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Appendix I

Phase solubility data of minoxidil in water with CDs at 30°C

Solubility data of minoxidil in water with β-CD at 30°C

Calibration curve data

Minoxidil conc^{n} (mol/l x 10^6)	3.841	6.146	9.219	12.292	15.365	18.439	24.585
Absorbance (229 nm)	0.155	0.234	0.339	0.453	0.553	0.656	0.866

$$y = 0.0247 + 3.4300 \times 10^4 x$$

$$r^2 = 0.9998$$

β-CD conc^{n} (mol/l x 10^2)	Absorbance (229 nm)	Minoxidil conc^{n} (mol/l x 10^2)	Dilution factor
0	0.176	1.103	2500
0.211	0.222	1.438	2500
0.409	0.253	1.664	2500
0.618	0.276	1.832	2500
0.807	0.300	2.006	2500
1.226	0.339	2.291	2500
1.475	0.345	2.334	2500
1.621	0.381	2.597	2500
1.818	0.448	3.085	2500
2.072	0.445	3.063	2500
2.578	0.426	2.925	2500
3.054	0.448	3.085	2500
4.046	0.437	3.005	2500
6.104	0.446	3.071	2500
8.012	0.457	3.151	2500
10.040	0.426	2.925	2500
12.157	0.209	1.343	2500
14.125	0.200	1.278	2500
18.120	0.197	1.256	2500
20.097	0.193	1.227	2500
22.053	0.202	1.292	2500
24.107	0.175	1.095	2500

Solubility data of minoxidil in water with HP-β-CD at 30°C

Calibration curve data

Minoxidil conc^{n} (mol/l x 10^6)	3.841	6.146	9.219	12.292	15.365	18.439	24.585
Absorbance (229 nm)	0.146	0.229	0.333	0.441	0.540	0.666	0.868

$$y = 0.0122 + 3.4902 \times 10^4 x$$

$$r^2 = 0.9995$$

HP-β-CD conc^{n} (mol/l x 10^2)	Absorbance (229 nm)	Minoxidil conc^{n} (mol/l x 10^2)	Dilution factor
0	0.202	1.359	2500
1.000	0.298	2.047	2500
2.018	0.405	2.813	2500
3.094	0.513	3.587	2500
4.065	0.316	4.351	5000
5.024	0.374	5.182	5000
6.051	0.411	5.712	5000
8.011	0.514	7.188	5000
10.123	0.586	8.219	5000
12.152	0.668	9.394	5000
14.094	0.787	11.099	5000
16.007	0.388	13.457	12500
17.982	0.420	14.603	12500
20.061	0.473	16.501	12500
21.985	0.493	17.218	12500
24.025	0.509	17.791	12500
26.022	0.531	18.579	12500
28.043	0.543	19.008	12500
30.036	0.571	20.011	12500

Appendix II

Stability data of minoxidil solutions containing variuos concentrations of EDTA sodium at 70°C

and

Stability data of minoxidil solutions containing variuos concentrations of CDs at room temperature and at 70°C

Stability data of minoxidil solutions in various concentrations of EDTA sodium at 70°C.

a. Minoxidil solutions containing β-CD 0.1% w/v

EDTA sodium (%w/v)	Time (day)	concentration of minoxidil remaining (mg/ml)			Average concentration*
0	0	19.91	20.40	19.64	19.98 ± 0.38
	14	18.40	19.29	19.73	19.14 ± 0.68
0.01	0	19.38	20.04	18.98	19.47 ± 0.53
	14	18.98	18.40	20.00	19.13 ± 0.81
0.05	0	18.93	17.69	20.71	19.11 ± 1.52
	14	19.11	18.49	19.07	18.89 ± 0.35
0.10	0	20.38	21.20	17.38	19.65 ± 2.01
	14	19.38	19.87	19.02	19.42 ± 0.43

b. Minoxidil solutions containing HP-β-CD 5% w/v

EDTA sodium (%w/v)	Time (day)	concentration of minoxidil remaining (mg/ml)			Average concentration*
0	0	19.28	20.89	18.36	19.51 ± 1.28
	14	18.53	19.69	20.89	19.70 ± 1.18
0.01	0	18.35	19.33	19.60	19.09 ± 0.66
	14	20.35	18.80	17.29	18.81 ± 1.53
0.05	0	19.96	18.50	19.82	19.43 ± 0.80
	14	18.44	20.18	19.73	19.45 ± 0.90
0.10	0	19.16	19.36	19.16	19.23 ± 0.11
	14	19.73	18.35	18.35	18.81 ± 0.80

* = Mean ± SD , n = 3

Stability data of minoxidil solutions containing no β-CD and ethanol 40% v/v (Rx 2).

a. At room temperature (30°C)

Time (days)	concentration of minoxidil remaining (mg/ml)			Average concentartion*
0	21.15	19.94	20.04	20.38 ± 0.67
14	19.13	20.38	18.83	19.45 ± 0.82
28	21.06	19.29	19.62	19.99 ± 0.94
42	19.56	19.64	17.60	18.93 ± 1.15
56	19.26	19.24	18.99	19.16 ± 0.15
70	19.33	19.00	18.90	19.08 ± 0.22
84	19.29	19.85	20.55	19.90 ± 0.63

$$\ln conc^{n} = 2.9864 + (-3.5714 \times 10^{-4}) \text{ time}$$

$$r^2 = 0.1713$$

$$r = -0.4139$$

b. At 70°C

Time (days)	concentration of minoxidil remaining (mg/ml)			Average concentration*
0	21.15	19.94	20.04	20.38 ± 0.67
14	20.58	17.69	19.64	19.30 ± 1.47
28	18.72	18.71	18.47	18.63 ± 0.14
42	19.07	19.20	17.24	18.50 ± 1.09
56	18.94	20.96	18.42	19.44 ± 1.34
70	19.90	17.70	18.50	18.70 ± 1.11
84	19.03	18.59	19.08	18.90 ± 0.27

$$\ln conc^{n} = 2.9736 + (-5.6122 \times 10^{-4}) \text{ time}$$

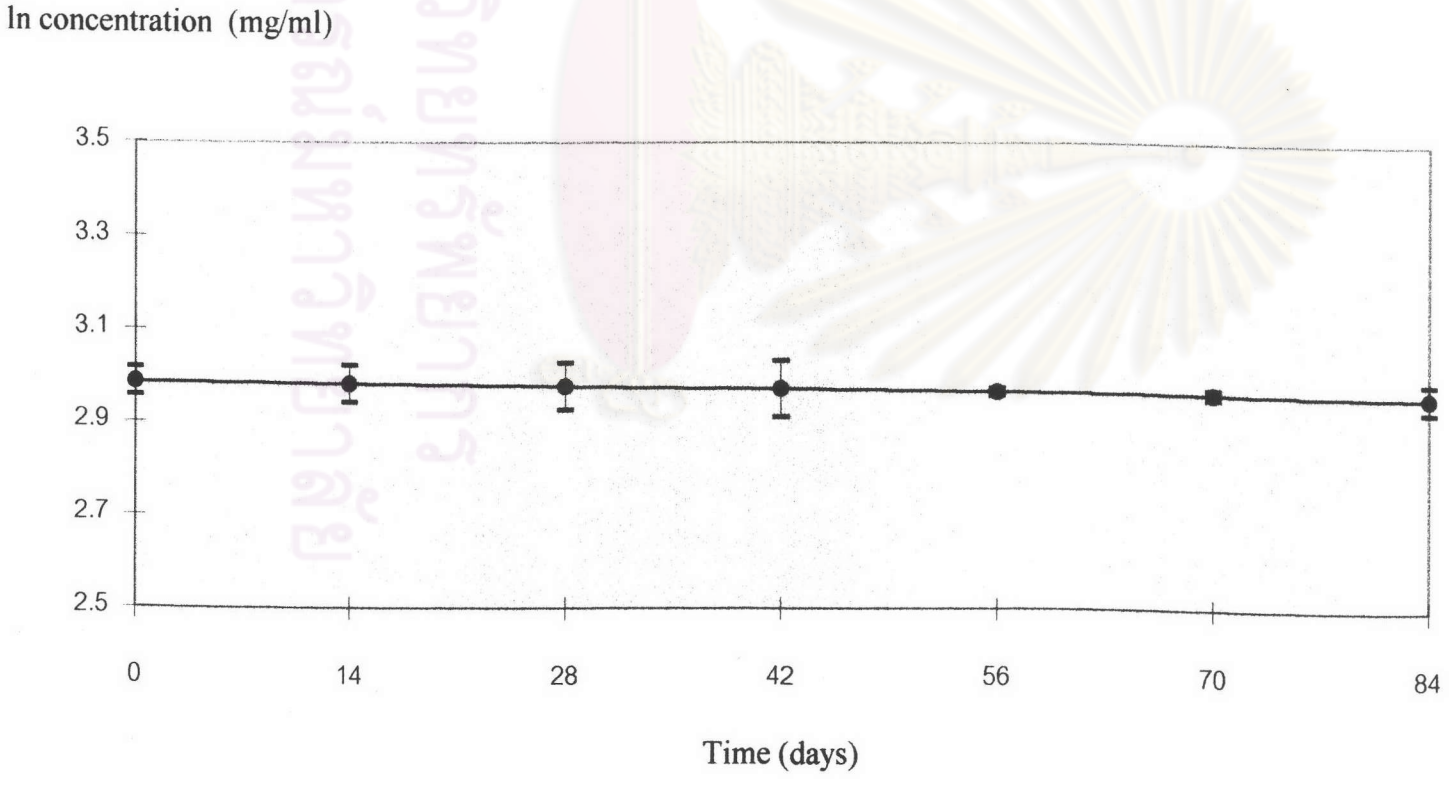
$$r^2 = 0.2701$$

$$r = -0.5197$$

* = Mean ± SD , n = 3

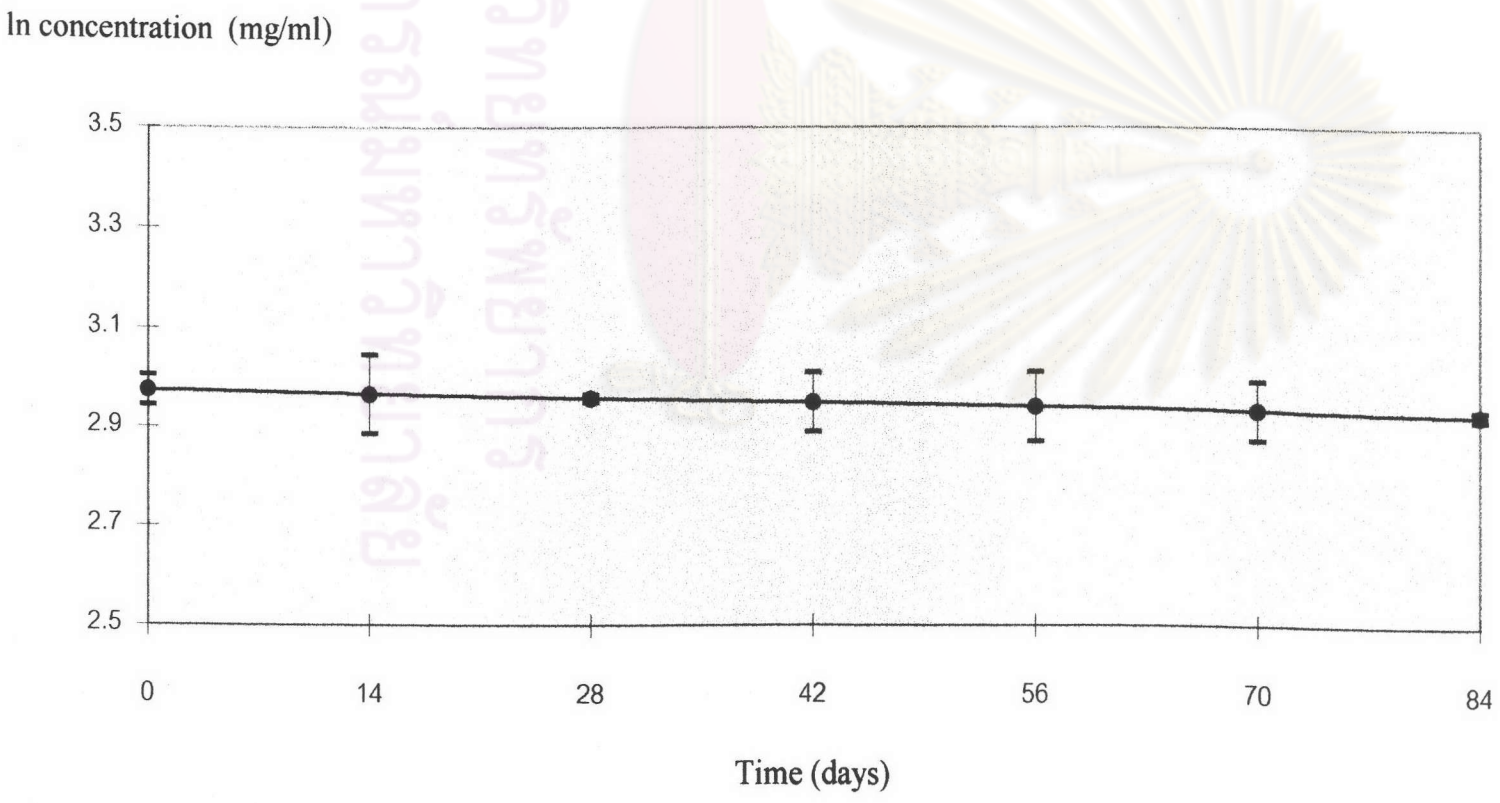
Stablity data of minoxidil solutions containing no β-CD and ethanol 40% v/v (Rx 2)

a. At room temperature (30°C)



Stablity data of minoxidil solutions containing no β-CD and ethanol 40% v/v (Rx 2)

b. At 70°C



Stability data of minoxidil solutions containing β-CD 0.1% w/v (Rx 3).

a. At room temperature (30°C)

Time (days)	concentration of minoxidil remaining (mg/ml)			Average concentration*
0	18.71	21.00	19.78	19.83 ± 1.14
14	17.95	18.98	19.73	18.89 ± 0.89
28	18.82	20.67	18.31	19.27 ± 1.24
42	18.56	19.84	17.79	18.73 ± 1.03
56	18.07	20.74	18.30	19.04 ± 1.48
70	20.20	19.40	17.18	18.93 ± 1.56
84	19.84	17.18	18.54	18.52 ± 1.33

$$\ln conc^{n} = 2.9707 + (-5.6122 \times 10^{-4})\ time$$

$$r^2 = 0.5500$$

$$r = -0.7416$$

b. At 70°C

Time (days)	concentration of minoxidil remaining (mg/ml)			Average concentration*
0	18.71	21.00	19.78	19.83 ± 1.14
14	19.02	19.78	19.33	19.38 ± 0.38
28	18.09	21.20	19.38	19.56 ± 1.56
42	20.82	20.80	18.78	20.13 ± 1.17
56	18.52	20.30	18.53	19.12 ± 1.02
70	19.40	18.80	20.40	19.53 ± 0.81
84	17.66	18.40	19.61	18.56 ± 0.98

$$\ln conc^{n} = 2.9882 + (-5.3571 \times 10^{-4})\ time$$

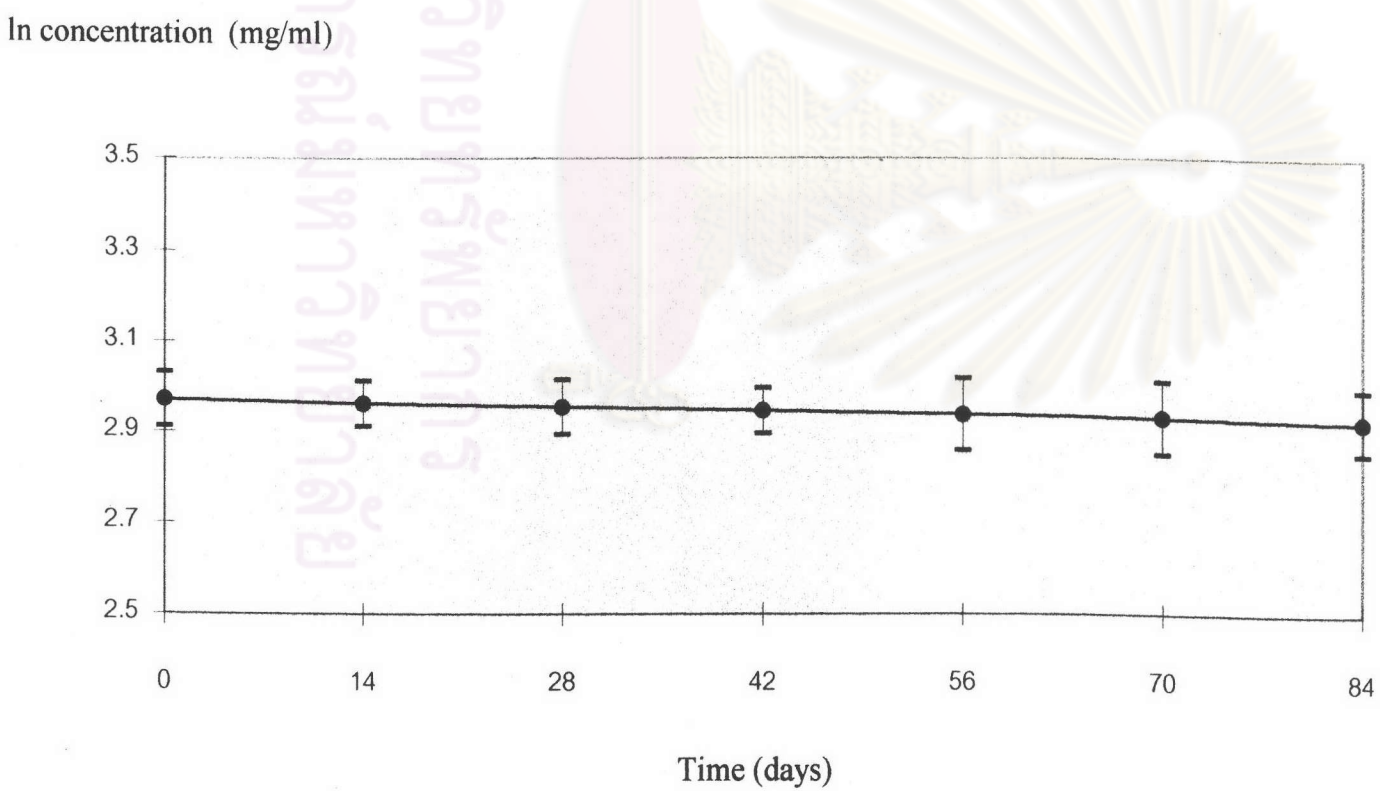
$$r^2 = 0.3776$$

$$r = -0.6145$$

* = Mean ± SD , n = 3

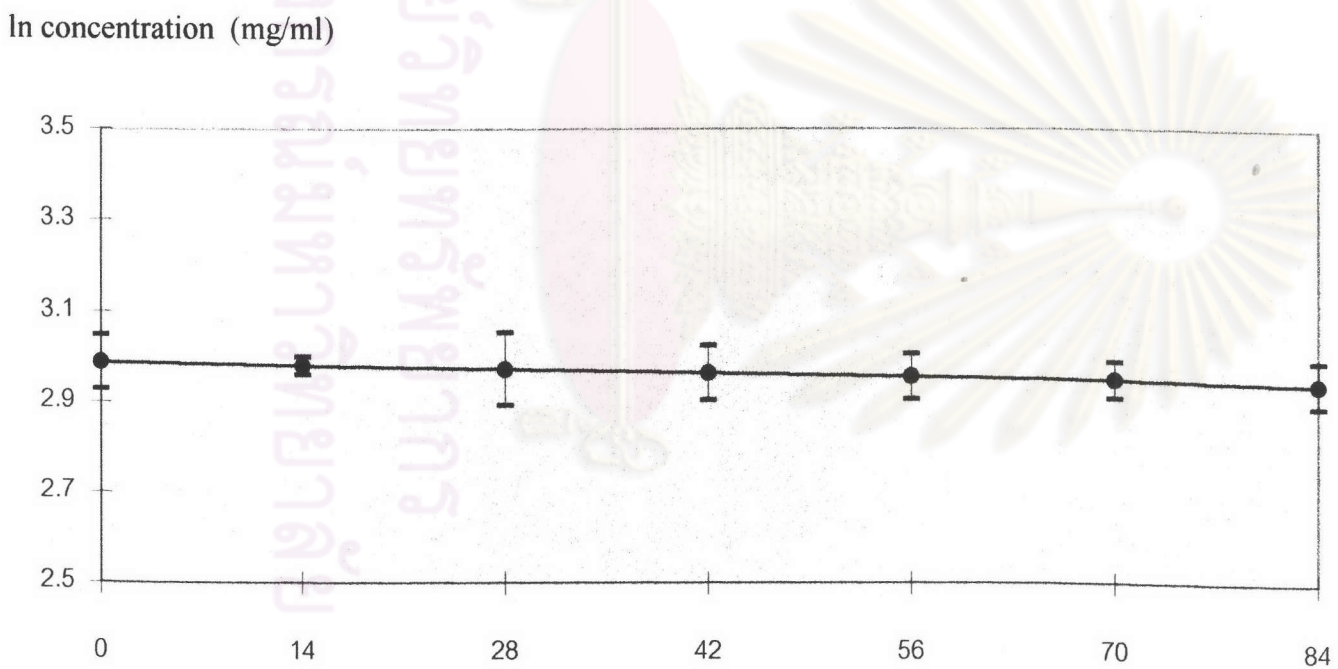
Stablity data of minoxidil solutions containing β-CD 0.1% w/v (Rx 3)

a. At room temperature (30°C)



Stablity data of minoxidil solutions containing β-CD 0.1% w/v (Rx 3)

b. At 70°C



Stability data of minoxidil solutions containing β-CD 0.4% w/v (Rx 4).

a. At room temperature (30°C)

Time (days)	concentration of minoxidil remaining (mg/ml)			Average concentration*
0	18.18	20.90	20.89	19.99 ± 1.57
14	18.20	20.47	19.33	19.33 ± 1.13
28	19.91	20.18	18.18	19.42 ± 1.08
42	19.51	20.80	19.56	19.96 ± 0.73
56	19.41	20.00	19.30	19.57 ± 0.38
70	20.10	19.15	20.80	20.02 ± 0.83
84	19.18	20.19	19.66	19.68 ± 0.50

$\ln conc^{n} = 2.9746 + (1.2755 \times 10^{-4})$ time

$r^2 = 0.0744$

$r = 0.2728$

b. At 70°C

Time (days)	concentration of minoxidil remaining (mg/ml)			Average concentration*
0	18.18	20.90	20.89	19.99 ± 1.57
14	18.89	20.18	20.67	19.91 ± 0.92
28	20.56	19.60	19.18	19.78 ± 0.71
42	19.16	19.56	18.36	19.03 ± 0.61
56	19.67	19.14	19.32	19.38 ± 0.27
70	18.00	20.20	21.10	19.77 ± 1.59
84	19.28	17.70	18.49	18.49 ± 0.79

$\ln conc^{n} = 2.9939 + (-6.3775 \times 10^{-4})$ time

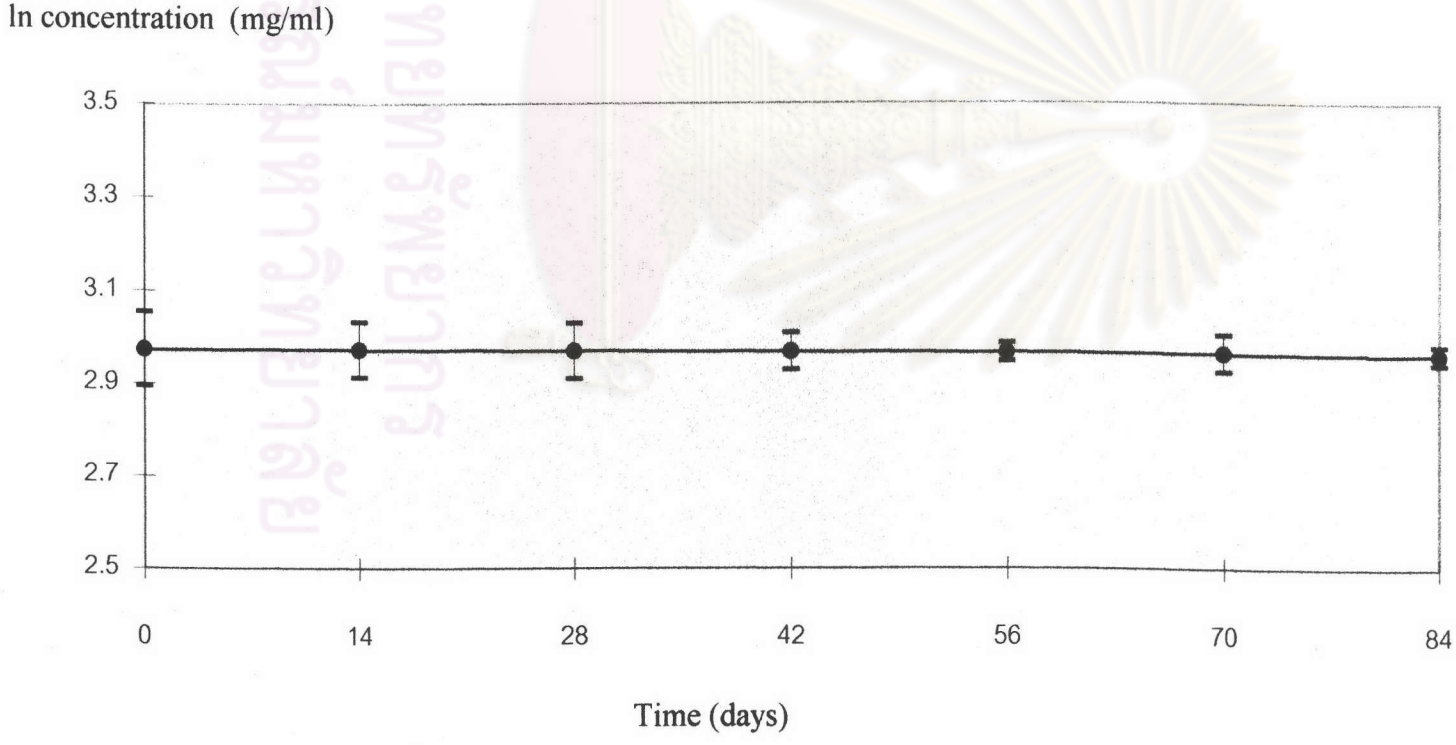
$r^2 = 0.5661$

$r = -0.7524$

* = Mean ± SD , n = 3

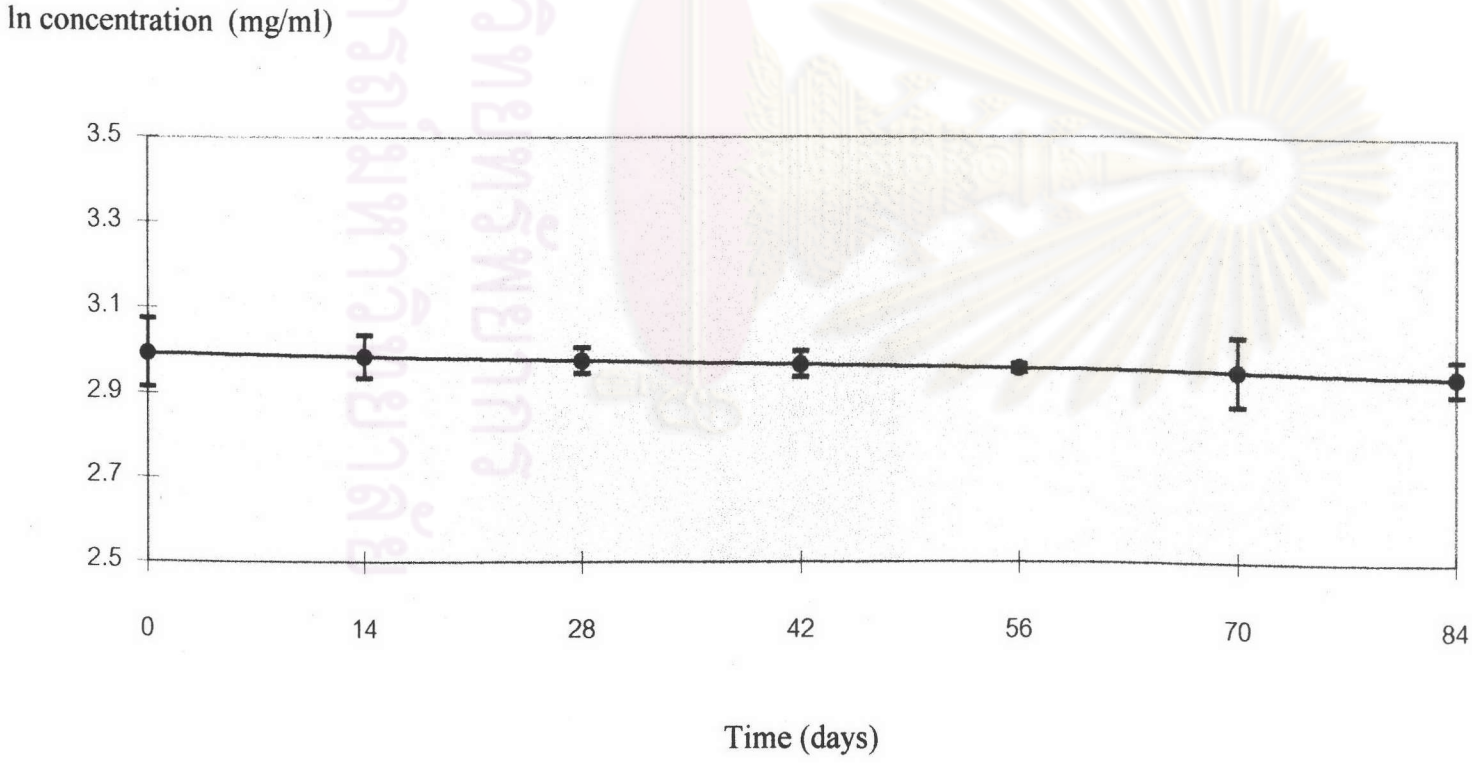
Stablity data of minoxidil solutions containing β-CD 0.4% w/v (Rx 4)

a. At room temperature (30°C)



Stablity data of minoxidil solutions containing β-CD 0.4% w/v (Rx 4)

b. At 70°C



Stability data of minoxidil solutions containing β-CD 0.7% w/v (Rx 5).

a. At room temperature (30°C)

Time (days)	concentration of minoxidil remaining (mg/ml)			Average concentration*
0	19.78	19.42	20.56	19.92 ± 0.58
14	19.60	20.13	20.00	19.91 ± 0.27
28	18.22	19.87	21.11	19.73 ± 1.45
42	20.60	19.47	18.60	19.56 ± 1.00
56	19.90	20.19	19.07	19.72 ± 0.58
70	17.56	20.40	18.58	18.85 ± 1.44
84	19.79	20.06	19.94	19.93 ± 0.13

$$\ln conc^{n} = 2.9878 + (-2.5510 \times 10^{-4}) \text{ time}$$

$$r^2 = 0.1838$$

$$r = -0.4287$$

b. At 70°C

Time (days)	concentration of minoxidil remaining (mg/ml)			Average concentration*
0	19.78	19.42	20.56	19.92 ± 0.58
14	20.44	19.82	18.58	19.61 ± 0.95
28	20.51	18.98	19.58	19.69 ± 0.77
42	20.13	19.16	20.84	20.04 ± 0.84
56	19.15	19.93	20.67	19.92 ± 0.76
70	19.47	18.50	20.70	19.56 ± 1.10
84	19.24	19.31	19.47	19.34 ± 0.12

$$\ln conc^{n} = 2.9921 + (-2.5510 \times 10^{-4}) \text{ time}$$

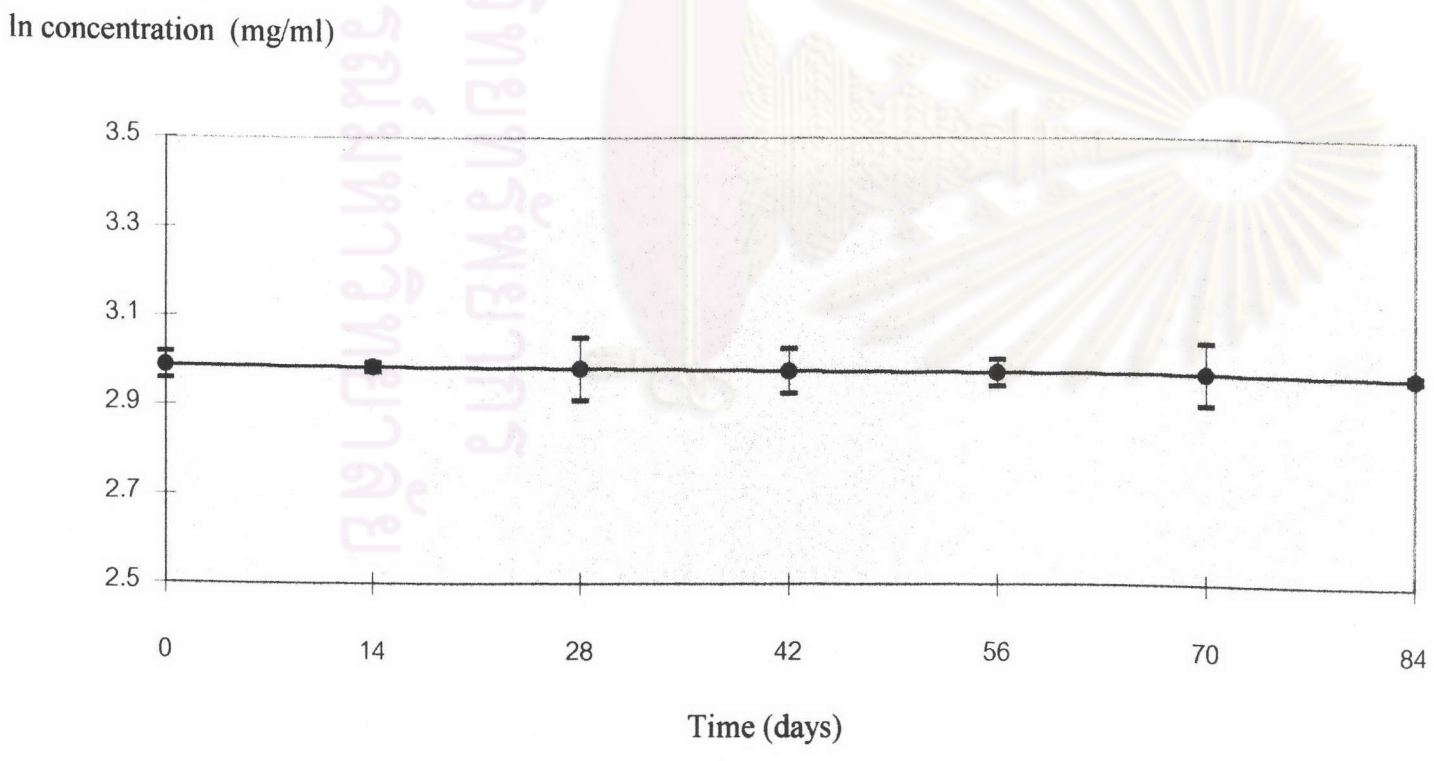
$$r^2 = 0.3289$$

$$r = -0.5735$$

* = Mean ± SD , n = 3

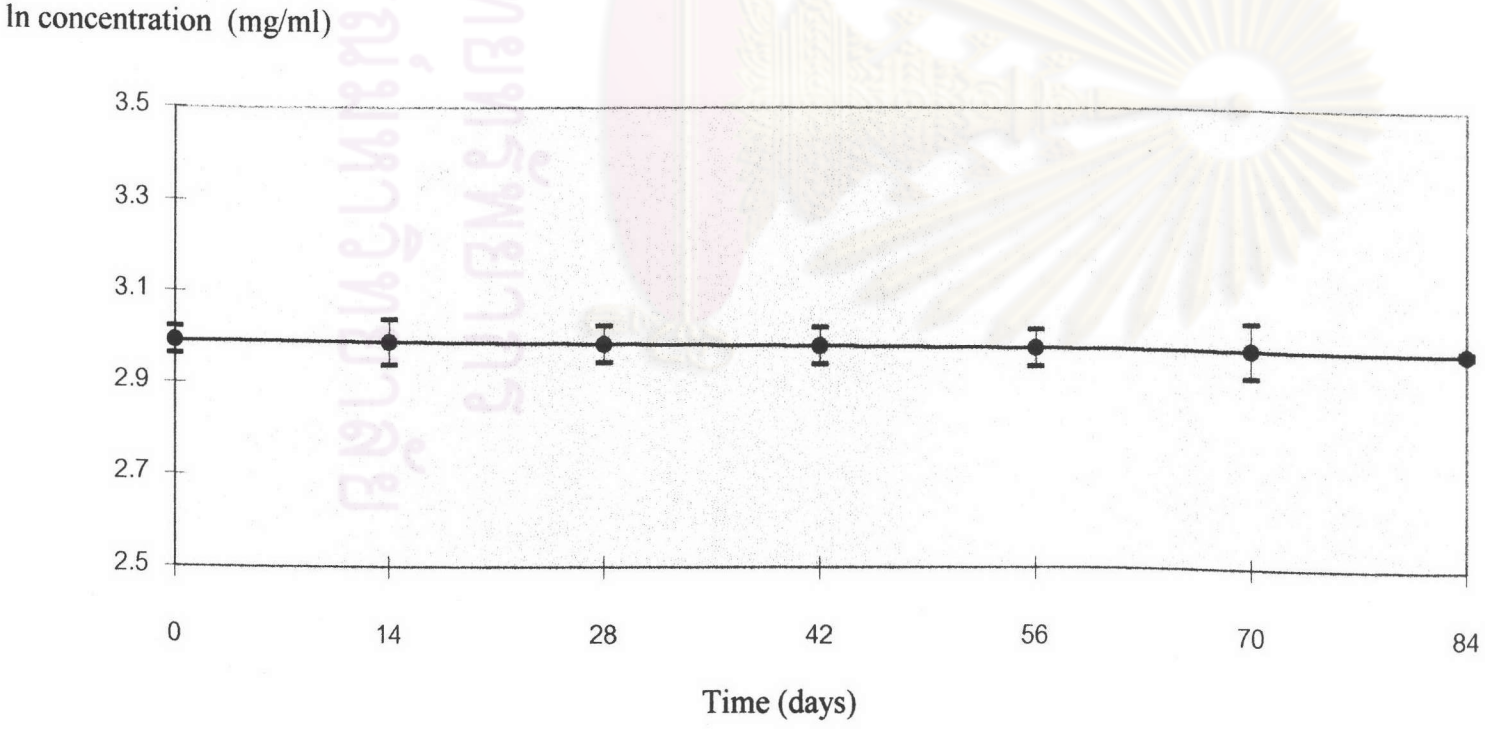
Stablity data of minoxidil solutions containing β-CD 0.7% w/v (Rx 5)

a. At room temperature (30°C)



Stablity data of minoxidil solutions containing β-CD 0.7% w/v (Rx 5)

b. At 70°C



Stability data of minoxidil solutions containing no HP-β-CD and ethanol 30% v/v (Rx 6).

a. At room temperature (30°C)

Time (days)	concentration of minoxidil remaining (mg/ml)			Average concentration*
0	18.82	21.29	21.84	20.65 ± 1.61
14	17.56	19.33	20.22	19.04 ± 1.30
28	18.40	19.02	20.93	19.45 ± 1.32
42	17.07	19.47	21.15	19.23 ± 2.05
56	20.40	21.07	20.75	20.74 ± 0.33
70	18.85	16.45	19.06	18.12 ± 1.45
84	19.07	17.30	16.98	17.78 ± 1.12

$$\ln conc^{n} = 3.0125 + (-1.2500 \times 10^{-3}) \text{ time}$$

$$r^2 = 0.4287$$

$$r = -0.6548$$

b. At 70°C

Time (days)	concentration of minoxidil remaining (mg/ml)			Average concentration*
0	18.82	21.29	21.84	20.65 ± 1.61
14	20.93	20.53	20.07	20.51 ± 0.43
28	19.73	18.22	19.56	19.17 ± 0.83
42	19.31	18.81	18.93	19.02 ± 0.26
56	20.67	21.02	20.04	20.58 ± 0.50
70	19.28	18.17	20.04	19.16 ± 0.94
84	19.19	19.55	19.85	19.53 ± 0.33

$$\ln conc^{n} = 3.0096 + (-6.3775 \times 10^{-4}) \text{ time}$$

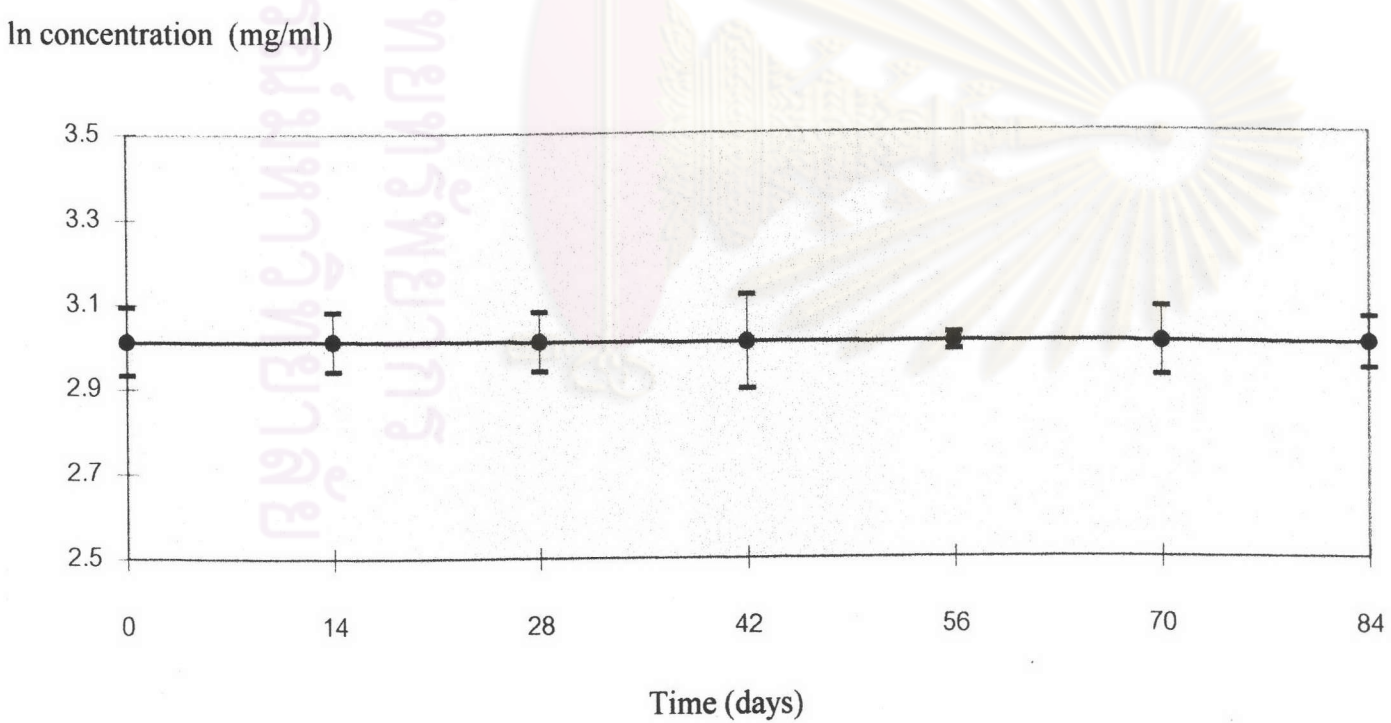
$$r^2 = 0.2441$$

$$r = -0.4941$$

* = Mean ± SD , n = 3

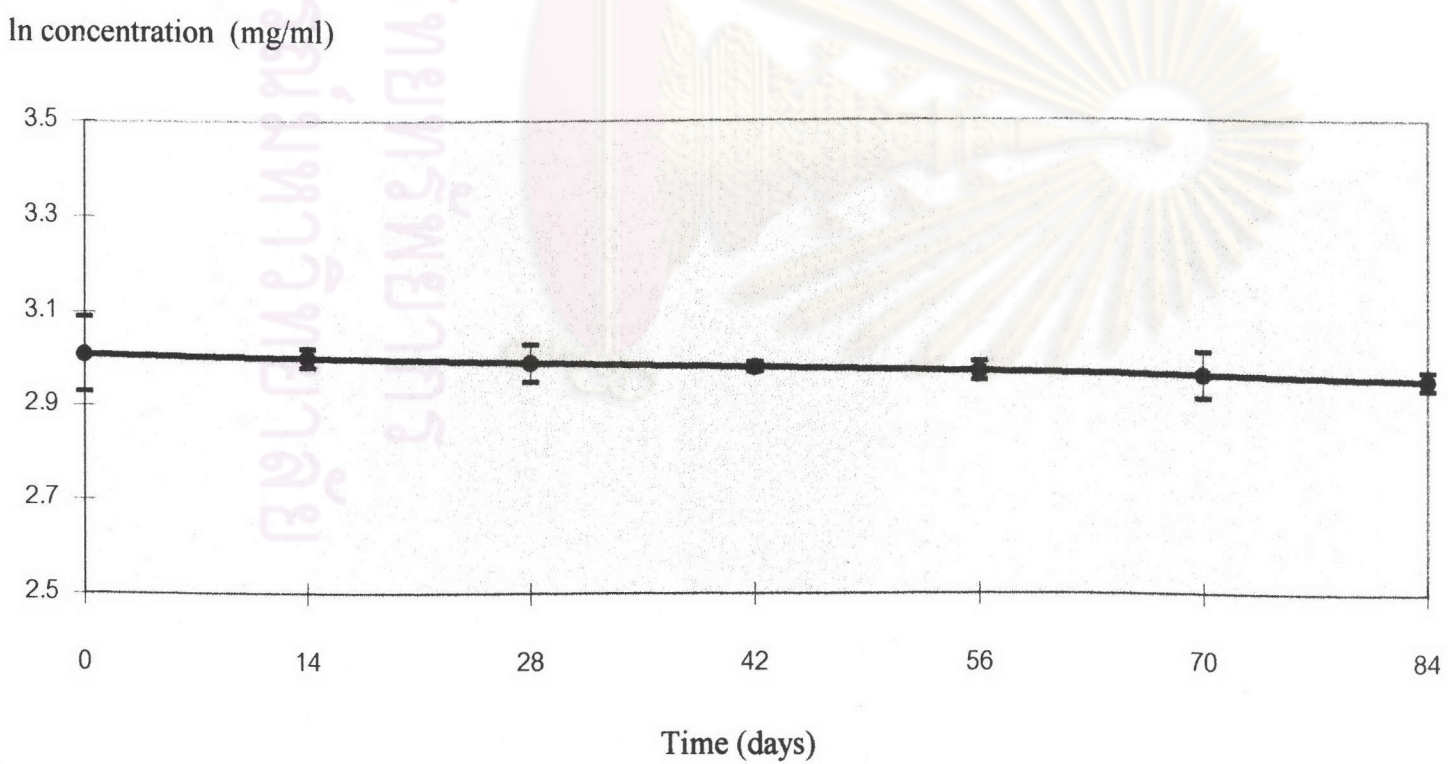
Stablity data of minoxidil solutions containing no HP-β-CD and ethanol 30% v/v (Rx 6)

a. At room temperature (30°C)



Stablity data of minoxidil solutions containing no HP-β-CD and ethanol 30% v/v (Rx 6)

b. At 70°C



Stability data of minoxidil solutions containing HP-β-CD 5% w/v (Rx 7).

a. At room temperature (30°C)

Time (days)	concentration of minoxidil remaining (mg/ml)			Average concentration*
0	20.04	20.53	19.89	20.15 ± 0.33
14	19.58	19.91	20.24	19.91 ± 0.33
28	19.69	19.29	20.62	19.87 ± 0.68
42	20.04	19.76	18.79	19.53 ± 0.66
56	20.00	18.98	20.06	19.68 ± 0.61
70	19.84	17.89	21.06	19.60 ± 1.60
84	18.29	18.11	19.06	18.49 ± 0.50

$$\ln \text{conc}^{n} = 3.0053 + (-7.3980 \times 10^{-4}) \text{ time}$$

$$r^2 = 0.7200$$

$$r = -0.8485$$

b. At 70°C

Time (days)	concentration of minoxidil remaining (mg/ml)			Average concentration*
0	20.04	20.53	19.89	20.15 ± 0.33
14	19.53	19.82	20.51	19.95 ± 0.50
28	18.71	19.29	18.69	18.90 ± 0.34
42	18.76	19.78	19.16	19.23 ± 0.51
56	18.71	20.75	19.91	19.79 ± 1.02
70	18.42	20.25	19.02	19.23 ± 0.93
84	20.17	18.18	18.89	19.08 ± 1.01

$$\ln \text{conc}^{n} = 2.9868 + (-4.3367 \times 10^{-4}) \text{ time}$$

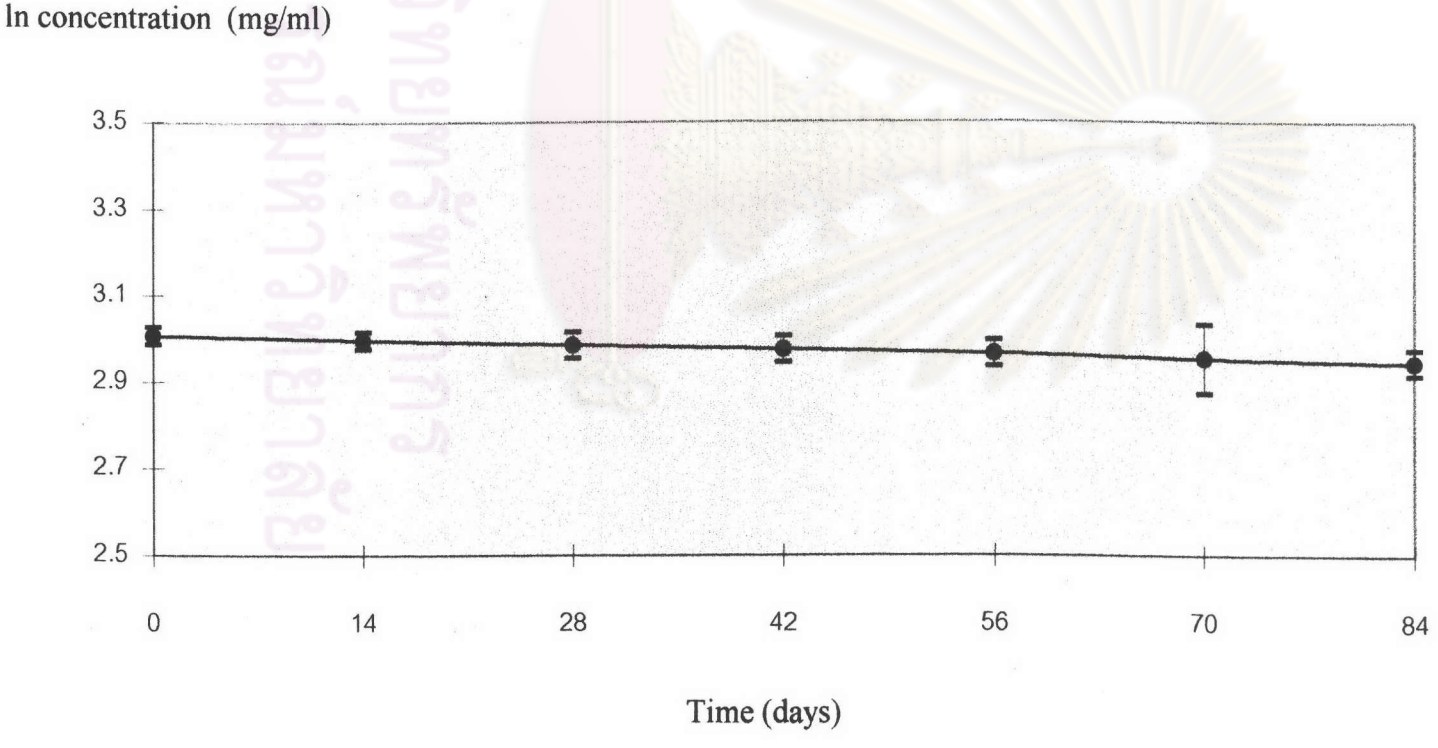
$$r^2 = 0.3577$$

$$r = -0.5980$$

* = Mean ± SD , n = 3

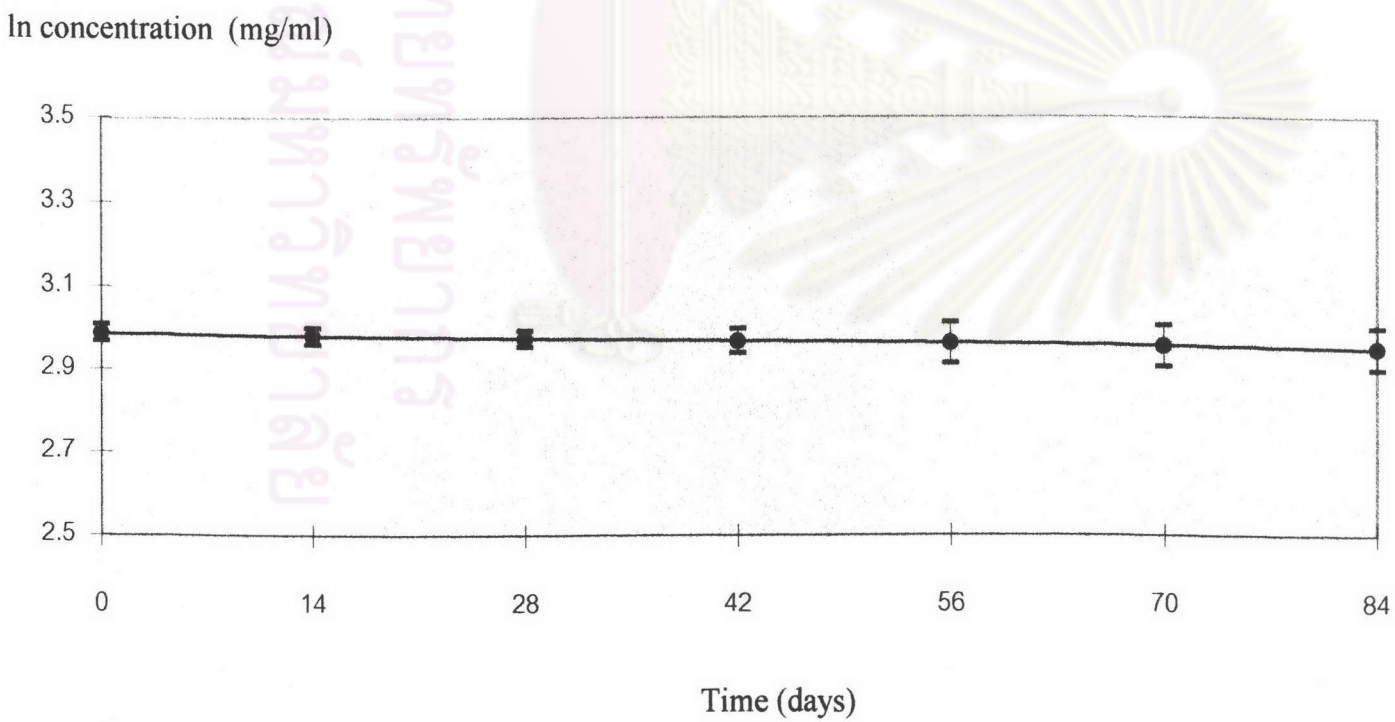
Stablity data of minoxidil solutions containing HP-β-CD 5% w/v (Rx 7)

a. At room temperature (30°C)



Stablity data of minoxidil solutions containing HP-β-CD 5% w/v (Rx 7)

b. At 70°C



Stability data of minoxidil solutions containing HP-β-CD 10% w/v (Rx 8).

a. At room temperature (30°C)

Time (days)	concentration of minoxidil remaining (mg/ml)			Average concentration*
0	21.24	20.84	18.27	20.12 ± 1.61
14	18.62	21.11	19.29	19.67 ± 1.29
28	18.36	19.11	19.47	18.98 ± 0.57
42	19.58	18.89	19.33	19.27 ± 0.35
56	21.07	21.11	20.33	20.84 ± 0.44
70	20.08	19.47	20.99	20.18 ± 1.76
84	17.90	18.52	18.90	18.44 ± 0.50

$$\ln conc^{n} = 2.9896 + (-3.3163 \times 10^{-4}) \text{ time}$$

$$r^2 = 0.0540$$

$$r = -0.2324$$

b. At 70°C

Time (days)	concentration of minoxidil remaining (mg/ml)			Average concentration*
0	21.24	20.84	18.27	20.12 ± 1.61
14	20.58	18.62	19.60	19.60 ± 0.89
28	19.51	19.11	19.73	19.45 ± 0.31
42	20.31	20.67	19.91	20.30 ± 0.38
56	20.58	20.67	20.98	20.74 ± 0.21
70	20.87	20.88	20.51	20.75 ± 0.21
84	19.49	19.52	19.08	19.36 ± 0.25

$$\ln conc^{n} = 2.9893 + (1.5306 \times 10^{-4}) \text{ time}$$

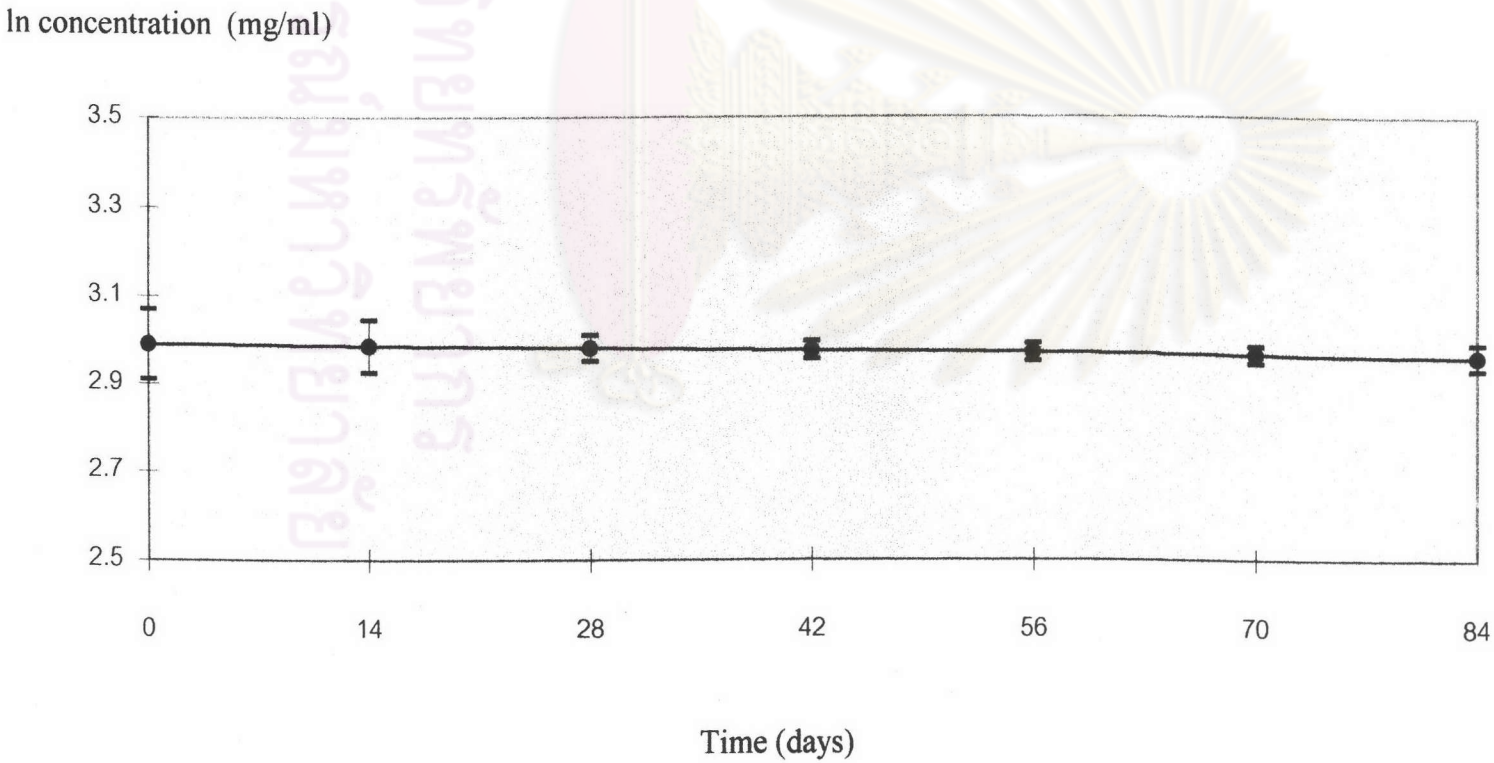
$$r^2 = 0.0249$$

$$r = 0.1577$$

* = Mean ± SD , n = 3

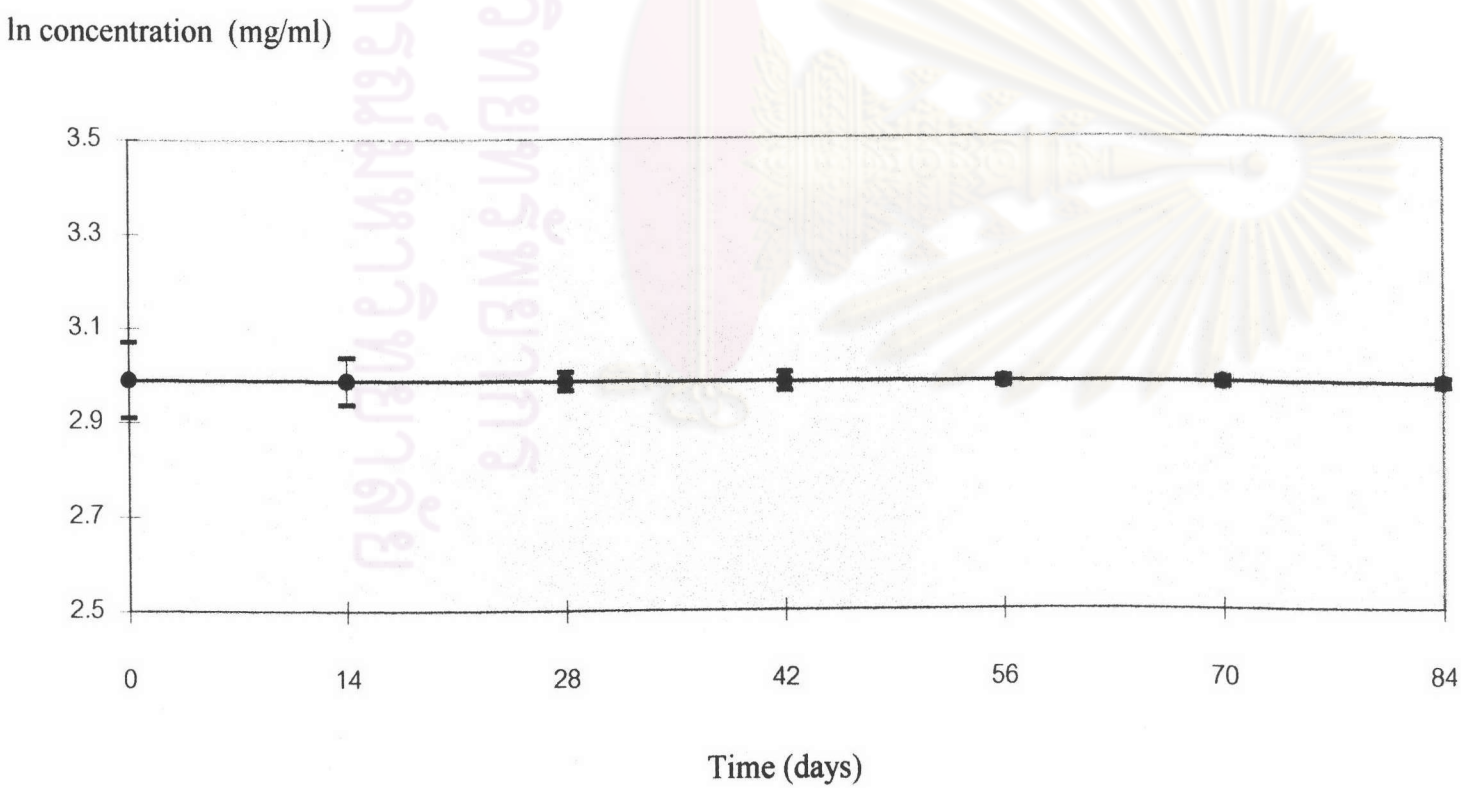
Stablity data of minoxidil solutions containing HP-β-CD 10% w/v (Rx 8)

a. At room temperature (30°C)



Stablity data of minoxidil solutions containing HP-β-CD 10% w/v (Rx 8)

b. At 70°C



Stability data of minoxidil solutions containing HP-β-CD 15% w/v (Rx 9).

a. At room temperature (30°C)

Time (days)	concentration of minoxidil remaining (mg/ml)			Average concentration*
0	20.40	20.49	19.55	20.15 ± 0.52
14	18.91	20.89	20.60	20.13 ± 1.96
28	18.44	20.56	19.71	19.57 ± 1.07
42	20.75	19.69	18.40	19.61 ± 1.18
56	20.80	20.33	20.29	20.47 ± 0.28
70	19.39	18.44	20.51	19.45 ± 1.04
84	19.04	18.69	19.34	19.02 ± 0.32

$$\ln \text{conc}^{n} = 3.0032 + (-4.8469 \times 10^{-4}) \text{ time}$$

$$r^2 = 0.3112$$

$$r = -0.5578$$

b. At 70°C

Time (days)	concentration of minoxidil remaining (mg/ml)			Average concentration*
0	20.40	20.49	19.55	20.15 ± 0.52
14	19.64	19.60	18.40	19.21 ± 0.70
28	20.16	17.69	18.13	18.66 ± 1.32
42	18.62	18.84	19.38	18.95 ± 0.39
56	20.82	20.91	20.93	20.89 ± 0.06
70	19.94	20.97	18.94	19.95 ± 1.01
84	18.54	19.39	20.55	19.49 ± 1.01

$$\ln \text{conc}^{n} = 2.9636 + (2.5510 \times 10^{-4}) \text{ time}$$

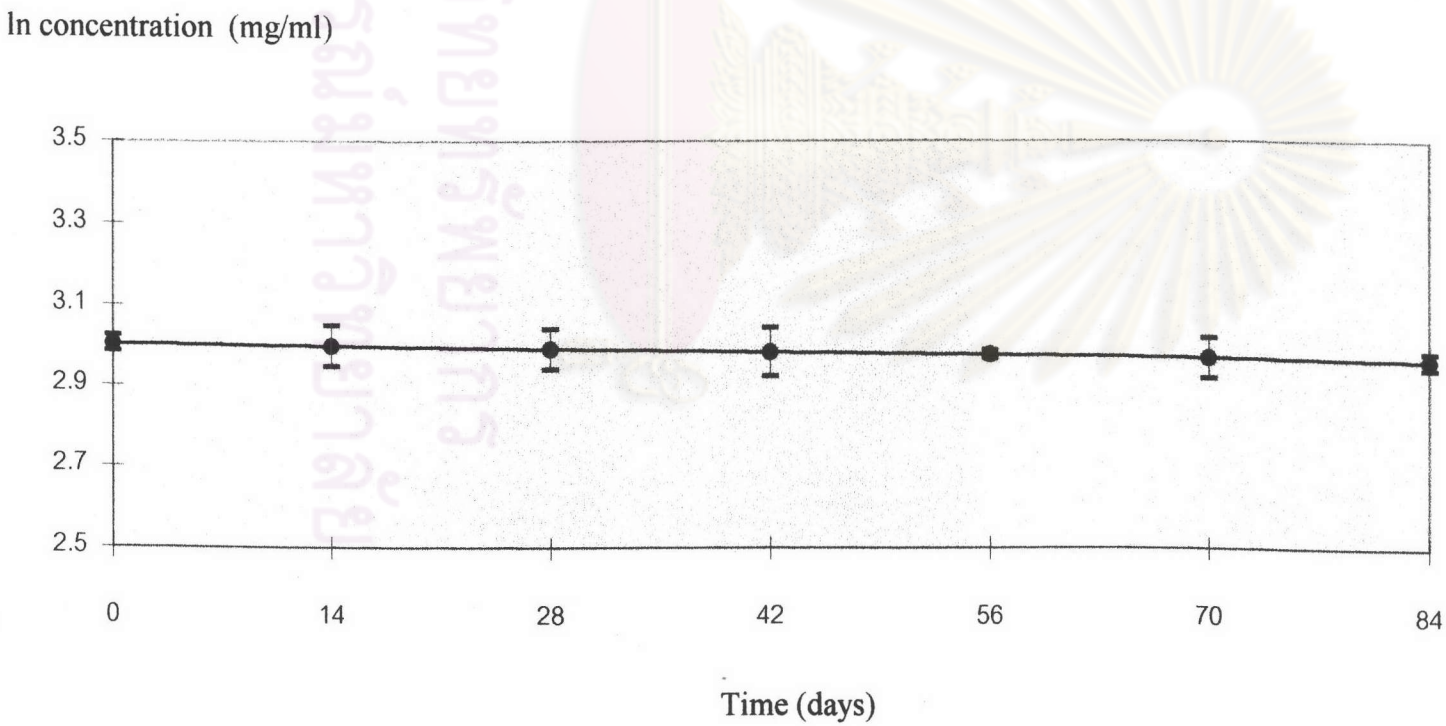
$$r^2 = 0.0398$$

$$r = 0.1995$$

* = Mean ± SD , n = 3

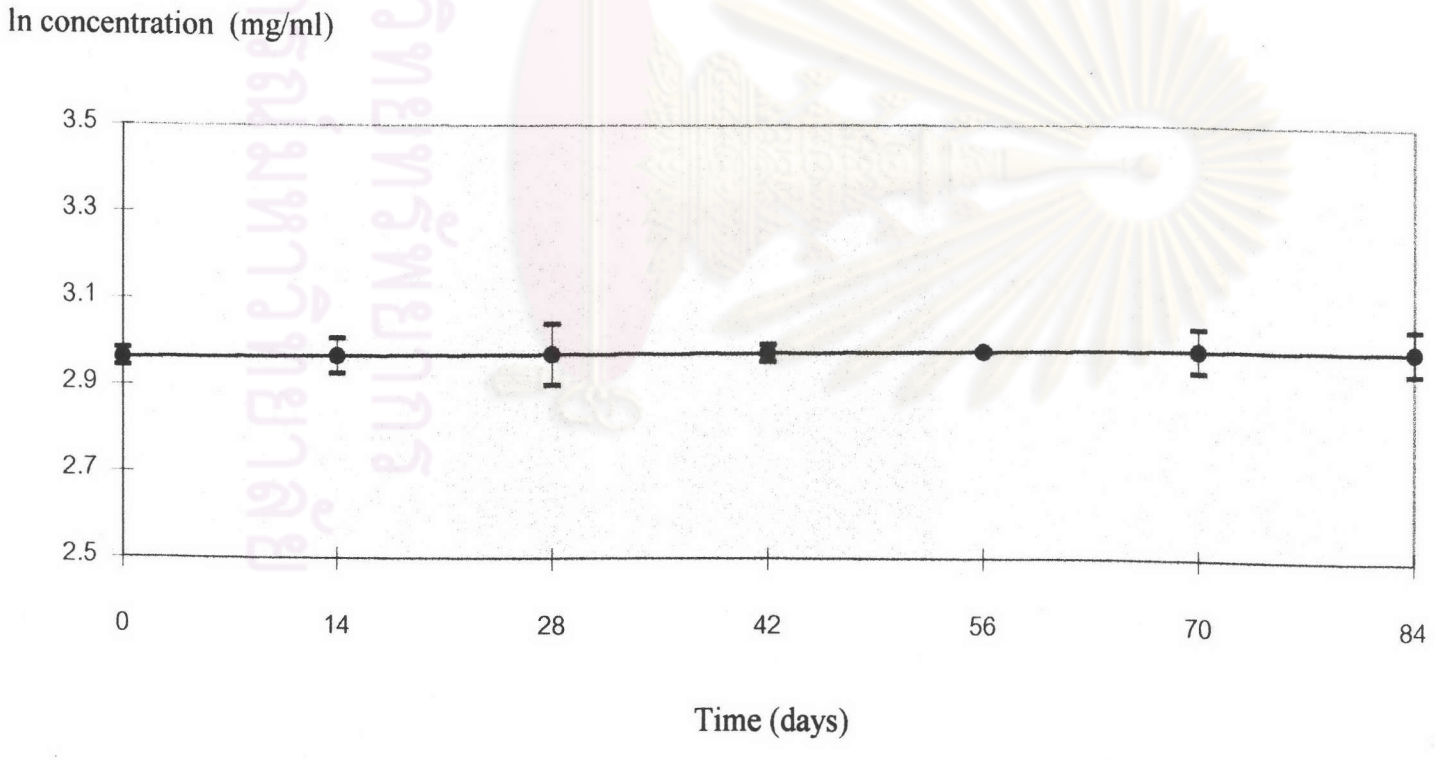
Stablity data of minoxidil solutions containing HP-β-CD 15% w/v (Rx 9)

a. At room temperature (30°C)



Stablity data of minoxidil solutions containing HP-β-CD 15% w/v (Rx 9)

b. At 70°C



Stability data of minoxidil solutions containing HP-β-CD 20% w/v (Rx 10).

a. At room temperature (30°C)

Time (days)	concentration of minoxidil remaining (mg/ml)			Average concentration*
0	21.40	20.38	19.22	20.33 ± 1.09
14	19.73	19.82	20.33	19.96 ± 0.32
28	20.76	19.33	17.60	19.23 ± 1.58
42	18.27	17.64	20.84	18.92 ± 1.69
56	20.27	20.08	20.47	20.27 ± 0.19
70	20.29	19.32	20.76	20.12 ± 0.73
84	19.51	18.40	18.50	18.80 ± 0.61

$\ln conc^{n} = 2.9953 + (-4.3367 \times 10^{-4})$ time

$r^2 = 0.1531$

$r = -0.3912$

b. At 70°C

Time (days)	concentration of minoxidil remaining (mg/ml)			Average concentration*
0	21.40	20.38	19.22	20.33 ± 1.09
14	19.22	19.84	18.93	19.33 ± 0.46
28	19.22	19.67	19.33	19.41 ± 0.23
42	18.76	19.58	19.10	19.15 ± 0.41
56	19.38	20.24	19.51	19.71 ± 0.46
70	20.59	20.11	20.43	20.38 ± 0.24
84	19.19	19.23	21.09	19.84 ± 1.08

$\ln conc^{n} = 2.9736 + (1.5306 \times 10^{-4})$ time

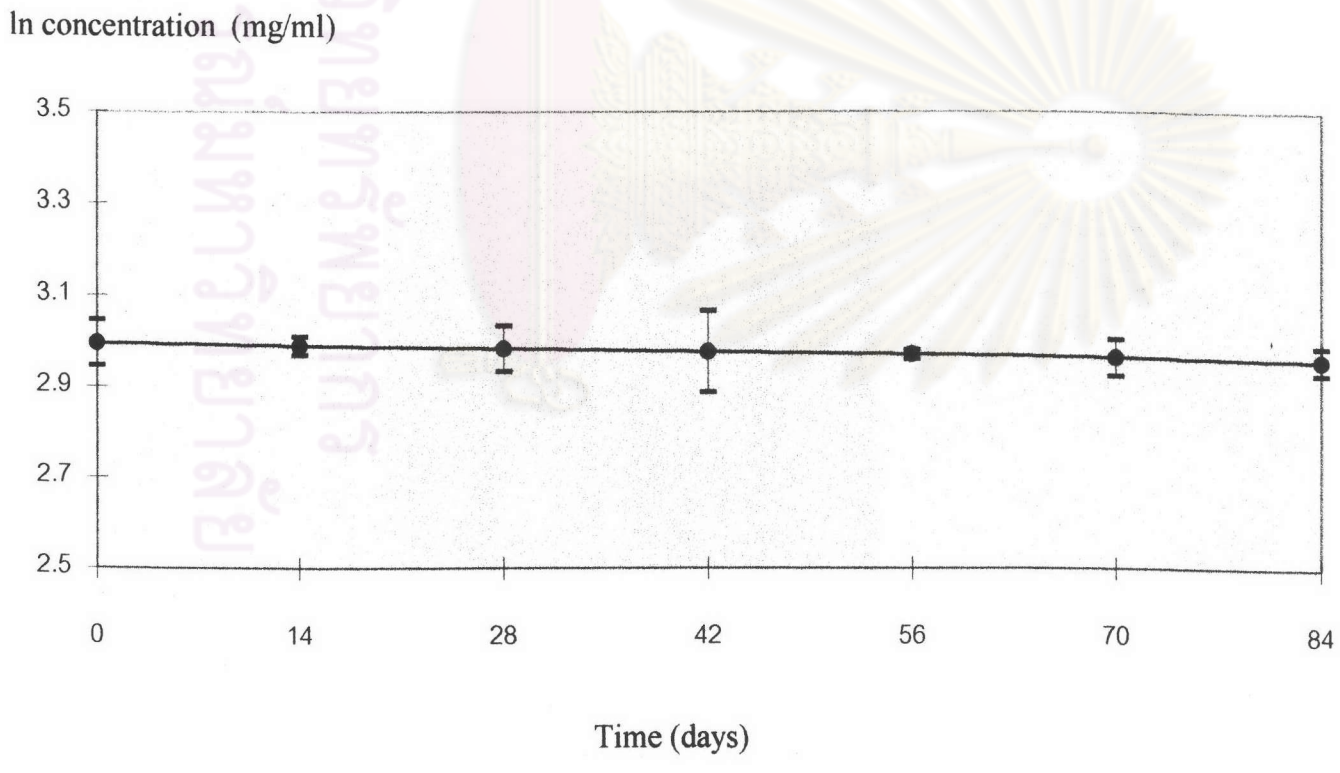
$r^2 = 0.0357$

$r = 0.1890$

* = Mean ± SD , n = 3

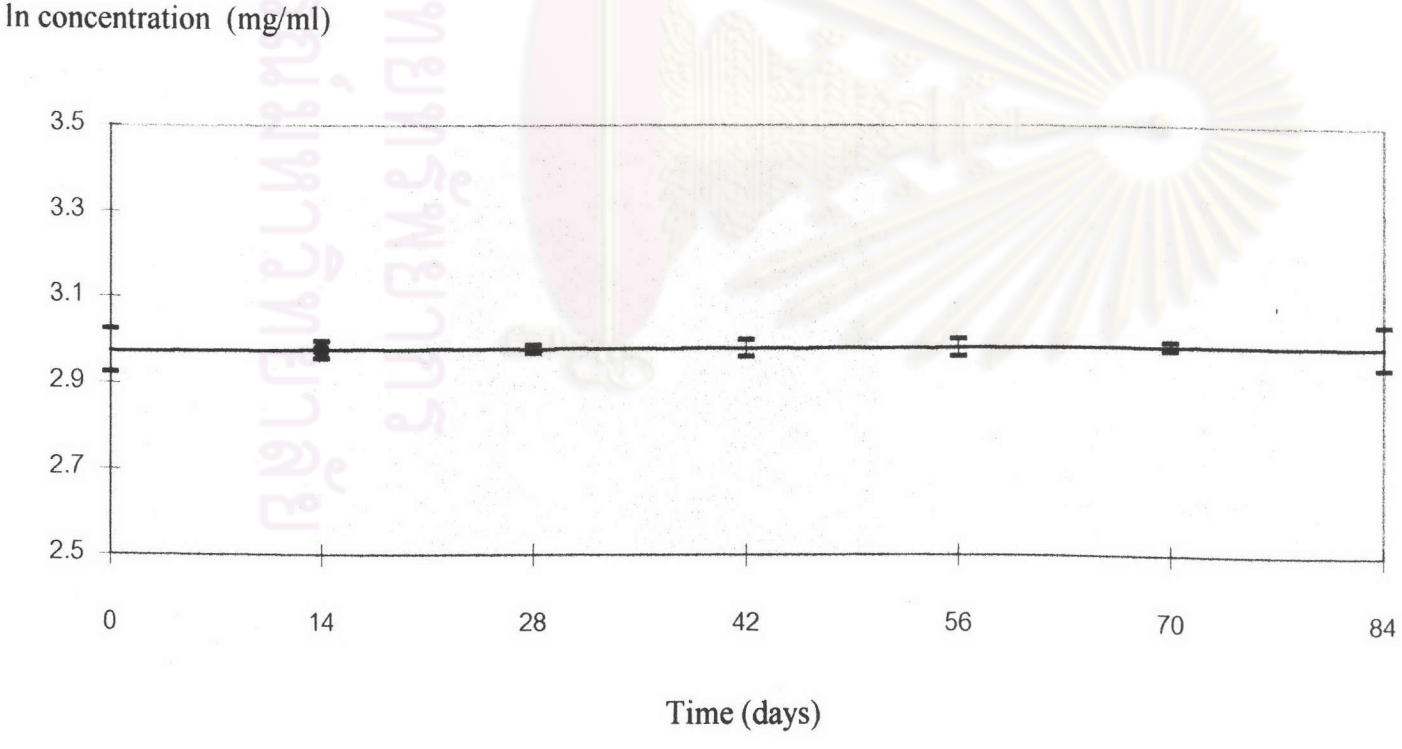
Stablity data of minoxidil solutions containing HP-β-CD 20% w/v (Rx 10)

a. At room temperature (30°C)



Stablity data of minoxidil solutions containing HP-β-CD 20% w/v (Rx 10)

b. At 70°C



Appendix III

One way ANOVA of stability data of minoxidil solutions containing variuos concentrations of EDTA sodium at 70°C

and

One way ANOVA of stability data of minoxidil solutions containing variuos concentrations of CDs at room temperature and at 70°C

One way ANOVA of stability data of minoxidil solutions containing β-CD 0.1% w/v in various concentrations of EDTA sodium at 70°C.

a. At the begining (D_0)

Source	df	SS	MS=SS/df	F
Amoung Groups	3	1.20	0.40	0.23
Within Group	8	13.57	1.70	
Total	11	14.77		

b. At D_{14}

Source	df	SS	MS=SS/df	F
Amoung Groups	3	0.44	0.15	0.43
Within Group	8	2.83	0.35	
Total	11	3.27		

$F_{table(3,8)} = 4.07$

Level of significant = 0.05

df = Degree of freedom

SS = Sum of square

MS = Mean square

F = Variance ratio

One way ANOVA of stability data of minoxidil solutions containing HP-β-CD 5% w/v in various concentrations of EDTA sodium at 70°C.

a. At the begining (D_0)

Source	df	SS	MS=SS/df	F
Amoung Groups	3	0.33	0.11	0.16
Within Group	8	5.47	0.68	
Total	11	5.80		

b. At D_{14}

Source	df	SS	MS=SS/df	F
Amoung Groups	3	1.85	0.62	0.48
Within Group	8	10.37	1.30	
Total	11	12.22		

$F_{table(3,8)} = 4.07$

Level of significant = 0.05

df = Degree of freedom

SS = Sum of square

MS = Mean square

F = Variance ratio

One way ANOVA of stability data of minoxidil solutions containing no β-CD and ethanol 40% v/v (Rx 2).

a. At room temperature (30°C)

Source	df	SS	MS=SS/df	F
Among Groups	6	5.29	0.88	1.63
Within Group	14	7.63	0.54	
Total	20	12.92		

b. At 70°C

Source	df	SS	MS=SS/df	F
Amoung Groups	6	7.68	1.28	1.29
Within Group	14	13.91	0.99	
Total	20	21.59		

$F_{table(6,15)} = 2.64$

Level of significant = 0.05

df = Degree of freedom

SS = Sum of square

MS = Mean square

F = Variance ratio

One way ANOVA of stability data of minoxidil solutions containing β-CD 0.1% w/v (Rx 3).

a. At room temperature (30°C)

Source	df	SS	MS=SS/df	F
Among Groups	6	3.23	0.54	0.34
Within Group	14	22.26	1.59	
Total	20	25.49		

b. At 70°C

Source	df	SS	MS=SS/df	F
Amoung Groups	6	4.63	0.77	0.68
Within Group	14	15.89	1.13	
Total	20	20.52		

$F_{table(6,15)} = 2.64$

Level of significant = 0.05

df = Degree of freedom

SS = Sum of square

MS = Mean square

F = Variance ratio

One way ANOVA of stability data of minoxidil solutions containing β-CD 0.4% w/v (Rx 4).

a. At room temperature (30°C)

Source	df	SS	MS=SS/df	F
Among Groups	6	1.44	0.24	0.26
Within Group	14	13.07	0.93	
Total	20	14.51		

b. At 70°C

Source	df	SS	MS=SS/df	F
Amoung Groups	6	5.45	0.91	0.86
Within Group	14	14.83	1.06	
Total	20	20.28		

$F_{table(6,15)} = 2.64$

Level of significant = 0.05

df = Degree of freedom

SS = Sum of square

MS = Mean square

F = Variance ratio

One way ANOVA of stability data of minoxidil solutions containing β-CD 0.7% w/v (Rx 5).

a. At room temperature (30°C)

Source	df	SS	MS=SS/df	F
Among Groups	6	2.66	0.44	0.52
Within Group	14	11.89	0.85	
Total	20	14.55		

b. At 70°C

Source	df	SS	MS=SS/df	F
Amoung Groups	6	1.10	0.18	0.29
Within Group	14	8.70	0.62	
Total	20	9.80		

$F_{table(6,15)} = 2.64$

Level of significant = 0.05

df = Degree of freedom

SS = Sum of square

MS = Mean square

F = Variance ratio

One way ANOVA of stability data of minoxidil solutions containing no HP-β-CD and ethanol 30% v/v (Rx 6).

a. At room temperature (30°C)

Source	df	SS	MS=SS/df	F
Among Groups	6	23.05	3.84	1.94
Within Group	14	27.70	1.98	
Total	20	50.75		

b. At 70°C

Source	df	SS	MS=SS/df	F
Amoung Groups	6	9.95	1.66	2.44
Within Group	14	9.53	0.68	
Total	20	19.48		

$F_{table(6,15)} = 2.64$

Level of significant = 0.05

df = Degree of freedom

SS = Sum of square

MS = Mean square

F = Variance ratio

One way ANOVA of stability data of minoxidil solutions containing HP-β-CD 5% w/v (Rx 7).

a. At room temperature (30°C)

Source	df	SS	MS=SS/df	F
Among Groups	6	5.18	0.86	1.41
Within Group	14	8.59	0.61	
Total	20	13.77		

b. At 70°C

Source	df	SS	MS=SS/df	F
Amoung Groups	6	4.19	0.70	1.32
Within Group	14	7.37	0.53	
Total	20	11.56		

$F_{table(6,15)} = 2.64$

Level of significant = 0.05

df = Degree of freedom

SS = Sum of square

MS = Mean square

F = Variance ratio

One way ANOVA of stability data of minoxidil solutions containing HP-β-CD 10% w/v (Rx 8).

a. At room temperature (30°C)

Source	df	SS	MS=SS/df	F
Among Groups	6	11.9	1.98	2.41
Within Group	14	11.47	0.82	
Total	20	13.37		

b. At 70°C

Source	df	SS	MS=SS/df	F
Amoung Groups	6	6.23	1.04	1.86
Within Group	14	7.90	0.56	
Total	20	14.13		

$F_{table(6,15)} = 2.64$

Level of significant = 0.05

df = Degree of freedom

SS = Sum of square

MS = Mean square

F = Variance ratio

One way ANOVA of stability data of minoxidil solutions containing HP-β-CD 15% w/v (Rx 9).

a. At room temperature (30°C)

Source	df	SS	MS=SS/df	F
Among Groups	6	4.48	0.75	1.01
Within Group	14	10.39	0.74	
Total	20	14.87		

b. At 70°C

Source	df	SS	MS=SS/df	F
Amoung Groups	6	10.64	1.77	2.64
Within Group	14	9.41	0.67	
Total	20	20.05		

$F_{table(6,15)} = 2.64$

Level of significant = 0.05

df = Degree of freedom

SS = Sum of square

MS = Mean square

F = Variance ratio

One way ANOVA of stability data of minoxidil solutions containing HP-β-CD 20% w/v (Rx 10).

a. At room temperature (30°C)

Source	df	SS	MS=SS/df	F
Among Groups	6	7.81	1.30	1.19
Within Group	14	15.26	1.09	
Total	20	23.07		

b. At 70°C

Source	df	SS	MS=SS/df	F
Amoung Groups	6	4.20	0.70	1.59
Within Group	14	6.17	0.44	
Total	20	10.37		

$F_{table(6,15)} = 2.64$

Level of significant = 0.05

df = Degree of freedom

SS = Sum of square

MS = Mean square

F = Variance ratio

Appendix IV

Thin layer chromatography (TLC) of minoxidil

Thin layer chromatography (TLC) of minoxidil (Gennaro, 1990).

System TA

Plates : Silica gel G, dipped in or spray with 0.1M potassium hydroxide in methanol and dried

Modile phase : Methanol : Strong ammonia solution (100 : 1.5)

Spraying reagent : Dragendorff reagent

Results : Orange spot

	a)	b)	c)	d)	e)	f)	g)
Rf value x 100	60	-	-	58	59	58	60

a) = minoxidil

b) = β-CD

c) = HP-β-CD

d) = minoxidil solution with β-CD at room temperature

e) = minoxidil solution with β-CD at 70°C

f) = minoxidil solution with HP-β-CD at room temperature

g) = minoxidil solution with HP-β-CD at 70°C

\- = any spots were not seen

System TC

Plates : Silica gel G, dipped in or spray with 0.1M potassium hydroxide in methanol and dried

Modile phase : Chloroform : Methanol (90 : 10)

Spraying reagent : Dragendorff reagent

Results : Orange spot

	a)	b)	c)	d)	e)	f)	g)
Rf value x 100	02	-	-	04	03	04	02

a) = minoxidil

b) = β-CD

c) = HP-β-CD

d) = minoxidil solution with β-CD at room temperature

e) = minoxidil solution with β-CD at 70°C

f) = minoxidil solution with HP-β-CD at room temperature

g) = minoxidil solution with HP-β-CD at 70°C

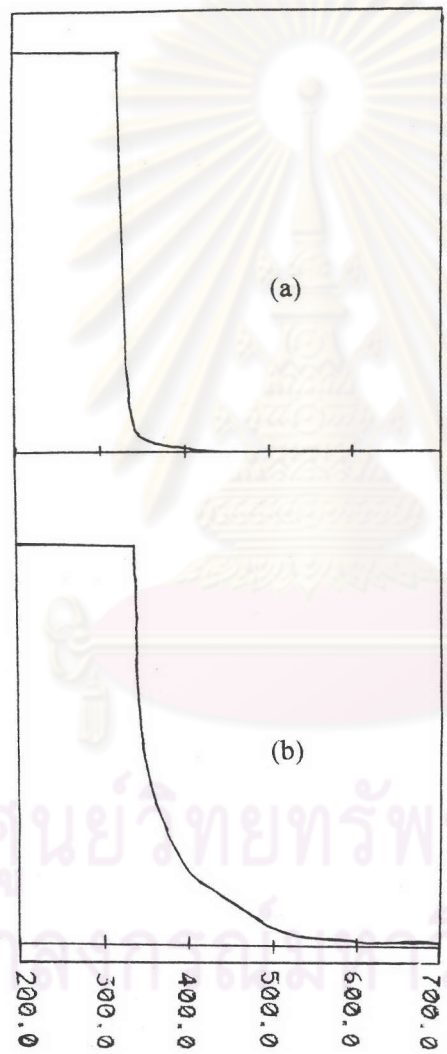
\- = any spots were not seen

Appendix V

The UV spectra of minoxidil sample solutions

The UV spectra of minoxidil

Sample	:	2% minoxidil solution (dilution 2 : 5)
Equipment	:	UV spectrophotometer, Hitachi 220A, Japan
Scan wavelength	:	200-700 nm.
Absorbance limit	:	0.0 - 1.0

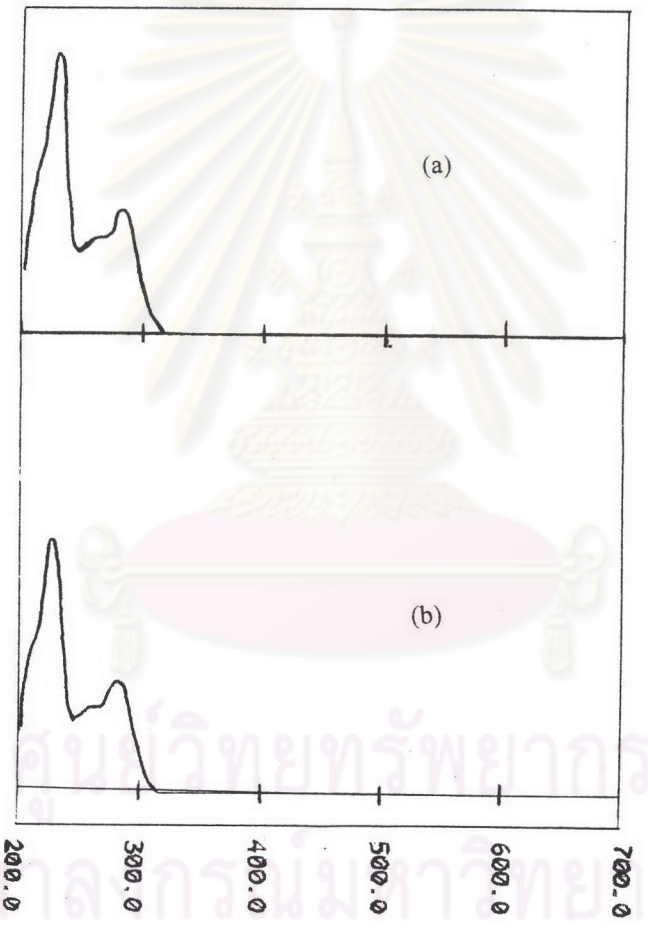


(a) minoxidil solution at room temperature

(b) minoxidil solution at 70°C

The UV spectra of minoxidil

Sample	:	2% minoxidil solution (dilution 1 : 5000)
Equipment	:	UV spectrophotometer, Hitachi 220A, Japan
Scan wavelength	:	200-700 nm.
Absorbance limit	:	0.0 - 1.0



(a) minoxidil solution at room temperature

(b) minoxidil solution at 70°C

Appendix VI

Data of the in vitro permeation of minoxidil through newborn pig skin

Rx 1 Regaine®

Calibration curve data

Concentration (mcg/ml)	0.0603	0.1005	0.2010	0.4020	0.6030	0.8040	1.0050
Peak area ratio	0.1186	0.2198	0.5211	1.0718	1.6056	2.2515	2.8714

$$y = -0.0755 + 2.8934x$$

$$r^2 = 0.9990$$

Permeation data

Permeation run	Run I		Run II		Run III	
Time (hour)	Peak area ratio	Amount (mcg)	Peak area ratio	Amount (mcg)	Peak area ratio	Amount (mcg)
0.33	0.4547	2.33	0.5671	2.89	0.5712	2.87
0.67	0.4437	2.28	1.0560	5.09	0.8257	4.01
1.0	0.6748	3.29	2.3439	10.88	1.2233	5.78
1.5	1.4382	6.65	2.1545	16.38	1.4229	10.88
2.0	1.4045	11.37	2.1060	16.02	1.7199	13.04
2.5	1.0865	12.50	1.1184	13.15	1.2029	13.93
3.5	0.9315	10.83	1.2334	14.42	2.0922	23.62
4.5	0.9154	10.66	1.3088	15.25	1.4329	21.91
6.0	0.6769	8.09	1.6349	18.84	1.7644	26.73
8.0	0.8453	6.60	1.1734	18.35	1.7962	27.19
12.0	1.0842	8.32	1.2028	18.78	2.3245	34.87
16.0	1.0698	8.21	0.6368	15.69	1.1728	27.20
20.0	0.8770	6.83	0.6453	15.88	0.8421	20.00
24.0	0.6929	5.51	0.4922	12.51	0.6205	15.17
Receptor volume (ml)	12.45		12.75		12.61	

Average amount of minoxidil in preparation = 19.05 ± 0.77 mg/ml

Permeation data per unit area

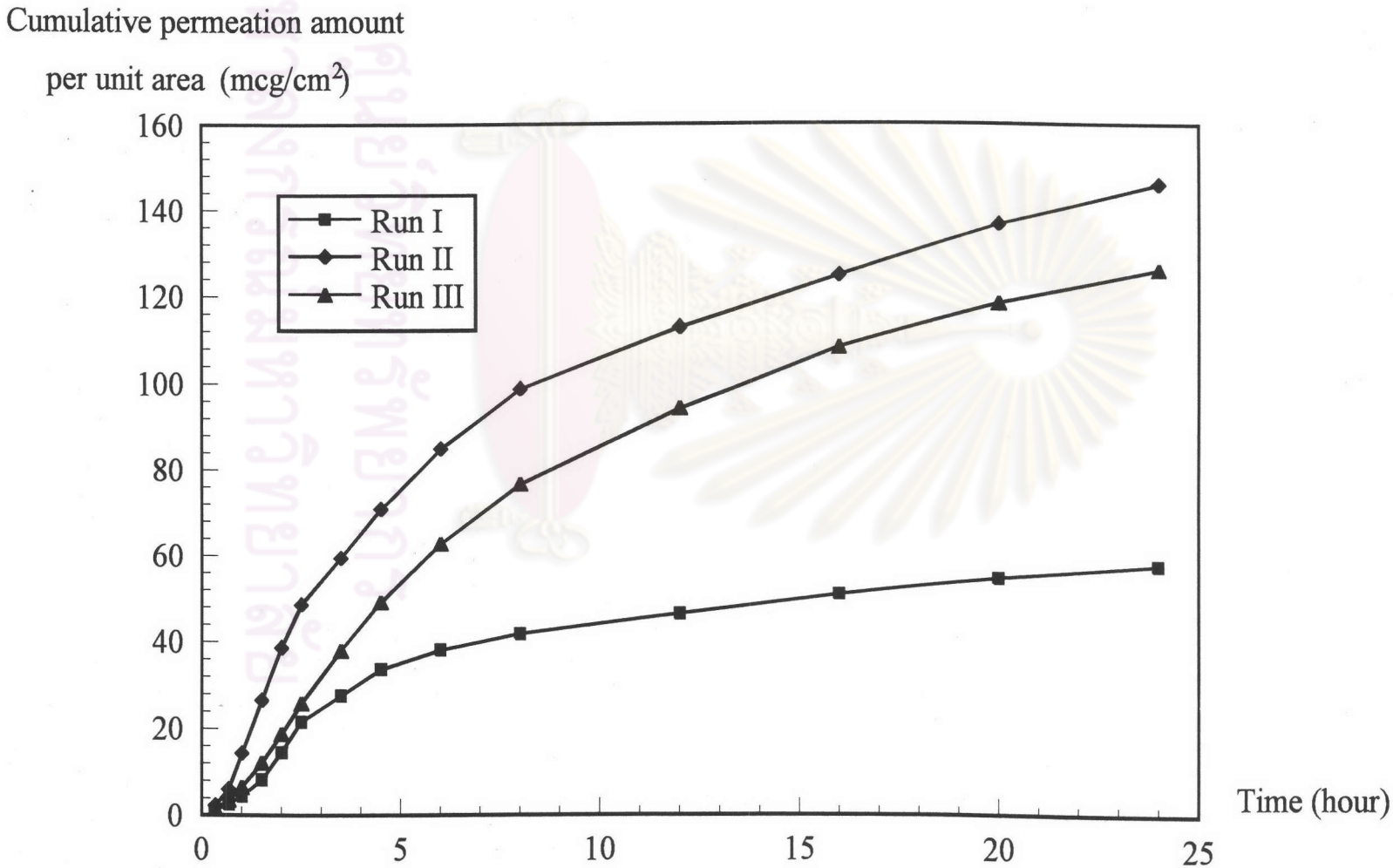
Permeation run	Run I	Run II	Run III
Time (hour)	Cumulative amount per unit area (mcg/cm^2)	Cumulative amount per unit area (mcg/cm^2)	Cumulative amount per unit area (mcg/cm^2)
0.33	1.30	2.17	1.46
0.67	2.57	6.0	3.51
1.0	4.41	14.18	6.46
1.5	8.13	26.50	12.01
2.0	14.48	38.54	18.66
2.5	21.46	48.43	25.77
3.5	27.51	59.27	37.82
4.5	33.47	70.74	49.0
6.0	37.99	84.90	62.64
8.0	41.67	98.70	76.51
12.0	46.32	112.82	94.30
16.0	50.91	124.62	108.18
20.0	54.73	136.56	118.38
24.0	57.80	145.96	126.12
Jss ($mcg/h/cm^2$) (1.5-4.5 h)	8.2009	14.1269	12.3279
r^2	0.9602	0.9697	0.9980
Permeation area (cm^2)	1.79	1.33	1.96
Membrane thickness (cm)	0.0273	0.0288	0.0283
Normalized Jss ($mcg/h/cm^2$)	8.2920	15.0687	12.9215

Average normalized Jss = 12.0941 ± 3.4633 ($mcg/h/cm^2$)

% cv = 28.64

Minoxidil flux from the commercial minoxidil solutions Rx 1 Regaine ®

through newborn pig skin



Rx 2 Containing no β-CD and ethanol 40% v/v

Calibration curve data

Concentration (mcg/ml)	0.0201	0.0603	0.1005	0.2010	0.4020	0.6030	0.8040	1.0050
Peak area ratio	0.0554	0.1535	0.2444	0.5218	1.0265	1.5097	2.0583	2.5386

$$y = 1.8265 \times 10^{-3} + 2.5325x$$

$$r^2 = 0.9998$$

Permeation data

Permeation run	Run I		Run II		Run III	
Time (hour)	Peak area ratio	Amount (mcg)	Peak area ratio	Amount (mcg)	Peak area ratio	Amount (mcg)
0.33	0.2123	1.06	1.6905	42.15	0.6061	3.07
0.67	1.2150	66.85	1.6671	41.92	0.5622	15.50
1.0	1.2757	31.59	0.8579	21.55	1.5743	39.15
1.5	1.4599	36.15	1.5256	38.36	2.4810	61.72
2.0	1.3814	34.21	1.8784	47.24	1.8784	46.72
2.5	1.1656	28.86	0.6029	15.13	1.4411	71.66
3.0	0.6589	16.29	0.3541	8.87	1.0067	50.04
4.0	1.0414	25.78	0.6910	17.35	1.6753	83.33
6.0	1.8063	44.74	0.5170	12.97	1.8820	93.62
8.0	1.0533	52.15	0.4815	12.07	2.0327	101.12
12.0	0.9505	47.05	0.5687	14.27	0.7329	72.81
16.0	0.6145	30.38	0.3408	8.53	0.5872	58.28
20.0	0.8366	41.40	0.5395	6.77	1.2275	61.03
24.0	0.4964	24.53	0.2886	3.61	0.5345	26.52
Receptor volume (ml)	12.56		12.75		12.61	

Average amount of minoxidil in preparation = 19.44 ± 1.05 mg/ml

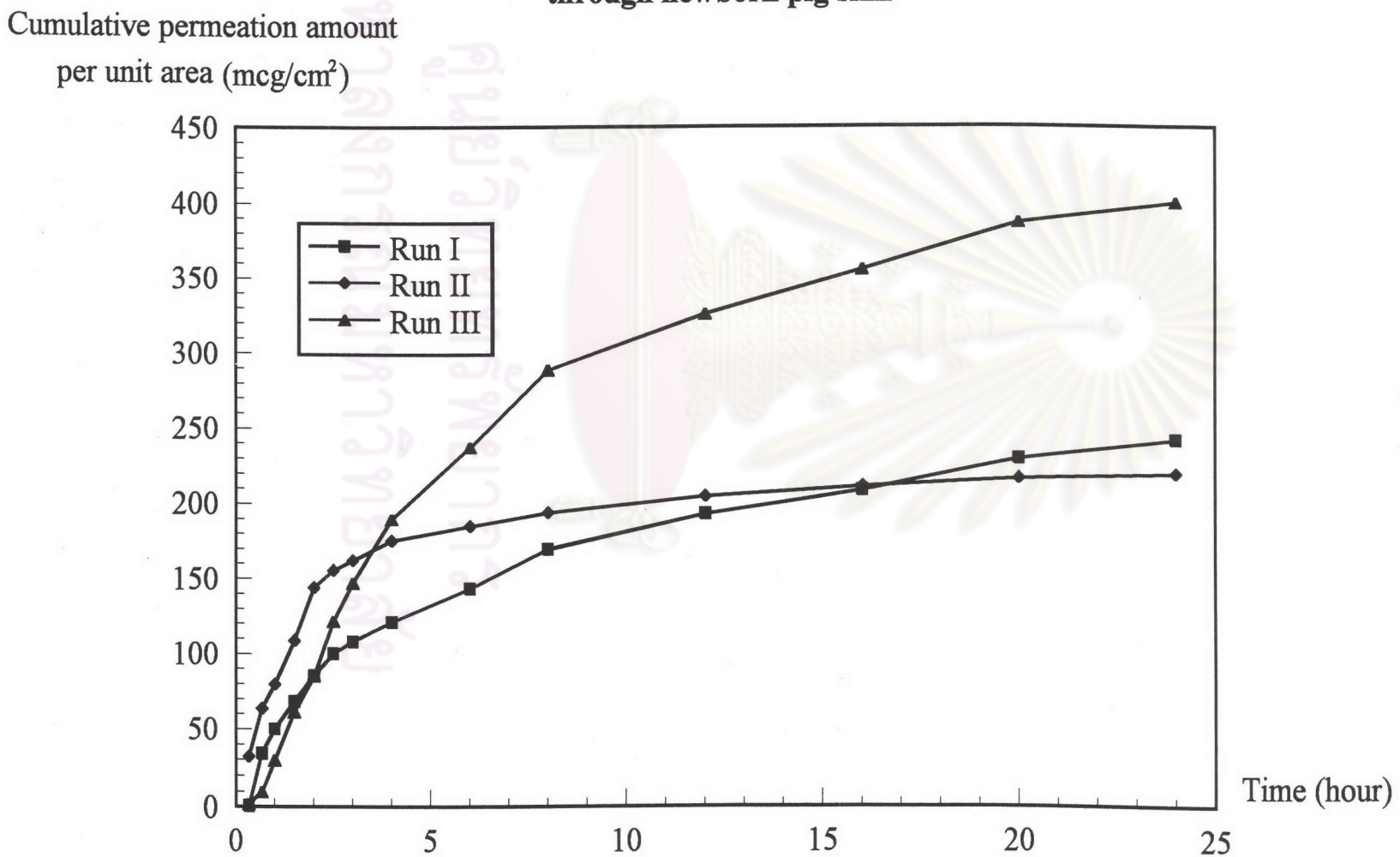
Permeation data per unit area

Permeation run	Run I	Run II	Run III
Time (hour)	Cumulative amount per unit area (mcg/cm^2)	Cumulative amount per unit area (mcg/cm^2)	Cumulative amount per unit area (mcg/cm^2)
0.33	0.53	31.96	1.57
0.67	34.12	63.48	9.47
1.0	50.00	79.68	29.45
1.5	68.16	108.53	60.94
2.0	85.36	144.04	84.77
2.5	99.86	155.42	121.34
3.0	108.04	162.09	146.88
4.0	121.00	175.13	189.38
6.0	143.48	184.89	237.15
8.0	169.69	193.96	288.74
12.0	193.33	204.69	325.89
16.0	208.60	211.10	355.62
20.0	229.40	219.19	386.76
24.0	241.73	218.91	400.29
Jss ($mcg/h/cm^2$) (1.5-3.0 h)	26.8280	34.4120	58.8780
r^2	0.9772	0.8671	0.9933
Permeation area (cm^2)	1.99	1.33	1.96
Membrane thickness (cm)	0.0283	0.0285	0.0266
Normalized Jss ($mcg/h/cm^2$)	28.1197	36.3238	58.0057

Average normalized Jss = 40.8164 ± 15.4412 ($mcg/h/cm^2$)

% cv = 37.83

Minoxidil flux from minoxidil solutions Rx 2 containing no β– CD and ethanol 40% v/v through newborn pig skin



Rx 3 Containing β-CD 0.1% w/v

Calibration curve data

Concentration (mcg/ml)	0.0402	0.0603	0.1005	0.2010	0.4020	0.6030	0.8040	1.0050
Peak area ratio	0.0528	0.1268	0.2320	0.5180	1.0385	1.7008	2.2769	2.8258

$$y = -0.0631 + 2.8845x$$

$$r^2 = 0.9994$$

Permeation data

Permeation run	Run I		Run II		Run III	
Time (hour)	Peak area ratio	Amount (mcg)	Peak area ratio	Amount (mcg)	Peak area ratio	Amount (mcg)
0.33	0.2100	1.20	0.1352	0.88	0.2943	1.57
0.67	0.6113	2.97	0.2598	1.43	0.7270	3.46
1.0	0.9902	4.64	0.4455	2.26	1.1529	5.33
1.5	1.7417	7.95	0.8169	3.91	2.1810	9.84
2.0	1.7499	13.04	1.2204	5.70	1.7202	12.76
2.5	2.0787	15.41	1.5057	6.97	1.2481	14.08
3.0	1.2941	14.46	1.8918	8.68	1.4159	15.88
4.0	1.4575	16.41	1.4297	13.00	1.9709	21.84
6.0	1.8596	20.74	1.4747	22.32	2.7719	30.44
8.0	1.5758	23.58	1.7041	25.65	1.8713	27.69
12.0	2.1217	31.43	1.7264	25.97	2.1477	31.65
16.0	1.3114	29.66	1.2020	27.54	1.3234	29.78
20.0	1.2562	28.47	1.1846	27.17	1.1720	26.53
24.0	1.0017	22.98	0.9885	22.90	0.9959	22.74
Receptor volume (ml)	12.45		12.56		12.39	

Average amount of minoxidil in preparation = 19.46 ± 1.01 mg/ml

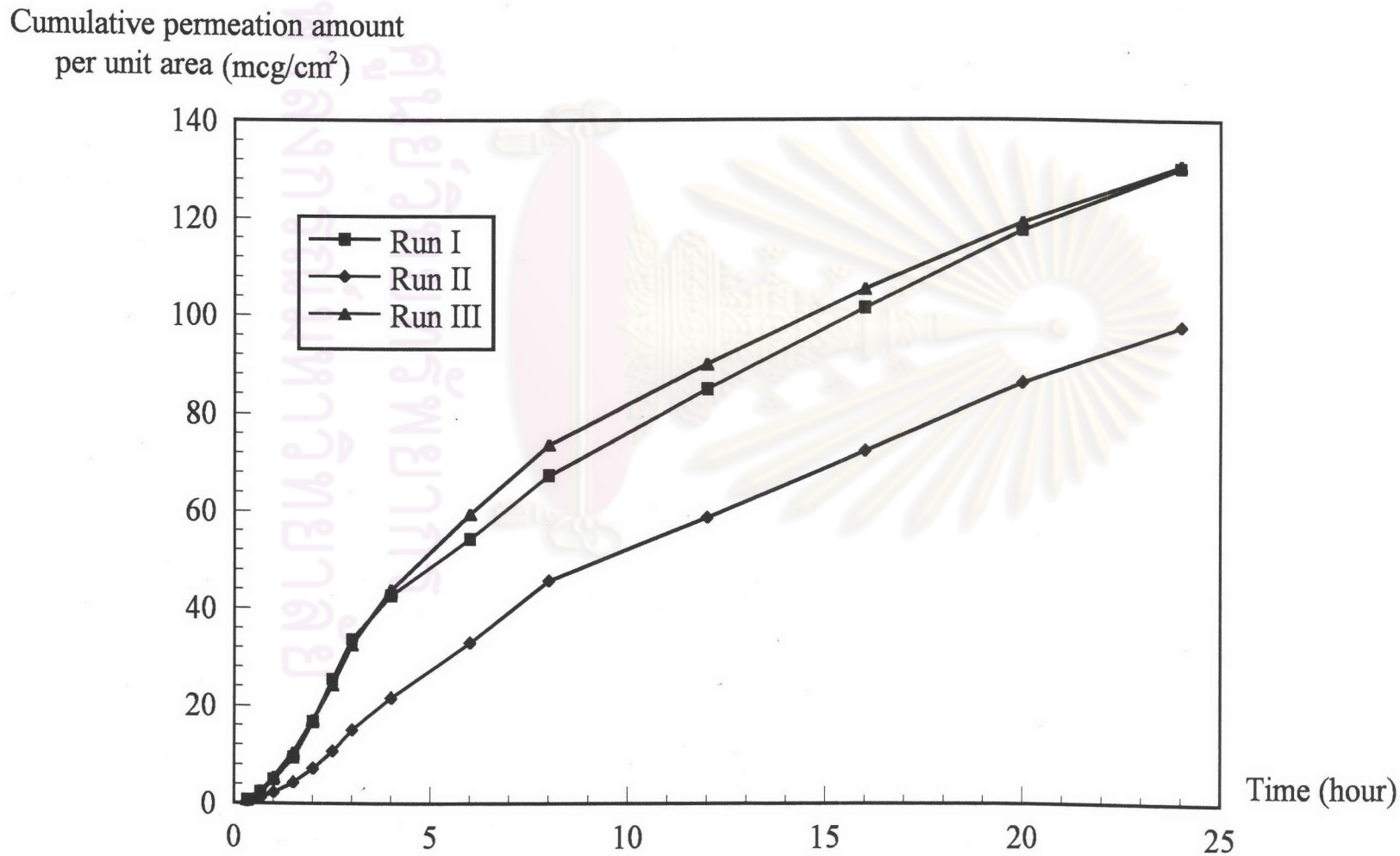
Permeation data per unit area

Permeation run	Run I	Run II	Run III
Time (hour)	Cumulative amount per unit area (mcg/cm^2)	Cumulative amount per unit area (mcg/cm^2)	Cumulative amount per unit area (mcg/cm^2)
0.33	0.67	0.44	0.81
0.67	2.33	1.16	2.59
1.0	4.92	2.30	5.34
1.5	9.36	4.26	10.41
2.0	16.65	7.12	16.99
2.5	25.26	10.63	24.25
3.0	33.43	14.99	32.43
4.0	42.60	21.52	43.69
6.0	54.19	32.74	59.38
8.0	67.36	45.63	73.65
12.0	84.92	58.68	89.97
16.0	101.49	72.52	105.32
20.0	117.40	86.17	118.99
24.0	130.23	97.68	130.72
Jss ($mcg/h/cm^2$) (1.5-4.0 h)	13.5676	7.0549	13.5319
r^2	0.9812	0.9969	0.9955
Permeation area (cm^2)	1.79	1.99	1.94
Membrane thickness (cm)	0.0261	0.0264	0.0282
Normalized Jss ($mcg/h/cm^2$)	13.1153	6.8981	14.1333

Average normalized Jss = 11.3822 ± 3.9166 ($mcg/h/cm^2$)

% cv = 34.41

Minoxidil flux from minoxidil solutions Rx 3 containing β-CD 0.1% w/v through newborn pig skin



Rx 4 Containing β-CD 0.4% w/v

Calibration curve data

Concentration (mcg/ml)	0.0402	0.0603	0.1005	0.2010	0.4020	0.6030	0.8040	1.0050
Peak area ratio	0.0528	0.1268	0.2320	0.5180	1.0385	1.7008	2.2769	2.8258

$$y = -0.0631 + 2.8845x$$
$$r^2 = 0.9994$$

Permeation data

Permeation run	Run I		Run II		Run III	
Time (hour)	Peak area ratio	Amount (mcg)	Peak area ratio	Amount (mcg)	Peak area ratio	Amount (mcg)
0.33	0.0663	0.57	0.1076	0.76	0.1702	1.04
0.67	0.1495	0.94	0.2551	1.41	0.4039	2.08
1.0	0.2009	1.16	0.3783	1.96	0.6664	3.25
1.5	0.4562	2.29	0.7297	3.52	1.2371	5.80
2.0	0.7356	3.52	1.0146	4.79	1.5073	7.00
2.5	0.8831	4.17	1.0567	4.97	1.6803	7.78
3.0	0.8753	4.13	1.0271	4.84	1.3812	7.89
4.0	1.0467	4.89	1.3032	6.07	1.6672	9.45
6.0	1.2598	5.83	1.5524	7.18	2.1617	12.16
8.0	1.2157	5.63	1.4965	6.93	2.2602	12.69
12.0	1.4671	8.25	2.4268	11.06	2.4621	18.40
16.0	1.3544	10.20	0.3703	14.51	1.6419	18.63
20.0	1.1402	8.66	0.6581	15.70	1.3263	15.18
24.0	1.0276	7.84	0.7352	17.38	0.9319	10.88
Receptor volume (ml)	12.45		12.56		12.61	

Average amount of minoxidil in preparation = 18.66 ± 0.33 mg/ml

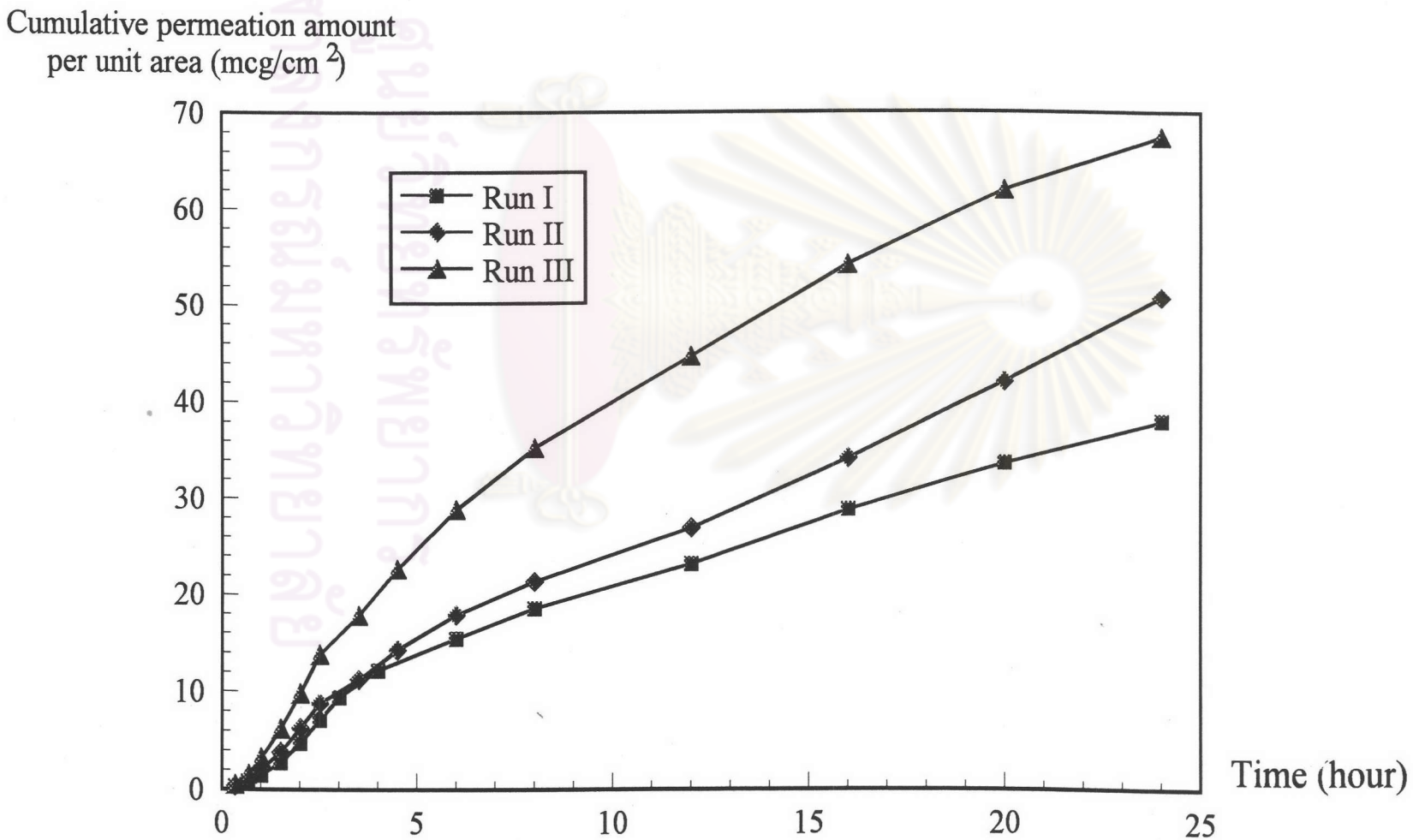
Permeation data per unit area

Permeation run	Run I	Run II	Run III
Time (hour)	Cumulative amount per unit area (mcg/cm^2)	Cumulative Amount per unit area (mcg/cm^2)	Cumulative Amount per unit area (mcg/cm^2)
0.33	0.32	0.38	0.53
0.67	0.84	1.09	1.59
1.0	1.49	2.07	3.25
1.5	2.77	3.84	6.21
2.0	4.74	6.25	9.78
2.5	7.07	8.75	13.75
3.0	9.37	11.18	17.77
4.0	12.11	14.23	22.60
6.0	15.36	17.84	28.80
8.0	18.51	21.32	35.27
12.0	23.12	26.88	44.66
16.0	28.82	34.17	54.17
20.0	33.65	42.06	61.91
24.0	38.03	50.79	67.46
Jss ($mcg/h/cm^2$) (1.5-3.0 h)	4.4260	4.9040	7.7300
r^2	0.9986	0.9999	0.9992
Permeation area (cm^2)	1.79	1.99	1.96
Membrane thickness (cm)	0.0332	0.0273	0.0229
Normalized Jss ($mcg/h/cm^2$)	5.4497	4.9585	6.5562

Average normalized Jss = 5.6548 ± 0.8183 ($mcg/h/cm^2$)

% cv = 14.47

Minoxidil flux from minoxidil solutions Rx 4 containing β-CD 0.4 % w/v Through newborn pig skin



Rx 5 Containing β-CD 0.7% w/v

Calibration curve data

Concentration (mcg/ml)	0.0603	0.1005	0.2010	0.4020	0.6030	0.8040	1.0050
Peak area ratio	0.1186	0.2198	0.5211	1.0718	1.6056	2.2515	2.8714

$$y = -0.0755 + 2.8934x$$
$$r^2 = 0.9990$$

Permeation data

Permeation run	Run I		Run II		Run III	
Time (hour)	Peak area ratio	Amount (mcg)	Peak area ratio	Amount (mcg)	Peak area ratio	Amount (mcg)
0.33	0.2796	1.56	0.1225	0.88	0.1207	0.88
0.67	0.4422	2.27	0.1717	1.09	0.1501	1.01
1.0	0.5836	2.89	0.2986	1.66	0.2295	1.37
1.5	1.0314	4.86	0.5485	2.76	0.4439	2.33
2.0	1.3823	6.40	0.6913	3.40	0.4898	2.54
2.5	1.5568	7.17	0.7942	3.85	0.5050	2.61
3.0	1.3225	7.52	0.8224	3.98	0.5015	2.59
4.0	1.6796	9.44	0.9027	4.33	0.5045	2.61
6.0	1.8514	13.84	1.2203	5.74	0.8572	4.19
8.0	1.8590	13.87	1.3712	6.41	1.0669	5.14
12.0	2.1371	15.87	1.5691	7.28	1.8128	8.49
16.0	2.0416	15.18	1.9066	8.78	1.6907	7.94
20.0	1.2321	14.06	1.3381	6.26	1.4572	6.89
24.0	1.1623	13.31	1.0505	4.99	1.1159	5.36
Receptor volume (ml)	12.45		12.56		12.75	

Average amount of minoxidil in preparation = 20.50 ± 1.26 mg/ml

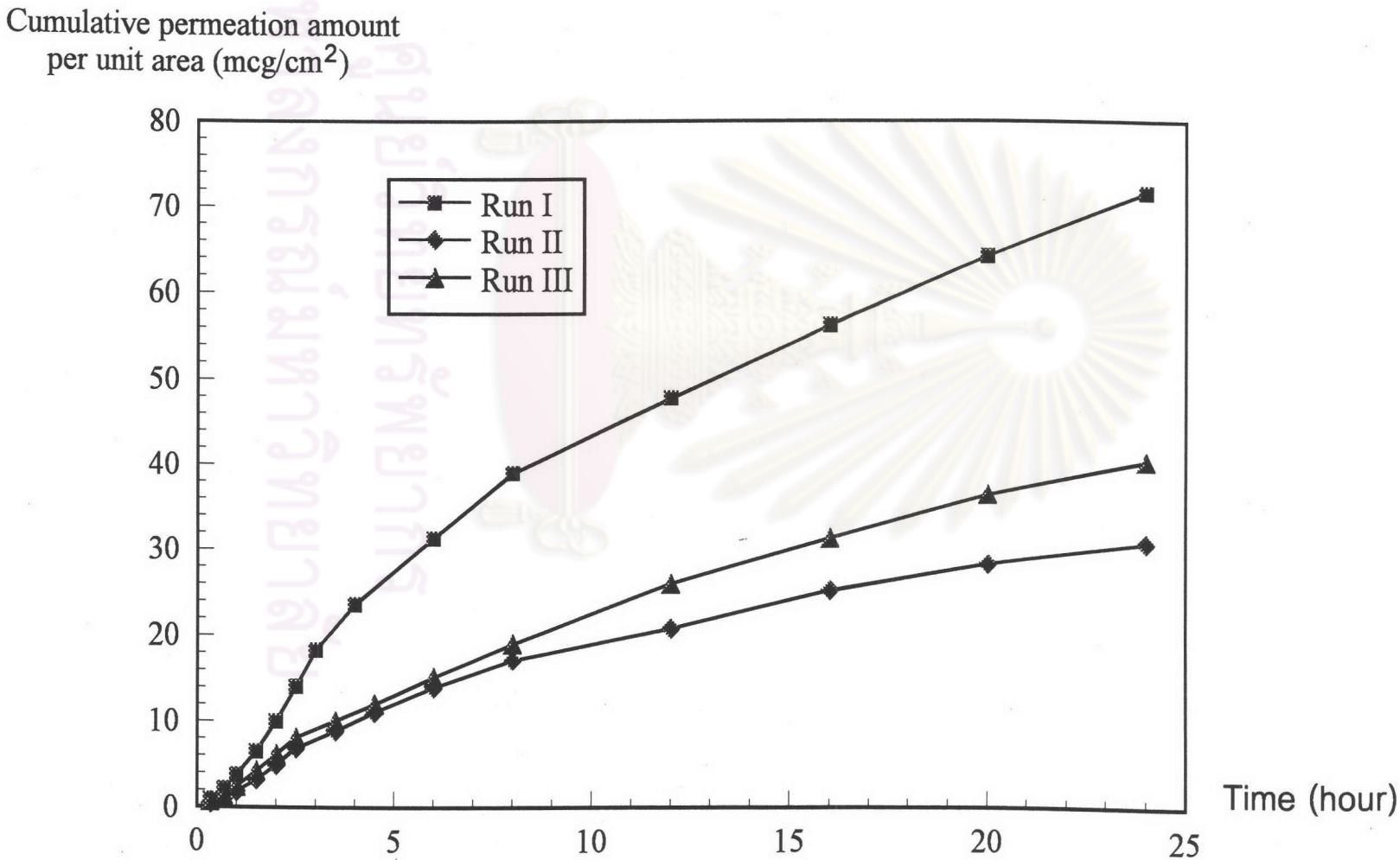
Permeation data per unit area

Permeation run	Run I	Run II	Run III
Time (hour)	Cumulative amount per unit area (mcg/cm^2)	Cumulative amount per unit area (mcg/cm^2)	Cumulative amount per unit area (mcg/cm^2)
0.33	0.87	0.44	0.66
0.67	2.14	0.99	1.42
1.0	3.75	1.82	2.45
1.5	6.47	3.21	4.20
2.0	10.04	4.92	6.11
2.5	14.05	6.85	8.07
3.0	18.25	8.85	10.02
4.0	23.52	11.03	11.98
6.0	31.26	13.91	15.13
8.0	39.00	17.13	19.00
12.0	47.87	20.79	25.97
16.0	56.35	25.21	31.35
20.0	64.21	28.35	36.53
24.0	71.64	30.86	40.56
Jss ($mcg/h/cm^2$) (1.5-3.0 h)	7.8700	3.7700	3.8840
r^2	0.9987	0.9987	0.9999
Permeation area (cm^2)	1.79	1.99	1.33
Membrane thickness (cm)	0.0230	0.0263	0.0248
Normalized Jss ($mcg/h/cm^2$)	6.7041	3.6722	3.5675

Average normalized Jss = 4.6479 ± 1.7815 ($mcg/h/cm^2$)

% cv = 38.33

Minoxidil flux from minoxidil solutions Rx 5 containing β-CD 0.7% w/v through newborn pig skin



Rx 6 Containing no HP-β-CD and ethanol 30% v/v

Calibration curve data

Concentration (mcg/ml)	0.1005	0.2010	0.4020	0.6030	0.8040	1.0050
Peak area ratio	0.2859	0.5326	1.0101	1.5483	1.9591	2.6562

$$y = 5.1427 \times 10^{-3} + 2.5554x$$
$$r^2 = 0.9955$$

Permeation data

Permeation run	Run I		Run II		Run III	
Time (hour)	Peak area ratio	Amount (mcg)	Peak area ratio	Amount (mcg)	Peak area ratio	Amount (mcg)
0.33	0.5912	9.51	0.4850	3.88	0.6025	3.27
0.67	0.4487	21.61	0.4355	10.43	0.6814	8.34
1.0	0.3912	26.87	0.6671	16.04	0.5396	13.18
2.0	0.6701	64.79	0.4497	43.12	0.6467	31.66
3.0	0.7459	72.18	0.9514	45.88	0.6706	32.84
4.0	0.7793	75.42	0.9550	46.05	0.5695	27.84
6.0	1.0354	100.40	1.2330	59.33	0.6356	31.00
8.0	1.2403	120.34	1.2182	58.81	0.5477	26.77
12.0	1.3626	132.27	1.4049	67.87	0.5785	28.30
16.0	1.8133	176.19	1.4322	69.18	0.5975	29.23
20.0	1.4663	142.38	1.6408	79.31	0.5436	26.57
24.0	1.0038	97.31	1.5631	75.54	0.3358	16.32
Receptor volume (ml)	12.45		12.39		12.61	

Average amount of minoxidil in preparation = 18.72 ± 1.93 mg/ml

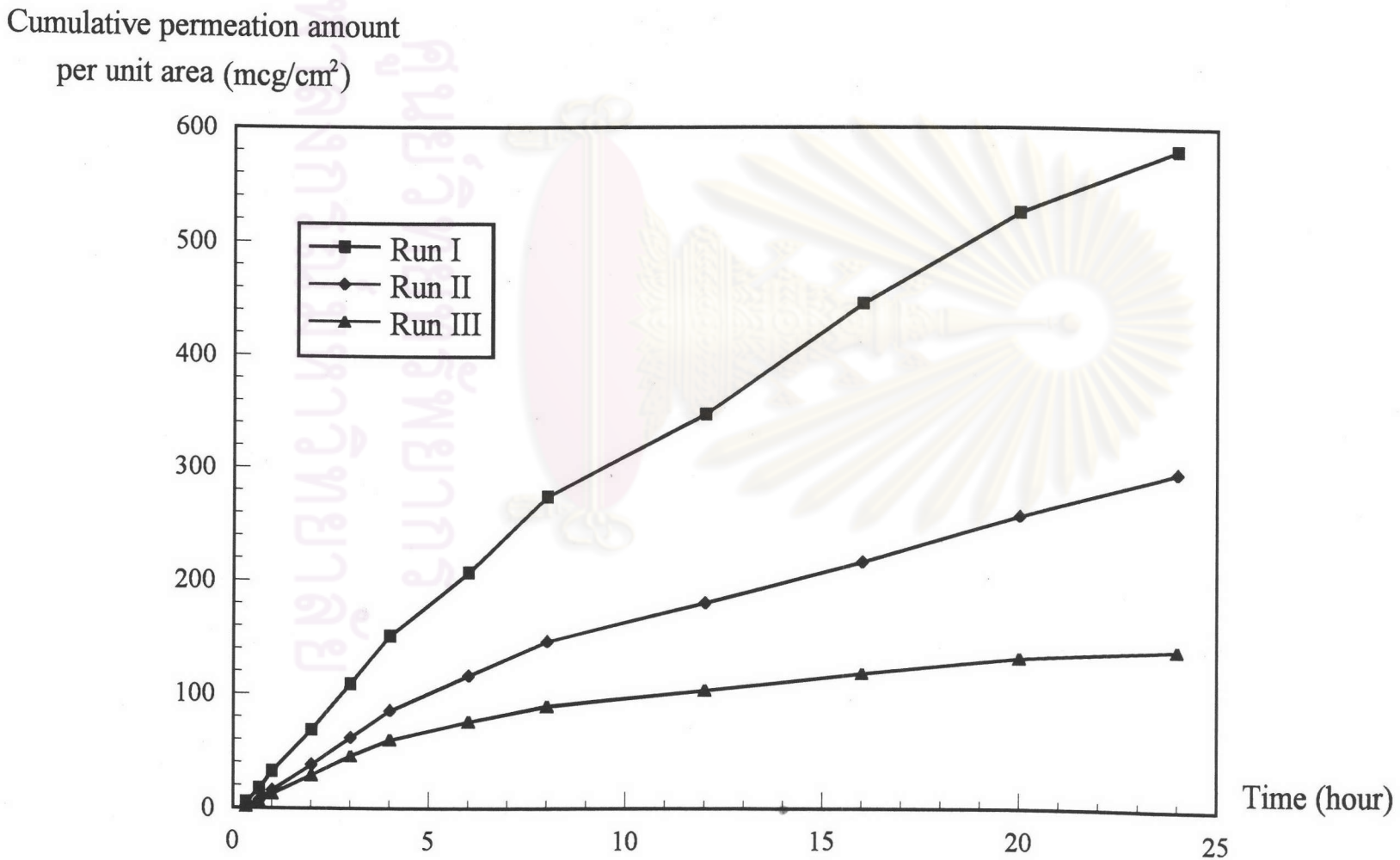
Permeation data per unit area

Permeation run	Run I	Run II	Run III
Time (hour)	Cumulative amount per unit area (mcg/cm^2)	Cumulative amount per unit area (mcg/cm^2)	Cumulative amount per unit area (mcg/cm^2)
0.33	5.31	2.00	1.67
0.67	17.38	7.38	5.92
1.0	32.40	15.64	12.65
2.0	68.59	37.87	28.80
3.0	108.92	61.52	45.56
4.0	151.05	85.26	59.76
6.0	207.14	115.94	75.63
8.0	274.37	146.26	89.29
12.0	348.26	181.24	103.73
16.0	446.69	216.90	118.64
20.0	526.23	257.78	132.20
24.0	580.60	296.72	140.52
Jss ($mcg/h/cm^2$) (1.0-4.0 h)	39.6280	23.2510	15.8090
r^2	0.9988	0.9997	0.9988
Permeation area (cm^2)	1.79	1.94	1.96
Membrane thickness (cm)	0.0242	0.0276	0.0237
Normalized Jss ($mcg/h/cm^2$)	35.5184	23.7677	13.8768

Average normalized Jss = 24.3876 ± 10.8341 ($mcg/h/cm^2$)

% cv = 44.42

Minoxidil flux from minoxidil solutions Rx 6 containing no HP- β-CD and ethanol 30% v/v through newborn pig skin



Rx 7 Containing HP-β-CD 5 % w/v

Calibration curve data

Concentration (mcg/ml)	0.1005	0.2010	0.4020	0.6030	0.8040	1.0050
Peak area ratio	0.2526	0.5013	1.0588	1.7437	2.0747	2.9391

$$y = -0.0717 + 2.8889x$$
$$r^2 = 0.9903$$

Permeation data

Permeation run	Run I		Run II		Run III	
Time (hour)	Peak area ratio	Amount (mcg)	Peak area ratio	Amount (mcg)	Peak area ratio	Amount (mcg)
0.33	0.3969	2.22	0.5215	3.18	0.7088	4.54
0.67	0.3600	18.71	0.3428	8.89	0.5208	12.92
1.0	0.5112	25.24	0.6081	14.58	0.6766	16.33
2.0	0.3343	35.17	0.6291	30.06	0.6643	32.10
3.0	0.5177	51.24	0.9768	44.96	1.0653	49.56
5.0	0.8312	38.84	1.7767	79.27	1.5978	72.88
6.0	0.7105	33.91	1.5120	67.92	0.6008	58.66
8.0	0.5418	26.63	2.0792	92.24	0.6225	60.53
12.0	1.0017	23.30	0.6253	99.65	1.2693	117.02
16.0	0.9300	21.77	0.7255	85.46	1.2045	111.37
20.0	0.8156	19.28	0.4668	57.74	0.8085	76.67
24.0	0.8037	19.02	0.5996	57.59	0.6028	58.76
Receptor volume (ml)	12.56		12.39		12.61	

Average amount of minoxidil in preparation = 18.39 ± 0.87 mg/ml

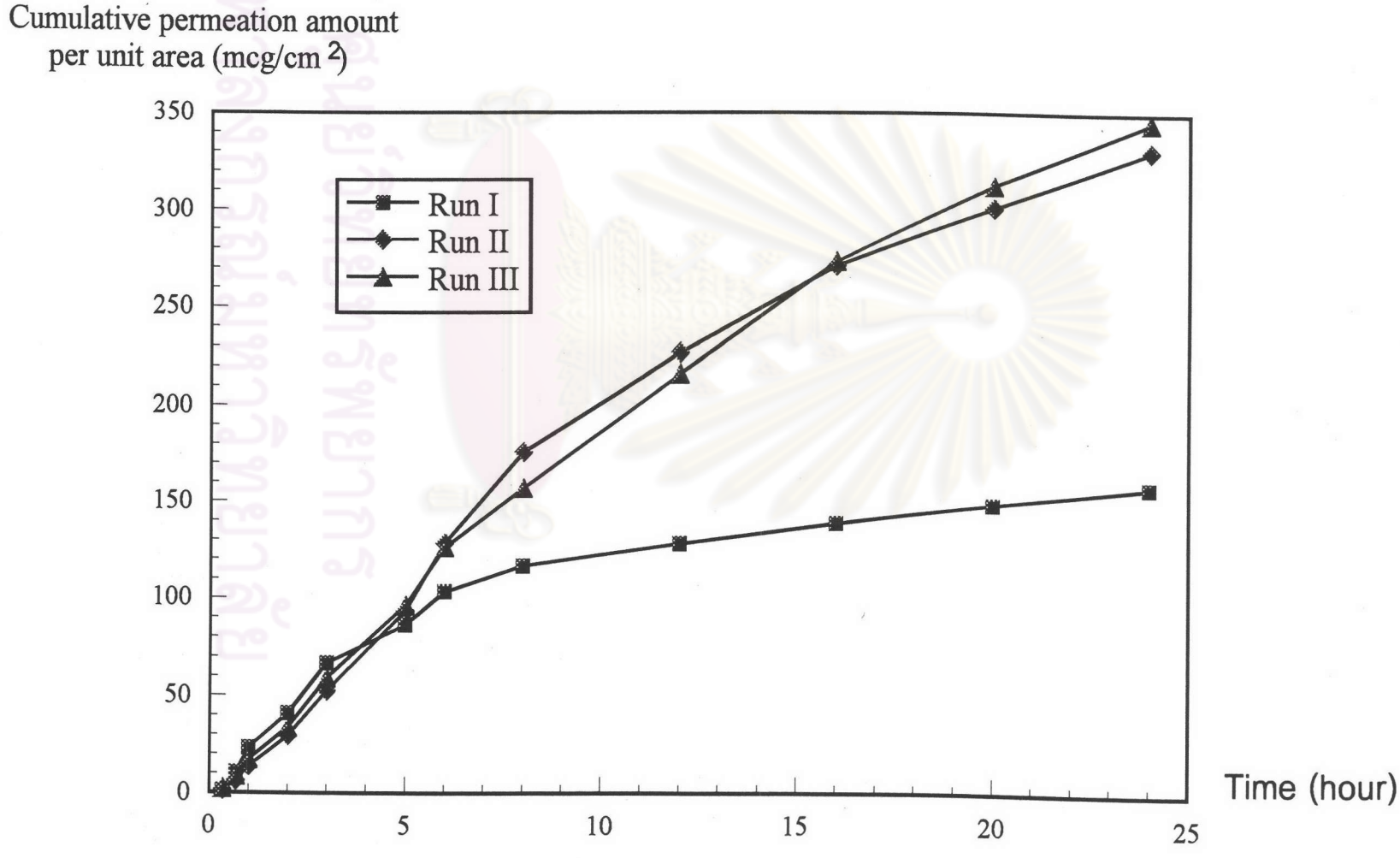
Permeation data per unit area

Permeation run	Run I	Run II	Run III
Time (hour)	Cumulative amount per unit area (mcg/cm^2)	Cumulative amount per unit area (mcg/cm^2)	Cumulative amount per unit area (mcg/cm^2)
0.33	1.11	1.64	2.32
0.67	10.52	6.22	8.91
1.0	23.20	13.74	17.24
2.0	40.87	29.23	33.62
3.0	66.62	52.41	58.90
5.0	86.14	93.27	96.09
6.0	103.18	128.28	126.01
8.0	116.56	175.82	156.90
12.0	128.27	227.19	216.60
16.0	139.21	271.24	273.42
20.0	148.90	301.00	312.54
24.0	158.46	330.69	345.52
Jss ($mcg/h/cm^2$) (1.0-8.0 hr)	15.4969	23.5089	20.5662
r^2	0.9761	0.9928	0.9947
Permeation area (cm^2)	1.99	1.94	1.96
Membrane thickness (cm)	0.0243	0.0245	0.0230
Normalized Jss ($mcg/h/cm^2$)	13.9472	21.3321	17.5193

Average normalized Jss = 17.5995 ± 3.6931 ($mcg/h/cm^2$)

% cv = 20.98

Minoxidil flux from minoxidil solutions Rx 7 containing HP- β-CD 5% w/v through newborn pig skin



Rx 8 Containing HP-β-CD 10 % w/v

Calibration curve data

Concentration (mcg/ml)	0.1005	0.2010	0.4020	0.6030	0.8040	1.0050
Peak area ratio	0.2526	0.5013	1.0588	1.7437	2.0747	2.9391

$$y = -0.0717 + 2.8889x$$
$$r^2 = 0.9903$$

Permeation data

Permeation run	Run I		Run II		Run III	
Time (hour)	Peak area ratio	Amount (mcg)	Peak area ratio	Amount (mcg)	Peak area ratio	Amount (mcg)
0.33	0.3144	1.84	0.6427	3.13	0.3360	2.22
0.67	0.4809	4.79	0.8680	5.04	0.6666	8.04
1.0	0.6609	7.87	1.4423	12.99	1.1886	13.74
2.0	1.9446	21.72	1.0717	24.52	1.9283	29.09
3.0	0.5245	34.66	0.8457	39.34	0.8679	40.98
4.0	0.8496	39.68	0.9917	45.16	1.1026	51.20
6.0	0.6497	62.00	1.3795	62.23	0.6807	65.57
8.0	0.7935	74.45	1.5401	69.12	0.8835	83.23
12.0	1.1201	102.59	2.0216	89.78	1.3146	121.05
16.0	0.9682	89.59	1.9201	85.43	1.2627	116.46
20.0	0.8417	78.68	1.8443	82.17	0.9984	93.31
24.0	0.5624	54.53	1.6186	72.49	0.7187	68.85
Receptor volume (ml)	12.45		12.39		12.61	

Average amount of minoxidil in preparation = 17.31 ± 0.44 mg/ml

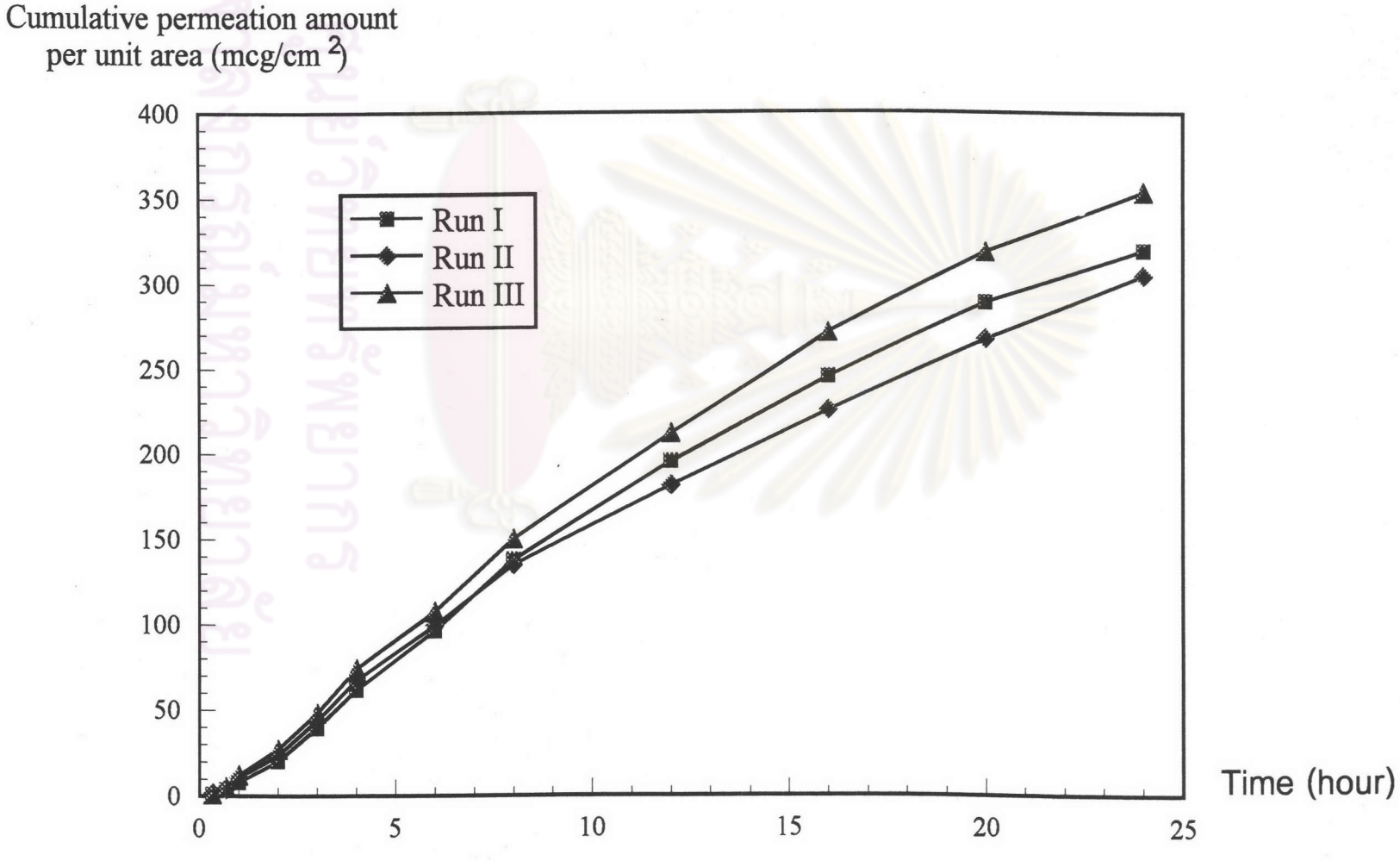
Permeation data per unit area

Permeation run	Run I	Run II	Run III
Time (hour)	Cumulative amount per unit area (mcg/cm^2)	Cumulative amount per unit area (mcg/cm^2)	Cumulative amount per unit area (mcg/cm^2)
0.33	1.03	1.61	1.13
0.67	3.68	4.21	5.23
1.0	8.08	10.91	12.24
2.0	20.21	23.55	27.09
3.0	39.57	43.82	47.99
4.0	61.74	67.33	74.12
6.0	96.38	99.41	107.57
8.0	137.97	135.04	150.03
12.0	195.28	181.32	211.79
16.0	245.33	225.35	271.21
20.0	289.29	267.71	318.82
24.0	319.75	305.08	353.95
Jss ($mcg/h/cm^2$) (2.0-8.0 h)	19.4452	18.3866	20.2059
r^2	0.9989	0.9963	0.9966
Permeation area (cm^2)	1.79	1.94	1.96
Membrane thickness (cm)	0.0277	0.0294	0.0284
Normalized Jss ($mcg/h/cm^2$)	19.9493	20.0210	21.2641

Average normalized Jss = 20.4115 ± 0.7393 ($mcg/h/cm^2$)

% cv = 3.62

Minoxidil flux from minoxidil solutions Rx 8 containing HP- β-CD 10% w/v through newborn pig skin



Rx 9 Containing HP-β-CD 15 % w/v

Calibration curve data

Concentration (mcg/ml)	0.2010	0.0603	0.1005	0.2010	0.4020	0.6030	0.8040	1.0050
Peak area ratio	0.0485	0.1474	0.2535	0.5296	1.0969	1.6138	2.1283	2.6678

$$y = -0.0044 + 2.6662x$$
$$r^2 = 0.9998$$

Permeation Data

Permeation run	Run I		Run II		Run III	
Time (hour)	Peak area ratio	Amount (mcg)	Peak area ratio	Amount (mcg)	Peak area ratio	Amount (mcg)
0.33	0.4654	2.26	0.4715	2.26	0.9460	4.59
0.67	0.8580	20.31	1.0668	5.08	0.5801	13.82
1.0	0.9612	22.74	1.8000	8.56	0.9576	22.75
1.5	0.8519	20.34	0.6588	15.41	0.7263	17.27
2.0	0.9022	21.35	0.7482	17.49	0.9225	21.92
2.5	0.7912	18.74	0.7283	17.02	1.0089	23.96
3.0	0.6532	15.49	0.7794	18.21	1.1166	26.51
4.0	1.4293	33.76	1.1323	26.41	1.6032	38.01
6.0	1.6671	39.37	1.9222	44.76	1.4676	34.81
8.0	1.2552	29.67	2.4108	56.11	1.7599	41.72
12.0	0.8196	19.40	1.6454	76.67	1.2199	28.95
16.0	0.4568	10.86	1.5111	70.42	1.3837	32.82
20.0	0.3576	8.53	0.9947	46.42	1.3461	31.93
24.0	0.5684	6.74	0.6550	30.64	1.0860	25.79
Receptor volume (ml)	12.56		12.39		12.61	

Average amount of minoxidil in preparation = 16.55 ± 0.99 mg/ml

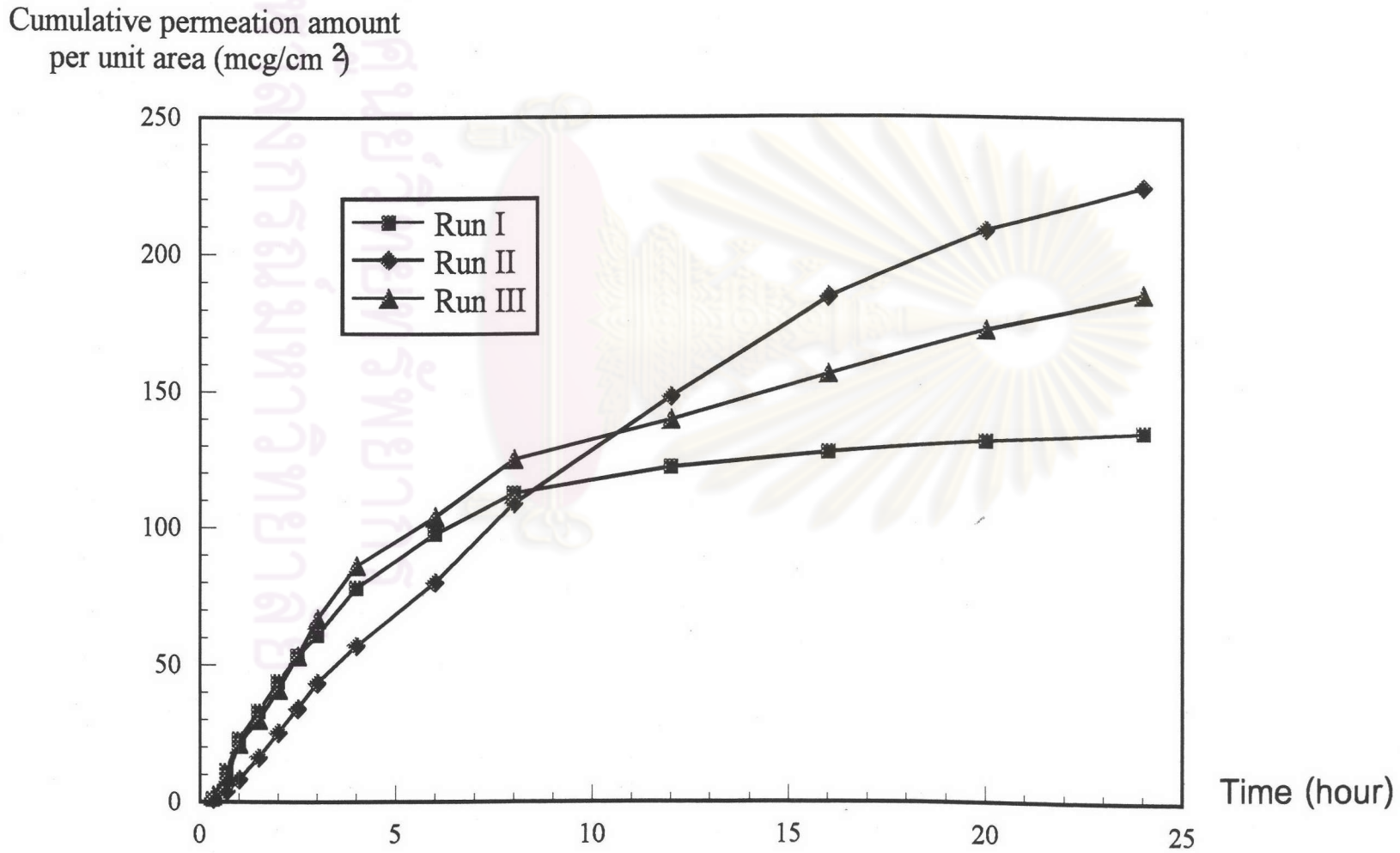
Permeation data per unit area

Permeation run	Run I	Run II	Run III
Time (hour)	Cumulative amount per unit area (mcg/cm^2)	Cumulative amount per unit area (mcg/cm^2)	Cumulative amount per unit area (mcg/cm^2)
0.33	1.13	1.16	2.34
0.67	11.34	3.78	9.39
1.0	22.77	8.20	21.22
1.5	32.99	16.14	29.81
2.0	43.72	25.15	40.99
2.5	53.13	33.93	53.22
3.0	60.92	43.31	66.74
4.0	77.88	56.93	86.14
6.0	97.67	80.00	103.90
8.0	112.58	108.92	125.18
12.0	122.33	148.44	139.95
16.0	127.78	184.74	156.70
20.0	132.07	208.67	172.99
24.0	135.46	224.46	186.15
Jss ($mcg/h/cm^2$) (1.5-4.0 h)	17.7205	16.4294	22.8608
r^2	0.9968	0.9949	0.9963
Permeation area (cm^2)	1.99	1.94	1.96
Membrane thickness (cm)	0.0305	0.0311	0.0271
Normalized Jss ($mcg/h/cm^2$)	20.0176	18.9242	22.9455

Average normalized Jss = 20.6291 ± 2.0792 ($mcg/h/cm^2$)

% cv = 10.08

Minoxidil flux from minoxidil solutions Rx 9 containing HP- β-CD 15% w/v through newborn pig skin



Rx 10 Containing HP-β-CD 20 % w/v

Calibration curve data

Concentration (mcg/ml)	0.2010	0.0603	0.1005	0.2010	0.4020	0.6030	0.8040	1.0050
Peak area ratio	0.0485	0.1474	0.2535	0.5296	1.0969	1.6138	2.1283	2.6678

$$y = -0.0044 + 2.6662x$$
$$r^2 = 0.9998$$

Permeation data

Permeation run	Run I		Run II		Run III	
Time (hour)	Peak area ratio	Amount (mcg)	Peak area ratio	Amount (mcg)	Peak area ratio	Amount (mcg)
0.33	0.0996	0.50	0.169	0.82	0.3761	1.84
0.67	0.5219	2.53	0.3551	1.71	0.5063	2.46
1.0	1.2167	5.87	0.5118	2.45	0.7092	3.44
1.5	0.6715	7.96	0.6109	3.67	0.4846	5.78
2.0	0.8320	7.88	0.9349	4.45	0.6662	6.34
2.5	0.7768	7.36	1.0801	5.14	0.7669	7.30
3.0	0.6441	6.11	0.6502	7.60	0.8311	7.90
4.0	0.5571	5.29	0.6795	7.94	1.5335	14.55
6.0	0.7439	7.05	0.5441	14.99	1.1063	29.18
8.0	0.8373	7.93	0.4943	16.55	1.3296	39.43
12.0	1.0941	10.35	0.2798	16.51	1.4514	57.37
16.0	1.2194	11.53	0.3867	15.51	1.3718	65.09
20.0	1.0464	9.90	0.5566	13.03	1.1846	56.23
24.0	0.7895	7.48	0.4258	9.99	0.6332	30.15
Receptor volume (ml)	12.56		12.39		12.61	

Average amount of minoxidil in preparation = 19.41 ± 0.45 mg/ml

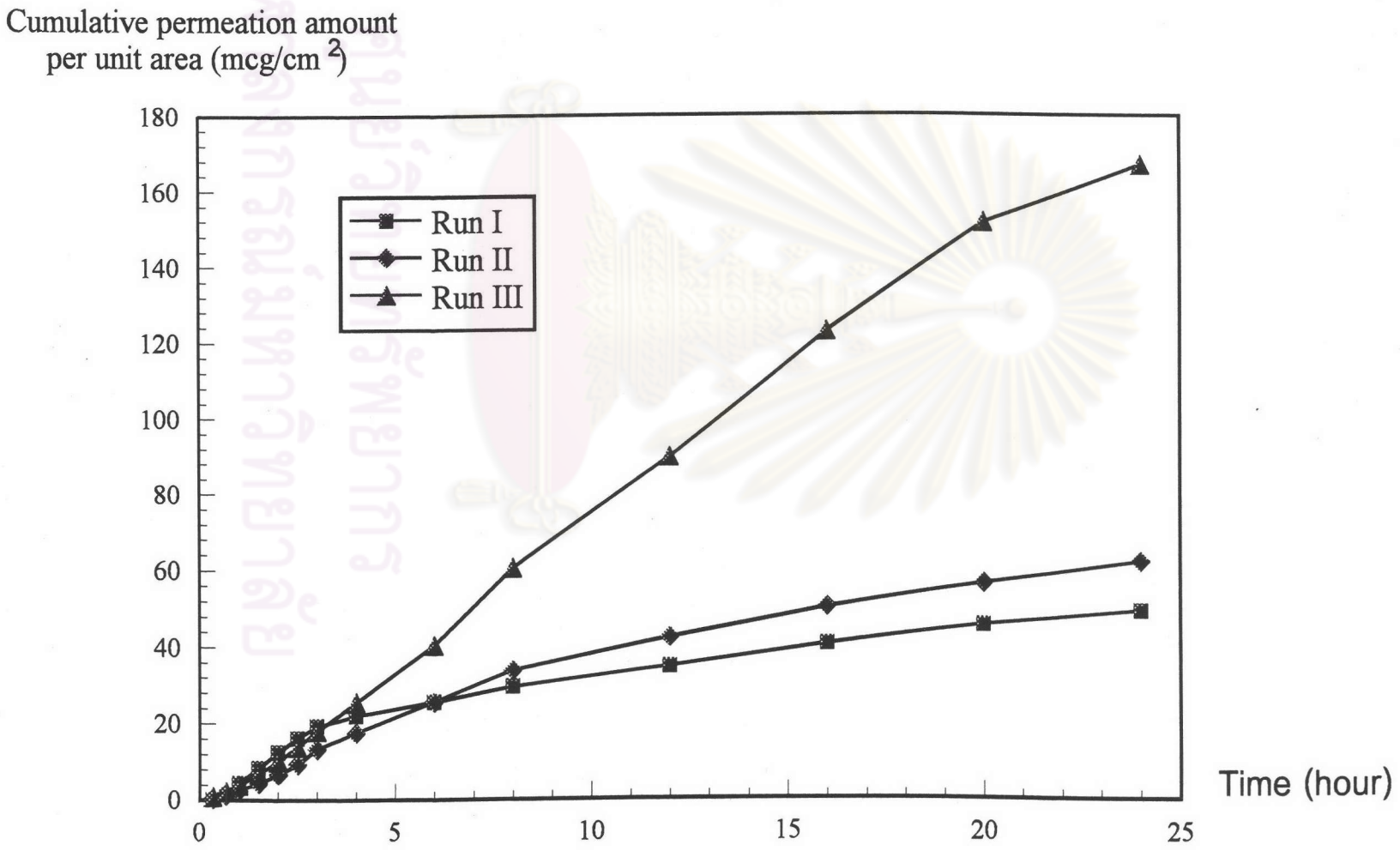
Permeation data per unit area

Permeation run	Run I	Run II	Run III
Time (hour)	Cumulative amount per unit area (mcg/cm^2)	Cumulative amount per unit area (mcg/cm^2)	Cumulative amount per unit area (mcg/cm^2)
0.33	0.25	0.42	0.94
0.67	1.52	1.30	2.19
1.0	4.47	2.57	3.95
1.5	8.47	4.46	6.90
2.0	12.43	6.75	10.13
2.5	16.13	9.40	13.86
3.0	19.20	13.32	17.89
4.0	21.86	17.41	25.31
6.0	25.40	25.41	40.20
8.0	29.39	33.67	60.32
12.0	34.59	42.18	89.59
16.0	40.38	49.99	122.80
20.0	45.36	56.17	151.48
24.0	49.11	61.86	166.87
Jss ($mcg/h/cm^2$) (1.0-3.0 h)	7.4240	5.2880	7.3452
r^2	0.9974	0.9792	0.9990
Permeation area (cm^2)	1.99	1.94	1.96
Membrane thickness (cm)	0.0267	0.0262	0.0285
Normalized Jss ($mcg/h/cm^2$)	7.3415	5.0921	7.7533

Average normalized Jss = 6.7290 ± 1.4324 ($mcg/h/cm^2$)

% cv = 21.29

Minoxidil flux from minoxidil solutions Rx 10 containing HP- β-CD 20% w/v through newborn pig skin



Appendix VII

One way ANOVA of the data of in vitro permeation of minoxidil through newborn pig skin

One way ANOVA of average normalized fluxes of minoxidil from the commercial minoxidil solution, Regaine® (Rx 1) and minoxidil solutions containing various concentrations of β-CD (Rx 2-5) through newborn pig skin.

Source	df	SS	MS=SS/df	F
Amoung Groups	4	2647.45	661.86	12.27
Within Group	10	539.22	53.92	
Total	14	3186.67		

$F_{table(4,10)} = 3.48$

Level of significant = 0.05

df = Degree of freedom

SS = Sum of square

MS = Mean square

F = Variance ratio

One way ANOVA of average normalized fluxes of minoxidil from the commercial minoxidil solution, Regaine® (Rx 1) and minoxidil solutions containing various concentrations of HP-β-CD (Rx 6-10) through newborn pig skin.

Source	df	SS	MS=SS/df	F
Amoung Groups	5	627.91	125.58	5.02
Within Group	12	299.86	27.99	
Total	17	927.77		

$F_{table(5,12)} = 3.11$

Level of significant = 0.05

df = Degree of freedom

SS = Sum of square

MS = Mean square

F = Variance ratio

One way ANOVA of average normalized fluxes of minoxidil from minoxidil solutions formulae Rx 1-10 through newborn pig skin.

Source	df	SS	MS=SS/df	F
Amoung Groups	9	3258.55	362.06	8.88
Within Group	20	815.09	40.75	
Total	29	4073.64		

$F_{table(8,20)} = 2.45$

Level of significant = 0.05

df = Degree of freedom

SS = Sum of square

MS = Mean square

F = Variance ratio

One way ANOVA of percent cumulative amounts of minoxidil in receiver compartment at 12 hours of the commercial minoxidil solution, Regaine ® (Rx 1) and minoxidil solutions containing various concentrations of β-CD (Rx 2-5).

Source	df	SS	MS=SS/df	F
Amoung Groups	4	189.45	47.36	8.90
Within Group	10	53.21	5.32	
Total	14	242.66		

$F_{table(4,10)} = 3.48$

Level of significant = 0.05

df = Degree of freedom

SS = Sum of square

MS = Mean square

F = Variance ratio

One way ANOVA of percent cumulative amounts of minoxidil in receiver compartment at 12 hours of the commercial minoxidil solution, Regaine ® (Rx 1) and minoxidil solutions containing various concentrations of HP-β-CD (Rx 6-10).

Source	df	SS	MS=SS/df	F
Amoung Groups	5	190.82	38.16	4.99
Within Group	12	91.67	7.64	
Total	17	282.49		

$F_{table(5,12)} = 3.11$

Level of significant = 0.05

df = Degree of freedom

SS = Sum of square

MS = Mean square

F = Variance ratio

One way ANOVA of percent cumulative amounts of minoxidil in receiver compartment at 12 hours of minoxidil solutions formulae Rx 1-10.

Source	df	SS	MS=SS/df	F
Amoung Groups	9	452.45	50.27	7.12
Within Group	20	141.19	7.06	
Total	29	593.64		

$F_{table(8,20)} = 2.45$

Level of significant = 0.05

df = Degree of freedom

SS = Sum of square

MS = Mean square

F = Variance ratio

One way ANOVA of percent cumulative amounts of minoxidil in receiver compartment at 24 hours of the commercial minoxidil solution, Regaine ® (Rx 1) and minoxidil solutions containing various concentrations of β-CD (Rx 2-5).

Source	df	SS	MS=SS/df	F
Amoung Groups	4	246.77	61.69	6.57
Within Group	10	93.90	9.39	
Total	14	340.67		

$F_{table(4,10)} = 3.48$

Level of significant = 0.05

df = Degree of freedom

SS = Sum of square

MS = Mean square

F = Variance ratio

One way ANOVA of percent cumulative amounts of minoxidil in receiver compartment at 24 hours of the commercial minoxidil solution, Regaine ® (Rx 1) and minoxidil solutions containing various concentrations of HP-β-CD (Rx 6-10).

Source	df	SS	MS=SS/df	F
Amoung Groups	5	516.17	103.23	3.91
Within Group	12	317.17	26.43	
Total	17	834.34		

$F_{table(5,12)} = 3.11$

Level of significant = 0.05

df = Degree of freedom

SS = Sum of square

MS = Mean square

F = Variance ratio

One way ANOVA of percent cumulative amounts of minoxidil in receiver compartment at 24 hours of minoxidil solutions formulae Rx 1-10.

Source	df	SS	MS=SS/df	F
Amoung Groups	9	989.42	109.93	5.44
Within Group	20	403.81	20.19	
Total	29	1393.23		

$F_{table(8,20)} = 2.45$

Level of significant = 0.05

df = Degree of freedom

SS = Sum of square

MS = Mean square

F = Variance ratio

VITA

Miss Ruttana Tuntiruttanasoontorn was born in November 13, 1967 in Bangkok, Thailand. She has received her Bachelor Degree of Science in Pharmacy from the Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok, Thailand since 1991. After graduation, she had been worked as a pharmacist in the pharmacy department in Loei Hospital, Loei province from 1991 to 1993. In 1993-1994, she worked at Bumrungrad Hospital, Bangkok before entering the Master's Degree programme in Pharmacy at Chulalongkorn University.