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APPENDICES

Appendix I

Absorbance of Tetracycline Hydrochloride Reference
Standard in water at 276 nm.

Concentration ($\mu\text{g/ml}$)	Absorbance
0	0.000
2	0.070
4	0.141
6	0.211
8	0.282
10	0.352
12	0.422

Correlation coefficient : 0.9993

$$Y = 0.0362X + 0.0063$$

Appendix II

Absorbance of Cimetidine Standard Solution in water at
218 nm.

Concentration ($\mu\text{g/ml}$)	Absorbance
0	0.000
2	0.185
4	0.369
6	0.554
8	0.738
10	0.923

Correlation coefficient : 0.9986

$$Y = 0.0923X + 0.0106$$

Appendix III



Absorbance of Mefenamic Acid Standard Solution in Phosphate Buffer pH 7.8 at 283.5 nm.

Concentration ($\mu\text{g/ml}$)	Absorbance
0	0.000
2	0.083
4	0.165
6	0.248
8	0.330
10	0.413
12	0.495

Correlation coefficient : 0.9999

$$Y = 0.0413X - 0.0032$$

Appendix IV

Statistics

Analysis of Variance (ANOVA)

Source of Variance	DF	SS	MS	F
Among Groups (Treatment)	k-1	SS _{among}	MS _{among} = SS _{among} / (k-1)	F = $\frac{MS_{among}}{MS_{within}}$
Within Groups (Error)	N-k	SS _{within}	MS _{within} = SS _{within} / (N-k)	MS _{within}
Total	N-1	SS _{total}		

DF = Degree of Freedom

SS = Sum of Squares

$$SS_{among} = \sum_{j=1}^k n_j (X_{.j} - X_{..})^2$$

$$SS_{within} = \sum_{j=1}^k \sum_{i=1}^k (X_{ij} - X_j)^2$$

$$SS_{total} = \sum_{j=1}^k \sum_{i=1}^k (X_{ij} - X_{..})^2$$

MS = Mean Square

F = Variance Ratio

where

k = number of treatments

n = sample sizes of each treatment

X_{ij} = Observed Value at Treatment j

i = 1, 2,, n

j = 1, 2,, k

$$T.j = \sum_{i=1}^{n_j} X_{ij}$$

$$X.j = T.j/n_j$$

$$T.. = \sum_{j=1}^k T.j$$

$$X.. = T../N$$

$$N = \sum_{j=1}^k n_j$$

Comparing the F value with the critical value F obtained from table at degree of freedom (k-1) and (N-k):

- if $F > F_{(table)}$: reject the null hypothesis that $\mu_1 = \mu_2 = \mu_3 = \dots = \mu_k$ and accept the alternative hypothesis.
- if $F < F_{(table)}$: accept the null hypothesis.

Appendix V

Correlation between Compressibility and Flowability

Compressibility	Flowability
5 - 15	Excellent
12 - 16	Good
18 - 21	Fair to Passable
23 - 35	Poor
33 - 38	Very Poor
> 40	Very Very Poor

Appendix VI

Results of dissolution test

Table 26

Results of dissolution test on Raw Material Tetracycline Hydrochloride I, II and III Capsules (% released at 60 min.)

Raw Material Used	capsule A	capsule B	capsule C
Tetracycline HCL I	88.97	86.47	85.69
Tetracycline HCL II	82.50	84.53	90.39
Tetracycline HCL III	86.89	91.76	92.97

Table 27

Results of dissolution test on Raw Material Tetracycline Hydrochloride I, II and III Capsules (time used in min. to release 70%)

Raw Material Used	capsule A	capsule B	capsule C
Tetracycline HCL I	2.78	3.48	3.65
Tetracycline HCL II	2.96	3.13	3.13
Tetracycline HCL III	2.78	3.13	3.48

Table 28

Results of dissolution test on Experimental Capsules of Tetracycline Hydrochloride I, II and III (% released at 60 min.)

Experimental Capsules	capsule A	capsule B	capsule C
Tetracycline HCL I	89.48	93.93	93.92
Tetracycline HCL II	85.26	88.72	80.61
Tetracycline HCL III	93.88	98.18	91.36

Table 29

Results of dissolution test on Experimental Capsules of Tetracycline Hydrochloride I, II and III (time used in min. to release 70%)

Experimental Capsules	capsule A	capsule B	capsule C
Tetracycline HCL I	6.67	7.78	7.80
Tetracycline HCL II	7.22	7.25	8.33
Tetracycline HCL III	46.67	47.78	40.00

Table 30

Results of dissolution test on Experimental Capsules of Tetracycline Hydrochloride II and Fixed-diluent Tetracycline Hydrochloride (I & III) Capsules (% released at 60 min.)

Experimental Capsules	capsule A	capsule B	capsule C
Tetracycline HCL II	85.26	88.72	80.61
Tetra I Fixed	85.18	87.12	89.65
Tetra III Fixed	73.74	80.29	75.82

Table 31

Results of dissolution test on Experimental Capsules of Tetracycline Hydrochloride II and Fixed-diluent Tetracycline Hydrochloride (I & III) Capsules (time used in min. to release 70%)

Experimental Capsules	capsule A	capsule B	capsule C
Tetracycline HCL II	7.22	7.25	8.33
Tetra I Fixed	16.00	18.00	22.67
Tetra III Fixed	42.00	42.00	52.00

Table 32

Results of dissolution test on Raw Material Cimetidine I, II, III, IV and V Capsules (% released at 15 min.)

Raw Material Used	capsule A	capsule B	capsule C
Cimetidine I	89.21	88.07	95.68
Cimetidine II	85.92	87.89	88.35
Cimetidine III	72.60	78.11	80.48
Cimetidine IV	88.64	92.94	86.59
Cimetidine V	90.53	91.59	92.83

Table 33

Results of dissolution test on Raw Material Cimetidine I, II, III, IV and V Capsules (time used in min. to release 75%)

Raw Material Used	capsule A	capsule B	capsule C
Cimetidine I	5.91	5.91	6.96
Cimetidine II	6.26	6.96	7.65
Cimetidine III	4.52	4.52	7.00
Cimetidine IV	7.30	8.35	8.70
Cimetidine V	4.87	4.87	5.22

Table 34

Results of dissolution test on Experimental Capsules of Cimetidine I, II, III, IV and V (% released at 15 min.)

Experimental Capsules	capsule A	capsule B	capsule C
Cimetidine I	96.98	98.29	99.49
Cimetidine II	95.33	94.88	89.82
Cimetidine III	89.26	88.99	88.02
Cimetidine IV	81.15	83.99	85.73
Cimetidine V	84.59	79.80	79.60

Table 35

Results of dissolution test on Experimental Capsules of Cimetidine I, II, III, IV and V (time used in min. to release 75%)

Experimental Capsules	capsule A	capsule B	capsule C
Cimetidine I	4.17	4.17	4.52
Cimetidine II	4.87	4.87	4.87
Cimetidine III	4.87	4.87	4.87
Cimetidine IV	5.56	6.26	6.26
Cimetidine V	10.78	11.48	13.22

Table 36

Results of dissolution test on Experimental Capsules of Cimetidine I and Fixed-diluent Cimetidine (II, III, IV & V) Capsules (% released at 15 min.)

Experimental Capsules	capsule A	capsule B	capsule C
Cimetidine I	.96.98	98.29	99.49
Cimetidine II Fixed	91.85	83.91	93.54
Cimetidine III Fixed	98.01	103.76	96.27
Cimetidine IV Fixed	98.71	100.29	100.89
Cimetidine V Fixed	97.74	99.92	106.75

Table 37

Results of dissolution test on Experimental Capsules of Cimetidine I and Fixed-diluent Cimetidine (II, III, IV & V) Capsules (time used in min. to release 75%)

Experimental Capsules	capsule A	capsule B	capsule C
Cimetidine I	4.67	4.00	4.00
Cimetidine II Fixed	4.90	7.00	9.10
Cimetidine III Fixed	4.55	6.30	6.30
Cimetidine IV Fixed	5.95	6.65	7.00
Cimetidine V Fixed	4.55	4.90	4.90

Table 38

Results of dissolution test on Raw Material Mefenamic Acid I, II and III Capsules (% released at 60 min.)

Raw Material Used	capsule A	capsule B	capsule C
Mefenamic Acid I	4.58	4.10	3.74
Mefenamic Acid II	4.69	5.69	6.21
Mefenamic Acid III	20.15	18.52	15.62

Table 39

Results of dissolution test on Experimental Capsules of Mefenamic Acid I, II and III (% released at 60 min.)

Experimental Capsules	capsule A	capsule B	capsule C
Mefenamic Acid I	34.67	27.07	29.47
Mefenamic Acid II	23.79	18.25	21.40
Mefenamic Acid III	65.14	57.78	72.55

Table 40

Results of dissolution test on Experimental Capsules of Mefenamic Acid III and Fixed-diluent Mefenamic Acid (I & II) Capsules (% released at 60 min.)

Experimental Capsules	capsule A	capsule B	capsule C
Mefen III	65.14	57.78	72.55
Mefen I Fixed	37.74	21.21	17.39
Mefen II Fixed	22.50	27.86	25.17

Appendix VII

Dissolution of various capsules

Table 41
Dissolution of Raw Material Tetracycline Hydrochloride Capsules

Time (min.)	Raw Material Capsules (% drug dissolved \pm SD) ^(a)		
	Tetra I	Tetra II	Tetra III
1	4.40 \pm 1.40	2.18 \pm 0.59	2.21 \pm 0.29
3	68.93 \pm 4.91	70.47 \pm 4.00	66.33 \pm 4.78
5	82.00 \pm 4.34	84.70 \pm 3.80	84.24 \pm 2.22
7	83.59 \pm 3.68	87.57 \pm 4.54	91.07 \pm 5.75
10	85.27 \pm 3.17	92.24 \pm 4.05	92.96 \pm 5.13
15	91.24 \pm 0.46	88.90 \pm 3.30	92.32 \pm 6.18
20	89.93 \pm 2.10	87.84 \pm 4.65	90.87 \pm 4.66
30	86.61 \pm 1.27	87.60 \pm 4.32	91.20 \pm 3.49
45	86.74 \pm 1.57	86.62 \pm 5.05	90.14 \pm 2.89
60	87.04 \pm 1.72	85.81 \pm 4.10	90.54 \pm 3.22
90	87.91 \pm 2.42	85.62 \pm 4.40	90.94 \pm 3.61

(a) averaged from three determinations

Table 42

Dissolution of Experimental Tetracycline Hydrochloride I, II and III Capsules

Time (min.)	Experimental Capsules (% drug dissolved \pm SD)		
	Tetra I	Tetra II	Tetra III
1	0.78 \pm 0.59	0.97 \pm 1.34	0.70 \pm 0.31
3	7.88 \pm 0.91	6.38 \pm 3.47	2.70 \pm 0.31
5	44.55 \pm 4.68	43.85 \pm 3.88	30.40 \pm 4.89
7	69.24 \pm 4.32	69.74 \pm 4.32	34.83 \pm 4.21
10	84.51 \pm 2.55	81.79 \pm 3.33	45.05 \pm 1.93
15	92.96 \pm 4.19	90.09 \pm 3.20	48.19 \pm 2.60
20	95.20 \pm 3.57	90.03 \pm 4.00	54.32 \pm 3.32
30	94.07 \pm 4.31	86.29 \pm 4.13	63.11 \pm 0.94
45	92.44 \pm 2.01	85.78 \pm 3.44	70.44 \pm 2.75
60	92.45 \pm 2.57	84.86 \pm 4.07	94.53 \pm 3.47
90	91.38 \pm 2.51	83.29 \pm 3.71	94.96 \pm 2.99

Table 43

Dissolution of Fixed-diluent Tetracycline Hydrochloride (I & II) Capsules compared with Experimental Tetracycline Hydrochloride II Capsules

Time (min.)	Experimental Capsules (% drug dissolved \pm SD)		
	Tetra II	Tetra I Fixed	Tetra III Fixed
1	0.97 \pm 1.34	0.17 \pm 0.00	0.25 \pm 0.14
3	6.38 \pm 3.47	3.43 \pm 4.05	1.31 \pm 1.77
5	43.85 \pm 3.88	13.98 \pm 4.37	10.18 \pm 2.47
7	69.74 \pm 4.32	22.29 \pm 3.74	16.81 \pm 1.16
10	81.79 \pm 3.33	46.27 \pm 3.51	23.71 \pm 1.93
15	90.09 \pm 3.20	65.16 \pm 2.78	31.13 \pm 1.26
20	90.03 \pm 4.00	72.28 \pm 5.49	37.93 \pm 6.58
30	86.29 \pm 4.13	83.11 \pm 3.03	51.60 \pm 7.47
45	85.78 \pm 3.44	87.91 \pm 1.39	67.41 \pm 5.40
60	84.86 \pm 4.07	87.32 \pm 2.24	76.62 \pm 3.35
90	83.29 \pm 3.71	87.05 \pm 2.40	76.63 \pm 1.73

Table 44

Dissolution of Raw Material Cimetidine Capsules

Time (min.)	Raw Material Capsules (% drug dissolved \pm SD)				
	Cimet I	Cimet II	Cimet III	Cimet IV	Cimet V
1	18.96 (1.76)	3.17 (0.78)	6.65 (0.66)	(0.89)	(0.25)
3	51.09 (5.81)	21.14 (1.60)	66.36 (1.19)	13.01 (3.14)	49.67 (1.37)
5	69.77 (2.21)	60.42 (3.27)	75.57 (3.27)	46.17 (4.49)	79.19 (2.65)
7	78.27 (3.36)	77.04 (4.85)	78.54 (4.29)	66.91 (4.84)	86.74 (4.08)
10	85.40 (4.01)	85.01 (1.10)	77.54 (3.46)	87.02 (3.84)	92.30 (0.92)
15	90.99 (4.11)	87.39 (1.29)	77.06 (4.04)	89.39 (3.24)	91.65 (1.15)
30	89.94 (4.79)	87.65 (2.26)	76.99 (3.96)	90.70 (4.27)	90.46 (0.99)
45	89.58 (5.16)	87.90 (1.99)	76.96 (4.66)	89.93 (3.66)	91.22 (0.96)

Table 45

Dissolution of Experimental Cimetidine I, II, III, IV & V Capsules

Time (min.)	Experimental Capsules (% drug dissolved \pm SD)				
	Cimet I	Cimet II	Cimet III	Cimet IV	Cimet V
1	5.89 (2.57)	1.32 (0.35)	6.66 (2.24)	1.47 (1.05)	1.71 (1.45)
3	51.50 (6.58)	30.93 (3.17)	24.50 (3.25)	20.28 (2.45)	18.33 (3.17)
5	86.09 (2.87)	76.95 (1.22)	77.99 (1.87)	68.04 (4.35)	40.59 (3.57)
7	93.76 (4.44)	85.84 (4.91)	82.01 (1.20)	79.53 (0.47)	62.89 (4.08)
10	100.50 (1.09)	94.71 (0.32)	86.20 (1.55)	82.22 (2.06)	70.25 (3.63)
15	100.47 (0.82)	93.34 (3.06)	88.76 (0.65)	83.62 (2.31)	81.33 (2.83)
30	100.81 (0.48)	93.13 (2.45)	87.38 (0.60)	81.24 (2.63)	81.59 (2.31)
45	100.35 (0.89)	91.75 (1.98)	86.42 (0.62)	81.74 (2.85)	81.17 (2.37)

Table 46

Dissolution of Fixed-diluent Cimetidine II, III, IV & V Capsules compared with Experimental Cimetidine I Capsules

Time (min.)	Experimental Capsules (% drug dissolved \pm SD)				
	Cimet I	Cimet II Fixed	Cimet III Fixed	Cimet IV Fixed	Cimet V Fixed
1	5.89 (2.57)	7.18 [*] (7.14)	4.41 (0.94)	4.11 (0.20)	5.34 (0.34)
3	51.50 (6.58)	32.44 (18.05)	36.48 (13.77)	19.14 (4.12)	45.61 (2.35)
5	86.09 (2.87)	47.32 (17.81)	62.96 (14.51)	54.75 (7.85)	78.15 (4.02)
7	93.76 (4.44)	76.82 (6.82)	87.08 (4.12)	80.36 (7.52)	93.68 (3.40)
10	100.50 (1.09)	85.80 (7.25)	93.27 (6.26)	95.08 (1.40)	98.43 (3.60)
15	100.47 (0.82)	89.77 (5.14)	96.27 (8.49)	99.96 (1.13)	101.47 (4.70)
30	100.81 (0.48)	90.76 (3.71)	98.70 (5.56)	101.50 (0.81)	105.39 (1.16)
45	100.35 (0.89)	91.18 (4.09)	99.39 (5.22)	101.84 (1.76)	107.18 (3.26)

Table 47

Dissolution of Raw Material Mefenamic Acid Capsules

Time (min.)	Raw Material Capsules (% drug dissolved \pm SD)		
	Mefen I	Mefen II	Mefen III
1	0.63 \pm 0.22	0.56 \pm 0.35	1.33 \pm 0.13
3	0.69 \pm 0.18	0.63 \pm 0.24	1.33 \pm 0.13
5	0.81 \pm 0.12	0.93 \pm 0.30	2.17 \pm 0.16
7	0.82 \pm 0.12	1.32 \pm 0.06	3.32 \pm 0.83
10	0.96 \pm 0.29	1.47 \pm 0.08	6.41 \pm 0.58
15	1.42 \pm 0.29	1.75 \pm 0.29	7.77 \pm 1.15
20	1.88 \pm 0.36	2.20 \pm 0.05	9.98 \pm 2.20
25	2.30 \pm 0.48	2.51 \pm 0.09	10.98 \pm 2.12
30	2.77 \pm 0.87	3.26 \pm 0.36	12.20 \pm 2.52
40	3.25 \pm 0.54	4.34 \pm 0.64	13.93 \pm 2.87
50	3.67 \pm 0.36	4.98 \pm 0.72	16.25 \pm 2.45
60	4.14 \pm 0.42	5.53 \pm 0.77	18.10 \pm 2.29
75	4.88 \pm 0.41	6.27 \pm 1.37	20.54 \pm 1.87
90	5.87 \pm 0.52	6.95 \pm 1.05	23.54 \pm 3.23
105	6.23 \pm 0.45	7.41 \pm 1.23	24.93 \pm 3.14
120	6.91 \pm 0.22	7.99 \pm 1.12	26.98 \pm 3.96

Table 48

Dissolution of Experimental Mefenamic Acid I, II & III Capsules

Time (min.)	Experimental Capsules (% drug dissolved \pm SD)		
	Mefen I	Mefen II	Mefen III
1	0.60 \pm 0.34	0.33 \pm 0.27	0.51 \pm 0.17
3	0.90 \pm 0.33	0.98 \pm 0.16	0.70 \pm 0.32
5	1.67 \pm 0.38	2.07 \pm 0.65	1.23 \pm 0.51
7	2.51 \pm 0.82	3.75 \pm 1.63	2.33 \pm 0.35
10	3.33 \pm 0.99	5.71 \pm 2.34	4.33 \pm 0.49
15	5.81 \pm 1.60	8.82 \pm 1.85	8.93 \pm 0.87
20	8.69 \pm 1.33	11.04 \pm 2.39	14.03 \pm 1.53
25	11.48 \pm 1.23	13.46 \pm 2.08	19.20 \pm 2.95
30	14.29 \pm 0.93	14.65 \pm 1.51	28.29 \pm 6.93
40	20.82 \pm 1.32	18.08 \pm 2.78	51.67 \pm 5.88
50	26.07 \pm 3.45	19.64 \pm 2.73	56.80 \pm 5.13
60	30.40 \pm 3.89	21.14 \pm 2.78	65.16 \pm 7.38
75	33.47 \pm 4.36	25.46 \pm 1.19	75.27 \pm 1.61
90	36.50 \pm 1.42	27.47 \pm 2.19	80.28 \pm 3.10
105	41.61 \pm 1.93	29.98 \pm 3.83	85.33 \pm 2.91
120	41.93 \pm 4.44	32.10 \pm 2.66	86.10 \pm 4.86

Table 49

Dissolution of Fixed-diluent Mefenamic Acid (I & II)
Capsules compared with Experimental Mefenamic Acid III
Capsules

Time (min.)	Experimental Capsules (% drug dissolved \pm SD)		
	Mefen I Fixed	Mefen II Fixed	Mefen III
1	1.12 \pm 0.46	1.09 \pm 0.43	0.51 \pm 0.17
3	1.88 \pm 0.98	2.81 \pm 1.74	0.70 \pm 0.32
5	2.57 \pm 0.47	3.48 \pm 1.72	1.23 \pm 0.51
7	3.78 \pm 0.55	5.52 \pm 2.01	2.33 \pm 0.35
10	5.91 \pm 0.88	8.80 \pm 2.55	4.33 \pm 0.49
15	7.16 \pm 0.87	11.20 \pm 3.06	8.93 \pm 0.87
20	9.62 \pm 1.43	13.46 \pm 2.61	14.03 \pm 1.53
25	12.20 \pm 2.75	15.84 \pm 3.11	19.20 \pm 2.95
30	14.25 \pm 3.15	17.72 \pm 1.85	28.29 \pm 6.93
40	17.65 \pm 4.58	20.28 \pm 2.33	51.67 \pm 5.88
50	22.67 \pm 8.57	23.56 \pm 2.37	56.80 \pm 5.13
60	25.45 \pm 10.81	25.18 \pm 2.68	65.16 \pm 7.38
75	31.33 \pm 14.70	27.93 \pm 2.38	75.27 \pm 1.61
90	38.36 \pm 16.64	31.03 \pm 2.48	80.28 \pm 3.10
105	41.29 \pm 15.94	33.52 \pm 2.97	85.33 \pm 2.91
120	50.52 \pm 15.74	37.65 \pm 1.13	86.10 \pm 4.86

VITAE

Major Supang Wongkhan was born on February 9, 1951, in Lopburi, Thailand. He got his degree in Bachelor of Pharmacy from Faculty of Pharmacy, Chulalongkorn University in 1975. He worked at Ananthamahidol Hospital, Lopburi for about nine year during 1975-1984. Since 1985, he has worked in Department of Pharmacy, Pramongkutkloao Hospital in Bangkok.

