

## **BAB V**

### **KESIMPULAN DAN SARAN**

#### **A. Kesimpulan**

Pertama, berdasarkan 4 formula *solid* SNEDDS naringenin diperoleh formula optimum dengan menggunakan  $2^2$  *Factorial Design* yaitu formula dengan perbandingan komponen stearin 1 bagian dan PEG 1000 3 bagian dengan memiliki karakterisasi waktu emulsifikasi 25,33 detik, % transmitan sebesar 33,13 %, AUC disolusi sebesar 2432,51,  $Q_{30}$  disolusi sebesar 102,93%, dan konstanta difusi sebesar 0,169.

Kedua, pengaruh komponen stearin dapat meningkatkan % transmitan dari formula *solid* SNEDDS naringenin, sedangkan pengaruh komponen PEG 1000 dapat menurunkan waktu emulsifikasi (*emulsification time*), AUC total dan  $Q_{30}$  uji disolusi serta dapat menurunkan konstanta difusi dari formulasi *solid* SNEDDS naringenin.

#### **B. Saran**

Pertama, perlu dilakukan penelitian lebih lanjut dalam karakterisasi *solid* SNEDDS naringenin untuk dapat melihat gambaran lebih jelas mengenai parameter kritis *solid* SNEDDS.

Kedua, perlu dilakukan pengujian aktivitas antioksidan untuk mengetahui perbandingan antara sediaan *solid* SNEDDS naringenin dengan naringenin murni agar mengetahui keefektifan aktivitas dari sediaan.

## DAFTAR PUSTAKA

- Azeem A, Rizwan M, Ahmad FJ, Iqbal Z, Khar RK, Aqil M, et al., 2009, Nanoemulsion Components Screening and Selection: a Technical Note. *AAPS PharmSciTech*, 10: 69–76.
- Astika DN. 2015. Pengaruh Penambahan Surfaktan Tween 80 terhadap Sifat Mutu Fisik Stabilitas Mikroemulsi Ketoprofen [Skripsi]. Jember: fakultas Farmasi, Universitas Jember.
- Balakumar K, Raghavan CV, Selvan NT, Prasad RH, dan Abdu S, 2013. Self Nanoemulsifying Drug Delivery System (SNEDDS) of Rosuvastatin Calcium: Design, Formulation, Bioavailability and Pharmacokinetic Evaluation. *Colloids and Surfaces B: Biointerfaces*, 112: 337–343.
- Bali B, Ali M, Ali J. (2010). Study Of Surfactant Combinations And Development of A Novel Nanoemulsion for Minimising Variations in Bioavailability of Ezetimibe. *Colloids Surfaces B: Biointerfaces* 76:410–20.
- Basiron Y. 2005. Palm oil. Dalam Shahidi F (Ed). *Bailey's Industrial Oil and Fat Product*. P. 333-429. *John Wiley & Sons Inc*. Hoboken.
- Benita, S., 2006, *Microencapsulation: Methods & Industrial Applications Vol 158*, 2nd Edition, 2-5.
- Bugianesi, R., G. Catasta, P. Spignoo, A. D'Uva, and G. Malani. 2002. Naringenin from cooked tomato paste is bioavailable in men. *J. Nutr* 132 (11) : 3349-3352.
- Bolton S. 1997. *Pharmaceutical Statistics, Practical and Clinical Applications*. Ed ke-3. New York: Marcel Dekker. hlm 326-352.
- Bolton S and Bon C. 2004. *Pharmaceutical Statistics*. New York: Marcell Dekker Inc. hlm 265-281.
- Date AA, Desai N, Dixit R, dan Nagarsenker M. 2010. Self-Nanoemulsifying Drug Delivery System: Formulation Insights, Applications and Advances, *Nanomedicine*, 5: 1595–1616.
- Debnath S, Satyanarayana, dan Kumar GV., 2011, *Nanoemulsion-A Method to Improve The Solubility of Lipophilic Drugs*, *Pharmanest.*, 2 (2-3), 72-76.
- Fudholi A. 2013. *Disolusi dan Pelepasan Obat In-vitro*, Pustaka Pelajar, Yogyakarta.

- Gupta S, Chavan S, dan Sawant KK. 2011, Self-Nanoemulsifying Drug Delivery System for Adefovir Dipivoxil: Design, Characterization, in Vitro and ex Vivo Evaluation, *Physicochem. Eng. Aspects*. 392, 145-155.
- Harmita. 2004. *Petunjuk Pelaksanaan Validasi Metode dan Cara Perhitungannya*. Majalah Ilmu Kefarmasian 1:117-135.
- Hsiu SL, Huang TY, Hou YC, Chin DH, Chao PD. 2001. Comparison of metabolic pharmacokinetics of naringin and naringenin in rabbits. *Life Sciences* 70, 1481-1489.
- Kaur G, Pankaj C, & Halikumar SL. 2013. Formulation Development of Self-Nanoemulsifying Drug Delivery System (SNEDDS) of Celecoxib for Improvement of Oral Bioavailability. *Pharmacophore*; 4(4); 120-133.
- Kommuru TR, Gurley B, Khan MA, Reddy IK. 2001. Self-Emulsifying Drug Delivery Systems (SEDDS) of Coenzyme Q10: Formulation Development and Bioavailability Assessment. *Int. J. Pharm.* 212, 233-246.
- Makadia HA, Bhatt AY, Parmar RB, Paun JS, dan Tank HM. 2013. Self-Nanoemulsifying Drug Delivery System (SNEDDS): Future Aspects, *Asian J Pharm Res*, 3(1) : 21-24.
- Martin A, Swatbrick J, & Cammarata A. 1993. *Farmasi Fisik Jilid 2* diterjemahkan oleh Yoshita Edisi III, UI-Press : Jakarta.
- Miryala V, Kurakula M. 2013. Self-Nanoemulsifying Drug Delivery System (SNEDDS) for Oral Delivery of Atorvastatin – Formulation and Bioavailability Studies. *J. Drug Deliv. Ther* 3,, 131-142.
- Patel J, Kevin G, Patel A, Raval M, dan Sheth N. 2011a, Design and Development of a Self-Nanoemulsifying Drug Delivery System for Telmisartan for Oral Drug Delivery, *Int J Pharm Investig*, 1: 112–118.
- Patel J, Patel A., Raval M, dan Sheth N., 2011b, Formulation and Development of a Self-Nanoemulsifying Drug Delivery System of Irbesartan, *J Adv Pharm Technol Res*, 2: 9–16.
- Pinto Reis C, Neufeld RJ, Ribeiro ANJ, dan Veiga F. 2006. Nanoencapsulation I, Methods for preparation of drug-loaded polymeric nanoparticles, *Nanomedicine : Nanotechnology, Biology and Medicine*, 2: 8-21.
- Pusat Nasional Informasi Bioteknologi. PubChem Compound Database; CID – 439246, <https://pubchem.ncbi.nlm.nih.gov/compound/439246> [14 Desember 2018].
- Rai MK, Yadaw AP, Gade AK. 2011. Biogenic nanoparticles: an introduction to what they are, how they are synthesized and their applications. In: Rai MK,

- Duran N (eds) Metal nanoparticles in microbiology, Springer-Verlag, Berlin, Heidelberg, Germany, pp 1-16
- Rao PV, Rohini P, Bhagyasree P. 2017. Flavonoid: A Review on Naringenin. *J. Pharmacology and Phytochemistry*. 6(5): 2778-2783.
- Rowe RC, Sheskey PJ, dan Quinn ME. 2009. *Handbook of Pharmaceutical Excipients, 6th Edition, sixth. Ed*, Pharmaceutical Press, London.
- Sahumena MH. 2014. Pengembangan Nanopartikel Ketoprofen dengan Teknik SNEDDS dan Uji Aktifitas Antiinflamasi. [Tesis program Pasca Sarjana]. Universitas Gadjah Mada, Yogyakarta.
- Shafiq-un-Nabi S, Shakeel F, Talegaonkar S, Ali J, Baboota S, Ahuja A, 2007, Formulation Development and Optimization using Nanoemulsion Technique: A technical note, *AAPS Pharm SciTech*, 8: E12 – E17.
- Shakeel F, Baboota S, Ahuja A, Ali J, Faisal MS, dan Shafiq S. 2008. Stability Evaluation of Celecoxib Nanoemulsion Containing Tween 80, *Thai Journal Pharm Sci*, 32: 4-9.
- Singh B, Bandopadhyay S, Kapil R, Singh R, dan Katare O. 2009. Self-emulsifying Drug Delivery System (SEDDS): Formulation Development, Characterization and Applications, *Crit Rev Ther Drug Carrier Syst*, 26: 427–521.
- Wang Y, Sun J, Zhang T, Liu H, He P, He Z. 2011. Enhanced Oral Bioavailability Of Selfmicroemulsifying Drug Delivery System of Oridonin. *Int. J. Pharm.* 355, 269-276.
- Zhang P, Liu Y, Feng N, Xu J. 2008. Preparation and evaluation of selfmicroemulsifying drug delivery system of oridonin. *Int. J. Pharm.* 355, 269–276.
- Zhang L, Song L, Zhang P, Liu T, Zhou L, Yang G, Lin R, Zhang J. 2015. Solubilities of Naringin and Naringenin in Different Solvents and Dissociation Constants of Naringenin. *J. Chem. Eng. Data*. 40.

**L**

**A**

**M**

**P**

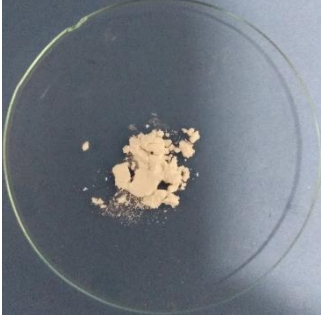

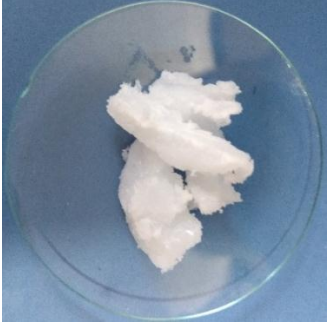

**I**



**R**

**A**

**N**

**Lampiran 1. Komponen Penyusun Solid SNEDDS Naringenin dan Alat**

<b>GAMBAR BAHAN</b>	<b>NAMA BAHAN</b>
	ZAT AKTIF NARINGENIN
	STEARIN (MINYAK)
	PEG 1000
	KOLLIPHOR EL

GAMBAR BAHAN	NAMA BAHAN
	MIKROPIPET
	MAGNETIC STIRRER

## Lampiran 2. Kurva Kalibrasi Dapar Fosfat Ph 7,4

### Penentuan Panjang Gelombang Maksimum Dapar Fosfat pH 7,4

Larutan induk naringenin 5000  $\mu\text{g/mL}$  = 50,0 mg Naringenin + 10 mL metanol

Larutan stok naringenin 100  $\mu\text{g/mL}$

$$V1 \times C1 = V2 \times C2$$

$$10000 \text{ mL} \times 100 \text{ ppm} = V2 \times 5000 \text{ ppm}$$

$$V2 = 200 \text{ mL}$$

(200 mL larutan induk naringenin 5000  $\mu\text{g/mL}$  + 9,8 mL lar. dapar fosfat pH 7,4)

Larutan naringenin 10  $\mu\text{g/mL}$

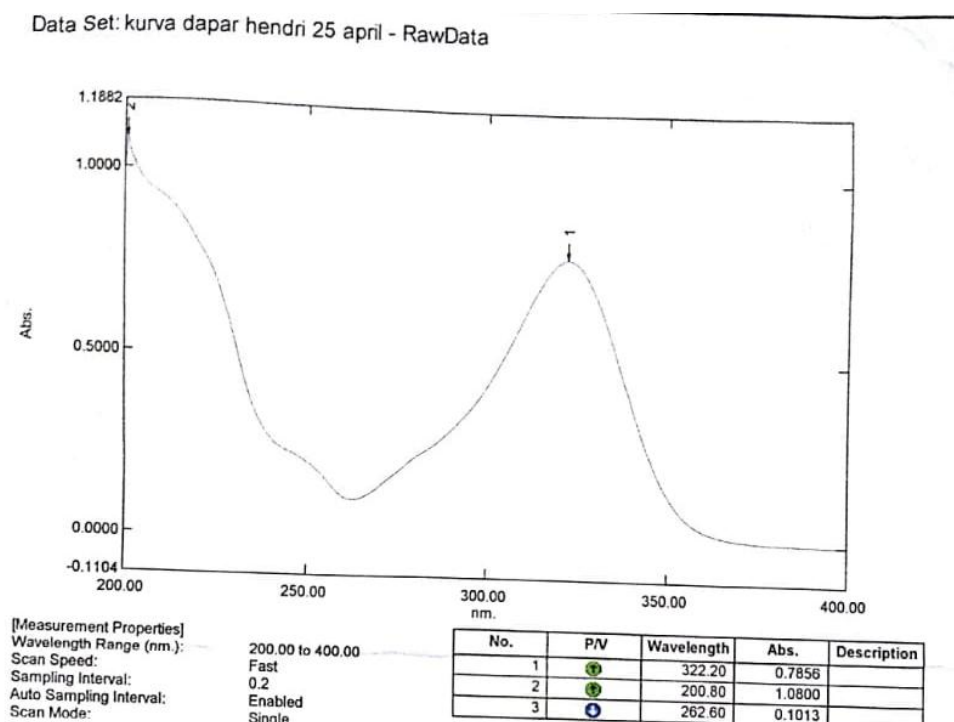
$$V1 \times C1 = V2 \times C2$$

$$10000 \text{ mL} \times 10 \mu\text{g/mL} = V2 \times 100 \mu\text{g/mL}$$

$$V2 = 1000 \text{ mL}$$

(1000 mL larutan stok naringenin + 9 mL larutan dapar fosfat pH 7,4)

Scanning panjang gelombang maksimum





<b>Konsentrasi (ppm)</b>	<b>Replikasi 1</b>	<b>Replikasi 2</b>	<b>Replikasi 3</b>	<b>Replikasi 4</b>	<b>Rata- rata</b>
1,92	0,166	0,176	0,163	0,164	0,167
3,70	0,325	0,328	0,349	0,354	0,339
5,36	0,457	0,461	0,451	0,457	0,457
6,90	0,636	0,637	0,649	0,654	0,644
8,33	0,762	0,767	0,785	0,784	0,775
9,68	0,909	0,915	0,944	0,946	0,929

### Lampiran 3. Kurva Kalibrasi HCl 0,1N

#### Penentuan Panjang Gelombang Maksimum HCl 0,1 N

Larutan induk naringenin 5060  $\mu\text{g/mL}$  = 50,6 mg Naringenin + 10 mL metanol

Larutan stok naringenin 101,2  $\mu\text{g/mL}$

$$V_1 \times C_1 = V_2 \times C_2$$

$$3000 \text{ mL} \times 100 \text{ ppm} = V_2 \times 5060 \text{ ppm}$$

$$V_2 = 59,29 \text{ mL}$$

(59 mL larutan induk naringenin 5000  $\mu\text{g/mL}$  + 3 mL lar. HCl 0,1 N)

Larutan naringenin 10  $\mu\text{g/mL}$

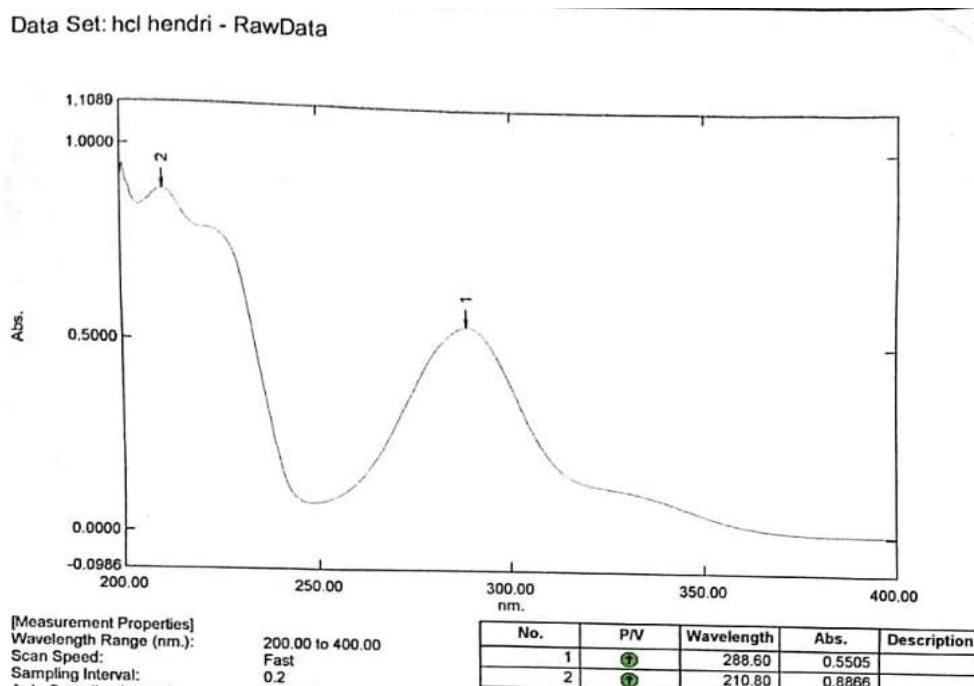
$$V_1 \times C_1 = V_2 \times C_2$$

$$3000 \text{ mL} \times 10 \mu\text{g/mL} = V_2 \times 101,2 \mu\text{g/mL}$$

$$V_2 = 296,44 \text{ mL}$$

(296,44 mL larutan stok naringenin + 3 mL larutan HCl 0,1 N)

Scanning panjang gelombang maksimum



**Tabel Kurva Kalibrasi HCl 0,1 N**

<b>Vol. Pengambilan</b>	<b>Vol. Pembuatan</b>	<b>F. Pengenceran</b>	<b>Kons.</b>	<b>Replikasi 1</b>	<b>Replikasi 2</b>	<b>Replikasi 3</b>	<b>Replikasi 4</b>	<b>Rata- rata</b>
59	3000	51,85	1,95	0,259	0,257	0,257	0,257	0,258
119	3000	26,21	3,86	0,315	0,318	0,317	0,318	0,317
178	3000	17,85	5,67	0,392	0,393	0,39	0,392	0,392
237	3000	13,66	7,41	0,455	0,456	0,455	0,455	0,455
296	3000	11,14	9,09	0,512	0,513	0,513	0,514	0,513
355	3000	9,45	10,71	0,565	0,567	0,564	0,567	0,566
474	3000	7,33	13,81	0,652	0,651	0,653	0,655	0,653

#### Lampiran 4. Validasi Metode Analisis

##### a. Dapar Fosfat pH 7,4

###### - 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%	
					<b>% Recovery</b>	<b>98,65%</b>

###### - Presisi

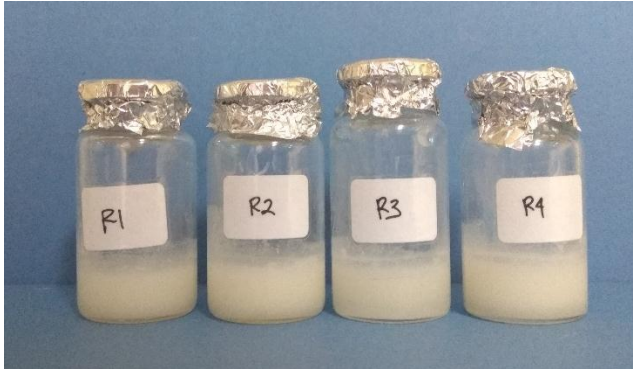
Replikasi	Absorbansi	Konsentrasi
1	0,420	4,633
2	0,439	4,828
3	0,443	4,869
4	0,442	4,858
5	0,444	4,879
6	0,447	4,910
7	0,433	4,766
8	0,439	4,828
9	0,445	4,889
10	0,457	5,012
<b>SD</b>	0,0987	
<b>Rata-rata</b>	4,8470	
<b>CV</b>	0,0204	

**b. HCl 0,1 N**  
**- Akurasi**

Konsentra si	Replika si	Absorban si	Konsentra si	Kons. Sebenarn ya	% Recover y	Rata- Rata	
80%	1	0,515	9,3936	9,088	103%	101,96 %	<b>100,29</b> %
	2	0,506	9,1295	9,088	100%		
	3	0,511	9,2762	9,088	102%		
100%	1	0,566	10,8771	10,708	102%	101,61 %	
	2	0,5658	10,8838	10,708	102%		
	3	0,56575	10,8823	10,708	102%		
120%	1	0,65278	13,4354	13,808	97%	97,30%	
	2	0,65273	13,4339	13,808	97%		
	3	0,65275	13,4345	13,808	97%		

**- Presisi**

REPLIKASI	ABS	KONSENTRASI
1	0,562	10,772
2	0,560	10,714
3	0,563	10,802
4	0,561	10,743
5	0,562	10,772
6	0,565	10,860
7	0,564	10,831
8	0,560	10,714
9	0,561	10,743
10	0,556	10,596
SD	0,073437	
Rata-rata	10,7547	
CV	0,006828	

**Lampiran 5. Bentuk Sediaan *Solid* SNEDDS Naringenin****- Sediaan *Solid* SNEDDS Naringenin****- Nanoemulsi Solid SNEDDS Naringenin**

**Lampiran 6. Data Waktu Emulsifikasi dan % Transmitan Solid SNEDDS Naringenin.**

- **Waktu Emulsifikasi**

<b>Waktu Emulsifikasi (detik)</b>				
<b>Replikasi</b>	<b>Formula 1</b>	<b>Formula 2</b>	<b>Formula 3</b>	<b>Formula 4</b>
1	26	15	18	51
2	26	15	17	52
3	24	16	17	51
<b>Rata-Rata</b>	25,33	15,33	17,33	51,33
<b>SD</b>	1,15	0,58	0,58	0,58
<b>RSD</b>	4,56	3,77	3,33	1,12

- **% Transmitan**

<b>% Transmittan</b>				
<b>Replikasi</b>	<b>Formula 1</b>	<b>Formula 2</b>	<b>Formula 3</b>	<b>Formula 4</b>
1	33	4,6	37,5	28
2	33,1	4,8	37,8	27,9
3	33,3	5	38	27,8
<b>Rata-Rata</b>	33,13	4,80	37,77	27,90
<b>SD</b>	0,15	0,20	0,25	0,10
<b>RSD</b>	0,46	4,17	0,67	0,36

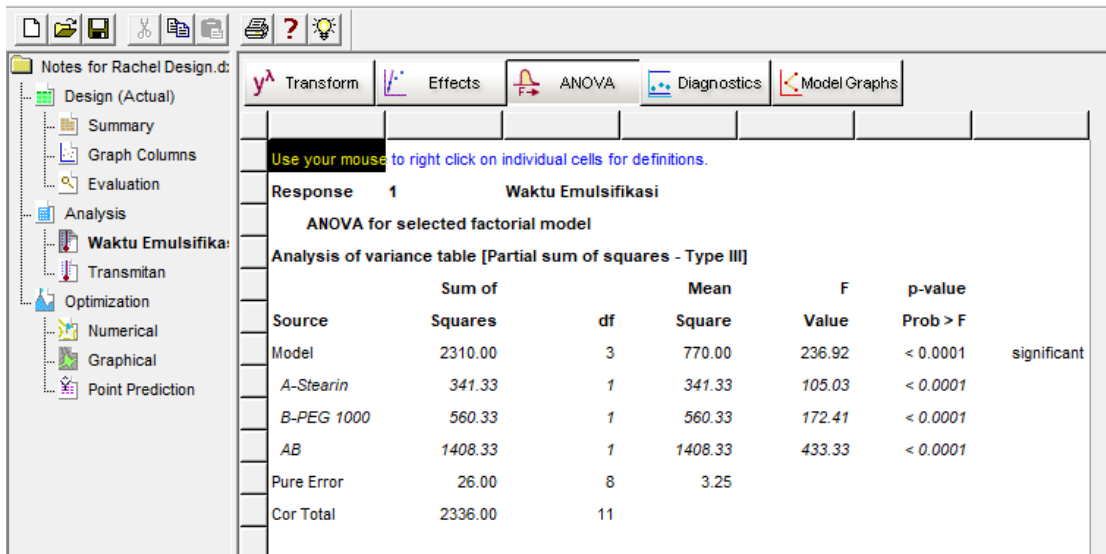
## Lampiran 7. Penentuan Formula Optimum Basis *Solid* SNEDDS Naringenin

Select	Std	Run	Factor 1 A:Stearin bagian	Factor 2 B:PEG 1000 bagian	Response 1 Waktu Emulsifikasi detik	Response 2 Transmitan %
1		8	1.00	3.00	20	30.7
2		1	1.00	3.00	21	29.9
3		12	1.00	3.00	24	29.8
4		7	3.00	3.00	13	2.5
5		9	3.00	3.00	9	2.4
6		3	3.00	3.00	10	2.4
7		10	1.00	6.00	14	30.2
8		11	1.00	6.00	13	29.2
9		6	1.00	6.00	14	29.5
10		5	3.00	6.00	48	26
11		2	3.00	6.00	46	25.8
12		4	3.00	6.00	44	25.7

### A. Waktu Emulsifikasi

Term	Stdized Effects	Sum of Squares	% Contribution
Intercept			
M A-Stearin	10.67	341.33	14.61
M B-PEG 1000	13.67	560.33	23.99
M AB	21.67	1408.33	60.29
Lack Of Fit		0.000	0.000
Pure Error		26.00	1.11
Lenth's ME	15.62		
Lenth's SME	20.18		

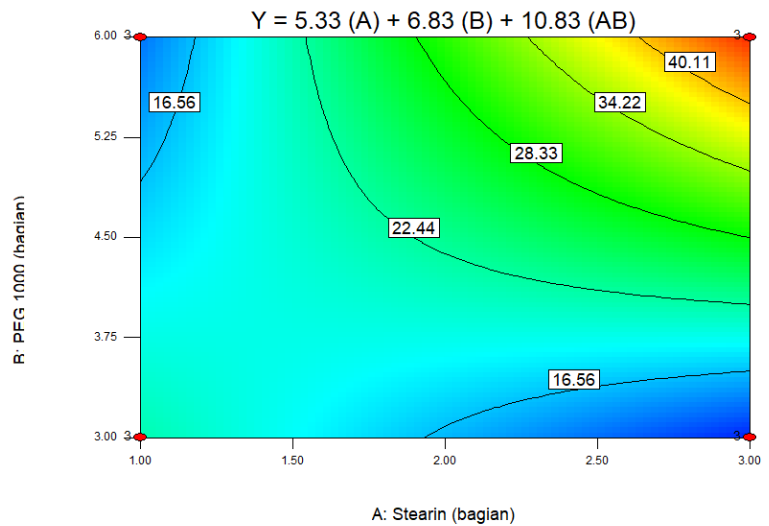




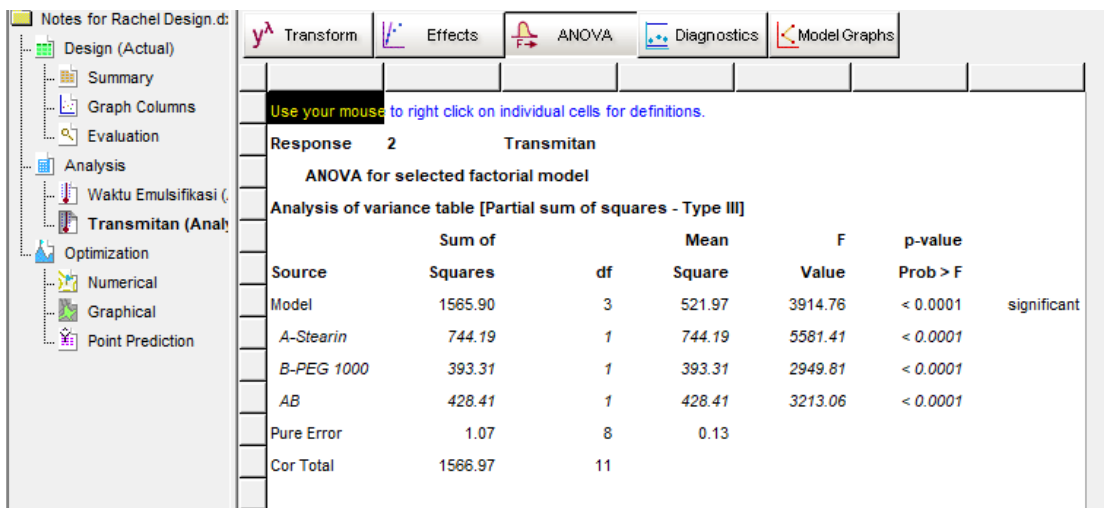
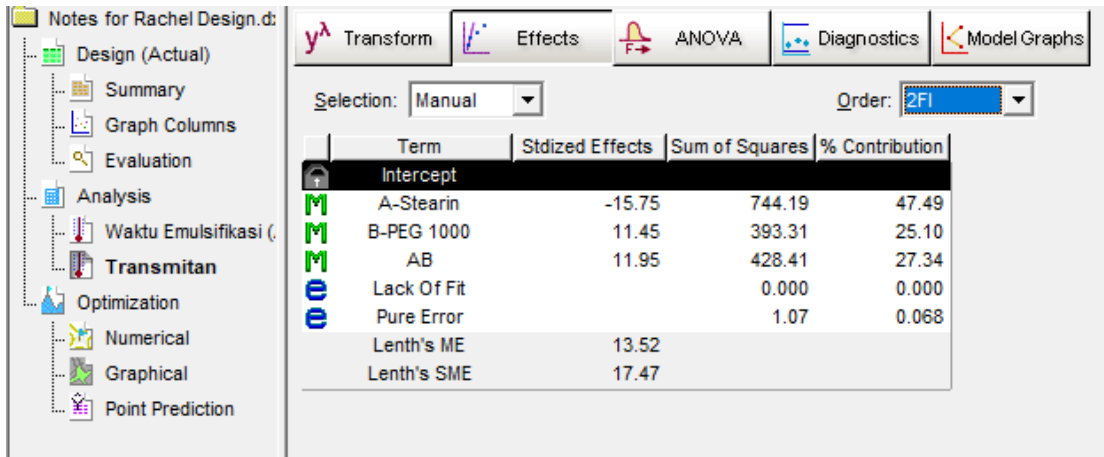
Design-Expert® Software

Waktu Emulsifikasi  
 ● Design Points  
 48  
 9

X1 = A: Stearin  
 X2 = B: PEG 1000



### B. % Transmitan



Design-Expert® Software

Transmitan

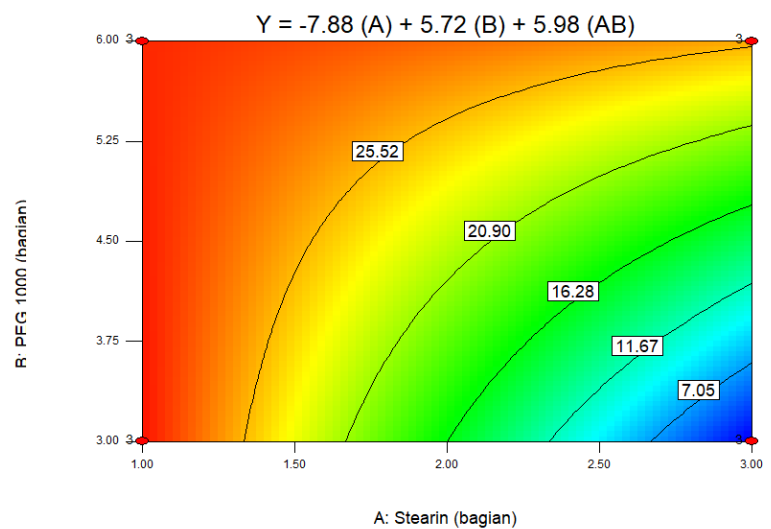
• Design Points

30.7

2.4

X1 = A: Stearin

X2 = B: PEG 1000



### C. Formula Optimum basis Solid SNEDDS Naringenin

Notes for Rachel Design.d

Design (Actual)

- Summary
- Graph Columns
- Evaluation
- Analysis
- Waktu Emulsifikasi (
- Transmitan (Analysi
- Optimization
- Numerical
- Graphical
- Point Prediction

Solutions Tool

- Report
- Ramps
- Bar Graph

Criteria Solutions Graphs

Solutions 1 2

Constraints		Lower	Upper	Lower	Upper		
Name	Goal	Limit	Limit	Weight	Weight	Importance	
Stearin	is in range	1	3	1	1	3	
PEG 1000	is in range	3	6	1	1	3	
Waktu Emulsifika	minimize	9	48	1	1	3	
Transmitan	maximize	2.4	30.7	1	1	3	

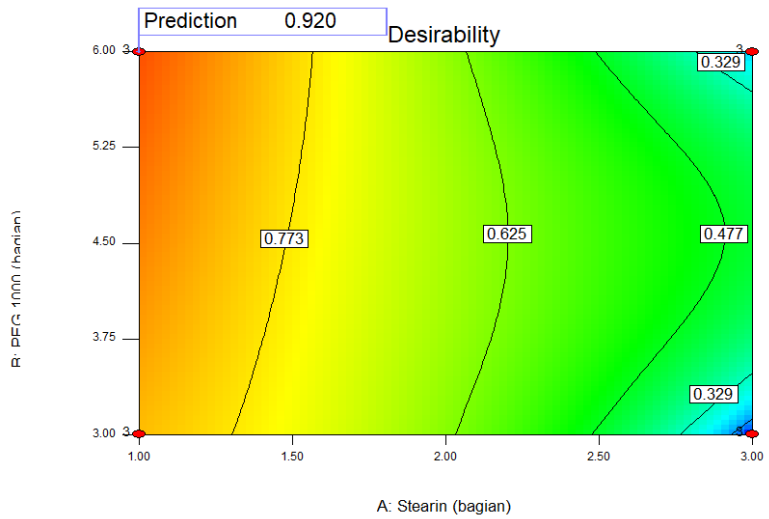
Solutions						
Number	Stearin	PEG 1000	Waktu Emulsifi	Transmitan	Desirability	
1	1.00	6.00	13.6667	29.6333	0.920	Selected
2	1.02	6.00	13.973	29.5973	0.916	

2 Solutions found

Design-Expert® Software

Desirability  
 ● Design Points  
 1  
 0

X1 = A: Stearin  
 X2 = B: PEG 1000



### Lampiran 8. Uji Disolusi Solid SNEDDS Naringenin

Waktu (menit)	Rata-rata (% Release)				SD			
	F1	F2	F3	F4	F1	F2	F3	F4
0	0	0	0	0	0	0	0	0
1	5,29	5,29	5,44	5,51	0,30	0,44	0,74	1,48
3	32,37	29,39	29,39	33,25	0,45	0,88	1,32	0,43
5	50,12	53,73	31,34	34,03	0,75	0,59	0,89	0,44
7	83,04	60,44	54,59	36,02	0,46	2,36	1,14	0,58
10	89,82	74,05	59,87	38,58	1,05	1,50	0,57	0,90
15	92,58	81,17	63,99	55,28	2,69	1,22	0,92	0,86
20	95,02	86,04	76,74	59,23	3,60	0,79	0,86	0,99
25	99,80	97,46	82,12	77,01	2,01	0,50	1,20	1,87
30	102,29	105,90	99,78	86,03	0,85	1,39	1,65	1,26
60	109,22	107,35	105,49	105,27	1,15	0,81	0,64	1,80

### Lampiran 9. Tabel Konstanta Difusi Solid SNEDDS Naringenin

Waktu	Konstanta Difusi				SD			
	F1	F2	F3	F4	F1	F2	F3	F4
0	0	0	0	0	0	0	0	0
1	8,017	8,109	11,935	7,835	0,00	0,46	0,09	0,18
3	9,009	9,283	12,692	8,734	0,18	0,27	0,00	0,28
5	9,462	10,013	13,729	9,276	0,18	0,36	0,36	0,19
7	10,193	11,387	15,959	10,096	0,09	0,18	0,46	0,18
10	11,386	12,500	17,482	11,348	0,46	0,09	0,55	0,21
15	12,589	14,352	19,656	12,005	0,08	0,55	0,19	0,27
20	14,442	15,493	20,665	13,517	0,17	0,28	0,26	0,66
25	15,947	17,828	21,501	14,072	0,45	0,28	0,19	0,47
30	17,830	19,183	22,616	15,420	0,36	0,38	0,17	1,11
60	22,372	20,458	24,013	18,663	0,54	0,20	0,26	0,16
90	24,043	22,929	25,058	20,298	0,37	0,07	0,19	0,02
120	28,644	24,056	27,478	22,585	0,17	0,07	0,35	0,61

## Lampiran 10. Hasil Optimasi Solid SNEDDS Naringenin

### A. Waktu Emulsifikasi

Selection:	Manual	Order:	2FI
Term	Stdized Effects	Sum of Squares	% Contribution
Intercept			
M A-Stearin	12.00	432.00	17.44
M B-PEG 1000	14.00	588.00	23.74
M AB	22.00	1452.00	58.63
e Lack Of Fit		0.000	0.000
e Pure Error		4.67	0.19
Lenth's ME	15.86		
Lenth's SME	20.50		

Response 1 Waktu Emulsifikasi

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	2472.00	3	824.00	1412.57	< 0.0001	significant
A-Stearin	432.00	1	432.00	740.57	< 0.0001	
B-PEG 1000	588.00	1	588.00	1008.00	< 0.0001	
AB	1452.00	1	1452.00	2489.14	< 0.0001	
Pure Error	4.67	8	0.58			
Cor Total	2476.67	11				

Final Equation in Terms of Coded Factors:

$$\begin{aligned} \text{Waktu Emulsifikasi} = & \\ & +27.33 \\ & +6.00 * A \\ & +7.00 * B \\ & +11.00 * A * B \end{aligned}$$

## B. % Transmitan

Selection: <b>Manual</b>		Order: <b>2FI</b>		
	Term	Stdized Effects	Sum of Squares	% Contribution
	Intercept			
M	A-Stearin	-19.10	1094.43	56.79
M	B-PEG 1000	13.87	576.85	29.93
M	AB	9.23	255.76	13.27
e	Lack Of Fit		0.000	0.000
e	Pure Error		0.27	0.014
	Lenth's ME	15.69		
	Lenth's SME	20.27		

Response 2 Transmitan

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	
Model	1927.05	3	642.35	18800.46	< 0.0001	significant
A-Stearin	1094.43	1	1094.43	32032.10	< 0.0001	
B-PEG 1000	576.85	1	576.85	16883.51	< 0.0001	
AB	255.76	1	255.76	7485.76	< 0.0001	
Pure Error	0.27	8	0.034			
Cor Total	1927.32	11				

Final Equation in Terms of Coded Factors:

$$\begin{aligned} \text{Transmitan} = & \\ & +25.90 \\ & -9.55 * A \\ & +6.93 * B \\ & +4.62 * A * B \end{aligned}$$

### C. AUC Disolusi

Selection: Manual		Order: 2FI		
	Term	Stdized Effects	Sum of Squares	% Contribution
	Intercept			
M	A-Stearin	-266.20	2.126E+005	16.02
M	B-PEG 1000	-606.47	1.103E+006	83.18
M	AB	-43.29	5622.07	0.42
e	Lack Of Fit		0.000	0.000
e	Pure Error		4972.49	0.37
	Lenth's ME	302.65		
	Lenth's SME	391.05		

Response 4 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	1.322E+006	3	4.405E+005	708.77	< 0.0001	significant
A-Stearin	2.126E+005	1	2.126E+005	342.02	< 0.0001	
B-PEG 1000	1.103E+006	1	1.103E+006	1775.24	< 0.0001	
AB	5622.07	1	5622.07	9.05	0.0169	
Pure Error	4972.49	8	621.56			
Cor Total	1.327E+006	11				

Final Equation in Terms of Coded Factors:



$$\begin{aligned} \text{AUC Disolusi} = & \\ & +2017.82 \\ & -133.10 * A \\ & -303.24 * B \\ & -21.64 * A * B \end{aligned}$$

### D. Q<sub>30</sub> Disolusi

Selection:	Manual	Order:	2FI
Term	Stdized Effects	Sum of Squares	% Contribution
Intercept			
M A-Stearin	-5.08	77.27	11.26
M B-PEG 1000	-11.19	375.54	54.70
M AB	-8.68	226.11	32.94
e Lack Of Fit		0.000	0.000
e Pure Error		7.57	1.10
Lenth's ME	9.89		
Lenth's SME	12.78		

Response 3 Q30 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	678.92	3	226.31	239.17	< 0.0001	significant
A-Stearin	77.27	1	77.27	81.66	< 0.0001	
B-PEG 1000	375.54	1	375.54	396.88	< 0.0001	
AB	226.11	1	226.11	238.97	< 0.0001	
Pure Error	7.57	8	0.95			
Cor Total	686.49	11				

Final Equation in Terms of Coded Factors:

$$\begin{aligned}
 \text{Q30 Disolusi} = & \\
 & +98.50 \\
 & -2.54 * A \\
 & -5.59 * B \\
 & -4.34 * A * B
 \end{aligned}$$



### E. Konstanta Difusi

Selection:	Manual	Order:	2FI
Term	Stdized Effects	Sum of Squares	% Contribution
Intercept			
M A-Stearin	-0.018	1.008E-003	17.91
M B-PEG 1000	-0.031	2.945E-003	52.31
M AB	0.023	1.587E-003	28.18
EE Lack Of Fit		0.000	0.000
EE Pure Error		9.000E-005	1.60
Lenth's ME	0.026		
Lenth's SME	0.034		

Response 5 Konst. 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	5.541E-003	3	1.847E-003	164.17	< 0.0001	significant
A-Stearin	1.008E-003	1	1.008E-003	89.63	< 0.0001	
B-PEG 1000	2.945E-003	1	2.945E-003	261.81	< 0.0001	
AB	1.587E-003	1	1.587E-003	141.07	< 0.0001	
Pure Error	9.000E-005	8	1.125E-005			
Cor Total	5.631E-003	11				

Final Equation in Terms of Coded Factors:

$$\begin{aligned} \text{Konst. Difusi} = & \\ & +0.13 \\ & -9.167E-003 * A \\ & -0.016 * B \\ & +0.012 * A * B \end{aligned}$$

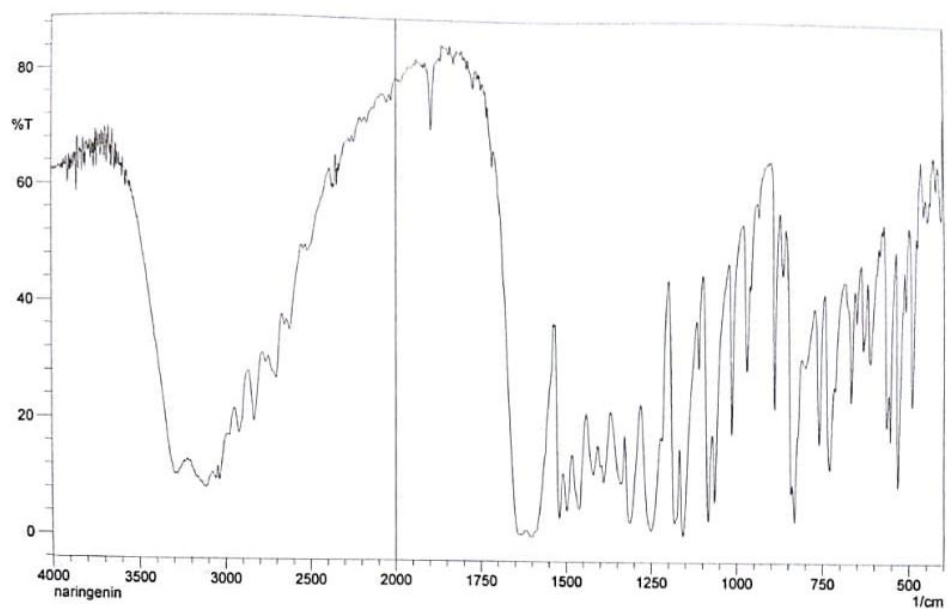
### Lampiran 11. Hasil Formula Optimum Solid SNEDDS Naringenin

Name	Goal	Lower Limit	Upper Limit	Lower Weight	Upper Weight	Importance
Stearin	is in range	1	3	1	1	3
PEG 1000	is in range	3	6	1	1	3
Waktu Emulsifikasi	minimize	15	52	1	1	3
Transmitan	maximize	4.6	38	1	1	3
Q30 Disolusi	maximize	85.18	106.94	1	1	3
AUC Disolusi	maximize	1548.62	2474.52	1	1	3
Konst. Difusi	maximize	0.111	0.169	1	1	3

#### Solutions

Number	Stearin	PEG 1000	Waktu Emulsifikasi	Transmitan	Q30 Disolusi	AUC Disolusi	Konst. Difusi	Desirability	Selectec
1	<u>1.00</u>	<u>3.00</u>	<u>25.3333</u>	<u>33.1333</u>	<u>102.293</u>	<u>2432.51</u>	<u>0.169</u>	<u>0.857</u>	Selectec

### Lampiran 12. FT-IR Naringenin



Lampiran 13. *Certificate Of Analysis (CO-A) Naringenin*

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

## CERTIFICATE OF ANALYSIS

<b>Product Name</b>	Naringenin	<b>Code</b>	BPBE-622-A																																																						
<b>Botanical Source</b>	Citrus Grandis (L.) Osbeck	<b>Used Part</b>	Fruit																																																						
<b>Batch No.</b>	H020862217A	<b>Mfg. Date</b>	Aug. 15, 2017																																																						
<b>Packing</b>	25kg/Drum	<b>Retest Date</b>	Aug. 14, 2019																																																						
<b>Quantity</b>	25g	<b>Report Date</b>	Aug. 21, 2017																																																						
<b>Specification</b>	98%(HPLC)																																																								
<table border="1"> <thead> <tr> <th>ITEM</th> <th>SPECIFICATION</th> <th>RESULT</th> </tr> </thead> <tbody> <tr> <td><b>Assay(HPLC)</b></td> <td>≥98.0%</td> <td>98.23%</td> </tr> <tr> <td><b>Appearance</b></td> <td>White powder</td> <td>Complies</td> </tr> <tr> <td><b>Odor</b></td> <td>Characteristic</td> <td>Complies</td> </tr> <tr> <td><b>Particle Size</b></td> <td>NLT 95% pass 80 mesh</td> <td>Complies</td> </tr> <tr> <td><b>Loss on Drying</b></td> <td>≤5.0%</td> <td>0.53%</td> </tr> <tr> <td><b>Sulphated Ash</b></td> <td>≤0.1%</td> <td>0.05%</td> </tr> <tr> <td><b>Heavy Metals</b></td> <td>≤10ppm</td> <td>Complies</td> </tr> <tr> <td>-Pb</td> <td>≤1ppm</td> <td>Complies</td> </tr> <tr> <td>-As</td> <td>≤1ppm</td> <td>Complies</td> </tr> <tr> <td>-Cd</td> <td>≤1ppm</td> <td>Complies</td> </tr> <tr> <td>-Hg</td> <td>≤0.1ppm</td> <td>Complies</td> </tr> <tr> <td><b>Total Plate Count</b></td> <td>≤1000cfu/g</td> <td>Complies</td> </tr> <tr> <td>-Yeast &amp; Mold</td> <td>≤100cfu/g</td> <td>Complies</td> </tr> <tr> <td>-E.Coli</td> <td>Negative</td> <td>Negative</td> </tr> <tr> <td>-Salmonella</td> <td>Negative</td> <td>Negative</td> </tr> <tr> <td><b>Conclusion</b></td> <td colspan="2">Comply with the Specification.</td> </tr> <tr> <td><b>Storage</b></td> <td colspan="2">Preserve in tight containers, protected from strong light and high heat. Store in dry cool place.</td> </tr> </tbody> </table>				ITEM	SPECIFICATION	RESULT	<b>Assay(HPLC)</b>	≥98.0%	98.23%	<b>Appearance</b>	White powder	Complies	<b>Odor</b>	Characteristic	Complies	<b>Particle Size</b>	NLT 95% pass 80 mesh	Complies	<b>Loss on Drying</b>	≤5.0%	0.53%	<b>Sulphated Ash</b>	≤0.1%	0.05%	<b>Heavy Metals</b>	≤10ppm	Complies	-Pb	≤1ppm	Complies	-As	≤1ppm	Complies	-Cd	≤1ppm	Complies	-Hg	≤0.1ppm	Complies	<b>Total Plate Count</b>	≤1000cfu/g	Complies	-Yeast & Mold	≤100cfu/g	Complies	-E.Coli	Negative	Negative	-Salmonella	Negative	Negative	<b>Conclusion</b>	Comply with the Specification.		<b>Storage</b>	Preserve in tight containers, protected from strong light and high heat. Store in dry cool place.	
ITEM	SPECIFICATION	RESULT																																																							
<b>Assay(HPLC)</b>	≥98.0%	98.23%																																																							
<b>Appearance</b>	White powder	Complies																																																							
<b>Odor</b>	Characteristic	Complies																																																							
<b>Particle Size</b>	NLT 95% pass 80 mesh	Complies																																																							
<b>Loss on Drying</b>	≤5.0%	0.53%																																																							
<b>Sulphated Ash</b>	≤0.1%	0.05%																																																							
<b>Heavy Metals</b>	≤10ppm	Complies																																																							
-Pb	≤1ppm	Complies																																																							
-As	≤1ppm	Complies																																																							
-Cd	≤1ppm	Complies																																																							
-Hg	≤0.1ppm	Complies																																																							
<b>Total Plate Count</b>	≤1000cfu/g	Complies																																																							
-Yeast & Mold	≤100cfu/g	Complies																																																							
-E.Coli	Negative	Negative																																																							
-Salmonella	Negative	Negative																																																							
<b>Conclusion</b>	Comply with the Specification.																																																								
<b>Storage</b>	Preserve in tight containers, protected from strong light and high heat. Store in dry cool place.																																																								
<b>Analyst:</b>	<b>QC Manager:</b>	<b>QA:</b>																																																							