

## DAFTAR PUSTAKA

- Alkilani, A. Z., McCrudden, M. T. C., & Donnelly, R. F. 2015. Transdermal drug delivery: Innovative pharmaceutical developments based on disruption of the barrier properties of the stratum corneum. *Pharmaceutics*.7(4): 438–470. doi: <https://doi.org/10.3390/pharmaceutics7040438>
- Álvarez, L. A., Van de Sijpe, G., Desmet, S., Metsemakers, W. J., Spriet, I., Allegaert, K., & Rozenski, J. 2022. Ways to Improve Insights into Clindamycin Pharmacology and Pharmacokinetics Tailored to Practice. *Antibiotics*.11(5). doi: <https://doi.org/10.3390/antibiotics11050701>
- Anjani, Q. K., Permana, A. D., Cárcamo-Martínez, Á., Domínguez-Robles, J., Tekko, I. A., Larrañeta, E., Vora, L. K., Ramadon, D., & Donnelly, R. F. 2021. Versatility of hydrogel-forming microneedles in in vitro transdermal delivery of tuberculosis drugs. *European Journal of Pharmaceutics and Biopharmaceutics*.158: 294 – 312. doi: <https://doi.org/10.1016/j.ejpb.2020.12.003>
- Cano, A., Ettcheto, M., Espina, M., López-Machado, A., Cajal, Y., Rabanal, F., Sánchez-López, E., Camins, A., García, M. L., & Souto, E. B. 2020. State-of-the-art polymeric nanoparticles as promising therapeutic tools against human bacterial infections. *Journal of Nanobiotechnology*.18 (1). doi: <https://doi.org/10.1186/s12951-020-00714-2>
- Hasan, N., Cao, J., Lee, J., Hlaing, S. P., Oshi, M. A., Naeem, M., Ki, M. H., Lee, B. L., Jung, Y., & Yoo, J. W. 2019. Bacteria-targeted clindamycin loaded polymeric nanoparticles: Effect of surface charge on nanoparticle adhesion to MRSA, antibacterial activity, and wound healing. *Pharmaceutics*. 11(5). doi: <https://doi.org/10.3390/pharmaceutics11050236>
- Hung, S. Y., Chiu, C. H., Huang, C. H., Lin, C. W., Yeh, J. T., Yang, H. M., & Huang, Y. Y. 2022. Impact of wound microbiology on limb preservation in patients with diabetic foot infection. *Journal of Diabetes Investigation*. 13(2): 336–343. doi: <https://doi.org/10.1111/jdi.13649>
- International Diabetes Federation. 2021. Five Question on the IDF Diabetes Atlas. *Diabetes Research and Clinical Practice*.102:147–148.
- Jung, J. H., & Jin, S. G. 2021. Microneedle for transdermal drug delivery: current trends and fabrication. *Journal of Pharmaceutical Investigation*. 51(5): 503–517. doi: <https://doi.org/10.1007/s40005-021-00512-4>
- Kang, N. W., Kim, S., Lee, J. Y., Kim, K. T., Choi, Y., Oh, Y., Kim, J., Kim, D. D., & Park, J. H. 2021. Microneedles for drug delivery: recent advances in materials and geometry for preclinical and clinical studies. *Expert Opinion on Drug Delivery*. 18 (7): 929–947. doi: <https://doi.org/10.1080/17425247.2021.1828860>
- Trevor, A. J. 2016. *Basic and Clinical Pharmacology*. 13<sup>th</sup> ed. Elsevier-Williams & Wilkins Inc.
- Z. A. A. , K. R. , dan S. A. 2023. *Prevalence of diabetes in new of IDF Diabetes Atlas 10th edition*. Bentham Science Publishers. doi: <https://doi.org/10.2174/1573399819666230413094200>



- Kurakula, M., & Rao, G. S. N. K. 2020. Pharmaceutical assessment of polyvinylpyrrolidone (PVP): As excipient from conventional to controlled delivery systems with a spotlight on COVID-19 inhibition. In *Journal of Drug Delivery Science and Technology* (60). doi: <https://doi.org/10.1016/j.jddst.2020.102046>
- Kwon, K. T., & Armstrong, D. G. 2018. Microbiology and antimicrobial therapy for diabetic foot infections. In *Infection and Chemotherapy*. 50(1): 11–20. Korean Society of Infectious Diseases, Korean Society for Chemotherapy. doi:<https://doi.org/10.3947/ic.2018.50.1.11>
- Larrañeta, E., Moore, J., Vicente-Pérez, E. M., González-Vázquez, P., Lutton, R., Woolfson, A. D., & Donnelly, R. F. 2014. A proposed model membrane and test method for microneedle insertion studies. *International Journal of Pharmaceutics*. 472(1–2): 65–73. doi: <https://doi.org/10.1016/j.ijpharm.2014.05.042>
- Li, W., Tang, J., Terry, R. N., Li, S., Brunie, A., Callahan, R. L., Noel, R. K., Rodríguez, C. A., Schwendeman, S. P., & Prausnitz, M. R. 2019. Long-acting reversible contraception by effervescent microneedle patch. *Sci. Adv* 5. doi: <http://advances.sciencemag.org/>
- Lipsky, B. A., Senneville, E., Abbas, Z. G., Aragon\_Sanchez, J., Diggle, M., Embil, J. M., Kono, S., Lavery, L. A., Malone, M., Van Asten, S. A., Urbancic-Rovan, V., & Peters, E. J. G. 2019. *IWGDF Guideline on the diagnosis and treatment of foot infection in persons with diabetes*. [www.iwgdfguidelines.org](http://www.iwgdfguidelines.org)
- Liu, T., Jiang, G., Song, G., Sun, Y., Zhang, X., & Zeng, Z. 2021. Fabrication of Rapidly Separable Microneedles for Transdermal Delivery of Metformin on Diabetic Rats. *Journal of Pharmaceutical Sciences*. 110(8): 3004–3010. doi:<https://doi.org/10.1016/j.xphs.2021.04.009>
- Macdonald, K. E., Boeckh, S., Stacey, H. J., & Jones, J. D. 2021. The microbiology of diabetic foot infections: a meta-analysis. *BMC Infectious Diseases*. 21(1). doi: <https://doi.org/10.1186/s12879-021-06516-7>
- Maqbool, I., Noreen, S., Pervaiz, F., Ijaz, M., & Farooq, I. 2019. Micro Particles: A Review of Recent Developments, Microencapsulation Method, and Therapeutic Strategies. *Global Pharmaceutical Sciences Review*. 4(1): 28–39. doi:[https://doi.org/10.31703/gpsr.2019\(iv-i\).04](https://doi.org/10.31703/gpsr.2019(iv-i).04)
- Mudjahid, M., Nainu, F., Utami, R. N., Sam, A., Marzaman, A. N. F., Roska, T. P., Asri, R. M., Himawan, A., Donnelly, R. F., & Permana, A. D. 2022. Enhancement in Site-Specific Delivery of Chloramphenicol Using Bacterially Sensitive Microparticle Loaded into Dissolving Microneedle: Potential for Enhanced Effectiveness Treatment of Cellulitis. *ACS Applied Materials Interfaces*. doi:<https://doi.org/10.1021/acsmi.2c16857>
- ..., C. G., and L. J. K. 2022. *Clindamycin*. Treasure Island: StatPearls Publishing.
- ..., M. A., Fitri Sultan, N. A., Saputra, N., Friandini, R. A., Natsir Djide, N. J., & Permana, A. D. 2022. Chitosan-chitosan hydrogel forming microneedle-mediated transdermal delivery of tadalafil citrate from direct-compressed tablet reservoir for



- potential improvement of pulmonary hypertension therapy. *International Journal of Pharmaceutics*. 631. doi: <https://doi.org/10.1016/j.ijpharm.2022.122549>
- Pavlović, N., Bogičević, I. A., Zaklan, D., Đanić, M., Goločorbin-Kon, S., Al-Salami, H., & Mikov, M. 2022. Influence of Bile Acids in Hydrogel Pharmaceutical Formulations on Dissolution Rate and Permeation of Clindamycin Hydrochloride. *Gels*. 8(1). doi: <https://doi.org/10.3390/gels8010035>
- Permana, A. D., Anjani, Q. K., Sartini, Utomo, E., Volpe-Zanutto, F., Paredes, A. J., Evary, Y. M., Mardikasari, S. A., Pratama, M. R., Tuany, I. N., & Donnelly, R. F. 2021a. Selective delivery of silver nanoparticles for improved treatment of biofilm skin infection using bacteria-responsive microparticles loaded into dissolving microneedles. *Materials Science and Engineering C*. 120. doi:<https://doi.org/10.1016/j.msec.2020.111786>
- Pünnel, L. C., & Lunter, D. J. 2021. Film-forming systems for dermal drug delivery. *Pharmaceutics*. 13(7). MDPI. doi: <https://doi.org/10.3390/pharmaceutics13070932>
- Ramirez-Acuña, J. M., Cardenas-Cadena, S. A., Marquez-Salas, P. A., Garza-Veloz, I., Perez-Favila, A., Cid-Baez, M. A., Flores-Morales, V., & Martinez-Fierro, M. L. (2019). Diabetic foot ulcers: Current advances in antimicrobial therapies and emerging treatments. *Antibiotics*. 8(4). doi: <https://doi.org/10.3390/antibiotics8040193>
- Rowe, R. C., Sheshey, P. J., & Quinn, M. E. 2009. *Handbook of Pharmaceutical Excipients* (6th ed.). Pharmaceutical Press and American Pharmacists Association.
- Syafika, N., Azis, S. B. A., Enggi, C. K., Qonita, H. A., Mahmud, T. R. A., Abizart, A., Asri, R. M., & Permana, A. D. 2023. Glucose-Responsive Microparticle-Loaded Dissolving Microneedles for Selective Delivery of Metformin: A Proof-of-Concept Study. *Molecular Pharmaceutics*. 20(2): 1269–1284. doi: <https://doi.org/10.1021/acs.molpharmaceut.2c00936>
- Tekko, I. A., Chen, G., Domínguez-Robles, J., Thakur, R. R. S., Hamdan, I. M. N., Vora, L., Larrañeta, E., McElnay, J. C., McCarthy, H. O., Rooney, M., & Donnelly, R. F. 2020. Development and characterisation of novel poly (vinyl alcohol)/poly (vinyl pyrrolidone)-based hydrogel-forming microneedle arrays for enhanced and sustained transdermal delivery of methotrexate. *International Journal of Pharmaceutics*. 586. doi: <https://doi.org/10.1016/j.ijpharm.2020.119580>
- Teodorescu, M., Bercea, M., & Morariu, S. 2019. Biomaterials of PVA and PVP in medical and pharmaceutical applications: Perspectives and challenges. *Technology Advances*. 37(1): 109–131. doi: <https://doi.org/10.1016/j.biotechadv.2018.11.008>
- vi, G., Dubey, S. K., Pandey, M. M., Gupta, G., Singh, M., & Donnelly, R. F. 2020. Microneedles: A smart approach and increasing potential for drug delivery system. In *Biomedicine and Pharmacotherapy*. 49–1258. Elsevier Masson SAS. doi: <https://doi.org/10.1016/j.biopha.2018.10.078>

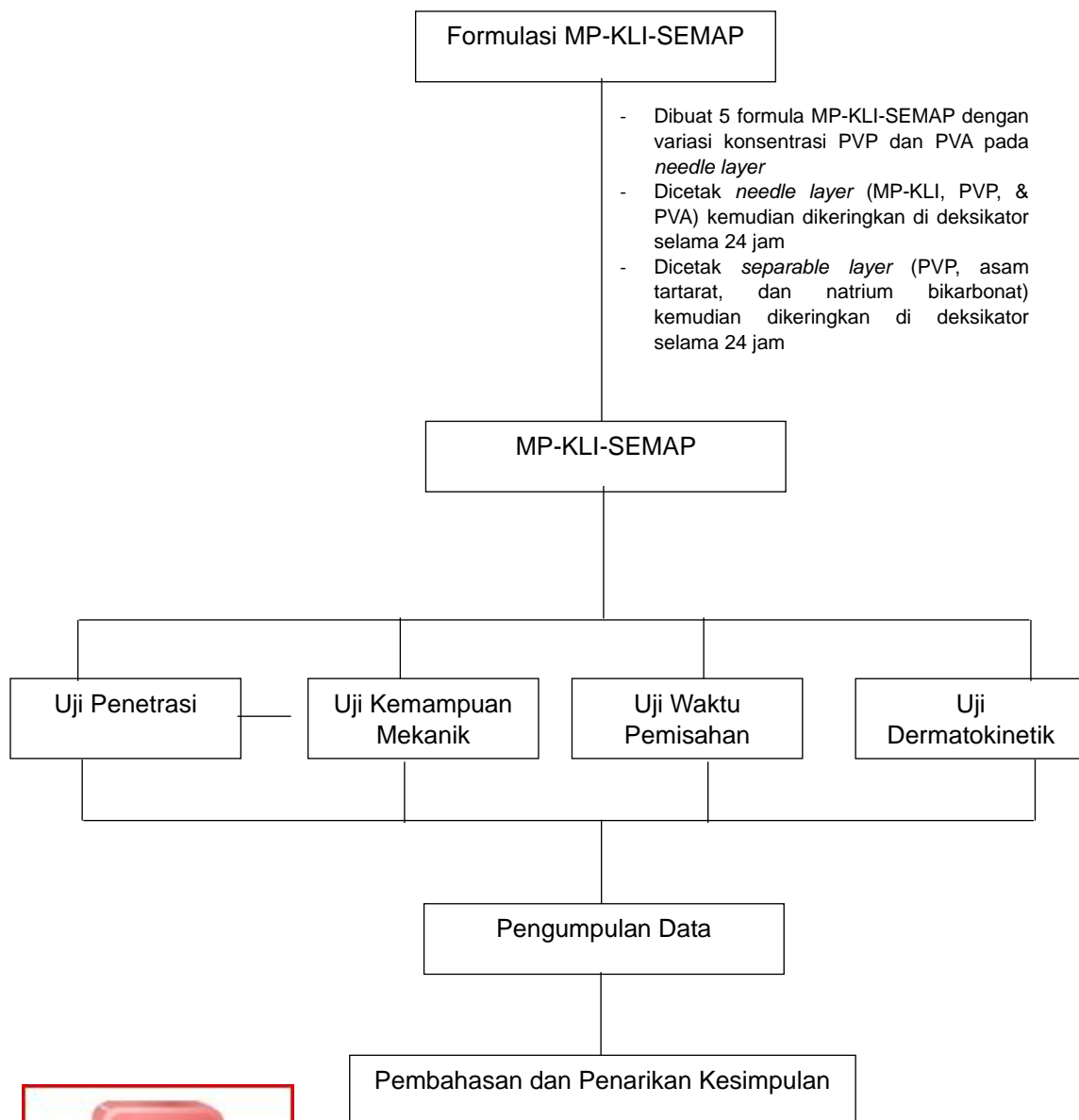


- Webber, S. 2013. International Diabetes Federation. *Diabetes Research and Clinical Practice*. 102(2): 147–148. doi: <https://doi.org/10.1016/j.diabres.2013.10.013>
- Yang, P., Lu, C., Qin, W., Chen, M., Quan, G., Liu, H., Wang, L., Bai, X., Pan, X., & Wu, C. (2020). Construction of a core-shell microneedle system to achieve targeted co-delivery of checkpoint inhibitors for melanoma immunotherapy. *Acta Biomaterialia*. 104: 147–157. doi: <https://doi.org/10.1016/j.actbio.2019.12.037>



## LAMPIRAN

### Lampiran 1. Skema Kerja



## Lampiran 2. Hasil uji morfologi, dan kekuatan mekanik MP-KLI-SEMAP

Tabel 4. Hasil uji kekuatan mekanik

Formula	Sebelum Uji Kekuatan Mekanik (Uji morfologi)		Setelah Uji Kekuatan Mekanik		% Penurunan tinggi jarum	Rata-rata $\pm$ SD
	Panjang ( $\mu\text{m}$ )	Rata-rata $\pm$ SD	Panjang ( $\mu\text{m}$ )	Rata-rata $\pm$ SD		
F1	707	703,33	540	537,33	23,62	23,60 $\pm$ 1,62
	701	$\pm$ 3,21	547	$\pm$ 11,23	21,97	
	702		525		25,21	
F2	705	703,33	674	669,33	4,40	4,83 $\pm$ 2,65
	704	$\pm$ 2,08	650	$\pm$	7,67	
	701		684	17,47	2,43	
F3	704	701,67	687	665	2,414	5,22 $\pm$ 2,65
	699	$\pm$ 2,52	660	$\pm$ 19,97	5,58	
	702		648		7,70	
F4	707	704,67	620	627,33	12,31	10,97 $\pm$ 1,16
	701	$\pm$ 3,21	630	$\pm$ 6,42	10,13	
	706		632		10,48	
F5	702	706,67	519	511	26,07	27,48 $\pm$ 1,29
	706	$\pm$ 2,31	510	$\pm$ 7,55	27,76	
	706		504		28,62	



### Lampiran 3. Hasil uji kemampuan penetrasi MP-KLI-SEMAP

**Tabel 5.** Hasil uji kemampuan penetrasi

Lapisan	Jumlah lubang yang terbentuk					%penetrasi				
	F1	F2	F3	F4	F5	F1	F2	F3	F4	F5
1	100	100	100	100	100	100	100	100	100	100
2	65	100	100	80	77	65	100	100	80	77
3	34	97	72	65	28	33,67	96,67	72	65,33	28
4	0	82	14	0	0	0	81,67	14,33	0	0
5	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0

Perhitungan:

- a. Contoh perhitungan presentase penurunan tinggi jarum

Diketahui untuk F1 replikasi pertama, tinggi *microneedle* sebelum dilakukan uji kekuatan mekanik adalah 707  $\mu\text{m}$  dan setelah dilakukan uji kekuatan mekanik tingginya menjadi 540  $\mu\text{m}$ , maka :

$$\begin{aligned} \text{Pengurangan ketinggian jarum} &= \frac{\text{Tinggi sebelum uji} - \text{Tinggi setelah uji}}{\text{Tinggi sebelum uji}} \times 100\% \\ &= \frac{707 - 540}{707} \times 100\% \\ &= 23,62\% \end{aligned}$$

- b. Contoh perhitungan presentase penetrasi lapisan ke-n

Diketahui untuk F1 lapisan ke-3 terbentuk 34 lubang dari 100 *needle*, maka

$$\begin{aligned} \text{Jumlah lubang dalam parafilm} &= \frac{\text{Jumlah lubang yang diamati}}{\text{Jumlah lubang keseluruhan}} \times 100\% \\ &= \frac{34}{100} \times 100\% \\ &= 34\% \end{aligned}$$



**Lampiran 4. Hasil uji waktu pemisahan****Tabel 6.** Uji waktu pemisahan MP-KLI-SEMAP

Formula	Replikasi			Rata-rata $\pm$ SD
	1 (detik)	2 (detik)	3 (detik)	
F1	59	53	62	58 $\pm$ 4,58
F2	54	63	51	56 $\pm$ 5,1
F3	55	58	60	57,67 $\pm$ 2,52
F4	58	57	59	58 $\pm$ 0,82
F5	61	59	52	57 $\pm$ 4,73





### Lampiran 5. Hasil Uji dermatokinetik secara *ex vivo* pada kulit normal

**Tabel 7.** Hasil uji dermatokinetik Krim-KLI

Waktu	Absorpsi	Konsentrasi mikrogram/mL	Volume	Faktor pengenceran	Jumlah KLI dalam kulit	Mikrogram/cm <sup>2</sup>	Rata-rata	SD
1	0	0	2	2	0	0	0	0
	0	0	2	2	0	0		
	0	0	2	2	0	0		
2	0	0	2	2	0	0	0	0
	0	0	2	2	0	0		
	0	0	2	2	0	0		
3	0	0	2	2	0	0	0	0
	0	0	2	2	0	0		
	0	0	2	2	0	0		
4	0.0205	0.79	2	2	3.16	1.96	1.74	0.26
	0.019	0.73	2	2	2.91	1.80		
	0.0155	0.58	2	2	2.33	1.45		
5	0.031	1.22	2	2	4.89	3.04	3.53	0.51
	0.041	1.64	2	2	6.55	4.06		
	0.0355	1.41	2	2	5.64	3.50		
6	0.021	0.81	2	2	3.24	2.01	2.28	0.24
	0.0245	0.95	2	2	3.82	2.37		
	0.0255	1.00	2	2	3.98	2.47		
	0.0205	0.79	2	2	3.16	1.96	1.87	0.08
	0.0195	0.75	2	2	2.99	1.86		
	0.019	0.73	2	2	2.91	1.80		
	0.0155	0.58	2	2	2.33	1.45	1.62	0.18
	0.019	0.73	2	2	2.91	1.80		
	0.017	0.64	2	2	2.58	1.60		



**Tabel 8.** Hasil uji dermatokinetik Krim MP-KLI

Waktu	Absorpsi	Konsentrasi mikrogram /mL	Volume	Faktor pengenceran	Jumlah KLI dalam kulit	Mikrogram/cm <sup>2</sup>	Rata-rata	SD
1	0	0	2	2	0	0	0	0
	0	0	2	2	0	0		
	0	0	2	2	0	0		
2	0	0	2	2	0	0	0	0
	0	0	2	2	0	0		
	0	0	2	2	0	0		
3	0	0	2	2	0	0	0	0
	0	0	2	2	0	0		
	0	0	2	2	0	0		
4	0.0205	0.016	0.60	2	2	2.41	1.96	0.42
	0.019	0.0215	0.83	2	2	3.32		
	0.0155	0.024	0.93	2	2	3.74		
5	0.031	0.027	1.06	2	2	4.23	2.93	0.34
	0.041	0.0295	1.16	2	2	4.64		
	0.0355	0.0335	1.33	2	2	5.31		
6	0.021	0.0395	1.57	2	2	6.30	4.16	0.32
	0.0245	0.041	1.64	2	2	6.55		
	0.0255	0.0455	1.82	2	2	7.29		
	0.0205	0.0215	0.83	2	2	3.32	1.98	0.11
	0.0195	0.021	0.81	2	2	3.24		
	0.019	0.0195	0.75	2	2	2.99		
	0.0155	0.0195	0.75	2	2	2.99	1.65	0.27
	0.019	0.0185	0.71	2	2	2.83		
	0.017	0.0145	0.54	2	2	2.17		



**Tabel 9.** Hasil uji dermatokinetik KLI-SEMAP pada kulit normal

Waktu	Absorpsi	Konsentrasi mikrogram /mL	Volume	Faktor pengenceran	Jumlah KLI dalam kulit	Mikrogram/cm <sup>2</sup>	Rata-rata	SD
1	0.117	4.78	2	2	19.11	11.85	14.21	2.20
	0.1595	6.53	2	2	26.13	16.21		
	0.1435	5.87	2	2	23.49	14.57		
2	0.3815	15.71	2	2	62.83	38.98	40.22	1.08
	0.4005	16.49	2	2	65.97	40.92		
	0.399	16.43	2	2	65.72	40.77		
3	0.2715	11.16	2	2	44.64	27.70	24.35	3.61
	0.2015	8.27	2	2	33.07	20.52		
	0.2435	10.00	2	2	40.02	24.83		
4	0.1295	5.29	2	2	21.17	13.14	13.68	0.56
	0.1405	5.75	2	2	22.99	14.26		
	0.1345	5.50	2	2	22.00	13.65		
5	0.051	2.05	2	2	8.20	5.09	6.18	1.05
	0.0715	2.90	2	2	11.59	7.19		
	0.0625	2.52	2	2	10.10	6.27		
6	0.046	1.84	2	2	7.37	4.57	4.51	0.16
	0.0465	1.86	2	2	7.45	4.62		
	0.0435	1.74	2	2	6.96	4.32		
	0.0195	0.75	2	2	2.99	1.86	2.25	0.36
	0.0065	1.04	2	2	4.15	2.57		
	0.0024	0.93	2	2	3.74	2.32		
	0.0015	0.83	2	2	3.32	2.06	2.08	0.28
	0.0045	0.95	2	2	3.82	2.37		
	0.0019	0.73	2	2	2.91	1.80		



**Tabel 10.** Hasil uji dermatokinetik MP-KLI-SEMAP pada kulit normal

Waktu	Absorpsi	Konsentrasi mikrogram /mL	Volume	Faktor pengenceran	Jumlah KLI dalam kulit	Mikrogram/cm <sup>2</sup>	Rata-rata	SD
1	0	0	2	2	0	0	0	0
	0	0	2	2	0	0		
	0	0	2	2	0	0		
	0	0	2	2	0	0		
2	0	0	2	2	0	0	0	0
	0	0	2	2	0	0		
	0	0	2	2	0	0		
	0	0	2	2	0	0		
3	0	0	2	2	0	0	0	0
	0	0	2	2	0	0		
	0	0	2	2	0	0		
	0	0	2	2	0	0		
4	0	0	2	2	0	0	0	0
	0	0	2	2	0	0		
	0	0	2	2	0	0		
	0	0	2	2	0	0		
5	0.031	1.22	2	2	4.89	3.04	3.24	0.44
	0.029	1.14	2	2	4.56	2.83		
	0.039	1.55	2	2	6.21	3.86		
	0.035	1.39	2	2	5.55	3.45		
6	0.038	1.51	2	2	6.05	3.75	3.51	0.17
	0.034	1.35	2	2	5.39	3.34		
	0.043	1.72	2	2	6.88	4.27		
	0.039	1.55	2	2	6.21	3.86		
	0.036	1.43	2	2	5.72	3.55	3.89	0.29
	0.036	1.43	2	2	5.72	3.55		
	0.037	1.47	2	2	5.88	3.65		
	0.038	1.51	2	2	6.05	3.75		



**Lampiran 6. Hasil uji dematokinetik secara ex vivo pada model kulit terinfeksi**

**Tabel 11.** Hasil uji dermatokinetik Krim KLI pada model kulit terinfeksi

Waktu	Absorpsi	Konsentrasi mikrogram /mL	Volume	Faktor pengenceran	Jumlah KLI dalam kulit	Mikrogram/cm <sup>2</sup>	Rata-rata	SD
1	0	0	2	2	0	0	0	0
	0	0	2	2	0	0		
	0	0	2	2	0	0		
	0	0	2	2	0	0		
2	0	0	2	2	0	0	0	0
	0	0	2	2	0	0		
	0	0	2	2	0	0		
	0	0	2	2	0	0		
3	0	0	2	2	0	0	0	0
	0	0	2	2	0	0		
	0	0	2	2	0	0		
	0	0	2	2	0	0		
4	0.027	4.14	2	2	16.55	10.26	10.37	0.42
	0.0245	4.36	2	2	17.45	10.83		
	0.016	4.03	2	2	16.13	10.01		
	0.039	9.32	2	2	37.29	23.13		
5	0.0405	8.17	2	2	32.66	20.26	21.48	1.49
	0.0315	8.48	2	2	33.9	21.03		
	0.022	15.29	2	2	61.17	37.95		
	0.0195	16.51	2	2	66.05	40.98		
6	0.0265	16.12	2	2	64.48	40	39.64	1.54
	0.0195	11.99	2	2	47.95	29.75		
	0.022	10	2	2	40.02	24.83		
	0.015	10.93	2	2	43.74	27.13		
	0.0165	9.92	2	2	39.69	24.62		
	0.02	9.47	2	2	37.87	23.49		
	0.0155	9.76	2	2	39.02	24.21		
	0.02	10.93	2	2	43.74	27.13		
0.015	9.92	2	2	39.69	24.62			
0.02	9.47	2	2	37.87	23.49			
0.0155	9.76	2	2	39.02	24.21			



**Tabel 12.** Hasil uji dermatokinetik Krim MP-KLI pada model kulit terinfeksi

Waktu	Absorpsi	Konsentrasi mikrogram /mL	Volume	Faktor pengenceran	Jumlah KLI dalam kulit	Mikrogram/cm <sup>2</sup>	Rata-rata	SD
1	0	0	2	2	0	0	0	0
	0	0	2	2	0	0		
	0	0	2	2	0	0		
2	0	0	2	2	0	0	0	0
	0	0	2	2	0	0		
	0	0	2	2	0	0		
3	0	0	2	2	0	0	0	0
	0	0	2	2	0	0		
	0	0	2	2	0	0		
4	0.016	4.14	2	2	16.55	10.26	10.37	0.42
	0.0215	4.36	2	2	17.45	10.83		
	0.024	4.03	2	2	16.13	10.01		
	0.027	9.32	2	2	37.29	23.13		
5	0.0295	8.17	2	2	32.66	20.26	21.48	1.49
	0.0335	8.48	2	2	33.9	21.03		
	0.0395	15.29	2	2	61.17	37.95		
6	0.041	16.51	2	2	66.05	40.98	39.64	1.54
	0.0455	16.12	2	2	64.48	40		
	0.0215	11.99	2	2	47.95	29.75		
	0.021	10	2	2	40.02	24.83		
7	0.0195	10.93	2	2	43.74	27.13	27.24	2.46
	0.0195	9.92	2	2	39.69	24.62		
	0.0185	9.47	2	2	37.87	23.49		
	0.0145	9.76	2	2	39.02	24.21		



**Tabel 13.** Hasil uji dermatokinetik KLI-SEMAP pada model kulit terinfeksi

Waktu	Absorpsi	Konsentrasi mikrogram /mL	Volume	Faktor pengenceran	Jumlah KLI dalam kulit	Mikrogram/cm <sup>2</sup>	Rata-rata	SD
1	0.1255	0.6	2	2	2.41	1.5	1.57	0.26
	0.149	0.54	2	2	2.17	1.34		
	0.1505	0.75	2	2	2.99	1.86		
2	0.4055	1.29	2	2	5.14	3.19	3.75	0.56
	0.3715	1.74	2	2	6.96	4.32		
	0.391	1.51	2	2	6.05	3.75		
3	0.216	2.71	2	2	10.84	6.73	7.51	0.73
	0.251	3.29	2	2	13.16	8.16		
	0.2435	3.08	2	2	12.33	7.65		
4	0.1325	4.14	2	2	16.55	10.26	10.37	0.42
	0.1215	4.36	2	2	17.45	10.83		
	0.1155	4.03	2	2	16.13	10.01		
5	0.0565	9.32	2	2	37.29	23.13	21.48	1.49
	0.067	8.17	2	2	32.66	20.26		
	0.0725	8.48	2	2	33.9	21.03		
6	0.0545	15.29	2	2	61.17	37.95	39.64	1.54
	0.0465	16.51	2	2	66.05	40.98		
	0.0505	16.12	2	2	64.48	40		
7	0.021	11.99	2	2	47.95	29.75	27.24	2.46
	0.015	10	2	2	40.02	24.83		
	0.019	10.93	2	2	43.74	27.13		
8	0.005	9.92	2	2	39.69	24.62	24.11	0.57
	0.045	9.47	2	2	37.87	23.49		
	0.085	9.76	2	2	39.02	24.21		



**Tabel 14.** Hasil uji dermatokinetik MP-KLI-SEMAP pada model kulit terinfeksi bakteri

Waktu	Absorpsi	Konsentrasi mikrogram /mL	Volume	Faktor pengenceran	Jumlah KLI dalam kulit	Mikrogram/cm <sup>2</sup>	Rata-rata	SD
1	0.016	0.60	2	2	2.41	1.50	1.57	0.26
	0.0145	0.54	2	2	2.17	1.34		
	0.0195	0.75	2	2	2.99	1.86		
2	0.0325	1.29	2	2	5.14	3.19	3.75	0.56
	0.0435	1.74	2	2	6.96	4.32		
	0.038	1.51	2	2	6.05	3.75		
3	0.067	2.71	2	2	10.84	6.73	7.51	0.73
	0.081	3.29	2	2	13.16	8.16		
	0.076	3.08	2	2	12.33	7.65		
4	0.1015	4.14	2	2	16.55	10.26	10.37	0.42
	0.107	4.36	2	2	17.45	10.83		
	0.099	4.03	2	2	16.13	10.01		
5	0.227	9.32	2	2	37.29	23.13	21.48	1.49
	0.199	8.17	2	2	32.66	20.26		
	0.2065	8.48	2	2	33.90	21.03		
6	0.3715	15.29	2	2	61.17	37.95	39.64	1.54
	0.401	16.51	2	2	66.05	40.98		
	0.3915	16.12	2	2	64.48	40.00		
7	0.2915	11.99	2	2	47.95	29.75	27.24	2.46
	0.35	10.00	2	2	40.02	24.83		
	0.36	10.93	2	2	43.74	27.13		
8	0.15	9.92	2	2	39.69	24.62	24.11	0.57
	0.05	9.47	2	2	37.87	23.49		
	0.75	9.76	2	2	39.02	24.21		





## Lampiran 7. Data Statistik

### Lampiran 7.1. Uji Kekuatan Mekanik

Tests of Normality							
	Formula	Kolmogorov-Smirnov <sup>a</sup>			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
Uji mekanik	F1	.176	3	.	1.000	3	.976
	F2	.232	3	.	.980	3	.727
	F3	.219	3	.	.987	3	.784
	F4	.328	3	.	.870	3	.295
	F5	.253	3	.	.964	3	.637

a. Lilliefors Significance Correction

ANOVA					
Uji mekanik					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	1329.672	4	332.418	84.003	.000
Within Groups	39.572	10	3.957		
Total	1369.244	14			

Multiple Comparisons							
Dependent Variable: uji mekanik							
	(I) formula	(J) formula	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Tukey HSD	F1	F2	18.77000*	1.62423	.000	13.4245	24.1155
		F3	18.37333*	1.62423	.000	13.0279	23.7188
		F4	12.63000*	1.62423	.000	7.2845	17.9755
		F5	-3.88000	1.62423	.195	-9.2255	1.4655
	F2	F1	-18.7700*	1.62423	.000	-24.1155	-13.4245
		F3	-.39667	1.62423	.999	-5.7421	4.9488
		F4	-6.14000*	1.62423	.023	-11.4855	-.7945
		F5	-22.6500*	1.62423	.000	-27.9955	-17.3045
	F3	F1	-18.3733*	1.62423	.000	-23.7188	-13.0279
		F2	.39667	1.62423	.999	-4.9488	5.7421
		F4	-5.74333*	1.62423	.034	-11.0888	-.3979
		F5	-22.2533*	1.62423	.000	-27.5988	-16.9079
		F1	-12.6300*	1.62423	.000	-17.9755	-7.2845
		F2	6.14000*	1.62423	.023	.7945	11.4855
		F3	5.74333*	1.62423	.034	.3979	11.0888
		F5	-16.5100*	1.62423	.000	-21.8555	-11.1645
F1	3.88000	1.62423	.195	-1.4655	9.2255		
F2	22.65000*	1.62423	.000	17.3045	27.9955		



		F3	22.25333*	1.62423	.000	16.9079	27.5988
		F4	16.51000*	1.62423	.000	11.1645	21.8555
Games-Howell	F1	F2	18.77000*	1.79580	.005	9.8720	27.6680
		F3	18.37333*	1.79822	.005	9.4570	27.2897
		F4	12.63000*	1.15568	.003	7.2128	18.0472
		F5	-3.88000	1.20095	.138	-9.3564	1.5964
	F2	F1	-18.7700*	1.79580	.005	-27.6680	-9.8720
		F3	-.39667	2.16744	1.000	-10.0322	9.2389
		F4	-6.14000	1.67326	.141	-15.6240	3.3440
		F5	-22.6500*	1.70484	.004	-31.9052	-13.3948
	F3	F1	-18.3733*	1.79822	.005	-27.2897	-9.4570
		F2	.39667	2.16744	1.000	-9.2389	10.0322
		F4	-5.74333	1.67585	.163	-15.2491	3.7625
		F5	-22.2533*	1.70739	.004	-31.5295	-12.9771
	F4	F1	-12.6300*	1.15568	.003	-18.0472	-7.2128
		F2	6.14000	1.67326	.141	-3.3440	15.6240
		F3	5.74333	1.67585	.163	-3.7625	15.2491
		F5	-16.5100*	1.00856	.000	-21.0194	-12.0006
F5	F1	3.88000	1.20095	.138	-1.5964	9.3564	
	F2	22.65000*	1.70484	.004	13.3948	31.9052	
	F3	22.25333*	1.70739	.004	12.9771	31.5295	
	F4	16.51000*	1.00856	.000	12.0006	21.0194	

\*. The mean difference is significant at the 0.05 level.

## Lampiran 7.2. Uji Kemampuan Penetrasi

Tests of Normality							
	Formula	Kolmogorov-Smirnov <sup>a</sup>			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
Kemampuan penetrasi	F1	.	3	.	.	3	.
	F2	.219	3	.	.987	3	.780
	F3	.321	3	.	.881	3	.328
	F4	.	3	.	.	3	.
	F5	.	3	.	.	3	.

a. Lilliefors Significance Correction

ANOVA					
Kemampuan penetrasi					
	Sum of Squares	df	Mean Square	F	Sig.
	15095.067	4	3773.767	463.988	.000
	81.333	10	8.133		
	15176.400	14			



Multiple Comparisons							
Dependent Variable: Kemampuan penetrasi							
	(I) Formula	(J) Formula	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Tukey HSD	F1	F2	-81.66667*	2.32857	.000	-89.3302	-74.0032
		F3	-14.33333*	2.32857	.001	-21.9968	-6.6698
		F4	.00000	2.32857	1.000	-7.6635	7.6635
		F5	.00000	2.32857	1.000	-7.6635	7.6635
	F2	F1	81.66667*	2.32857	.000	74.0032	89.3302
		F3	67.33333*	2.32857	.000	59.6698	74.9968
		F4	81.66667*	2.32857	.000	74.0032	89.3302
		F5	81.66667*	2.32857	.000	74.0032	89.3302
	F3	F1	14.33333*	2.32857	.001	6.6698	21.9968
		F2	-67.33333*	2.32857	.000	-74.9968	-59.6698
		F4	14.33333*	2.32857	.001	6.6698	21.9968
		F5	14.33333*	2.32857	.001	6.6698	21.9968
	F4	F1	.00000	2.32857	1.000	-7.6635	7.6635
		F2	-81.66667*	2.32857	.000	-89.3302	-74.0032
		F3	-14.33333*	2.32857	.001	-21.9968	-6.6698
		F5	.00000	2.32857	1.000	-7.6635	7.6635
	F5	F1	.00000	2.32857	1.000	-7.6635	7.6635
		F2	-81.66667*	2.32857	.000	-89.3302	-74.0032
		F3	-14.33333*	2.32857	.001	-21.9968	-6.6698
		F4	.00000	2.32857	1.000	-7.6635	7.6635
Games-Howell	F1	F2	-81.66667*	1.45297	.001	-92.8460	-70.4874
		F3	-14.33333	3.38296	.151	-40.3622	11.6956
		F4	.00000	.00000	.	.0000	.0000
		F5	.00000	.00000	.	.0000	.0000
	F2	F1	81.66667*	1.45297	.001	70.4874	92.8460
		F3	67.33333*	3.68179	.002	46.2503	88.4164
		F4	81.66667*	1.45297	.001	70.4874	92.8460
		F5	81.66667*	1.45297	.001	70.4874	92.8460
	F3	F1	14.33333	3.38296	.151	-11.6956	40.3622
		F2	-67.33333*	3.68179	.002	-88.4164	-46.2503
		F4	14.33333	3.38296	.151	-11.6956	40.3622
		F5	14.33333	3.38296	.151	-11.6956	40.3622
	F4	F1	.00000	.00000	.	.0000	.0000
		F2	-81.66667*	1.45297	.001	-92.8460	-70.4874
		F3	-14.33333	3.38296	.151	-40.3622	11.6956
		F5	.00000	.00000	.	.0000	.0000
	F5	F1	.00000	.00000	.	.0000	.0000
		F2	-81.66667*	1.45297	.001	-92.8460	-70.4874
		F3	-14.33333	3.38296	.151	-40.3622	11.6956
		F4	.00000	.00000	.	.0000	.0000

ce is significant at the 0.05 level.



### Lampiran 7.3. Uji Waktu Pemisahan

Tests of Normality							
	Formula	Kolmogorov-Smirnov <sup>a</sup>			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
Waktupemisahan	F1	.253	3	.	.964	3	.637
	F2	.292	3	.	.923	3	.463
	F3	.219	3	.	.987	3	.780
	F4	.175	3	.	1.000	3	1.000
	F5	.304	3	.	.907	3	.407

a. Lilliefors Significance Correction

ANOVA					
Waktu pemisahan					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	8.267	4	2.067	.115	.974
Within Groups	179.333	10	17.933		
Total	187.600	14			

Multiple Comparisons								
Dependent Variable: Waktu pemisahan								
	(I) Formula	(J) Formula	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval		
						Lower Bound	Upper Bound	
Tukey HSD	F1	F2	2.00000	3.45768	.975	-9.3795	13.3795	
		F3	.33333	3.45768	1.000	-11.046	11.7128	
		F4	.00000	3.45768	1.000	-11.379	11.3795	
		F5	.66667	3.45768	1.000	-10.712	12.0462	
	F2	F1	-2.00000	3.45768	.975	-13.379	9.3795	
		F3	-1.66667	3.45768	.987	-13.046	9.7128	
		F4	-2.00000	3.45768	.975	-13.379	9.3795	
		F5	-1.33333	3.45768	.995	-12.712	10.0462	
	F3	F1	-.33333	3.45768	1.000	-11.712	11.0462	
		F2	1.66667	3.45768	.987	-9.7128	13.0462	
		F4	-.33333	3.45768	1.000	-11.712	11.0462	
		F5	.33333	3.45768	1.000	-11.046	11.7128	
			F1	.00000	3.45768	1.000	-11.379	11.3795
			F2	2.00000	3.45768	.975	-9.3795	13.3795
			F3	.33333	3.45768	1.000	-11.046	11.7128
			F5	.66667	3.45768	1.000	-10.712	12.0462
		F1	-.66667	3.45768	1.000	-12.046	10.7128	
		F2	1.33333	3.45768	.995	-10.046	12.7128	
		F3	-.33333	3.45768	1.000	-11.712	11.0462	
		F4	-.66667	3.45768	1.000	-12.046	10.7128	



Games-Howell	F1	F2	2.00000	4.47214	.988	-18.838	22.8389
		F3	.33333	3.01846	1.000	-15.291	15.9580
		F4	.00000	2.70801	1.000	-18.871	18.8710
		F5	.66667	3.80058	1.000	-16.237	17.5709
	F2	F1	-2.00000	4.47214	.988	-22.838	18.8389
		F3	-1.66667	3.88730	.989	-24.485	21.1522
		F4	-2.00000	3.65148	.972	-28.569	24.5695
		F5	-1.33333	4.52155	.998	-22.224	19.5579
	F3	F1	-.33333	3.01846	1.000	-15.958	15.2913
		F2	1.66667	3.88730	.989	-21.152	24.4855
		F4	-.33333	1.56347	.999	-9.5601	8.8934
		F5	.33333	3.09121	1.000	-15.872	16.5389
	F4	F1	.00000	2.70801	1.000	-18.871	18.8710
		F2	2.00000	3.65148	.972	-24.569	28.5695
		F3	.33333	1.56347	.999	-8.8934	9.5601
		F5	.66667	2.78887	.999	-18.872	20.2057
	F5	F1	-.66667	3.80058	1.000	-17.570	16.2375
		F2	1.33333	4.52155	.998	-19.557	22.2245
		F3	-.33333	3.09121	1.000	-16.538	15.8722
		F4	-.66667	2.78887	.999	-20.205	18.8723

#### Lampiran 7.4. Uji dermatokinetik secara ex vivo pada kulit normal

Tests of Normality							
	Waktu	Kolmogorov-Smirnov <sup>a</sup>			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
Krim KLI	1 jam	.	3	.	.	3	.
	2 jam	.	3	.	.	3	.
	3 jam	.	3	.	.	3	.
	4 jam	.263	3	.	.956	3	.595
	5 jam	.193	3	.	.997	3	.892
	6 jam	.307	3	.	.904	3	.398
	7 jam	.232	3	.	.980	3	.726
	8 jam	.204	3	.	.993	3	.843
Krim MP-KLI	1 jam	.	3	.	.	3	.
	2 jam	.	3	.	.	3	.
	3 jam	.	3	.	.	3	.
	4 jam	.261	3	.	.957	3	.602
	5 jam	.230	3	.	.981	3	.734
	6 jam	.294	3	.	.921	3	.455
	7 jam	.292	3	.	.923	3	.463
	8 jam	.309	3	.	.900	3	.386
	9 jam	.232	3	.	.980	3	.729
	10 jam	.360	3	.	.808	3	.133
	11 jam	.219	3	.	.987	3	.780
	12 jam	.190	3	.	.997	3	.902
	13 jam	.199	3	.	.995	3	.864
	14 jam	.328	3	.	.871	3	.298



	7 jam	.244	3	.	.972	3	.677
	8 jam	.190	3	.	.997	3	.903
MP-KLI-SEMAP	1 jam	.	3	.	.	3	.
	2 jam	.	3	.	.	3	.
	3 jam	.	3	.	.	3	.
	4 jam	.	3	.	.	3	.
	5 jam	.312	3	.	.895	3	.371
	6 jam	.284	3	.	.933	3	.501
	7 jam	.203	3	.	.994	3	.847
	8 jam	.175	3	.	1.000	3	1.000
a. Lilliefors Significance Correction							

ANOVA						
		Sum of Squares	df	Mean Square	F	Sig.
KrimKLI	Between Groups	34.790	8	4.349	89.788	.000
	Within Groups	.872	18	.048		
	Total	35.661	26			
Krim MP-KLI	Between Groups	49.001	8	6.125	115.656	.000
	Within Groups	.953	18	.053		
	Total	49.954	26			
SEMAP-KLI	Between Groups	4048.561	8	506.070	219.082	.000
	Within Groups	41.579	18	2.310		
	Total	4090.141	26			
MP-KLI-SEMAP	Between Groups	81.732	8	10.217	167.974	.000
	Within Groups	1.095	18	.061		
	Total	82.827	26			

### Lampiran 7.5 . Uji Dermatokinetik secara *ex vivo* pada model kulit terinfeksi

Tests of Normality						
aktu	Kolmogorov-Smirnov <sup>a</sup>			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
am	.	3	.	.	3	.
am	.	3	.	.	3	.
am	.	3	.	.	3	.
am	.267	3	.	.952	3	.577
am	.284	3	.	.933	3	.501



	6 jam	.258	3	.	.960	3	.616
	7 jam	.184	3	.	.999	3	.928
	8 jam	.238	3	.	.976	3	.700
Krim MP-KLI	1 jam	.	3	.	.	3	.
	2 jam	.	3	.	.	3	.
	3 jam	.	3	.	.	3	.
	4 jam	.267	3	.	.952	3	.577
	5 jam	.284	3	.	.933	3	.501
	6 jam	.258	3	.	.960	3	.616
	7 jam	.184	3	.	.999	3	.928
	8 jam	.238	3	.	.976	3	.700
SEMAP-KLI	1 jam	.265	3	.	.953	3	.583
	2 jam	.175	3	.	1.000	3	.990
	3 jam	.241	3	.	.973	3	.687
	4 jam	.267	3	.	.952	3	.577
	5 jam	.284	3	.	.933	3	.501
	6 jam	.258	3	.	.960	3	.616
	7 jam	.184	3	.	.999	3	.928
	8 jam	.238	3	.	.976	3	.700
MP-KLI-SEMAP	1 jam	.265	3	.	.953	3	.583
	2 jam	.175	3	.	1.000	3	.990
	3 jam	.241	3	.	.973	3	.687
	4 jam	.267	3	.	.952	3	.577
	5 jam	.284	3	.	.933	3	.501
	6 jam	.258	3	.	.960	3	.616
	7 jam	.184	3	.	.999	3	.928
	8 jam	.238	3	.	.976	3	.700
a. Lilliefors Significance Correction							

ANOVA						
		Sum of Squares	df	Mean Square	F	Sig.
Krim KLI	Between Groups	4733.503	8	591.688	388.978	.000
	Within Groups	27.380	18	1.521		
	Total	4760.883	26			
Krim MP-KLI	Between Groups	4733.503	8	591.688	388.978	.000
	Within Groups	27.380	18	1.521		
	Total	4760.883	26			
	Between Groups	3721.791	8	465.224	286.672	.000
	Within Groups	29.211	18	1.623		
	Total	3751.002	26			



MP-KLI-SEMAP	Between Groups	3721.791	8	465.224	286.672	.000
	Within Groups	29.211	18	1.623		
	Total	3751.002	26			



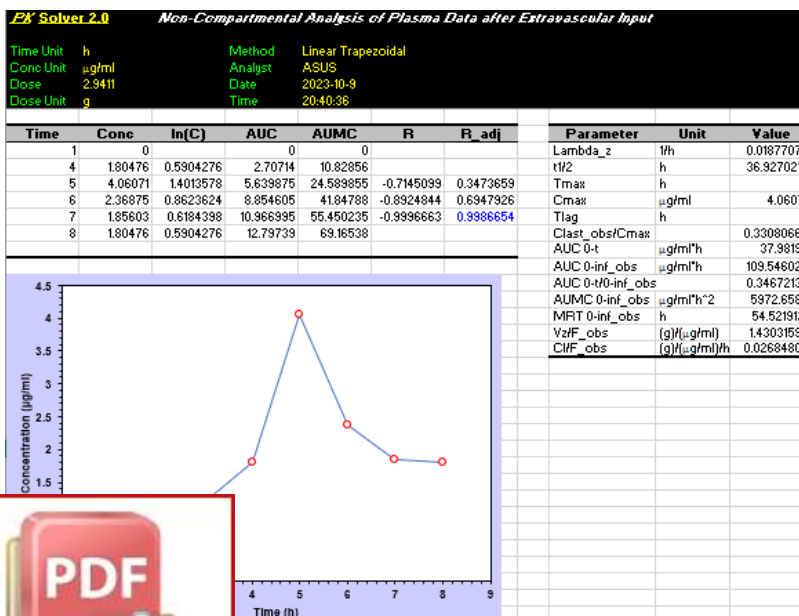
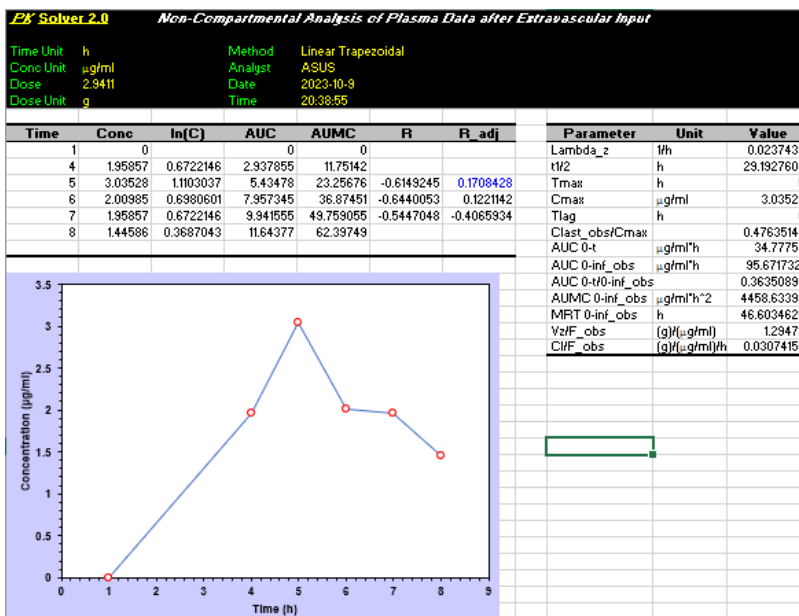
Optimization Software:  
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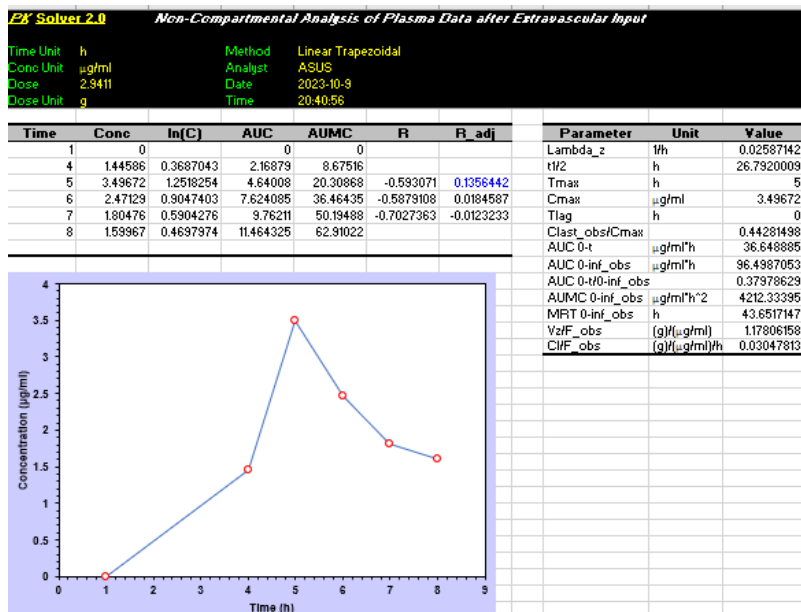


## Lampiran 8. Analisis PK Solver

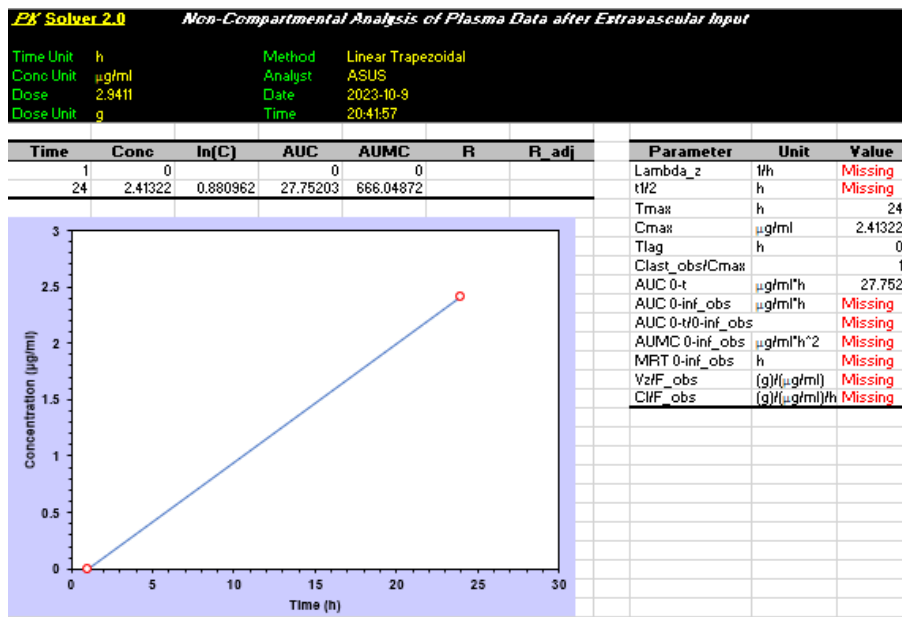
### Lampiran 8.1 Uji dermatokinetik secara ex vivo pada kulit normal

#### 1. Krim KLI

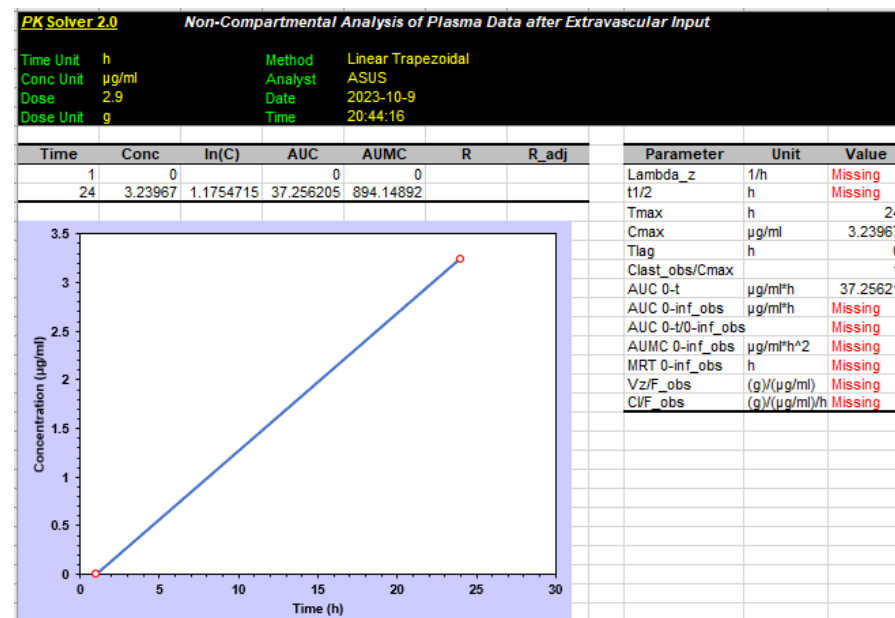
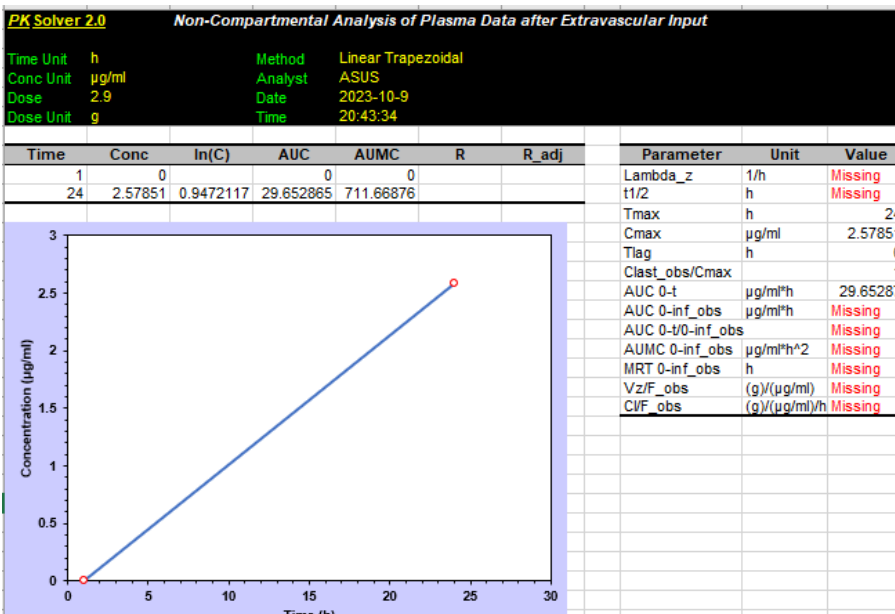




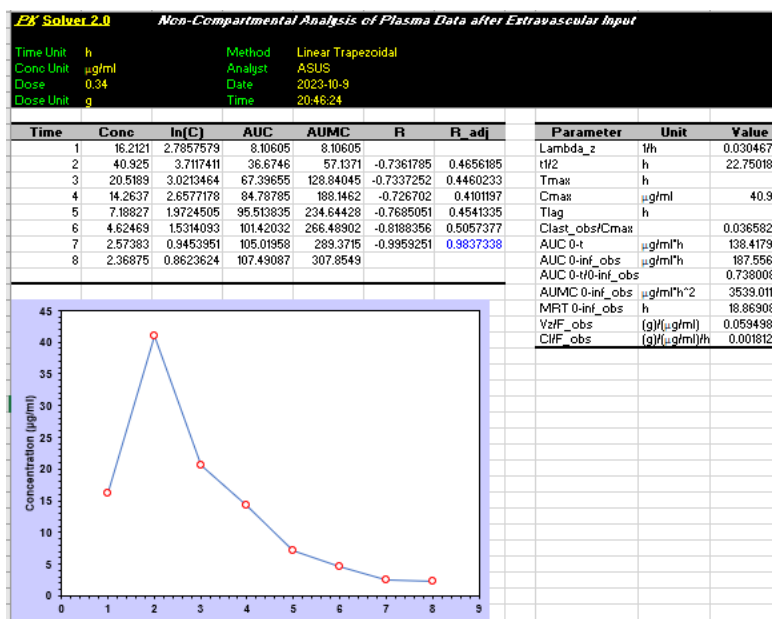
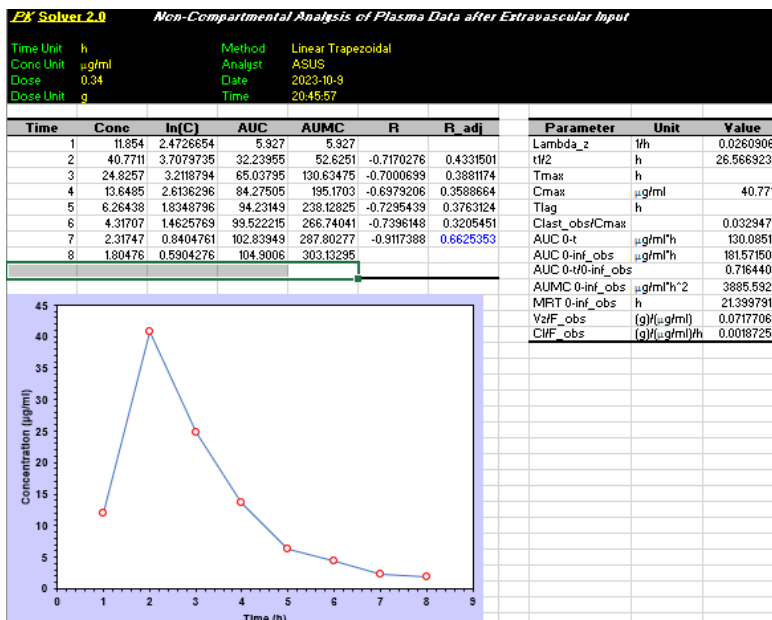
## 2. Krim-MP-KLI

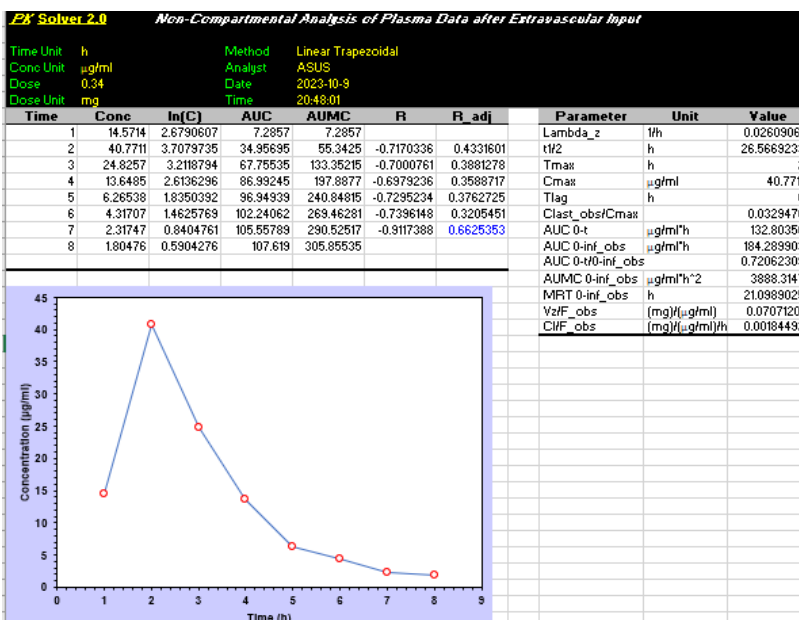


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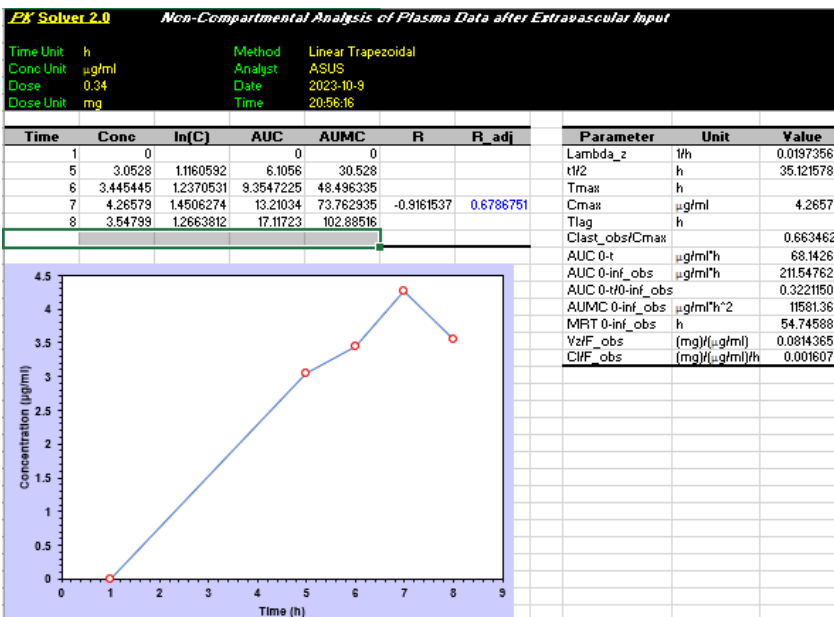


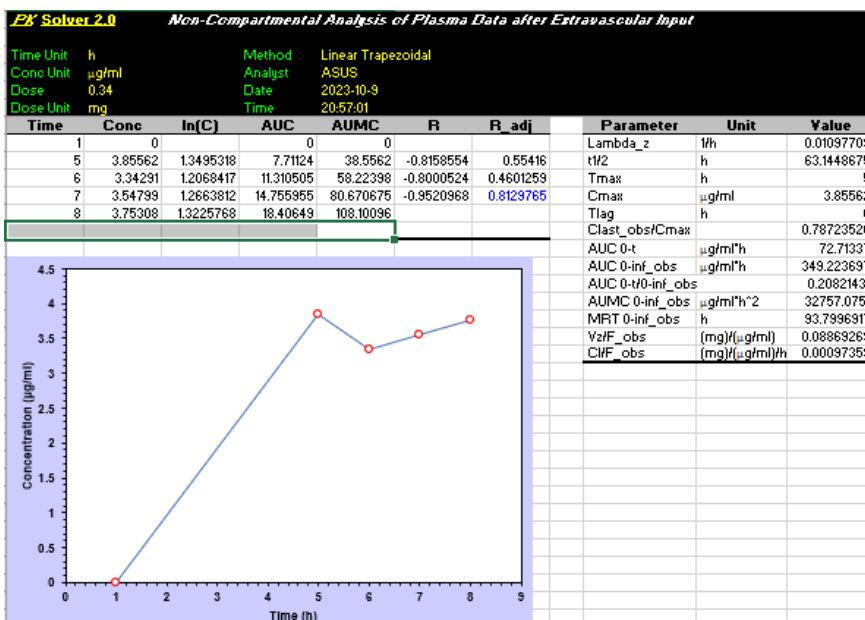
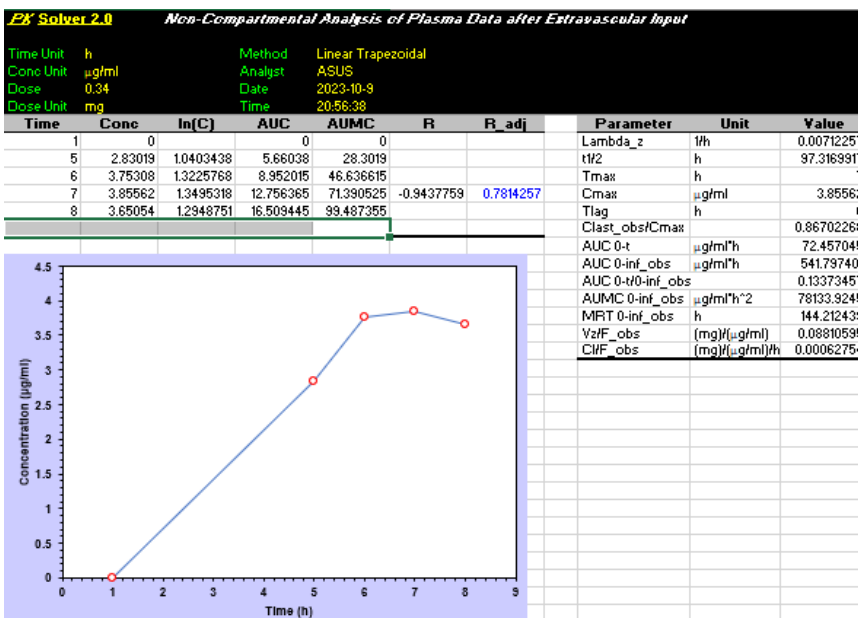
### 3. SEMAP-KLI





4. MP-KLI-SEMAP

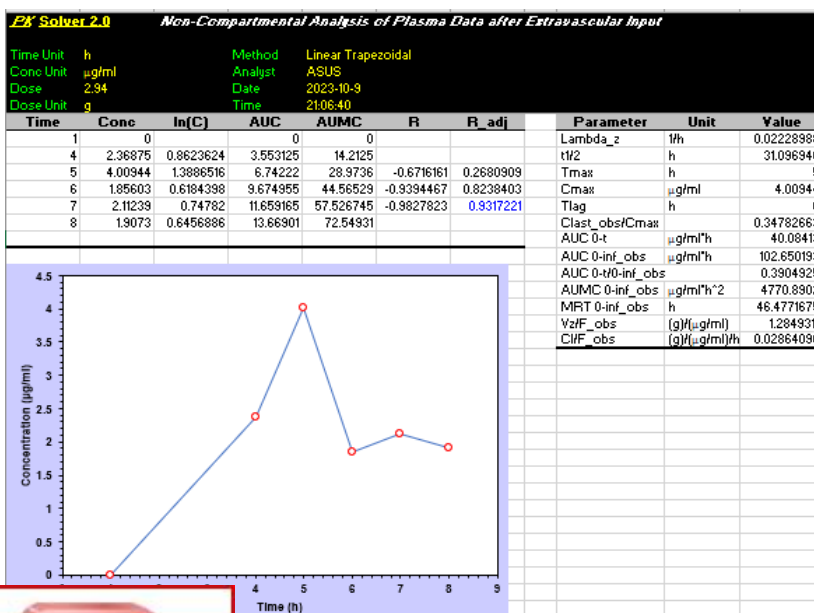
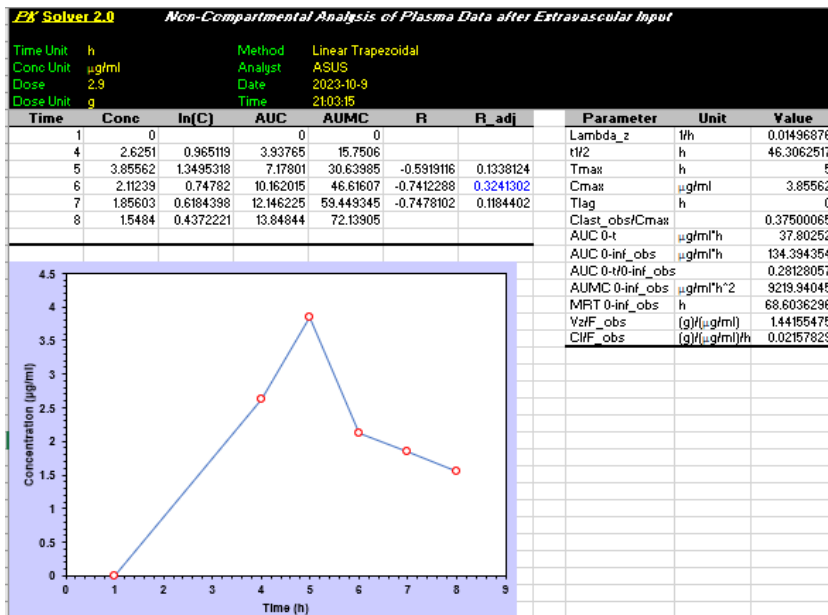


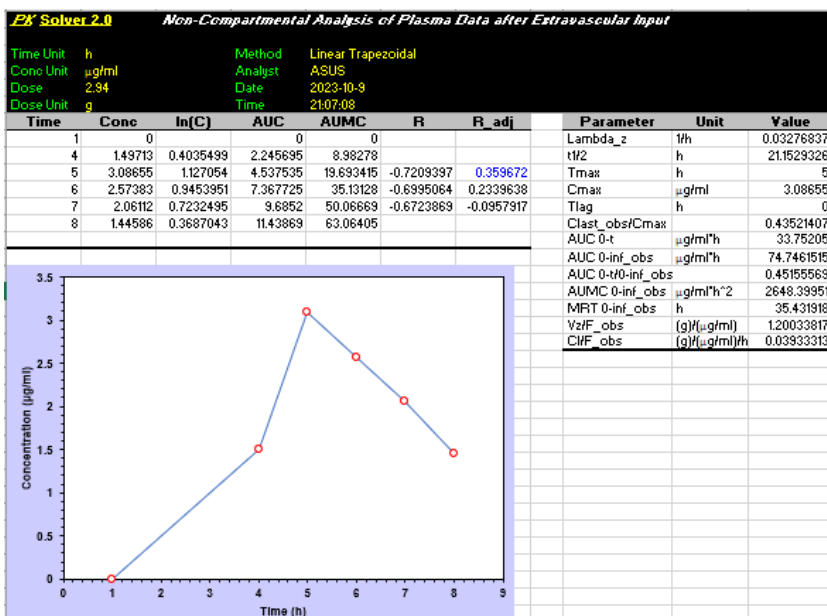


**Optimization Software:**  
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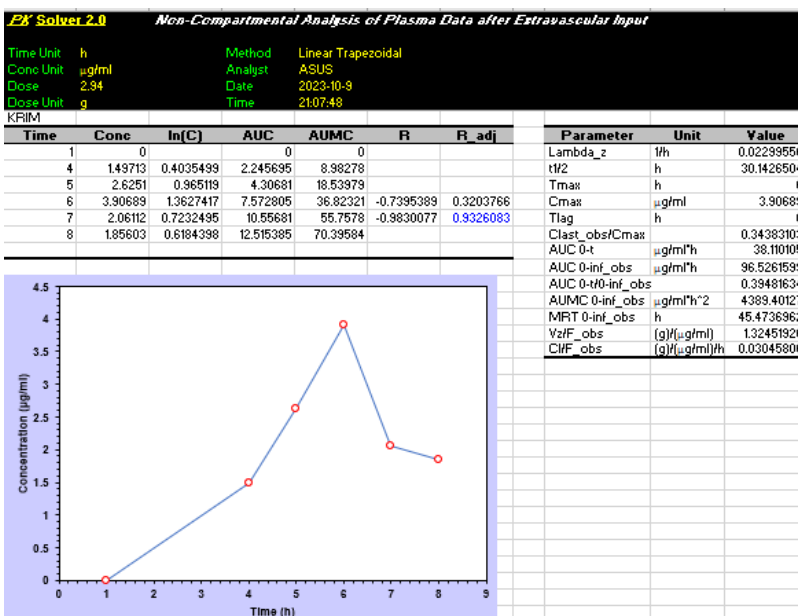
## Lampiran 8.2 Uji dermatokinetik secara ex vivo pada kulit normal

### 1. Krim KLI

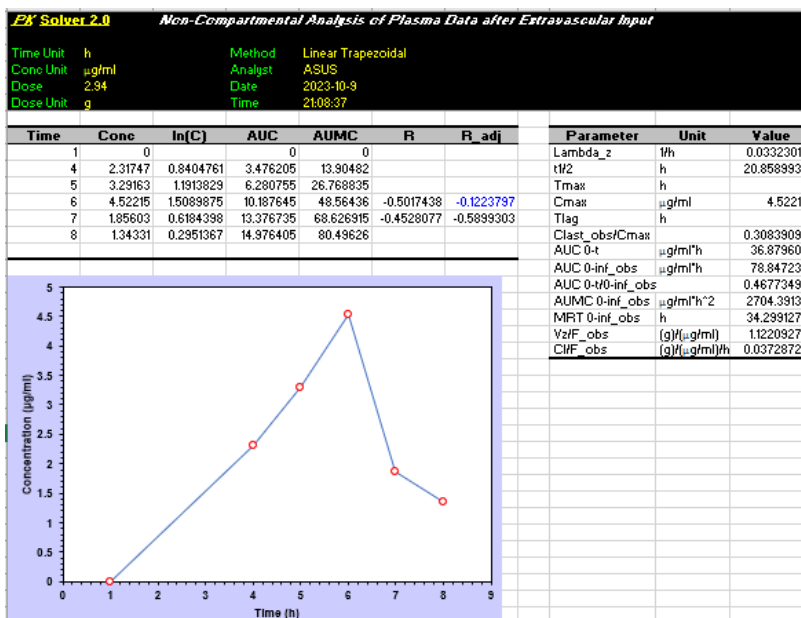
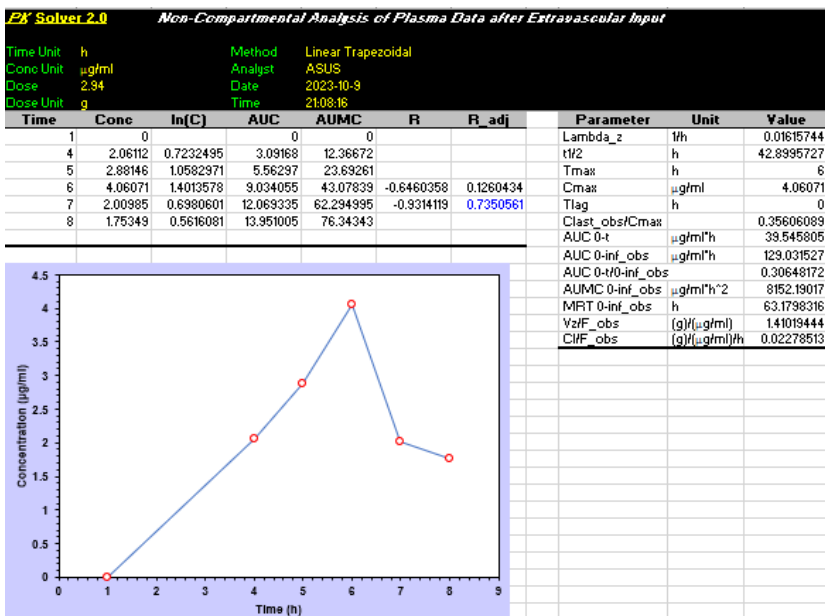




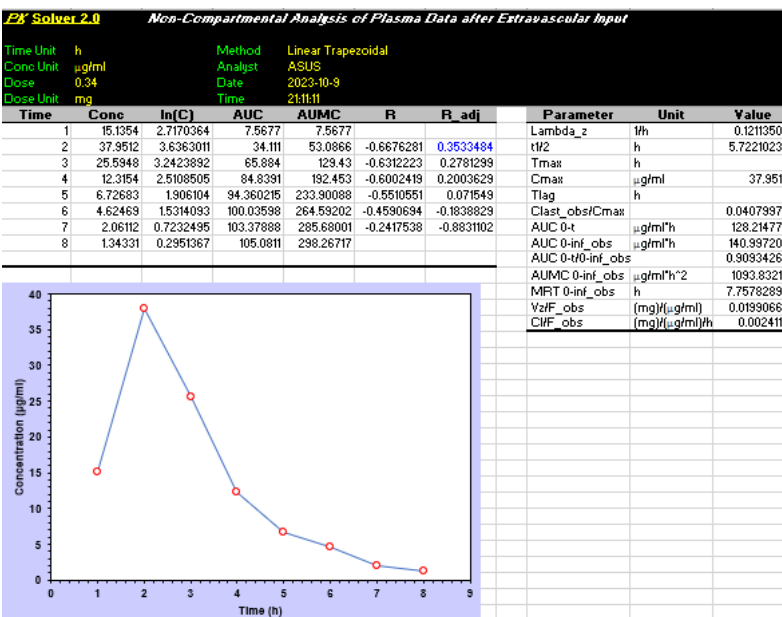
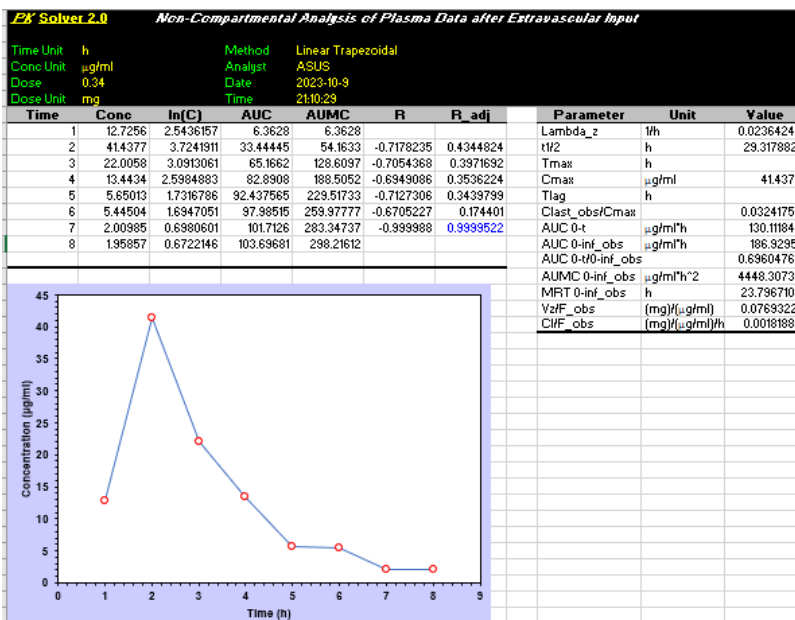
## 2. Krim-MP-KL

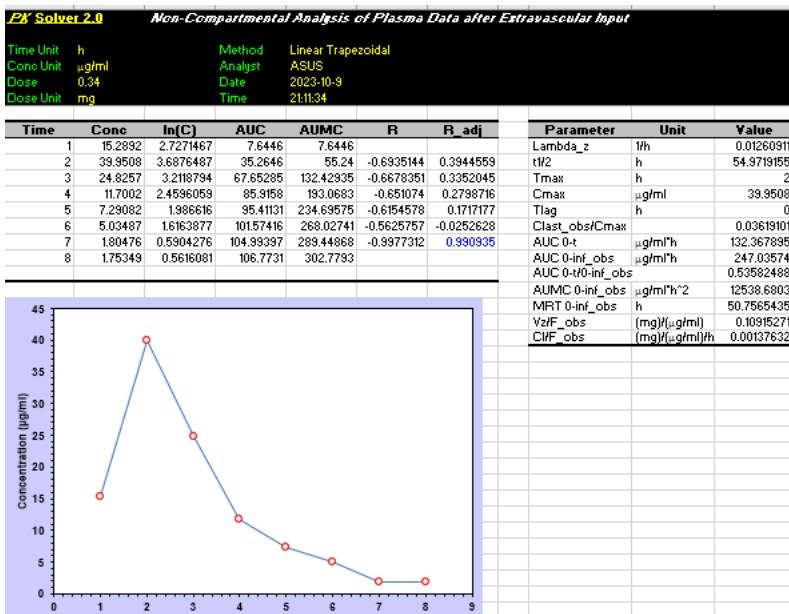




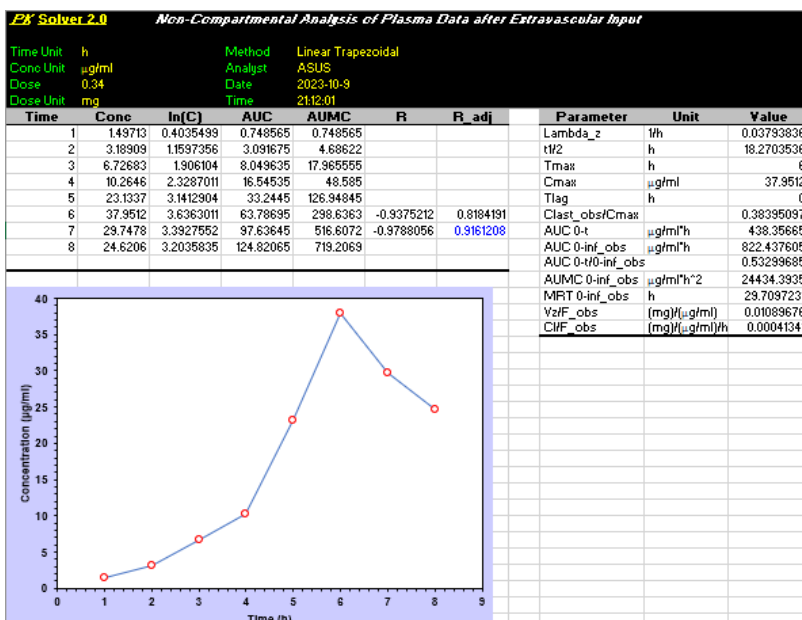


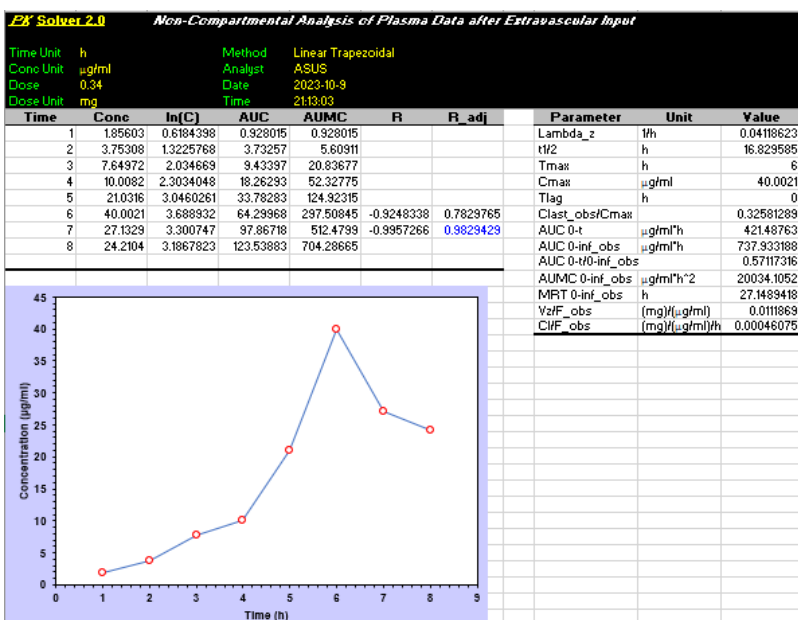
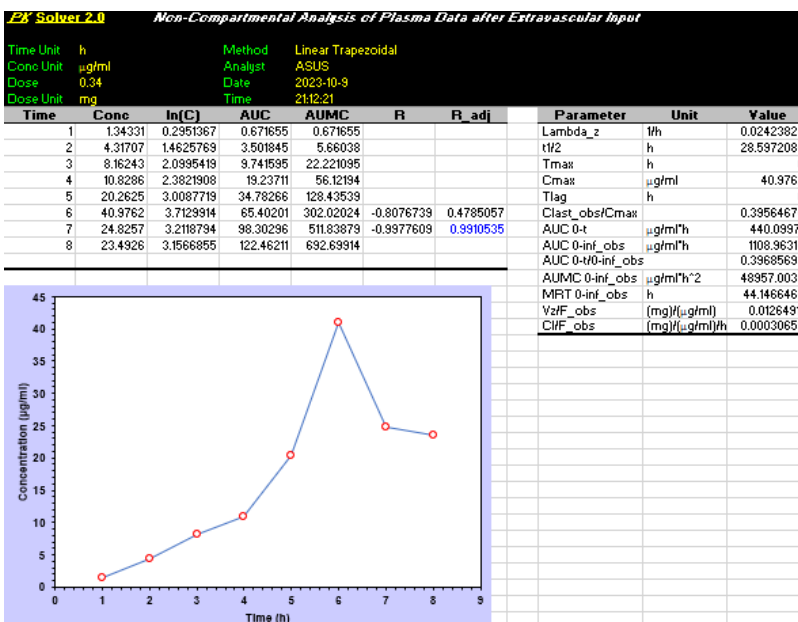
### 3. SEMAP-KLI





4. MP-KLI-SEMAP





**Optimization Software:**  
[www.balesio.com](http://www.balesio.com)

**Lampiran 9. Dokumentasi Kegiatan**

Analisis menggunakan Spektrofotometer UV-Vis



Formulasi MP-KLI-SEMAP



Karakterisasi MP-KLI



Uji dermatokinetik secara *ex vivo*



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