REFERENCES

Ahuja, S., and Ashman, S. 1990. Terbutaline sulphate. In K.Florey (ed.), Analytical profiles of drug substances, Vol.19, pp.602-625. New York : Academic Press.

Baert, L., and Remon, J.P. 1993. Influence of amount of granulation liquid on the drug release rate from pellets made by extrusion spheronization. Int. J. Pharm. 95 : 135-141.

Batailie, B., Ligarski, K., Jacob, M., Thomas, C., and Duru, C. 1993. Study of the influence of spheronization and drying conditions on the physico-mechanical properties of neutral spheroids containing Avicel PH101^{R} and lactose. Drug Dev. Ind. Pharm. 19 (6) : 653-671.

Bianchini, R., Bruni, G., Gazzaniga, A., and Vecchio, C. 1992. Influence of extrusion-spheronization processing on the physical properties of d-Indobufen pellets containing pH adjusters. Drug Dev. Ind. Pharm. 18(14) : 1485-1503.

_____.1993. d-Indobufen extended-release pellets prepared by coating with aqueous polymer dispersions. Drug Dev. Ind. Pharm. 19 (16) : 2021-2041.

Chariot, M., Frances, J., Lewis, G.A., Methieu, D., Phan Tan Luu,R., and Stevens, H.N.E. 1987. A factorial approach to process variables of extrusion-spheronization of wet powder masses. Drug Dev. Ind. Pharm. 13(9-11) : 1639-1649.

Chetty, D.J., and Dangor, C.M. 1994. The development of an oral controlled release pellets formulation of diethylpropion hydrochloride. Drug Dev. Ind. Pharm. 20 (6) : 993-1005.

Coupe, A.J., Davis, S.S., and Wilding, I.R. 1991. Variation in gastro-intestinal transit of pharmaceutical dosage forms in healthy subjects, Pharm. Res. 8(3):360-364.

Davis, S.S., Hardy, J.G., Taylor, M.J., Whalley, D.R., and Wilson, C.G. 1984. A comparative study of the gastrointestinal transit of a pellet and tablet formulation. Int. J. Pharm. 21: 167-177.

Doshi, H.A., and Shrivastava, R. 1993. Preparation of pellets: Extruding and spheronizing machines study. Indian J. Pharm. Sci. 55 (2) : 55-58.

Elbers, J.A.C., Bakkenes,H.W., and Fokkens, J.G. 1992. Effect of amount and composition of granulation liquid on mixing, extrusion and spheronization. Drug Dev. Ind. Pharm. 18 (5):501-517.

Funck, J.A.B., Schwartz, J.B., Reilly, W.T.,and Ghali, E.S. 1991. Binder effectiveness for beads with high drug levels. Drug Dev. Ind. Pharm. 17(9):1143-1156.

Ghali, E.S., Klinger, G.H., and Schwartz, J.B. 1989. Modified drug release from beads prepared with combinations of two grades of microcrystalline cellulose. Drug Dev. Ind. Pharm. 15 (9): 1455-1473.

Ghebre-Sellassie, I (ed.).1989. Pharmaceutical pelletization technology. pp.1-14. New York:Marcel Dekker INC.

Gilligan, C.A., and Li Wan Po, A. 1991. Factors affecting drug release from a pellet system coated with an aqueous colloidal dispersion. Int. J. Pharm 73 : 51-68.

Goskonda, S.R., and Upadrashta, S.M. 1993. Avicel RC-591/chitosan beads by extrusion-spheronization technology. Drug Dev. Ind. Pharm. 19 (8) : 915-927.

_____., and Hileman, G.A. 1994. Development of matrix controlled release beads by extrusion-spheronization technology using a statistical screening design. Drug Dev. Ind. Pharm. 20 (3) : 279-292.

Harris, M.R., and Ghebre-Sellassie, I. 1989. Formulation variables. In I.Ghebre-Sellassie (ed.), Pharmaceutical pelletization techonology. pp.217-239. New York : Marcel Dekker INC.

Hasznos, L., Langer, I.,and Gyarmathy, M. 1992. Some factors influencing pellet characteristics made by an extrusion-spheronization process part I : Effects on size characteristics and moisture content decrease of pellets. Drug Dev. Ind. Pharm. 18 (4) : 409-437.

Hicks, D.C., and Freese, H.J. 1989. Extrusion and spheronizing equipment. In I. Ghebre-Sellassie (ed.), Pharmaceutical pelletization techonology. pp.71-100. New York: Marcel Dekker INC.

Hileman, G.A., goskonda, S.R., Spalitto, A.J.,and Upadrashta, S.M. 1993. A factorial approach to high dose product development by an extrusion/spheronization process. Drug Dev. Ind. Pharm. 19 (4) : 483-491.

Hossain, M., and Ayres, J.W.1990. Variables that influence coat integrity in a laboratory spray coater. Pharm. Tech. October : 72,74,76-78,80,82.

Jalal, I.M., Malinowski, H.J., and Smith, W.E.1972. Tablet granulations composed of spherical-shape particles. J. Pharm. Sci. 61 (9) : 1466-1468.

Jones, D.M.1985. Factors to consider in fluid-bed processing. Pharm. Tech. 3 : 50-62.

Kavee Chanprapaph. 1990. The studies of durian rind extracts as the aqueous binders for tablet preparation. Master's Thesis, Department of Manufacturing Pharmacy, Graduate School, Chulalongkorn University.

Kleinebudde, P., and Lindner, H. 1993. Experiments with an instrumented twin-screw extruder using a single-step granulation/extrusion process. Int. J. Pharm. 94 : 49-58.

Ku,C.C., Joshi, Y.M., Bergum, J.S., and Jain, N.B.1993. Bead manufacture by extrusion/spheronization-a statistical design for process optimization. Drug Dev. Ind. Pharm. 19(13) : 1505 -1519.

Li, S.P., Metha, G.N., Buchler, J.D., Grim, W.M., and Harwood, R.J.1990. The effect of film-coating additives on the in-vitro dissolution release rate of ethylcellulose-coated theophylline granules. Pharm. Tech. March : 20,22-24.

Lovgren, K., and Lundberg, P.J. 1989. Determination of sphericity of pellets prepared by extrusion/spheronization and the impactof some process parameters. Drug Dev. Ind. Pharm. 15(14-16): 2375-2392.

Malinowski, H.J., and Smith, W.E. 1974. Effects of spheronization process variables on selected tablet properties. J. Pharm. Sci. 63 (2):285-288.

_____., 1975. Used of factorial design to evaluate granulations prepared by spheronization. J. Pharm. Sci 64(10) : 1688-1692.

Metha, A.M. 1988. Scale up considerations in the fluid-bed process for controlled release products. Pharm. Tech 2:46-52.

_____.1989. Evaluation and characterization of pellets. In I. Ghebre-Sellassie (ed.), Pharmaceutical pelletization technology. pp.241-265. New York : Marcel Dekker

Millili, G.P., and Schwartz, J.B. 1990. The strength of microcrystalline cellulose pellets : The effect of granulating with water/ethanol mixture. Drug Dev. Ind. Pharm. 16(18) : 1411-1426.

Munday., D.L., and Fassihi, A.R.1991. Changes in drug release rate : effect of stress storage conditions on film coated mini-tablets. Drug Dev. Ind. Pharm. 17 (15) : 2135-2143.

Newton, J.M., Chow, A.K., and Jeewa, K.B.1993. The effect of excipient source on spherical granules made by extrusion/spheronization. Pharm. Tech. March: 166,168,170,172,174.

O'Connor, R.E., and Schwartz, J.B.1985. Spheronization II: drug release from drug-diluent mixtures. Drug Dev. Ind. Pharm. 11(9&10) : 1837-1857.

O'Reilly, S., Wilson, C.G., and Hardy, J.G. 1987. The influence of food on the gastric emptying of multiparticulate dosage form Int. J. Pharm. 34 : 213-216.

Parikh, D.M. 1991. Air flow in batch fluid-bed processing. Pharm. Tech. March:100,102,104,106,108,110.

Porter, S.C., and Bruno, C.H. 1982. Coating of pharmaceutical solid dosage forms. In H.A.Lieberman, L. Lachman, and J.B. Schwartz (ed.), Pharmaceutical dosage forms : Tablet Vol.3. pp. 77-125. New York : Marcel Dekker INC.

Price, J.M.C., Davis, S.S., and Wilding, I.R. 1991. The effect of fiber on gastrointestinal transit times in vegetarians and omnivores. Int. J. Pharm. 76 : 123-131.

Ragnarsson, G., and Johanasson., M.O. 1988. Coated drug cores in multiple unit preparations influence of particle size. Drug Dev. Ind. Pharm. 14(15-17):2285-2297.

_____., Sandberg, A., and Lindstedt, B. 1992. In vitro release characteristics of a membrane-coated pellet formulation-influence of drug solubility and particle size. Int. J. Pharm. 79 : 223-232.

Remon, J.P., and Schwartz, J.B. 1987. Effect of raw materials and processing on the quality of granules prepared from micro-crystalline cellulose-lactose mixtures. Drug Dev. Ind. Pharm. 13(1) : 1-14.

Reynolds, A.D. 1970. A new technique for the production of spherical particles. Manu. Chem. & Aerosol News. June : 40-43.

Rockvillie. ed. 1990. USPXXII NFXVII. pp. 1578-1580. The United States of America : Mack printing company.

Ruiz, R., Sakr, A., and Sprockel, O.L. 1990. A study on the manufacture and in vitro dissolution of terbutaline sulphate microcapsules and their tablets. Drug Dev. Ind. Pharm. 16(11): 1829-1842.

Sakellariou, P., Rowe, R.C., and White, E.F.T. 1986. Polymer/polymer interaction in blends of ethylcellulose with both cellulose derivatives and polyethylene glycol 6000. Int. J. Pharm. 34 : 93-103.

Sheen, P.C., Sabol, P.J., Alcorn, G.J., and Feld, K.M. 1992. Aqueous film coating studied of sustained release nicotinic acid pellets : an in vitro evaluation. Drug Dev. Ind. Pharm. 18 (8) : 851-860.

Wesdyk, R., Joshi, Y.M., Jain, N.B., Morris, K., and Newman, A. 1990. The effect of size and mass on the film thickness of beads coated in fluidized bed equipment. Int. J. Pharm. 65 : 69-76.

Woodruff, C.W., and Nuessle, N.O. 1972. Effect of processing variables on particles obtained by extrusion-spheronization processing. J. Pharm. Sci. 61(5) : 787-790.

Yuen, K.H., Deshmukh, A.A., and Newton, J.M. 1993. Development and in vitro evaluation of a multiparticulate sustained release theophylline formulation. Drug Dev. Ind. Pharm. 19(8):855-874.

Zhang, G., Schwartz, J.B., and Schmaare, R.L. 1990. Effect of spheronization technique on drug released from uncoated beads. Drug Dev. Ind. Pharm. 16 (7): 1171-1184.

_____. 1991. Bead coating : I. Change in release kinetics (and machanism) due to coating levels. Pharm. Res. 8(3) : 331-335.

_____., Wigent, R.J., and Sugita, E.T. 1991. Bead coating:II. Effect of spheronization technique on drug release from coated spheres. Drug Dev. Ind. Pharm. 17 (6):817-830.

APPENDIX

Statistic

Analysis of variance of each physical property of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations, binder types and amount of water are presented in Tables 34-41. And comparison of each physical property of lactose-Avicel PH101^{R} pellets prepared with various spheronization timer, binder concentrations, binder types and amount of water are shown in Tables 42-49.

The code of each formulation consisted of three parts. The first part was binder type which E,L,A and M were Methocel E-15LV^{R}, Methocel A4M^{R} and HPC-M^{R}, respectively. The second part was binder concentration which 033,067,133,167,200 and 233 were 0.33% w/v,1.33% w/w, 1.67% w/w,2.00% w/w and 2.33% w/w, rspectively. And the thrid part was spheronization time which 05, 10 and 15 were 5 min, 10 min and 15 min, respectively. The code of factor which tested for analysis of variance was T.

Table 34 Analysis of variance of granule size of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types

Formulation	Variance Ratio	F-Ratio	Statistical Significance
E 133TT	81.79	9.55	S
E 167TT	6.43	9.55	NS
E 200TT	3.21	9.55	NS
L 133TT	10.40	9.55	S
L 167TT	239.03	9.55	S
L 200TT	10.25	9.55	S
A 033TT	3.52	9.55	NS
A 067TT	34.26	9.55	S
M 133TT	24.90	9.55	S
M 167TT	0.22	9.55	NS
M 200TT	10.04	9.55	S
M 233TT	28.01	9.55	S
E TTT05	130.71	9.55	S
E TTT10	190.45	9.55	S
E TTT15	153.39	9.55	S
L TTT05	5.32	9.55	NS
L TTT10	14.88	9.55	S
L TTT15	72.83	9.55	S

Table 34 Analysis of variance of granule size of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types (continued)

Formulation	Variance Ratio	F-Ratio	Statistical Significance
A TTT05	13.16	18.51	NS
A TTT10	587.93	18.51	S
A TTT15	62.90	18.51	S
M TTT05	9.30	6.59	S
M TTT10	2.02	6.59	NS
M TTT15	1.56	6.59	NS
T 13305	3.43	9.55	NS
T 13310	0.58	9.55	NS
T 13315	16.71	9.55	S
T 16705	88.05	9.55	S
T 16710	147.10	9.55	S
T 16715	268.60	9.55	S
T 20005	58.71	9.55	S
T 20010	12.96	9.55	S
T 20015	15.14	9.55	S

S = significant at $P < 0.05$

NS = not significant at $P > 0.05$

Table 35 Analysis of variance of percent sieve fraction on 14/20 mesh cut of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types

Formulation	Variance Ratio	F-Ratio	Statistical Significance
E 133TT	9.33	9.55	NS
E 167TT	6.08	9.55	NS
E 200TT	4.84	9.55	NS
L 133TT	2.08	9.55	NS
L 167TT	73.34	9.55	S
L 200TT	9.73	9.55	S
A 033TT	0.39	9.55	NS
A 067TT	7.80	9.55	NS
M 133TT	18.24	9.55	S
M 167TT	0.76	9.55	NS
M 200TT	0.57	9.55	NS
M 233TT	6.11	9.55	NS
E TTT05	121.94	9.55	S
E TTT10	42.50	9.55	S
E TTT15	120.77	9.55	S
L TTT05	5.22	9.55	NS
L TTT10	7.44	9.55	NS
L TTT15	154.78	9.55	S

Table 35 Analysis of variance of percent sieve fraction on 14/20 mesh cut of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types (continued)

Formulation	Variance Ratio	F-Ratio	Statistical Significance
A TTT05	1.49	18.51	NS
A TTT10	74.36	18.51	S
A TTT15	31.15	18.51	S
M TTT05	8.48	6.59	S
M TTT10	42.90	6.59	S
M TTT15	28.64	6.59	S
T 13305	18.25	9.55	S
T 13310	18.80	9.55	S
T 13315	8.73	9.55	NS
T 16705	314.65	9.55	S
T 16710	172.93	9.55	S
T 16715	63.88	9.55	S
T 20005	28.77	9.55	S
T 20010	61.79	9.55	S
T 20015	265.30	9.55	S

S = significant at $P < 0.05$

NS = not significant at $P > 0.05$

Table 36 Analysis of varianceof bulk density of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types

Formulation	Variance Ratio	F-Ratio	Statistical Significance
E 133TT	0.27	5.14	NS
E 167TT	8.23	5.14	S
E 200TT	1.47	5.14	NS
L 133TT	5.69	5.14	S
L 167TT	1.01	5.14	NS
L 200TT	10.95	5.14	S
A 033TT	1.81	5.14	NS
A 067TT	0.34	5.14	NS
M 133TT	3.31	5.14	NS
M 167TT	4.42	5.14	NS
M 200TT	10.24	5.14	S
M 233TT	23.33	5.14	S
E TTT05	30.48	5.14	S
E TTT10	2.73	5.14	NS
E TTT15	27.93	5.14	S
L TTT05	2.41	5.14	NS
L TTT10	14.23	5.14	S
L TTT15	5.04	5.14	NS

Table 36 Analysis of varianceof bulk density of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types (continued)

Formulation	Variance Ratio	F-Ratio	Statistical Significance
A TTT05	0.04	7.71	NS
A TTT10	0.15	7.71	NS
A TTT15	7.83	7.71	S
M TTT05	11.87	4.07	S
M TTT10	2.05	4.07	NS
M TTT15	2.77	4.07	NS
T 13305	6.37	5.14	S
T 13310	4.41	5.14	NS
T 13315	0.94	5.14	NS
T 16705	1.12	5.14	NS
T 16710	0.85	5.14	NS
T 16715	8.61	5.14	S
T 20005	201.00	5.14	S
T 20010	17.76	5.14	S
T 20015	111.52	5.14	S

S = significant at $P < 0.05$

NS = not significant at $P > 0.05$

Table 37 Analysis of variance of tapped density of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentration and binder types

Formulation	Variance Ratio	F-RAtio	Statistical Significance
E 133TT	0.73	5.14	NS
E 167TT	5.82	5.14	S
E 200TT	1.96	5.14	NS
L 133TT	0.88	5.14	NS
L 167TT	10.59	5.14	S
L 200TT	10.43	5.14	S
A 033TT	1.01	5.14	NS
A 067TT	0.16	5.14	NS
M 133TT	8.06	5.14	S
M 167TT	10.95	5.14	S
M 200TT	17.78	5.14	S
M 233TT	0.12	5.14	NS
E TTT05	7.01	5.14	S
E TTT10	26.07	5.14	S
E TTT15	24.42	5.14	S
L TTT05	6.98	5.14	S
L TTT10	34.66	5.14	S
L TTT15	12.62	5.14	S

Table 37 Analysis of variance of tapped density of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentration and binder types (continued)

Formulation	Variance Ratio	F-RAtio	Statistical Significance
A TTT05	1.20	7.71	NS
A TTT10	0.53	7.71	NS
A TTT15	0.08	7.71	NS
M TTT05	14.06	4.07	S
M TTT10	2.26	4.07	NS
M TTT15	1.53	4.07	NS
T 13305	13.51	5.14	S
T 13310	15.68	5.14	S
T 13315	0.96	5.14	NS
T 16705	7.76	5.14	S
T 16710	4.09	5.14	NS
T 16715	12.70	5.14	S
T 20005	21.61	5.14	S
T 20010	45.61	5.14	S
T 20015	165.00	5.14	S

S = significant at $P < 0.05$

NS = not significant at $P > 0.05$

Table 38 Analysis of variance of flow rate of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types

Formulation	Variance Ratio	F-Ratio	Statistical Significance
E 133TT	20.21	5.14	S
E 167TT	18.15	5.14	S
E 200TT	4.45	5.14	NS
L 133TT	53.57	5.14	S
L 167TT	3.59	5.14	NS
L 200TT	1.43	5.14	NS
A 033TT	1.48	5.14	NS
A 067TT	8.14	5.14	S
M 133TT	7.45	5.14	S
M 167TT	5.13	5.14	NS
M 200TT	7.94	5.14	S
M 233TT	0.83	5.14	NS
E TTT05	5.32	5.14	S
E TTT10	4.15	5.14	NS
E TTT15	3.11	5.14	NS
L TTT05	2.03	5.14	NS
L TTT10	74.94	5.14	S
L TTT15	5.36	5.14	S
A TTT05	0.07	7.71	NS

Table 38 Analysis of variance of flow rate of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types (continued)

Formulation	Variance Ratio	F-Ratio	Statistical Significance
A TTT10	107.04	7.71	S
A TTT15	15.77	7.71	S
M TTT05	0.30	4.07	NS
M TTT10	9.35	4.07	S
M TTT15	7.85	4.07	S
T 13305	4.28	5.14	NS
T 13310	12.38	5.14	S
T 13315	27.18	5.14	S
T 16705	5.77	5.14	S
T 16710	1.07	5.14	NS
T 16715	14.92	5.14	S
T 20005	0.05	5.14	NS
T 20010	15.52	5.14	S
T 20015	19.14	5.14	S

S = significant at $P < 0.05$

NS = not significant at $P > 0.05$

Table 39 Analysis of variance of angle of repose of lactose-Avicel PH101^{R} pellets prepared with various spheronization times,binder concentrations and binder types

Formulation	Variance Ratio	F-Ratio	Statistical Significance
E 133TT	25.06	5.14	S
E 167TT	3.72	5.14	NS
E 200TT	0.01	5.14	NS
L 133TT	1.04	5.14	NS
L 167TT	1.61	5.14	NS
L 200TT	10.86	5.14	S
A 033TT	12.20	5.14	S
A 067TT	12.47	5.14	S
M 133TT	3.65	5.14	NS
M 167TT	0.93	5.14	NS
M 200TT	15.13	5.14	S
M 233TT	3.02	5.14	NS
E TTT05	13.26	5.14	S
E TTT10	0.19	5.14	NS
E TTT15	5.07	5.14	NS
L TTT05	12.51	5.14	S
L TTT10	5.19	5.14	S
L TTT15	11.86	5.14	S

Table 39 Analysis of variance of angle of repose of lactose-Avicel PH101^{R} pellets prepared with various spheronization times,binder concentrations and binder types(continued)

Formulation	Variance Ratio	F-Ratio	Statistical Significance
A TTT05	1.82	7.71	NS
A TTT10	3.25	7.71	NS
A TTT15	18.96	7.71	S
M TTT05	2.85	4.07	NS
M TTT10	17.05	4.07	S
M TTT15	9.24	4.07	S
T 13305	18.19	5.14	S
T 13310	17.05	5.14	S
T 13315	26.93	5.14	S
T 16705	25.91	5.14	S
T 16710	20.47	5.14	S
T 16715	16.32	5.14	S
T 20005	0.94	5.14	NS
T 20010	12.72	5.14	S
T 20015	9.96	5.14	S

S = significant at $P < 0.05$

NS = not significant at $P > 0.05$

Table 40 Analysis of variance of percent friability of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types

Formulation	Variance Ratio	F-Ratio	Statistical Significance
E 133TT	0.02	9.55	NS
E 167TT	4.13	9.55	NS
E 200TT	0.51	9.55	NS
L 133TT	0.14	9.55	NS
L 167TT	5.41	9.55	NS
L 200TT	62.03	9.55	S
A 033TT	0.14	9.55	NS
A 067TT	0.09	9.55	NS
M 133TT	1.11	9.55	NS
M 167TT	4.53	9.55	NS
M 200TT	4.36	9.55	NS
M 233TT	3.32	9.55	NS
E TTT05	7.51	9.55	NS
E TTT10	0.26	9.55	NS
E TTT15	0.41	9.55	NS
L TTT05	0.67	9.55	NS
L TTT10	3.74	9.55	NS
L TTT15	0.27	9.55	NS

Table 40 Analysis of variance of percent friability of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types (continued)

Formulation	Variance Ratio	F-Ratio	Statistical Significance
A TTT05	0.00	18.51	NS
A TTT10	0.17	18.51	NS
A TTT15	0.00	18.51	NS
M TTT05	21.12	6.59	S
M TTT10	18.28	6.59	S
M TTT15	8.85	6.59	S
T 13305	16.37	9.55	S
T 13310	13.41	9.55	S
T 13315	7.85	9.55	NS
T 16705	4.77	9.55	NS
T 16710	11.69	9.55	S
T 16715	17.75	9.55	S
T 20005	1.13	9.55	NS
T 20010	15.32	9.55	S
T 20015	3.28	9.55	NS

S = significant at $P < 0.05$

NS = not significant at $P > 0.05$

Table 41 Analysis of variance of physical properties of lactose-Avicel PH101^{R} pellets prepared with various amount of water (percent base on dry weight)

Properties	Variance Ratio	F-Ratio	Statistical Significance
Mean partical size	6.48	9.55	NS
percent sieve fraction on 14/20 mesh cut	10.20	9.55	S
percent friability	2.94	9.55	NS
bulk density	23.00	5.14	S
tapped density	15.80	5.14	S
flow rate	37.95	5.14	S
angle of repose	0.00	5.14	NS

S = significant at $P < 0.05$

NS = not significant at $P > 0.05$

Table 42 Comparison of granule size of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types using Duncan's new multiple range test

Formulation	Difference between means	LSR	Statistical Significance
E 13315 VS E 13305	0.07	0.02	S
E 13315 VS E 13310	0.02	0.02	S
E 13310 VS E 13305	0.05	0.02	S
L 13315 VS L 13305	0.24	0.17	S
L 13315 VS L 13310	0.15	0.17	NS
L 13310 VS L 13305	0.09	0.17	NS
L 16715 VS L 16705	0.77	0.11	S
L 16715 VS L 16710	0.38	0.11	S
L 16710 VS L 16705	0.39	0.11	S
L 20015 VS L 20005	0.39	0.27	S
L 20015 VS L 20010	0.19	0.27	NS
L 20010 VS L 20005	0.20	0.27	NS
A 06715 VS A 06705	0.47	0.18	S
A 06715 VS A 06710	0.15	0.18	NS
A 06710 VS A 06705	0.32	0.18	S
M 13315 VS M 13305	0.17	0.08	S
M 13315 VS M 13310	0.07	0.08	NS

Table 42 Comparison of granule size of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types using Duncan's new multiple range test(continued)

Formulation	Difference between means	LSR	Statistical Significance
M 13310 VS M 13305	0.10	0.08	S
M 20015 VS M 20005	0.16	0.11	S
M 20015 VS M 20010	0.09	0.11	NS
M 20010 VS M 20005	0.07	0.11	NS
M 23315 VS M 23305	0.07	0.03	S
M 23315 VS M 23310	0.03	0.03	NS
M 23310 VS M 23305	0.04	0.03	S
E 20005 VS E 13305	0.25	0.11	S
E 20005 VS E 16705	0.33	0.11	S
E 16705 VS E 13305	0.58	0.11	S
E 20010 VS E 13310	0.27	0.10	S
E 20010 VS E 16710	0.37	0.10	S
E 16710 VS E 13310	0.64	0.10	S
E 20015 VS E 13315	0.16	0.13	S
E 20015 VS E 16715	0.54	0.13	S
E 16715 VS E 13315	0.70	0.13	S
L 20010 VS L 13310	0.15	0.26	NS

Table 42 Comparison of granule size of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types using Duncan's new multiple range test(continued)

Formulation	Difference between means	LSR	Statistical Significance
L 20010 VS L 16710	0.28	0.26	S
L 16710 VS L 13310	0.43	0.26	S
L 20015 VS L 13315	0.20	0.18	S
L 20015 VS L 16715	0.47	0.18	S
L 16715 VS L 13315	0.66	0.18	S
A 06710 VS A 03310	0.40	0.07	S
A 06715 VS A 03310	0.55	0.30	S
M 23305 VS M 13305	0.04	0.06	NS
M 23305 VS M 16705	0.04	0.06	NS
M 23305 VS M 20005	0.06	0.06	NS
M 20005 VS M 13305	0.02	0.06	NS
M 20005 VS M 16705	0.10	0.06	S
M 16705 VS M 13305	0.08	0.06	S
M 13315 VS E 13315	0.04	0.10	NS
M 13315 VS L 13315	0.13	0.10	S
L 13315 VS E 13315	0.17	0.10	S
M 16705 VS E 16705	0.56	0.14	S

Table 42 Comparison of granule size of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types using Duncan's new multiple range test(continued)

Formulation	Difference between means	LSR	Statistical Significance
M 16705 VS L 16705	0.11	0.14	NS
L 16705 VS E 16705	0.45	0.14	S
M 16710 VS E 16710	0.17	0.13	S
M 16710 VS L 16710	0.49	0.13	S
L 16710 VS E 16710	0.66	0.13	S
M 16715 VS E 16715	0.73	0.13	S
M 16715 VS L 16715	0.86	0.13	S
L 16715 VS E 16715	0.13	0.13	S
M 20005 VS E 20005	0.34	0.10	S
M 20005 VS L 20005	0.13	0.10	S
L 20005 VS E 20005	0.21	0.10	S
M 20010 VS E 20010	0.33	0.22	S
M 20010 VS L 20010	0.25	0.22	S
L 20010 VS E 20010	0.08	0.22	NS
M 20015 VS E 20015	0.16	0.21	NS

Table 42 Comparison of granule size of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types using Duncan's new multiple range test(continued)

Formulation	Difference between means	LSR	Statistical Significance
M 20015 VS L 20015	0.36	0.21	S
L 20015 VS E 20015	0.20	0.21	NS

S = significant at $P < 0.05$

NS = not significant at $P > 0.05$

Table 43 Comparison of percent sieve fraction on 14/20 mesh cut of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types using Duncan's new multiple range test

Formulation	Difference between means	LSR	Statistical Significance
L 16715 VS L 16705	11.24	2.97	S
L 16715 VS L 16710	4.46	2.97	S
L 16710 VS L 16705	6.78	2.97	S
L 20015 VS L 20005	5.09	4.44	S
L 20015 VS L 20010	0.45	4.44	NS
L 20010 VS L 20005	5.54	4.44	S
M 13315 VS M 13305	4.95	2.68	S
M 13315 VS M 13310	3.49	2.68	S
M 13310 VS M 13305	1.46	2.68	NS
E 20005 VS E 13305	11.41	3.25	S
E 20005 VS E 16705	3.97	3.25	S
E 16705 VS E 13305	15.38	3.25	S
E 20010 VS E 13310	14.91	6.25	S
E 20010 VS E 16710	1.44	6.25	NS
E 16710 VS E 13310	16.35	6.25	S
E 20015 VS E 13315	19.79	5.01	S
E 20015 VS E 16715	1.61	5.01	NS

Table 43 Comparison of percent sieve fraction on 14/20 mesh cut of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types using Duncan's new multiple range test (continued)

Formulation	Difference between means	LSR	Statistical Significance
E 16715 VS E 13315	21.39	5.01	S
L 20015 VS L 13315	5.11	3.21	S
L 20015 VS L 16715	12.14	3.21	S
L 16715 VS L 13315	17.26	3.21	S
A 06710 VS A 03310	6.34	3.17	S
A 06715 VS A 03315	8.68	6.69	S
M 23305 VS M 13305	13.31	7.87	S
M 23305 VS M 16705	10.00	7.85	S
M 23305 VS M 20005	6.44	7.69	NS
M 20005 VS M 13305	6.88	7.85	NS
M 20005 VS M 16705	3.57	7.69	NS
M 16705 VS M 13305	3.31	7.69	NS
M 23310 VS M 13310	18.23	5.10	S
M 23310 VS M 16710	16.82	5.09	S
M 23310 VS M 20010	10.18	4.99	S
M 20010 VS M 13310	8.06	5.09	S
M 20010 VS M 16710	6.64	4.99	S

Table 43 Comparison of percent sieve fraction on 14/20 mesh cut of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types using Duncan's new multiple range test (continued)

Formulation	Difference between means	LSR	Statistical Significance
M 16710 VS M 13310	1.41	4.99	NS
M 23315 VS M 13315	20.52	6.85	S
M 23315 VS M 16715	14.38	6.83	S
M 23315 VS M 20015	5.58	6.69	NS
M 20015 VS M 13315	14.94	6.83	S
M 20015 VS M 16715	8.80	6.69	S
M 16715 VS M 13315	6.15	6.69	NS
M 13305 VS E 13305	5.70	5.99	NS
M 13305 VS L 13305	11.38	5.99	S
L 13305 VS E 13305	5.69	5.99	NS
M 13310 VS E 13310	6.04	5.99	S
M 13310 VS L 13310	11.54	5.99	S
L 13310 VS E 13310	5.49	5.99	NS
M 16705 VS E 16705	24.39	3.18	S
M 16705 VS L 16705	17.18	3.18	S
L 16705 VS E 16705	7.21	3.18	S
M 16710 VS E 16710	23.81	4.42	S

Table 43 Comparison of percent sieve fraction on 14/20 mesh cut of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types using Duncan's new multiple range test (continued)

Formulation	Difference between means	LSR	Statistical Significance
M 16710 VS L 16710	20.61	4.42	S
L 16710 VS E 16710	3.21	4.42	NS
M 16715 VS E 16715	27.07	8.68	S
M 16715 VS L 16715	26.31	8.68	S
L 16715 VS E 16715	0.76	8.68	NS
M 20005 VS E 20005	23.98	10.15	S
M 20005 VS L 20005	14.75	10.15	S
L 20005 VS E 20005	9.23	10.15	NS
M 20010 VS E 20010	29.02	8.50	S
M 20010 VS L 20010	20.01	8.50	S
L 20010 VS E 20010	9.00	8.50	S
M 20015 VS E 20015	33.27	5.38	S
M 20015 VS L 20015	22.96	5.38	S
L 20015 VS E 20015	10.31	5.38	S

S = significant at $P < 0.05$

NS = not significant at $P > 0.05$

Table 44 Comparison of bulk density of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types using Duncan's new multiple range test

Formulation	Difference between means	LSR	Statistical Significance
E 16715 VS E 16705	0.00	0.01	NS
E 16715 VS E 16710	0.02	0.01	S
E 16710 VS E 16705	0.02	0.01	S
L 13315 VS L 13305	0.00	0.02	NS
L 13315 VS L 13310	0.03	0.02	S
L 13310 VS L 13305	0.02	0.02	S
L 20015 VS L 20005	0.02	0.01	S
L 20015 VS L 20010	0.01	0.01	S
L 20010 VS L 20005	0.00	0.01	NS
M 20010 VS M 20005	0.03	0.02	S
M 20015 VS M 20010	0.01	0.02	NS
M 20010 VS M 20005	0.02	0.02	S
M 23315 VS M 23305	0.04	0.02	S
M 23315 VS M 23310	0.02	0.01	S
M 23310 VS M 23305	0.02	0.01	S
E 20005 VS E 13305	0.05	0.02	S
E 20005 VS E 16705	0.04	0.02	S

Table 44 Comparison of bulk density of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types using Duncan's new multiple range test(continued)

Formulation	Difference between means	LSR	Statistical Significance
E 16705 VS E 13305	0.01	0.02	NS
E 20015 VS E 13315	0.04	0.01	S
E 20015 VS E 16715	0.03	0.01	S
E 16715 VS E 13315	0.01	0.01	NS
L 20010 VS L 13310	0.04	0.02	S
L 20010 VS L 16710	0.02	0.02	S
L 16710 VS L 13310	0.01	0.02	NS
A 06715 VS A 03315	0.02	0.02	S
M 23305 VS M 13305	0.01	0.01	S
M 23305 VS M 16705	0.01	0.01	NS
M 23305 VS M 20005	0.02	0.01	S
M 20005 VS M 13305	0.00	0.01	NS
M 20005 VS M 16705	0.02	0.01	S
M 16705 VS M 13305	0.02	0.01	S
M 13305 VS E 13305	0.01	0.01	NS
M 13305 VS L 13305	0.02	0.01	S
L 13305 VS E 13305	0.01	0.01	NS

Table 44 Comparison of bulk density of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types using Duncan's new multiple range test(continued)

Formulation	Difference between means	LSR	Statistical Significance
M 16715 VS E 16715	0.03	0.02	S
M 16715 VS L 16715	0.03	0.02	S
L 16715 VS E 16715	0.00	0.02	NS
M 20005 VS E 20005	0.06	0.01	S
M 20005 VS L 20005	0.01	0.01	S
L 20005 VS E 20005	0.05	0.01	S
M 20010 VS E 20010	0.04	0.02	S
M 20010 VS L 20010	0.01	0.02	NS
L 20010 VS E 20010	0.05	0.02	S
M 20015 VS E 20015	0.02	0.01	S
M 20015 VS L 20015	0.03	0.01	S
L 20015 VS E 20015	0.06	0.01	S

S = significant at $P < 0.05$

NS = not significant at $P > 0.05$

Table 45 Comparison of tapped density of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types using Duncan's new multiple range test

Formulation	Difference between means	LSR	Statistical Significance
E 16715 VS E 16705	0.01	0.02	NS
E 16715 VS E 16710	0.02	0.02	S
E 16710 VS E 16705	0.02	0.02	NS
L 16715 VS L 16705	0.03	0.02	S
L 16715 VS L 16710	0.02	0.02	S
L 16710 VS L 16705	0.01	0.02	NS
L 20015 VS L 20005	0.03	0.02	S
L 20015 VS L 20010	0.02	0.02	NS
L 20010 VS L 20005	0.02	0.02	S
M 13315 VS M 13305	0.04	0.03	S
M 13315 VS M 13310	0.01	0.03	NS
M 13310 VS M 13305	0.03	0.03	S
M 16715 VS M 16705	0.04	0.02	S
M 16715 VS M 16710	0.02	0.02	NS
M 16710 VS M 16705	0.02	0.02	NS
M 20015 VS M 20005	0.04	0.02	S
M 20015 VS M 20010	0.01	0.02	NS

Table 45 Comparison of tapped density of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types using Duncan's new multiple range test(continued)

Formulation	Difference between means	LSR	Statistical Significance
M 20010 VS M 20005	0.03	0.02	S
E 20005 VS E 13305	0.04	0.03	S
E 20005 VS E 16705	0.04	0.03	S
E 16705 VS E 13305	0.00	0.03	NS
E 20010 VS E 13310	0.06	0.02	S
E 20010 VS E 16710	0.04	0.02	S
E 16710 VS E 13310	0.03	0.02	S
E 20015 VS E 13315	0.04	0.02	S
E 20015 VS E 16715	0.04	0.02	S
E 16715 VS E 13315	0.00	0.02	NS
L 20005 VS L 13305	0.03	0.02	S
L 20005 VS L 16705	0.03	0.02	S
L 16705 VS L 13305	0.00	0.02	NS
L 20010 VS L 13310	0.07	0.02	S
L 20010 VS L 16710	0.04	0.02	S
L 16710 VS L 13310	0.03	0.02	S
L 20015 VS L 13315	0.07	0.03	S

Table 45 Comparison of tapped density of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types using Duncan's new multiple range test(continued)

Formulation	Difference between means	LSR	Statistical Significance
L 20015 VS L 16715	0.03	0.03	NS
L 16715 VS L 13315	0.04	0.03	S
M 23305 VS M 13305	0.04	0.02	S
M 23305 VS M 16705	0.03	0.02	S
M 23305 VS M 20005	0.04	0.02	S
M 20005 VS M 13305	0.00	0.02	NS
M 20005 VS M 16705	0.01	0.02	NS
M 16705 VS M 13305	0.02	0.02	NS
M 13305 VS E 13305	0.03	0.02	S
M 13305 VS L 13305	0.05	0.02	S
L 13305 VS E 13305	0.01	0.02	NS
M 13310 VS E 13310	0.00	0.02	NS
M 13310 VS L 13310	0.04	0.02	S
L 13310 VS E 13310	0.04	0.02	S
M 16705 VS E 16705	0.02	0.02	S
M 16705 VS L 16705	0.03	0.02	S
L 16705 VS L 16705	0.01	0.02	NS

Table 45 Comparison of tapped density of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types using Duncan's new multiple range test(continued)

Formulation	Difference between means	LSR	Statistical Significance
M 16715 VS E 16715	0.03	0.02	S
M 16715 VS L 16715	0.05	0.02	S
L 16715 VS E 16715	0.01	0.02	NS
M 20005 VS E 20005	0.07	0.03	S
M 20005 VS L 20005	0.01	0.03	NS
L 20005 VS E 20005	0.06	0.03	S
M 20010 VS E 20010	0.06	0.02	S
M 20010 VS L 20010	0.04	0.02	S
L 20010 VS E 20010	0.09	0.02	S
M 20015 VS E 20015	0.02	0.01	S
M 20015 VS L 20015	0.06	0.01	S
L 20015 VS E 20015	0.08	0.01	S

S = significant at $P < 0.05$

NS = not significant at $P > 0.05$

Table 46 Comparison of flow rate of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types using Duncan's new multiple range test

Formulation	Difference between means	LSR	Statistical Significance
E 13315 VS E 13305	41.70	23.43	S
E 13315 VS E 13310	59.27	24.24	S
E 13310 VS E 13305	17.58	23.43	NS
E 16715 VS E 16705	8.25	14.04	NS
E 16715 VS E 16710	24.95	14.04	S
E 16710 VS E 16705	33.20	14.52	S
L 13315 VS L 13305	13.38	10.85	S
L 13315 VS L 13310	31.33	10.85	S
L 13310 VS L 13305	44.71	11.22	S
A 06715 VS A 06705	19.70	16.26	S
A 06715 VS A 06710	5.87	16.26	NS
A 06710 VS A 06705	25.59	16.82	S
M 13315 VS M 13305	37.02	24.80	S
M 13315 VS M 13310	25.18	23.97	S
M 13310 VS M 13305	11.84	23.97	NS
M 20015 VS M 20005	33.31	24.29	S
M 20015 VS M 20010	0.36	23.48	NS
M 20010 VS M 20005	32.95	23.48	S

Table 46 Comparison of flow rate of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types using Duncan's new multiple range test(continued)

Formulation	Difference between means	LSR	Statistical Significance
E 20005 VS E 13305	17.49	25.14	NS
E 20005 VS E 16705	16.01	25.14	NS
E 16705 VS E 13305	33.50	26.01	S
L 20010 VS L 13310	52.46	10.88	S
L 20010 VS L 16710	29.87	10.52	S
L 16710 VS L 13310	22.59	10.52	S
L 20015 VS L 13315	26.69	20.62	S
L 20015 VS L 16715	14.00	19.93	NS
L 16715 VS L 13315	12.68	19.93	NS
A 06710 VS A 03310	30.42	8.17	S
A 06715 VS A 03315	27.24	19.06	S
M 23310 VS M 13310	0.91	23.36	NS
M 23310 VS M 16710	13.47	24.30	NS
M 23310 VS M 20010	30.04	24.87	S
M 20010 VS M 13310	29.09	24.30	S
M 20010 VS M 16710	16.57	23.36	NS
M 16710 VS M 13310	12.51	23.36	NS
M 23315 VS M 13315	19.98	16.55	S

Table 46 Comparison of flow rate of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types using Duncan's new multiple range test(continued)

Formulation	Difference between means	LSR	Statistical Significance
M 23315 VS M 16715	24.37	17.62	S
M 23315 VS M 20015	24.25	17.21	S
M 20015 VS M 13315	4.26	16.55	NS
M 20010 VS M 16715	0.13	16.55	NS
M 16715 VS M 13315	4.39	17.21	NS
M 13310 VS E 13310	31.01	22.64	S
M 13310 VS L 13310	43.15	22.64	S
L 13310 VS E 13310	12.15	21.88	NS
M 13315 VS E 13315	53.44	19.43	S
M 13315 VS L 13315	13.35	18.78	NS
L 13315 VS E 13315	40.09	18.78	S
M 16705 VS E 16705	18.98	23.29	NS
M 16705 VS L 16705	13.19	23.29	NS
L 16705 VS E 16705	32.17	24.10	S
M 16715 VS E 16715	41.39	19.87	S
M 16715 VS L 16715	30.43	19.21	S
L 16715 VS E 16715	10.96	19.21	NS
M 20010 VS E 20010	12.38	17.21	NS

Table 46 Comparison of flow rate of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types using Duncan's new multiple range test(continued)

Formulation	Difference between means	LSR	Statistical Significance
M 20010 VS L 20010	38.39	17.81	S
L 20010 VS E 20010	26.01	17.21	S
M 20015 VS E 20015	39.53	19.22	S
M 20015 VS L 20015	44.27	19.89	S
L 20015 VS E 20015	4.75	19.22	NS

S = significant at $P < 0.05$

NS = not significant at $P > 0.05$

Table 47 Comparison of angle of repose of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types using Duncan's new multiple range test

Formulation	Difference between means	LSR	Statistical Significance
E 13315 VS E 13305	5.18	1.85	S
E 13315 VS E 13310	2.84	1.79	S
E 13310 VS E 13305	2.34	1.79	S
L 20015 VS L 20005	3.99	2.49	S
L 20015 VS L 20010	0.06	2.40	NS
L 20010 VS L 20005	3.93	2.40	S
A 03315 VS A 03305	2.88	1.63	S
A 03315 VS A 03310	0.27	1.57	NS
A 03310 VS A 03305	2.61	1.57	S
A 06715 VS A 06705	2.17	2.93	NS
A 06715 VS A 06710	3.75	2.93	S
A 06710 VS A 06705	5.92	3.04	S
M 20015 VS M 20005	0.72	2.41	NS
M 20015 VS M 20010	4.28	2.41	S
M 20010 VS M 20005	5.01	2.49	S
E 20005 VS E 13305	2.65	1.38	S
E 20005 VS E 16705	2.13	1.33	S

Table 47 Comparison of angle of repose of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types using Duncan's new multiple range test (continued)

Formulation	Difference between means	LSR	Statistical Significance
E 16705 VS E 13305	0.52	1.33	NS
L 20005 VS L 13305	5.37	3.08	S
L 20005 VS L 16705	5.54	3.19	S
L 16705 VS L 13305	0.17	3.08	NS
L 20010 VS L 13310	1.21	2.41	NS
L 20010 VS L 16710	3.15	2.50	S
L 16710 VS L 13310	1.94	2.41	NS
L 20015 VS L 13315	4.71	2.50	S
L 20015 VS L 16715	1.56	2.41	NS
L 16715 VS L 13315	3.15	2.41	S
A 06715 VS A 03315	2.49	1.59	S
M 23310 VS M 13310	3.70	2.16	S
M 23310 VS M 16710	3.36	2.08	S
M 23310 VS M 20010	1.72	2.08	NS
M 20010 VS M 13310	5.42	2.21	S
M 20010 VS M 16710	5.08	2.16	S
M 16710 VS M 13310	0.34	2.08	NS

Table 47 Comparison of angle of repose of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types using Duncan's new multiple range test (continued)

Formulation	Difference between means	LSR	Statistical Significance
M 23315 VS M 13315	2.95	2.13	S
M 23315 VS M 16715	4.80	2.27	S
M 23315 VS M 20015	3.04	2.22	S
M 20015 VS M 13315	0.09	2.13	NS
M 20015 VS M 16715	1.76	2.13	NS
M 16715 VS M 13315	1.84	2.22	NS
M 13305 VS E 13305	4.80	2.85	S
M 13305 VS L 13305	2.05	2.85	NS
L 13305 VS E 13305	6.85	2.95	S
M 13310 VS E 13310	0.03	2.06	NS
M 13310 VS L 13310	4.25	2.06	S
L 13310 VS E 13310	4.28	2.14	S
M 13315 VS E 13315	1.59	2.30	NS
M 13315 VS L 13315	6.60	2.38	S
L 13315 VS E 13315	5.01	2.30	S
M 16705 VS E 16705	0.73	2.42	NS
M 16705 VS L 16705	5.77	2.42	S

Table 47 Comparison of angle of repose of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types using Duncan's new multiple range test (continued)

Formulation	Difference between means	LSR	Statistical Significance
L 16705 VS E 16705	6.50	2.50	S
M 16710 VS E 16710	0.19	2.54	NS
M 16710 VS L 16710	5.85	2.63	S
L 16710 VS E 16710	5.66	2.54	S
M 16715 VS L 16715	0.84	2.43	NS
M 16715 VS E 16715	5.29	2.52	S
L 16715 VS E 16715	4.45	2.43	S
M 20010 VS L 20010	5.05	2.54	S
M 20010 VS L 20010	2.38	2.45	NS
L 20010 VS E 20010	2.67	2.45	S
M 20015 VS E 20015	0.73	1.53	NS
M 20015 VS L 20015	1.97	1.53	S
L 20015 VS E 20015	2.70	1.58	S

S = significant at $P < 0.05$

NS = not significant at $P > 0.05$

Table 48 Comparison of percent friability of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types using Duncan's new multiple range test

Formulation	Difference between means	LSR	Statistical Significance
L 20015 VS L 20005	0.09	0.06	S
L 20015 VS L 20010	0.11	0.06	S
L 20010 VS L 20005	0.20	0.06	S
M 23305 VS M 13305	0.58	0.22	S
M 23305 VS M 16705	0.27	0.22	S
M 23305 VS M 20005	0.15	0.21	NS
M 20005 VS M 13305	0.43	0.22	S
M 20005 VS M 16705	0.12	0.21	NS
M 16705 VS M 13305	0.32	0.21	S
M 23310 VS M 13310	0.46	0.19	S
M 23310 VS M 16710	0.37	0.19	S
M 23310 VS M 20010	0.35	0.19	S
M 20010 VS M 13310	0.11	0.19	NS
M 20010 VS M 13710	0.02	0.19	NS
M 16710 VS M 13310	0.09	0.19	NS
M 23315 VS M 13315	0.35	0.21	S
M 23315 VS M 16715	0.28	0.20	S

Table 48 Comparison of percent friability of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types using Duncan's new multiple range test (continued)

Formulation	Difference between means	LSR	Statistical Significance
M 23315 VS M 20015	0.28	0.21	S
M 20015 VS M 13315	0.07	0.20	NS
M 20015 VS M 16715	0.00	0.20	NS
M 16715 VS M 13315	0.07	0.21	NS
M 13305 VS E 13305	0.33	0.25	S
M 13305 VS L 13305	0.43	0.25	S
L 13305 VS E 13305	0.11	0.25	NS
M 13310 VS E 13310	0.25	0.24	S
M 13310 VS L 13310	0.39	0.24	S
L 13310 VS E 13310	0.14	0.24	NS
M 16710 VS E 16710	0.16	0.26	NS
M 16710 VS L 16710	0.39	0.26	S
L 16710 VS E 16710	0.23	0.26	NS
M 16715 VS E 16715	0.05	0.18	NS
M 16715 VS L 16715	0.31	0.18	S
L 16715 VS E 16715	0.26	0.18	S
M 20010 VS E 20010	0.07	0.24	NS

Table 48 Comparison of percent friability of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types using Duncan's new multiple range test (continued)

Formulation	Difference between means	LSR	Statistical Significance
M 20010 VS L 20010	0.40	0.24	S
L 20010 VS E 20010	0.33	0.24	S

S = significant at $P < 0.05$

NS = not significant at $P > 0.05$

Table 49 Comparison of properties of lactose-Avicel PH101^{R} pellets prepared with various spheronization times, binder concentrations and binder types using Duncan's new multiple range test

Formulation	Difference between means	LSR	Statistical Significance
SF 44 VS SF 40	3.70	2.74	S
SF 44 VS SF 42	0.81	2.74	NS
SF 42 VS SF 40	2.89	2.74	S
BD 44 VS BD 40	0.04	0.01	S
BD 44 VS BD 42	0.02	0.01	S
BD 42 VS BD 40	0.02	0.01	S
TD 44 VS TD 40	0.04	0.02	S
TD 44 VS TD 42	0.02	0.02	S
TD 42 VS TD 40	0.01	0.02	NS
FR 44 VS FR 40	35.49	10.86	S
FR 44 VS FR 42	8.93	10.49	NS
FR 42 VS FR 40	26.56	10.49	S

S = significant at $P < 0.05$

NS = not significant at $P > 0.05$

SF, BD, TD AND FR were percent sieve fraction on 14/20 mesh cut, bulk density, tapped density and flow rate, respectively.

40, 42 and 44 were 40% w/w, 42% w/w and 44% w/w of water base on dry weight.

Calibration Curve

The concentration versus absorbance of terbutaline sulphate in 0.01 N hydrochloric acid at 278 nm is presented in Table 50. The standard curve of terbutaline sulphate after regression analysis is illustrated in Figure 85.

The spectrum of terbutaline sulphate in 0.01 N hydrochrolic acid at 278 nm is shown in Figure 86. And high performance liquid chromatogram of terbutaline sulphate and pindolol at an excitation wavelength (λex) of 280 nm and an emission wavelength (λem) of nm is shown in Figure 87.

Table 50 Absorbance of terbutaline sulphate standard solution in 0.01 N hydrochloric acid at 278 nm

Concentration (mg/ml)	Absorbance at 278 nm
0	0
0.02	0.130
0.04	0.264
0.06	0.396
0.08	0.528
0.10	0.658
0.12	0.796

Y = 6.6343 X - 0.0024

r = 0.99997

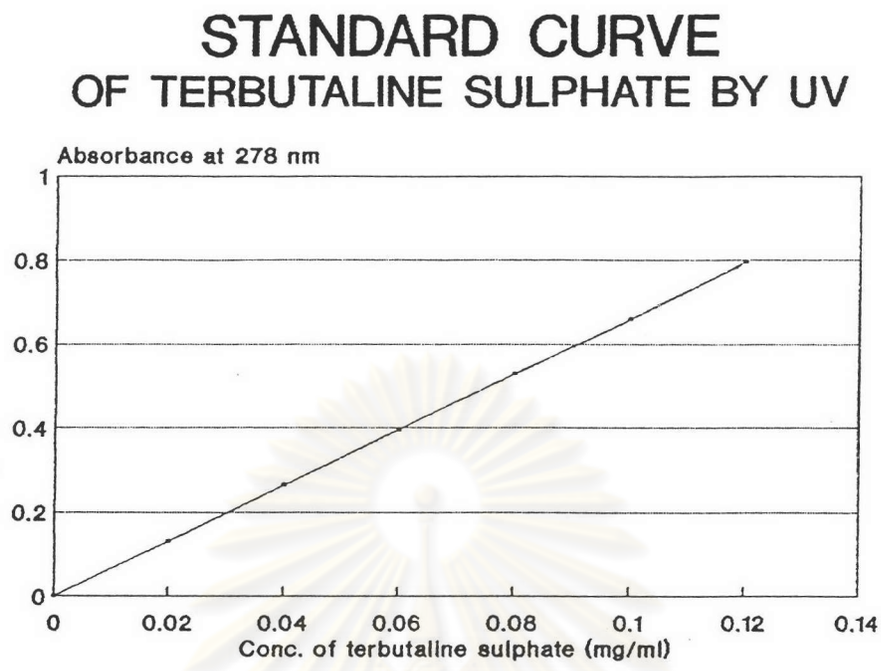

Figure 85 Standard curve of terbutaline sulphate in 0.01 N hydrochloric acid at 278 nm

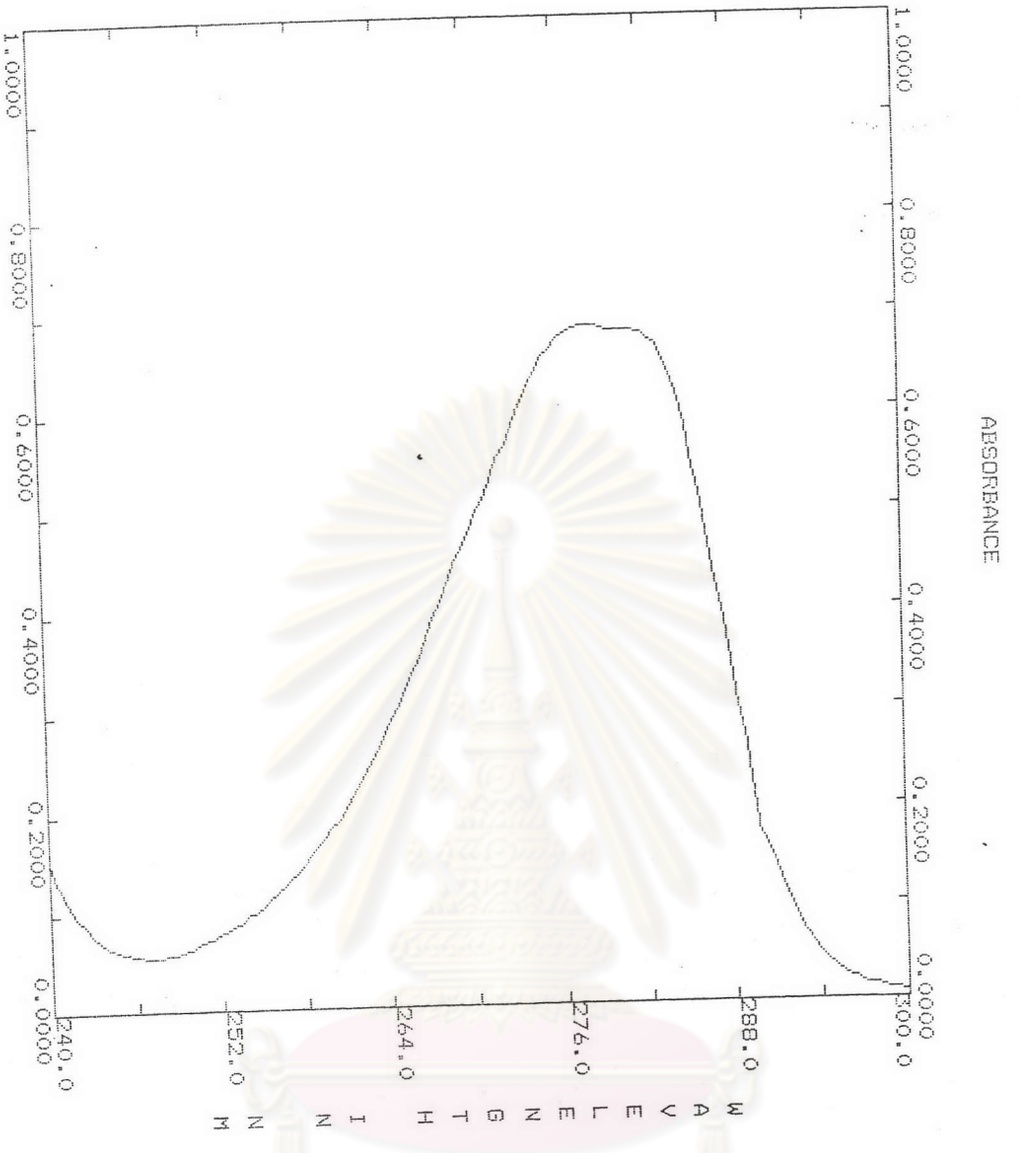

Figure 86 Spectrum of terbutaline sulphate in 0.01 N hydrochloric acid at 278 nm

Figure 87 High pressure liquid chromatogram of terbutaline sulphated and pindolol at an excitation wavelength (λex) of 280 nm and an emission wavelength (λem) of 310 nm

Drug Content

Amount of terbutaline sulphate in uncoated terbutaline sulphate pellets and in film coated terbutaline sulphate pellets are presented in Tables 51-63.

Table 51 Amount of terbutaline sulphate in uncoated terbutaline sulphate pellets (lot 1)

Sample No.	Amount of drug in 300 mg pellets (mg)
1	5.37
2	5.31
3	5.36
4	5.38
5	5.36
6	5.31
7	5.37
8	5.30
9	5.36
10	5.36
X	5.35
SD	0.03

Table 52 Amount of terbutaline sulphate in uncoated terbutaline sulphate pellets (lot 2)

Sample No.	Amount of drug in 300 mg pellets (mg)
1	5.24
2	5.17
3	5.20
4	5.30
5	5.35
6	5.35
7	5.33
8	5.24
9	5.33
10	5.31
X	5.28
SD	0.06

Table 53 Amount of terbutaline sulphate in uncoated terbutaline sulphate pellets (lot 3)

Sample No.	Amount of drug in 300 mg pellets (mg)
1	5.25
2	5.28
3	5.26
4	5.28
5	5.26
6	5.23
7	5.23
8	5.26
9	5.25
10	5.24
X	5.25
SD	0.02

Table 54 Amount of terbutaline sulphate in 5.4 % w/w coating level of film coated terbutaline sulphate pellets formulation 2

Sample No.	Amount of drug in 300 mg pellets (mg)
1	4.96
2	5.02
3	5.00
4	5.04
5	5.08
6	5.00
7	5.09
8	5.05
9	5.05
10	4.85
X	5.01
SD	0.07

$$F = \frac{(U-C)}{C} \times 100$$

$$= \frac{(5.28-5.01)}{5.01} \times 100$$

$$= 5.39\%$$

The percent ethylcellulose film based on weight increased was 5.39.

Table 55 Amount of terbutaline sulphate in 5.4 % w/w coating level of film coated terbutaline sulphate pellets formulation 1

Sample No.	Amount of drug in 300 mg pellets (mg)
1	5.00
2	4.94
3	5.00
4	4.96
5	5.00
6	5.00
7	5.01
8	4.97
9	4.98
10	4.92
X	4.98
SD	0.03

$$F = \frac{(U-C)}{C} \times 100$$

$$= \frac{(5.25-4.98)}{4.98} \times 100$$

$$= 5.42\%$$

The percent ethylcellulose film based on weight increased was 5.42.

Table 56 Amount of terbutaline sulphate in 3.2 % w/w coating level of film coated terbutaline sulphate pellets formulation 1

Sample No.	Amount of drug in 300 mg pellets (mg)
1	5.06
2	5.19
3	5.30
4	5.31
5	5.19
6	5.17
7	5.13
8	5.17
9	5.08
10	5.23
X	5.18
SD	0.08

$$F = \frac{(U-C)}{C} \times 100$$

$$= \frac{(5.35-5.18)}{5.18} \times 100$$

$$= 3.28\%$$

The percent ethylcellulose film based on weight increased was 3.28.

Table 57 Amount of terbutaline sulphate in 1.5 % w/w coating level of film coated terbutaline sulphate pellets formulation 1

Sample No.	Amount of drug in 300 mg pellets (mg)
1	5.28
2	5.20
3	5.26
4	5.34
5	5.19
6	5.26
7	5.29
8	5.37
9	5.24
10	5.26
X	5.27
SD	0.06

$$F = \frac{(U-C)}{C} \times 100$$

$$= \frac{(5.35-5.27)}{5.27} \times 100$$

$$= 1.52\%$$

The percent ethylcellulose film based on weight increased was 1.52.

Table 58 Amount of terbutaline sulphate in 1.1 % w/w coating level of film coated terbutaline sulphate pellets formulation 1 (lot 1)

Sample No.	Amount of drug in 300 mg pellets (mg)
1	5.32
2	5.26
3	5.30
4	5.28
5	5.29
6	5.28
7	5.30
8	5.28
9	5.32
10	5.25
X	5.29
SD	0.02

$$F = \frac{(U-C)}{C} \times 100$$

$$= \frac{(5.35-5.29)}{5.29} \times 100$$

$$= 1.13\%$$

The percent ethylcellulose film based on weight increased was 1.13.

Table 59 Amount of terbutaline sulphate in 3.2 % w/w coating level of film coated terbutaline sulphate pellets formulation 3

Sample No.	Amount of drug in 300 mg pellets (mg)
1	5.14
2	5.03
3	5.04
4	5.04
5	5.02
6	5.12
7	5.12
8	5.14
9	5.14
10	5.08
X	5.09
SD	0.05

$$F = \frac{(U-C)}{C} \times 100$$

$$= \frac{(5.35-5.09)}{5.09} \times 100$$

$$= 3.14\%$$

The percent ethylcellulose film based on weight increased was 3.14.

Table 60 Amount of terbutaline sulphate in 3.2 % w/w coating level of film coated terbutaline sulphate pellets formulation 4

Sample No.	Amount of drug in 300 mg pellets (mg)
1	5.12
2	5.08
3	5.08
4	5.08
5	5.04
6	5.13
7	5.09
8	5.10
9	5.10
10	5.09
X	5.09
SD	0.02

$$F = \frac{(U-C)}{C} \times 100$$

$$= \frac{(5.25-5.09)}{5.09} \times 100$$

$$= 3.14\%$$

The percent ethylcellulose film based on weight increased was 3.14.

Table 61 Amount of terbutaline sulphate in 3.2 % w/w coating level of film coated terbutaline sulphate pellets formulation 5

Sample No.	Amount of drug in 300 mg pellets (mg)
1	5.07
2	5.16
3	5.26
4	5.04
5	5.05
6	5.04
7	5.03
8	5.03
9	5.12
10	5.08
X	5.09
SD	0.07

$$F = \frac{(U-C)}{C} \times 100$$

$$= \frac{(5.25-5.09)}{5.09} \times 100$$

$$= 3.14\%$$

The percent ethylcellulose film based on weight increased was 3.14.

Table 62 Amount of terbutaline sulphate in 1.1 % w/w coating level of film coated terbutaline sulphate pellets formulation 1 (lot2)

Sample No.	Amount of drug in 300 mg pellets (mg)
1	5.19
2	5.23
3	5.26
4	5.21
5	5.25
6	5.26
7	5.21
8	5.19
9	5.22
10	5.17
X	5.22
SD	0.03

$$F = \frac{(U-C)}{C} \times 100$$

$$= \frac{(5.28-5.22)}{5.22} \times 100$$

$$= 1.15\%$$

The percent ethylcellulose film based on weight increased was 1.15.

Table 63 Amount of terbutaline sulphate in 1.1 % w/w coating level of film coated terbutaline sulphate pellets formulation 1 (lot 3)

Sample No.	Amount of drug in 300 mg pellets (mg)
1	5.26
2	5.26
3	5.13
4	5.20
5	5.14
6	5.18
7	5.22
8	5.15
9	5.21
10	5.15
X	5.19
SD	0.05

$$F = \frac{(U-C)}{C} \times 100$$

$$= \frac{(5.25-5.19)}{5.19} \times 100$$

$$= 1.16\%$$

The percent ethylcellulose film based on weight increased was 1.16

VITAE

Miss Padungkwan Chitropas was born on November 7, 1969. She got her degree in Bachelor of Science in Pharmacywith second honors in 1992 from Faculty of Pharmaceutical Science, Mahidol University, Thailand.