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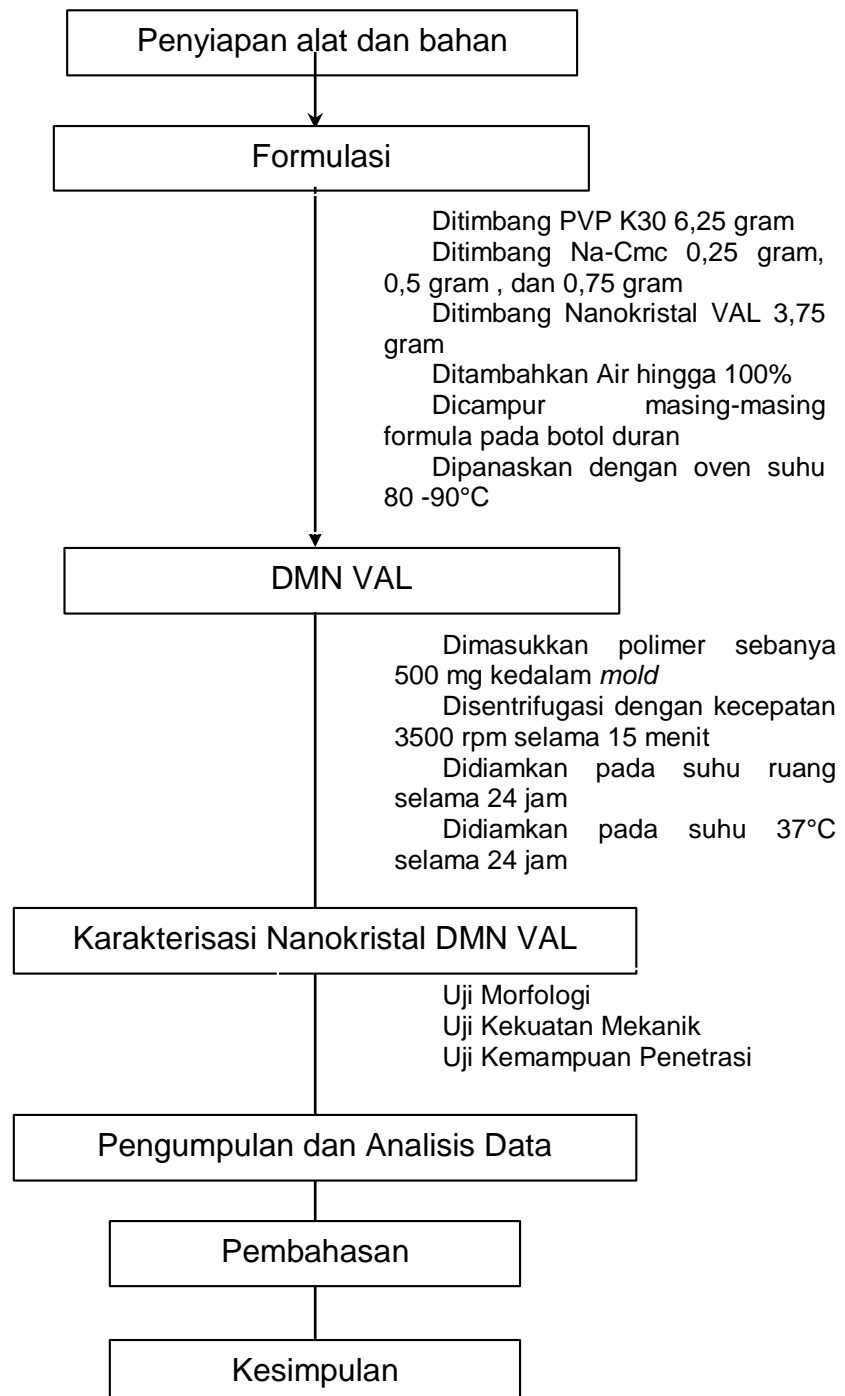
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LAMPIRAN

Lampiran 1. Skema Kerja



Lampiran 2. Hasil uji morfologi, kekuatan mekanik dan kemampuan penetrasi *dissolving microneedle* nanokristal VAL

Tabel 9. Persentase penurunan panjang DMN nanokristal VAL

For Mula	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	688,14	687,14 ± 0,22	370,58	370,54 ± 0,02	46,14	46,07 ± 0,14
	684,99		370,53		46,16	
	688,31		370,53		45,90	
	701,2		476,38		32,06	
F2	700,95	700,97 ± 1,84	479,51	478,47 ± 1,81	31,59	31,74 ± 0,27
	700,76		479,53		31,57	
	710,45		501,39		29,42	
F3	709,73	710,18 ± 0,39	467,09	483,73 ± 17,17	34,18	31,88 ± 2,38
	710,38		482,71		32,04	

Tabel 10. Persentase penetrasi DMN nanokristal VAL

Lapisan	Jumlah Lubang yang terbentuk			%penetrasi		
	F1	F2	F3	F1	F2	F3
1	100	100	100	100	100	100
2	100	100	100	100	100	100
3	47	67	95	47	67	95
4	0	20	82	0	80	82
5	0	0	0	0	0	0
6	0	0	0	0	0	0
7	0	0	0	0	0	0
8	0	0	0	0	0	0

a. Contoh perhitungan persentase penurunan tinggi *needle*

Diketahui untuk F1 replikasi pertama, *microneedle* berukuran 687,14 µm dan setelah dilakukan uji mekanik, tingginya menjadi 370,54 µm, maka :

$$\begin{aligned} \%Kompresi &= \frac{\text{Tinggi sebelum uji} - \text{Tinggi setelah uji}}{\text{Tinggi sebelum uji}} \times 100\% \\ &= \frac{687,14 - 370,54}{687,14} \times 100\% \end{aligned}$$

$$= 46,07\%$$

b. Perhitungan persentase penetrasi lapisan ke-n

Diketahui untuk F1 lapisan ke-3, terbentuk 40 lubang sedangkan *needle* berjumlah 100, maka

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

$$= \frac{40}{100} \times 100\%$$

$$= 40\%$$

Lampiran 3. Hasil penentuan Densitas

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

Bahan	F1	F3	F3
PVP K30 K30	6,25	6,25	6,25
Na-CMC	0,25	0,5	0,75
Nanokristal-VAL	2,5	2,5	2,5
Air	16	15,75	15,5

Tabel 12. Berat basah dan berat kering sampel balok pipih tiap formula (mg)

Replikasi	F1		F2		F3	
	Basah	Kering	Basah	Kering	Basah	Kering
1	500	330	500	310	500	290
2	500	330	500	320	500	290
3	500	320	500	320	500	390

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
F1	10	10	4,98	498	1,00	0,99 ± 0,01
	10	10	5,12	512	0,97	
	10	10	4,97	497	1,00	
F2	10	10	4,91	491	1,01	1,02 ± 0,00
	10	10	4,89	489	1,02	
	10	10	4,92	492	1,01	
F3	10	10	5,54	554	0,90	0,90 ± 0,01
	10	10	5,49	549	0,91	
	10	10	5,60	560	0,98	

Contoh perhitungan densitas

Diketahui : Berat basah F1 replikasi pertama = 500 mg

Berat kering F1 replikasi pertama = 330

Panjang sisi 1 = 10 mm

Panjang sisi 2 = 10 mm

$$\text{Tinggi} = 4,98$$

Berat nanokristal VAL dalam formula =10 mg

$$\text{Volume 1 needle} = 0,00933 \text{ mm}^3$$

Maka,

$$\text{Volume} = \text{sisi 1} \times \text{sisi 2} \times \text{tinggi}$$

$$10 \text{ mm} \times 10 \text{ mm} \times 4,98 \text{ mm} = 498 \text{ mm}^3$$

$$\text{Densitas} = \frac{330 \text{ mg}}{498 \text{ mm}^3}$$

$$= 0,67 \text{ mg/mm}^3$$

Lampiran 4. Hasil penentuan LOD dan persentase jumlah nanokristal dalam massa kering

Tabel 14. Persentase kehilangan air

Replikasi	F1 (%)	F2 (%)	F3 (%)
1	34	38	42
2	36	36	42
3	36	36	42

Tabel 15. Persentase nanokristal VAL dalam massa kering

Replikasi	F1 (%)	F2 (%)	F3 (%)
1	15,15	16,12	17,24
2	15,62	15,62	17,24
3	15,62	15,62	17,24

Contoh perhitungan LOD dan persentase jumlah nanokristal dalam massa kering

Diketahui : Berat basah F1 replikasi pertama = 500 mg

Berat kering F1 replikasi pertama = 330

$$\begin{aligned} \%LOD &= \frac{\text{Bobot basah} - \text{Bobot kering}}{\text{Bobot basah}} \times 100\% \\ &= \frac{500 \text{ mg} - 330 \text{ mg}}{500 \text{ mg}} \times 100\% \\ &= 34\% \end{aligned}$$

Persentase nanokristal VAL dalam massa kering

$$\begin{aligned} &= \frac{\text{Konsentrasi nanokristal VAL}}{100\% - \%LOD} \times 100\% \\ &= \frac{10\%}{100\% - 34\%} \times 100 \\ &= 15,15\% \end{aligned}$$

Lampiran 5. Hasil penentuan volume, berat jarum, dan berat jarum nanokristal VAL

Tabel 16. Berat 100 *needle* dalam massa kering

Replikasi	F1	F2	F3
1	0,93	0,95	0,84
2	0,91	0,95	0,84
3	0,93	0,94	0,83

Tabel 17. Jumlah nonokristal VAL dalam 100 *needle*

Formula	Jumlah nanokristal VAL	Rata-rata \pm SD
	0,26	
F1	0,25	0,26 \pm 0,004
	0,26	
	0,27	
F2	0,27	0,27 \pm 0,000
	0,27	
	0,28	
F3	0,29	0,28 \pm 0,002
	0,28	

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

$$\text{Volume satu } needle = 0,00933 \text{ mm}^3$$

$$\text{Volume 100 } needle = 0,00933 \text{ mm}^3 \times 100 = 0,933 \text{ mm}^3$$

$$\text{Berat untuk 100 } needle = \text{volume 100 } needle \times \text{densitas}$$

$$= 0,933 \text{ mm}^3 \times 1,00$$

$$= 0,93$$

Diketahui VAL dalam nanokristal (95,5%)

Maka,

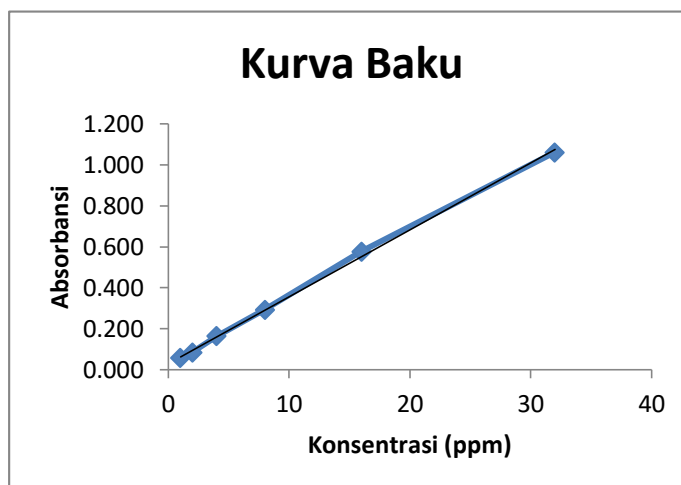
Jumlah nanokristal VAL dalam formula F1 replikasi 1 adalah:

$$= \%VAL \times \text{berat nanokristal dalam 100 } \textit{needle}$$

$$= 0,955 \times 0,26$$

$$= 0,25 \text{ mg}$$

Lampiran 6. Hasil penentuan kandungan obat VAL pada sistem DMN



Gambar 11. Kurva baku VAL

Tabel 18. Kurva baku VAL

Konsentrasi (ppm)	Abs 1	Abs 2	Abs 3	Rata-Rata \pm SD
0	0	0	0	0 ± 0
1	0.056	0.063	0.052	$0.057 \pm 0,006$
2	0.071	0.095	0.088	$0.085 \pm 0,012$
4	0.161	0.165	0.168	$0.165 \pm 0,003$
0,8	0.291	0.284	0.306	$0.294 \pm 0,011$
16	0.553	0.573	0.604	$0.577 \pm 0,026$
32	1.061	1.043	1.083	$1.062 \pm 0,020$

Tabel 19. Kandungan nanokrsital VAL dalam *needle*

Formula	Abs	Konsentrasi (ppm)	Jumlah VAL (mg)	%kandungan obat	Rata-Rata \pm SD
F1	0,812	23,97	0,26	97,90	$97,98 \pm 0,07$
	0,813	24,00	0,26	98,03	
	0,813	24,00	0,26	98,03	
F2	0,876	25,93	0,25	98,82	$99,12 \pm 0,27$
	0,880	26,05	0,24	99,28	
	0,880	26,05	0,25	99,28	
F3	0,910	26,97	0,27	99,60	$99,98 \pm 0,32$
	0,915	27,13	0,27	100	
	0,915	27,13	0,27	100	

Contoh perhitungan kandungan nanokristal VAL dalam DMN

Untuk 100 gram formula terdapat 10 gram nanokristal VAL, dalam nanokristal terdapat 95,5% VAL. Untuk 1 kali pengerjaan cukup dibuat 25 gram maka dalam 25 gram terdapat 2,3875 gram VAL. Setiap 25 gram formula dapat dibuat 50 DMN @ 500 mg dengan berat kering 330 mg. Jadi secara teoritis, didalam 330 mg DMN terdapat VAL 2,3875 gram/50 DMN = 0,04775 gram atau 47,75 mg/500 berat basah. Untuk perhitungan kandungan obat dari 330 mg DMN dikeruk bagian jarum diperoleh 0,26 mg kemudian dilarutkan menggunakan 1 ml etanol dan diukur absorbansinya.

Diketahui : Abs F1 replikasi 1= 0,812

Persamaan kurva baku $y = 0,0326x + 0,0307$

Berat 100 jarum yang dikeruk = 0,25 mg

Maka, konsentrasi VAL :

$$0,812 = 0,0326x + 0,0307$$

$$x = \frac{0,812 - 0,0307}{0,0326}$$

$$x = 23,97 \mu\text{g/mL}$$

Jadi terdapat 23,97 $\mu\text{g/mL}$ /0,26 mg sediaan

Sehingga,

Jumlah nanokristal VAL dalam formula F1 =

Dalam 1 DMN terdapat 47,75 mg VAL, untuk F1

$$\frac{47,75 \text{ mg}}{330 \text{ mg}} = 0,144 \text{ mg VAL}$$

$0,144 \times 0,25 = 0,036 \text{ mg VAL}/0,25 \text{ mg}$ apabila *drug loading* 100%

Sehingga,

$0,02397 \text{ mg/mL} \times 0,036 \text{ mg} = 0,6658 = 66,58\%$

Kandungan nanokristal VAL dalam F1 adalah 66,58%

Lampiran 7. Hasil uji waktu melarut

Tabel 20. Uji waktu melarut DMN nanokristal VAL

Waktu	F1		F2		F3	
	Panjang (µm)	Rata-rata±SD	Panjang (µm)	Rata-rata± SD	Panjang (µm)	Rata-rata±SD
2 menit	309,13		292,70		267,77	
	315,11	313,94 ±4,34	242,88	276,11±28,77	274,07	275,06±7,82
	317,59		292,75		283,33	
4 menit	261,73		118,73		180,71	
	280,24	273,03±9,91	104,06	108,67±8,71	190,05	187,93±6,43
	277,13		103,23		193,04	
6 menit	136,99		82,65		99,85	
	133,92	135,98±1,78	71,35	81,41±9,50	84,07	95,55±10,1
	137,04		90,24		102,74	
8 menit	84,33		56,58		46,82	
	96,56	92,49±7,06	62,62	62,59±6,00	59,16	54,04±6,43
	95,57		68,58		56,14	
10 menit	71,69		21,34		0	
	84,66	79,12±6,68	22,56	21,80	0	0±0
	81,02		21,50		0	

Lampiran 8. Hasil uji permeasi *ex vivo*

Tabel 21. Data permeasi *Ex vivo* F1

Waktu (jam)	Serapan	Konsentrasi ($\mu\text{g/ml}$)	1 ml (μg)	Faktor pengenceran	13 ml (μg)	Faktor Koreksi	VAL yang terpermeasi (μg)	Permeat Kumulatif ($\mu\text{g/cm}^2$)	Rata-rata \pm SD
	0	0,00	0,00	1	0	0	0	0	
0,25	0	0,00	0,00	1	0	0	0	0	$0 \pm 0,00$
	0	0,00	0,00	1	0	0	0	0	
	0,053	0,68	0,68	1	8,89	0	8,89	5,29	
0,50	0,054	0,71	0,71	1	9,29	0	9,29	5,53	$5,53 \pm 0,24$
	0,055	0,75	0,75	1	9,69	0	9,69	5,77	
0,75	0,057	0,81	0,81	1	10,49	0,68	11,17	6,65	
	0,059	0,87	0,87	1	11,29	0,71	12,00	7,14	$7,06 \pm 0,38$
	0,06	0,90	0,90	1	11,68	0,75	12,43	7,40	
1,00	0,061	0,93	0,93	1	12,08	1,49	13,57	8,08	$8,76 \pm 0,64$

Waktu (jam)	Serapan	Konsentrasi ($\mu\text{g/ml}$)	1 ml (μg)	Faktor pengenceran	13 ml (μg)	Faktor Koreksi	VAL yang terpermeasi (μg)	Permeat Kumulatif ($\mu\text{g/cm}^2$)	Rata-rata \pm SD
2,00	0,064	1,02	1,02	1	13,28	1,58	14,86	8,85	14,98 \pm 0,81
	0,066	1,08	1,08	1	14,08	1,64	15,72	9,36	
	0,084	1,63	1,63	1	21,25	2,42	23,67	14,09	
	0,088	1,76	1,76	1	22,85	2,60	25,45	15,15	
	0,09	1,82	1,82	1	23,65	2,73	26,37	15,70	
3,00	0,087	1,73	1,73	1	22,45	4,06	26,51	15,78	16,65 \pm 0,85
	0,09	1,82	1,82	1	23,65	4,36	28,01	16,67	
	0,093	1,91	1,91	1	24,84	4,55	29,39	17,49	
4,00	0,094	1,94	1,94	1	25,24	5,78	31,02	18,47	18,99 \pm 0,56
	0,095	1,97	1,97	1	25,64	6,18	31,82	18,94	
	0,097	2,03	2,03	1	26,44	6,46	32,90	19,58	

Waktu (jam)	Serapan	Konsentrasi ($\mu\text{g/ml}$)	1 ml (μg)	Faktor pengenceran	13 ml (μg)	Faktor Koreksi	VAL yang terpermeasi (μg)	Permeat Kumulatif ($\mu\text{g/cm}^2$)	Rata-rata \pm SD
5,00	0,12	2,74	2,74	1	35,61	7,72	43,33	25,79	26,74 \pm 0,94
	0,123	2,83	2,83	1	36,81	8,15	44,96	26,76	
	0,126	2,92	2,92	1	38,00	8,49	46,49	27,67	
6,00	0,128	2,98	2,98	1	38,80	10,46	49,26	29,32	30,33 \pm 0,99
	0,131	3,08	3,08	1	40,00	10,98	50,98	30,35	
	0,134	3,17	3,17	1	41,19	11,41	52,61	31,31	
7,00	0,149	3,63	3,63	1	47,17	13,45	60,62	36,08	37,06 \pm 0,93
	0,152	3,72	3,72	1	48,37	14,06	62,43	37,16	
	0,154	3,78	3,78	1	49,17	14,58	63,75	37,95	
8,00	0,163	4,06	4,06	1	52,76	17,08	69,83	41,57	42,44 \pm 0,86
	0,165	4,12	4,12	1	53,56	17,78	71,34	42,46	

Waktu (jam)	Serapan	Konsentrasi ($\mu\text{g/ml}$)	1 ml (μg)	Faktor pengenceran	13 ml (μg)	Faktor Koreksi	VAL yang terpermeasi (μg)	Permeat Kumulatif ($\mu\text{g/cm}^2$)	Rata-rata \pm SD
24,00	0,167	4,18	4,18	1	54,35	18,37	72,72	43,28	56,20 \pm 1,25
	0,209	5,47	5,47	1	71,10	21,13	92,24	54,90	
	0,213	5,59	5,59	1	72,70	21,90	94,60	56,31	
	0,216	5,68	5,68	1	73,89	22,55	96,44	57,40	

Tabel 22. Data permeasi *Ex vivo* F2

Waktu (jam)	Serapan	Konsentrasi ($\mu\text{g/ml}$)	1 ml (μg)	Faktor pengenceran	13 ml (μg)	Faktor Koreksi	VAL yang terpermeasi (μg)	Permeat Kumulatif ($\mu\text{g/cm}^2$)	Rata-rata \pm SD
0,25	0	0,75	0,75	1	0	0	0	0	6,00 \pm 0,24
	0	0,78	0,78	1	0	0	0	0	
	0	0,81	0,81	1	0	0	0	0	
	0,055	0,84	0,84	1	9,69	0	9,69	5,77	

Waktu (jam)	Serapan	Konsentrasi ($\mu\text{g/ml}$)	1 ml (μg)	Faktor pengenceran	13 ml (μg)	Faktor Koreksi	VAL yang terpermeasi (μg)	Permeat Kumulatif ($\mu\text{g/cm}^2$)	Rata-rata \pm SD
0,50	0,056	0,87	0,87	1	10,09	0	10,09	6,01	
	0,057	0,93	0,93	1	10,49	0	10,49	6,24	
0,75	0,058	1,05	1,05	1	10,89	0,75	11,63	6,92	
	0,059	1,17	1,17	1	11,29	0,78	12,06	7,18	7,26 \pm 0,38
	0,061	1,24	1,24	1	12,08	0,81	12,89	7,67	
1,00	0,065	1,45	1,45	1	13,68	1,58	15,26	9,08	
	0,069	1,51	1,51	1	15,27	1,64	16,92	10,07	9,91 \pm 0,77
	0,071	1,54	1,54	1	16,07	1,74	17,81	10,60	
2,00	0,078	1,67	1,67	1	18,86	2,63	21,50	12,80	
	0,08	1,76	1,76	1	19,66	2,82	22,48	13,38	13,29 \pm 0,81
	0,081	1,82	1,82	1	20,06	2,97	23,03	13,71	

Waktu (jam)	Serapan	Konsentrasi ($\mu\text{g/ml}$)	1 ml (μg)	Faktor pengenceran	13 ml (μg)	Faktor Koreksi	VAL yang terpermeasi (μg)	Permeat Kumulatif ($\mu\text{g/cm}^2$)	Rata-rata \pm SD
3,00	0,085	2,00	2,00	1	21,65	4,09	25,74	15,32	16,09 \pm 0,72
	0,088	2,06	2,06	1	22,85	4,33	27,18	16,18	
	0,09	2,13	2,13	1	23,65	4,52	28,16	16,76	
4,00	0,096	2,16	2,16	1	26,04	5,75	31,79	18,92	19,58 \pm 0,67
	0,098	2,28	2,28	1	26,84	6,09	32,93	19,60	
	0,1	2,40	2,40	1	27,63	6,33	33,97	20,22	
5,00	0,101	3,51	3,51	1	28,03	7,75	35,79	21,30	22,47 \pm 1,56
	0,105	3,57	3,57	1	29,63	8,15	37,78	22,49	
	0,109	3,66	3,66	1	31,22	8,46	39,68	23,62	
6,00	0,145	3,81	3,81	1	45,58	9,91	55,49	33,03	33,89 \pm 0,88
	0,147	3,94	3,94	1	46,38	10,43	56,81	33,82	

Waktu (jam)	Serapan	Konsentrasi ($\mu\text{g/ml}$)	1 ml (μg)	Faktor pengenceran	13 ml (μg)	Faktor Koreksi	VAL yang terpermeasi (μg)	Permeat Kumulatif ($\mu\text{g/cm}^2$)	Rata-rata \pm SD
7,00	0,15	4,00	4,00	1	47,57	10,86	58,44	34,78	38,62 \pm 1,05
	0,155	4,03	4,03	1	49,57	13,42	62,98	37,49	
	0,159	4,06	4,06	1	51,16	14,00	65,16	38,79	
8,00	0,161	4,12	4,12	1	51,96	14,52	66,48	39,57	42,13 \pm 0,74
	0,162	8,54	8,54	1	52,36	17,23	69,59	41,42	
	0,163	8,69	8,69	1	52,76	17,94	70,69	42,08	
24,00	0,165	8,75	8,75	1	53,56	18,52	72,07	42,90	80,08 \pm 1,26
	0,309	0,75	0,75	1	110,9 8	21,26	132,24	78,71	
	0,314	0,78	0,78	1	112,9 7	21,99	134,97	80,34	
	0,316	0,81	0,81	1	113,7 7	22,64	136,41	81,20	

Tabel 23. Data permeasi *ex vivo* F3

Waktu (jam)	Serapan	Konsentrasi ($\mu\text{g/ml}$)	1 ml (μg)	Faktor pengenceran	13 ml (μg)	Faktor Koreksi	VAL yang terpermeasi (μg)	Permeat Kumulatif ($\mu\text{g/cm}^2$)	Rata-rata \pm SD
0,25	0,051	0,62	0,62	1	8,10	0	8,10	4,82	$5,13 \pm 0,36$
	0,052	0,65	0,65	1	8,49	0	8,49	5,06	
	0,054	0,71	0,71	1	9,29	0	9,29	5,53	
0,50	0,061	0,93	0,93	1	12,08	0,62	12,71	7,56	$8,22 \pm 0,62$
	0,064	1,02	1,02	1	13,28	0,65	13,93	8,29	
	0,066	1,08	1,08	1	14,08	0,71	14,79	8,80	
0,75	0,072	1,27	1,27	1	16,47	1,55	18,02	10,73	$11,35 \pm 0,67$
	0,074	1,33	1,33	1	17,27	1,67	18,94	11,27	
	0,077	1,42	1,42	1	18,46	1,80	20,26	12,06	
1,00	0,087	1,73	1,73	1	22,45	2,82	25,27	15,04	$15,94 \pm 0,84$
	0,091	1,85	1,85	1	24,05	3,00	27,05	16,10	

Waktu (jam)	Serapan	Konsentrasi ($\mu\text{g/ml}$)	1 ml (μg)	Faktor pengenceran	13 ml (μg)	Faktor Koreksi	VAL yang terpermeasi (μg)	Permeat Kumulatif ($\mu\text{g/cm}^2$)	Rata-rata \pm SD
	0,093	1,91	1,91	1	24,84	3,22	28,06	16,70	
2,00	0,104	2,25	2,25	1	29,23	4,55	33,78	20,10	
	0,107	2,34	2,34	1	30,43	4,85	35,28	21,00	20,91 \pm 0,77
	0,109	2,40	2,40	1	31,22	5,13	36,35	21,64	
3,00	0,124	2,86	2,86	1	37,21	6,79	44,00	26,19	
	0,127	2,95	2,95	1	38,40	7,19	45,60	27,14	27,13 \pm 0,93
	0,13	3,05	3,05	1	39,60	7,53	47,13	28,05	
4,00	0,152	3,72	3,72	1	48,37	9,66	58,03	34,54	
	0,157	3,87	3,87	1	50,37	10,15	60,51	36,02	35,85 \pm 1,23
	0,16	3,97	3,97	1	51,56	10,58	62,14	36,99	
5,00	0,242	6,48	6,48	1	84,26	13,38	97,64	58,12	59,74 \pm 1,94

Waktu (jam)	Serapan	Konsentrasi ($\mu\text{g/ml}$)	1 ml (μg)	Faktor pengenceran	13 ml (μg)	Faktor Koreksi	VAL yang terpermeasi (μg)	Permeat Kumulatif ($\mu\text{g/cm}^2$)	Rata-rata \pm SD
	0,245	6,57	6,57	1	85,46	14,02	99,48	59,21	
	0,255	6,88	6,88	1	89,44	14,54	103,99	61,90	
6,00	0,255	6,88	6,88	1	89,44	19,86	109,30	65,06	
	0,258	6,97	6,97	1	90,64	20,60	111,24	66,21	66,15 \pm 1,06
	0,26	7,03	7,03	1	91,44	21,42	112,86	67,18	
7,00	0,291	7,98	7,98	1	103,80	26,74	130,54	77,70	
	0,294	8,08	8,08	1	105,00	27,57	132,56	78,91	78.84 \pm 1,11
	0,296	8,14	8,14	1	105,79	28,46	134,25	79,91	
8,00	0,335	9,33	9,33	1	121,35	34,72	156,07	92,90	
	0,338	9,43	9,43	1	122,54	35,64	158,19	94,16	94,24 \pm 1,38
	0,342	9,55	9,55	1	124,14	36,60	160,73	95,67	

Waktu (jam)	Serapan	Konsentrasi ($\mu\text{g/ml}$)	1 ml (μg)	Faktor pengenceran	13 ml (μg)	Faktor Koreksi	VAL yang terpermeasi (μg)	Permeat Kumulatif ($\mu\text{g/cm}^2$)	Rata-rata \pm SD
24,00	0,443	12,65	12,65	1	164,41	44,06	208,47	124,09	125,57 \pm 1,45
	0,447	12,77	12,77	1	166,01	45,07	211,08	125,64	
	0,45	12,86	12,86	1	167,21	46,14	213,35	126,99	

Contoh Perhitungan Jumlah Obat yang Terpermeasi

Persamaan: $y = 0,0326x + 0,0307$

Keterangan:

y = serapan $a = 0,0307$

x = konsentrasi $b = 0,0326$

F3 Replikasi ke-1, jam ke-24 diperoleh serapan = 0,443. Sehingga, untuk mendapatkan konsentrasi:

$$x = \frac{y - a}{b}$$

$$x = \frac{0,443 - 0,0307}{0,0326}$$

$$x = 12,64 \mu\text{g/mL}$$

Permeasi kumulatif dihitung dengan menggunakan rumus:

$$Q = \frac{C_n \cdot V + \sum_{i=1}^{n-1} C_i \cdot S}{A}$$

$$C_n = 12,64 \mu\text{g/mL}$$

$$\sum_{i=1}^{n-1} = 44,06$$

$$V = 13 \text{ mL } \mu\text{g/mL}$$

$$S = 1 \text{ mL}$$

$$A = 1,68 \text{ cm}^2$$

$$Q = \frac{12,64 \times 13 + 44,06 \times 1}{1,68}$$

$$= 124,09 \mu\text{g/cm}^2$$

Contoh perhitungan Fluks Tiap Jam

Rumus:
$$J = \frac{Q}{T}$$

F3 replikasi ke-1, jam ke-24 diperoleh permeasi kumulatif $124,09 \mu\text{g}/\text{cm}^2$

Maka,

$$J = \frac{124,09}{24}$$

$$= 5,17 \mu\text{g}/\text{cm}^2.\text{jam}$$

Contoh Penentuan Nilai Fluks Rata-Rata

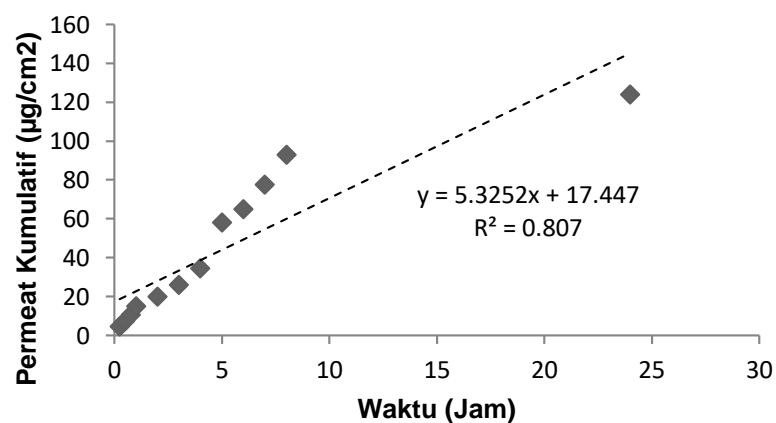
Persamaan : $y = bx + a$

Keterangan :

a = intersep

b= slope

Dari hasil Uji permeasi DMN nanokristal VAL F3, didapatkan grafik berikut:



Gambar 12. Grafik Permeat Kumulatif F3 Replikasi 1

Nilai fluks rata-rata dapat diambil dari nilai slope dari persamaan yang didapatkan

Maka, nilai fluks masing-masing replikasi adalah

1. $y = 5,3252x + 17.447 \rightarrow J_1 = 5,3252$
2. $y = 5.3644x + 18.259 \rightarrow J_2 = 5.3644$
3. $y = 5.4001x + 19.111 \rightarrow J_3 = 5.4001$

Fluks rata-rata F3 adalah $5,3632 \mu\text{g}/\text{cm}^2.\text{jam}$

Contoh Perhitungan *Lag time*

Persamaan : $y = bx + a$

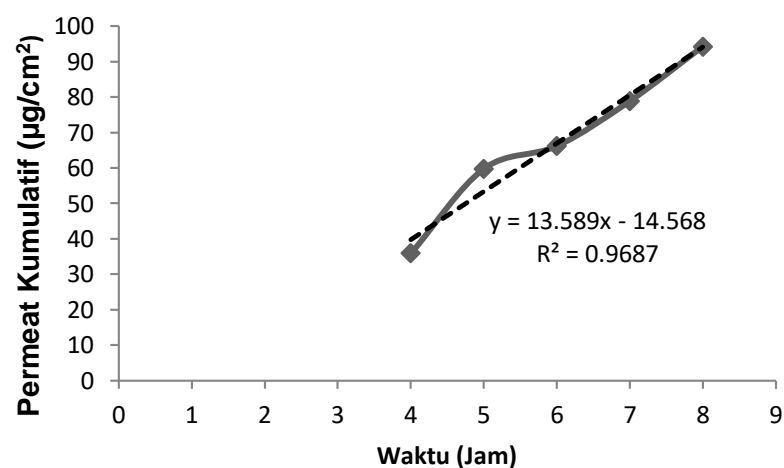
Keterangan :

a = intersep

b= slope

Dari hasil uji permeasi DMN nanokrsital VAL F3 pada waktu ke 4,5,6,7,8,

didapatkan grafik berikut:



Gambar 13. Grafik Permeat Kumulatif F1

Nilai *lag time* dapat dihitung menggunakan persamaan garis pada gambar

13:

$y = bx - a$

$$a = 14,568; b = 13,589$$

Maka, *lagtime* dapat diperoleh sebagai berikut :

Jika $y = 0$, maka x (*lagtime*)

$$y = bx - a$$

$$x = \frac{y + a}{b}$$

$$x = \frac{0+14,568}{13,589} = 1,07 \text{ jam}$$

Lampiran 9. Data Statistik

Lampiran 9.1. Uji Kekutan Mekanik

Normality test

	F1	F2	F3
Test for normal distribution			
Anderson-Darling test			
A2*	N too small	N too small	N too small
P value			
Passed normality test (alpha=0.05)?			
P value summary			
D'Agostino & Pearson test			
K2	N too small	N too small	N too small
P value			
Passed normality test (alpha=0.05)?			
P value summary			
Shapiro-Wilk test			
W	0.8073	0.7806	0.9966
P value	0.1321	0.0689	0.8889
Passed normality test (alpha=0.05)?	Yes	Yes	Yes
P value summary	ns	ns	ns
Kolmogorov-Smirnov test			
KS distance	N too small	N too small	N too small
P value			
Passed normality test (alpha=0.05)?			
P value summary			
Number of values	3	3	3

ANOVA

Table Analyzed	%penurunan tinggi				
Repeated measures ANOVA summary					
Assume sphericity?	No				
F	96.21				
P value	0.0102				
P value summary	*				
Statistically significant (P < 0.05)?	Yes				
Geisser-Greenhouse's epsilon	0.5001				
R squared	0.9796				
Was the matching effective?					
F	0.7364				
P value	0.5342				
P value summary	ns				
Is there significant matching (P < 0.05)?	No				
R squared	0.007442				
ANOVA table	SS	DF	MS	F (DFn, DFd)	P value
Treatment (between columns)	406.5	2	203.3	F (1.000, 2.000) = 96.21	P=0.0102
Individual (between rows)	3.112	2	1.556	F (2, 4) = 0.7364	P=0.5342
Residual (random)	8.451	4	2.113		
Total	418.1	8			
Data summary					
Number of treatments (columns)	3				
Number of subjects (rows)	3				
Number of missing values	0				

Multiple Comparisons (Tukey HSD)

Number of families	1							
Number of comparisons per family	3							
Alpha	0.05							
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value			
F1 vs. F2	14.33	13.49 to 15.16	Yes	****	<0.0001	A-B		
F1 vs. F3	14.19	6.069 to 22.30	Yes	*	0.0169	A-C		
F2 vs. F3	-0.1400	-9.087 to 8.807	No	ns	0.9953	B-C		
Test details	Mean 1	Mean 2	Mean Diff.	SE of diff.	n1	n2	q	DF
F1 vs. F2	46.07	31.74	14.33	0.1415	3	3	143.2	2
F1 vs. F3	46.07	31.88	14.19	1.378	3	3	14.56	2
F2 vs. F3	31.74	31.88	-0.1400	1.519	3	3	0.1304	2

Lampiran 9.2. Uji Waktu melarut

Normality test

	F1	F2	F3
Test for normal distribution			
Anderson-Darling test			
A2*	N too small	N too small	N too small
P value			
Passed normality test (alpha=0.05)?			
P value summary			
D'Agostino & Pearson test			
K2	N too small	N too small	N too small
P value			
Passed normality test (alpha=0.05)?			
P value summary			
Shapiro-Wilk test			
W	0.7507	1.000	0.9201
P value	0.0015	0.9926	0.4526
Passed normality test (alpha=0.05)?	No	Yes	Yes
P value summary	**	ns	ns
Kolmogorov-Smirnov test			
KS distance	N too small	N too small	N too small
P value			
Passed normality test (alpha=0.05)?			
P value summary			
Number of values	3	3	3

ANOVA

Table Analyzed	Waktu Melarut					
Repeated measures ANOVA summary						
Assume sphericity?	No					
F	207.2					
P value	0.0041					
P value summary	**					
Statistically significant (P < 0.05)?	Yes					
Geisser-Greenhouse's epsilon	0.5186					
R squared	0.9904					
Was the matching effective?						
F	19.03					
P value	0.0090					
P value summary	**					
Is there significant matching (P < 0.05)?	Yes					
R squared	0.08335					
ANOVA table	SS	DF	MS	F (DFn, DFd)	P value	
Treatment (between columns)	2355	2	1177	F (1.037, 2.074) = 207.2	P=0.0041	
Individual (between rows)	216.2	2	108.1	F (2, 4) = 19.03	P=0.0090	
Residual (random)	22.73	4	5.681			
Total	2594	8				
Data summary						
Number of treatments (columns)	3					
Number of subjects (rows)	3					
Number of missing values	0					

Multiple Comparisons (Tukey HSD)

Number of families	1								
Number of comparisons per family	3								
Alpha	0.05								
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value				
F1 vs. F2	29.23	18.21 to 40.24	Yes	**	0.0074	A-B			
F1 vs. F3	37.78	32.57 to 42.99	Yes	****	<0.0001	A-C			
F2 vs. F3	8.553	-7.125 to 24.23	No	ns	0.1502	B-C			
Test details	Mean 1	Mean 2	Mean Diff.	SE of diff.	n1	n2	q	DF	
F1 vs. F2	91.82	62.59	29.23	1.870	3	3	22.11	2	
F1 vs. F3	91.82	54.04	37.78	0.8850	3	3	60.37	2	
F2 vs. F3	62.59	54.04	8.553	2.662	3	3	4.545	2	

Lampiran 9.4. Uji permeasi Ex vivo

Normality test

	F1	F2	F3
Test for normal distribution			
Anderson-Darling test			
A2*	N too small	N too small	N too small
P value			
Passed normality test (alpha=0.05)?			
P value summary			
D'Agostino & Pearson test			
K2	N too small	N too small	N too small
P value			
Passed normality test (alpha=0.05)?			
P value summary			
Shapiro-Wilk test			
W	0.9946	0.9691	0.9984
P value	0.8591	0.6626	0.9240
Passed normality test (alpha=0.05)?	Yes	Yes	Yes
P value summary	ns	ns	ns
Kolmogorov-Smirnov test			
KS distance	N too small	N too small	N too small
P value			
Passed normality test (alpha=0.05)?			
P value summary			
Number of values	3	3	3

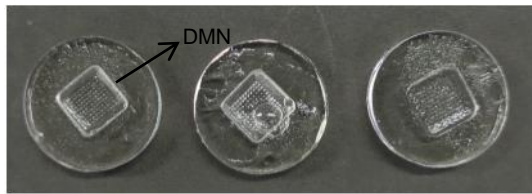
ANOVA

Table Analyzed	Ex Vivo					
Repeated measures ANOVA summary						
Assume sphericity?	No					
F	175750					
P value	<0.0001					
P value summary	****					
Statistically significant (P < 0.05)?	Yes					
Geisser-Greenhouse's epsilon	0.6640					
R squared	1.000					
Was the matching effective?						
F	246.9					
P value	<0.0001					
P value summary	****					
Is there significant matching (P < 0.05)?	Yes					
R squared	0.001403					
ANOVA table	SS	DF	MS	F (DFn, DFd)	P value	
Treatment (between columns)	7452	2	3726	F (1.328, 2.656) = 175750	P<0.0001	
Individual (between rows)	10.47	2	5.234	F (2, 4) = 246.9	P<0.0001	
Residual (random)	0.08480	4	0.02120			
Total	7462	8				
Data summary						
Number of treatments (columns)	3					
Number of subjects (rows)	3					
Number of missing values	0					

Multiple Comparisons (Tukey HSD)

Number of families	1								
Number of comparisons per family	3								
Alpha	0.05								
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value				
F1 vs. F2	-23.88	-24.32 to -23.44	Yes	****	<0.0001	A-B			
F1 vs. F3	-69.37	-70.06 to -68.68	Yes	****	<0.0001	A-C			
F2 vs. F3	-45.49	-46.38 to -44.60	Yes	****	<0.0001	B-C			
Test details	Mean 1	Mean 2	Mean Diff.	SE of diff.	n1	n2	q	DF	
F1 vs. F2	56.20	80.08	-23.88	0.07506	3	3	450.0	2	
F1 vs. F3	56.20	125.6	-69.37	0.1172	3	3	837.1	2	
F2 vs. F3	80.08	125.6	-45.49	0.1518	3	3	423.9	2	

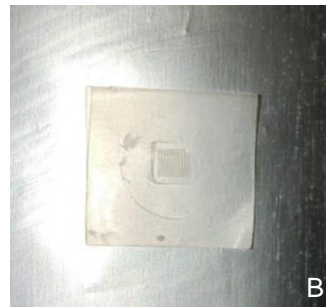
Lampiran 10. Dokumentasi Penelitian



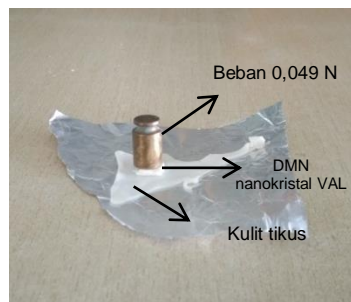
Gambar 15. Formulasi DMN nanokristal VAL



Gambar 16. Proses sentrifugasi DMN nanokristal VAL



Gambar 17. (A) Evaluasi kekuatan mekanik dan (B) kemampuan penetrasi



Gambar 18. Uji waktu melarut (durasi 10 menit)



Gambar 19. Uji permeasi *Ex vivo*

