DAFTAR PUSTAKA

Ahad, A., Aqil, M., Kohli, K., Sultana, Y., Mujeeb, M. 2014. Design, formulation and optimization of valsartan transdermal gel containing iso-eucalyptol as novel permeation enhancer: Preclinical assessment of pharmacokinetics in Wistar albino rats. *Expert Opinion on Drug Delivery*. 11(8):1149–1162.

Ahad, A., Al-Mohizea, A.M., Al-Jenoobi, F.I., Aqil, M. 2016. Transdermal delivery of angiotensin II receptor blockers (ARBs), angiotensin-converting enzyme inhibitors (ACEIs) and others for management of hypertension. *Drug Delivery.* 23(2): 579-590.

Akram, M.R., Ahmad, M., Abrar, A., Sarfraz, R.M., Mahmood, A. 2018. Formulation design and development of matrix diffusion controlled transdermal drug delivery of glimepiride. *Drug Des. Devel. Ther*. 12(1): 349–364.

Ali, H.S.M., Hanafy, A.F. 2017. Glibenclamide Nanocrystals in a Biodegradable Chitosan Patch for Transdermal Delivery: Engineering, Formulation, and Evaluation. *J. Pharm. Sci.* 106(1):402–410.

Ali, H.E., Abdel-Aziz, M., Ibrahiem, A.M., Sayed, M.A., Abd-Rabboh, H.S.M., Awwad, N.S., Algarni, H., Shkir, M., Khairy, M.Y. 2022. Microstructure Study and Linear/Nonlinear Optical Performance of Bi-Embedded PVP/PVA Films for Optoelectronic and Optical Cut-Off Applications. *Polymers.*

Al-Japarai, K.A.S., Mahmood, S., Almurisi, S.H., Venugopal, J.R., Hilles, A.R., Azmana, M., Raman, S. 2020. Current trends in polymer microneedle for transdermal drug delivery. *International Journal of Pharmaceutics.*

Astuti, R.D. 2021. Patch Formulation of Celery Leaves Extract (Apium Graveolens L.) As Mosquito Repellent. *Atlantis Press.* 521(1).

Battegay, E.J., Lip, G.Y.H., Bakris, G.L. 2005. *Hypertension: Principles and Practice*. Informa Healthcare.

Bhosale, S.S., Avachat, A.M. 2013. Design and development of ethosomal transdermal drug delivery system of valsartan with preclinical assessment in Wistar albino rats. *J. Liposome Res*. 23(1):119–125.

Dhaliwal, K., Dosanjh, P. 2018. Biodegradable Polymers and their Role in Drug Delivery Systems. *Biomed J Sci & Tech Res.* 11(1).

Frohlich, E.D., Ventura, H.O. 2009. *An Atlas of Investigation and Management Hypertension, Clinical Publishing*. Atlas Medical Publishing Ltd, Mill Street, Oxford.

Gaaz, T. S., Sulong, A. B., Akhtar, M. N., Kadhum, A. A. H., Mohamad, A. B., Al-Amiery, A. A., McPhee, D. J. 2015. Properties and applications of polyvinyl alcohol, halloysite nanotubes and their nanocomposites. *Molecules*. 20(12):22833-22847.

Garland, M.J., Caffarel-salvador, E., Migalska, K., Woolfson, A.D., Donnelly, R.F. 2012. Dissolving polymeric microneedle arrays for electrically assisted transdermal drug delivery. *J. Control. Release.* 159(1):52-59

Gigliobianco, M.R., Casadidio, C., Censi, R., Di-Martino, P. 2018. Nanocrystals of poorly soluble drugs: Drug bioavailability and physicochemical stability. *Pharmaceutics.*

Guillot, A.J., Cordeiro, A.S., Donnelly, R.F., Monstesinos, M.C., Garrigues, T.M., Melero, A. 2020. Microneedle-Based Delivery: An Overview of Current Applications and Trends. *Pharmaceutics.*

González-Vázquez, P., Larrañeta, E., McCrudden, M.T.C., Jarrahian, C., Rein-Weston, A., Quintanar-Solares, M., Zehrung, D., McCarthy, H., Courtenay, A.J., Donnelly, R.F. 2017. Transdermal delivery of gentamicin using dissolving microneedle arrays for potential treatment of neonatal sepsis. *J. Control. Release*. 265(1):30–40.

He, J., Zhang, Z., Zheng, X., Li, L., Qi, J., Wu, W., Lu, Y. 2021. Design and Evaluation of Dissolving Microneedles for Enhanced Dermal Delivery of Propranolol Hydrochloride. *Pharmaceutics.*

He, X., Sun, J., Zhuang, J., Xu, H., Liu, Y., Wu, D. 2019. Microneedle System for Transdermal Drug and Vaccine Delivery: Devices, Safety, and Prospects. *Dose-Response: An International Journal.*

Helberg, R.M.L., Dai, Z., Ansaloni, L., Deng, L. 2020. PVA/PVP blend polymer matrix for hosting carriers in facilitated transport membranes: Synergistic enhancement of CO_2 separation performance. *Green Energy & Environment.* 5(1):59-68.

Himawan, A., Djide, N.J.N., Mardikasari, S.A., Utami, R.N., Arjuna, A., Donnelly, R.F., Permana, A.D., 2021. A Novel In Vitro Approach to Investigate the Effect of Food Intake on Release Profile of Valsartan in Solid Dispersion-Floating Gel In-Situ Delivery System. *Eur. J. Pharm*. *Sci.*

Jaspreet, S.K., Quek, T.C., Soon, W.J., Choi, J., Zou, S., Kang, L. 2013.

Effect of Microneedle Geometry and Supporting Substrate on Microneedle Array Penetration into Skin. *Journal of Pharmaceutical Sciences.* 102(11): 4100-4108.

Jaspreet, K., Sandeep, K. 2018. Development of Nanocrystal Formulation With Improved Dissolution. *Journal of Drug Delivery and Therapeutics.* 8(5): 118-129.

Jeong, W.Y., Kwon, M., Choi, H.E., Kim, K.S., 2021. Recent advances in transdermal drug delivery systems. *Biomater. Res*. 25(1):1–15.

Jiang, X., Zhao, H., Li, W. 2022. Microneedle-Mediated Transdermal Delivery of Drug-Carrying Nanoparticles. *Front. Bioeng. Biotechnol.*

Jung, J.H., Jin, S.G. 2021. Microneedle for transdermal drug delivery: current trends and fabrication. *J. Pharm. Investig*. 51(1):503–517.

Katzung, B.G., Masters, S.B., Trevor, A.J., 2012. F*armakologi Dasar & Klinik Vol 2*. Diterjemahkan oleh Ricky Soeharsono, EGC : Jakarta.

Kementerian Kesehatan RI. 2020. *Profil Kesehatan Indonesia Tahun 2019*. Kementerian Kesehatan RI.

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. *Journal of Drug Delivery Science and Technology.* 60(1).

Lalitha, N., Sanjay, P.P.N., Vyshak, M.G., Kadri, U. 2010. Stability-indicating reverse phase HPLC method for the determination of cefazolin. *Trop. J. Pharm. Res*. 9(1):45–50.

Liu, H.Y., Du, L., Zhao, Y.T., Tian, W.Q. 2015. In vitro hemocompatibility and cytotoxicity evaluation of halloysite nanotubes for biomedical application. *J. Nanomater*.

Luzuriaga, M.A., Berry, D.R., Reagan, J.C., Smaldone, R.A., Gassensmith. J.J. 2018. Biodegradable 3D Printed Polymer Microneedles for Transdermal Drug Delivery. *Lab Chip.* 16(1).

Merici, A., Fitri, L.K., Budiarti, N. 2020. The Effect of Artesunate and Brotowali (Tinospora Crispa) Combination on Histopathological, and Expression of Nuclear Factor Kappa B (NF-kβ) in Renal Tubules of Mice Infected With Plasmodium Berghei. *Clinical and Research Journal in Internal Medicine.* 1(1): 2723-5130.

Mil, K.M., Gryciuk, M.E., Pawlukianiec, C., Żendzian-Piotrowska, M., Ładny,

J.R., Zalewska, A., Maciejczyk, M. 2021. Pleiotropic Properties of Valsartan: Do They Result from the Antiglycooxidant Activity? Literature Review and in Vitro Study. *Oxid. Med. Cell. Longev*.

Mogusala, N.R., Devadasu, V.R., Venisetty, R.K. 2015. Fabrication of Microneedle Molds and Polymer Based Biodegradable Microneedle Patches: A Novel Method. *American Journal of Drug Delivery and Therapeutics.* 2(2).

Nagarkar, R., Patel, J. 2019. Polyvinyl Alcohol: A Comprehensive Study. *Acta Scientific Pharmaceutical Sciences.* 3(4).

Oparil, S., Acelajado, M.C., Bakris, G.L., Berlowitz, D.R., Cifkova, R., Dominiczak, A.F., Grassi, G., Jordan, J., Poulter, N.R., Rodgers, A., Whelton, P.K. 2019. Hypertension. *Nat Rev Dis Primers.*

Parmar, P.K., Bansal, A.K. 2021. Novel nanocrystal-based formulations of apremilast for improved topical delivery. *Drug Deliv. Transl. Res*. 11(1): 966–983.

Permana, A.D., Paredes, A.J., Volpe-Zanutto, F., Anjani, Q.K., Utomo, E., Donnelly, R.F. 2020. Dissolving microneedle-mediated dermal delivery of itraconazole nanocrystals for improved treatment of cutaneous candidiasis. *Eur. J. Pharm. Biopharm*. 154(1):50–61.

Permana, A.D., Paredes, A.J., Zanutto, F.V., Amir, M.N., Ismail, I., Bahar, M.A., Sumarheni, Palma, S.D., Donnelly, R.F. 2021. Albendazole Nanocrystal-Based Dissolving Microneedles with Improved Pharmacokinetic Performance for Enhanced Treatment of Cystic Echinococcosis. *ACS Appl. Mater. Interfaces.* 13(1):38745–38760.

Putri, R.M., Setiaji, B., Masra, F., Budiati, E., 2021. Factors Related to The Incidence of Hypertension. I*ndones. J. Glob. Heal. Res*. 3(1):305–316.

Ruela, A.L.M., Perissinato, A.G., Lino, M.E.S., Mudrik, P.S., Pereira, G.R. 2016. Evaluation of skin absorption of drugs from topical and transdermal formulations. *Brazilian Journal of Pharmaceutical Sciences.* 52(3).

Sadeqi, A., Kiaee, G., Zeng, W., Nejad, H.R., Sonkusale, S. 2022. Hard polymeric porous microneedles on stretchable substrate for transdermal drug delivery. *Scientific reports.*

Shikka, S., Ravi, S., Gyan, P.S. 2017. Prevalence and Associated Risk Factors of Hypertension: A Cross-Sectional Study in Urban Varanasi. Int. *J. Hypertens.*

Shim, W.S., Hwang, Y.M., Park, S.G., Lee, C.K., Kang, N.G. 2018. Role of

Polyvinylpyrrolidone in Dissolving Microneedle for Efficient Transdermal Drug Delivery: In vitro and Clinical Studies. *Bulletin Korean Chemical Society.*

Sukandar, E.Y., Andrajati, R., Sigit, J.I., Adynyana, I.K., Setiadi, A.A.P., Kusnandar, 2008. *ISO Farmakoterapi, 1st ed*. PT. ISFI Penerbitan, Jakarta Barat.

Tajane, T.S. 2018. Estimation of Valsartan in Pharmaceutical Formulation by Area under Curve Spectrophotometric Method. *International Journal of Advances in Pharmaceutics.* 7(1):1-4.

Teodorescu, M., Bercea, M. 2015. Poly(vinylpyrrolidone) – A Versatile Polymer for Biomedical and Beyond Medical Applications. *Polymer-Plastics Technology and Engineering*. 54(1): 923–943.

Tuan-Mahmood, T.M., McCrudden, M.T.C., Torrisi, B.M., McAlister, E., Garland, M.J., Singh, T.R.R., Donnelly, R.F. 2013. Microneedles for intradermal and transdermal drug delivery. *European Journal of Pharmaceutical Sciences.*

Vora, L. K., Vavia, P. R., Larrrañeta, E., Bell, S. E. J., and Donelly, R. F. 2018. Novel nanosuspension-based dissolving microneedle arrays for transdermal delivery of a hydrophobic drug. *Journal of Interdisciplinary Nanomedicine.* 3(2).

Vora, L. K., Courtenay, A. J., Tekko, I. A., Larrañeta, E., & Donnelly, R. F. 2019. Pullulan-based dissolving microneedle arrays for enhanced transdermal delivery of small and large biomolecules*. International Journal of Biological Macromolecules.*

Wang, Q.L., Zhu, D.D., Liu, X.B., Chen, B.Z., Guo, X.D. 2016. Microneedles with Controlled Bubble Sizes and Drug Distributions for Efficient Transdermal Drug Delivery. *Scientific Reports.*

Waghule, T., Singhvi, G., Dubey, S.K., Pandey, M.M., Gupta, G., Singh, M., Dua, K. 2019. Microneedles: A smart approach and increasing potential for transdermal drug delivery system. *Biomedicine & Pharmacotherapy.* 109(1): 1249-1258.

Wati, I.F., Kuswandi, B., Pratoko, D.K. 2021. Development of Plastic Microzone Plate Biosensor for Antidiabetic Activity Screening in Medicinal Plant Extract. *J. Pustaka Kesehatan.* 9(1).

Wishart, D.S,, Guo, A.C., Oler E. 2022. HMDB 5.0: the Human Metabolome Database for 2022. *Nucleic Acids Res*. 7(50).

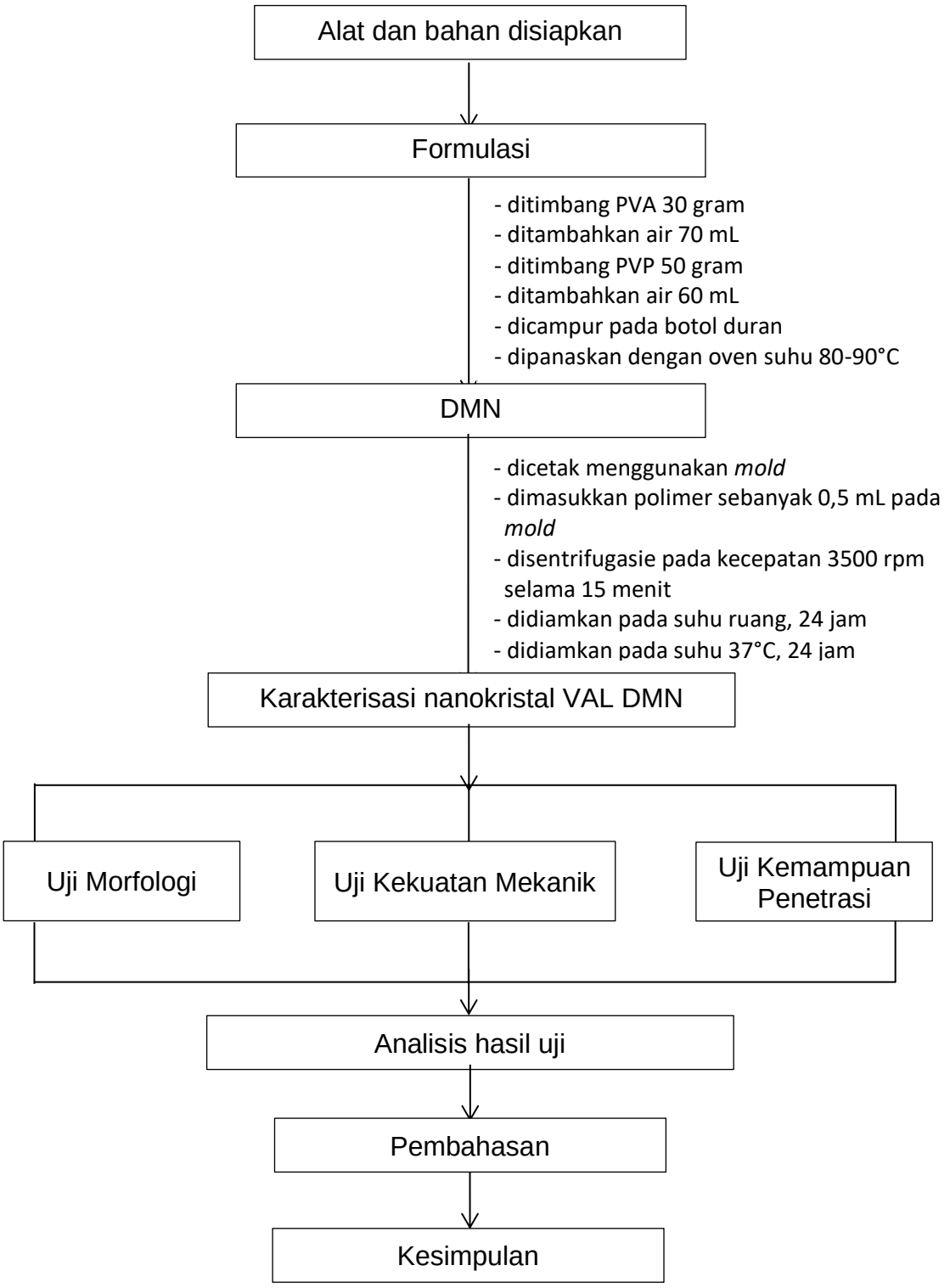
Zanela, J., Bilck, A.P., Casagrande, M., Grossmann, M.V.E., Yamashita, F. 2018. Polyvinyl alcohol (PVA) molecular weight and extrusion temperature in starch/PVA biodegradable sheets. *Polimeros.* 28(3).

Zhang, N., Zhou, X., Liu, L., Zhao, L., Xie, H., Yang, Z. 2021. Dissolving Polymer Microneedles for Transdermal Delivery of Insulin. *Front. Pharmacol*.

Zullfi, F., Dahlan, K., Sugita, P. 2014. Karakteristik Fluks Membran Dalam Filtrasi Limbah Cair Industri Pelapisan Logam. *Jurnal Biofisika.*

LAMPIRAN

Lampiran 1. Skema Kerja Umum



Lampiran 2. Hasil Uji Morfologi, Kekuatan Mekanik dan Kemampuan Penetrasi DMN

Tabel 9. Persentase penurunan panjang DMN dengan kandungan nanokristal VAL

Formula	Sebelum Uji Kekuatan Mekanik (Uji morfologi)			Setelah Uji Kekuatan Mekanik			% Penurunan Panjang *needle*	Rata-Rata	SD
	Panjang (µm)	Rata-rata	SD	Panjang (µm)	Rata-rata	SD			
F1	697	697	0	604	603	11.53	13.34	13.49	1.65
	697			591			15.21		
	697			614			11.91		
F2	699	697.67	6.11	603	601	11.14	13.73	13.86	0.84
	703			611			13.09		
	691			589			14.76		
F3	698	699	1	661	642.33	16.92	5.30	8.11	2.51
	699			628			10.16		
	700			638			8.86		
F4	697	698	2.65	602	590.67	16.28	13.63	15.37	2.63
	701			572			18.40		
	696			598			14.08		
F5	698	698.67	2.08	417	406	9.85	40.26	41.89	1.43
	697			398			42.90		
	701			403			42.51		

Tabel 10. Jumlah lubang DMN dengan kandungan nanokristal VAL yang terbentuk

Lapisan	Jumlah lubang yang terbentuk				
	F1	F2	F3	F4	F5
1	100	100	100	100	100
2	81	82	100	86	66
3	26	27	100	26	0
4	10	11	78	18	0
5	0	0	31	0	0
6	0	0	0	0	0
7	0	0	0	0	0
8	0	0	0	0	0

a. Contoh perhitungan persentase penurunan tinggi *needle*

Diketahui untuk F1 replikasi pertama, *microneedle* berukuran 697 µm dan setekah dilakukan uji mekanik, tingginya menjadi 604 µm. maka:

$$\% \text{ kompresi} = \frac{\text{tinggi sebelum uji} - \text{tinggi sesudah uji}}{\text{tinggi sebelum uji}} \times 100\%$$

$$= \frac{697-604}{697} \times 100\%$$

$$= 13.34\%$$

b. Perhitungan persentase penetrasi lapisan ke-n

Diketahui untuk F1 lapisan ke-4, terbentuk 10 lubang sedangkan *needle* berjumlah 100, maka:

$$\%\text{penetrasi lapisan ke-n} = \frac{\text{Jumlah lubang pada lapisan ke} - \text{n}}{\text{Jumlah lubang total}} \times 100\%$$

$$= \frac{10}{100} \times 100\%$$

$$= 10\%$$

Lampiran 3. Hasil Penentuan Densitas

Tabel 11. Bobot setiap bahan dalam tiap formula (% b/b)

Bahan	F1	F2	F3	F4	F5
PVA	9.6	7.2	4.8	2.4	0
PVP	24	28	32	36	40
Nanokristal-VAL	20	20	20	20	20
Air	46.4	44.8	43.2	41.6	40

Tabel 12. Bobot basah dan bobot kering sampel balok pipih tiap formula (mg)

Replikasi	F1		F2		F3		F4		F5	
	Basah	Kering	Basah	Kering	Basah	Kering	Basah	Kering	Basah	Kering
1	503	291	521	368	511	348	505	368	503	372
2	512	312	516	337	506	357	502	347	505	357
3	505	336	517	337	517	361	511	359	518	368

Tabel 13. Volume balok pipih tiap formula

Formula	Sisi 1 (mm)	Sisi 2 (mm)	Tinggi (mm)	Volume (mm^3)	BJ (mg/mm^3)	Rata-rata	SD
	10	10	5.74	574	1.01		
F1	10	10	5.89	589	1.01	1.01	0.002
	10	10	5.91	591	1.01		
	10	10	5.56	556	1.01		
F2	10	10	5.64	564	1.01	1.02	0.008
	10	10	5.68	568	1.03		
	10	10	5.21	521	1.00		
F3	10	10	5.19	519	1.04	1.02	0.019
	10	10	5.22	522	1.02		
F4	10	10	4.91	491	1.04	1.03	0.014

	10	10	4.98	498	1.02		
	10	10	5.03	503	1.02		
	10	10	4.72	472	1.02		
F5	10	10	4.64	464	1.03	1.03	0.014
	10	10	4.81	481	1.05		

Contoh perhitungan densitas

Diketahui: Bobot basah F1 replikasi pertama= 503 mg

Bobot kering F1 replikasi pertama= 291 mg

Panjang sisi 1 = 10 mm

Panjang sisi 2 = 10 mm

Tinggi = 5.74 mm

Bobot nanokristal VAL dalam formula = 20 g

Volume 1 *needle* = 0,00933 mm^3

Maka,

Volume = sisi 1 x sisi 2 x tinggi

= 10 mm x 10 mm x 5.74 mm

= 574 mm^3

Densitas = $\frac{\text{Bobot kering}}{\text{Volume}}$

= $\frac{291\ \text{mg}}{574\ \text{mm}^3}$

= 1.01 mg/mm^3

Lampiran 4. Hasil Penentuan LOD dan Persentase Jumlah Nanokristal VAL dalam Massa Kering

Tabel 14. Persentase kehilangan air

Replikasi	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)
1	42.15	29.37	31.90	27.13	26.04
2	39.06	34.69	29.45	30.88	29.31
3	33.46	34.82	30.17	29.75	28.96

Tabel 15. Persentase nanokristal VAL dalam massa kering

Replikasi	F1	F2	F3	F4	F5
1	34.57	28.31	29.37	27.45	27.04
2	32.82	30.62	28.35	28.93	28.29
3	30.06	30.68	28.64	28.47	28.15

Contoh perhitungan LOD dan persentase jumlah nanokristal VAL dalam massa kering

Diketahui: Bobot basah F1 replikasi pertama = 503 mg

Bobot kering F1 replikasi pertama = 291 mg

$$\%\text{Kehilangan air} = \frac{\text{Bobot basah} - \text{bobot kering}}{\text{Bobot basah}} \times 100\%$$

$$= \frac{503 - 291\ \text{mg}}{593\ \text{mg}} \times 100\%$$

$$= 42.15\%$$

$$\%\text{Jumlah nanokristal VAL dalam massa kering} = \frac{\text{Bobot nanokristal VAL}}{100\% - \%\text{kehilangan air}} \times 100$$

$$= \frac{20\ \text{mg}}{100\% - 42.15\%} \times 100$$

$$= 34.57\%$$

Lampiran 5. Hasil Penentuan Volume, Bobot Jarum (*Needle*), dan Bobot Nanokristal VAL

Tabel 16. Bobot 100 *needle* dalam massa kering (mg)

Replikasi	F1	F2	F3	F4	F5
1	0.94	0.94	0.94	0.97	0.95
2	0.94	0.95	0.97	0.95	0.96
3	0.94	0.96	0.95	0.95	0.98

Tabel 17. Jumlah nanokristal VAL dalam 100 *needle*

Formula	Jumlah nanokristal VAL	Rata-rata	SD
1	0.31	0.31	0.000
	0.31		
	0.31		
2	0.28	0.28	0.002
	0.28		
	0.29		
3	0.27	0.27	0.005
	0.28		
	0.27		
4	0.28	0.27	0.003
	0.27		
	0.27		
5	0.26	0.27	0.003
	0.27		
	0.27		

Contoh perhitungan penentuan volume, bobot jarum (*needle*), dan bobot nanokristal VAL

Volume satu *needle* = 0.00933 mm^3

Volume 100 *needle* = 0.00933mm^3 x 100 = 0.933 mm^3

Bobot untuk 100 *needle* = volume 100 *needle* x densitas

= 0.933 mm^3 x 1,01 mg/mm^3

= 0.94 mg

Diketahui: VAL dalam nanokristal (95.5%)

Maka,

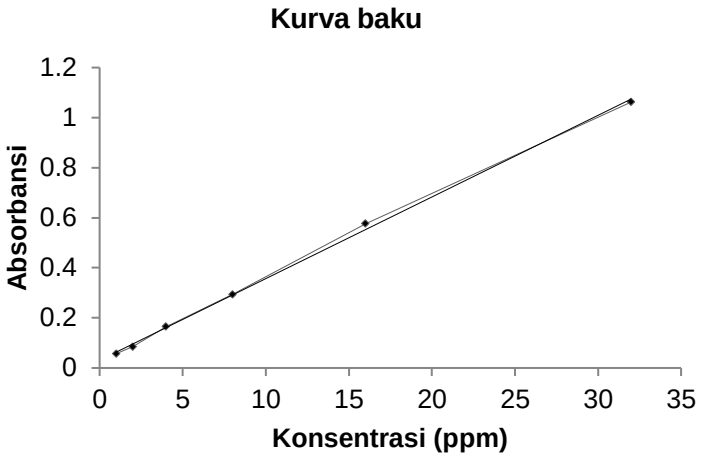
Jumlah nanokrsital VAL dalam formulasi F1 replikasi 1

= %VAL x bobot nanokristal dalam 100 *needle*

= 0.955 x 0.31

= 0.30 mg

Lampiran 6. Hasil Penentuan Kandungan VAL pada Sistem DMN



Gambar 13. Kruva baku VAL

Tabel 18. Pembuatan kurva baku

Konsentrasi	Abs1	Abs2	Abs3	Rata-rata	SD
0	0	0	0	0	0
1	0.056	0.063	0.052	0.057	0.006
2	0.071	0.095	0.088	0.085	0.012
4	0.161	0.165	0.168	0.165	0.003
8	0.291	0.284	0.306	0.294	0.011
16	0.553	0.573	0.604	0.577	0.026
32	1.061	1.043	1.083	1.062	0.020

Tabel 19. Kandungan nanokristal VAL dalam *needle*

Formula	Abs	Konsentrasi (µg/mL)	Jumlah VAL (mg)	%kandungan obat	Rata-rata	SD
F1	1.021	30.4	0.29	100	98.7	2.2
	1.019	30.3	0.29	99.8		
	0.982	29.2	0.29	96.1		

	0.904	26.8	0.27	95.1		
F2	0.912	27.1	0.27	95.9	96.3	1.3
	0.928	27.5	0.27	97.7		
F3	0.892	26.4	0.26	96.7		
	0.881	26.1	0.27	95.5	97.1	1.8
	0.913	27.1	0.26	99.1		
F4	0.893	26.5	0.26	98.2		
	0.911	27.0	0.26	100	98.3	1.9
	0.878	26.0	0.26	96.5		
F5	0.903	26.8	0.25	100		
	0.879	26.0	0.25	97.7	98.8	1.5
	0.883	26.2	0.26	98.2		

Contoh perhitungan kandungan nanokristal VAL dalam 100 *needle*

Diketahui: Abs F1 replikasi 1 = 1.021

Persamaan kurva baku y = 0.0326x + 0.030

Bobot rata-rata nanokristal VAL dalam formula = 0.27 mg

Maka,

1.021 = 0.0326x + 0.030

$x = \frac{1.021-0.030}{0.0326}$

x = 30.4 µg/mL

jumlah nanokristal VAL dalam *needle*

= %VAL dalam nanokristal x jumlah nanokristal VAL dalam massa kering

= 0.955 x 0.31 mg

= 0.29 mg

Lampiran 7. Hasil Uji Permeasi *Ex Vivo*

Tabel 20. Persentase permeasi F1

Waktu (jam)	Replikasi	Abs	Konsentrasi (µg/ml)	0.5 ml (µg)	8 ml (µg)	Faktor koreksi	VAL ter-permeasi	% Permeasi	Rata-rata	SD
	1	0	0.00	0.00	0	0	0	0		
0.25	2	0	0.00	0.00	0	0	0	0	0	0
	3	0	0.00	0.00	0	0	0	0		
	1	0.061	0.43	0.43	0.003	0.0000	0.00343	1.1828		
0.5	2	0.055	0.19	0.19	0.002	0.0000	0.00154	0.531	0.00206	0.00111
	3	0.054	0.15	0.15	0.001	0.0000	0.00123	0.4241		
	1	0.069	0.74	0.74	0.006	0.0004	0.00638	2.2		
0.75	2	0.071	0.82	0.82	0.007	0.0001	0.00678	2.3379	0.00610	0.00008
	3	0.066	0.63	0.63	0.005	0.0001	0.00516	1.7793		
	1	0.082	1.26	1.26	0.01	0.0011	0.01122	3.869		
1	2	0.092	1.65	1.65	0.013	0.0010	0.01421	4.9	0.01418	0.00029
	3	0.102	2.04	2.04	0.016	0.0007	0.01713	5.9069		
	1	0.112	2.44	2.44	0.019	0.0024	0.02193	7.5621		
2	2	0.143	3.66	3.66	0.029	0.0026	0.03193	11.01	0.02423	0.00068
	3	0.101	2.00	2.00	0.016	0.0028	0.01885	6.5		
	1	0.132	3.22	3.22	0.026	0.0048	0.03066	10.572		
3	2	0.187	5.39	5.39	0.043	0.0063	0.04944	17.048	0.03596	0.0117
	3	0.123	2.87	2.87	0.023	0.0048	0.02779	9.5828		
	1	0.241	7.52	7.52	0.06	0.0080	0.06822	23.524		
4	2	0.218	6.61	6.61	0.053	0.0117	0.06459	22.272	0.06456	0.00036
	3	0.219	6.65	6.65	0.053	0.0076	0.06089	20.997		
	1	0.256	8.11	8.11	0.065	0.0156	0.08046	27.745		
5	2	0.279	9.01	9.01	0.072	0.0183	0.09042	31.179	0.07926	0.0117
	3	0.217	6.57	6.57	0.053	0.0143	0.06691	23.072		
	1	0.265	8.46	8.46	0.068	0.0237	0.0914	31.517		
6	2	0.287	9.33	9.33	0.075	0.0273	0.10195	35.155	0.09881	0.00064
	3	0.311	10.27	10.27	0.082	0.0209	0.10309	35.548		
	1	0.388	13.30	13.30	0.106	0.0321	0.1386	47.793		
7	2	0.313	10.35	10.35	0.083	0.0366	0.11946	41.193	0.12464	0.0122
	3	0.319	10.59	10.59	0.085	0.0311	0.11588	39.959		
	1	0.298	9.76	9.76	0.078	0.0454	0.12356	42.607		
8	2	0.387	13.26	13.26	0.106	0.0470	0.15312	52.8	0.13532	0.0156
	3	0.328	10.94	10.94	0.088	0.0417	0.1293	44.586		

Tabel 21. Persentase permeasi F2

Waktu (jam)	Replikasi	Abs	Konsentrasi (µg/ml)	0.5 ml (µg)	8 ml (µg)	Faktor koreksi	VAL ter-permeasi	% Permeasi	Rata-rata	SD
	1	0	0.00	0	0	0	0	0		
0.25	2	0	0.00	0	0	0	0	0	0	0
	3	0	0.00	0	0	0	0	0		
0.5	1	0.055	0.19	0.19	0.001	0.0000	0.0015	0.5556		

	2	0.059	0.35	0.35	0.002	0.0000	0.0028	1.037	0.00	0.0
	3	0.057	0.27	0.27	0.002	0.0000	0.0022	0.8148	2	006
	1	0.073	0.90	0.90	0.007	0.0001	0.0074	2.7407	0.01	0.0
0.75	2	0.081	1.22	1.22	0.009	0.0003	0.0101	3.7407	1	04
	3	0.098	1.89	1.89	0.015	0.0002	0.0154	5.7037		
	1	0.098	1.89	1.89	0.015	0.0010	0.0162	6	0.01	0.0
1	2	0.102	2.04	2.04	0.016	0.0015	0.0179	6.6296	6	021
	3	0.087	1.45	1.45	0.011	0.0021	0.0138	5.1111		
	1	0.132	3.22	3.22	0.025	0.0029	0.0288	10.667	0.02	0.0
2	2	0.091	1.61	1.61	0.012	0.0036	0.0165	6.1111	3	062
	3	0.113	2.48	2.48	0.019	0.0036	0.0234	8.6667		
	1	0.159	4.29	4.29	0.034	0.0062	0.0405	15	0.04	0.0
3	2	0.178	5.04	5.04	0.040	0.0052	0.0455	16.852	3	025
	3	0.167	4.60	4.60	0.036	0.0060	0.0429	15.889		
	1	0.222	6.77	6.77	0.054	0.0109	0.0646	23.926	0.06	0.0
4	2	0.203	6.02	6.02	0.048	0.0102	0.0584	21.63		04
	3	0.198	5.82	5.82	0.046	0.0106	0.0573	21.222		
	1	0.287	9.33	9.33	0.074	0.0172	0.0919	34.037	0.08	0.0
5	2	0.279	9.01	9.01	0.072	0.0162	0.0884	32.741	3	123
	3	0.217	6.57	6.57	0.052	0.0165	0.0691	25.593		
	1	0.219	6.65	6.65	0.053	0.0265	0.0798	29.556	0.09	0.0
6	2	0.278	8.97	8.97	0.071	0.0252	0.0971	35.963	3	113
	3	0.298	9.76	9.76	0.078	0.0230	0.1012	37.481		
	1	0.382	13.07	13.07	0.104	0.0332	0.1378	51.037	0.12	0.0
7	2	0.298	9.76	9.76	0.078	0.0342	0.1123	41.593	5	127
	3	0.345	11.61	11.61	0.092	0.0328	0.1257	46.556		
	1	0.318	10.55	10.55	0.084	0.0463	0.1307	48.407	0.14	0.0
8	2	0.398	13.70	13.70	0.109	0.0440	0.1536	56.889	3	117
	3	0.372	12.67	12.67	0.101	0.0444	0.1458	54		

Tabel 22. Persentase permeasi F3

Waktu (jam)	Replikasi	Abs	Konsentrasi (µg/ml)	0.5 ml (µg)	8 ml (µg)	Faktor koreksi	VAL ter-permeasi	% Permeasi	Rata-rata	SD
	1	0.054	0.15	0.15	0.001	0	0.0012	0.4615	0.00	0.0
0.25	2	0.061	0.43	0.43	0.003	0	0.0034	1.3077	22	01
	3	0.056	0.23	0.23	0.001	0	0.0019	0.7308		
	1	0.076	1.02	1.02	0.008	0.0001	0.0083	3.1923	0.00	0.0
0.5	2	0.081	1.22	1.22	0.009	0.0004	0.0102	3.9231	86	01
	3	0.073	0.90	0.90	0.007	0.0002	0.0074	2.8462		
	1	0.091	1.61	1.61	0.012	0.0011	0.0141	5.4231	0.01	0.0
0.75	2	0.102	2.04	2.04	0.016	0.0016	0.018	6.9231	61	02
	3	0.098	1.89	1.89	0.015	0.0011	0.0162	6.2308		
	1	0.122	2.83	2.83	0.022	0.0027	0.0254	9.7692	0.02	0.0
1	2	0.142	3.62	3.62	0.028	0.0036	0.0326	12.538	89	04
	3	0.131	3.19	3.19 2	0.025	0.0030	0.0285	10.962		

	1	0.187	5.39	5.39	0.043	0.0056	0.0487	18.731	0.04	0.0
	2	0.192	5.59	5.59	0.044	0.0073	0.052	20	83	04
	3	0.171	4.76	4.76	0.038	0.0062	0.0443	17.038		
	1	0.21	6.30	6.30	0.050	0.0110	0.0614	23.615	0.08	0.0
3	2	0.298	9.76	9.76	0.078	0.0128	0.091	35	18	1
	3	0.311	10.27	10.27	0.082	0.0109	0.0931	35.808		
	1	0.382	13.07	13.07	0.104	0.0172	0.1218	46.846	0.10	0.0
4	2	0.318	10.55	10.55	0.084	0.0226	0.107	41.154	8	13
	3	0.288	9.37	9.37	0.074	0.0212	0.0962	37		
	1	0.398	13.70	13.70	0.109	0.0303	0.1399	53.808	0.13	0.0
5	2	0.319	10.59	10.59	0.084	0.0332	0.1179	45.346	27	1
	3	0.398	13.70	13.70	0.109	0.0306	0.1402	53.923		
	1	0.429	14.92	14.92	0.119	0.0440	0.1634	62.846	0.16	0.0
6	2	0.398	13.70	13.70	0.109	0.0437	0.1534	59	7	17
	3	0.499	17.67	17.67	0.141	0.0442	0.1857	71.423		
	1	0.503	17.83	17.83	0.142	0.0589	0.2016	77.538	0.18	0.0
7	2	0.439	15.31	15.31	0.122	0.0574	0.18	69.231	97	11
	3	0.449	15.70	15.70	0.125	0.0619	0.1876	72.154		
	1	0.483	17.04	17.04	0.136	0.0768	0.2132	82	0.23	0.0
8	2	0.598	21.57	21.57	0.172	0.0727	0.2454	94.385	11	16
	3	0.549	19.64	19.64	0.157	0.0776	0.2348	90.308		

Tabel 23. Persentase permeasi F4

Waktu (jam)	Replikasi	Abs	Konsentrasi (µg/ml)	0.5 ml (µg)	8 ml (µg)	Faktor koreksi	VAL ter-permeasi	% Permeasi	Rata-rata	SD
	1	0	0.00	0.00	0	0	0	0		
0.25	2	0	0.00	0.00	0	0	0	0	0	0
	3	0	0.00	0.00	0	0	0	0		
	1	0.055	0.19	0.19	0.001	0.0000	0.0015	0.5769	0.00	0.0
0.5	2	0.061	0.43	0.43	0.003	0.0000	0.0034	1.3077	2	01
	3	0.053	0.11	0.11	0.000	0.0000	0.0009	0.3462		
	1	0.068	0.70	0.70	0.005	0.0001	0.0058	2.2308	0.00	0.0
0.75	2	0.071	0.82	0.82	0.006	0.0004	0.007	2.6923	8	03
	3	0.088	1.49	1.49	0.011	0.0001	0.0121	4.6538		
	1	0.092	1.65	1.65	0.013	0.0008	0.0141	5.4231	0.01	0.0
1	2	0.098	1.89	1.89	0.015	0.0012	0.0163	6.2692	5	01
	3	0.089	1.53	1.53	0.012	0.0016	0.0139	5.3462		
	1	0.119	2.71	2.71	0.021	0.0025	0.0242	9.3077	0.02	0.0
2	2	0.102	2.04	2.04	0.016	0.0031	0.0195	7.5	3	03
	3	0.118	2.67	2.67	0.021	0.0031	0.0245	9.4231		
	1	0.165	4.52	4.52	0.036	0.0052	0.0414	15.923	0.04	0.0
3	2	0.187	5.39	5.39	0.043	0.0051	0.0483	18.577	4	04
	3	0.167	4.60	4.60	0.036	0.0058	0.0426	16.385		
	1	0.198	5.82	5.82	0.046	0.0097	0.0564	21.692	0.05	0.0
4	2	0.201	5.94	5.94	0.047	0.0105	0.0581	22.346	5	03
	3	0.182	5.19	5.19	0.041	0.0104	0.052	20		
5	1	0.298	9.76	9.76	0.078	0.0156	0.0937	36.038		

	2	0.189	5.47	5.47	0.043	0.0165	0.0603	23.192	0.074	0.018
	3	0.213	6.41	6.41	0.051	0.0156	0.0669	25.731		
	1	0.311	10.27	10.27	0.082	0.0253	0.1075	41.346		
6	2	0.287	9.33	9.33	0.074	0.0219	0.0966	37.154	0.107	0.01
	3	0.352	11.89	11.89	0.095	0.0220	0.1171	45.038		
	1	0.411	14.21	14.21	0.113	0.0356	0.1493	57.423		
7	2	0.383	13.11	13.11	0.104	0.0313	0.1362	52.385	0.141	0.007
	3	0.379	12.95	12.95	0.103	0.0339	0.1375	52.885		
	1	0.487	17.20	17.20	0.137	0.0498	0.1875	72.115		
8	2	0.398	13.70	13.70	0.109	0.0444	0.154	59.231	0.167	0.018
	3	0.404	13.93	13.93	0.111	0.0468	0.1583	60.885		

Tabel 24. Persentase permeasi F5

Waktu (jam)	Replikasi	Abs	Konsentrasi (µg/ml)	0.5 ml (µg)	8 ml (µg)	Faktor koreksi	VAL ter-permeasi	% Permeasi	Rata-rata	SD
	1	0	0.00	0.00	0	0	0	0		
0.25	2	0	0.00	0.00	0	0	0	0	0	0
	3	0	0.00	0.00	0	0	0	0		
	1	0	0.00	0.00	0	0.0000	0	0		
0.5	2	0	0.00	0.00	0	0.0000	0	0	0	0
	3	0	0.00	0.00	0	0.0000	0	0		
	1	0	0.00	0.00	0	0.0000	0	0		
0.75	2	0	0.00	0.00	0	0.0000	0	0	0	0
	3	0	0.00	0.00	0	0.0000	0	0		
	1	0.054	0.15	0.15	0.001	0.0000	0.001	0.3846		
1	2	0.056	0.23	0.23	0.002	0.0000	0.002	0.7692	0.003	0.003
	3	0.073	0.90	0.90	0.007	0.0000	0.007	2.6923		
	1	0.098	1.89	1.89	0.015	0.0001	0.015	5.7692		
2	2	0.087	1.45	1.45	0.012	0.0002	0.012	4.6154	0.014	0.002
	3	0.099	1.93	1.93	0.015	0.0009	0.016	6.1538		
	1	0.111	2.40	2.40	0.019	0.0020	0.021	8.0769		
3	2	0.132	3.22	3.22	0.026	0.0016	0.027	10.385	0.027	0.005
	3	0.143	3.66	3.66	0.029	0.0028	0.032	12.308		
	1	0.152	4.01	4.01	0.032	0.0044	0.037	14.231		
4	2	0.176	4.96	4.96	0.04	0.0049	0.045	17.308	0.038	0.006
	3	0.132	3.22	3.22	0.026	0.0064	0.032	12.308		
	1	0.198	5.82	5.82	0.047	0.0084	0.055	21.154		
5	2	0.167	4.60	4.60	0.037	0.0098	0.047	18.077	0.052	0.004
	3	0.188	5.43	5.43	0.043	0.0097	0.053	20.385		
	1	0.211	6.33	6.33	0.051	0.0142	0.065	25		
6	2	0.178	5.04	5.04	0.04	0.0144	0.055	21.154	0.063	0.007
	3	0.221	6.73	6.73	0.054	0.0151	0.069	26.538		
	1	0.262	8.34	8.34	0.067	0.0206	0.087	33.462		
7	2	0.267	8.54	8.54	0.068	0.0195	0.088	33.846	0.085	0.005
	3	0.232	7.16	7.16	0.057	0.0218	0.079	30.385		
	1	0.298	9.76	9.76	0.078	0.0289	0.107	41.154		
8	2	0.287	9.33	9.33	0.075	0.0280	0.103	39.615	0.103	0.003

3	0.277	8.93	8.93	0.071	0.0290	0.1	38.462

Lampiran 8. Data Analisis Statistik

Lampiran 8.1. Uji Kekuatan Mekanik DMN

Tests of Normality

		Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	formula	Statistic	df	Sig.	Statistic	df	Sig.
persentasi_penurunan_needle	formula 1	.201	3	.	.994	3	.856
	formula 2	.226	3	.	.983	3	.751
	formula 3	.284	3	.	.933	3	.500
	formula 4	.355	3	.	.820	3	.164
	formula 5	.335	3	.	.857	3	.260

a. Lilliefors Significance Correction

ANOVA

persentasi_penurunan_needle

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	2134.611	4	533.653	142.331	.000
Within Groups	37.494	10	3.749		
Total	2172.105	14			

Post Hoc Tests

Multiple Comparisons

Dependent Variable: persentasi_penurunan_needle

	(I) formula	(J) formula	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Tukey HSD	formula 1	formula 2	-.37426057	1.58100651	.999	-5.5774829	4.8289617
		formula 3	5.38124678*	1.58100651	.042	.1780245	10.5844691
		formula 4	-1.88449131	1.58100651	.756	-7.0877136	3.3187310
		formula 5	-28.4025344*	1.58100651	.000	-33.6057566	-23.1993121
	formula 2	formula 1	.37426057	1.58100651	.999	-4.8289617	5.5774829
		formula 3	5.75550735*	1.58100651	.029	.5522851	10.9587296
		formula 4	-1.51023074	1.58100651	.869	-6.7134530	3.6929915
		formula 5	-28.0282738*	1.58100651	.000	-33.2314961	-22.8250515
	formula 3	formula 1	-5.38124678*	1.58100651	.042	-10.5844691	-.1780245
		formula 2	-5.75550735*	1.58100651	.029	-10.9587296	-.5522851
		formula 4	-7.26573809*	1.58100651	.007	-12.4689604	-2.0625158
		formula 5	-33.7837811*	1.58100651	.000	-38.9870034	-28.5805588
	formula 4	formula 1	1.88449131	1.58100651	.756	-3.3187310	7.0877136
		formula 2	1.51023074	1.58100651	.869	-3.6929915	6.7134530
		formula 3	7.26573809*	1.58100651	.007	2.0625158	12.4689604
		formula 5	-26.5180430*	1.58100651	.000	-31.7212653	-21.3148208
	formula 5	formula 1	28.40253435*	1.58100651	.000	23.1993121	33.6057566
		formula 2	28.02827378*	1.58100651	.000	22.8250515	33.2314961
		formula 3	33.78378113*	1.58100651	.000	28.5805588	38.9870034
		formula 4	26.51804304*	1.58100651	.000	21.3148208	31.7212653
Games-Howell	formula 1	formula 2	-.37426057	1.07248731	.995	-6.0969944	5.3484732
		formula 3	5.38124678	1.73764871	.168	-3.0044593	13.7669529
		formula 4	-1.88449131	1.79634818	.823	-10.7030130	6.9340304
		formula 5	-28.4025344*	1.26100616	.000	-34.0725631	-22.7325056
	formula 2	formula 1	.37426057	1.07248731	.995	-5.3484732	6.0969944
		formula 3	5.75550735	1.53118182	.151	-3.8305475	15.3415622
		formula 4	-1.51023074	1.59748600	.863	-11.6604342	8.6399727
		formula 5	-28.0282738*	.95667721	.000	-32.8317966	-23.2247509
	formula 3	formula 1	-5.38124678	1.73764871	.168	-13.7669529	3.0044593
		formula 2	-5.75550735	1.53118182	.151	-15.3415622	3.8305475
		formula 4	-7.26573809	2.10265440	.109	-16.6240041	2.0925279
		formula 5	-33.7837811*	1.66865972	.001	-42.3089233	-25.2586389
	formula 4	formula 1	1.88449131	1.79634818	.823	-6.9340304	10.7030130
		formula 2	1.51023074	1.59748600	.863	-8.6399727	11.6604342
		formula 3	7.26573809	2.10265440	.109	-2.0925279	16.6240041
		formula 5	-26.5180430*	1.72970201	.002	-35.5263998	-17.5096863
	formula 5	formula 1	28.40253435*	1.26100616	.000	22.7325056	34.0725631
		formula 2	28.02827378*	.95667721	.000	23.2247509	32.8317966
		formula 3	33.78378113*	1.66865972	.001	25.2586389	42.3089233
		formula 4	26.51804304*	1.72970201	.002	17.5096863	35.5263998

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

Lampiran 8.2. Uji Kemampuan Penetrasi DMN

Tests of Normality

		Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Lapisan_4	Statistic	df	Sig.	Statistic	df	Sig.
Persen_penetrasi	Formula 1	.292	3	.	.923	3	.463
	Formula 2	.292	3	.	.923	3	.463
	Formula 3	.196	3	.	.996	3	.878
	Formula 4	.276	3	.	.942	3	.537
	Formula 5	.	3	.	.	3	.

a. Lilliefors Significance Correction

ANOVA

Persen_penetrasi

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	11781.733	4	2945.433	142.982	.000
Within Groups	206.000	10	20.600		
Total	11987.733	14			

Post Hoc Test

Multiple Comparisons

Dependent Variable: Persen_penetrasi

			Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
	(I) Lapisan_4	(J) Lapisan_4				Lower Bound	Upper Bound
Tukey HSD	Formula 1	Formula 2	-.333	3.706	1.000	-12.53	11.86
		Formula 3	-68.000*	3.706	.000	-80.20	-55.80
		Formula 4	-7.667	3.706	.303	-19.86	4.53
		Formula 5	10.333	3.706	.108	-1.86	22.53
	Formula 2	Formula 1	.333	3.706	1.000	-11.86	12.53
		Formula 3	-67.667*	3.706	.000	-79.86	-55.47
		Formula 4	-7.333	3.706	.341	-19.53	4.86
		Formula 5	10.667	3.706	.094	-1.53	22.86
	Formula 3	Formula 1	68.000*	3.706	.000	55.80	80.20
		Formula 2	67.667*	3.706	.000	55.47	79.86
		Formula 4	60.333*	3.706	.000	48.14	72.53
		Formula 5	78.333*	3.706	.000	66.14	90.53
	Formula 4	Formula 1	7.667	3.706	.303	-4.53	19.86
		Formula 2	7.333	3.706	.341	-4.86	19.53
		Formula 3	-60.333*	3.706	.000	-72.53	-48.14
		Formula 5	18.000*	3.706	.005	5.80	30.20
	Formula 5	Formula 1	-10.333	3.706	.108	-22.53	1.86
		Formula 2	-10.667	3.706	.094	-22.86	1.53
		Formula 3	-78.333*	3.706	.000	-90.53	-66.14
		Formula 4	-18.000*	3.706	.005	-30.20	-5.80

Games-Howell	Formula 1	Formula 2	-.333	1.700	1.000	-7.89	7.22
		Formula 3	-68.000*	5.344	.013	-104.85	-31.15
		Formula 4	-7.667	2.404	.167	-19.86	4.53
		Formula 5	10.333*	1.202	.040	1.09	19.58
	Formula 2	Formula 1	.333	1.700	1.000	-7.22	7.89
		Formula 3	-67.667*	5.344	.014	-104.52	-30.82
		Formula 4	-7.333	2.404	.185	-19.53	4.86
		Formula 5	10.667*	1.202	.038	1.42	19.91
	Formula 3	Formula 1	68.000*	5.344	.013	31.15	104.85
		Formula 2	67.667*	5.344	.014	30.82	104.52
		Formula 4	60.333*	5.608	.011	27.32	93.35
		Formula 5	78.333*	5.207	.013	38.27	118.40
	Formula 4	Formula 1	7.667	2.404	.167	-4.53	19.86
		Formula 2	7.333	2.404	.185	-4.86	19.53
		Formula 3	-60.333*	5.608	.011	-93.35	-27.32
		Formula 5	18.000*	2.082	.040	1.98	34.02
	Formula 5	Formula 1	-10.333*	1.202	.040	-19.58	-1.09
		Formula 2	-10.667*	1.202	.038	-19.91	-1.42
		Formula 3	-78.333*	5.207	.013	-118.40	-38.27
		Formula 4	-18.000*	2.082	.040	-34.02	-1.98

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

Lampiran 8.3. Penentuan Jumlah Obat pada Sistem DMN

Tests of Normality

		Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	formula	Statistic	df	Sig.	Statistic	df	Sig.
bobot_nanokristalVAL	Formula 1	.356	3	.	.818	3	.157
	Formula 2	.266	3	.	.952	3	.579
	Formula 3	.175	3	.	1.000	3	.989
	Formula 4	.332	3	.	.863	3	.276
	Formula 5	.325	3	.	.876	3	.312

a. Lilliefors Significance Correction

ANOVA

bobot_nanokristalVAL

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	.003	4	.001	55.800	.000
Within Groups	.000	10	.000		
Total	.003	14			

Post Hoc Tests

Multiple Comparisons

Dependent Variable: bobot_nanokristalVAL

	(I) formula	(J) formula	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Tukey HSD	Formula 1	Formula 2	.0220667*	.0028610	.000	.012651	.031482
		Formula 3	.0306667*	.0028610	.000	.021251	.040082
		Formula 4	.0345667*	.0028610	.000	.025151	.043982
		Formula 5	.0375000*	.0028610	.000	.028084	.046916
	Formula 2	Formula 1	-.0220667*	.0028610	.000	-.031482	-.012651
		Formula 3	.0086000	.0028610	.078	-.000816	.018016
		Formula 4	.0125000*	.0028610	.010	.003084	.021916
		Formula 5	.0154333*	.0028610	.002	.006018	.024849
	Formula 3	Formula 1	-.0306667*	.0028610	.000	-.040082	-.021251
		Formula 2	-.0086000	.0028610	.078	-.018016	.000816
		Formula 4	.0039000	.0028610	.662	-.005516	.013316
		Formula 5	.0068333	.0028610	.196	-.002582	.016249
	Formula 4	Formula 1	-.0345667*	.0028610	.000	-.043982	-.025151
		Formula 2	-.0125000*	.0028610	.010	-.021916	-.003084
		Formula 3	-.0039000	.0028610	.662	-.013316	.005516
		Formula 5	.0029333	.0028610	.838	-.006482	.012349
	Formula 5	Formula 1	-.0375000*	.0028610	.000	-.046916	-.028084
		Formula 2	-.0154333*	.0028610	.002	-.024849	-.006018
		Formula 3	-.0068333	.0028610	.196	-.016249	.002582
		Formula 4	-.0029333	.0028610	.838	-.012349	.006482
Games-Howell	Formula 1	Formula 2	.0220667*	.0014915	.009	.011882	.032251
		Formula 3	.0306667*	.0029941	.027	.008336	.052997
		Formula 4	.0345667*	.0022341	.011	.018300	.050833
		Formula 5	.0375000*	.0021572	.008	.021855	.053145
	Formula 2	Formula 1	-.0220667*	.0014915	.009	-.032251	-.011882
		Formula 3	.0086000	.0033079	.276	-.009390	.026590
		Formula 4	.0125000	.0026399	.053	-.000248	.025248
		Formula 5	.0154333*	.0025751	.025	.003152	.027715
	Formula 3	Formula 1	-.0306667*	.0029941	.027	-.052997	-.008336
		Formula 2	-.0086000	.0033079	.276	-.026590	.009390
		Formula 4	.0039000	.0037026	.821	-.013299	.021099
		Formula 5	.0068333	.0036567	.458	-.010331	.023998
	Formula 4	Formula 1	-.0345667*	.0022341	.011	-.050833	-.018300
		Formula 2	-.0125000	.0026399	.053	-.025248	.000248
		Formula 3	-.0039000	.0037026	.821	-.021099	.013299
		Formula 5	.0029333	.0030656	.862	-.010704	.016571
	Formula 5	Formula 1	-.0375000*	.0021572	.008	-.053145	-.021855
		Formula 2	-.0154333*	.0025751	.025	-.027715	-.003152
		Formula 3	-.0068333	.0036567	.458	-.023998	.010331
		Formula 4	-.0029333	.0030656	.862	-.016571	.010704

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

Lampiran 8.4. Penentuan Kandungan Obat pada Sistem DMN

Tests of Normality

		Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	formula	Statistic	df	Sig.	Statistic	df	Sig.
kandungan_obat	formula 1	.369	3	.	.788	3	.087
	formula 2	.253	3	.	.964	3	.637
	formula 3	.248	3	.	.968	3	.659
	formula 4	.191	3	.	.997	3	.900
	formula 5	.328	3	.	.871	3	.298

a. Lilliefors Significance Correction

ANOVA

kandungan_obat

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	14.417	4	3.604	1.145	.390
Within Groups	31.478	10	3.148		
Total	45.895	14			

Homogeneous Subsets

kandungan_obat

	formula	N	Subset for alpha = 0.05
			1
Tukey HSD[a]	formula 2	3	96.2715138
	formula 3	3	97.1097069
	formula 4	3	98.3270293
	formula 1	3	98.6656248
	formula 5	3	98.7852900
	Sig.		.457

Means for groups in homogeneous subsets are displayed.

a. Uses Harmonic Mean Sample Size = 3.000.

Post Hoc Tests

Multiple Comparisons

Dependent Variable: kandungan_obat

	(I) formula	(J) formula	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Tukey HSD	formula 1	formula 2	2.39411100	1.44862727	.500	-2.3734404	7.1616624
		formula 3	1.55591793	1.44862727	.816	-3.2116334	6.3234693
		formula 4	.33859549	1.44862727	.999	-4.4289559	5.1061468
		formula 5	-.11966522	1.44862727	1.000	-4.8872166	4.6478861
	formula 2	formula 1	-2.39411100	1.44862727	.500	-7.1616624	2.3734404
		formula 3	-.83819307	1.44862727	.975	-5.6057444	3.9293583
		formula 4	-2.05551551	1.44862727	.630	-6.8230669	2.7120358
		formula 5	-2.51377622	1.44862727	.457	-7.2813276	2.2537751
	formula 3	formula 1	-1.55591793	1.44862727	.816	-6.3234693	3.2116334
		formula 2	.83819307	1.44862727	.975	-3.9293583	5.6057444
		formula 4	-1.21732245	1.44862727	.912	-5.9848738	3.5502289
		formula 5	-1.67558315	1.44862727	.774	-6.4431345	3.0919682
	formula 4	formula 1	-.33859549	1.44862727	.999	-5.1061468	4.4289559
		formula 2	2.05551551	1.44862727	.630	-2.7120358	6.8230669
		formula 3	1.21732245	1.44862727	.912	-3.5502289	5.9848738
		formula 5	-.45826071	1.44862727	.997	-5.2258121	4.3092906
	formula 5	formula 1	.11966522	1.44862727	1.000	-4.6478861	4.8872166
		formula 2	2.51377622	1.44862727	.457	-2.2537751	7.2813276
		formula 3	1.67558315	1.44862727	.774	-3.0919682	6.4431345
		formula 4	.45826071	1.44862727	.997	-4.3092906	5.2258121
Games-Howell	formula 1	formula 2	2.39411100	1.49267591	.573	-5.0635261	9.8517481
		formula 3	1.55591793	1.65778634	.869	-5.9575596	9.0693955
		formula 4	.33859549	1.67844558	.999	-7.2274241	7.9046150
		formula 5	-.11966522	1.53901886	1.000	-7.5103900	7.2710596
	formula 2	formula 1	-2.39411100	1.49267591	.573	-9.8517481	5.0635261
		formula 3	-.83819307	1.30351124	.959	-6.9240656	5.2476794
		formula 4	-2.05551551	1.32968625	.594	-8.3203341	4.2093031
		formula 5	-2.51377622	1.14867969	.339	-7.6505573	2.6230049
	formula 3	formula 1	-1.55591793	1.65778634	.869	-9.0693955	5.9575596
		formula 2	.83819307	1.30351124	.959	-5.2476794	6.9240656
		formula 4	-1.21732245	1.51269287	.917	-7.9453220	5.5106771
		formula 5	-1.67558315	1.35633301	.738	-7.8406595	4.4894932
	formula 4	formula 1	-.33859549	1.67844558	.999	-7.9046150	7.2274241
		formula 2	2.05551551	1.32968625	.594	-4.2093031	8.3203341
		formula 3	1.21732245	1.51269287	.917	-5.5106771	7.9453220
		formula 5	-.45826071	1.38150759	.996	-6.7794438	5.8629224
	formula 5	formula 1	.11966522	1.53901886	1.000	-7.2710596	7.5103900
		formula 2	2.51377622	1.14867969	.339	-2.6230049	7.6505573
		formula 3	1.67558315	1.35633301	.738	-4.4894932	7.8406595
		formula 4	.45826071	1.38150759	.996	-5.8629224	6.7794438

Lampiran 8.5. Uji Waktu Melarut

Lampiran 8.6. Uji Permeasi *Ex Vivo* pada Waktu 8 Jam

Tests of Normality[a]

		Kolmogorov-Smirnov[b]			Shapiro-Wilk		
	formula	Statistic	df	Sig.	Statistic	df	Sig.
persen_permeasi	Formula 1	.260	2	.			
	Formula 2	.250	3	.	.966	3	.648
	Formula 3	.256	3	.	.962	3	.625
	Formula 4	.342	3	.	.845	3	.228
	Formula 5	.254	3	.	.963	3	.633

a. persen_permeasi is constant when formula = 1. It has been omitted.

b. Lilliefors Significance Correction

ANOVA

persen_permeasi

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	.027	4	.007	34.380	.000
Within Groups	.002	10	.000		
Total	.029	14			

Homogeneous Subsets

persen_permeasi

			Subset for alpha = 0.05		
	formula	N	1	2	3
Tukey HSD[a]	Formula 5	3	.1033924		
	Formula 1	3	.1353268	.1353268	
	Formula 2	3		.1433714	
	Formula 4	3		.1665866	
	Formula 3	3			.2311102
	Sig.		.111	.121	1.000

Means for groups in homogeneous subsets are displayed.

a. Uses Harmonic Mean Sample Size = 3.000.

Post Hoc Tests

Multiple Comparisons

Dependent Variable: persen_permeasi

	(I) formula	(J) formula	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Tukey HSD	Formula 1	Formula 2	-.00804462	.01150919	.952	-.0459223	.0298331
		Formula 3	-.09578346*	.01150919	.000	-.1336612	-.0579058
		Formula 4	-.03125984	.01150919	.121	-.0691375	.0066179
		Formula 5	.03193438	.01150919	.111	-.0059433	.0698121
	Formula 2	Formula 1	.00804462	.01150919	.952	-.0298331	.0459223
		Formula 3	-.08773885*	.01150919	.000	-.1256165	-.0498611
		Formula 4	-.02321522	.01150919	.324	-.0610929	.0146625
		Formula 5	.03997900*	.01150919	.038	.0021013	.0778567
	Formula 3	Formula 1	.09578346*	.01150919	.000	.0579058	.1336612
		Formula 2	.08773885*	.01150919	.000	.0498611	.1256165
		Formula 4	.06452362*	.01150919	.002	.0266459	.1024013
		Formula 5	.12771785*	.01150919	.000	.0898401	.1655956
	Formula 4	Formula 1	.03125984	.01150919	.121	-.0066179	.0691375
		Formula 2	.02321522	.01150919	.324	-.0146625	.0610929
		Formula 3	-.06452362*	.01150919	.002	-.1024013	-.0266459
		Formula 5	.06319423*	.01150919	.002	.0253165	.1010719
	Formula 5	Formula 1	-.03193438	.01150919	.111	-.0698121	.0059433
		Formula 2	-.03997900*	.01150919	.038	-.0778567	-.0021013
		Formula 3	-.12771785*	.01150919	.000	-.1655956	-.0898401
		Formula 4	-.06319423*	.01150919	.002	-.1010719	-.0253165
Games-Howell	Formula 1	Formula 2	-.00804462	.01127808	.942	-.0604047	.0443155
		Formula 3	-.09578346*	.01310626	.009	-.1541133	-.0374537
		Formula 4	-.03125984	.01386842	.320	-.0936216	.0311019
		Formula 5	.03193438	.00925287	.199	-.0328525	.0967213
	Formula 2	Formula 1	.00804462	.01127808	.942	-.0443155	.0604047
		Formula 3	-.08773885*	.01162439	.011	-.1424444	-.0330333
		Formula 4	-.02321522	.01247740	.466	-.0840265	.0375960
		Formula 5	.03997900	.00699772	.068	-.0059708	.0859288
	Formula 3	Formula 1	.09578346*	.01310626	.009	.0374537	.1541133
		Formula 2	.08773885*	.01162439	.011	.0330333	.1424444
		Formula 4	.06452362*	.01415149	.047	.0012659	.1277813
		Formula 5	.12771785*	.00967197	.013	.0594789	.1959568
	Formula 4	Formula 1	.03125984	.01386842	.320	-.0311019	.0936216
		Formula 2	.02321522	.01247740	.466	-.0375960	.0840265
		Formula 3	-.06452362*	.01415149	.047	-.1277813	-.0012659
		Formula 5	.06319423	.01068205	.073	-.0133108	.1396993
	Formula 5	Formula 1	-.03193438	.00925287	.199	-.0967213	.0328525
		Formula 2	-.03997900	.00699772	.068	-.0859288	.0059708
		Formula 3	-.12771785*	.00967197	.013	-.1959568	-.0594789
		Formula 4	-.06319423	.01068205	.073	-.1396993	.0133108

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

Lampiran 9. Dokumentasi Penelitian

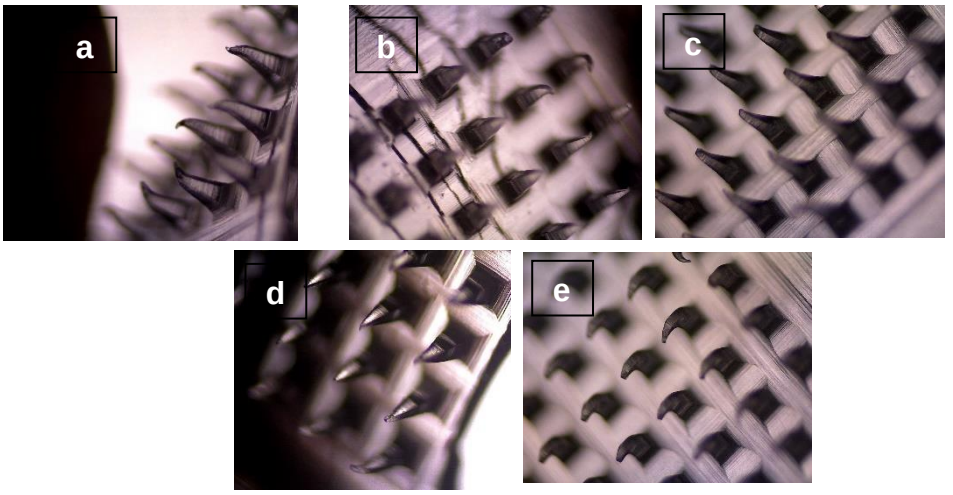
Gambar 14. Proses pembuatan polimer

Gambar 15. Polimer dengan kandungan nanokristal VAL

Gambar 16. Proses pencetakan DMN dan proses sentrifugasi

Gambar 17. Proses pengeringan DMN pada suhu 37°C menggunakan oven

Gambar 18. Pengukuran Panjang gelombang dengan spektrofotometer UV-Vis



Gambar 19. Morfologi *needle* DMN (a) F1; (b) F2; (c) F3; (d) F4; (e) F5 setelah uji kekuatan mekanik

Gambar 20. Uji *ex vivo* menggunakan apparatus sel difusi Franz