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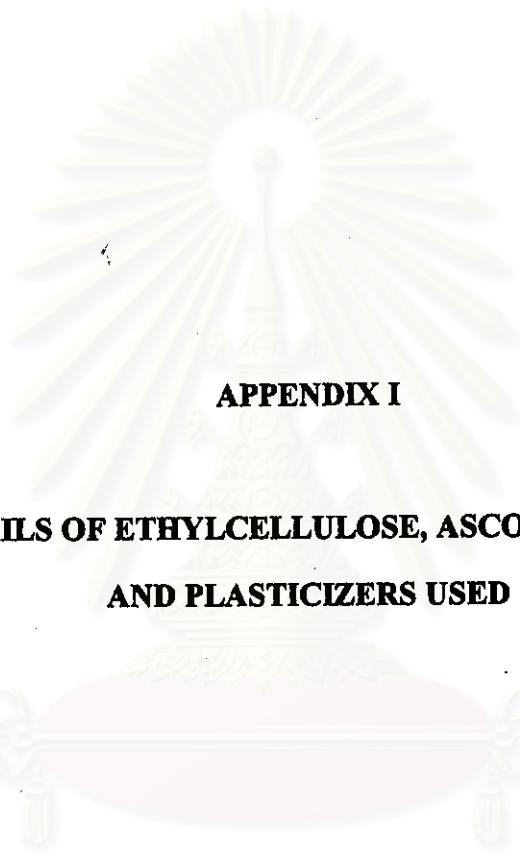
APPENDIX I

DETAILS OF ETHYLCELLULOSE, ASCORBIC ACID,
AND PLASTICIZERS USED

Ethylcellulose

Ethylcellulose is an ethyl ether of cellulose. It is a long-chain polymer consisting of anhydroglucose units joined together by acetal linkages. Each anhydroglucose unit has three replaceable hydroxyl groups which are substituted to the extent of 2.25-2.60 ethoxyl groups (OC_2H_5) per unit, equivalent to an ethoxyl content of 44-51% (Wade and Weller, 1994c; Rekhi and Jambhekar, 1995).
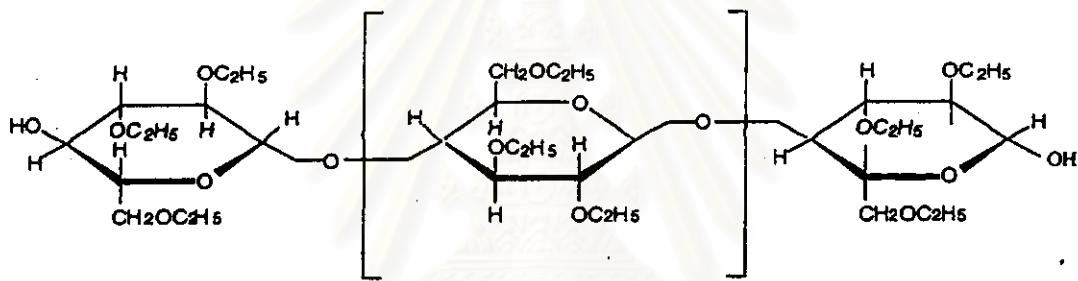
Figure 53. Structural formula of ethylcellulose.

Ethylcellulose resins are a tasteless, odorless, nonionic charge, free-flowing, white to light-tan granular powders. The differences in physical properties of the ethylcellulose products result largely from variation in the degree of etherification.

Properties of Ethylcellulose (Wade and Weller, 1994c)

Density (bulk) : 0.4 g/cm.

Glass transition temperature : 130-133°C.

Hygroscopicity : Ethylcellulose absorbs very little water at high relative humidities or during immersion; any absorbed water evaporates readily.

Solubility : Ethylcellulose is practically insoluble in hexanes, glycerin, propylene glycol and water. Ethylcellulose that contains less than 46.5% of ethoxyl groups is freely soluble in chloroform, methyl acetate, tetrahydrofuran, and in mixtures of aromatic hydrocarbons with ethanol (95%). Ethylcellulose that contains not less than 46.5% of ethoxyl groups is freely soluble in chloroform, ethanol (95%), ethyl acetate, methanol, and toluene.

Specific gravity : 1.12-1.15.

Viscosity : Various grades of ethylcellulose are commercially available which differ in their ethoxyl content and degree of polymerization. They may be used to produce 5%w/v solutions in organic solvents with viscosities of 6-110 mPas (cP). The viscosity of solutions increases with an increase in concentration of ethylcellulose and as the length of the polymer molecule increases.

Stability : Ethylcellulose is a stable, slightly hygroscopic material. It is chemically resistant to alkalis, both dilute and concentrated, and to salt solutions, although it is more sensitive to acidic materials than cellulose esters. Ethylcellulose is subject to oxidative degradation in the presence of sunlight or UV light at elevated temperatures but light, visible or UV, has no discoloring action on ethylcellulose.

Incompatibility : Ethylcellulose is incompatible with paraffin wax and microcrystalline wax.

L-Ascorbic Acid
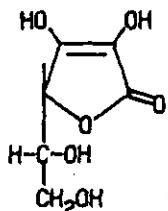
Empirical formula $C_6H_8O_6$

MW 176.12

Figure 54. Structural formula of L-ascorbic acid.

Ascorbic acid is an enolic form of 3-oxo-L-gulofuranolactone. It is white or slight yellow, nonhygroscopic, odorless or almost odorless, pleasant sharp acidic taste crystals or powder (Al-Meshal and Hassan, 1982; Connors et al.,1986; Wade and Weller, 1994a). It may be prepared synthetically or obtained by extraction from various vegetable sources.

Properties of L-Ascorbic Acid (Al-Meshal and Hassan, 1982; Connors et al., 1986; Wade and Weller, 1994a)

Acidity/alkalinity : pH = 2.1-2.6 (5%w/v aqueous solution).

Density (bulk) : 0.7-0.9 g/cm³ for crystalline material; 0.5-0.7 g/cm³ for powder.

Density (particle) : 1.65 g/cm³.

Density (tapped) : 1.0-1.2 g/cm³ for crystalline material; 0.9-1.1 g/cm³ for powder.

Dissociation constant : pK_{a1} = 4.17; pK_{a2} = 11.57.

Melting point : 190-191°C with decomposition.

Solubility : At 20°C; 1 g dissolves in 3.5 ml of water, 25 ml of alcohol (95%), 50 ml of absolute alcohol, 100 ml of glycerol, and 20 ml of propylene glycol.

Practically insoluble in ether, chloroform, benzene and light petroleum.

Incompatibility :   L-ascorbic acid is incompatible with alkalis, heavy metal ions, especially copper, iron, zinc, and manganese, oxidizing agents, methenamine, phenylephrine hydrochloride, pyrilamine maleate, salicylamide, sodium nitrite, sodium salicylate, and theobromine salicylate (Botha, Lotter, and Preez, 1987).

L-Ascorbic acid has many important functions (Ovesen, 1984; Block et al., 1991). Ascorbic acid is essential for the formation of collagen and intercellular material, and hence for the development of cartilage, bone, and teeth, and for the healing of wounds. For its antioxidant properties, it can reduce ferrous iron to ferric iron with the promotion of nonheme iron absorption. It is necessary for the prevention and cure of the deficiency disease scurvy. In addition, its antioxidant properties may be important in the prevention of cancer, heart disease, age-related eye disease, and other conditions. However, the connection between ascorbic acid and these processes remain to be established. There was little convincing evidence to support the claims of clinically important efficacy of ascorbic acid in the prophylaxis and therapy of the common cold (Dykes and Meier, 1975). Ascorbic acid is also used as an antioxidant in aqueous pharmaceutical formulations at a concentration of 0.01-0.1%w/v. It is also widely used in foods as an antioxidant (Wade and Weller, 1994a).

Stability of L-Ascorbic Acid

In an aqueous solution, the degradation of ascorbic acid occurs under both aerobic and anaerobic conditions (Connors et al., 1986). The pH-rate profiles for both aerobic and anaerobic degradations show maxima around pH 4 (near pK_1). Maximum stability occurs near pH 3 and pH 6.

Under aerobic conditions, ascorbic acid is easily oxidized (reversibly) to give dehydroascorbic acid. The oxidation rate is dependent on pH and oxygen concentration and is catalyzed by light and metal ions, especially by Cu^{2+} and Fe^{3+}. The dehydroascorbic acid can undergo further hydrolysis to give the irreversible degradation products, 2,3-diketogulonic acid, which then oxidizes to threonic acid and oxalic acid as shown in figure 55(a). Under anaerobic conditions, it undergoes dehydration and hydrolysis to give furfural and carbon dioxide as shown in figure 55(b). The dehydration reaction is faster in acidic than in basic media due to hydrogen ion catalysis.

Ascorbic acid in solid dosage forms is stable provided that moisture content is controlled. Stability tests showed that commercial tablets of ascorbic acid maintained claimed levels for five years at room temperature and a relative humidity of 55 to 65% (Rubin et al., 1976). Degradation of ascorbic acid in tablets as a function of initial moisture, other tablet excipients, and relative humidity and temperature of storage conditions (Asker and Harris, 1990).

Ascorbic acid, crystals or fine powder, is fairly stable to air if it is protected from humidity, but it darkens slowly on exposure to air and light. In the absence of oxygen and other oxidizing agents it is also heat stable. On prolonged storage, a slight yellow discoloration may occur which, however, does not affect the biological activity but if it hydrolyses to diketogulonic acid, the activity will be lost (Vanderveen, E. and Vanderveen, J.E., 1995).

Investigations into the oxidation of ascorbic acid and efforts that have been made to improve its storage stability, e.g., exclusion of air/oxygen, adjustment of pH, reduced metal ion contamination, and avoidance of light, have been reviewed by

(a) under aerobic conditions.

(b) under anaerobic conditions.
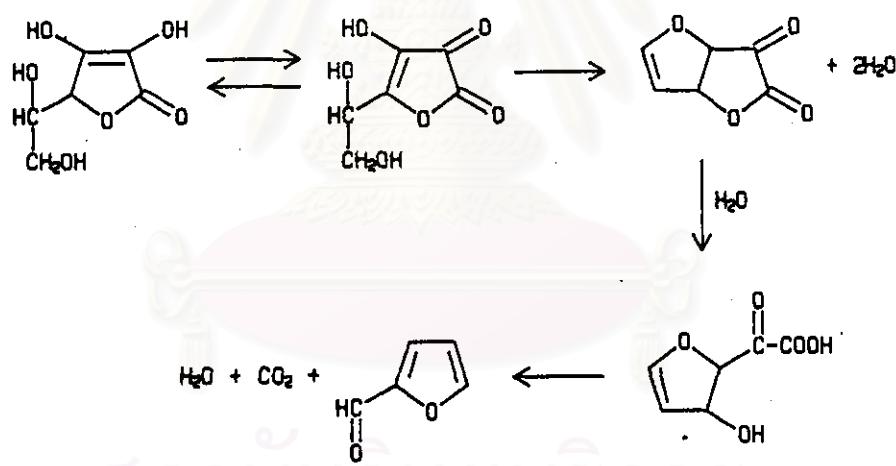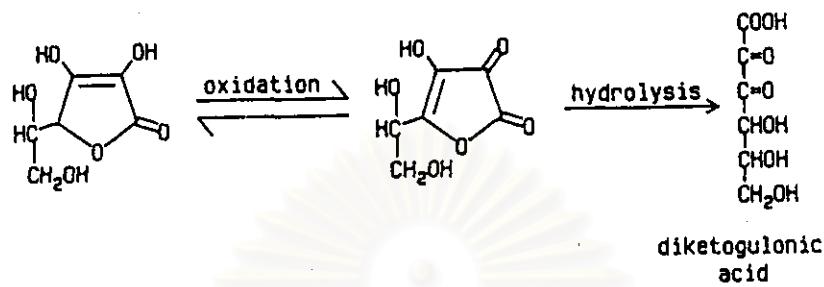
Figure 55. Steps of degradation of ascorbic acid in an aqueous solution.

Hajratwala (1985). Additives such as antioxidants, chelating agents and surfactants have been used. Solvents other than water (e.g., propylene glycol) may also be utilized to stabilize ascorbic acid. Increasing concentrations of sodium chloride in solution is associated with a lower concentration of dissolved oxygen which can improve stability of ascorbic acid. Improvement by use of disodium edetate results from the chelation of the heavy metal ions which cause decomposition of ascorbic acid. There are optimal concentrations of the chelating agent dependent upon the amounts of heavy metal ions present.

Dibutyl Sebacate

$C_4H_9OCO(CH_2)_8COOC_4H_9$

Empirical formula $C_{18}H_{34}O_4$
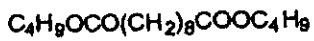
MW 314.47

Figure 56. Structural formula of dibutyl sebacate.

Dibutyl sebacate consists of the esters of n-butanol and saturated dibasic acids, principally sebacic acid. It is a clear, colorless, oily liquid with a bland to slight butyl odor. It is used in oral pharmaceutical formulations as a plasticizer for film coatings on tablets, beads and granules, at concentrations of 10-30% by weight of polymer. It is also used in cosmetics and foods as a synthetic flavor and flavor adjuvant and is generally regarded as nontoxic and nonirritant material.

Properties of Dibutyl Sebacate (Wade and Weller, 1994b)

Acid value : 0.02.

Boiling point : 344-349°C.

Melting point : -10°C.

Specific gravity : 0.937 at 20°C.

Solubility : Dibutyl sebacate is soluble in ethanol, propan-2-ol and mineral oil, and practically insoluble in water.

Stability : Dibutyl sebacate is stable. It is not reactive with water and hazardous polymerization does not occur. Dibutyl sebacate should be stored in a well-closed container, in a cool and dry place.

Incompatibility : Dibutyl sebacate is incompatible with strong oxidizing agents.

Triacetin

$$CH_2OCOCH_3$$
$$H—C—OCOCH_3$$
$$CH_2OCOCH_3$$
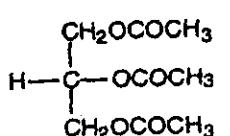
Empirical formula $C_9H_{14}O_6$

MW 218.21

Figure 57. Structural formula of triacetin.

Triacetin or glycerol triacetate is a colorless, viscous liquid with a slightly fatty odor. It is used as a hydrophilic plasticizer in both aqueous and solvent-based polymeric coating of capsules, tablets, beads, and granules; typical concentrations used are 10-35 %w/w. It is also reported to possess fungistatic properties due to the liberation of acetic acid and has been used as a 25%w/w cream or ointment in the treatment of superficial fungal conditions. In addition, it is used in cosmetics, perfumery and foods as a solvent and as a fixative in the formulation of perfumes and flavors.

Properties of Triacetin (Wade and Weller, 1994d)

Boiling point : 258°C.

Melting point : -78°C.

Density : 1.16 g/cm^3 at 25°C.

Solubility : Triacetin is miscible with chloroform, ethanol (95%), and ether. It is soluble 1 in 14 of water.

Stability : Triacetin is stable and should be stored in a well-closed, nonmetallic container, in a cool and dry place.

Incompatibilities : Triacetin is incompatible with metals and may react with oxidizing agents.

Triethyl citrate

$$CH_2COOC_2H_5$$
$$HO-C-COOC_2H_5$$
$$CH_2COOC_2H_5$$
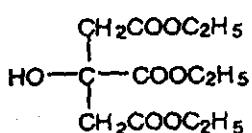
Empirical formula $C_{12}H_{20}O_7$

MW 276.29

Figure 58. Structural formula of triethyl citrate.

Triethyl citrate is a bitter tasting, odorless, practically colorless, oily liquid. It is used as plasticizers for aqueous based coatings in oral sustained release or enteric coated capsules and tablet formulations. It is also used in food products as a sequestrant and in cosmetics as a deodorizing agent. It is generally regarded as nontoxic and nonirritant materials.

Properties of Triethyl Citrate (Wade and Weller, 1994e)

Boiling point : 288°C.

Specific gravity : 1.135-1.139.

Solubility : Soluble 1 in 125 of peanut oil, 1 in 15 of water. Miscible with ethanol (95%) and ether.

Stability : Triethyl citrate is stable if stored in a well-closed container in a cool and dry place.

Incompatibilities : Triethyl citrate can react with oxidizing materials and strong alkalis.
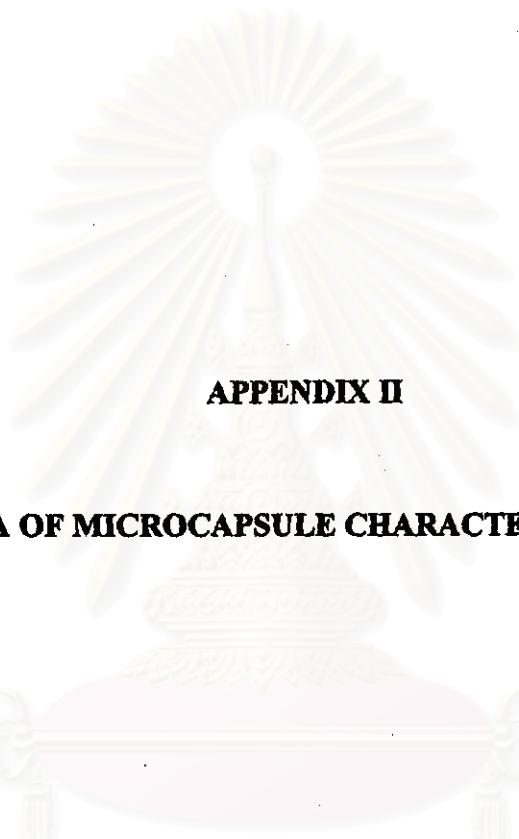
APPENDIX II

DATA OF MICROCAPSULE CHARACTERIZATION

Table 19. Cumulative percent frequency undersize of ascorbic acid microcapsules prepared by temperature induced coacervation technique.

size (µm)	Cumulative % frequency undersize of formulation no.							
	2	3	4	5	6	7	8	9
400	0.00	0.76	0.92	0.23	0.00	0.30	0.56	0.83
600	9.22	21.52	8.90	4.57	6.98	7.14	13.37	10.19
800	33.41	68.10	32.21	24.43	31.67	26.49	42.06	43.53
1000	59.22	90.63	65.64	55.71	59.60	52.68	68.80	72.45
1200	81.57	96.71	87.12	79.91	81.80	77.68	84.96	88.71
1400	92.40	99.49	94.48	92.01	94.26	91.07	95.82	96.14
1600	98.39	100.00	98.47	97.49	98.25	96.73	99.44	99.45
1800	99.31	100.00	99.69	99.32	99.25	99.11	99.72	99.72
2000	99.77	100.00	100.00	99.77	99.75	100.00	100.00	100.00
2200	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
mean (µm) (SD)	953.46 (288.82)	745.57 (198.85)	925.15 (265.76)	993.15 (274.80)	956.86 (275.97)	997.62 (294.01)	890.53 (274.87)	877.96 (256.54)

Table 20. Cumulative percent frequency undersize of ascorbic acid microcapsules prepared by solvent evaporation technique.

size (μm)	Cumulative % frequency undersize of formulation no.										
	10	11	12	13	14	15	16	17	18	19	20
300	0.27	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
600	11.35	9.25	1.76	0.00	0.00	0.94	0.00	6.24	0.00	0.38	0.00
900	30.00	47.69	25.92	2.40	0.32	3.20	7.33	42.08	0.34	1.73	0.59
1200	51.35	68.21	74.08	55.52	20.96	8.29	66.72	75.20	3.02	9.04	9.88
1500	71.35	88.73	95.84	95.20	73.60	19.21	91.30	93.92	8.05	22.69	32.21
1800	86.22	97.11	98.40	98.24	90.08	44.07	95.27	98.40	18.46	43.27	54.94
2100	93.24	99.13	99.68	98.88	92.64	62.52	98.78	99.84	36.91	62.69	73.52
2400	97.30	100.00	100.00	99.68	96.32	80.04	100.00	100.00	58.72	78.85	86.96
2700	98.65	100.00	100.00	99.84	98.24	88.70	100.00	100.00	77.18	89.23	93.48
3000	99.19	100.00	100.00	100.00	98.88	94.73	100.00	100.00	87.25	95.96	97.23
3300	99.46	100.00	100.00	100.00	99.84	97.36	100.00	100.00	93.29	98.65	97.83
3600	99.46	100.00	100.00	100.00	100.00	98.68	100.00	100.00	97.99	98.85	99.41
3900	99.73	100.00	100.00	100.00	100.00	100.00	100.00	100.00	99.66	99.62	100.00
4200	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
mean (μm) (SD)	1237.30 (561.53)	1019.65 (380.66)	1062.96 (267.96)	1200.72 (227.31)	1437.36 (382.62)	1956.78 (602.79)	1171.83 (272.60)	1002.96 (315.61)	2307.38 (597.49)	1947.12 (589.06)	1811.86 (543.54)

Table 21.   Yield of ascorbic acid microcapsules prepared by temperature induced coacervation technique.

Formulation no.	Variables		Observed Wt (g)	Theoretical Wt (g)	Yield (%)
	Core to wall ratio	Plasticizer (% w/w)			
1	1:2	-	*	*	*
2	1:1	-	5.7000	6	95.00
3	3:2	-	7.1802	7.5	95.74
4	1:1	20% TA	5.7211	6	95.35
5	1:1	30% TA	5.7407	6	95.68
6	1:1	20% TEC	5.7281	6	95.47
7	1:1	30% TEC	5.7223	6	95.37
8	1:1	20% DBS	5.6935	6	94.89
9	1:1	30% DBS	5.6949	6	94.92

* The microcapsules could not be obtained

Table 22. Yield of ascorbic acid microcapsules prepared by solvent evaporation technique.

Formulation no.	Variables			Observed Wt (g)	Theoretical Wt (g)	Yield (%)
	%EC conc.	Core to wall ratio	% Surfactant			
10	4	1:2	1.0%Span80	4.4379	4.8	92.46
11	5	1:2	1.0%Span80	5.8829	6	98.05
12	6	1:2	1.0%Span80	7.3296	7.2	101.80
13	6	1:1	1.0%Span80	9.3721	9.6	97.63
14	6	3:2	1.0%Span80	11.2954	12	94.13
15	6	1:2	-	6.3505	7.2	88.20
16	6	1:2	0.5%Span80	6.8728	7.2	95.46
17	6	1:2	1.5%Span80	7.4676	7.2	103.72
18	6	1:2	0.5%Tween80	7.0726	7.2	98.23
19	6	1:2	1.0%Tween80	8.0280	7.2	111.50
20	6	1:2	1.5%Tween80	9.0788	7.2	126.09

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Table 23. Drug content and drug entrapment of ascorbic acid microcapsules prepared by the temperature induced coacervation technique (n = 4).

Formulation no.	Observed content (%w/w)				Mean (SD)	Theoretical content (%w/w)	Entrapment (SD) (%)
	1	2	3	4			
2	50.98	50.49	51.17	50.49	50.78 (0.35)	50	101.57 (0.70)
3	60.12	60.09	61.05	60.36	60.40 (0.45)	60	100.67 (0.75)
4	49.21	49.65	51.50	51.08	50.36 (1.10)	50	100.72 (2.20)
5	50.29	50.58	50.94	50.44	50.56 (0.28)	50	101.12 (0.56)
6	52.80	51.02	52.15	52.54	52.13 (0.79)	50	104.25 (1.58)
7	50.42	50.92	52.24	51.63	51.30 (0.80)	50	102.61 (1.60)
8	51.43	50.94	49.77	51.12	50.82 (0.73)	50	101.63 (1.45)
9	51.82	51.92	52.01	52.00	51.94 (0.09)	50	103.87 (0.18)

Table 24. Drug content and drug entrapment of ascorbic acid microcapsules prepared by the solvent evaporation technique (n = 4).

Formulation no.	Observed content (%w/w)				Mean (SD)	Theoretical content (%w/w)	Entrapment (SD) (%)
	1	2	3	4			
10	21.92	23.58	26.50	26.60	24.65 (2.30)	33.33	73.96 (6.89)
11	22.25	30.20	25.95	25.77	26.04 (3.25)	33.33	78.14 (9.76)
12	26.31	27.32	29.93	30.66	28.56 (2.07)	33.33	85.67 (6.22)
13	44.30	45.85	44.05	43.75	44.49 (0.94)	50	88.98 (1.87)
14	54.04	55.34	54.11	54.64	54.53 (0.60)	60	90.89 (1.00)
15	31.41	31.03	31.15	31.15	31.19 (0.16)	33.33	93.56 (0.48)
16	31.53	29.98	33.54	29.65	31.18 (1.78)	33.33	93.53 (5.33)
17	27.79	25.69	25.86	25.24	26.15 (1.13)	33.33	78.44 (3.38)
18	29.00	28.11	27.20	26.64	27.74 (1.04)	33.33	83.22 (3.11)
19	19.62	19.82	21.98	20.74	20.54 (1.08)	33.33	61.63 (3.23)
20	17.80	19.01	17.79	18.96	18.39 (0.69)	33.33	55.18 (2.06)

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Table 25. The summary of the release rate constants[a] (K) of Higuchi equation plots and the correlation coefficients (r) at a selected time range (min) of the microcapsules prepared by temperature induced coacervation technique (n = 3).

Formulation no.	Time range (min)	% Released range	r	K (% min$^{-1/2}$)			Mean (SD)
				1	2	3	
2	5-30	6-72%	0.9997	20.13	20.85	20.38	20.45 (0.37)
3	5-30	9-82%	0.9997	23.10	22.82	21.78	22.57 (0.69)
4	5-30	6-73%	0.9989	20.63	21.02	21.18	20.94 (0.28)
5	5-30	6-71%	0.9994	20.45	20.45	19.62	20.17 (0.48)
6	5-30	5-69%	0.9961	19.94	20.75	19.57	20.09 (0.60)
7	5-30	5-66%	0.9961	20.40	18.38	18.28	19.02 (1.19)
8	5-30	4-58%	0.9969	17.21	16.35	16.29	16.62 (0.51)
9	5-30	3-50%	0.9942	14.11	14.35	14.29	14.25 (0.13)

[a] Determined by least squares method.

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Table 26. The summary of the release rate constants[a] (K) of Higuchi equation plots and the correlation coefficients (r) at a selected time range (min) (n = 3) of the microcapsules prepared by solvent evaporation technique.

Formulation no.	Time range (min)	% Released range	r	K (% min$^{-1/2}$)			Mean (SD)
				1	2	3	
10	5-20	17-45%	0.9774	13.25	13.12	13.49	13.29 (0.19)
11	5-30	22-73%	0.9816	15.22	15.68	16.03	15.64 (0.41)
12	5-45	11-65%	0.9998	12.25	12.54	11.25	12.01 (0.67)
13	5-20	17-50%	0.9910	14.74	14.92	14.41	14.69 (0.26)
14	5-20	19-57%	0.9939	16.06	16.29	17.00	16.45 (0.49)
15	5-60	7-52%	0.9961	8.31	7.97	7.72	8.00 (0.29)
16	5-45	10-50%	0.9955	9.30	9.33	8.15	8.93 (0.67)
17	5-30	17-69%	0.9957	16.00	15.40	16.27	15.89 (0.45)
18	5-20	13-42%	0.9931	13.79	13.37	11.98	13.05 (0.94)
19	10-180	17-64%	0.9996	4.39	4.56	4.69	4.55 (0.15)
20	10-180	15-58%	0.9995	4.20	4.33	4.17	4.23 (0.09)

[a] Determined by least squares method.

Table 27. Percent drug released from microcapsules prepared by temperature induced coacervation technique (formulation no. 2) (n = 3).

Time (min)	0	5	10	20	30	45	60	90	120	180	240	K
1	0	5.84	21.28	48.63	70.61	88.40	96.49	98.92	99.88	100.00	99.48	20.13
2	0	5.75	23.10	54.03	71.87	88.62	95.58	98.18	98.93	99.26	100.00	20.85
3	0	6.53	25.67	51.89	72.76	87.27	95.97	98.61	98.30	99.25	100.00	20.38
mean	0	6.04	23.35	51.52	71.75	88.10	96.01	98.57	99.04	99.50	99.83	20.45
SD	0	0.43	2.21	2.72	1.08	0.73	0.46	0.37	0.80	0.43	0.30	0.37

Table 28. Percent drug released from microcapsules prepared by temperature induced coacervation technique (formulation no. 3) (n = 3).

Time (min)	0	5	10	20	30	45	60	90	120	180	240	K
1	0	10.10	32.43	63.76	84.57	98.60	98.49	98.81	100.00	99.67	99.77	23.10
2	0	8.40	28.35	59.75	81.74	96.87	99.16	98.83	99.58	99.46	100.00	22.82
3	0	8.13	28.12	58.61	77.97	92.53	97.23	99.44	98.72	99.26	100.00	21.78
mean	0	8.88	29.63	60.71	81.43	96.00	98.29	99.03	99.44	99.46	99.92	22.57
SD	0	1.07	2.42	2.70	3.31	3.13	0.98	0.36	0.65	0.21	0.13	0.69

Table 29. Percent drug released from microcapsules prepared by temperature induced coacervation technique (formulation no. 4) (n = 3).

Time (min)	0	5	10	20	30	45	60	90	120	180	240	K
1	0	5.49	20.19	49.57	71.34	90.70	95.71	99.67	99.78	99.25	100.00	20.63
2	0	5.74	22.85	52.04	73.17	89.93	95.52	98.81	98.93	99.68	100.00	21.02
3	0	6.62	23.28	52.44	74.65	91.06	95.14	97.56	98.09	98.83	100.00	21.18
mean	0	5.95	22.11	51.35	73.05	90.56	95.46	98.68	98.93	99.25	100.00	20.94
SD	0	0.59	1.67	1.55	1.66	0.58	0.29	1.06	0.84	0.42	0.00	0.28

Table 30. Percent drug released from microcapsules prepared by temperature induced coacervation technique (formulation no. 5) (n = 3).

Time (min)	0	5	10	20	30	45	60	90	120	180	240	K
1	0	6.78	22.72	50.72	72.51	87.74	94.22	97.60	98.58	100.00	99.65	20.45
2	0	4.87	19.90	47.55	70.74	85.36	93.28	97.24	100.00	99.21	99.52	20.45
3	0	5.65	24.55	49.96	69.37	84.36	93.79	97.74	97.83	98.58	100.00	19.62
mean	0	5.77	22.39	49.41	70.87	85.82	93.76	97.53	98.80	99.26	99.72	20.17
SD	0	0.96	2.34	1.65	1.57	1.74	0.47	0.26	1.10	0.71	0.25	0.48

Table 31. Percent drug released from microcapsules prepared by temperature induced coacervation technique (formulation no. 6) (n = 3).

Time (min)	0	5	10	20	30	45	60	90	120	180	240	K
1	0	3.62	16.56	44.31	67.50	83.24	94.36	98.40	98.09	98.62	100.00	19.94
2	0	4.71	18.61	48.02	70.97	85.71	93.72	98.29	98.62	100.00	99.06	20.75
3	0	5.19	17.34	45.51	67.49	85.77	94.63	97.97	98.08	99.04	100.00	19.57
mean	0	4.51	17.50	45.95	68.65	84.91	94.24	98.22	98.26	99.22	99.69	20.09
SD	0	0.80	1.04	1.90	2.00	1.45	0.47	0.22	0.31	0.71	0.54	0.60

Table 32. Percent drug released from microcapsules prepared by temperature induced coacervation technique (formulation no. 7) (n = 3).

Time (min)	0	5	10	20	30	45	60	90	120	180	240	K
1	0	6.25	21.77	50.82	71.37	88.42	93.55	99.13	98.83	100.00	99.27	20.40
2	0	4.23	16.50	42.33	63.03	80.24	92.94	97.54	98.29	98.82	100.00	18.38
3	0	4.92	14.95	38.92	63.98	86.52	93.49	97.14	98.09	99.46	100.00	18.28
mean	0	5.13	17.74	44.02	66.13	85.06	93.33	97.94	98.40	99.43	99.76	19.02
SD	0	1.02	3.57	6.13	4.56	4.28	0.34	1.05	0.38	0.59	0.42	1.19

Table 33. Percent drug released from microcapsules prepared by temperature induced coacervation technique (formulation no. 8) (n = 3).

Time (min)	0	5	10	20	30	45	60	90	120	180	240	K
1	0	4.74	16.88	39.85	60.26	79.96	92.23	97.96	98.28	99.46	100.00	17.21
2	0	4.01	16.39	38.02	56.87	77.35	89.39	96.49	96.81	98.19	100.00	16.35
3	0	3.93	15.13	36.74	56.52	78.49	90.14	95.89	97.05	98.21	100.00	16.29
mean	0	4.22	16.14	38.20	57.88	78.60	90.59	96.78	97.38	98.62	100.00	16.62
SD	0	0.45	0.90	1.56	2.07	1.31	1.47	1.06	0.79	0.73	0.00	0.51

Table 34. Percent drug released from microcapsules prepared by temperature induced coacervation technique (formulation no. 9) (n = 3).

Time (min)	0	5	10	20	30	45	60	90	120	180	240	K
1	0	3.84	13.90	32.01	49.64	70.92	83.02	95.85	97.45	97.98	100.00	14.11
2	0	3.95	13.85	31.73	50.73	69.69	82.51	91.56	97.00	99.46	100.00	14.35
3	0	2.51	11.98	30.04	48.99	69.85	83.62	91.25	97.45	99.04	100.00	14.29
mean	0	3.43	13.24	31.26	49.79	70.16	83.05	92.89	97.30	98.83	100.00	14.25
SD	0	0.80	1.10	1.06	0.88	0.67	0.55	2.57	0.26	0.77	0.00	0.13

Table 35. Percent drug released from microcapsules prepared by solvent evaporation technique (formulation no. 10) (n = 3).

Time (min)	0	5	10	20	30	45	60	90	120	180	240	300	360	420	480	K
1	0	16.77	34.76	47.01	51.38	55.03	56.63	59.88	62.03	63.07	65.09	66.98	68.60	69.66	71.15	13.25
2	0	19.57	38.56	49.65	53.92	57.84	59.59	62.42	63.74	65.19	67.64	68.69	69.20	71.93	70.92	13.12
3	0	15.60	33.18	46.32	51.88	56.52	59.20	63.19	65.44	65.48	67.10	68.58	68.78	69.94	69.83	13.49
mean	0	17.31	35.50	47.66	52.39	56.46	58.47	61.83	63.74	64.58	66.61	68.08	68.86	70.51	70.64	13.29
SD	0	2.04	2.77	1.76	1.35	1.41	1.61	1.73	1.71	1.32	1.34	0.96	0.31	1.24	0.70	0.19

Table 36. Percent drug released from microcapsules prepared by solvent evaporation technique (formulation no. 11) (n = 3).

Time (min)	0	5	10	20	30	45	60	90	120	180	240	300	360	420	480	K
1	0	21.46	43.38	62.56	71.26	77.02	80.54	82.73	83.32	85.79	86.11	87.11	87.17	87.63	88.63	15.22
2	0	23.90	46.24	65.74	75.30	81.12	82.86	86.31	86.65	87.11	88.36	88.18	89.04	88.47	89.06	15.68
3	0	21.56	44.00	66.15	73.25	79.88	82.28	85.68	86.52	86.86	88.31	88.91	90.24	90.72	91.20	16.03
mean	0	22.31	44.54	64.82	73.27	79.34	81.90	84.91	85.49	86.59	87.60	88.07	88.82	88.94	89.63	15.64
SD	0	1.38	1.51	1.97	2.02	2.10	1.21	1.91	1.89	0.70	1.28	0.90	1.55	1.60	1.37	0.41

Table 37. Percent drug released from microcapsules prepared by solvent evaporation technique (formulation no. 12) (n = 3).

Time (min)	0	5	10	20	30	45	60	90	120	180	240	300	360	420	480	K
1	0	9.98	22.21	38.94	50.20	64.94	72.91	82.14	86.52	89.44	90.66	91.15	92.38	93.36	94.59	12.25
2	0	12.69	25.30	41.85	53.25	69.32	77.57	86.12	89.21	91.45	91.69	92.31	93.30	93.80	93.80	12.54
3	0	11.46	22.24	37.47	48.32	61.78	69.92	78.72	83.85	87.77	89.49	91.08	91.94	92.18	93.29	11.25
mean	0	11.38	23.25	39.42	50.59	65.35	73.47	82.33	86.53	89.55	90.61	91.51	92.54	93.11	93.89	12.01
SD	0	1.36	1.77	2.23	2.49	3.78	3.86	3.70	2.68	1.84	1.10	0.69	0.70	0.84	0.66	0.67

Table 38. Percent drug released from microcapsules prepared by solvent evaporation technique (formulation no. 13) (n = 3).

Time (min)	0	5	10	20	30	45	60	90	120	180	240	300	360	420	480	K
1	0	18.39	36.04	51.78	59.88	67.17	71.82	77.13	80.44	85.29	88.02	90.13	91.99	94.00	93.23	14.74
2	0	16.04	33.64	49.82	59.63	67.20	72.42	78.72	82.82	87.20	89.11	90.77	91.26	93.84	91.58	14.92
3	0	18.38	36.13	51.08	59.24	66.52	71.66	78.21	81.15	85.11	86.95	90.56	91.68	92.54	93.16	14.41
mean	0	17.60	35.27	50.89	59.58	66.96	71.97	78.02	81.47	85.87	88.03	90.49	91.64	93.46	92.66	14.69
SD	0	1.35	1.41	0.99	0.32	0.39	0.40	0.81	1.22	1.16	1.08	0.33	0.37	0.80	0.93	0.26

Table 39. Percent drug released from microcapsules prepared by solvent evaporation technique (formulation no. 14) (n = 3).

Time (min)	0	5	10	20	30	45	60	90	120	180	240	300	360	420	480	K
1	0	19.98	37.80	56.21	66.43	74.95	81.53	87.29	91.59	93.94	95.44	97.43	97.21	98.47	96.89	16.06
2	0	22.28	41.18	59.12	70.35	79.08	84.90	91.78	94.85	96.65	97.17	97.94	98.34	98.60	98.22	16.29
3	0	17.50	37.69	56.00	65.85	76.17	81.70	88.24	91.84	94.45	96.21	97.59	98.11	98.51	97.66	17.00
mean	0	19.92	38.89	57.11	67.54	76.73	82.71	89.11	92.76	95.01	96.27	97.66	97.89	98.53	97.59	16.45
SD	0	2.39	1.98	1.75	2.45	2.12	1.90	2.37	1.81	1.44	0.87	0.26	0.60	0.07	0.67	0.49

Table 40. Percent drug released from microcapsules prepared by solvent evaporation technique (formulation no. 15) (n = 3).

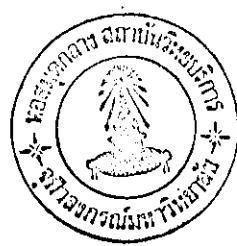| Time (min)	0	5	10	20	30	45	60	90	120	180	240	300	360	420	480	K
1	0	6.94	17.17	29.08	37.20	45.77	53.33	61.95	68.20	75.69	79.72	82.81	84.70	86.48	86.46	8.31
2	0	7.36	17.15	29.15	37.19	45.04	51.57	60.89	66.78	75.60	78.56	80.60	83.12	84.73	84.95	7.97
3	0	7.56	16.52	28.09	35.35	43.57	50.45	59.33	65.61	72.62	77.03	79.97	82.69	84.28	85.88	7.72
mean	0	7.29	16.95	28.77	36.58	44.79	51.79	60.72	66.87	74.64	78.44	81.13	83.50	85.16	85.76	8.00
SD	0	0.32	0.37	0.59	1.06	1.12	1.45	1.32	1.30	1.75	1.35	1.49	1.06	1.17	0.76	0.29

Table 41. Percent drug released from microcapsules prepared by solvent evaporation technique (formulation no. 16) (n = 3).

Time (min)	0	5	10	20	30	45	60	90	120	180	240	300	360	420	480	K
1	0	10.09	21.57	34.46	42.46	52.11	57.71	66.39	71.10	77.89	80.73	82.49	84.63	86.41	87.47	9.30
2	0	9.79	21.35	33.04	44.94	50.76	56.85	66.73	72.06	79.00	80.64	83.38	84.55	85.85	86.79	9.33
3	0	10.53	20.29	30.82	38.65	47.33	53.18	62.04	66.93	74.00	77.76	81.53	82.09	84.92	85.86	8.15
mean	0	10.14	21.07	32.77	42.02	50.07	55.91	65.06	70.03	76.96	79.71	82.47	83.76	85.73	86.71	8.93
SD	0	0.38	0.68	1.84	3.17	2.47	2.41	2.61	2.73	2.62	1.69	0.92	1.44	0.75	0.81	0.67

Table 42. Percent drug released from microcapsules prepared by solvent evaporation technique (formulation no. 17) (n = 3).

Time (min)	0	5	10	20	30	45	60	90	120	180	240	300	360	420	480	K
1	0	19.37	37.89	58.02	71.64	82.08	86.32	89.86	91.20	92.43	91.95	93.30	93.30	93.55	93.31	16.00
2	0	17.54	35.88	55.57	67.74	78.39	83.31	87.38	89.88	91.38	90.28	89.75	90.23	90.13	89.15	15.40
3	0	15.18	35.06	55.35	68.43	79.48	83.39	87.07	90.28	90.89	91.13	91.00	91.36	92.09	91.95	16.27
mean	0	17.36	36.28	56.32	69.27	79.98	84.34	88.10	90.45	91.57	91.12	91.35	91.63	91.92	91.47	15.89
SD	0	2.10	1.46	1.48	2.08	1.89	1.72	1.53	0.68	0.79	0.83	1.80	1.55	1.72	2.12	0.45

Table 43. Percent drug released from microcapsules prepared by solvent evaporation technique (formulation no. 18) (n = 3).

Time (min)	0	5	10	20	30	45	60	90	120	180	240	300	360	420	480	K
1	0	12.24	28.87	43.48	50.92	58.49	62.73	71.76	78.85	85.84	88.35	89.65	90.68	92.66	93.70	13.79
2	0	10.64	26.10	40.86	46.91	54.23	59.20	68.65	73.39	82.13	85.75	87.94	89.86	93.52	93.36	13.37
3	0	16.07	29.71	43.14	49.81	58.50	63.62	71.47	78.38	84.51	87.68	89.65	90.67	92.38	93.68	11.98
mean	0	12.98	28.23	42.50	49.22	57.08	61.85	70.63	76.88	84.16	87.26	89.08	90.40	92.85	93.58	13.05
SD	0	2.79	1.89	1.43	2.07	2.46	2.34	1.72	3.02	1.88	1.35	0.99	0.47	0.60	0.19	0.94

Table 44. Percent drug released from microcapsules prepared by solvent evaporation technique (formulation no. 19) (n = 3).

Time (min)	0	5	10	20	30	45	60	90	120	180	240	300	360	420	480	K
1	0	10.53	19.03	25.10	29.77	34.88	39.34	48.55	53.46	63.74	69.16	74.30	78.82	83.85	86.04	4.39
2	0	6.59	15.50	22.32	26.41	30.81	34.39	42.48	51.24	63.22	67.89	73.86	78.74	81.57	86.33	4.56
3	0	6.10	17.01	25.29	30.09	37.91	40.92	49.29	55.11	66.15	70.97	76.80	80.02	83.10	87.18	4.69
mean	0	7.74	17.18	24.24	28.76	34.53	38.22	46.77	53.27	64.37	69.34	74.99	79.20	82.84	86.52	4.55
SD	0	2.42	1.77	1.66	2.04	3.56	3.41	3.74	1.94	1.56	1.55	1.59	0.72	1.16	0.59	0.15

Table 45. Percent drug released from microcapsules prepared by solvent evaporation technique (formulation no. 20) (n = 3).

Time (min)	0	5	10	20	30	45	60	90	120	180	240	300	360	420	480	K
1	0	8.70	14.63	20.26	24.11	28.59	32.70	40.71	46.74	58.00	66.54	73.55	79.51	83.69	85.71	4.20
2	0	7.84	14.73	20.70	24.79	29.46	33.68	41.83	49.15	58.96	67.27	74.21	79.64	83.81	85.29	4.33
3	0	8.53	14.35	19.98	23.70	28.32	32.22	39.91	46.75	57.30	65.46	73.42	78.48	82.70	86.09	4.17
mean	0	8.36	14.57	20.31	24.20	28.79	32.87	40.82	47.54	58.09	66.42	73.73	79.21	83.40	85.70	4.23
SD	0	0.45	0.20	0.36	0.55	0.60	0.74	0.96	1.39	0.83	0.91	0.42	0.64	0.61	0.40	0.09

Table 46. Percent drug remaining of pure ascorbic acid powders stored at 40°C and 75% R.H. (n = 4).

Time (days)	0	6	13	21	34	48	69	91	112	154
1	100.00	99.30	99.67	97.97	99.01	94.06	95.20	96.80	91.71	93.45
2	100.00	100.34	101.96	97.34	98.40	95.72	95.83	96.45	94.72	92.72
3	100.00	101.56	96.39	96.79	96.40	95.13	95.75	94.94	92.52	90.57
4	100.00	98.50	101.79	97.91	97.82	96.32	94.34	95.49	95.68	90.69
Mean	100.00	99.93	99.95	97.50	97.91	95.31	95.28	95.92	93.66	91.86
SD	0.00	1.32	2.59	0.55	1.12	0.96	0.69	0.86	1.85	1.45

Table 47. Percent drug remaining of formulation no. 9 microcapsules stored at 40°C and 75% R.H. (n = 4).

Time (days)	0	6	13	21	34	48	69	91	112	154
1	51.82	49.55	50.59	51.81	49.88	52.59	51.95	49.82	50.13	50.06
2	51.92	51.27	50.79	51.42	50.78	50.87	51.26	50.53	50.46	49.53
3	50.69	50.95	49.66	51.41	49.51	49.68	50.51	50.68	50.57	49.55
4	50.99	49.68	53.03	52.97	49.21	51.19	51.16	51.03	51.62	50.17
Mean	51.35	50.36	51.02	51.90	49.85	51.08	51.22	50.52	50.70	49.83
SD	0.61	0.87	1.43	0.74	0.68	1.20	0.59	0.51	0.64	0.34
%	100.00	98.07	99.34	101.07	97.06	99.47	99.74	98.37	98.72	97.03
SD	0.00	1.70	2.78	1.43	1.33	2.33	1.15	0.99	1.25	0.65

Table 48. Percent drug remaining of formulation no. 16 microcapsules stored at 40°C and 75% R.H. (n = 4).

Time (days)	0	6	13	21	34	48	69	91	112	154
1	26.62	28.69	30.26	28.78	25.90	26.12	26.01	28.17	24.36	26.62
2	25.17	27.53	28.05	29.30	29.26	25.59	27.28	26.16	26.88	27.07
3	28.52	26.84	30.51	29.88	29.25	25.40	26.21	25.89	25.33	25.32
4	30.25	26.47	28.20	26.01	27.12	25.73	27.48	26.20	25.85	26.28
Mean	27.64	27.38	29.26	28.49	27.88	25.71	26.75	26.61	25.61	26.32
SD	2.22	0.98	1.31	1.71	1.66	0.30	0.74	1.05	1.05	0.74
%	100.00	99.07	105.84	103.08	100.88	93.02	96.76	96.26	92.64	95.23
SD	0.00	3.53	4.74	6.20	6.01	1.10	2.69	3.81	3.80	2.69

Table 49. Percent drug remaining of formulation no. 20 microcapsules stored at 40°C and 75% R.H. (n = 4).

Time (days)	0	6	13	21	34	48	69	91	112	154
1	15.43	16.51	15.47	15.41	16.62	14.13	12.91	11.17	9.30	8.56
2	16.09	15.44	14.71	14.10	13.41	13.40	11.52	11.15	9.08	9.13
3	16.86	15.90	15.68	13.21	15.88	14.01	11.58	10.00	10.02	7.72
4	16.36	16.26	16.60	15.36	14.38	12.94	11.60	9.97	10.16	8.05
Mean	16.19	16.03	15.62	14.52	15.07	13.62	11.90	10.57	9.64	8.37
SD	0.60	0.46	0.78	1.06	1.45	0.55	0.67	0.68	0.53	0.62
%	100.00	99.03	96.48	89.71	93.13	84.15	73.54	65.32	59.56	51.68
SD	0.00	2.87	4.81	6.57	8.95	3.43	4.16	4.19	3.28	3.81
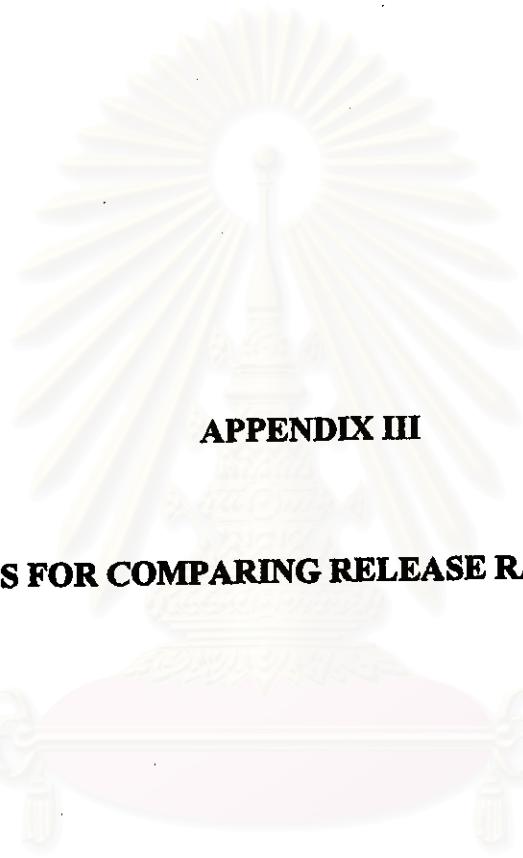
APPENDIX III

STATISTICS FOR COMPARING RELEASE RATE CONSTANTS

Analysis of Covariance (ANCOVA) was used for comparing the drug release rate constants of the formulation studied and performed by using SPSS® 7.5 program. A null hypothesis, i.e. there is no difference in the slopes or release rate constants compared, was tested against an alternative hypothesis, i.e. at least one pair of the slopes is not equal (a significance level, $\alpha = 0.05$).

The assumption of equality of regression slopes calculated from the plots of percent drug released and square root of time can be tested by fitting a model containing main effects of formulation no. (N) and time ($min^{1/2}$, T), as well as the N*T interaction. The interaction term provides the test of the null hypothesis of equal slopes as presented in tables 50-53 and 54-57 for the formulations prepared by the temperature induced coacervation technique and the solvent evaporation technique, respectively.

Table 50. Tests of the effect of the studied core to wall ratio on the drug release rate from the microcapsules prepared by the temperature induced coacervation technique.

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Noncent. Parameter	Observed Power[a]
Corrected Model	5766.705[b]	3	1922.235	2040.747	.000	6122.240	1.000
Intercept	1257.253	1	1257.253	1334.767	.000	1334.767	1.000
N1	.235	1	.235	.250	.643	.250	.068
T1	5655.111	1	5655.111	6003.766	.000	6003.766	1.000
N1 * T1	13.664	1	13.664	14.506	.019	14.506	.809
Error	3.768	4	.942				
Total	19657.42	8					
Corrected Total	5770.473	7					

a. Computed using alpha = .05

b. R Squared = .999 (Adjusted R Squared = .999)

Table 51. Tests of the effect of the used amount of triacetin on the drug release rate from the microcapsules prepared by the temperature induced coacervation technique.

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Noncent. Parameter	Observed Power[a]
Corrected Model	7727.766[b]	5	1545.553	1014.135	.000	5070.673	1.000
Intercept	1893.623	1	1893.623	1242.525	.000	1242.525	1.000
N2	.951	2	.475	.312	.743	.624	.081
T2	7723.070	1	7723.070	5067.592	.000	5067.592	1.000
N2 * T2	1.863	2	.931	.611	.573	1.222	.112
Error	9.144	6	1.524				
Total	24879.97	12					
Corrected Total	7736.910	11					

a. Computed using alpha = .05

b. R Squared = .999 (Adjusted R Squared = .998)

Table 52. Tests of the effect of the used amount of triethyl citrate on the drug release rate from the microcapsules prepared by the temperature induced coacervation technique.

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Noncent. Parameter	Observed Power[a]
Corrected Model	7290.099[b]	5	1458.020	242.880	.000	1214.400	1.000
Intercept	1897.571	1	1897.571	316.101	.000	316.101	1.000
N3	2.182	2	1.091	.182	.838	.364	.068
T3	7228.684	1	7228.684	1204.169	.000	1204.169	1.000
N3 * T3	6.730	2	3.365	.561	.598	1.121	.106
Error	36.018	6	6.003				
Total	22186.85	12					
Corrected Total	7326.117	11					

a. Computed using alpha = .05

b. R Squared = .995 (Adjusted R Squared = .991)

Table 53. Tests of the effect of the used amount of dibutyl sebacate on the drug release rate from the microcapsules prepared by the temperature induced coacervation technique.

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Noncent. Parameter	Observed Power[a]
Corrected Model	5876.618[b]	5	1175.324	278.517	.000	1392.583	1.000
Intercept	1389.352	1	1389.352	329.235	.000	329.235	1.000
N4	19.083	2	9.542	2.261	.185	4.522	.298
T4	5367.016	1	5367.016	1271.822	.000	1271.822	1.000
N4 * T4	119.541	2	59.770	14.164	.005	28.328	.957
Error	25.320	6	4.220				
Total	17115.01	12					
Corrected Total	5901.938	11					

a. Computed using alpha = .05

b. R Squared = .996 (Adjusted R Squared = .992)

From table 50, the interaction term (N1*T1) shows rejection of the equal slopes assumption (P = 0.019). Therefore, there is a statistical difference between drug release rate from the microcapsules with core to wall ratio of 1:1 and 3:2, prepared by the temperature induced coacervation technique. The interaction terms (N2*T2 and N3*T3) presented in tables 51 and 52, respectively, show that triacetin and triethyl citrate do not significantly affect the drug release rate from the microcapsules (P = 0.573 and 0.598, respectively). The interaction term, N4*T4, shown in table 53 indicates that there are statistically significant difference among the drug release rates from the microcapsules prepared by the temperature induced coacervation technique with various dibutyl sebacate amounts (P = 0.005).

Table 54. Tests of the effect of the ethylcellulose concentration on the drug release rate from the microcapsules prepared by the solvent evaporation technique.

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Noncent. Parameter	Observed Power[a]
Corrected Model	4405.300[b]	5	881.060	66.124	.000	330.622	1.000
Intercept	128.645	1	128.645	9.655	.021	9.655	.736
N1	9.682	2	4.841	.363	.710	.727	.086
T1	2620.127	1	2620.127	196.643	.000	196.643	1.000
N1 * T1	54.288	2	27.144	2.037	.211	4.074	.272
Error	79.946	6	13.324				
Total	24937.01	12					
Corrected Total	4485.245	11					

a. Computed using alpha = .05

b. R Squared = .982 (Adjusted R Squared = .967)

Table 55. Tests of the effect of the core to wall ratio on the drug release rate from the microcapsules prepared by the solvent evaporation technique.

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Noncent. Parameter	Observed Power[a]
Corrected Model	3091.147[b]	5	618.229	155.221	.000	776.105	1.000
Intercept	179.456	1	179.456	45.057	.001	45.057	.999
N2	.348	2	.174	.044	.958	.087	.054
T2	2135.551	1	2135.551	536.180	.000	536.180	1.000
N2 * T2	50.458	2	25.229	6.334	.043	12.669	.635
Error	19.914	5	3.983				
Total	18368.29	11					
Corrected Total	3111.061	10					

a. Computed using alpha = .05

b. R Squared = .994 (Adjusted R Squared = .987)

Table 56. Tests of the effect of the Span80 concentration on the drug release rate from the microcapsules prepared by the solvent evaporation technique.

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Noncent. Parameter	Observed Power[a]
Corrected Model	6385.403[b]	7	912.200	307.361	.000	2151.524	1.000
Intercept	311.428	1	311.428	104.934	.000	104.934	1.000
N3	27.735	3	9.245	3.115	.067	9.345	.574
T3	5482.504	1	5482.504	1847.298	.000	1847.298	1.000
N3 * T3	366.135	3	122.045	41.122	.000	123.367	1.000
Error	35.614	12	2.968				
Total	31729.78	20					
Corrected Total	6421.017	19					

a. Computed using alpha = .05

b. R Squared = .994 (Adjusted R Squared = .991)

Table 57. Tests of the effect of the Tween80 concentration on the drug release rate from the microcapsules prepared by the solvent evaporation technique.

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Noncent. Parameter	Observed Power[a]
Corrected Model	5376.882[b]	7	768.126	642.335	.000	4496.344	1.000
Intercept	49.633	1	49.633	41.505	.000	41.505	1.000
N4	117.473	3	39.158	32.745	.000	98.235	1.000
T4	1906.185	1	1906.185	1594.021	.000	1594.021	1.000
N4 * T4	426.693	3	142.231	118.939	.000	356.816	1.000
Error	20.329	17	1.196				
Total	33918.34	25					
Corrected Total	5397.211	24					

a. Computed using alpha = .05

b. R Squared = .996 (Adjusted R Squared = .995)

From table 54, the interaction term (N1*T1) shows that the drug release rates from the microcapsules prepared by the solvent evaporation technique with various ethylcellulose concentrations are not significantly different (P = 0.211). The interaction terms (N2*T2, N3*T3, and N4*T4) presented in tables 55-57 show that there are statistically significant difference among the drug release rates from the microcapsules prepared by the solvent evaporation technique with various core to wall ratios, Span80 concentrations, and Tween80 concentrations (P = 0.043, 0.000 and 0.000, respectively). At least one pair of the drug release rates from the microcaspules prepared with each of factor is significantly different.

VITA

Miss Dusadee Vanichtanunkul was born on 5th September 1972, in Bangkok, Thailand. She graduated the Bachelor of Science in Pharmacy with a second class honors in 1994 from the Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok, Thailand. Following Graduation, she received the University Development Committee (U.D.C.) scholarship to study the Master's Degree program in Pharmaceutical Sciences at Chulalongkorn University in 1995.