1:1)	25.45	-29.75 to 80.65	No	ns	0.6229	B-C
isoproterenol vs. EVOO:VCO (1:2)	43.98	-11.23 to 99.18	No	ns	0.1528	B-D
isoproterenol vs. EVOO:VCO (2:1)	43.23	-11.98 to 98.43	No	ns	0.1638	B-E
EVOO:VCO (1:1) vs. EVOO:VCO (1:2)	18.53	-36.68 to 73.73	No	ns	0.8348	C-D
EVOO:VCO (1:1) vs. EVOO:VCO (2:1)	17.78	-37.43 to 72.98	No	ns	0.8538	C-E
EVOO:VCO (1:2) vs. EVOO:VCO (2:1)	-0.7500	-55.95 to 54.45	No	ns	>0.9999	D-E

Lampiran 4. Dokumentasi Penelitian



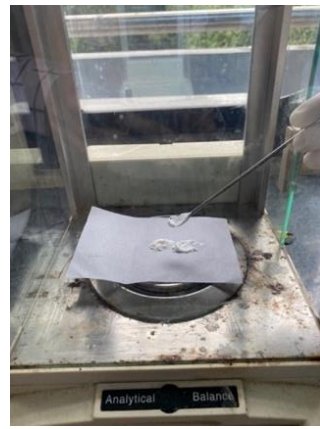
Gambar 6. Aklimatisasi hewan coba



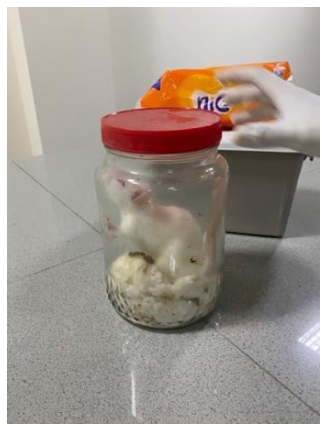
Gambar 7. Isoproterenol



Gambar 8. Reagen kit



Gambar 9. Penimbangan isoproterenol



Gambar 10. Pembusuan hewan coba



Gambar 11. Pengambilan darah



Gambar 12. Sentrifugasi sampel darah



Gambar 13. Serum dalam tabung *ependorf*



Gambar 14. Pengukuran biomarker dengan *humalyzer*



Gambar 15. Data hasil pengukuran

Lampiran 5. Surat Rekomendasi Persetujuan Etik

KEMENTERIAN PENDIDIKAN, KEBUDAYAAN, RISET DAN TEKNOLOGI
UNIVERSITAS HASANUDDIN FAKULTAS KEDOKTERAN
KOMITE ETIK PENELITIAN UNIVERSITAS HASANUDDIN
RSPTN UNIVERSITAS HASANUDDIN
RSUP Dr. WAHIDIN SUDIROHUSODO MAKASSAR
Sekretariat : Lantai 2 Gedung Laboratorium Terpadu
JL.PERINTIS KEMERDEKAAN KAMPUS TAMALANREA KM.10 MAKASSAR 90245.
Contact Person: dr. Agussalim Bukhari.,MMed,PhD, SpGK TELP. 081241850858, 0411 5780103, Fax : 0411-581431






REKOMENDASI PERSETUJUAN ETIK

Nomor : 278/UN4.6.4.5.31/ PP36/ 2023

Tanggal: 8 Mei 2023

Dengan ini Menyatakan bahwa Protokol dan Dokumen yang Berhubungan Dengan Protokol berikut ini telah mendapatkan Persetujuan Etik :

No Protokol	UH23030206	No Sponsor Protokol	
Peneliti Utama	Nur Rahmi	Sponsor	
Judul Peneliti	Uji Efek Protektif Kombinasi Extra Virgin Olive Oil (EVOO) dan Virgin Coconut Oil (VCO) Terhadap Peningkatan Kadar SGOT dan SGPT Pada Tikus Yang Diinduksi Isoproterenol		
No Versi Protokol	1	Tanggal Versi	28 Maret 2023
No Versi PSP		Tanggal Versi	
Tempat Penelitian	Laboratorium Fakultas Farmasi Universitas Hasanuddin Makassar		
Jenis Review	<input type="checkbox"/> Exempted <input checked="" type="checkbox"/> Expedited <input type="checkbox"/> Fullboard Tanggal	Masa Berlaku 8 Mei 2023 sampai 8 Mei 2024	Frekuensi review lanjutan
Ketua KEP Universitas Hasanuddin	Nama Prof.Dr.dr. Suryani As'ad, M.Sc.,Sp.GK (K)	Tanda tangan 	
Sekretaris KEP Universitas Hasanuddin	Nama dr. Agussalim Bukhari, M.Med.,Ph.D.,Sp.GK (K)	Tanda tangan 	

Kewajiban Peneliti Utama:

- Menyerahkan Amandemen Protokol untuk persetujuan sebelum di implementasikan
- Menyerahkan Laporan SAE ke Komisi Etik dalam 24 Jam dan dilengkapi dalam 7 hari dan Laporan SUSAR dalam 72 Jam setelah Peneliti Utama menerima laporan
- Menyerahkan Laporan Kemajuan (progress report) setiap 6 bulan untuk penelitian resiko tinggi dan setiap setahun untuk penelitian resiko rendah
- Menyerahkan laporan akhir setelah Penelitian berakhir
- Melaporkan penyimpangan dari prokol yang disetujui (protocol deviation / violation)
- Mematuhi semua peraturan yang ditentukan