DAFTAR PUSTAKA

Agustina, R. 2021. *Metabolomic Study of Food Derived Compounds Interacting with ABC Transporters*. Kanazawa.

Astuti, SD. 2009. Efek Ekstrak Etanol 70% Daun Pepaya (Carica papaya, Linn.) terhadap Aktivitas Ast & Alt Pada Tikus Galur Wistar Setelah Pemberian Obat Tuberkulosis (Isoniazid & Rifampisin). Surakarta: Fakultas Farmasi Universitas Setia Budi.

Botelho, A., Pierezan, F., Soto-Blanco, B., & Melo, M. M. 2019*. A review of cardiac glycosides: Structure, toxicokinetics, clinical signs, diagnosis and antineoplastic potential. Toxicon : official journal of the International Society on Toxinology*, 158, 63–68.

Chakraborty, P. and Ramakrishnan, M. 2016. '*Role of P-glycoprotein in Chemotherapeutic Drug Resistance and Mechanisms of Pump Deactivation to Overcome MDR in Cancer Cells – A Critical Review',* 1(2), pp. 31–38.

Chen, H., Shien, K., Suzawa, K., Tsukuda, K., Tomida, S., Sato, H., … Toyooka, S. 2017. *Elacridar, a third-generation ABCB1 inhibitor, overcomes resistance to docetaxel in non-small cell lung cancer. Oncology Letters*, 14(4), 4349–4354.

Chen, M., Zhou, S. Y., Fabriaga, E., Zhang, P. H., & Zhou, Q. 2018. *Food-drug interactions precipitated by fruit juices other than grapefruit juice: An update review. Journal of food and drug analysis*, 26(2S), S61–S71.

D'Alessandro, C., Benedetti, A., Di Paolo, A., Giannese, D., & Cupisti, A. 2022. *Interactions between Food and Drugs, and Nutritional Status in Renal Patients: A Narrative Review. Nutrients*, 14(1), 212.

Fasinu, P. S., & Rapp, G. K. 2019. *Herbal Interaction With Chemotherapeutic Drugs-A Focus on Clinically Significant Findings. Frontiers in oncology,* 9, 1356.

Ferreira, R.J.; Santos, D.J.D.; Ferreira, M.-J.U. 2015. *P-glycoprotein and membrane roles in multidrug resistance. Future Med. Chem*, 7, 929–946.

Fujiwara Y, Yahara S, Ikeda T, Ono M, Nohara T. 2003. *Cytotoxic major saponin from tomato fruits. Chemical and Pharmaceutical Bulletin*, 51, 234-235.

Fujiwara, Y., Kiyota, N., Hori, M., Matsushita, S., Iijima, Y., Aoki, K., Nagai, R. 2007. *Esculeogenin A, a new tomato sapogenol, ameliorates hyperlipidemia and athero- sclerosis in ApoE-deficient mice by inhibiting ACAT. Arteriosclerosis, Thrombosis, and Vascular Biology*, 27(11), 2400–2406.

Goodman, Gilman. 2008. *Manual of Pharmacology and Therapeutics*. New York, USA: The Mc Graw Hill;

Hendera dan Sri Rahayu. 2018. Interaksi Antar Obat pada Peresepan Pasien Rawat Inap Pediatrik Rumah Sakit X dengan Menggunakan Aplikasi *Medscape*. *Journal Of Current Pharmaceutical Sciences*. Vol 1(2): 75-80.

Juliano, R.L.; Ling, V. 1976 *A surface glycoprotein modulating drug permeability in Chinese hamster ovary cell mutants. Biochim. Biophys. Acta Biomembr,* 455, 152–162.

Katzung B.G.(Ed.), (2017). *Basic & Clinical Pharmacology*, 14e. McGraw Hill.

Kim, Y.; Chen, J. 2018. *Molecular structure of human P-glycoprotein in the ATP-bound, outward-facing conformation. Science*, 359, 915–919.

Kou, L.; Sun, R.; Bhutia, Y.D.; Yao, Q.; 2018, *Chen, R. Emerging advances in P-glycoprotein inhibitory nanomaterials for drug delivery. Expert Opin. Drug Deliv*. 15, 869–879.

Latif, S.M.; Rusdiana, T.; Gozali, D. 2018. Artikel Tinjauan: Pengaruh P-glycoprotein (P-gp) terhadap Bioavalabilitas Atorvastatin. *Farmaka. Suplemen*., 15(3).

Lawati, H. 2022. A *Review of the Pharmacokinetics of Cyclosporin. IJFMR* Volume 4(6). 10.36948/ijfmr.2022.v04i06.975

Liu, Ruijuan & Li, Xia & Wei, Jingyao & Liu, Shuaibing & Chang, Yuanyuan & Zhang, Jiali & Zhang, Ji & Zhang, Xiaojian & Fuhr, Uwe & Taubert, Max & Tian, Xin. 2019. *A Single Dose of Baicalin Has No Clinically Significant Effect on the Pharmacokinetics of Cyclosporine A in Healthy Chinese Volunteers. Frontiers in Pharmacology*.

Mangunsong, S., Assiddiqy, R., Sari, E., Marpaung, P., & Sari, R. 2019. Penentuan β-karoten dalam buah wortel (Daucus Carota) secara kromatografi cair kinerja tinggi (U-HPLC). *AcTion: Aceh Nutrition Journal*, 4(1), 36-41. doi:http://dx.doi.org/10.30867/action.v4i1.151

Mealey, K.L.; Waiting, D.; Raunig, D.L.; Schmidt, K.R.; Nelson, F.R. *Oral bioavailability of P-glycoprotein substrate drugs do not differ between ABCB1-1Δ and ABCB1 wild type dogs. J. Vet. Pharmacol. Ther.* 2010, 33, 453–460.

Melfi MT, Nardiello D, Cicco N, Candido V, Centonze D. 2018. *Simultaneous determination of water-and fat-soluble vitamins, lycopene and beta-carotene in tomato samples and pharmaceutical formulations: Double injection single run by reverse-phase liquid chromatography with uv detection. Journal of Food Composition and Analysis*: 70: 9-17

Nakonechnaya,O., Kholin, A., Subbotin, E., Grishchenko, O., Burkovsaya, E., Khrolenko, Yu., Burdukovskii, M., Micheeva, A., Gatfitskaya, I., Orlovskaya, I., & Kulchin, Yu. 2020. *Tomato (cv. Bonsai) plant development under different light spectra. Fifth Asian School-Conference on Physics an Technology of Nanostructured Materials. Vladivostok*.

Nanayakkara, A.K.; Follit, C.A.; Chen, G.; Williams, N.S.; Vogel, P.D.; Wise, J.G.2018. *Targeted inhibitors of P-glycoprotein increase*

chemotherapeutic-induced mortality of multidrug resistant tumor cells. Sci. Rep. , 8, 967.

Naveen, P., Lingaraju, H. B., Deepak, M., Medhini, B., & Prasad, K. S. (2018b). *Method development and validation for the determination of caffeine: an alkaloid from coffea arabica by high-performance liquid chromatography method. Pharmacognosy Research*, 10(1), 88.

Nguyen, T. T., Duong, V. A., & Maeng, H. J. 2021. *Pharmaceutical Formulations with P-Glycoprotein Inhibitory Effect as Promising Approaches for Enhancing Oral Drug Absorption and Bioavailability. Pharmaceutics*, 13(7), 1103.

Petric, Z., Žuntar, I., Putnik, P., & Bursać Kovačević, D. 2020. *Food-Drug Interactions with Fruit Juices. Foods (Basel, Switzerland)*, 10(1), 33.

Salim, M. M. R., Rashid, M. H., Hossain, M. M., & Zakaria, M. (2018). *Morphological characterization of tomato (Solanum lycopersicum L.) genotypes. Journal of the Saudi Society of Agricultural Sciences.* doi:10.1016/j.jssas.2018.11.001

Schinkel, A.H.; Jonker, J.W. 2012. *Mammalian drug efflux transporters of the ATP binding cassette (ABC) family: An overview. Adv. Drug Deliv. Rev*., 64, 138–153.

Shargel Leon & Yu Andrew BC. 2012. *Applied Biopharmaceutics and Pharmacokinetics 7th Edition*. New York: McGrawHills Education.

Son, Ki-Ho & Kim, Eun-Young & Oh, Myung-Min. 2018. *Growth and Development of Cherry Tomato Seedlings Grown under Various Combined Ratios of Red to Blue LED Lights and Fruit Yield and Quality after Transplanting. Protected Horticulture and Plant Factory.* 27. 54-63. 10.12791/KSBEC.2018.27.1.54.

Thanacoody, R. 2019 *Drug interactions. In Clinical Pharmacy and Therapeutics; Whittlesea, C., Hodson, K., Eds.; Elsevier*: Amsterdam, The Netherlands,; pp. 53–65.

Trivedi, A., Sohn, W., Hsu, C. P., Jafarinasabian, P., Zhang, H., Hutton, S., Flach, S., Abbasi, S., Dutta, S., & Lee, E. 2022. *Pharmacokinetic Drug-Drug Interaction Study of Omecamtiv Mecarbil With Amiodarone and Digoxin in Healthy Subjects. Clinical pharmacology in drug development*, 11(3), 388–396.

Yamanaka, Takao & Vincken, Jean-Paul & Waard, Pieter & Sanders, Mark & Takada, Norihisa & Gruppen, Harry. 2008. *Isolation, Characterization, and Surfactant Properties of the Major Triterpenoid Glycosides from Unripe Tomato Fruits. Journal of agricultural and food chemistry*. 56. 11432-40. 10.1021/jf802351c.

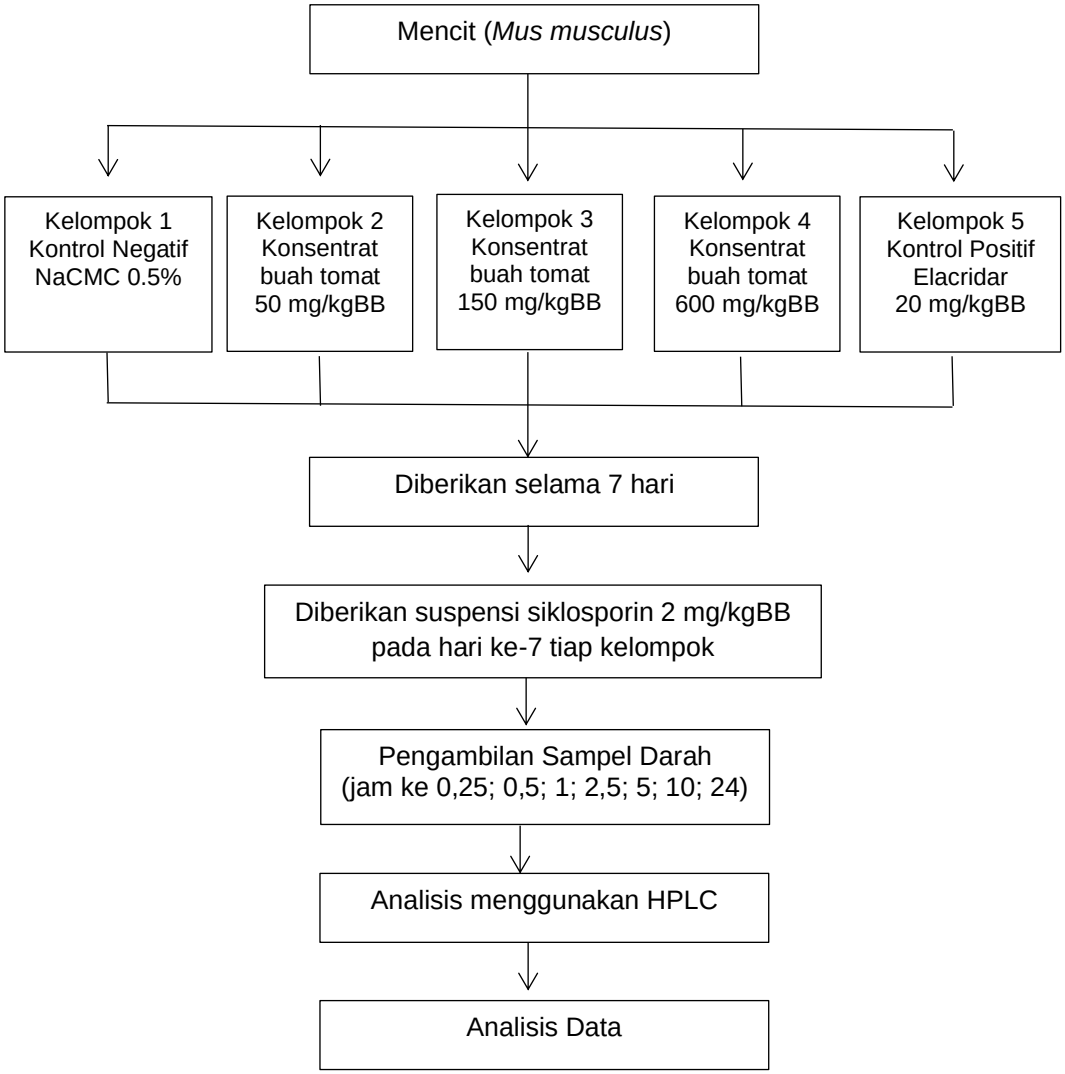
Yoshikawa, Yuko & Katayanagi, Yuki & Kamiya, Manatsu & Yamamoto, Yuri & Fukutomi, Ryuuta & Imai, Shinjiro & Miyoshi, Noriyuki & Ohashi, Norio. 2018. *Tomato saponin supplementation ameliorates the development of experimental arthritis by regulating inflammatory responses. Journal of Functional Foods*. 49. 458-464.

Zhang, Zhiqi & Zhou, Ying. 2023. *Intelligent Pharmacy's applications of cyclosporine. Intelligent Pharmacy.* 10.1016/j.ipha.2023.04.014.

Zhou, Jianrong & Kimura, Souta & Nohara, Toshihiro & Yokomizo, Kazumi. 2018. *Competitive Inhibition of Mammalian Hyaluronidase by Tomato Saponin, Esculeoside A. Natural Product Communications*. 13. 1461-1463.

LAMPIRAN

Lampiran 1. Skema Kerja



Lampiran 2. Perhitungan Dosis

Produk jus buah tomat yang beredar diketahui mengandung 160 g buah tomat dalam 200 mL, sehingga

Dosis manusia = 160 g/60 kgBB
= 2,7 g/kgBB

Konversi dosis mencit = 2,7 g/Kg x 12,3
= 33,2 g/kgBB → 30 g/kgBB

Sebanyak 10 kg tomat segar menghasilkan 189 g konsentrat kering tomat (faktor pembagi = 53)

Konsentrat tomat 30 g/kgBB = 30.000 mg/53
= 566 mg → 600 mg/kgBB

- Variasi Dosis
  a) Dosis 1 (50 mg/kgBB)
     Dosis 1 ekor mencit (35 g) = 50 mg/kgBB
     = 50 mg/1000 gBB
     = 1,75 mg/ 35 g/ 0,35 ml
     Dosis 1 kelompok mencit = 1,75 mg x 7
     = 12,25 mg/ 2,45 ml NaCMC
  b) Dosis 1 (150 mg/kgBB)
     Dosis 1 ekor mencit (35 g) = 150 mg/kgBB
     = 150 mg/1000 gBB
     = 5,25 mg/ 35 g/ 0,35 ml
     Dosis 1 kelompok mencit = 5,25 mg x 7
     = 36,75 mg/ 2,45 ml NaCMC
  c) Dosis 1 (600 mg/kgBB)
     Dosis 1 ekor mencit (35 g) = 600 mg/kgBB
     = 600 mg/1000 gBB
     = 21 mg/ 35 g/ 0,35 ml
     Dosis 1 kelompok mencit = 21 mg x 7
     = 147 mg/ 2,45 ml NaCMC

- Siklosporin 2 mg/kgBB

  Dosis yang diberikan = 35 g x 0.002 mg/gBB
  = 0.07 mg

  Siklosporin yang ditimbang = (0.07 mg x 26 ekor) dalam (0,35 ml x 26 ekor)
  = 1.82 mg dalam 9,1 ml NaCMC

- Elacridar 20 mg/kgBB

  Dosis yang diberikan = 35 g x 0.02 mg/gBB
  = 0.7 mg

  Siklosporin yang ditimbang = (0.7 mg x 5 ekor) dalam (0,35 ml x 5 ekor)
  = 3.5 mg dalam 1.75 ml NaCMC

Lampiran 3. Bobot Badan Mencit Pada Tiap Kelompok

Tabel 2. Bobot badan mencit pada kelompok I

Mice	H1	H2	H3	H4	H5	H6	H7
Mice 1	33	36,6	36,6	34,1	34	34,2	34
Mice 2	28,4	31,5	30,7	28,2	28,2	28,8	28,4
Mice 3	25,6	26	25,5	24,3	25,1	25,1	24,4
Mice 4	29	30,9	30,7	29	29,4	29,8	29,1
Mice 5	35	35,3	35,5	33,5	33,7	33,2	33,2

Tabel 3. Bobot badan mencit pada kelompok II

Mice	H1	H2	H3	H4	H5	H6	H7
Mice 1	27,6	28,3	28,1	27,5	27,6	27,9	28,8
Mice 2	26,1	26,9	26,7	26,4	26,4	26,1	28,2
Mice 3	36,7	27,4	26,8	26,7	27,3	27,6	29,9
Mice 4	30	30,8	30,2	29,4	29,9	29,8	31,8

Tabel 4. Bobot badan mencit pada kelompok III

Mice	H1	H2	H3	H4	H5	H6	H7
Mice 1	30,3	33,4	31,1	29,8	30,7	29,3	31,2
Mice 2	31,1	33,8	32	31,7	32,4	30,5	32,3
Mice 3	27,3	29,4	27,6	27	27,8	25,2	27,8
Mice 4	31,2	33,5	32,3	31,6	32,5	30,7	32,4
Mice 5	28,3	30,8	28,7	28,2	28,3	27,1	29,2

Tabel 5. Bobot badan mencit pada kelompok IV

Mice	H1	H2	H3	H4	H5	H6	H7
Mice 1	26,1	28,5	26,4	26,3	27,3	27,9	27,8
Mice 2	31,4	32,3	31	30,4	30,6	31	32,5
Mice 3	29	31,4	29,6	28,8	29,6	29,9	30,4

Tabel 6. Bobot badan mencit pada kelompok V

Mice	H1	H2	H3	H4	H5	H6	H7
Mice 1	27,3	29,2	27,2	26,8	28,7	29,1	31,7
Mice 2	26	26,6	25,6	24,7	25,7	26,6	28,2
Mice 3	23,4	25,3	23,1	21,8	22,3	22,1	24,8
Mice 4	27,3	29,2	26,4	26	27,5	28,4	31,3
Mice 5	25,5	27	25,6	25,4	26,5	27,6	30,4

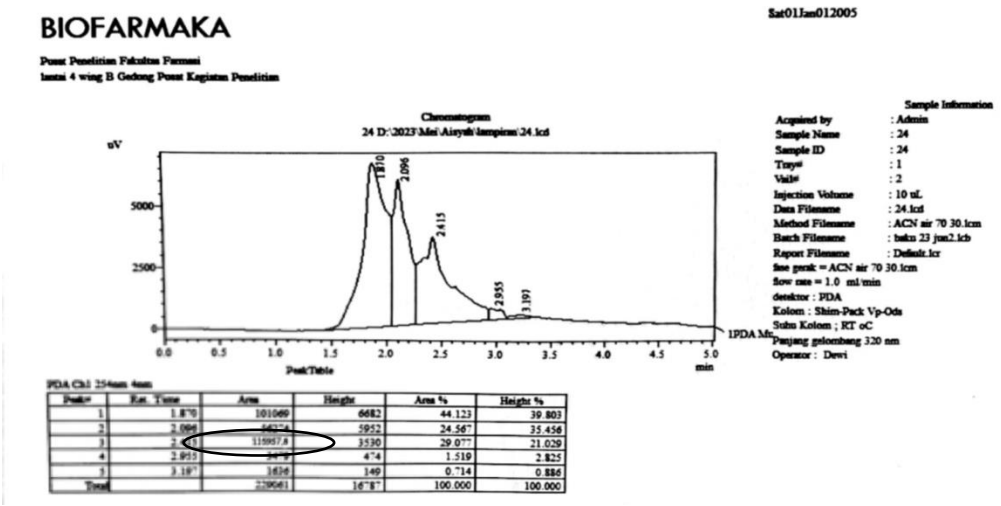
Lampiran 4. Luas Area Kromatogram Siklosporin Pada Beberapa Seri Kadar

Tabel 7. Luas Area Kromatogram Siklosporin Pada Beberapa Seri Kadar

No	Seri konsentrasi (µl/mL)	Luas Area
1	24	115957,8
2	72	385323,8
3	240	771810,8
4	720	1716398
5	2400	6740672

Lampiran 5. Kromatogram Standar Siklosporin

1. Kromatogram Standar Siklosporin pada konsentrasi 24 ppm

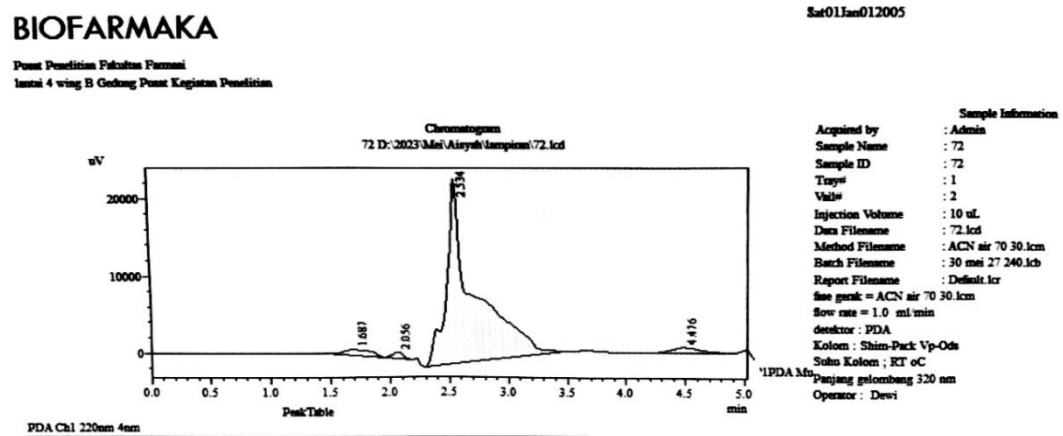


PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	1.870	101069	6682	44.123	39.803
2	2.094	66374	5952	24.567	35.456
3	2.413	115957.8	3530	29.077	21.029
4	2.955	4774	474	1.519	2.825
5	3.197	1626	149	0.714	0.886
Total		229681	16787	100.000	100.000

Gambar 7. Kromatogram Standar Siklosporin pada konsentrasi 24 ppm

2. Kromatogram Standar Siklosporin pada konsentrasi 72 ppm

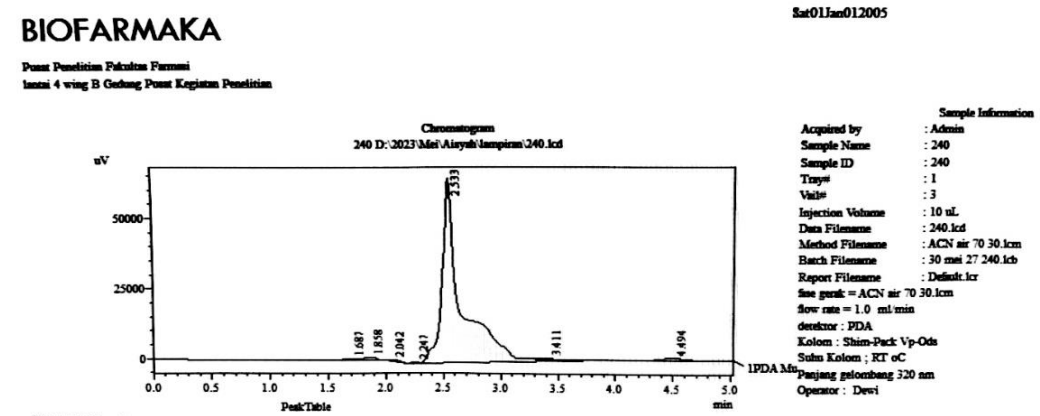


PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	1.687	13295	828	3.203	3.147
2	2.056	5367	830	1.290	3.152
3	2.334	385324	23969	92.828	91.067
4	4.476	11119	693	2.679	2.634
Total		415094	26320	100.000	100.000

Gambar 8. Kromatogram Standar Siklosporin pada konsentrasi 72 ppm

3. Kromatogram Standar Siklosporin pada konsentrasi 240 ppm

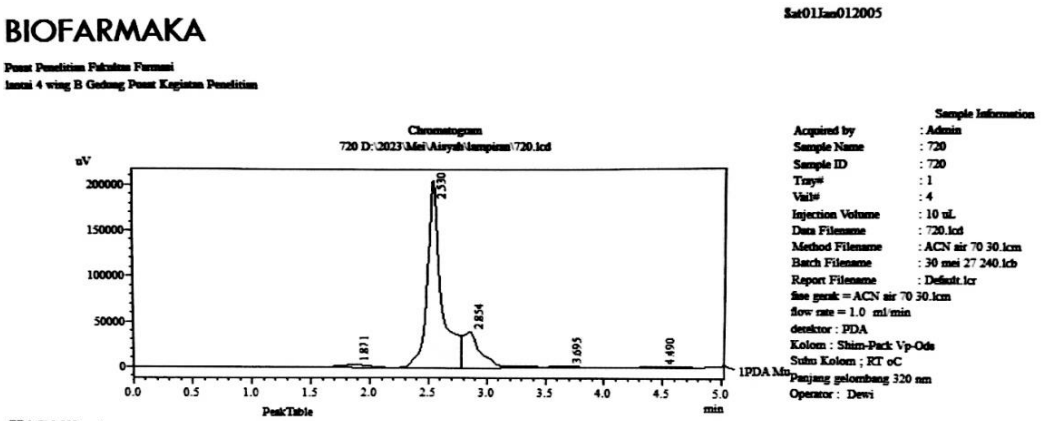


PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	1.687	3267	402	0.406	0.582
2	1.858	9112	1026	1.131	1.488
3	2.042	2830	376	0.351	0.545
4	2.247	1336	392	0.166	0.569
5	2.533	771811	65653	95.795	95.212
6	3.411	1127	163	0.140	0.236
7	4.494	16209	943	2.012	1.367
Total		805693	68954	100.000	100.000

Gambar 9. Kromatogram Standar Siklosporin pada konsentrasi 240 ppm

4. Kromatogram Standar Siklosporin pada konsentrasi 720 ppm

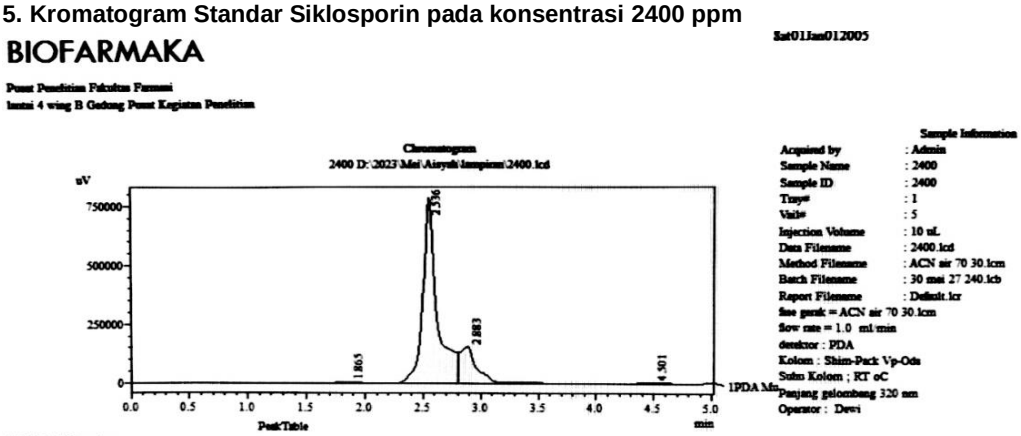


PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	1.871	58310	3531	2.585	1.404
2	2.530	1716398	206286	76.078	82.049
3	2.854	433475	39617	19.213	15.758
4	3.695	27250	1022	1.208	0.406
5	4.490	20658	962	0.916	0.383
Total		2256101	251418	100.000	100.000

Gambar 10. Kromatogram Standar Siklosporin pada konsentrasi 720 ppm

5. Kromatogram Standar Siklosporin pada konsentrasi 2400 ppm



PDA Ch1 220nm 4nm

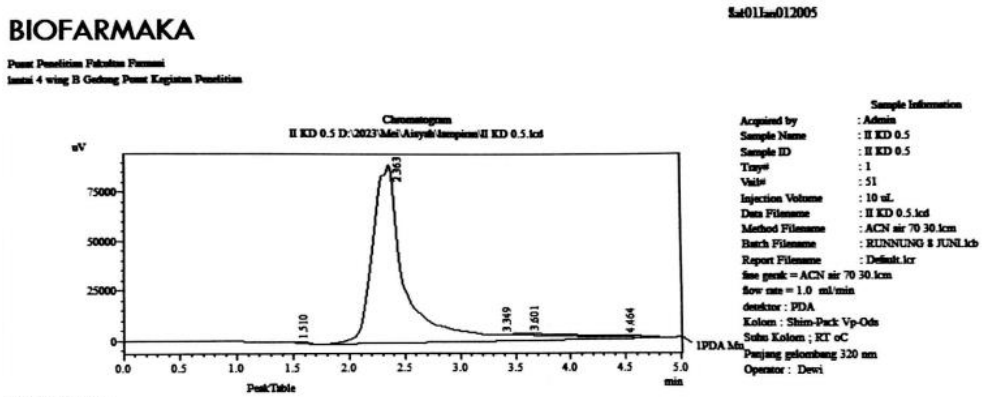
Peak#	Ret. Time	Area	Height	Area %	Height %
1	1.865	56943	3631	0.676	0.383
2	2.536	6740672	787593	80.081	83.128
3	2.883	1600149	155452	19.081	16.407
4	4.501	13551	774	0.161	0.082
Total		8417315	947450	100.000	100.000

Gambar 11. Kromatogram Standar Siklosporin pada konsentrasi 2400 ppm

Lampiran 6. Kromatogram Sampel Pengukuran Kadar Siklosporin

Data dibawah mewakili masing-masing kelompok

1. Kromatogram Sampel Pengukuran Siklosporin dalam plasma pada kelompok I

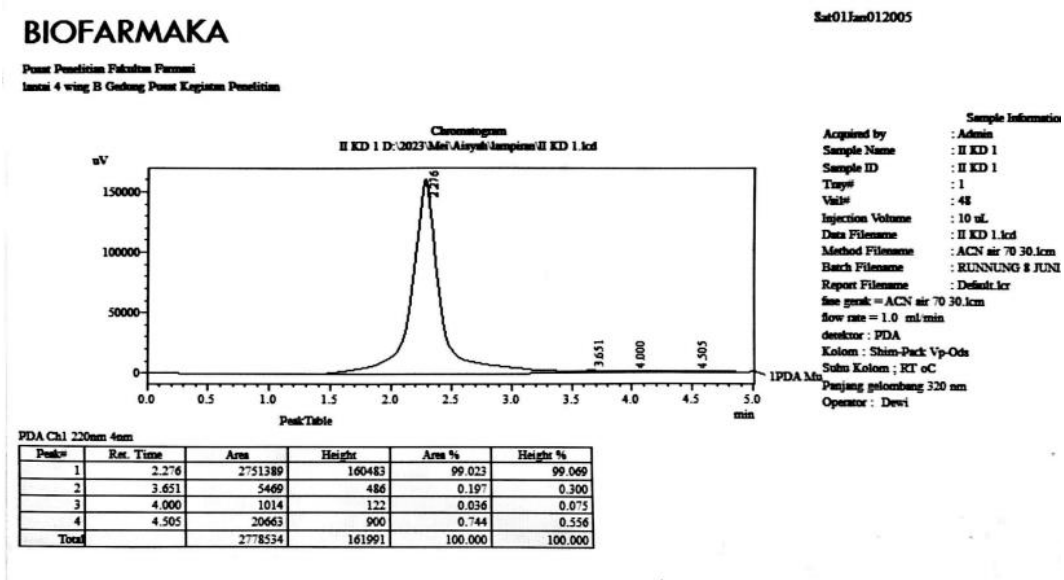


PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	1.510	3762	295	0.187	0.319
2	2.363	1963379	90329	97.527	97.771
3	3.349	3976	307	0.198	0.332
4	3.601	27007	779	1.342	0.843
5	4.464	15049	679	0.748	0.735
Total		2013174	92388	100.000	100.000

Gambar 12. Kromatogram Sampel Pengukuran Siklosporin dalam plasma pada kelompok I

2. Kromatogram Sampel Pengukuran Siklosporin dalam plasma pada kelompok II

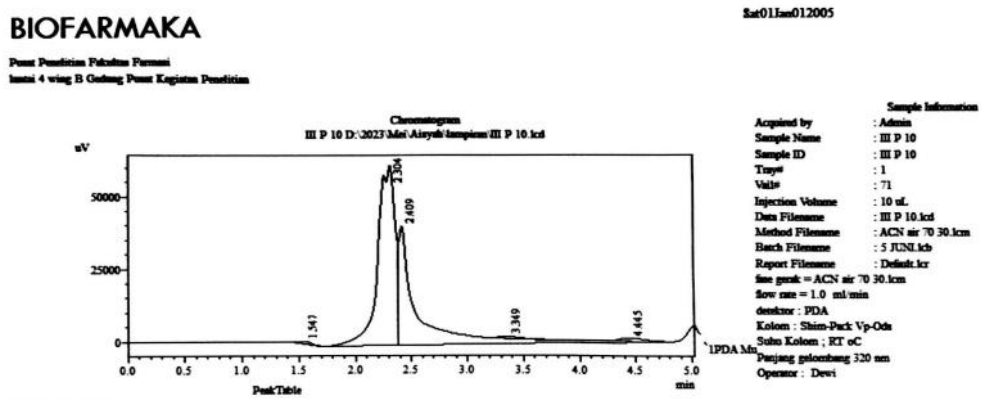


PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	2.276	2751389	160483	99.023	99.069
2	3.651	5469	486	0.197	0.300
3	4.000	1014	122	0.036	0.075
4	4.505	20663	900	0.744	0.556
Total		2778534	161991	100.000	100.000

Gambar 13. Kromatogram Sampel Pengukuran Siklosporin dalam plasma pada kelompok II

3. Kromatogram Sampel Pengukuran Siklosporin dalam plasma pada kelompok III

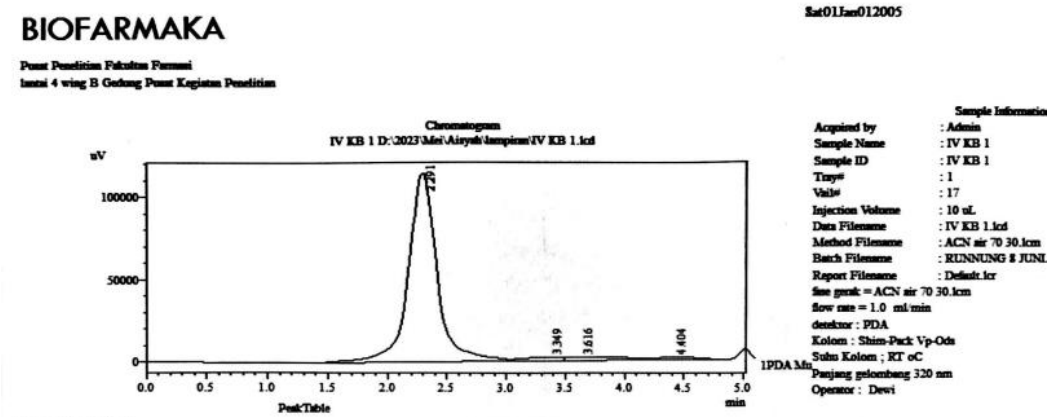


PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	1.547	5921	723	0.498	0.684
2	2.304	664305	61986	55.908	58.661
3	2.409	493062	41068	41.496	38.865
4	3.349	7241	675	0.609	0.639
5	4.445	17683	1216	1.488	1.151
Total		1188212	105668	100.000	100.000

Gambar 14. Kromatogram Sampel Pengukuran Siklosporin dalam plasma pada kelompok III

4. Kromatogram Sampel Pengukuran Siklosporin dalam plasma pada kelompok IV

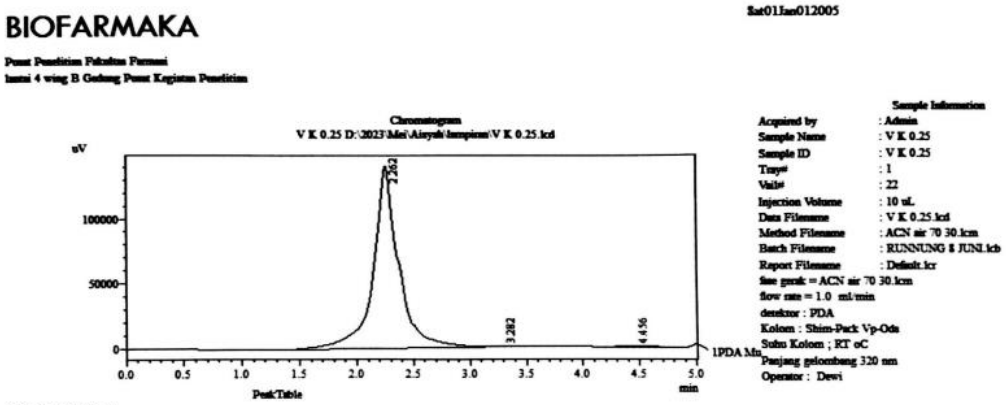


PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	2.291	1954527	114382	91.287	94.340
2	3.349	59121	2456	2.761	2.026
3	3.616	85048	2416	3.972	1.992
4	4.404	42386	1991	1.980	1.642
Total		2141081	121245	100.000	100.000

Gambar 15. Kromatogram Sampel Pengukuran Siklosporin dalam plasma pada kelompok IV

5. Kromatogram Sampel Pengukuran Siklosporin dalam plasma pada kelompok V



PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	2.262	2253271	140321	98.979	99.120
2	3.282	2388	187	0.105	0.132
3	4.456	20861	1059	0.916	0.748
Total		2276520	141567	100.000	100.000

Gambar 16. Kromatogram Sampel Pengukuran Siklosporin dalam plasma pada kelompok V

Lampiran 7. Kadar Siklosporin dalam darah pada tiap-tiap kelompok

Kelompok I NaCMC 0,5%

Tabel 8. Kadar Siklosporin dalam darah pada kelompok I

Time Point		Mice		
		1	2	3
0,25	luas area	947865,60	422999,30	2414174,50
	Conc (nM)	329,32	139,04	860,90
	Conc (ng/mL)	396,05	167,22	1035,33
	Ave (ng/mL)		532,87	
0,5	luas area	2210392,10	1624284,20	1127627,20
	Conc (nM)	787,03	574,55	394,49
	Conc (ng/mL)	946,49	690,95	474,42
	Ave (ng/mL)		703,95	
1	luas area	982222,8	1044589,90	1698085,90
	Conc (nM)	341,78	364,39	601,30
	Conc (ng/mL)	411,03	438,22	723,13
	Ave (ng/mL)		524,12	
2,5	luas area	479643,90	704361,80	1624284,20
	Conc (nM)	159,58	241,05	574,55
	Conc (ng/mL)	191,91	289,88	690,95
	Ave (ng/mL)		390,92	
5	luas area	721731,3	519651,80	331867,80
	Conc (nM)	247,34	174,08	106,01
	Conc (ng/mL)	297,46	209,35	127,48
	Ave (ng/mL)		211,43	
10	luas area	775719,60	369362,7	295033,50
	Conc (nM)	266,92	119,60	92,65
	Conc (ng/mL)	321,00	143,83	111,43
	Ave (ng/mL)		192,08	
24	luas area	466494,8	473763,50	346491,70
	Conc (nM)	154,81	157,45	111,31
	Conc (ng/mL)	186,18	189,35	133,86
	Ave (ng/mL)		169,80	

Kelompok II Konsentrat tomat 50 mg/kgBB

Tabel 9. Kadar Siklosporin dalam darah pada kelompok II

time point		mice			
		1	2	3	4
0,25	Area	2107280,20	1664687,10	2487522,50	2141233,30
	Conc (nM)	749,65	589,19	887,49	761,95
	Conc (ng/mL)	901,53	708,57	1067,31	916,33
	Ave (ng/mL)	898,44			
0,5	Area	1714413,70	1963379,30	1876332,90	2868525,20
	Conc (nM)	607,22	697,48	665,92	1025,62
	Conc (ng/mL)	730,25	838,79	800,84	1233,42
	Ave (ng/mL)	900,83			
1	Area	2549850,00	2751388,70	2598634,70	1868338,20
	Conc (nM)	910,09	983,15	927,78	663,02
	Conc (ng/mL)	1094,48	1182,35	1115,75	797,36
	Ave (ng/mL)	1047,49			
2,5	Area	1815664,00	1652208,30	1538624,70	2033295,80
	Conc (nM)	643,93	584,67	543,49	722,82
	Conc (ng/mL)	774,39	703,13	653,61	869,27
	Ave (ng/mL)	750,10			
5	Area	2259638,30	1760340,80	3555462,20	2161495,30
	Conc (nM)	804,88	623,87	1274,65	769,30
	Conc (ng/mL)	967,96	750,27	1532,91	925,17
	Ave (ng/mL)	1044,08			
10	Area	1993614,80	1783460,90	2347980,60	3305579,50
	Conc (nM)	708,44	632,25	836,91	1184,06
	Conc (ng/mL)	851,97	760,35	1006,47	1423,97
	Ave (ng/mL)	1010,69			
24	Area	2262971,30	2126372,60	1810085,50	1919571,20
	Conc (nM)	806,09	756,57	641,90	681,60
	Conc (ng/mL)	969,41	909,85	771,96	819,69
	Ave (ng/mL)	867,73			

Kelompok III Konsentrat tomat 150 mg/kgBB

Tabel 10. Kadar Siklosporin dalam darah pada kelompok III

time point		mice				
		1	2	3	4	5
0,25	height	622453,10	971753,70	1404109,9	1903103,1	661286,90
	Conc (nM)	211,35	337,98	494,73	675,63	225,43
	Conc (ng/mL)	254,17	406,46	594,96	812,51	271,11
	Ave (ng/mL)			467,84		
0,5	height	1664475,00	742560,90	545486,20	1433916,70	371326,80
	Conc (nM)	589,12	254,89	183,45	505,53	120,31
	Conc (ng/mL)	708,48	306,54	220,62	607,96	144,69
	Ave (ng/mL)			397,66		
1	height	357209,90	325602,90	473612,50	716787,80	1936399,40
	Conc (nM)	115,19	103,74	157,39	245,55	687,70
	Conc (ng/mL)	138,53	124,75	189,28	295,30	827,03
	Ave (ng/mL)			314,98		
2,5	height	634978,20	383649,10	717415,50	364210,70	338527,20
	Conc (nM)	215,89	124,78	245,78	117,73	108,42
	Conc (ng/mL)	259,64	150,06	295,58	141,59	130,39
	Ave (ng/mL)			195,45		
5	height	363413,90	1957442,50	400306,90	424512,10	564219,80
	Conc (nM)	117,44	695,32	130,82	139,59	190,24
	Conc (ng/mL)	141,24	836,20	157,32	167,88	228,79
	Ave (ng/mL)			306,29		
10	height	580161,40	539839,70	360258,70	1280484,00	493062,20
	Conc (nM)	196,02	181,40	116,30	449,91	164,44
	Conc (ng/mL)	235,74	218,16	139,86	541,06	197,76
	Ave (ng/mL)			266,52		
24	height	476996,10	354535,60	1082029,30	268948,00	1079871,90
	Conc (nM)	158,62	114,22	377,96	83,20	377,18
	Conc (ng/mL)	190,76	137,37	454,54	100,05	453,60
	Ave (ng/mL)			267,26		

Kelompok IV Konsentrat tomat 600 mg/kgBB

Tabel 11. Kadar Siklosporin dalam darah pada kelompok IV

time point		mice		
		1	2	3
0,25	height	487496,20	439064,50	433273,30
	Conc (nM)	162,43	144,87	142,77
	Conc (ng/mL)	195,34	174,22	171,70
	Ave (ng/mL)		180,42	
0,5	height	2177486,70	176874,40	1813532,10
	Conc (nM)	775,10	49,82	643,15
	Conc (ng/mL)	932,14	59,91	773,46
	Ave (ng/mL)		588,50	
1	height	1954526,50	875542,50	628386,50
	Conc (nM)	694,27	303,10	213,50
	Conc (ng/mL)	834,93	364,52	256,76
	Ave (ng/mL)		485,40	
2,5	height	481491,40	692300,60	631932,00
	Conc (nM)	160,25	236,67	214,79
	Conc (ng/mL)	192,72	284,63	258,31
	Ave (ng/mL)		245,22	
5	height	574745,40	373346,60	346806,80
	Conc (nM)	194,06	121,04	111,42
	Conc (ng/mL)	233,37	145,57	134,00
	Ave (ng/mL)		170,98	
10	height	709764,40	375372,60	469025,70
	Conc (nM)	243,01	121,78	155,73
	Conc (ng/mL)	292,24	146,45	187,28
	Ave (ng/mL)		208,66	
24	height	343030,50	243511,20	206060,30
	Conc (nM)	110,05	73,97	60,40
	Conc (ng/mL)	132,35	88,96	72,64
	Ave (ng/mL)		97,98	

Kelompok V Elacridar 20 mg/kgBB

Tabel 12. Kadar Siklosporin dalam darah pada kelompok V

time point		mice				
		1	2	3	4	5
0,25	height	751844,50	1528147,20	1750720,90		
	Conc (nM)	258,26	539,69	620,38		
	Conc (ng/mL)	310,59	649,04	746,08		
	Ave (ng/mL)			568,57		
0,5	height	1255234,10	1220098,00	1215223,00		
	Conc (nM)	440,75	428,02	426,25		
	Conc (ng/mL)	530,05	514,74	512,61		
	Ave (ng/mL)			519,13		
1	height	1215223,00	1760368,00	338819,10		
	Conc (nM)	426,25	623,88	108,53		
	Conc (ng/mL)	512,61	750,28	130,52		
	Ave (ng/mL)			162,71		
2,5	height	346062,80	902719,50	2167222,50	452525,50	
	Conc (nM)	111,15	312,96	771,38	149,75	
	Conc (ng/mL)	133,67	376,37	927,66	180,09	
	Ave (ng/mL)			404,45		
5	height	403272,90	215829,80	431700,10	344440,20	725485,80
	Conc (nM)	131,89	63,94	142,20	110,56	248,70
	Conc (ng/mL)	158,62	76,89	171,01	132,97	299,09
	Ave (ng/mL)			167,72		
10	height	356754,80	789175,30	395687,90	357532,00	
	Conc (nM)	115,03	271,79	129,14	115,31	
	Conc (ng/mL)	138,33	326,86	155,31	138,67	
	Ave (ng/mL)			189,79		
24	height	189277,20	310675,30	339194,40	448938,20	457851,20
	Conc (nM)	54,31	98,32	108,66	148,45	151,68
	Conc (ng/mL)	65,32	118,25	130,68	178,53	182,41
	Ave (ng/mL)			135,04		

Lampiran 8. Perhitungan *Area Under Curve* (AUC)

Tabel 13. Perhitungan *Area Under Curve* (AUC)

Treated	Mice	Time(min)								AUC(ng.min/mL)	AUC(ng/mL.hr)	Average	STd
		0	15	30	60	150	300	600	1440				
NaCMC	Mice1	0	396,05	946,49	411,03	191,91	297,46	321,00	186,18	587083,0047	9784,716745	8352,428	1309,161
	Mice2	0	167,22	690,95	438,22	289,88	209,35	143,83	189,35	433054,6696	7217,577826		
	Mice3	0	1035,33	474,42	723,13	690,95	127,48	111,43	133,86	483299,2911	8054,988186		
Tomat 50 mg/kgBB	Mice1	0	901,53	730,25	1094,48	774,39	967,96	851,97	969,41	1819729,961	30328,83268	32028,57	4079,605
	Mice2	0	708,57	838,79	1182,35	703,13	750,27	760,35	909,85	1626221,403	27103,69005		
	Mice3	0	1067,31	800,84	1115,75	653,61	1532,91	1006,47	771,96	2081495,931	34691,59885		
	Mice4	0	916,33	1233,42	797,36	869,27	925,17	1423,97	819,69	2159410,051	35990,16752		
Tomat 150 mg/kgBB	Mice1	0	254,17	708,48	138,53	259,64	141,24	235,74	190,76	428035,8437	7133,930729	9193,141	1627,172
	Mice2	0	406,46	306,54	124,75	150,06	836,20	218,16	137,37	661935,0248	11032,25041		
	Mice3	0	594,96	220,62	189,28	295,58	157,32	139,86	454,54	474907,9303	7915,132172		
	Mice4	0	812,51	607,96	295,30	141,59	167,88	541,06	100,05	616094,5207	10268,24201		
	Mice5	0	271,11	144,69	827,03	130,39	228,79	197,76	453,60	576968,875	9616,147917		
Tomat 600 mg/kgBB	Mice1	0	195,34	932,14	834,93	192,72	233,37	292,24	132,35	562339,8424	9372,330707	6910,294	2146,947
	Mice2	0	174,22	59,91	364,52	284,63	145,57	146,45	88,96	325677,3368	5427,955613		
	Mice3	0	171,70	773,46	256,76	258,31	134,00	187,28	72,64	355835,6637	5930,594395		
Elacridar	Mice 1	0	310,59	310,59			158,62	138,33	65,32	217047,041	3617,450684	6575,05	2114,263
	Mice 2	0	649,04	530,05		133,67	76,89	326,86	118,25	385275,7834	6421,263057		
	Mice 3	0	746,08	514,74	512,61	376,37	171,01	155,31	130,68	429857,2381	7164,287301		
	Mice 4	0		512,61	750,28	927,66	132,97	138,67	178,53	570401,3864	9506,689774		
	Mice 5	0			130,52	180,09	299,09	138,67	182,41	369933,5943	6165,559904		

Lampiran 9. Analisis Statistik

Tabel 2. ANOVA *Summary*

ANOVA summary	
F	20.22
P value	<0,0001
P value summary	****
Significant diff. among means (P < 0.05)?	Yes
R square	0,7294

Tabel 3. *Dunnett's Multiple Comparison*

Dunnett's multiple comparisons test	Mean Diff,	95,00% CI of diff,	Significant?	Summary	Adjusted P Value
NaCMC vs. tomat 50 mg/kgBB	-542	-761,5 to –322,5	Yes	****	<0,0001
NaCMC vs. Tomat 150 mgkgBB	72,74	-146,8 to 292,3	No	ns	0,8074
NaCMC vs. Tomat 600 mg/kgBB	106,9	-112,7 to 326,4	No	ns	0,5386
NaCMC vs. Elacridar	48,34	-171,2 to 267,8	No	ns	0,9442

Tabel 4. ANOVA *Summary* Cmax

ANOVA summary	
F	2.809
P value	0,0700
P value summary	ns
Significant diff. among means (P < 0.05)?	No
R square	0,4636

Tabel 5. *Dunnett's Multiple Comparison* Cmax

Dunnett's multiple comparisons test	Mean Diff,	95,00% CI of diff,	Significant?	Summary	Adjusted P Value
NaCMC vs. tomat 50 mg/kgBB	-343,5	-915,5 to 228,4	No	ns	0,3149
NaCMC vs. Tomat 150 mgkgBB	236,1	-310,8 to 783,0	No	ns	0,5771
NaCMC vs. Tomat 600 mg/kgBB	115,5	-496,0 to 726,9	No	ns	0,9524
NaCMC vs. Elacridar	135,4	-476,0 to 746,8	No	ns	0,9204

Tabel 6. ANOVA *Summary* AUC

ANOVA summary	
F	78,28
P value	<0,0001
P value summary	****
Significant diff. among means (P < 0.05)?	Yes
R square	0,9543

Tabel 7. *Dunnett's Multiple Comparison* AUC

Dunnett's multiple comparisons test	Mean Diff,	95,00% CI of diff,	Significant?	Summary	Adjusted P Value
NaCMC vs. tomat 50 mg/kgBB	-23676	-28752 to -18601	Yes	****	<0,0001
NaCMC vs. Tomat 150 mgkgBB	-840,7	-5694 to 4012	No	ns	0,9647
NaCMC vs. Tomat 600 mg/kgBB	1442	-3984 to 6868	No	ns	0,8653
NaCMC vs. Elacridar	1777	-3076 to 6630	No	ns	0,6991

Lampiran 10. Dokumentasi Penelitian

Gambar 17. Konsentrat Buah Tomat

Gambar 18. Siklosporin

Gambar 19. Elacridar

Gambar 20. Aklimatisasi hewan uji

Gambar 21. Penimbangan hewan coba

Gambar 22. Penyiapan sediaan uji

Gambar 23. Pemberian perlakuan hewan coba

Gambar 24. Pengambilan darah hewan coba

Gambar 25. Sentrifugasi sampel darah

Gambar 26. Preparasi sampel plasma

Gambar 27. Pengukuran kadar siklosporin menggunakan HPLC

Lampiran 11. Surat 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 : 314/UN4.6.4.5.31/ PP36/ 2023

Tanggal: 13 Mei 2023

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

No Protokol	UH23040250	No Sponsor	
Peneliti Utama	**Aisyatul Islamiyah Ridwan**	Sponsor	
Judul Peneliti	Pengaruh Inhibisi Transporter P-Glikoprotein (P-gp) Oleh Konsentrat Buah Tomat (Solanum lycopersicum) terhadap Profil Farmakokinetika Siklosporin Pada Mencit (Mus musculus).		
No Versi Protokol	**1**	Tanggal Versi	**14 April 2023**
No Versi PSP		Tanggal Versi	
Tempat Penelitian	Laboratorium Fakultas Farmasi Universitas Hasanuddin Makassar		
Jenis Review	☐ Exempted ☒ Expedited ☐ Fullboard Tanggal	Masa Berlaku **13 Mei 2023** sampai **13 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 Lapor 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