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APPENDICES

APPENDIX A

Analysis of AZT and its method validation

1.1 Spectrophotometric analysis of AZT

Table 1A Absorbtivity of five concentrations of AZT in 0.01M phosphate buffer pH 7.4 at the λ_{max} 267 nm.

Conc. (mole/L)	Abs of AZT at 267 nm in Phosphate buffer
1.51 E-5	0.1579
3.03 E-05	0.3205
6.05 E-05	0.6298
9.08 E-05	0.9420
1.21 E-05	1.2445

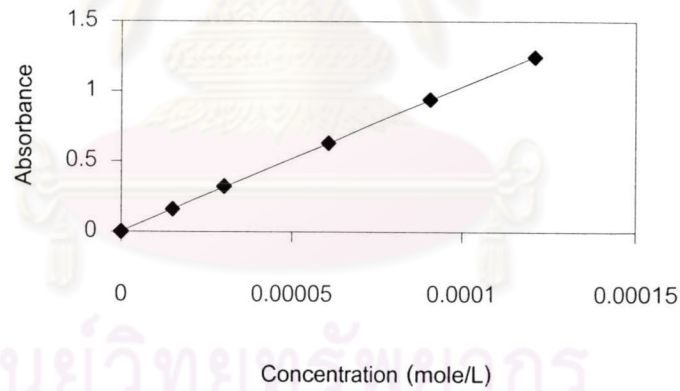


Figure 1A Representative of five concentrations of AZT in phosphate buffer vs. absorbance, slope of this line is molar absorptivity (ε) was determined from the slope to be: 10285 cm^2/mole, $Y = 10285x + 0.0043$, $r^2 = 0.9999$.

1.2 High-performance liquid chromatographic technique for drug analysis

AZT was analyzed by reversed phase HPLC and the design chromatographic condition were previously mentioned. Chromatograms of HPLC are shown in Figure 2A.

Analysis method validation parameters of AZT were summarized in Table 2A. The result of analytical method validation parameters for AZT accepted. Limit of quantitation of AZT was 0.0396 mcg/ml, it can be determined with acceptable accuracy, precision and linearity. The limit of quantitation was necessary for determination AZT in permeation study.

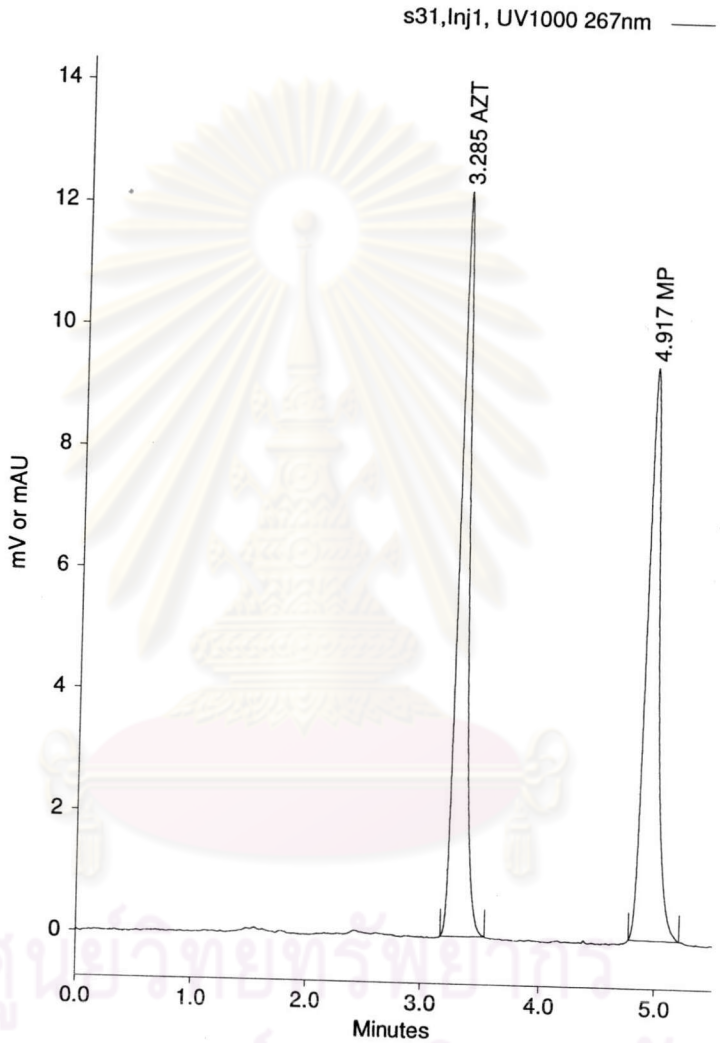


Figure 2A HPLC chromatogram of AZT and methyl paraben (internal standard) have a good resolution, which have retention time 3.29 and 4.92 min, respectively.

Figure 2A HPLC chromatogram of AZT and methyl paraben (internal standard) have a good resolution, which have retention time 3.29 and 4.92 min, respectively.

Table 2A Analytical method validation parameter of HPLC for AZT

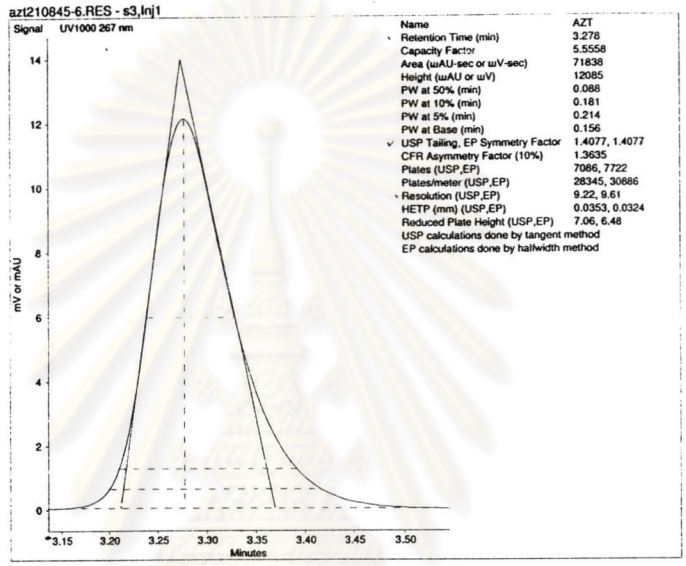
Parameter	Result value	Limited of acceptability
	AZT	
1. System suitability - Tailing factor - Resolution factor (from internal standard) - Repeatability of peak area - RSD (%)	 1.42 9.02 0.45	 < 2 > 2 > 2[a]
2. Specificity	No other peak interfere	No other peak interfere major peak [a]
3. Accuracy - recovery % (SD)	98.42 (1.89)	80-110% [b]
4. Precision - RSD (%)	1.89	≤ 2 [b]
5. linearity - the correlation coefficient (r^2)	0.99984	> 0.999 [b]
6. LOQ	0.0396 mcg/ml (% recovery = 91.74, %RSD = 1.44 linearity = 0.9995)	The minimum level of known concentration can be determined with acceptable accuracy, precision and linearity [a]

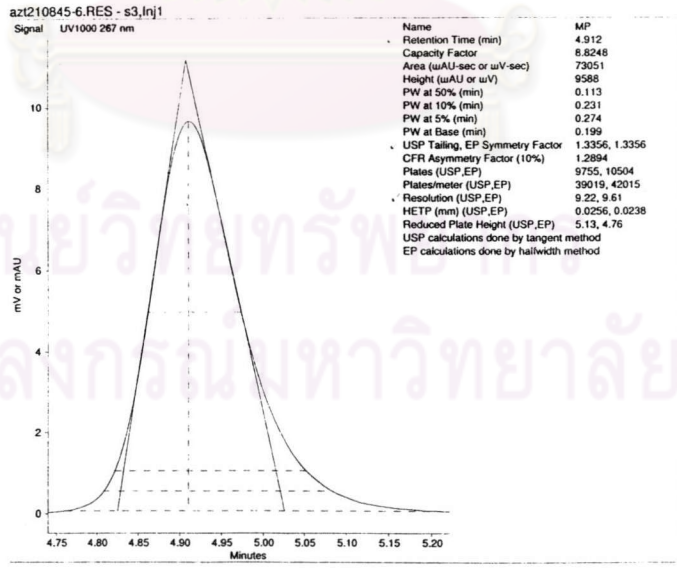
[a] USP XXIV

[b] Jenke, 1996

Table 3A System suitability of the analytical method of AZT

parameter	AZT	Methyl paraben
Tailing factor ± % CV	1.42 ± 0.38	1.35 ± 0.94
Resolution factor ± % CV	9.02 ± 0.41	





Calculating tailing factor and resolution factor of AZT and MP (methyl paraben) peak

Table 4A The repeatability of peak areas of AZT

Set No.	Peak area ratio
1	0.4506
2	0.4486
3	0.4479
4	0.4521
5	0.4507
Average	0.4499
SD	0.0017
%CV	0.45

Table 5A The analytical recovery of AZT

Known concentration (mcg/ml)	Calculated concentration from calibration curve (mcg/ml)	% Recovery
0.1586	0.1563	98.53
	0.1578	99.50
	0.1551	97.77
	0.1554	97.99
	0.1544	97.35
	0.1541	97.13
4.1245	4.0173	97.40
	4.2152	102.20
	4.0753	98.81
	4.0796	98.91
	4.0251	97.59
	4.0092	97.21
7.2973	7.2069	98.76
	7.5227	103.09
	7.0219	96.23
	7.0897	97.15
	7.3085	100.15
	6.9879	95.76
Average		98.42
SD		1.89
% CV		1.92
95% confidence interval		97.48-99.36

Table 6A The intraday precision

AZT concentration (mcg/ml)	Calculated concentration from calibration curve (mcg/ml)							
	No.1	No.2	No.3	No.4	No.5	No.6	average	% CV
0.1586	0.1563	0.1578	0.1551	0.1554	0.1544	0.1541	0.1555	0.88
4.1245	4.0173	4.2152	4.0753	4.0796	4.0251	4.0092	4.0703	1.89
7.2973	7.2069	7.5227	7.0219	7.0897	7.3085	6.9879	7.1896	2.81

Table 7A The interday precision

Day .	Calculated concentration from calibration curve							
	No.1	No.2	No.3	No.4	No.5	No.6	average	% CV
1	4.0173	4.2152	4.0753	4.0796	4.0251	4.0092	4.0703	1.89
2	4.0834	4.0293	4.0713	4.0133	4.0078	4.1863	4.0652	1.64
Average between day	4.0678							
% CV between day	0.07							
95 % Confidence interval	4.0278-4.1078							

Table 8A Linearity of AZT

AZT concentration (mcg/ml)	Peak area ratio				
	Set No.1	Set No.2	Set No.3	average	%CV
0	0	0	0	0	0
0.0793	0.0597	0.0576	0.0572	0.0582	2.31
0.3966	0.2338	0.2260	0.2249	0.2282	2.13
1.5864	0.9919	1.0029	1.0128	1.0025	1.04
3.9659	2.2758	2.2529	2.2524	2.2604	0.59
7.9318	4.6891	4.6603	4.6745	4.6746	0.31

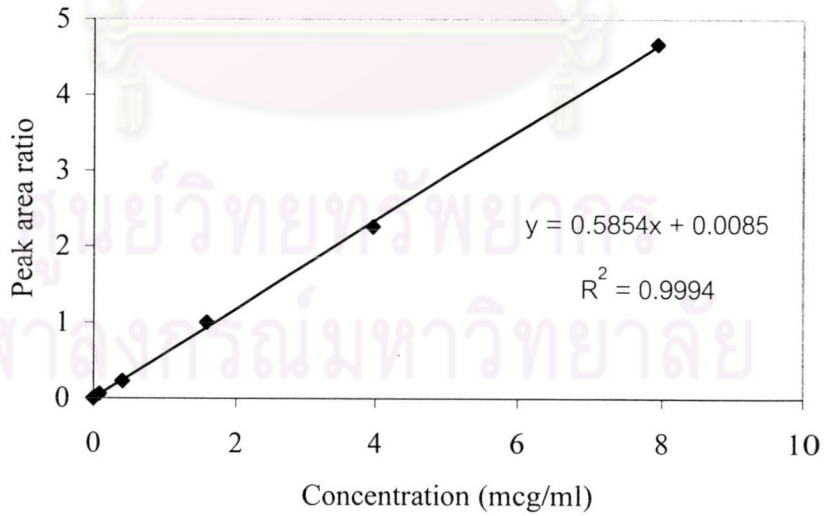


Figure 3A The calibration curve of AZT

Table 9A LOQ (Limit of quantitation) of AZT

Known concentration (mcg/ml)	Peak area ratio	Calculated concentration from calibration curve (mcg/ml)	% Recovery
0.0396	0.0305	0.0376	94.90
	0.0294	0.0357	90.16
	0.0293	0.0355	89.73
	0.0298	0.0364	81.88
	0.0297	0.0362	91.45
	0.0299	0.0366	92.31
Average	0.0298	0.0363	91.74
SD	0.00	0.00	1.84
% CV	1.44	2.01	2.01

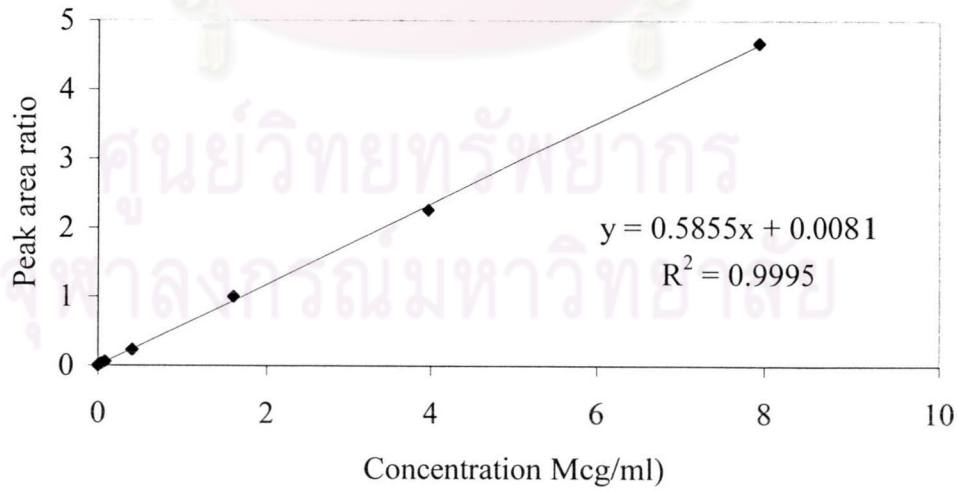


Figure 4A The linearity of AZT, concentration range of AZT were 0.0396 - 7.9318 mcg/ml

APPENDIX B

Selection of appropriate combination of vehicles for AZT preformulation

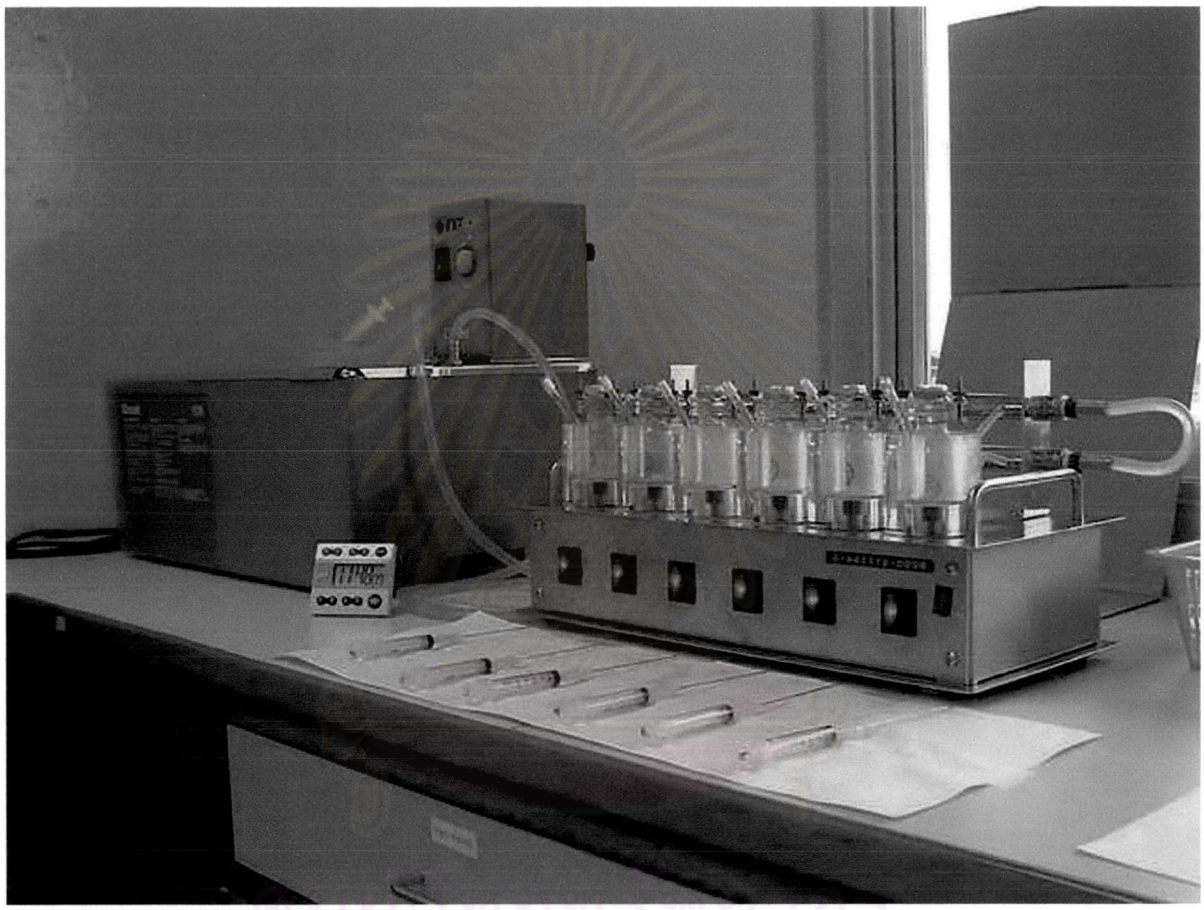


Figure 1B Modified Franz diffusion cells for *in vitro* permeation studies

Figure 2B Female newborn pig (local pig, 1.1-1.4 kg.) were obtained from Nakornpathom province of Thailand.

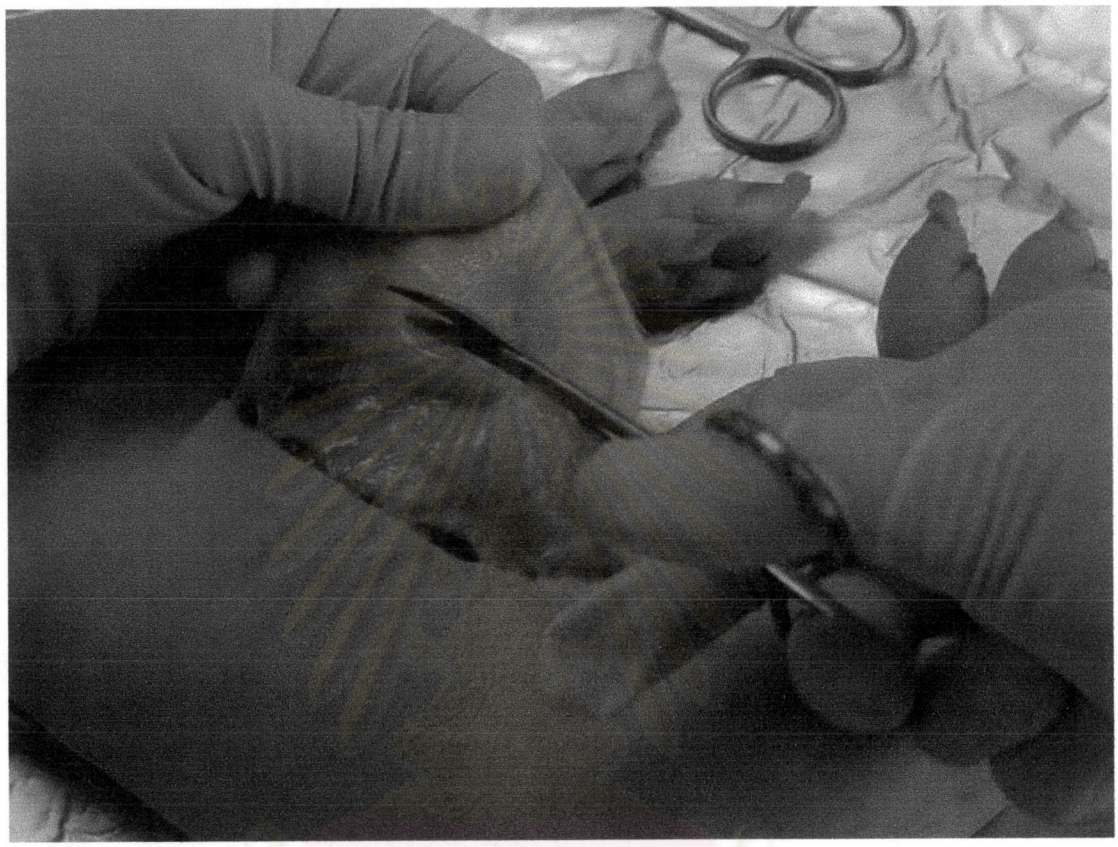


Figure 3B Subcutaneous fat and other extraneous tissues adhering to the dermis were completely removed and trimmed if necessary using forceps and scissors.

Figure 4B An excised full thickness skin was used for the penetration studies. An abdominal skin of a newborn pig was carefully excised and inspected for any defects.

Permeation of AZT in 70% saturated solution of ethanol/water (50/50) binary vehicles across newborn pig skin (AZT concentration in donor = 111.04 mg/ml)

Calibration curve data

Concentration(mcg/ml)	0	0.0793	0.3966	1.5864	3.9659	7.9318
Peak area ratio	0	0.0587	0.2494	0.9854	2.3073	4.5472

$$Y = 0.57x + 0.0383$$

$$R^2 = 0.9998$$

Time (hours)	Cumulative amount (mcg/cm^2)				Average (mcg/cm^2)	SE
	1	2	3	4		
1.5	3.79	0.65	2.74	0.27	1.86	0.73
3	4.36	4.98	3.06	0.50	3.22	0.86
4.5	18.26	13.72	3.17	1.68	9.21	3.49
6	31.37	30.58	23.44	24.65	27.51	1.75
7.5	52.21	50.64	50.19	50.26	50.82	0.41
9	68.89	56.59	60.40	66.58	63.12	2.44
10.5	75.89	69.57	77.93	68.08	72.87	2.07
12	101.29	84.55	92.73	86.14	91.18	3.30
Flux (mcg/cm^2)/h (6-12 h)	10.90	8.46	11.09	9.35	9.96	0.63
(R^2)	0.9755	0.9779	0.9805	0.9206		
Lag time (h)	2.95	2.10	3.50	2.67	2.86	0.29
Permeability x 10^3(cm/h)	0.09	0.08	0.10	0.08	0.09	0.01

Permeation of AZT in 70% saturated solution of IPA/water (50/50) binary vehicles across newborn pig skin (AZT concentration in donor = 145.81 mg/ml)

Calibration curve data

Concentration(mcg/ml)	0	0.0793	1.5864	3.9659	7.9318
Peak area ratio	0	0.0490	0.8958	2.2586	4.3537

$Y = 0.55602x + 0.0100$
$R^2 = 0.9996$

Time (hours)	Cumulative amount (mcg/cm^2)				Average (mcg/cm^2)	SE
	1	2	3	4		
1.5	1.66	1.17	1.53	1.72	1.52	0.12
3	2.27	3.55	3.19	5.41	3.61	0.66
4.5	3.29	7.66	5.99	7.62	6.14	1.03
6	13.82	26.16	21.99	14.74	19.18	2.96
7.5	33.13	44.55	41.98	35.16	38.71	2.72
9	42.85	63.89	54.53	58.65	54.98	4.47
10.5	60.28	84.48	74.25	70.44	72.36	5.00
12	65.13	94.91	85.99	74.33	80.09	6.53
Flux (mcg/cm^2)/h (6-12 h)	8.65	11.83	10.61	10.3	10.35	0.67
(R^2)	0.9694	0.9907	0.9927	0.9371		
Lag time (h)	4.02	3.69	3.81	4.08	3.90	0.09
Permeability x 10^3 (cm/h)	0.06	0.08	0.07	0.07	0.07	0.08

Permeation of AZT in 70% saturated solution of PEG/water (50/50) binary vehicles across newborn pig skin (AZT concentration in donor = 36.80 mg/ml)

Calibration curve data

Concentration(mcg/ml)	0	0.0793	0.3966	1.5864	3.9659	7.9318
Peak area ratio	0	0.0595	0.2587	0.9784	2.3545	4.5568

$Y = 0.5742x + 0.0321$

$R^2 = 0.9997$

Time (hours)	Cumulative amount (mcg/cm^2)				Average (mcg/cm^2)	SE
	1	2	3	4		
0.25	1.13	1.08	0.98	1.03	1.05	0.03
0.5	1.45	1.33	1.69	1.33	1.45	0.08
0.75	2.59	2.06	2.82	2.58	2.51	0.16
1	5.69	4.63	6.45	4.96	5.43	0.41
2.5	12.98	14.96	16.32	15.93	15.05	0.75
4	20.04	23.29	28.55	19.85	22.93	2.03
5.5	33.72	32.52	45.62	30.99	35.71	3.35
7	50.91	52.06	59.56	48.36	52.72	2.41
9.5	102.66	100.67	112.45	91.03	101.70	4.39
12	137.35	125.46	147.87	120.38	132.77	6.16
Flux (mcg/cm^2)/h (5.5-12 h)	16.57	14.86	16.48	14.16	15.52	0.60
(R^2)	0.9909	0.9827	0.9872	0.9837		
Lag time (h)	3.60	3.27	2.96	3.36	3.29	0.13
Permeability x 10^3 (cm/h)	0.45	0.40	0.45	0.38	0.42	0.02

Permeation of AZT in 70% saturated solution of ethanol/IPM(50/50) binary vehicles across newborn pig skin (AZT concentration in donor = 28.05 mg/ml)

Calibration curve data

Concentration(mcg/ml)	0	0.0793	0.3966	1.5864	3.9659	7.9318
Peak area ratio	0	0.0595	0.2339	1.0371	2.4059	4.7576

$Y = 0.599x + 0.0219$
$R^2 = 0.9997$

Time (hours)	Cumulative amount (mcg/cm^2)				Average (mcg/cm^2)	SE
	1	2	3	4		
1.5	2.72	3.25	2.63	2.49	2.77	0.14
3	6.48	8.84	5.83	5.99	6.79	0.60
4.5	11.36	12.65	8.44	9.01	10.36	0.86
6	14.83	21.37	18.23	13.37	16.95	1.55
7.5	31.74	35.11	40.35	30.91	34.53	1.86
9	73.02	149.07	132.19	74.91	107.30	16.94
10.5	198.48	258.71	276.66	317.26	262.78	21.38
12	668.48	632.02	746.17	605.30	662.99	26.50
$Flux_{int}$ (mcg/cm^2)/h (9-12 h)	198.49	160.98	204.66	176.80	185.23	10.05
(R^2)	0.8996	0.9096	0.9146	0.9975		
Lag time (h)	8.91	8.35	8.62	8.61	8.64	0.14
Permeability x 10^3 (cm/h)	7.08	5.73	7.30	6.30	6.60	0.33

APPENDIX C

Preformulation of AZT in suitable binary vehicles

Permeation of AZT saturated in ethanol/IPM (20/80) binary vehicles across newborn pig skin (AZT concentration in donor = 9.55 mg/ml)

Calibration curve data

Concentration(mcg/ml)	0	0.0793	0.3966	1.5864	3.9659	7.9318
Peak area ratio	0	0.0141	0.2311	0.9127	2.2589	4.3549

$Y = 0.5520x + 0.011$
$R^2 = 0.9995$

Time (hours)	Cumulative amount (mcg/cm^2)					Average (mcg/cm^2)	SE
	1	2	3	4	5		
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.25	0.24	0.03	0.01	0.03	0.00	0.06	0.04
0.5	1.03	0.36	0.26	0.16	0.00	0.36	0.18
0.75	1.95	0.66	0.76	0.15	0.00	0.70	0.34
1	3.04	1.45	0.69	0.53	0.00	1.14	0.53
2.5	10.41	6.29	4.76	3.50	0.77	5.15	1.60
4	38.26	9.41	8.43	11.18	2.75	14.01	6.23
5.5	225.64	12.02	19.97	64.47	19.14	68.25	40.43
7	476.07	78.93	61.91	155.56	75.87	169.67	78.33
9.5	926.13	369.94	352.00	358.89	285.00	458.39	117.87
12	1200.07	792.53	693.08	656.92	514.79	771.48	116.04
16	1546.57	1180.92	1027.82	959.75	831.64	1109.34	122.97
20	2352.22	1551.03	1446.37	1415.32	1188.45	1590.68	199.36
24	3265.47	2515.32	2069.52	2016.20	1505.34	2274.37	294.98
$Flux_{ss}$ (mcg/cm^2)/h (9.5-24 h)	159.11	136.64	113.24	84.09	110.36	120.69	12.71
(R^2)	0.9628	0.9618	0.9879	0.9995	0.986	-	-
Lag time (h)	4.62	6.92	6.43	6.01	6.50	6.10	0.40
Permeability x 10^3 (cm/h)	16.66	14.31	11.86	8.81	11.56	12.64	1.33

Permeation of AZT saturated in ethanol/IPM (30/70) binary vehicles across newborn pig skin (AZT concentration in donor = 19.64 mg/ml)

Calibration curve data

Concentration(mcg/ml)	0	0.0793	0.3966	1.5864	3.9659	7.9318
Peak area ratio	0	0.0434	0.2413	0.9033	2.2588	4.4848

$Y = 0.5653 x + 0.0067$
$R^2 = 1$

Time (hours)	Cumulative amount (mcg/cm^2)					Average (mcg/cm^2)	SE
	1	2	3	4	5		
0.25	0.19	0.21	0.22	0.56	5.26	1.29	1.00
0.5	0.74	0.21	0.26	3.04	8.47	2.54	1.57
0.75	1.02	0.59	0.30	5.33	14.55	4.36	2.71
1	1.80	0.51	1.08	9.82	21.47	6.93	4.01
2.5	9.86	3.50	9.64	16.97	28.86	13.77	4.34
4	28.05	7.92	18.57	26.91	30.45	22.38	4.13
5.5	51.76	12.93	38.61	47.55	34.65	37.10	6.77
7	147.49	24.72	87.96	57.89	78.41	79.29	20.20
9.5	496.82	104.45	169.93	638.88	393.36	360.69	99.76
12	1032.42	574.98	613.73	1520.04	815.43	911.32	172.64
16	2059.40	1530.59	1551.77	2551.37	1958.75	1930.37	187.91
20	2922.28	2050.34	2705.54	3816.11	2935.04	2885.86	282.81
24	3853.94	3082.23	3626.85	4809.49	4234.10	3921.32	290.00
$Flux_{ss}$ (mcg/cm^2)/h (9.5-24 h)	232.60	200.85	244.39	286.70	266.28	246.16	14.64
(R^2)	0.9993	0.9917	0.9963	0.9977	0.9941		
Lag time (h)	7.39	8.99	9.21	7.00	8.54	8.23	0.44
Permeability x 10^3 (cm/h)	11.84	10.23	12.44	14.59	13.56	12.53	0.74

Permeation of AZT saturated in ethanol/IPM(40/60) binary vehicles across newborn pig skin (AZT concentration in donor = 27.44 mg/ml)

Calibration curve data

Concentration(mcg/ml)	0	0.0793	0.3966	1.5864	3.9659	7.9318
Peak area ratio	0	0.0614	0.2317	0.9541	2.2544	4.4165

$Y = 0.5561x + 0.0259$
$R^2 = 0.9997$

Time (hours)	Cumulative amount (mcg/cm^2)					Average (mcg/cm^2)	SE
	1	2	3	4	5		
0.25	0.96	1.68	0.68	0.40	0.75	0.89	0.22
0.5	4.33	5.20	0.93	0.95	2.42	2.77	0.87
0.75	6.91	8.56	1.93	2.01	3.32	4.54	1.35
1	9.92	10.50	3.00	3.06	4.69	6.23	1.65
2.5	29.59	33.08	9.10	7.30	12.33	18.28	5.42
4	47.97	45.94	21.65	13.74	26.24	31.11	6.78
5.5	59.04	55.46	20.94	20.71	30.40	37.31	8.34
7	69.39	68.03	23.92	28.17	24.99	42.90	10.56
9.5	135.70	106.77	41.83	79.54	52.95	83.36	17.25
12	234.73	278.89	96.33	115.66	94.17	163.96	38.72
16	990.21	976.91	1914.72	706.26	413.01	1000.22	251.81
20	2777.85	2509.96	3428.42	1817.93	1810.45	2468.92	306.19
24	3724.66	3767.47	4971.76	3347.59	3110.44	3784.39	320.83
$Flux_{ss}$ (mcg/cm^2)/h (16-24 h)	341.81	348.82	382.13	330.17	337.18	348.02	9.05
(R^2)	0.9694	0.9968	1	0.9917	0.9996		
Lag time (h)	12.69	13.07	11.00	14.07	14.73	13.11	0.64
Permeability x 10^3 (cm/h)	12.46	12.71	13.93	12.03	12.29	12.68	0.33

Permeation of AZT saturated in ethanol/FIN(20/80) binary vehicles across newborn pig skin (AZT concentration in donor = 17.08 mg/ml)

Calibration curve data

Concentration(mcg/ml)	0	0.0793	0.3966	1.5864	3.9659	7.9318
Peak area ratio	0	0.0476	0.2313	0.8927	2.4501	4.9909

$Y = 0.6301x - 0.0307$
$R^2 = 0.9996$

Time (hours)	Cumulative amount (mcg/cm^2)					Average (mcg/cm^2)	SE
	1	2	3	4	5		
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.25	0.57	0.36	0.50	0.95	0.43	0.56	0.10
0.5	0.66	0.45	0.66	1.21	0.68	0.73	0.13
0.75	0.81	0.53	1.72	1.44	0.88	1.07	0.22
1	0.95	0.61	2.62	1.98	1.05	1.44	0.37
2.5	3.38	0.99	2.85	2.74	2.79	2.55	0.41
4	9.53	2.13	9.02	4.36	7.03	6.41	1.40
5.5	34.78	10.35	40.02	15.45	10.59	22.24	6.31
7	84.09	14.70	112.06	28.25	50.16	57.85	17.92
9.5	191.65	91.32	286.91	127.83	160.98	171.74	33.29
12	269.32	168.48	433.94	291.34	300.75	292.76	42.42
16	597.93	347.96	876.26	587.29	576.55	597.20	83.82
20	911.73	547.62	1001.40	890.39	921.74	854.58	79.00
24	1423.39	752.26	1286.70	1191.62	1025.23	1135.84	115.74
$Flux_{ss}$ (mcg/cm^2)/h (9.5-24 h)	46.22	69.18	73.82	63.45	84.85	67.50	6.38
(R^2)	0.9952	0.9729	0.9996	0.9783	0.9725	-	-
Lag time (h)	8.04	5.07	7.93	6.89	8.30	7.25	0.59
Permeability x 10^3 (cm/h)	2.71	4.05	4.32	3.72	4.97	3.95	0.37

Permeation of AZT saturated in ethanol/MCT (20/80) binary vehicles across newborn pig skin (AZT concentration in donor = 19.55 mg/ml)

Calibration curve data

Concentration(mcg/ml)	0	0.0793	0.3966	1.5864	3.9659	7.9318
Peak area ratio	0	0.0564	0.2251	0.8919	2.2423	4.4523

$Y = 0.5612x + 0.0056$
$R^2 = 1$

Time (hours)	Cumulative amount (mcg/cm^2)					Average (mcg/cm^2)	SE
	1	2	3	4	5		
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.25	1.95	0.48	0.26	0.43	0.97	0.82	0.31
0.5	7.00	1.03	0.66	0.65	2.06	2.28	1.21
0.75	11.95	2.20	0.75	4.25	3.79	4.5	1.94
1	16.65	3.57	1.03	6.50	4.73	6.50	2.69
2.5	82.86	5.73	2.80	30.23	5.69	25.46	15.18
4	89.17	11.41	5.75	35.29	11.17	30.56	15.52
5.5	120.03	14.37	6.94	47.05	15.62	40.80	20.97
7	163.30	18.98	10.47	64.29	22.71	55.95	28.40
9.5	260.11	39.93	29.18	109.88	40.49	95.92	43.48
12	409.11	155.88	121.36	201.39	73.22	192.19	58.15
16	738.36	503.72	427.39	499.06	329.65	499.64	67.50
20	1142.20	936.03	805.84	835.07	552.03	854.23	95.82
24	1611.43	1378.35	1281.36	1297.49	989.06	1311.54	99.87
$Flux_{ss}$ (mcg/cm^2)/h (9.5-24 h)	100.27	102.49	96.46	90.61	74.25	92.82	5.06
(R^2)	0.9939	0.9970	0.9904	0.9892	0.9751		
Lag time (h)	8.27	10.75	11.17	10.18	11.45	10.36	0.57
Permeability x 10^3 (cm/h)	5.13	5.24	4.93	4.63	3.80	4.75	0.26

Permeation of AZT saturated in ethanol/IPP (20/80) binary vehicles across newborn pig skin (AZT concentration in donor = 11.63 mg/ml)

Calibration curve data

Concentration(mcg/ml)	0	0.0793	0.3966	1.5864	3.9659	7.9318
Peak area ratio	0	0.0437	0.2060	0.9056	2.1856	4.1451

$Y = 0.5252x + 0.0258$
$R^2 = 0.9991$

Time (hours)	Cumulative amount (mcg/cm^2)					Average (mcg/cm^2)	SE
	1	2	3	4	5		
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.25	0.00	0.13	3.31	1.80	0.19	1.09	0.65
0.5	0.03	0.27	7.15	0.69	0.47	1.72	1.36
0.75	0.19	0.74	11.26	1.05	0.88	2.83	2.11
1	0.53	1.34	19.41	1.45	1.15	4.78	3.66
2.5	5.78	4.37	71.40	8.44	5.18	19.03	13.11
4	17.75	7.02	122.10	10.88	9.44	33.44	22.24
5.5	34.93	18.49	144.94	27.64	11.76	47.55	24.66
7	114.45	53.45	203.49	33.55	23.88	85.76	33.38
9.5	255.26	191.57	316.08	188.07	64.42	203.08	41.88
12	433.31	379.14	444.27	243.10	121.07	324.18	62.12
16	807.12	799.43	733.86	467.79	357.47	633.13	92.57
20	1217.84	1208.22	1016.60	814.29	641.61	979.71	112.24
24	1475.67	1452.90	1154.10	1325.67	929.30	1267.53	102.06
$Flux_{ss}$ (mcg/cm^2)/h (9.5-24 h)	87.28	60.73	78.06	61.42	90.60	75.62	6.28
(R^2)	0.9949	0.9868	0.9468	0.9842	0.9922	-	-
Lag time (h)	6.70	4.23	8.51	9.42	7.40	7.25	0.89
Permeability x 10^3 (cm/h)	7.50	5.22	6.71	5.28	7.79	6.50	0.54

Permeation of AZT saturated in ethanol/ADI (20/80) binary vehicles across newborn pig skin (AZT concentration in donor = 23.50 mg/ml)

Calibration curve data

Concentration(mcg/ml)	0	0.0793	0.3966	1.5864	3.9659	7.9318
Peak area ratio	0	0.1268	0.2337	0.9353	2.1203	4.0814

$Y = 0.514x + 0.0404$
$R^2 = 0.9991$

Time (hours)	Cumulative amount (mcg/cm^2)					Average (mcg/cm^2)	SE
	1	2	3	4	5		
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.25	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.5	0.42	0.95	0.40	0.00	0.38	0.43	0.15
0.75	1.42	4.00	1.61	0.00	1.04	1.61	0.66
1	0.95	4.90	2.10	0.00	2.58	2.11	0.83
2.5	8.35	12.26	41.67	1.42	9.86	14.71	6.98
4	17.68	34.21	22.04	4.22	18.55	19.34	4.80
5.5	21.38	47.25	27.14	5.73	23.20	24.94	6.66
7	46.13	68.37	41.88	12.23	28.94	39.51	9.32
9.5	114.04	139.04	91.92	56.93	58.95	92.17	15.84
12	219.34	277.56	192.03	155.41	118.18	192.50	27.25
16	631.84	581.55	524.31	352.59	281.84	474.43	67.33
20	1051.79	1179.52	896.49	799.86	657.51	917.04	91.80
24	1650.28	1684.85	1447.18	1321.93	1170.20	1454.89	97.43
$Flux_{ss}$ (mcg/cm^2)/h (9.5-24 h)	117.82	120.50	98.67	88.29	103.44	105.74	6.01
(R^2)	0.9910	0.9851	0.9654	0.9530	0.985	-	-
Lag time (h)	10.46	10.27	11.34	11.69	10.60	10.87	0.27
Permeability x 10^3 (cm/h)	5.01	5.13	4.20	3.76	4.40	4.50	0.26

APPENDIX D

Data on the addition of enhancers into preformulated AZT

Permeation of AZT saturated in ethanol/IPM(20/80) binary vehicles with 1% v/v NMP across newborn pig skin (AZT concentration in donor = 14.05 mg/ml)

Calibration curve data

Concentration(mcg/ml)	0	0.0793	0.3966	1.5864	3.9659	7.9318
Peak area ratio	0	0.0841	0.2242	0.9389	2.2291	4.3358

$Y = 0.5454x + 0.033$
$R^2 = 0.9997$

Time (hours)	Cumulative amount (mcg/cm^2)					Average (mcg/cm^2)	SE
	1	2	3	4	5		
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.25	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.5	0.00	0.50	0.69	0.00	0.00	0.24	0.14
0.75	0.00	0.34	1.74	0.00	0.00	0.42	0.31
1	0.00	0.13	3.40	0.00	0.00	0.71	0.61
2.5	0.08	1.32	5.63	1.00	1.44	1.89	0.88
4	1.78	4.57	10.78	4.65	8.29	6.02	1.44
5.5	6.95	14.04	26.60	24.16	33.84	21.12	4.34
7	28.91	40.93	76.76	61.88	98.38	61.37	11.33
9.5	117.99	134.29	365.05	249.31	354.79	244.29	47.82
12	254.95	308.90	540.02	507.17	579.55	438.12	59.65
16	575.00	687.23	953.29	869.23	938.46	804.64	67.91
20	838.38	1067.20	1340.17	1271.87	1242.48	1152.02	82.54
24	982.77	1209.88	1797.27	1347.26	1392.16	1345.87	121.83
$Flux_{ss}$ (mcg/cm^2)/h (9.5-24 h)	64.68	81.45	93.80	87.90	95.99	84.76	5.62
(R^2)	0.9873	0.9821	0.9984	0.9974	0.9977	-	-
Lag time (h)	7.29	7.40	6.59	5.59	6.08	6.59	0.35
Permeability x 10^3 (cm/h)	4.61	5.80	6.68	6.26	6.83	6.04	0.40

Permeation of AZT saturated in ethanol/IPM(20/80) binary vehicles with 5% v/v NMP across newborn pig skin (AZT concentration in donor = 27.56 mg/ml)

Calibration curve data

Concentration(mcg/ml)	0	0.0793	0.3966	1.5864	3.9659	7.9318
Peak area ratio	0	0.0508	0.2450	0.9761	0.4085	4.7039

$Y = 0.5938x + 0.0157$
$R^2 = 0.9998$

Time (hours)	Cumulative amount (mcg/cm^2)					Average (mcg/cm^2)	SE
	1	2	3	4	5		
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.25	0.03	0.31	0.10	0.80	0.15	0.28	0.14
0.5	0.08	0.46	0.13	1.21	0.19	0.42	0.21
0.75	0.10	0.85	0.30	1.72	0.32	0.66	0.29
1	0.23	1.34	0.49	2.10	0.50	0.93	0.35
2.5	1.61	5.94	3.02	6.03	1.99	3.72	0.95
4	6.64	16.03	8.84	13.67	4.98	10.03	2.09
5.5	24.67	45.38	27.80	32.36	14.49	28.94	5.05
7	79.53	135.09	79.37	69.04	37.66	80.14	15.73
9.5	342.54	419.44	327.98	71.53	212.28	274.75	60.65
12	626.94	815.54	624.20	431.27	634.97	626.58	60.80
16	1138.12	1589.02	1126.12	914.80	968.82	1147.38	118.65
20	1670.95	1949.58	1645.29	1399.90	1599.56	1653.06	88.11
24	2036.88	2697.29	2153.80	2023.02	2228.86	2227.97	123.35
$Flux_{ss}$ (mcg/cm^2)/h (9.5-24 h)	118.63	123.48	119.64	129.00	150.95	128.34	5.94
(R^2)	0.9974	0.9988	0.9792	0.9883	0.9924	-	-
Lag time (h)	6.47	6.71	7.91	7.41	6.35	6.97	0.30
Permeability x 10^3 (cm/h)	4.30	4.48	4.34	4.68	5.44	4.65	0.21

Permeation of AZT saturated in ethanol/IPM(20/80) binary vehicles with 10% v/v NMP across new born pig skin (AZT concentration in donor = 42.27 mg/ml)

Calibration curve data

Concentration(mcg/ml)	0	0.0793	0.3966	1.5864	3.9659	7.9318
Peak area ratio	0	0.0516	0.2365	0.9324	0.3215	4.8515

$Y = 0.6088x + 0.0176$
$R^2 = 0.9995$

Time (hours)	Cumulative amount (mcg/cm^2)					Average (mcg/cm^2)	± SE
	1	2	3	4	5		
0.25	0.3	0.27	0.24	0.54	0.64	0.40	0.08
0.5	1.68	0.76	0.81	1.70	1.89	1.37	0.24
0.75	2.84	1.95	1.11	2.95	3.26	2.42	0.39
1	3.76	3.35	1.39	4.23	15.79	5.71	2.57
2.5	12.58	15.92	5.89	12.65	34.27	16.26	4.79
4	52.63	61.96	16.97	30.32	67.39	45.85	9.60
5.5	158.66	270.36	64.91	75.27	278.63	169.56	45.83
7	359.85	768.54	216.42	266.96	603.61	443.08	105.12
9.5	857.96	1671.63	604.18	861.70	907.23	980.54	180.80
12	1498.79	2511.36	1242.74	1517.46	1508.33	1655.74	220.01
16	2418.36	3726.08	2077.97	2645.53	2564.86	2686.56	277.43
20	3758.44	5193.88	2971.30	4082.51	3987.19	3998.67	356.99
24	4205.73	5877.37	3314.99	4605.94	5759.88	4752.78	483.06
$Flux_{ss}$ (mcg/cm^2)/h (9.5-20 h)	272.09	332.20	222.86	305.53	291.91	284.92	18.34
(R^2)	0.9923	0.9984	0.9989	0.9949	0.9921	-	-
Lag time (h)	6.53	4.51	6.64	6.92	6.89	6.25	0.45
Permeability x 10^3 (cm/h)	6.44	7.86	5.27	7.23	6.91	6.74	0.43

Permeation of AZT saturated in ethanol/IPM(20/80) binary vehicles with 1% v/v oleic acid across newborn pig skin (AZT concentration in donor = 10.31 mg/ml)

Calibration curve data

Concentration(mcg/ml)	0	0.0793	0.3966	1.5864	3.9659	7.9318
Peak area ratio	0	0.0377	0.2142	0.8926	2.1773	4.2969

$Y = 0.5425x + 0.0077$

$R^2 = 0.9999$

Time (hours)	Cumulative amount (mcg/cm^2)					Average (mcg/cm^2)	SE
	1	2	3	4	5		
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.25	3.01	1.54	0.28	0.71	0.32	1.17	0.51
0.5	3.94	3.52	0.42	0.95	1.07	1.98	0.73
0.75	6.51	4.61	0.49	1.34	2.14	3.02	1.11
1	9.77	6.83	0.85	2.76	2.90	4.62	1.61
2.5	85.89	21.62	6.82	31.92	15.93	32.44	13.97
4	147.22	40.17	34.33	100.08	49.65	74.29	21.62
5.5	201.74	65.66	81.20	155.99	101.75	121.27	25.26
7	313.95	148.85	184.93	276.56	186.95	222.25	31.13
9.5	486.05	260.52	341.30	409.52	340.98	367.67	37.85
12	610.66	417.16	522.51	495.05	511.00	511.28	30.92
16	750.04	562.63	737.26	846.27	676.16	714.47	46.73
20	1078.07	859.83	1168.23	1143.26	942.35	1038.35	59.39
24	1635.59	1311.11	1638.34	1438.53	1297.44	1464.20	74.10
$Flux_{ss}$ (mcg/cm^2)/h (9.5-24 h)	70.28	81.13	69.08	62.03	63.06	69.12	3.41
(R^2)	0.9533	0.9796	0.9922	0.9905	0.9666	-	-
Lag time (h)	3.11	5.20	3.57	4.09	5.22	4.24	0.43
Permeability x 10^3 (cm/h)	6.82	7.87	6.70	6.02	6.12	6.71	0.33

Permeation of AZT saturated in ethanol/IPM (20/80) binary vehicles with 5% v/v oleic acid across newborn pig skin (AZT concentration in donor = 15.36 mg/ml)

Calibration curve data

Concentration(mcg/ml)	0	0.0793	0.3966	1.5864	3.9659	7.9318
Peak area ratio	0	0.0508	0.2452	1.0499	2.3430	4.5725

$Y = 0.5754x + 0.038$
$R^2 = 0.9991$

Time (hours)	Cumulative amount (mcg/cm^2)					Average (mcg/cm^2)	SE
	1	2	3	4	5		
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.25	0.03	0.00	0.04	0.54	0.49	0.22	0.12
0.5	0.78	0.00	0.51	0.62	0.94	0.57	0.16
0.75	1.43	0.00	1.28	1.16	1.58	1.09	0.28
1	2.10	0.00	2.06	1.71	2.34	1.64	0.42
2.5	8.69	1.39	10.00	8.31	9.08	7.49	1.55
4	21.23	4.99	24.28	21.19	21.26	18.59	3.45
5.5	45.31	16.50	52.64	38.39	51.82	40.93	6.63
7	128.44	76.38	125.46	73.39	130.73	106.88	13.10
9.5	401.17	353.46	445.21	311.87	456.55	393.65	27.36
12	773.29	806.07	830.33	702.08	829.33	788.22	23.90
16	1374.91	1349.20	1347.92	1231.77	1413.63	1343.49	30.36
20	1852.10	1876.85	1624.47	1564.07	1905.10	1764.52	70.65
24	2023.70	2237.68	1834.11	1871.05	2031.51	1999.61	71.48
$Flux_{ss}$ (mcg/cm^2)/h (9.5-24 h)	143.08	112.83	119.52	138.46	139.12	130.60	6.04
(R^2)	0.9958	0.9742	0.9834	0.9980	0.9970	-	-
Lag time (h)	6.71	4.92	6.41	6.06	6.47	6.11	0.32
Permeability x 10^3 (cm/h)	9.32	7.35	7.78	9.01	9.06	8.50	0.39

Permeation of AZT saturated in ethanol/IPM (20/80) binary vehicles with 10% v/v oleic acid across newborn pig skin (AZT concentration in donor = 9.67 mg/ml)

Calibration curve data

Concentration(mcg/ml)	0	0.0793	0.3966	1.5864	3.9659	7.9318
Peak area ratio	0	0.0797	0.2432	1.0049	2.3279	4.7150

$Y = 0.5907x + 0.0207$
$R^2 = 0.9997$

Time (hours)	Cumulative amount (mcg/cm^2)					Average (mcg/cm^2)	SE
	1	2	3	4	5		
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.25	0.39	0.06	0.98	3.70	1.91	1.41	0.65
0.5	0.13	0.26	2.28	4.12	2.56	1.87	0.75
0.75	0.16	0.60	4.41	6.19	3.65	3.00	1.15
1	0.39	1.18	6.39	8.12	5.33	4.28	1.50
2.5	2.29	4.79	32.16	14.41	50.07	20.74	9.01
4	6.07	9.00	191.87	33.45	202.02	88.48	44.56
5.5	12.20	19.14	514.73	172.89	506.45	245.08	112.14
7	99.87	136.88	973.27	201.95	896.42	461.68	194.24
9.5	167.06	264.58	1371.42	839.62	1152.44	759.02	237.82
12	322.03	485.43	1509.96	1116.51	1516.91	990.17	251.47
16	581.72	751.38	2010.94	1477.15	1863.86	1337.01	288.51
20	878.20	1040.72	2209.41	2223.47	2111.82	1692.73	301.06
24	1105.10	1398.92	2516.41	2301.14	2372.27	1938.77	286.30
$Flux_{ss}$ (mcg/cm^2)/h (9.5-24 h)	67.61	72.74	85.17	128.17	89.29	88.60	10.65
(R^2)	0.9984	0.9976	0.9674	0.9708	0.9695	-	-
Lag time (h)	7.17	5.64	6.47	3.34	4.23	5.37	0.71
Permeability x 10^3 (cm/h)	6.99	7.52	8.81	13.25	9.23	9.16	1.10

Permeation of AZT saturated in ethanol/IPM (20/80) binary vehicles with 1% v/v lauric acid across newborn pig skin (AZT concentration in donor = 10.29 mg/ml)

Calibration curve data

Concentration(mcg/ml)	0	0.0793	0.3966	1.5864	3.9659	7.9318
Peak area ratio	0	0.0562	0.2142	0.9326	2.1773	4.4821

$Y = 0.5623x + 0.0022$
$R^2 = 0.9997$

Time (hours)	Cumulative amount (mcg/cm^2)					Average (mcg/cm^2)	SE
	1	2	3	4	5		
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.25	0.16	0.82	0.00	0.17	0.24	0.28	0.13
0.5	0.53	2.28	0.33	0.58	0.54	0.85	0.33
0.75	0.91	6.45	0.44	0.99	1.03	1.96	1.03
1	1.74	10.66	1.25	1.64	1.92	3.44	1.65
2.5	9.40	52.89	8.15	12.97	10.23	18.73	7.83
4	44.57	138.58	44.65	60.78	34.47	64.61	17.31
5.5	96.18	249.77	67.84	130.80	98.27	128.57	29.12
7	175.43	350.01	136.07	184.17	164.16	201.97	34.59
9.5	238.80	505.59	211.64	347.90	305.08	321.80	47.33
12	406.88	738.55	323.88	488.38	473.33	486.20	63.41
16	680.85	914.42	559.19	695.57	594.60	688.92	56.53
20	945.10	1360.64	802.23	886.75	755.12	949.97	98.42
24	1058.51	1619.38	950.47	1073.14	868.13	1113.93	120.30
$Flux_{ss}$ (mcg/cm^2)/h (9.5-24 h)	55.58	74.64	49.61	51.82	42.23	54.78	5.42
(R^2)	0.9869	0.9913	0.9925	0.9976	0.9823	-	-
Lag time (h)	4.17	2.45	4.64	2.93	2.40	3.32	0.46
Permeability x 10^{-3} (cm/h)	5.40	7.25	4.82	5.04	4.10	5.32	0.53

ermeation of AZT saturated in ethanol/IPM (20/80) binary vehicles with 5% v/v lauric acid across newborn pig skin (AZT concentration in donor = 13.26 mg/ml)

Calibration curve data

Concentration(mcg/ml)	0	0.0793	0.3966	1.5864	3.9659	7.9318
Peak area ratio	0	0.0763	0.2704	1.0320	2.5747	5.0925

$Y = 0.641x + 0.0163$
$R^2 = 1$

Time (hours)	Cumulative amount (mcg/cm^2)					Average (mcg/cm^2)	SE
	1	2	3	4	5		
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.25	0.15	0.00	0.15	0.27	0.13	0.14	0.04
0.5	0.48	0.00	1.03	1.09	1.25	0.77	0.23
0.75	0.82	0.00	1.33	3.07	2.19	1.48	0.53
1	1.08	0.00	2.59	5.29	4.24	2.64	0.97
2.5	3.12	0.07	7.80	21.55	16.47	9.82	4.03
4	8.29	2.73	26.35	49.74	62.26	29.88	11.53
5.5	15.47	9.58	69.10	81.58	123.44	59.83	21.33
7	38.27	31.99	79.99	143.85	186.62	96.15	30.16
9.5	141.27	114.94	262.58	342.91	415.78	255.50	57.53
12	362.97	327.13	518.94	547.06	593.24	469.87	52.62
16	589.31	615.86	871.38	863.99	1248.23	837.75	118.59
20	740.65	1095.53	1338.22	1257.12	1697.10	1225.72	156.22
24	968.45	1656.60	2477.02	1825.46	2241.10	1833.73	260.76
$Flux_{ss}$ (mcg/cm^2)/h (9.5-24 h)	54.42	104.76	143.30	99.88	129.05	106.28	13.60
(R^2)	0.9847	0.9816	0.9296	0.9837	0.9940	-	-
Lag time (h)	6.00	9.03	8.67	6.62	6.69	7.40	0.61
Permeability x 10^3 (cm/h)	4.10	7.90	10.81	7.53	9.73	8.01	1.15

Permeation of AZT saturated in ethanol/IPM (20/80) binary vehicles with 10% v/v lauric acid across newborn pig skin (AZT concentration in donor = 9.31 mg/ml)

Calibration curve data

Concentration(mcg/ml)	0	0.0793	0.3966	1.5864	3.9659	7.9318
Peak area ratio	0	0.0747	0.2316	0.9434	2.2861	4.4929

$Y = 0.5654x + 0.0225$
$R^2 = 0.9999$

Time (hours)	Cumulative amount (mcg/cm^2)					Average (mcg/cm^2)	SE
	1	2	3	4	5		
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.25	0.87	0.05	0.01	0.67	0.00	0.40	0.22
0.5	1.06	0.72	0.09	2.38	0.00	1.06	0.48
0.75	1.41	1.98	0.30	3.67	0.02	1.84	0.70
1	3.52	2.47	0.42	5.05	0.24	2.87	0.97
2.5	3.89	12.36	2.65	23.60	19.52	10.63	4.83
4	10.01	30.80	14.03	152.62	224.94	51.87	33.89
5.5	34.79	39.29	182.37	568.86	556.82	206.33	125.61
7	39.85	70.51	405.00	851.51	1005.24	341.72	188.98
9.5	108.25	226.84	750.00	1166.58	1425.18	562.92	244.79
12	324.67	472.67	1024.00	1539.10	1702.32	840.11	277.35
16	597.81	804.29	1526.00	1860.26	2063.14	1197.09	297.41
20	810.05	1218.35	1787.63	2089.08	2511.41	1476.28	286.19
24	883.15	1298.15	2299.00	2390.67	3072.27	1717.74	372.30
$Flux_{ss}$ (mcg/cm^2)/h (9.5-24 h)	66.41	93.14	85.28	101.88	118.84	93.11	8.70
(R^2)	0.9904	0.9980	0.9606	0.9980	0.9995	-	-
Lag time (h)	7.44	7.07	5.13	4.52	3.25	5.48	0.78
Permeability x 10^3 (cm/h)	7.13	10.00	9.16	10.94	12.76	9.99	0.93

Permeation of AZT saturated in ethanol/IPM (30/70) binary vehicles with 1% v/v NMP across newborn pig skin (AZT concentration in donor = 23.44 mg/ml)

Calibration curve data

Concentration(mcg/ml)	0	0.0793	0.3966	1.5864	3.9659	7.9318
Peak area ratio	0	0.0614	0.2528	0.9542	2.2267	4.4668

$Y = 0.5601x + 0.0239$
$R^2 = 0.9998$

Time (hours)	Cumulative amount (mcg/cm^2)					Average (mcg/cm^2)	SE
	1	2	3	4	5		
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.25	0.82	2.13	2.08	1.19	0.17	1.28	0.38
0.5	2.31	6.42	4.04	4.28	0.57	3.52	0.99
0.75	3.68	11.08	5.15	4.17	1.51	5.12	1.60
1	5.69	16.44	6.90	5.94	2.99	7.59	2.31
2.5	26.64	48.55	18.84	26.77	12.23	26.61	6.12
4	51.59	69.36	36.80	52.63	82.60	58.59	7.91
5.5	80.00	97.24	50.33	108.07	117.88	90.70	11.89
7	129.29	140.18	69.87	360.09	223.42	184.57	50.25
9.5	271.74	460.58	161.63	897.00	522.20	462.63	126.34
12	888.44	1142.08	543.43	1625.13	1079.83	1055.78	176.45
16	2286.77	2165.14	1414.47	2876.79	1856.59	2119.95	241.84
20	3275.17	2891.50	2565.50	3999.25	3048.78	3156.04	240.35
24	4449.39	4263.35	3471.24	4899.36	4234.92	4263.65	231.01
Flux (mcg/cm^2)/h (9.5-24 h)	290.45	252.79	234.84	279.91	254.99	262.60	9.99
(R^2)	0.9974	0.9916	0.9936	0.9964	0.9916		
Lag time (h)	8.61	7.66	9.35	6.08	7.87	7.91	0.55
Permeability x 10^3 (cm/h)	12.39	10.78	10.02	11.94	10.88	11.20	0.43

Permeation of AZT saturated in ethanol/IPM (30/70) binary vehicles with 5% v/v NMP across newborn pig skin (AZT concentration in donor = 33.35 mg/ml)

Calibration curve data

Concentration(mcg/ml)	0.0793	0.3966	1.5864	3.9659	7.9318
Peak area ratio	0.0514	0.2456	0.8760	2.2469	4.4673

$Y = 0.5627x + 0.0052$

$R^2 = 0.9999$

Time (hours)	Cumulative amount (mcg/cm^2)					Average (mcg/cm^2)	SE
	1	2	3	4	5		
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.25	1.35	1.58	2.68	1.24	5.52	2.48	0.80
0.5	1.65	2.70	4.49	2.99	7.92	3.95	1.09
0.75	2.48	3.34	5.85	5.23	10.60	5.50	1.41
1	2.59	4.43	7.34	8.95	13.00	7.26	1.81
2.5	6.48	13.54	16.23	30.06	26.51	18.56	4.31
4	9.62	22.09	21.28	48.55	35.78	27.46	6.71
5.5	10.95	30.67	28.74	62.52	51.01	36.78	9.04
7	14.73	53.17	40.48	81.41	59.73	49.90	11.01
9.5	554.67	585.15	542.13	501.70	588.56	554.44	15.88
12	1599.56	1685.58	1245.83	1212.66	1222.48	1393.22	102.84
16	3338.04	3271.19	2877.94	2928.33	2745.14	3032.13	115.68
20	4359.54	4692.46	3981.46	3950.74	4509.75	4298.79	145.77
24	5829.22	5902.48	5085.56	5368.44	5629.26	5562.99	151.05
Flux (mcg/cm^2)/h (9.5-24 h)	358.23	367.22	319.18	337.09	362.47	348.84	9.03
(R^2)	0.9926	0.9957	0.9939	0.9948	0.9941		
Lag time (h)	7.56	7.51	7.70	8.02	8.19	7.80	0.13
Permeability x 10^3 (cm/h)	10.74	11.01	9.57	10.10	10.87	10.46	0.27

Permeation of AZT saturated in ethanol/IPM (30/70) binary vehicles with 10% v/v NMP across newborn pig skin (AZT concentration in donor = 56.39 mg/ml)

Calibration curve data

Concentration(mcg/ml)	0.0793	0.3966	1.5864	3.9659	7.9318
Peak area ratio	0.0332	0.2179	0.9154	2.3983	4.5990

$Y = 0.5843x + 0.0012$

$R^2 = 0.9995$

Time (hours)	Cumulative amount (mcg/cm^2)					Average (mcg/cm^2)	SE
	1	2	3	4	5		
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.25	0.44	1.27	0.74	0.77	1.22	0.89	0.16
0.5	0.71	2.51	0.93	1.28	2.85	1.66	0.43
0.75	1.28	3.82	1.45	5.41	5.24	3.44	0.89
1	1.69	5.24	5.76	8.82	8.30	5.96	1.27
2.5	4.38	16.27	16.98	23.46	39.32	20.08	5.71
4	14.33	34.76	38.91	52.71	55.02	39.15	7.32
5.5	39.15	54.80	70.02	98.44	89.15	70.31	10.86
7	190.84	99.48	220.73	131.55	200.98	168.71	22.81
9.5	1381.07	1082.92	1016.11	1056.05	1167.22	1140.68	65.00
12	2873.71	2151.23	1955.09	2428.70	2542.45	2390.24	158.88
16	5430.87	4425.57	3723.35	3848.05	4023.72	4290.31	308.81
20	7321.75	6018.23	5964.40	5752.57	6303.73	6272.14	276.75
24	8833.08	8117.71	7604.89	6841.76	7468.77	7773.24	333.96
Flux (mcg/cm^2)/h (9.5-24 h)	509.48	484.99	465.84	400.49	440.90	460.34	18.72
(R^2)	0.9910	0.9976	0.9967	0.9909	0.9908		
Lag time (h)	9.65	7.31	7.60	6.35	6.54	7.49	0.59
Permeability x 10^3 (cm/h)	9.03	8.60	8.26	7.10	7.82	8.16	0.33

APPENDIX E

Evaluation of AZT transdermal delivery system

The release of AZT from ethanol/IPM(20/80) across polyethylene microporous membrane (AZT concentration in donor = 42.85 mg/ml)

Calibration curve data

Concentration(mcg/ml)	0	0.0793	0.3966	1.5864	3.9659	7.9318
Peak area ratio	0	0.0469	0.2275	0.9224	2.3129	4.4521

$Y = 0.5634x + 0.0161$
$R^2 = 0.9996$

Time (hours)	Cumulative amount (mcg/cm^2)			Average (mcg/cm^2)	SE
	1	2	3		
0	0	0	0	0	0
0.25	1177.02	958.39	888.59	1008.00	86.88
0.5	2423.50	2239.45	1682.19	2115,04	222.85
0.75	3156.81	2700.77	2913.47	2923.68	131.74
1	3371.87	3139.73	3219.10	3243.57	68.12
2.5	5299.13	5155.04	4134.08	4862.75	366.69
4	5863.46	5600.72	4777.99	5414.06	326.95
5.5	5923.00	5848.44	4730.60	5500.68	385.63
7	5118.45	6094.19	5389.10	5533.91	290.82
9.5	6714.05	6275.48	5677.43	6222.32	300.42
12	6992.58	6381.65	6084.26	6486.16	267.36
16	7256.36	6575.78	6193.06	6675.07	310.93
20	7676.45	6732.97	6531.68	611.17	352.85
24	7844.85	6967.02	6933.76	7248.54	298.30
$Flux_{ss}$ (mcg/cm^2)/h (0-0.75 h)	4286.80	3753.40	3813.60	3951.27	168.67
R^2	0.9886	0.9720	0.9905		
Permeability x 10^3 (cm/h)	100.04	87.59	88.99	92.21	3.94
$Flux_{ss}$ (mcg/cm^2)/h (9.5-24 h)	79.156	46.959	79.321	68.47	10.76
R^2	0.9831	0.9961	0.9637		
Permeability x 10^3 (cm/h)	1.85	1.00	1.85	1.57	0.28

The release of AZT from ethanol/IPM(20/80) across 9% EVA nonoporous membrane (AZT concentration in donor = 42.85 mg/ml)

Calibration curve data

Concentration(mcg/ml)	0	0.0793	0.3966	1.5864	3.9659	7.9318
Peak area ratio	0	0.0579	0.2552	0.9950	2.2236	4.6196

$Y = 0.5769x + 0.0162$
$R^2 = 0.9993$

Time (hours)	Cumulative amount (mcg/cm^2)			Average (mcg/cm^2)	SE
	1	2	3		
0	0	0	0	0	0
0.25	0.05	0.05	1.21	0.44	0.27
0.5	0.66	0.64	1.50	0.93	0.20
0.75	1.16	0.96	2.73	1.62	0.39
1	1.26	1.42	2.47	1.72	0.27
2.5	4.47	3.93	6.29	4.90	0.51
4	6.22	7.23	9.00	7.48	0.58
5.5	9.82	9.11	11.21	10.05	0.44
7	10.87	11.06	13.51	11.82	0.60
9.5	14.30	15.53	16.78	15.54	0.51
12	18.27	17.49	19.97	18.58	0.52
16	23.28	23.36	27.32	24.65	0.94
20	28.80	30.78	30.16	29.91	0.41
24	33.40	30.81	30.98	31.73	0.59
$Flux_{ss}$ (mcg/cm^2)/h (0-24 h)	1.4183	1.5126	1.5363	1.4891	0.0400
R^2	0.9961	0.9959	0.9872		
Permeability x 10^3 (cm/h)	0.0300	0.0400	0.0400	0.0400	0.0030

Permeation of AZT from ethanol/IPM (20/80) across polyethylene microporous membrane adhered on newborn pig skin (AZT concentration in donor = 42.74 mg/ml)

Calibration curve data

Concentration(mcg/ml)	0	0.0793	0.3966	1.5864	3.9659	7.9318
Peak area ratio	0	0.0546	0.2496	0.9420	2.3108	4.5034

$Y = 0.5647 x + 0.0225$
$R^2 = 0.9998$

Time (hours)	Cumulative amount (mcg/cm^2)					Average (mcg/cm^2)	SE
	1	2	3	4	5		
0	0	0	0	0	0	0	0
0.25	0.12	0.12	0.00	0.02	0.07	0.06	0.02
0.5	0.46	0.90	0.22	0.21	0.48	0.45	0.13
0.75	1.52	2.40	0.72	0.58	1.18	1.28	0.33
1	2.99	4.70	1.26	0.99	2.06	2.40	0.67
2.5	24.32	34.10	6.92	0.58	15.63	16.31	5.99
4	81.97	122.85	23.65	15.63	46.36	58.09	19.86
5.5	210.91	306.13	115.48	51.77	147.65	166.39	43.35
7	384.93	515.29	355.79	163.48	342.93	352.48	56.29
9.5	718.85	869.48	734.81	488.27	452.85	652.85	79.08
12	1019.61	1194.74	1113.14	847.52	853.56	1005.71	69.15
16	1434.63	1745.73	1631.52	1439.21	1356.80	1521.58	72.05
20	1906.08	2275.00	2170.53	1855.16	1905.63	2022.48	83.93
24	2243.47	2589.47	2471.45	2279.68	2321.49	2379.31	65.92
Flux (mcg/cm^2)/h (7-24 h)	109.15	125.00	126.83	126.10	122.89	121.99	3.28
(R^2)	0.9959	0.9930	0.9903	0.9948	0.9927		
Lag time (h)	2.99	2.50	3.61	5.40	3.89	3.89	0.56
Permeability x 10^3 (cm/h)	2.55	2.92	2.97	2.95	2.88	2.86	0.08

Permeation of AZT from ethanol/IPM (20/80) across polyethylene microporous membrane adhered on newborn pig skin (AZT concentration in donor = 42.59 mg/ml)

Calibration curve data

Concentration(mcg/ml)	0	0.0793	0.3966	1.5864	3.9659	7.9318
Peak area ratio	0	0.0484	0.2616	0.9987	2.4471	4.8113

$Y = 0.6066x + 0.0165$
$R^2 = 0.9999$

Time (hours)	Cumulative amount (mcg/cm^2)					Average (mcg/cm^2)	SE
	1	2	3	4	5		
0	0	0	0	0	0	0	0
0.25	6.08	1.14	0.98	1.14	5.29	2.33	1.25
0.5	4.65	2.41	1.04	2.09	3.56	2.55	0.76
0.75	4.42	3.19	1.19	2.61	4.02	2.85	0.67
1	6.00	3.62	1.67	5.09	5.84	4.09	0.95
2.5	11.24	16.50	7.74	11.76	15.26	11.81	1.80
4	28.84	26.64	35.12	26.95	27.43	29.39	1.97
5.5	168.57	108.80	138.81	40.00	169.48	114.04	27.53
7	340.92	228.24	321.98	168.53	320.63	264.92	40.49
9.5	499.86	351.49	584.31	341.88	485.96	444.38	59.02
12	647.18	645.06	1068.69	781.87	746.24	785.70	99.61
16	1082.88	891.56	1536.63	1108.57	1245.22	1154.91	136.14
20	1374.09	1226.25	1844.16	1653.50	1547.96	1524.50	138.56
24	2008.76	1479.23	2554.06	2022.47	2114.23	2016.13	219.42
Flux (mcg/cm^2)/h (7-24 h)	95.78	75.51	127.34	112.08	105.55	103.25	8.63
(R^2)	0.9759	0.9943	0.9879	0.9929	0.9920		
Lag time (h)	4.39	4.11	4.39	5.71	4.55	4.63	0.28
Permeability x 10^3 (cm/h)	2.25	1.77	2.99	2.63	2.48	2.42	0.20

Permeation of AZT from ethanol/IPM (30/70) across polyethylene microporous membrane adhered on newborn pig skin (AZT concentration in donor = 56.25 mg/ml)

Calibration curve data

Concentration(mcg/ml)	0	0.0793	0.3966	1.5864	3.9659	7.9318
Peak area ratio	0	0.0596	0.2592	0.9868	2.3473	4.5811

$Y = 0.5766x + 0.0308$
$R^2 = 0.9997$

Time (hours)	Cumulative amount (mcg/cm^2)					Average (mcg/cm^2)	SE
	1	2	3	4	5		
0	0	0	0	0	0	0	0
0.25	0.55	0.21	0.43	0.89	2.04	0.82	0.32
0.5	1.12	0.69	1.47	1.94	4.14	1.87	0.60
0.75	1.17	2.32	2.92	4.96	6.74	3.62	0.99
1	1.86	5.50	4.38	8.85	10.45	6.21	1.54
2.5	8.99	16.26	16.55	19.47	32.42	18.74	3.83
4	8.88	16.26	16.55	19.47	32.42	18.74	3.83
5.5	175.23	108.36	75.49	134.28	178.08	134.29	19.65
7	565.94	233.67	142.05	319.09	334.69	319.09	70.65
9.5	941.93	673.66	604.65	793.37	853.21	773.37	60.66
12	1397.71	1468.19	1159.11	1401.46	1404.88	1366.27	53.39
16	2506.15	2416.49	1780.77	2287.67	2247.65	2247.75	125.48
20	3405.55	3276.03	2774.21	3083.87	3079.73	3123.88	106.84
24	4097.18	4051.92	3626.95	3874.04	3778.13	3885.65	86.89
Flux (mcg/cm^2)/h (7-24 h)	224.83	230.06	07.27	211.41	202.97	215.31	5.20
(R^2)	0.9938	0.9933	0.9953	0.9984	0.9984		
Lag time (h)	5.32	5.97	6.70	5.48	5.10	5.71	0.29
Permeability x 10^3 (cm/h)	3.99	4.08	3.68	3.75	3.60	3.22	0.56

VITA

Mrs. Nuntakan Suwanpidokkul was born on March 30, 1964 in Khonkaen, Thailand. She obtained her Bachelor degree in Pharmacy (B.Pharm.) from the Faculty of Pharmacy, Khonkaen University, Khonkaen in 1987. In 1990, she received her second degree in Master of Pharmacy from the Department of Pharmaceutical Chemistry, Chulalongkorn University, Bangkok. After the graduation, she worked as a lecturer in the Faculty of Pharmacy, Khonkaen University for one and a half years. From 1992, she has been working as a reseach scientist as Head of Pharmaceutical Chemistry Section at Research and Development Institute, Government Pharmaceutical Organization, Bangkok. She has joined the graduate program for the Doctor of Philosophy degree in Pharmacy at Chulalongkorn University in 1998.