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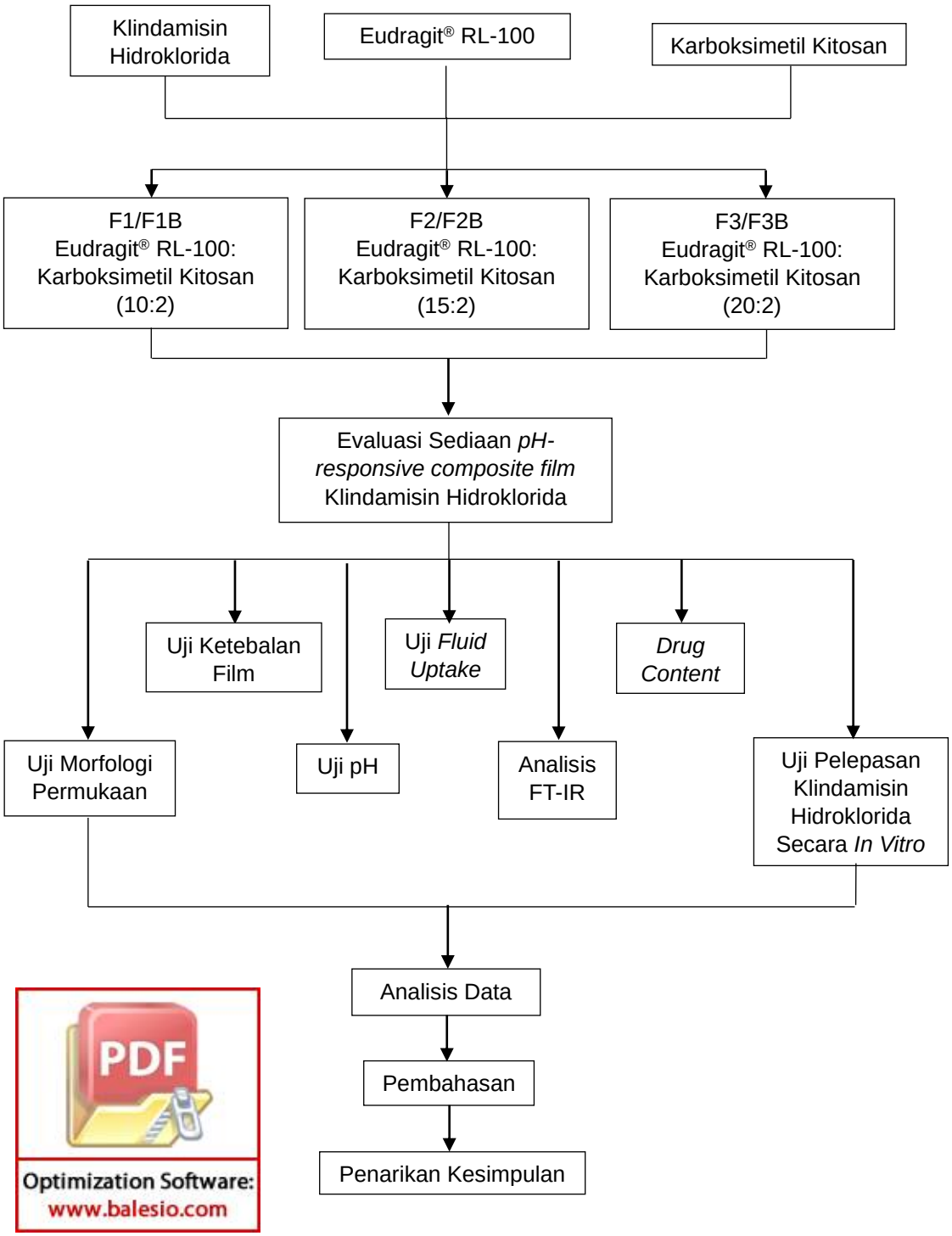
LAMPIRAN

Lampiran 1. Skema kerja

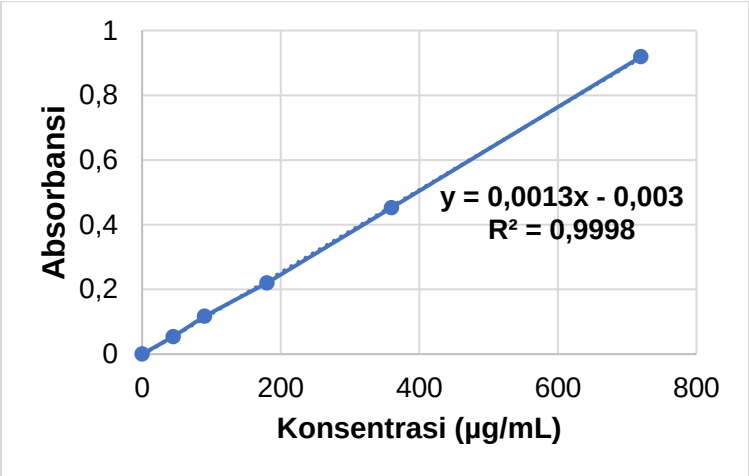


Lampiran 2. Preparasi cairan vaginal buatan (CVB)

Cairan vaginal buatan (CVB) dibuat dengan menimbang 5 g glukosa, 3,51 g NaCl, 2 g asam laktat, 1,4 g KOH, 1 g asam asetat, 0,4 g urea, 0,222 kalsium hidroksida, dan 0,016 g gliserin. Campuran tersebut lalu dilarutkan dengan *aquadest* hingga 1 L. Setelah itu, pH larutan diukur dan di*adjust* dengan 0,1 N HCl atau 0,1 N NaOH untuk memperoleh pH 4,9.

Lampiran 3. Penetapan kurva baku klindamisin HCl

Konsentrasi (µg/mL)	Absorbansi
0	0
45	0,054
90	0,117
180	0,22
360	0,452
720	0,919



Gambar 9. Kurva baku klindamisin HCl dalam CVB pH 4,9

Lampiran 4. Perhitungan data

Lampiran 4.1 Contoh perhitungan *fluid uptake* sediaan pH-*responsive composite film* klindamisin HCl

F1, replikasi 1 pada menit ke-10

)ot film kering (W_o) = 0,258 gram

)ot film yang bengkak pada menit ke-10 (W_{t10}) = 0,648 gram

uid uptake = ?

Penyelesaian :

Fluid Uptake (%) = $\frac{W_t - W_o}{Wt}$ x 100 %

= $\frac{0,648-0,258}{0,258}$ x 100 % = 151,162%

Lampiran 4.2 Contoh perhitungan kadar klindamisin HCl pada sediaan pH-*responsive composite film* klindamisin HCl

F1, replikasi 1

Diketahui : Persamaan kurva baku y = 0,0013x – 0,003
Absorbansi F1 replikasi 1 = 0,918
Faktor pengenceran = 1
Volume larutan = 5 mL
Bobot *film* yang digunakan = 50 mg
Bobot *film* utuh = 7,159 g
Bobot *film* sebelum di*coating* = 0,422 g
Bobot *film* setelah di*coating* = 0,239 g

Ditanyakan : % Efisiensi kadar obat = ?

Penyelesaian :

Jumlah klindamisin HCl pada *film* yang belum dipotong = $\frac{\text{Jumlah teoritis klindamisin HCL}}{\text{Bobot } film \text{ utuh}}$

= $\frac{0,3\text{ g}}{7,159\text{ g}}$ = 0,042 g/g

Terdapat 0,042 g dalam 1 g *film*, sehingga = $\frac{0,042\text{ g x bobot } film \text{ sebelum di} coating}{\text{Bobot } film \text{ setelah di} coating}$

= $\frac{0,042\text{ g x }0,422\text{ g}}{0,239\text{ g}}$ = $\frac{0,01772\text{ g}}{0,239\text{ g}}$

= $\frac{17,72\text{ mg}}{239\text{ mg}}$ = 0,074 mg/mg

Jadi, secara teoritis F1 mengandung klindamisin HCl sebesar 0,074 mg dalam 1 mg *film*.

Maka,

0,918 = 0,0013x – 0,003

x = $\frac{(0,918+0,003)}{0,0013}$

= 708,462 µg/mL = 0,708 mg/mL

Jumlah aktual klindamisin HCl:

=> $\frac{\text{kadar terukur x faktor pengenceran x jumlah media}}{\text{Bobot yang ditimbang}}$

= $\frac{0,708\text{ mg x 1 x 5 mL}}{}$ = 0,0708 mg klindamisin HCl/mg *film* F1

t = $\frac{\text{Jumlah aktual klindamisin HCl}}{\text{Jumlah teoritis klindamisin HCl}}$ x 100%

= $\frac{0,0708\text{ mg}}{0,074\text{ mg}}$ x 100% = 95,53 %

Lampiran 4.3 Contoh perhitungan pelepasan klindamisin HCl pada sediaan pH-*responsive composite film* klindamisin HCl

Diketahui : Persamaan kurva baku y = 0,0013x – 0,003
Absorbansi F1 replikasi 1 pada jam ke-1 = 0,089
Faktor pengenceran = 1
Volume larutan = 30 mL
Bobot *film* yang digunakan = 100 mg
Rata-rata kadar klindamisin HCl F1 dalam 1 mg *film* = 0,0706 mg

Ditanyakan : % kadar = ?

Penyelesaian :

F1 memiliki total aktual klindamisin HCl yaitu sebesar = 0,0706 mg x 100 mg = 7,06 mg

Maka,

0,089 = 0,0013x – 0,003

$$x = \frac{(0,089+0,003)}{0,0013}$$

=70,769 µg/mL

Faktor koreksi = Konsentrasi obat pada jam sebelumnya (jam ke-0,5)
= 35,385 µg/mL = 0,0354 mg

Jumlah klindamisin HCl dalam 30 mL:

=> kadar terukur x faktor pengenceran x jumlah media pelepasan
= 70,769 µg/mL x 1 x 30 = 2123 µg = 2,123 mg

Total klindamisin HCl yang terlepas = 2,123 mg + 0,0354 mg = 2,158 mg

$$\% \text{ Pelepasan obat} = \frac{\text{Total klindamisin HCl yang terlepas}}{\text{Total aktual klindamisin HCl}} \times 100\%$$

$$= \frac{2,158 \text{ mg}}{7,06 \text{ mg}} \times 100\% = 30,57\ \%$$

Lampiran 5. Tabel Hasil Evaluasi

Lampiran 5.1 Hasil Uji Ketebalan Film

Formula	Ketebalan Film (mm)	Rata-rata ± SD
F1	0,80 0,70 0,60 0,60 0,70	0,68 ± 0,08
F1B	0,60 0,40 0,30 0,40 0,40	0,42 ± 0,11
F2	0,90 0,80 0,70 0,70 0,80	0,78 ± 0,08
F2B	0,90 0,70 0,60 0,60 0,70	0,70 ± 0,12
F3	1,00 1,00 0,80 1,00 0,90	0,94 ± 0,09
F3B	0,90 0,80 0,80 0,80 0,80	0,82 ± 0,04

Lampiran 5.2 Hasil Uji pH Permukaan

Formula	pH	Rata-rata ± SD
F1	5,80 5,91 6,09	5,93 ± 0,15
F1B	5,67 5,87 5,93	5,82 ± 0,14
F2	5,74 5,89 6,18	5,94 ± 0,22
F2B	5,87 5,99 6,07	5,98 ± 0,10
F3	5,61 5,91 6,09	5,87 ± 0,24
F3B	5,77 5,81 6,13	5,90 ± 0,20

Lampiran 5.3 Hasil Uji *Fluid Uptake*

Lampiran 5.3.1 Bobot sediaan pH-responsive *composite film* klindamisin HCl

Waktu (menit) ke-	Bobot *film*					
	F1	**F1B**	**F2**	**F2B**	**F3**	**F3B**
0	0,258	0,214	0,372	0,366	0,369	0,385
	0,260	0,215	0,381	0,363	0,373	0,38
	0,255	0,218	0,379	0,371	0,378	0,377
Rata-rata ± SD	0,258 ± 0,003	0,216 ± 0,002	0,377 ± 0,005	0,367 ± 0,004	0,373 ± 0,005	0,381 ± 0,004
10	0,648	0,438	0,761	0,675	0,73	0,773
	0,653	0,442	0,777	0,673	0,734	0,758
	0,644	0,445	0,776	0,683	0,746	0,752
Rata-rata ± SD	0,648 ± 0,005	0,442 ± 0,004	0,771 ± 0,009	0,677 ± 0,005	0,737 ± 0,008	0,761 ± 0,011
30	0,673	0,461	0,843	0,712	0,750	0,772
	0,679	0,461	0,861	0,709	0,763	0,765
	0,666	0,467	0,860	0,721	0,770	0,759
Rata-rata ± SD	0,673 ± 0,007	0,463 ± 0,003	0,855 ± 0,010	0,714 ± 0,006	0,761 ± 0,010	0,765 ± 0,007
60	0,685	0,482	0,870	0,752	0,781	0,805
	0,692	0,483	0,885	0,749	0,787	0,793
	0,678	0,488	0,882	0,763	0,798	0,790
Rata-rata ± SD	0,685 ± 0,007	0,484 ± 0,003	0,879 ± 0,008	0,755 ± 0,007	0,789 ± 0,009	0,796 ± 0,008
120	0,687	0,486	0,874	0,796	0,814	0,826
	0,693	0,489	0,893	0,790	0,822	0,820
	0,680	0,497	0,890	0,807	0,832	0,810
Rata-rata ± SD	0,687 ± 0,007	0,491 ± 0,006	0,886 ± 0,010	0,798 ± 0,009	0,823 ± 0,009	0,819 ± 0,008

Lampiran 5.3.2 Hasil *% fluid uptake* sediaan pH-*responsive composite film* klindamisin HCl

Waktu (menit) ke-	*Fluid Uptake (%)*					
	F1	F1B	F2	F2B	F3	F3B
10	151,62 ± 0,80	104,79 ± 0,73	104,42 ± 0,43	84,64 ± 0,68	97,32 ± 0,53	99,91 ± 0,75
30	161,06 ± 0,18	114,69 ± 0,64	126,50 ± 0,47	94,73 ± 0,52	103,84 ± 0,66	101,05 ± 0,46
60	165,85 ± 0,33	124,58 ± 0,69	132,96 ± 0,82	105,82 ± 0,48	111,25 ± 0,35	109,11 ± 0,43
120	166,49 ± 0,37	127,51 ± 0,44	134,72 ± 0,30	117,55 ± 0,55	120,36 ± 0,25	115,06 ± 0,65

Lampiran 5.4 Hasil analisis kadar klindamisin HCl dalam sediaan pH-*responsive composite film* klindamisin HCl

Formula	Abs	Konsentrasi (µg/mL)	Total klindamisin HCL (mg)	%Kadar	%Rata-rata ± SD
F1	0,918	708,462	3,542	95,53	95,32 ± 1,98
	0,896	691,538	3,458	93,25	
	0,934	720,769	3,604	97,19	
F2	0,862	665,385	3,327	98,43	96,84 ± 3,06
	0,865	667,692	3,338	98,77	
	0,817	630,769	3,154	93,31	
F3	0,668	516,154	2,581	88,32	89,29 ± 3,40
	0,704	543,846	2,719	93,06	
	0,654	505,385	2,527	86,48	

Lampiran 5.5 Hasil uji pelepasan klindamisin HCl secara *in vitro* pada F1 sediaan pH-*responsinve composite film*

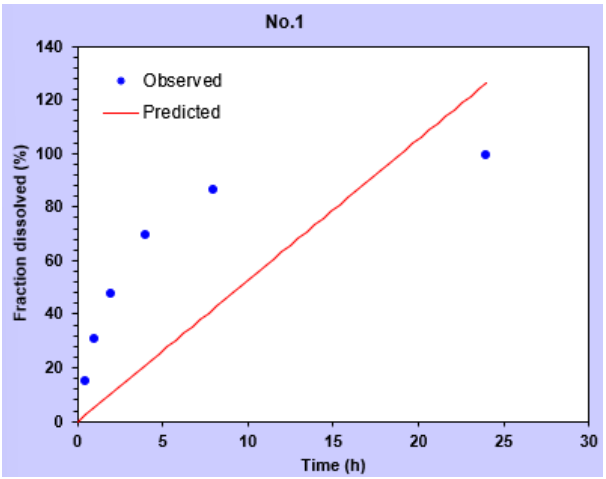
Waktu (jam)	Abs	Konsentrasi (µg/mL)	Jumlah klindamisin HCL yang terlepas dalam 30 mL (mg)	Faktor Koreksi (mg)	Faktor Pengenceran	Total klindamisin HCL yang terlepas (mg)	%Release	%Rata-rata ± SD
0,5	0,043	35,385	1,062	0	1	1,062	13,44	14,71 ± 2,14
	0,035	29,231	0,877	0	1	0,877	11,10	
	0,048	39,231	1,177	0	1	1,177	14,90	
1	0,089	70,769	2,123	0,0354	1	2,158	27,32	30,45 ± 3,50
	0,078	62,308	1,869	0,0292	1	1,898	24,03	
	0,099	78,462	2,354	0,0392	1	2,393	30,29	
2	0,13	102,308	3,069	0,1062	1	3,175	40,19	47,58 ± 2,31
	0,141	110,769	3,323	0,0915	1	3,415	43,22	
	0,143	112,308	3,369	0,1177	1	3,487	44,14	
4	0,193	150,769	4,523	0,2085	1	4,732	59,89	69,71 ± 2,48
	0,203	158,462	4,754	0,2023	1	4,956	62,74	
	0,207	161,538	4,846	0,2300	1	5,076	64,26	
8	0,241	187,692	5,631	0,3592	1	5,990	75,82	86,31 ± 1,48
	0,25	194,615	5,838	0,3608	1	6,199	78,47	
	0,244	190,000	5,700	0,3915	1	6,092	77,11	
24	0,298	231,538	6,531	0,5469	1	7,078	100,25	99,04 ± 1,45
	0,301	233,846	6,323	0,5554	1	6,878	97,43	
		235,385	6,438	0,5815	1	7,020	99,43	

F1 = 7,06 mg klindamisin HCl

Lampiran 5.6 Hasil uji kinetika model pelepasan klindamisin HCl secara *in vitro* menggunakan *add-ins* Microsoft Excel (DDsolver)

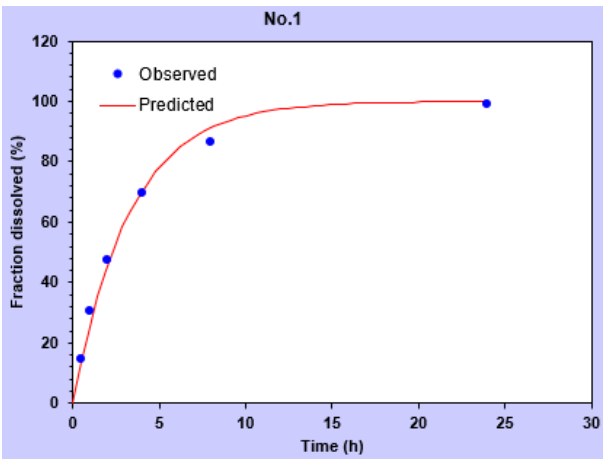
Lampiran 5.6.1 Hasil uji kinetika orde nol pelepasan klindamisin HCl secara *in vitro*

Goodness of Fit	
Parameter	**No.1**
N_observed	6
DF	5
R_obs-pre	0,811
Rsqr	-0,346
Rsqr_adj	-0,346
MSE	1443,761
MSE_root	38,00
Weighting	1,00
SS	7218,81
WSS	7218,81
AIC	55,31
MSC	-0,63



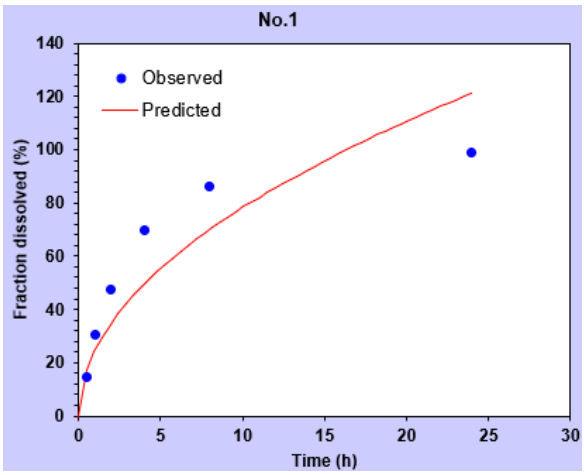
Lampiran 5.6.2 Hasil uji kinetika orde pertama pelepasan klindamisin HCl secara *in vitro*

Goodness of Fit	
Parameter	**No.1**
N_observed	6
DF	5
R_obs-pre	0,998
Rsqr	0,991
Rsqr_adj	0,991
MSE	9,547
MSE_root	3,09
Weighting	1,00
SS	47,73
WSS	47,73
AIC	25,19
MSC	4,39



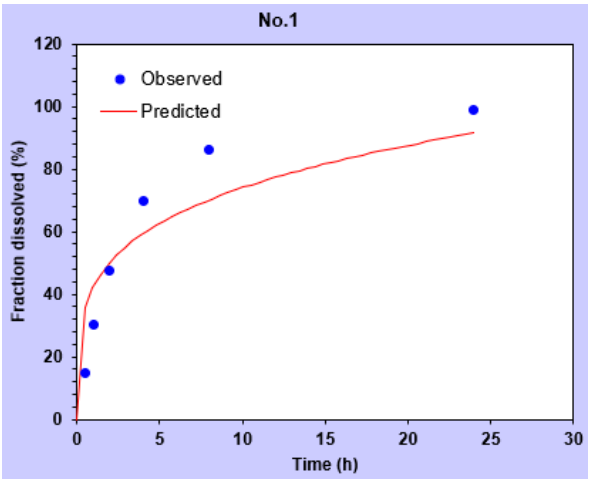
Lampiran 5.6.3 Hasil uji kinetika orde Higuchi pelepasan klindamisin HCl secara *in vitro*

Goodness of Fit	
Parameter	**No.1**
N_observed	6
DF	5
R_obs-pre	0,915
Rsqr	0,745
Rsqr_adj	0,745
MSE	273,22
MSE_root	16,53
Weighting	1,00
SS	1366,09
WSS	1366,09
AIC	45,32
MSC	1,03



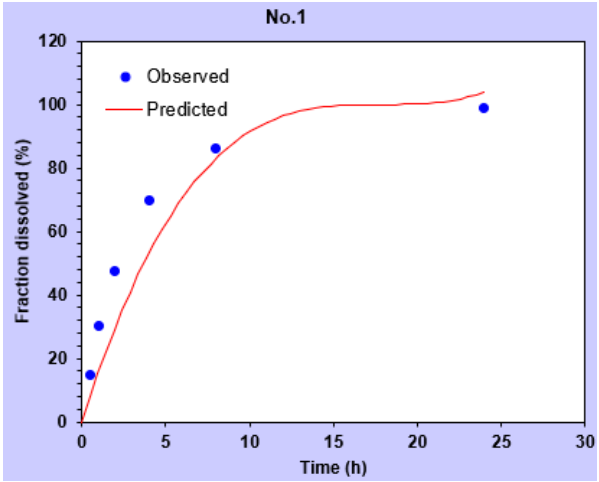
Lampiran 5.6.4 Hasil uji kinetika orde Korsmeyer-Peppas pelepasan klindamisin HCl secara *in vitro*

Goodness of Fit	
Parameter	**No.1**
N_observed	6
DF	4
R_obs-pre	0,962
Rsqr	0,809
Rsqr_adj	0,761
MSE	256,34
MSE_root	16,01
Weighting	1,00
SS	1025,36
WSS	1025,36
AIC	45,60
MSC	0,99



Lampiran 5.6.5 Hasil uji kinetika orde Hixson-Crowell pelepasan klindamisin HCl secara *in vitro*

Goodness of Fit	
Parameter	**No.1**
N_observed	6
DF	5
R_obs-pre	0,981
Rsqr	0,836
Rsqr_adj	0,836
MSE	175,55
MSE_root	13,25
Weighting	1,00
SS	877,74
WSS	877,74
AIC	42,66
MSC	1,48



Lampiran 6. Data hasil uji analisis statistik

Lampiran 6.1 Analisis statistik uji ketebalan *film*

Tests of Normality

		Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Formula	**Statistic**	**df**	**Sig.**	**Statistic**	**df**	**Sig.**
Ketebalan Film	**F1**	.231	5	.200*	.881	5	.314
	F1B	.372	5	.022	.828	5	.135
	F2	.231	5	.200*	.881	5	.314
	F2B	.300	5	.161	.833	5	.146
	F3	.349	5	.046	.771	5	.046
	F3B	.473	5	.001	.552	5	.000

*. This is a lower bound of the true significance.
a. Lilliefors Significance Correction

Kruskal-Wallis Test

Ranks

	Formula	N	Mean Rank
Ketebalan Film	F1	5	11.70
	F1B	5	3.40
	F2	5	17.90
	F2B	5	12.90
	F3	5	26.40
	F3B	5	20.70
	Total	30	

Test Statistics[a,b]

	Ketebalan Film
Kruskal-Wallis H	21.340
df	5
Asymp. Sig.	.001

a. Kruskal Wallis Test
b. Grouping Variable: Formula

Pairwise Comparisons of Formula

Sample 1-Sample 2	Test Statistic	Std. Error	Std. Test Statistic	Sig.	Adj. Sig.[a]
F1B-F1	8.300	5.470	1.517	.129	1.000
F1B-F2B	-9.500	5.470	-1.737	.082	1.000
F1B-F2	-14.500	5.470	-2.651	.008	.120
F1B-F3B	-17.300	5.470	-3.163	.002	.023
F1B-F3	-23.000	5.470	-4.205	.000	.000
F1-F2B	-1.200	5.470	-.219	.826	1.000
F1-F2	-6.200	5.470	-1.134	.257	1.000
F1-F3B	-9.000	5.470	-1.645	.100	1.000
F1-F3	-14.700	5.470	-2.688	.007	.108
F2B-F2	5.000	5.470	.914	.361	1.000
F2B-F3B	-7.800	5.470	-1.426	.154	1.000
F2B-F3	-13.500	5.470	-2.468	.014	.204
F2-F3B	-2.800	5.470	-.512	.609	1.000
F2-F3	-8.500	5.470	-1.554	.120	1.000
F3B-F3	5.700	5.470	1.042	.297	1.000

The significance level is .05.
a. Significance values have been adjusted by the Bonferroni correction for multiple tests.

Lampiran 6.2 Analisis statistik uji *surface* pH

Tests of Normality

		Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Formula	Statistic	df	Sig.	Statistic	df	Sig.
pH	F1	.230	3	.	.981	3	.736
	F1B	.301	3	.	.912	3	.424
	F2	.249	3	.	.967	3	.653
	F2B	.219	3	.	.987	3	.780
	F3	.232	3	.	.980	3	.726
	F3B	.349	3	.	.832	3	.194

ANOVA

pH

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	.044	5	.009	.269	.921
Within Groups	.396	12	.033		
Total	.440	17			

Lampiran 6.3 Analisis statistik uji *fluid uptake*

Tests of Normality

		Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Formula	Statistic	df	Sig.	Statistic	df	Sig.
Fluid Uptake	F1	.245	3	.	.971	3	.671
	F1B	.355	3	.	.818	3	.159
	F2	.310	3	.	.899	3	.382
	F2B	.299	3	.	.914	3	.432
	F3	.193	3	.	.997	3	.892
	F3B	.293	3	.	.922	3	.460

a. Lilliefors Significance Correction

ANOVA

Fluid Uptake

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	5528.527	5	1105.705	593.703	.000
Within Groups	22.349	12	1.862		
Total	5550.875	17			

Multiple Comparisons

Dependent Variable: Fluid Uptake

	(I) Formula	(J) Formula	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound
Tukey HSD	F1	F1B	40.655667*	1.114267	.000	36.91293	44.39840
		F2	31.779000*	1.114267	.000	28.03626	35.52174
		F2B	48.952333*	1.114267	.000	45.20960	52.69507
		F3	46.139000*	1.114267	.000	42.39626	49.88174
		F3B	51.435333*	1.114267	.000	47.69260	55.17807
	F1B	F1	-40.655667*	1.114267	.000	-44.39840	-36.91293
		F2	-8.876667*	1.114267	.000	-12.61940	-5.13393
		F2B	8.296667*	1.114267	.000	4.55393	12.03940
		F3	5.483333*	1.114267	.004	1.74060	9.22607
		F3B	10.779667*	1.114267	.000	7.03693	14.52240
	F2	F1	-31.779000*	1.114267	.000	-35.52174	-28.03626
		F1B	8.876667*	1.114267	.000	5.13393	12.61940
		F2B	17.173333*	1.114267	.000	13.43060	20.91607
		F3	14.360000*	1.114267	.000	10.61726	18.10274
		F3B	19.656333*	1.114267	.000	15.91360	23.39907
	F2B	F1	-48.952333*	1.114267	.000	-52.69507	-45.20960
		F1B	-8.296667*	1.114267	.000	-12.03940	-4.55393
		F2	-17.173333*	1.114267	.000	-20.91607	-13.43060
		F3	-2.813333	1.114267	.191	-6.55607	.92940
		F3B	2.483000	1.114267	.293	-1.25974	6.22574
	F3	F1	-46.139000*	1.114267	.000	-49.88174	-42.39626
		F1B	-5.483333*	1.114267	.004	-9.22607	-1.74060
		F2	-14.360000*	1.114267	.000	-18.10274	-10.61726
		F2B	2.813333	1.114267	.191	-.92940	6.55607
		F3B	5.296333*	1.114267	.005	1.55360	9.03907
	F3B	F1	-51.435333*	1.114267	.000	-55.17807	-47.69260
		F1B	-10.779667*	1.114267	.000	-14.52240	-7.03693
		F2	-19.656333*	1.114267	.000	-23.39907	-15.91360
		F2B	-2.483000	1.114267	.293	-6.22574	1.25974
		F3	-5.296333*	1.114267	.005	-9.03907	-1.55360

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

Lampiran 6.4 Analisis statitstik uji *drug content*

Tests of Normality

		Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Formula	Statistic	df	Sig.	Statistic	df	Sig.
Drug Content	F1	.208	3	.	.992	3	.826
	F2	.365	3	.	.797	3	.107
	F3	.279	3	.	.939	3	.525

a. Lilliefors Significance Correction

ANOVA

Drug Content

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	95.439	2	47.720	5.771	.040
Within Groups	49.615	6	8.269		
Total	145.055	8			

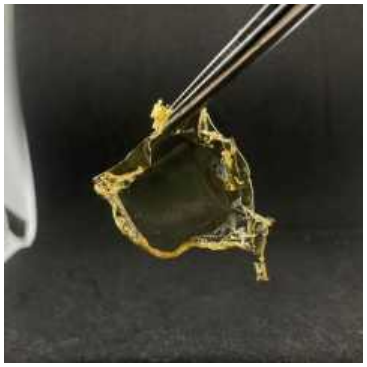
Multiple Comparisons

Dependent Variable: Drug Content

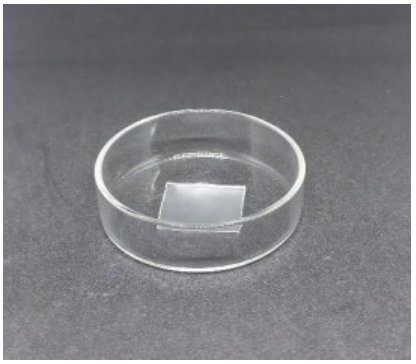
	(I) Formula	(J) Formula	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound
Tukey HSD	F1	F2	-1.724000	2.347940	.753	-8.92812	5.48012
		F3	5.882667	2.347940	.101	-1.32146	13.08679
	F2	F1	1.724000	2.347940	.753	-5.48012	8.92812
		F3	7.606667*	2.347940	.041	.40254	14.81079
	F3	F1	-5.882667	2.347940	.101	-13.08679	1.32146
		F2	-7.606667*	2.347940	.041	-14.81079	-.40254

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

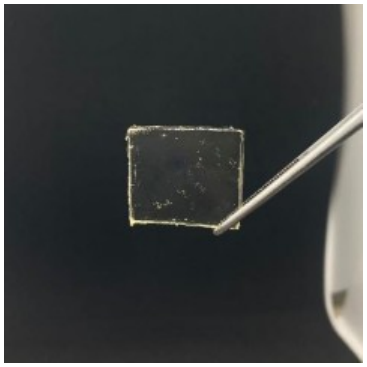
Lampiran 7. Dokumentasi



Gambar 11. Orientasi formula pH-*responsive composite film*



Gambar 12. Sediaan pH-*responsive composite film* sebelum *coating*



Gambar 13. Sediaan pH-*responsive composite film* setelah *coating*

Gambar 14. Proses uji ketebalan film

s uji *fluid uptake*

Gambar 16. Proses uji pelepasan klindamisin hidroklorida secara *in vitro*

Gambar 17. Proses pengukuran konsentrasi pelepasan klindamisin hidroklorida secara *in vitro*

Gambar 18. Alat mikroskop

Gambar 19. Alat spektrofotometer UV-Vis