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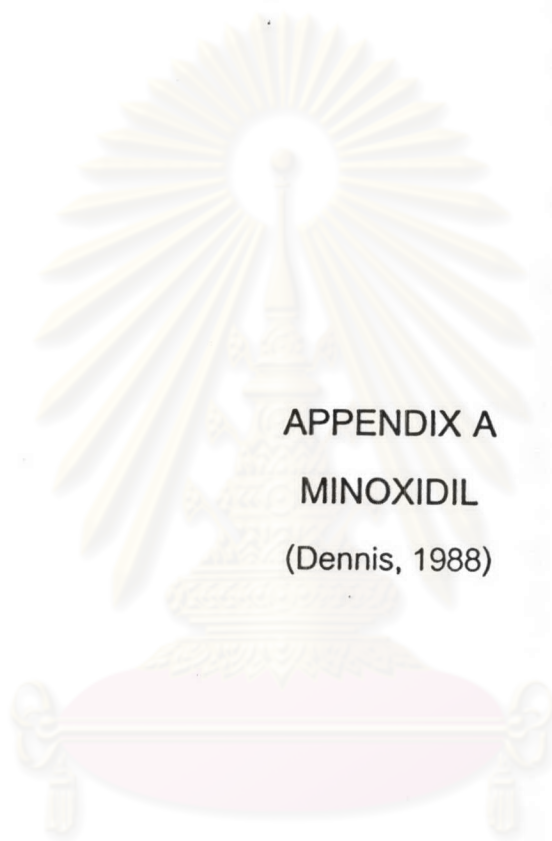
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APPENDICES

ศูนย์วิทยทรัพยากร
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APPENDIX A

MINOXIDIL

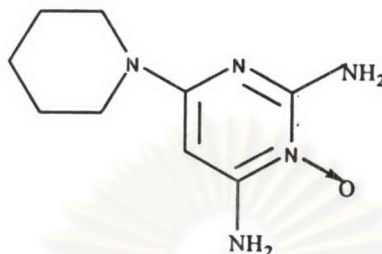
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Minoxidil

Chemical name: minoxidil: 2,6-Diamino-4-piperidinopyrimidine 1-oxide

Structure: $C_9H_{15}N_5O$



MW: 209.25

MP: 225 °C

Soluble: 1:500 in water, readily soluble in ethanol and propylene glycol, practically insoluble in chloroform

pK_a : 4.61


K: 1.24 (octanol-water partition coefficient)

Adverse effects: Incidence less frequent is contact dermatitis (itching or skin rash). Allergic reaction and systemic reaction are rare.

Topical dosage form: 2% and 5% minoxidil in mixed solvent of 20% propylene glycol, 60% ethanol, and 20% water. Also in phospholipid-base liposomes at 1.5 and 4.5%.

Stability and storage: The degradation of minoxidil in solution (20°C, pH 7.0, phosphate buffer) follows first-order degradation kinetics with a rate constant of $9.646 \times 10^{-3} \text{ day}^{-1}$ and a calculated activation energy of 11.7 Kcal/mole. Degradation is acid-base dependent showing the greatest stability at pH 5.0

Minoxidil solution should be stored in tightly closed container and at controlled temperature from 15-30°C.



APPENDIX B
PROPERTIES OF SOME SELECTED MATERIALS

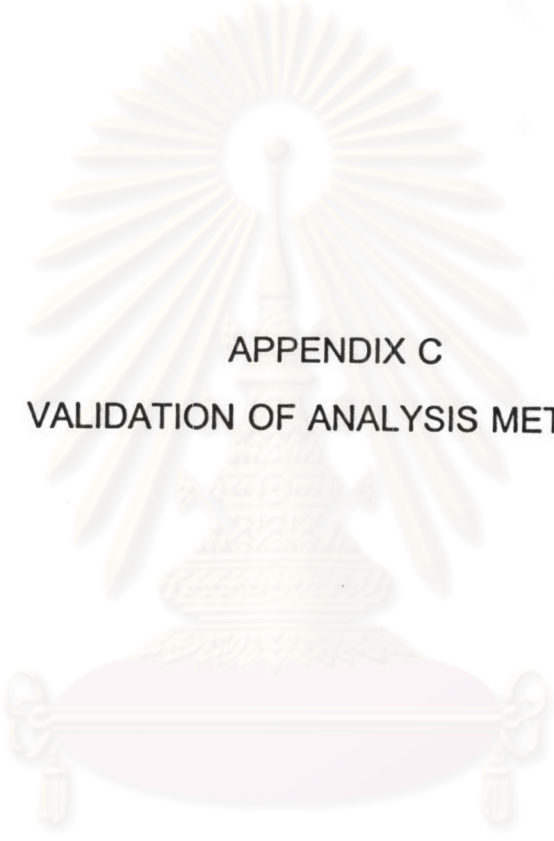
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Properties of some selected materials

Material	Formula	Property
Acetic acid	$C_2H_4O_2$	MW: 60.1
Boric acid	H_3BO_3	MW: 61.83 MP: 171°C pH of solution: 3.8-4.8
Brij [®] 76 (POE-10)	$C_{38}H_{78}O_{11}$	MW: 710 MP: 38°C HLB: 12.4
Cholesterol	$C_{27}H_{46}O$	MW: 386.67 MP: 147-150°C BP: 360°C
Dicetylphosphate	$C_{32}H_{67}O_4P$	MW: 546.86 MP: 76-80°C
Minoxidil	$C_9H_{15}N_5O$	MW: 209.3 MP: 225°C Solubility: 1:500 in W pKa: 4.61 K: 1.24
Propylene glycol	$C_3H_8O_2$	MW: 76.09 BP: 188°C
Potassium chloride	KCl	MW: 74.55 MP: 773°C
Sodium acetate	$NaC_2H_3O_2 \cdot 3H_2O$	MW: 136.08 MP: 58°C
Sodium hydroxide	NaOH	MW: 40
Solulan [®] C24 (cholesteryl poly-24-oxyethylene ether)	-	MW: 1,443 HLB: 8-9 Cloud point: 88-95°C

Material	Formula	Property
Span [®] 20	$C_{18}H_{34}O_6$	MW: 346 HLB: 8.6
Span [®] 40	$C_{22}H_{42}O_6$	MP: 44-48°C HLB: 6.7
Span [®] 60	$C_{24}H_{46}O_6$	MP: 53-57°C HLB: 4.7
Span [®] 80	$C_{24}H_{44}O_6$	MW: 429 HLB: 4.3
Span [®] 85	$C_{60}H_{108}O_8$	MW: 958 HLB: 1.8
Tween [®] 20	$C_{58}H_{114}O_{26}$	MW: 1,128 HLB: 16.7
Tween [®] 80	$C_{64}H_{124}O_{26}$	MW: 1,310 HLB: 15

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APPENDIX C
VALIDATION OF ANALYSIS METHOD

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Validation for the quantitative determination of MN solution in isopropanol by UV Spectroscopy

1. Accuracy

MN and surfactant/CHO mixtures at 1.0, 1.5, and 2.5 mg/mL MN and 100 mg/mL lipid mixture were prepared. Three sets of each concentration were prepared. Each individual sample was analyzed by UV spectrophotometry, and percent analytical recovery of each sample was calculated.

2. Precision

2.1 Within Run Precision

The within run precision was determined by analyzing of three sets of the calibration curve in the same day. Inverse concentrations of three other concentrations (7.2, 10.8, 14.4 $\mu\text{g/mL}$) of MN were compared, and the percent coefficient of variation (% CV) for each concentration was calculated.

2.2 Between Run Precision

The between run precision was determined in a similar manner to that in 2.1 but on different days. The percent coefficient of variation (% CV) for each concentration was calculated.

3. Linearity

Linear regression analysis of the absorbances versus the corresponding concentrations was performed, and the coefficient of determination was calculated.

4. Specificity

Specificity expresses how much the results obtained by the method for a given analyte are influenced by the presence of foreign substances. The UV spectra from UV spectrophotometer of niosome formulas without drug are shown in Figures 4-17, Appendix D.

The results of validation process are shown in the following tables:

C.1. Accuracy

Table C.1. Accuracy Data

Expected concentration (mg/mL)	Analytical concentration (mg/mL)	% Recovery
2.5	2.55	102.00
	2.57	102.80
	2.58	103.20
1.5	1.49	99.33
	1.47	98.00
	1.46	97.33
1.0	0.96	96.30
	0.99	99.20
	1.02	101.50

Mean % Recovery = 99.96

SD = 2.51,

% CV = 2.51

C.2. Precision

C.2.1. Within Run Precision

Table C.2.1. Within Run Precision Data

conc ($\mu\text{g/mL}$)	absorbance					
	1	2	3	4	5	6
7.2	0.369	0.369	0.37	0.364	0.361	0.365
10.8	0.549	0.562	0.563	0.547	0.549	0.554
14.4	0.725	0.754	0.735	0.722	0.726	0.726

conc ($\mu\text{g/mL}$)	inversed concentration ($\mu\text{g/mL}$)						mean	SD	%CV
	1	2	3	4	5	6			
7.2	7.2146	7.1842	7.1434	7.2544	7.1681	7.2035	7.1947	0.04338	0.60296
10.8	10.8583	10.812	10.9159	10.8639	10.8551	10.9022	10.8679	0.02504	0.23043
14.4	14.4211	14.4211	14.2554	14.3156	14.3517	14.2681	14.3388	0.04193	0.29242

C.2.2. Between Run Precision

Table C.2.2. Between Run Precision Data

conc ($\mu\text{g/mL}$)	absorbance								
	day 1			day 2			day 3		
	1	2	3	1	2	3	1	2	3
7.2	0.378	0.351	0.37	0.373	0.374	0.38	0.378	0.37	0.367
10.8	0.57	0.531	0.563	0.554	0.55	0.554	0.562	0.552	0.549
14.4	0.757	0.701	0.735	0.729	0.728	0.744	0.748	0.738	0.735

conc ($\mu\text{g/mL}$)	absorbance								
	day 4			day 5			day 6		
	1	2	3	1	2	3	1	2	3
7.2	0.372	0.379	0.375	0.384	0.382	0.375	0.37	0.377	0.377
10.8	0.557	0.566	0.57	0.57	0.574	0.57	0.568	0.563	0.574
14.4	0.738	0.753	0.755	0.752	0.752	0.752	0.742	0.747	0.755

conc ($\mu\text{g/mL}$)	inversed concentration ($\mu\text{g/mL}$)								
	day 1			day 2			day 3		
	1	2	3	1	2	3	1	2	3
7.2	7.2162	7.1523	7.1434	7.2555	7.2016	7.2868	7.2686	7.1618	7.2485
10.8	10.8252	10.856	10.9352	10.8683	10.7862	10.7053	10.7733	10.7096	10.8102
14.4	14.3402	14.3539	14.3143	14.3613	14.4114	14.4381	14.3162	14.3353	14.4501

conc ($\mu\text{g/mL}$)	inversed concentration ($\mu\text{g/mL}$)									mean	SD	%CV
	day 4			day 5			day 6					
	1	2	3	1	2	3	1	2	3			
7.2	7.2896	7.2708	7.217	7.2597	7.2207	7.2208	7.1724	7.2743	7.154	7.223	0.0494	0.6907
10.8	10.861	10.8125	10.8962	10.8643	10.906	10.9	10.9655	10.8171	10.8992	10.844	0.0712	0.653
14.4	14.3552	14.3542	14.3868	14.3915	14.3225	14.334	14.2989	14.3219	14.3403	14.357	0.0428	0.2986

C.3. Linearity

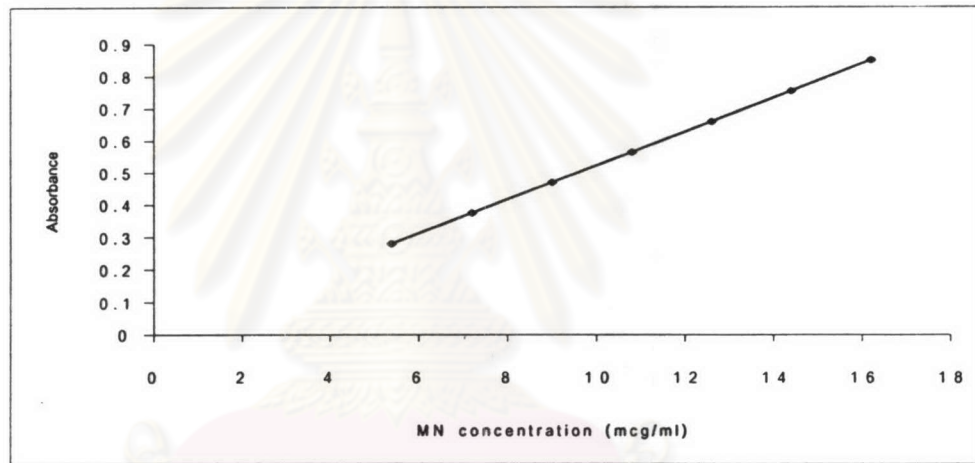
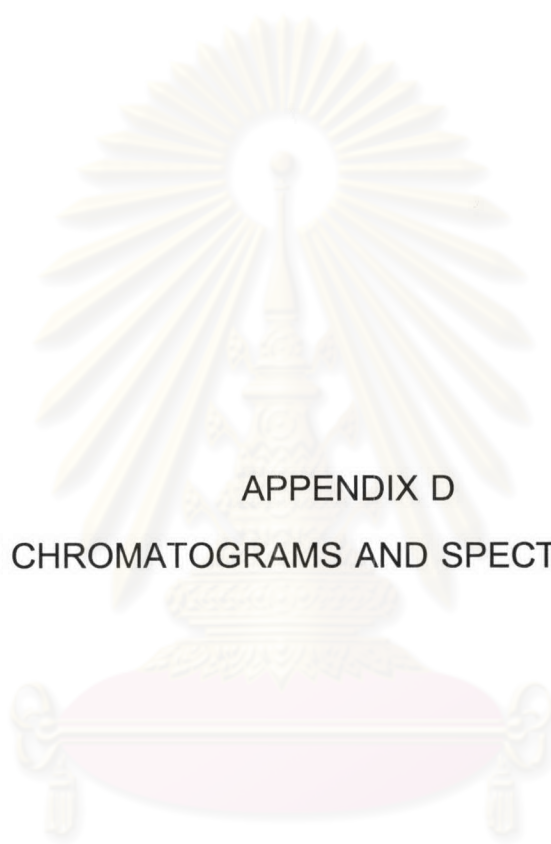


Figure C.3. A representation of calibration curve of standard solutions of MN

Where $y = 0.0528x - 0.0049$; $r^2 = 0.9999$

y = Absorbance

X = MN concentration ($\mu\text{g/mL}$)



APPENDIX D

HPLC CHROMATOGRAMS AND SPECTRA OF MN

ศูนย์วิจัยทรัพยากร
จุฬาลงกรณ์มหาวิทยาลัย

Stability of MN solution at room temperature (24-25°C), 70°C, and 100°C for 2 hours by HPLC

Condition: Analytical column = Hypersil®C₁₈ reverse column

internal standard = triamcinolone acetonide

flow rate = 1 mL/min

setting time = 10 min

speed = 1

attend = 6

wave length = 254 nm

injection volume = 20 µL

mobile phase = Methanol: W: Glacial acetic acid: Dicetylsulfosuccinate
80: 20: 1: 0.3



Figure 1. At room temperature (peak area ratio = 1.8276)



Figure 2. At 70°C (peak area ratio = 1.8489)

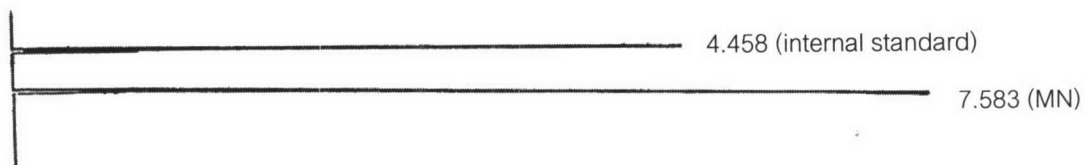


Figure 3. At 100°C (peak area ratio = 1.8724)

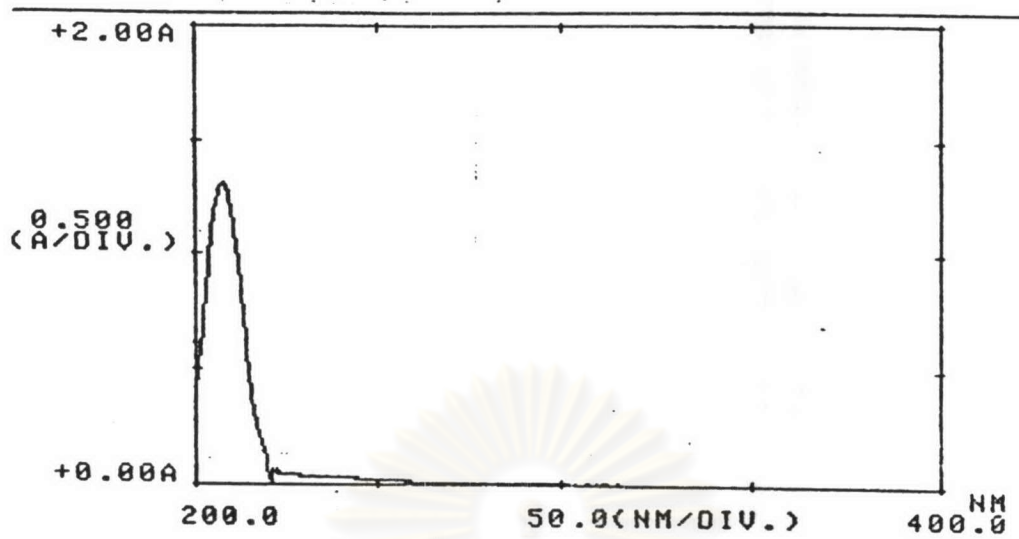


Figure 4. UV spectrum of Span[®] 40:CHO niosomes without drug (total lipid 100 mg/mL) dissolved in isopropanol

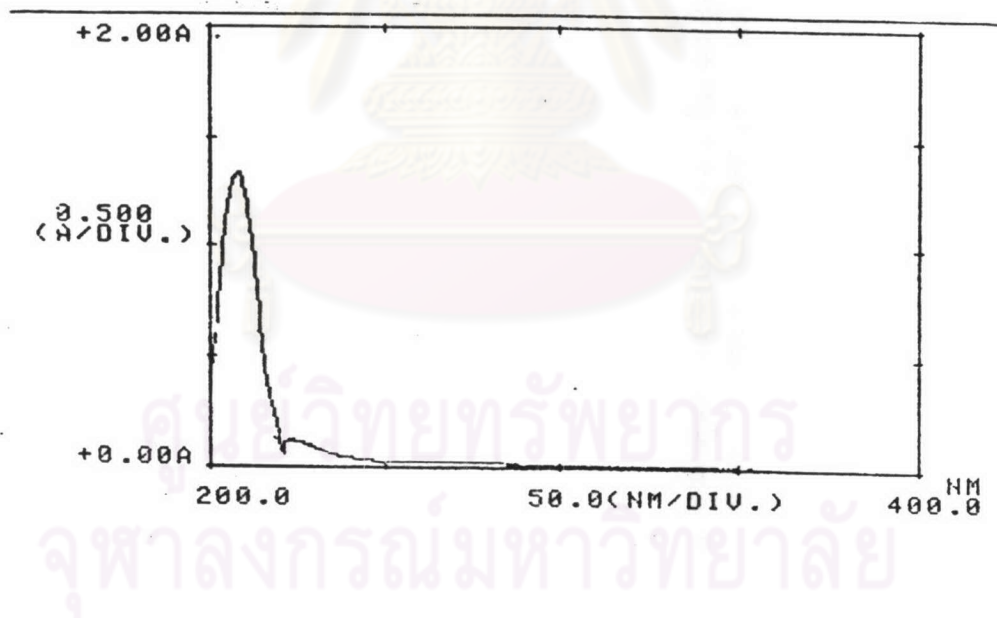


Figure 5. UV spectrum of Span[®] 60:CHO niosomes without drug (total lipid 100 mg/mL) dissolved in isopropanol

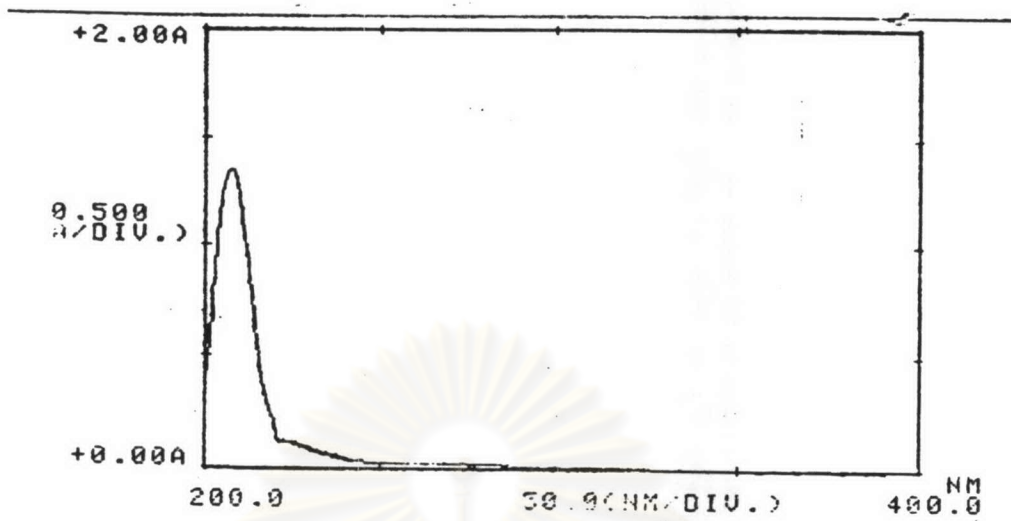


Figure 6. UV spectrum of POE-10:CHO niosomes without drug (total lipid 100 mg/mL) dissolved in isopropanol

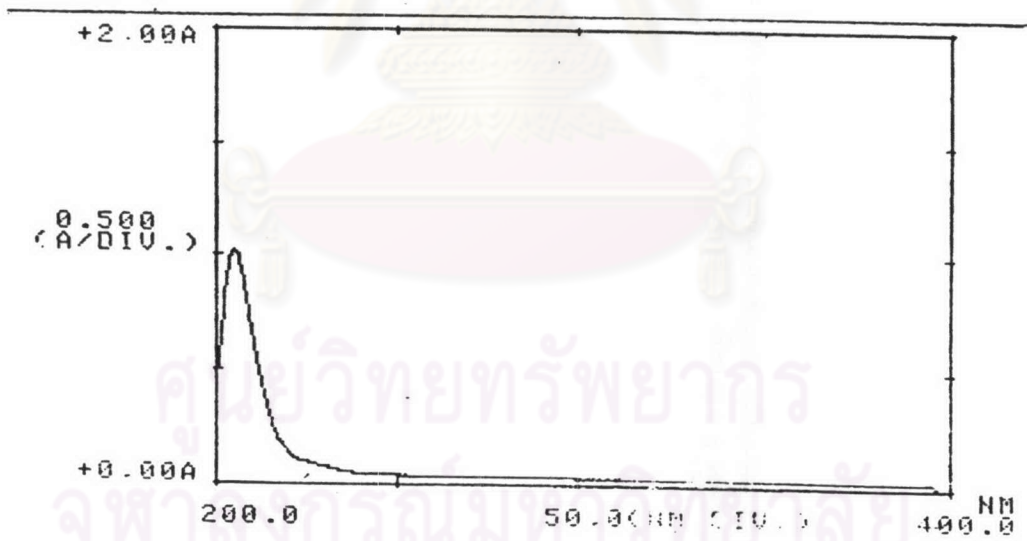


Figure 7. UV spectrum of Span[®] 40:CHO niosomes without drug (total lipid 100 mg/mL) in 15% PG in W dissolved in isopropanol

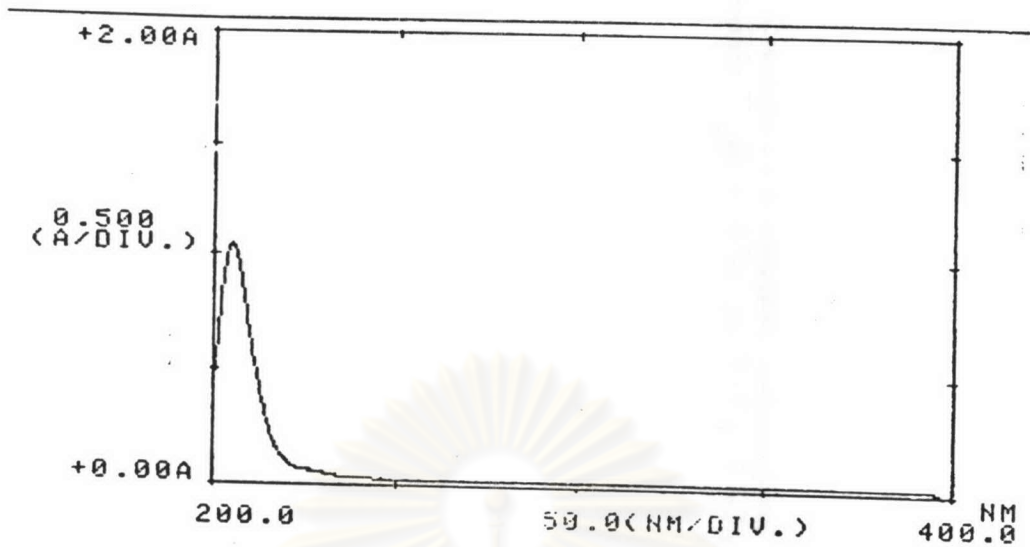


Figure 8. UV spectrum of Span[®] 60:CHO niosomes without drug (total lipid 100 mg/mL) in 15% PG in W dissolved in isopropanol

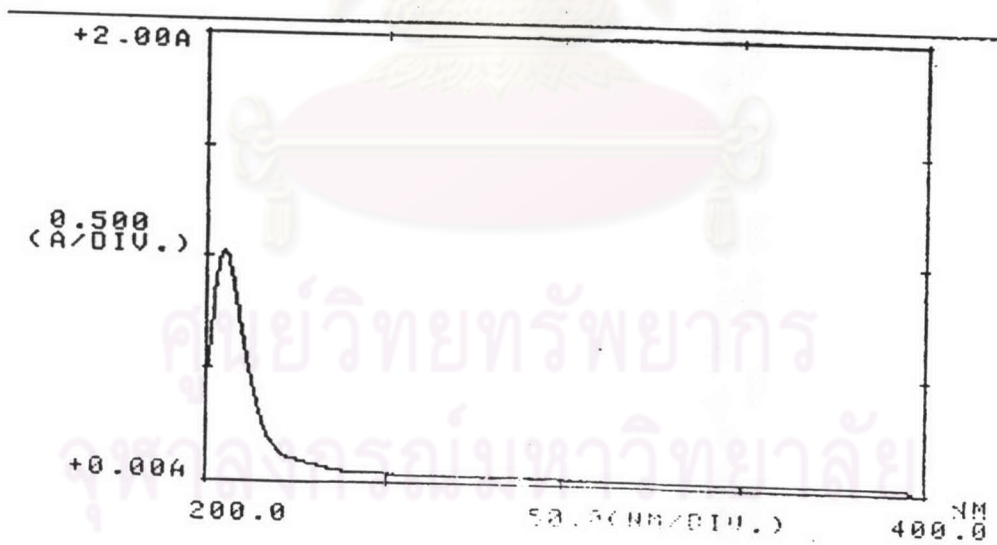


Figure 9. UV spectrum of POE-10:CHO niosomes without drug (total lipid 100 mg/mL) in 15% PG in W dissolved in isopropanol

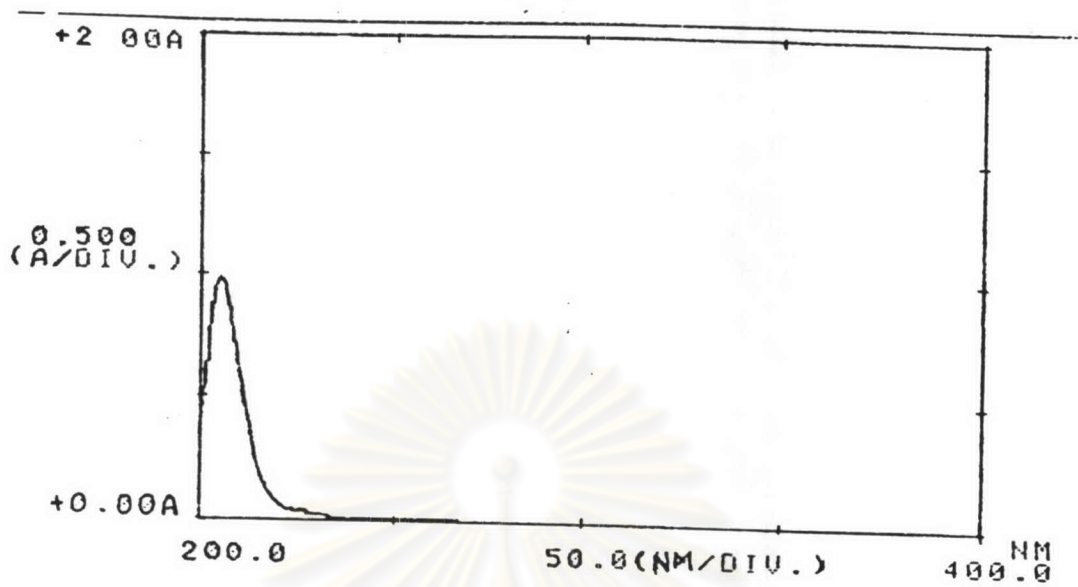


Figure 10. UV spectrum of POE-10:CHO niosomes without drug (total lipid 100 mg/mL) in acetate buffer pH 4.6 dissolved in isopropanol

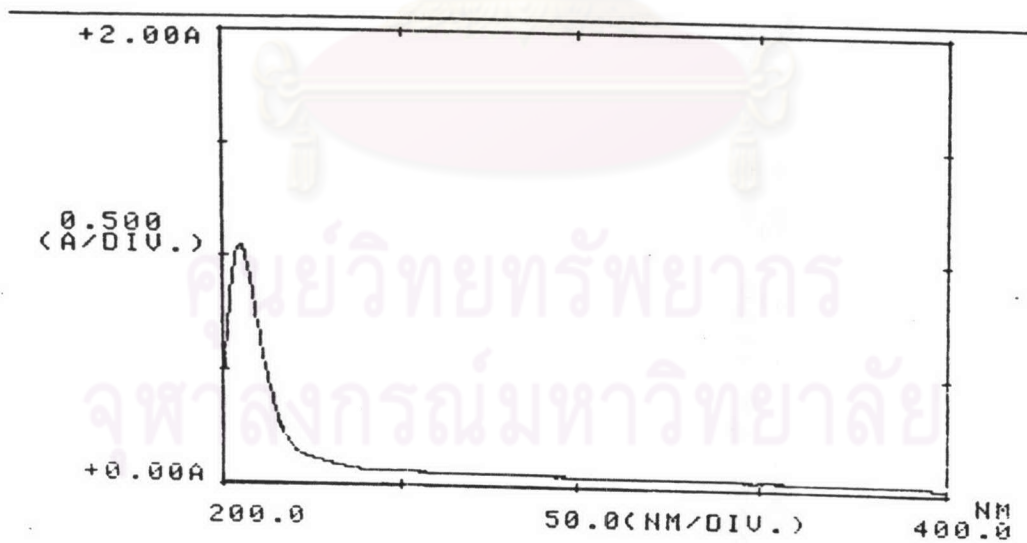


Figure 11. UV spectrum of Span[®] 40:CHO niosomes without drug (total lipid 100 mg/mL) in borate buffer pH 7.0 dissolved in isopropanol

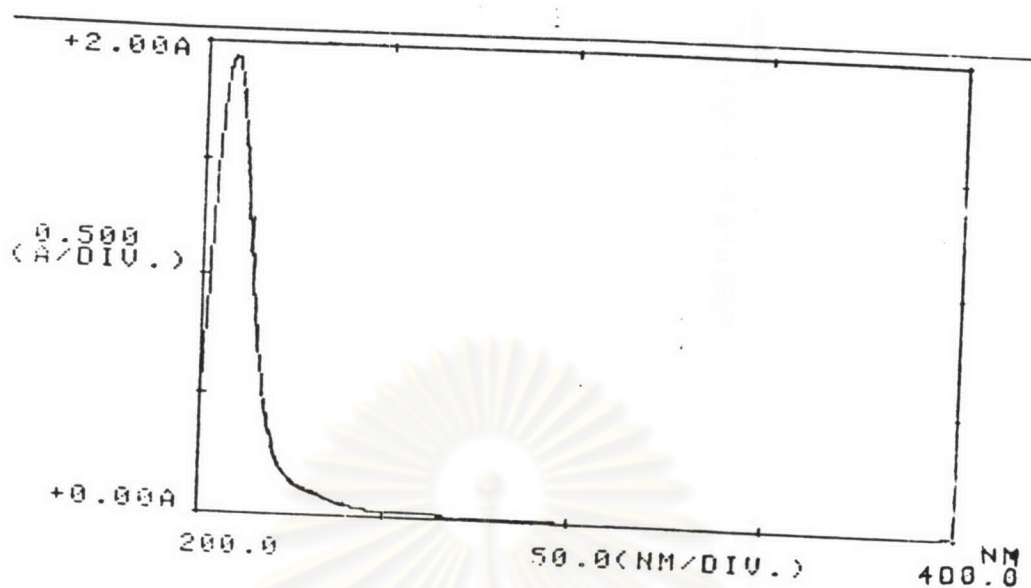


Figure 12. UV spectrum of Span[®] 60:CHO niosomes without drug (total lipid 100 mg/mL) in borate buffer pH 7.0 dissolved in isopropanol

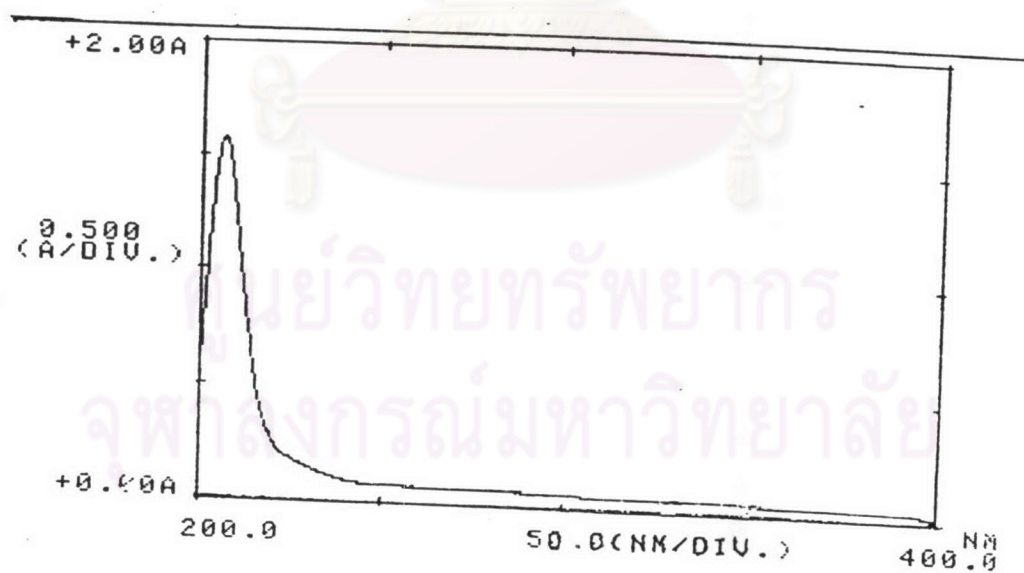


Figure 13. UV spectrum of POE-10:CHO niosomes without drug (total lipid 100 mg/mL) in borate buffer pH 7.0 dissolved in isopropanol

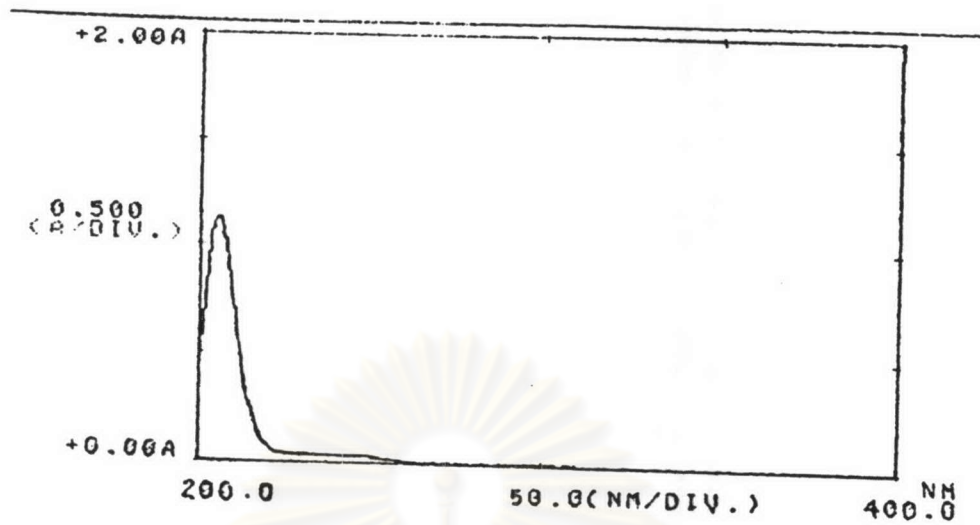


Figure 14. UV spectrum of Span[®] 40:CHO:DCP niosomes without drug (total lipid 100 mg/mL) dissolved in isopropanol

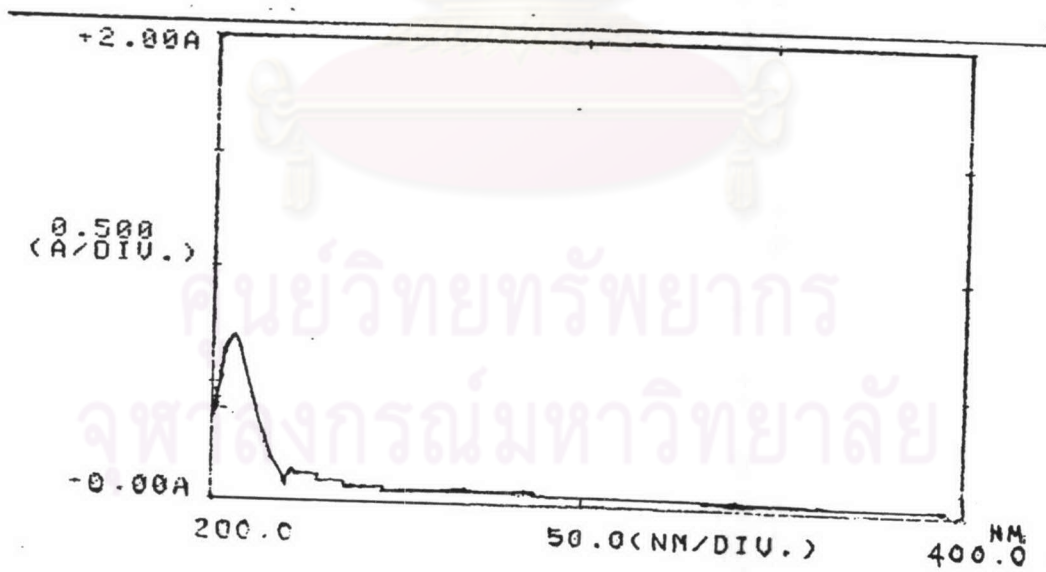


Figure 15. UV spectrum of Span[®] 40:CHO:Solulan[®] C24 niosomes without drug (total lipid 100 mg/mL) dissolved in isopropanol

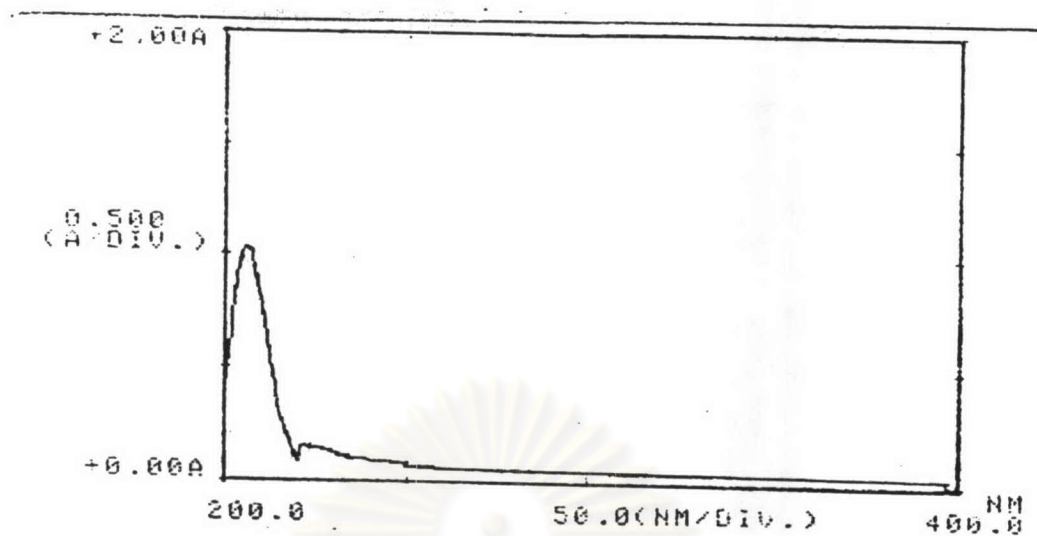


Figure 16. UV spectrum of Span[®] 60:CHO:Solulan[®] C24 niosomes without drug (total lipid 100 mg/mL) dissolved in isopropanol

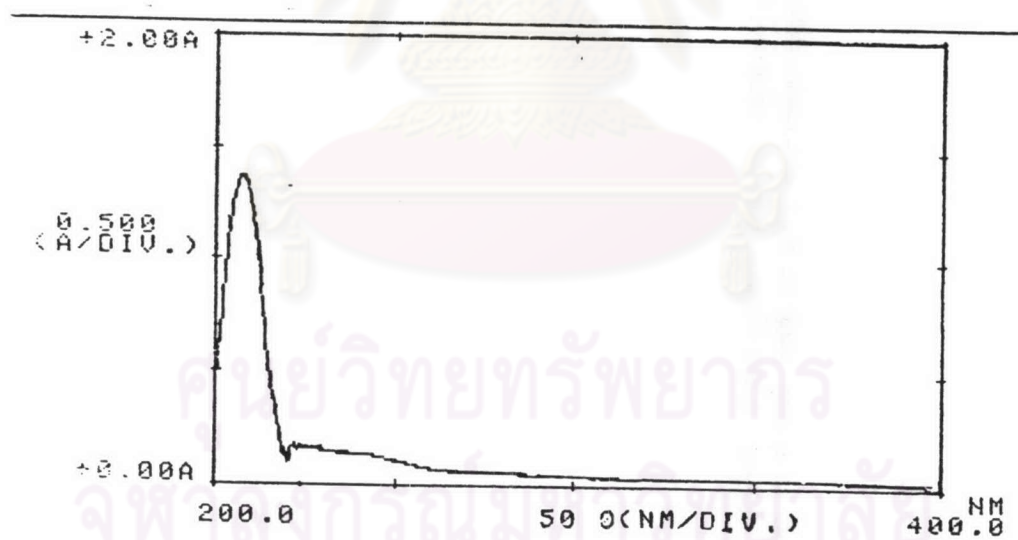
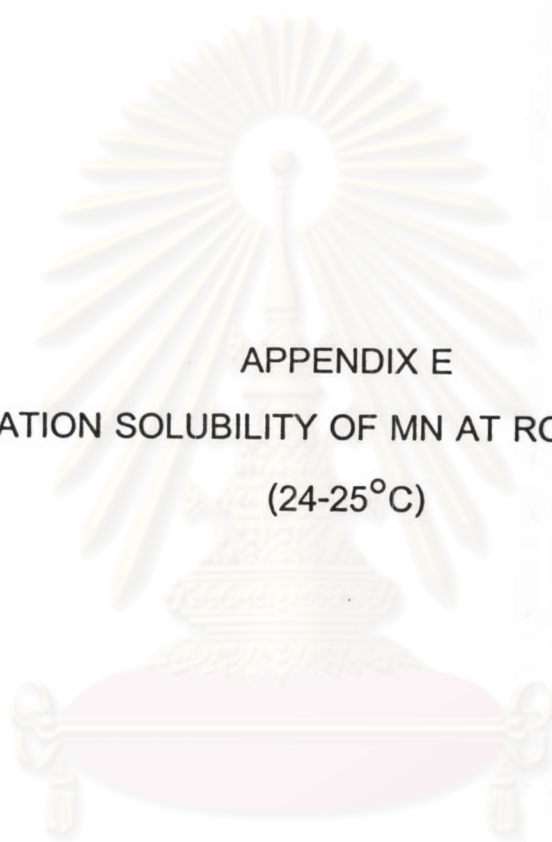


Figure 17. UV spectrum of POE-10:CHO:Solulan[®] C24 niosomes without drug (total lipid 100 mg/mL) dissolved in isopropanol



APPENDIX E
THE SATURATION SOLUBILITY OF MN AT ROOM TEMPERATURE
(24-25°C)

ศูนย์วิทยทรัพยากร
จุฬาลงกรณ์มหาวิทยาลัย

The saturation solubility of MN at room temperature (24-25°C)

a) Water

Time (h)	Absorbance			Saturation solubility (mg/mL)			Mean	SD
1	0.535	0.542	0.53	2.34	2.31	2.32	2.32	0.0153
3	0.532	0.543	0.54	2.33	2.38	2.3	2.34	0.0404
6	0.56	0.547	0.534	2.46	2.34	2.34	2.38	0.0693
9	0.526	0.548	0.547	2.31	2.4	2.34	2.35	0.0458
12	0.533	0.548	0.57	2.36	2.4	2.45	2.4	0.0451
24	0.546	0.554	0.568	2.39	2.42	2.49	2.43	0.0513
48	0.526	0.552	0.559	2.3	2.42	2.45	2.39	0.0794
54	0.548	0.556	0.549	2.4	2.44	2.4	2.41	0.0231
66	0.571	0.57	0.561	2.51	2.5	2.46	2.49	0.0265
90	0.559	0.585	0.558	2.45	2.57	2.44	2.49	0.0723

b) Acetate buffer pH 4.6

Time (h)	Absorbance			Saturation solubility (mg/mL)			Mean	SD
1	0.296	0.357	0.325	2.56	3.36	2.94	2.953	0.3983
3	0.329	0.43	0.387	2.99	4.31	3.75	3.6841	0.6617
6	0.377	0.45	0.415	3.62	4.57	4.11	4.1018	0.4766
9	0.427	0.463	0.443	4.27	4.74	4.48	4.4978	0.2355
12	0.477	0.506	0.489	4.92	5.3	5.08	5.1027	0.1902
24	0.492	0.5	0.495	5.12	5.22	5.16	5.168	0.0528
48	0.499	0.476	0.497	5.21	4.91	5.19	5.1027	0.1663
54	0.501	0.499	0.501	5.24	5.21	5.24	5.2289	0.0151
66	0.499	0.502	0.497	5.21	5.25	5.19	5.2158	0.0329
90	0.497	0.495	0.502	5.19	5.16	5.25	5.1984	0.0471

c) Borate buffer pH 7.0

Time (h)	Absorbance			Saturation solubility (mg/mL)			Mean	SD
1	0.549	0.498	0.525	2.68	2.44	2.57	2.5636	0.1239
3	0.606	0.576	0.58	2.96	2.82	2.83	2.871	0.0791
6	0.607	0.619	0.609	2.97	3.02	2.98	2.9892	0.0265
9	0.64	0.637	0.641	3.13	3.11	3.13	3.1235	0.0101
12	0.644	0.633	0.64	3.15	3.09	3.13	3.1218	0.027
24	0.642	0.636	0.639	3.14	3.11	3.12	3.1233	0.0158
48	0.645	0.637	0.642	3.15	3.11	3.14	3.1332	0.0196
54	0.642	0.637	0.635	3.14	3.11	3.1	3.117	0.0175
66	0.644	0.639	0.634	3.15	3.12	3.1	3.1218	0.0243
90	0.636	0.636	0.645	3.11	3.11	3.15	3.1218	0.0252

d) 15% PG in Water

Time (h)	Absorbance			Saturation solubility (mg/mL)			Mean	SD
1	0.245	0.247	0.243	4.49	4.53	4.45	4.4913	0.0433
3	0.256	0.254	0.255	4.73	4.69	4.71	4.7078	0.0216
6	0.27	0.275	0.278	5.18	5.14	5.14	5.1551	0.0231
9	0.28	0.28	0.278	5.25	5.25	5.21	5.2345	0.0231
12	0.281	0.28	0.283	5.27	5.25	5.31	5.2767	0.0306
24	0.283	0.281	0.284	5.31	5.27	5.33	5.3033	0.0306
48	0.282	0.281	0.283	5.29	5.27	5.31	5.29	0.02
54	0.281	0.283	0.285	5.27	5.31	5.36	5.3133	0.0451
66	0.28	0.281	0.281	5.25	5.27	5.27	5.2633	0.0115
90	0.279	0.282	0.282	5.23	5.29	5.25	5.2567	0.0306

e) 30% PG in Water

Time (h)	Absorbance			Saturation solubility (mg/mL)			Mean	SD
1	0.425	0.423	0.419	8.57	8.53	8.45	8.52	0.06
3	0.437	0.435	0.429	8.82	8.78	8.66	8.75	0.08
6	0.441	0.442	0.445	8.91	8.93	8.99	8.94	0.04
9	0.459	0.457	0.453	9.28	9.24	9.16	9.23	0.06
12	0.472	0.471	0.474	9.56	9.53	9.6	9.56	0.04
24	0.475	0.474	0.473	9.62	9.6	9.58	9.6	0.02
48	0.474	0.475	0.474	9.6	9.62	9.6	9.6	0.02
54	0.479	0.472	0.474	9.7	9.56	9.6	9.62	0.07
66	0.47	0.474	0.475	9.51	9.6	9.62	9.58	0.06
90	0.478	0.471	0.473	9.68	9.53	9.58	9.6	0.08

ศูนย์วิทยทรัพยากร
จุฬาลงกรณ์มหาวิทยาลัย



APPENDIX F
CALIBRATION DATA

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จุฬาลงกรณ์มหาวิทยาลัย

a) Calibration data for MN solution and MN niosomes in borate buffer pH 7.0, diluted with isopropanol

Conc.($\mu\text{g/mL}$)	5	7	9	11	13	15	17
Abs. at 280 nm	0.256	0.389	0.499	0.631	0.754	0.875	0.996

$$Y = 0.0616X - 0.0485, R^2 = 0.9997$$

b) Calibration data for MN solution and MN niosomes in borate buffer pH 7.0, diluted with isopropanol

Conc.($\mu\text{g/mL}$)	5	7	9	11	13	15	17
Abs. at 280 nm	0.257	0.385	0.512	0.625	0.761	0.874	0.991

$$Y = 0.0612X - 0.0443, R^2 = 0.9996$$

c) Calibration data for MN solution and MN niosomes in acetate buffer pH4.6, diluted with isopropanol

Conc.($\mu\text{g/mL}$)	5	7	9	11	13	15	17
Abs. at 280 nm	0.298	0.398	0.497	0.587	0.678	0.779	0.875

$$Y = 0.0477X - 0.0625, R^2 = 0.9997$$

d) Calibration data for MN solution and MN niosomes in 15% PG:W, diluted with isopropanol

Conc.($\mu\text{g/mL}$)	5	7	9	11	13	15	17
Abs. at 280 nm	0.244	0.354	0.455	0.554	0.654	0.759	0.864

$$Y = 0.0512X - 0.0087, R^2 = 0.9998$$

e) Calibration data for MN solution and MN niosomes in water, MN niosomes with 5% DCP and/or Solulan C24, diluted with isopropanol

Conc.($\mu\text{g/mL}$)	5	7	9	11	13	15	17
Abs. at 280 nm	0.259	0.365	0.470	0.576	0.682	0.787	0.893

$$Y = 0.0528X - 0.0049, R^2 = 0.9999$$

VITA

Miss Plookchit Chetratanont was born on May 16, 1974 in Chonburi, Thailand. She received her Bachelor of Science in Pharmacy from the Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok, Thailand in 1997. She worked at Somdej Na Sriracha Hospital, Chonburi for two years before entering the master's degree program in Pharmacy at Chulalongkorn University.



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