BAB V
KESIMPULAN DAN SARAN

A. Kesimpulan

Pertama, Proporsi formula optimum Stearin dan Kolliphor EL dalam pembuatan basis *solid* SNEDDS Naringenin yaitu 1 bagian stearin dan 4 bagian Kolliphor-EL dengan parameter *emulsification time* sebesar 17,67 detik, persen transmitan 40,27%, persen disolusi 100,148% pada menit ke-10, AUC disolusi 683,94 hingga menit ke-10, dan konstanta difusi 0,1548

Kedua, Komponen Stearin memberikan pengaruh yang lebih besar pada parameter *emulsification time* (54.08%) dan uji difusi (87,90%), sedangkan Kolliphor-EL memberikan pengaruh lebih besar terhadap parameter persen transmitan (48,39%) dan uji disolusi (59,66%) *solid* SNEDDS Naringenin.

B. Saran

Pertama, perlu dilakukan penelitian lebih lanjut dalam pembuatan *solid* SNEDDS Naringenin dengan perbandingan bahan dan karakterisasi serta uji fisik yang lebih mendetail.

Kedua, perlu dilakukan penelitian lebih lanjut mengenai Optimasi *solid* SNEDDS Naringenin dalam pembuatan ke dalam bentuk sediaan obat.

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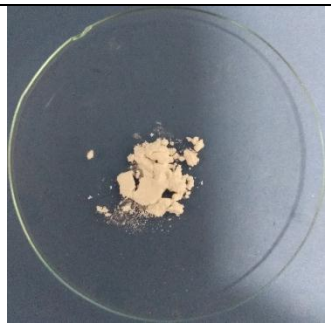
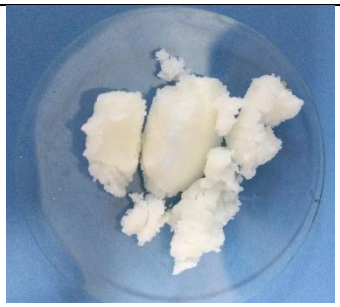
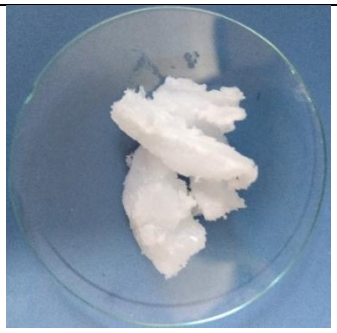
LAMPIRAN

Lampiran 1. Komponen Penyusun Solid SNEDDS Naringenin

GAMBAR BAHAN	NAMA BAHAN
	ZAT AKTIF NARINGENIN
	STEARIN (MINYAK)
	PEG 1000
	KOLLIPHOR EL

Lampiran 2. Alat-alat yang digunakan dalam praktikum

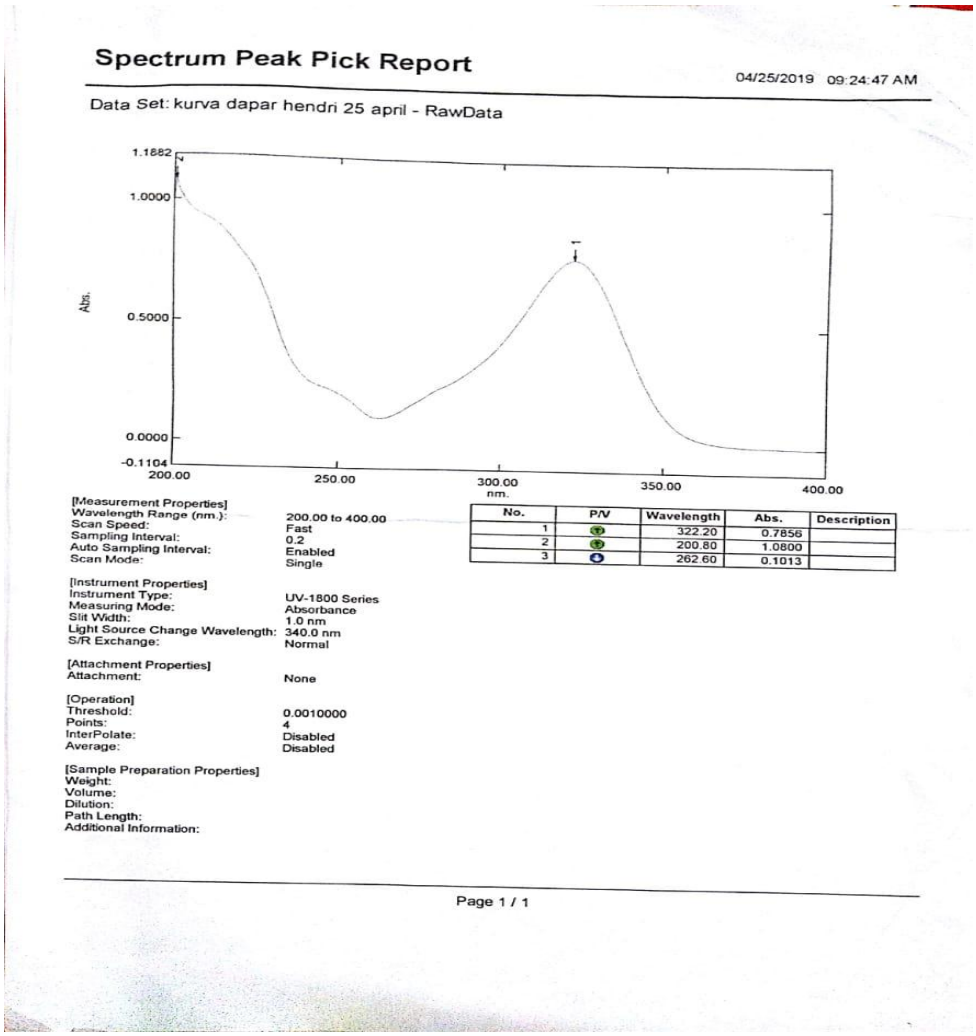
No	Alat	Nama Alat	Kegunaan
1		Neraca analitik	Menimbang bahan, baik bahan baku maupun *eksipien*.
2		Mikropipet	Megukur dan mengambil bahan, baik bahan baku maupun eksipien berupa cairan
3.		*Spektrofotometer UV-Vis*	Membaca serapan bahan aktif dan pembacaan *transmitan*

No	Alat	Nama Alat	Kegunaan
4.		*Stopwatch*	Untuk alat mesin hitung waktu
5.		Sentrifugasi	*Centrifuge* sample
6		Magnetic stirrer	Mencampur dan menghomogenkan komponen

Lampiran 3. Pembuatan kurva kalibrasi dan validasi metode analisis

a. Penentuan panjang gelombang maksimum Naringenin

Panjang gelombang maksimum diperoleh dari *scanning* larutan Naringenin konsentrasi 10 µg/mL dengan pelarut dapar fosfat pH 7,4. Hasil yang diperroleh yaitu panjang gelombang maksimum sebesar 322 nm dengan serapan 0,7856 µg/mL.



Spectrum Peak Pick Report

04/25/2019 09:24:47 AM

Data Set: kurva dapar hendri 25 april - RawData

No.	P/V	Wavelength	Abs.	Description
1	P	322.20	0.7856	
2	P	200.80	1.0800	
3	V	262.60	0.1013	

[Measurement Properties]
Wavelength Range (nm.): 200.00 to 400.00
Scan Speed: Fast
Sampling Interval: 0.2
Auto Sampling Interval: Enabled
Scan Mode: Single

[Instrument Properties]
Instrument Type: UV-1800 Series
Measuring Mode: Absorbance
Slit Width: 1.0 nm
Light Source Change Wavelength: 340.0 nm
S/R Exchange: Normal

[Attachment Properties]
Attachment: None

[Operation]
Threshold: 0.0010000
Points: 4
InterPolate: Disabled
Average: Disabled

[Sample Preparation Properties]
Weight:
Volume:
Dilution:
Path Length:
Additional Information:

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b. Kurva Kalibrasi

Konsentrasi (µg/mL)	Pembacaan 1	Pembacaan 2	Pembacaan 3	Pembacaan 4	Rata-rata
2	0,166	0,176	0,163	0,164	0,167
4	0,325	0,328	0,349	0,354	0,339
6	0,457	0,461	0,451	0,457	0,457
8	0,636	0,637	0,649	0,654	0,644
10	0,762	0,767	0,785	0,784	0,775
12	0,909	0,915	0,944	0,946	0,929

a = -0,0320

b = 0,0976

r = 0,9979

PERSAMAAN

y = - 0,0320 + 0,0976x

KETERANGAN

x = konsentrasi (µg/mL

y = serapan

c. Akurasi dan Presisi

- Akurasi

Konsentrasi	Replikasi	Absorbansi	Konsentrasi	Kons. sebenarnya	% Recovery	Rata-Rata
80%	1	0,343	3,84	3,7	104%	103,23%
	2	0,340	3,81	3,7	103%	
	3	0,339	3,80	3,7	103%	
100%	1	0,451	4,95	5,36	92%	92,36%
	2	0,445	4,89	5,36	91%	
	3	0,457	5,01	5,36	94%	
120%	1	0,647	6,96	6,9	101%	100,37%
	2	0,640	6,89	6,9	100%	
	3	0,644	6,93	6,9	100%	
					% Recovery	98,65%

Keterangan :

Kadar = (rata-rata serapan – (-0,0320)/ 0,0976

% *recovery* = $\frac{kadar\ terukur}{kadar\ sebenarnya}$ x 100 %

- Presisi

Replikasi	Absorbansi	Konsentrasi
1	0,420	4,633
2	0,439	4,828
3	0,443	4,869
4	0,442	4,858
5	0,444	4,879
6	0,447	4,910
7	0,433	4,766
8	0,439	4,828
9	0,445	4,889
10	0,457	5,012
SD	0,0987	
Rata-rata	4,8470	
CV	0,0204	

Lampiran 4. Hasil Contour Plot basis *solid* SNEDDS (tanpa obat)

Constraints

Name	Goal	Lower Limit	Upper Limit	Lower Weight	Upper Weight	Importance
Stearin	is in range	1	3	1	1	3
Kolliphor	is in range	1	4	1	1	3
WE	minimize	8	47	1	1	3
%T	maximize	8.3	58.8	1	1	3

Solutions

Number	Stearin	Kolliphor	WE	%T	Desirability	
1	1.00	4.00	9.66667	58.4667	0.975	Selected
2	1.00	3.88	9.63905	57.9275	0.970	
3	1.00	3.77	9.61567	57.4714	0.966	

a. Emulsification time

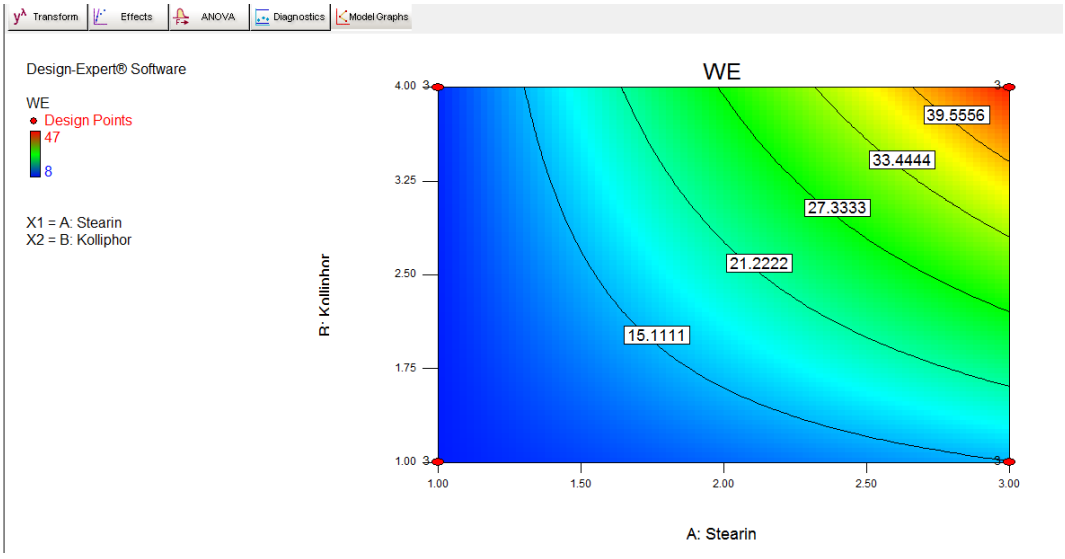
Factor	Coefficient Estimate	df	Standard Error	95% CI Low	95% CI High	VIF
Intercept	19.83	1	0.28	19.20	20.47	
A-Stearin	10.50	1	0.28	9.86	11.14	1.00
B-Kolliphor	7.83	1	0.28	7.20	8.47	1.00
AB	7.50	1	0.28	6.86	8.14	1.00

Final Equation in Terms of Coded Factors:

WE =
+19.83
+10.50 * A
+7.83 * B
+7.50 * A * B

Selection: Manual Order: 2FI

Term	Stdized Effects	Sum of Squares	% Contribution
Intercept			
A-Stearin	21.00	1323.00	48.26
B-Kolliphor	15.67	736.33	26.86
AB	15.00	675.00	24.62
Lack Of Fit		0.000	0.000
Pure Error		7.33	0.27
Lenth's ME	17.76		
Lenth's SME	22.95		



b. Persen transmitan

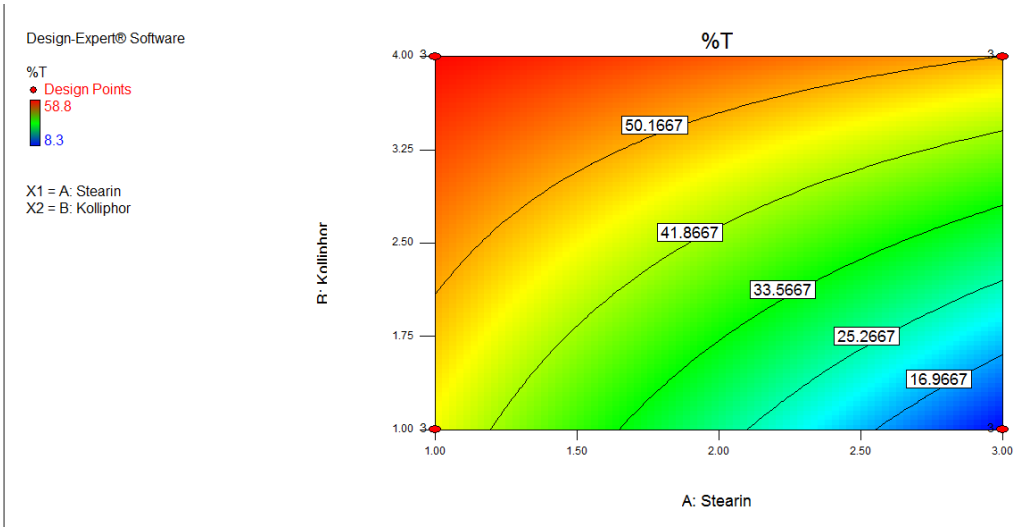
Factor	Coefficient Estimate	df	Standard Error	95% CI Low	95% CI High	VIF
Intercept	40.68	1	0.14	40.35	41.00	
A-Stearin	-11.29	1	0.14	-11.61	-10.97	1.00
B-Kolliphor	13.61	1	0.14	13.29	13.93	1.00
AB	7.11	1	0.14	6.79	7.43	1.00

Final Equation in Terms of Coded Factors:

%T =
+40.68
-11.29 * A
+13.61 * B
+7.11 * A * B

Selection: Manual Order: 2FI

Term	Stdized Effects	Sum of Squares	% Contribution
Intercept			
A-Stearin	-22.58	1530.02	35.09
B-Kolliphor	27.22	2222.24	50.96
AB	14.22	606.34	13.91
Lack Of Fit		0.000	0.000
Pure Error		1.86	0.043
Lenth's ME	25.55		
Lenth's SME	33.01		



Lampiran 5. Hasil optimasi solid SNEDDS Naringenin berdasarkan *emulsification time*, persen transmitan, uji disolusi, dan uji difusi.

Constraints

Name	Goal	Lower Limit	Upper Limit	Lower Weight	Upper Weight	Importance
Stearin	is in range	1	3	1	1	3
Kolliphor-EL	is in range	1	4	1	1	3
WE	minimize	14	50	1	1	3
% transmitan	maximize	5	40.5	1	1	3
AUC disolusi	maximize	599.315	702.931	1	1	3
Q disolusi	maximize	90.27	103.38	1	1	3
Konstanta difi	maximize	0.121834	0.162655	1	1	3

Solutions

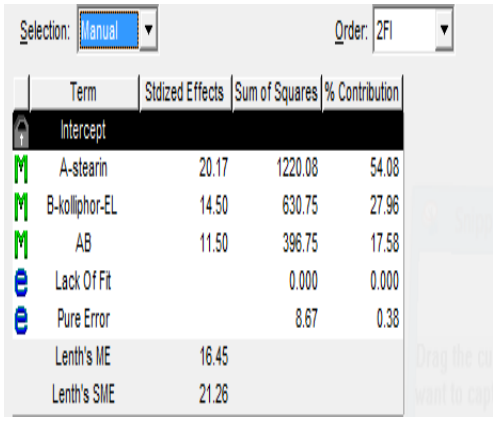
Number	Stearin	Kolliphor-EL	WE	% transmitan	AUC disolusi	Q disolusi	Konstanta di	Desirability	
1	1.00	4.00	17.6667	40.2667	683.941	100.148	0.154822	0.850	Selected
2	1.00	3.70	17.3673	39.6379	677.965	99.5155	0.155228	0.827	

a. Emulsification time

Factor	Coefficient Estimate	df	Standard Error	95% CI Low	95% CI High	VIF
Intercept	26.25	1	0.30	25.56	26.94	
A-stearin	10.08	1	0.30	9.39	10.78	1.00
B-kolliphor-EL	7.25	1	0.30	6.56	7.94	1.00
AB	5.75	1	0.30	5.06	6.44	1.00

Final Equation in Terms of Coded Factors:

WE =
+26.25
+10.08 * A
+7.25 * B
+5.75 * A * B



Use your mouse to right click on individual cells for definitions.

Response 1 WE

ANOVA for selected factorial model

Analysis of variance table [Partial sum of squares - Type III]

Source	Sum of Squares	df	Mean Square	F Value	p-value Prob > F	
Model	2247.58	3	749.19	691.56	< 0.0001	significant
A-Stearin	*1220.08*	*1*	*1220.08*	*1126.23*	*< 0.0001*	
B-Kolliphor-I	*630.75*	*1*	*630.75*	*582.23*	*< 0.0001*	
AB	*396.75*	*1*	*396.75*	*366.23*	*< 0.0001*	
Pure Error	8.67	8	1.08			
Cor Total	2256.25	11				

b. Persen transmitan

Factor	Coefficient Estimate	df	Standard Error	95% CI Low	95% CI High	VIF
Intercept	29.45	1	0.084	29.26	29.64	
A-stearin	-7.67	1	0.084	-7.86	-7.47	1.00
B-kolliphor-El	9.88	1	0.084	9.69	10.08	1.00
AB	6.73	1	0.084	6.54	6.93	1.00

Final Equation in Terms of Coded Factors:

%T =
+29.45
-7.67 * A
+9.88 * B
+6.73 * A * B

Selection: Manual Order: 2FI

Term	Stdized Effects	Sum of Squares	% Contribution
Intercept			
A-stearin	-15.33	705.33	29.12
B-kolliphor-EL	19.77	1172.16	48.39
AB	13.47	544.05	22.46
Lack Of Fit		0.000	0.000
Pure Error		0.68	0.028
Lenth's ME	17.35		
Lenth's SME	22.41		

Use your mouse to right click on individual cells for definitions.

Response 2 T

ANOVA for selected factorial model

Analysis of variance table [Partial sum of squares - Type III]

Source	Sum of Squares	df	Mean Square	F Value	p-value Prob > F	
Model	2421.55	3	807.18	9496.27	< 0.0001	significant
A-Stearin	*705.33*	*1*	*705.33*	*8298.04*	*< 0.0001*	
B-Kolliphor-l	*1172.16*	*1*	*1172.16*	*13790.16*	*< 0.0001*	
AB	*544.05*	*1*	*544.05*	*6400.63*	*< 0.0001*	
Pure Error	0.68	8	0.085			
Cor Total	2422.23	11				

c. Uji Disolusi (AUC)

Factor	Coefficient Estimate	df	Standard Error	95% CI Low	95% CI High	VIF
Intercept	657.35	1	5.61	644.41	670.29	
A-Stearin	3.35	1	5.61	-9.59	16.29	1.00
B-Kolliphor-El	21.98	1	5.61	9.04	34.92	1.00
AB	-7.96	1	5.61	-20.90	4.98	1.00

Final Equation in Terms of Coded Factors:

AUC disolusi =
+657.35
+3.35 * A
+21.98 * B
-7.96 * A * B

Selection: Manual Order: 2FI

Term	Stdized Effects	Sum of Squares	% Contribution
Intercept			
A-Stearin	6.70	134.53	1.38
B-Kolliphor-EL	43.96	5796.23	59.66
AB	-15.92	760.42	7.83
Lack Of Fit		0.000	0.000
Pure Error		3023.97	31.13
Lenth's ME	29.96		
Lenth's SME	38.71		

Use your mouse to right click on individual cells for definitions.

Response 3 AUC disolusi

ANOVA for selected factorial model

Analysis of variance table [Partial sum of squares - Type III]

Source	Sum of Squares	df	Mean Square	F Value	p-value Prob > F	
Model	6691.18	3	2230.39	5.90	0.0200	significant
A-Stearin	*134.53*	*1*	*134.53*	*0.36*	*0.5673*	
B-Kolliphor-I	*5796.23*	*1*	*5796.23*	*15.33*	*0.0044*	
AB	*760.42*	*1*	*760.42*	*2.01*	*0.1938*	
Pure Error	3023.97	8	378.00			
Cor Total	9715.15	11				

d. Disolusi (Q_{10})

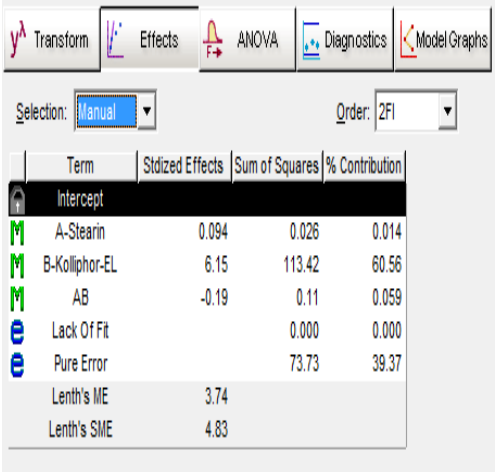
The "Pred R-Squared" of 0.1142 is not as close to the "Adj R-Squared" of 0.4587 as one might normally expect. This may indicate a large block effect or a possible problem with your model and/or data. Things to consider are model reduction, response tranformation, outliers, etc.

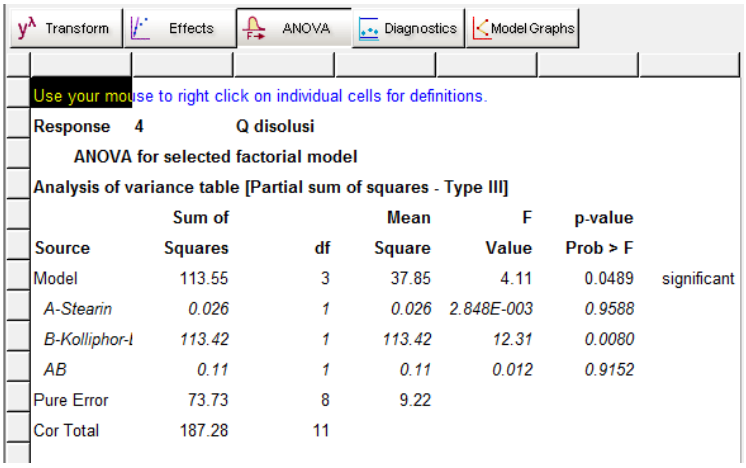
"Adeq Precision" measures the signal to noise ratio. A ratio of 3.62 indicates an inadequate signal and we should not use this model to navigate the design space.

Factor	Coefficient Estimate	df	Standard Error	95% CI Low	95% CI High	VIF
Intercept	97.02	1	0.88	95.00	99.05	
A-Stearin	0.047	1	0.88	-1.97	2.07	1.00
B-Kolliphor-El	3.07	1	0.88	1.05	5.10	1.00
AB	-0.096	1	0.88	-2.12	1.92	1.00

Final Equation in Terms of Coded Factors:

Q disolusi =
+97.02
+0.047 * A
+3.07 * B
-0.096 * A * B





e. Difusi (Konstanta difusi)

The "Pred R-Squared" of 0.9628 is in reasonable agreement with the "Adj R-Squared" of 0.9773.

"Adeq Precision" measures the signal to noise ratio. A ratio greater than 4 is desirable. Your ratio of 26.930 indicates an adequate signal. This model can be used to navigate the design spa

Factor	Coefficient Estimate	df	Standard Error	95% CI Low	95% CI High	VIF
Intercept	0.14	1	6.828E-004	0.14	0.14	
A-Stearin	-0.014	1	6.828E-004	-0.016	-0.013	1.00
B-Kolliphor-El	2.264E-003	1	6.828E-004	6.895E-004	3.839E-003	1.00
AB	4.299E-003	1	6.828E-004	2.724E-003	5.873E-003	1.00

Final Equation in Terms of Coded Factors:

Konstanta difusi =
+0.14
-0.014 * A
+2.264E-003 * B
+4.299E-003 * A * B

Transform | Effects | ANOVA | Diagnostics | Model Graphs

Selection: Manual Order: 2FI

Term	Stdized Effects	Sum of Squares	% Contribution
Intercept			
A-Stearin	-0.028	2.382E-003	87.90
B-Kolliphor-EL	4.528E-003	6.151E-005	2.27
AB	8.597E-003	2.217E-004	8.18
Lack Of Fit		0.000	0.000
Pure Error		4.476E-005	1.65
Lenth's ME	0.010		
Lenth's SME	0.013		

Transform | Effects | ANOVA | Diagnostics | Model Graphs

Use your mouse to right click on individual cells for definitions.

Response 5 Konstanta difusi

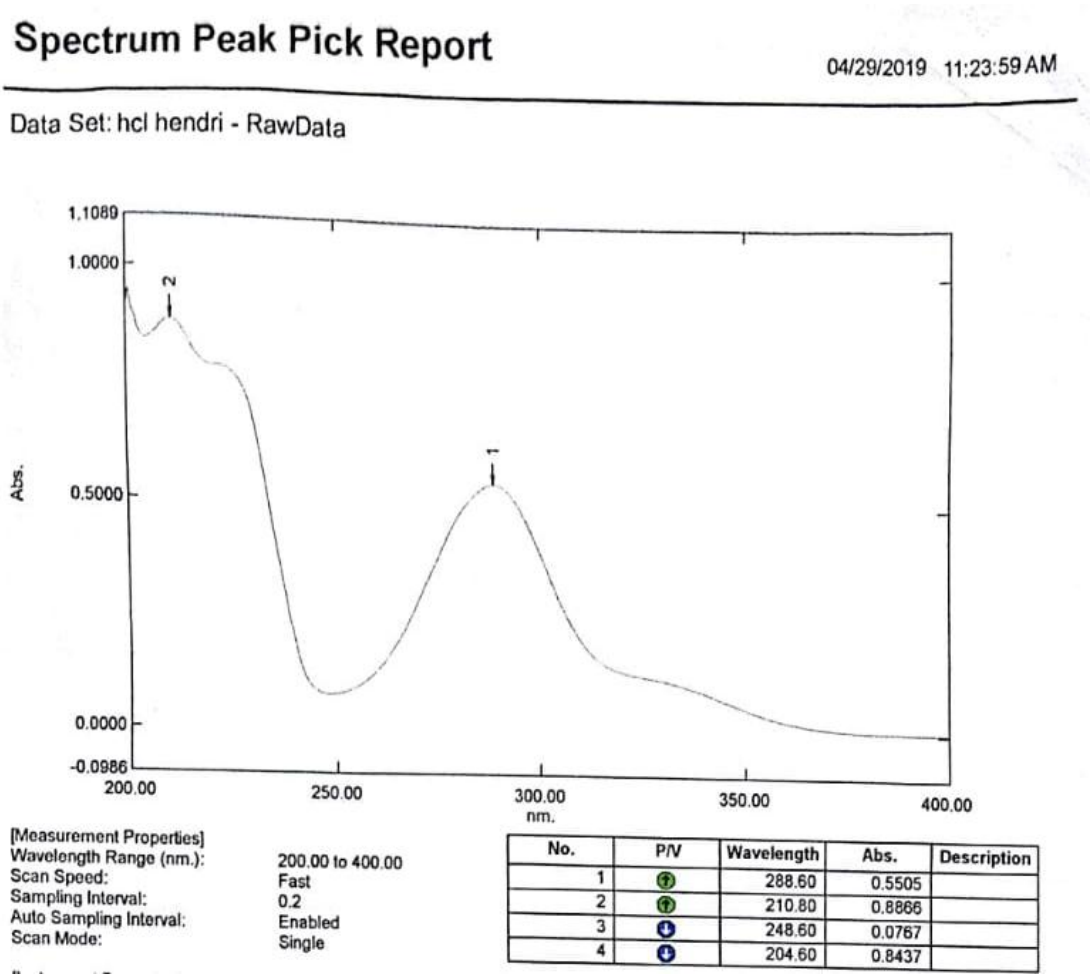
ANOVA for selected factorial model

Analysis of variance table [Partial sum of squares - Type III]

Source	Sum of Squares	df	Mean Square	F Value	p-value Prob > F	
Model	2.666E-003	3	8.885E-004	158.81	< 0.0001	significant
A-Stearin	*2.382E-003*	*1*	*2.382E-003*	*425.80*	*< 0.0001*	
B-Kolliphor-I	*6.151E-005*	*1*	*6.151E-005*	*10.99*	*0.0106*	
AB	*2.217E-004*	*1*	*2.217E-004*	*39.63*	*0.0002*	
Pure Error	4.476E-005	8	5.595E-006			
Cor Total	2.710E-003	11				

Lampiran 6. Uji Disolusi

a. Penentuan Panjang Gelombang maksimum HCl 0,1N



No.	P/V	Wavelength	Abs.	Description
1	↑	288.60	0.5505	
2	↑	210.80	0.8866	
3	↓	248.60	0.0767	
4	↓	204.60	0.8437	

b. Kurva Kalibrasi HCl 0,1 N

Konsentrasi (µg/mL)	Replikasi 1	Replikasi 2	Replikasi 3	Replikasi 4	Rata-rata
1,95	0,259	0,257	0,257	0,257	0,258
3,86	0,315	0,318	0,317	0,318	0,317
5,67	0,392	0,393	0,390	0,392	0,392
7,41	0,455	0,456	0,455	0,455	0,455
9,09	0,512	0,513	0,513	0,514	0,513
10,71	0,565	0,567	0,564	0,567	0,566
13,81	0,652	0,651	0,653	0,655	0,653

a = 0,1948
b = 0,0341
r = 0,9981

PERSAMAAN

y = 0,1948 + 0,0341x

KETERANGAN

x = konsentrasi (µg/mL

y = serapan

c. Akurasi dan Presisi

- **Akurasi**

Konsentrasi	Replikasi	Absorbansi	Konsentrasi	Kons. Sebenarnya	% Recovery	Rata-Rata
80%	1	0,515	9,3936	9,08835	103%	101,96%
	2	0,506	9,1295	9,08835	100%	
	3	0,511	9,2762	9,08835	102%	
100%	1	0,566	10,8771	10,7082	102%	101,61%
	2	0,5658	10,8838	10,7082	102%	
	3	0,56575	10,8823	10,7082	102%	
120%	1	0,65278	13,4354	13,8079	97%	97,30%
	2	0,65273	13,4339	13,8079	97%	
	3	0,65275	13,4345	13,8079	97%	
					% Recovery	**100,29%**

- **Presisi**

Replikasi	Absorbansi	Konsentrasi
1	0,562	9,1376
2	0,56	9,0935
3	0,563	9,1596
4	0,561	9,1155
5	0,562	9,1376
6	0,565	9,2037
7	0,564	9,1817
8	0,56	9,0935
9	0,561	9,1155
10	0,556	9,0053
SD	0,0734	
Rata-rata	10,7547	
CV	0,0068	

d. Data Disolusi *solid* SNEDDS Naringenin

Menit ke-	%Terdisolusi			
	F1	F2	F3	F4
0	0	0	0	0
1	6,72	7,46	10,93	9,51
3	52,05	56,65	60,65	59,92
5	70,58	74,26	79,84	78,91
7	83,43	90,17	96,82	95,74
10	90,27	92,52	102,30	98,94
15	91,46	94,07	104,36	99,05
20	91,85	94,21	106,62	99,34
25	92,78	95,37	107,94	100,21
30	92,86	95,63	109,26	101,33
60	95,89	101,32	111,26	103,54

Menit ke-	AUC			
	F1	F2	F3	F4
0	0	0	0	0
1	3,36	3,73	5,47	4,76
3	58,77	64,11	71,58	69,43
5	122,63	130,91	140,49	138,83
7	154,01	164,43	176,66	174,65
10	260,55	274,04	298,68	292,01
TOTAL AUC	**599,31**	**637,21**	**692,87**	**679,68**
DE_{10}	**59,93**	**63,72**	**69,29**	**67,97**

e. Data Disolusi Naringenin

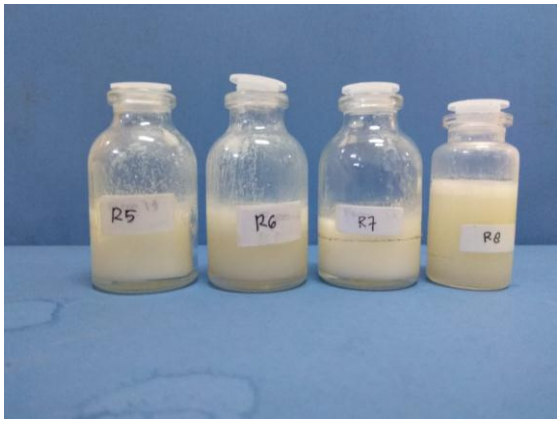
Menit ke-	%Terdisolusi	AUC
0	0	0
1	1,61	0,81
3	6,58	8,19
5	14,79	21,37
7	22,63	37,42
10	26,65	73,92
15	31,38	145,08
20	39,76	177,85
25	36,54	190,75
30	40,94	193,70
60	55,93	1453,05
TOTAL AUC	**2302,13**	
DE_{60}	**38,37**	

Lampiran 7. Uji difusi

Data Jumlah dan Konstanta Terdifusi

Menit ke-	Jumlah Terdifusi (µg/cm2)			
	F1	F2	F3	F4
0	0	0	0	0
1	9,24	8,97	10,52	10,89
3	10,16	10,06	11,91	12,00
5	11,27	10,53	11,94	12,67
7	11,65	11,18	13,06	13,35
10	13,41	12,85	14,56	13,84
15	13,63	13,43	15,34	14,80
20	15,23	14,20	16,13	15,86
25	16,93	16,35	17,56	17,01
30	19,38	16,87	18,65	19,29
60	21,67	17,30	25,59	19,72
90	24,16	22,77	26,84	23,03
120	29,70	24,36	28,29	29,29
Konstanta Difusi	1. 0,1626 2. 0,1551 3 0,1205	1. 0,0122 2. 0,1218 3. 0,1425	1. 0,1536 2. 0,1565 3. 0,1554	1. 0,1377 2. 0,1328 3. 0,1352

Lampiran 8. Bentuk Sediaan *Solid* SNEDDS Naringenin



Lampiran 9. Certificate Of Analysis (CO-A) Naringenin

泽世化学 THANEN CHEMICALS
ADDRESS: RM1707, BLDG 5, CHANGFA, 101-1# TAIHU ROAD, 213022, P.R.CHINA
TEL: +86 519 89880626 FAX: +86-519-89880629 Email:tcc@thanenchem.com

CERTIFICATE OF ANALYSIS

Product Name	Naringenin	**Code**	BPBE-622-A
Botanical Source	Citrus Grandis (L.) Obsbeck	**Used Part**	Fruit
Batch No.	H020862217A	**Mfg. Date**	Aug. 15, 2017
Packing	25kg/Drum	**Retest Date**	Aug. 14, 2019
Quantity	25g	**Report Date**	Aug. 21, 2017
Specification	98%(HPLC)		

ITEM	SPECIFICATION	RESULT
Assay(HPLC)	≥98.0%	98.23%
Appearance	White powder	Complies
Odor	Characteristic	Complies
Particle Size	NLT 95% pass 80 mesh	Complies
Loss on Drying	≤5.0%	0.53%
Sulphated Ash	≤0.1%	0.05%
Heavy Metals	≤10ppm	Complies
-Pb	≤1ppm	Complies
-As	≤1ppm	Complies
-Cd	≤1ppm	Complies
-Hg	≤0.1ppm	Complies
Total Plate Count	≤1000cfu/g	Complies
-Yeast & Mold	≤100cfu/g	Complies
-E.Coli	Negative	Negative
-Salmonella	Negative	Negative
Conclusion	Comply with the Specification.	
Storage	Preserve in tight containers, protected from strong light and high heat. Store in dry cool place.	

Analyst: QC Manager: QA: