CHAPTER III

RESULTS

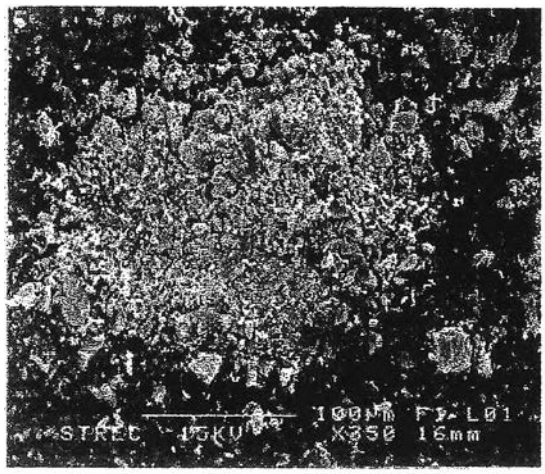
1. Morphology of Spray Dried Powders

The observation of size, shape and surface topography was done by scanning electron microscopy. The scanning electron photomicrographs of diclofenac sodium powders and Aerosil®200 in different magnifications are revealed in Figure 4. Diclofenac sodium powders were of irregular crystal shapes, rough surface, various sizes and adhering together. Aerosil® 200 was collapsed microball of different sizes with rough surface.

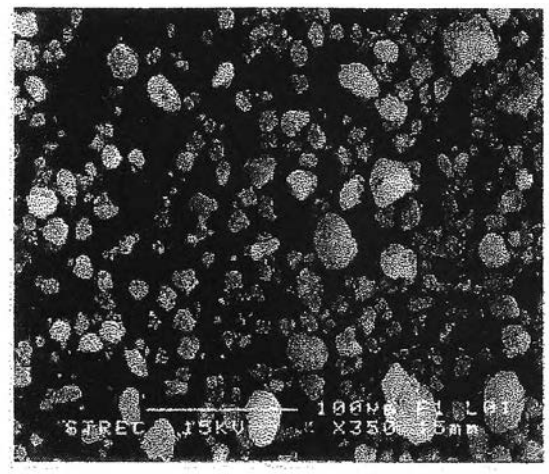
Figure 5 shows the scanning electron photomicrographs of Eudragit® RD 100 and NaCMC in different magnifications. Eudragit® RD 100 was round shape similar to microball with different sizes and smooth surface but had some fine powder adhering to the surface of polymer. NaCMC was irregular flakes with different sizes with rough surface.

The photomicrographs of diclofenac sodium spray dried powder without polymer at various inlet temperatures at 130°C and 160°C are shown in Figure 6 (Formulation 1-2). The powder obtained from the inlet temperature at 160°C composed of irregular thick crystal shapes in various sizes. The surface of powder was rough and had pores. No remarkable morphological difference was evident in the case of the particles prepared with the different inlet temperature. But by observation, shrinkage in the surface of the particles prepared using inlet temperature of 160°C were partly shrunken.

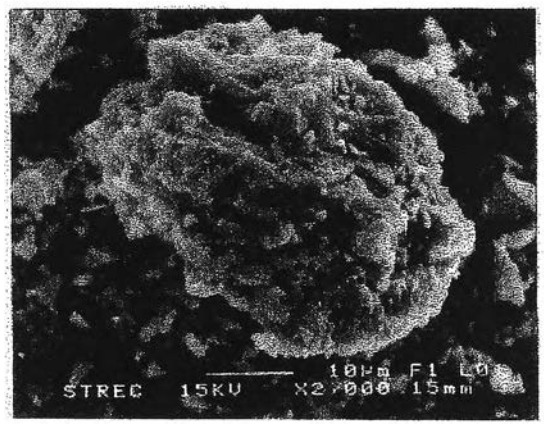
The photomicrographs of the spray dried powder produced by Eudragit® RD 100 (K(1)-K(3)) and Eudragit®RL 30D with NaCMC (L(1)-L(3)) at the ratio of 1:9 are shown in Figure 7 (Formulation 3-4). Some of the small



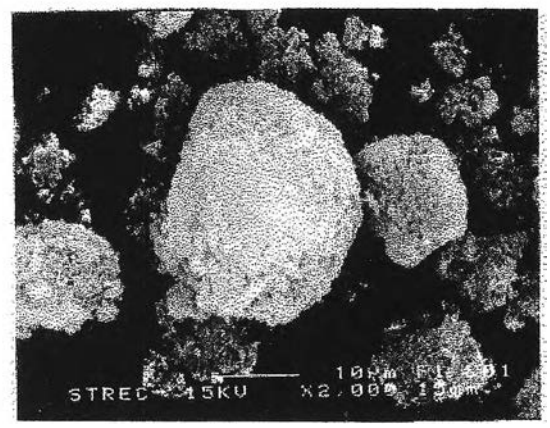
A



C

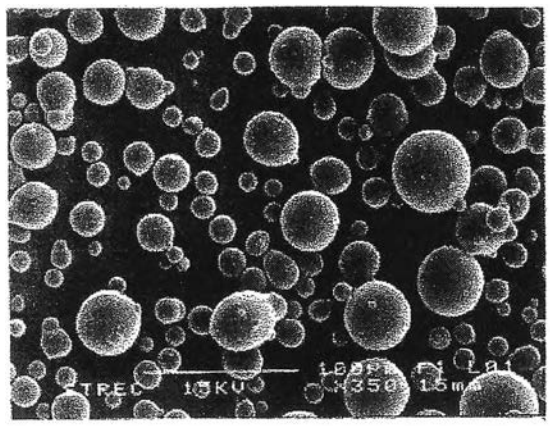


B

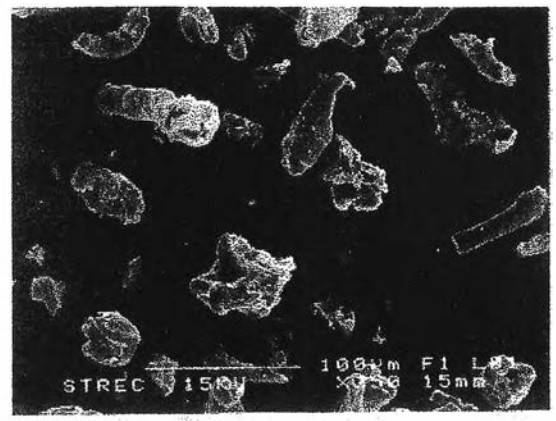


D

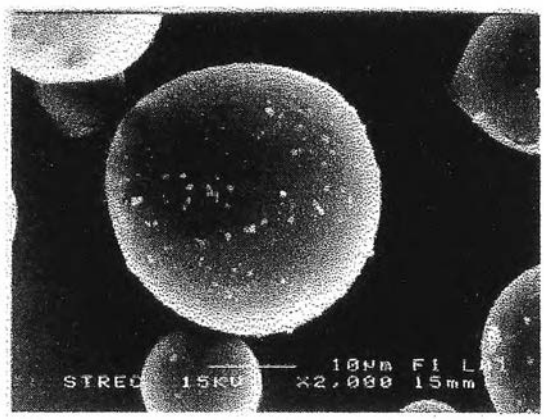
Figure 4 Scanning electron photomicrographs of diclofenac sodium powder (Ax 350, Bx 2,000) and Aerosil ®200 (C x 350, D x 2,000).



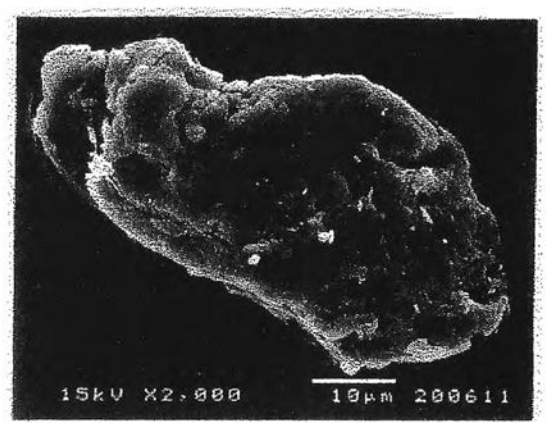
E



G

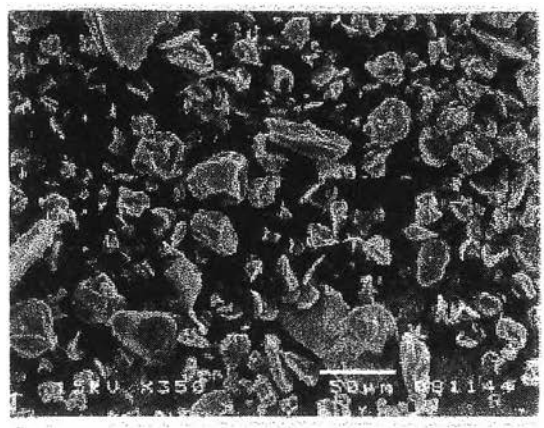


F

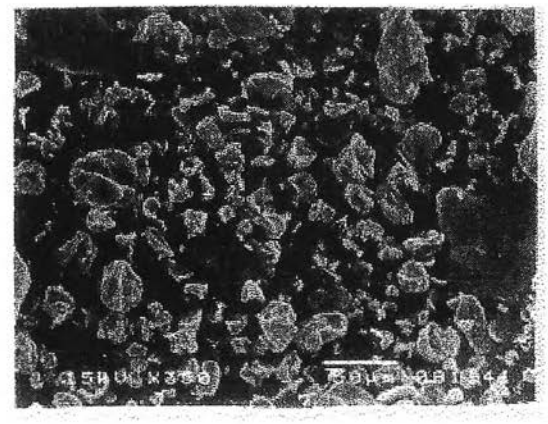


H

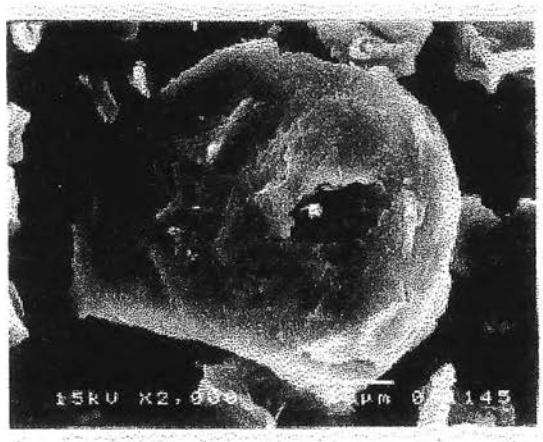
Figure 5 Scanning electron photomicrographs of Eudragit® RD 100 (E x 350, F x 2,000) and NaCMC (G x 350 , H x 2,000).



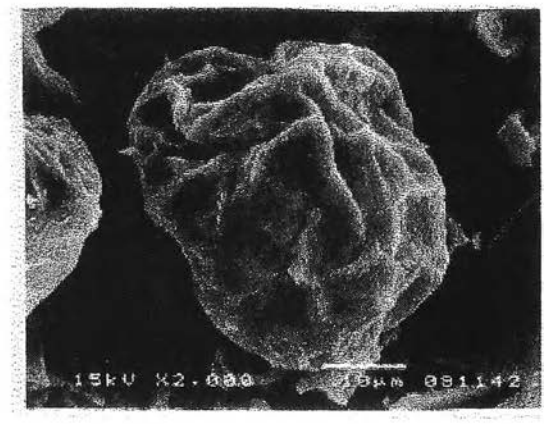
I (1)



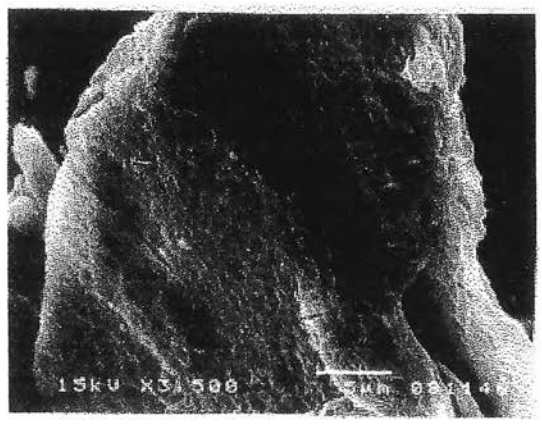
J(1)



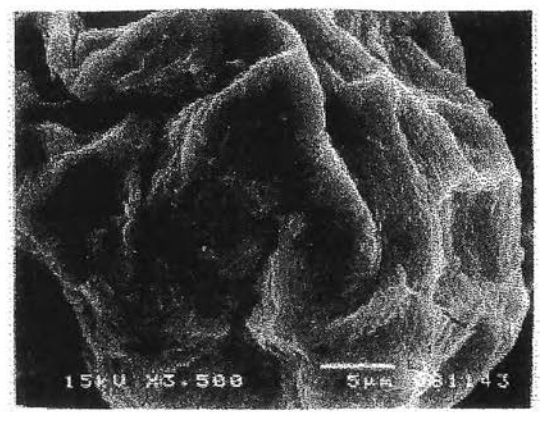
I (2)



J(2)



I(3)



J(3)

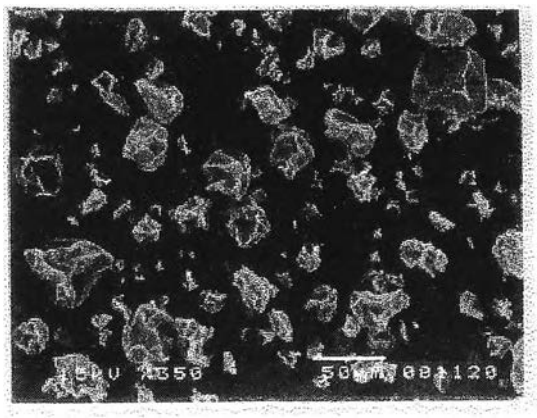
Figure 6 Scanning electron photomicrographs of spray- dried diclofenac sodium without polymer at various inlet temperature. I = 130°C J= 160°C (1) x 350 , (2) x 2,000, (3) x 3,500

particles were adhered to each other and / or attached to the large particles. The microparticles had rough surface. The particles seem to shrink and collapse. The size of spray dried powders using Eudragit®RD 100 was smaller than that of containing Eudragit® RL30D and NaCMC and had broader size distribution.

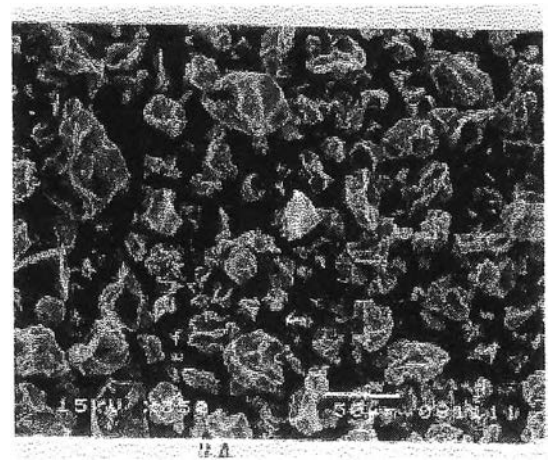
The photomicrographs of the spray dried diclofenac sodium powder produced by Eudragit at the ratio of 1 :4 with two different types of Eudragit. Eudragit ® RD100 (M (1)-M (3)) or Eudragit ®RL 30 D with NaCMC (N(1)-N(3)) are shown in Figure 8 (Formulation 5-6). The microparticle of two formulations with these two polymers had irregular shape with rough surface. The particles seem to shrink and collapse. All spray dried exhibited unspherical shape. The microparticles showed rosette aggregates. The size of spray dried powders using Eudragit®RD 100 was slightly bigger than that of containing Eudragit®RL 30D and NaCMC.

The microscopic images of spray dried diclofenac sodium powder produced by Eudragit® RD 100 (O(1)-O(3)) and Eudragit® RL 30D with NaCMC (P(1) - P(3)) at the same ratio of 1:2.33 are shown in Figure 9 (Formulation 7-8). The size of spray dried powders using Eudragit ®RD 100 had narrow size distribution include slightly bigger than that of using Eudragit®RL 30D and NaCMC. The surface of particles which contained Eudragit®RD 100 exhibited fairly rough surface and seem to be shrunken. The surface which containing Eudragit®RL 30D and NaCMC exhibited rough surface and was partly shrunken. The particles was collapsed and twisted.

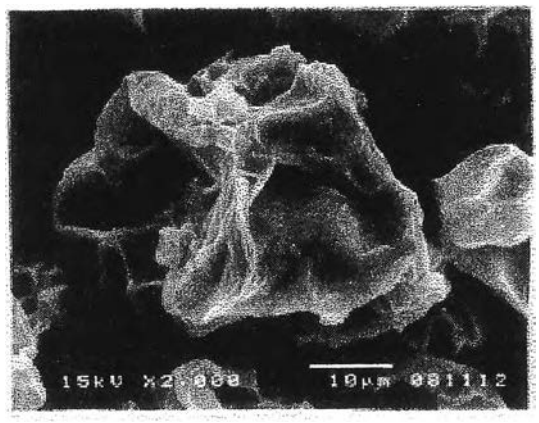
The microscopic appearance of spray dried diclofenac sodium powders produced by Eudragit®RD 100 (Q(1)-Q(3)) and Eudragit®RL 30D with NaCMC (R (1)-R(3)) at the same ratio 1:1.5 are displayed in Figure 10 (Formulation 9-10). Some of the small particles adhered to each other and attached to the large particles. The surface exhibited roughness and the particles seem to be hollow in shape. Some particles were shrunken with rosette aggregates and some of them were cracked. The agglomerated particles of spray dried diclofenac sodium with Eudragit ® RL 30D and NaCMC consisted of bigger, irregularly shaped microparticles and had wider size distribution.



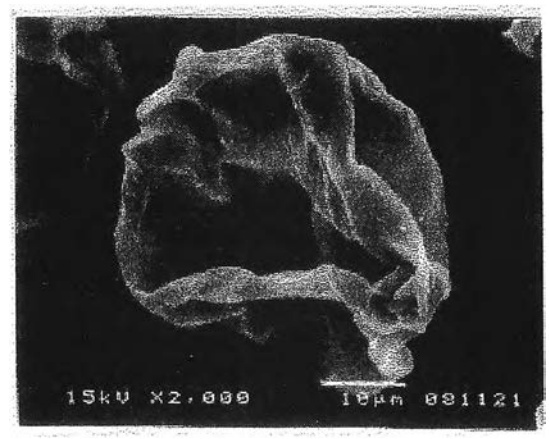
K(1)



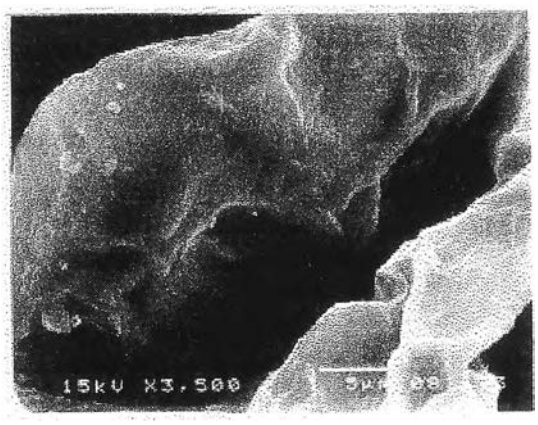
L(1)



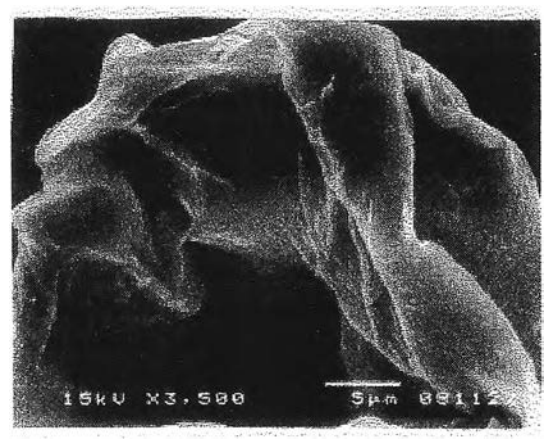
K(2)



L(2)

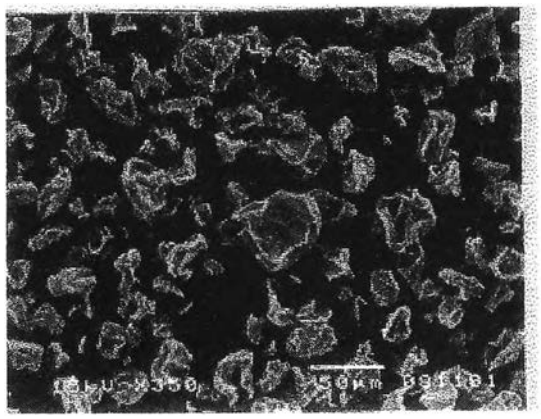


K(3)

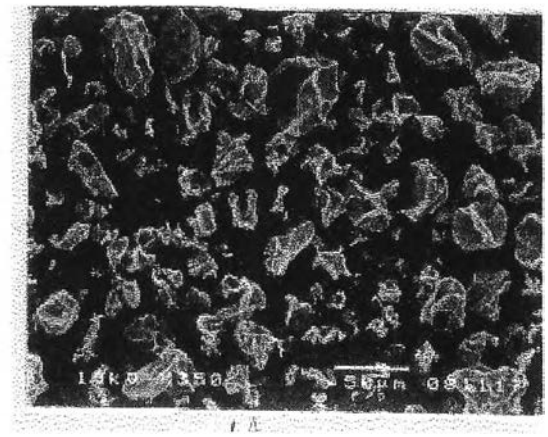


L (3)

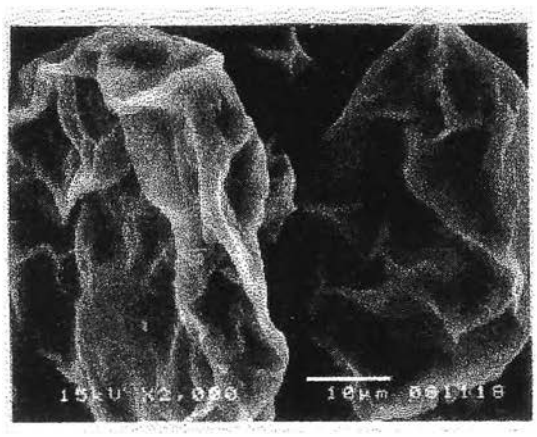
Figure 7 Scanning electron photomicrographs of spray- dried diclofenac sodium with various polymer. K = RD 1:9, L = RL and NaCMC 1:9 (1) x 350 , (2) x 2,000 , (3) x 3,500



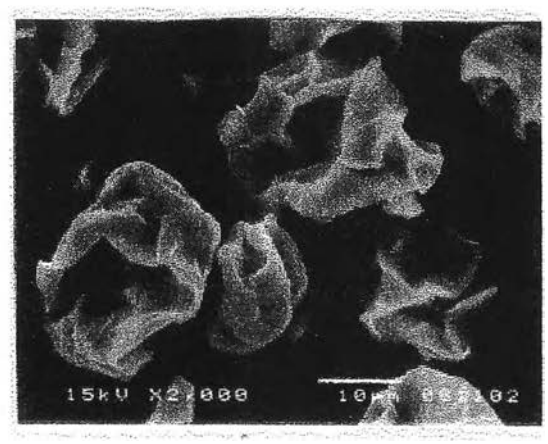
M(1)



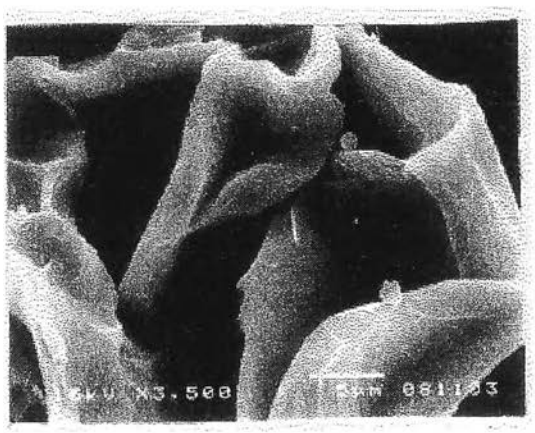
N(1)



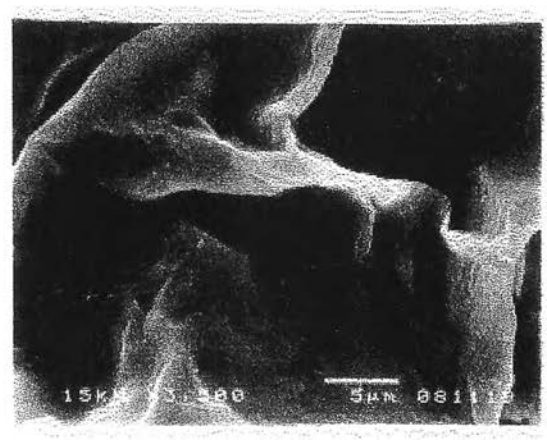
M(2)



N(2)

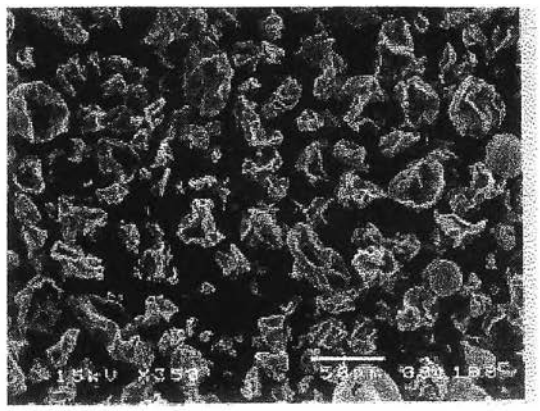


M(3)

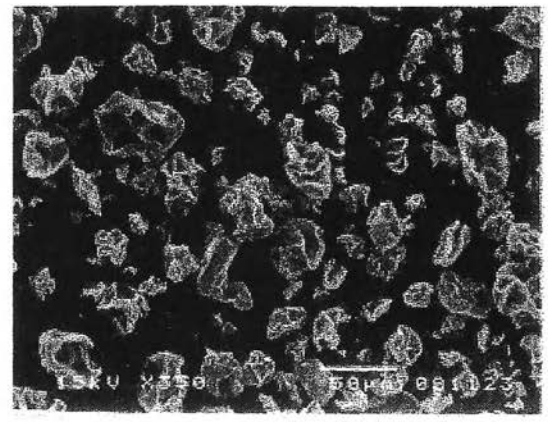


N(3)

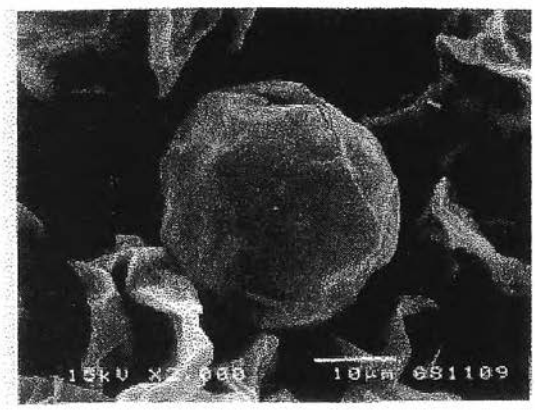
Figure 8 Scanning electron photomicrographs of spray - dried diclofenac sodium with various polymer. M = RD 1:4 , N = RL and NaCMC 1:4 (1) x 350 , (2) x 2,000 , (3) x 3,500



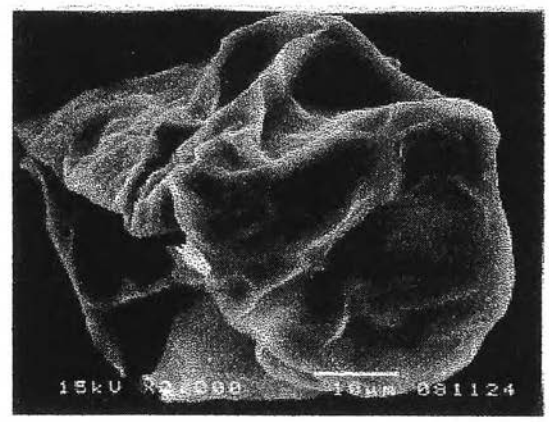
O(1)



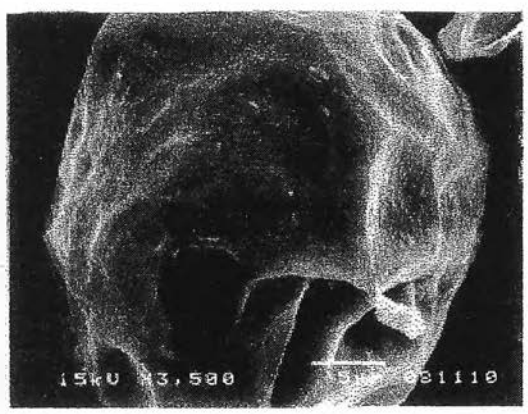
P(1)



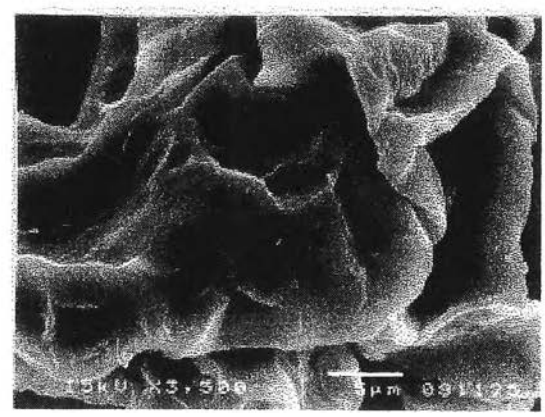
O(2)



P(2)

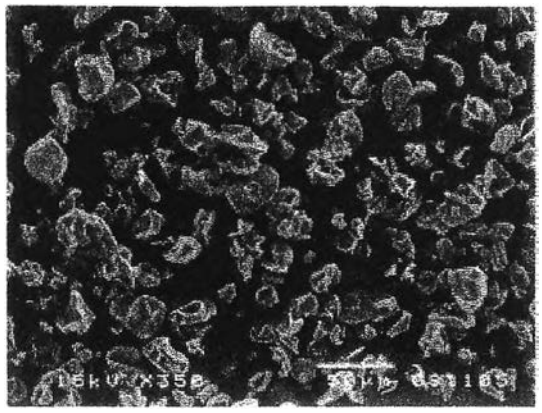


O(3)

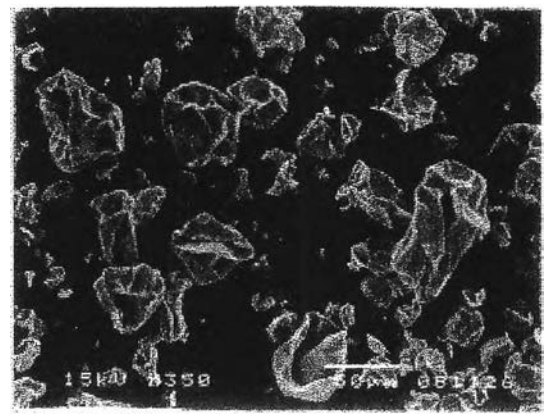


P(3)

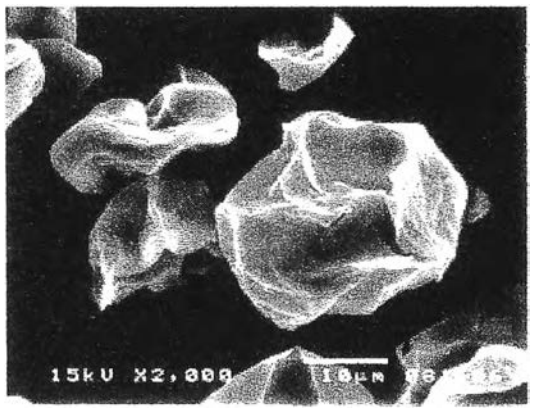
Figure 9 Scanning electron photomicrographs of spray - dried diclofenac sodium with various polymer. K = RD 1:2.33, L = RL and NaCMC 1:2.33 (1) x 350 , (2) x 2,000 , (3) x 3,500



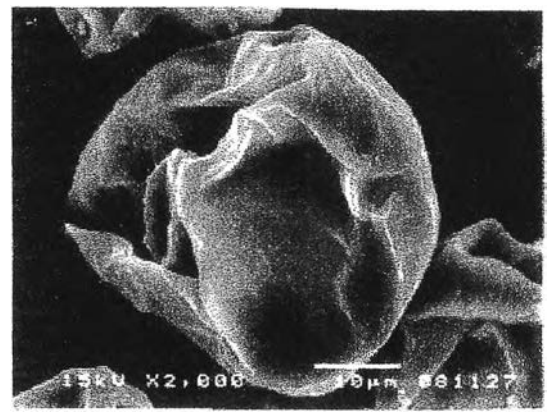
Q(1)



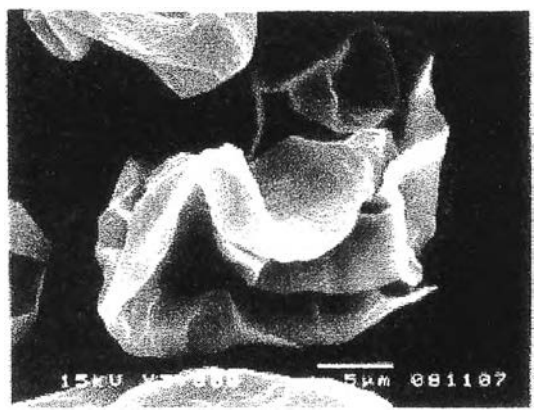
R(1)



Q(2)



R(2)



Q(3)

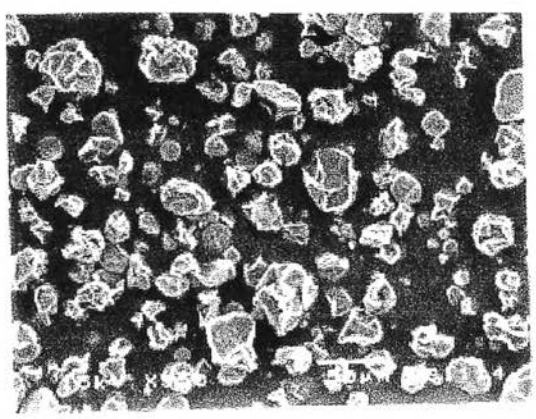
R(3)

Figure 10 Scanning electron photomicrographs of spray - dried diclofenac sodium with various polymer. Q = RD 1:1.5, R = RL and NaCMC 1:1.5 (1) x 350 , (2) x 2,000 , (3) x 3,500

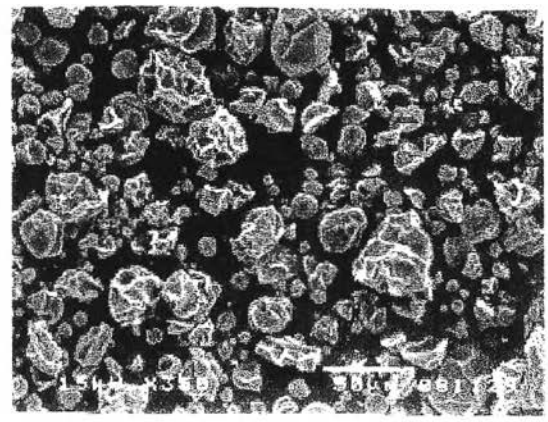
The microscopic views of spray dried diclofenac sodium powder produced by Eudragit®RD 100 (S(1)-S(3)) and Eudragit®RL 30D with NaCMC (T(1)-T(3)) at the same ratio of 1:1.5 with the aid of Aerosil® 200 are displayed in Figure 11. The two formulations that contained Aerosil ®200 in the amount of 15% of drug and polymer content. The photomicrographs of formulation that contained Eudragit® RD 100 showed porous surface of the microparticles. Aerosil®200 in the amount of 15% presented microparticles with more spherical shape than the other formulation, which did not have Aerosil®200 at the same ratio Figure 10 (Q-R).

The photomicrograph of the formulations containing Eudragit®RD 100 at the same ratio of polymer to drug ratio of 1:1.5 with the aid of Aerosil®200 at 30% of drug and polymer content are displayed in Figure 12 (Formulation 13-14). The agglomerated particles at inlet temperature 160°C (V(1)-V(3)) consisted of smaller and rounder shape and the surface area were smoother than those obtained from inlet temperature of 130°C (U(1)-U(3)). The surface of spray dried powder at inlet temperature of 130°C had porous surface include varied sizes of microparticles, whereas the particles of spray dried at the inlet temperature of 160°C consisted of compact shape and had narrow size distribution.

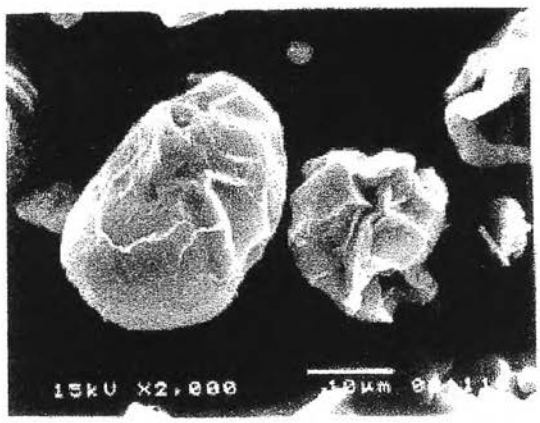
The photomicrograph of the formulations containing Eudragit®RD 100 at the same ratio of polymer to drug of 1:1.5 with the aid of Aerosil ®200 30% of drug and polymer content are displayed in Figure 13 (Formulation 14-15). When inlet temperature was 160°C and varying the feed rate, feed rate level used 12 rpm (W(1)-W(3)) and 9 rpm (X(1)-X(3)) were successful in the spray drying process of diclofenac sodium suspension . Most products obtained were microparticles with smooth surface. As the feed rate was decreased from 12 rpm to 9 rpm, the powder was slightly smaller than those produced at 12 rpm. The scanning electron photomicrographs of spray dried diclofenac sodium with Eudragit®RL30D and NaCMC, Eudragit®RL30D without NaCMC are presented in Figure 14. The agglomerated particle obtained from Eudragit®RL30D with NaCMC(Y(1)-Y(3)) included bigger irregularly shaped particles. The surface of particles was rough and shrunken and some of them were cracked.



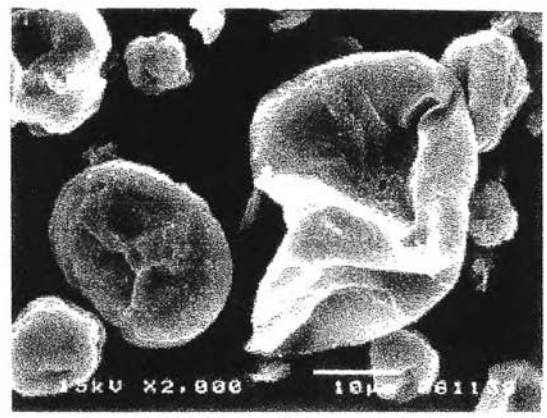
S(1)



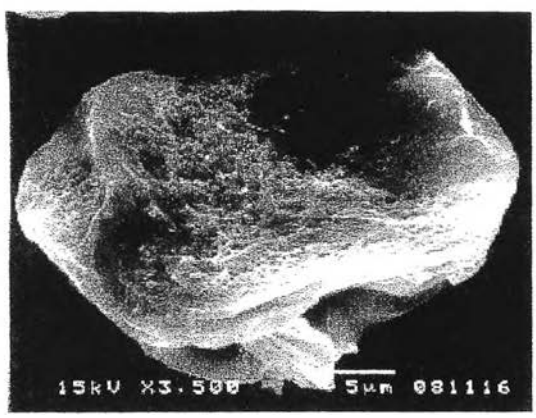
T(2)



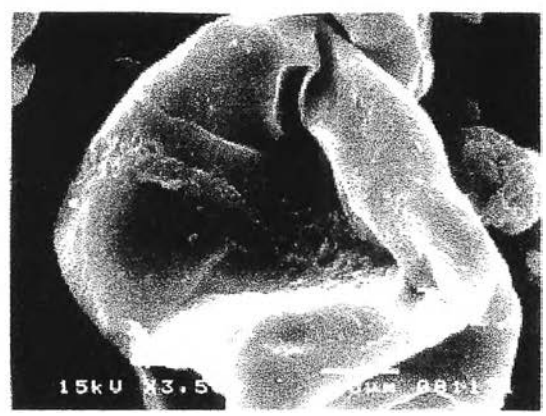
S(2)



T(2)

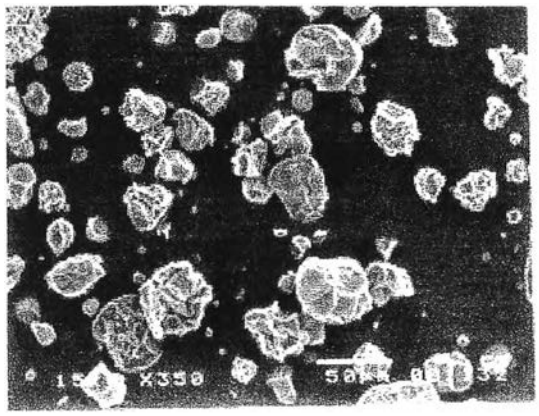


S(3)

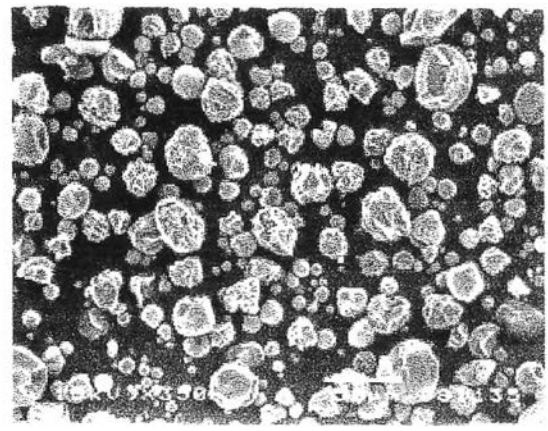


T(3)

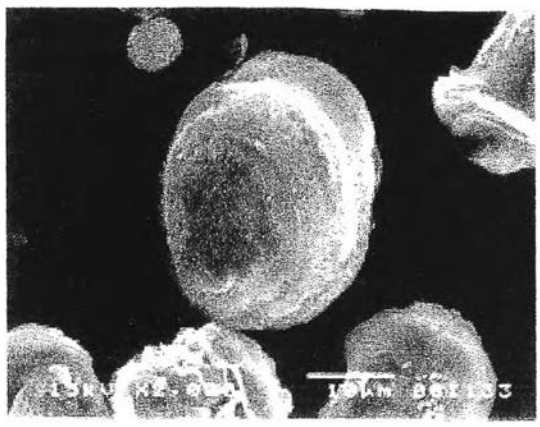
Figure 11 Scanning electron photomicrographs of spray - dried diclofenac sodium with various polymer. Q = RD 1:1.5, R = RL and NaCMC 1:1.5 and 15% w/w Aerosil®200. (1) x 350 , (2) x 2,000 , (3) x 3,500



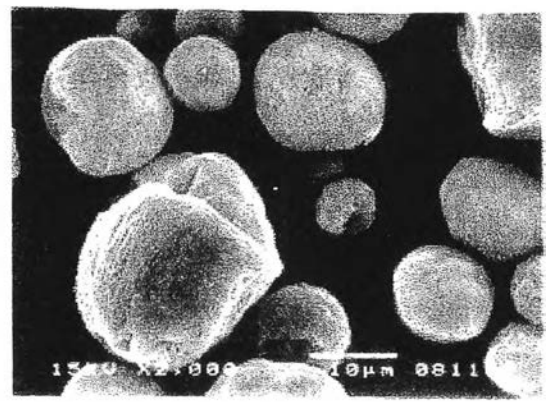
U(1)



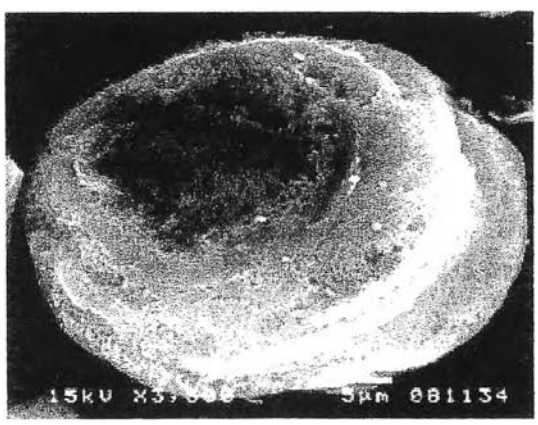
V(1)



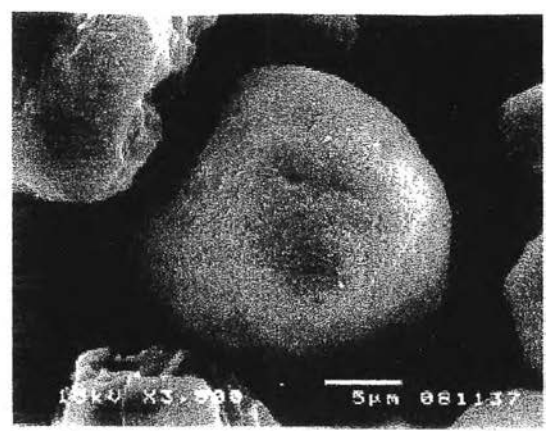
U(2)



V(2)



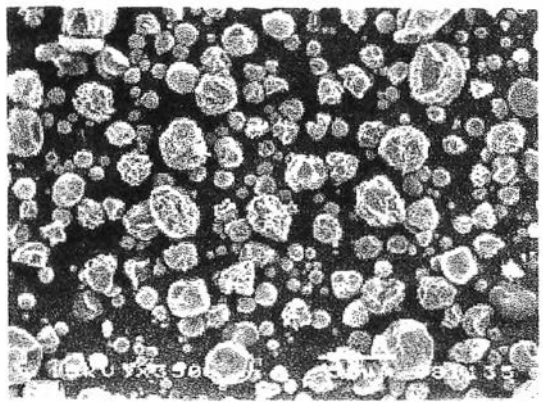
U(3)



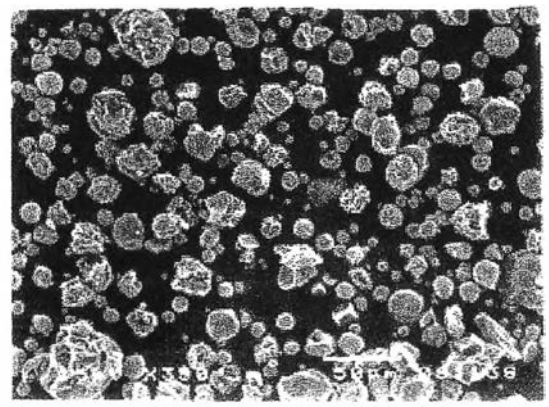
V(3)

Figure 12 Scanning Electron Photomicrographs of spray- dried diclofenac sodium with Eudragit® RD100 and Aerosil®200 30% w/w, feed rate 12 rpm (20 ml/min) at various inlet temperature. U=130° C., V =160° C.

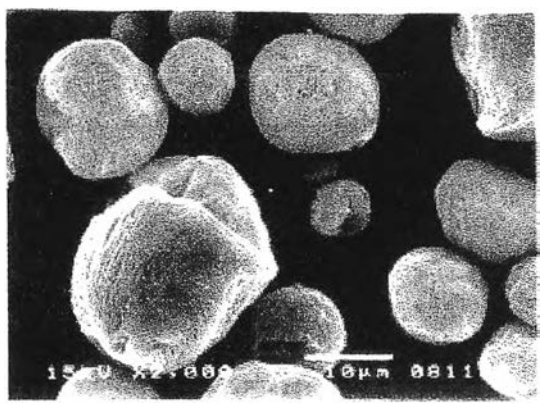
(1) x 350 , (2) x 2,000 , (3) x 3,500



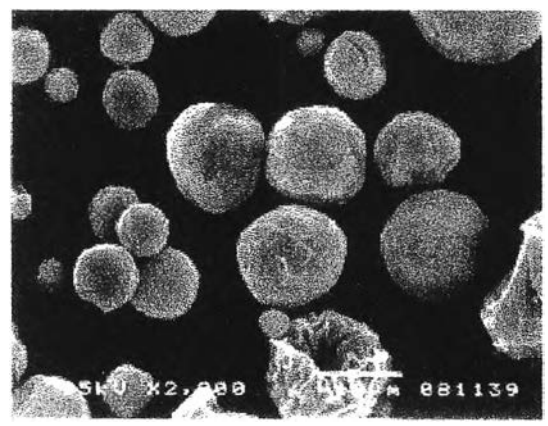
W(1)



X(1)

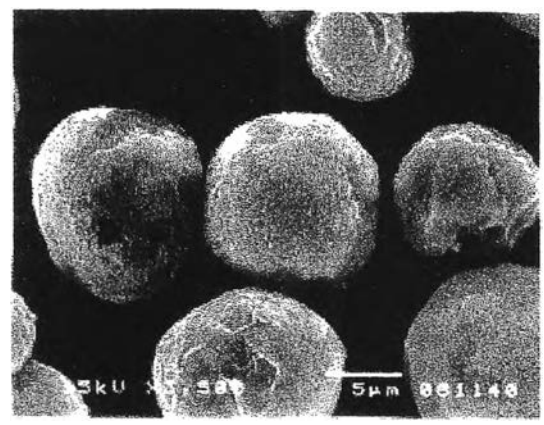


W(2)



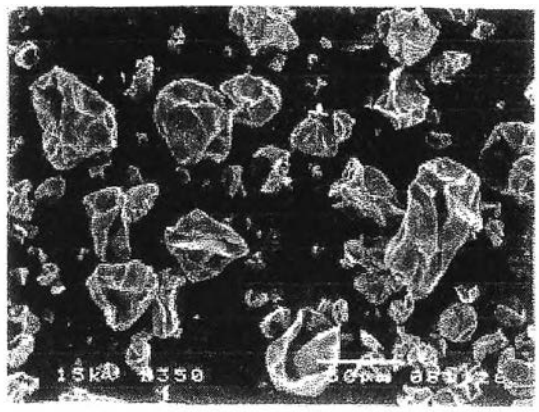
X(2)

W(3)

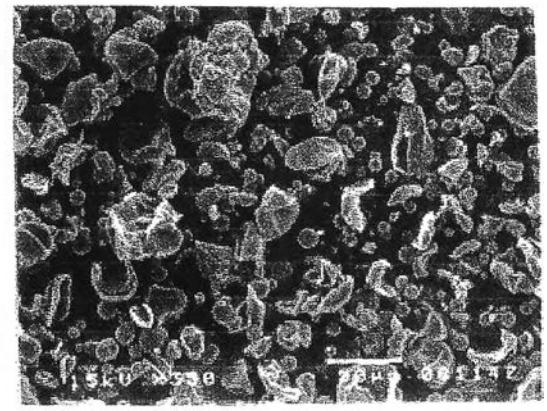


X(3)

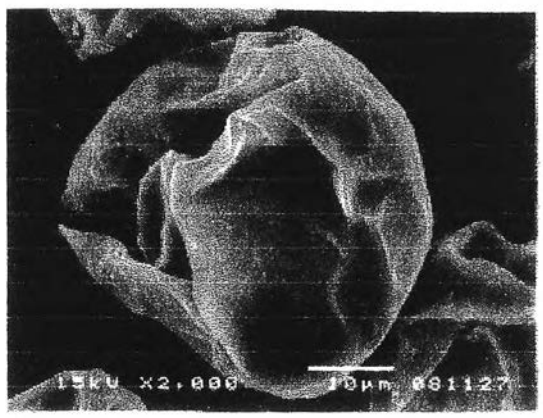
Figure 13 Scanning electron photomicrographs of spray- dried diclofenac sodium with Eudragit RD® 100 and 30% w/w Aerosil® 200, inlet temp.=160°C at various feed rate. W=12 rpm (20 ml/min) , X =9 rpm (15 ml/min)
(1) x 350 , (2) x 2,000 , (3) x 3,500



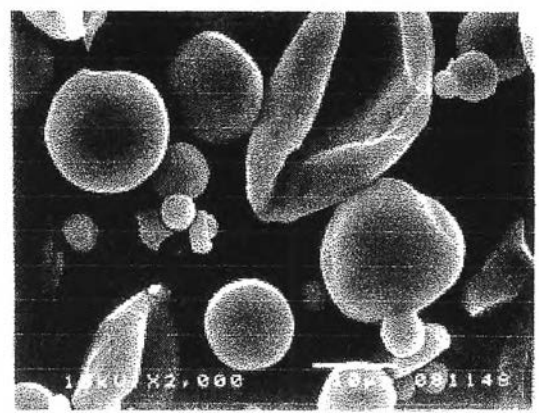
Y(1)



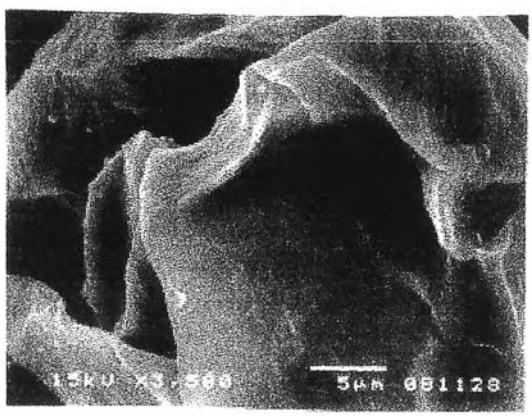
Z(1)



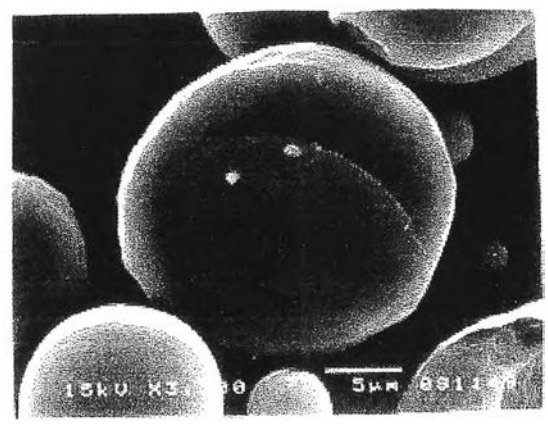
Y(2)



Z(2)



Y(3)



Z(3)

Figure 14 Scanning electron photomicrographs of spray- dried diclofenac sodium with Eudragit® RL30D. Y = RL and NaCMC 1:1.5 , Z = RL 1:1.5 (1) x 350 , (2) x 2,000 , (3) x 3,500

The Formulation which containing Eudragit®RL30D without NaCMC (Z (1)-Z (3)) showed the particles of ball shaped with relatively smaller sizes and had narrower size distribution.

The photomicrographs of diclofenac sodium, which formulated with Aerosil® 200 (S(1)-T(3)) that contained 15%w/w of drug and polymer content are shown in Figure 11 (Formulation11-12). Most products seemed to be spherical and dense shape. Varying the weight of Aerosil®200 (U(1)-X(3)) to 30%w/w of drug and polymer content (Formulation 13-15) was successful in the spray drying of diclofenac sodium suspension. Most products obtained were microparticles with smooth surface as the weight of Aerosil®200 was increased from 15 to 30 % w/w of drug and polymer content. The surface of the particles was smooth.

2. Particle size distribution

The particle size distribution of the spray dried powders are shown in Table 12. The particle size distributions are illustrated in Figures 15-26.

2.1 The spray dried diclofenac sodium at various inlet temperature

The particle size distribution of spray dried diclofenac sodium at various inlet air temperatures are shown in Figure 15 (Formulation 1-2). It was found that the size of microparticles from inlet temperature at 160°C was slightly bigger than that of using inlet air temperature at 130°C. The size of particles from using inlet temperature at 130°C that are bigger than 150 micrometers was more than 80% whereas from inlet temperature at 160°C bigger than 150 micrometers was more than 85%.

2.2 Effect of both polymeric formulations at the same polymer to drug ratio

2.2.1 The polymer to drug ratio of 1:9

The particle size distribution of diclofenac sodium from spray dried

Table 12 Particle size distribution of spray dried powders

Formulation	Inlet air Temp (°C)	Flow rate (rpm)*	Polymer to drug ratio	Aerosil (%w/w)	% Weight retained					
					Pan	106 µm	150 µm	180 µm	250 µm	425 µm
1	130	12	0:1	-	3.49	5.51	8.14	60.25	19.73	2.88
2	160	12	0:1	-	3.80	3.76	3.44	32.19	55.48	1.33
3	130	12	RD1: 9	-	3.2	20.84	51	18.92	2.52	1.56
4	130	12	RL+NaCMC1:9	-	1.48	4.72	23.52	64.12	3.96	1.8
5	130	12	RD1:4	-	0.36	1.04	2.76	28.36	64.96	2.2
6	130	12	RL+NaCMC 1:4	-	84.96	0.76	5.04	5.88	2.76	0.40
7	130	12	RD1:2.33	-	1.48	1.16	5.48	46.28	40.6	1.88
8	130	12	RL+NaCMC1:2.33	-	85.72	1.64	5.64	2.68	2.40	1.92
9	130	12	RD1:1.5	-	77.88	0.08	2.28	7.48	2.16	9.52
10	130	12	RL+NaCMC 1:1.5	-	78.32	2.56	8.36	8.16	0.4	2.12
11	130	12	RD1:1.5	15	82.56	3.68	6.28	2.96	2.36	1.16
12	130	12	RL+NaCMC 1:1.5	15	80.12	4.12	7.79	3.43	3.13	1.50
13	130	12	RD1:1.5	30	71.68	3.94	7.53	6.33	5.22	5.30
14	160	12	RD1:1.5	30	72.02	8.16	8.12	4.74	4	2.95
15	160	9	RD1:1.5	30	89.22	1.9	3.93	3.53	0.89	0.53
16	130	12	RL 1:1.5	-	80.24	3.56	4.32	7.71	3.68	0.49

* 12 rpm =20ml/min, 9rpm=15 ml/min

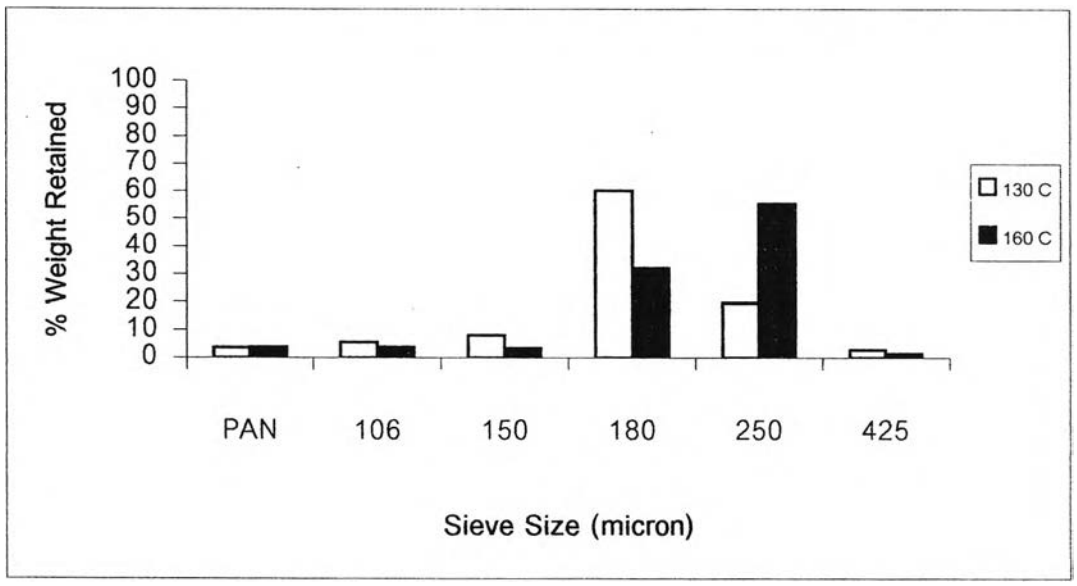


Figure 15 Particle size distribution of spray dried diclofenac sodium without polymer at various inlet air temperature.

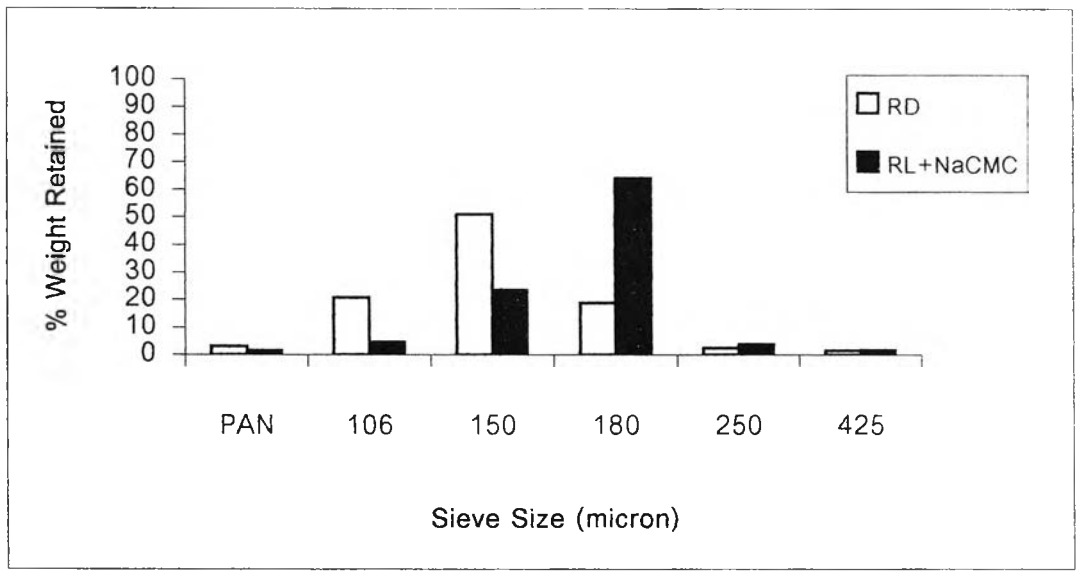


Figure 16 Particle size distribution of spray dried diclofenac sodium with Eudragit® RD 100, Eudragit® RL 30D and NaCMC at the same ratio of 1:9.

microparticles prepared by Eudragit® RD 100 compared with Eudragit® RL30D and NaCMC at the polymer to drug ratio of 1:9 are shown in Figure 16 (Formulation 3-4). It was found that the size of microparticles from Eudragit® RD 100 was smaller than that of using Eudragit ® RL30D and NaCMC. The size of particles using Eudragit® RD100 that was bigger than 106 micrometers more than 80% whereas that of using Eudragtit® RL30D and NaCMC was more than 90%.

2.2.2 The polymer to drug ratio of 1:4

The particle size distribution of diclofenac sodium from spray dried microparticles prepared by Eudragit®RD 100 compared with Eudragit®RL30D and NaCMC at the polymer to drug ratio of 1:4 are shown in Figure 17 (Formulation 5-6). It was found that the size of microparticles from Eudragit®RD 100 was bigger than that of Eudragit® RL30D and NaCMC. The size of particles containing Eudragit® RD100 that was bigger than 150 micrometers was more than 90%. In contrast that contained Eudragit®RL30D and NaCMC smaller than 106 micrometers was more than 80%.

2.2.3 The polymer to drug ratio of 1:2.33

The particle size distribution of diclofenac sodium from spray dried microparticles prepared by Eudragit® RD 100 compared with Eudragit® RL30D and NaCMC at the polymer to drug ratio of 1:2.33 are shown in Figure 18 (Formulation 7-8). It was found that the size of microparticles from Eudragit® RD 100 was bigger than that of Eudragit® RL30D combined with NaCMC. The size of particles containing Eudragit® RD100 bigger than 150 micrometers was more than 85%. In contrast that of containing Eudragit®RL30D and NaCMC smaller than 106 micrometers was more than 85%.

2.2.4 The polymer to drug ratio of 1:1.5

The particle size distribution of diclofenac sodium from spray dried

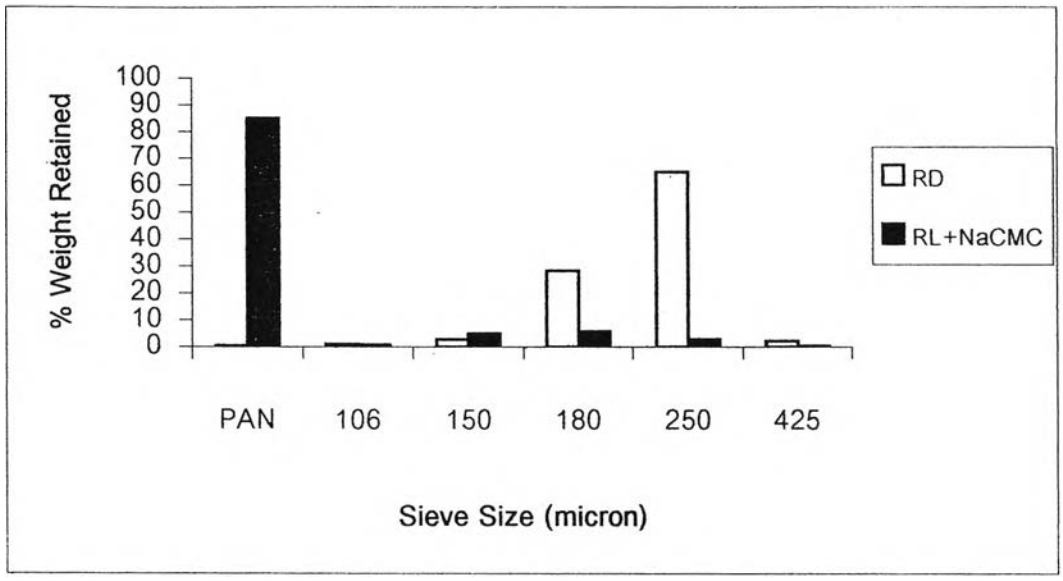


Figure 17 Particle size distribution of spray dried diclofenac sodium with Eudragit®RD 100, Eudragit® RL 30D and NaCMC at the same ratio of 1:4.

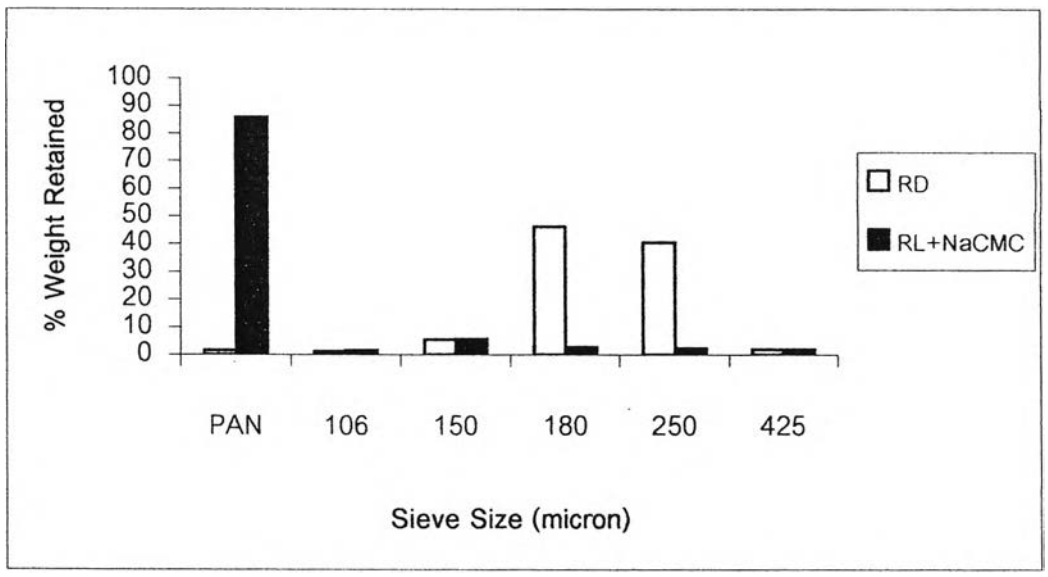


Figure 18 Particle size distribution of spray dried diclofenac sodium with Eudragit® RD 100 , Eudragit®RL 30D and NaCMC at the same ratio of 1:2.33.

microparticles prepared by Eudragit®RD 100 compared with Eudragit®RL30D and NaCMC at the polymer to drug ratio of 1:1.5 was shown in Figure 19 (Formulation 9-10). It was found that the size of microparticles from Eudragit® RD 100 was slightly bigger than that of Eudragit®RL30D and NaCMC. The size of microparticles containing Eudragit®RL30D and NaCMC smaller than 106 micrometers was more than 75%. Nevertheless, no statistically significant difference ($p>0.05$) between the size of these two formulations was observed from the paired – samples t- test (Appendix C, Table 31).

2.2.5 The polymer to drug ratio of 1:1.5 with 15% w/w Aerosil

The picture of the particle size distribution of the formulations contained diclofenac sodium with Eudragit®RD 100 compared with Eudragit® RL 30D and NaCMC at the polymer to drug ratio of 1:1.5 and the aid of Aerosil®200 at 15% w/w content of drug and polymer are shown in Figure 20. The size of spray dried powders containing both of polymers seem to be similar. The size smaller than 106 micrometers was more than 80%. Nevertheless, no statistically significant difference ($p>0.05$) between the size of these two formulations was observed from the paired – samples t- test. (Appendix C, Table 32).

2.3 Effect of inlet air temperature

The particle size distribution of diclofenac sodium from spray dried diclofenac sodium with Eudragit®RD 100 at the same ratio 1:1.5 by the aid of Aerosil® 200 30% content of drug and polymer prepared at two levels of inlet air temperature (130°C and 160°C) are displayed in Figure 21 .

The size of spray dried diclofenac sodium using inlet air temperature at 160°C was smaller than that of using 130°C. The size using inlet air temperature at 160°C smaller than 150 micrometers was more than 80%. Nevertheless, no statistically significant difference ($p>0.05$) between the size of these two formulations was observed from the paired –samples t- test (Appendix C, Table 33).

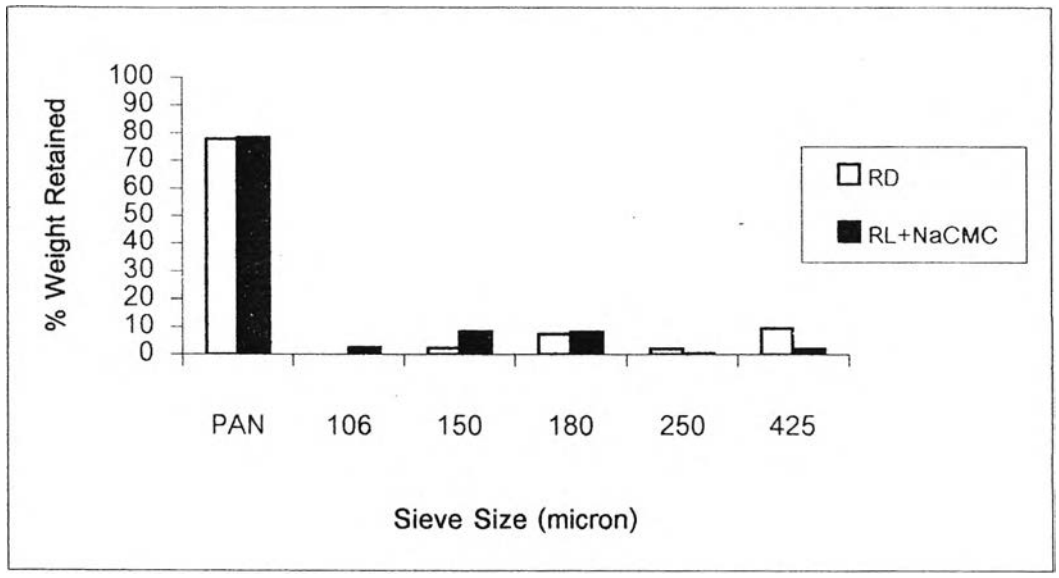


Figure 19 Particle size distribution of spray dried diclofenac sodium with Eudragit ® RD 100 , Eudragit® RL 30D and NaCMC at the same ratio of 1:1.5.

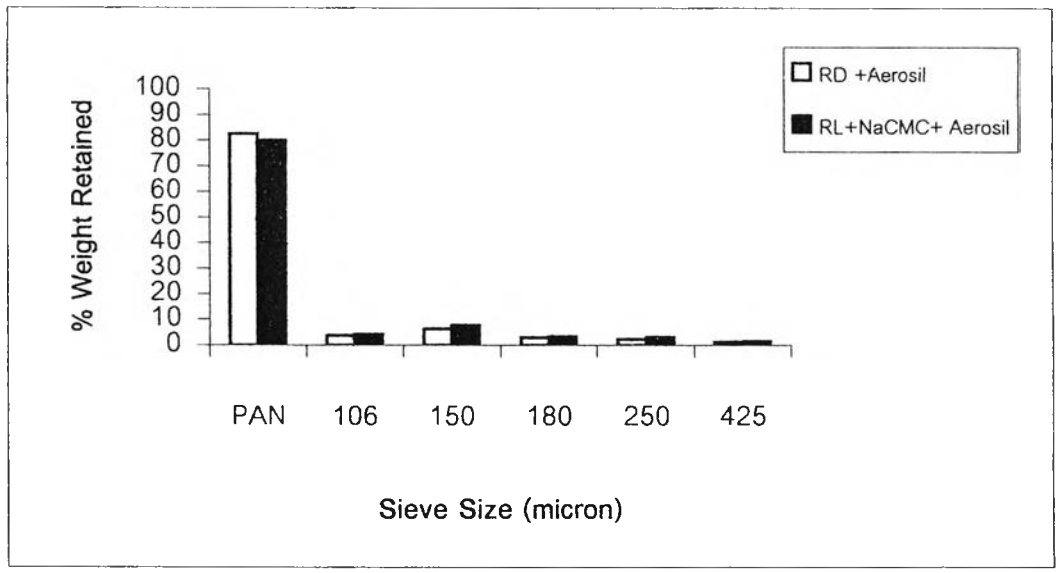


Figure 20 Particle size distribution of spray dried diclofenac sodium with Eudragit ® RD 100 , Eudragit® RL 30D and NaCMC at the same ratio of 1:1.5 and the aid 15% w/w Aerosil®200.

2.4 Effect of feed rate

The particle size distributions of diclofenac sodium from spray dried diclofenac sodium with Eudragit®RD100 at the same ratio 1:1.5 by the aid of Aerosil® 200 30% content of drug and polymer prepared at two levels of feed rate (12 rpm and 9 rpm) are displayed in Figure 22.

The size of spray dried diclofenac sodium using feed rate at 9 rpm was smaller than that of using feed rate 12 rpm. The size using feed rate at 9 rpm that was smaller than 106 micrometers was more than 89%. Nevertheless no statistically significant difference ($p>0.05$) between the size of these two Formulations was observed from the paired t- test(Appendix C, Table 34). In contrast, when tested with the independent – sample t test, the statistic test showed statistically significant difference ($p<0.05$) between the size of particles that smaller than 106 micrometers of these two formulations(Appendix C, Table35).

2.5 Effect of NaCMC

The picture of the particle size distribution of the formulations contained diclofenac sodium with Eudragit ® RL30D and NaCMC compared between with and without NaCMC at the same ratio 1:1.5 are shown in Figure 23.

The size of spray dried diclofenac sodium containing Eudragit® RL30D without NaCMC was smaller than that of using NaCMC. The size using Eudragit® RL30D without NaCMC that was smaller than 106 micrometers was more than 89% . Nevertheless, no statistically significant difference ($p>0.05$) between the size of these two formulations was observed from the paired –samples t- Test (Appendix C, Table 36).

2.6 Effect of amount of Aerosil

The picture of the particle size distribution of spray dried diclofenac sodium with Eudragit®RD100 with the aid of Aerosil® 200 0, 15, 30 % content of drug and polymer are shown in Figure 24. It was found that when increasing the amount of

Aerosil® 200 from 0 to 15 % w/w content of drug and polymer, the size of particles seemed to be smaller. The size of particles containing Aerosil® 200 15 % content of drug and polymer smaller than 106 micrometers was more than 80% but increasing the amount of Aerosil® 200 from 15 to 30 % w/w content of drug and polymer, the size of particles seemed to be much bigger. The size of particles using Aerosil®200 30 % content of drug and polymer smaller than 106 micrometers was more than 70%. Nevertheless, no statistically significant difference ($p>0.05$) between the size of these three formulations was observed from the two-way anova test (Appendix C,Table37).

2.7 Effect of polymer to drug ratio

2.7.1 Eudragit® RD100

The particle size distribution of the spray dried particles prepared from Eudragit®RD100 at different polymer to drug ratio (1:9=Formulation3, 1:4=Formulation 5, 1:2.33=Formulation 7, 1:1.5= Formulation 9) exhibited the smallest particle size when Eudragit®RD100 was formulated in the ratio of 1:1.5. Spray dried powders from Eudragit ® RD100 at the ratio 1:4 had the biggest size. The pictures of these particle size distributions of diclofenac sodium are shown in Figure 25.

2.7.2 Eudragit® RL30D and NaCMC

The particle size distribution of the spray dried particles prepared from Eudragit ® RL30D and NaCMC at different polymer to drug ratio (1:9=Formulation4, 1:4=Formulation 6, 1:2.33=Formulation 8, 1:1.5 = Formulation 10) exhibited the smallest particle size when Eudragit ® RL30D and NaCMC were formulated in the ratio of 1:2.33. Spray dried powders from Eudragit ® RL30D and NaCMC at the ratio 1:9 had the biggest size. The pictures of the particle size distributions of diclofenac sodium are shown in Figure26.

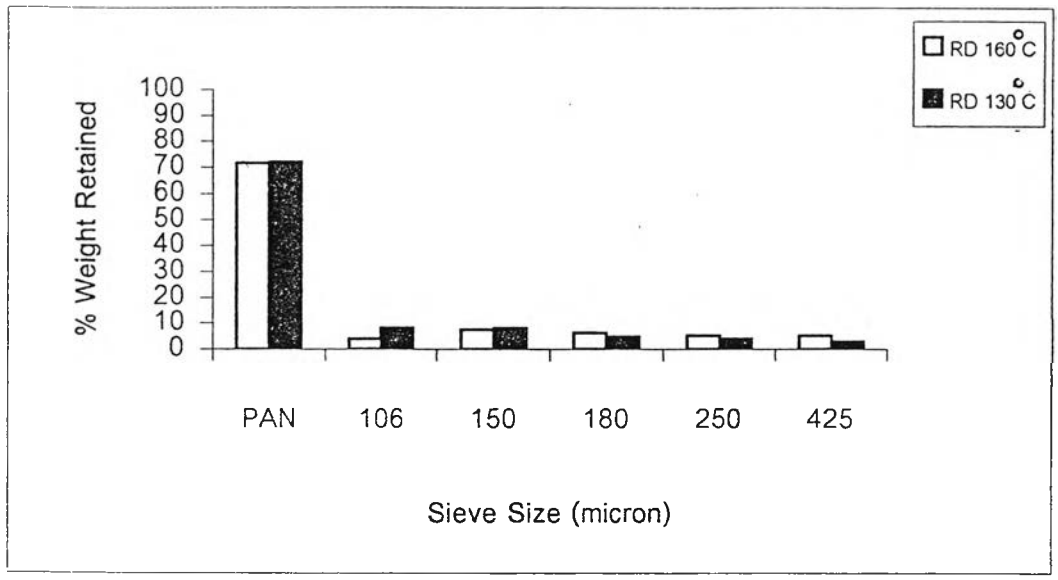


Figure 21 Particle size distribution of spray dried diclofenac sodium with Eudragit ® RD 100 (RD 1:1.5) and 30% w/w Aerosil® 200, feed rate 20 ml/min (12 rpm) at various inlet air temperature.

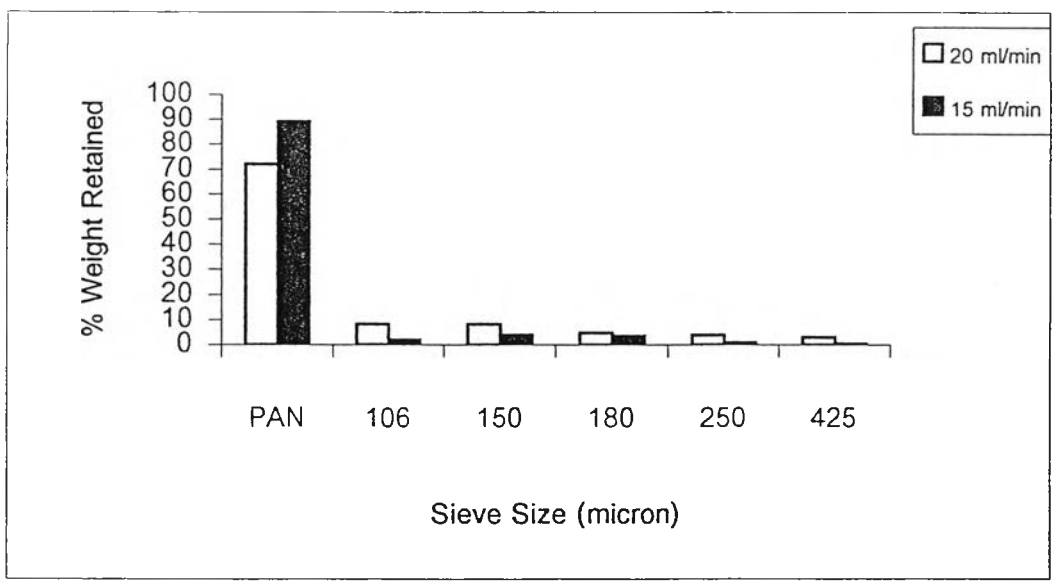


Figure 22 Particle size distribution of spray dried diclofenac sodium with Eudragit ®RD 100 (RD 1:1.5) and Aerosil ®200 30% w/w inlet temperature=160°C, at various feed rate.

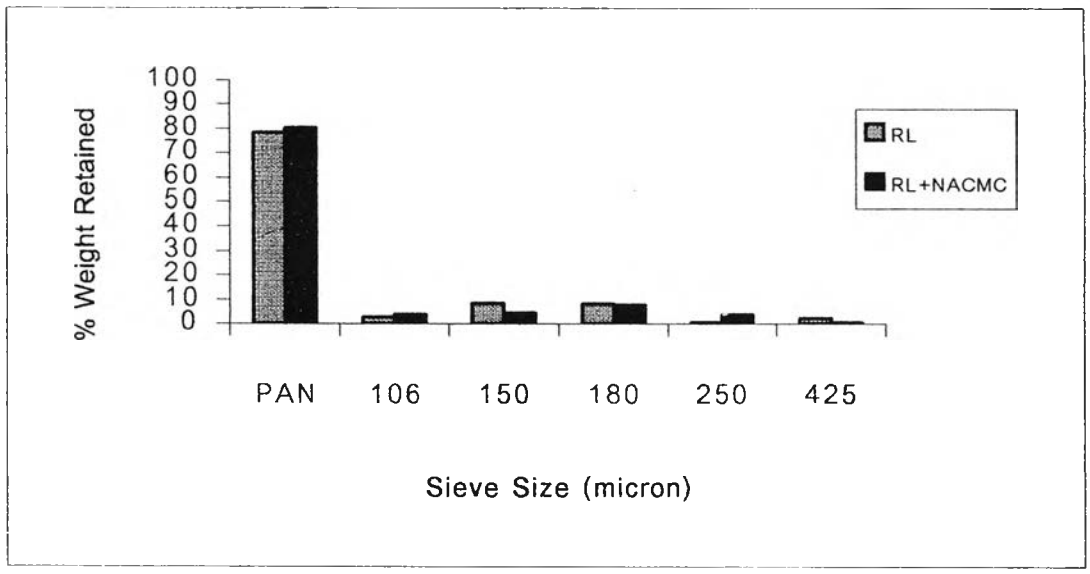


Figure 23 Particle size distribution of spray dried diclofenac sodium with Eudragit® RL 30D and Eudragit® RL 30D and NaCMC at the same ratio of 1:1.5.

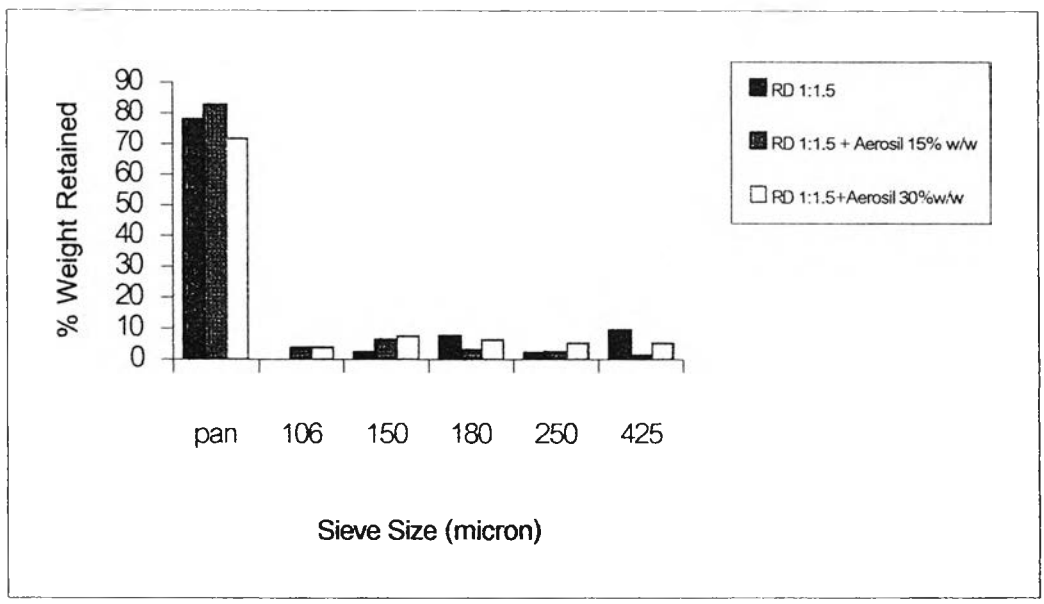


Figure 24 Particle size distribution of spray dried diclofenac sodium with Eudragit® RD 100 , with the aid of Aerosil ® 200 = 0, 15, 30 % w/w at the same ratio of 1:1.5.

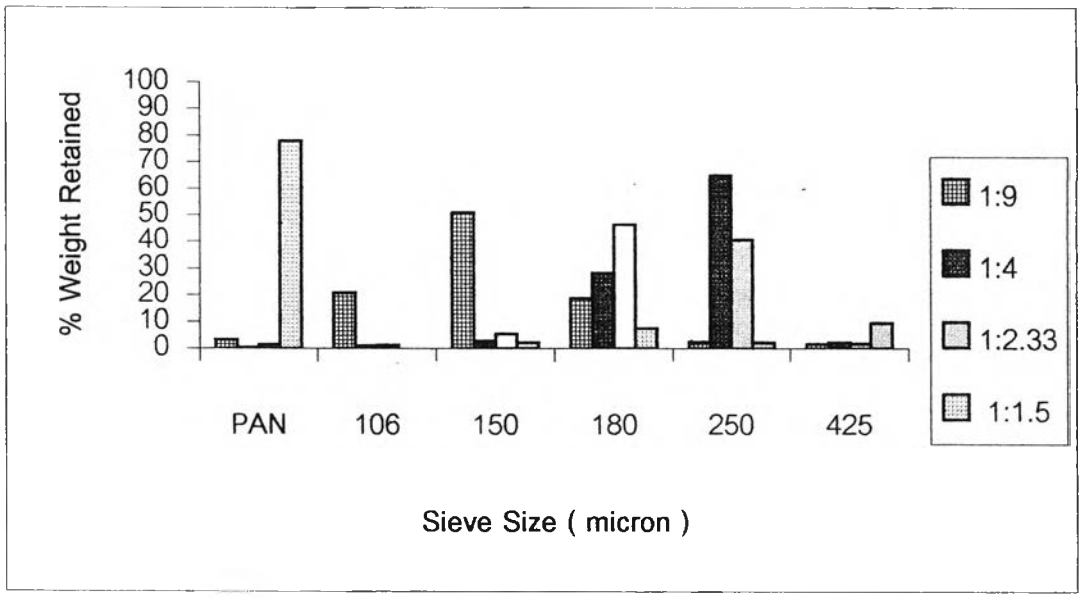


Figure 25 Particle size distribution of spray dried diclofenac sodium with Eudragit ® RD 100 at various polymer to drug ratios.

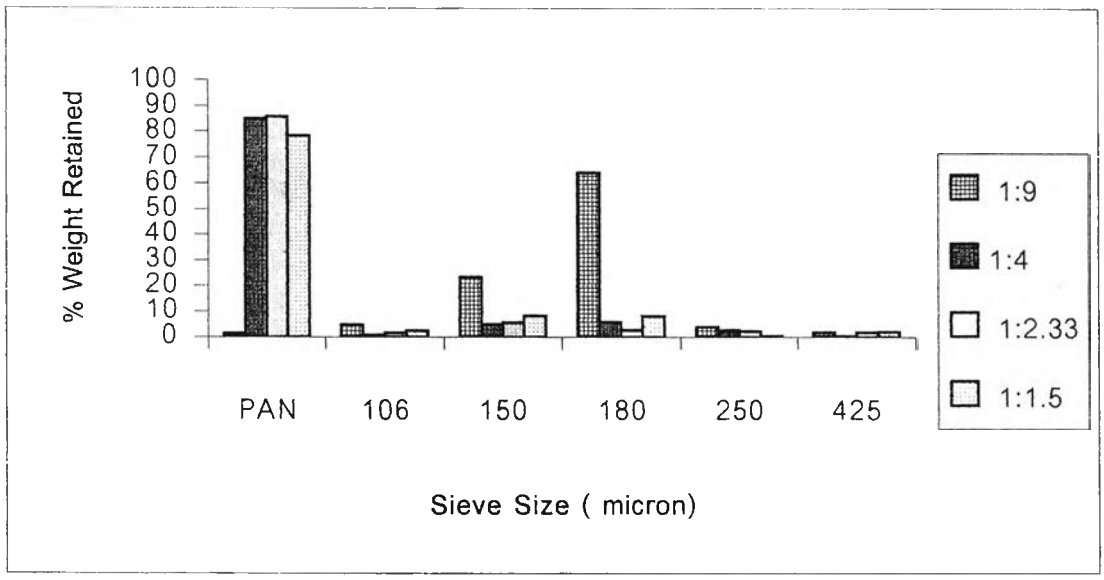


Figure 26 Particle size distribution of spray dried diclofenac sodium with Eudragit ® RL 30 D and NaCMC at various polymer to drug ratios.

3. Flow rate

The flow rate of spray dried powder in every formulations could be determined. Except Formulations 11 , 12 ,13, 14 and 15 because the powder did not flow out to form a conical heap on the cup so the time and the height of graph could not be detected by Mc Lab. The result showed that formulations 13, 14 and15 gave higher flow rate than Formulations 11,12 because the three former formulations had Aerosil ®200 of 30 % w/w but Formulations 11, 12 had less amount of Aerosil® 200. Flow rate of spray dried powders are displayed in Table 13. Other formulations the flow rate could not be measured by Mc-Lab. It might be due to the absence of Aerosil®200 in these formulations.

4. Angle of repose

Angle of repose from the spray dried powder produced by Eudragit® RD100 at the polymer to drug ratio of 1:1.5 with Aerosil® 200 of 30% were lower than 30 degrees (Formulations 13-15).

Angle of repose from the spray dried powder produced by Eudragit® RD100, Eudragit® RL30D and NaCMC at the polymer to drug ratio of 1:1.5 with Aerosil® 200 of 15% were 42.05 and 40.16 degrees, respectively. They exhibited larger angle of repose than the Formulations 13-15 but had smaller angle of repose than the other formulation without Aerosil®200. Angle of repose of spray dried powders are displayed in Table 13.

5. Bulk, Tapped densities and Percent Compressibility

The bulk and tapped densities of all preparations could be clearly concluded. When these densities were calculated to percent compressibility, the new results could be interpreted and showed the effects of Aerosil ®200. Bulk density, tapped density and percent compressibility of the spray dried powder prepared from different formulations are shown in Table 14.

Table 13 Angle of repose and flow rate of spray dried powders.

Formulation	Polymer to drug ratio	Aerosil (%w/w)	Angleof repose (°)**	Flow rate (g/sec)***
1	Spray - dried diclofenac sodium at 130°C	-	48.20 (0.06)	*
2	Spray - dried diclofenac sodium at 160°C	-	45.20 (0.06)	*
3	RD 1:9	-	46.20 (0.26)	*
4	RL+NaCMC 1:9	-	48.00 (0.10)	*
5	RD 1:4	-	47.45 (0.43)	*
6	RL+NaCMC 1:4	-	46.07 (0.05)	*
7	RD 1:2.33	-	47.39 (0.45)	*
8	RL+NaCMC 1:2.33	-	48.29 (0.09)	*
9	RD 1:1.5	-	44.30 (0.25)	*
10	RL+NaCMC 1:1.5	-	42.65 (0.05)	*
11	RD 1:1.5	15	42.05 (0.08)	21.72 (0.66)
12	RL+NaCMC 1:1.5	15	40.16 (0.05)	19.43 (0.67)
13	RD 1:1.5	30	28.65 (0.04)	25.23 (0.82)
14	RD 1:1.5	30	30.20 (0.02)	30.83 (0.98)
15	RD 1:1.5	30	28.13 (0.10)	28.04 (0.44)
16	RL 1:1.5	-	45.26 (0.08)	*

* can not measure flow rate by Mc Lab

** standard deviation from 3 determinations

*** standard deviation from 6 determinations

Formulation 14-15 spray dried at inlet temperature = 160 °C

Formulation 15 spray dried at feed rate 15 ml/min (9 rpm)

The bulk and tapped densities of both polymeric formulations (Eudragit® RD100, Eudragit® RL30D+NaCMC) at the same ratio of (1:9, 1:4, 1:2.33, 1:1.5) showed no significant differences. These values were obviously increased with increasing the polymer to drug ratio. Comparision between the formulations prepared from Eudragit® RL30D with and without NaCMC (Formulation 10, 16) showed that the formulation without NaCMC gave lower bulk and tapped densities than those of with NaCMC. Increasing the amount of Aerosil® 200 into the formulation showed the increasing of bulk and tapped densities. The process variables such as inlet temperature and feed rate did not affect bulk and tapped densities.

Percent compressibility values of the spray dried powders prepared from both polymeric formulation were compared. When the polymer to drug ratios were 1:9, 1:4, 1:2.33, 1:1.5, percent compressibility showed no differences between these formulations at the same ratio. Comparision between the formulations prepared from Eudragit® RL30D with and without NaCMC (Formulation 10, 16) showed that the formulation without NaCMC gave lower percent compressibility than those of with NaCMC. Increasing the amount of Aerosil®200 into formulation showed that the percent compressibility decreased. Thus, there was a tendency that the percent compressibility withld decrease when the percent of Aerosil®200 in the formulation increased. The process variables such as inlet air temperature and feed rate did not affect the percent compressibility because there was no significant difference in these values of these three formulations (13, 14, 15).

6. Viscosity

The viscosity of suspension feed of both polymeric formulations at the various ratio are displayed in Table15. The viscosity of suspension feed prepared from both polymeric formulations (Eudragit® RD100, Eudragit® RL30D and NaCMC) at the same polymer to drug ratio of 1:9 (Formulation 3-4), 1:4 (Formulation 5-6) were not significantly different. Increasing the polymer to drug ratio to 1:2.33(Formulation 7-8)

Table 14 The bulk density, tapped density and percent compressibility of the spray dried products prepared from different formulations.

Formulation	Polymer:Drug Ratio	Bulk density (g/ml)*	Tapped density (g/ml)*	%Compressibility (%)
1	0:1, 130°C	0.2538	0.4348	41.63
2	0:1, 160°C	0.2825	0.4717	40.11
3	RD1:9	0.2174	0.3289	33.90
4	RL+NaCMC1:9	0.2137	0.3311	35.46
5	RD1:4	0.2304	0.3632	36.56
6	RL+NaCMC1:4	0.2370	0.3676	35.53
7	RD1:2.33	0.2427	0.3704	34.48
8	RL+NaCMC1:2.33	0.2432	0.3821	36.35
9	RD1:1.5	0.3145	0.4710	33.23
10	RL+NaCMC1:1.5	0.3106	0.4764	34.80
11	RD1:1.5+A15%w/w	0.3950	0.5651	30.10
12	RL+NaCMC1:1.5 +A 15%w/w	0.3937	0.5682	30.71
13	RD1:1.5+A30%w/w	0.4202	0.5682	26.05
14**	RD1:1.5+A30%w/w	0.4132	0.5624	26.53
15***	RD1:1.5+A30%w/w	0.4137	0.5650	26.78
16	RL 1:1.5	0.2925	0.4032	32.21

* Average from three determinations

** Formulation 14 , inlet temperature = 160°C, feed rate = 20 ml/min

*** Formulation 15, inlet temperature = 160°C, feed rate = 15 ml/min

Formulation 1-13, 16, inlet temperature = 130°C, feed rate = 20 ml/min

A=Aerosil ®200

and 1:1.5 (Formulation 9-10), showed significantly different between the viscosity of suspension feed. At the polymer to drug ratio 1:1.5 and 1:2.33, the viscosity suspension feed prepared from Eudragit® RL30D and NaCMC was higher than that prepared from Eudragit® RD100. Comparision between the viscosity of suspension prepared from Eudragit® RL30D with and without NaCMC showed that the viscosity without NaCMC (Formulation 16), was lower than that with NaCMC (Formulation10). Increasing polymer to drug ratio of both polymeric formulation from 1:9 to 1:1.5 increased the viscosity of the suspension feed.

Table 15 The viscosity of suspension feed of both polymeric formulation at the various ratios.

Formulation	Eudragit® RD100 (g)	Eudragit® RL30D (g)	NaCMC (g)	DI water qs.to (g)	Viscosity (Cps)*
3	5	-	-	500	12.78
4	-	4.55	0.45	500	13.08
5	10	-	-	500	16.39
6	-	9.1	0.9	500	16.48
7	15	-	-	500	22.29
8		13.65	1.35	500	32.89
9	20	-	-	500	24.49
10	-	18.2	1.8	500	70.10
16	-	20.0	-	500	11.88

* =Average from three determinations

7. Porosity Determination

The surface area and the total pore volume of spray- dried particles were measured by BET method. The specific surface area and the total pore volume of

spray-dried diclofenac sodium with both polymeric formulations in different inlet air temperatures and feed rates are displayed in Table 16.

Table 16 The specific surface area and the total pore volume of spray-dried powders.

Formulation	Polymer to Drug Ratio	Inlet Air Temperature (°C)	Feed Rate (rpm) **	Specific Surface Area (m^2/g)	Total Pore Volume (cm^3/g)
9	RD:1.5	130	12	1.33 ± 0.02	0.31
10	RL+ NaCMC1:1.5	130	12	0.90 ± 0.01	0.21
13*	RD1:1.5	130	12	13.23 ±0.14	3.04
14*	RD1:1.5	160	12	10.43± 0.11	2.40
15*	RD1:1.5	160	9	11.01± 0.05	2.53
16	RL1:1.5	130	12	0.78 ± 0.01	0.18

* Formulation 13-15 had Aerosil 200 30%w/w of content of drug and polymer

** 12 rpm = 20 ml/min, 9 rpm=15 ml/min

Comparison between the products produced from both polymeric formulation (Eudragit® RD100, Eudragit® RL 30D and NaCMC) at the same ratio of 1:1.5, the formulation that prepared from Eudragit® RL 30D and NaCMC had a lower specific surface area and also lower pore volume (Formulation 9, 10). Comparison between the formulation that prepared from Eudragit® RL 30D with and without NaCMC showed that the products without NaCMC had a lower specific surface area and also lower total pore volume (Formulation 10, 16). Comparison between the formulation prepared from Eudragit® RD 100 that contained the polymer to drug ratio of 1:1.5 and Aerosil® 200 30% at feed rate was 12 rpm, (Formulation 13=130°C, Formulation 14=160°C) showed that the formulation which used inlet air temperature of 160 °C gave lower specific surface area and also total pore volume than those used inlet air temperature of 130°C. There was a tendency to decrease in the specific surface area

and total pore volume when increasing the inlet air temperature. Comparision between the formulation prepared from Eudragit®RD 100 that contained the polymer to drug ratio 1:1.5 and Aerosil® 200 30% with inlet air temperature of 160°C, and various feed rate (Formulation 14=12 rpm, Formulation 15=9 rpm) showed that the formulation which used feed rate of 9 rpm gave higher specific surface area and also total pore volume than those used feed rate of 12 rpm. There was a tendency to increase in the specific surface area and total pore volume when decreasing the feed rate.

8. Drug content

The percentage of drug content of the spray dried powder prepared from various formulations are displayed in Table 17. The standard deviation shown implied the uniformity of drug distribution in spray dried product.

Table 17 The percentage of drug content in spray dried products.

Formulation	% Drug content	% Drug amount*
1	97.68	97.68 (0.11)**
2	99.80	99.80 (0.06)
3	90.15	100.17 (0.11)
4	91.56	101.73 (0.08)
5	82.02	102.52 (0.37)
6	79.90	99.88 (0.07)
7	70.39	100.56 (0.15)
8	69.43	99.18 (0.15)
9	60.17	100.29 (0.17)
10	59.89	99.82 (0.08)
11	52.81	101.22 (0.23)
12	53.72	102.98 (0.07)
13	45.38	98.34 (0.13)
14	45.34	98.24 (0.08)
15	45.01	97.54 (0.09)
16	59.80	99.66 (0.21)

* Average from three determinations (based on theoretical amount)

** Standard deviation

9. The Yield of Production

In spray drying process the liquid was atomized into droplets and the droplets were transformed into the dried particles. The products were collected from the collector. The percentage recovery from the collector is displayed in Table 18. The yield of production was expressed as the weight percentage of the final product harvested with respect to the initial amount of polymer and drug sprayed. The total product yield was good, particularly in the low quantity of polymer used for preparation. When increasing the concentration of polymer in the formulation, the product yield decreased. Large amount of powder adhered to the wall of drying chamber and could not be harvested. When increasing the amount of Aerosil® 200 into formulation the percent yield increased markedly. It was clearly shown that the inlet air temperature, the feed rate and the atomizing air pressure did not affect to the total percentage recovery of the spray dried products.

Table 18 The percent yield of spray-dried products from collector.

Formulation	Percent of production yield
1	91.76
2	92.35
3	87.73
4	85.56
5	80.72
6	79.90
7	75.48
8	77.91
9	62.42
10	64.45
11	66.38
12	68.47
13	76.43
14	77.49
15	76.46
16	69.39

10. Infrared Spectra

The IR spectra of diclofenac sodium and spray dried diclofenac sodium at 130^0C and 160^0C are shown in Figure 27. The principle peaks were observed at wavenumbers 749, 769, 1285, 1308, 1507 and 1577 cm^{-1}. The peaks at 749 and 769 cm^{-1} resulted from C-H out of plane bending. The IR adsorption bands at 1285 and 1308 cm^{-1} resulted from C-N stretching and the peaks at 1507 and 1577 cm^{-1} resulted from C=C stretching.

Figure 28 exhibits the IR spectra of Eudragit® RL30D and Eudragit® RD100. The IR spectra of Eudragit® RL30D showed the characteristic bands for the esters groups at 1150-1190 and 1240-1270 cm^{-1} and the C=O ester vibration at 1730 cm^{-1}. The IR absorption spectra at 1385, 1450, 1475 and 2950-3000 cm^{-1} resulted from CH_x vibration. The IR spectra of Eudragit® RD100 similarly showed the characteristic bands for the esters groups at 1150-1190 and 1240-1270 cm^{-1} and the C=O ester vibration at 1730 cm^{-1}. The IR absorption spectra at 1385, 1450, 1475 and 2950-3000 cm^{-1} resulted from CH_x vibration. The characteristic bands at 1604 resulted from carboxylate bond, and further OH vibration at 3450 and C=O bond at 950-1100 cm^{-1}.

Figure 29 exhibits the IR spectra of NaCMC and Aerosil® 200. The IR spectra of NaCMC showed the characteristic bands for the esters groups at 1240-1270 cm^{-1}, the carboxylate bone at 1604 and further OH vibration at 3450 cm^{-1}. The IR spectra of Aerosil 200 showed the characteristic bands for Si-O-Si at 1095-1015 cm^{-1}.

The IR spectra of spray dried diclofenac sodium with Eudragit® RD100 at the different polymer to drug ratios are illustrated in Figure 30. The spray dried powders showed the spectra of diclofenac sodium and Eudragit® RD100 in every drug to polymer ratios, and also revealed that the eminent peaks of both diclofenac sodium and Eudragit® RD100 did not shift. This indicated that the interaction between

diclofenac sodium and Eudragit® RD100 was scarced. Increasing the polymer to drug ratio signified the intensities of the IR absorption peak at 1730 cm^{-1}.

As the same result from as Eudragit® RD100, the IR spectra of spray dried diclofenac sodium with Eudragit® RL 30D and NaCMC at the different polymer to drug ratios are illustrated in Figure 31. The spray dried powders showed the spectra of diclofenac sodium and Eudragit® RL 30D and NaCMC in every drug and polymer ratio, and also revealed that the eminent peaks of both diclofenac sodium and Eudragit® RL30D did not shift. These indicated that the interaction between diclofenac sodium and Eudragit RL® 30D with NaCMC was scarced. Increasing the polymer to drug ratio signified the intensities of the IR absorption peaks at 1730cm^{-1}.

Figure 32 depicts the IR spectra of spray dried diclofenac sodium with Eudragit® RD100 with Aerosil 30% w/w at the same ratio of polymer to drug 1:1.5 from various inlet temperature (Formulation 13-14). Increasing the inlet air temperature from 130°C to 160°C, the IR absorption peaks of both inlet air temperatures seemed to be similar. The spray dried powders showed the combined spectra of diclofenac sodium and Eudragit® RD 100. The observation indicated no difference in the positions of the spectra and still revealed the eminent peaks both of drug and polymer. Comparision with spray dried diclofenac sodium without polymer showed that the C-N stretching peaks of diclofenac sodium at 1308 cm^{-1} were disappeared and the IR absorption peaks of both temperatures at 1095 cm^{-1} were higher intensities. Comparision between spray dried diclofenac sodium without polymer and spray dried with Eudragit® RD 100 at the same inlet temperature of 130° C, the IR peaks at 1577 cm^{-1} of spray dried diclofenac sodium with Eudragit RD 100 were higher intensities. At the inlet air temperature at 160°C, there was no difference between IR peak at 1577 cm^{-1} from using inlet temperature at 130°C

Figure 33 depicts the IR spectra of spray dried diclofenac sodium with Eudragit® RD100 with Aerosil 30% w/w at the same ratio of polymer to drug 1:1.5 from various feed rate. (Formulation 14-15). Decreasing the feed rate from 12 to 9 rpm, there was difference between the IR absorption peaks of the two feed rates because the IR absorption peak at 1577 cm^{-1} was of lower intensities. The spray

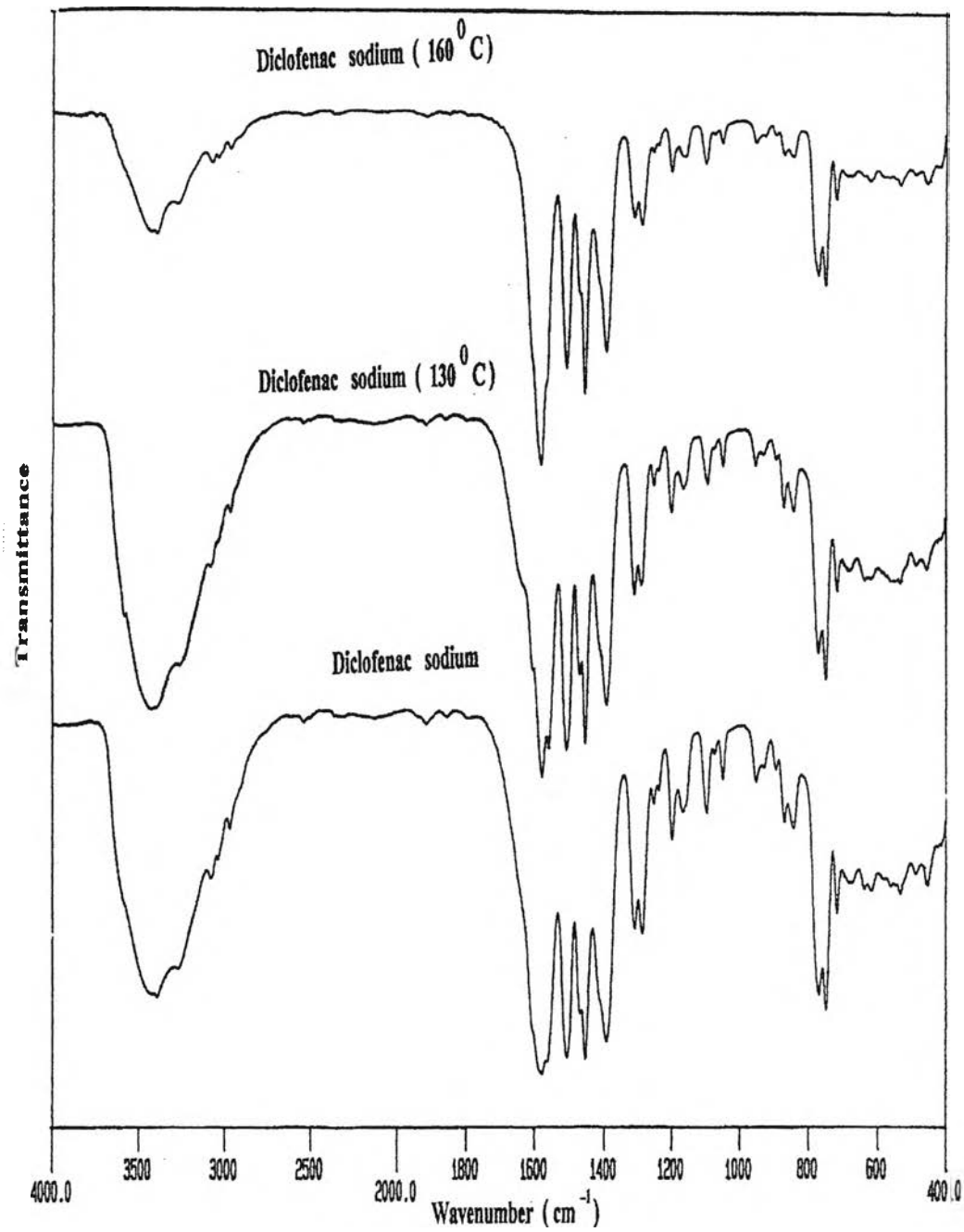


Figure 27 IR spectra of diclofenac sodium and spray dried diclofenac sodium at various inlet temperature.

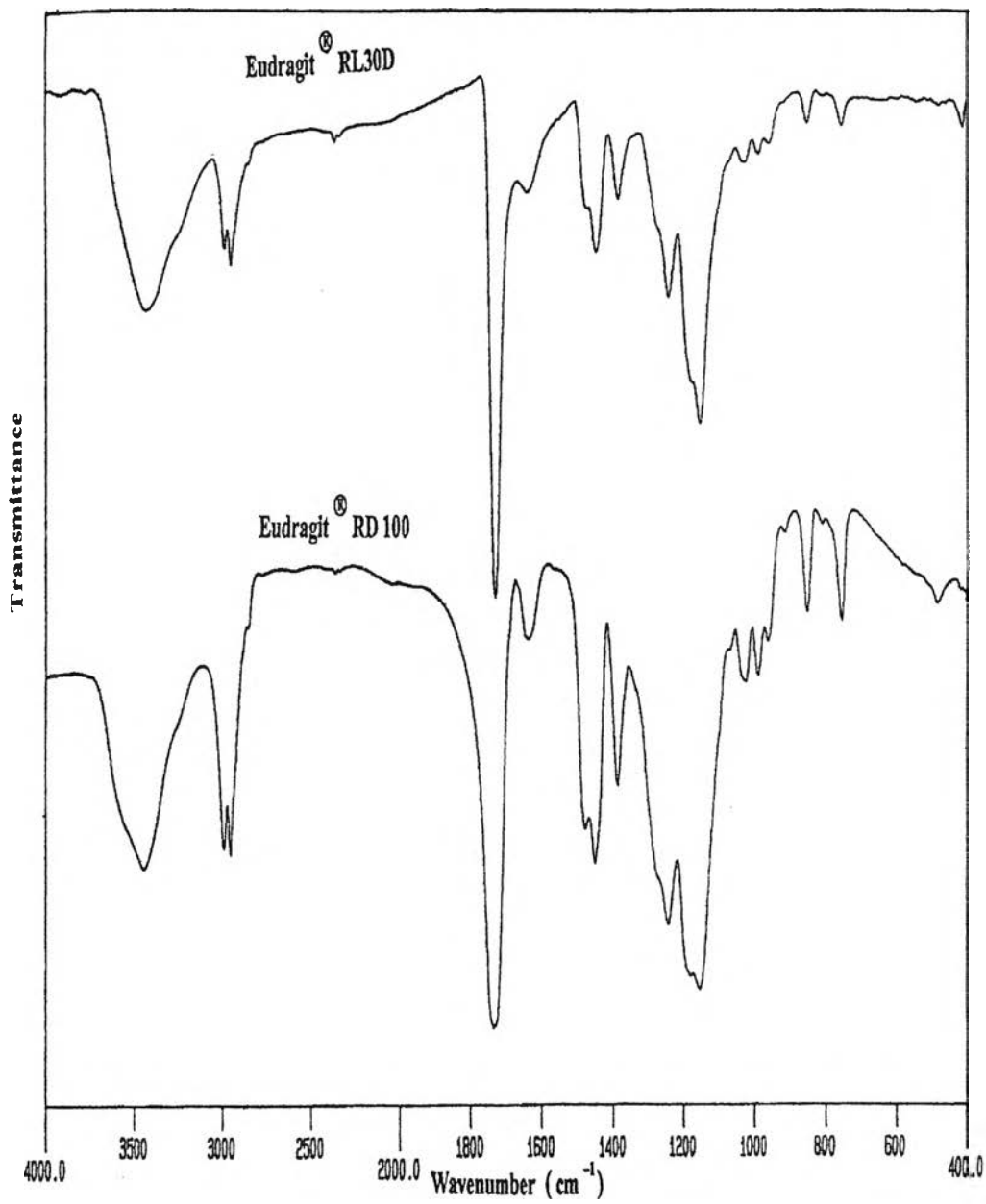


Figure 28 IR spectra of Eudragit®RL30D and Eudragit® RD100.

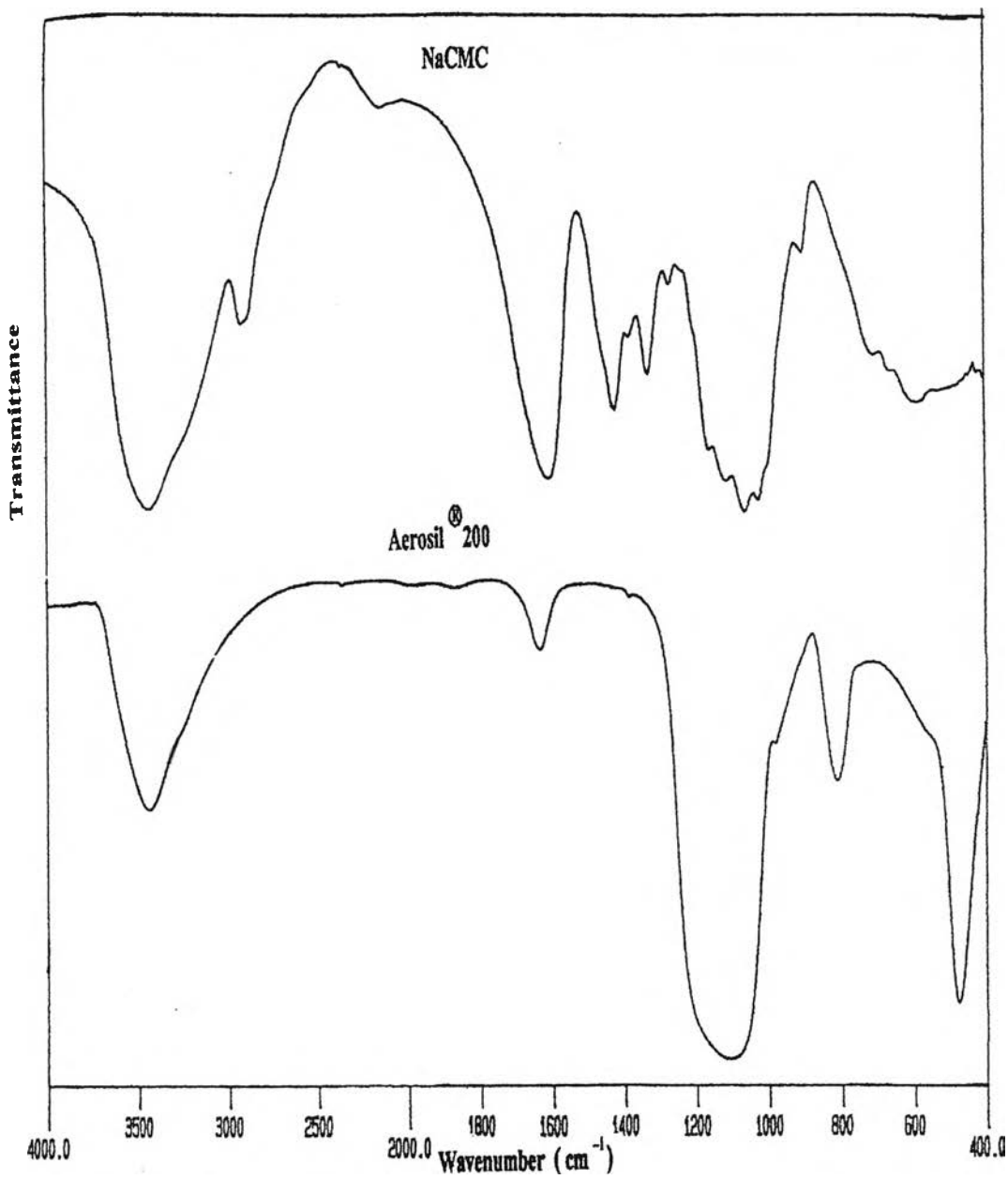


Figure 29 IR spectra of NaCMC and Aerosil® 200.

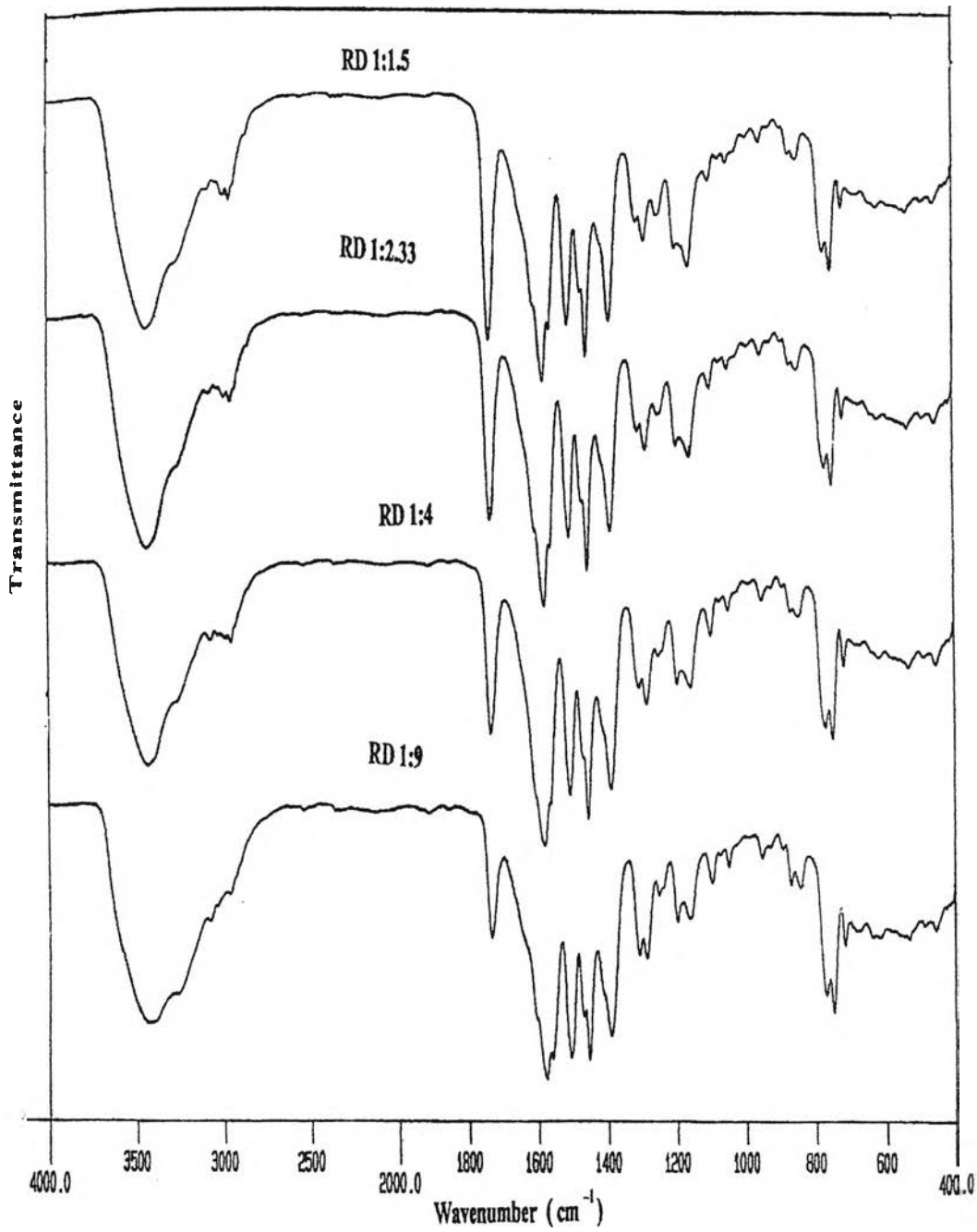


Figure 30 IR spectra of spray dried diclofenac sodium with Eudragit®RD100 at various polymer to drug ratios.

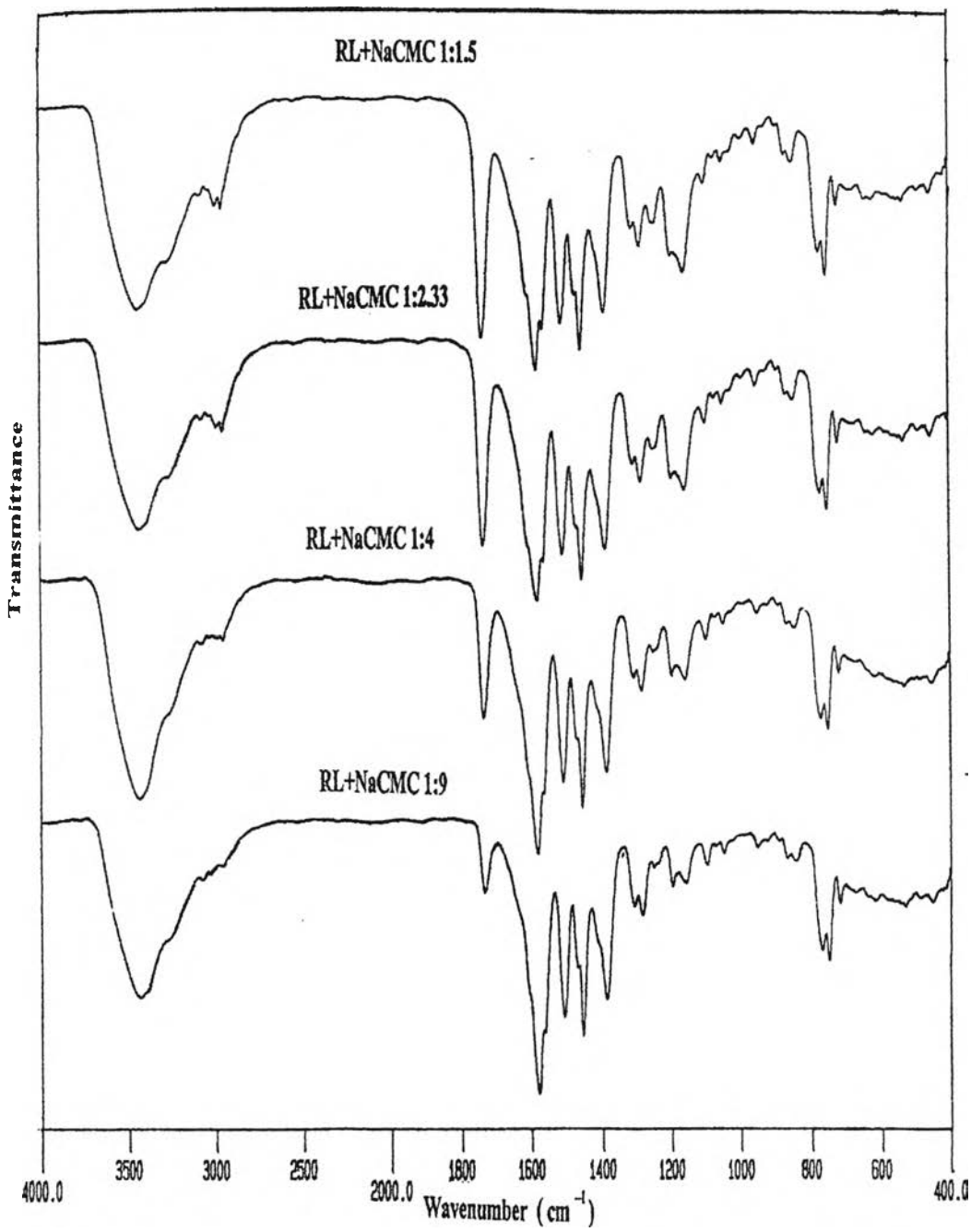


Figure 31 IR spectra of spray dried diclofenac sodium with Eudragit® RL30D and NaCMC at various polymer to drug ratios.

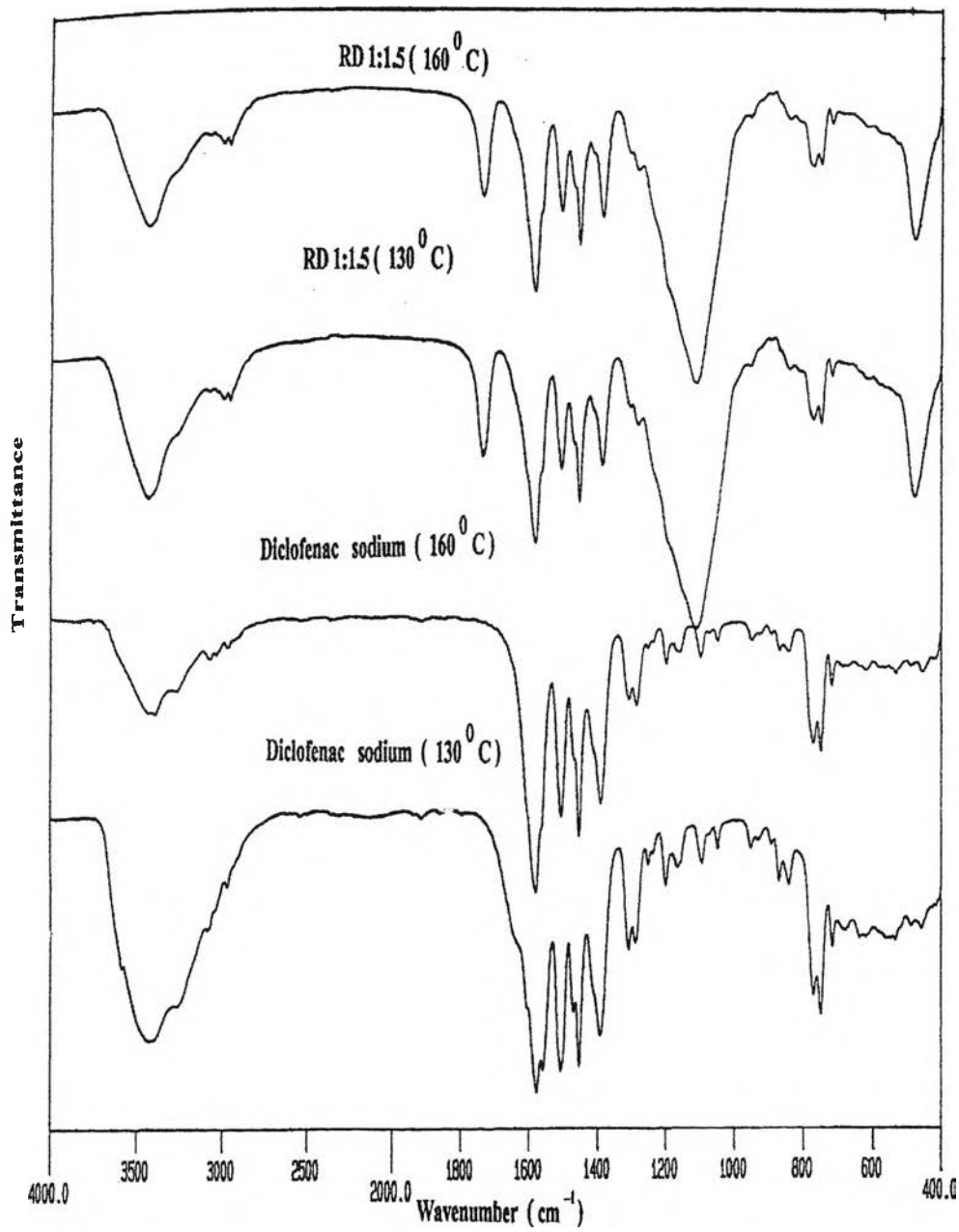


Figure 32 IR spectra of spray dried diclofenac sodium with Eudragit®RD100 (RD1:1.5) and 30%w/w Aerosil®200 at various inlet temperature, feed rate 12 rpm = 20 ml/min).

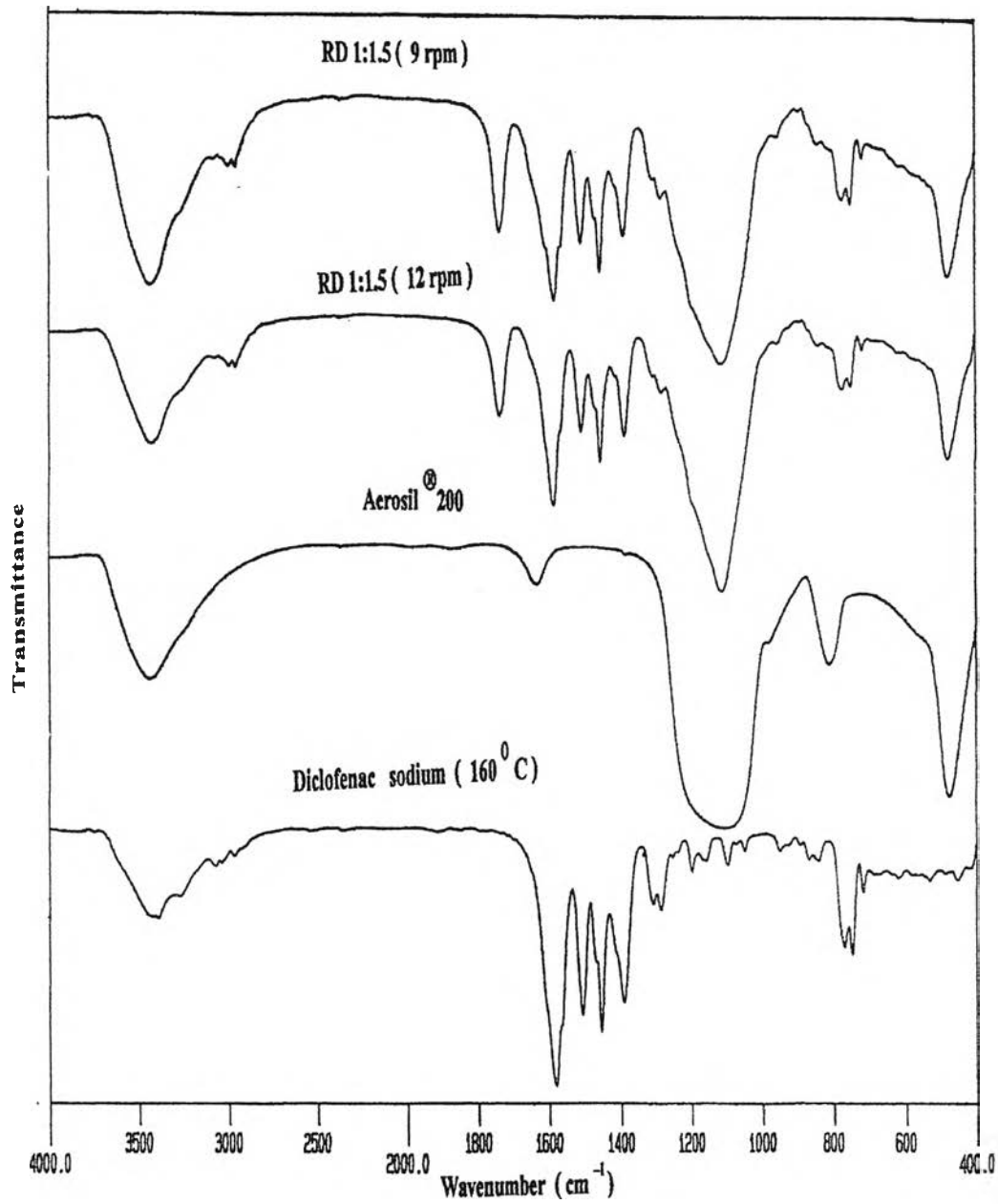


Figure 33 IR spectra of spray dried diclofenac sodium with Eudragit® RD100 (RD1:1.5) and Aerosil® 200 30%w/w at various feed rate, inlet temperature = 160 °C (12 rpm=20ml/min, 9 rpm=15 ml/min).

dried powders showed the combined spectra of diclofenac sodium and Eudragit® RD100 . The observation indicated no difference in the pattern spectra and still revealed the eminent peaks both of drug and polymer. Comparision with spray dried diclofenac sodium without polymer showed that the C-N stretching peaks of diclofenac sodium at 1308 cm^{-1} was disappeared.

The IR spectra of the formulation used Eudragit® RL 30D with or without NaCMC are depicted in Figure 34. The characteristic peaks of the formulation that with NaCMC were not shifted from their positions compared to the IR spectra of the formulation without NaCMC. Comparision between two formulations with and without NaCMC , the IR absorption peaks of the formulation with NaCMC at 1385, 1450, 1577 and 1730 cm^{-1} were of lower intensities. The observation indicated no difference in pattern spectra and still revealed the eminent peaks both of drug and polymer.

The IR spectra of the spray dried powders of the formulations produced by Eudragit ® RD100 compared with Eudragit ® RL30D and NaCMC at the ratio 1:9. and 1:4 are shown in Figure 35 . From both polymer to drug ratio, the IR absorption peaks of the formulation produced by Eudragit®RD 100 at 1450 and 1577 cm^{-1} were of lower intensities but at 1730 cm^{-1} was of higher intensities. There was no difference between the principle spectra of the formulation containing Eudragit ® RD100 and Eudragit®RL30D and NaCMC. These results indicated that the interaction between drug and polymer was hardly seen and commercial grade of polymer had no effect on the IR spectra.

The IR spectra of the spray dried powders of the Formulations produced by Eudragit® RD100 compared with Eudragit® RL30D and NaCMC at the ratio 1:2.33 and 1:1.5 are shown in Figure 36 . From both polymer to drug ratio, the IR absorption peaks of the formulation produced by Eudragit® RD 100 at 1450 and 1577 and 1730 cm^{-1} were of higher intensities. These results indicated that the eminent peaks of drug and polymer were still found.

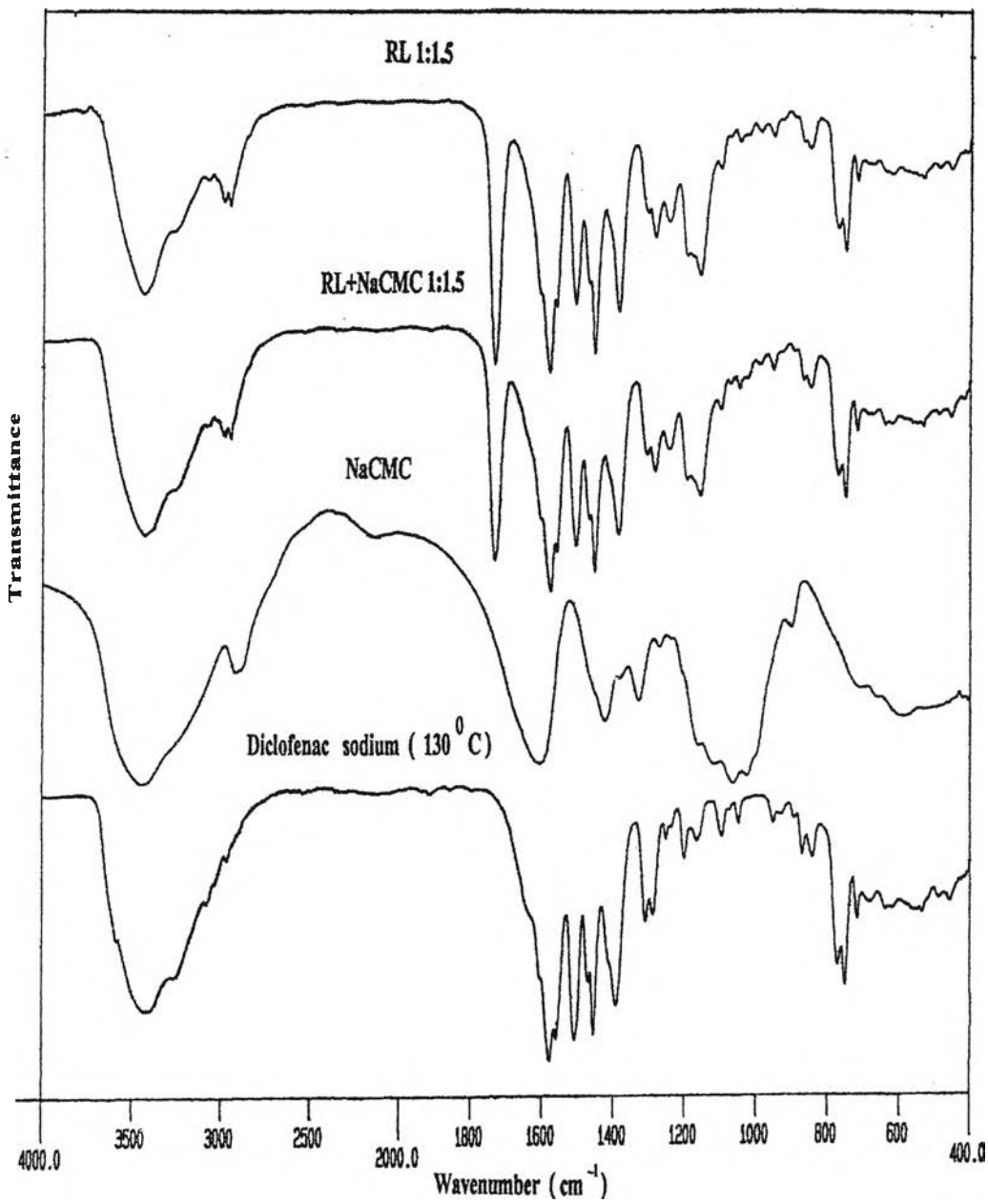


Figure 34 IR spectra of spray dried diclofenac sodium with Eudragit®RL30D, Eudragit® RL30D and NaCMC at the same ratio of 1:1.5.

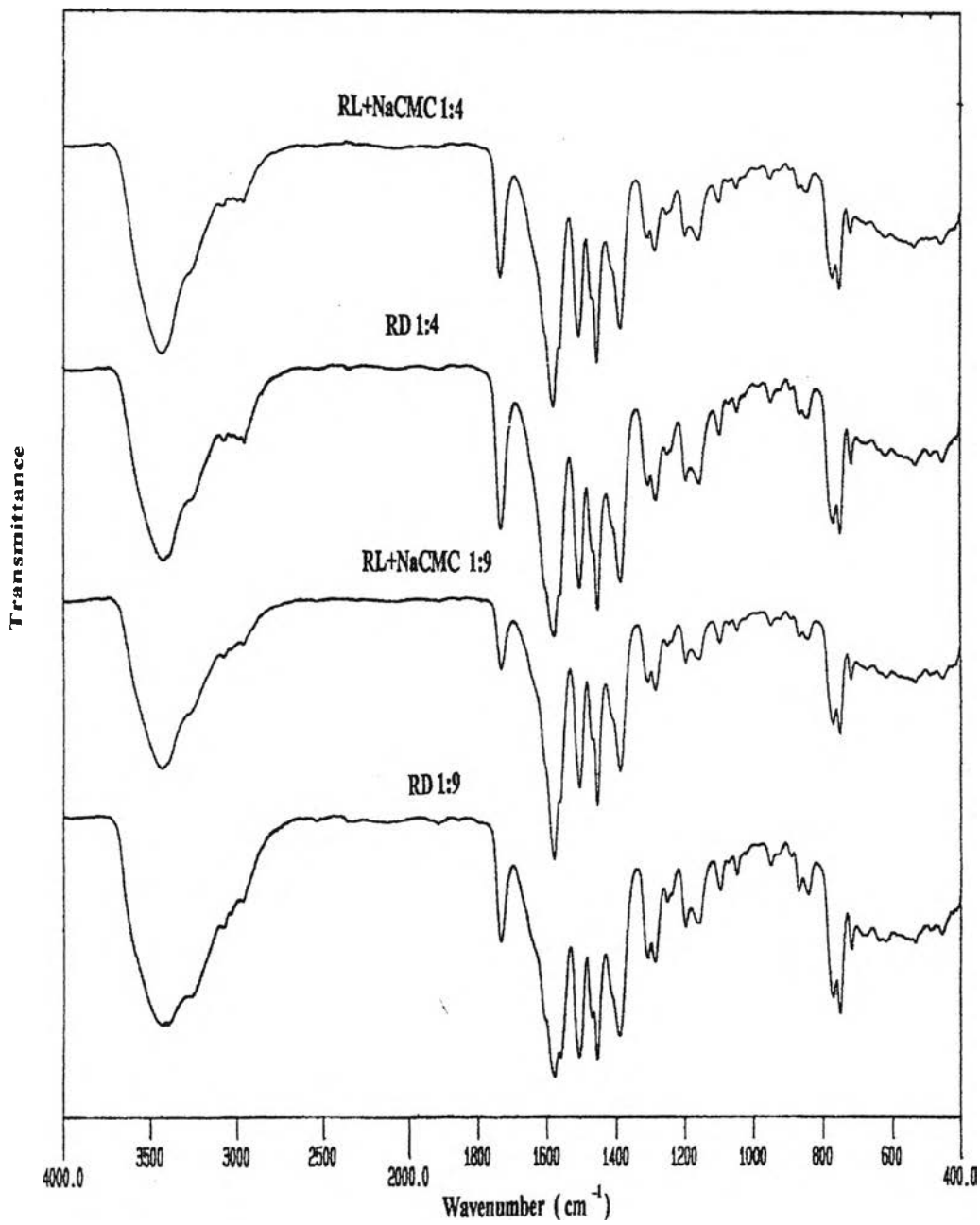


Figure 35 IR spectra of spray dried diclofenac sodium with Eudragit® RD100, Eudragit® RL30D and NaCMC at the same ratio of 1:9 and 1:4.

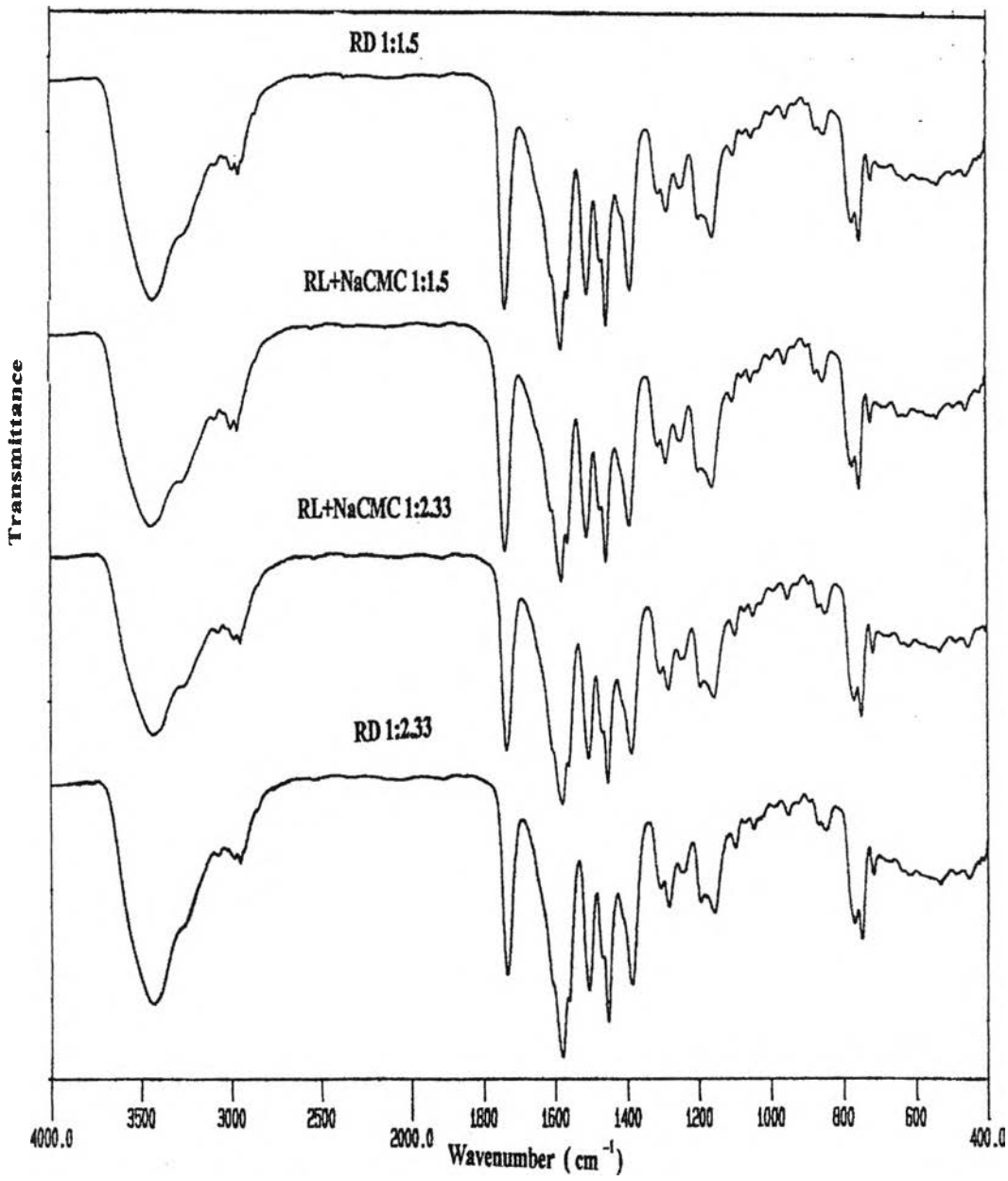


Figure 36 IR spectra of spray dried diclofenac sodium with Eudragit ® RD100, Eudragit®RL30D and NaCMC at the same ratio of 1:2.33 and 1:1.5.

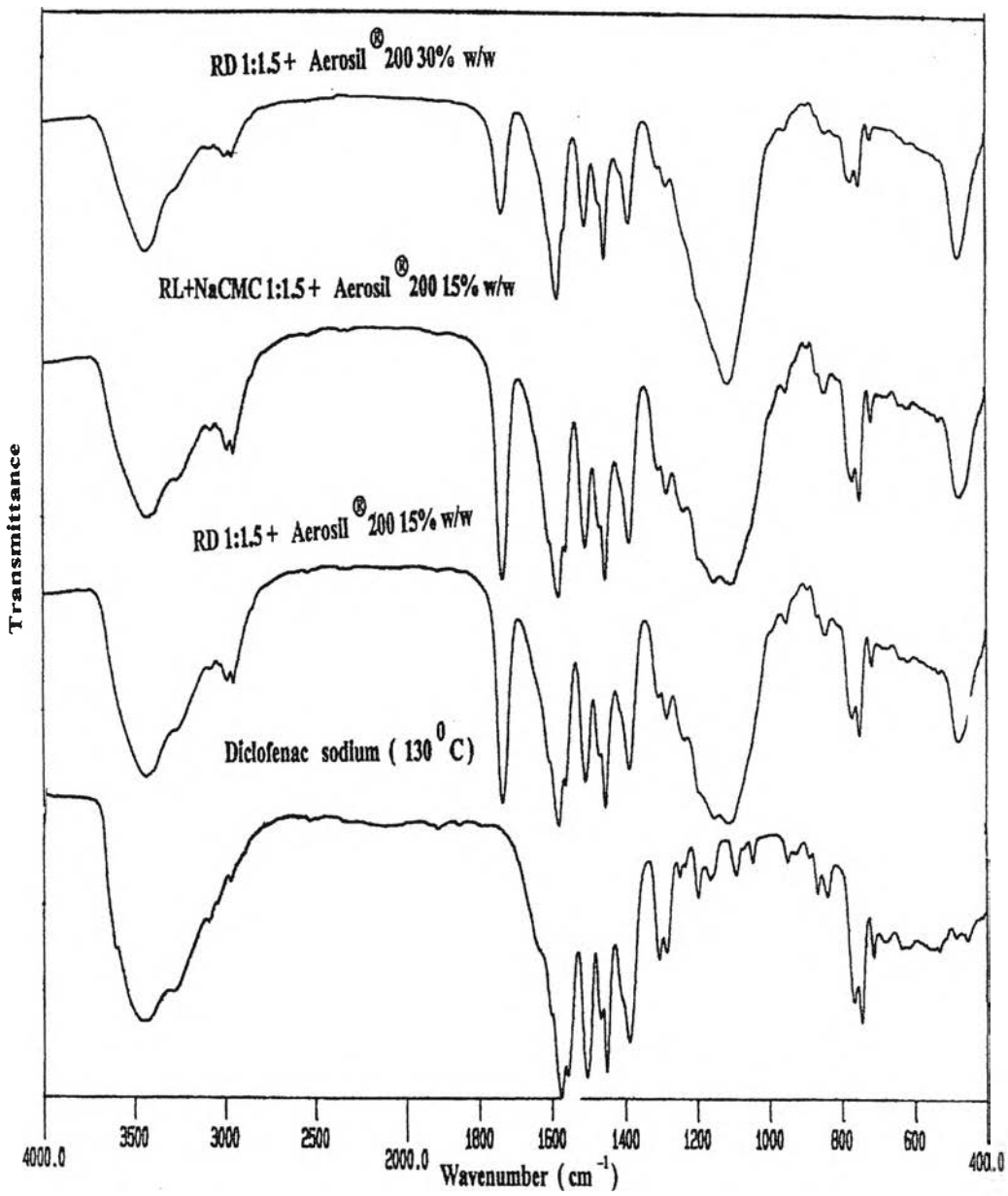


Figure 37 IR spectra of spray dried diclofenac sodium with Eudragit® RD100, Eudragit®RL30D and NaCMC with 15, 30 w/w Aerosil®200.

The IR spectra of the formulation with the addition of Aerosil ®200 15 to 30 % w/w are depicted in Figure 37. No difference between the characteristic peaks of the formulations but these formulations with Aerosil ® 200 30% w/w exhibited that C-N streching peaks of diclofenac sodium at 1308 cm^{-1} was disappeared. Comparision between product from Eudragit® RD 100 and Eudragit® RL30D with NaCMC by adding Aerosil® 200 15% w/w showed that the IR absorption patterns seemed to be similar. Increasing the amount of Aeriosil ®200 from 15 to 30% decreased the intensities of the IR absorption peak at 1450, 1730 cm^{-1} but increased the intensities at 1095, 1577 cm^{-1}. The IR peaks of spectra of all spray dried products with drug and polymer are shown in Table 19.

Table 19 Principle peaks of IR spectra of diclofenac sodium and of diclofenac sodium spray dried products.

Process variable	**Principle peak (cm^{-1})**					
Diclofenac sodium	749	769	1285	1308	1507	1577
Spray dried DS* at 130 ^{O}C	749	771	1288	1308	1508	1576
Spray dried DS at 160 ^{O}C	748	769	1285	1307	1507	1579
Polymer : Drug ratio						
RD 1:9	749	770	1286	1308	1507	1577
RL+NaCMC 1:9	749	769	1285	1308	1507	1578
RD 1:4	749	769	1284	1307	1507	1580
RL+NaCMC1:4	749	769	1284	1307	1507	1579
RD 1:2.33	749	769	1284	1306	1507	1579
RL+NaCMC 1:2.33	749	769	1283	1306	1507	1579
RD 1:1.5	749	770	1284	1307	1507	1578
RL+NaCMC 1:1.5	749	769	1284	1307	1507	1578
RD 1:1.5+ A15 %w/w	749	770	1283	1306	1507	1578
RL+NaCMC1:1.5 + A 15%w/w	749	769	1283	1305	1508	1579
RD1:1.5 +A30 %w/w(130^{0}C,12rpm)	749	771	1281	-	1507	1581
RD1:1.5+A30 %w/w(160^{0}C,12rpm)	750	773	1280	-	1507	1583
RD1:1.5+A 30%w/w (130^{0}C,9rpm)	749	772	1282	-	1507	1580
RL 1:1.5	749	770	1283	1304	1507	1579

* = Diclofenac sodium A= Aerosil 200, [1] = 20 ml/min [2] = 15 ml/min

11. Powder X-ray Diffraction

The X-ray diffraction patterns of diclofenac sodium, Eudragit® RD 100, Eudragit® RL30D, NaCMC and Aerosil® 200 and spray dried powders from various formulations are separated into related groups and illustrated in Figure 38-45.

The X-ray diffraction patterns of diclofenac sodium alone showed characteristic peaks at 6.44, 8.68, 11.36 , 15.36, 17.32, 20.04, 23.64, 27.24 (2θ) and small peaks at the diffraction angle between 15-30°(2θ). The X-ray diffraction patterns of spray dried diclofenac sodium without polymer at 130°C (Formulation 1) showed that diclofenac sodium was still in crystalline form but remarkably with much intense peaks. A slightly lower baseline was detected when compared with diclofenac sodium that was not spray dried. The X-ray diffraction patterns of spray dried diclofenac sodium without polymer at 160°C (Formulation 2) showed the same pattern as diclofenac sodium which spray dried at 130°C but had fewer intense peaks and a slightly higher baseline was detected. The characteristic peak at 6.44 (2θ) of spray dried diclofenac sodium without polymer at 130°C (Formulation 1) has higher intensities than spray dried diclofenac sodium without polymer at 160°C (Formulation 2) and diclofenac sodium (raw material). The characteristics peaks at 15.36 (2θ) of both spray dried diclofenac sodium at various inlet air temperature was of higher intensities but peaks at 26.08, 27.24(2θ) were of lower intensities and peaks at 21.16 (2θ) disappeared when compared with diclofenac sodium. It was found that the principle peaks of diclofenac sodium existed but the intensities of the peaks changed. The X-ray diffraction patterns of diclofenac sodium and spray dried diclofenac sodium at various temperature are shown in Figure 38.

Figure 39 depicts the X-ray diffraction patterns of diclofenac sodium with Eudragit® RD100 in various polymer to drug ratios (Formulation 3, 5, 7, 9). The characteristic peaks of Eudragit® RD100 was shown at 13.76 and 31.72(2θ). These four formulations exhibited lower intensities of diclofenac sodium peaks and crystallinity of drug existed because the principle peaks of diclofenac

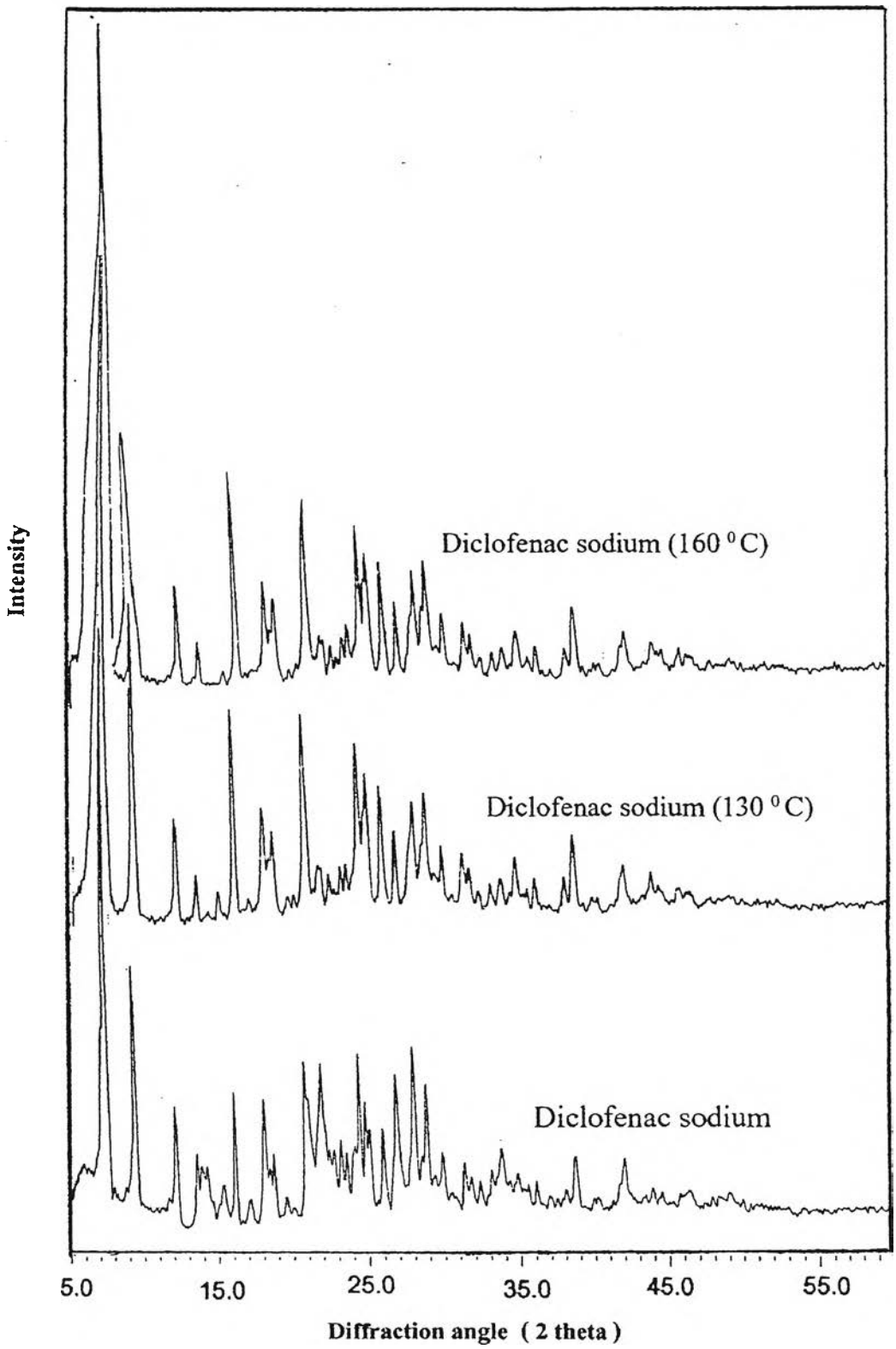


Figure 38 X-ray diffractograms of diclofenac sodium and spray dried diclofenac sodium without polymer at various inlet air temperature.

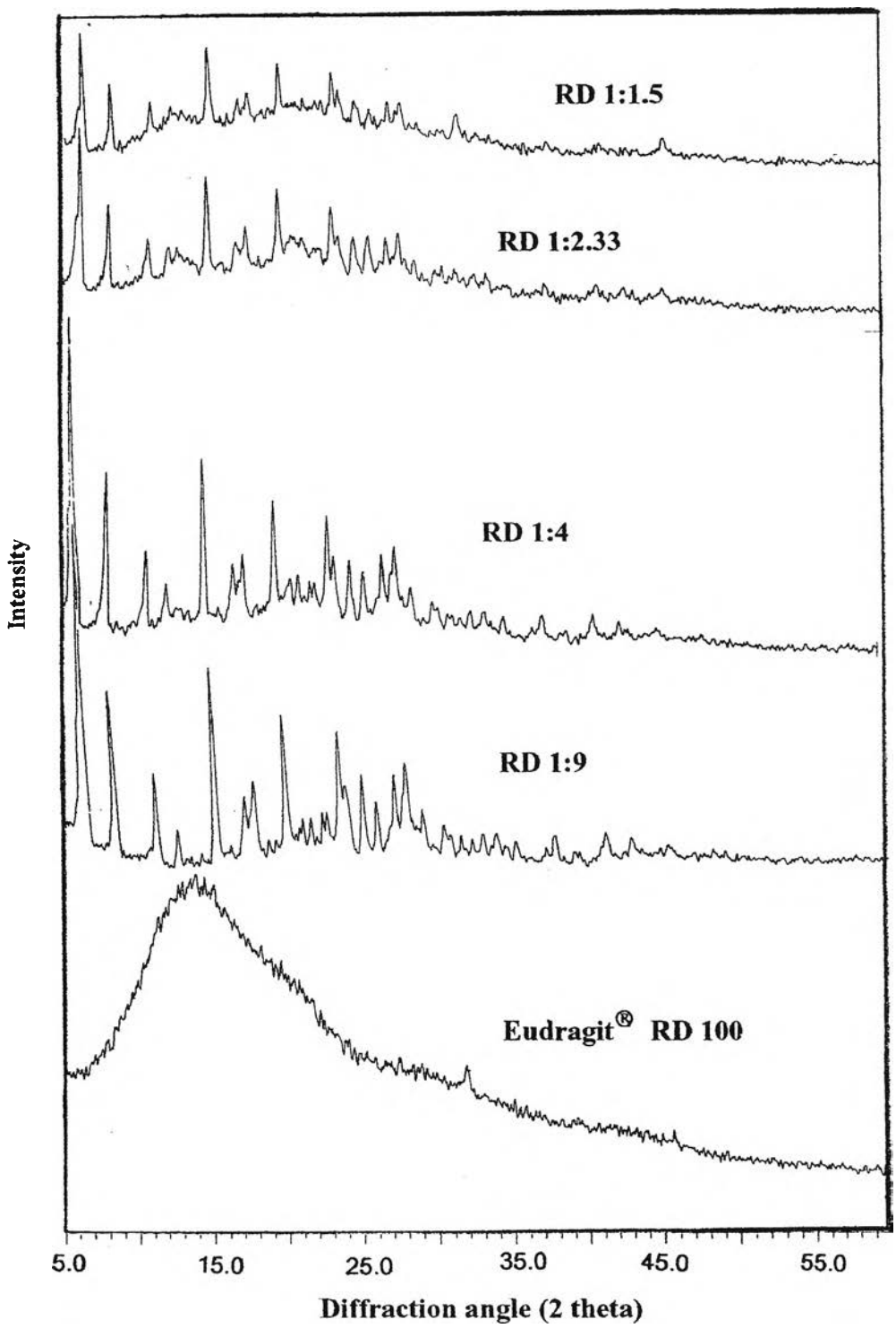


Figure 39 X-ray diffractograms of spray dried diclofenac sodium with Eudragit ® RD100 at various polymer to drug ratios.

sodium appeared and did not shift. Increasing polymer to drug ratio increased the amorphism of diclofenac sodium. However, dilution of drug by polymer might result on the lower intensities of drug.

The X-ray diffraction patterns of diclofenac sodium with Eudragit® RL 30D and NaCMC in various of polymer to drug ratios (Formulation 4, 6, 8, 10) are illustrated in Figure 40. The characteristic peaks of Eudragit®RL30D was shown at 13.12°(2θ). It was observed that the intensities of the diffraction peaks of spray dried diclofenac sodium and Eudragit® RL30D with NaCMC were weaker than those of diclofenac sodium alone. It exhibited that the principle peaks of diclofenac sodium existed and did not shift.

No difference was observed between the X-ray diffraction patterns of diclofenac sodium formulated with Eudragit® RD100 and diclofenac sodium formulated with Eudragit® RL30D and NaCMC when compared in the same polymer to drug ratio both with or without Aerosil® 200 (Formulation 3=4 , 5=6 ,7=8 ,9=10, 11=12). It was found that the principle peaks of diclofenac sodium existed and did not shift but the intensities of peaks changed. Crystallinity of drug still appeared. The X-ray diffraction patterns are shown in Figure 41-42.

The diffraction peaks of the spray dried powders of formulations with Aerosil® 200 are presented in Figure 43. The characteristic peaks Aerosil® 200 was shown at 21.60°(2θ). These peaks were weaker than those of formulation without Aerosil® 200. Slightly higher baseline was detected but the eminent peaks were still found . Some of diclofenac sodium change to amorphous form. Increasing amount of Aerosil 200 into the formulation increased the amorphous form of diclofenac sodium (Formulation 9-13).

The X-ray diffraction patterns of spray dried diclofenac sodium with varying inlet air temparature and feed rate are shown in Figure 44. When increasing the inlet air temperature from 130°C to 160°C (Formulation 13-14), the diffractograms showed the same pattern but the spray dried diclofenac sodium using inlet temperature at

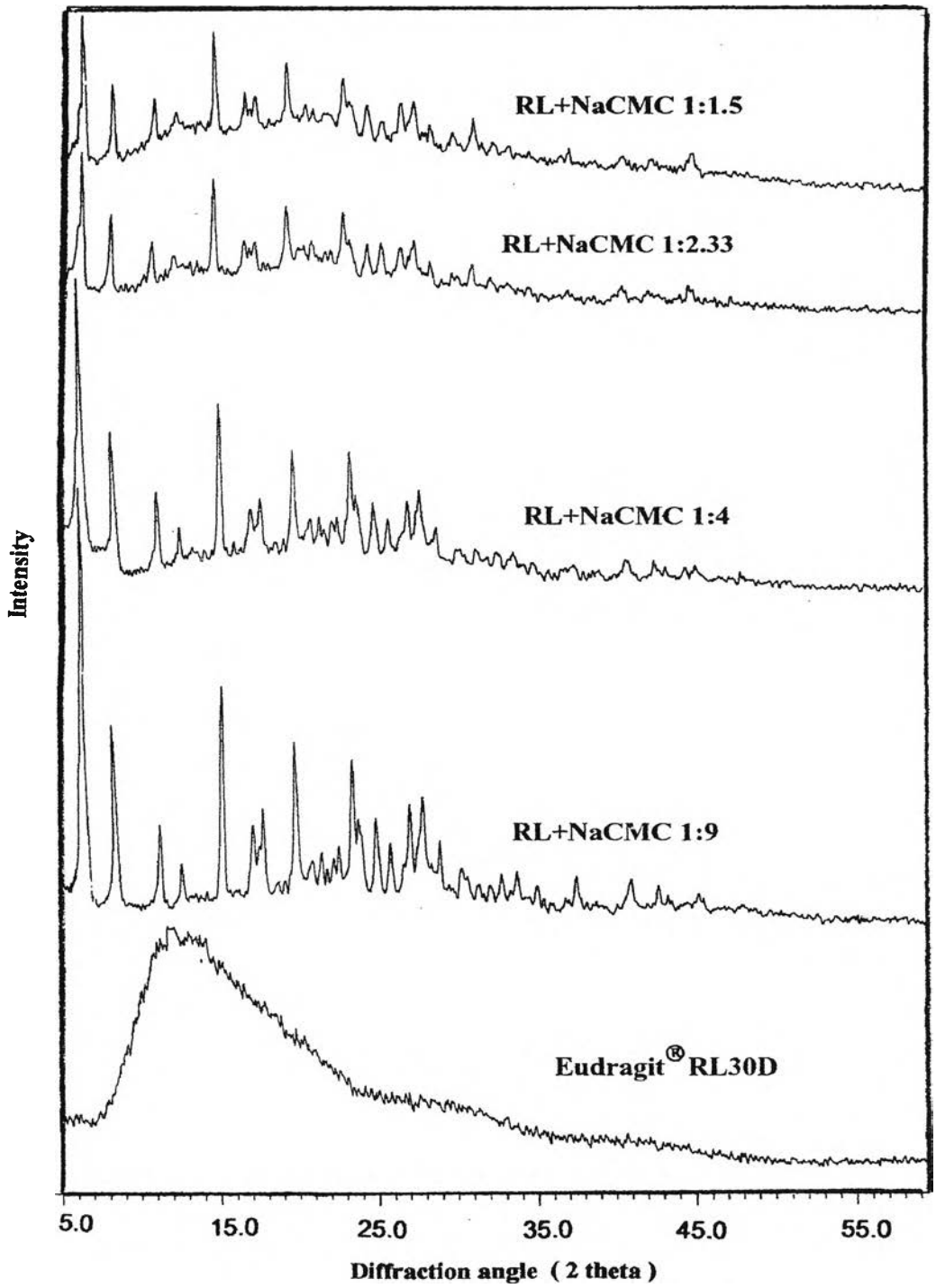


Figure 40 X ray diffractograms of spray dried diclofenac sodium with Eudragit® RL30D and NaCMC at various polymer to drug ratios.

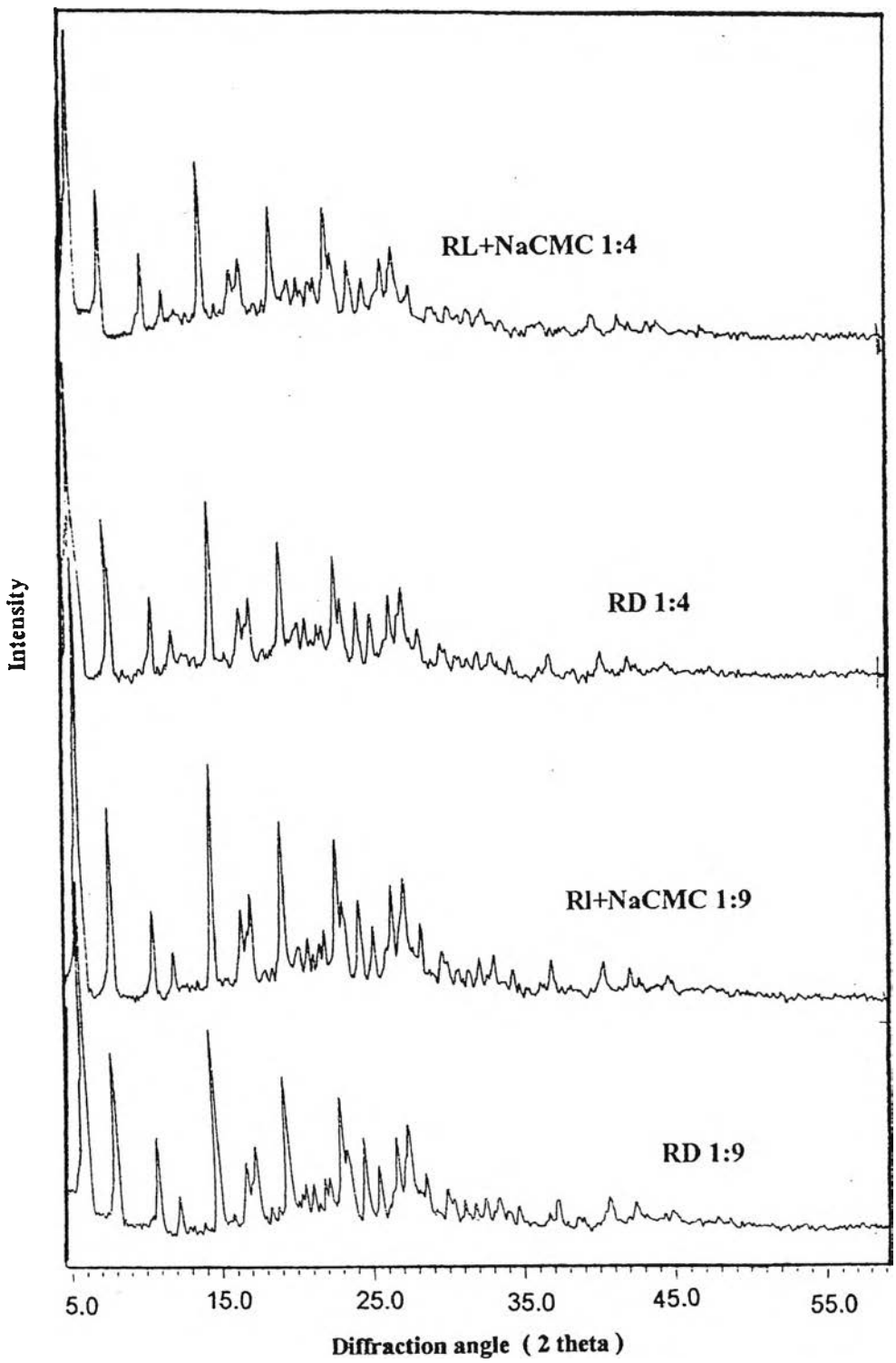


Figure 41 X-ray diffractograms of spray dried diclofenac sodium with Eudragit® RD100, Eudragit® RL30D and NaCMC at the same ratio of 1:9 and 1:4.

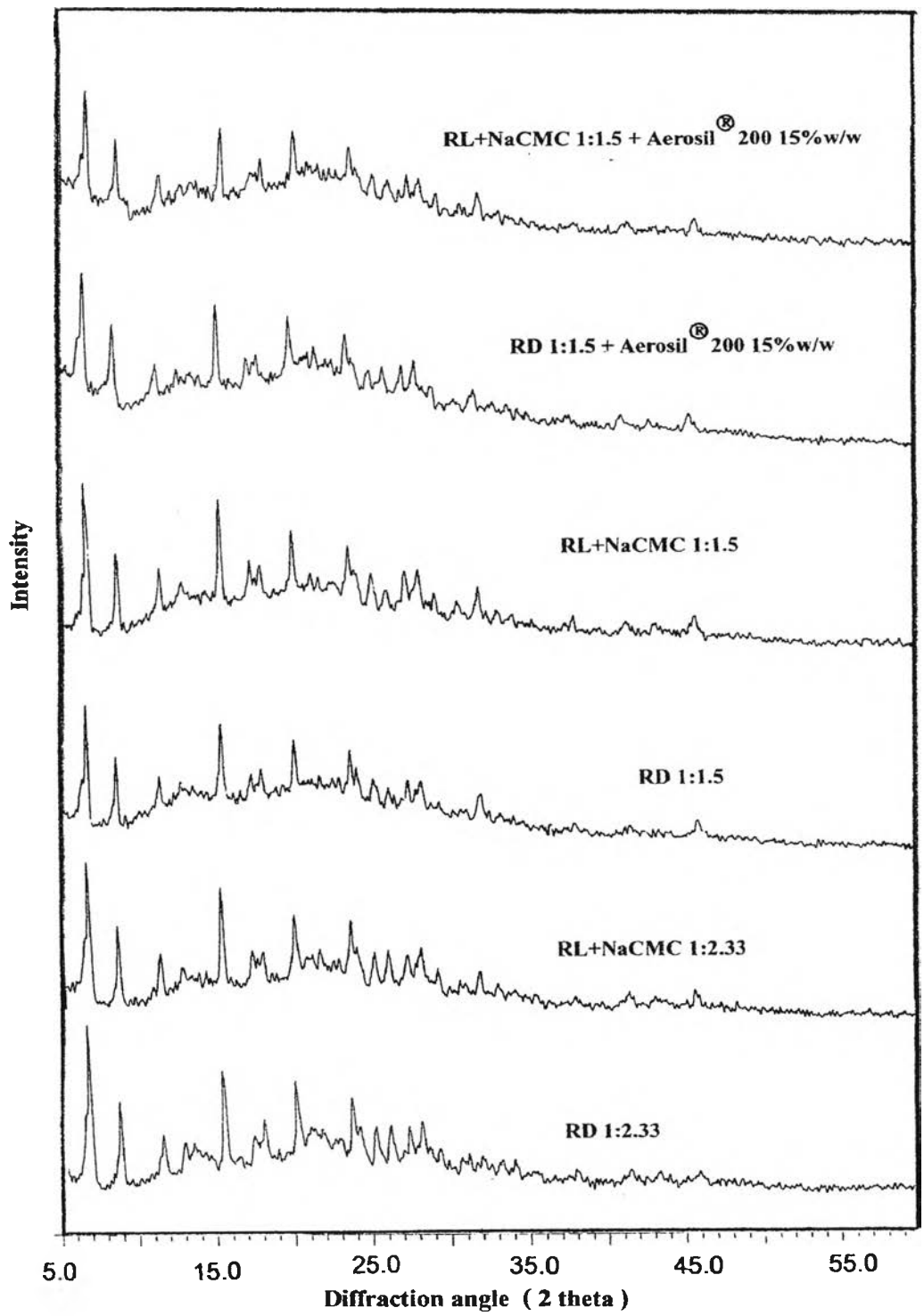


Figure 42 X ray diffractograms of spray dried diclofenac sodium with Eudragit® RD100, Eudragit® RL30D and NaCMC at the same ratio of 1:2.33 and 1:1.5, 1:1.5 with 15% w/w Aerosil® 200.

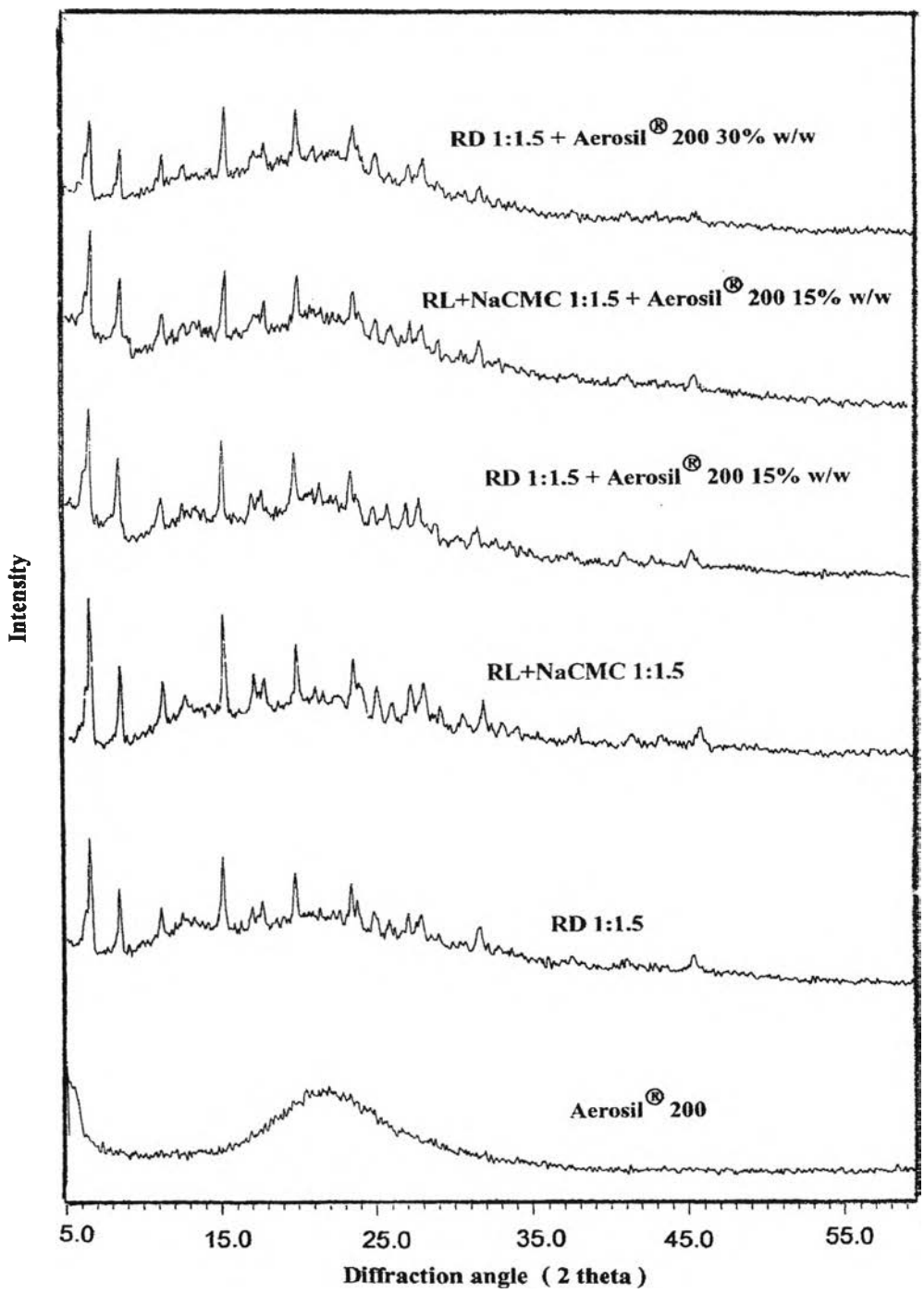


Figure 43 X-ray diffractograms of spray dried diclofenac sodium with Eudragit® RD100, Eudragit® RL30D and NaCMC and 0, 15, 30 % w/w Aerosil® 200.

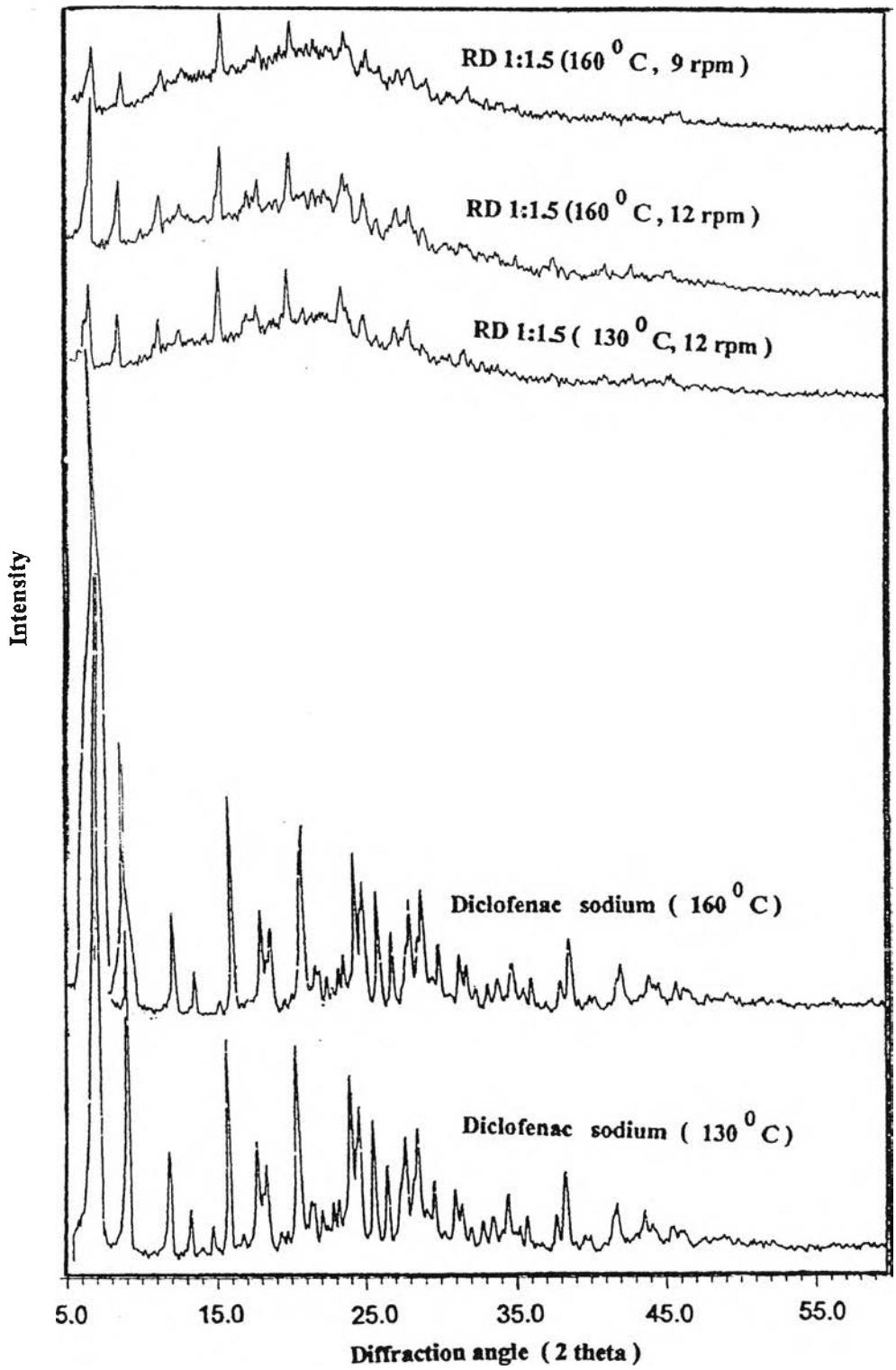


Figure 44 X ray diffractograms of spray dried diclofenac sodium with Eudragit ® RD100 (RD 1:1.5) and 30% w/w Aerosil® 200 at various inlet temperature and feed rate.
(12 rpm =20 ml/min , 9 rpm=15 ml/min)

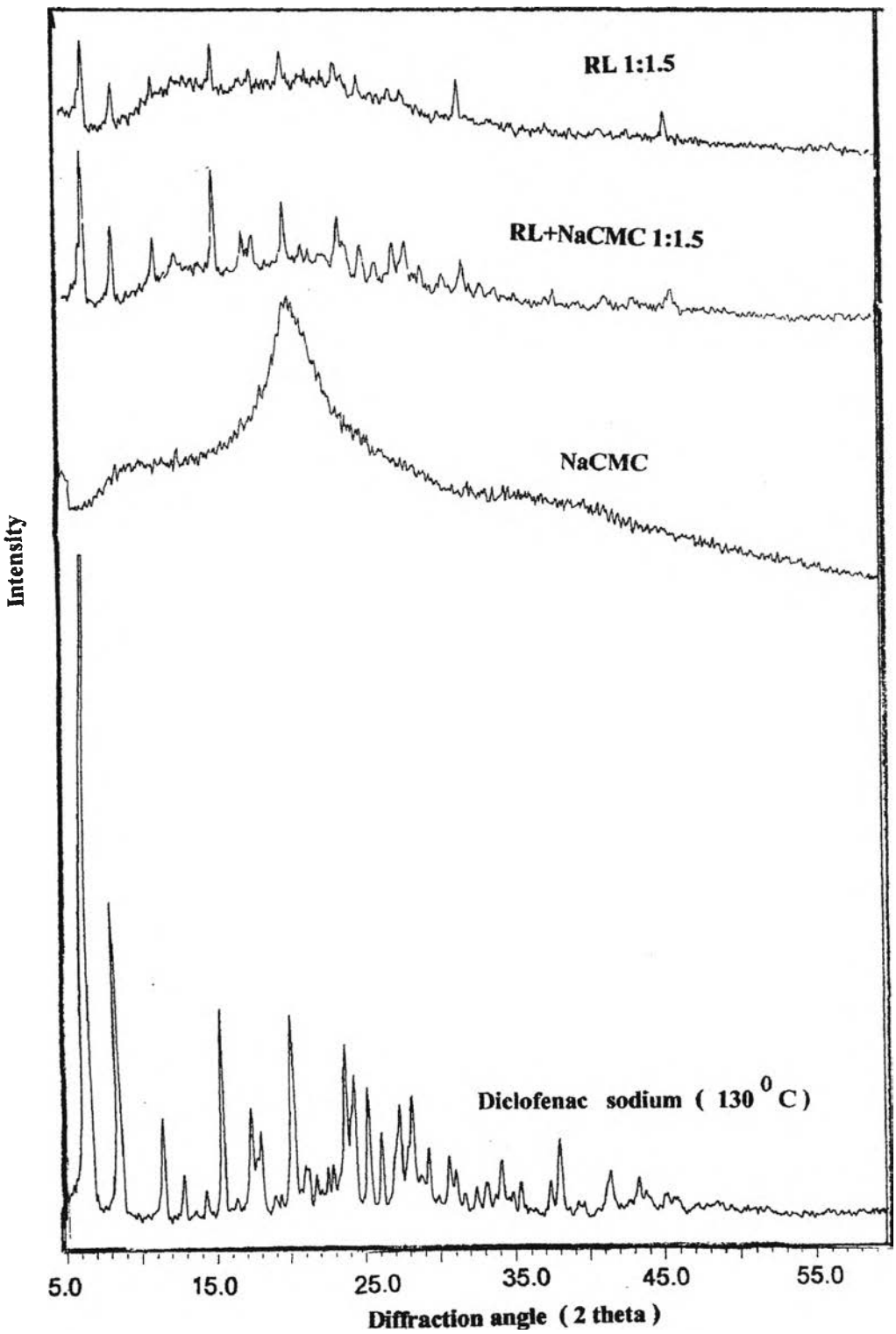


Figure 45 X-ray diffractograms of spray dried diclofenac sodium with Eudragit® RL30D, Eudragit ® RL30D and NaCMC at the same

130°C (Formulation13) had lower intensity peak at 6.44°and 8.34°(2θ). When comparison with using inlet temperature at 160°C (Formulation14). Therefore in Formulation13 some diclofenac sodium was changed to amorphous form but crystallinity of drug was still found. Moreover when compared to diclofenac sodium alone these two formulations exhibited crystallinity of drug because the principle peaks were still found and did not shift. When decreasing the feed rate from 12 rpm to 9 rpm (Formulation 14-15) the diffractogram still exhibited crystallinity of drug when compared with diclofenac sodium alone but with decreasing feed rate, the amorphous form of diclofenac sodium increased. The characteristics peaks at 6.44 and 8.34°(2θ) had lower intensity. Decreasing the inlet air temperature and decreasing the feed rate affected the crystallinity of drug the eminent peaks of diclofenac sodium were still found but crystallinity of drug decreased and amorphism of drug increased.

The X-ray diffraction patterns of spray dried diclofenac sodium with Eudragit® RL30D and NaCMC or without NaCMC are shown in Figure 45. The characteristic peaks NaCMC was shown at 20.04°(2θ). It was observed that the intensities of the diffraction peaks of spray dried diclofenac sodium without NaCMC(Formulation 16) were weaker than those with NaCMC (Formulation 10). So, the reduction of peak intensities of spray dried product indicated that some crystal in product was converted to an amorphous form. The eminent peaks of diclofenac sodium were still found.

12. DSC (Differential Scanning Calorimetry)

The DSC thermogram of pure diclofenac sodium gave an exotherm at 280.5°C, followed by an endotherm at 284.9°C, In addition spray dried diclofenac sodium at 130°C and 160°C had the same patterns of DSC peak. The DSC thermograms of diclofenac sodium and spray dried pure diclofenac sodium at various inlet air temperatures are shown in Figure 46.

The DSC thermograms of Eudragit ®RD100 revealed two endothermic peaks at 51.4°C and 192.6°C, whereas Eudragit ®RL30D showed two endothermic peaks at 57.5°C and 199.5°C. The DSC thermograms of Eudragit®RD100 and Eudragit ®

RL30D are presented in Figure 47. NaCMC presented the endotherm at 72.4°C, whereas Aerosil®200 showed endotherm at 49.4°C. The DSC thermograms of NaCMC and Aerosil®200 are presented in Figure 48.There was no difference between the DSC thermogram patterns of diclofenac sodium alone and those of the formulations prepared by spray drying process but the difference in DSC peak temperatures were detected .

Comparison of the formulation between two types of polymer revealed that there was no difference between the DSC thermogram patterns of those prepared by Eudragit®RD100 and Eudragit ® RL30D with NaCMC at the same ratio of (1:9, 1:4). The exothermic temperatures and endothermic temperatures of diclofenac sodium spray dried with Eudragit®RD100 were slightly lower than spray dried with Eudragit® RL 30D and NaCMC. At the ratio of 1:9, the exothermic peaks increased from 266.5 to 267.2°C whereas the endothermic increased from 271.6 to 272.4°C. At the ratio of 1:4 the exothermic temperatures increased from 259.9 to 260.3°C whereas the endothermic increased from 267.0 to 267.1°C. Their DSC thermograms are shown in Figure 49.

Comparison of the formulations between two types of polymer revealed that there was no difference between the DSC thermogram patterns of those prepared by Eudragit®RD100 and Eudragit®RL30D with NaCMC at the same ratio (1:2.33, 1:1.5). The exothermic temperatures and endothermic temperatures of diclofenac sodium spray dried with Eudragit® RD100 were slightly higher than spray dried with Eudragit® RL 30D and NaCMC. At the ratio of 1:2.33, the exothermic temperatures decreased from 256.2 to 254.2°C whereas the endothermic increased from 263.0 to 261.9°C. At the ratio of 1:1.5 the exothermic temperatures increased from 249.9 to 248.9°C whereas the endothermic decreased from 257.8 to 257.4°C. Their DSC thermograms are shown in Figure 50.

By observation, the exotherm of all formulations which had Aerosil®200 were shifted to the higher temperature at the ratio 1:1.5 with 15% Aerosil 200. There were differences in temperatures between products of Eudragit®RD100 and Eudragit ®

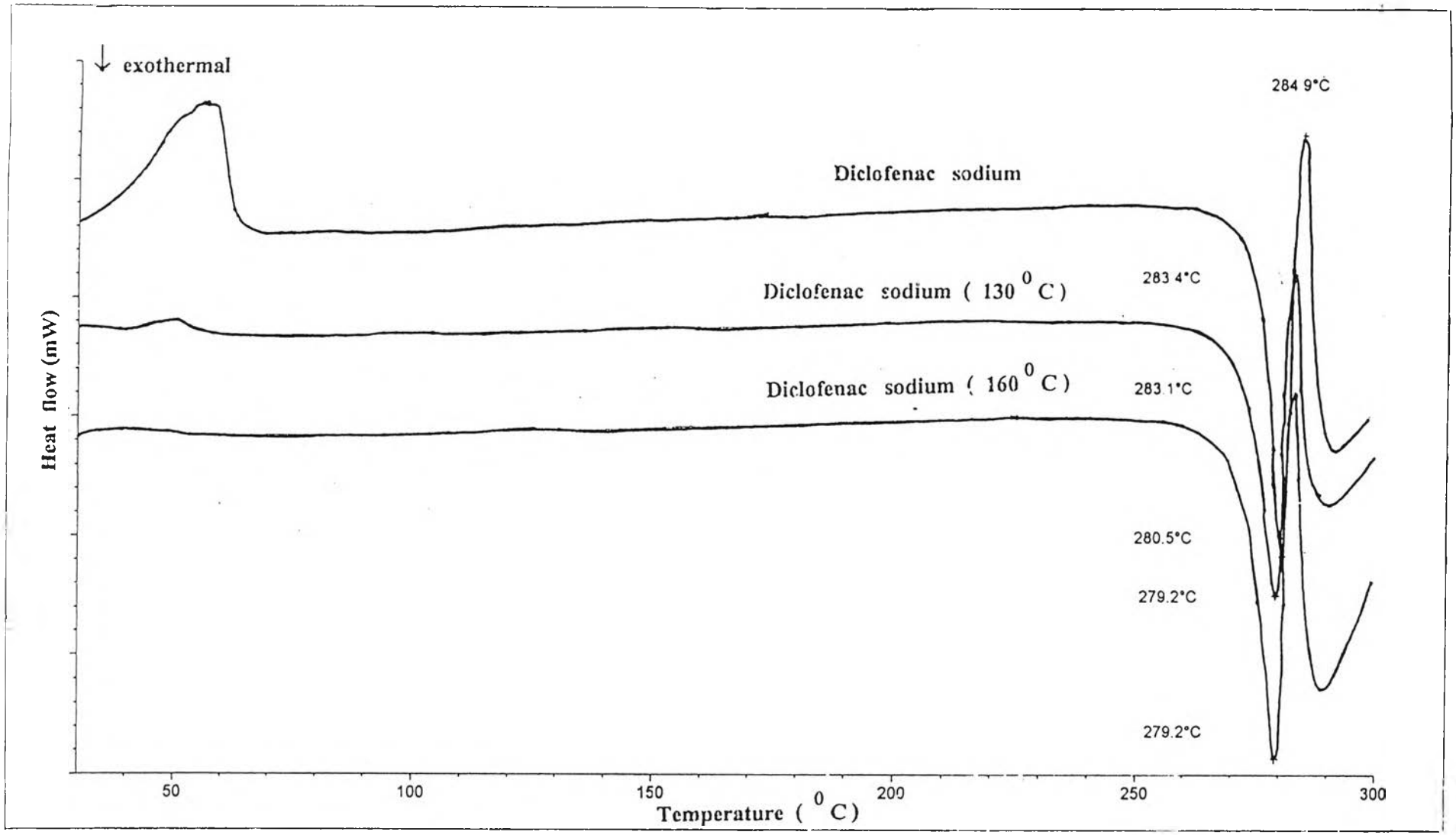


Figure 46 DSC thermograms of diclofenac sodium and spray dried diclofenac sodium without polymer at various inlet temperature.

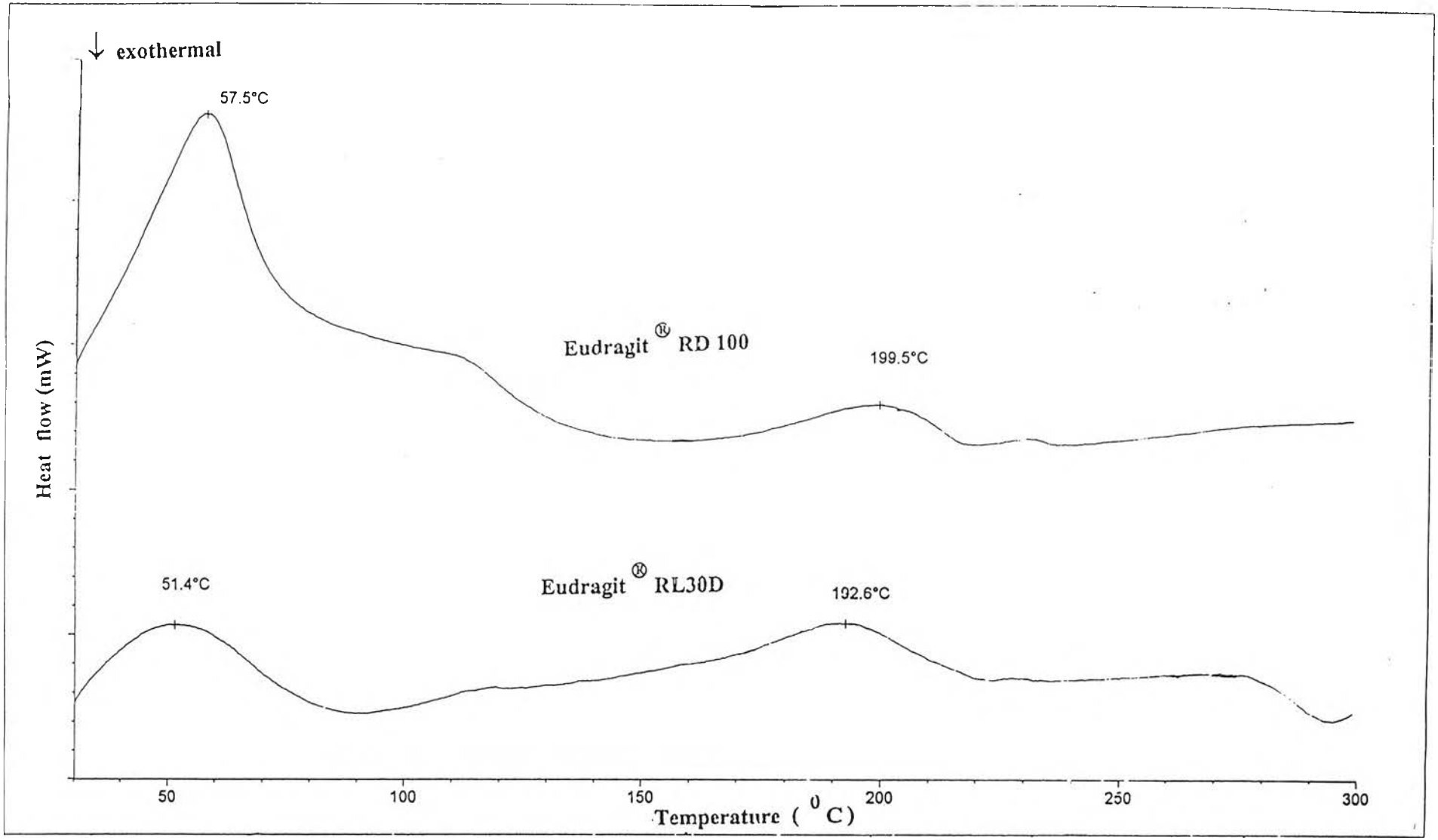


Figure 47 DSC Thermograms of Eudragit ® RD100 and Eudragit® RL30D.

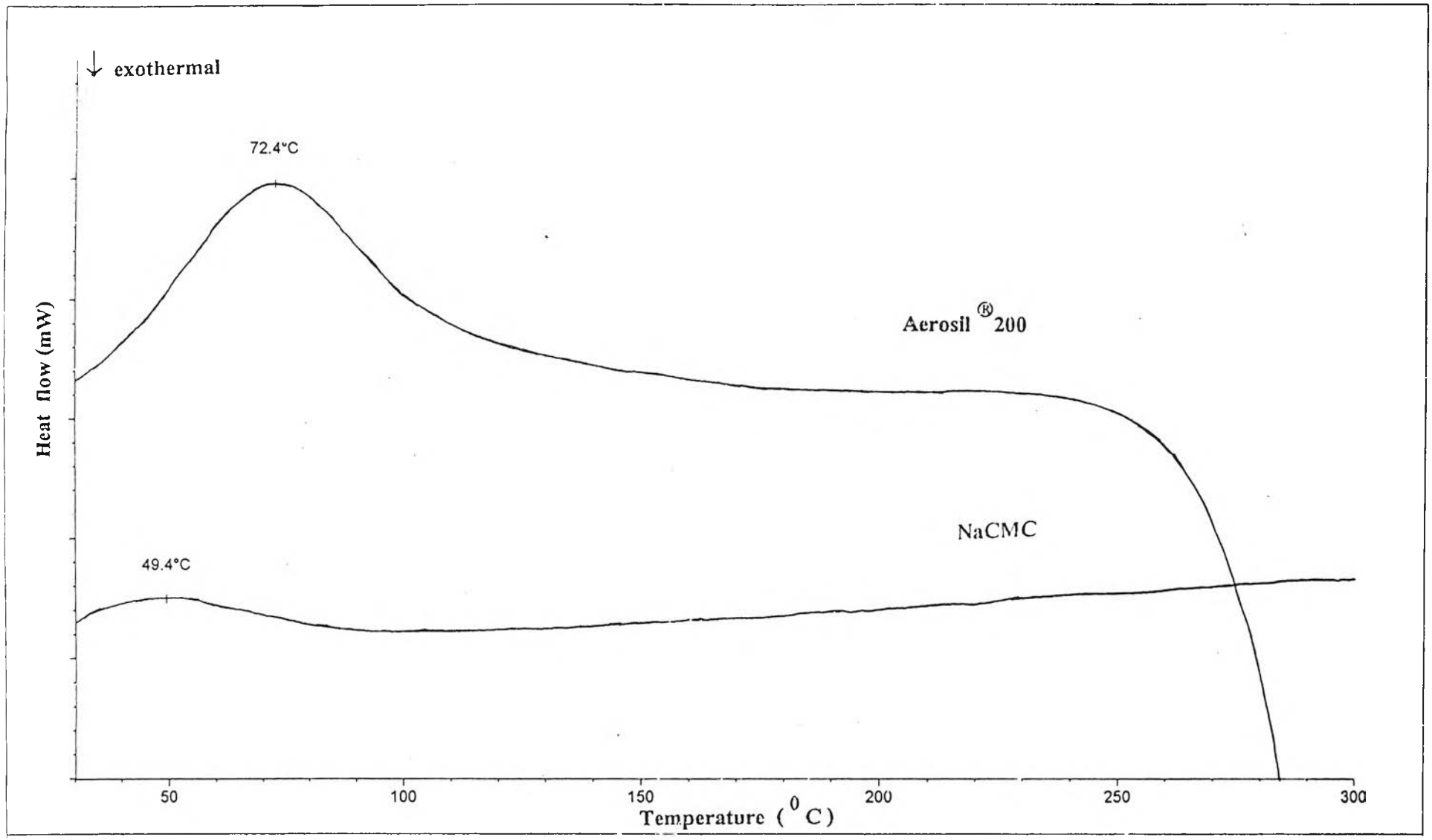


Figure 48 DSC Thermograms of Aerosil®200 and NaCMC.

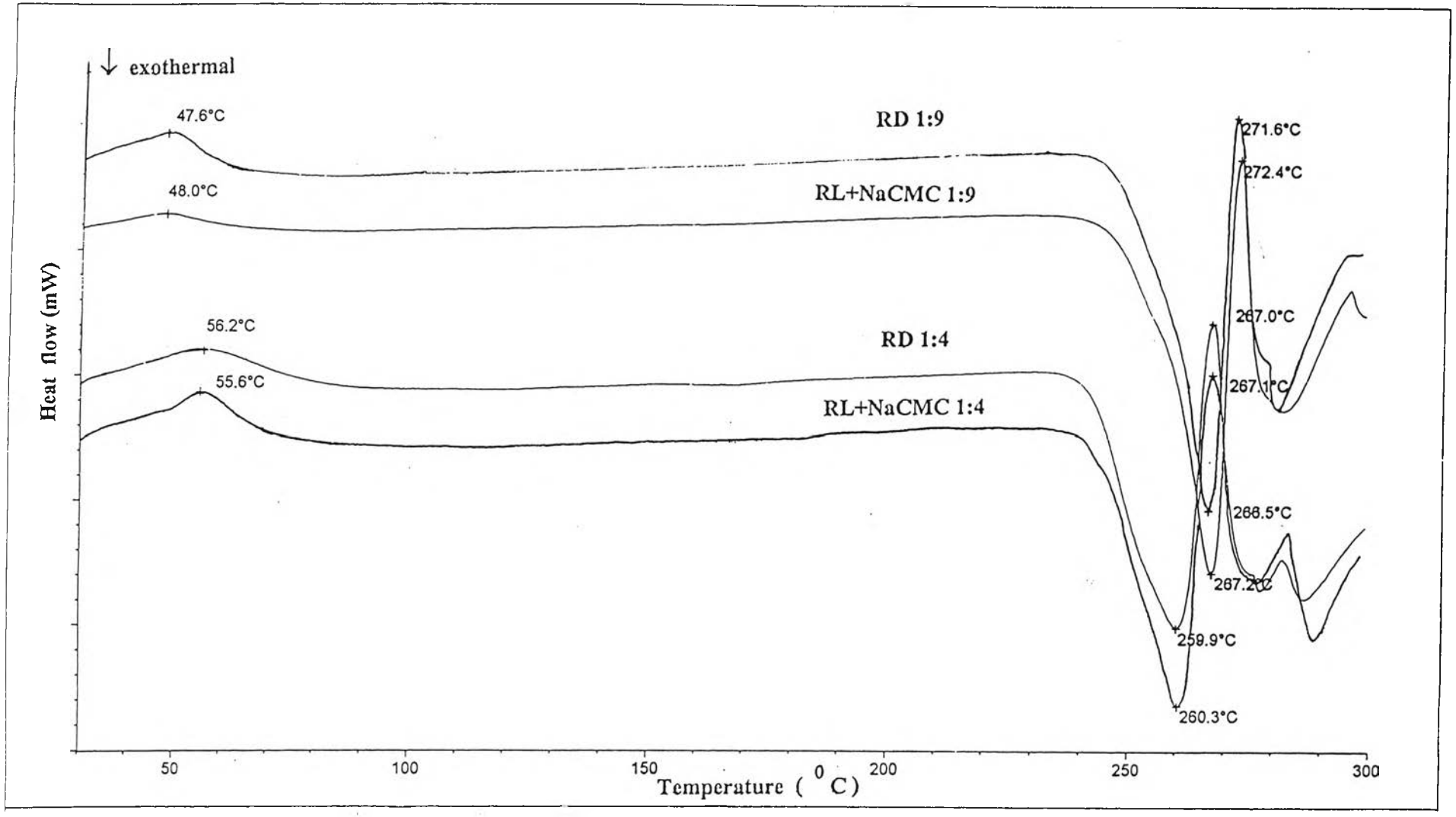


Figure 49 DSC Thermograms of spray dried diclofenac sodium with Eudragit ®RD100, Eudragit®RL30D and NaCMC at the same ratio of 1:9 and 1:4.

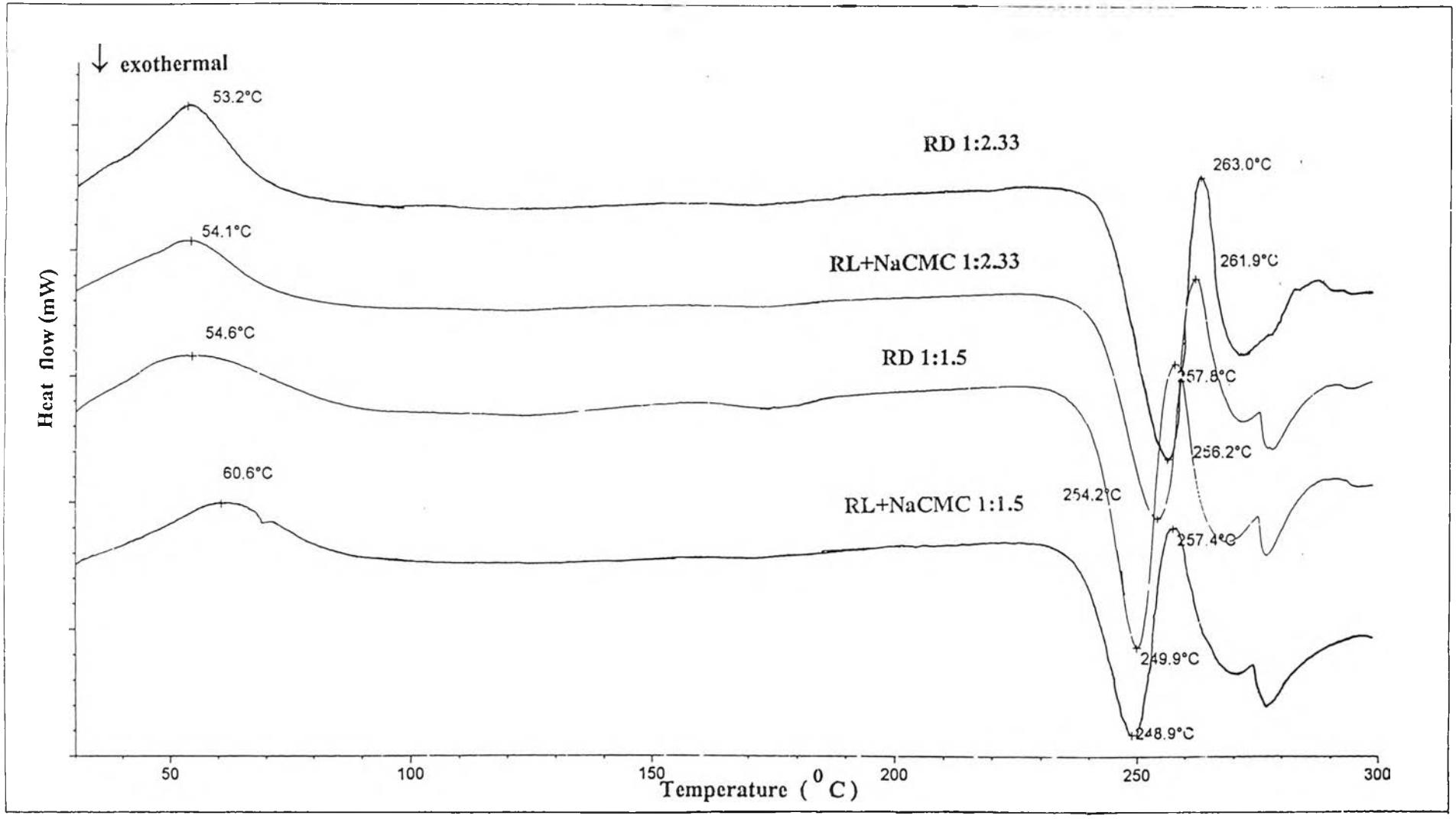


Figure 50 DSC Thermograms of spray dried diclofenac sodium with Eudragit ®RD100, Eudragit®RL30D and NaCMC at the same ratio of 1:2.33 and 1:1.5.

RL30D with NaCMC. The exothermic temperature when containing Eudragit® RD100 was higher about 2°C. By containing Eudragit® RD100, increasing amount of Aerosil®200 from 15 to 30% revealed that the endothermic peak increased from 264.9 to 272.7°C. The endothermic peaks of these formulations disappeared. These exothermic temperatures were higher as the amount of Aerosil®200 in these formulations increased. Their DSC thermograms are shown in Figure 51.

Increasing the inlet tempreature from 130°C to 160°C exhibited no difference between the exothermic temperatures of two formulations (Formulation 13-14). Increasing the inlet temperature from 130°C to 160°C revealed the exothermic decreased from 272.7 to 271.8°C. The endothermic peaks of these formulations disappeared. The DSC thermograms of spray dried diclofenac sodium with varying air inlet temperature are shown in Figure 52. In addition , decreasing the feed rate from 12 rpm to 9 rpm, the exothermic temperatures decreased from 271.8 to 270.6°C. The endothermic peaks of these formulations disappeared. Their DSC thermograms of spray dried diclofenac sodium with varying feed rate are shown in Figure 53.

The exotherm and endotherm of the formulation without NaCMC was shifted to the lower temperature when compared with formulation which add NaCMC. The exothermic temperature decreased from 248.9 to 243.5°C and the endothermic temperature decreased from 257.4 to 254.8 °C. Their DSC thermograms of spray dried diclofenac sodium are shown in Figure 54.

Varying polymer to drug ratios of Eudragit® RD100 revealed that when increasing the polymer to drug ratios, the exothermic and endothermic peaks were shifted to the lower temperature when compared with diclofenac sodium alone. When spray dried with Eudragit® RD100 at the ratio 1:9 to 1:4. The exothermic temperatures decreased from 266.5 to 259.9°C respectively and the endothermic peaks decreased from 271.6 to 267.0°C, respectively. When spray dried with Eudragit® RD100 at the ratio 1:2.33 to 1:1.5. The exothermic temperatures decreased from 256.2 to 249.9°C, respectively and the endothermic peaks decreased from 263.0 to 257.8°C, respectively. Their DSC thermograms are shown in Figure 55.

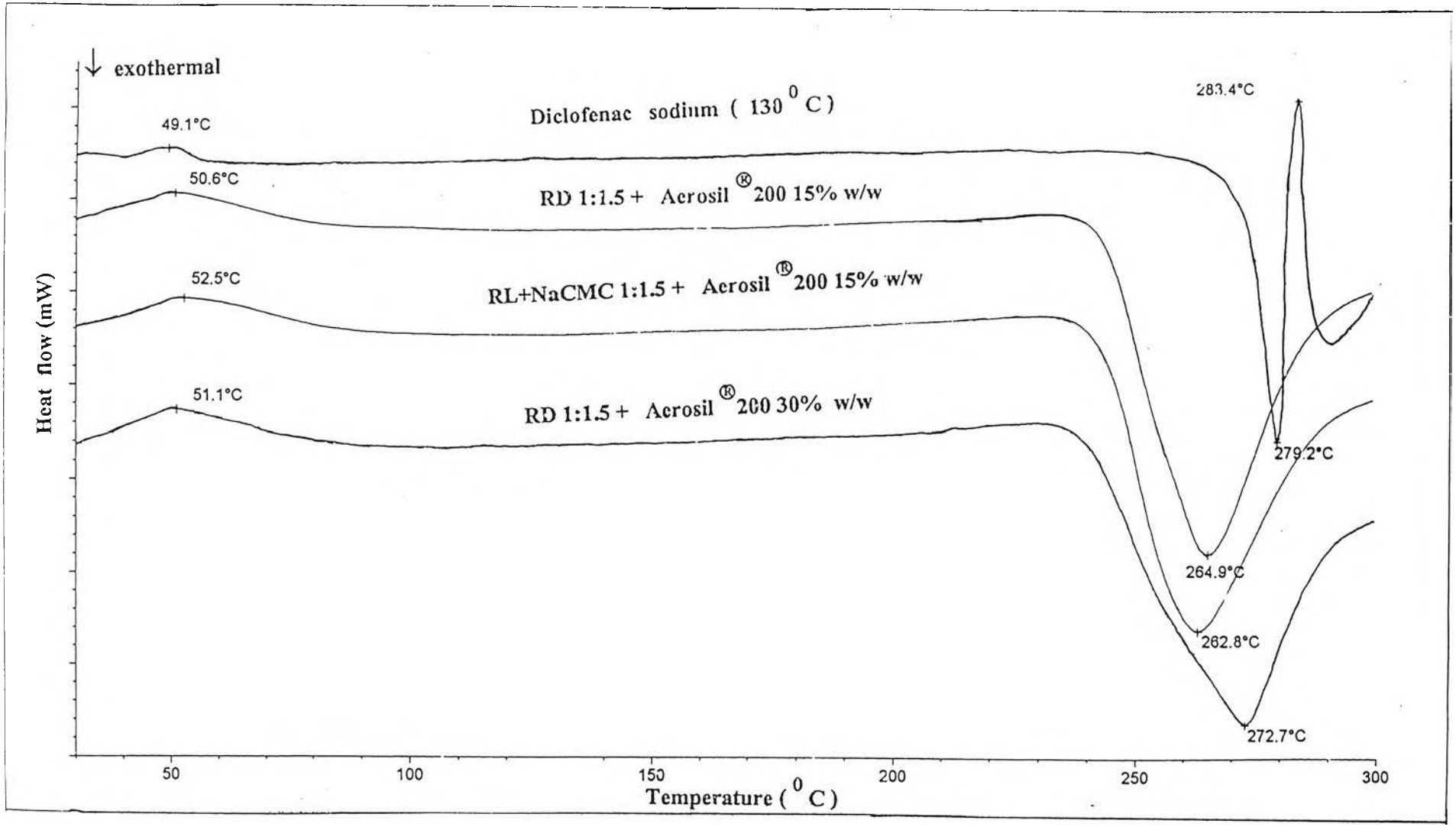


Figure 51 DSC Thermograms of spray dried diclofenac sodium with Eudragit ® RD100, Eudragit®RL30D and NaCMC and 15, 30%w/w Aerosil®200 at the same ratio of 1:1.5.

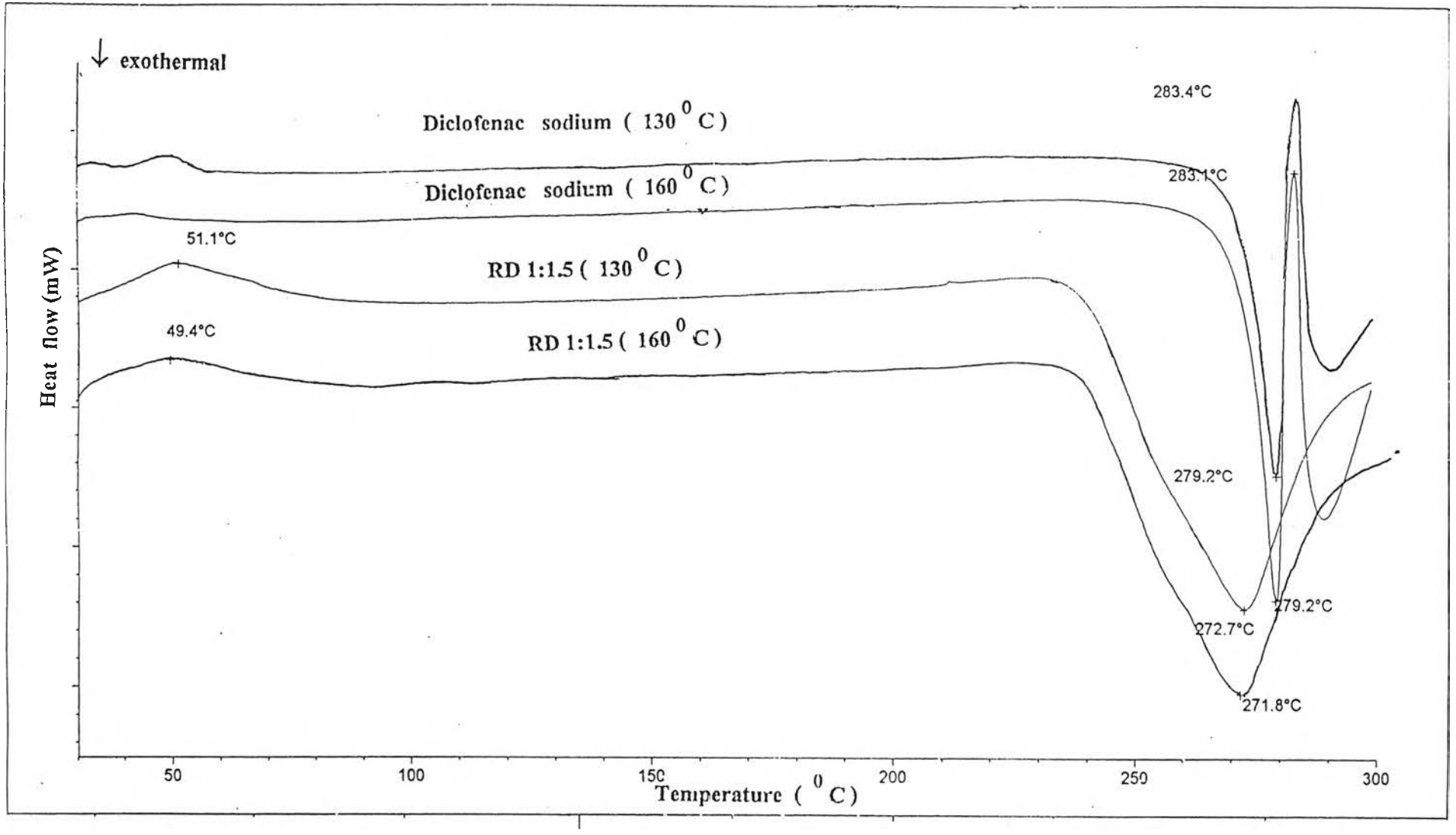


Figure 52 DSC Thermograms of spray dried diclofenac sodium with Eudragit® RD100 (RD 1:1.5) and 30% w/w Aerosil ®200 at various inlet air temperature, feed rate 12 rpm (20 ml/min).

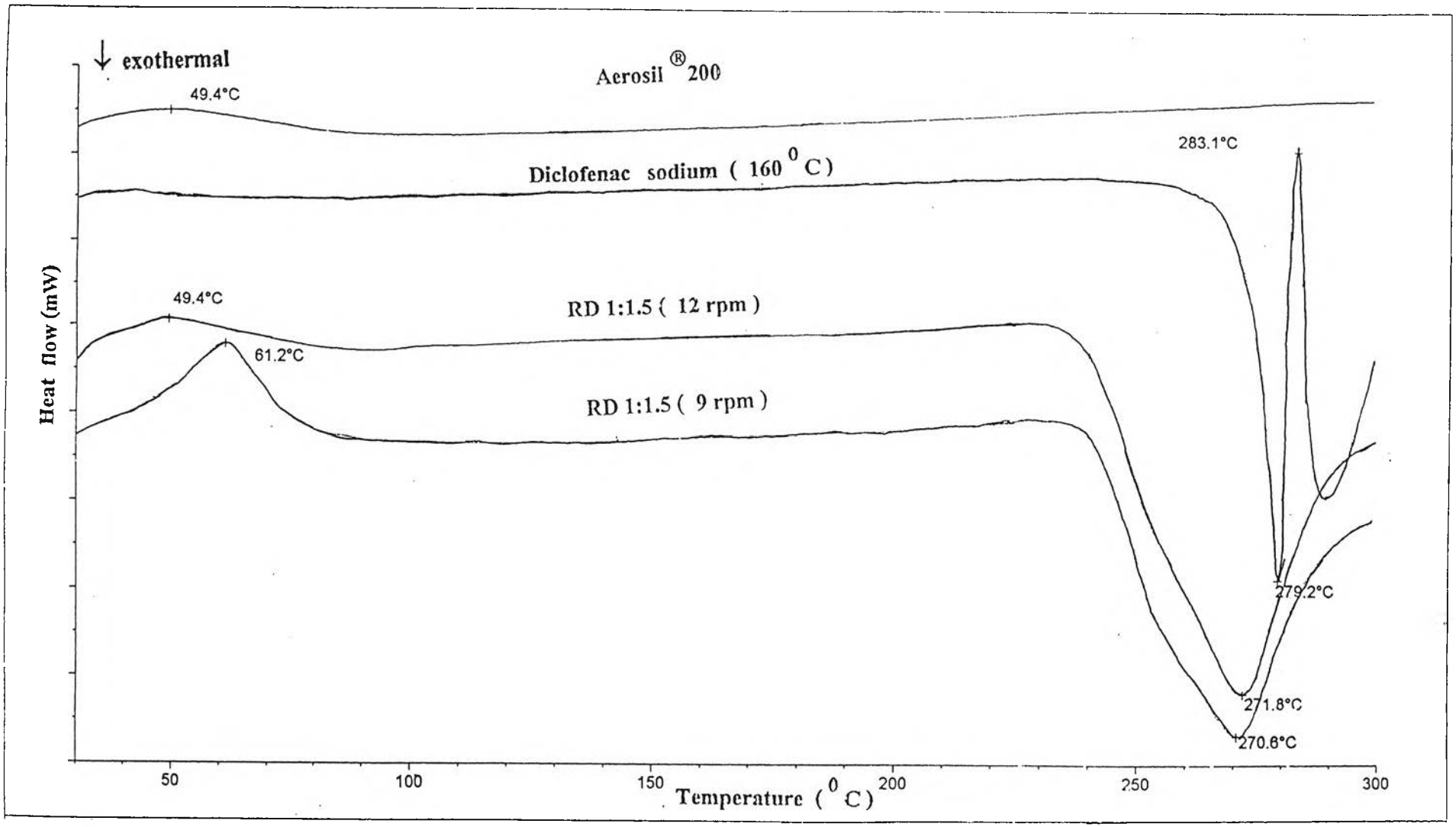


Figure 53 DSC Thermograms of spray dried diclofenac sodium with Eudragit® RD100 (RD 1:1.5) and 30% w/w Aerosil 200 at various feed rate, inlet air temperature 160°C. 12 rpm = 20 ml/min, 9 rpm= 15ml/min.

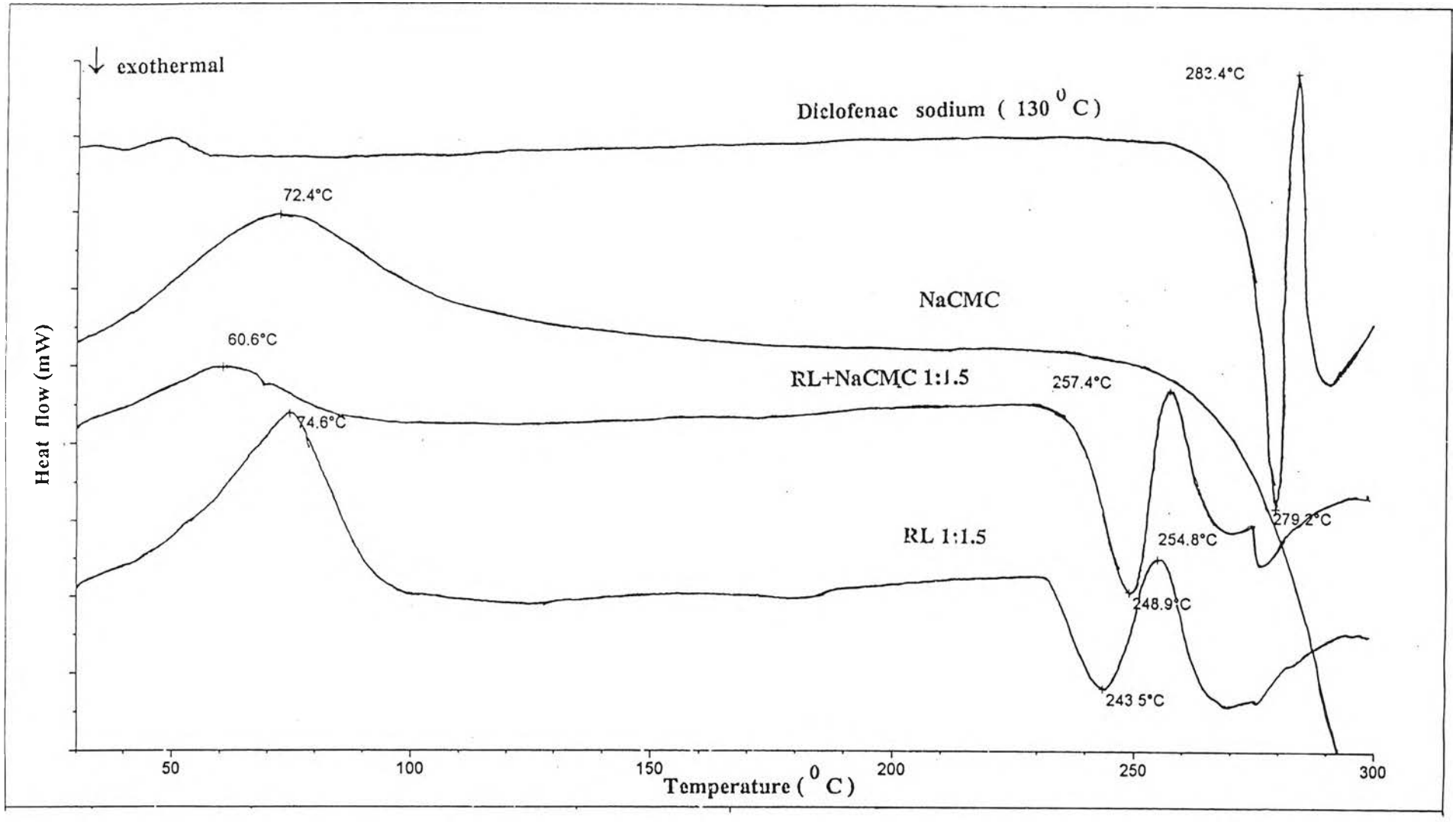


Figure 54 DSC Thermograms of spray dried diclofenac sodium with Eudragit ®RL30D, Eudragit®RL30D and NaCMC at the same ratio of 1:1.5.

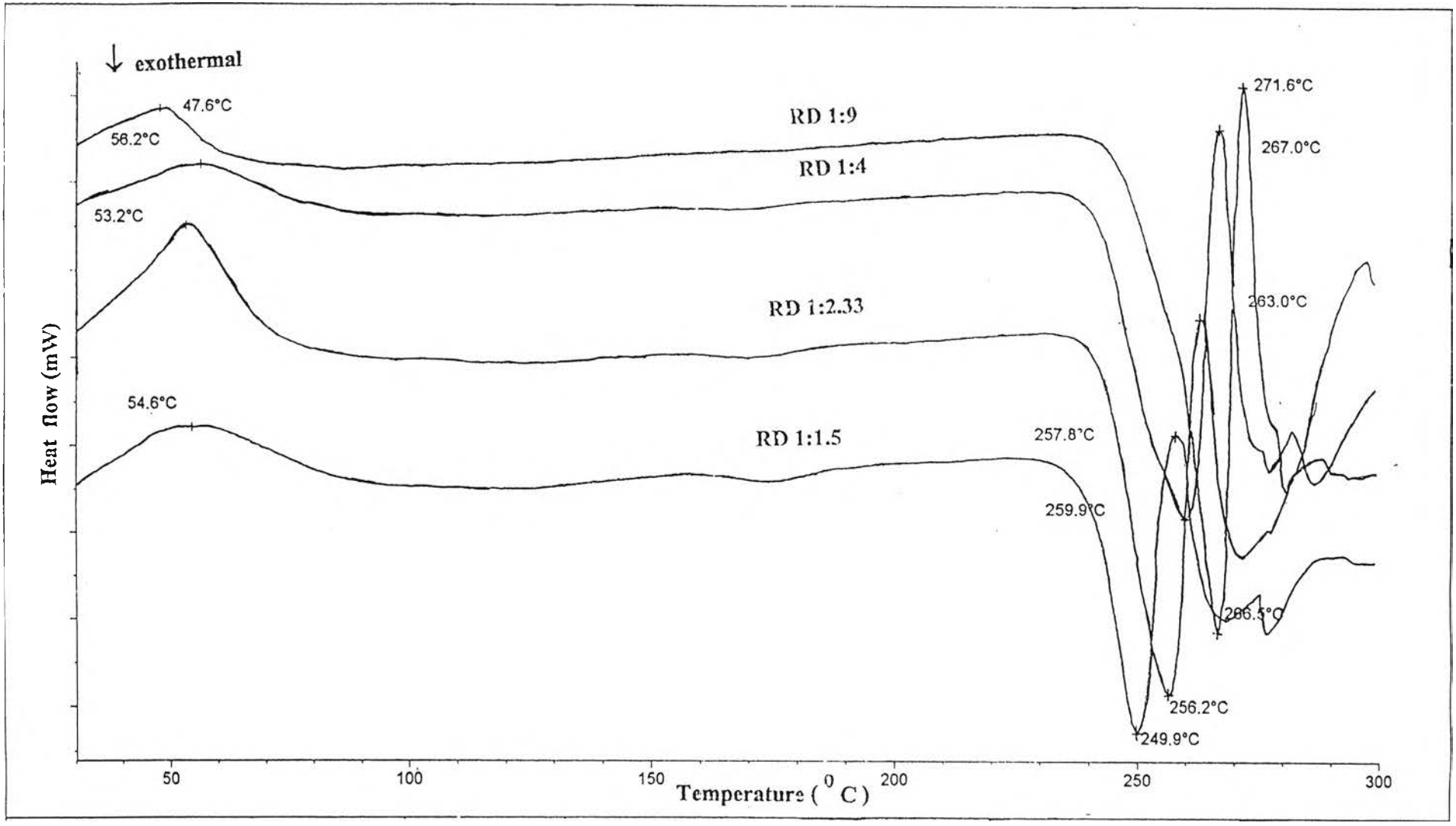


Figure 55 DSC Thermograms of spray dried diclofenac sodium with Eudragit® RD100 at various polymer to drug ratios.

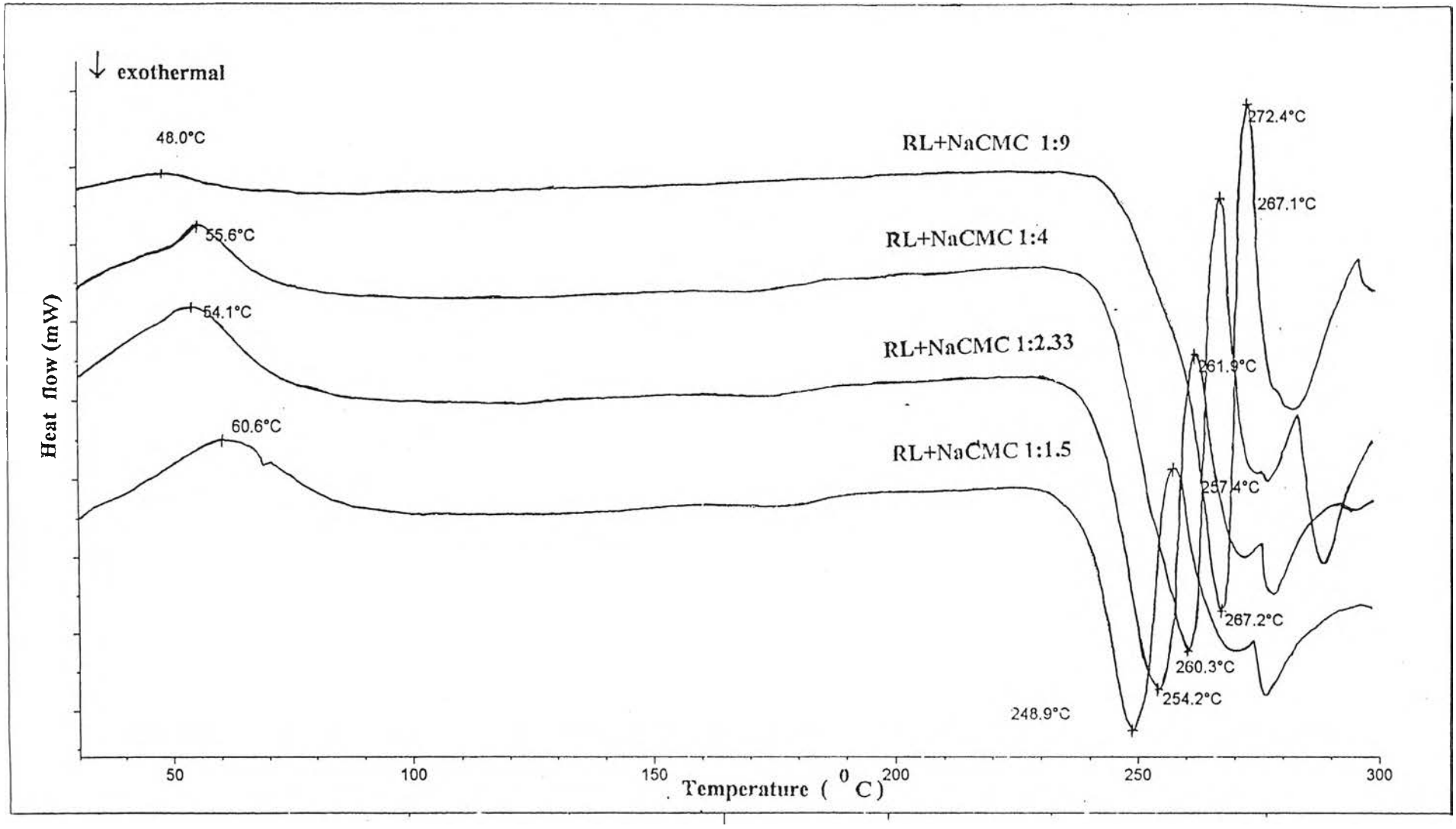


Figure 56 DSC Thermograms of spray dried diclofenac sodium with Eudragit® RL30D and NaCMC at various polymer to drug ratios.

Varying polymer to drug ratios of Eudragit® RL30D and NaCMC revealed that when increasing polymer to drug ratios , the exothermic and endothermic peaks were shifted to the lower temperature when compared with diclofenac sodium alone. When spray dried with Eudragit®RL30D and NaCMC at the ratio 1:9 to 1:4. The exothermic temperatures decreased from 267.2 to 260.3°C respectively and the endothermic peaks decreased from 272.4 to 267.1°C, respectively. When spray dried with Eudragit® RL30D and NaCMC at the ratio 1:2.33 to 1:1.5. The exothermic temperatures decreased from 254.2 to 248.9°C, respectively and the endothermic peaks decreased from 261.9 to 257.4°C, respectively. The DSC thermograms are shown in Figure 56. Their DSC temperatures of all spray dried products with drug and polymers are listed in Table 20.

Table 20 The exothermic and endothermic temperatures of spray dried products produced by different types and proportion of polymers.

Formulation	DSC Temperatures (degree celcius)	
	Exotherm	Endotherm
Diclofenac sodium	280.5	284.9
Eudragit ® RD100	-	51.4 . 192.6
Eudragit ® RL30D	-	57.5 ,199.5
Aerosil ® 200	-	49.4
NaCMC	-	72.4
1	279.2	283.4
2	279.2	283.1
3	266.5	271.6
4	267.2	272.4
5	259.9	267.0
6	260.3	267.1
7	256.2	263.0
8	254.2	261.9
9	249.9	257.8
10	248.9	257.4
11	264.9	-
12	262.8	-
13	272.7	-
14	271.8	-
15	270.6	-
16	243.5	254.8

13. Dissolution Study

From the experimental data; the dissolution or the release profiles was plotted between the amount of drug released against time. The dissolution of these formulations are described in Tables 25-30 (Appendix B).

Spray dried diclofenac sodium without polymer and spray dried diclofenac sodium with polymer from every formulation that filled into capsules were evaluated in the pH change system. For the capsules that contained spray dried diclofenac sodium and diclofenac sodium with various polymers spray dried powders tested in acid stage (0.1 N HCl, pH 1.2) for 2 hours, the percentage of drug release from all formulations were less than 3%. Then the pH of the dissolution medium was adjusted to 6.8. The capsules were continuously tested until 24 hrs.

13.1 Controlled diclofenac sodium capsule (Formulation 1-2)

The dissolution profile of capsules containing only spray dried diclofenac sodium at various inlet air temperature are shown in Figure 57 (Formulation 1-2). The capsules were tested in acid stage for 2 hours and the percentage of drug release from the sample was less than 2%. In pH 6.8, the drug released was more than 80% within the first 2 hours. This result indicated that diclofenac sodium was more soluble in phosphate buffer pH 6.8 than in 0.1 N HCl. The amount of drug that released in 6 hrs was more than 95% so the amount of drug released in 24 hours was 100.51% for drug spray dried using inlet temperature of 130°C and also100.56% when using products obtained from the inlet temperature of 160°C.

13.2 Commercial Voltaren® SR Tablet

The commercial product used was Voltaren® SR (as 100mg tablet). The amount of drug release at any time interval are presented in Table 25 (Appendix B). The release of diclofenac sodium from Voltaren® SR Tablet was affected by dissolution medium as illustrated in Figure 57. In pH change system, the percentage of drug release from Voltaren® SR at the first 2 hours (acid stage) was less than 1%.

Whereas the percentage of drug release at the first 6 hours in phosphate buffer pH 6.8 were more than 25 %. The amount of drug that released in 24 hours was 79.67%. After the drug was released for 24 hours, the polymer keeping the original shape of tablet remained undissolved.

13.3 Effect of polymer to drug ratio on dissolution profiles.

13.3.1 Polymer to drug ratio of 1:9 (Formulation 3-4)

The dissolution profiles of diclofenac sodium from spray dried microparticles prepared by Eudragit®RD 100 compared with Eudragit®RL 30 D and NaCMC in 0.1 N HCl and phosphate buffer pH 6.8 by pH change method are shown in Figure58 (Table 26, Appendix B). In pH change system, at the first 2 hours, the percentage of drug release from two formulations were less than 4 %. The product which prepared by Eudragit ®RD 100 released the drug of more than 80% at the 12 th hour and product which prepared using Eudragit ®RL 30 D and NaCMC releaseded the drug more than 75 % at the same hours. The dissolution profile of microparticles prepared by various polymers but at the same polymer to drug ratio of 1:9 seemed to be similar. The p-values from paired-samples t- test showed no statistically significant difference ($p > 0.05$) in the release patterns of both formulations (Table 38 , Appendix C). Complete drug release was seen on the 24 th hour of the experiment.

13.3.2 Polymer to drug ratio of 1:4 (Formulation 5-6)

The dissolution profiles of diclofenac sodium from spray dried microparticles prepared by Eudragit®RD 100 compared with Eudragit®RL 30 D and NaCMC in 0.1 N HCl and phosphate buffer pH 6.8 by pH change method are shown in Figure59 (Table 26-27, Appendix B). Both formulations gave the same release profile with a maximum drug release of more than 75 % at 18 th hour. The amount of drug that released in 24 hours were 94.59% and 94.99%, with Eudragit®RD 100 compared with Eudragit®RL30D and NaCMC, respectively. The dissolution profile of microparticles prepared by various polymers but at the same polymer to drug ratio of 1:4 seemed to be similar. The p - values from paired – samples t- test showed no

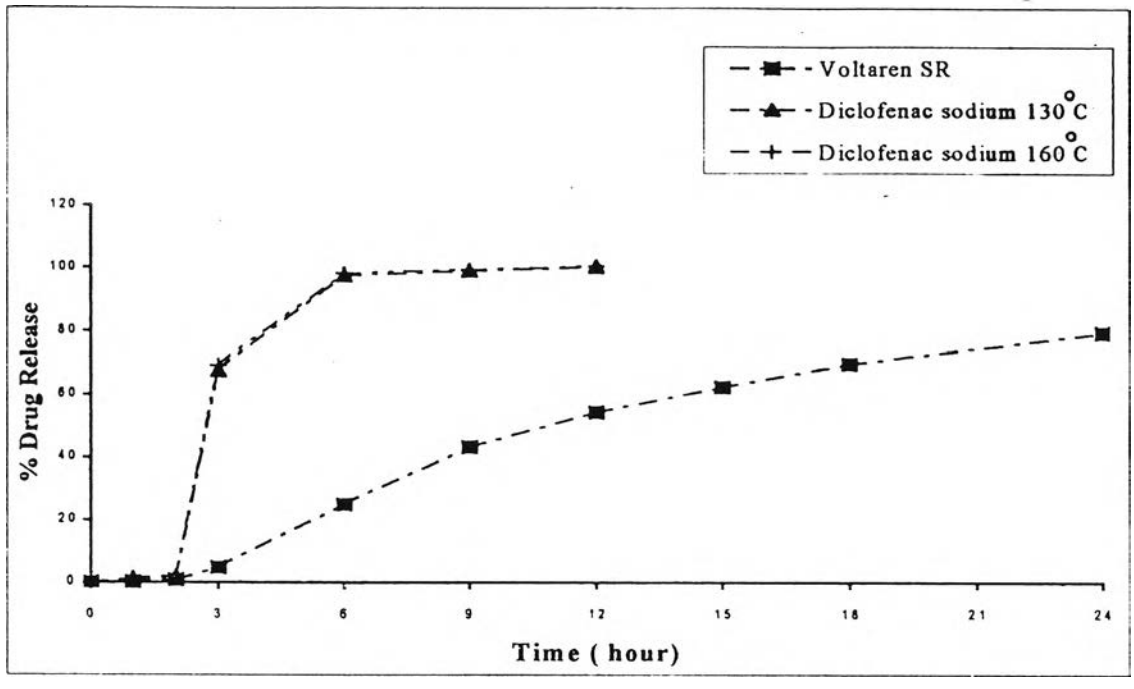


Figure 57 The release profiles of spray dried diclofenac sodium at various inlet air temperature and Voltaren® SR tablet.

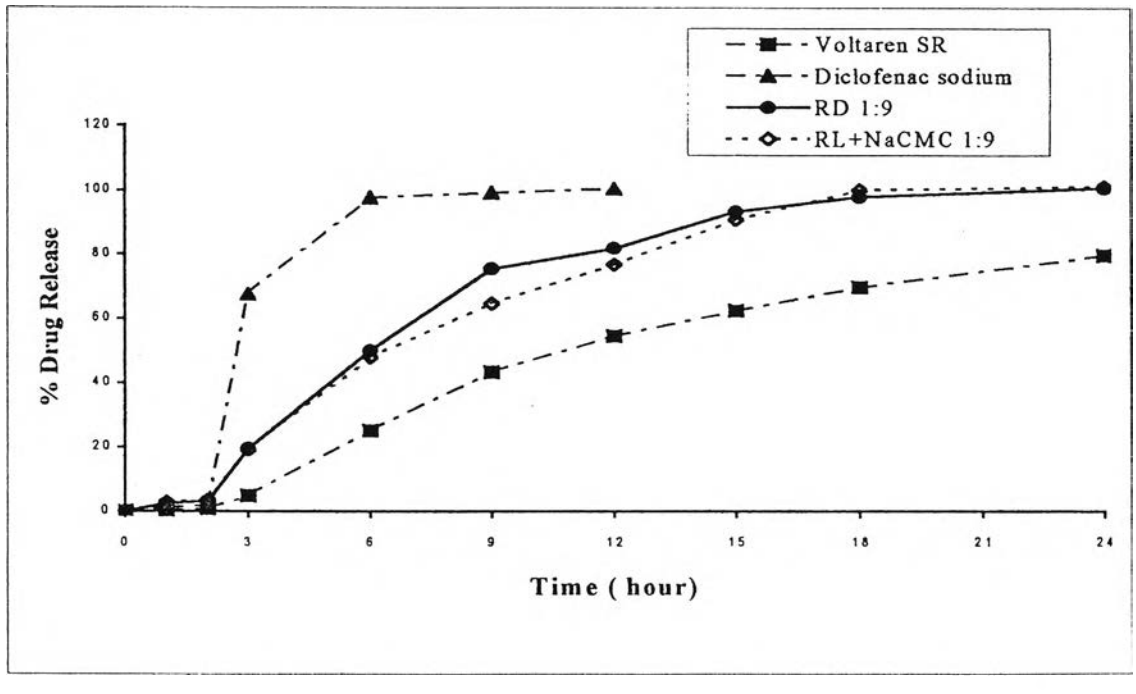


Figure 58 The release profiles of spray dried diclofenac sodium with Eudragit® RD 100, Eudragit ®RL30D and NaCMC at the same ratio of 1:9.

statistically significant difference ($p>0.05$) in the release patterns of both formulations (Table 39 , Appendix C).

13.3.3 Polymer to drug ratio of 1:2.33 (Formulation 7-8)

From Figure 60, the release profiles of the spray dried powders formulations prepared from Eudragit ®RD 100 to drug ratio of 1:2.33 was compared to those of formulation prepared from Eudragit ®RL 30 D and NaCMC at the same ratio. These release profiles are illustrated in (Table 27, Appendix B). Controlled release of drug was observed in pH change system. A very low percentage of drug release was found in the first 2 hours (acid stage). The formulation which contained Eudragit ®RD 100 showed similar dissolution profile when compared with product from Eudragit ®RL 30 D and NaCMC at the same ratio. The amout of drug that released in 24 hours were 87.80 % and 86.88 %, for powders made from Eudragit®RD 100 compared with Eudragit®RL 30 D and NaCMC, respectively. The p-values from paired-samples t-test showed no statistically significant difference ($p> 0.05$) in the release patterns of both formulations (Table 40 , Appendix C).

13.3.4 The polymer to drug ratio of 1:1.5 (Formulation 9-10)

The dissolution profiles of diclofenac sodium from spray dried microparticles prepared by Eudragit ®RD 100 compared with Eudragit ®RL 30 D and NaCMC at the polymer to drug ratio of 1:1.5 in 0.1 N HCl and phosphate buffer pH 6.8 by pH change method are shown in Figure 61 (Table 28 , Appendix B). The dissolution profiles of microparticles prepared with these two polymers seemed to be similar. But the formulation which contained Eudragit®RD100 showed slightly higher dissolution profile than using Eudragit ®RL 30 D and NaCMC. The amount of drug that released in 24 hours were 58.97 % and 58.77 %, respectively. The p-values from paired-samples t- test showed no statistically significant difference($p> 0.05$) in the release patterns of both formulations (Table 41 , Appendix C).

13.3.5 The polymer to drug ratio of 1:1.5 and 15%w/w Aerosil®200 (Formulation 11-12)

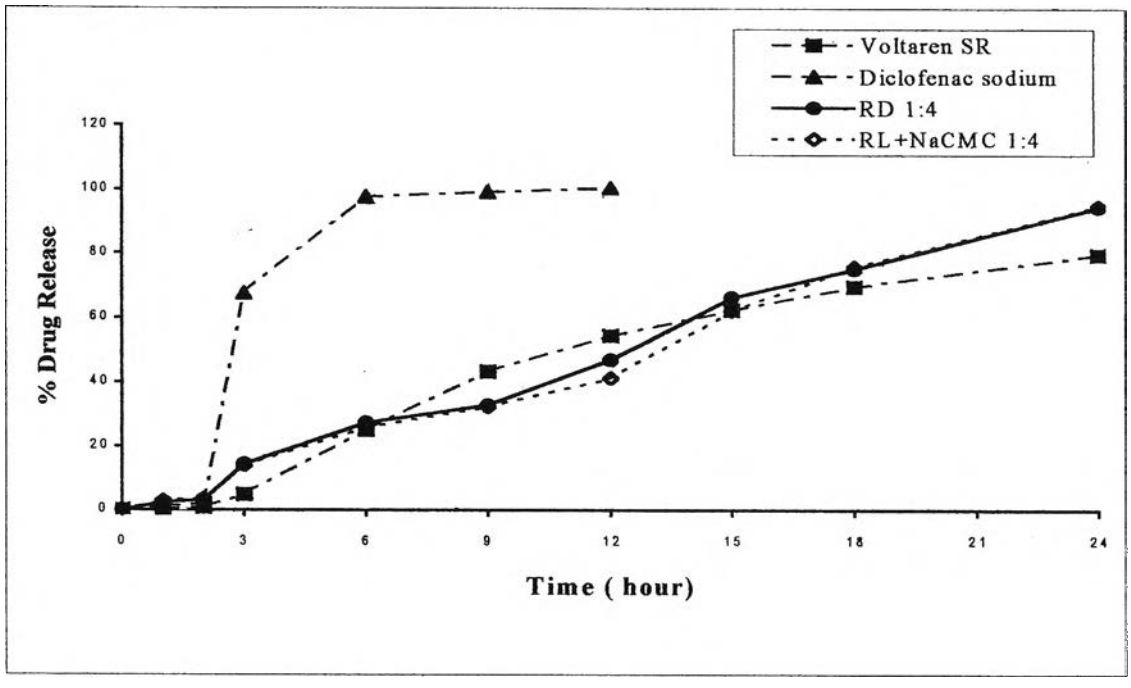


Figure 59 The release profiles of spray dried diclofenac sodium with Eudragit ® RD 100, Eudragit ®RL30D and NaCMC at the same ratio of 1:4.

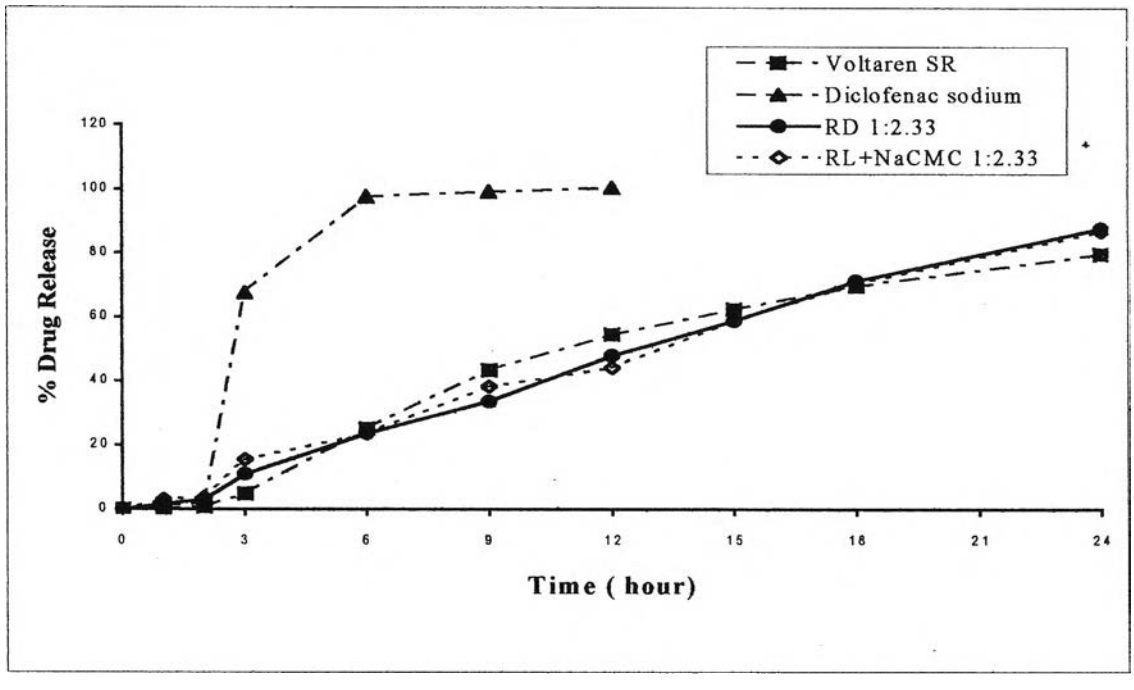


Figure 60 The release profiles of spray dried diclofenac sodium with Eudragit® RD 100, Eudragit ®RL30D and NaCMC at the same ratio of 1:2.33.

The formulations contained diclofenac sodium with spray dried Eudragit®RD100 compared with Eudragit ®RL 30D and NaCMC. The aid using Aerosil 200 15 %w/w content of drug in both formulations. The pictures of the release of diclofenac sodium are shown in Figure 62 (Table 28-29, Appendix B). Patterns of dissolution profile were similar. The p-values from paired-samples t- test showed no statistically significant difference($p>0.05$) in the release patterns of both Formulations (Table 42 , Appendix C).

13.4 Effect of NaCMC (Formulation 10-16)

The release of diclofenac sodium from spray dried diclofenac sodium with Eudragit ®RL 30 D and NaCMC at the ratio 1:1.5 compared with without NaCMC are displayed in Figure 63 (Table 28 and 30, Appendix B).

The amount of drug released from the formulation prepared by Eudragit ®RL 30 D without NaCMC was higher than formulation had NaCMC in every hour by pH change system. Nevertheless, The p-values from paired samples t- test showed statistically significant difference ($p<0.05$) in the release pattern of these two formulations (Table 43, Appendix C).

13.5 Effect of inlet temperature (Formulation 13-14)

The release of diclofenac sodium from spray dried diclofenac sodium with Eudragit®RD 100 at the same ratio 1:1.5 by the aid of Aerosil 200 30% content of drug and polymer prepared at two levels of inlet air temparature (130°C and 160°C) using pH change system are displayed in Figure 64 (Table 29,Appendix B).

The amount of drug that released in 24 hours were 77.32% and 78.92%, respectively. Patterns of dissolution profile were superimposed. The p-values from two way anova - test showed no statistically significant difference ($p> 0.05$) in the release patterns of these two formulations (Formulation 13-14) (Table 44,Appendix C).

The amount of drug that released in 24 hours were 77.32 % and 78.92 % and 79.67% for formulation 13, 14 and Voltaren® SR, respectively. Nevertheless, no statistically significant difference ($p>0.05$) between the release patterns of formulation 13 and Voltaren® SR when using the two way anova - test (Table 44, Appendix C). In contrast , Statically significant difference was observed from the two way anova- test ($p<0.05$) between the release patterns of these two formulations (Formulation 14 and Voltaren® SR) (Table 44 , Appendix C).

13.6 Effect of feed rate (Formulation 14-15)

The release of diclofenac sodium from spray dried diclofenac sodium with Eudragit ®RD 100 at the same ratio 1:1.5 by the aid of Aerosil 200 30% content of drug and polymer prepared at various feed rate (12 rpm , 9 rpm) are shown in Figure 65 (Table 29-30 , Appendix B).

The amount of drug released from the formulation prepared at feed rate of 12 rpm was slightly lower than the formulation, which prepared at feed rate 9 rpm in pH change system. Nevertheless, The p-values from two way anova - test showed no statistically significant difference ($p> 0.05$) in the release patterns of these two formulations (Formulation 14-15) (Table 44, AppendixC). In contrast, when tested with the independent – samples t test, the statistic test also showed statistically significant difference ($p<0.05$) between the release at 24 th hour of microparticles of these two formulations (Formulation 14-15) (Table 46, AppendixC)..

Statistically significant difference was observed from the two way anova- test ($p<0.05$) between the release patterns of formulation 15 and Voltaren® SR (Table 44, Appendix C). The amount of drug that released in 24 hours were 78.92 % and 86.83 % and 79.67% for formulation 14 , 15 and Voltaren ® SR, respectively. In conclusion, when tested with statistic between four formulations (Voltaren SR, Formulation13, Formulation 14, Formulation 15), The p-values from two way anova - test showed statistically significant difference ($p< 0.05$) in the release patterns of these four formulations (Table 45, Appendix C).

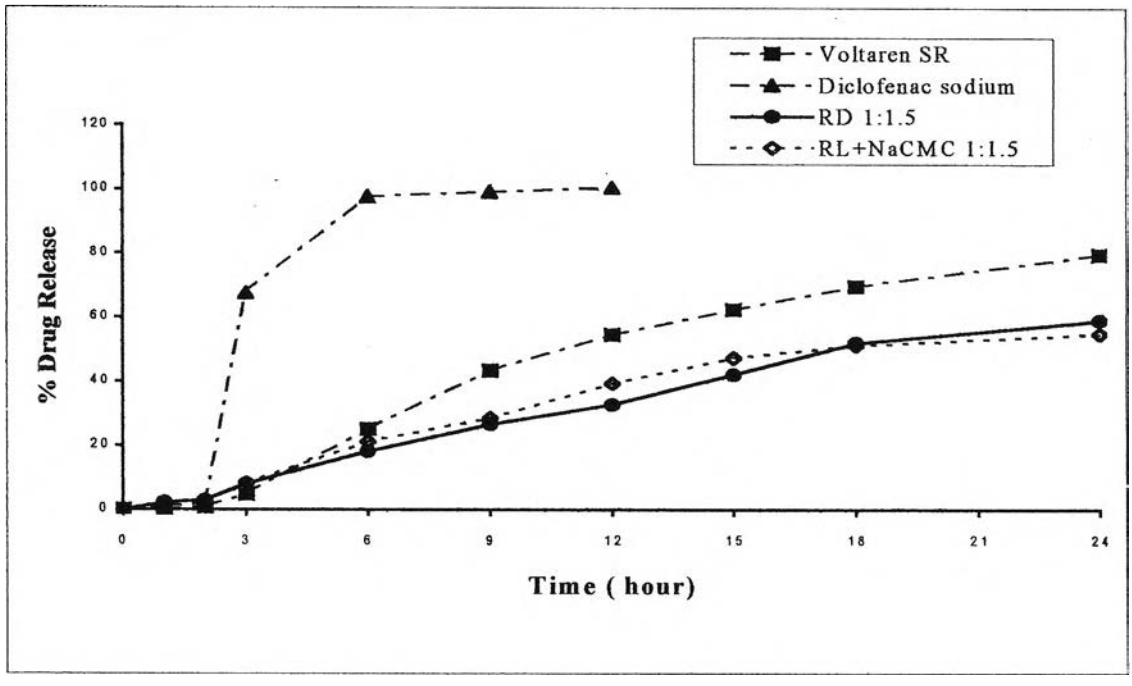


Figure 61 The release profiles of spray dried diclofenac sodium with Eudragit® RD 100, Eudragit ®RL30D and NaCMC at the same ratio of 1:1.5.

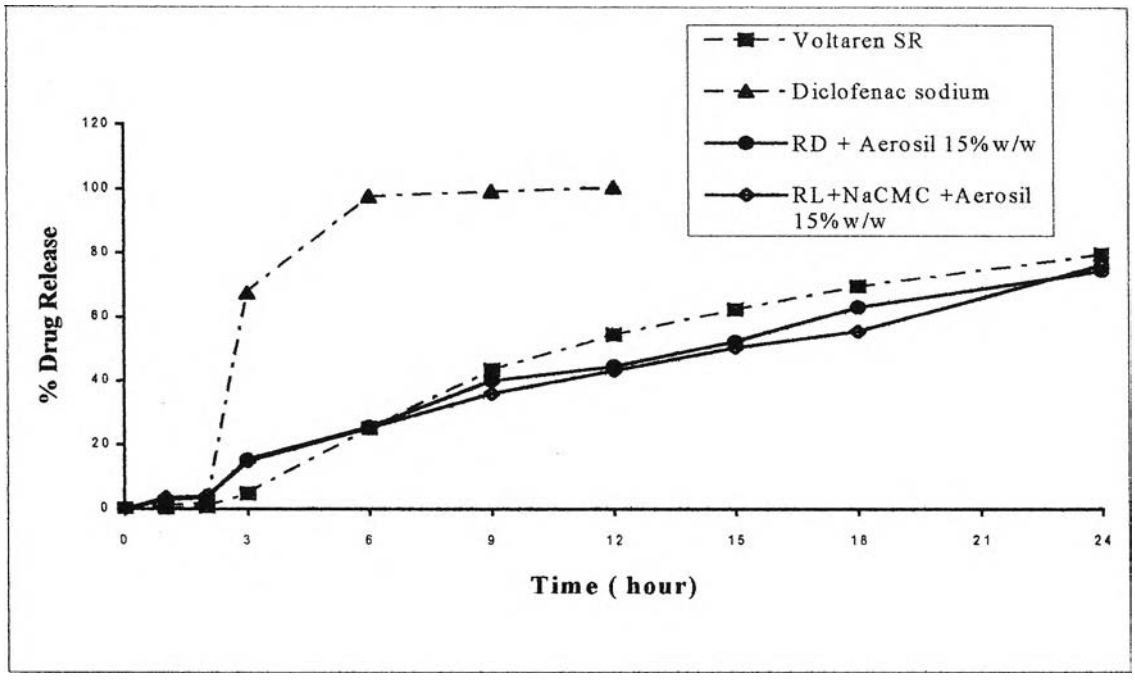


Figure 62 The release profiles of spray dried diclofenac sodium with Eudragit® RD 100, Eudragit ®RL30D and NaCMC and the aid of Aerosil® 200 15% w/w at he same ratio of 1:1.5.

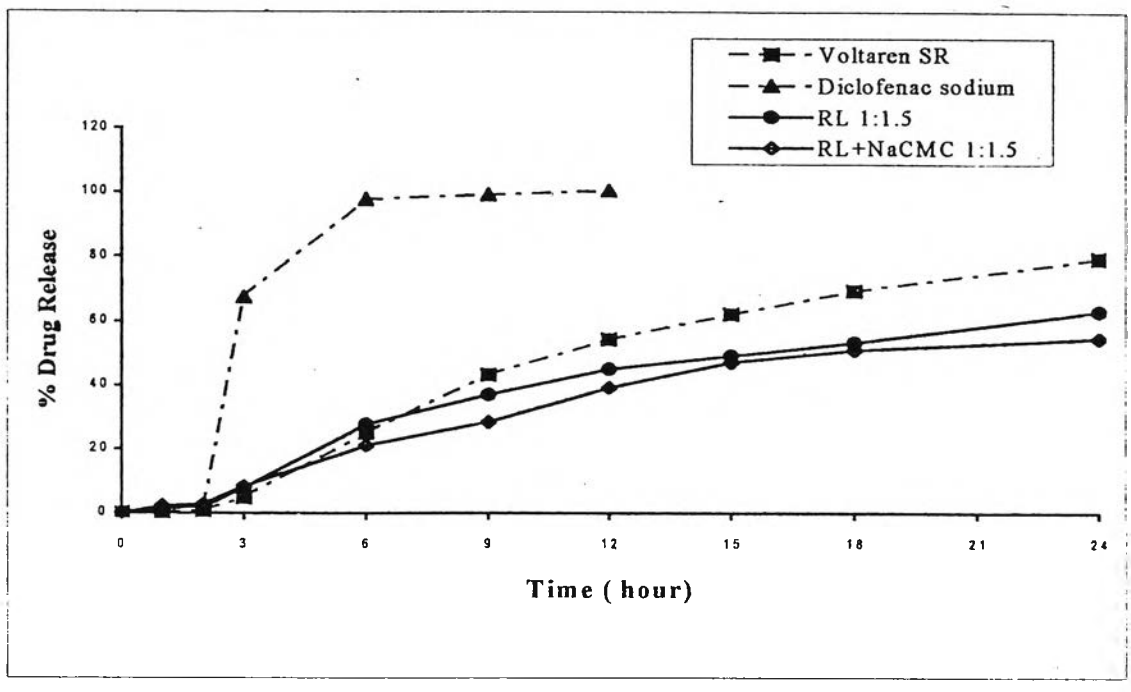


Figure 63 The release profiles of spray dried diclofenac sodium with Eudragit® RL30D, Eudragit ® RL30D and NaCMC at the same ratio of 1:1.5.

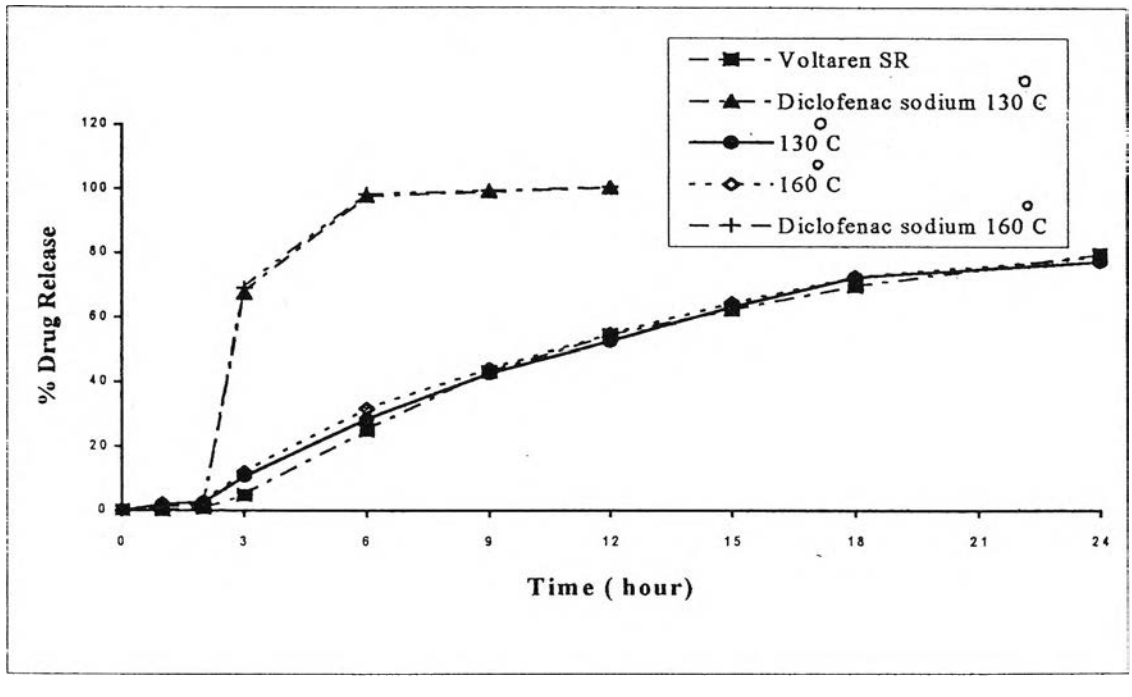


Figure 64 The release profiles of spray dried diclofenac sodium with Eudragit® RD 100 (RD 1:1.5) and Aerosil® 200 30%w/w at various inlet air temperature, feed rate = 12 rpm (20 ml/min).

13.7 Effect of the polymer to drug ratio

13.7.1 Eudragit ® RD100 (Formulation 3,5,7,9)

The dissolution profiles of diclofenac sodium from diclofenac sodium with Eudragit ®RD 100 spray dried powder with various polymers to drug ratios into a pH change system are shown in Figure 66. The percentages of diclofenac sodium released at 24 hours were decreased from 100.72%, 94.59%, 87.80%, to 58.97% when the proportions of polymer in the formulations increased from the polymer to drug ratios of 1:9 to 1:4 to 1:2.33 and 1:1.5, respectively. The release of diclofenac sodium decreased with the increasing of the amount of polymer in the formulation as expected. The concentration of Eudragit®RD 100 in the formulation was the determining factor in controlling release rate of drug.

13.7.2 Eudragit®RL30D and NaCMC (Formulation 4,6,8,10)

These formulations contained diclofenac sodium with Eudragit ®RL 30D and NaCMC at various ratios into a pH changing system are shown in Figure 67. In pH change system, the highest amount of diclofenac sodium released in 24 hours obtained from Formulation 4 that had polymer to drug ratio of 1:9. The percentage of diclofenac sodium released at 24 hours was 101.24%. The release profile of this formulation was also faster than other formulations (Formulation 6, 8, 10).

13.8 Effect of Amount of Aerosil®200 (Formulation 9-13)

The release profiles of the formulation containing Eudragit®RD 100 and Eudragit®RL 30D and NaCMC to diclofenac sodium at the ratio of 1:1.5 with and without Aerosil® 200 are exhibited in Figure 68. Percent release of the formulation, which had Aerosil®200 was higher than those of without Aerosil® 200 into formulation. At 0%, 15% and 30% of Aerosil® 200 were added to the formulation. The percentages of drug released from the microparticles were 58.97%, 54.77%,

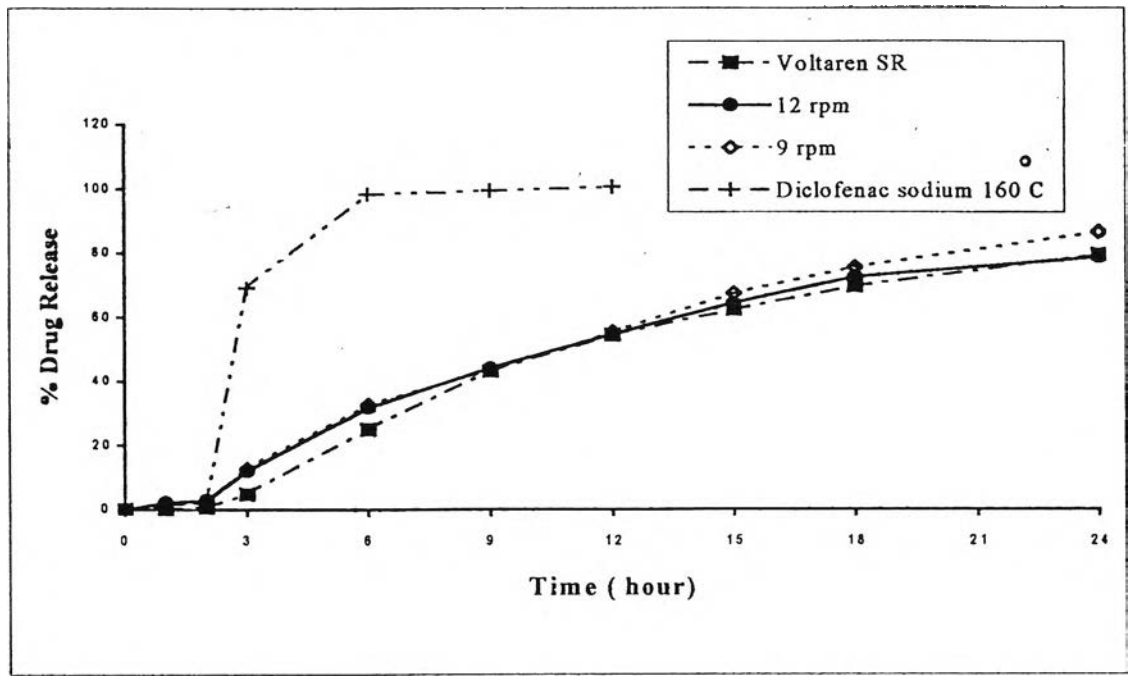


Figure 65 The release profiles of spray dried diclofenac sodium with Eudragit® RD 100 (RD 1:1.5) and Aerosil® 200 30% w/w at various feed rate, inlet air temperature 160°C.

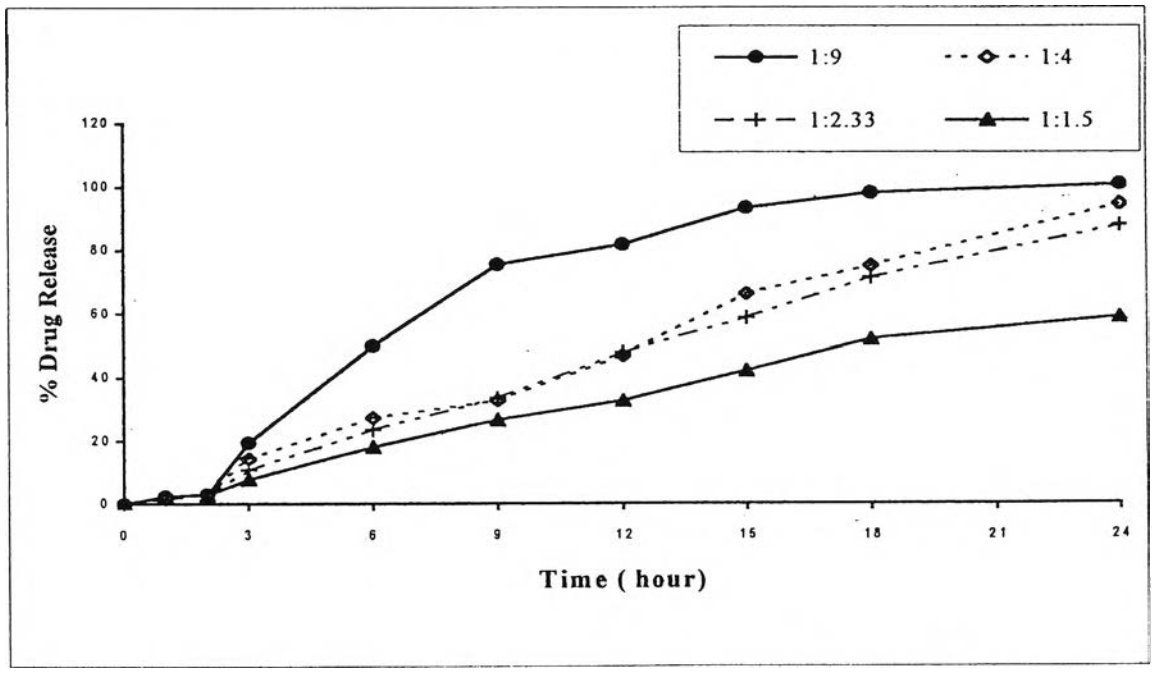


Figure 66 The release profiles of spray dried diclofenac sodium with Eudragit® RD 100 at various polymer to drug ratios.

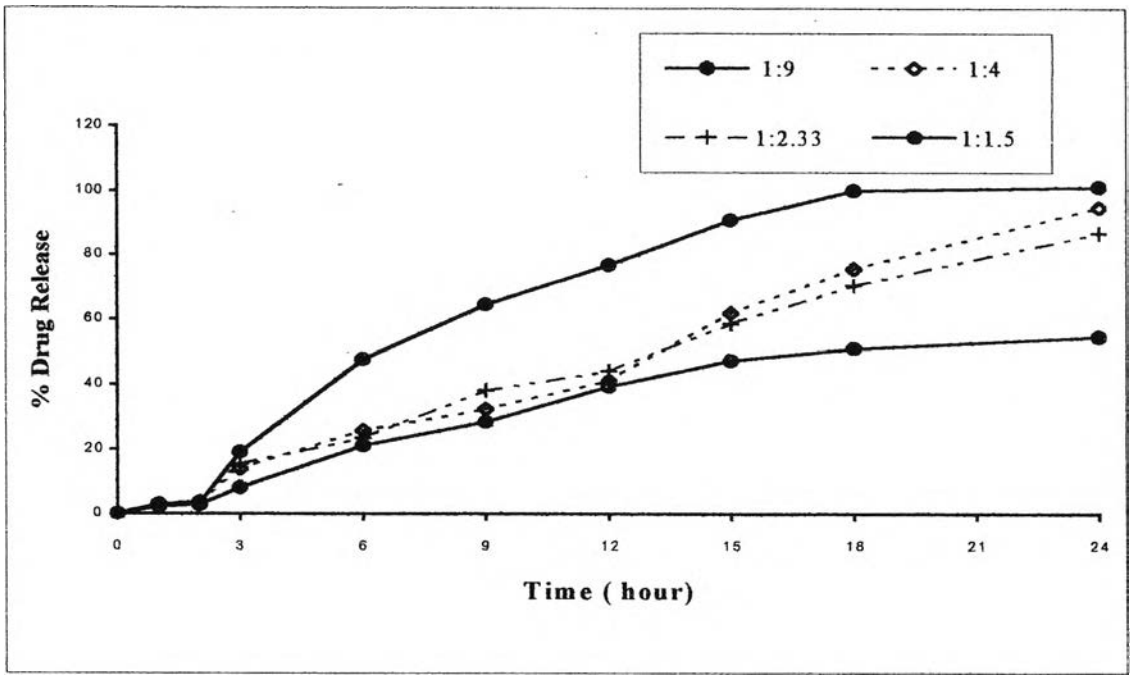


Figure 67 The release profiles of spray dried diclofenac sodium with Eudragit ® RL30D and NaCMC at various polymer to drug ratios.

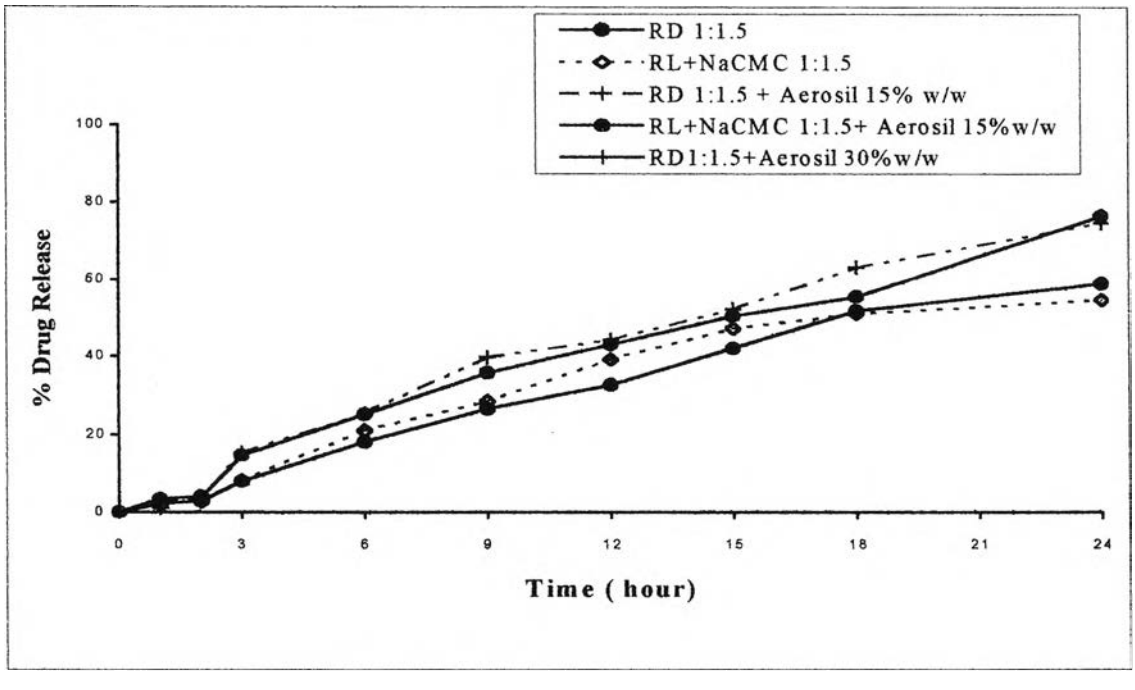


Figure 68 The release profiles of spray dried diclofenac sodium with Eudragit® RD100, Eudragit ®RL30D and NaCMC with or without Aerosil 200.

74.67%, 76.40%, 77.32%. Higher amount of Aerosil® 200 showed the higher percent of dissolution profile of diclofenac sodium.

The Elucidation of drug release model

In order to determine the effect of type of polymer and formulation on the model of drug release, analysis of all dissolution data was carried out to elucidate release model (zero order, first order, and Higuchi model). The plots between percentage of drug released versus square root of time (Higuchi model), percentage of drug released against time (zero order), log percent of drug remained versus time(first order). The correlation coefficients are presented in Table 21.

a) The Voltaren® SR Tablet

From the pH change method, the highest correlation coefficient was 0.9970 obtained from the first order plot The first order model might possibly be operative.

b) The control diclofenac sodium capsule

From the pH change method, the first order plots was linear with the correlation coefficient values greater than 0.97. However, the highest correlation coefficients of Formulation 1 and 2 were 0.9819 and 0.9979, respectively. The resulted indicated that the release data might have followed the first order model.

c) The Formulation 3-4 microparticles (RD1:9, RL30D and NaCMC 1:9)

From the pH change method, the two formulations showed similar release model. The first order plot was linear with the correlation coefficient values greater than 0.96. The highest correlation coefficients of Formulation 3 and 4 were 0.9664 and 0.9771, respectively. The highest correlation coefficient was obtained from the first order plot.

d) The Formulation 5-6 microparticle (RD1:4, RL30D and NaCMC 1:4)

All these Formulations showed similar release model. The highest correlation was obtained from zero order model of pH change system. For Formulation 5, the correlation coefficient of release was 0.9861 whereas from Formulation 6 was 0.9859. In conclusion, the resulted indicated that the release data might have followed the zero order model.

e) The Formulation7-8 microparticle (RD1:2.33, RL30D and NaCMC 1:2.33)

For the test of pH-changing system, the zero order plot were linear with the correlation coefficient values greater than 0.98. For Formulation 7 and 8 the highest correlation coefficients were 0.9919 and 0.9875 from the zero order plot.

f) The Formulation 9-10 microparticle (RD1:1.5, RL30D and NaCMC 1:1.5)

From the pH change method, the highest correlation coefficient, as presented in Table 21 was obtained from the Higuchi model. By observation, Formulation 9, both the first order plot and the Higuchi plot were of interested because the correlation coefficient from Formulation 9 were 0.9917 and 0.9912, respectively but the highest correlation coefficient from Formulation 10 was 0.9803 from the Higuchi plot. If these formulations showed similar release model in pH change system. This indicated that the Higuchi model would be possibly followed.

g) The Formulation 11-12 microparticle (RD1:1.5, RL30D and NaCMC 1:1.5 with 15% w/w Aerosil)

These two Formulations showed similar release model in pH change system. The Higuchi plot was linearity with the correlation coefficient values greater than 0.98. For Formulation 11 and 12, the highest correlation coefficients were 0.9917 and 0.9861 from the Higuchi plot, In the conclusion, the Formulation 11-12 might have been followed the Higuchi model.

h) The Formulation 13-15 microparticles (RD100 1:1.5 with 30%w/wAerosil)

From the pH change method, Formulations 13-15, the highest correlation coefficient as presented in Table 21, both the first order plot and the Higuchi plot were of interested because these two models plots were linear with the correlation coefficient values greater than 0.98. For Formulation 13 (inlet temperature=130C, feed rate=12 rpm) the highest correlation coefficients were 0.9864 and 0.9865 from the first order plot and the Higuchi plot, respectively. As the same way, Formulation 15 (inlet temperature=160C, feed rate=9 rpm)the highest correlation coefficients were 0.9940 and 0.9946 from the first order plot and the Higuchi plot, respectively. For Formulation 14(inlet temperature=160C, feed rate=12 rpm)the highest correlation coefficient was 0.9911 from the first order plot. These three formulations showed similar release model in the pH change system. This indicated that the first order model would be possibly followed.

i) The Formulation 16 microparticle (RL30D 1:1.5)

For the test of pH-change system, the Higuchi plot was linear with the highest correlation coefficient values of 0.9754, the formulation might have followed the Higuchi model.

Table 21 Correlation coefficient of the relation ships between percentage drug released versus time.

Formulation	Correlation coefficient		
	pH change system		
	Zero	First	Higuchi
Voltaren SR	0.9315	0.9970	0.9864
1	0.5209	0.9819	0.6230
2	0.5042	0.9779	0.6062
3	0.8187	0.9664	0.9241
4	0.8726	0.9711	0.9577
5	0.9861	0.8883	0.9740
6	0.9859	0.8622	0.9589
7	0.9919	0.9525	0.9891
8	0.9875	0.9490	0.9827
9	0.9793	0.9917	0.9912
10	0.9228	0.9580	0.9803
11	0.9646	0.9897	0.9917
12	0.9776	0.9601	0.9861
13	0.9306	0.9864	0.9865
14	0.9246	0.9911	0.9856
15	0.9505	0.9940	0.9946
16	0.9049	0.9692	0.9754