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APPENDIX

Table 25   Absorbance of Theophylline in 0.1 N HCl
            Determined at 268.5 nm.

Concentration (µg/ml)	Absorbance
0	0.000
4	0.216
6	0.322
8	0.430
10	0.537
12	0.645
14	0.747

Correlation coefficient = 0.999958 ;
Y =0.053453X + 0.001141

Table 26   Absorbance of Theophylline in Phosphate Buffer
            pH 6.8 Determined at 270.3 nm.

Concentration (µg/ml)	Absorbance
0	0.000
4	0.226
6	0.335
8	0.449
10	0.561
12	0.670
14	0.783

Correlation coefficient = 0.999973 ;
Y =0.055852X + 0.000852

Table 27 Particle Size Distribution of Spray-Dried Powders
Prepared from Various Spray Drying Conditions

Process Variable /Level	% Weight Retained on Sieve Size					
	Pan	45 µm	75 µm	106 µm	125 µm	250 µm
Inlet Temperature (°C)						
120	15.97	47.88	6.97	10.99	11.77	6.41
130	3.22	66.5	5.98	10.22	8.65	5.42
150	0.12	13.82	11.85	33.49	17.72	23.01
170	63.23	10.78	5.22	6.84	9.32	4.62
Feed rate (ml/min)						
18	0.88	46.01	28.28	9.63	9.79	5.41
24	3.22	66.5	5.98	10.22	8.65	5.42
27	53.81	20.76	8.1	7.28	6.46	3.6
30	41.45	31.68	5.6	8.06	10.72	2.5
Atomization pressure						
2 bar	58.91	19.62	6.93	6	4.98	3.56
3 bar	33.04	26.39	9.62	17.14	9.74	4.07
4 bar	3.22	66.5	5.98	10.22	8.65	5.42
6 bar	0.16	28.73	42.42	9.23	13.32	6.13
Concentration of Solution (%)						
10	1	68.52	7.79	9.58	9.51	3.61
13	3.22	66.5	5.98	10.22	8.65	5.42
20	18	42.93	17.89	8.53	8.25	4.39
25	52.74	19.53	5.23	7.74	8.55	6.21

Table 28 Cumulative % Frequency Undersize and Z Value of Spray-Dried Powder Produced
at Different Inlet Temperature

Temperature / Size Range (micron)	120°C		130°C		150°C		170°C	
	CUM%	Z	CUM%	Z	CUM%	Z	CUM%	Z
0-45	15.97	-0.9958	3.22	-1.8500	0.12	-3.0400	63.23	0.3379
45-75	63.85	0.3545	69.72	0.5163	13.94	-1.0832	74.01	0.6436
75-106	70.82	0.5482	75.70	0.6968	25.79	-0.6490	79.23	0.8145
106-125	81.81	0.9081	85.92	1.0768	59.28	0.2347	86.07	1.0836
125-250	93.58	1.5208	94.57	1.6045	77.00	0.7387	95.39	1.6840
>=250	100.00		100.00		100.00		100.00	

CUM% = Cumulative % Frequency Undersize

Table 29 Cumulative % Frequency Undersize and Z Value of Spray-Dried Powder Produced
at Different Feed Rate of Solution

Feed Rate / Size Range (micron)	18 ml/min		24 ml/min		27 ml/min		30 ml/min	
	CUM%	Z	CUM%	Z	CUM%	Z	CUM%	Z
0-45	0.88	-2.3750	3.22	-1.8500	53.81	0.0956	41.45	-0.2159
45-75	46.89	-0.0780	69.72	0.5163	74.57	0.6609	73.13	0.6167
75-106	75.17	0.6800	75.70	0.6968	82.67	0.9412	78.73	0.7972
106-125	84.80	1.0279	85.92	1.0768	89.95	1.2788	86.79	1.1167
125-250	94.59	1.6864	94.57	1.6045	96.41	1.8000	97.51	1.9617
>=250	100.00		100.00		100.00		100.00	

CUM% = Cumulative % Frequency Undersize

Table 30 Cumulative % Frequency Undersize and Z Value of Spray-Dried Powder Produced
at Various Atomization Pressure

Atomization Pressure / Size Range (micron)	2 bar		3 bar		4 bar		6 bar	
	CUM%	Z	CUM%	Z	CUM%	Z	CUM%	Z
0-45	58.91	0.2251	33.04	-0.4389	3.22	-1.8500	0.16	-2.9400
45-75	78.53	0.7903	59.43	0.2387	69.72	0.5163	28.89	-0.5566
75-106	85.46	1.0565	69.05	0.4972	75.70	0.6968	71.31	0.5624
106-125	91.46	1.3694	86.19	1.0891	85.92	1.0768	80.54	0.8611
125-250	96.44	1.8038	95.93	1.7425	94.57	1.6045	93.86	1.5433
>=250	100.00		100.00		100.00		100.00	

CUM% = Cumulative % Frequency Undersize

Table 31 Cumulative % Frequency Undersize and Z Value of Spray-Dried Powder Produced
from Various Concentration of Solution

Size Range (micron) / Concentration of Solution	10% CUM%	10% Z	13% CUM%	13% Z	20% CUM%	20% Z	25% CUM%	25% Z
0-45	1.00	-2.3217	3.22	-1.8500	18	-0.9154	52.74	0.0687
45-75	69.52	0.5106	69.72	0.5163	60.93	0.2774	72.27	0.5909
75-106	77.31	0.7490	75.70	0.6968	78.82	0.8003	77.50	0.7553
106-125	86.89	1.1214	85.92	1.0768	87.35	1.1430	85.24	1.0470
125-250	96.40	1.7988	94.57	1.6045	95.6	1.7060	93.79	1.5375
>=250	100.00		100.00		100		100.00	

CUM% = Cumulative % Frequency Undersize

Table 32 Geometric Mean Diameter of Spary-Dried Product Prepared from Different Conditions

Process Variable /Level	D50* μm
Inlet Temperature (°C)	
120	73.40
130	82.30
150	144.83
170	32.30
Feed rate (ml/min)	
18	94.23
24	82.30
27	39.47
30	51.22
Atomization pressure	
2 bar	33.05
3 bar	63.00
4 bar	82.30
6 bar	106.54
Concentration of Solution (%)	
10	86.62
13	82.30
20	68.81
25	39.99

*Geometric mean diameter

Table 33   Amount of Theophylline Release from
          Spray-Dried Matrices Prepared at Different
          Inlet Air Temperature

Temperature (°C)	Time (hr)	%*	SD**
120	0.00	0.00	0.00
	0.25	7.91	0.36
	0.50	13.56	0.76
	0.75	18.25	0.60
	1.00	22.18	0.95
	2.00	37.17	1.61
	3.00	45.53	1.55
	4.00	54.03	1.12
	5.00	60.29	0.90
	6.00	63.56	1.73
	7.00	68.58	2.28
	8.00	71.23	1.77
	10.00	77.38	0.68
	12.00	83.84	0.88
130	0.00	0.00	0.00
	0.25	7.88	0.51
	0.50	13.22	0.64
	0.75	17.91	0.82
	1.00	21.55	0.65
	2.00	36.05	1.29
	3.00	43.29	0.59
	4.00	51.20	1.03
	5.00	55.73	0.64
	6.00	60.81	1.71
	7.00	63.98	2.13
	8.00	70.84	0.88
	10.00	78.76	0.62
	12.00	87.43	0.82
150	0.00	0.00	0.00
	0.25	6.42	0.31
	0.50	11.29	0.35
	0.75	15.29	0.86
	1.00	19.17	0.87
	2.00	31.25	2.41
	3.00	37.21	1.28
	4.00	42.31	1.08
	5.00	47.45	1.73
	6.00	51.75	1.84
	7.00	55.89	2.03
	8.00	60.70	3.46
	10.00	63.96	2.19
	12.00	68.59	1.30
170	0.00	0.00	0.00
	0.25	7.35	0.90
	0.50	11.87	1.02
	0.75	15.61	0.86
	1.00	18.80	0.96
	2.00	28.89	1.12
	3.00	34.52	0.65
	4.00	40.49	1.05
	5.00	44.89	1.54
	6.00	48.39	1.57
	7.00	52.26	1.94
	8.00	53.67	2.37
	10.00	59.75	3.16
	12.00	66.55	3.31

* Mean of six determinations (%)
** Standard deviation

Table 34 Amount of Theophylline Release from Spray-Dried Matrices Prepared at Different Feed Rate

Feedrate (ml/min)	Time (hr)	%*	SD**
18	0.00	0.00	0.00
	0.25	8.08	0.33
	0.50	13.29	0.70
	0.75	17.51	0.78
	1.00	21.03	0.86
	2.00	34.39	1.43
	3.00	43.88	1.52
	4.00	51.60	2.05
	5.00	59.69	2.19
	6.00	62.57	1.49
	7.00	69.13	2.40
	8.00	69.41	0.73
	10.00	77.81	2.10
	12.00	82.44	1.99
24	0.00	0.00	0.00
	0.25	7.88	0.51
	0.50	13.22	0.64
	0.75	17.91	0.82
	1.00	21.55	0.65
	2.00	36.05	1.29
	3.00	43.29	0.59
	4.00	51.20	1.03
	5.00	55.73	0.64
	6.00	60.81	1.71
	7.00	63.98	2.13
	8.00	70.84	0.88
	10.00	78.76	0.62
	12.00	87.43	0.82
27	0.00	0.00	0.00
	0.25	7.52	0.52
	0.50	12.49	0.89
	0.75	17.27	0.77
	1.00	21.48	1.05
	2.00	36.56	0.93
	3.00	47.42	1.11
	4.00	54.86	1.58
	5.00	60.86	0.50
	6.00	66.80	0.52
	7.00	71.34	0.77
	8.00	74.88	0.47
	10.00	81.52	1.24
	12.00	86.05	1.49
30	0.00	0.00	0.00
	0.25	8.24	0.49
	0.50	13.52	0.71
	0.75	18.64	0.96
	1.00	23.72	1.02
	2.00	38.84	1.34
	3.00	48.12	1.40
	4.00	54.95	1.54
	5.00	60.26	2.11
	6.00	64.52	2.26
	7.00	67.56	2.36
	8.00	71.75	2.36
	10.00	77.79	2.15
	12.00	84.54	1.82

* Mean of six determinations (%)
** Standard deviation

Table 35   Amount of Theophylline Release from Spray-Dried Matrices Prepared at Various Atomization Pressure

Atomization pressure (bar)	Time (hr)	%*	SD**
2	0.00	0.00	0.00
	0.25	7.81	0.82
	0.50	12.23	0.91
	0.75	16.20	0.92
	1.00	19.97	0.82
	2.00	33.56	0.95
	3.00	42.98	0.56
	4.00	50.05	0.61
	5.00	56.67	0.36
	6.00	61.35	0.77
	7.00	64.07	0.72
	8.00	68.71	1.42
	10.00	78.36	1.64
	12.00	83.40	1.43
3	0.00	0.00	0.00
	0.25	8.16	0.58
	0.50	13.77	1.24
	0.75	18.35	0.89
	1.00	23.09	1.87
	2.00	35.50	2.00
	3.00	43.48	1.44
	4.00	50.55	1.92
	5.00	55.07	1.98
	6.00	59.73	1.90
	7.00	63.85	1.99
	8.00	68.05	2.73
	10.00	75.47	3.37
	12.00	82.51	3.70
4	0.00	0.00	0.00
	0.25	7.88	0.51
	0.50	13.22	0.64
	0.75	17.91	0.82
	1.00	21.55	0.65
	2.00	36.05	1.29
	3.00	43.29	0.59
	4.00	51.20	1.03
	5.00	55.73	0.64
	6.00	60.81	1.71
	7.00	63.98	2.13
	8.00	70.84	0.88
	10.00	78.76	0.62
	12.00	87.43	0.82
6	0.00	0.00	0.00
	0.25	7.86	0.29
	0.50	13.56	0.27
	0.75	17.85	0.26
	1.00	21.73	0.34
	2.00	34.99	0.78
	3.00	45.58	1.12
	4.00	51.76	0.88
	5.00	60.98	2.14
	6.00	64.43	0.47
	7.00	68.53	1.42
	8.00	72.84	1.60
	10.00	79.82	1.54
	12.00	84.85	1.78

*   Mean of six determinations (%)
** Standard deviation

Table 36   Amount of Theophylline Release from
            Spray-Dried Matrices Prepared at Different
            Concentration of Solution

Concentration of solution (%)	Time (hr)	%*	SD**
10	0.00	0.00	0.00
	0.25	7.78	0.49
	0.50	13.51	0.94
	0.75	17.73	0.48
	1.00	21.56	0.43
	2.00	34.61	0.40
	3.00	44.13	0.33
	4.00	52.02	0.84
	5.00	57.63	0.93
	6.00	62.58	1.23
	7.00	66.84	0.59
	8.00	69.95	1.05
	10.00	77.66	1.64
	12.00	82.80	1.24
13	0.00	0.00	0.00
	0.25	7.88	0.51
	0.50	13.22	0.64
	0.75	17.91	0.82
	1.00	21.55	0.65
	2.00	36.05	1.29
	3.00	43.29	0.59
	4.00	51.20	1.03
	5.00	55.73	0.64
	6.00	60.81	1.71
	7.00	63.98	2.13
	8.00	70.84	0.88
	10.00	78.76	0.62
	12.00	87.43	0.82
20	0.00	0.00	0.00
	0.25	6.81	0.35
	0.50	12.08	0.60
	0.75	16.85	0.84
	1.00	20.22	0.97
	2.00	32.85	0.53
	3.00	42.57	0.70
	4.00	52.99	0.48
	5.00	55.39	0.70
	6.00	61.22	1.36
	7.00	65.68	0.74
	8.00	70.52	0.80
	10.00	78.64	1.97
	12.00	83.69	1.87
25	0.00	0.00	0.00
	0.25	8.12	0.92
	0.50	14.23	1.61
	0.75	18.81	2.08
	1.00	23.92	1.96
	2.00	39.74	2.34
	3.00	50.20	2.14
	4.00	58.13	2.43
	5.00	63.61	3.42
	6.00	68.60	2.25
	7.00	73.28	1.95
	8.00	77.18	1.82
	10.00	81.13	2.27
	12.00	86.20	1.28

* Mean of six determinations (%)
** Standard deviation

Table 37   Analysis of Variance of T50% at Different Inlet Air Temperature

SOURCE	SUM OF SQUARES	DF	MEAN SQUARE	F	PROBABILITY
Between groups	42.841	3	14.28	41.403	0.000
Within groups	6.898	20	0.345		

DUNCAN MULTIPLE RANGE TESTS

ORDERED MEANS DIFFER AT ALPHA=0.05		ORDERED MEANS DIFFER AT ALPHA=0.01	
Gap order	Difference	Gap order	Difference
2	0.708	2	0.967
3	0.743	3	1.007
4	0.765	4	1.034

Table 38   Analysis of Variance of T80% at Different Inlet Air Temperature

SOURCE	SUM OF SQUARES	DF	MEAN SQUARE	F	PROBABILITY
Between groups	174.649	3	58.216	65.171	0.000
Within groups	17.866	20	0.893		

DUNCAN MULTIPLE RANGE TESTS

ORDERED MEANS DIFFER AT ALPHA=0.05		ORDERED MEANS DIFFER AT ALPHA=0.01	
Gap order	Difference	Gap order	Difference
2	1.139	2	1.556
3	1.195	3	1.621
4	1.231	4	1.664

Table 39   Analysis of Variance of T50% at Different Feed Rate

SOURCE	SUM OF SQUARES	DF	MEAN SQUARE	F	PROBABILITY
Between groups	1.039	3	0.346	3.776	0.027
Within groups	1.834	20	0.092		

DUNCAN MULTIPLE RANGE TESTS
ORDERED MEANS DIFFER AT ALPHA=0.05

Gap order	Difference
2	0.365
3	0.383
4	0.394

Table 40   Analysis of Variance of T80% at Different Feed Rate

SOURCE	SUM OF SQUARES	DF	MEAN SQUARE	F	PROBABILITY
Between groups	4.402	3	1.467	4.964	0.010
Within groups	5.912	20	0.296		

DUNCAN MULTIPLE RANGE TESTS

ORDERED MEANS DIFFER AT ALPHA=0.05		ORDERED MEANS DIFFER AT ALPHA=0.01	
Gap order	Difference	Gap order	Difference
2	0.655	2	0.895
3	0.687	3	0.932
4	0.708	4	0.957

Table 41   Analysis of Variance of T50% at Various Atomization Pressure

SOURCE	SUM OF SQUARES	DF	MEAN SQUARE	F	PROBABILITY
Between groups	0.234	3	0.078	1.578	0.226
Within groups	0.988	20	0.049		

DUNCAN MULTIPLE RANGE TESTS
ORDERED MEANS DIFFER AT ALPHA=0.05

Gap order	Difference
2	0.268
3	0.281
4	0.289

Table 42   Analysis of Variance of T80% at Various Atomization Pressure

SOURCE	SUM OF SQUARES	DF	MEAN SQUARE	F	PROBABILITY
Between groups	3.488	3	1.163	2.910	0.060
Within groups	7.992	20	0.400		

DUNCAN MULTIPLE RANGE TESTS
ORDERED MEANS DIFFER AT ALPHA=0.05

Gap order	Difference
2	0.762
3	0.799
4	0.823

Table 43   Analysis of Variance of T50% at Different Concentration of Solution

SOURCE	SUM OF SQUARES	DF	MEAN SQUARE	F	PROBABILITY
Between groups	2.526	3	0.842	29.099	0.000
Within groups	0.579	20	0.029		

DUNCAN MULTIPLE RANGE TESTS
ORDERED MEANS DIFFER AT ALPHA=0.05   ORDERED MEANS DIFFER AT ALPHA=0.01

Gap order	Difference	Gap order	Difference
2	0.205	2	0.280
3	0.215	3	0.292
4	0.222	4	0.300

Table 44   Analysis of Variance of T80% at Different Concentration of Solution

SOURCE	SUM OF SQUARES	DF	MEAN SQUARE	F	PROBABILITY
Between groups	8.146	3	2.715	9.745	0.000
Within groups	5.572	20	0.279		

DUNCAN MULTIPLE RANGE TESTS
ORDERED MEANS DIFFER AT ALPHA=0.05   ORDERED MEANS DIFFER AT ALPHA=0.01

Gap order	Difference	Gap order	Difference
2	0.636	2	0.896
3	0.667	3	0.905
4	0.687	4	0.930

Table 45   Effect of Magnesium Stearate on Amount of
Theophylline Release from Spray-Dried Matrices

Formulation	Time (hr)	%*	SD**
0% Mg	0.00	0.00	0.00
	0.25	7.81	0.54
	0.50	12.98	0.62
	0.75	17.18	0.97
	1.00	21.15	1.42
	2.00	36.42	1.51
	3.00	46.21	1.32
	4.00	54.90	1.22
	5.00	61.55	0.92
	6.00	66.80	1.37
	7.00	70.85	0.92
	8.00	74.88	0.68
	10.00	80.60	0.87
	12.00	88.41	1.05
+0.75%Mg	0.00	0.00	0.00
	0.25	8.24	0.65
	0.50	14.43	0.51
	0.75	19.08	0.51
	1.00	23.11	0.52
	2.00	34.49	0.47
	3.00	43.59	0.69
	4.00	50.17	1.52
	5.00	57.64	0.65
	6.00	62.82	0.33
	7.00	66.74	0.06
	8.00	70.95	0.34
	10.00	78.42	0.63
	12.00	85.45	0.13
+1.5%Mg	0.00	0.00	0.00
	0.25	5.54	0.09
	0.50	9.90	0.37
	0.75	12.62	0.20
	1.00	15.24	0.15
	2.00	24.63	0.70
	3.00	30.00	0.29
	4.00	36.32	0.59
	5.00	38.67	0.34
	6.00	42.65	0.32
	7.00	44.62	0.54
	8.00	47.07	0.16
	10.00	52.64	0.31
	12.00	57.31	0.60

* Mean of six determinations (%)
** Standard deviation

Table 46   Amount of Theophylline Release from Matrices
            Prepared at Different Compressional Force
            with Carver Laboratory Press

Compressional Force (lb)	Time (hr)	%*	SD**
500	0.00	0.00	0.00
	0.25	7.81	0.54
	0.50	12.98	0.62
	0.75	17.18	0.97
	1.00	21.15	1.42
	2.00	36.42	1.51
	3.00	46.21	1.32
	4.00	54.90	1.22
	5.00	61.55	0.92
	6.00	66.80	1.37
	7.00	70.85	0.92
	8.00	74.88	0.68
	10.00	80.60	0.87
	12.00	88.41	1.05
1000	0.00	0.00	0.00
	0.25	8.46	0.11
	0.50	14.41	0.17
	0.75	19.73	0.22
	1.00	25.20	0.42
	2.00	41.47	0.74
	3.00	49.93	0.68
	4.00	57.72	0.17
	5.00	62.70	0.60
	6.00	67.39	0.26
	7.00	71.79	0.42
	8.00	74.51	0.20
	10.00	81.86	0.50
	12.00	87.63	0.62
1500	0.00	0.00	0.00
	0.25	8.01	0.85
	0.50	13.37	0.70
	0.75	17.43	0.64
	1.00	21.26	0.88
	2.00	35.75	1.04
	3.00	45.23	2.37
	4.00	51.81	1.63
	5.00	56.41	1.23
	6.00	62.01	1.11
	7.00	65.08	1.41
	8.00	69.59	1.93
	10.00	76.15	1.60
	12.00	80.73	1.54

* Mean of six determinations (%)
** Standard deviation

Table 47   Amount of Theophylline Release from Matrices
            Prepared at Different Compressional Force
            with Instrumented Single Machine

Compressional Force (lb)	Time (hr)	%*	SD**
	0.00	0.00	0.00
	0.25	7.21	0.49
	0.50	12.33	0.89
	0.75	17.61	1.06
	1.00	22.76	0.97
	2.00	37.70	0.92
300	3.00	45.17	0.91
	4.00	52.18	0.88
	5.00	58.62	0.96
	6.00	62.76	0.74
	7.00	66.25	0.80
	8.00	69.50	0.41
	10.00	76.31	0.40
	12.00	81.17	0.65
	0.00	0.00	0.00
	0.25	7.66	0.40
	0.50	12.30	0.59
	0.75	16.43	0.61
	1.00	20.47	0.48
	2.00	35.66	0.67
500	3.00	45.62	1.18
	4.00	53.48	1.51
	5.00	58.97	1.17
	6.00	64.00	1.14
	7.00	67.98	1.21
	8.00	71.49	1.03
	10.00	76.78	1.28
	12.00	82.10	1.07
	0.00	0.00	0.00
	0.25	7.89	0.19
	0.50	12.82	0.47
	0.75	17.14	0.39
	1.00	20.93	0.54
	2.00	36.93	0.72
700	3.00	44.97	1.45
	4.00	53.55	2.18
	5.00	61.29	2.34
	6.00	66.55	2.20
	7.00	69.73	2.97
	8.00	74.00	2.77
	10.00	80.94	2.98
	12.00	86.52	2.20

* Mean of six determinations (%)
** Standard deviation

Table 48   Amount of Theophylline Release from
            Spray-Dried Matrices of Batch I-III

Formulation	Time (hr)	%*	SD**
Batch I	0.00	0.00	0.00
	0.25	7.61	0.17
	0.50	12.83	0.23
	0.75	17.10	0.31
	1.00	21.14	0.59
	2.00	35.45	1.17
	3.00	43.88	0.86
	4.00	51.56	0.55
	5.00	56.58	0.62
	6.00	61.38	0.79
	7.00	65.84	0.69
	8.00	69.49	0.68
	10.00	76.71	0.95
	12.00	81.70	1.31
Batch II	0.00	0.00	0.00
	0.25	7.66	0.40
	0.50	12.30	0.59
	0.75	16.43	0.61
	1.00	20.47	0.48
	2.00	35.66	0.67
	3.00	45.62	1.18
	4.00	53.48	1.51
	5.00	58.97	1.17
	6.00	64.00	1.14
	7.00	67.98	1.21
	8.00	71.49	1.03
	10.00	76.78	1.28
	12.00	82.10	1.07
Batch III	0.00	0.00	0.00
	0.25	7.62	0.21
	0.50	12.39	0.37
	0.75	16.90	0.38
	1.00	21.31	1.04
	2.00	37.01	1.83
	3.00	46.31	1.20
	4.00	54.33	1.85
	5.00	60.25	1.80
	6.00	65.07	1.73
	7.00	69.35	1.53
	8.00	72.66	1.70
	10.00	78.93	1.38
	12.00	83.42	0.44

* Mean of six determinations (%)
** Standard deviation

Table 49   Amount of Theophylline Release from
            Spray-Dried Matrices of Scale-up Batch,
            Nuelin[R] T/SR and Theodur[R]

Formulation	Time (hr)	%*	SD**
Scale-up Batch	0.00	0.00	0.00
	0.25	7.27	0.66
	0.50	12.80	0.97
	0.75	17.47	1.20
	1.00	22.58	1.46
	2.00	38.41	1.20
	3.00	45.22	1.45
	4.00	53.14	1.61
	5.00	60.49	1.10
	6.00	65.08	1.38
	7.00	68.92	1.37
	8.00	72.18	1.76
	10.00	78.41	2.05
	12.00	83.54	1.57
Nuelin [R]	0.00	0.00	0.00
	0.25	8.04	0.31
	0.50	12.19	0.32
	0.75	15.47	0.32
	1.00	18.38	0.37
	2.00	25.85	0.45
	3.00	35.19	1.08
	4.00	42.87	1.43
	5.00	48.86	1.44
	6.00	53.05	0.92
	7.00	56.74	1.64
	8.00	61.27	1.26
	10.00	67.80	1.79
	12.00	76.09	2.08
Theodur [R]	0.00	0.00	0.00
	0.25	5.59	0.29
	0.50	8.11	0.47
	0.75	10.14	0.53
	1.00	12.01	0.41
	2.00	17.54	0.72
	3.00	26.03	1.30
	4.00	39.62	2.57
	5.00	50.39	2.00
	6.00	56.69	2.70
	7.00	65.43	3.86
	8.00	71.09	4.28
	10.00	79.72	3.87
	12.00	87.06	2.15

* Mean of six determinations (%)
** Standard deviation

Table 50   Analysis of Variance of T50% at Different Magnesium Stearate
            Percent of Spray-Dried Matrices

SOURCE	SUM OF SQUARES	DF	MEAN SQUARE	F	PROBABILITY
Between groups	122.661	2	61.331	4490.166	0.000
Within groups	0.205	15	0.014		

DUNCAN MULTIPLE RANGE TESTS

ORDERED MEANS DIFFER AT ALPHA=0.05		ORDERED MEANS DIFFER AT ALPHA=0.01	
Gap order	Difference	Gap order	Difference
2	0.144	2	0.199
3	0.151	3	0.208

Table 51   Analysis of Variance of T80% at Different Magnesium Stearate
            Percent of Spray-Dried Matrices

SOURCE	SUM OF SQUARES	DF	MEAN SQUARE	F	PROBABILITY
Between groups	560.675	2	280.338	4479.802	0.000
Within groups	0.934	15	0.062		

DUNCAN MULTIPLE RANGE TESTS

ORDERED MEANS DIFFER AT ALPHA=0.05		ORDERED MEANS DIFFER AT ALPHA=0.01	
Gap order	Difference	Gap order	Difference
2	0.307	2	0.426
3	0.322	3	0.443

Table 52   Analysis of Variance of T50% at Different Compressional
            Pressure (500lb-1500lb)

SOURCE	SUM OF SQUARES	DF	MEAN SQUARE	F	PROBABILITY
Between groups	1.740	2	0.870	35.858	0.000
Within groups	0.364	15	0.024		

DUNCAN MULTIPLE RANGE TESTS

ORDERED MEANS DIFFER AT ALPHA=0.05		ORDERED MEANS DIFFER AT ALPHA=0.01	
Gap order	Difference	Gap order	Difference
2	0.192	2	0.266
3	0.201	3	0.277

Table 53   Analysis of Variance of T80% at Different Compressional
          Pressure (500lb-1500lb)

SOURCE	SUM OF SQUARES	DF	MEAN SQUARE	F	PROBABILITY
Between groups	15.742	2	7.871	74.943	0.000
Within groups	1.575	15	0.105		

DUNCAN MULTIPLE RANGE TESTS
ORDERED MEANS DIFFER AT ALPHA=0.05   ORDERED MEANS DIFFER AT ALPHA=0.01

Gap order	Difference		Gap order	Difference
2	0.399		2	0.553
3	0.418		3	0.575

Table 54   Analysis of Variance of T50% at Different Compressional
          Pressure (300lb-700lb)

SOURCE	SUM OF SQUARES	DF	MEAN SQUARE	F	PROBABILITY
Between groups	0.066	2	0.033	1.214	0.324
Within groups	0.405	15	0.027		

DUNCAN MULTIPLE RANGE TESTS
ORDERED MEANS DIFFER AT ALPHA=0.05   ORDERED MEANS DIFFER AT ALPHA=0.01

Gap order	Difference		Gap order	Difference
2	0.202		2	0.280
3	0.212		3	0.292

Table 55   Analysis of Variance of T80% at Different Compressional
          Pressure (300lb-700lb)

SOURCE	SUM OF SQUARES	DF	MEAN SQUARE	F	PROBABILITY
Between groups	10.086	2	5.043	24.703	0.000
Within groups	3.062	15	0.204		

DUNCAN MULTIPLE RANGE TESTS
ORDERED MEANS DIFFER AT ALPHA=0.05   ORDERED MEANS DIFFER AT ALPHA=0.01

Gap order	Difference		Gap order	Difference
2	0.556		2	0.771
3	0.583		3	0.802

Table 56 Analysis of Variance of T50% from Batch I-III

SOURCE	SUM OF SQUARES	DF	MEAN SQUARE	F	PROBABILITY
Between groups	0.282	2	0.141	6.761	0.008
Within groups	0.313	15	0.021		

DUNCAN MULTIPLE RANGE TESTS

ORDERED MEANS DIFFER AT ALPHA=0.05		ORDERED MEANS DIFFER AT ALPHA=0.01	
Gap order	Difference	Gap order	Difference
2	0.178	2	0.246
3	0.186	3	0.257

Table 57 Analysis of Variance of T80% from Batch I-III

SOURCE	SUM OF SQUARES	DF	MEAN SQUARE	F	PROBABILITY
Between groups	3.138	2	1.569	8.158	0.004
Within groups	2.885	15	0.192		

DUNCAN MULTIPLE RANGE TESTS

ORDERED MEANS DIFFER AT ALPHA=0.05		ORDERED MEANS DIFFER AT ALPHA=0.01	
Gap order	Difference	Gap order	Difference
2	0.540	2	0.748
3	0.566	3	0.779

Table 58 Analysis of Variance of T50% from Batch I-III and Scale-up Batch

SOURCE	SUM OF SQUARES	DF	MEAN SQUARE	F	PROBABILITY
Between groups	0.290	3	0.097	3.345	0.040
Within groups	0.579	20	0.029		

DUNCAN MULTIPLE RANGE TESTS

ORDERED MEANS DIFFER AT ALPHA=0.05		ORDERED MEANS DIFFER AT ALPHA=0.01	
Gap order	Difference	Gap order	Difference
2	0.205	2	0.280
3	0.215	3	0.292
4	0.222	4	0.300

Table 59   Analysis of Variance of T80% from Batch I-III and Scale-up
           Batch

SOURCE	SUM OF SQUARES	DF	MEAN SQUARE	F	PROBABILITY
Between groups	4.246	3	1.415	5.439	0.007
Within groups	5.205	20	0.260		

DUNCAN MULTIPLE RANGE TESTS
ORDERED MEANS DIFFER AT ALPHA=0.05   ORDERED MEANS DIFFER AT ALPHA=0.01

Gap order	Difference		Gap order	Difference
2	0.615		2	0.840
3	0.645		3	0.875
4	0.664		4	0.898

Table 60   Analysis of Variance of T50% from Spray-Dried Matrices
           Nuelin and Theodur

SOURCE	SUM OF SQUARES	DF	MEAN SQUARE	F	PROBABILITY
Between groups	9.973	2	4.987	62.966	0.000
Within groups	1.188	15	0.079		

DUNCAN MULTIPLE RANGE TESTS
ORDERED MEANS DIFFER AT ALPHA=0.05   ORDERED MEANS DIFFER AT ALPHA=0.01

Gap order	Difference		Gap order	Difference
2	0.347		2	0.480
3	0.363		3	0.500

Table 61   Analysis of Variance of T80% from Spray-Dried Matrices
           Nuelin and Theodur

SOURCE	SUM OF SQUARES	DF	MEAN SQUARE	F	PROBABILITY
Between groups	27.276	2	13.638	23.199	0.000
Within groups	8.813	15	0.588		

DUNCAN MULTIPLE RANGE TESTS
ORDERED MEANS DIFFER AT ALPHA=0.05   ORDERED MEANS DIFFER AT ALPHA=0.01

Gap order	Difference		Gap order	Difference
2	0.944		2	1.308
3	0.989		3	1.362

Table 62 Particle Size Distribution of Spray-Dried Powder
from Consecutive-Three Batch and Scale-up Batch.

Formulation	% Weight Retained on Sieve Size					
	Pan	45 um	75 um	106 um	125 um	250 um
Batch I	68.56	16.34	3.80	3.99	4.28	3.02
Batch II	56.51	20.45	4.54	8.54	4.98	4.98
Batch II	66.14	15.01	5.18	5.37	5.43	2.88
Scale-up Batch	56.21	19.05	7.90	6.36	6.97	3.50

Table 63 Cumulative % Frequency Undersize and Z Value of Spray-Dried Powder
from Batch I-III and Scale-up Batch

Batch Size Range (micron)	I		II		III		Scale-up Batch	
	CUM%	Z	CUM%	Z	CUM%	Z	CUM%	Z
0-45	68.56	0.4834	59.05	0.2287	66.14	0.4162	56.21	0.1563
45-75	84.90	1.0322	77.59	0.7583	81.15	0.8833	75.26	0.6828
75-106	88.70	1.2105	82.44	0.9323	86.33	1.0955	83.16	0.9604
106-125	92.69	1.4531	89.74	1.2667	91.70	1.3853	89.52	1.2544
125-250	96.97	1.8767	94.71	1.6173	97.13	1.9000	96.49	1.8100
>=250	100.00		100.00		100.00		100.00	

CUM% = Cumulative % Frequency Undersize

Table 64   The In Vitro Release Specification of
            Theophylline Product Prepared from
            Ready Made Granule manufactured by
            Boehringer Ingelheim KG

Time (hr.)	Amount of Drug Release
1	15-30%
3	40-60%
5	55-75%
7	65-85%
9	70-90%
11	75-95%

Table 65   The Values of Release Exponent (n), Kinetic
            Constant (k) and Correlation Coefficient (r^2)
            following Linear Regression of Dissolution Data
            for Values of M_t/M_∞

Batch	n Release exponent	k Kinetic constant	r^2 Correlation coefficient
I	0.52	0.2350	0.9910
II	0.52	0.2398	0.9847
III	0.52	0.2415	0.9856
Scale-up	0.52	0.2427	0.9876
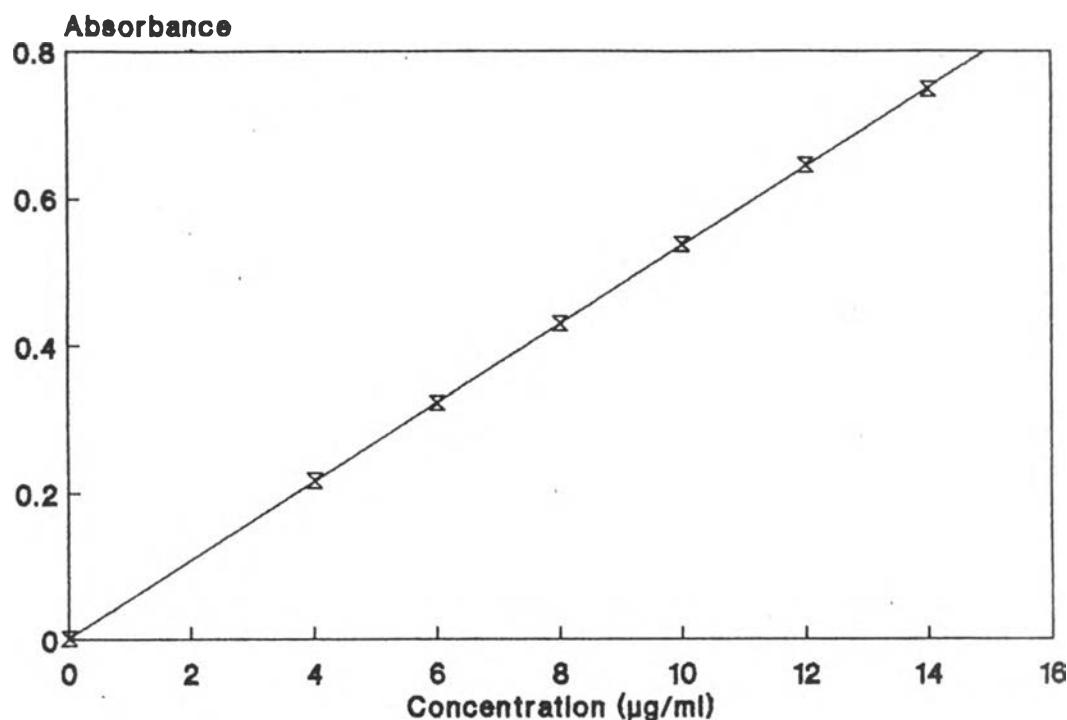
Figure 63   Calibration Curve of Theophylline in 0.1 N HCl at 268.5 nm.
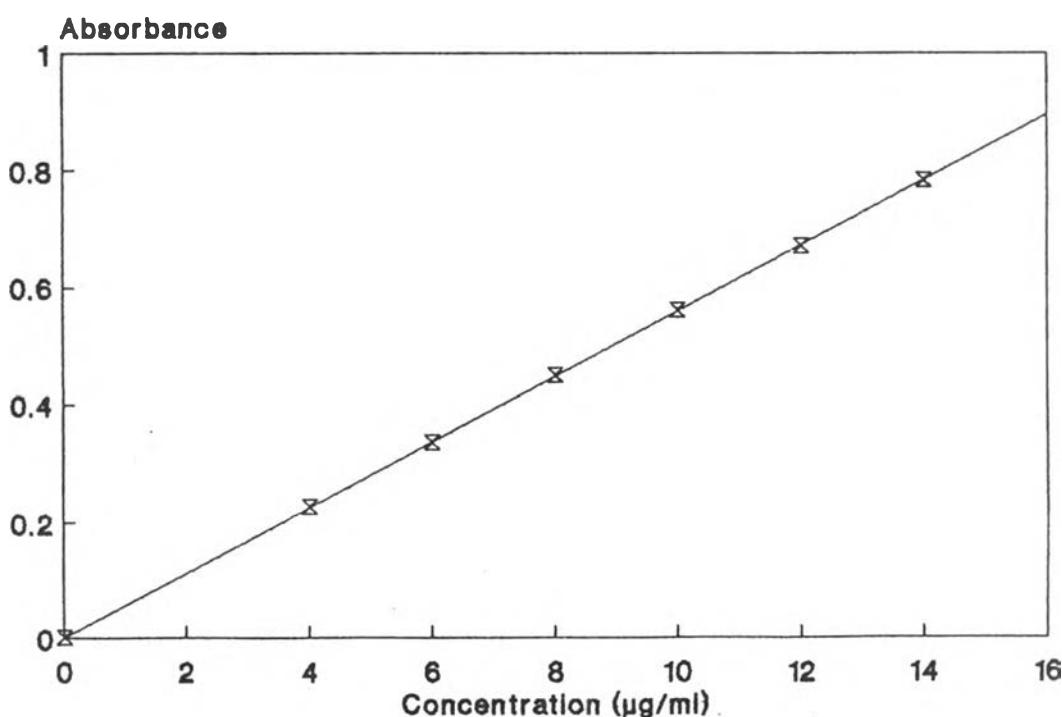
Figure 64   Calibration Curve of Theophylline in Phosphaste Buffer pH 6.8 at 270.3 nm.

Cumulative % frequency undersize
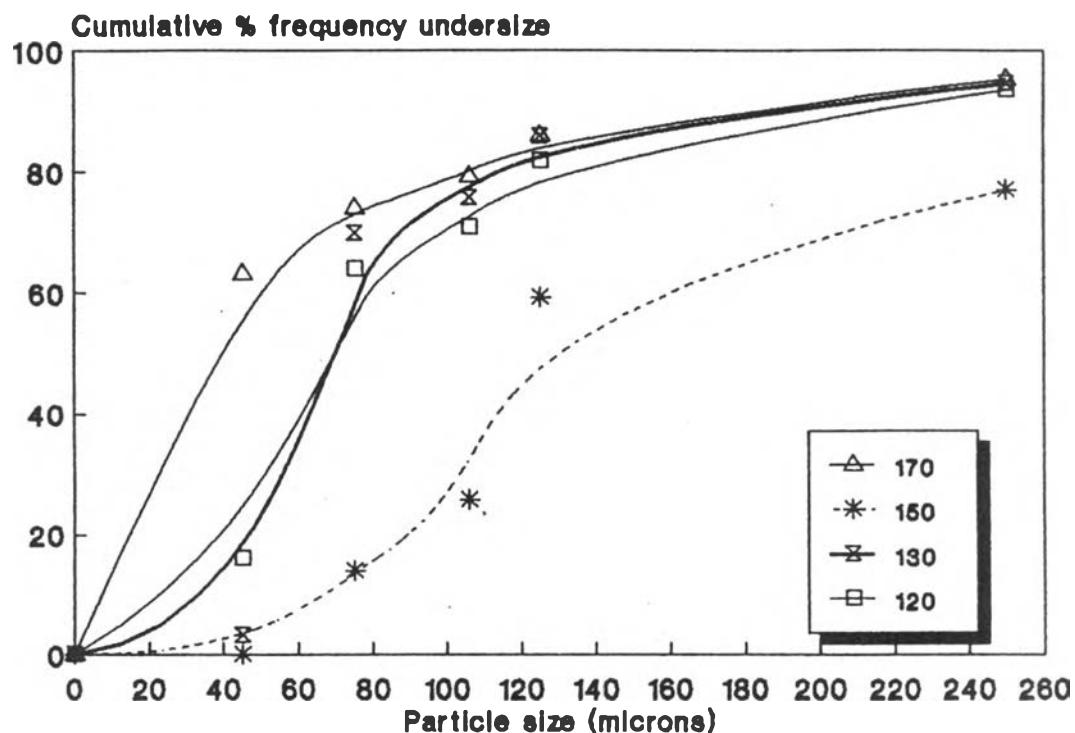
Figure 65   The Plot of Cumulative % Frequency Undersize
             of Spray-Dried Powders Prepared at Different
             Inlet Air Temperature

**Cumulative % F undersize(Prob.scale,z)**
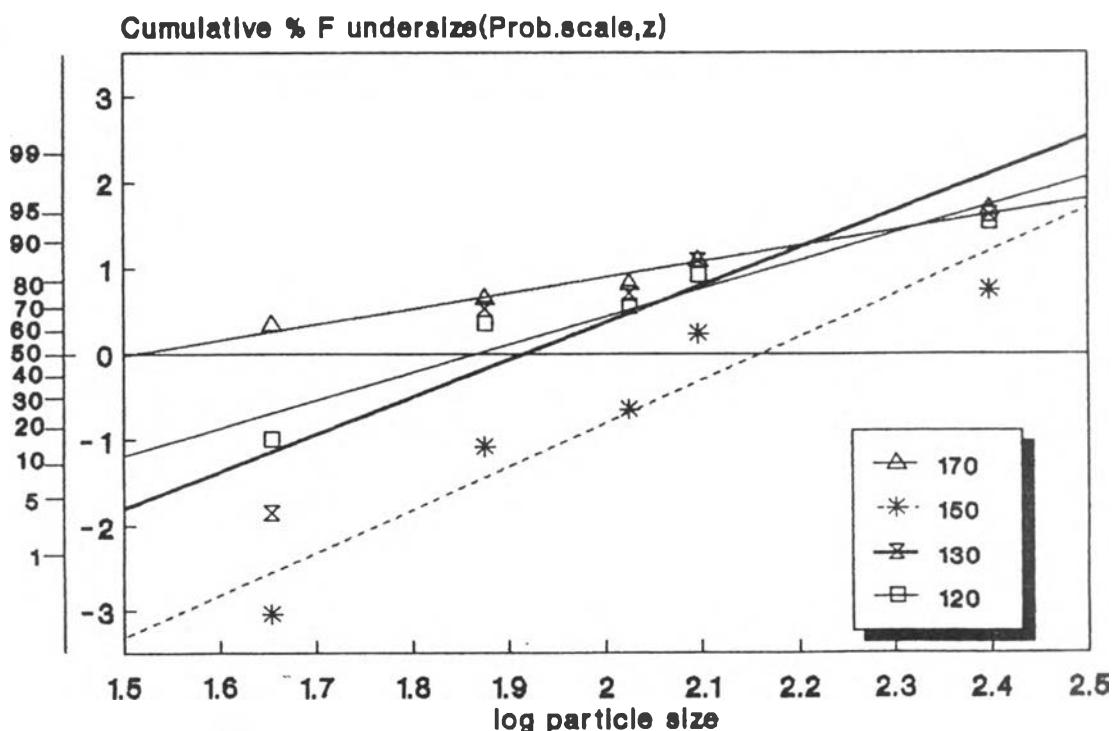
Figure 66   The Plot of Cumulative % Frequency Undersize
             on Probability Scale Versus Log Particle Size
             of Spray Dried Powders Prepared at Different
             Inlet Air Temperature

Cumulative % frequency undersize
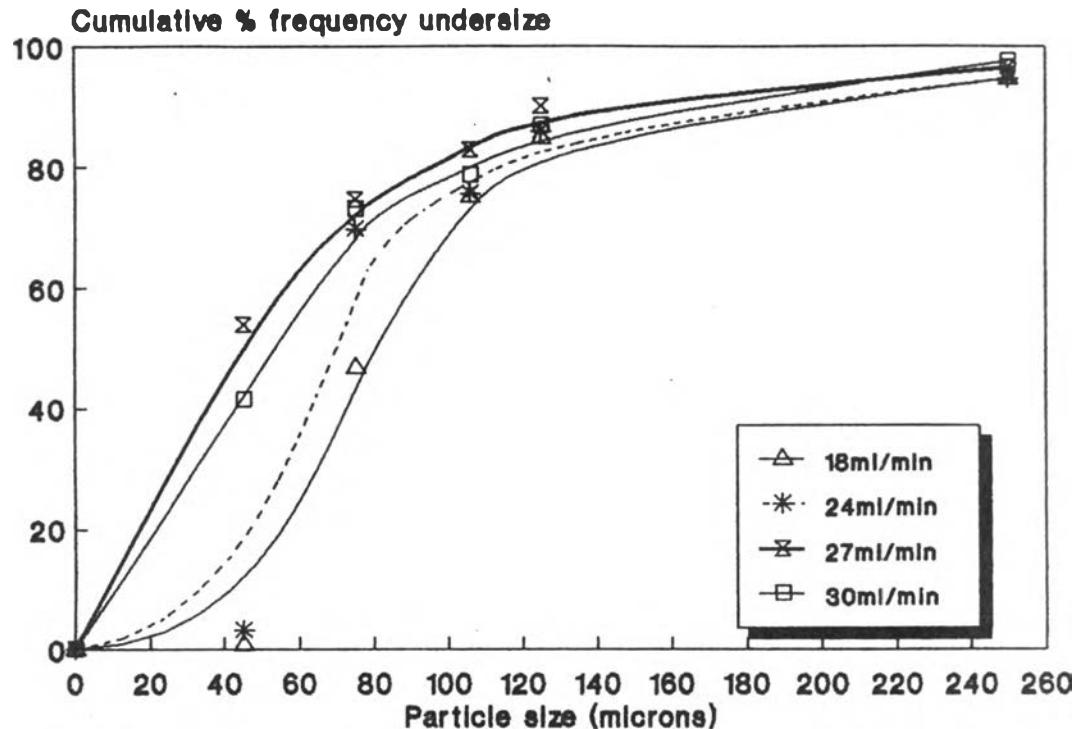
Figure 67   The Plot of Cumulative % Frequency Undersize
of Spray-Dried Powders Prepared at Different
Feed Rate

Cumulative % F undersize(Prob.sacle,z)
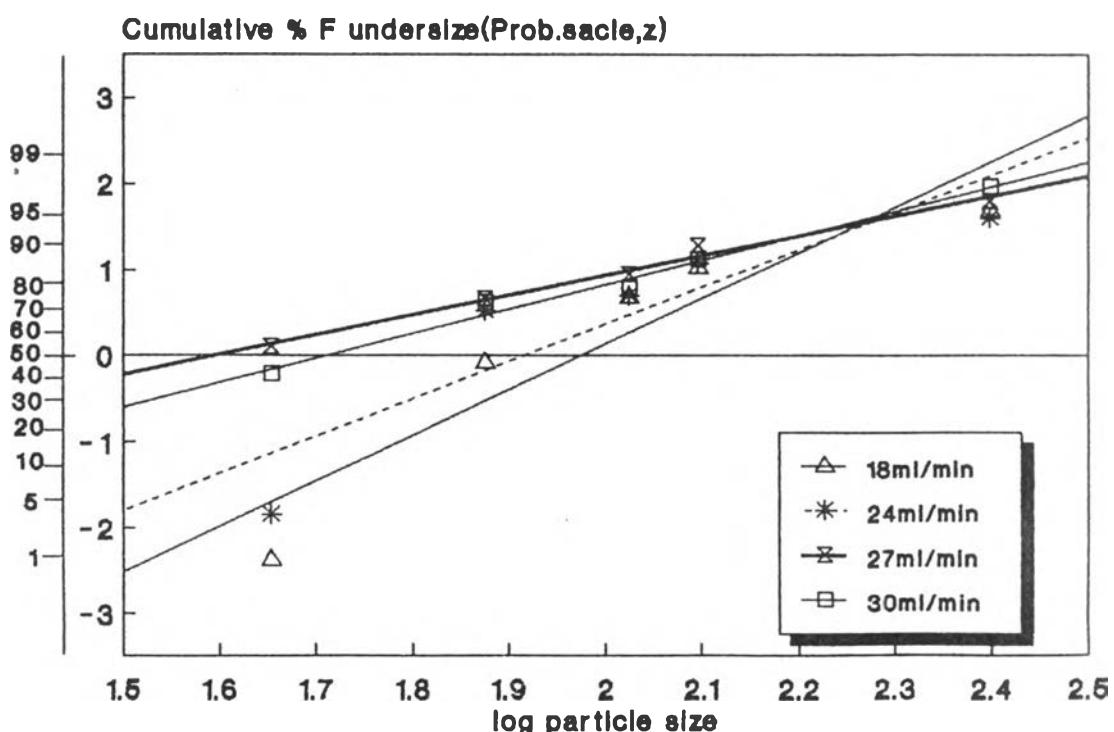
Figure 68   The Plot of Cumulative % Frequency Undersize
on Probability Scale Versus Log Particle Size
of Spray Dried Powders Prepared at Different
Feed Rate
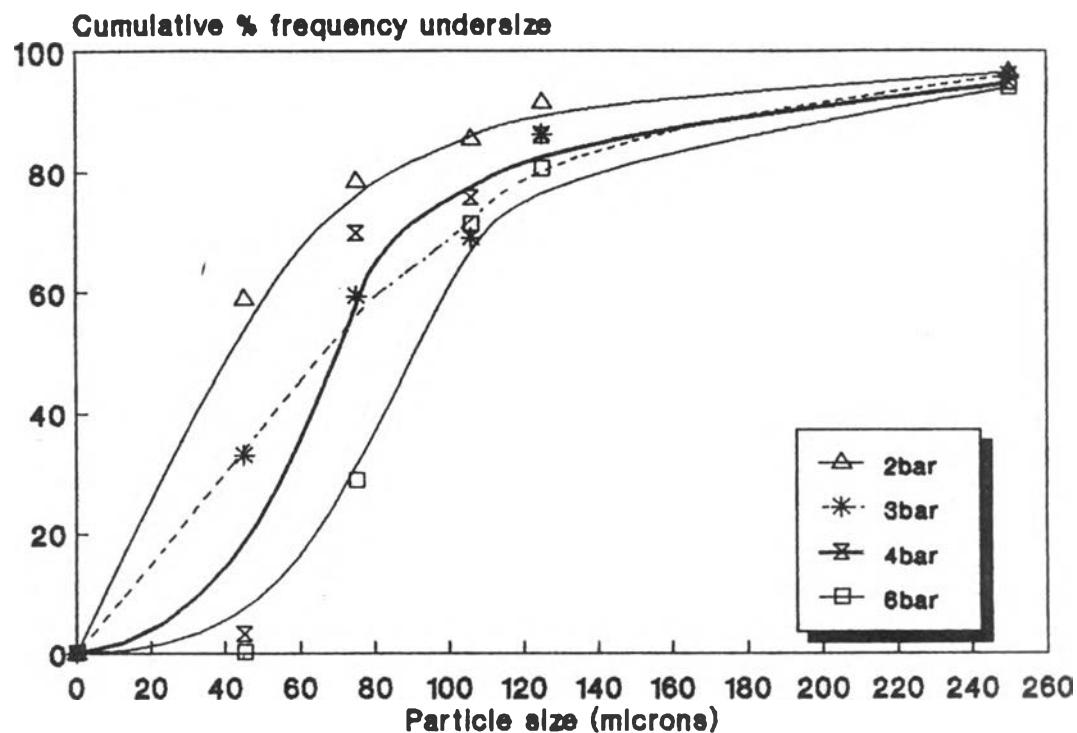
Figure 69 The Plot of Cumulative % Frequency Undersize of Spray-Dried Powders Prepared at Various Atomizing Air Pressure
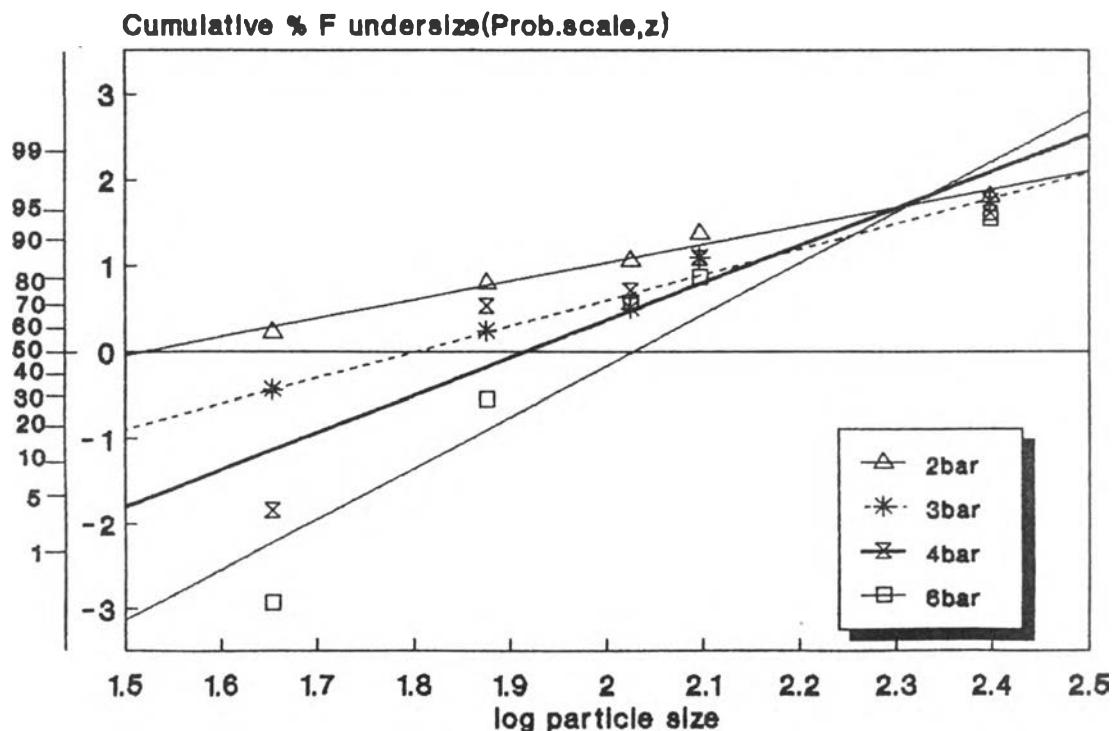
Figure 70 The Plot of Cumulative % Frequency Undersize on Probability Scale Versus Log Particle Size of Spray Dried Powders Prepared at Various Atomizing Air Pressure
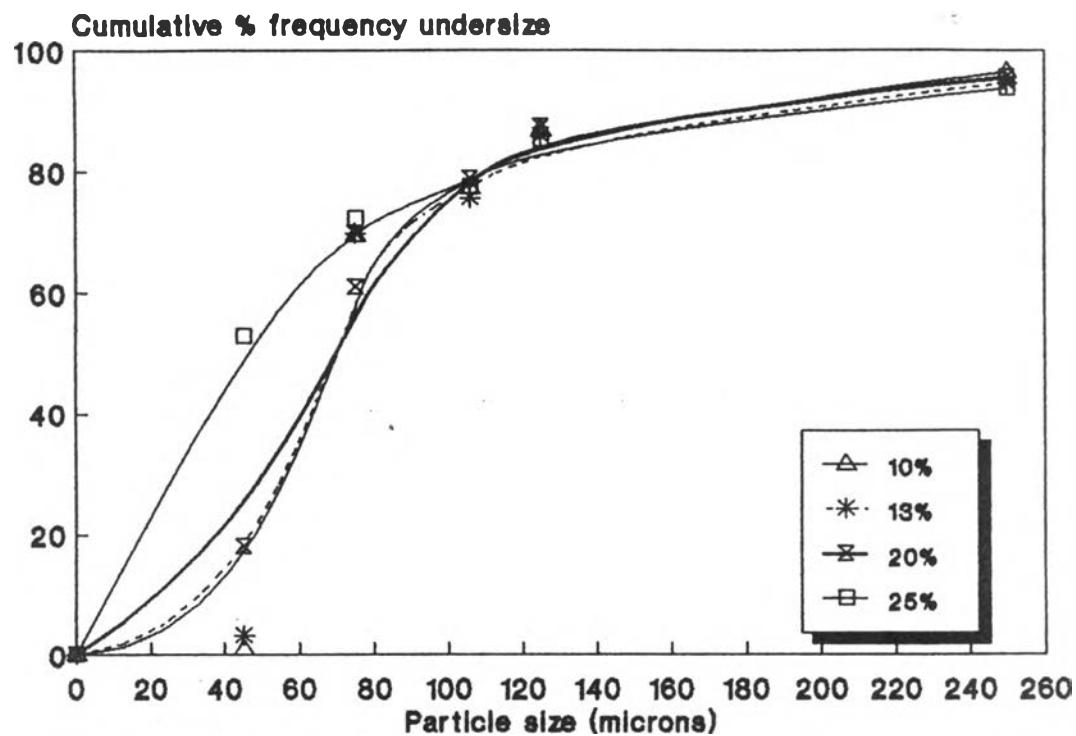
Figure 71   The Plot of Cumulative % Frequency Undersize
of Spray-Dried Powders Prepared from Various
Feed Concentration
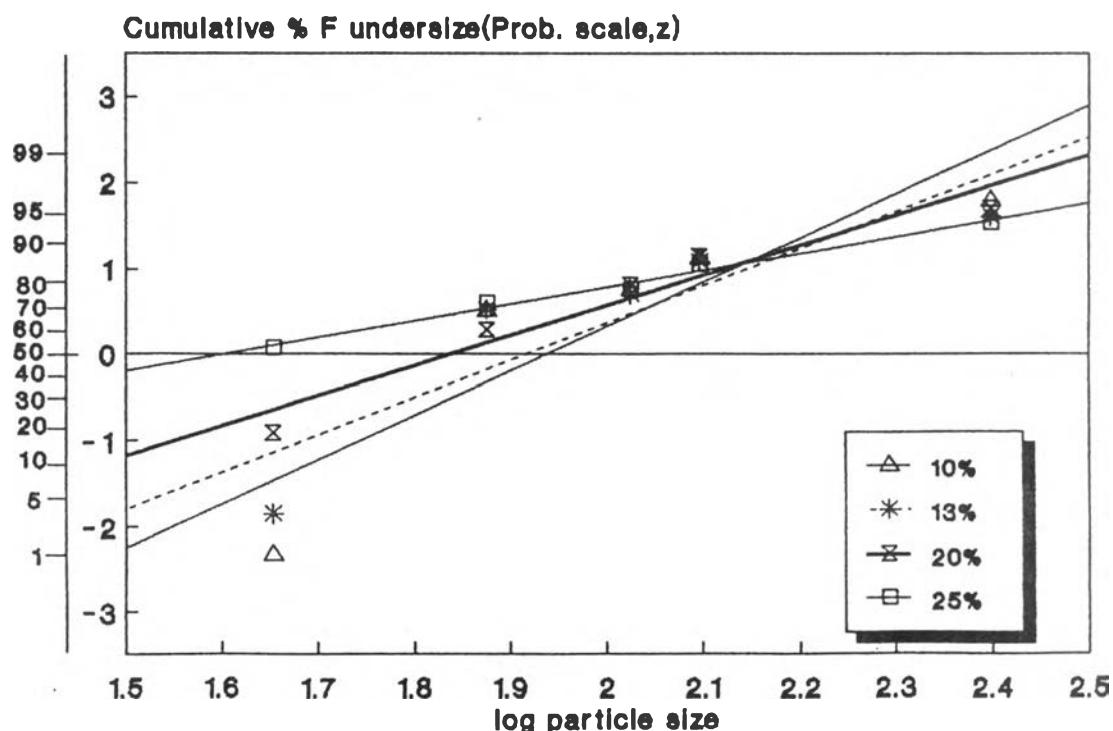
Figure 72   The Plot of Cumulative % Frequency Undersize
on Probability Scale Versus Log Particle Size
of Spray Dried Powders Prepared from Various
Feed Concentration
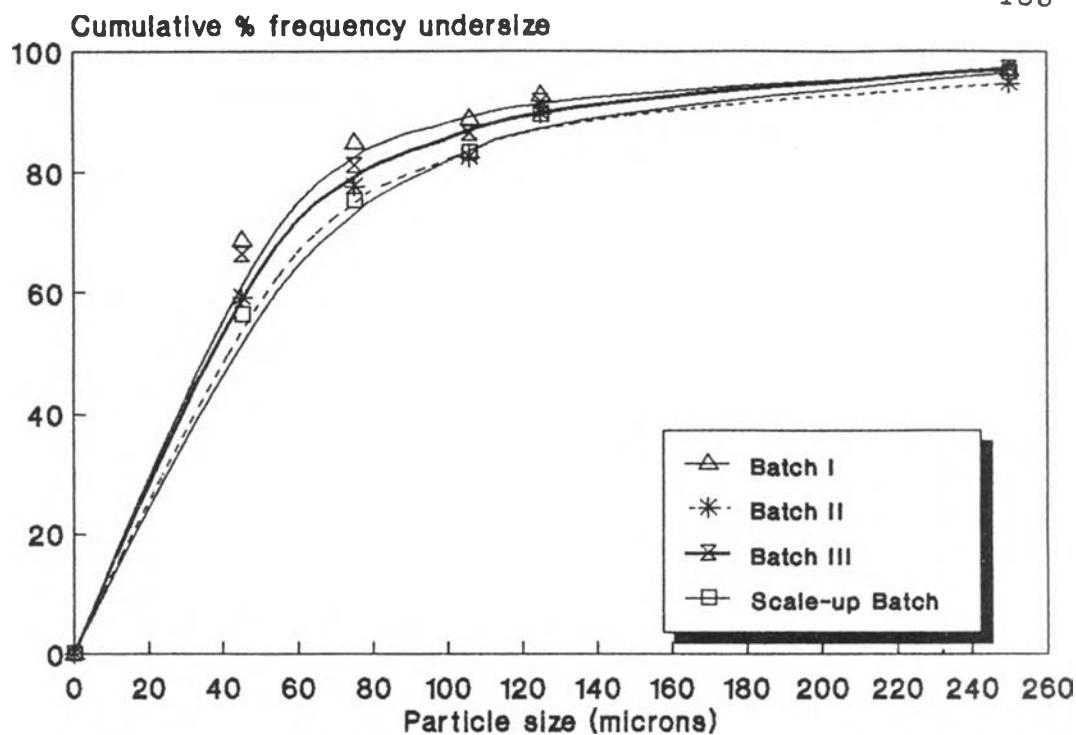
Figure 73   The Plot of Cumulative % Frequency Undersize
   of Consecutive-Three Batch and Scale-up Batch
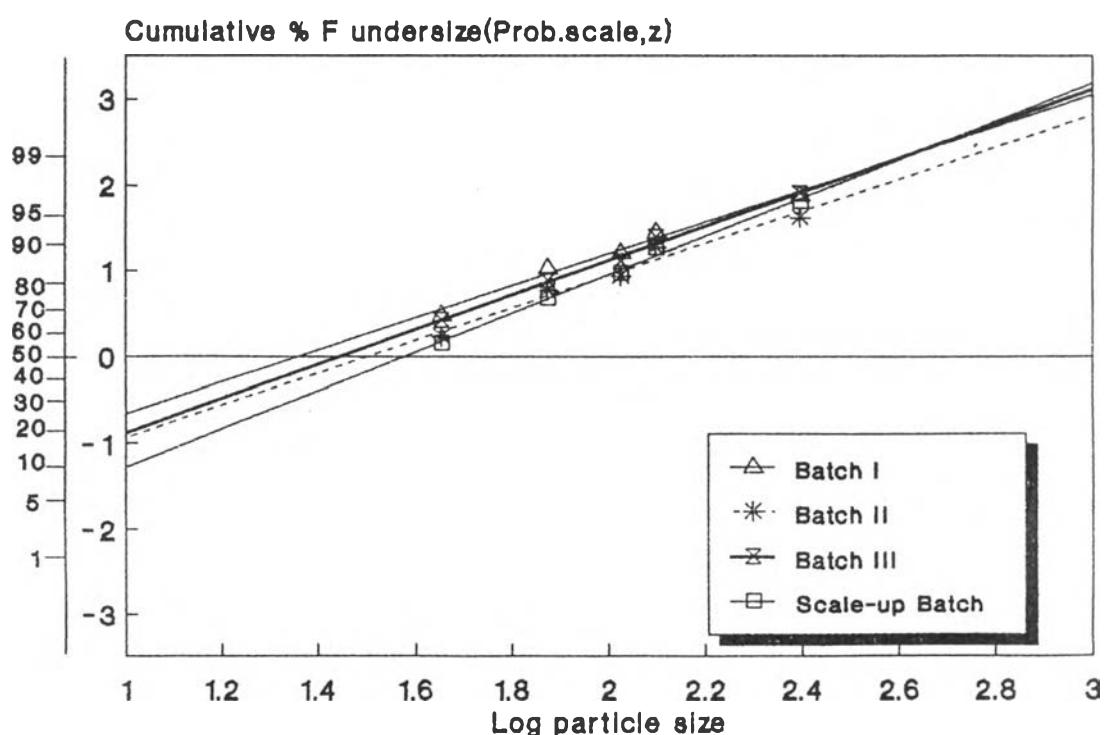

Figure 74   The Plot of Cumulative % Frequency Undersize
             on Probability Scale Versus Log Particle Size
             of Spray Dried Powders of Consecutive-Three
             Batch and Scale-up Batch

THEOPHYLLINE SR 12-TABLETS
Batch to batch-variation

Theophylline SR 12-tablets, batch A ✳   Theophylline SR 12-tablets, batch B ✕

Theophylline SR 12-tablets, batch C △   SR 12-granules, unprocessed ▱
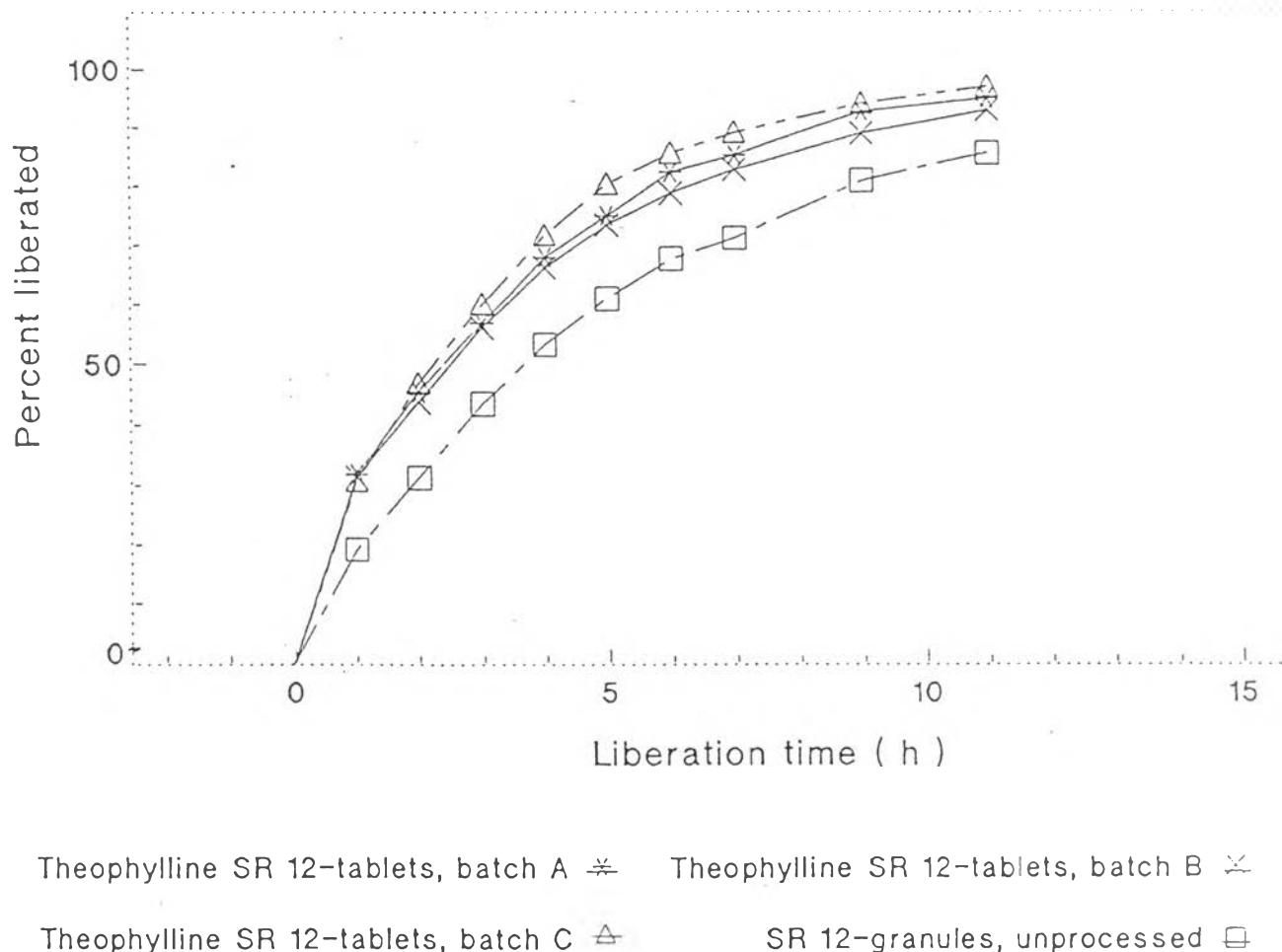
Figure 75   The Batch to Batch Variation of
             Dissolution Profiles of Theophylline SR12
             Tablets

Biography

Miss Vipaluk Patomchaiviwat was born on October 23, 1967. She got her degree in Bachelor of Science in Pharmacy with honors in 1990 from Faculty of Pharmacy, Mahidol University, Bangkok, Thailand.