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APPENDIX A

DETAILS OF SODIUM CARBOXYMETHYLCELLULOSE AND POLYVINYL ALCOHOL

Sodium Carboxymethylcellulose

(Wade and Weller, 1994)

Nonproprietary Names

USP : Carboxymethylcellulose sodium

BP : Carmellose sodium; sodium carboxymethylcellulose

Synonyms

Akucell; Blanose; Cekol; cellulose gum; CMC sodium; Courlose; E466; Nymcel;

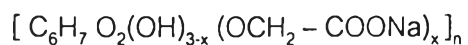
SCMC; sodium carboxymethylcellulose ; sodium cellulose glycolate; sodium

CMC; Tylose CB.

Chemical Names and CAS Registry Number

Cellulose, carboxymethyl ether, sodium salt (9004-32-4)

Empirical Formula



Molecular Weight

90,000 – 700,000

Structural Formula

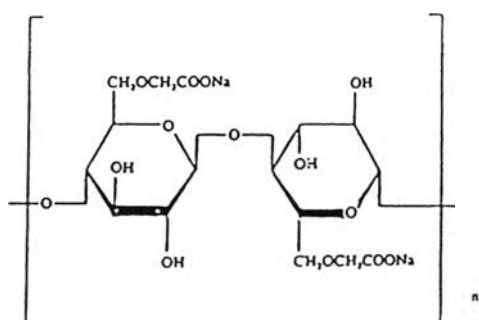


Figure 19 Structure of Sodium Carboxymethylcellulose

Functional Category

USP : Suspending and/or viscosity-increasing agent; tablet binder; coating agent

BP : Pharmaceutical aid

Others : Disintegrant; thickener; suspension stabilizer

Description

Carboxymethylcellulose sodium occurs as a white to almost white colored, odorless, granular powder.

Typical Properties

Density : 0.75 g/cm³

Dissociation constant : $pK_a = 4.30$

Melting point : browns at approximately 227°C, chars at approximately 252°C

Solubility : practically insoluble in acetone, ethanol, ether and toluene. Easily dispersed in water at all temperatures, forming clear, coloidal solution.

Viscosity : various grades of carboxymethylcellulose sodium are commercially available which have differing aqueous viscosities; aqueous 1% w/v solutions with viscosities of 5-4000 mPa s (5-4000 cP) may be obtained. An increase in concentration results in an increase in aqueous solution viscosity.

Polyvinyl Alcohol

(Wade and Weller, 1994)

Nonproprietary Name

USP : Polyvinyl alcohol

Synonyms

Airvol; Elvanol; Polyviol; PVA; vinyl alcohol polymer.

Chemical Names and CAS Registry Number

Ethenol, homopolymer [9002-89-5]

Empirical Formula

$(C_2H_4O)_n$

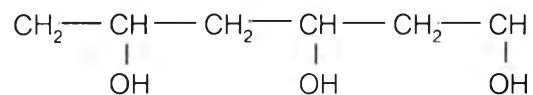
Molecular Weight

High viscosity : 200,000 (avg)

Medium viscosity : 130,000 (avg)

Low viscosity : 30,000 (avg)

Structural Formula



Functional Category

Coating agent; nonionic surfactant; viscosity-increasing agent.

Description

White to cream-colored granular powder or granules. Odorless.

Typical Properties

Melting point :

228 °C for fully hydrolyzed grades.

180-190 °C for partially hydrolyzed grades.

Solubility : soluble in hot or cold water; solubility in water increases as the molecular weight decreases.

Viscosity :

Grade	Dynamic viscosity of 4% w/w aqueous solution at 20°C (mPas)
High viscosity	40-65
Medium viscosity	21-33
Low viscosity	4-7

APPENDIX B

DATA OF COMPARATIVE PERCENT YIELD, CONTENT,
ENTRAPMENT OF MICROCAPSULES

Table 21 The percent yield, percent content, and percent entrapment of minocycline hydrochloride microcapsules prepared by the w/o/w solvent evaporation technique with different polymers and sodium carboxymethylcellulose concentrations

Coating polymer	SCMC concentration (%W/V)	% Yield	% Content					% Theoretical content	% Entrapment				
			N1	N2	N3	Mean	SD		N1	N2	N3	Mean	SD
L-PLA	0%	83.22	0.84	0.83	0.84	0.84	0.01	16.78	5.01	4.95	5.01	4.99	0.03
	0.05%	97.70	0.47	0.47	0.47	0.47	0.00	16.39	2.87	2.87	2.87	2.87	0.00
	0.10%	81.10	0.24	0.24	0.24	0.24	0.00	16.57	1.45	1.45	1.45	1.45	0.00
	0.20%	82.27	0.25	0.24	0.24	0.24	0.01	16.72	1.50	1.44	1.44	1.46	0.03
DL-PLA	0%	79.67	0.71	0.70	0.71	0.71	0.01	16.94	4.19	4.13	4.19	4.17	0.03
	0.05%	82.80	0.09	0.09	0.09	0.09	0.00	16.79	0.54	0.54	0.54	0.54	0.00
	0.10%	78.63	0.15	0.15	0.15	0.15	0.00	16.52	0.91	0.91	0.91	0.91	0.00
	0.20%	84.08	0.15	0.15	0.15	0.15	0.00	16.75	0.90	0.90	0.90	0.90	0.00
PLGA (75:25)	0%	72.97	0.83	0.82	0.82	0.82	0.01	16.89	4.91	4.85	4.85	4.87	0.03
	0.05%	71.48	0.38	0.38	0.39	0.38	0.01	16.78	2.26	2.26	2.31	2.28	0.03
	0.10%	76.33	0.78	0.78	0.78	0.78	0.00	16.67	4.68	4.68	4.68	4.68	0.00
	0.20%	91.39	0.23	0.23	0.22	0.23	0.01	16.56	1.39	1.39	1.33	1.37	0.03

Table 21 (continued)

Coating polymer	SCMC concentration (%W/V)	% Yield	% Content					% Theoretical content	% Entrapment				
			N1	N2	N3	Mean	SD		N1	N2	N3	Mean	SD
PLGA (50:50)	0%	81.85	0.49	0.50	0.49	0.49	0.01	16.50	2.97	3.03	2.97	2.99	0.03
	0.05%	74.16	0.29	0.30	0.30	0.30	0.01	16.78	1.73	1.79	1.79	1.77	0.03
	0.10%	81.37	0.14	0.14	0.14	0.14	0.00	16.54	0.85	0.85	0.85	0.85	0.00
	0.20%	81.52	0.13	0.13	0.14	0.13	0.01	16.50	0.79	0.79	0.85	0.81	0.03

Table 22 The percent yield, percent content, and percent entrapment of minocycline hydrochloride microcapsules prepared by the w/o/w solvent evaporation technique with different polymers and core to wall ratios

Coating polymer	Core to wall ratio	% Yield	% Content					% Theoretical content	% Entrapment				
			N1	N2	N3	Mean	SD		N1	N2	N3	Mean	SD
L-PLA [SCMC 0%]	1 : 5	83.22	0.84	0.83	0.84	0.84	0.01	16.78	5.01	4.95	5.01	4.99	0.03
	1 : 1	52.00	0.02	0.03	0.02	0.02	0.01	49.75	0.04	0.06	0.04	0.05	0.01
	5 : 1	23.81	-	-	-	-	-	-	-	-	-	-	-
DL-PLA [SCMC 0%]	1 : 5	79.67	0.71	0.70	0.71	0.71	0.01	16.94	4.19	4.13	4.19	4.17	0.03
	1 : 1	49.88	0.02	0.02	0.02	0.02	0.00	49.63	0.04	0.04	0.04	0.04	0.00
	5 : 1	26.03	-	-	-	-	-	-	-	-	-	-	-
PLGA (75:25) [SCMC 0%]	1 : 5	72.97	0.83	0.82	0.82	0.82	0.01	16.89	4.91	4.85	4.85	4.87	0.03
	1 : 1	46.38	0.03	0.03	0.03	0.03	0.00	49.87	0.06	0.06	0.06	0.06	0.00
	5 : 1	17.43	-	-	-	-	-	-	-	-	-	-	-
PLGA (50:50) [SCMC 0%]	1 : 5	81.85	0.49	0.50	0.49	0.49	0.01	16.50	2.97	3.03	2.97	2.99	0.03
	1 : 1	46.91	0.03	0.03	0.03	0.03	0.00	49.63	0.06	0.06	0.06	0.06	0.00
	5 : 1	16.67	-	-	-	-	-	-	-	-	-	-	-

APPENDIX C

DATA OF PARTICLE SIZE AND SIZE DISTRIBUTION OF MICROCAPSULES

Table 23 Particle size of minocycline hydrochloride microcapsules using L-PLA with 1:5 core to wall ratio

System Details							
Range Lens: 300RF mm		Beam Length: 2.40 mm		Sampler: MS1		Obscuration: 4.8 %	
Presentation: 30HD		(Particle R.I. = (1.5295, 0.1000);		Dispersant R.I. = 1.3300]		Residual: 0.602 %	
Analysis Model: Polydisperse		Killed Data Channels: Low 0; High 2					
Modifications: Active -							
Result Statistics							
Distribution Type: Volume		Concentration = 0.0352 %Vol		Density = 1.000 g / cub. cm		Specific S.A. = 0.1263 sq. m / g	
Mean Diameters:		D (v, 0.1) = 54.68 um		D (v, 0.5) = 115.96 um		D (v, 0.9) = 336.66 um	
D [4, 3] = 158.46 um		D [3, 2] = 47.51 um		Span = 2.432E+00		Uniformity = 7.200E-01	

Size Low (um)	In %	Size High (um)	Under%	Size Low (um)	In %	Size High (um)	Under%
0.05	0.00	0.06	0.00	6.63	0.04	7.72	1.29
0.06	0.00	0.07	0.00	7.72	0.06	9.00	1.36
0.07	0.00	0.08	0.00	9.00	0.08	10.48	1.44
0.08	0.00	0.09	0.00	10.48	0.09	12.21	1.53
0.09	0.00	0.11	0.00	12.21	0.09	14.22	1.62
0.11	0.00	0.13	0.00	14.22	0.07	16.57	1.69
0.13	0.00	0.15	0.00	16.57	0.06	19.31	1.75
0.15	0.00	0.17	0.00	19.31	0.08	22.49	1.84
0.17	0.00	0.20	0.00	22.49	0.19	26.20	2.02
0.20	0.00	0.23	0.00	26.20	0.41	30.53	2.43
0.23	0.00	0.27	0.01	30.53	0.80	35.56	3.23
0.27	0.01	0.31	0.01	35.56	1.42	41.43	4.64
0.31	0.01	0.36	0.03	41.43	2.39	48.27	7.03
0.36	0.02	0.42	0.04	48.27	3.79	56.23	10.82
0.42	0.02	0.49	0.07	56.23	5.69	65.51	16.51
0.49	0.04	0.58	0.10	65.51	7.72	76.32	24.23
0.58	0.05	0.67	0.15	76.32	9.23	88.91	33.46
0.67	0.06	0.78	0.21	88.91	9.68	103.58	43.14
0.78	0.08	0.91	0.29	103.58	9.18	120.67	52.32
0.91	0.10	1.06	0.40	120.67	8.20	140.58	60.51
1.06	0.13	1.24	0.52	140.58	7.04	163.77	67.56
1.24	0.14	1.44	0.66	163.77	5.97	190.80	73.53
1.44	0.14	1.68	0.81	190.80	5.11	222.28	78.64
1.68	0.13	1.95	0.94	222.28	4.52	258.95	83.16
1.95	0.11	2.28	1.05	258.95	4.11	301.68	87.27
2.28	0.07	2.65	1.12	301.68	3.75	351.46	91.01
2.65	0.05	3.09	1.17	351.46	3.25	409.45	94.27
3.09	0.03	3.60	1.19	409.45	2.61	477.01	96.87
3.60	0.01	4.19	1.21	477.01	1.82	555.71	98.70
4.19	0.01	4.88	1.21	555.71	1.04	647.41	99.74
4.88	0.01	5.69	1.23	647.41	0.26	754.23	100.00
5.69	0.02	6.63	1.25	754.23	0.00	878.67	100.00

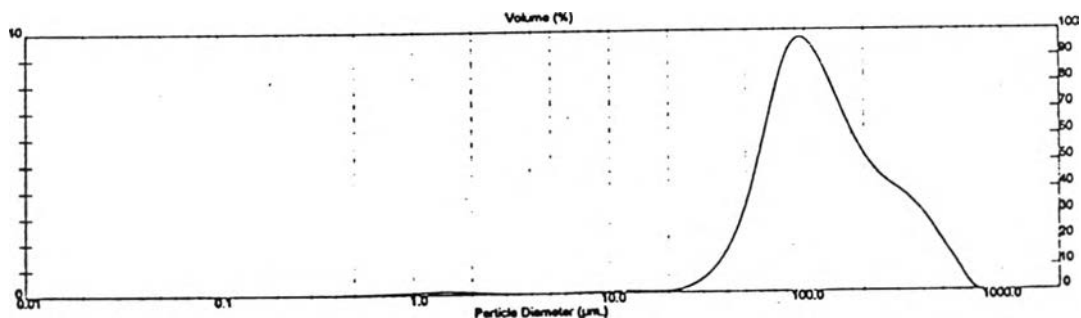


Figure 20 Particle size distribution of minocycline hydrochloride microcapsules using L-PLA with 1:5 core to wall ratio.

Table 23 (continued)

System Details			
Range Lens: 300RF mm	Beam Length: 2.40 mm	Sampler: MS1	Obscuration: 5.3 %
Presentation: 30HD	[Particle R.I. = (1.5295, 0.1000);	Dispersant R.I. = 1.3300]	Residual: 0.665 %
Analysis Model: Polydisperse	Killed Data Channels: Low 0; High 2		
Modifications: Active -			

Result Statistics			
Distribution Type: Volume	Concentration = 0.0396 %Vol	Density = 1.000 g / cub. cm	Specific S.A. = 0.1253 sq. m / g
Mean Diameters:	D (v, 0.1) = 55.08 um	D (v, 0.5) = 120.74 um	D (v, 0.9) = 352.73 um
D [4, 3] = 166.25 um	D [3, 2] = 47.87 um	Span = 2.465E+00	Uniformity = 7.426E-01

Size Low (um)	In %	Size High (um)	Under%	Size Low (um)	In %	Size High (um)	Under%
0.05	0.00	0.06	0.00	6.63	0.04	7.72	1.27
0.06	0.00	0.07	0.00	7.72	0.06	9.00	1.33
0.07	0.00	0.08	0.00	9.00	0.08	10.48	1.41
0.08	0.00	0.09	0.00	10.48	0.09	12.21	1.49
0.09	0.00	0.11	0.00	12.21	0.08	14.22	1.58
0.11	0.00	0.13	0.00	14.22	0.07	16.57	1.64
0.13	0.00	0.15	0.00	16.57	0.06	19.31	1.70
0.15	0.00	0.17	0.00	19.31	0.08	22.49	1.78
0.17	0.00	0.20	0.00	22.49	0.18	26.20	1.96
0.20	0.00	0.23	0.00	26.20	0.39	30.53	2.35
0.23	0.01	0.27	0.01	30.53	0.78	35.56	3.13
0.27	0.01	0.31	0.02	35.56	1.40	41.43	4.53
0.31	0.01	0.36	0.03	41.43	2.35	48.27	6.89
0.36	0.02	0.42	0.05	48.27	3.71	56.23	10.59
0.42	0.02	0.49	0.08	56.23	5.46	65.51	16.06
0.49	0.04	0.58	0.11	65.51	7.30	76.32	23.36
0.58	0.05	0.67	0.16	76.32	8.67	88.91	32.03
0.67	0.06	0.78	0.22	88.91	9.14	103.58	41.16
0.78	0.08	0.91	0.30	103.58	8.80	120.67	49.96
0.91	0.10	1.06	0.40	120.67	8.03	140.58	58.00
1.06	0.12	1.24	0.52	140.58	7.11	163.77	65.10
1.24	0.14	1.44	0.66	163.77	6.21	190.80	71.32
1.44	0.14	1.68	0.80	190.80	5.45	222.28	76.76
1.68	0.12	1.95	0.92	222.28	4.87	258.95	81.63
1.95	0.10	2.28	1.02	258.95	4.39	301.68	86.01
2.28	0.07	2.65	1.09	301.68	3.90	351.46	89.92
2.65	0.05	3.09	1.14	351.46	3.33	409.45	93.24
3.09	0.03	3.60	1.17	409.45	2.67	477.01	95.91
3.60	0.01	4.19	1.18	477.01	2.02	555.71	97.93
4.19	0.01	4.88	1.19	555.71	1.36	647.41	99.29
4.88	0.01	5.69	1.20	647.41	0.71	754.23	100.00
5.69	0.02	6.63	1.23	754.23	0.00	878.67	100.00

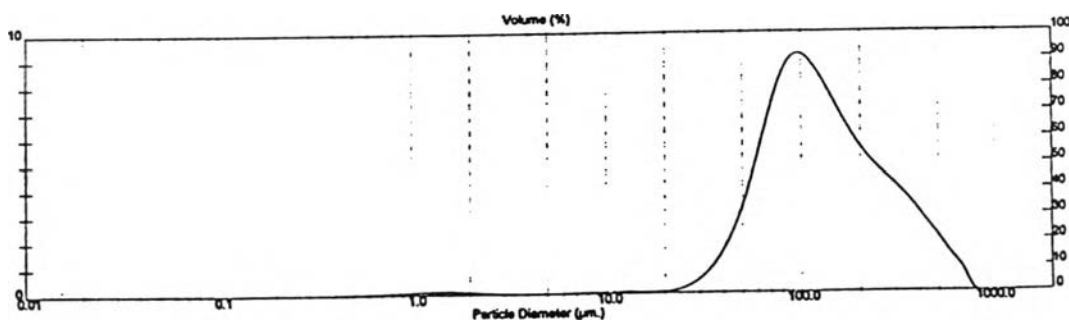


Figure 20 (continued)

Table 23 (continued)

System Details							
Range Lens: 300RF mm	Beam Length: 2.40 mm	Sampler: MS1		Obscuration: 3.9 %			
Presentation: 30HD	[Particle R.I. = (1.5295, 0.1000);	Dispersant R.I. = 1.3300]		Residual: 0.606 %			
Analysis Model: Polydisperse	Killed Data Channels: Low 0; High 2						
Modifications: Active -							
Result Statistics							
Distribution Type: Volume	Concentration = 0.0275 %Vol	Density = 1.000 g / cub. cm	Specific S.A. = 0.1296 sq. m / g				
Mean Diameters:	D (v, 0.1) = 54.91 um	D (v, 0.5) = 111.54 um	D (v, 0.9) = 273.44 um				
D [4, 3] = 140.50 um	D [3, 2] = 46.30 um	Span = 1.959E+00	Uniformity = 5.952E-01				
Size Low (um)	In %	Size High (um)	Under%	Size Low (um)	In %	Size High (um)	Under%
0.05	0.00	0.06	0.00	6.63	0.04	7.72	1.33
0.06	0.00	0.07	0.00	7.72	0.06	9.00	1.39
0.07	0.00	0.08	0.00	9.00	0.08	10.48	1.47
0.08	0.00	0.09	0.00	10.48	0.09	12.21	1.56
0.09	0.00	0.11	0.00	12.21	0.09	14.22	1.65
0.11	0.00	0.13	0.00	14.22	0.07	16.57	1.73
0.13	0.00	0.15	0.00	16.57	0.06	19.31	1.78
0.15	0.00	0.17	0.00	19.31	0.07	22.49	1.86
0.17	0.00	0.20	0.00	22.49	0.16	26.20	2.02
0.20	0.00	0.23	0.00	26.20	0.37	30.53	2.40
0.23	0.00	0.27	0.01	30.53	0.75	35.56	3.15
0.27	0.01	0.31	0.01	35.56	1.38	41.43	4.53
0.31	0.01	0.36	0.03	41.43	2.36	48.27	6.89
0.36	0.02	0.42	0.04	48.27	3.83	56.23	10.71
0.42	0.02	0.49	0.07	56.23	5.87	65.51	16.59
0.49	0.04	0.58	0.10	65.51	8.17	76.32	24.75
0.58	0.05	0.67	0.15	76.32	9.89	88.91	34.65
0.67	0.06	0.78	0.21	88.91	10.42	103.50	45.07
0.78	0.08	0.91	0.30	103.50	9.95	120.67	55.02
0.91	0.11	1.06	0.40	120.67	9.02	140.58	64.04
1.06	0.13	1.24	0.53	140.58	7.99	163.77	72.03
1.24	0.15	1.44	0.68	163.77	6.59	190.80	78.62
1.44	0.15	1.68	0.82	190.80	5.46	222.28	84.07
1.68	0.14	1.95	0.96	222.28	4.52	258.95	88.59
1.95	0.11	2.28	1.07	258.95	3.71	301.68	92.30
2.28	0.08	2.65	1.15	301.68	2.99	351.46	95.29
2.65	0.05	3.09	1.20	351.46	2.26	409.45	97.56
3.09	0.03	3.60	1.23	409.45	1.54	477.01	99.10
3.60	0.01	4.19	1.24	477.01	0.81	555.71	99.91
4.19	0.01	4.88	1.25	555.71	0.09	647.41	100.00
4.88	0.01	5.69	1.26	647.41	0.00	754.23	100.00
5.69	0.02	6.63	1.29	754.23	0.00	878.67	100.00

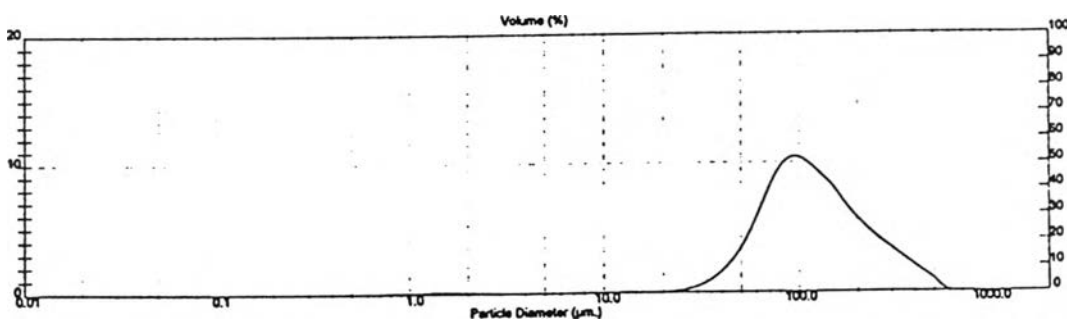


Figure 20 (continued)

Table 24 Particle size of minocycline hydrochloride microcapsules using DL-PLA with 1:5 core to wall ratio

System Details							
Range Lens: 300RF mm	Beam Length: 2.40 mm	Sampler: MS1		C%curacion: 6.4 %			
Presentation: 3OHD	[Particle R.L. = (1.5295, 0.1000);	Dispersant R.I. = 1.3300]		Residual: 0.496 %			
Analysis Model: Polydisperse	Killed Data Channels: Low 0; High 2						
Modifications: Active --							
Result Statistics							
Distribution Type: Volume	Concentration = 0.0295 %Vol	Density = 1.000 g / cub. cm	Specific S.A. = 0.1905 sq. m / g				
Mean Diameters:	D (v, 0.1) = 35.03 um	D (v, 0.5) = 71.34 um	D (v, 0.9) = 186.74 um				
D [4, 3] = 94.89 um	D [3, 2] = 31.50 um	Span = 2.126E+00	Uniformity = 6.686E-01				
Size Low (um)	In %	Size High (um)	Under%	Size Low (um)	In %	Size High (um)	Under%
0.05	0.00	0.06	0.00	6.63	0.12	7.72	2.39
0.06	0.00	0.07	0.00	7.72	0.12	9.00	2.52
0.07	0.00	0.08	0.00	9.00	0.10	10.48	2.62
0.08	0.00	0.09	0.00	10.48	0.08	12.21	2.70
0.09	0.00	0.11	0.00	12.21	0.08	14.22	2.78
0.11	0.00	0.13	0.00	14.22	0.14	16.57	2.92
0.13	0.00	0.15	0.00	16.57	0.32	19.31	3.24
0.15	0.00	0.17	0.00	19.31	0.64	22.49	3.88
0.17	0.00	0.20	0.00	22.49	1.17	26.20	5.05
0.20	0.00	0.23	0.00	26.20	2.01	30.53	7.06
0.23	0.00	0.27	0.00	30.53	3.34	35.56	10.40
0.27	0.00	0.31	0.00	35.56	5.30	41.43	15.70
0.31	0.00	0.36	0.00	41.43	7.73	48.27	23.43
0.36	0.01	0.42	0.01	48.27	9.84	56.23	33.27
0.42	0.02	0.49	0.03	56.23	10.79	65.51	44.07
0.49	0.04	0.58	0.07	65.51	10.43	76.32	54.50
0.58	0.07	0.67	0.14	76.32	9.41	88.91	63.91
0.67	0.10	0.78	0.24	88.91	8.26	103.58	72.17
0.78	0.13	0.91	0.38	103.58	6.48	120.67	78.65
0.91	0.18	1.06	0.55	120.67	4.98	140.58	83.63
1.06	0.21	1.24	0.76	140.58	3.80	163.77	87.43
1.24	0.24	1.44	1.00	163.77	2.95	190.80	90.38
1.44	0.25	1.68	1.25	190.80	2.40	222.28	92.78
1.68	0.23	1.95	1.48	222.28	2.05	258.95	94.83
1.95	0.18	2.28	1.66	258.95	1.76	301.68	96.59
2.28	0.13	2.65	1.79	301.68	1.45	351.46	98.04
2.65	0.09	3.09	1.88	351.46	1.05	409.45	99.09
3.09	0.07	3.60	1.94	409.45	0.65	477.01	99.74
3.60	0.06	4.19	2.00	477.01	0.26	555.71	100.00
4.19	0.07	4.88	2.07	555.71	0.00	647.41	100.00
4.88	0.09	5.69	2.16	647.41	0.00	754.23	100.00
5.69	0.11	6.63	2.27	754.23	0.00	878.67	100.00

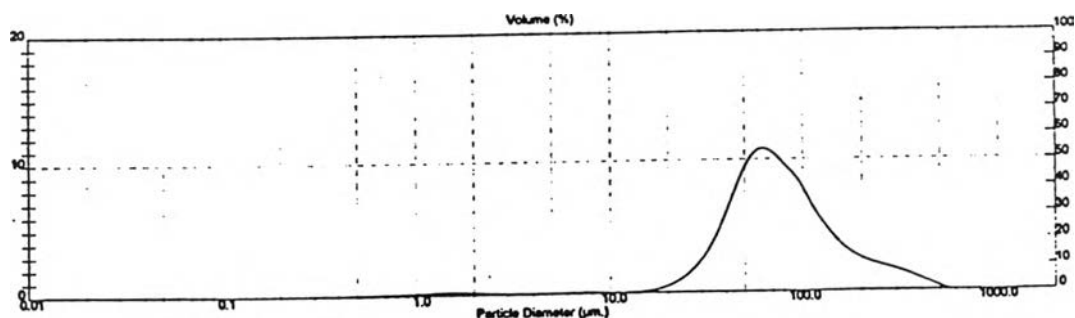


Figure 21 Particle size distribution of minocycline hydrochloride microcapsules using DL-PLA with 1:5 core to wall ratio.

Table 24 (continued)

System Details							
Range Lens: 300RF mm		Beam Length: 2.40 mm		Sampler: MS1		Obscuration: 5.9 %	
Presentation: 3OHD		[Particle \bar{r}_i = (1.5295, 0.1000); Dispersant R.I. = 1.3300]				Residual: 0.572 %	
Analysis Model: Polydisperse		Killed Data Channels: Low C; High 2					
Modifications: Active -							
Result Statistics							
Distribution Type: Volume		Concentration = 0.0272 %Vol		Density = 1.000 g/cub. cm		Specific S.A. = 0.1910 sq. m/g	
Mean Diameters:		D (v, 0.1) = 34.65 um		D (v, 0.5) = 71.57 um		D (v, 0.9) = 172.22 um	
D [4, 3] = 90.04 um		D [3, 2] = 31.41 um		Span = 1.012E+00		Uniformity = 5.963E-01	
Size Low (um)	In %	Size High (um)	Under%	Size Low (um)	In %	Size High (um)	Under%
0.05	0.00	0.06	0.00	6.63	0.12	7.72	2.38
0.06	0.00	0.07	0.00	7.72	0.11	9.00	2.50
0.07	0.00	0.08	0.00	9.00	0.09	10.48	2.59
0.08	0.00	0.09	0.00	10.48	0.07	12.21	2.66
0.09	0.00	0.11	0.00	12.21	0.07	14.22	2.74
0.11	0.00	0.13	0.00	14.22	0.14	16.57	2.88
0.13	0.00	0.15	0.00	16.57	0.32	19.31	3.20
0.15	0.00	0.17	0.00	19.31	0.67	22.49	3.86
0.17	0.00	0.20	0.00	22.49	1.23	26.20	5.10
0.20	0.00	0.23	0.00	26.20	2.13	30.53	7.23
0.23	0.00	0.27	0.00	30.53	3.48	35.56	10.71
0.27	0.00	0.31	0.00	35.56	5.38	41.43	16.09
0.31	0.00	0.36	0.00	41.43	7.61	48.27	23.71
0.36	0.01	0.42	0.01	48.27	9.50	56.23	33.20
0.42	0.02	0.49	0.03	56.23	10.41	65.51	43.62
0.49	0.04	0.58	0.07	65.51	10.25	76.32	53.87
0.58	0.07	0.67	0.14	76.32	9.49	88.91	63.36
0.67	0.10	0.78	0.24	88.91	8.57	103.58	71.93
0.78	0.14	0.91	0.38	103.58	6.98	120.67	78.91
0.91	0.18	1.06	0.56	120.67	5.55	140.58	84.46
1.06	0.22	1.24	0.77	140.58	4.34	163.77	88.79
1.24	0.24	1.44	1.01	163.77	3.38	190.80	92.18
1.44	0.24	1.68	1.26	190.80	2.66	222.28	94.84
1.68	0.22	1.95	1.48	222.28	2.08	258.95	96.92
1.95	0.18	2.28	1.66	258.95	1.55	301.68	98.47
2.28	0.13	2.65	1.78	301.68	1.03	351.46	99.50
2.65	0.09	3.09	1.87	351.46	0.50	409.45	100.00
3.09	0.07	3.60	1.94	409.45	0.00	477.01	100.00
3.60	0.06	4.19	2.00	477.01	0.00	555.71	100.00
4.19	0.07	4.88	2.07	555.71	0.00	647.41	100.00
4.88	0.09	5.69	2.16	647.41	0.00	754.23	100.00
5.69	0.11	6.63	2.27	754.23	0.00	878.67	100.00

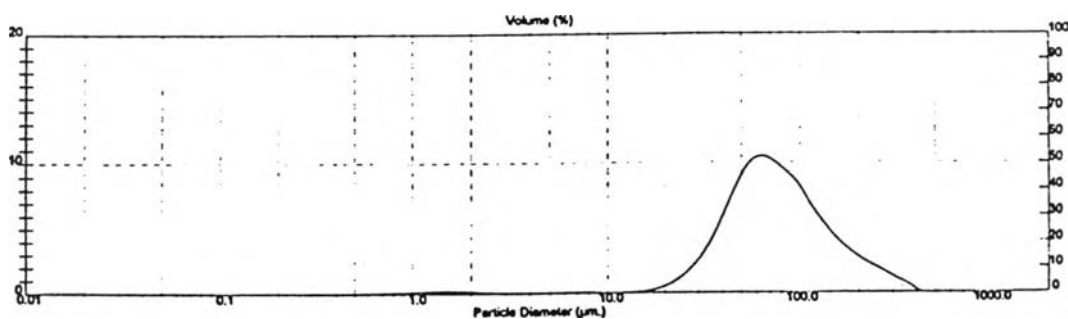


Figure 21 (continued)

Table 24 (continued)

System Details			
Range Lens: 300RF mm	Beam Length: 2.40 mm	Sampler: MS1	Obscuration: 6.6 %
Presentation: 3OHD	[Particle R.I. = (1.5295, 0.1000);	Dispersant R.I. = 1.3300]	Residual: 0.605 %
Analysis Model: Polydisperse	Killed Data Channels: Low 0; High 2		
Modifications: Active -			

Result Statistics			
Distribution Type/Volume	Concentration = 0.0307 %Vol	Density = 1.000 g / cub. cm	Specific S.A. = 0.1884 sq. m / g
Mean Diameters:	D (v, 0.1) = 34.65 um	D (v, 0.5) = 73.02 um	D (v, 0.9) = 190.58 um
D [4, 3] = 95.42 um	D [3, 2] = 31.84 um	Span = 2.136E+00	Uniformity = 6.581E-01

Size Low (um)	In %	Size High (um)	Under%	Size Low (um)	In %	Size High (um)	Under%
0.05	0.00	0.06	0.00	6.63	0.12	7.72	2.35
0.06	0.00	0.07	0.00	7.72	0.12	9.00	2.47
0.07	0.00	0.08	0.00	9.00	0.10	10.48	2.56
0.08	0.00	0.09	0.00	10.48	0.08	12.21	2.64
0.09	0.00	0.11	0.00	12.21	0.08	14.22	2.72
0.11	0.00	0.13	0.00	14.22	0.15	16.57	2.87
0.13	0.00	0.15	0.00	16.57	0.33	19.31	3.19
0.15	0.00	0.17	0.00	19.31	0.67	22.49	3.87
0.17	0.00	0.20	0.00	22.49	1.24	26.20	5.11
0.20	0.00	0.23	0.00	26.20	2.13	30.53	7.24
0.23	0.00	0.27	0.00	30.53	3.47	35.56	10.71
0.27	0.00	0.31	0.00	35.56	5.32	41.43	16.02
0.31	0.00	0.36	0.00	41.43	7.47	48.27	23.49
0.36	0.01	0.42	0.01	48.27	9.26	56.23	32.75
0.42	0.02	0.49	0.03	56.23	10.12	65.51	42.87
0.49	0.04	0.58	0.07	65.51	9.94	76.32	52.81
0.58	0.07	0.67	0.14	76.32	9.21	88.91	62.02
0.67	0.10	0.78	0.24	88.91	8.30	103.58	70.32
0.78	0.14	0.91	0.38	103.58	6.73	120.67	77.06
0.91	0.18	1.06	0.55	120.67	5.35	140.58	82.41
1.06	0.21	1.24	0.76	140.58	4.22	163.77	86.63
1.24	0.23	1.44	1.00	163.77	3.39	190.80	90.02
1.44	0.24	1.68	1.23	190.80	2.82	222.28	92.84
1.68	0.22	1.95	1.45	222.28	2.37	258.95	95.21
1.95	0.17	2.28	1.62	258.95	1.94	301.68	97.15
2.28	0.13	2.65	1.75	301.68	1.45	351.46	98.59
2.65	0.09	3.09	1.84	351.46	0.95	409.45	99.54
3.09	0.07	3.60	1.90	409.45	0.46	477.01	100.00
3.60	0.06	4.19	1.97	477.01	0.00	555.71	100.00
4.19	0.07	4.88	2.04	555.71	0.00	647.41	100.00
4.88	0.09	5.69	2.13	647.41	0.00	754.23	100.00
5.69	0.11	6.63	2.23	754.23	0.00	878.67	100.00

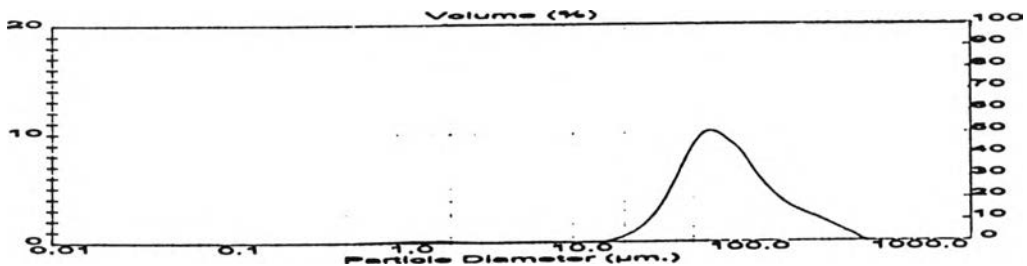


Figure 21 (continued)

Table 25 Particle size of minocycline hydrochloride microcapsules using PLGA 75:25 with 1:5 core to wall ratio

System Details							
Range Lens: 300RF mm	Beam Length: 2.40 mm	Sampler: MS1		Obscuration: 6.2 %			
Presentation: 30HD	(Particle R.I. = (1.5295, 0.1000);	Dispersant R.L = 1.3300]		Residual: 0.585 %			
Analysis Model: Polydisperse	Killed Data Channels: Low 0; High 2						
Modifications: Active -							
Result Statistics							
Distribution Type: Volume	Concentration = 0.0285 %Vol	Density = 1.000 g / cub. cm	Specific S.A. = 0.2962 sq. m / g				
Mean Diameters:	D (v, 0.1) = 40.03 um	D (v, 0.5) = 109.13 um	D (v, 0.9) = 316.62 um				
D [4, 3] = 147.01 um	D [3, 2] = 20.26 um	Span = 2.535E+00	Uniformity = 7.714E-01				
Size Low (um)	In %	Size High (um)	Under%	Size Low (um)	In %	Size High (um)	Under%
0.05	0.00	0.06	0.00	6.63	0.10	7.72	1.87
0.06	0.00	0.07	0.00	7.72	0.12	9.00	1.99
0.07	0.00	0.08	0.01	9.00	0.14	10.48	2.13
0.08	0.01	0.09	0.02	10.48	0.16	12.21	2.29
0.09	0.01	0.11	0.03	12.21	0.18	14.22	2.47
0.11	0.01	0.13	0.04	14.22	0.23	16.57	2.70
0.13	0.02	0.15	0.06	16.57	0.33	19.31	3.03
0.15	0.03	0.17	0.09	19.31	0.53	22.49	3.56
0.17	0.04	0.20	0.13	22.49	0.86	26.20	4.42
0.20	0.06	0.23	0.20	26.20	1.35	30.53	5.77
0.23	0.09	0.27	0.29	30.53	2.04	35.56	7.81
0.27	0.10	0.31	0.39	35.56	2.94	41.43	10.75
0.31	0.10	0.36	0.49	41.43	4.03	48.27	14.77
0.36	0.10	0.42	0.59	48.27	5.17	56.23	19.95
0.42	0.09	0.49	0.68	56.23	6.21	65.51	26.16
0.49	0.09	0.58	0.77	65.51	6.93	76.32	33.09
0.58	0.09	0.67	0.86	76.32	7.26	88.91	40.35
0.67	0.09	0.78	0.95	88.91	7.23	103.58	47.58
0.78	0.09	0.91	1.04	103.58	6.96	120.67	54.54
0.91	0.09	1.06	1.13	120.67	6.57	140.58	61.11
1.06	0.10	1.24	1.22	140.58	6.14	163.77	67.25
1.24	0.09	1.44	1.32	163.77	5.75	190.80	73.00
1.44	0.08	1.68	1.40	190.80	5.51	222.28	78.51
1.68	0.07	1.95	1.47	222.28	5.25	258.95	83.76
1.95	0.05	2.28	1.52	258.95	4.83	301.68	88.60
2.28	0.04	2.65	1.56	301.68	4.18	351.46	92.77
2.65	0.02	3.09	1.58	351.46	3.29	409.45	96.06
3.09	0.02	3.60	1.60	409.45	2.30	477.01	98.36
3.60	0.02	4.19	1.62	477.01	1.31	555.71	99.67
4.19	0.03	4.88	1.65	555.71	0.33	647.41	100.00
4.88	0.05	5.69	1.70	647.41	0.00	754.23	100.00
5.69	0.07	6.63	1.77	754.23	0.00	878.67	100.00

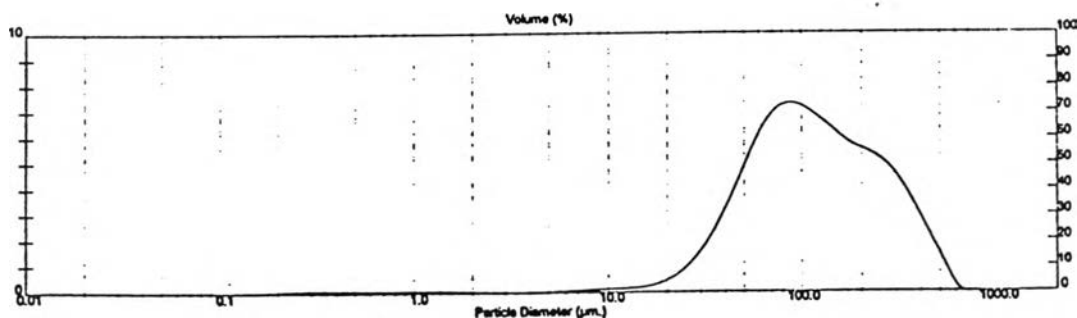


Figure 22 Particle size distribution of minocycline hydrochloride microcapsules using PLGA 75:25 with 1:5 core to wall ratio.

Table 25 (continued)

System Details			
Range Lens: 300RF mm	Beam Length: 2.40 mm	Sampler: MS1	Obscuration: 5.2 %
Prerotation: 30HD	[Particle R.I. = (1.5295, 0.1000)];	Dispersant R.I. = 1.3300]	Residual: 0.441 %
Analysis Model: Polydisperse	Killed Data Channel: Low 0; High 2		
Modifications: Active -			

Result Statistics			
Distribution Type: Volume	Concentration = 0.0284 %Vol	Density = 1.000 g / cub. cm	Specific S.A. = 0.2830 sq. m / g
Mean Diameters:	D (v, 0.1) = 40.98 um	D (v, 0.5) = 107.58 um	D (v, 0.9) = 322.21 um
D [4, 3] = 147.79 um	D [3, 2] = 21.20 um	Span = 2.614E+00	Uniformity = 7.881E-01

Size Low (um)	In %	Size High (um)	Under%	Size Low (um)	In %	Size High (um)	Under%
0.05	0.00	0.06	0.00	6.63	0.09	7.72	1.85
0.06	0.00	0.07	0.00	7.72	0.11	9.00	1.96
0.07	0.00	0.08	0.00	9.00	0.13	10.48	2.09
0.08	0.00	0.09	0.01	10.48	0.15	12.21	2.24
0.09	0.01	0.11	0.01	12.21	0.17	14.22	2.40
0.11	0.01	0.13	0.02	14.22	0.21	16.57	2.61
0.13	0.01	0.15	0.03	16.57	0.31	19.31	2.92
0.15	0.02	0.17	0.06	19.31	0.49	22.49	3.42
0.17	0.04	0.20	0.09	22.49	0.80	26.20	4.22
0.20	0.06	0.23	0.15	26.20	1.27	30.53	5.49
0.23	0.09	0.27	0.25	30.53	1.93	35.56	7.42
0.27	0.12	0.31	0.36	35.56	2.83	41.43	10.24
0.31	0.12	0.36	0.48	41.43	3.95	48.27	14.20
0.36	0.11	0.42	0.59	48.27	5.20	56.23	19.40
0.42	0.10	0.49	0.69	56.23	6.38	65.51	25.78
0.49	0.10	0.58	0.79	65.51	7.22	76.32	33.00
0.58	0.09	0.67	0.87	76.32	7.61	88.91	40.61
0.67	0.09	0.78	0.96	88.91	7.56	103.58	48.17
0.78	0.09	0.91	1.05	103.58	7.22	120.67	55.38
0.91	0.09	1.06	1.14	120.67	6.72	140.58	62.11
1.06	0.09	1.24	1.24	140.58	6.15	163.77	68.26
1.24	0.09	1.44	1.33	163.77	5.60	190.80	73.86
1.44	0.08	1.68	1.41	190.80	5.18	222.28	79.04
1.68	0.07	1.95	1.48	222.28	4.81	258.95	83.85
1.95	0.05	2.28	1.54	258.95	4.40	301.68	88.25
2.28	0.04	2.65	1.57	301.68	3.88	351.46	92.14
2.65	0.02	3.09	1.60	351.46	3.19	409.45	95.33
3.09	0.02	3.60	1.61	409.45	2.38	477.01	97.71
3.60	0.02	4.19	1.63	477.01	1.56	555.71	99.27
4.19	0.03	4.88	1.65	555.71	0.73	647.41	100.00
4.88	0.04	5.69	1.70	647.41	0.00	754.23	100.00
5.69	0.06	6.63	1.76	754.23	0.00	878.67	100.00

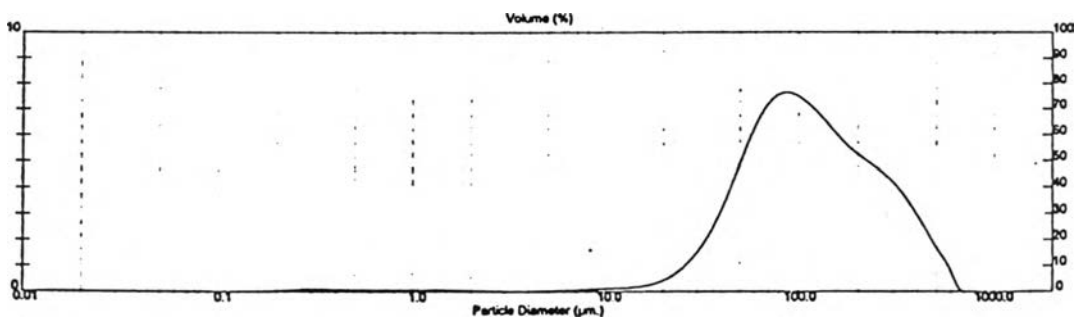


Figure 22 (continued)

Table 25 (continued)

System Details							
Range Lens: 300RF mm		Beam Length: 2.40 mm		Sampler: MS1		Obscuration: 4.9 %	
Presentation: 3OHD		[Particle R.I. = (1.5295, 0.1000);		Dispersant R.I. = 1.3300]		Residual: 0.474 %	
Analysis Model: Polydisperse		Killed Data Channels: Low 0; High 2					
Modifications: Active -							
Result Statistics							
Distribution Type: Volume		Concentration = 0.0273 %Vol		Density = 1.000 g / cub. cm		Specific S.A. = 0.2823 sq. m / g	
Mean Diameters:		D (v, 0.1) = 42.00 um		D (v, 0.5) = 107.54 um		D (v, 0.9) = 341.38 um	
D [4, 3] = 152.66 um		D [3, 2] = 21.25 um		Span = 2.784E+00		Uniformity = 8.270E-01	
Size Low (um)	In %	Size High (um)	Under%	Size Low (um)	In %	Size High (um)	Under%
0.05	0.00	0.06	0.00	6.63	0.09	7.72	1.82
0.06	0.00	0.07	0.00	7.72	0.11	9.00	1.94
0.07	0.00	0.08	0.00	9.00	0.13	10.48	2.07
0.08	0.00	0.09	0.01	10.48	0.14	12.21	2.21
0.09	0.01	0.11	0.01	12.21	0.16	14.22	2.36
0.11	0.01	0.13	0.02	14.22	0.19	16.57	2.55
0.13	0.01	0.15	0.04	16.57	0.27	19.31	2.82
0.15	0.02	0.17	0.06	19.31	0.44	22.49	3.26
0.17	0.04	0.20	0.09	22.49	0.73	26.20	3.98
0.20	0.06	0.23	0.16	26.20	1.17	30.53	5.16
0.23	0.09	0.27	0.25	30.53	1.82	35.56	6.98
0.27	0.12	0.31	0.37	35.56	2.72	41.43	9.70
0.31	0.12	0.36	0.49	41.43	3.87	48.27	13.57
0.36	0.11	0.42	0.60	48.27	5.17	56.23	18.73
0.42	0.10	0.49	0.70	56.23	8.43	65.51	25.16
0.49	0.10	0.58	0.79	65.51	7.36	76.32	32.52
0.58	0.09	0.67	0.88	76.32	7.82	88.91	40.34
0.67	0.09	0.78	0.97	88.91	7.79	103.58	48.14
0.78	0.09	0.91	1.05	103.58	7.39	120.67	55.53
0.91	0.09	1.06	1.14	120.67	6.77	140.58	62.30
1.06	0.09	1.24	1.23	140.58	6.03	163.77	68.33
1.24	0.09	1.44	1.32	163.77	5.31	190.80	73.64
1.44	0.08	1.68	1.40	190.80	4.77	222.28	78.41
1.68	0.07	1.95	1.47	222.28	4.39	258.95	82.80
1.95	0.05	2.28	1.52	258.95	4.10	301.68	86.91
2.28	0.03	2.65	1.55	301.68	3.79	351.46	90.69
2.65	0.02	3.09	1.58	351.46	3.32	409.45	94.01
3.09	0.01	3.60	1.59	409.45	2.67	477.01	96.68
3.60	0.02	4.19	1.61	477.01	1.89	555.71	98.57
4.19	0.02	4.88	1.63	555.71	1.11	647.41	99.67
4.88	0.04	5.69	1.67	647.41	0.33	754.23	100.00
5.69	0.06	6.63	1.74	754.23	0.00	878.67	100.00

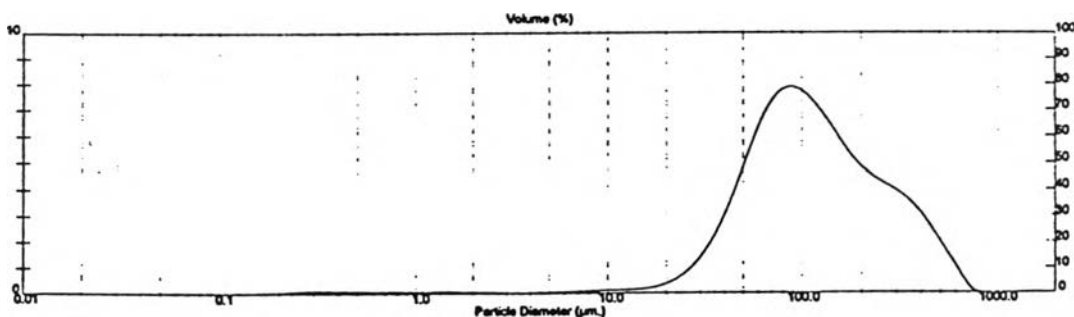


Figure 22 (continued)

Table 26 Particle size of minocycline hydrochloride microcapsules using PLGA 50:50 with 1:5 core to wall ratio

System Details							
Range Lens: 300RF mm	Beam Length: 2.40 mm	Sampler: MS1		Obscuration: 4.7 %			
Presentation: 30HD	[Particle R.I. = (1.5295, 0.1000);	Dispersant R.I. = 1.3300]		Residual: 0.495 %			
Analysis Model: Polydisperse	Killed Data Channels: Low 0; High 2						
Modifications: Active -							
Result Statistics							
Distribution Type: Volume	Concentration = 0.0250 %Vol	Density = 1.000 g / cub. cm	Specific S.A. = 0.1821 sq. m / g				
Mean Diameters:	D (v, 0.1) = 32.92 um	D (v, 0.5) = 128.05 um	D (v, 0.9) = 413.34 um				
D [4, 3] = 181.70 um	D [3, 2] = 32.95 um	Span = 2.973E+00	Uniformity = 0.484E-01				
Size Low (um)	In %	Size High (um)	Under%	Size Low (um)	In %	Size High (um)	Under%
0.05	0.00	0.08	0.00	6.63	0.13	7.72	2.13
0.06	0.00	0.07	0.00	7.72	0.14	9.00	2.27
0.07	0.00	0.08	0.00	9.00	0.15	10.48	2.41
0.08	0.00	0.09	0.00	10.48	0.18	12.21	2.59
0.09	0.00	0.11	0.00	12.21	0.26	14.22	2.85
0.11	0.00	0.13	0.00	14.22	0.40	16.57	3.25
0.13	0.00	0.15	0.00	16.57	0.64	19.31	3.89
0.15	0.00	0.17	0.00	19.31	1.01	22.49	4.90
0.17	0.00	0.20	0.00	22.49	1.52	26.20	6.41
0.20	0.00	0.23	0.00	26.20	2.20	30.53	8.61
0.23	0.00	0.27	0.00	30.53	3.02	35.56	11.64
0.27	0.02	0.31	0.02	35.56	3.89	41.43	15.53
0.31	0.03	0.36	0.05	41.43	4.60	48.27	20.13
0.36	0.04	0.42	0.09	48.27	4.97	56.23	25.10
0.42	0.06	0.49	0.14	56.23	5.01	65.51	30.10
0.49	0.08	0.58	0.22	65.51	4.85	76.32	34.96
0.58	0.10	0.67	0.32	76.32	4.64	88.91	39.60
0.67	0.12	0.78	0.44	88.91	4.43	103.58	44.03
0.78	0.14	0.91	0.58	103.58	4.30	120.67	48.33
0.91	0.16	1.06	0.74	120.67	4.30	140.58	52.64
1.06	0.17	1.24	0.91	140.58	4.44	163.77	57.08
1.24	0.16	1.44	1.07	163.77	4.73	190.80	61.81
1.44	0.15	1.68	1.22	190.80	5.14	222.28	66.95
1.68	0.13	1.95	1.35	222.28	5.64	258.95	72.59
1.95	0.10	2.28	1.45	258.95	5.93	301.68	78.52
2.28	0.08	2.65	1.53	301.68	5.85	351.46	84.38
2.65	0.06	3.09	1.59	351.46	5.30	409.45	89.68
3.09	0.06	3.60	1.64	409.45	4.36	477.01	94.04
3.60	0.06	4.19	1.71	477.01	3.17	555.71	97.21
4.19	0.08	4.88	1.79	555.71	1.99	647.41	99.20
4.88	0.10	5.69	1.89	647.41	0.80	754.23	100.00
5.69	0.12	6.63	2.00	754.23	0.00	878.67	100.00

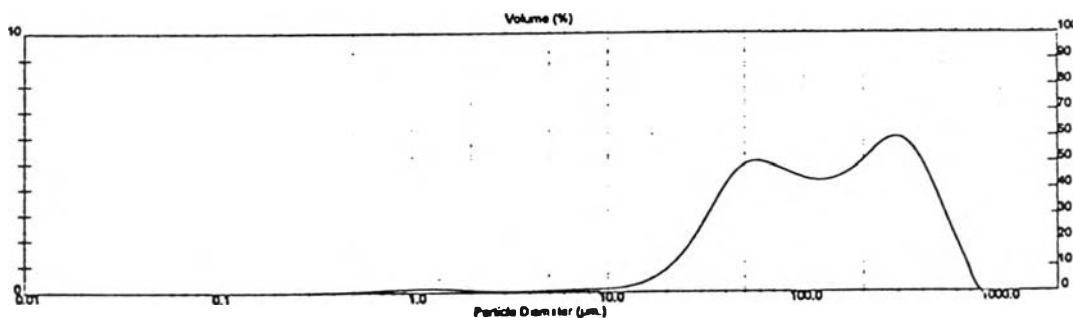


Figure 23 Particle size distribution of minocycline hydrochloride microcapsules using PLGA 50:50 with 1:5 core to wall ratio.

Table 26 (continued)

System Details			
Range Lens: 300RF mm	Beam Length: 2.40 mm	Sampler: MS1	Obscuration: 2.9 %
Presentation: 30HD	(Particle R.I. = (1.5295, 0.1000);	Dispersant R.I. = 1.3300]	
Analysis Model: Polydisperse			Residual: 0.593 %
Modifications: Active -	Killed Data Channels: Low 0; High 2		

Result Statistics			
Distribution Type: Volume	Concentration = 0.0160 %Vol	Density = 1.000 g / cub. cm	Specific S.A. = 0.1859 sq. m / g
Mean Diameters:	D (v, 0.1) = 34.63 um	D (v, 0.5) = 126.88 um	D (v, 0.9) = 408.35 um
D [4, 3] = 179.22 um	D [3, 2] = 32.28 um	Span = 2.945E+00	Uniformity = 9.158E-01

Size Low (um)	In %	Size High (um)	Under%	Size Low (um)	In %	Size High (um)	Under%
0.05	0.00	0.06	0.00	6.63	0.12	7.72	2.04
0.06	0.00	0.07	0.00	7.72	0.12	9.00	2.16
0.07	0.00	0.08	0.00	9.00	0.13	10.48	2.29
0.08	0.00	0.09	0.00	10.48	0.15	12.21	2.44
0.09	0.00	0.11	0.00	12.21	0.21	14.22	2.65
0.11	0.00	0.13	0.00	14.22	0.33	16.57	2.98
0.13	0.00	0.15	0.00	16.57	0.56	19.31	3.54
0.15	0.00	0.17	0.00	19.31	0.90	22.49	4.44
0.17	0.00	0.20	0.00	22.49	1.38	26.20	5.81
0.20	0.01	0.23	0.01	26.20	1.99	30.53	7.80
0.23	0.02	0.27	0.03	30.53	2.72	35.56	10.53
0.27	0.03	0.31	0.05	35.56	3.49	41.43	14.02
0.31	0.04	0.36	0.09	41.43	4.18	48.27	18.20
0.36	0.05	0.42	0.14	48.27	4.68	56.23	22.88
0.42	0.06	0.49	0.20	56.23	4.97	65.51	27.85
0.49	0.08	0.58	0.28	65.51	5.10	76.32	32.95
0.58	0.10	0.67	0.37	76.32	5.13	88.91	38.08
0.67	0.12	0.78	0.49	88.91	5.12	103.58	43.20
0.78	0.13	0.91	0.62	103.58	5.11	120.67	48.32
0.91	0.14	1.06	0.76	120.67	5.13	140.58	53.45
1.06	0.15	1.24	0.91	140.58	5.18	163.77	58.63
1.24	0.15	1.44	1.06	163.77	5.25	190.80	63.88
1.44	0.14	1.68	1.20	190.80	5.36	222.28	69.24
1.68	0.12	1.95	1.31	222.28	5.47	258.95	74.71
1.95	0.09	2.28	1.41	258.95	5.44	301.68	80.16
2.28	0.07	2.65	1.48	301.68	5.21	351.46	85.37
2.65	0.06	3.09	1.54	351.46	4.71	409.45	90.08
3.09	0.05	3.60	1.59	409.45	3.94	477.01	94.02
3.60	0.06	4.19	1.65	477.01	2.97	555.71	96.98
4.19	0.07	4.88	1.72	555.71	1.99	647.41	98.98
4.88	0.09	5.69	1.82	647.41	1.02	754.23	100.00
5.69	0.11	6.63	1.92	754.23	0.00	878.67	100.00

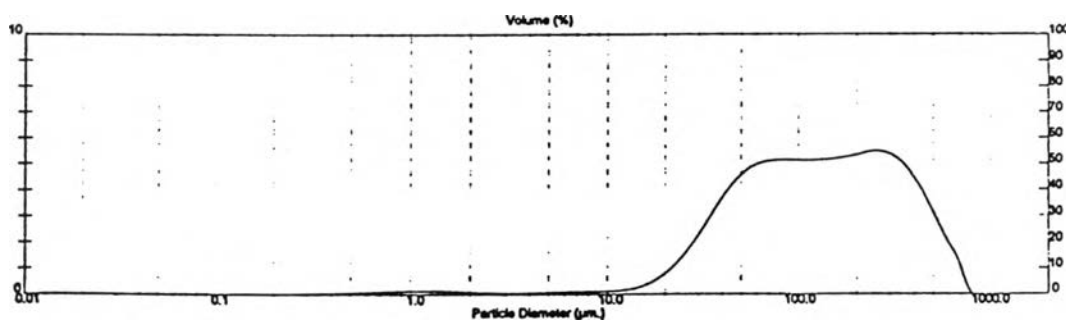


Figure 23 (continued)

Table 26 (continued)

System Details			
Range Lens: 300RF mm	Beam Length: 2.40 mm	Sampler: MS1	Obscuration: 3.2 %
Presentation: 30HD	(Particle R.I. = (1.5295, 0.1000); Dispersant R.I. = 1.3300)		Residual: 0.388 %
Analysis Model: Polydisperse			
Modifications: Active -	Killed Data Channels: Low 0; High 2		

Result Statistics			
Distribution Type: Volume	Concentration = 0.0170 %Vol	Density = 1.000 g / cub. cm	Specific S.A. = 0.1849 sq. m / g
Mean Diameters:	D (v, 0.1) = 34.80 um	D (v, 0.5) = 119.66 um	D (v, 0.9) = 373.95 um
D [4, 3] = 167.12 um	D [3, 2] = 32.46 um	Span = 2.834E+00	Uniformity = 8.981E-01

Size Low (um)	In %	Size High (um)	Under%	Size Low (um)	In %	Size High (um)	Under%
0.05	0.00	0.06	0.00	6.63	0.13	7.72	2.12
0.06	0.00	0.07	0.00	7.72	0.14	9.00	2.25
0.07	0.00	0.08	0.00	9.00	0.14	10.48	2.40
0.08	0.00	0.09	0.00	10.48	0.16	12.21	2.55
0.09	0.00	0.11	0.00	12.21	0.21	14.22	2.76
0.11	0.00	0.13	0.00	14.22	0.33	16.57	3.09
0.13	0.00	0.15	0.00	16.57	0.52	19.31	3.61
0.15	0.00	0.17	0.00	19.31	0.83	22.49	4.44
0.17	0.00	0.20	0.00	22.49	1.28	26.20	5.72
0.20	0.00	0.23	0.00	26.20	1.93	30.53	7.65
0.23	0.01	0.27	0.01	30.53	2.81	35.56	10.45
0.27	0.02	0.31	0.03	35.56	3.84	41.43	14.30
0.31	0.03	0.36	0.07	41.43	4.79	48.27	19.09
0.36	0.04	0.42	0.11	48.27	6.37	56.23	24.46
0.42	0.06	0.49	0.17	56.23	8.51	65.51	29.97
0.49	0.08	0.58	0.25	65.51	11.39	76.32	35.36
0.58	0.10	0.67	0.34	76.32	15.17	88.91	40.53
0.67	0.12	0.78	0.46	88.91	19.95	103.58	45.48
0.78	0.13	0.91	0.59	103.58	27.78	120.67	50.26
0.91	0.15	1.06	0.75	120.67	38.47	140.58	54.99
1.06	0.16	1.24	0.91	140.58	52.80	163.77	59.80
1.24	0.17	1.44	1.08	163.77	71.04	190.80	64.83
1.44	0.15	1.68	1.23	190.80	94.54	222.28	70.23
1.68	0.13	1.95	1.36	222.28	124.83	258.95	76.06
1.95	0.10	2.28	1.46	258.95	163.02	301.68	82.08
2.28	0.07	2.65	1.54	301.68	209.77	351.46	87.85
2.65	0.06	3.09	1.59	351.46	265.00	409.45	92.85
3.09	0.05	3.60	1.65	409.45	328.75	477.01	96.60
3.60	0.06	4.19	1.71	477.01	400.38	555.71	98.98
4.19	0.07	4.88	1.78	555.71	480.10	647.41	100.00
4.88	0.09	5.69	1.87	647.41	567.00	754.23	100.00
5.69	0.11	6.63	1.99	754.23	660.00	878.67	100.00

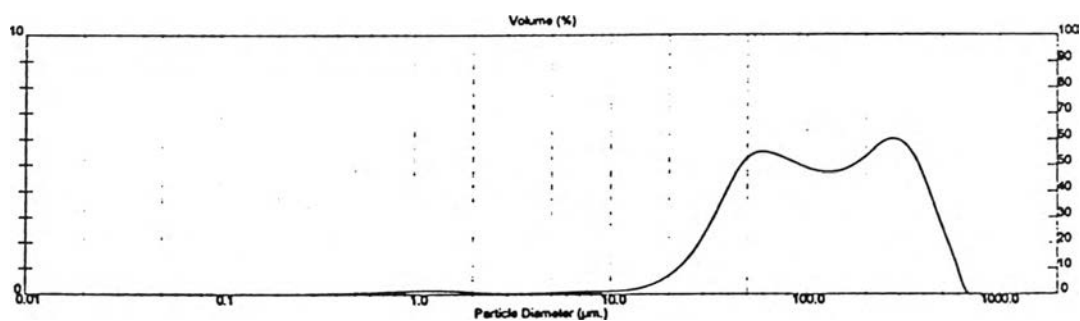


Figure 23 (continued)

APPENDIX D

DATA OF MINOCYCLINE HYDROCHLORIDE RELEASED
FROM MICROCAPSULES

Table 27 The percent release of minocycline hydrochloride from minocycline hydrochloride microcapsules prepared from poly (L-lactide) with 1:5 core to wall ratio in isotonic borate buffer pH 7.5 ± 0.1 (n=6)

Time(hours)	%Release 1	%Release 2	%Release 3	%Release 4	%Release 5	%Release 6	Mean	SD
0.5	3.63	3.48	3.78	3.57	3.51	3.69	3.61	0.11
1.0	4.66	4.50	4.88	4.52	4.54	4.70	4.63	0.15
1.5	4.81	4.75	5.05	4.81	4.76	4.85	4.84	0.11
2.0	5.05	4.95	5.21	5.03	4.98	5.09	5.05	0.09
3.0	5.23	5.14	5.38	5.25	5.12	5.27	5.23	0.09
4.0	5.53	5.52	5.69	5.60	5.42	5.57	5.56	0.09
5.0	5.66	5.60	5.85	5.68	5.55	5.64	5.66	0.10
6.0	5.71	5.66	5.87	5.74	5.63	5.67	5.71	0.09
7.0	5.78	5.71	5.96	5.82	5.70	5.53	5.75	0.14
9.0	6.01	5.90	6.23	5.98	5.84	6.01	6.00	0.13
11.0	6.27	6.16	6.41	6.30	6.08	6.32	6.26	0.12
13.0	6.45	6.46	6.62	6.46	6.29	6.52	6.47	0.11
16.0	6.66	6.61	6.88	6.69	6.54	6.77	6.69	0.12
19.0	6.77	6.78	7.00	6.87	6.65	6.85	6.82	0.12

Table 27 (continued)

Time(hours)	%Release 1	%Release 2	%Release 3	%Release 4	%Release 5	%Release 6	Mean	SD
22.0	6.97	6.97	7.16	7.08	6.88	7.01	7.01	0.10
26.0	7.07	7.13	7.29	7.19	7.03	7.17	7.15	0.09
30.0	7.27	7.41	7.47	7.32	7.20	7.36	7.34	0.10
34.0	7.50	7.56	7.66	7.45	7.45	7.55	7.53	0.08
41.0	7.70	7.68	7.88	7.62	7.72	7.71	7.72	0.09
48.0	8.01	7.94	8.17	8.00	7.93	7.95	8.00	0.09

Table 28 The percent release of minocycline hydrochloride from minocycline hydrochloride microcapsules prepared from poly (DL-lactide) with 1:5 core to wall ratio in isotonic borate buffer pH 7.5 ± 0.1 (n=6)

Time(hours)	%Release 1	%Release 2	%Release 3	%Release 4	%Release 5	%Release 6	Mean	SD
0.5	3.17	3.05	3.08	3.20	2.93	3.08	3.09	0.10
1.0	4.09	3.93	3.88	4.12	3.69	3.85	3.93	0.16
1.5	4.12	4.02	3.95	4.31	3.79	3.94	4.02	0.18
2.0	4.21	4.22	4.15	4.53	3.90	4.09	4.18	0.21
3.0	4.41	4.45	4.38	4.82	4.11	4.30	4.41	0.23
4.0	4.55	4.50	4.42	4.94	4.18	4.38	4.50	0.25
5.0	4.63	4.56	4.63	5.08	4.25	4.41	4.59	0.28
6.0	4.65	4.60	4.81	5.11	4.27	4.48	4.65	0.29
7.0	4.71	4.61	4.90	5.20	4.33	4.50	4.71	0.31
9.0	4.94	4.86	5.16	5.31	4.50	4.62	4.90	0.31
11.0	5.11	5.07	5.31	5.52	4.66	4.80	5.08	0.32
13.0	5.48	5.44	5.61	5.84	4.99	5.21	5.43	0.30
16.0	5.72	5.68	5.83	5.97	5.31	5.45	5.66	0.24
19.0	5.85	5.75	5.87	6.07	5.59	5.55	5.78	0.19

Table 28 (continued)

Time(hours)	%Release 1	%Release 2	%Release 3	%Release 4	%Release 5	%Release 6	Mean	SD
22.0	6.08	5.88	6.02	6.25	5.85	5.69	5.96	0.20
26.0	6.44	6.27	6.36	6.62	6.18	5.84	6.29	0.27
30.0	6.85	6.73	6.84	6.95	6.46	6.27	6.68	0.26
34.0	7.00	6.85	7.06	7.01	6.67	6.49	6.85	0.23
41.0	7.29	7.16	7.42	7.26	7.04	6.67	7.14	0.26
48.0	7.63	7.48	7.75	7.47	7.37	6.92	7.44	0.29

Table 29 The percent release of minocycline hydrochloride from minocycline hydrochloride microcapsules prepared from poly (DL-lactide-co-glycolide) 75:25 with 1:5 core to wall ratio in isotonic borate buffer pH 7.5 ± 0.1 (n=6)

Time(hours)	%Release 1	%Release 2	%Release 3	%Release 4	%Release 5	%Release 6	Mean	SD
0.5	5.55	5.49	5.61	5.46	5.31	5.64	5.51	0.12
1.0	6.57	6.52	6.62	6.43	6.33	6.68	6.53	0.13
1.5	6.75	6.65	6.79	6.63	6.49	6.87	6.70	0.13
2.0	6.91	6.80	6.98	6.83	6.62	7.00	6.86	0.14
3.0	7.00	6.91	7.04	6.95	6.75	7.04	6.95	0.11
4.0	7.26	7.06	7.23	7.19	7.03	7.32	7.18	0.11
5.0	7.35	7.15	7.28	7.27	7.15	7.42	7.27	0.11
6.0	7.57	7.35	7.43	7.49	7.35	7.65	7.47	0.12
7.0	7.74	7.52	7.56	7.67	7.55	7.85	7.65	0.13
9.0	7.84	7.64	7.61	7.79	7.68	7.95	7.75	0.13
11.0	7.85	7.69	7.62	7.84	7.70	8.00	7.78	0.14
13.0	8.06	7.94	7.87	8.09	7.91	8.28	8.03	0.15
16.0	8.27	8.19	8.14	8.16	8.06	8.50	8.22	0.15
19.0	8.43	8.29	8.29	8.31	8.23	8.69	8.37	0.17

Table 29 (continued)

Time(hours)	%Release 1	%Release 2	%Release 3	%Release 4	%Release 5	%Release 6	Mean	SD
22.0	8.55	8.43	8.49	8.44	8.39	8.85	8.53	0.17
26.0	8.70	8.61	8.57	8.61	8.58	9.03	8.68	0.18
30.0	8.94	8.89	8.82	8.89	8.83	9.31	8.95	0.18
34.0	9.21	9.14	9.12	9.12	9.18	9.62	9.23	0.19
41.0	9.50	9.43	9.49	9.52	9.44	9.89	9.55	0.17
48.0	9.75	9.64	9.66	9.76	9.64	10.10	9.76	0.18

Table 30 The percent release of minocycline hydrochloride from minocycline hydrochloride microcapsules prepared from poly (DL-lactide-co-glycolide) 50:50 with 1:5 core to wall ratio in isotonic borate buffer pH 7.5 ± 0.1 (n=6)

Time(hours)	%Release 1	%Release 2	%Release 3	%Release 4	%Release 5	%Release 6	Mean	SD
0.5	2.41	2.59	2.07	2.29	2.50	2.71	2.43	0.23
1.0	3.04	3.24	2.65	2.92	3.19	3.39	3.07	0.26
1.5	3.26	3.48	2.85	3.15	3.54	3.67	3.33	0.30
2.0	3.41	3.64	2.99	3.32	3.77	3.89	3.50	0.33
3.0	3.52	3.72	3.04	3.41	3.81	3.99	3.58	0.34
4.0	3.61	3.73	3.11	3.46	3.90	4.00	3.64	0.32
5.0	3.74	3.83	3.22	3.59	3.99	4.06	3.74	0.31
6.0	3.93	4.03	3.39	3.71	4.21	4.29	3.93	0.33
7.0	4.18	4.23	3.67	3.98	4.36	4.47	4.15	0.29
9.0	4.41	4.48	3.98	4.31	4.54	4.56	4.38	0.22
11.0	4.64	4.75	4.19	4.54	4.82	4.79	4.62	0.24
13.0	4.72	4.80	4.32	4.63	4.94	4.90	4.72	0.23
16.0	4.97	5.05	4.62	4.83	5.11	5.19	4.96	0.21
19.0	5.12	5.20	4.81	4.94	5.24	5.38	5.12	0.21

Table 30 (continued)

Time(hours)	%Release 1	%Release 2	%Release 3	%Release 4	%Release 5	%Release 6	Mean	SD
22.0	5.39	5.50	5.08	5.14	5.53	5.66	5.38	0.23
26.0	5.45	5.59	5.18	5.24	5.63	5.72	5.47	0.22
30.0	5.66	5.75	5.34	5.44	5.79	5.93	5.65	0.22
34.0	5.99	5.88	5.65	5.79	6.14	6.29	5.96	0.23
41.0	6.36	6.27	5.99	6.14	6.58	6.70	6.34	0.27
48.0	6.56	6.43	6.18	6.30	6.79	6.97	6.54	0.30

APPENDIX E

DATA OF STATISTICS FOR COMPARISON
OF CORE ENTRAPMENT

Table 31 Test of split-plot design on the effect of stabilising agent concentration on percent entrapment of minocycline hydrochloride microcapsules prepared with 1:5 core to wall ratio

Source of Variation	Degree of Freedom	Sum of Square	Mean Square	F _{cal}	F _{table}
Main plots:					
Polymer type	3	25.01	8.34	3.36	6.99
SCMC concentration	3	65.72	21.91	8.83*	6.99
Main plot error	9	22.34	2.48		
Sub plots:					
% entrapment	2	0	0	0	5.61
% entrapment* polymer type	6	0.01	0.0017	4.25*	3.67
Sub plot error	4	0.01	0.0004		

* = Significant when computed using alpha 0.05

Table 32 Test of randomized block design on the effect of stabilising agent concentration on percent entrapment of minocycline hydrochloride microcapsules prepared from poly (L-lactide) with 1:5 core to wall ratio

Source of Variation	Degree of Freedom	Sum of Square	Mean Square	F _{cal}	F _{table}
Total	11	25.1234	-	-	-
%entrapment	2	0.0018	0.0009	1.8	5.14
SCMC conc.	3	25.1186	8.3729	16,745.80*	4.76
Error	6	0.003	0.0005		

* = Significant when computed using alpha 0.05

Table 33 Test of John Tukey's Honestly significant difference on the effect of stabilising agent concentration on percent entrapment of minocycline hydrochloride microcapsules prepared from poly (L-lactide) with 1:5 core to wall ratio

SCMC conc.	Mean	Pairwise Difference		
		0.05% (2.87)	0.10% (1.45)	0.20% (1.46)
0%	4.99	2.12*	3.54*	3.53*
0.05%	2.87	-	1.42*	1.41*
0.10%	1.45	-	-	0.01
0.20%	1.46	-	-	-

* = Significant when computed using alpha 0.05

Table 34 Test of randomized block design on the effect of stabilising agent concentration on percent entrapment of minocycline hydrochloride microcapsules prepared from poly (DL-lactide) with 1:5 core to wall ratio

Source of Variation	Degree of Freedom	Sum of Square	Mean Square	F _{cal}	F _{table}
Total	11	26.0754	-	-	-
%entrapment	2	0.0006	0.0003	1	5.14
SCMC conc.	3	26.0730	8.6910	28,970*	4.76
Error	6	0.0018	0.0003		

* = Significant when computed using alpha 0.05



Table 35 Test of John Tukey's Honestly significant difference on the effect of stabilising agent concentration on percent entrapment of minocycline hydrochloride microcapsules prepared from poly (DL-lactide) with 1:5 core to wall ratio

SCMC conc.	Mean	Pairwise Difference		
		0.05% (0.54)	0.10% (0.91)	0.20% (0.90)
0%	4.17	3.63*	3.26*	3.27*
0.05%	0.54	-	0.37*	0.36*
0.10%	0.91	-	-	0.01
0.20%	0.90	-	-	-

* = Significant when computed using alpha 0.05

Table 36 Test of randomized block design on the effect of stabilising agent concentration on percent entrapment of minocycline hydrochloride microcapsules prepared from poly (DL-lactide-co-glycolide) 75:25 with 1:5 core to wall ratio

Source of Variation	Degree of Freedom	Sum of Square	Mean Square	F _{cal}	F _{table}
Total	11	27.4307	-	-	-
%entrapment	2	0.0009	0.00035	0.3608	5.14
SCMC conc.	3	27.4242	9.1414	9,424.1237*	4.76
Error	6	0.0058	0.00097		

* = Significant when computed using alpha 0.05

Table 37 Test of John Tukey's Honestly significant difference on the effect of stabilising agent concentration on percent entrapment of minocycline hydrochloride microcapsules prepared from poly (DL-lactide-co-glycolide) 75:25 with 1:5 core to wall ratio

SCMC conc.	Mean	Pairwise Difference		
		0.05% (2.28)	0.10% (4.68)	0.20% (1.37)
0%	4.87	2.59*	0.19*	3.50*
0.05%	2.28	-	2.40*	0.91*
0.10%	4.68	-	-	3.31*
0.20%	1.37	-	-	-

* = Significant when computed using alpha 0.05

Table 38 Test of randomized block design on the effect of stabilising agent concentration on percent entrapment of minocycline hydrochloride microcapsules prepared from poly (DL-lactide-co-glycolide) 50:50 with 1:5 core to wall ratio

Source of Variation	Degree of Freedom	Sum of Square	Mean Square	F _{cal}	F _{table}
Total	11	9.4497	-	-	-
%entrapment	2	0.0024	0.0012	1.5	5.14
SCMC conc.	3	9.4425	3.1475	3,934.3750*	4.76
Error	6	0.0048	0.0008		

* = Significant when computed using alpha 0.05

Table 39 Test of John Tukey's Honestly significant difference on the effect of stabilising agent concentration on percent entrapment of minocycline hydrochloride microcapsules prepared from poly (DL-lactide-co-glycolide) 50:50 with 1:5 core to wall ratio

SCMC conc.	Mean	Pairwise Difference		
		0.05% (1.77)	0.10% (0.85)	0.20% (0.81)
0%	2.99	1.22 [*]	2.14 [*]	2.18 [*]
0.05%	1.77	-	0.92 [*]	0.96 [*]
0.10%	0.85	-	-	0.04
0.20%	0.81	-	-	-

^{*} = Significant when computed using alpha 0.05

Table 40 Test of randomized block design on the effect of polymers on percent entrapment of minocycline hydrochloride microcapsules prepared by using 0% SCMC with 1:5 core to wall ratio

Source of Variation	Degree of Freedom	Sum of Square	Mean Square	F _{cal}	F _{table}
Total	11	7.5873	-	-	-
%entrapment	2	0.0018	0.0009	0.6923	5.14
Type of polymer	3	7.5777	2.5259	1,943*	4.76
Error	6	0.0078	0.0013		

* = Significant when computed using alpha 0.05

Table 41 Test of John Tukey's Honestly significant difference on the effect of polymers on percent entrapment of minocycline hydrochloride microcapsules prepared by using 0% SCMC with 1:5 core to wall ratio

Type of polymer	Mean	Pairwise Difference		
		DL-PLA (4.17)	PLGA 75:25 (2.99)	PLGA 50:50 (4.87)
L-PLA	4.99	0.82*	2.00*	0.12*
DL-PLA	4.17	-	1.18*	0.70*
PLGA 75:25	2.99	-	-	1.88*
PLGA 50:50	4.87	-	-	-

* = Significant when computed using alpha 0.05

Table 42 Test of randomized block design on the effect of core to wall ratio on percent entrapment of minocycline hydrochloride microcapsules prepared from poly (L-lactide)

Source of Variation	Degree of Freedom	Sum of Square	Mean Square	F _{cal}	F _{table}
Total	5	36.6575	-	-	-
%entrapment	2	0.0006	0.0003	0.2857	19.00
C:W	1	36.6548	36.6548	34,909.333*	18.51
Error	2	0.0021	0.00105		

* = Significant when computed using alpha 0.05

Table 43 Test of randomized block design on the effect of core to wall ratio on percent entrapment of minocycline hydrochloride microcapsules prepared from poly (DL-lactide)

Source of Variation	Degree of Freedom	Sum of Square	Mean Square	F _{cal}	F _{table}
Total	5	25.5877	-	-	-
%entrapment	2	0.0012	0.0006	1	19.00
C:W	1	25.5853	25.5853	42,642.1667*	18.51
Error	2	0.0012	0.0006		

* = Significant when computed using alpha 0.05

Table 44 Test of randomized block design on the effect of core to wall ratio on percent entrapment of minocycline hydrochloride microcapsules prepared from poly (DL-lactide-co-glycolide) 75:25

Source of Variation	Degree of Freedom	Sum of Square	Mean Square	F _{cal}	F _{table}
Total	5	34.7065	-	-	-
%entrapment	2	0.0012	0.0006	1	19.00
C:W	1	34.7041	34.7141	57,840.1667*	18.51
Error	2	0.0012	0.0006		

* = Significant when computed using alpha 0.05

Table 45 Test of randomized block design on the effect of core to wall ratio on percent entrapment of minocycline hydrochloride microcapsules prepared from poly (DL-lactide-co-glycolide) 50:50

Source of Variation	Degree of Freedom	Sum of Square	Mean Square	F _{cal}	F _{table}
Total	5	12.8797	-	-	-
%entrapment	2	0.0012	0.0006	1	19.00
C:W	1	12.8773	12.8773	21,462.1667*	18.51
Error	2	0.0012	0.0006		

* = Significant when computed using alpha 0.05



VITA

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