CHAPTER III

RESULTS

1. Preliminary Investigation on Suitable Coating Conditions and Coating Dispersion

Suitable coating conditions and coating dispersion were investigated by coating theophylline granules with aqueous polymeric dispersion which had various amount of Cab-O-Sil as previously presented in Table 3. The amount of Cab-O-Sil in the dispersion that suited for coating the granules in this study was 30 % w/w of polymer content calculated on the dry polymer basis. The suitable coating conditions and coating dispersion using top spraying method was previously described in Tables 4 and 5, respectively.

2. Evaluation of Theophylline Granules

The theophylline granules were coated with various levels of Eudragit® NE 30D using top spray and bottom spray method. The levels of coating were calculated on the basis of Eudragit®NE 30D content in aqueous polymeric coating used and were shown as percent of polymer coated based on weight of granules.

2.1 Morphology of Theophylline Granules

The theophylline granules were examined using scanning electron microscope (SEM) at different magnifications. The x 35 and x 500 magnifications were used to investigate the shape and surface topography of granules. The cross-section of theophylline granule was also observed for the film morphology at x 2000 magnification.

2.1.1 Uncoated Granules

The shape and surface topography of uncoated theophylline granules are shown in Figure 9. The granules exhibited cylindrical shape and rough surface at both low and high magnifications.

2.1.2 Eudragit®NE 30D Coated Granules Using Different Spraying Method

To study the effect of spraying method, top spray and bottom spray method were used to investigated. For top spray method, the granules were coated with Eudragit®NE 30D lot A and lot B. The surface and cross-sectioned morphology of the granules coated with various percent coating levels of these polymers are shown in Figures 10-22. Figures 10-15 illustrate granules coated with Eudragit ®NE 30D lot A at coating levels of 1.55 %, 4.66 %, 5.40 %, 8.75 %, 10.83 % and 13.25 % respectively whereas Figures 16-22 are granules coated with 4.28 %, 7.18 %, 7.85 %, 8.75 %, 10.60 %, 13.51 % and 21.20 % coating levels of Eudragit®NE 30D lot B, respectively.

The photomicrographs of all top-spray coated granules were notable that coated with lower percent coating level exhibited thinner film than those with higher percent coating level of Eudragit®NE 30D. Edge and corner of theophylline granules were decreased with increasing of percent coating level of Eudragit® NE 30D.

In addition, it was observed that granules coated with Eudragit®NE 30D lot A appeared to provide a smooth and continuous film of the polymer as shown in Figures

10-15, as compared to a rough and porous surface of granules coated with Eudragit® NE 30D lot B as shown in Figures 16-22.

For bottom spray method, theophylline granules were coated with Eudragit® NE 30D lot B. Figures 23-27 illustrate the surface and cross-sectioned morphology of the granules coated with this polymer at coating level of 4.16 %, 6.61 %, 7.97 %, 8.78 % and 11.49 % respectively.

The photomicrographs of all bottom-spray coated granules were notable that the granules coated with higher percent coating level exhibited thicker film than those with lower percent coating level. Edge and corner of theophylline granules were decreased with increasing of the percent coating level of Eudragit®NE 30D. Some formulations of them had fine particles of theophylline granules embedding into the layers of the films. Comparison to the top-spray coated granules which used the same Lot No. of Eudragit®NE 30D as shown in Figures 16-22, it appeared that the bottom-spray coated granules demonstrated smoother surface characteristics and more continuous film.

2.1.3 Eudragit®NE 30D Coated Granules Using Different Atomizing Air Pressure

Top spray method was used to coat theophylline granules with Eudragit®NE 30D lot A at 10 % coating level using various atomizing air pressure. Figures 21-23 illustrate the surface and cross-sectioned morphology of the granules which were coated at 1, 2 and 3 bar of atomizing air pressure respectively.

The photomicrographs of all granules were notable that the surface of granules coated with higher atomizing air pressure exhibited rougher film than those with lower atomizing air pressure. Moreover, the cross-sectioned morphology of granules were demonstrated that granules which were coated at higher atomizing air pressure exhibited less continuous film than those coated at lower atomizing air pressure.

2.1.4 Granules Coated with Polymer Blends.

A. Eudragit®NE 30D/HPMC Coated Granules

Theophylline granules were coated with polymer blends containing various ratios of Eudragit®NE 30D/HPMC using top spray method at the same coating level (about 10 % of core granules). Figures 31-37 illustrate the surface and cross-sectioned morphology of the granules which were coated with this blend in ratios of 3:2 , 3:1.5 , 3:1 , 3:0.5 , 12.5:1 , 12.5:0.5 and 100:1 respectively.

The photomicrographs of all Eudragit®NE 30D/HPMC coated granules were notable that coated with this blend containing higher HPMC content exhibited smoother and less porous surface than those containing lower HPMC content.

B. Eudragit®NE 30D/RL 30D Coated Granules

Theophylline granules were coated with polymer blends containing various ratios of Eudragit®NE 30D/RL 30D using top spray method at the same coating level (about 10 % of core granules). Figures 38-41 illustrate the surface and cross-sectioned morphology of the granules which were coated with this blend in ratios of 50:50 , 80:20 , 90:10 and 95:5 respectively.

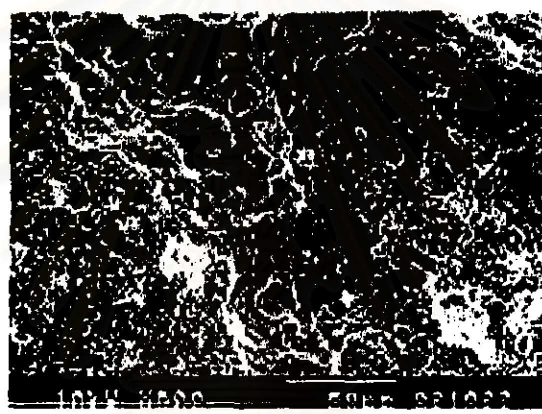
The photomicrographs of all Eudragit®NE 30D/RL 30D coated granules were notable that more porous and sponge-like surface was found when increasing the amount of Eudragit®RL 30D in the coating formulation.

(A)

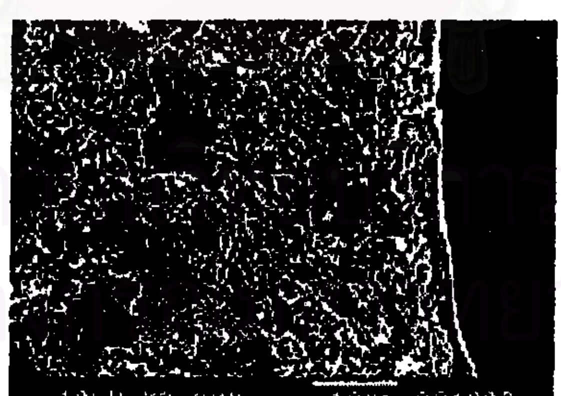
(B)

Figure 9 **The photomicrographs of uncoated theophylline granules (A : theophylline granules x 35, B: theophylline surface x 500).**

(A)

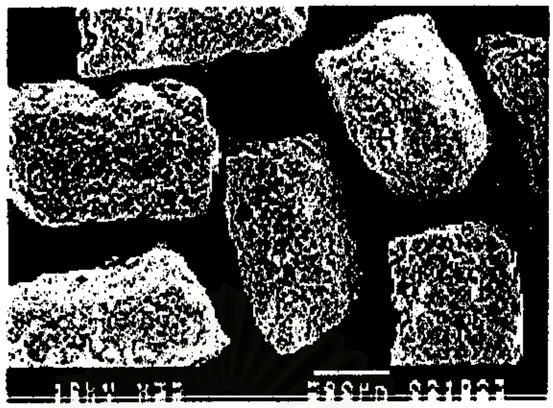


(B)

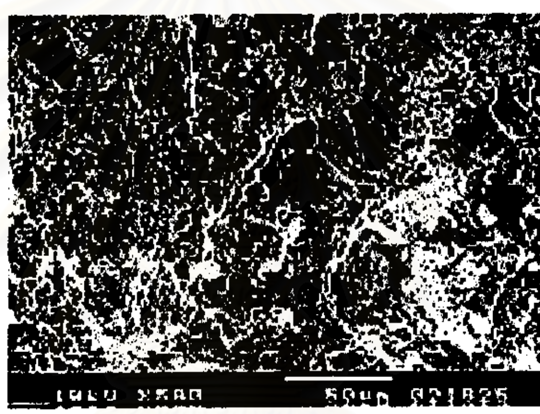


(C)

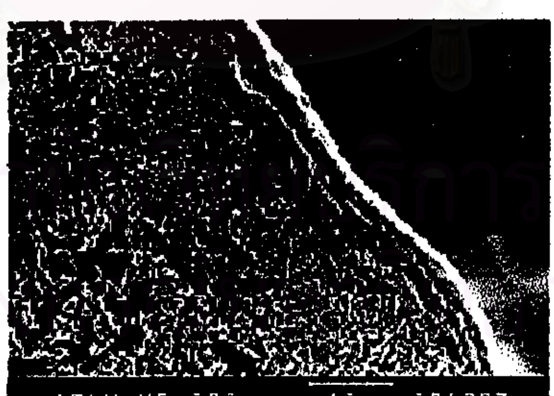
Figure 10 The photomicrographs of 1.55 % Eudragit®NE 30D lot A coated granules using top spray method. (A : coated granules x 35 , B : coated surface x 500, C : cross-section x 2000).



(A)



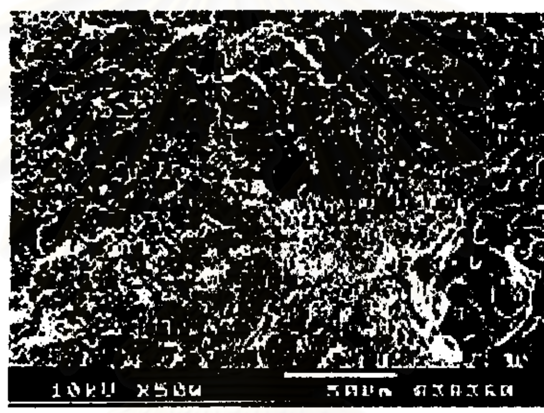
(B)



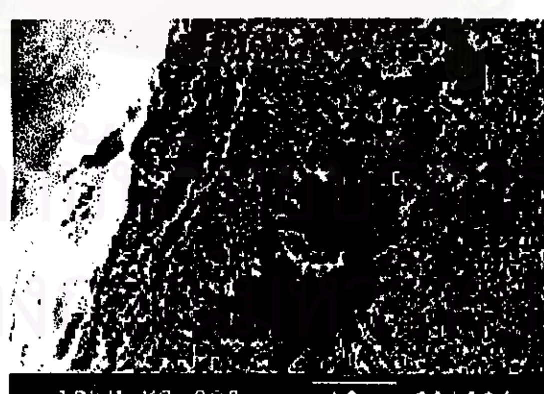
(C)

Figure 11 The photomicrographs of 4.66 % Eudragit®NE 30D lot A coated granules using top spray method. (A : coated granules x 35 , B : coated surface x 500, C : cross-section x 2000).

(A)



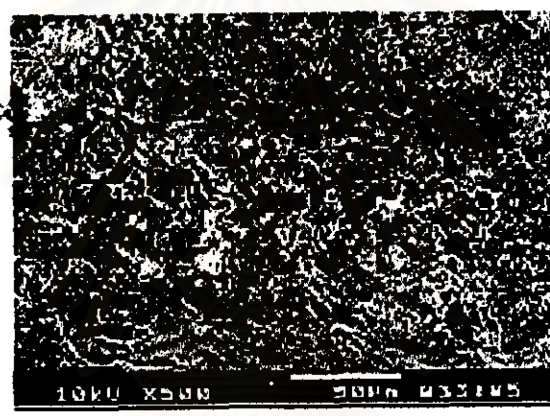
(B)



(C)

Figure 12 The photomicrographs of 5.40 % Eudragit®NE 30D lot A coated granules using top spray method. (A : coated granules x 35 , B : coated surface x 500, C : cross-section x 2000).

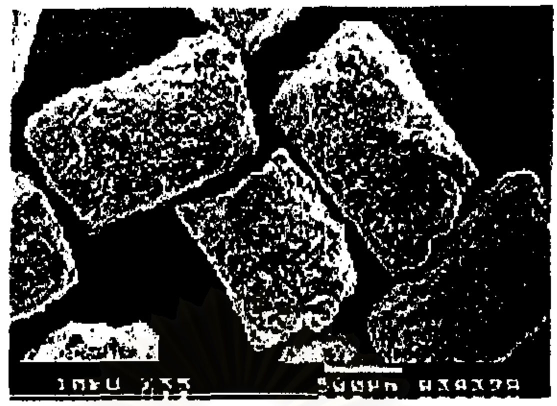
(A)



(B)

(C)

Figure 13 The photomicrographs of 8.75 % Eudragit® NE 30D lot A coated granules using top spray method. (A : coated granules x 35 , B : coated surface x 500, C : cross-section x 2000).

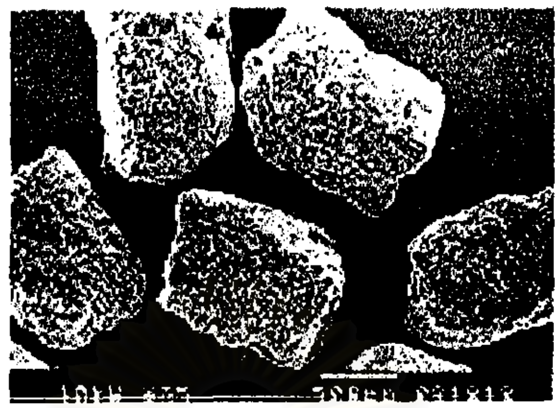


(A)

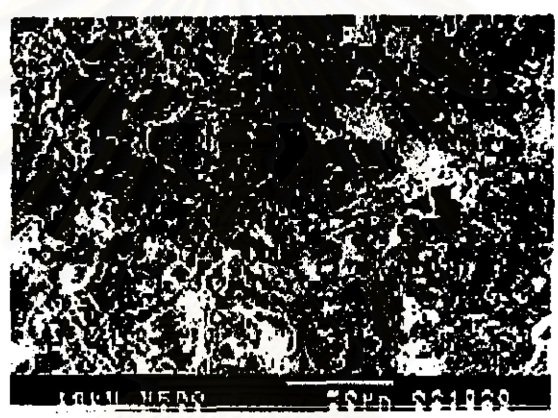
(B)

(C)

Figure 14 The photomicrographs of 10.83 % Eudragit®NE 30D lot A coated granules using top spray method. (A : coated granules x 35 , B : coated surface x 500, C : cross-section x 2000).



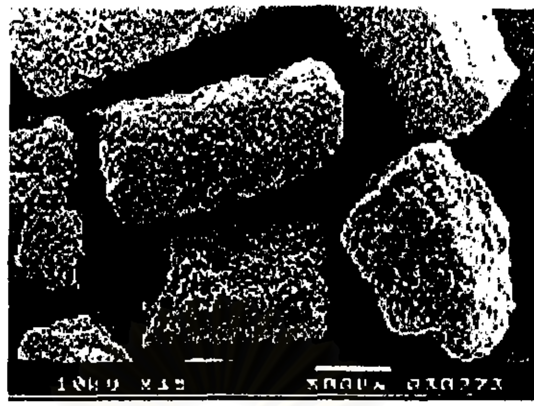
(A)



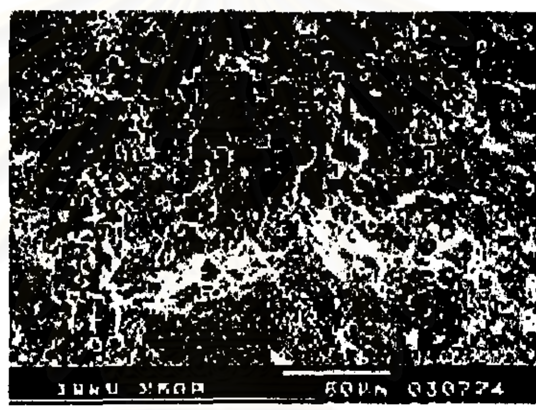
(B)

(C)

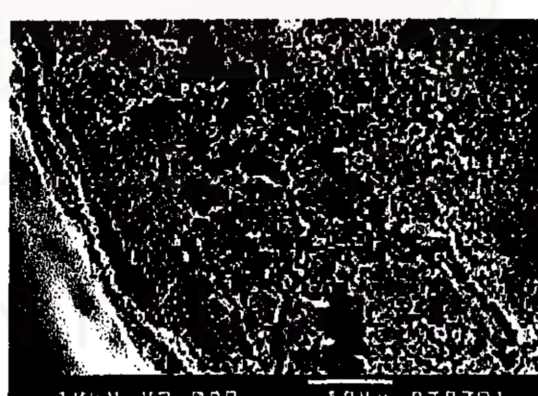
Figure 15 The photomicrographs of 13.25 % Eudragit®NE 30D lot A coated granules using top spray method. (A : coated granules x 35 , B : coated surface x 500, C : cross-section x 2000).



(A)



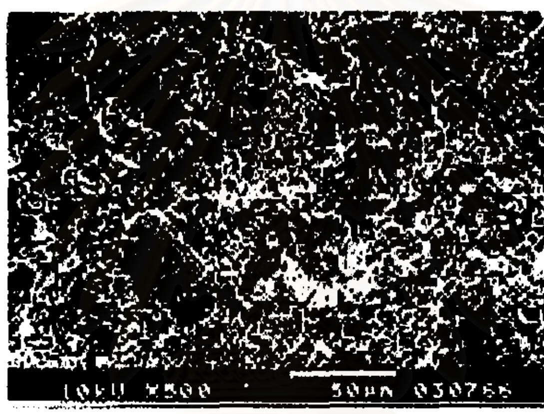
(B)



(C)

Figure 16 The photomicrographs of 4.28 % Eudragit®NE 30D lot B coated granules using top spray method. (A : coated granules x 35 , B : coated surface x 500, C : cross-section x 2000).

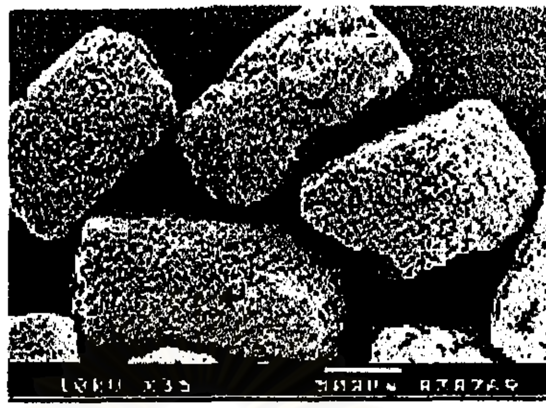
(A)



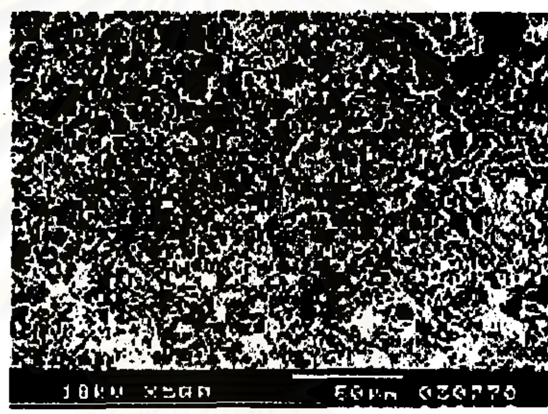
(B)

(C)

Figure 17 The photomicrographs of 7.18 % Eudragit®NE 30D lot B coated granules using top spray method. (A : coated granules x 35 , B : coated surface x 500, C : cross-section x 2000).



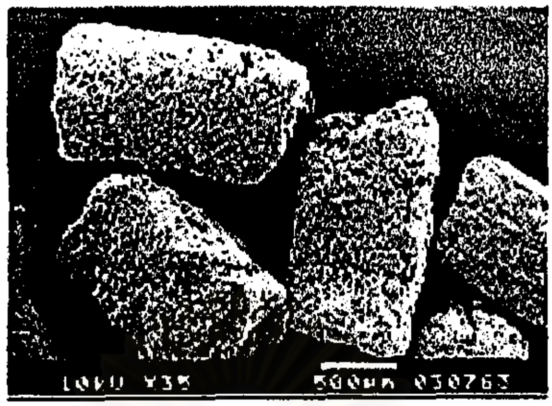
(A)



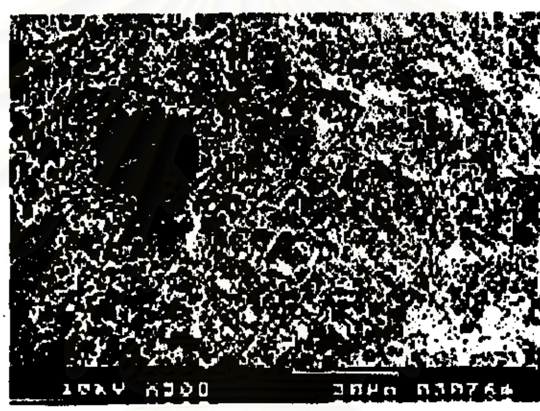
(B)

(C)

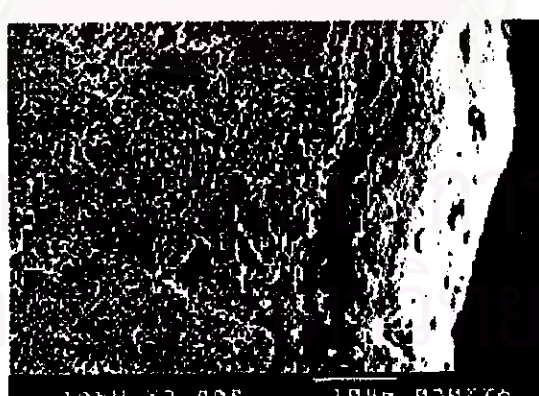
Figure 18 The photomicrographs of 7.85 % Eudragit®NE 30D lot B coated granules using top spray method. (A : coated granules x 35 , B : coated surface x 500, C : cross-section x 2000).



(A)

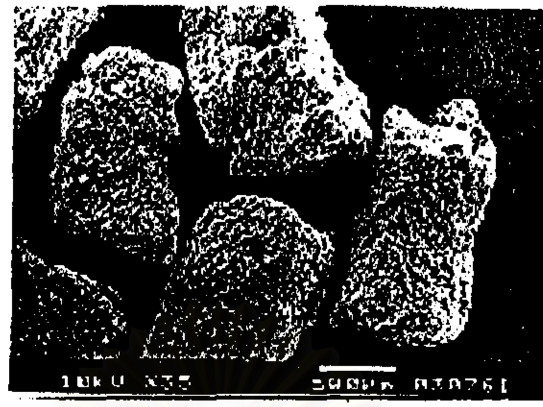


(B)

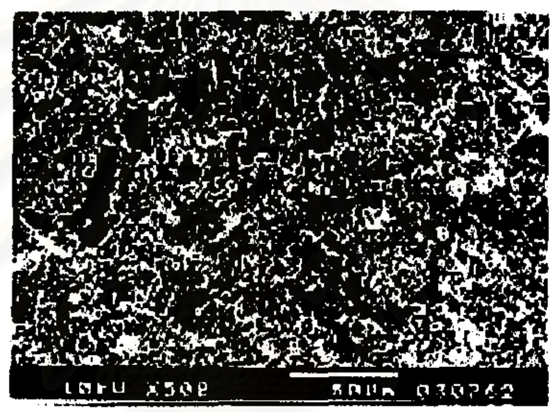


(C)

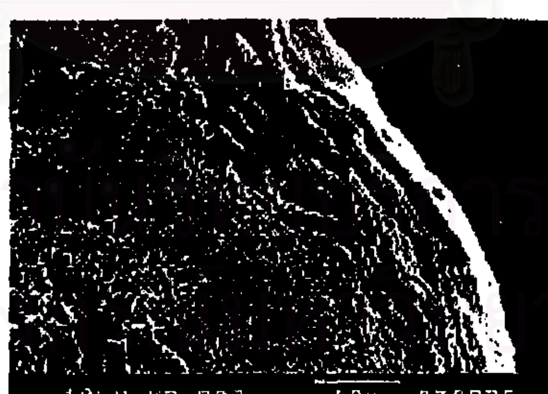
Figure 19 The photomicrographs of 8.75 % Eudragit®NE 30D lot B coated granules using top spray method. (A : coated granules x 35 , B : coated surface x 500, C : cross-section x 2000).



(A)



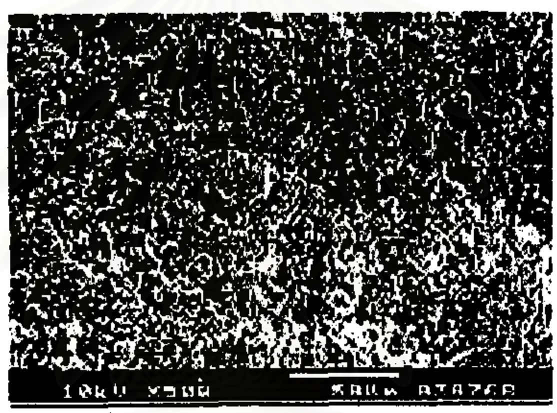
(B)



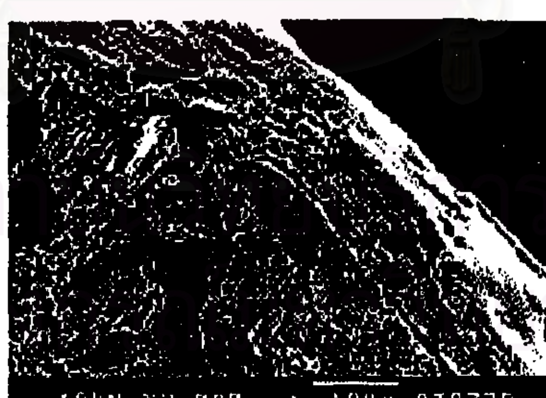
(C)

Figure 20 The photomicrographs of 10.60 % Eudragit®NE 30D lot B coated granules using top spray method. (A : coated granules x 35 , B : coated surface x 500, C : cross-section x 2000).

(A)

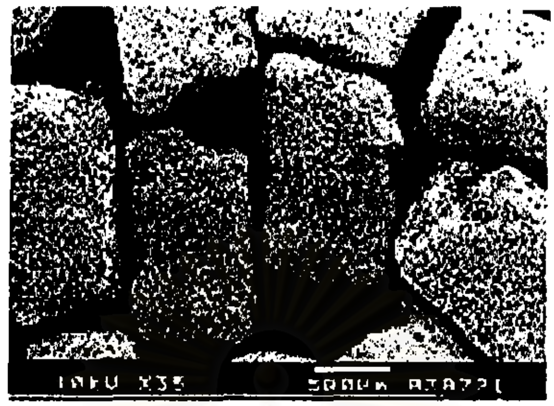


(B)

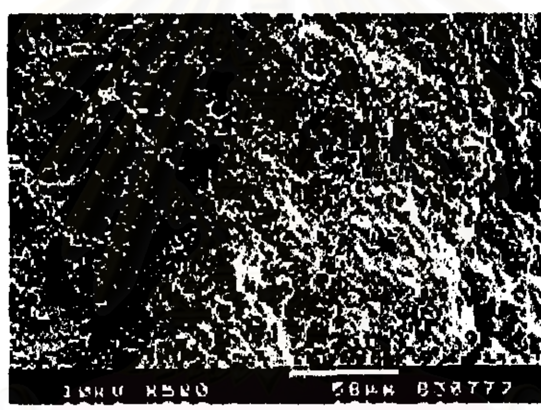


(C)

Figure 21 The photomicrographs of 13.51 % Eudragit®NE 30D lot B coated granules using top spray method. (A : coated granules x 35 , B : coated surface x 500, C : cross-section x 2000).



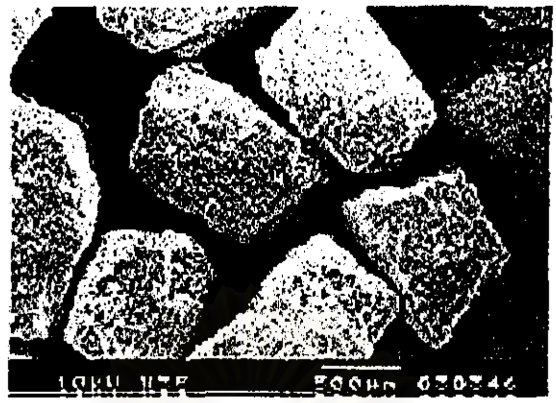
(A)



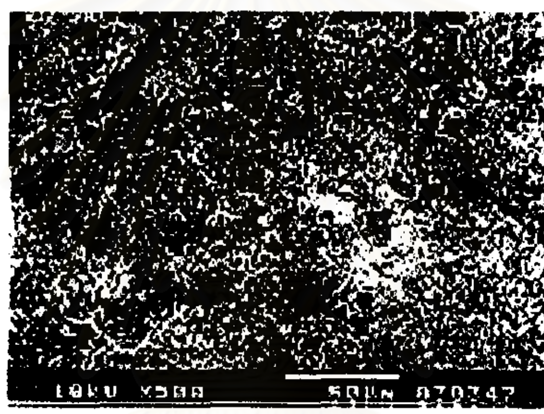
(B)

(C)

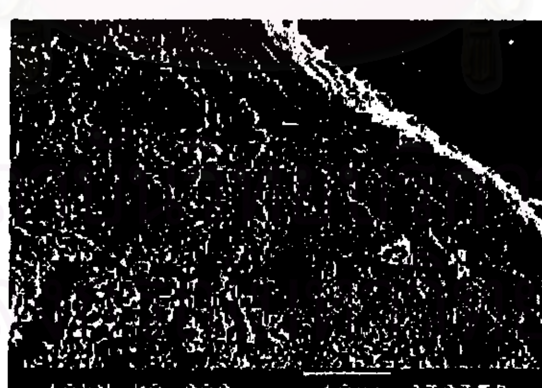
Figure 22 The photomicrographs of 21.20 % Eudragit®NE 30D lot B coated granules using top spray method. (A : coated granules x 35 , B : coated surface x 500, C : cross-section x 2000).



(A)



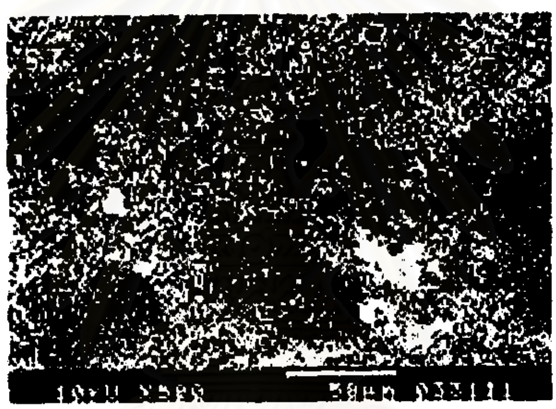
(B)



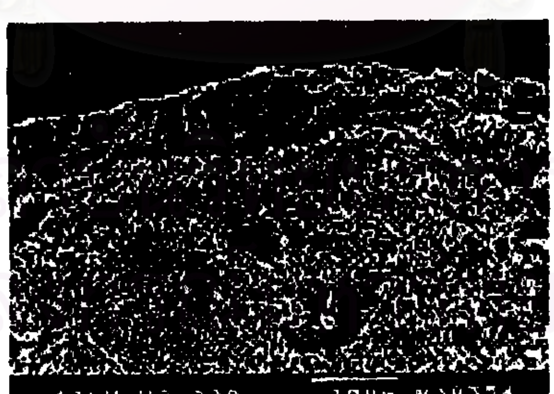
(C)

Figure 23 The photomicrographs of 4.16 % Eudragit®NE 30D lot B coated granules using bottom spray method. (A : coated granules x 35 , B : coated surface x 500, C : cross-section x 2000).

(A)



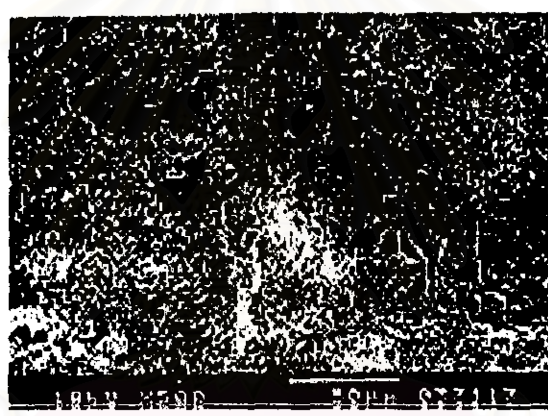
(B)



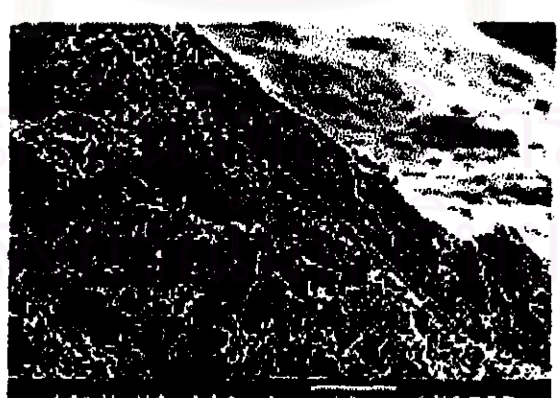
(C)

Figure 24 The photomicrographs of 6.61 % Eudragit®NE 30D lot B coated granules using bottom spray method. (A : coated granules x 35 , B : coated surface x 500, C : cross-section x 2000).

(A)



(B)

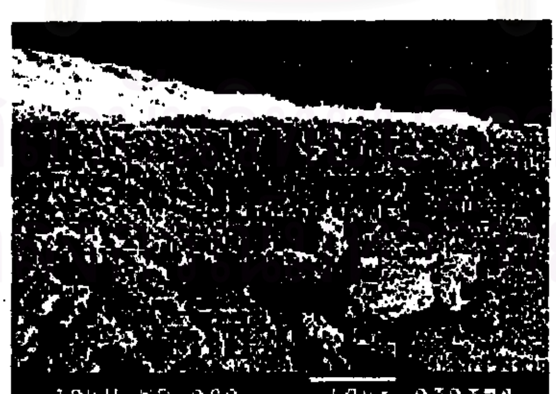


(C)

Figure 25 The photomicrographs of 7.97 % Eudragit®NE 30D lot B coated granules using bottom spray method. (A : coated granules x 35 , B : coated surface x 500, C : cross-section x 2000).

(A)

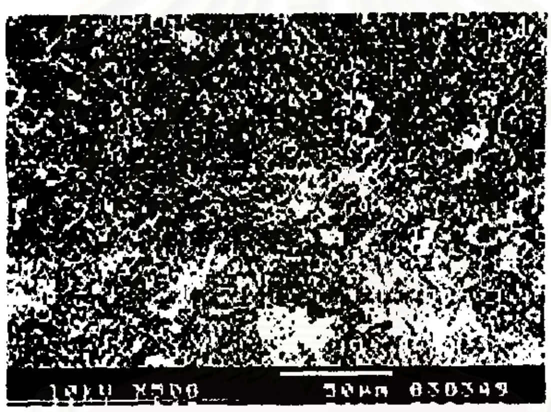
(B)



(C)

Figure 26 The photomicrographs of 8.78 % Eudragit®NE 30D lot B coated granules using bottom spray method. (A : coated granules x 35 , B : coated surface x 500, C : cross-section x 2000).

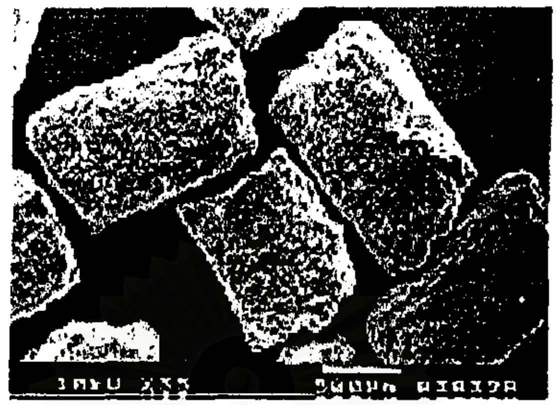
(A)



(B)

(C)

Figure 27 The photomicrographs of 11.49 % Eudragit®NE 30D lot B coated granules using bottom spray method. (A : coated granules x 35 , B : coated surface x 500, C : cross-section x 2000).

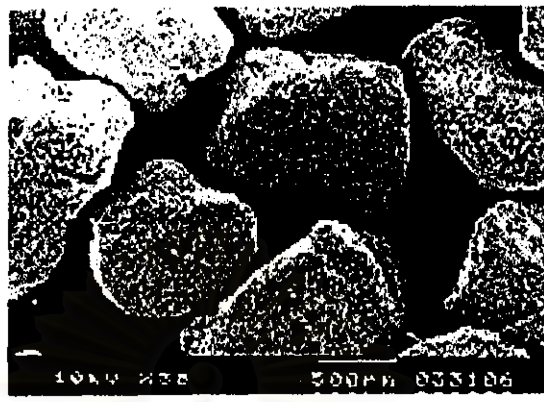


(A)

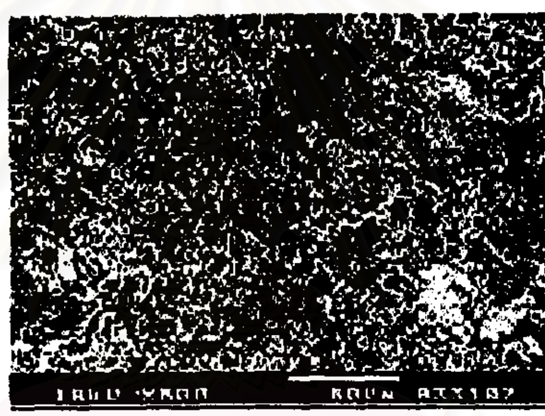
(B)

(C)

Figure 28 The photomicrographs of 10 % Eudragit®NE 30D coated granules using atomizing air pressure at 1 bar. (A : coated granules x 35 , B : coated surface x 500 , C : cross-section x 2000).



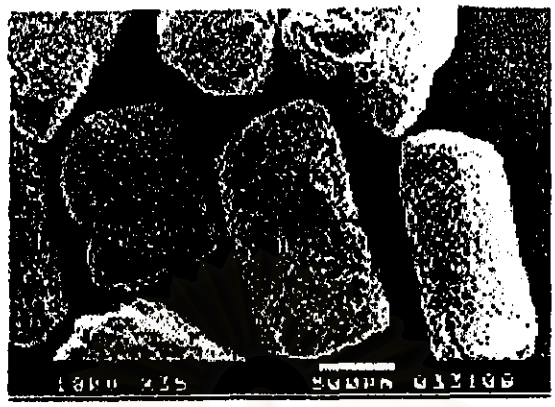
(A)



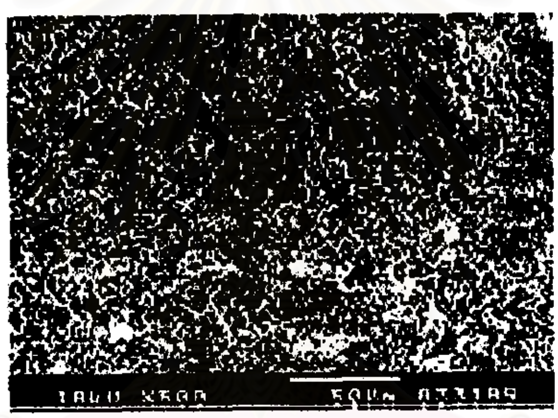
(B)

(C)

Figure 29 The photomicrographs of 10 % Eudragit®NE 30D coated granules using atomizing air pressure at 2 bar. (A : coated granules x 35 , B : coated surface x 500 , C : cross-section x 2000).



(A)

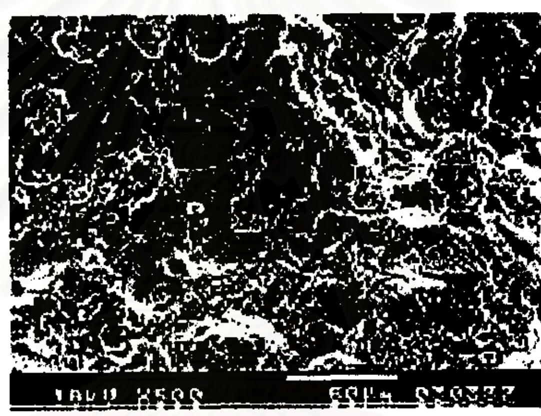


(B)

(C)

Figure 30 The photomicrographs of 10 % Eudragit®NE 30D coated granules using atomizing air pressure at 3 bar. (A : coated granules x 35 , B : coated surface x 500 , C : cross-section x 2000).

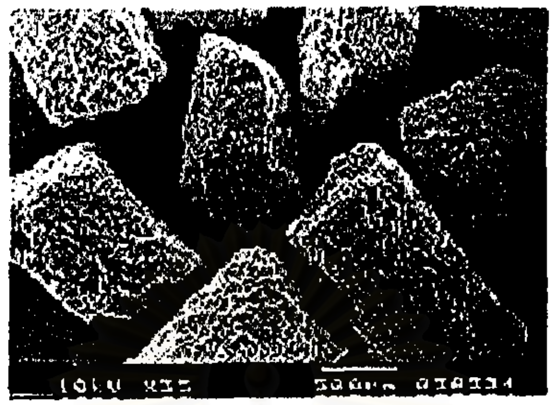
(A)



(B)

(C)

Figure 31 The photomicrographs of 10 % Eudragit® NE 30D / HPMC in ratio 3:2 coated granules. (A : coated granules x 35 , B : coated surface x 500 , C : cross-section x 2000).

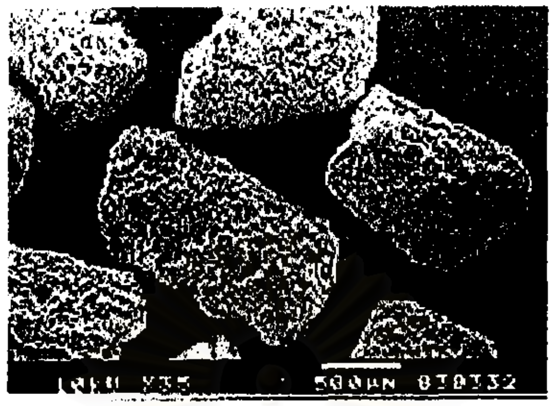


(A)

(B)

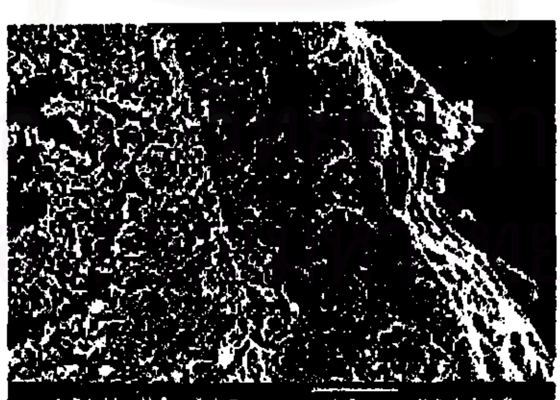
(C)

Figure 32 The photomicrographs of 10 %Eudragit® NE 30D / HPMC in ratio 3:1.5 coated granules. (A : coated granules x 35 , B : coated surface x 500 , C : cross-section x 2000).



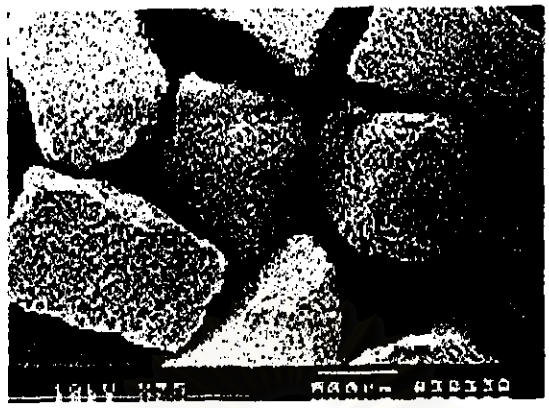
(A)

(B)

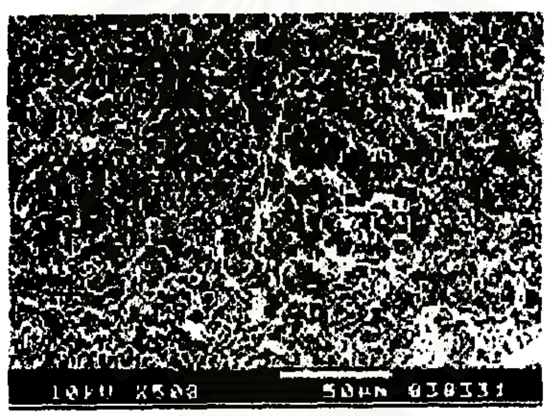


(C)

Figure 33 The photomicrographs of 10 % Eudragit® NE 30D / HPMC in ratio 3:1 coated granules. (A : coated granules x 35 , B : coated surface x 500 , C : cross-section x 2000).



(A)



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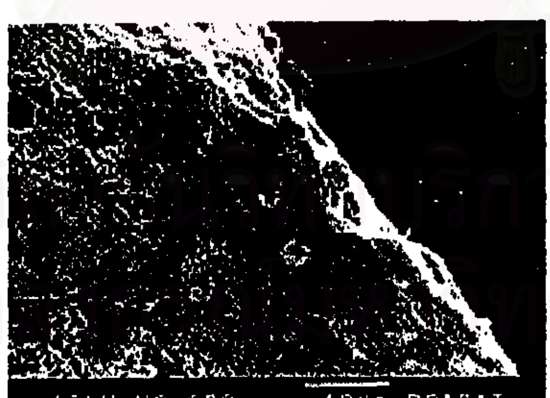
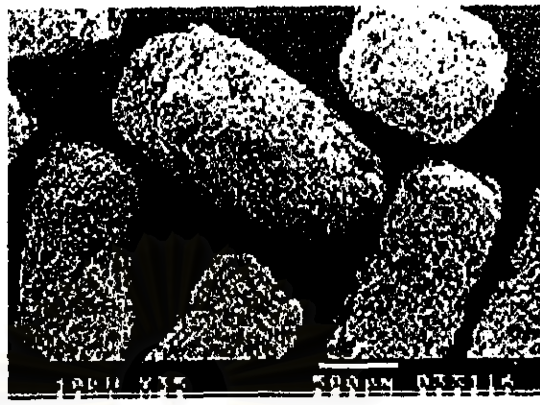
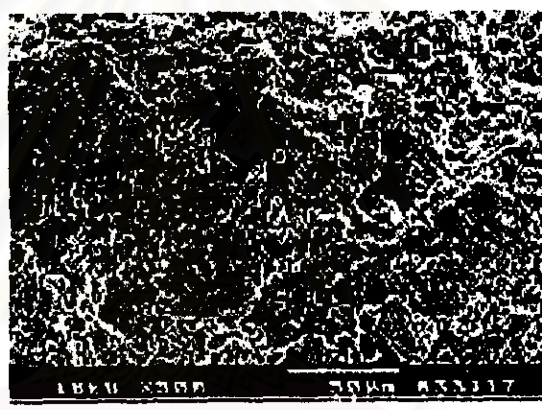


(C)

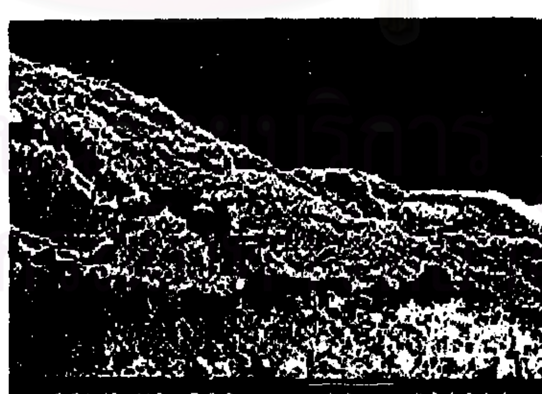
Figure 34 The photomicrographs of 10 % Eudragit® NE 30D / HPMC in ratio 3:0.5 coated granules. (A : coated granules x 35 , B : coated surface x 500 , C : cross-section x 2000).



(A)

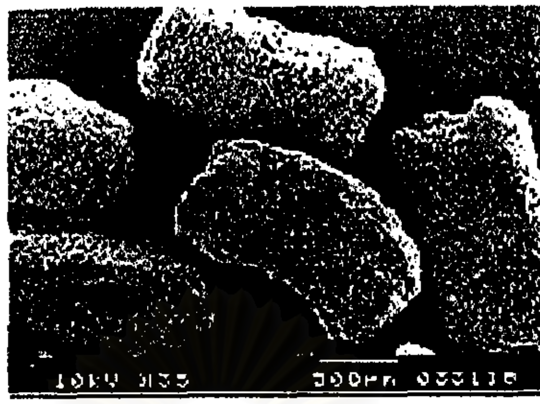


(B)

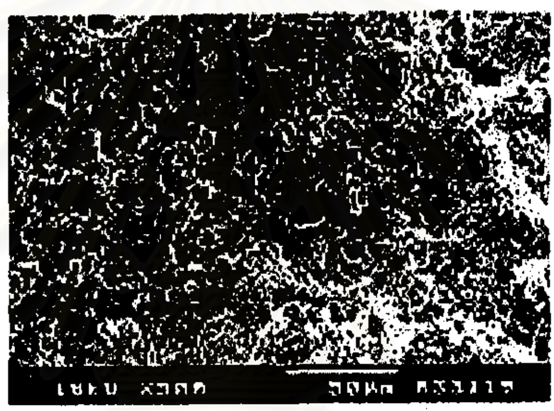


(C)

Figure 35 The photomicrographs of 10 % Eudragit®NE 30D / HPMC in ratio 12.5:1 coated granules. (A : coated granules x 35 , B : coated surface x 500 , C : cross-section x 2000).



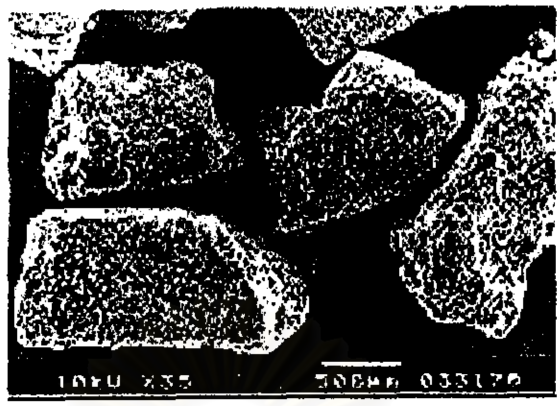
(A)



(B)

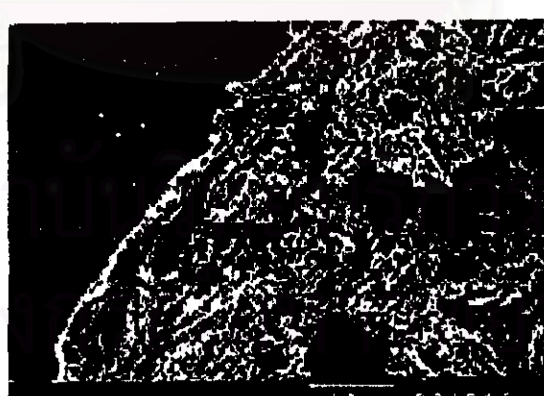
(C)

Figure 36 The photomicrographs of 10 % Eudragit®NE 30D/HPMC in ratio12.5:0.5 coated granules. (A : coated granules x 35 , B : coated surface x 500 , C : cross-section x 2000).



(A)

(B)

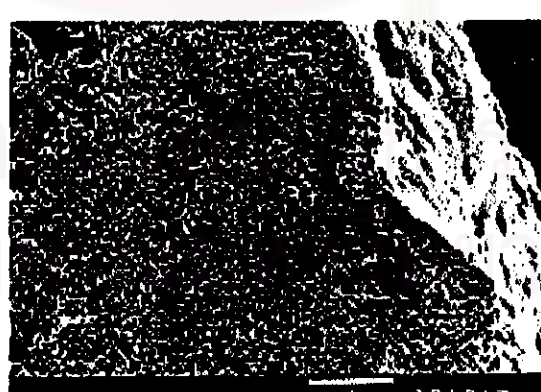


(C)

Figure 37 The photomicrographs of 10 % Eudragit®NE 30D / HPMC in ratio 100:1 coated granules. (A : coated granules x 35 , B : coated surface x 500 , C : cross-section x 2000).

(A)

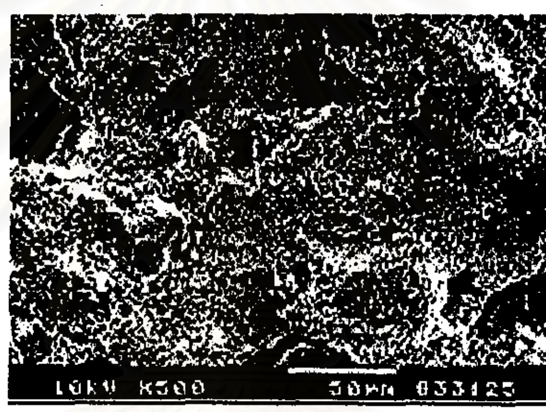
(B)



(C)

Figure 38 The photomicrographs of 10 % Eudragit®NE 30D / RL 30D in ratio 50:50 coated granules. (A : coated granules x 35 , B : coated surface x 500 , C : cross-section x 2000).

(A)



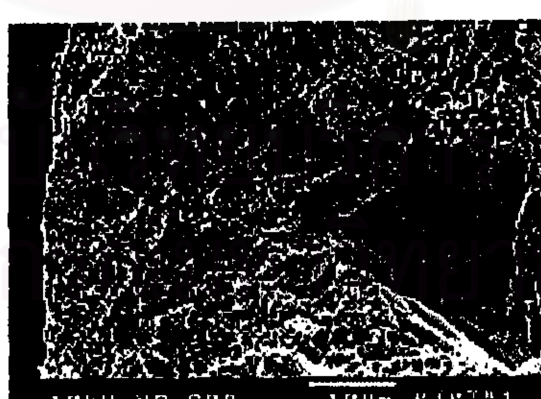
(B)

(C)

Figure 39 The photomicrographs of 10 % Eudragit® NE 30D / RL 30D in ratio 80:20 coated granules. (A : coated granules x 35 , B : coated surface x 500 , C : cross-section x 2000).

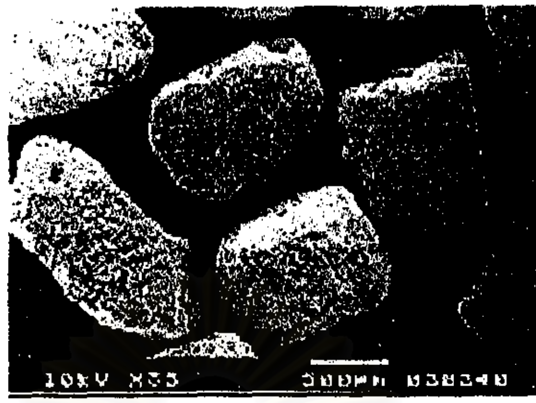
(A)

(B)

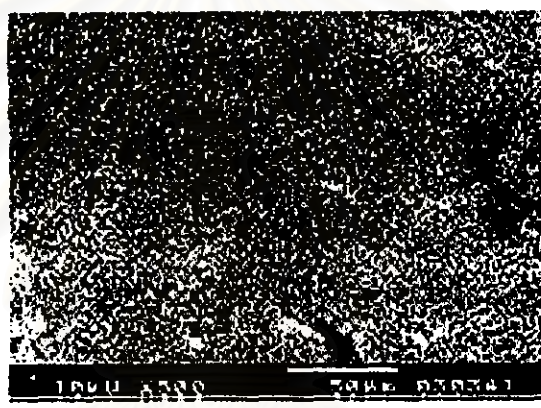


(C)

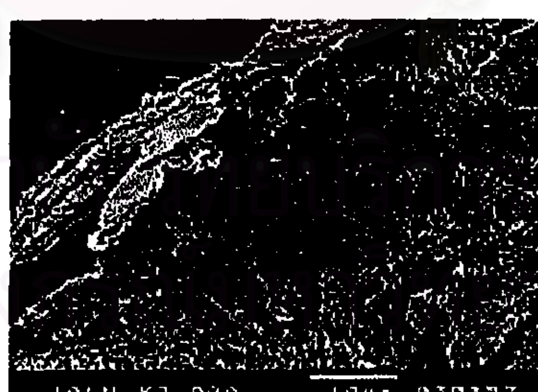
Figure 40 The photomicrographs of 10 % Eudragit® NE 30D / RL 30D in ratio 90:10 coated granules. (A : coated granules x 35 , B : coated surface x 500 , C : cross-section x 2000).



(A)



(B)



(C)

Figure 41 The photomicrographs of 10 % Eudragit®NE 30D / RL 30D in ratio 95:5 coated granules. (A : coated granules x 35 , B : coated surface x 500 , C : cross-section x 2000).

2.2 Bulk Densities, Tapped Densities and Carr's Compressibilities of Theophylline Granules

The bulk density and tapped density of uncoated theophylline granules were 0.54 and 0.56 g/ml, respectively as shown in Table 6. For coated granules, the bulk densities and tapped densities of granules coated with various levels of Eudragit®NE 30D using top spray and bottom spray method were not much affected as shown in Tables 7 and 8.

The bulk densities and tapped densities of granules coated with different atomizing air pressure were illustrated in Table 9. It was observed that the atomizing air pressure had no effect on both of densities.

In addition, the bulk densities and tapped densities of granules coated with polymer blends containing various ratios of Eudragit®NE 30D/HPMC or Eudragit® NE 30D/RL 30D were also not apparently different as presented in Tables 10 and 11, respectively.

The percent compressibility of uncoated granules was 4.15 % and those of all coated granules are shown in Tables 7-11. For these obtained results, it could not be concluded .

2.3 Moisture Contents of Theophylline Granules

The moisture content of uncoated granules was 0.61% as shown in Table 6. When granules were coated with different levels and lot of Eudragit®NE 30D using top spray and bottom spray method or coated with polymer blends containing various ratios of Eudragit® NE 30D/HPMC or Eudragit®NE 30D/RL 30D, their moisture contents were not much different and were in a range of 0.62-0.76% as presented in Tables 7-11.

2.4 Flow Rates and Angles of Repose of Theophylline Granules

The flow rate of uncoated was 10.83 g/sec. as presented in Table 6 and those of all Eudragit®NE 30D coated granules are shown in Tables 7 and 8. It was notable that the coating level had no effect on the flow rate for both of spraying methods. However, the bottom-spray coated granules were found to have faster flow rates when it was compared with the top-spray coated granules.

For granules coated with different atomizing air pressure, their flow rates were not much affected as shown in Table 9.

When coated with polymer blends containing various ratios of Eudragit®NE 30D/HPMC or Eudragit®NE 30D/RL 30D, their flow rates were also not apparently different as illustrated in Tables 10 and 11.

The angles of repose of uncoated and all Eudragit®NE 30D coated granules are reported in Tables 6-9. It was found that the angles of repose of top-spray coated granules were within a range of 30-38° which indicated good flow whereas those of bottom-spray coated granules were within a range of 25-30° which indicated excellent flow as shown in Table 12.

The angles of repose of granules coated with polymer blends containing various ratios of Eudragit®NE 30D/HPMC or Eudragit®NE 30D/RL 30D are shown in Tables 10 and 11. They were not much different and were within a range of 25-30° which indicated excellent flow as shown in Table 12.

Table 6 Physical properties of uncoated theophylline granules.

Physical properties	Mean value (SD)
Bulk density (g/ml)	0.54 (0.01)
Tapped density (g/ml)	0.56 (0.02)
Carr's index (%)	4.15
Flow rate (g/sec.)	10.83 (0.18)
Angle of repose (x °)	30.39 (0.44)
Moisture content (%)	0.61 (0.05)

Table 7 **Physical properties of top-spray Eudragit®NE 30D coated granules.**

Lot of Eudragit	Percent coated	Bulk density (g/ml)	Tapped density (g/ml)	Carr's index (%)	Flow rate (g/sec.)	Angle of repose (x °)	Moisture content (%)
A	1.55	0.51(0.01)	0.52(0.00)	2.73	12.87(0.53)	32.95(0.28)	0.69(0.01)
	4.66	0.52(0.01)	0.54(0.00)	3.20	12.23(0.29)	32.05(1.47)	0.72(0.02)
	5.40	0.52(0.01)	0.53(0.02)	2.77	12.05(0.33)	32.07(0.80)	0.74(0.01)
	8.75	0.52(0.02)	0.53(0.02)	3.38	11.72(0.57)	32.52(1.01)	0.76(0.03)
	10.83	0.52(0.01)	0.53(0.03)	2.87	12.95(0.64)	32.77(0.20)	0.75(0.01)
	13.25	0.52(0.02)	0.54(0.01)	3.70	11.83(0.57)	32.76(0.88)	0.76(0.02)
B	4.28	0.53(0.01)	0.55(0.01)	3.91	13.00(0.45)	31.58(0.93)	0.73(0.07)
	7.18	0.53(0.02)	0.55(0.01)	3.84	11.62(0.41)	33.10(0.74)	0.69(0.04)
	7.85	0.52(0.01)	0.54(0.01)	3.62	13.28(0.75)	32.75(0.88)	0.72(0.05)
	8.75	0.53(0.01)	0.55(0.04)	3.61	11.78(0.49)	33.10(0.74)	0.71(0.05)
	10.60	0.54(0.03)	0.57(0.01)	4.08	11.31(0.62)	32.14(0.56)	0.70(0.01)
	13.51	0.54(0.01)	0.56(0.03)	3.06	12.68(0.91)	32.00(0.84)	0.68(0.06)
	21.20	0.54(0.04)	0.56(0.02)	3.99	12.08(1.09)	32.03(0.53)	0.71(0.04)

*** (SD in parenthesis)**

Table 8 **Physical properties of bottom-spray Eudragit®NE 30D coated granules.**

Percent coated	Bulk density (g/ml)	Tapped density (g/ml)	Carr's index (%)	Flow rate (g/sec.)	Angle of repose (x °)	Moisture content (%)
4.16	0.56(0.00)	0.58(0.02)	3.45	16.93(0.98)	29.59(0.90)	0.68(0.01)
6.61	0.56(0.01)	0.58(0.02)	3.74	17.26(0.76)	27.85(1.19)	0.67(0.03)
7.97	0.58(0.03)	0.60(0.01)	3.36	18.97(0.89)	28.36(0.79)	0.76(0.02)
8.78	0.57(0.02)	0.60(0.01)	4.08	17.97(0.19)	27.55(0.18)	0.76(0.03)
11.49	0.57(0.02)	0.59(0.03)	3.98	16.46(0.41)	29.35(1.18)	0.70(0.03)

*** (SD in parenthesis)**

Table 9 Physical properties of Eudragit®NE 30D coated granules using different atomizing air pressure.

Atomizing pressure (bar)	Bulk density (g/ml)	Tapped density (g/ml)	Carr's index (%)	Flow rate (g/sec.)	Angle of repose (x°)	Moisture content (%)
1	0.52(0.01)	0.53(0.01)	2.87	12.95(0.64)	32.77(0.20)	0.75(0.01)
2	0.55(0.02)	0.57(0.01)	3.45	12.56(0.89)	30.81(0.39)	0.75(0.02)
3	0.55(0.02)	0.58(0.01)	3.68	13.10(0.57)	30.28(1.30)	0.75(0.01)

* (SD in parenthesis)

Table 10 Physical properties of Eudragit®NE 30D/HPMC coated granules.

Ratio of Eudragit / HPMC	Bulk density (g/ml)	Tapped density (g/ml)	Carr's index (%)	Flow rate (g/sec.)	Angle of repose (x°)	Moisture content (%)
3:2	0.53(0.02)	0.57(0.01)	6.92	12.32(1.47)	28.05(0.87)	0.65(0.04)
3:1.5	0.53(0.01)	0.56(0.03)	5.15	11.49(1.07)	29.39(0.01)	0.66(0.06)
3:1	0.55(0.01)	0.59(0.02)	7.01	12.65(0.78)	28.69(0.63)	0.70(0.07)
3:0.5	0.56(0.04)	0.59(0.02)	5.41	13.00(0.74)	29.18(0.85)	0.62(0.07)
12.5:1	0.53(0.02)	0.56(0.03)	5.76	13.54(0.40)	28.78(0.61)	0.64(0.05)
12.5:0.5	0.54(0.02)	0.56(0.01)	4.47	13.37(1.46)	29.54(0.89)	0.66(0.03)
100:1	0.54(0.01)	0.56(0.01)	3.41	11.49(1.09)	29.62(0.89)	0.65(0.02)

* (SD in parenthesis)

Table 11 Physical properties of Eudragit®NE 30D/RL 30D coated granules.

Ratio of NE 30D / RL 30D	Bulk density (g/ml)	Tapped density (g/ml)	Carr's index (%)	Flow rate (g/sec.)	Angle of repose (x°)	Moisture content (%)
50:50	0.54(0.01)	0.58(0.01)	7.27	11.43(0.38)	28.97(0.28)	0.75(0.05)
80:20	0.51(0.01)	0.55(0.02)	7.51	11.02(0.32)	28.59(1.17)	0.71(0.03)
90:10	0.56(0.01)	0.61(0.02)	8.62	11.71(0.78)	29.75(0.87)	0.62(0.04)
95:5	0.55(0.02)	0.60(0.03)	8.31	10.62(0.30)	26.19(0.32)	0.64(0.01)

* (SD in parenthesis)

Table 12 The angle of repose of the granules.

Angle of repose (x°)	Flowability
25 - 30	excellent flow
30 - 38	good flow
38 - 45	fair flow
45 - 55	poor flow
55 - 70	very poor flow
> 70	very very poor flow

2.5 Specific Surface Area of Theophylline Granules

The specific surface area of theophylline granules coated with various levels of Eudragit®NE 30D lot B using different spraying method, top spray and bottom spray method, are presented in Table 13. Increasing the level of coating decreased the specific surface area of bottom-spray coated granules. It could be seen that the coating level might affect the specific surface area of coated granules. In case of top-spray coated granules, the specific surface area were decreased from 1.26 to 1.03 and 0.95 m^2/g when the coating levels were increased from 4.28% to 8.75% and 10.60% respectively. However, at higher coating level of top-spray coated granules, the specific surface area were increased as the coating level increased. The highest specific surface area of top-spray coated granules was obtained from the 21.20% coated granules.

Comparison to the bottom-spray coated granules which were coated at the same level, it seem to be that the top-spray coated granules demonstrated higher specific surface area.

Table 13 Specific surface area of Eudragit®NE 30D lot B coated granules.

Spraying method	Percent coated	Specific surface area ($m^2/g \pm SD$)
Top spray method	4.28	1.26 ± 0.04
	8.75	1.03 ± 0.01
	10.60	0.95 ± 0.02
	13.51	1.07 ± 0.03
	21.20	1.30 ± 0.01
Bottom spray method	4.16	1.03 ± 0.01
	8.78	0.91 ± 0.01
	11.49	0.77 ± 0.20

2.6 Dissolution Study of Theophylline Granules

The dissolution data of all theophylline granules studied by basket method in phosphate buffer pH 6.6 are shown in Tables 26-33 (Appendix B). From these data, the dissolution or the release profiles could be plotted between the percentage of amount of drug release against time. Then, the change of release rate profile was constructed from the dissolution profile to elucidate the release rate at various time interval during the cause of drug dissolution from granules.

The release rate was calculated by dividing the difference of percent drug release at various time interval with the time utilized to release that certain amount of the drug. The release rate data of all granules are tabulated in Tables 34-40 (Appendix B). The rate, then, was plotted with the mid point of the time interval.

2.6.1 Uncoated Granules

The dissolution data of theophylline from uncoated granules are listed in Table 26 (Appendix B) and are shown graphically in Figure 42. The average percentage of drug release was nearly 100 % within 15 minutes. The release rate profile of uncoated granules is tabulated in Table 34 (Appendix B) and shown graphically in Figure 43.

2.6.2 Eudragit®NE 30D Coated Granules Using Different Spraying Method

The dissolution profiles of theophylline from granules coated with various levels of Eudragit®NE 30D using different spraying method are shown in Figures 44, 46 and 48 (Tables 28-30 , Appendix B). Figures 44 and 46 illustrate the dissolution profiles of top-spray coated granules which were applied with different lot of Eudragit®NE 30D, that is, lot A and lot B, respectively whereas Figure 48 is the

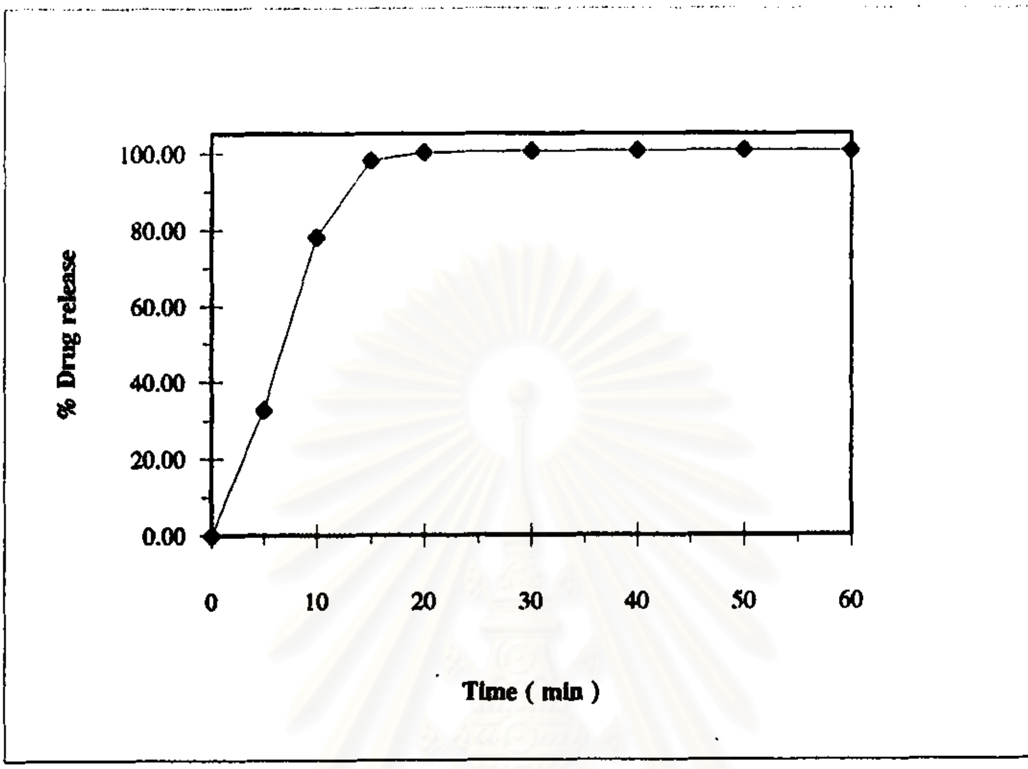


Figure 42 The release profile of uncoated theophylline granules.

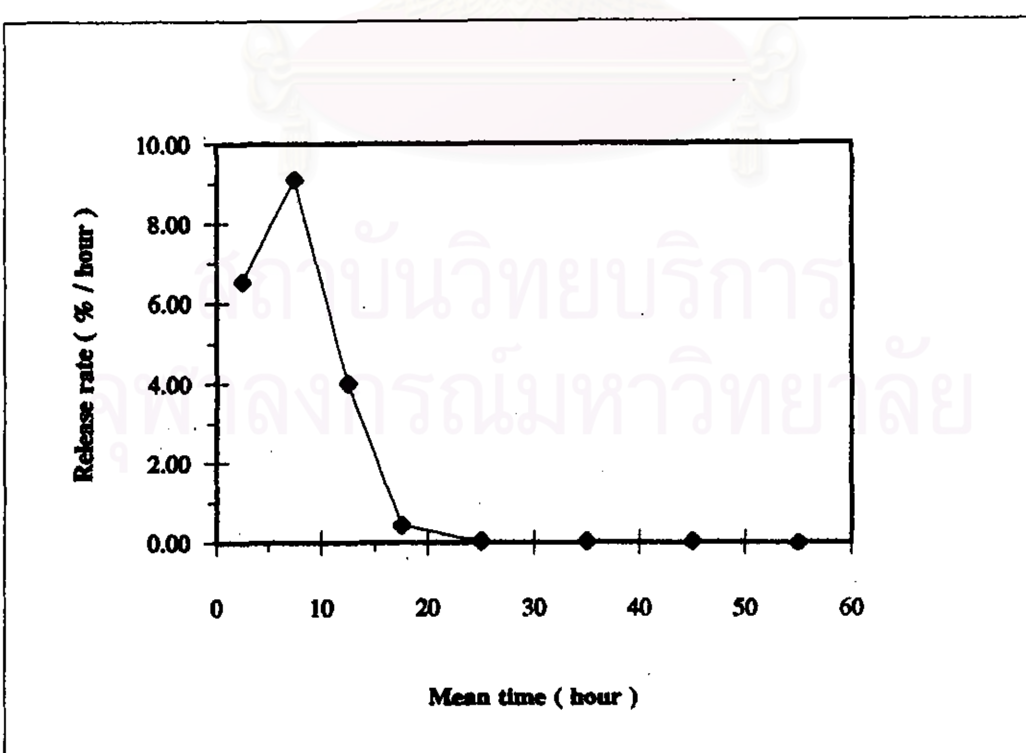


Figure 43 The release rate profile of uncoated theophylline granules.

dissolution profiles of bottom-spray coated granules. The release rate profiles of these coated granules are shown in Figures 45, 47 and 49 (Tables 35-37, Appendix B).

In Figure 44, it was notable that increasing the percent coating level resulted in a corresponding decrease of the drug release from the top-spray Eudragit®NE 30D lot A coated granules. This result were similar to that obtained from the top-spray Eudragit®NE 30D lot B coated granules and bottom-spray coated granules as shown in Figures 46 and 48, respectively. However, complete drug release was not received on the 24th hours of experiment from the granules coated with Eudragit®NE 30D lot A at 8.75 %, 10.83 % and 13.25 % coating level using top spray method as shown in Figure 45. Whereas, the percentages of theophylline release from top-spray Eudragit® NE 30D lot B coated granules were more than 90 % of total capacity within 12 hours in every coating levels as shown in Figure 46.

The release rate profiles of top-spray Eudragit®NE 30D lot A coated granules are shown in Figure 45. It was observed that the release rate of 1.55 %, 4.66 % and 5.40 % coated granules decreased as the time increased whereas that of 8.75 %, 10.83 % and 13.25 % coated granules was nearly constant. The release rate of top-spray Eudragit®NE 30D lot B coated granules and bottom-spray coated granules decreased with the time increased as shown in Figures 47 and 49 respectively.

A. Influence of Different Lot of Eudragit®NE 30D on the Dissolution Profiles of Coated Granules

Theophylline granules coated with Eudragit®NE 30D lot A and lot B using top spray method were evaluated for the influence of different lot of polymer on the release profiles of the same level of coated granules. The comparative release profiles of Eudragit®NE 30D lot A and lot B coated granules at the same coating level are shown graphically in Figures 50-52. Figure 50 shows release profiles of theophylline granules coated with approximately 4 % coating level (4.66 % and

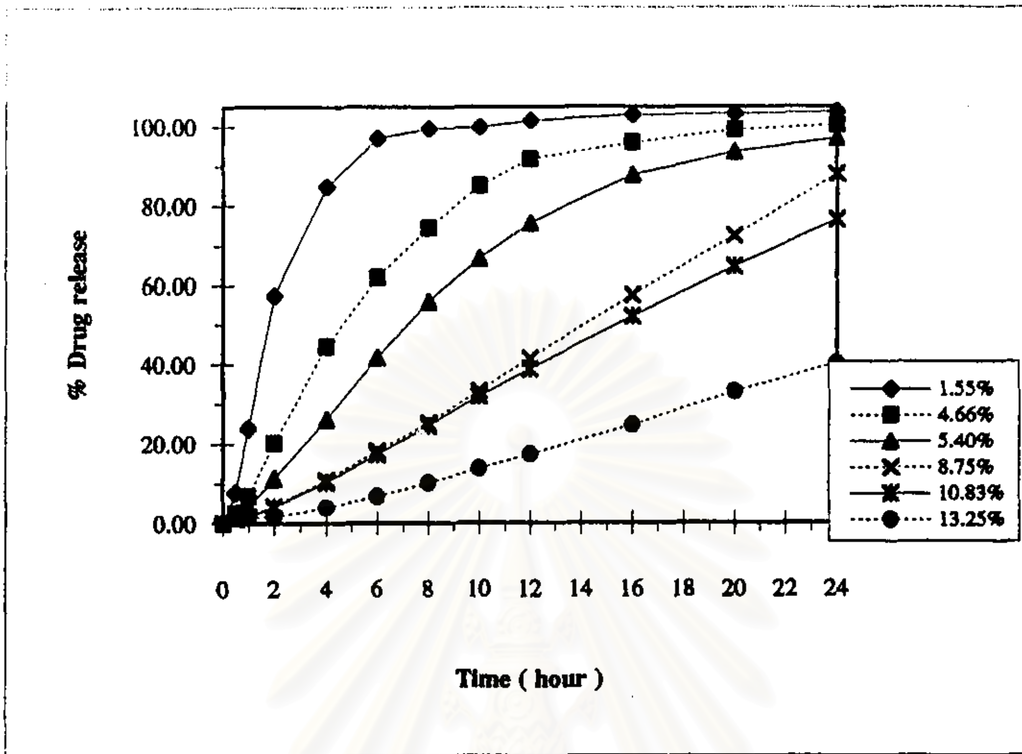


Figure 44 The release profiles of theophylline granules coated with Eudragit(R) NE 30D lot A using top spray method.

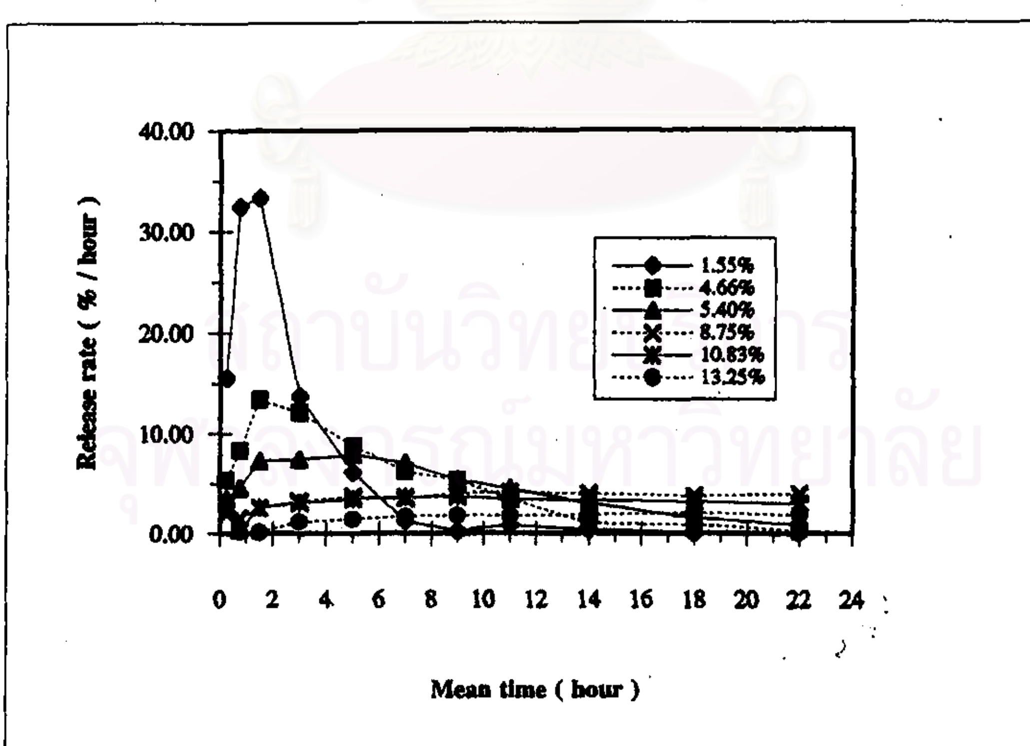


Figure 45 The release rate profiles of theophylline granules coated with Eudragit(R) NE 30D lot A using top spray method.

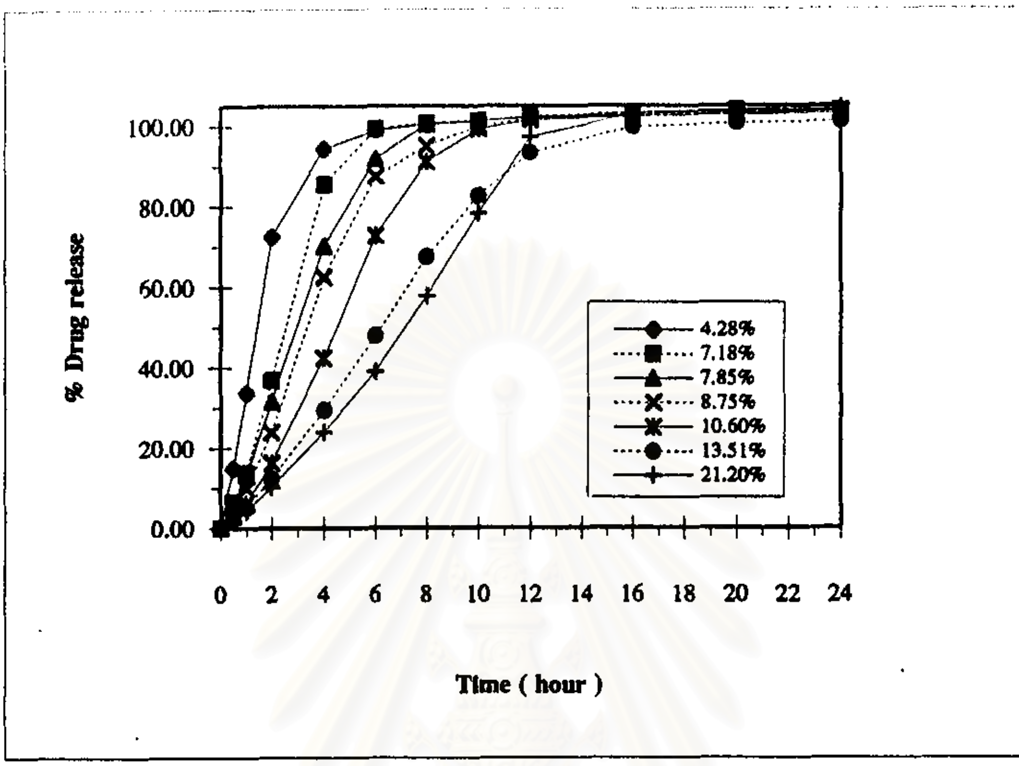


Figure 46 The release profiles of theophylline granules coated with Eudragit(R) NE 30D lot B using top spray method.

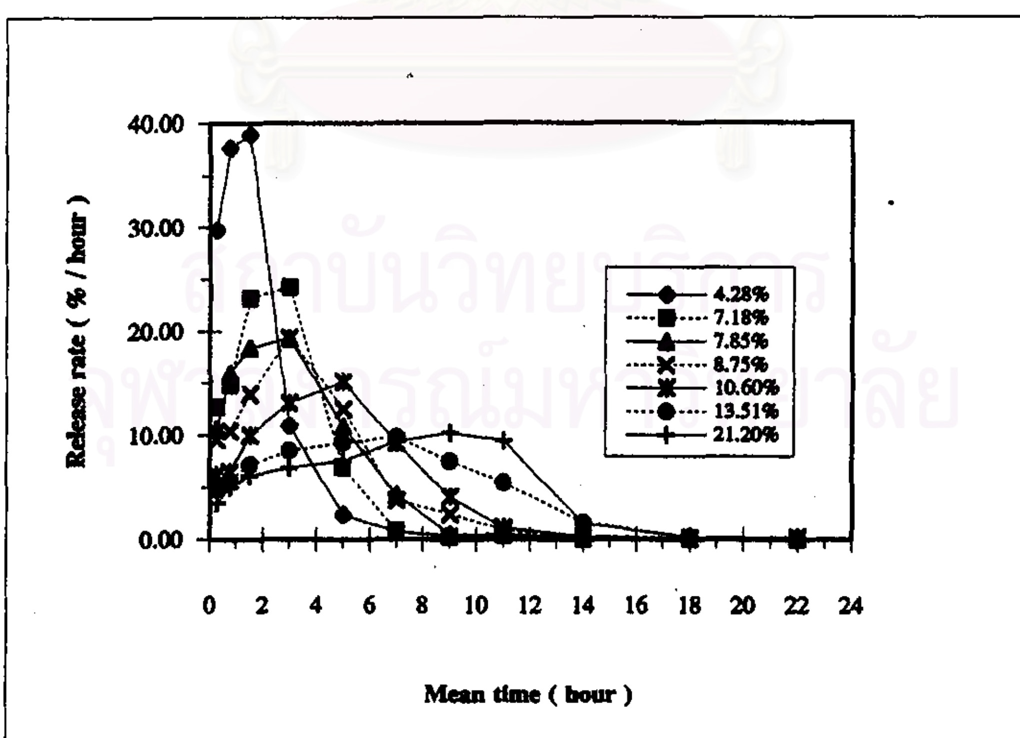


Figure 47 The release rate profiles of theophylline granules coated with Eudragit(R) NE 30D lot B using top spray method.

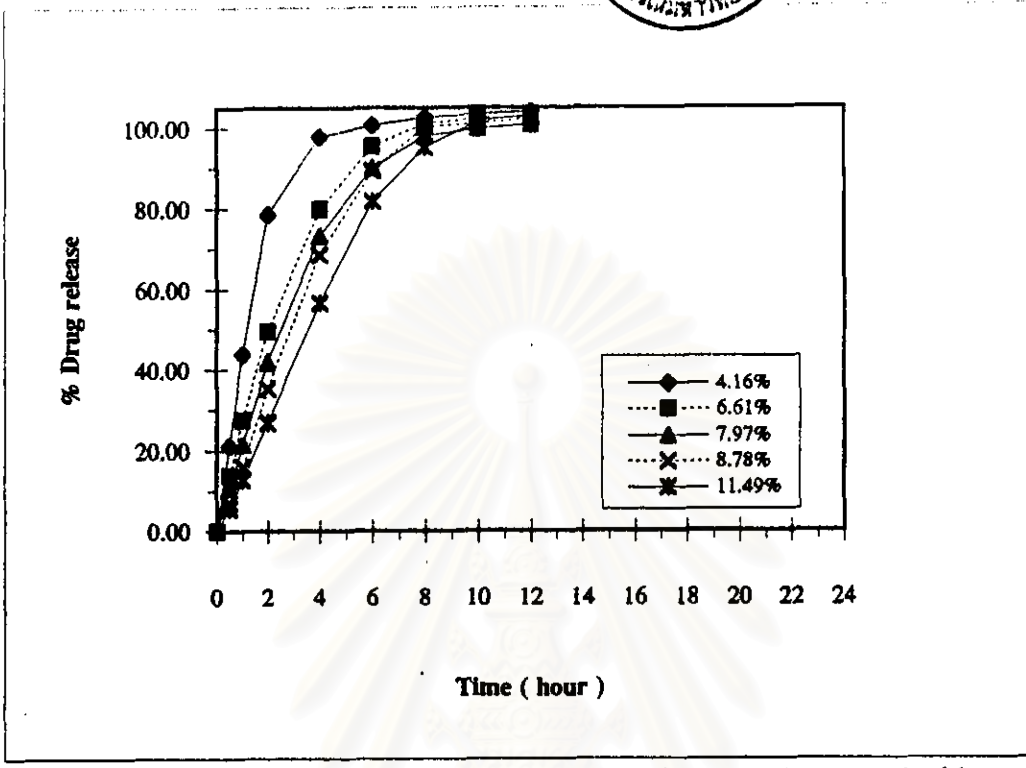


Figure 48 The release profiles of theophylline granules coated with Eudragit$^{(R)}$ NE 30D lot B using bottom spray method.

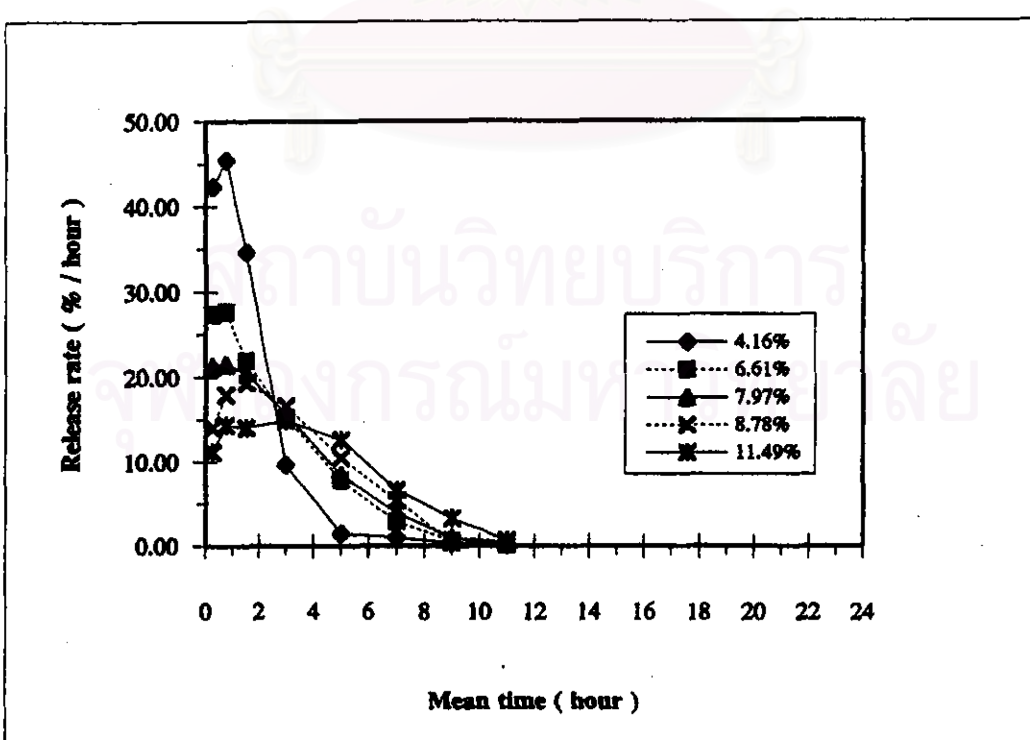


Figure 49 The release rate profiles of theophylline granules coated with Eudragit$^{(R)}$ NE 30D lot B using bottom spray method.

4.28 %), Figure 51 illustrates release profiles of theophylline granules coated with approximately 8 % coating level (8.75 % and 8.75 %) and Figure 52 is release profiles of theophylline granules coated with approximately 10 % coating level (10.83 % and 10.60 %).

Each pair of drug release profiles showed statistical significance as shown in Table 51 (Appendix C). From the resultant data, slower release profile was obtained from theophylline granules coated with Eudragit®NE 30D lot A.

B. Influence of Different Spray Method on the Dissolution Profiles of Eudragit®NE 30D Coated Granules

Top-spray and bottom-spray Eudragit®NE 30D lot B coated granules were evaluated for the influence of different spraying method on the release profiles of the same level of coated granules. The comparative release profiles of top-spray and bottom-spray coated granules at the same coating level are shown graphically in Figures 53-55. Figure 53 shows release profiles of theophylline granules coated with approximately 4 % coating level (4.28 % and 4.16 %), Figure 54 illustrates release profiles of theophylline granules coated with approximately 7 % coating level (7.85 % and 7.97 %) and Figure 55 is release profiles of theophylline granules coated with approximately 8 % (8.75 % and 8.78 %).

Each pair of drug release profiles showed no statistical significance as shown in Table 52 (Appendix C). From the obtained results, the release profile of drug from top-spray coated granules had no difference to that from bottom-spray coated granules.

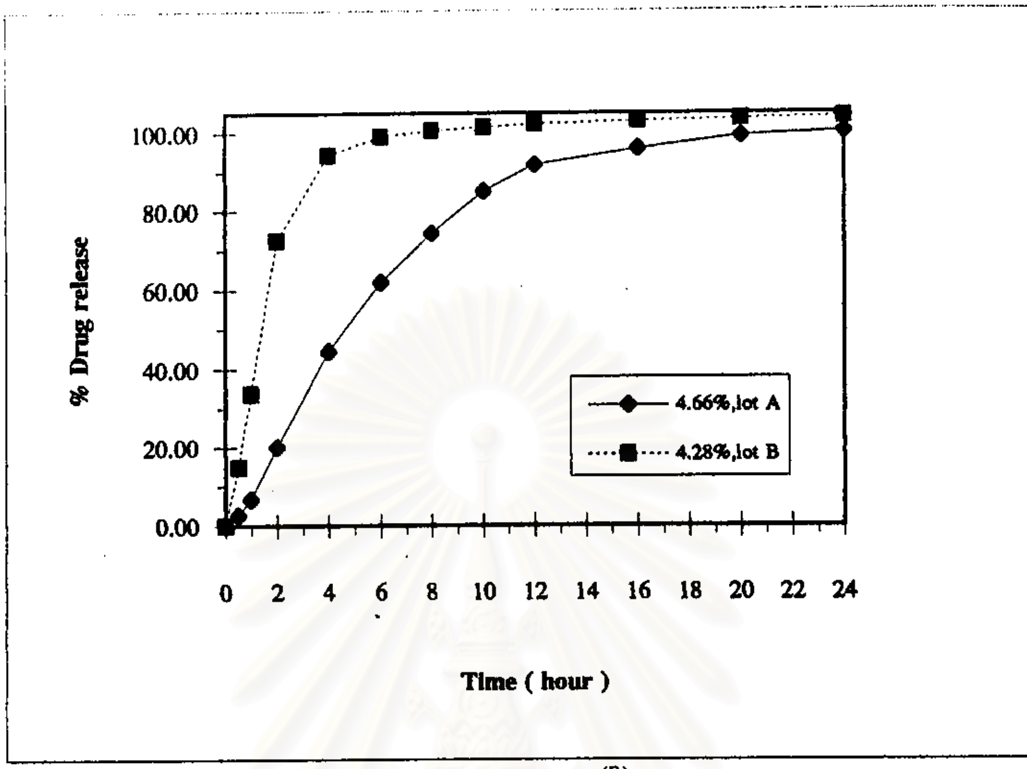


Figure 50 Influence of different lot of Eudragit(R)NE 30D in about 4% coating level on the theophylline granules release profiles from coated granules.

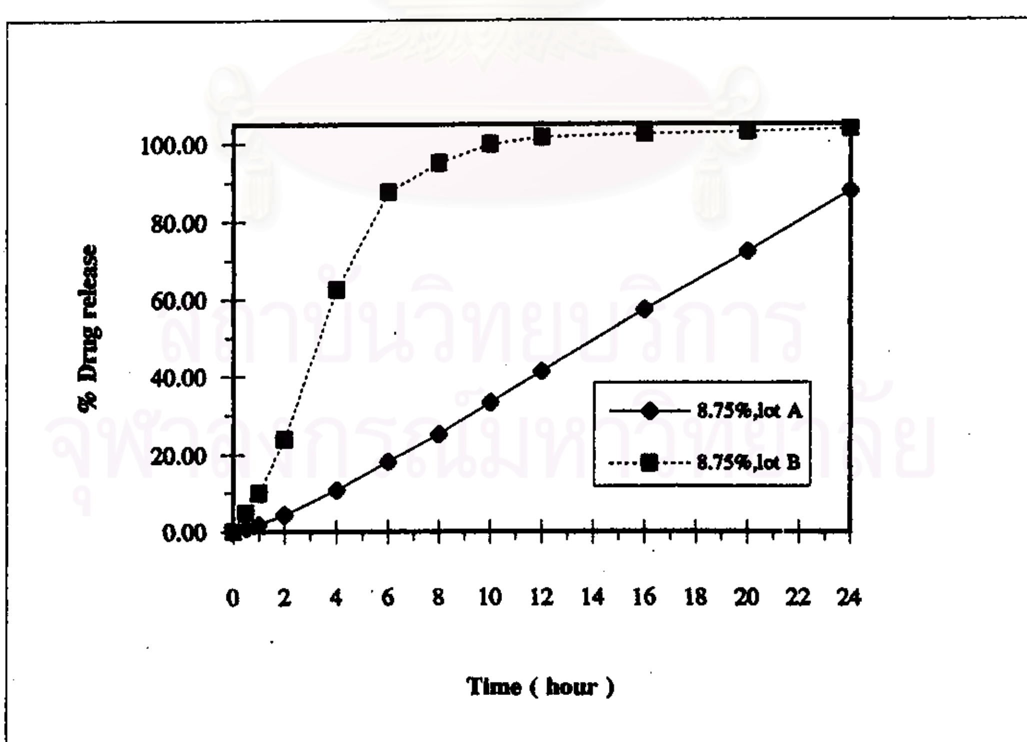


Figure 51 Influence of different lot of Eudragit(R)NE 30D in about 8% coating level on the theophylline granules release profiles from coated granules.

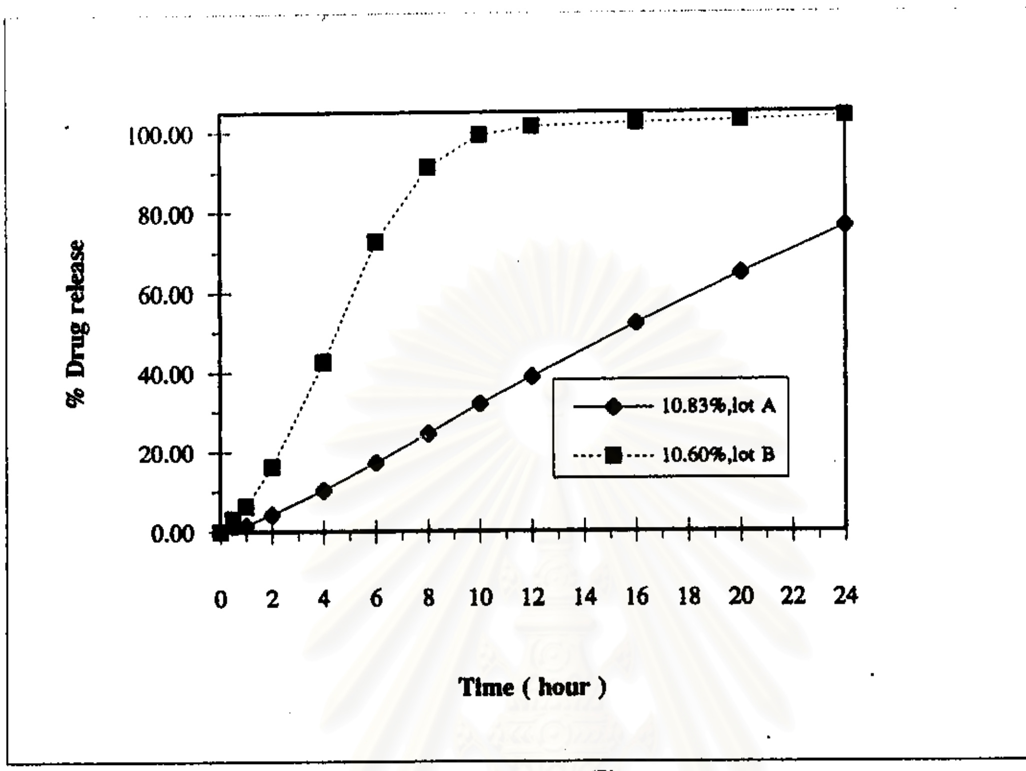


Figure 52 Influence of different lot of Eudragit(R) NE 30D in about 10% coating level on the theophylline granules release profiles from coated granules.

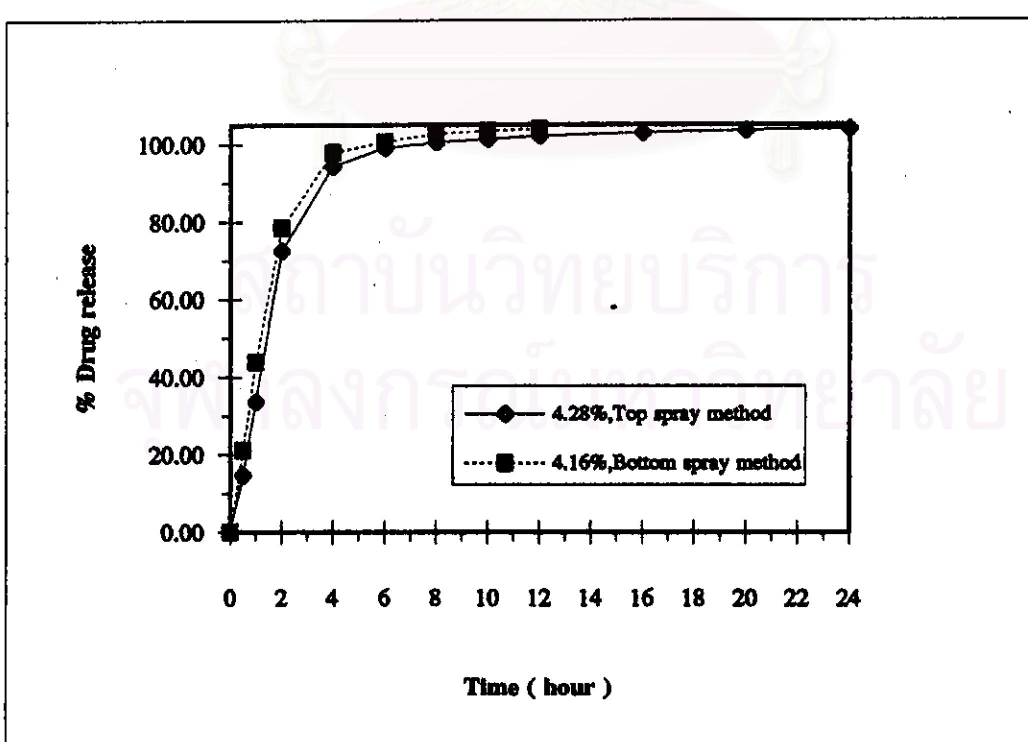


Figure 53 Influence of different spraying method in about 4% coating level of Eudragit NE 30D on the theophylline granules release profiles from coated granules.

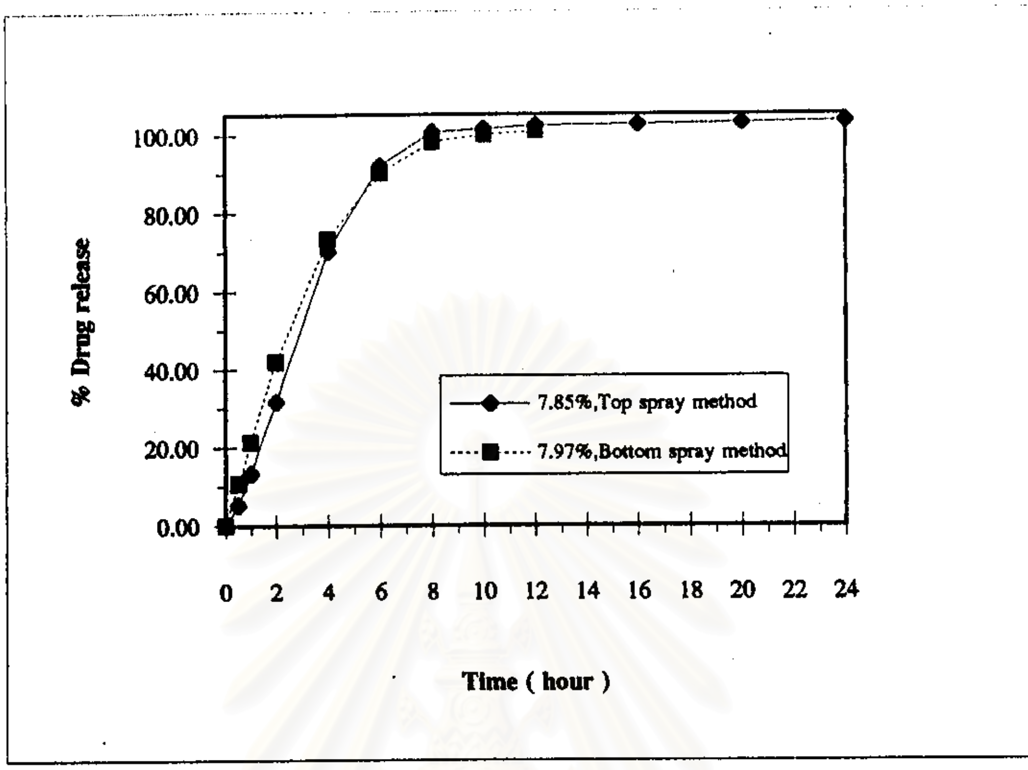


Figure 54 Influence of different spraying method in about 7% coating level of Eudragit NE 30D on the theophylline granules release profiles from coated granules.

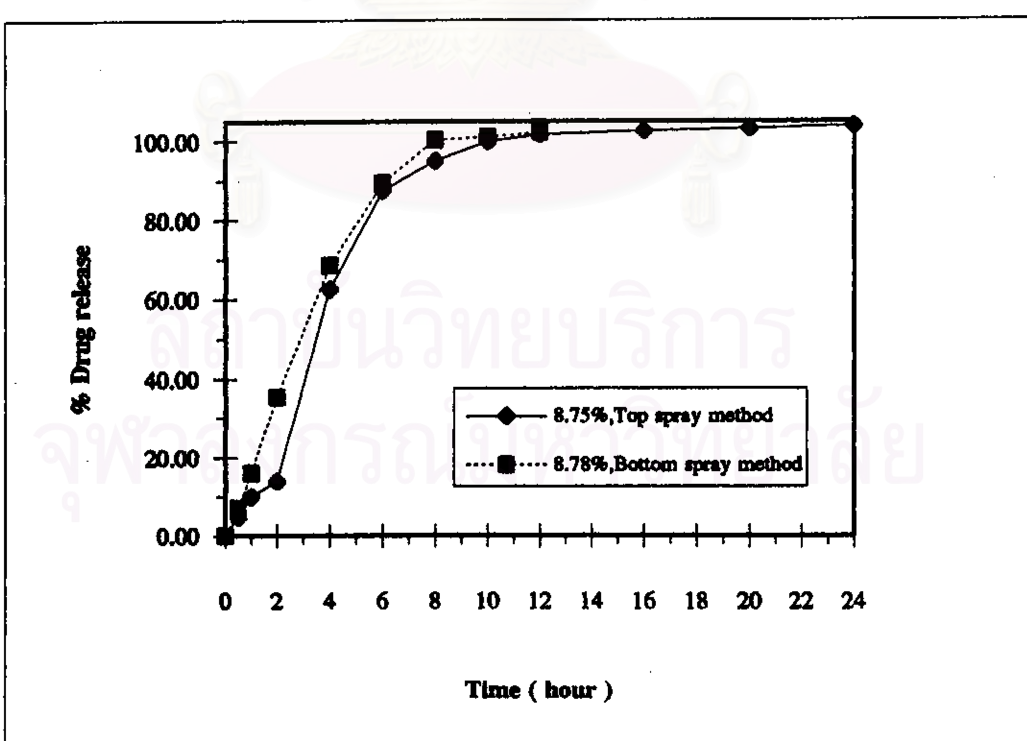


Figure 55 Influence of different spraying method in about 8% coating level of Eudragit NE 30D on the theophylline granules release profiles from coated granules.

2.6.3 Eudragit®NE 30D Coated Granules Using Different Atomization Air Pressure

The dissolution profiles of theophylline from granules coated with Eudragit® NE 30D lot A at 10 % coating level using different atomizing air pressure are demonstrated in Figure 56 (Table 31, Appendix B). The release rate profiles of these granules are shown in Figure 57 (Table 38, Appendix B).

The percentage of theophylline release from coated granules at 24 hours were increased from 76.44 % to 97.11 % and 104.50 % when the atomizing air pressure used were increased from 1 to 2 and 3 bar respectively. As shown in Figure 57, a practically constant theophylline release rate was obtained from the 1-bar atomizing air pressure coated granules whereas the 2-bar atomizing air pressure coated granules exhibited the inconstant release rate. The release rate of 3-bar atomizing air pressure coated granules was faster than the granules coated using lower atomizing air pressure. For the 3-bar atomizing air pressure coated granules, the initial rapid release of drug in the first 4 hours followed by slower release until 12th hour of experiment which complete drug release was received.

2.6.4 Granules Coated with Polymer Blends

A. Eudragit® NE 30D / HPMC Coated Granules

The dissolution profiles of theophylline from granules coated with blends containing various ratios of Eudragit® NE 30D/HPMC at 10% coating level are shown in Figure 58 (Table 32, Appendix B). The release rate was decreased with the time increased as shown in Figure 59 (Table 39, Appendix B).

In Figure 58, when the proportion of HPMC presented in the polymer blends of Eudragit®NE 30D/HPMC was decreased from 3:2 to 3:1.5, 3:1, 3:0.5, 12.5:1,

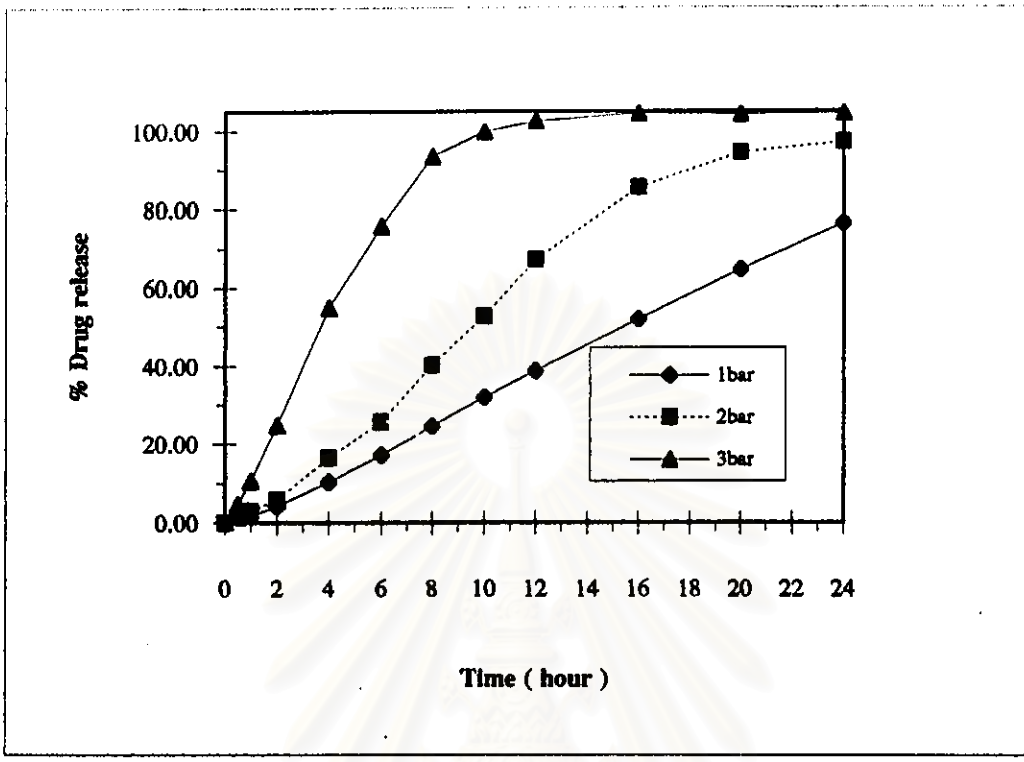


Figure 56 The release profiles of theophylline granules coated with 10% Eudragit(R) NE 30D using different atomizing air pressure.

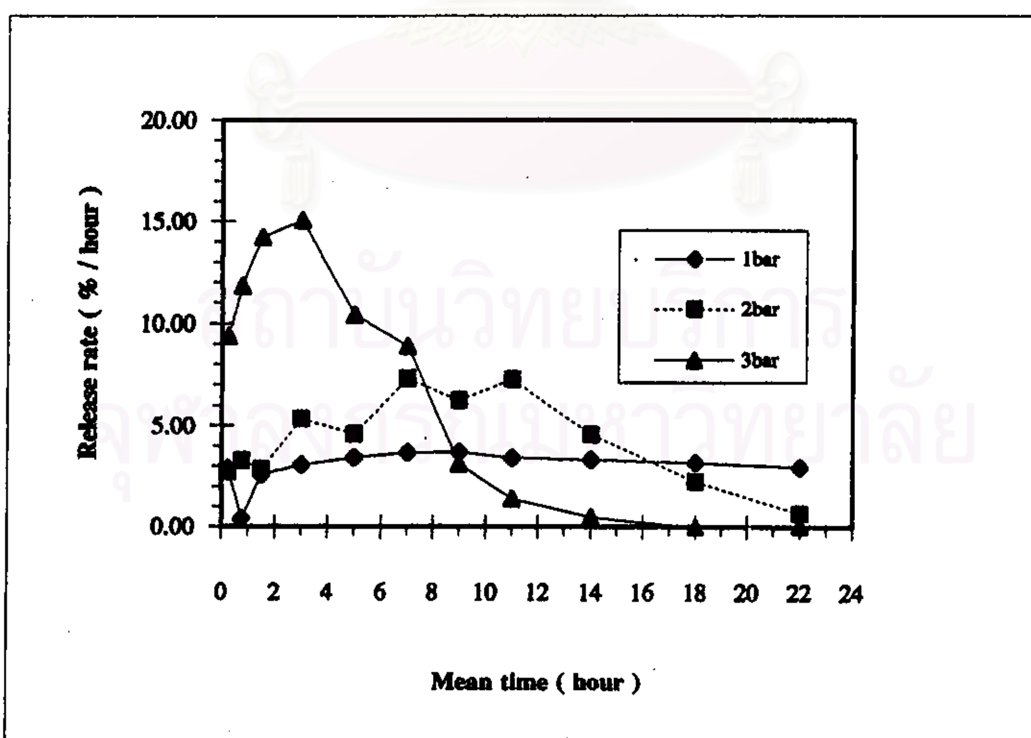


Figure 57 The release rate profiles of theophylline granules coated with 10 % Eudragit(R) NE 30D using different atomizing air pressur

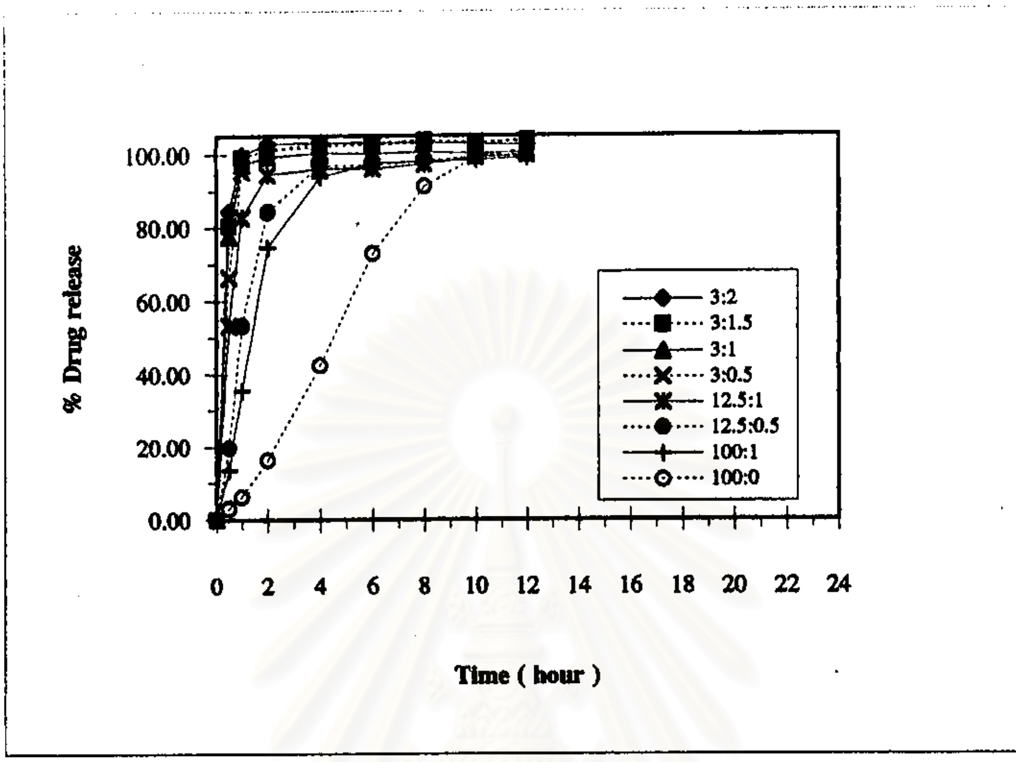


Figure 58 The release profiles of theophylline granules coated with 10% of blends containing various ratios of Eudragit[(R)]NE 30D/HPMC.

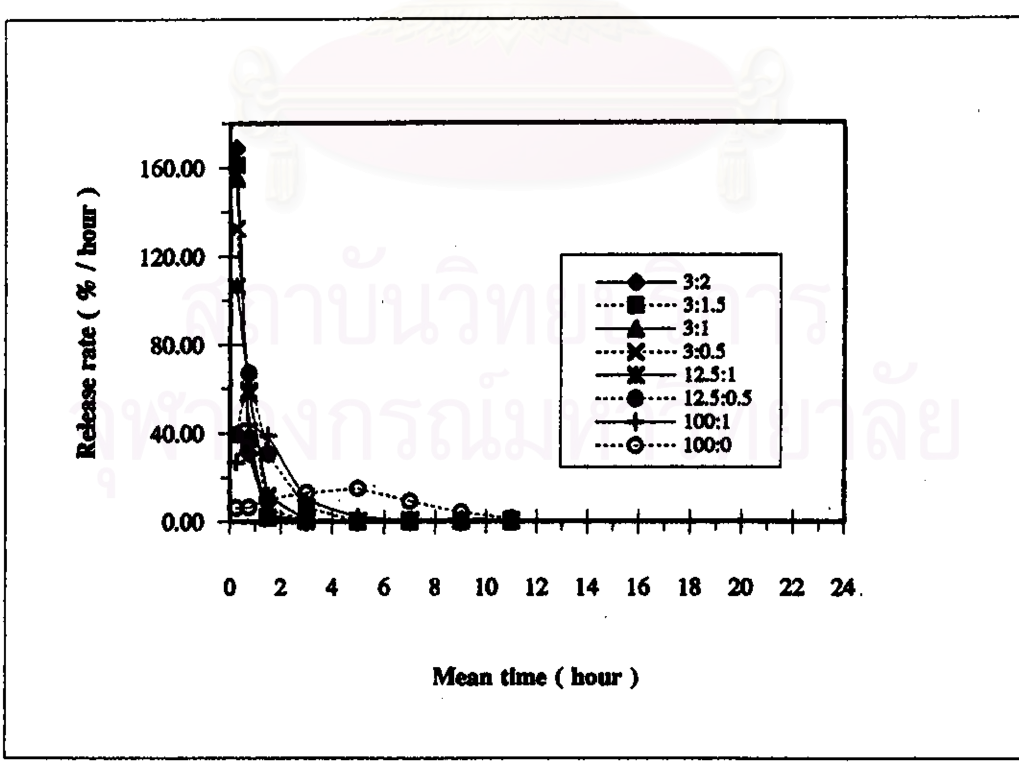


Figure 59 The release rate profiles of theophylline granules coated with 10% of blends containing various ratios of Eudragit[(R)]NE 30D/HPMC.

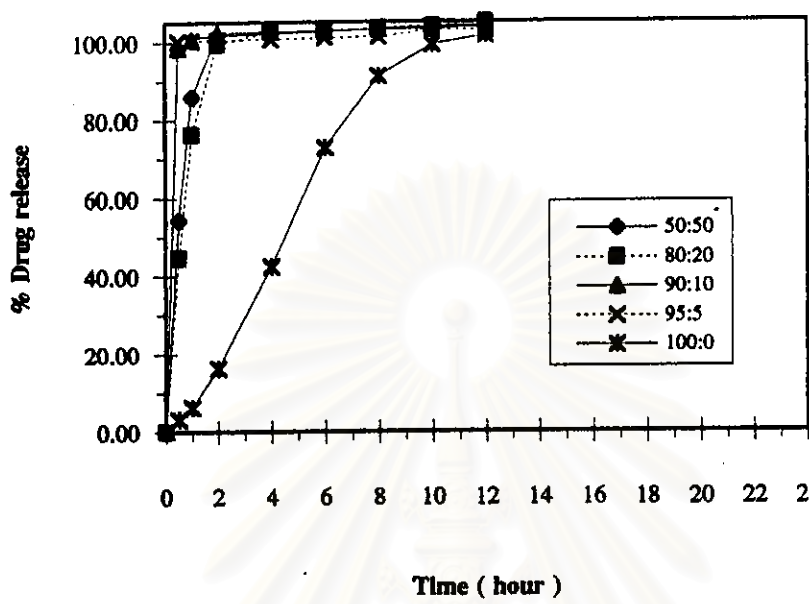


Figure 60 The release profiles of theophylline granules coated with 10% of blends containing various ratios of Eudragit(R)NE 30D/RL 30D.

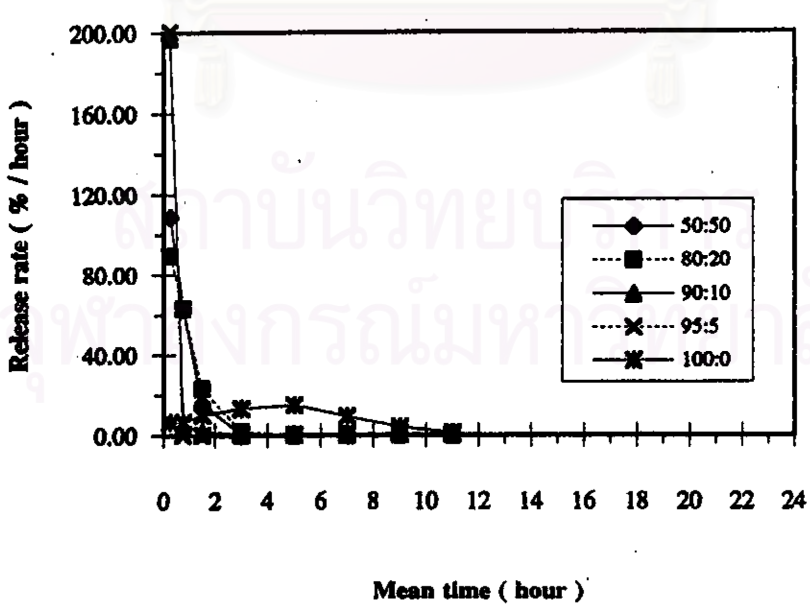


Figure 61 The release rate profiles of theophylline granules coated with 10% of blends containing various ratios of Eudragit(R)NE 30D/RL 30D.

12.5:0.5 and 100:1, the release rate of drug from coated granules decreased. However, it was notable that the granules coated with this blend showed no capability to control the drug release. Every formulation release the drug completely on the 4th hour of the experiment, even when the ratio was 100:1. The release rate of all Eudragit®NE 30D/HPMC coated granules were faster than those coated with only Eudragit®NE 30D at the same coating level.

B. Eudragit® NE 30D / RL 30D Coated Granules

The dissolution profiles of theophylline from granules coated with blends containing various ratios of Eudragit®NE 30D/RL 30D at 10 % coating level are shown in Figure 60 (Table 33, Appendix B). The release rate was decreased with the time increased as shown in Figure 61 (Table 40, Appendix B).

In Figure 60, when the proportion of Eudragit®RL 30D presented in the polymer blends of Eudragit®NE 30D/RL 30D was decreased from 50:50 to 80:20, 90:10 and 95:5, the release rate of drug did not decreased as the same as the Eudragit® NE 30D/HPMC coated granules. Only granules coated with blends of Eudragit®NE 30D/RL 30D in ratios of 50:50 and 80:20, decreasing the proportion of Eudragit®RL 30D in the polymer blends resulted in a corresponding decrease of the release of drug. The granules coated at ratios of 90:10 and 95:5 released the drug immediately on the half hour of experiment followed by slightly increased release up to 12 hours. The release rate of all Eudragit®NE 30D/RL 30D coated granules were also faster than those coated with only Eudragit®NE 30D at the same coating level.

2.6.5 Theo-24® (Commercial Product)

The dissolution data of theophylline from the commercial product, Theo-24®, are listed in Table 27 (Appendix B) and are shown graphically in Figure 62. The release rate profile of this product is tabulated in Table 34 (Appendix B) and shown

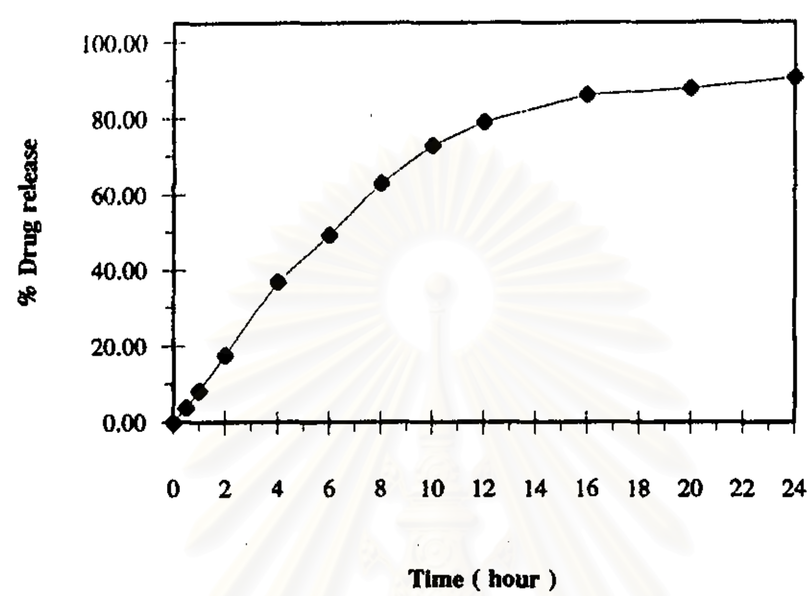


Figure 62 The release profile of Theo-24(R).

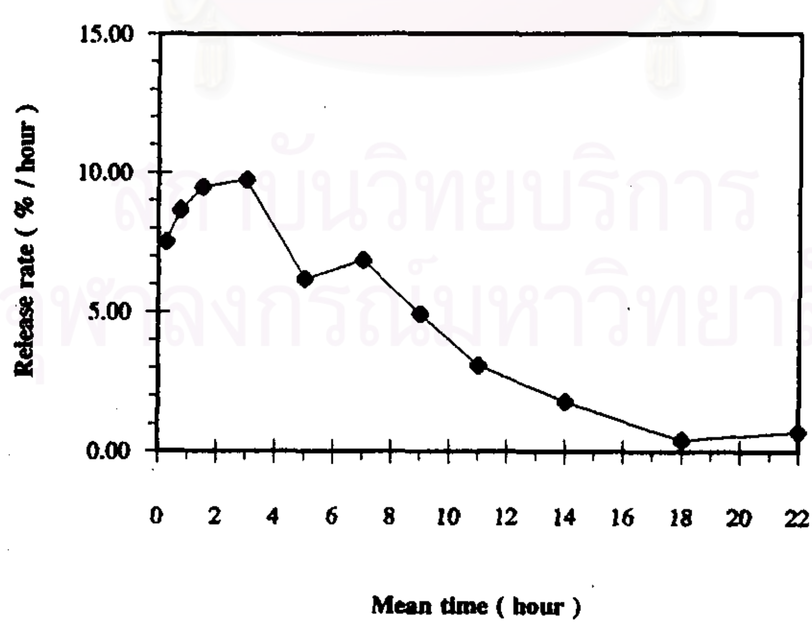


Figure 63 The release rate profile of Theo-24(R).

graphically in Figure 63. The release rate decreased as the time increased was observed.

2.6.6 Dissolution Profiles of Selected Formulations Compared with the Commercial Product

The satisfactory formulations were selected and compared their dissolution profiles with the commercial product, Theo-24®. The selection of formulation was based on the drug release at 24 hours interval of not less than 80 % with the small standard deviation and cumulative percent release of drug conforming to the USP XXIII requirement for the theophylline extended release capsules as presented in Table 14.

Table 14 USP XXIII requirement and cumulative percent release of drug from selected formulations of top-spray Eudragit®NE 30D coated granules.

Time (hours)	% Release		
	USP range	4.66% Eudragit® NE 30D lot A	13.51% Eudragit® NE 30D lot B
0	-	0.00	0.00
0.5	-	2.66	2.37
1	5-15	6.81	5.21
2	12-30	20.22	12.32
4	25-50	44.49	29.36
5	30-60	53.20	38.65
6	-	61.90	47.95
8	55-75	74.30	67.53
10	-	84.95	82.50
12	-	91.79	93.33
16	-	95.87	99.68
20	-	99.18	100.57
24	-	100.27	101.10

Figure 64 showed the profiles of the selected formulations, 4.66 % Eudragit® NE 30D lot A and 13.51 % Eudragit® NE 30D lot B coated granules using top spray method, compared with that of requirement specified in the USP XXIII. The profiles of them when compared with Theo-24® are illustrated in Figure 64. The selected

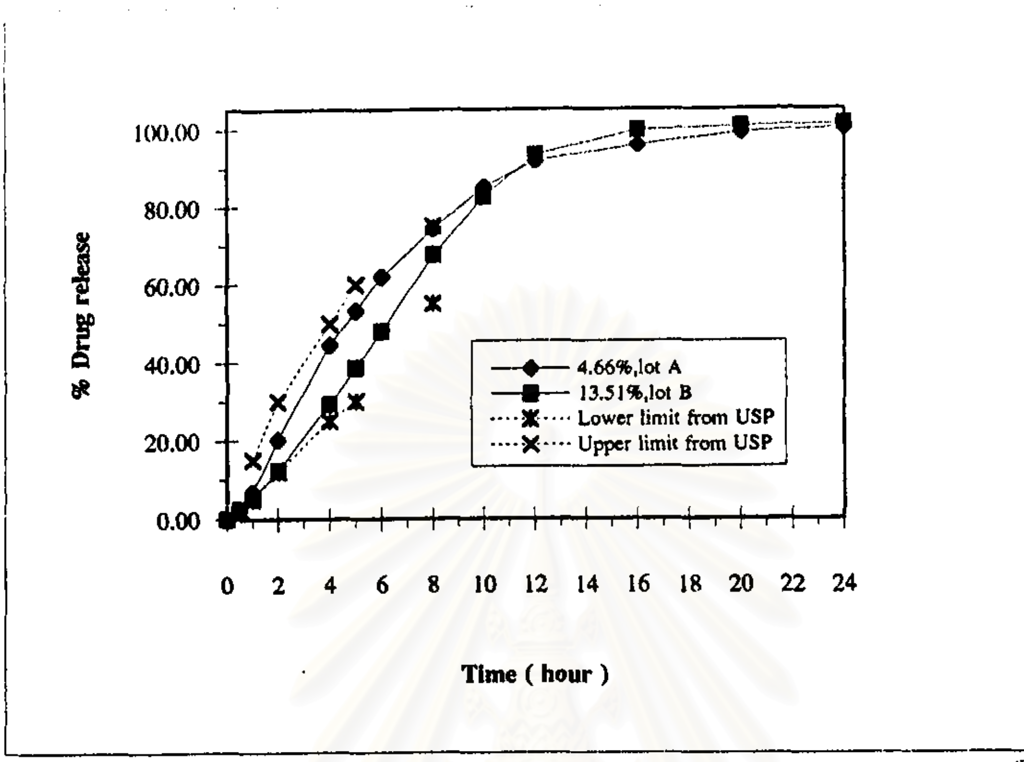


Figure 64 The release profiles from the selected formulations of top-spray Eudragit(R) NE 30D coated granules compared with the USP XXIII requirement.

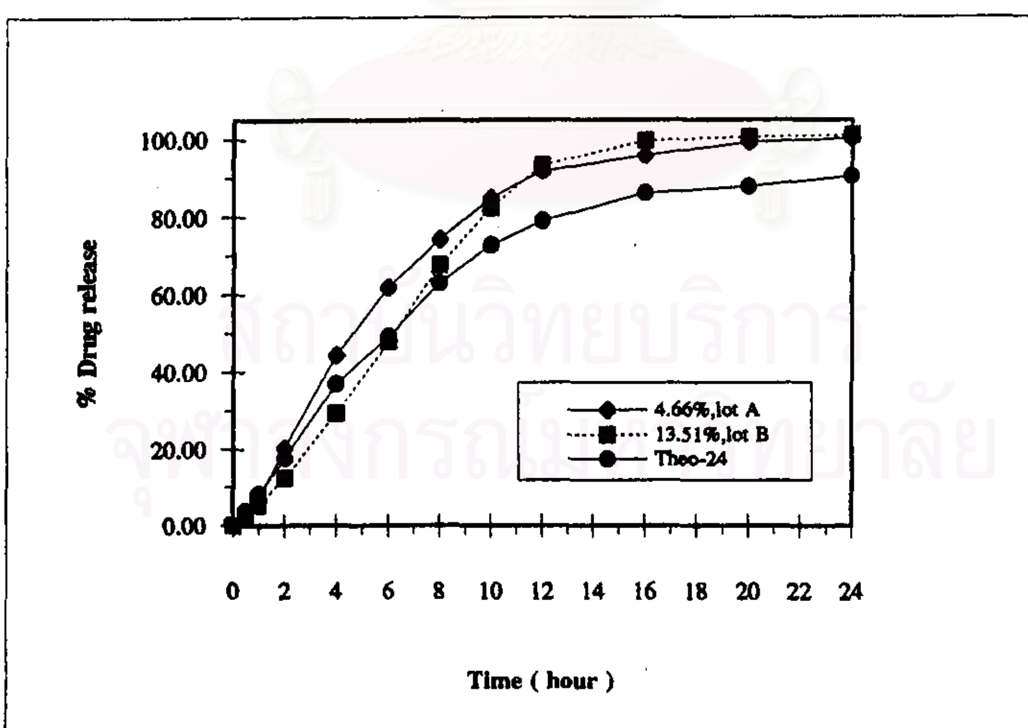


Figure 65 The release profiles from the selected formulations of top-spray Eudragit(R)NE 30D coated granules compared with Theo-24(R).

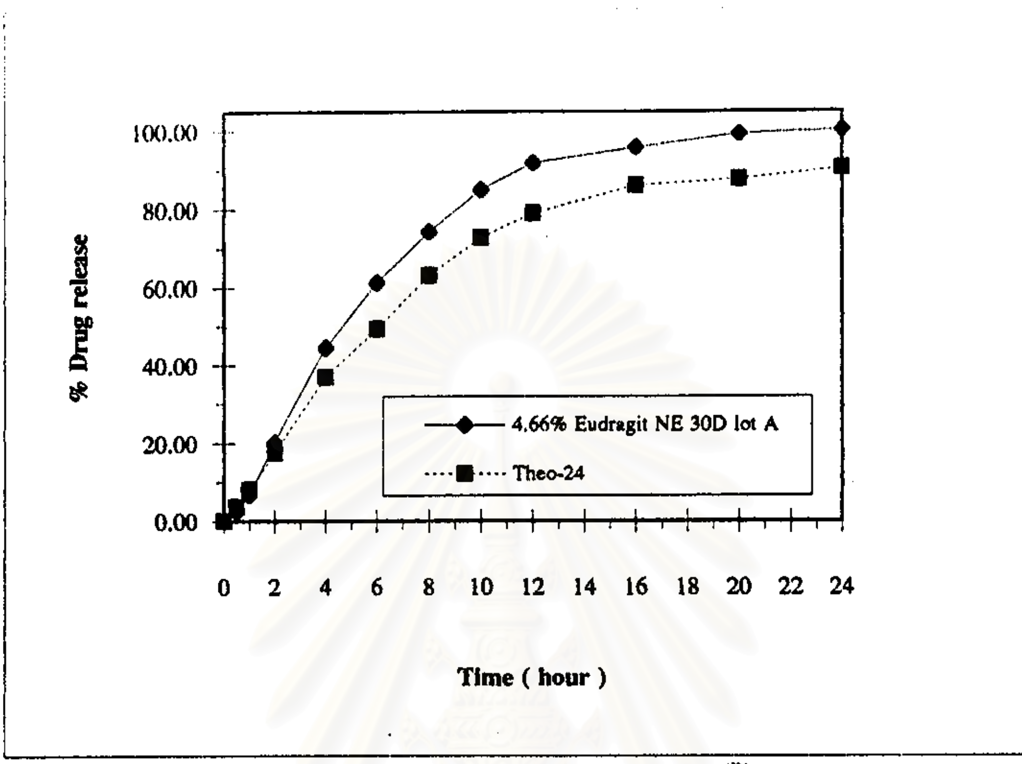


Figure 66 The release profiles from 4.66% Eudragit$^{(R)}$NE 30D lot A coated granules compared with Theo-24$^{(R)}$.

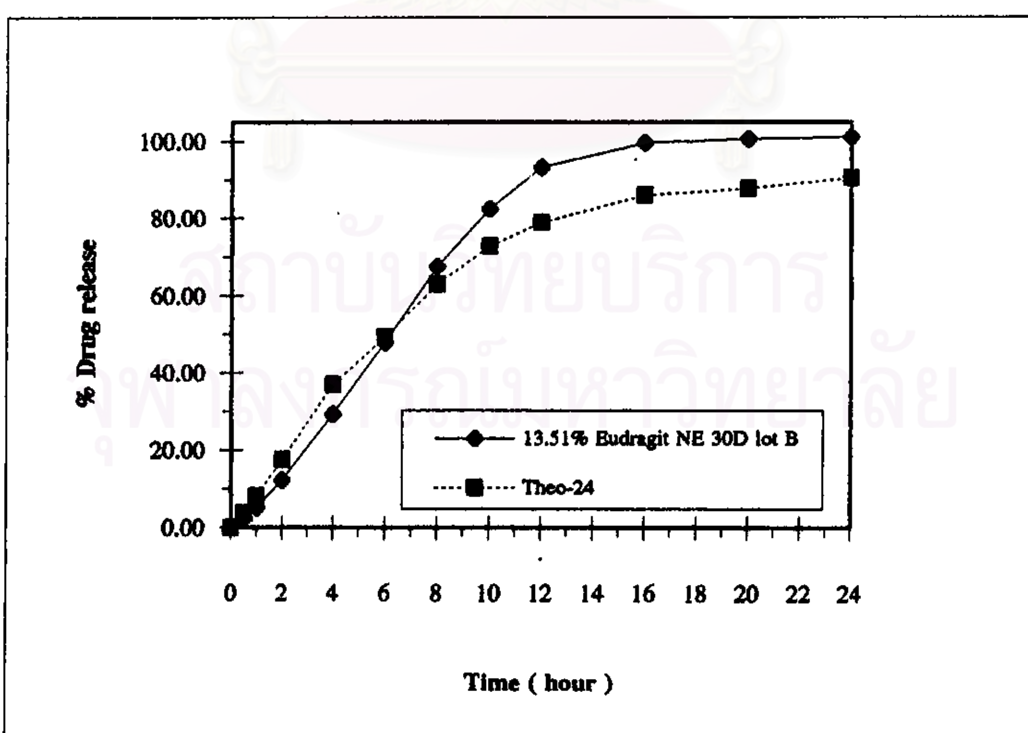


Figure 67 The release profiles from 13.51% Eudragit$^{(R)}$NE 30D lot B coated granules compared with Theo-24$^{(R)}$.

release profile than Theo-24® as shown in Figure 65 whereas that of 13.51 % Eudragit® NE 30D lot B shows slower release profile than Theo-24® in the first 6 hours followed by higher release until 24th hour of experiment as illustrated in Figure 67.

Nevertheless, each pair of drug release profiles showed no statistical significance as shown in Table 53 (Appendix C). From the obtained results, the release profile of theophylline from each selected formulation had no difference with that from and Theo-24®.

2.7 Elucidation of Drug Release Model

In order to determine the effect of type of polymer and formulation difference on the model of drug release, analysis of all dissolution data was carried out to elucidate what model (zero-order, first-order and Higuchi model) could be fitted by the data. The plots between percentage of drug released against time (zero-order), log percent of drug remained versus time (first-order) and percentage of drug released versus square root of time (Higuchi model) were, therefore, constructed and the one which was the most linear was the accepted model of drug release.

For some formulations, the values of correlation coefficient were undifferentiated between the first-order and Higuchi plots. Then, it was necessary to distinguish between the models. The further treatment was based upon the use of the different forms of the first-order and Higuchi equations. The plots of rate of release versus 1/Q were linear when the release was fitted with the Higuchi model. If the plots of rate of release versus Q were linear, they indicated that the first-order model was operative. The correlation coefficients of rate of release against reciprocal amount (1/Q) and amount (Q) of theophylline released from all granules are shown in Tables 19-22 (data from Tables 41-47, Appendix B).

Table 15 Correlation coefficient of the relationships between percentage drug release versus time (A), percent drug released versus square root time (B), and log percentage drug remained versus time (C) from uncoated theophylline granules and Theo-24®.

Product	A	B	C
uncoated granule	0.4912	0.7439	0.8870
Theo-24®	0.8490	0.9582	0.9720

Table 16 Correlation coefficient of the relationships between percentage drug release versus time (A), percent drug released versus square root time (B), and log percentage drug remained versus time (C) from theophylline granules coated with Eudragit®NE 30D using different spraying method.

Spraying method	lot of Eudragit®	Percent coated	A	B	C
Top spray	A	1.55	0.5658	0.7957	0.9827
		4.66	0.8112	0.9401	0.9803
		5.40	0.9205	0.9664	0.9858
		8.75	0.9976	0.9006	0.9067
		10.83	0.9987	0.9174	0.9641
		13.25	0.9876	0.8646	0.9713
	B	4.28	0.5003	0.7434	0.9942
		7.18	0.5795	0.7945	0.9113
		7.85	0.6304	0.8336	0.9547
		8.75	0.6750	0.8596	0.5599
		10.60	0.7399	0.8876	0.8636
		13.51	0.8564	0.9373	0.8512
		21.20	0.8849	0.9292	0.7710
Bottom spray	B	4.16	0.6633	0.8610	0.9861
		6.61	0.8221	0.9474	0.9757
		7.97	0.8571	0.9561	0.9322
		8.78	0.8801	0.9528	0.9706
		11.49	0.9313	0.9601	0.9436

Table 17 Correlation coefficient of the relationships between percentage drug release versus time (A), percent drug released versus square root time (B), and log percentage drug remained versus time (C) from theophylline granules coated with Eudragit®NE 30D using different atomizing air pressure (10% coating level).

Atomizing air pressure (bar)	A	B	C
1	0.9987	0.9174	0.9641
2	0.9658	0.9353	0.9454
3	0.7232	0.8920	0.8362

Table 18 Correlation coefficient of the relationships between percentage drug release versus time (A), percent drug released versus square root time (B), and log percentage drug remained versus time (C) from theophylline granules coated with various ratio of polymer blends (10% coating level).

Type of polymer blend	Ratio of polymer blend	A	B	C
Eudragit®NE 30D : HPMC	3:2	0.2395	0.4587	0.9290
	3:1.5	0.2694	0.4945	0.9673
	3:1	0.2636	0.4883	0.9369
	3:0.5	0.3271	0.5648	0.9726
	12.5:1	0.4088	0.6509	0.8798
	12.5:0.5	0.5917	0.8056	0.9463
	100:1	0.6652	0.8519	0.9142
Eudragit®NE 30D : RL 30D	50:50	0.3984	0.6431	0.9867
	80:20	0.4669	0.7098	0.9454
	90:10	0.1984	0.3958	-
	95:5	0.1909	0.3819	-

Table 19 Comparison of linearity between plots of rate of release against reciprocal amount (1/Q) and amount (Q) of theophylline released from uncoated granules and Theo-24®.

Product	Correlation coefficient of rate (dQ / dt)	
	Versus Q	Versus 1/Q
uncoated granule	0.4890	0.3151
Theo-24®	0.7646	0.1871

Table 20 Comparison of linearity between plots of rate of release against reciprocal amount (1/Q) and amount (Q) of theophylline released from granules coated with Eudragit®NE 30D using different spraying method.

Spraying method	lot of Eudragit® NE 30D	Percent coated	Correlation coefficient of rate (dQ / dt)	
			Versus Q	Versus 1/Q
Top spray	A	1.55	0.6090	0.1261
		4.66	0.4933	0.0102
		5.40	0.3167	0.0108
		8.75	0.5060	0.7258
		10.83	0.1495	0.4892
		13.25	0.1883	0.1533
	B	4.28	0.7134	0.3648
		7.18	0.4283	0.1168
		7.85	0.5471	0.1116
		8.75	0.4255	0.1865
		10.60	0.2565	0.0083
		13.51	0.2478	0.0000
		21.20	0.0633	0.0259
Bottom spray	B	4.16	0.8410	0.5411
		6.61	0.9304	0.5882
		7.97	0.8702	0.4703
		8.78	0.6494	0.1723
		11.49	0.5510	0.1018

Table 21 Comparison of linearity between plots of rate of release against reciprocal amount (1/Q) and amount (Q) of theophylline released from granules coated with Eudragit®NE 30D using different atomizing air pressure (10% coating level).

Atomizing air pressure (bar)	Correlation coefficient of rate (dQ / dt)	
	Versus Q	Versus 1/Q
1	0.1495	0.4892
2	0.0103	0.1034
3	0.5947	0.1159

Table 22 Comparison of linearity between plots of rate of release against reciprocal amount (1/Q) and amount (Q) of theophylline released from granules coated with various ratios of polymer blends (10% coating level).

Type of polymer blend	Ratio of polymer blend	Correlation coefficient of rate (dQ / dt)	
		Versus Q	Versus 1/Q
Eudragit®NE 30D : HPMC	3:2	0.9975	0.9963
	3:1.5	0.9901	0.9879
	3:1	0.9828	0.9765
	3:0.5	0.9485	0.9185
	12.5:1	0.9513	0.8962
	12.5:0.5	0.6197	0.2775
	100:1	0.5872	0.2139
Eudragit®NE 30D : RL 30D	50:50	0.9486	0.8831
	80:20	0.9362	0.8302
	90:10	0.7227	0.7344
	95:5	0.1350	0.1371

2.7.1 Uncoated Granules

The correlation coefficients of uncoated theophylline granules were obtained as tabulated in Table 15. The highest correlation coefficient was 0.8870 received from the plots of log percent of drug remained versus time. In addition, the correlation coefficient of rate versus Q was higher than those of rate versus 1/Q as presented in Table 19. Therefore, the theophylline release from uncoated granules was likely to be the first-order model.

2.7.2 Eudragit®NE 30D Coated Granules Using Different Spraying Method

A. Top-Spray Coated Granules

The correlation coefficients of Eudragit®NE 30D lot A and lot B coated granules are tabulated in Table 16.

For the Eudragit®NE 30D lot A coated granules, The highest correlation coefficient of 1.55 % coated granules was obtained from the first-order plot. Both the first-order and Higuchi plots of 4.66 % and 5.40 % coated granules were linear with the correlation coefficient values greater than 0.94. However, the highest correlation coefficients of 4.66 % and 5.40 % coated granules were 0.9803 and 0.9858 obtained from the first-order plot, respectively. This results indicated that the release data might have followed the first-order model. The further treatment revealed that the correlation coefficients of rate of release against Q of them were higher than those against 1/Q as exhibited in Table 20. Therefore, the theophylline release from these granules were likely to be the first-order model. In case of 8.75 %, 10.83 % and 13.25 % coated granules, The highest correlation coefficients were obtained from the plot of percent of drug released against time. Hence, the zero-order model might possibly be operative.

For the top-spray Eudragit®NE 30D lot B coated granules, The highest correlation coefficients of 4.28 %, 7.18 % and 7.85 % coated granules were obtained from the plot of log percent of drug remained versus time. The results indicated that the theophylline release from these granules were likely to be the first-order model. Other coated granules exhibited similarly high correlation coefficient in both first-order and Higuchi plots. The further treatment revealed that the correlation coefficients of rate of release versus Q were higher than those versus 1/Q as exhibited in Table 20. Therefore, the release from these granules were followed the first-order model.

B. Bottom-Spray Coated Granules

The correlation coefficients of bottom-spray Eudragit® NE 30D coated granules are tabulated in Table 16. For the 4.16 % coated granules, the first-order plot was linear with the correlation coefficient values of greater than 0.99. High correlation coefficients of other coated granules were undifferentiated between the first-order and Higuchi plots. The further treatment revealed that the correlation coefficients of rate of release against Q were higher than those against 1/Q as presented in Table 20. It was indicated that the release profiles of these coated granules might have followed the first-order model.

2.7.3 Eudragit®NE 30D Coated Granules Using Different Atomizing Air Pressure

The correlation coefficients of Eudragit®NE 30D coated granules using different atomizing air pressure are tabulated in Table 17. The highest correlation coefficients of 1-bar and 2-bar atomizing air pressure coated granules were obtained from the plot of percentage of drug released versus time whereas the correlation coefficients of 3-bar coated granules were similar in both first-order and Higuchi plots. The further treatment revealed that the correlation coefficient of release rate against Q of 3-bar coated granules was higher than that against 1/Q as illustrated in Table 21. Therefore, the release profiles of 1-bar and 2-bar coated granules were likely to be zero-order model while that of 3-bar coated granules might have followed the Higuchi model.

2.7.4 Coated Granules with Polymer Blends

A. Eudragit®NE 30D/HPMC Coated Granules

The correlation coefficients of granules with blends containing various ratios of Eudragit®NE 30D/HPMC at 10 % coating level are tabulated in Table 18. All these coated granules showed similar release model. The highest correlation coefficient was obtained from the first-order plots. The correlation coefficient of release rate versus Q was higher than those versus 1/Q as presented in Table 22. These results indicated that the theophylline release from all Eudragit®NE30D/HPMC coated granules might have followed the first-order model.

B. Eudragit®NE 30D/RL 30D Coated Granules

The correlation coefficients of granules with blends containing various ratios of Eudragit®NE 30D/RL 30D at 10% coating level are tabulated in Table 18. For the granules coated with Eudragit®NE 30D/RL 30D in ratios of 50:50 and 80:20, the first-order plot was linear with the correlation coefficient values of greater than 0.94. In addition, the correlation coefficient of release rate versus Q was higher than those versus 1/Q as showed in Table 22. Therefore, the first-order model might possibly be operative for these coated granules. In case of granules coated with this blend in ratios of 90:10 and 95:5, the correlation coefficient of release rate against Q did not show difference from those against 1/Q. This results indicated that the release model of granules coated with this blend in ratios of 50:50 and 80:20 might have followed the first-order model whereas those of 90:10 and 95:5 could not be specified.

2.7.5 Theo-24® (Commercial Product)

The correlation coefficients were obtained as tabulated in Table 15. The highest correlation coefficient was 0.9720 obtained from the first-order plot. In addition, the correlation coefficient of rate versus Q was higher than those of rate versus 1/Q as shown in Table 19. The first-order model might possibly be operative.

3. Evaluation of Aqueous Polymeric Films

3.1 Water Sorption of Aqueous Polymeric Films

3.1.2 Eudragit®NE 30D Film

The percent water sorption of Eudragit®NE 30D film containing Cab-O-Sil of 30 % w/w of polymer was 34.83 % as shown in Table 23.

Table 23 Percent water sorption, percent elongation at break and tensile strength of aqueous polymeric films.

Type of polymer	Percent water sorption	Percent elongation at break	Tensile strength (N/mm^2)
Eudragit®NE 30D	34.83 ± 3.05	578.68 ± 14.12	2.91 ± 0.30
Eudragit®NE 30D / HPMC in ratio			
3:2	50.03 ± 2.04	12.24 ± 1.92	13.09 ± 1.05
3:1.5	47.60 ± 5.79	28.03 ± 7.54	12.36 ± 1.02
3:1	45.86 ± 4.67	58.02 ± 5.69	11.25 ± 0.61
3:0.5	39.61 ± 4.60	179.13 ± 6.69	7.67 ± 0.26
12.5:1	35.68 ± 3.28	143.58 ± 5.39	4.26 ± 0.27
12.5:0.5	33.96 ± 1.46	575.57 ± 9.82	3.82 ± 0.05
100:1	34.71 ± 1.21	517.79 ± 9.14	3.12 ± 0.45

3.1.2 Eudragit®NE 30D/HPMC Films

The percent water sorption of aqueous polymeric films containing various ratios of Eudragit®NE 30D/HPMC are shown in Table 23. For the ratios of 3:2, 3:1.5, 3:1 and 3:0.5 films, it was notable that the percent water sorption of these films were higher than that of Eudragit®NE 30D film and were apparently decreased as the proportion of HPMC in the film decreased. However, other ratios of Eudragit®NE 30D/HPMC film, their percent water sorption were not apparently different as shown in Table 23.

3.2 Percent Elongation at Break and Tensile Strength of Aqueous Polymeric Films

3.2.1 Eudragit®NE 30D Film

The percent elongation at break and tensile strength of Eudragit®NE 30D film containing Cab-O-Sil of 30 % w/w of polymer were 578.68 % and 2.91 $N/mm.^2$ respectively as shown in Table 23.

3.2.2 Eudragit®NE 30D/HPMC Films

The percent elongation at break and tensile strength of aqueous polymeric films containing various ratios of Eudragit®NE 30D/HPMC are shown in Table 23. It could be seen that the tensile strength was decreased as the proportion of HPMC in the film decreased. In the Eudragit®NE 30D/HPMC which had high proportion of HPMC, their percent elongation at break were lower than that of only Eudragit®NE 30D film and were increased as the proportion of HPMC decreased. While the percent elongation at break of films which had low amount of HPMC were not much different.

3.3 Infrared Spectrometry

The IR spectra of the Eudragit®NE 30D lot A and lot B are depicted in Figure 68. The principle peaks of Eudragit®NE 30D were at the wavenumbers of 1150-1180, 1240-1260, 1385, 1450, 1730 and 2950-3000 cm^{-1} (Rohm GmbH, 1996 ; Gopferich and Lee, 1992). The peak of Eudragit® NE 30D at 1730 cm^{-1} resulted from C=O stretching of the ester groups. The IR absorption bands at 1180 and 1240 cm^{-1} were resulted from C-O stretching. The peaks at 1385 and 1450 cm^{-1} were resulted from C-H bending. The C-H stretching was observed at 2950 cm^{-1} . From the obtained data, it could be seen that the spectrum of Eudragit®NE 30D lot A was similar to that of lot B. Nonetheless, comparison the peak intensities of C-H stretching at 2950 cm^{-1} to C=O stretching at 1730 cm^{-1} was conducted in order to estimate the polymer chain length. It was found that Eudragit®NE 30D lot A had higher peak ratio indicating of higher monomers or shorter chains than Eudragit® NE 30D lot B.

The IR spectra of polymer blend containing Eudragit®NE 30D lot B and HPMC in ratio of 1:1 and HPMC alone are also depicted in Figure 68. The prominent peaks spectra did not shift which reveal that no interaction or slight interaction between these polymers occurred.

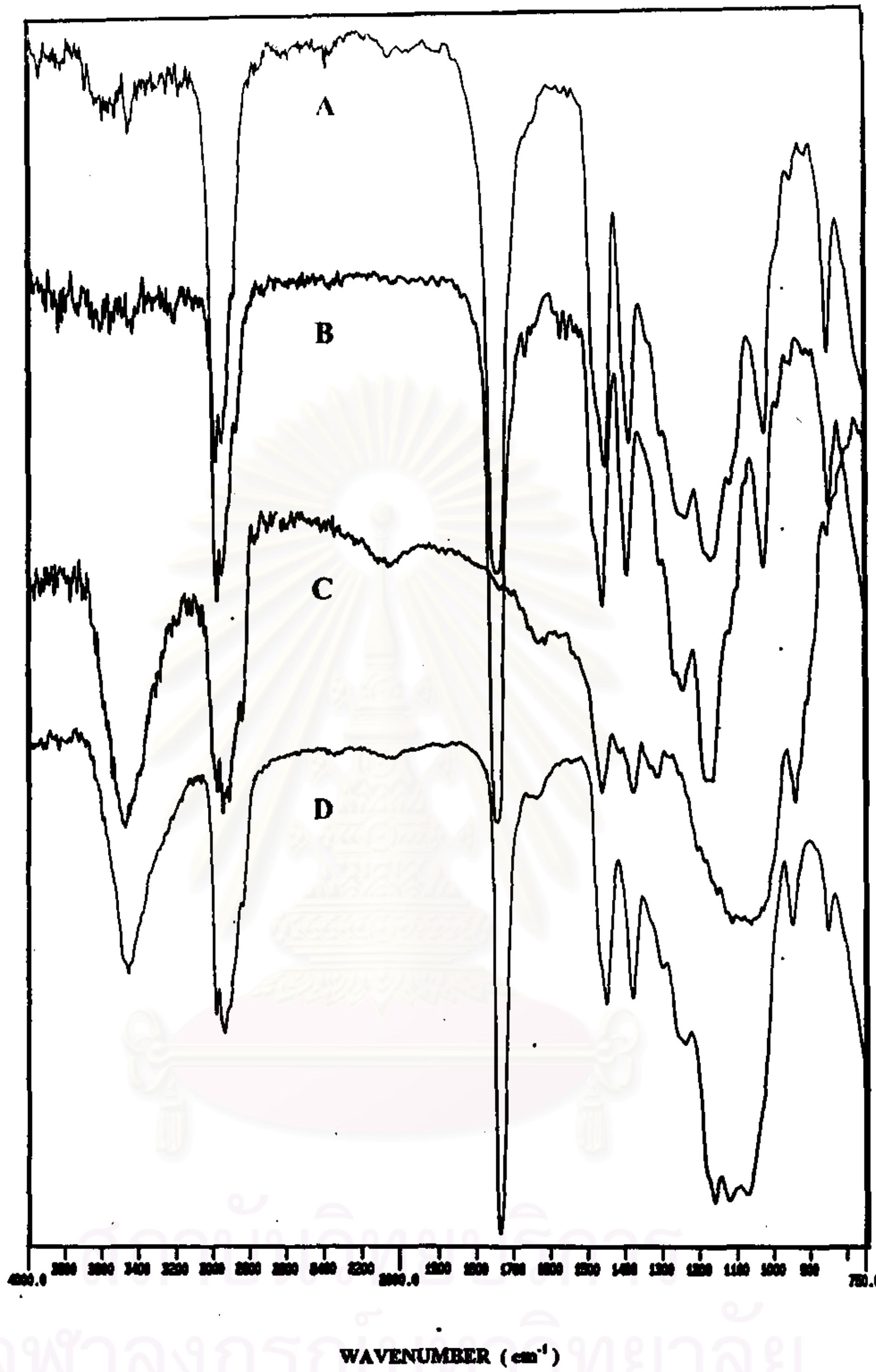


Figure 68 IR spectra of polymer.

Key : A - Eudragit®NE 30D lot A

: B - Eudragit®NE 30D lot B

: C - HPMC

: D - Eudragit®NE 30D lot B/HPMC in ratio 1:1