

## DAFTAR PUSTAKA

- Ananda, P. W. R. *et al.* (2021) 'Combination of transdermal patches and solid microneedles for improved transdermal delivery of primaquine', *International Journal of Pharmaceutics*, 609(August), p. 121204. doi: 10.1016/j.ijpharm.2021.121204.
- Anjani, Q. K. *et al.* (2022) 'Metronidazole nanosuspension loaded dissolving microarray patches: An engineered composite pharmaceutical system for the treatment of skin and soft tissue infection', *Biomaterials Advances*, 140(June). doi: 10.1016/j.bioadv.2022.213073.
- Barbosa, A. I. *et al.* (2023) 'Evaluating the Skin Interactions and Permeation of Alginate/Fucoidan Hydrogels Per Se and Associated with Different Essential Oils', *Pharmaceutics*, 15(1), pp. 1–17. doi: 10.3390/pharmaceutics15010190.
- Dharadhar, S. *et al.* (2019a) 'Microneedles for transdermal drug delivery: a systematic review', *Drug Development and Industrial Pharmacy*, 45(2), pp. 188–201. doi: 10.1080/03639045.2018.1539497.
- Dharadhar, S. *et al.* (2019b) 'Microneedles for transdermal drug delivery: a systematic review', *Drug Development and Industrial Pharmacy*, 45(2), pp. 188–201. doi: 10.1080/03639045.2018.1539497.
- Ding, A. J. *et al.* (2017) 'Current Perspective in the Discovery of Anti-aging Agents from Natural Products', *Natural Products and Bioprospecting*, 7(5), pp. 335–404. doi: 10.1007/s13659-017-0135-9.
- Fallacara, A. *et al.* (2018) 'Hyaluronic acid in the third millennium', *Polymers*, 10(7). doi: 10.3390/polym10070701.
- Fernando, I. P. S. *et al.* (2020) 'Fucoidan refined by *Sargassum confusum* indicate protective effects suppressing photo-oxidative stress and skin barrier perturbation in UVB-induced human keratinocytes', *International Journal of Biological Macromolecules*, 164, pp. 149–161. doi: 10.1016/j.ijbiomac.2020.07.136.
- Flatt, T. (2012) 'A new definition of aging?', *Frontiers in Genetics*, 3(AUG), pp. 1–2. doi: 10.3389/fgene.2012.00148.
- Ganceviciene, R. *et al.* (2012a) 'Skin anti-aging strategies', *Dermato-Endocrinology*, 4(3). doi: 10.4161/derm.22804.
- Ganceviciene, R. *et al.* (2012b) 'Skin anti-aging strategies', *Dermato-Endocrinology*, 4(3). doi: 10.4161/derm.22804.

- Geng, R. *et al.* (2021) 'Boosting the photoaged skin: The potential role of dietary components', *Nutrients*, 13(5), pp. 1–27. doi: 10.3390/nu13051691.
- Gomaa, M. *et al.* (2018) 'Use of seaweed and filamentous fungus derived polysaccharides in the development of alginate-chitosan edible films containing fucoidan: Study of moisture sorption, polyphenol release and antioxidant properties', *Food Hydrocolloids*, 82, pp. 239–247. doi: 10.1016/j.foodhyd.2018.03.056.
- Gomaa, Y. A. *et al.* (2010) 'Effects of microneedle length, density, insertion time and multiple applications on human skin barrier function: Assessments by transepidermal water loss', *Toxicology in Vitro*, 24(7), pp. 1971–1978. doi: 10.1016/j.tiv.2010.08.012.
- Gruber, F. *et al.* (2020) 'Cell aging and cellular senescence in skin aging — Recent advances in fibroblast and keratinocyte biology', *Experimental Gerontology*, 130(August 2019), p. 110780. doi: 10.1016/j.exger.2019.110780.
- Gu, Y. *et al.* (2020) 'Biomarkers, oxidative stress and autophagy in skin aging', *Ageing Research Reviews*, 59(February), p. 101036. doi: 10.1016/j.arr.2020.101036.
- He, J. *et al.* (2021) 'Design and evaluation of dissolving microneedles for enhanced dermal delivery of propranolol hydrochloride', *Pharmaceutics*, 13(4), pp. 1–15. doi: 10.3390/pharmaceutics13040579.
- Hou, X. *et al.* (2022) 'Application and Efficacy of Melatonin Elastic Liposomes in Photoaging Mice', *Oxidative Medicine and Cellular Longevity*, 2022. doi: 10.1155/2022/7135125.
- Kim, Y. I. *et al.* (2018) 'Anti-photoaging effects of low molecular-weight fucoidan on ultraviolet B-irradiated mice', *Marine Drugs*, 16(8), pp. 1–13. doi: 10.3390/md16080286.
- Krug, J. (2005) *Kinetic pattern formation at solid surfaces, Collective Dynamics of Nonlinear and Disordered Systems*. doi: 10.1007/3-540-26869-3\_2.
- Larrañeta, E. *et al.* (2014) 'A proposed model membrane and test method for microneedle insertion studies', *Elsevier B.V.*, pp. 1–9. doi: 10.1016/j.ijpharm.2014.05.042.
- Lee, H., Hong, Y. and Kim, M. (2021) 'Structural and functional changes and possible molecular mechanisms in aged skin', *International Journal of Molecular Sciences*, 22(22). doi: 10.3390/ijms222212489.
- Lee, J. W., Park, J. H. and Prausnitz, M. R. (2008a) 'Dissolving microneedles for transdermal drug delivery', *Biomaterials*, 29(13), pp. 2113–2124. doi: 10.1016/j.biomaterials.2007.12.048.

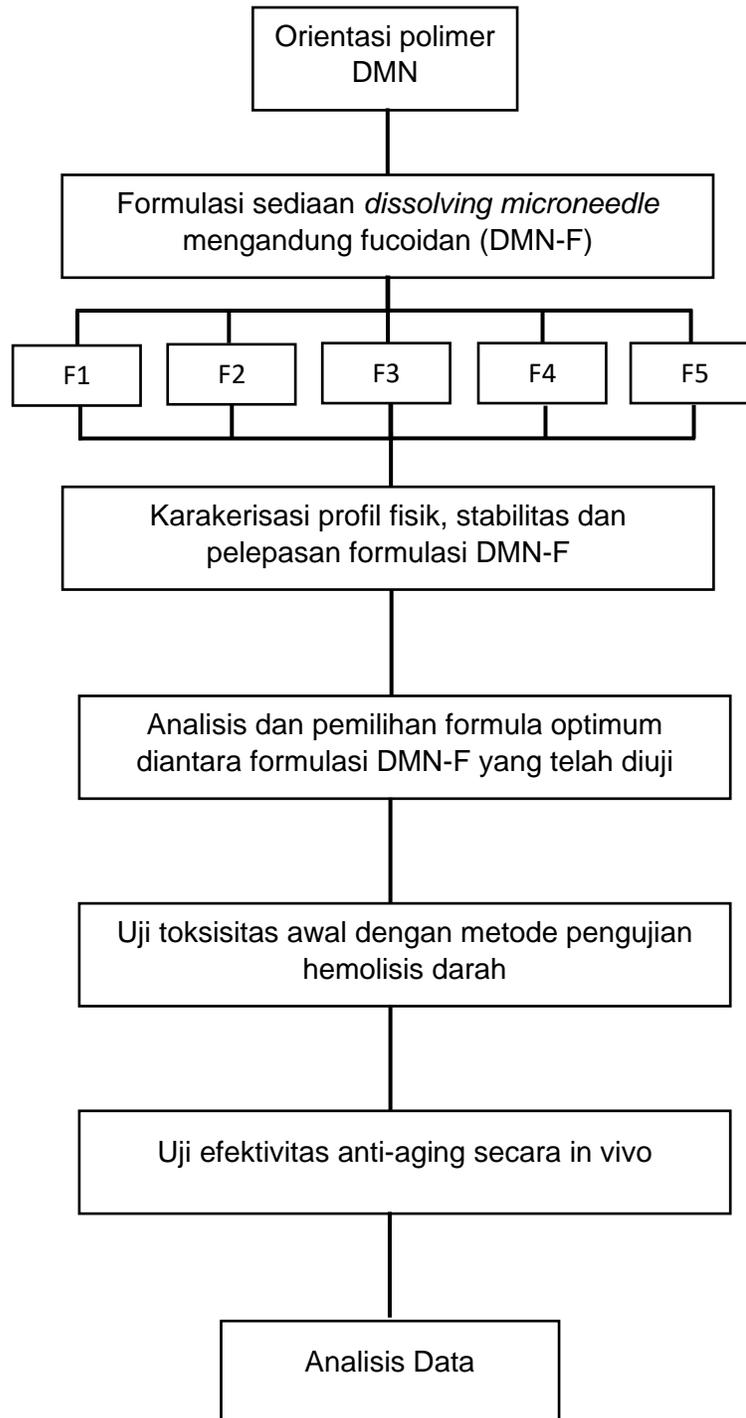
- Lee, J. W., Park, J. H. and Prausnitz, M. R. (2008b) 'Dissolving microneedles for transdermal drug delivery', *Biomaterials*, 29(13), pp. 2113–2124. doi: 10.1016/j.biomaterials.2007.12.048.
- Li, B. *et al.* (2008) 'Fucoidan: Structure and bioactivity', *Molecules*, 13(8), pp. 1671–1695. doi: 10.3390/molecules13081671.
- Liu, M. *et al.* (2016) 'Combined multi-modal photoacoustic tomography, optical coherence tomography (OCT) and OCT angiography system with an articulated probe for in vivo human skin structure and vasculature imaging', *Biomedical Optics Express*, 7(9), p. 3390. doi: 10.1364/boe.7.003390.
- Luthuli, S. *et al.* (2019) 'marine drugs Therapeutic Effects of Fucoidan : A Review on Recent Studies', *Mdpi*.
- Mabate, B. *et al.* (2021) 'Fucoidan structure and its impact on glucose metabolism: Implications for diabetes and cancer therapy', *Marine Drugs*, 19(1), pp. 1–20. doi: 10.3390/md19010030.
- Makrantonaki, E. and Zouboulis, C. C. (2007) 'Characteristics and pathomechanisms of endogenously aged skin', *Dermatology*, 214(4), pp. 352–360. doi: 10.1159/000100890.
- Markiewicz-Tomczyk, A., Budzisz, E. and Erkiert-Polguj, A. (2023) 'A Subjective and Objective Assessment of Combined Methods of Applying Chemical Peels and Microneedling in Antiaging Treatments', *Journal of Clinical Medicine*, 12(5). doi: 10.3390/jcm12051869.
- Mensah, E. O. *et al.* (2023) 'Marine fucoidans: Structural, extraction, biological activities and their applications in the food industry', *Food Hydrocolloids*, 142(April), p. 108784. doi: 10.1016/j.foodhyd.2023.108784.
- Michalak, M. *et al.* (2021) 'Bioactive compounds for skin health: A review', *Nutrients*, 13(1), pp. 1–31. doi: 10.3390/nu13010203.
- Mir, M. *et al.* (2020) 'Microneedle liquid injection system assisted delivery of infection responsive nanoparticles: A promising approach for enhanced site-specific delivery of carvacrol against polymicrobial biofilms-infected wounds', *International Journal of Pharmaceutics*, 587(April), p. 119643. doi: 10.1016/j.ijpharm.2020.119643.
- Mostafa, D. K. *et al.* (2022) 'Modulation of autophagy, apoptosis and oxidative stress: a clue for repurposing metformin in photoaging', *Inflammopharmacology*, 30(6), pp. 2521–2535. doi: 10.1007/s10787-022-01041-8.
- Nasiri, M. I. *et al.* (2022) 'Nanoemulsion-based dissolving microneedle arrays for enhanced intradermal and transdermal delivery', *Drug Delivery and Translational Research*, 12(4), pp. 881–896. doi: 10.1007/s13346-021-01107-0.

- Pangestuti, R., Siahaan, E. A. and Kim, S. K. (2018) 'Photoprotective substances derived from marine algae', *Marine Drugs*, 16(11). doi: 10.3390/md16110399.
- Paredes, A. J. *et al.* (2021) 'Novel tip-loaded dissolving and implantable microneedle array patches for sustained release of finasteride', *International Journal of Pharmaceutics*, 606(June), p. 120885. doi: 10.1016/j.ijpharm.2021.120885.
- Permana, A. D. *et al.* (2019) 'Solid lipid nanoparticle-based dissolving microneedles: A promising intradermal lymph targeting drug delivery system with potential for enhanced treatment of lymphatic filariasis', *Journal of Controlled Release*, 316(September), pp. 34–52. doi: 10.1016/j.jconrel.2019.10.004.
- Permana, A. D., Mir, M., *et al.* (2020) 'Bacterially sensitive nanoparticle-based dissolving microneedles of doxycycline for enhanced treatment of bacterial biofilm skin infection: A proof of concept study', *International Journal of Pharmaceutics: X*, 2(December 2019), p. 100047. doi: 10.1016/j.ijpx.2020.100047.
- Permana, A. D., Paredes, A. J., *et al.* (2020) 'Dissolving microneedle-mediated dermal delivery of itraconazole nanocrystals for improved treatment of cutaneous candidiasis', *European Journal of Pharmaceutics and Biopharmaceutics*, 154(April), pp. 50–61. doi: 10.1016/j.ejpb.2020.06.025.
- Pham, T. L. B. *et al.* (2022) 'Anti-Aging Effects of a Serum Based on Coconut Oil Combined with Deer Antler Stem Cell Extract on a Mouse Model of Skin Aging', *Cells*, 11(4). doi: 10.3390/cells11040597.
- Pozharitskaya, O. N. *et al.* (2019) 'The pharmacokinetics of fucoidan after topical application to rats', *Marine Drugs*, 17(12), pp. 1–9. doi: 10.3390/md17120687.
- Proksch, E. (2018) 'pH in nature, humans and skin', *Journal of Dermatology*, 45(9), pp. 1044–1052. doi: 10.1111/1346-8138.14489.
- Puizina-Ivic, N. (2014) 'Skin aging SKIN AGING', *Acta Dermatoven*, 17(2), pp. 47–53.
- Pyo, I. S. *et al.* (2020) 'Mechanisms of Aging and the Preventive Effects of', *Molecules*, 25(20), p. 4649.
- Resende, D. I. S. P. *et al.* (2021) 'Trends in the use of marine ingredients in anti-aging cosmetics', *Algal Research*, 55(December 2020). doi: 10.1016/j.algal.2021.102273.
- Roska, T. P. *et al.* (2022) 'Development of chloramphenicol wound dressing protein-based microparticles in chitosan hydrogel system for improved effectiveness of dermal wound therapy', *Biomaterials Advances*, 143(October), p. 213175. doi: 10.1016/j.bioadv.2022.213175.

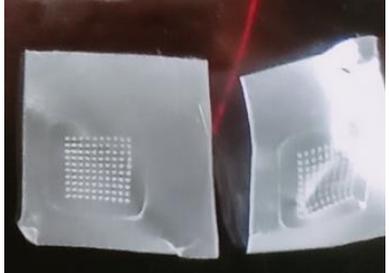
- Sæbø, I. P. *et al.* (2023) 'Optimization of the Hemolysis Assay for the Assessment of Cytotoxicity', *International Journal of Molecular Sciences*, 24(3). doi: 10.3390/ijms24032914.
- Sartawi, Z., Blackshields, C. and Faisal, W. (2022) 'Dissolving microneedles: Applications and growing therapeutic potential', *Journal of Controlled Release*, 348(April), pp. 186–205. doi: 10.1016/j.jconrel.2022.05.045.
- Schommer, N. N. and Gallo, R. L. (2013) 'Structure and function of the human skin microbiome', *Trends in Microbiology*, 21(12), pp. 660–668. doi: 10.1016/j.tim.2013.10.001.
- Singh, A. and Bali, A. (2016) 'Formulation and characterization of transdermal patches for controlled delivery of duloxetine hydrochloride', *Journal of Analytical Science and Technology*, 7(1). doi: 10.1186/s40543-016-0105-6.
- Tobin, D. J. (2017) 'Introduction to skin aging', *Journal of Tissue Viability*, 26(1), pp. 37–46. doi: 10.1016/j.jtv.2016.03.002.
- Vona, D. *et al.* (2023) 'Drug Delivery through Epidermal Tissue Cells by Functionalized Biosilica from Diatom Microalgae', *Marine Drugs*, 21(8). doi: 10.3390/md21080438.
- Vora, L. K. *et al.* (2018) 'Novel nanosuspension-based dissolving microneedle arrays for transdermal delivery of a hydrophobic drug', *Journal of Interdisciplinary Nanomedicine*, 3(2), pp. 89–101. doi: 10.1002/jin2.41.
- Waghule, T. *et al.* (2019) 'Microneedles: A smart approach and increasing potential for transdermal drug delivery system', *Biomedicine and Pharmacotherapy*, 109(October 2018), pp. 1249–1258. doi: 10.1016/j.biopha.2018.10.078.
- Wang, J. *et al.* (2013) 'Chemical composition and moisture-absorption/retention ability of polysaccharides extracted from five algae', *International Journal of Biological Macromolecules*, 57, pp. 26–29. doi: 10.1016/j.ijbiomac.2013.03.001.
- Wang, N. *et al.* (2021) 'Fucoidan hydrogels induced by  $\kappa$ -carrageenan: Rheological, thermal and structural characterization', *International Journal of Biological Macromolecules*, 191(July), pp. 514–520. doi: 10.1016/j.ijbiomac.2021.09.111.
- Zayed, A. *et al.* (2020) 'Fucoidan characterization: Determination of purity and physicochemical and chemical properties', *Marine Drugs*, 18(11), pp. 1–31. doi: 10.3390/md18110571.
- Zhang, S. and Duan, E. (2018) 'Fighting against Skin Aging: The Way from Bench to Bedside', *Cell Transplantation*, 27(5), pp. 729–738. doi: 10.1177/0963689717725755.

## LAMPIRAN

### Lampiran 1. Alur Penelitian.



## Lampiran 2. Dokumentasi Penelitian.

	
<p>Penyiapan dan formulasi DMN-F</p>	<p>Karakterisasi DMN-F</p>
	
	<p>Pengujian pH</p>
	
<p>Pengujian WVT</p>	<p>Pembuatan Kurva baku</p>
	
<p>Induksi dan penyiapan in vivo</p>	<p>Treatment Hewan Coba</p>

### Lampiran 3. Data Statistik.

#### Uji kekuatan mekanik dan kemampuan penetrasi

Number of values	1	1	1	1	1
Minimum	11.19	25.13	32.68	1.260	5.090
25% Percentile	11.19	25.13	32.68	1.260	5.090
Median	11.19	25.13	32.68	1.260	5.090
75% Percentile	11.19	25.13	32.68	1.260	5.090
Maximum	11.19	25.13	32.68	1.260	5.090
Mean	11.19	25.13	32.68	1.260	5.090
Std. Deviation	2.710	2.090	2.300	1.180	1.160
Std. Error	1.565	1.207	1.328	0.6813	0.6697
Lower 95% CI	4.458	19.94	26.97	-1.671	2.208
Upper 95% CI	17.92	30.32	38.39	4.191	7.972

P value	< 0.0001		
P value summary	***		
Are means signif. different? (P < 0.05)	Yes		
Number of groups	5		
F	136.1		
R square	0.9820		
ANOVA Table	SS	df	MS
Treatment (between columns)	2150	4	537.5
Residual (within columns)	39.48	10	3.948
Total	2190	14	

Tukey's Multiple Comparison Test	Mean Diff.	q	Significant? P < 0.05?	Summary	95% CI of diff
F1 vs F2	-13.94	12.15	Yes	***	-19.28 to -8.601
F1 vs F3	-21.49	18.73	Yes	***	-26.83 to -16.15
F1 vs F4	9.930	8.656	Yes	***	4.591 to 15.27
F1 vs F5	6.100	5.317	Yes	*	0.7610 to 11.44
F2 vs F3	-7.550	6.581	Yes	**	-12.89 to -2.211
F2 vs F4	23.87	20.81	Yes	***	18.53 to 29.21
F2 vs F5	20.04	17.47	Yes	***	14.70 to 25.38
F3 vs F4	31.42	27.39	Yes	***	26.08 to 36.76
F3 vs F5	27.59	24.05	Yes	***	22.25 to 32.93
F4 vs F5	-3.830	3.339	No	ns	-9.169 to 1.509

### Water Loss On drying

R square	0.5886				
ANOVA Table					
	SS	df	MS		
Treatment (between columns)	106.2	4	26.56		
Residual (within columns)	74.24	10	7.424		
Total	180.5	14			
Tukey's Multiple Comparison Test					
	Mean Diff.	q	Significant? F	Summary	95% CI of diff
F1 vs F2	0.3089	0.1963	No	ns	-7.012 to 7.630
F1 vs F3	5.414	3.442	No	ns	-1.907 to 12.74
F1 vs F4	1.708	1.086	No	ns	-5.614 to 9.029
F1 vs F5	6.453	4.102	No	ns	-0.8685 to 13.77
F2 vs F3	5.105	3.245	No	ns	-2.216 to 12.43
F2 vs F4	1.399	0.8892	No	ns	-5.922 to 8.720
F2 vs F5	6.144	3.906	No	ns	-1.177 to 13.47
F3 vs F4	-3.706	2.356	No	ns	-11.03 to 3.615
F3 vs F5	1.039	0.6603	No	ns	-6.262 to 8.360
F4 vs F5	4.745	3.016	No	ns	-2.576 to 12.07

### Surface pH

ANOVA Table					
	SS	df	MS		
Treatment (between columns)	2.332	4	0.5829		
Residual (within columns)	0.2052	10	0.02052		
Total	2.537	14			
Tukey's Multiple Comparison Test					
	Mean Diff.	q	Significant? F	Summary	95% CI of diff
F1 vs F2	0.4289	5.166	Yes	*	0.04400 to 0.8138
F1 vs F3	1.074	12.99	Yes	***	0.6896 to 1.459
F1 vs F4	0.7300	8.627	Yes	***	0.3451 to 1.115
F1 vs F5	0.9956	12.04	Yes	***	0.6107 to 1.380
F2 vs F3	0.6456	7.806	Yes	**	0.2607 to 1.030
F2 vs F4	0.3011	3.641	No	ns	-0.06377 to 0.6860
F2 vs F5	0.5667	6.852	Yes	**	0.1818 to 0.9516
F3 vs F4	-0.3444	4.165	No	ns	-0.7293 to 0.04044
F3 vs F5	-0.07889	0.9539	No	ns	-0.4638 to 0.3060
F4 vs F5	0.2656	3.211	No	ns	-0.1193 to 0.6504

### Uji permeasi dan retensi secar Ex vivo

Bartlett's test for equal variances					
Bartlett's statistic (corrected)	13.57				
P value	0.0088				
P value summary	**				
Do the variances differ signif. (P < 0.05)	Yes				
ANOVA Table					
	SS	df	MS		
Treatment (between columns)	13670	4	3417		
Residual (within columns)	26332	60	438.9		
Total	40002	64			
Tukey's Multiple Comparison Test					
	Mean Diff.	q	Significant? F	Summary	95% CI of diff
F1 vs F2	6.612	1.138	No	ns	-16.50 to 29.72
F1 vs F3	13.98	2.402	No	ns	-9.149 to 37.07
F1 vs F4	-28.68	4.937	Yes	**	-51.79 to -5.576
F1 vs F5	-4.918	0.8464	No	ns	-28.02 to 18.19
F2 vs F3	7.346	1.264	No	ns	-15.76 to 30.45
F2 vs F4	-35.30	6.075	Yes	***	-58.40 to -12.19
F2 vs F5	-11.53	1.984	No	ns	-34.64 to 11.58
F3 vs F4	-42.64	7.339	Yes	***	-65.75 to -19.53
F3 vs F5	-18.88	3.249	No	ns	-41.98 to 4.231
F4 vs F5	23.77	4.090	Yes	*	0.8584 to 48.87

Table Analyzed			
dosis Retensi			
One-way analysis of variance			
P value	< 0.0001		
P value summary	***		
Are means signif. different? (P < 0.05)	Yes		
Number of groups	5		
F	62658		
R square	0.9941		
Bartlett's test for equal variances			
Bartlett's statistic (corrected)	452.5		
P value	< 0.0001		
P value summary	***		
Do the variances differ signif. (P < 0.05)	Yes		
ANOVA Table			
	SS	df	MS
Treatment (between columns)	16027	4	4007
Residual (within columns)	95.60	1495	0.06395
Total	16123	1499	

Tukey's Multiple Comparison Test	Mean Diff.	q	Significant? P	Summary	95% CI of diff
F1 vs F2	-3.317	227.2	Yes	***	-3.374 to -3.260
F1 vs F3	-9.271	635.0	Yes	***	-9.328 to -9.214
F1 vs F4	-0.6824	46.74	Yes	***	-0.7392 to -0.6257
F1 vs F5	-3.124	214.0	Yes	***	-3.181 to -3.067
F2 vs F3	-5.954	407.8	Yes	***	-6.011 to -5.897
F2 vs F4	2.635	180.5	Yes	***	2.578 to 2.691
F2 vs F5	0.1930	13.22	Yes	***	0.1362 to 0.2498
F3 vs F4	8.589	588.3	Yes	***	8.532 to 8.645
F3 vs F5	6.147	421.0	Yes	***	6.090 to 6.204
F4 vs F5	-2.442	167.2	Yes	***	-2.498 to -2.385

## Lampiran 4. Perhitungan.

### Pembuatan kurva baku Fucoidan

Sebanyak 1 mg fucoidan ditimbang seksama kemudian larutkan menggunakan labu tentukur 10 mL dan dicukupkan dengan akuades hingga tanda batas untuk menghasilkan konsentrasi akhir sebesar 100 ppm. Larutan baku ini kemudian diencerkan menjadi seri pengenceran 1,25, 2,5, 5, 10, 20, 40, dan 80 ppm.

Untuk pengenceran 80 ppm, dilakukan dengan labu tentukur 5 mL

$$V_1N_1=V_2N_2$$

$$80 \text{ ppm} \times 5 \text{ ml} = 100 \text{ ppm} \times N_2$$

$$400/100 = N_2$$

$$N_2 = 4 \text{ ml}$$

Jadi 4 ml dicuplik dari larutan baku 100 ppm kemudian dicukupkan hingga tanda batas pada labu tentukur 5 ml.

### Pengukuran kadar Aktual Fucoidan dalam sistem DMN-F

Setelah melarutkan DMN-F dengan 13 ml aquadest, sebanyak 1ml dicuplik dan diukur. Data absorbansi hasil pengukuran dapat dilihat pada lampiran tabel 5D.

$$y=0,0114x + 0,0436$$

$$0.1525 - 0.0436 = 0,0114x$$

$$0.1089 / 0.0114 = x$$

$$x = 9,55 \text{ ug/ml}$$

$$13 \text{ ml} * 9,55 \text{ ug/ml} = 124,19 \text{ ug}$$

### Penentuan Kandungan Fucoidan dalam sistem DMN

Microneedle dikeruk kemudian diukur dengan spektrofotometri UV-VIS, hasil pengukuran kemudian dibandingkan dengan kandungan teoritis.

$$\%Dosis \text{ muat} = \frac{\text{konsentrasi hasil pengukuran}}{\text{Jumlah Teoritis}} \times 100$$

$$\%Dosis\ muat = \frac{117,06}{120,596} \times 100$$

$$\%Dosis\ muat = \frac{117,06}{120,596} \times 100$$

$$= 97\%$$

Jadi efisiensi peng-inkorporasian fucoidan dalam sistem DMN-F untuk F1 yaitu sebesar 97 % dari dosis awal/teoritisnya.

### Perhitungan uji permeasi dan retensi

Perhitungan kadar permeasi fucoidan dalam sistem DMN-F menggunakan persamaan yang dari hasil pembuatan kurva baku yang dapat dilihat pada lampiran 5F.

$$y=0.0114x+0.0436$$

-Permeasi F1 jam ke-0,25

1 ml sampel diukur asil pengukuran diperoleh abs= 0,422.

$$0,0623-0,0436=0,0114x$$

$$0.0252=0,0114x$$

$$x= 1,640 \mu\text{g/ml}$$

karena total cairan dalam sistem sel difusi franz sebanyak 13 ml, kemudian ditambahkan dengan faktor koreksi (fc) hasil pencuplikan interval waktu sebelumnya maka

$$(1,640 \mu\text{g} \times 13) + 0 = 21,32 \mu\text{g}$$

Konsentrasi yang diperoleh kemudian dihitung dengan menggunakan persamaan dibawah ini.

$$Permeasi(\%) = \frac{Hasil\ pengukuran\ waktu\ ke - n}{kadar\ aktual\ fucoidan\ dalam\ DMN} * 100$$

$$Permeasi(\%) = \frac{21,32 \mu\text{g}}{119,32 \mu\text{g}} * 100$$

$$\text{Permeasi}(\%) = 17,86\%$$

Perhitungan kadar Fucoidan yang teretensi dalam jaringan kulit dilakukan dengan menggunakan rumus seperti diatas. 2 g jaringan kulit yang telah dihaluskan dan diekstraksi dengan 2ml PBS.

Hasil F1:

$$0,0521 - 0,0436 = 0,0114x$$

$$0,0085 = 0,0114x$$

$$x = 0,7456 \mu\text{g}$$

selanjutnya konsentrasi di bagi dengan jumlah sampling kulit

$$\text{Retensi} = 0,7456 \mu\text{g} / 2 \text{ cm}^2 = 0,372$$

### Hemolisis darah

$$\text{Hemolysis}(\%) = \frac{\text{Abs}(\text{Test sample}) - \text{Abs}(\text{Negative control})}{\text{Abs}(\text{positive control}) - \text{Abs}(\text{Negative control})} * 100$$

Hasil uji menggunakan spektrofotometer UV-Vis diketahui:

Kontrol positif	Kontrol negatif	5 ppm	50 ppm	500 ppm
1,973	0,0973	0,102	0,112	0,117
		0,109	0,113	0,138
		0,110	0,111	0,141
Rata-rata		0,107	0,112	0,132

- 5 ppm

$$\text{Hemolysis}(\%) = \frac{0,107 - 0,0973}{1,973 - 0,0973} * 100$$

$$\text{Hemolysis}(\%) = 0,515$$

- 50 ppm

$$\text{Hemolysis}(\%) = \frac{0,112 - 0,0973}{1,973 - 0,0973} * 100$$

$$\text{Hemolysis}(\%) = 0,781$$

- 500 ppm

$$\text{Hemolysis}(\%) = \frac{0,132 - 0,0973}{1,973 - 0,0973} * 100$$

$$\text{Hemolysis}(\%) = 1,848$$

### Perhitungan dosis fucoidan sebagai anti-aging untuk pengujian in-vivo.

Pada F4 DMN-F mengandung 115.80 µg yang terukur pada instrument spektrofotometer. Untuk pengaplikasian DMN-F pada punggung kulit tikus akan diberikan sebanyak 2 patch DMN-F agar mampu memberikan efek pada area yang lebih luas sehingga total dosis yang diterima setiap hewan uji setiap hari adalah

$$115,80 \times 2 = 231,6 \mu\text{g}$$

## Lampiran 5. Tabel Data.

### A. Uji kekuatan mekanik

Formula	Tinggi awal (µm)	Tinggi akhir(µm)	Height Reduction (%)
F1	631,77 ± 1,57	566,90 ± 4,02	11,19 ± 2,71
F2	708,09 ± 3,98	533,35 ± 3,64	25,13 ± 2,09
F3	660,96 ± 1,37	442,09 ± 3,61	32,68 ± 2,30
F4	682,04 ± 0,80	673,43 ± 1,43	1,26 ± 1,18
F5	645,62 ± 4,10	612,94 ± 5,0	5,09 ± 1,16

### B. Uji Kelarutan

Formula	Time (menit)				
	0	2	4	6	8
F1	0	40,42 ± 1,97	71,69 ± 2,76	88,02 ± 5,04	100
F2	0	38,47 ± 1,96	70,61 ± 3,50	86,14 ± 5,91	100
F3	0	34,04 ± 1,66	70,29 ± 1,32	86,75 ± 4,45	100
F4	0	40,89 ± 1,89	68,10 ± 4,73	84,99 ± 4,84	100
F5	0	32,51 ± 1,38	62,06 ± 3,24	88,76 ± 3,78	100

### C. Water loss on drying dan bobot teoritis fucoidan

Formula	Bobot awal (g)	Bobot akhir (g)	%LOD	Kandungan toritis fucoidan (µg)
---------	----------------	-----------------	------	---------------------------------

F1	$0,5029 \pm 0,0079$	$0,2251 \pm 0,0148$	$55,24 \pm 3,31$	$120,60 \pm 22,62$
F2	$0,5049 \pm 0,0030$	$0,2275 \pm 0,0013$	$54,93 \pm 0,08$	$217,94 \pm 34,51$
F3	$0,5047 \pm 0,0043$	$0,2532 \pm 0,0052$	$49,83 \pm 0,68$	$276,21 \pm 39,66$
F4	$0,5029 \pm 0,0002$	$0,2336 \pm 0,0184$	$53,53 \pm 3,66$	$116,59 \pm 26,66$
F5	$0,4989 \pm 0,0055$	$0,2553 \pm 0,0153$	$48,79 \pm 3,50$	$196,06 \pm 32,72$

**D. Tabel konsentrasi fucoidan yang diukur menggunakan spektrofotometer UV-Vis**

Formula	absorbansi	Kons ( $\mu\text{g/ml}$ )	13 ml	rata-rata	SD
F1	0,1525	9,55	124,19	119,24	4,45
	0,1430	8,72	113,40		
	0,1489	9,24	120,12		
F2	0,2163	15,15	196,96	211,86	10,92
	0,2328	16,60	215,80		
	0,2390	17,13	222,81		
F3	0,2682	19,70	256,12	262,47	20,98
	0,2545	18,50	240,55		
	0,2986	22,36	290,75		
F4	0,1410	8,54	111,12	115,80	5,05
	0,1431	8,72	113,46		
	0,1513	9,44	122,81		
F5	0,1949	13,26	172,49	188,63	12,80
	0,2099	14,58	189,60		
	0,2223	15,67	203,80		

### E. Water Vapor Transmission

Formula	WVT (g/cm <sup>2</sup> d)	Rata- rata	SD
F1	0,107924	0,134974	0,020014
	0,141281		
	0,155716		
F2	0,127274	0,122897	0,003135
	0,121319		
	0,120097		
F3	0,127715	0,127174	0,001936
	0,129228		
	0,12458		
F4	0,122978	0,11487	0,006726
	0,115125		
	0,106508		
F5	0,117411	0,111078	0,015423
	0,089835		
	0,125987		

### F. Surface pH

Formula	pH	Rata- rata	SD
F1	6,58	6,40	0,21
	6,46		
	6,16		
F2	6,95	6,83	0,11
	6,73		
	6,81		
F3	5,90	5,75	0,14
	5,75		
	5,61		
F4	6,23	6,10	0,15
	6,13		
	5,93		
F5	5,87	5,83	0,04
	5,85		
	5,79		

### G. MAA

Tabel MAA RH 33%

Formula	Waktu (hari)								
	0	2	4	6	8	10	12	14	
F1	Rata-rata	0	1,1335	1,3447	1,8501	2,0197	2,1278	2,2010	2,3390
	SD	0	0,1374	0,2152	0,1749	0,0502	0,0185	0,1375	0,1124
F2	Rata-rata	0	2,6794	3,0315	3,3081	3,4451	3,6339	3,7692	3,8526
	SD	0	0,1734	0,1953	0,1863	0,1828	0,1999	0,2094	0,2071
F3	Rata-rata	0	5,2596	5,6506	6,0126	6,1010	6,2185	6,4424	6,5308
	SD	0	0,2486	0,2853	0,2712	0,3194	0,3226	0,3707	0,3761
F4	Rata-rata	0	0,7902	1,0713	1,4379	1,4662	1,6021	1,6589	1,8706
	SD	0	0,2434	0,1924	0,4267	0,0700	0,1692	0,1399	0,3244
F5	Rata-rata	0	1,7068	2,1440	2,6007	2,7572	2,9304	3,1008	3,3522
	SD	0	0,1685	0,1606	0,1872	0,1913	0,2096	0,2103	0,1496

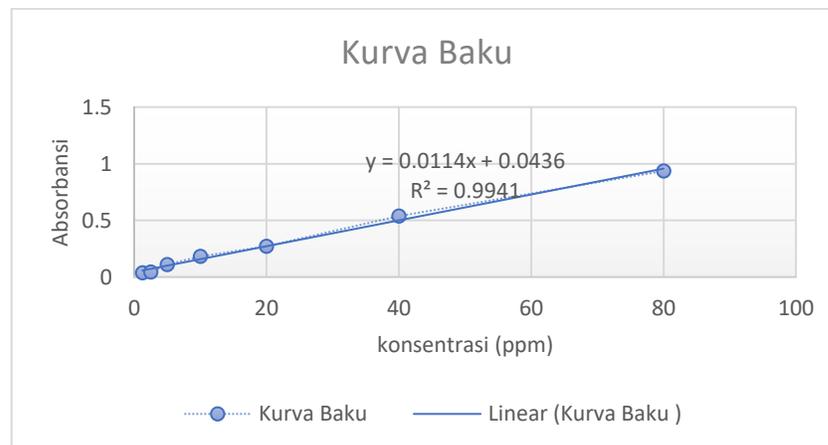
Tabel MAA RH 65%

Formula	Waktu (hari)								
	0	2	4	6	8	10	12	14	
F1	Rata-rata	0	5,8576	7,7346	8,5874	9,5834	9,5881	10,3269	11,5998
	SD	0	0,4037	0,3518	0,2836	0,5522	0,2593	0,3116	0,3677
F2	Rata-rata	0	6,5160	7,0570	7,9170	8,9979	9,2389	10,3344	11,4860
	SD	0	0,1738	0,1940	0,3052	0,4545	0,4022	0,0987	0,8064
F3	Rata-rata	0	4,3355	5,3764	6,2931	7,1715	7,2196	7,9831	9,3350
	SD	0	0,6997	0,5377	0,3140	0,4383	0,3989	0,6743	0,6876
F4	Rata-rata	0	5,7833	6,5397	8,2643	8,6698	8,8067	9,1804	10,0943
	SD	0	0,4884	0,5874	0,7180	0,3442	0,1394	0,3109	0,1505
F5	Rata-rata	0	6,3480	6,6116	7,5057	8,4089	8,4329	9,1733	10,6111
	SD	0	0,7684	0,7669	0,7896	0,9130	0,6804	0,7715	0,7442

#### H. Penyiapan Kurva Baku

Konsentrasi (ppm)	Absorbansi			
	1	2	3	Rata-rata
1,25	0,0360	0,0370	0,0380	0,0370
2,5	0,0430	0,0430	0,0430	0,0430
5	0,1080	0,1090	0,1140	0,1103
10	0,1800	0,1830	0,1850	0,1827
20	0,2710	0,2710	0,2710	0,2710
40	0,5370	0,5370	0,5380	0,5373
80	0,9350	0,9360	0,9370	0,9360

Persamaan kurva baku dari hasil pengukuran menggunakan spektrofotometer UV-Vis yaitu  $y=0.0114x+0.0436$ , dimana kurva nya dapat dilihat pada gambar dibawah ini.



## I. Permeasi dan retensi

Tabel data Permeasi F1

Waktu (jam)	abs	Kons (µg/ml)	13 ml (µg)	FK	Kons. total (µg)	rata-rata (µg)	permeasi (%)	rata-rata (%)	SD
0.25	0,0623	1,6404	21,3246	0,0000	21,3246	17,9795	17,8852	15,06	5,37
	0,0566	1,1404	14,8246	0,0000	14,8246		12,4336		
	0,0592	1,3684	17,7895	0,0000	17,7895		14,9203		
0.50	0,0745	2,7105	35,2368	1,6404	36,8772	32,1687	30,9295	26,98	2,76
	0,0693	2,2535	29,2956	1,1404	30,4360		25,5271		
	0,0680	2,1404	27,8246	1,3684	29,1930		24,4846		
0.75	0,0696	2,2807	29,6491	4,3509	34,0000	35,4909	28,5163	29,75	1,84
	0,0690	2,2281	28,9649	3,3939	32,3588		27,1398		
	0,0757	2,8158	36,6053	3,5088	40,1140		33,6442		
1	0,0709	2,3947	31,1316	4,3532	35,4847	39,4846	29,7616	33,11	3,34
	0,0750	2,7544	35,8070	3,3961	39,2031		32,8802		
	0,0789	3,0965	40,2544	3,5116	43,7660		36,7072		
2	0,0800	3,1930	41,5088	6,7479	48,2567	48,4785	40,4736	40,66	3,33
	0,0781	3,0289	39,3763	6,1505	45,5268		38,1840		
	0,0831	3,4649	45,0439	6,6081	51,6519		43,3213		
3	0,0834	3,4912	45,3860	9,9409	55,3268	54,8396	46,4035	45,96	1,65
	0,0808	3,2632	42,4211	9,1794	51,6005		43,2781		
	0,0853	3,6553	47,5184	10,0730	57,5914		48,3028		
4	0,0832	3,4737	45,1579	13,4321	58,5900	59,5752	49,1403	49,39	7,02
	0,0831	3,4649	45,0439	12,4426	57,4864		48,214		
	0,0865	3,7632	48,9211	13,7283	62,6493		52,5449		

	<u>0,0831</u>	<u>3,4649</u>	<u>45,0439</u>	<u>16,9058</u>	<u>61,9496</u>		<u>51,9581</u>		
<b>5</b>	<u>0,0859</u>	<u>3,7105</u>	<u>48,2368</u>	<u>15,9075</u>	<u>64,1443</u>	64,8530	<u>53,7988</u>	55,94	2,45
	<u>0,0883</u>	<u>3,9211</u>	<u>50,9737</u>	<u>17,914</u>	<u>68,4651</u>		<u>57,4227</u>		
	<u>0,0811</u>	<u>3,2895</u>	<u>42,7632</u>	<u>20,3707</u>	<u>63,1339</u>		<u>52,9513</u>		
<b>6</b>	<u>0,0829</u>	<u>3,4474</u>	<u>44,8158</u>	<u>19,6180</u>	<u>64,4338</u>	66,6893	<u>54,0416</u>	55,9333	7,74
	<u>0,0884</u>	<u>3,9298</u>	<u>51,0877</u>	<u>21,4125</u>	<u>72,5002</u>		<u>60,8070</u>		
	<u>0,0794</u>	<u>3,1404</u>	<u>40,8246</u>	<u>23,6602</u>	<u>64,4847</u>		<u>54,0843</u>		
<b>7</b>	<u>0,0812</u>	<u>3,2939</u>	<u>42,8202</u>	<u>23,0654</u>	<u>65,8856</u>	67,1165	<u>55,2592</u>	56,29	7,76
	<u>0,0836</u>	<u>3,5105</u>	<u>45,6368</u>	<u>25,3423</u>	<u>70,9791</u>		<u>59,5313</u>		
	<u>0,0790</u>	<u>3,1053</u>	<u>40,3684</u>	<u>26,8005</u>	<u>67,1689</u>		<u>56,3356</u>		
<b>8</b>	<u>0,0816</u>	<u>3,3333</u>	<u>43,3333</u>	<u>26,3592</u>	<u>69,6926</u>	69,1504	<u>58,4522</u>	57,99	4,80
	<u>0,0802</u>	<u>3,2105</u>	<u>41,7368</u>	<u>28,8528</u>	<u>70,5897</u>		<u>59,2046</u>		
	<u>0,0760</u>	<u>2,8421</u>	<u>36,9474</u>	<u>29,9058</u>	<u>66,8532</u>		<u>56,0708</u>		
<b>24</b>	<u>0,0778</u>	<u>3,0000</u>	<u>39,0000</u>	<u>29,6926</u>	<u>68,6926</u>	70,0481	<u>57,6135</u>	58,75	4,30
	<u>0,0809</u>	<u>3,2719</u>	<u>42,5351</u>	<u>32,0633</u>	<u>74,5984</u>		<u>62,5668</u>		

### Tabel Retensi

FORMULA	ABSORBANSI	Kons ( $\mu\text{g}$ )	RATA-RATA	SD
F1	0,0453	0,1491	0,3596	0,1571
	0,0482	0,4035		
	0,0496	0,5263		
F2	0,0810	3,2807	3,6784	0,3413
	0,0905	4,1140		
	0,0851	3,6404		
F3	0,1512	9,4386	9,6316	0,2251
	0,1570	9,9474		
	0,1520	9,5088		
F4	0,0548	0,9825	1,0380	0,3069
	0,0600	1,4386		
	0,0515	0,6930		
F5	0,0848	3,6140	3,4854	0,1075
	0,0834	3,4912		
	0,0818	3,3509		

### J. Jumlah kerutan

Kelompok	Replikasi			Rata-rata	SD
	I	II	III		
Kontrol Sehat (G1)	6	4	4	4,67	0,94
Kontrol Positif (G2)	6	7	7	6,67	0,47
Treatment DMN-F (G3)	7	9	10	8,67	1,25
MN Blank (G4)	21	15	17	17,67	2,49
Kontrol Negatif (G5)	18	28	22	22,67	4,11

### K. Elastisitas Kulit

Kelompok	Replikasi			Rata-rata	SD
	I	II	III		
Kontrol Sehat (G1)	6,89	4,07	5,76	5,57	1,16
Kontrol Positif (G2)	4,14	7,13	6,39	5,89	1,27
Treatment DMN-F (G3)	9,5	5,79	7,99	7,76	1,52
MN Blank (G4)	19,97	14,19	15,89	16,68	2,43
Kontrol Negatif (G5)	19,21	15,29	16,76	17,09	1,62

**L. Tingkat Kelembaban Kulit**

Kelompok	Replikasi			Rata-rata	SD
	I	II	III		
Kontrol Sehat (G1)	49,3	57,7	56,5	54,50	4,54
Kontrol Positif (G2)	56,0	58,6	52,6	55,73	3,01
Treatment DMN-F (G3)	53,6	54,8	54,4	54,27	0,61
MN Blank (G4)	45,4	46,9	41,3	44,53	2,90
Kontrol Negatif (G5)	43,3	41,3	36,6	40,40	3,44

## Lampiran 6. Izin Kode Etik Penelitian.

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, SpCK TELP. 081241850658, 0411 5780103. Fax : 0411-581431

**REKOMENDASI PERSETUJUAN ETIK**  
Nomor : 549/UN4.6.4.5.31/ PP36/ 2023

Tanggal: 7 Agustus 2023

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

No Protokol	UH23050314	No Sponsor	
Peneliti Utama	apt Alghifary Anas Achmad, S.Si	Sponsor	
Judul Peneliti	UJI AKTIVITAS FUCOIDAN SEBAGAI ANTI-AGING DALAM FORMULASI PENGHANTARAN TRANSDERMAL DISSOLVING MICRONEEDLES		
No Versi Protokol	2	Tanggal Versi	7 Agustus 2023
No Versi PSP		Tanggal Versi	
Tempat Penelitian	Fakultas Farmasi Universitas Hasanuddin Makassar		
Jenis Review	<input type="checkbox"/> Exempted <input checked="" type="checkbox"/> Expedited <input type="checkbox"/> Fullboard Tanggal	Masa Berlaku 7 Agustus 2023 sampai 7 Agustus 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 Lapnr 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