CHAPTER III

RESULTS

A. Part I-Prednisolone

1. Prednisolone-dextrose System

1.1 Tablet Disintegration Studies

The average disintegration times of prednisolone tablets containing drug and dextrose were presented in Table 6. Prednisolone control tablets exhibited slowest disintegration time of 4.77 minutes. The tablets containing coprecipitates gave disintegration times less than 2 minutes while the tablets containing physical mixtures gave disintegration times between 1-4 minutes. For 1:1 prednisolone: dextrose ratio, tablets containing coprecipitate exhibited faster disintegration time than tablets containing physical mixture. For 1:3 and 1:5 drug:dextrose ratios, the disintegration times of tablets containing coprecipitates or physical mixtures were comparable ($\alpha = 0.05$).

1.2 Tablet Dissolution Studies

The dissolution parameters and dissolution profiles of prednisolone tablets containing drug and dextrose were demonstrated in Table 7 and Figures 4-8. The tablets containing coprecipitates gave higher prednisolone dissolution than the tablets containing

Table 6. Average Disintegration Times of the Tablets Containing Various Ratios of Prednisolone:Dextrose System

PREDNISOLONE TABLETS CONTAINING	AVERAGE DISINTEGRATION TIME* ± S.D. (MIN)
1:0 Prednisolone:carrier coprecipitate	4.77 ± 1.39
1:1 Prednisolone:dextrose coprecipitate	1.79 ± 0.73
1:1 Prednisolone:dextrose physical mixture	3.43 ± 0.78
1:3 Prednisolone:dextrose coprecipitate	1.21 ± 0.52
1:3 Prednisolone:dextrose physical mixture	1.71 ± 0.46
1:5 Prednisolone:dextrose coprecipitate	1.56 ± 1.30
1:5 Prednisolone:dextrose physical mixture	2.66 ± 0.61

* From 6 tablets

Table 7. The Dissolution Parameters of Prednisolone Tablets Containing Various Ratios of Drug:Dextrose System

PREDNISOLONE TABLETS CONTAINING	C_{20} [1]	C_{60} [2]	T_{60} [3] (MIN)	T_{90} [4] (MIN)
1:0 Prednisolone:carrier coprecipitate	79.4±1.52	88.0±1.34	7.5	>60
1:1 Prednisolone:dextrose coprecipitate	76.5±3.38	100.1±1.78	12.5	34.5
1:1 Prednisolone:dextrose physical mixture	72.2±1.14	89.8±2.10	12.0	>60
1:3 Prednisolone:dextrose coprecipitate	87.1±1.92	96.3±0.88	5.0	25.5
1:3 Prednisolone:dextrose physical mixture	86.9±1.81	93.7±1.73	6.0	27.5
1:5 Prednisolone:dextrose coprecipitate	91.8±0.79	97.1±0.66	4.5	17.5
1:5 Prednisolone:dextrose physical mixture	87.4±0.05	92.3±0.15	3.5	30.0

[1] C_{20} = % Prednisolone dissolved obtained at the time of 20 minutes.

[2] C_{60} = % Prednisolone dissolved obtained at the time of 60 minutes.

[3] T_{60} = The time required for 60% prednisolone dissolution.

[4] T_{90} = The time required for 90% prednisolone dissolution.

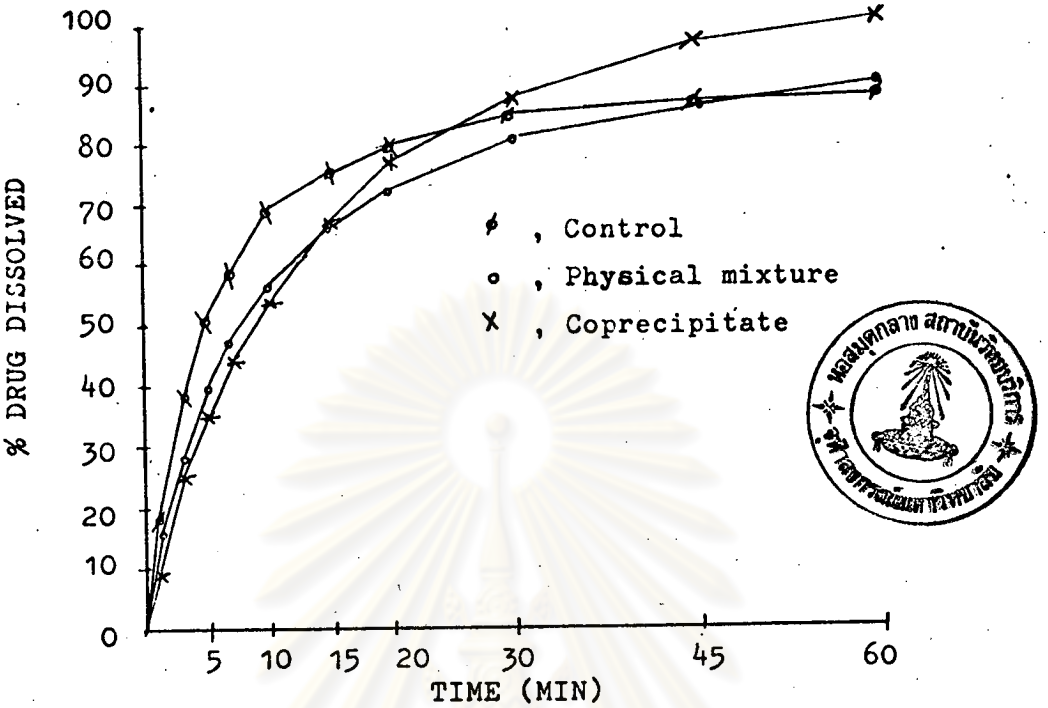

Figure 4. Dissolution profiles of tablets containing 1:1 prednisolone:dextrose.

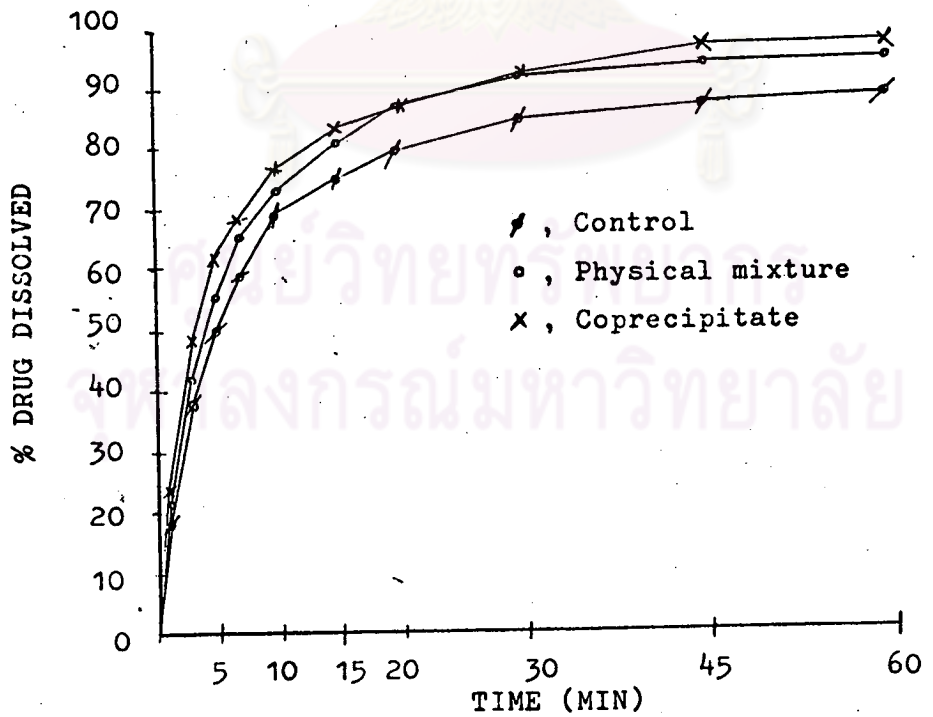

Figure 5. Dissolution profiles of tablets containing 1:3 prednisolone:dextrose.

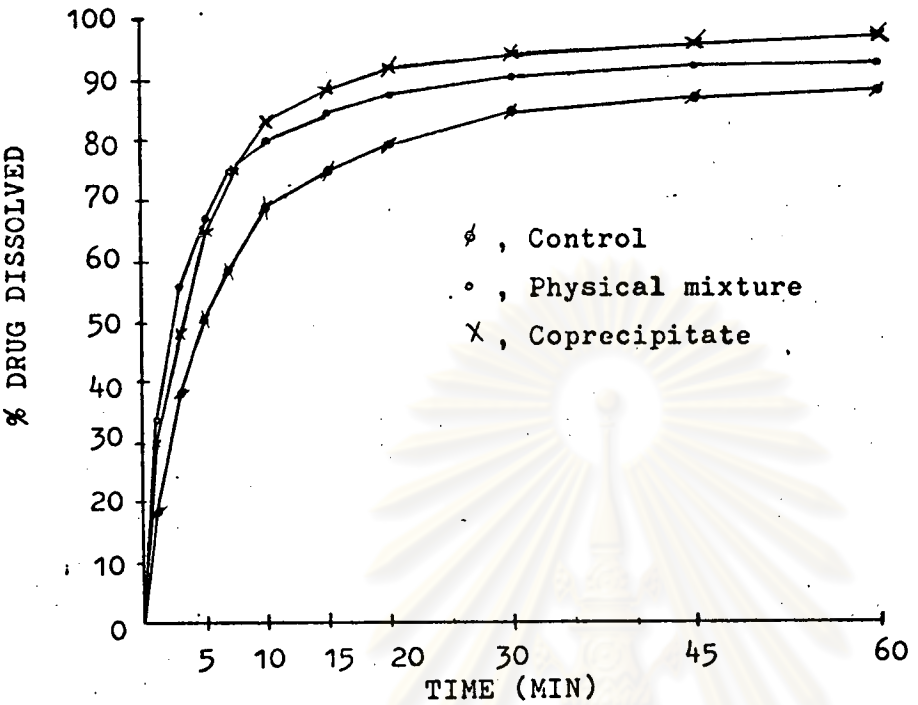

Figure 6. Dissolution profiles of tablets containing 1:5 prednisolone:dextrose.

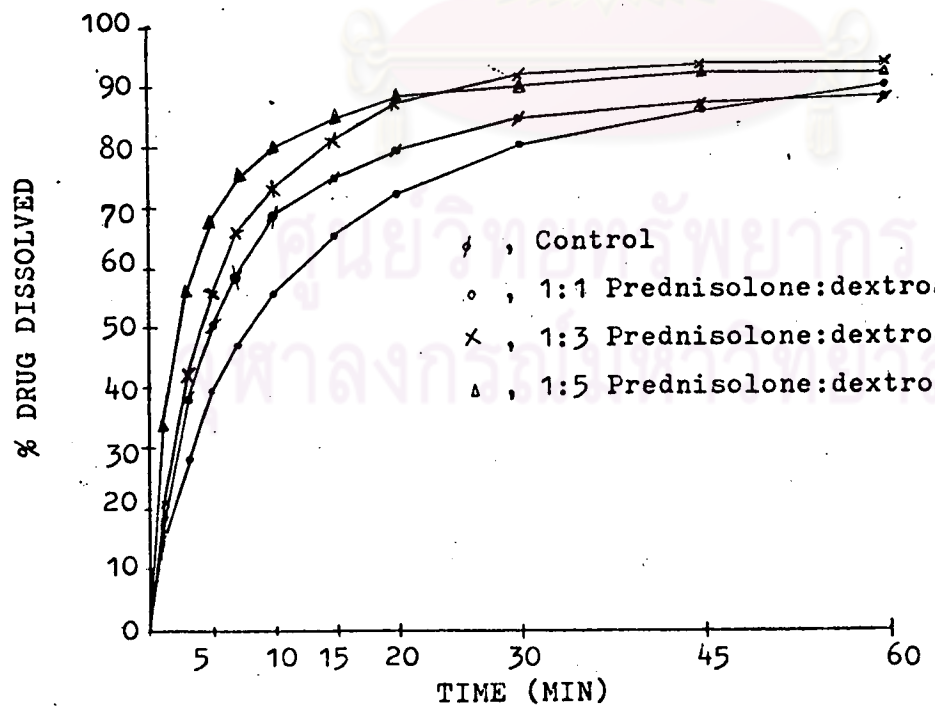

Figure 7. Dissolution profiles of tablets containing various ratios of prednisolone:dextrose physical mixtures.

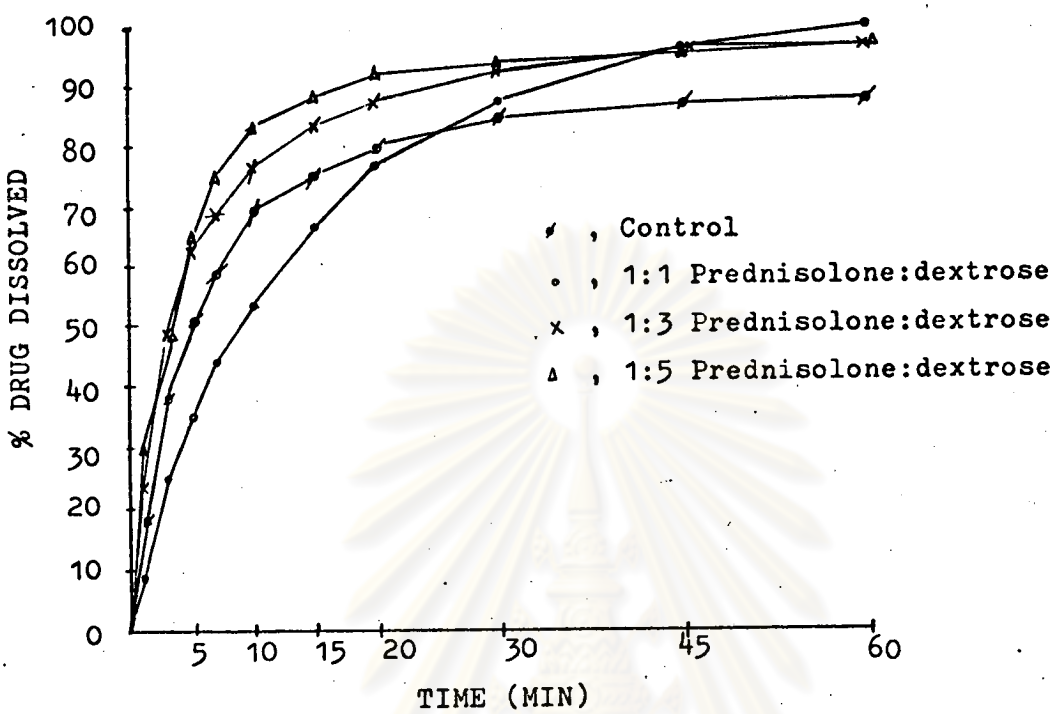

Figure 8. Dissolution profiles of tablets containing various ratios of prednisolone:dextrose coprecipitates.

physical mixtures at every drug:dextrose ratio within 60 minutes. The dissolution of drug increased as the content of dextrose increased in both coprecipitates and physical mixtures.

The tablets containing prednisolone and dextrose showed faster dissolution rates of prednisolone than the prednisolone control tablets, except the tablets containing 1:1 prednisolone: dextrose physical mixture. The T_{90} (time required for 90% prednisolone dissolved) of the tablets containing 1:5 prednisolone: dextrose was the lowest of 17.5 minutes, while more than 60 minutes were obtained from recrystallized prednisolone tablets.

2. Prednisolone-PEG 4000 System

2.1 Tablet Disintegration Studies

The average disintegration times of prednisolone tablets containing drug and PEG 4000 were presented in Table 8. The disintegration times of the tablets containing coprecipitate and the tablets containing physical mixture having the same drug:carrier ratio were comparable ($\alpha = 0.05$).

Increasing content of PEG 4000 significantly increased the disintegration time of prednisolone tablets. However, the tablets containing 1:1 prednisolone:PEG 4000 seemed to exhibit faster disintegration times than the prednisolone control tablets but the tablets of 1:3 or 1:5 prednisolone:PEG 4000 significantly exhibited slower disintegration times than the prednisolone control tablets.

Table 8. Average Disintegration Times of the Tablets Containing Various Ratios of Prednisolone:PEG 4000 System

PREDNISOLONE TABLETS CONTAINING	AVERAGE DISINTEGRATION TIME* ± S.D. (MIN)
1:0 Prednisolone:carrier coprecipitate	4.77 ± 1.39
1:1 Prednisolone:PEG 4000 coprecipitate	3.22 ± 0.52
1:1 Prednisolone:PEG 4000 physical mixture	2.35 ± 0.83
1:3 Prednisolone:PEG 4000 coprecipitate	11.18 ± 3.46
1:3 Prednisolone:PEG 4000 physical mixture	9.67 ± 1.57
1:5 Prednisolone:PEG 4000 coprecipitate	17.72 ± 1.67
1:5 Prednisolone:PEG 4000 physical mixture	16.93 ± 4.05

* From 6 tablets

2.2 Tablet Dissolution Studies

The dissolution parameters and dissolution profiles of prednisolone tablets containing drug and PEG 4000 were presented in Table 9 and Figures 9-13. No enhancement in prednisolone dissolution was observed in the tablets containing physical mixtures compared to prednisolone control tablets. In addition, the tablets of 1:3 and 1:5 prednisolone:PEG 4000 physical mixtures produced slower dissolution rates than the prednisolone control tablets.

For 1:1 and 1:3 drug:PEG 4000 ratios the tablets containing coprecipitates exhibited the same prednisolone dissolution as the tablets containing physical mixtures within 60 minutes. At 1:5 drug:PEG 4000 ratio, tablets containing coprecipitate showed slower dissolution than tablets containing physical mixture in the initial part of dissolution profile, followed by subsequent higher prednisolone dissolution rate in the latter part of the dissolution profile.

The tablets of 1:5 prednisolone:PEG 4000 coprecipitate produced the highest rate of 99% prednisolone dissolution within 60 minutes while the prednisolone control tablets produced 88% prednisolone dissolution.

Table 9. The Dissolution Parameters of Prednisolone Tablets Containing Various Ratios of Drug:PEG 4000 System

PREDNISOLONE TABLETS CONTAINING	C_{20} [1]	C_{60} [2]	T_{60} [3] (MIN)	T_{90} [4] (MIN)
1:0 Prednisolone:carrier	79.4±1.52	88.0±1.34	7.5	>60
1:1 Prednisolone:PEG 4000 coprecipitate	69.7±3.19	88.7±3.09	13.5	>60
1:1 Prednisolone:PEG 4000 physical mixture	79.3±2.54	90.6±1.81	8.5	56.5
1:3 Prednisolone:PEG 4000 coprecipitate	53.8±1.34	88.9±0.42	24.0	>60
1:3 Prednisolone:PEG 4000 physical mixture	59.8±0.59	86.2±1.15	20.0	>60
1:5 Prednisolone:PEG 4000 coprecipitate	50.1±7.46	98.8±4.15	23.5	41.0
1:5 Prednisolone:PEG 4000 physical mixture	60.8±6.16	90.0±0.57	19.5	60.0

[1] C_{20} = % Prednisolone dissolved obtained at the time of 20 minutes.

[2] C_{60} = % Prednisolone dissolved obtained at the time of 60 minutes.

[3] T_{60} = The time required for 60% prednisolone dissolution.

[4] T_{90} = The time required for 90% prednisolone dissolution.

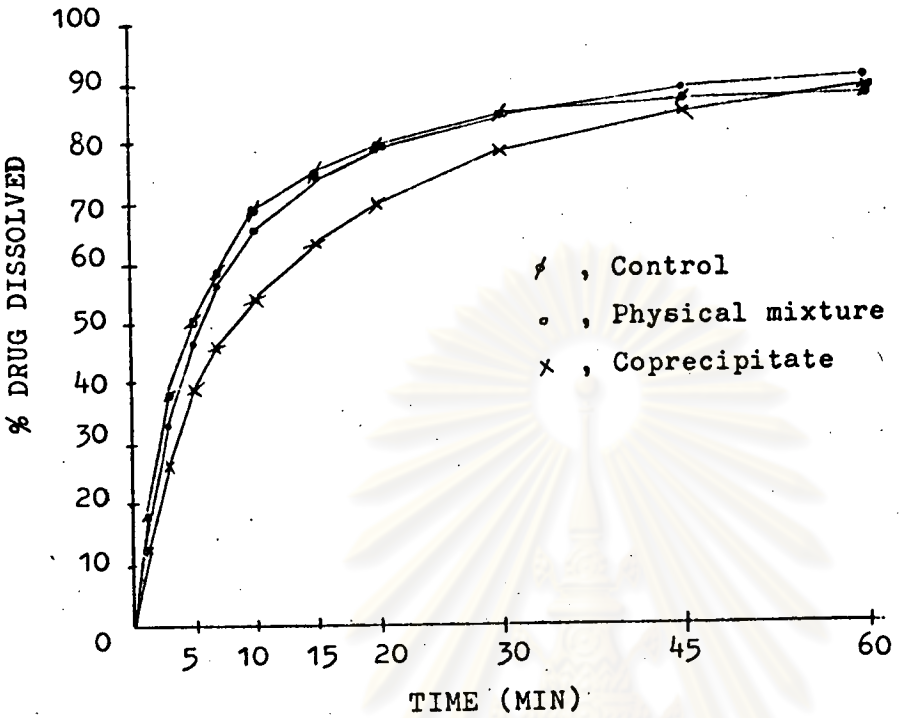

Figure 9. Dissolution profiles of tablets containing 1:1 prednisolone:PEG 4000.

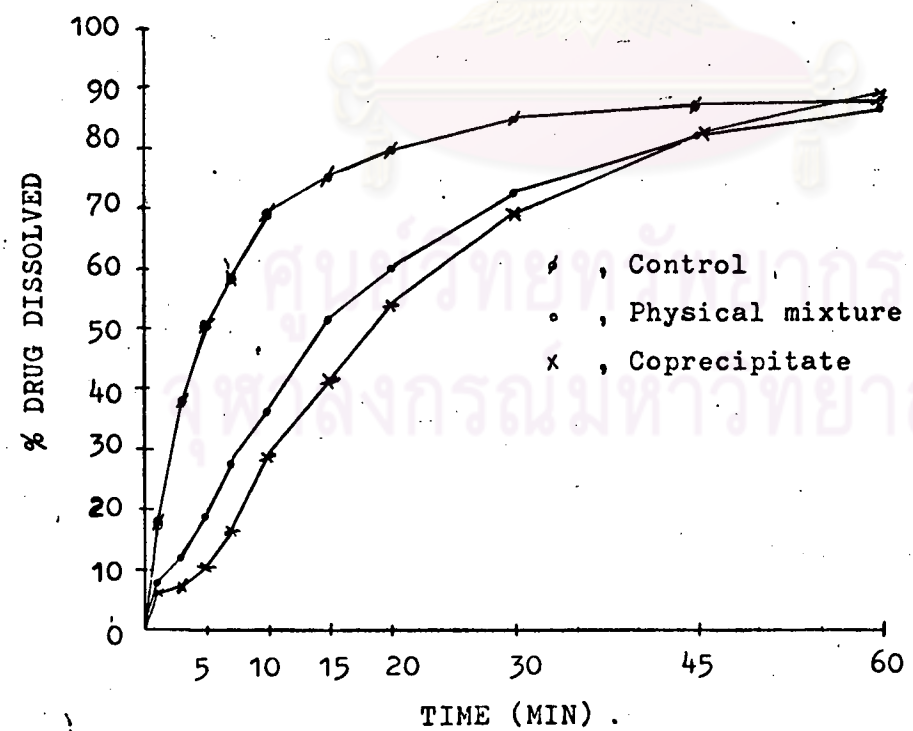

Figure 10. Dissolution profiles of tablets containing 1:3 prednisolone:PEG 4000.

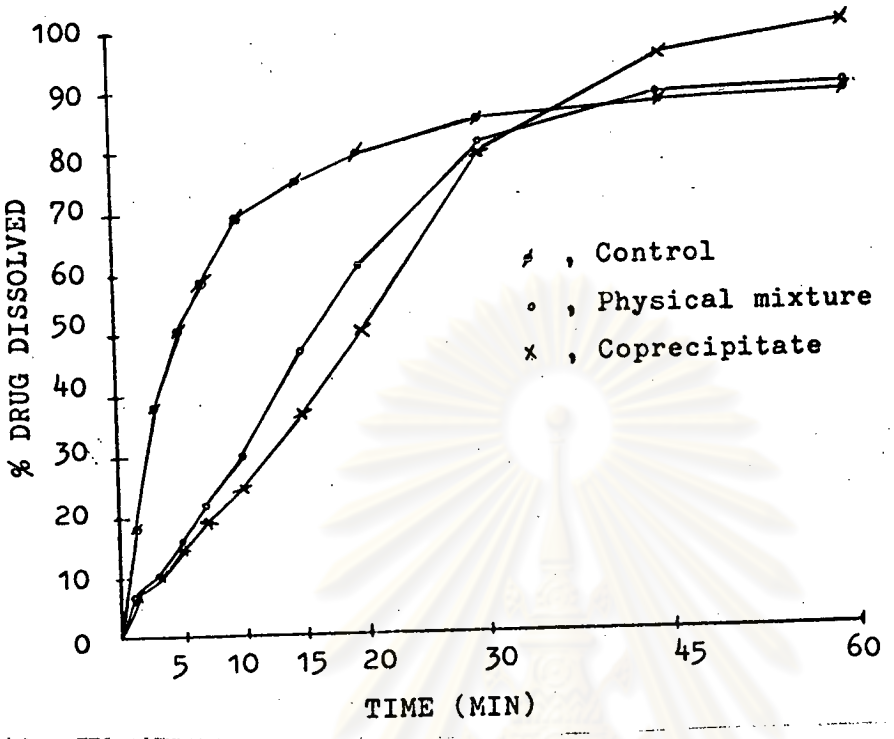

Figure 11. Dissolution profiles of tablets containing 1:5 prednisolone:PEG 4000.

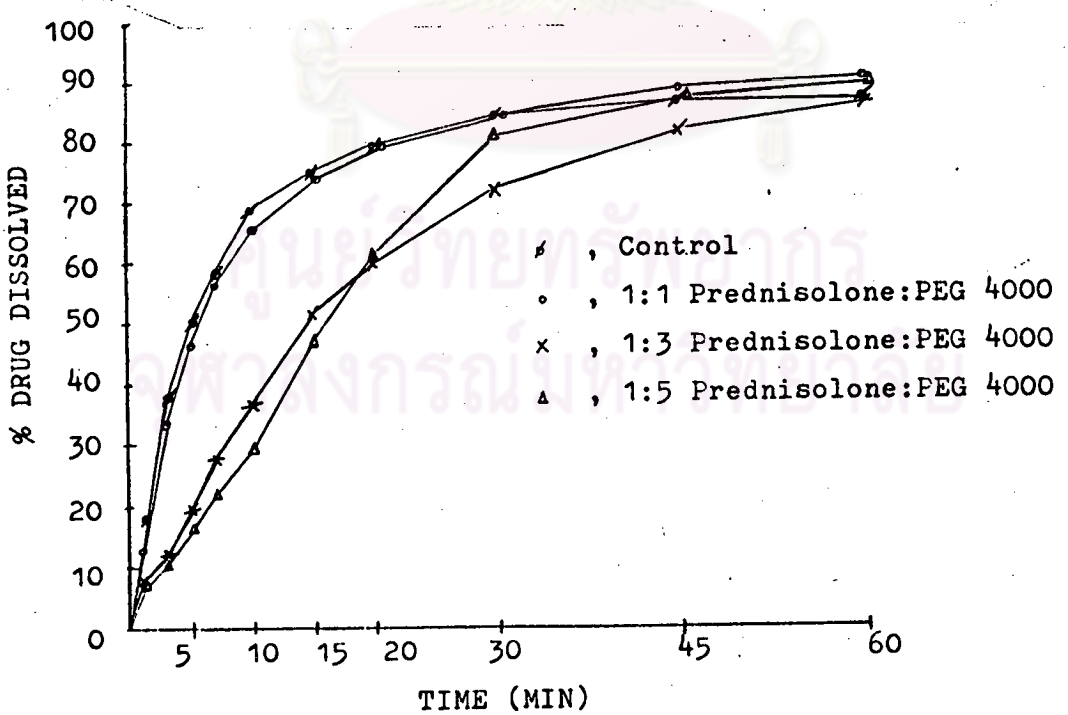

Figure 12. Dissolution profiles of tablets containing various ratios of prednisolone:PEG 4000 physical mixtures.

3. Prednisolone-SLS System

3.1 Tablet Disintegration Studies

The average disintegration times of prednisolone tablets containing drug and SLS were presented in Table 10. The tablets containing prednisolone-SLS coprecipitate produced faster disintegration time than the tablets containing prednisolone-SLS physical mixture having the same ratio of drug:carrier. All tablets containing prednisolone-SLS, except the tablets of 1:1 prednisolone:SLS coprecipitate, exhibit slower disintegration times than the prednisolone control tablets. The tablets of 1:1 prednisolone:SLS coprecipitate gave comparable disintegration time to the prednisolone control tablets ($\alpha = 0.05$).

Among the tablets containing coprecipitates, the tablets of 1:1 prednisolone:SLS ratio showed the fastest disintegration time, while the comparable disintegration times were obtained between the tablets of 1:3 prednisolone:SLS coprecipitate and the tablets of 1:5 prednisolone:SLS coprecipitate ($\alpha = 0.05$). The same result was obtained among the tablets containing physical mixtures.

3.2 Tablet Dissolution Studies

The dissolution parameters and dissolution profiles of prednisolone tablets containing drug and SLS were shown in Table 11 and Figures 14-18. Comparing to the tablets containing physical mixture, the tablets containing coprecipitate of the same ratio of

Table 10. Average Disintegration Times of the Tablets Containing Various Ratios of Prednisolone:SLS System

PREDNISOLONE TABLETS CONTAINING	AVERAGE DISINTEGRATION TIME* ± S.D. (MIN)
1:0 Prednisolone:carrier coprecipitate	4.77 ± 1.39
1:1 Prednisolone:SLS coprecipitate	3.88 ± 0.54
1:1 Prednisolone:SLS physical mixture	12.75 ± 3.31
1:3 Prednisolone:SLS coprecipitate	14.08 ± 2.75
1:3 Prednisolone:SLS physical mixture	19.46 ± 2.37
1:5 Prednisolone:SLS coprecipitate	17.07 ± 3.16
1:5 Prednisolone:SLS physical mixture	21.96 ± 2.64

* From 6 tablets

Table 11. The Dissolution Parameters of Prednisolone Tablets Containing Various Ratios of Drug:SLS System

PREDNISOLONE TABLETS CONTAINING	C_{20} [1]	C_{60} [2]	T_{60} [3] (MIN)	T_{90} [4] (MIN)
1:0 Prednisolone:carrier coprecipitate	79.4±1.52	88.0±1.34	7.5	>60
1:1 Prednisolone:SLS coprecipitate	92.1±2.60	99.1±1.61	5.0	18.5
1:1 Prednisolone:SLS physical mixture	83.6±1.35	97.8±0.79	14.0	25.5
1:3 Prednisolone:SLS coprecipitate	76.5±7.09	99.3±1.50	16.5	28.0
1:3 Prednisolone:SLS physical mixture	46.0±4.56	99.9±0.55	24.0	37.5
1:5 Prednisolone:SLS coprecipitate	53.3±2.45	102.0±1.10	16.5	26.5
1:5 Prednisolone:SLS physical mixture	74.0±6.26	101.2±0.35	23.0	39.0

[1] C_{20} = % Prednisolone dissolution obtained at the time of 20 minutes.

[2] C_{60} = % Prednisolone dissolution obtained at the time of 60 minutes.

[3] T_{60} = The time required for 60% prednisolone dissolution.

[4] T_{90} = The time required for 90% prednisolone dissolution.

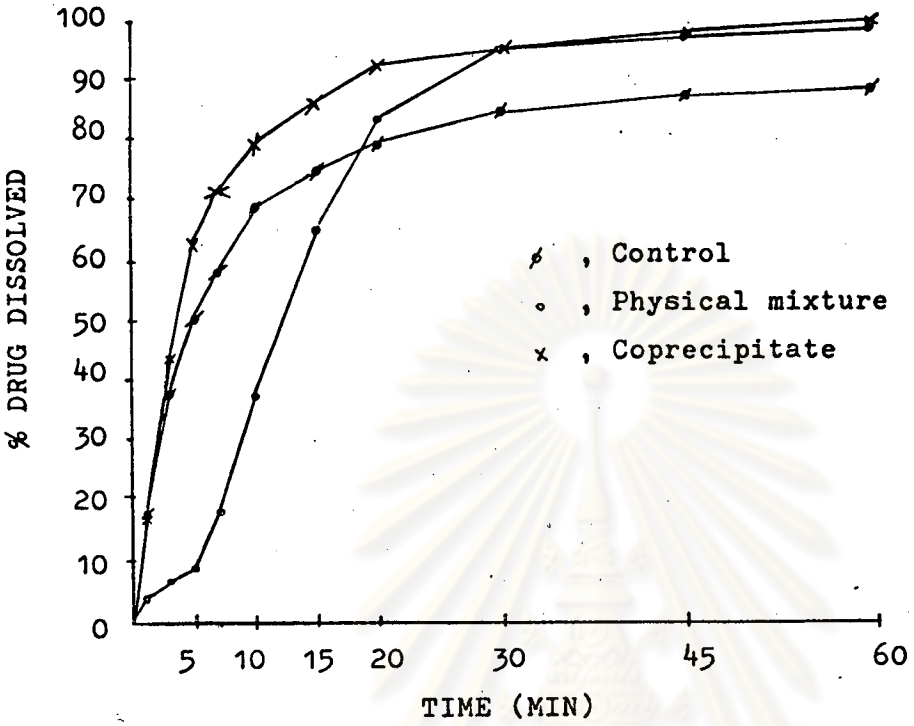

Figure 14. Dissolution profiles of tablets containing 1:1 prednisolone:SLS.

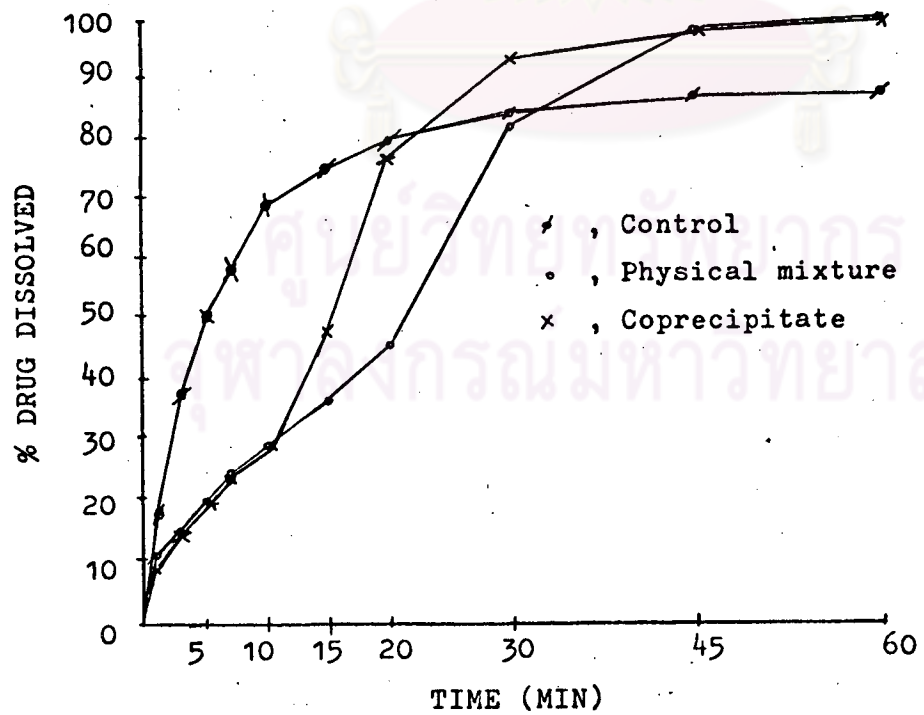

Figure 15. Dissolution profiles of tablets containing 1:3 prednisolone:SLS

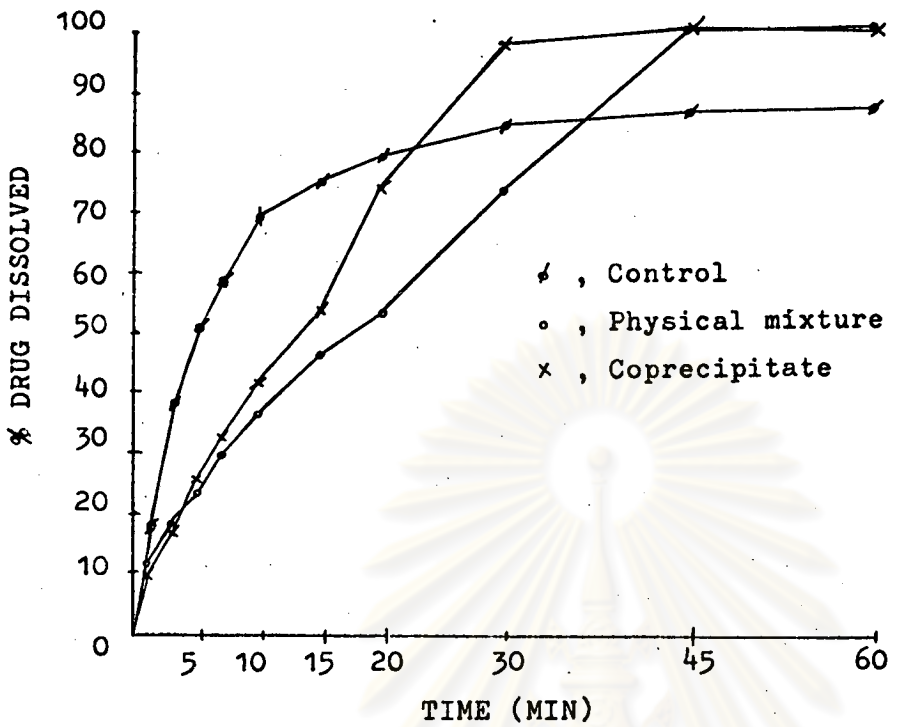

Figure 16. Dissolution profiles of tablets containing 1:5 prednisolone:SLS.

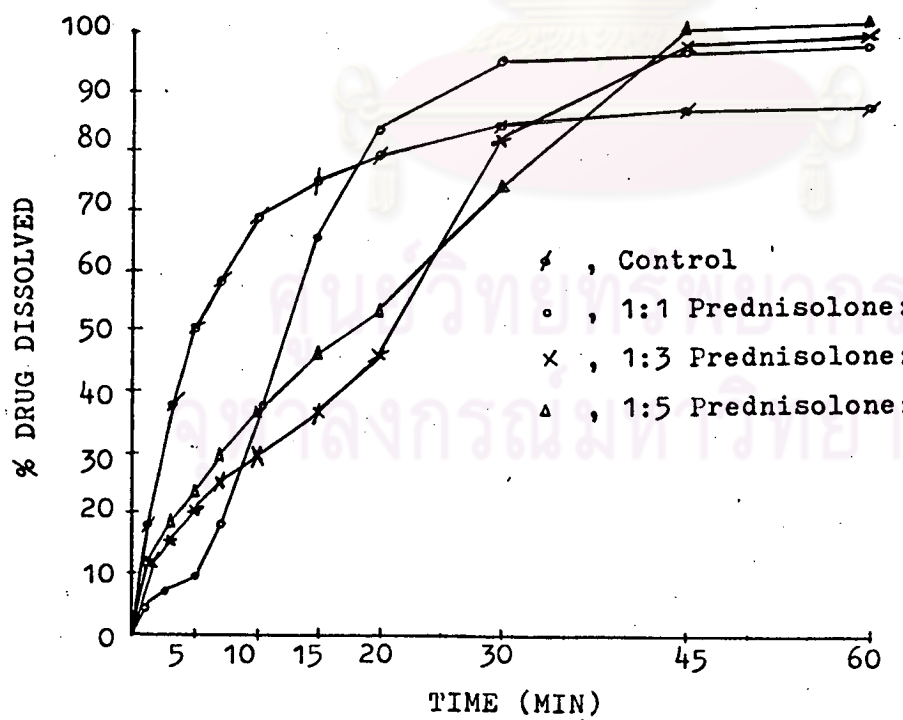

Figure 17. Dissolution profiles of tablets containing various ratios of prednisolone:SLS physical mixtures.

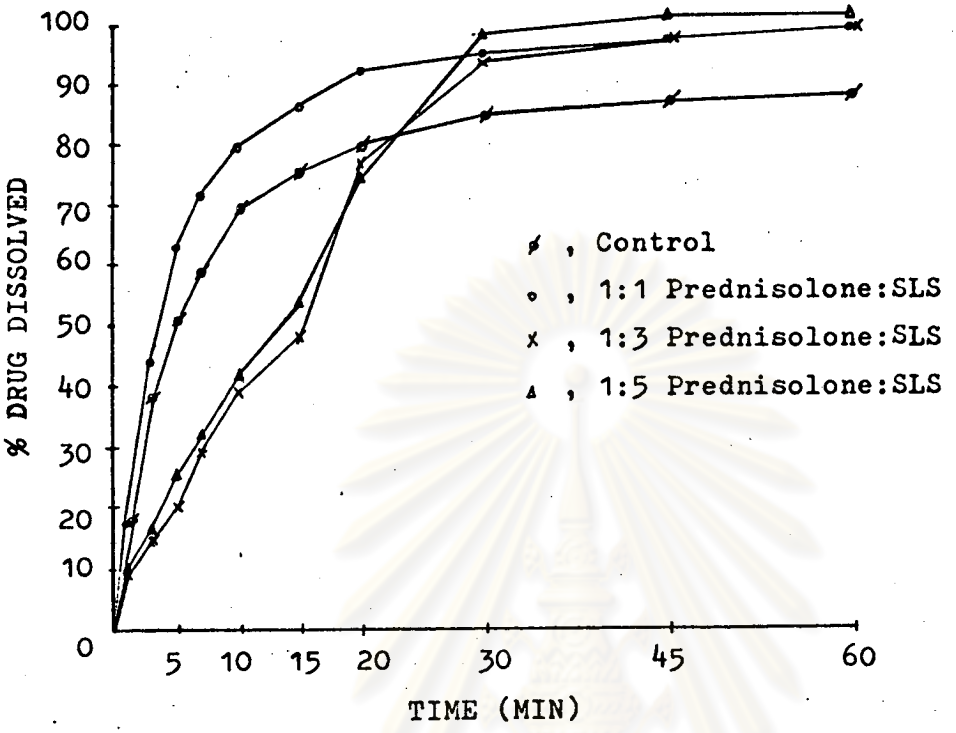

Figure 18. Dissolution profiles of tablets containing various ratios of prednisolone:SLS coprecipitates.

drug:carrier gave faster prednisolone dissolution rate. The complete prednisolone dissolutions were obtained from the tablets of coprecipitates and physical mixtures while only 88% prednisolone dissolution was obtained from the prednisolone control tablets after 60 minutes in dissolution medium. However, the initial prednisolone dissolution rates of the tablets containing 1:3 and 1:5 prednisolone:SLS coprecipitates and the tablets containing 1:1, 1:3, and 1:5 prednisolone:SLS physical mixtures were slower than the prednisolone control tablets, followed by the subsequent higher prednisolone dissolution rates.

The similar dissolution profiles were obtained between the tablets containing 1:3 prednisolone:SLS coprecipitate and the tablets containing 1:5 prednisolone:SLS coprecipitate, and between the tablets containing 1:3 prednisolone:SLS physical mixture and the tablets containing 1:5 prednisolone:SLS physical mixture.

The tablets of 1:1 prednisolone:SLS coprecipitate gave the fastest T_{90} of 18.5 minutes. The tablets of 1:1 prednisolone:SLS physical mixture exhibited fastest dissolution rate among the prednisolone tablets containing physical mixtures and they also yielded faster dissolution rate than the prednisolone tablets containing coprecipitate of 1:3 or 1:5 drug:SLS ratio.

4. 1:5 Prednisolone:(dextrose-PEG 4000) Systems

4.1 Tablet Disintegration Studies

The average disintegration times of prednisolone tablets containing 1:5 drug:(dextrose-PEG 4000) were listed in Table 12.

Table 12. Average Disintegration Times of the Tablets Containing Various Systems of 1:5 Prednisolone:(dextrose-PEG 4000)

PREDNISOLONE TABLETS CONTAINING	AVERAGE DISINTEGRATION TIME* ± S.D. (MIN)
1:0 Prednisolone:carrier coprecipitate	4.77 ± 1.39
1:(0+5) Prednisolone:(dextrose+PEG 4000) coprecipitate	17.72 ± 1.67
1:(0+5) Prednisolone:(dextrose+PEG 4000) physical mixture	16.93 ± 4.05
1:(1+4) Prednisolone:(dextrose+PEG 4000) coprecipitate	15.17 ± 1.35
1:(1+4) Prednisolone:(dextrose+PEG 4000) physical mixture	10.43 ± 2.78
1:(2+3) Prednisolone:(dextrose+PEG 4000) coprecipitate	5.51 ± 2.58
1:(2+3) Prednisolone:(dextrose+PEG 4000) physical mixture	7.17 ± 1.88
1:(3+2) Prednisolone:(dextrose+PEG 4000) coprecipitate	3.38 ± 1.02
1:(3+2) Prednisolone:(dextrose+PEG 4000) physical mixture	2.90 ± 0.72
1:(4+1) Prednisolone:(dextrose+PEG 4000) coprecipitate	2.26 ± 0.95
1:(4+1) Prednisolone:(dextrose+PEG 4000) physical mixture	3.56 ± 1.67
1:(5+0) Prednisolone:(dextrose+PEG 4000) coprecipitate	1.56 ± 1.30
1:(5+0) Prednisolone:(dextrose+PEG 4000) physical mixture	2.66 ± 0.61

* From 6 tablets

It was apparent that the presence of more dextrose and less PEG 4000 in the prednisolone tablets caused decreasing in disintegration times of the tablets containing coprecipitates or physical mixtures. For 1:(2+3), 1:(3+2), 1:(4+1) drug:(dextrose+PEG 4000) there was no significant difference in disintegration time (α = 0.05) occured between the tablets containing coprecipitates and the tablets containing physical mixtures. However, for 1:(1+4) drug:(dextrose +PEG 4000) the tablets of coprecipitate gave slower disintegration time than the tablets of physical mixture.

The tablets of 1:(1+4) prednisolone:(dextrose+PEG 4000) coprecipitate or physical mixture exhibited slower disintegration time than the prednisolone control tablets. Faster or comparable disintegration times were obtained from the prednisolone tablets containing prednisolone:(dextrose+PEG 4000) of 1:(2+3), 1:(3+2), and 1:(4+1) ratios, compared to prednisolone control tablets.

4.2 Tablet Dissolution Studies

The dissolution parameters and dissolution profiles of prednisolone tablets containing 1:5 drug:(dextrose+PEG 4000) were presented in Table 13 and Figures 19-24. Tablets containing drug: carriers exhibited faster dissolution than prednisolone control tablets. All four formulations of the tablets containing coprecipitates gave 100% prednisolone dissolution within 60 minutes, while the tablets containing physical mixtures and the prednisolone control tablets gave prednisolone dissolutions of 92-95% and 88% respectively.

Table 13. The Dissolution Parameters of Prednisolone Tablets Containing Various Systems of 1:5 Drug: (dextrose-PEG 4000)

PREDNISOLONE TABLETS CONTAINING	C_{20} [1]	C_{60} [2]	T_{60} [3] (MIN)	T_{90} [4] (MIN)
1:0 Prednisolone:carrier coprecipitate	79.4±1.52	88.0±1.34	7.5	>60
1:(1+4) Prednisolone:(dextrose+PEG 4000) coprecipitate	42.6±0.31	104.5±5.44	26.5	43.5
1:(1+4) Prednisolone:(dextrose+PEG 4000) physical mixture	70.1±1.88	93.0±0.53	16.0	45.0
1:(2+3) Prednisolone:(dextrose+PEG 4000) coprecipitate	103.1±2.33	110.5±0.48	5.0	10.5
1:(2+3) Prednisolone:(dextrose+PEG 4000) physical mixture	90.0±0.83	92.5±0.45	4.5	20.0
1:(3+2) Prednisolone:(dextrose+PEG 4000) coprecipitate	102.0±0.44	110.4±0.44	3.0	9.0
1:(3+2) Prednisolone:(dextrose+PEG 4000) physical mixture	90.3±0.39	94.2±0.22	3.0	19.5
1:(4+1) Prednisolone:(dextrose+PEG 4000) coprecipitate	96.8±1.93	104.7±0.49	5.0	15.0
1:(4+1) Prednisolone:(dextrose+PEG 4000) physical mixture	91.2±0.72	94.1±0.32	4.0	16.5

[1] C_{20} = % Prednisolone dissolved obtained at the time of 20 minutes.
[2] C_{60} = % Prednisolone dissolved obtained at the time of 60 minutes.
[3] T_{60} = The time required for 60% prednisolone dissolution.
[4] T_{90} = The time required for 90% prednisolone dissolution.

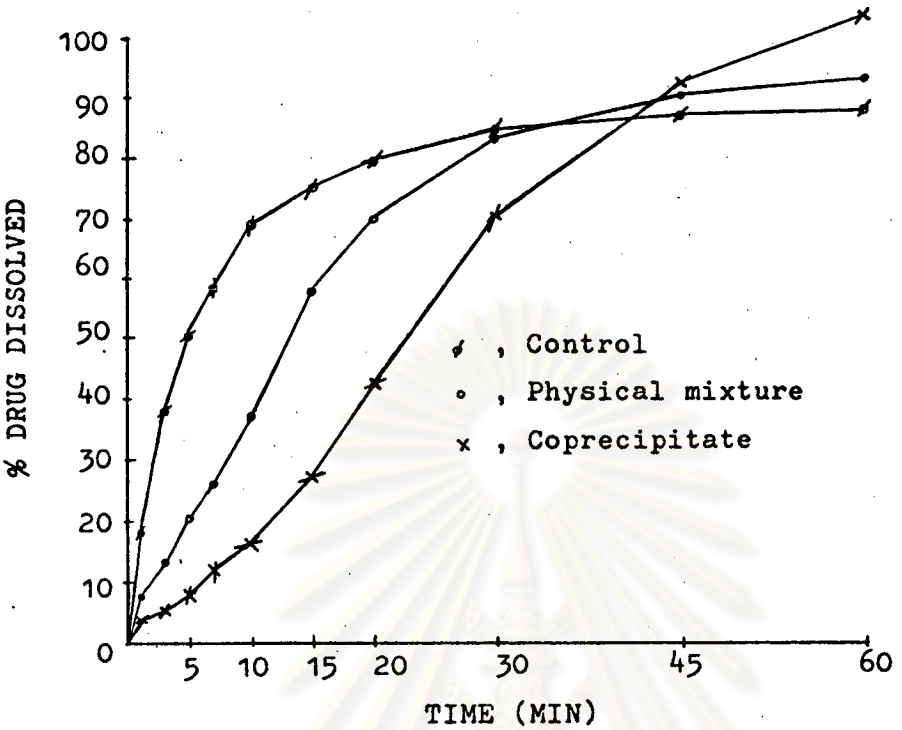

Figure 19. Dissolution profiles of tablets containing 1:(1+4) prednisolone:(dextrose+PEG 4000).

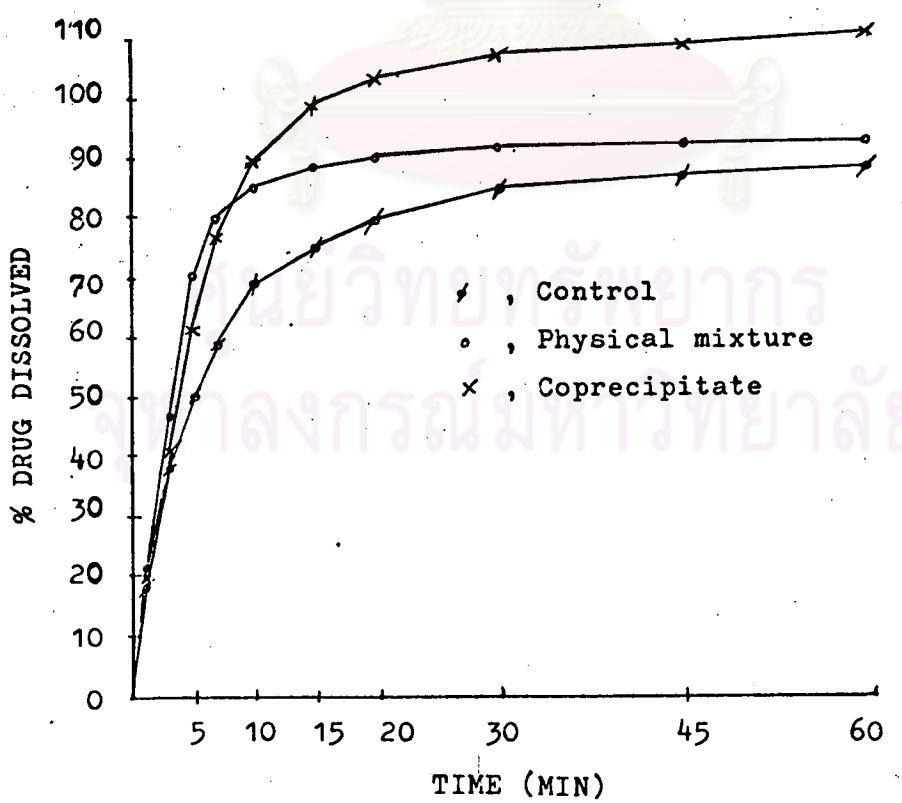

Figure 20. Dissolution profiles of tablets containing 1:(2+3) prednisolone:(dextrose+PEG 4000).

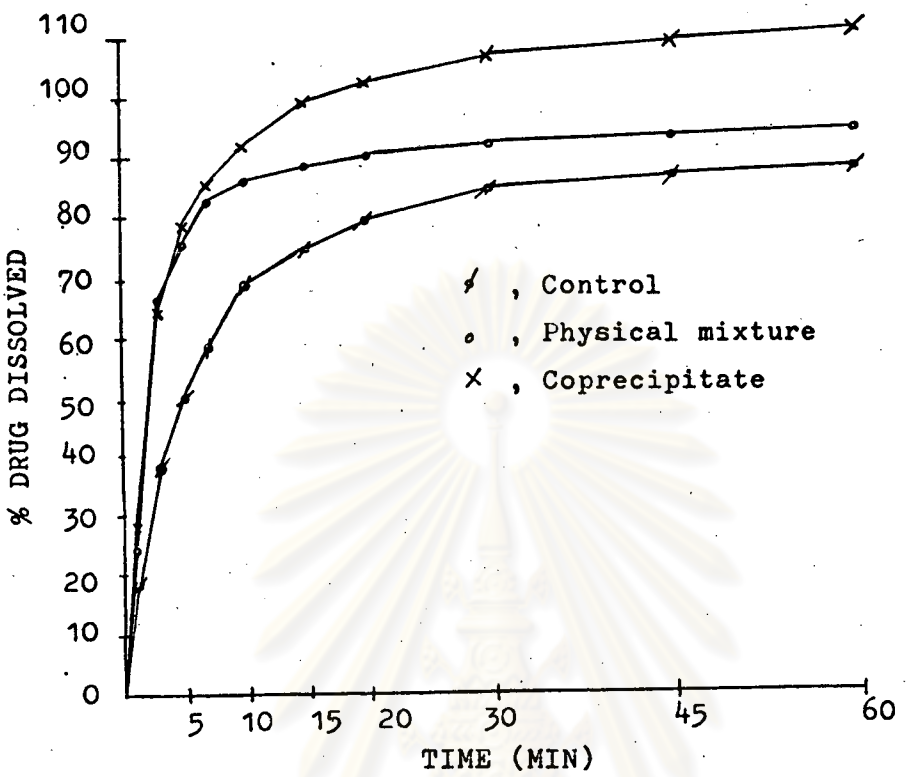

Figure 21. Dissolution profiles of tablets containing 1:(3+2) prednisolone:(dextrose+PEG 4000).

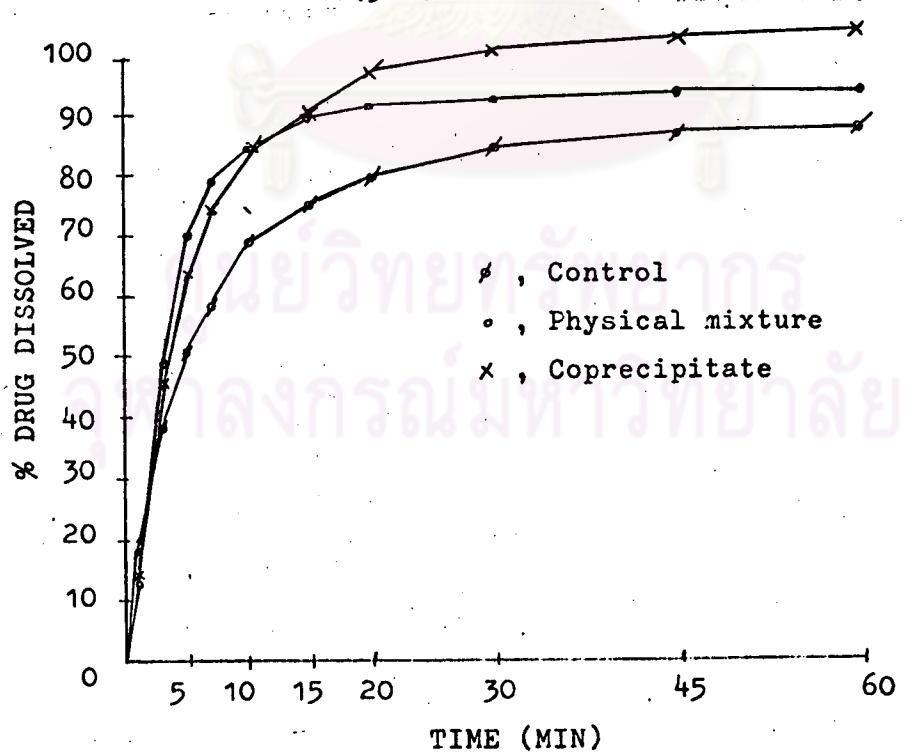

Figure 22. Dissolution profiles of tablets containing 1:(4+1) prednisolone:(dextrose+PEG 4000).

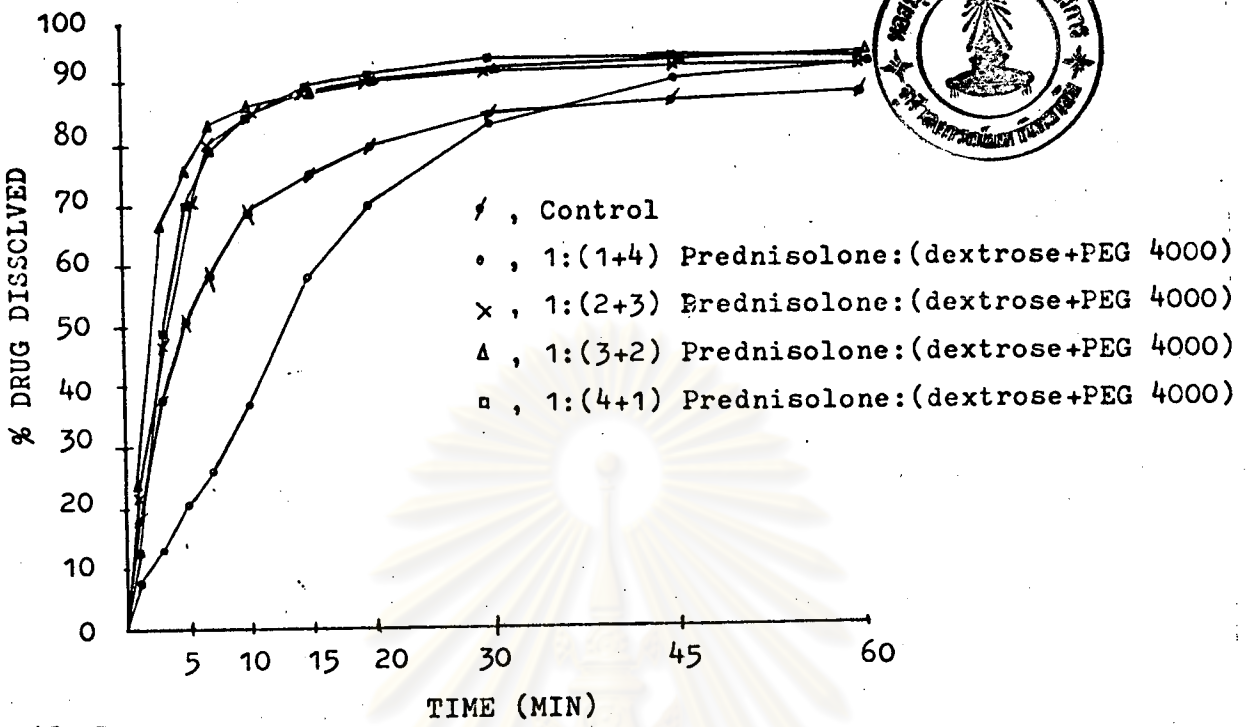

Figure 23. Dissolution profiles of tablets containing various systems of 1:5 prednisolone:(dextrose-PEG 4000) physical mixtures.

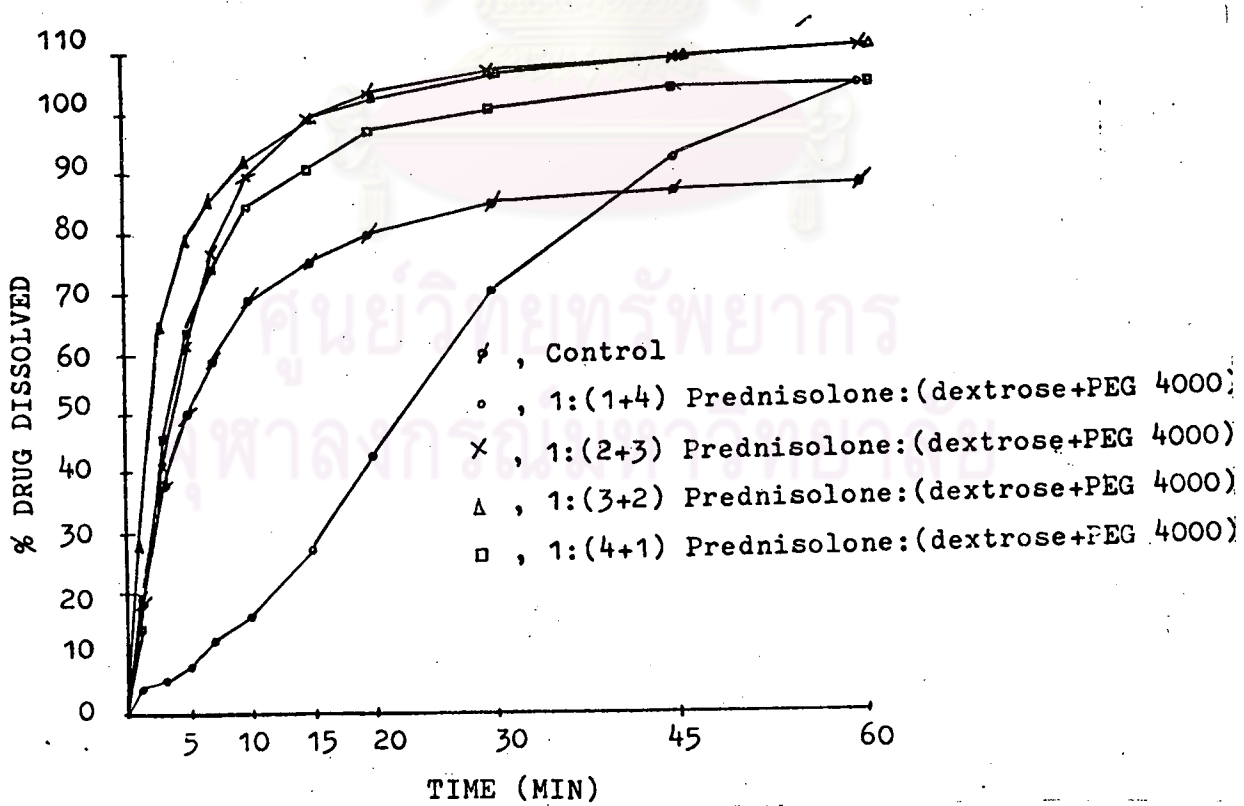

Figure 24. Dissolution profiles of tablets containing various systems of 1:5 prednisolone:(dextrose-PEG 4000) coprecipitates.

However, the tablets containing 1:(1+4) prednisolone: (dextrose+PEG 4000) coprecipitate or physical mixture initially showed slower dissolution rates than the prednisolone control tablets, followed by subsequent faster dissolution rates.

The tablets of 1:(2+3), 1:(3+2), and 1:(4+1) prednisolone: (dextrose+PEG 4000) physical mixtures gave comparable dissolution rates. Among the tablets containing coprecipitates, the tablets of 1:(3+2) prednisolone:(dextrose+PEG 4000) yielded the fastest T_{90} of 9.0 minutes, followed by the tablets of 1:(2+3) prednisolone: (dextrose+PEG 4000), the tablets of 1:(4+1) prednisolone:(dextrose +PEG 4000), and the tablets of 1:(1+4) prednisolone:(dextrose+ PEG 4000) which have T_{90} of 10.5, 15.0, and 43.5 minutes respectively. The prednisolone control tablets gave T_{90} of more than 60 minutes.

5. Prednisolone:(dextrose-SLS) Systems

5.1 Tablet Disintegration Studies

The average disintegration times of the prednisolone tablets containing 1:5 drug:(dextrose-SLS) were shown in Table 14. Increasing amount of SLS and decreasing amount of dextrose in the prednisolone tablets resulted in increasing disintegration time. No significant difference in disintegration time was observed between the tablets containing coprecipitate and the tablets containing physical mixture having the same ratio of drug:carriers of 1:(2+3), 1:(3+2), or 1:(4+1) respectively (α = 0.05). The tablets of 1:(1+4) prednisolone:(dextrose+SLS) coprecipitate gave faster disintegration time than the tablets of 1:(1+4) prednisolone:(dextrose+SLS) physical mixture.

Table 14. Average Disintegration Times of the Tablets Containing Various Systems of 1:5 Prednisolone:(dextrose-SLS)

PREDNISOLONE TABLETS CONTAINING	AVERAGE DISINTEGRATION TIME* ± S.D. (MIN)
1:0 Prednisolone:carrier coprecipitate	4.77 ± 1.39
1:(0+5) Prednisolone:(dextrose+SLS) coprecipitate	17.07 ± 3.16
1:(0+5) Prednisolone:(dextrose+SLS) physical mixture	21.96 ± 2.64
1:(1+4) Prednisolone:(dextrose+SLS) coprecipitate	12.67 ± 1.01
1:(1+4) Prednisolone:(dextrose+SLS) physical mixture	18.97 ± 3.43
1:(2+3) Prednisolone:(dextrose+SLS) coprecipitate	14.28 ± 1.33
1:(2+3) Prednisolone:(dextrose+SLS) physical mixture	13.96 ± 1.51
1:(3+2) Prednisolone:(dextrose+SLS) coprecipitate	9.60 ± 2.17
1:(3+2) Prednisolone:(dextrose+SLS) physical mixture	9.53 ± 2.40
1:(4+1) Prednisolone:(dextrose+SLS) coprecipitate	4.71 ± 0.77
1:(4+1) Prednisolone:(dextrose+SLS) physical mixture	5.85 ± 1.53
1:(5+0) Prednisolone:(dextrose+SLS) coprecipitate	1.56 ± 1.30
1:(5+0) Prednisolone:(dextrose+SLS) physical mixture	2.66 ± 0.61

* From 6 tablets

All tablets containing 1:5 prednisolone:(dextrose-SLS) coprecipitates or physical mixtures, except the tablets of 1:(4+1) prednisolone:(dextrose+SLS), produced slower disintegration times than the prednisolone control tablets. The tablets containing 1:(4+1) prednisolone:(dextrose+SLS) coprecipitate and physical mixture exhibited comparable disintegration times to the prednisolone control tablets (α = 0.05).

5.2 Tablet Dissolution Studies

The dissolution parameters and dissolution profiles of prednisolone tablets containing 1:5 drug:(dextrose-SLS) were presented in Table 15 and Figures 25-30. For 1:(1+4) or 1:(2+3) prednisolone:(dextrose+SLS) ratio, there was no significant difference in dissolution rate between the tablets of coprecipitate and the tablet of physical mixture. However, for 1:(4+1) or 1:(3+2) prednisolone:(dextrose+SLS) ratio, the tablets containing coprecipitate produced faster dissolution rate than the tablets containing physical mixture.

All tablets containing drug:carriers gave higher prednisolone dissolution than the prednisolone control tablets. Within 60 minutes the tablets containing coprecipitates and physical mixtures of 1:5 prednisolone:(dextrose-SLS) in the ratio of 1:(1+4), 1:(2+3), and 1:(3+2) exhibited over 96% prednisolone dissolutions while the prednisolone control tablets gave 88% prednisolone dissolution. The tablets containing 1:(4+1) prednisolone:(dextrose+SLS) coprecipitate or physical mixture gave 91% or 89% prednisolone dissolution respectively.

Table 15. The Dissolution Parameters of Prednisolone Tablets Containing Various Systems of 1:5 Drug: (dextrose-SLS)

PREDNISOLONE TABLETS CONTAINING	C_{20} [1]	C_{60} [2]	T_{60} [3] (MIN)	T_{90} [4] (MIN)
1:0 Prednisolon:carrier coprecipitate	79.4±1.52	88.0±1.34	7.5	>60
1:(1+4) Prednisolone:(dextrose+SLS) coprecipitate	61.5±7.00	100.9±0.47	19.5	29.0
1:(1+4) Prednisolone:(dextrose+SLS) physical mixture	56.1±5.55	96.3±0.12	21.0	30.0
1:(2+3) Prednisolone:(dextrose+SLS) coprecipitate	79.2±1.05	98.1±0.85	17.5	27.0
1:(2+3) Prednisolone:(dextrose+SLS) physical mixture	73.2±5.86	97.8±0.32	18.0	27.5
1:(3+2) Prednisolone:(dextrose+SLS) coprecipitate	94.2±4.90	97.9±2.73	9.5	16.0
1:(3+2) Prednisolone:(dextrose+SLS) physical mixture	92.5±0.55	97.5±1.32	13.5	19.5
1:(4+1) Prednisolone:(dextrose+SLS) coprecipitate	80.9±2.38	91.0±0.15	10.0	45.0
1:(4+1) Prednisolone:(dextrose+SLS) physical mixture	64.6±4.48	89.5±1.12	18.0	>60

[1] C_{20} = % Prednisolone dissolved obtained at the time of 20 minutes.
[2] C_{60} = % Prednisolone dissolved obtained at the time of 60 minutes.
[3] T_{60} = The time required for 60% prednisolone dissolution.
[4] T_{90} = The time required for 90% prednisolone dissolution.

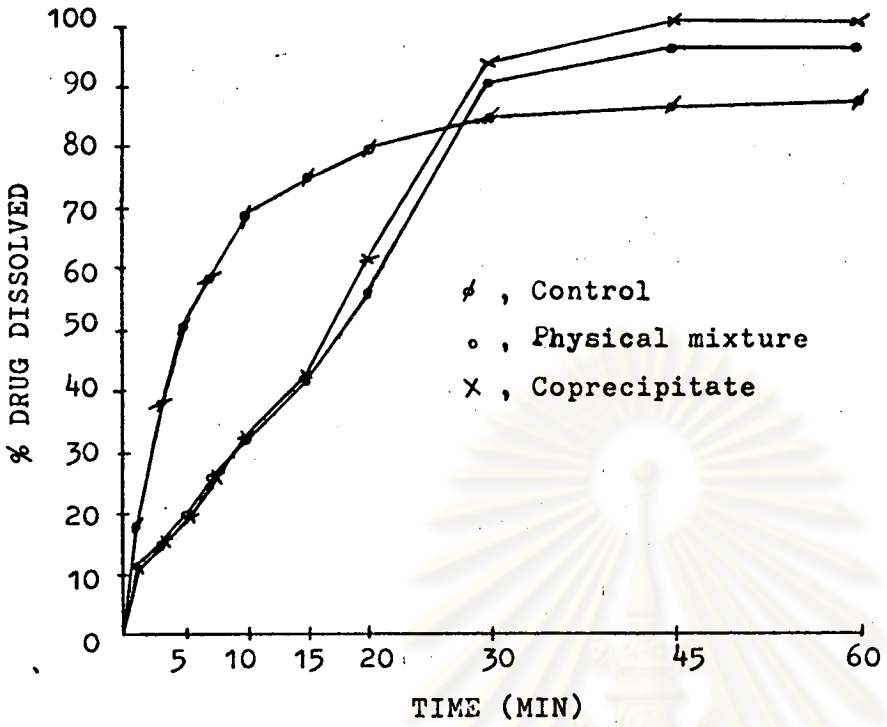

Figure 25. Dissolution profiles of tablets containing 1:(1+4) prednisolone:(dextrose+SLS)

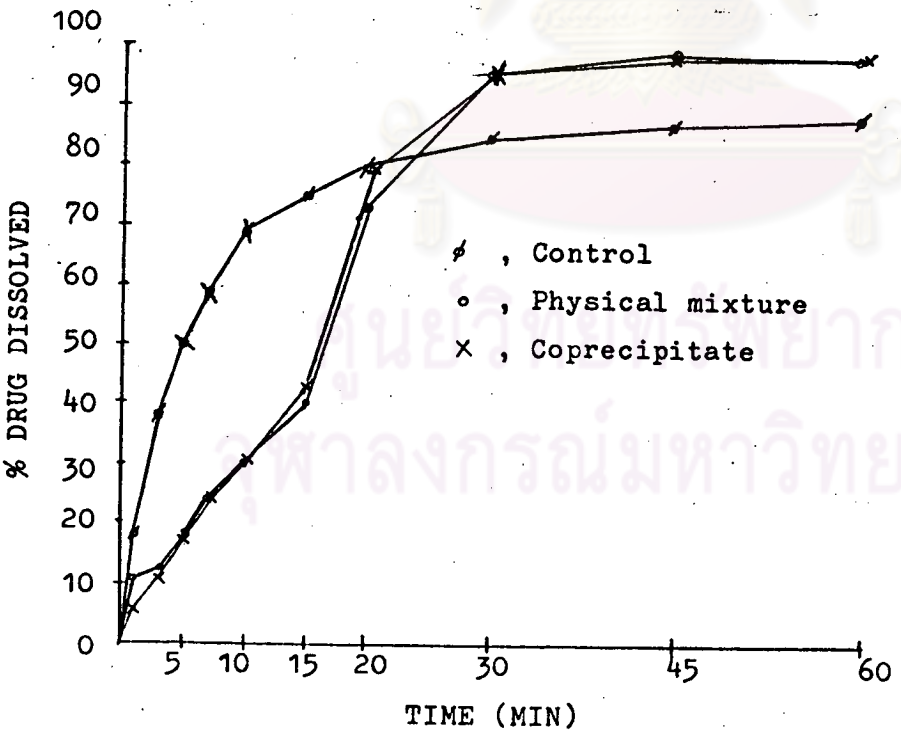

Figure 26. Dissolution profiles of tablets containing 1:(2+3) prednisolone:(dextrose+SLS).

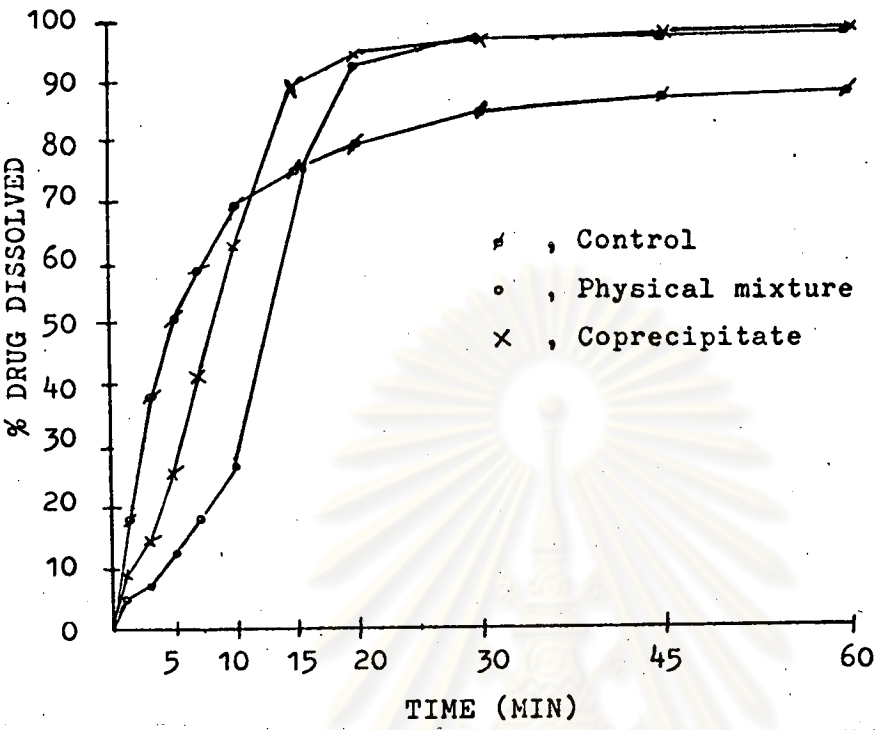

Figure 27. Dissolution profiles of tablets containing 1:(3+2) prednisolone:(dextrose+SLS).

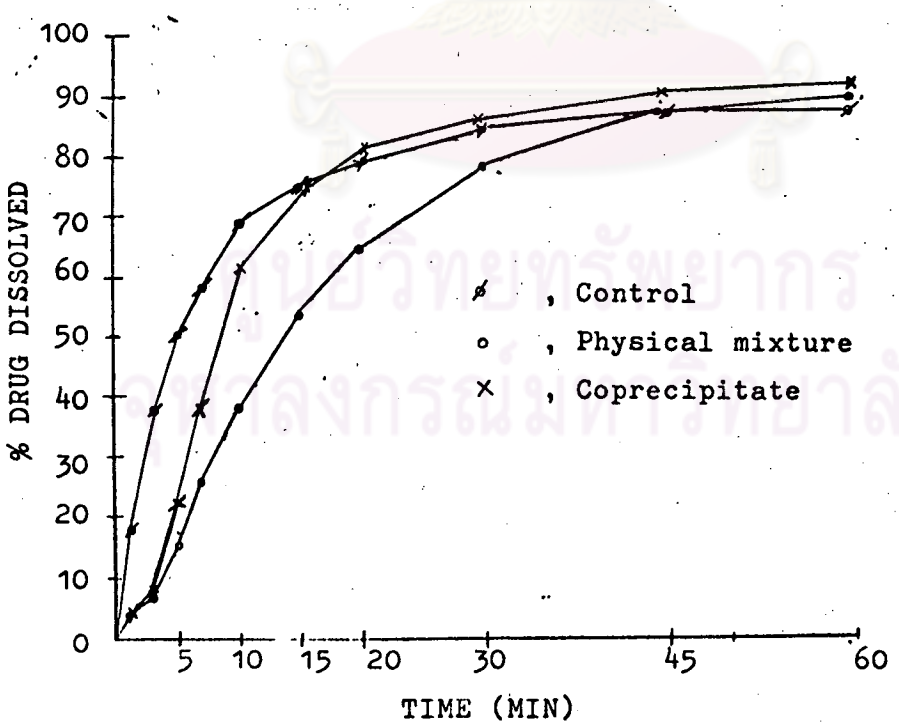

Figure 28. Dissolution profiles of tablets containing 1:(4+1) prednisolone:(dextrose+SLS).

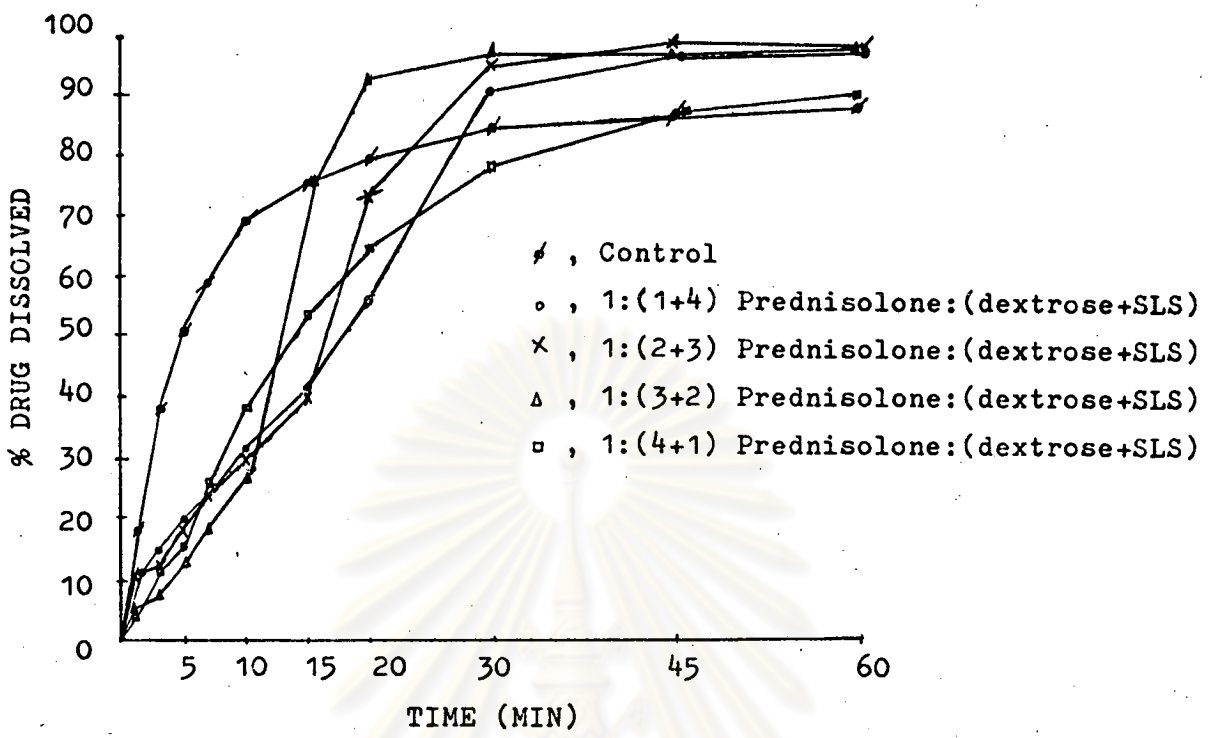

Figure 29. Dissolution profiles of tablets containing various systems of 1:5 prednisolone:(dextrose-SLS) physical mixtures.

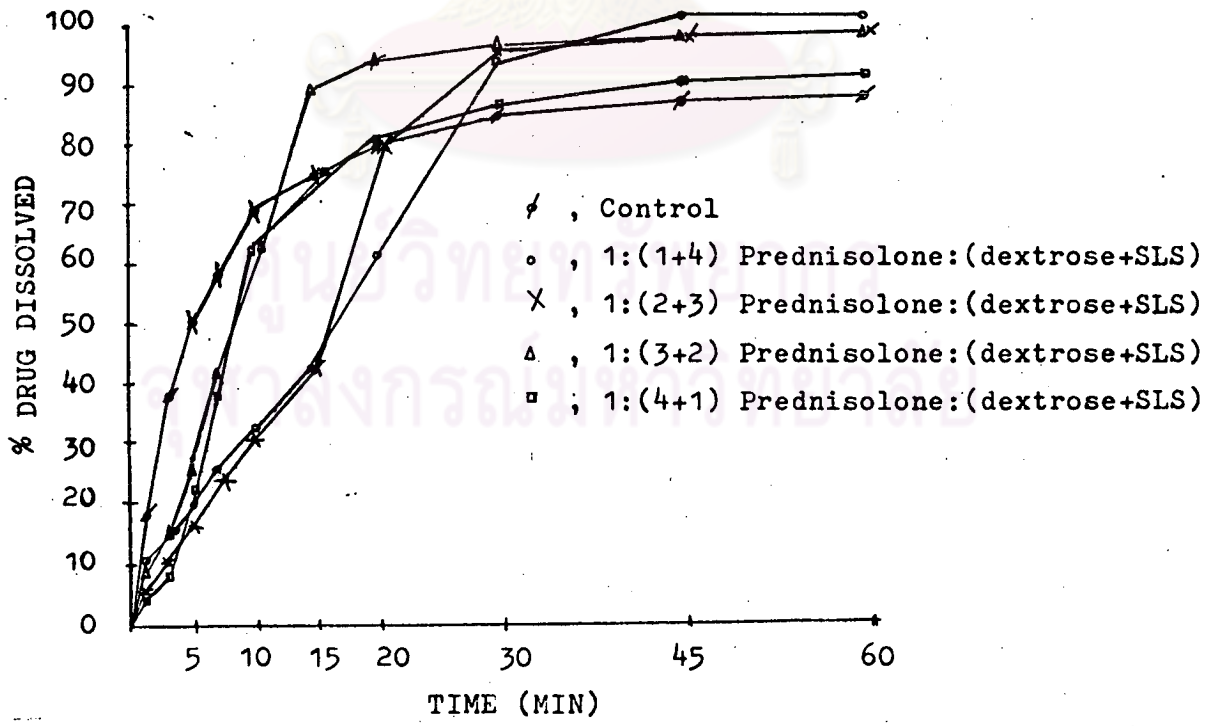

Figure 30. Dissolution profiles of tablets containing various systems of 1:5 prednisolone:(dextrose-SLS) coprecipitates.

Comparing to the prednisolone control tablets, the dissolution rates of the tablets containing 1:5 prednisolone:(dextrose-SLS) coprecipitates or physical mixtures were initially slower, followed by subsequent higher dissolution rates.

Among the prednisolone tablets containing coprecipitates the system of 1:(3+2) prednisolone:(dextrose+SLS) was the best system for improving prednisolone dissolution, followed by the system of 1:(2+3), 1:(1+4), and 1:(4+1) prednisolone:(dextrose+SLS) respectively. The same result was observed among the prednisolone tablets containing the physical mixture.

B. Part II-Indomethacin

1. 1:1 Indomethacin-Single Carrier Systems

1.1 Tablet Disintegration Studies

The average disintegration times of indomethacin tablets containing 1:1 drug-single carrier were exhibited in Table 16. The tablets containing 1:1 indomethacin:dextrose coprecipitate and the tablet containing 1:1 indomethacin:dextrose physical mixture yielded comparable disintegration times ($\alpha = 0.05$), and both exhibited faster disintegration times than the indomethacin control tablets.

The tablets containing 1:1 indomethacin:PEG 4000 coprecipitate gave slower disintegration time than the tablets containing 1:1 indomethacin:PEG 4000 physical mixture. The indomethacin control tablets gave faster disintegration time than the tablets containing PEG 4000 coprecipitate or physical mixture.

Table 16. Average Disintegration Times of the Tablets Containing 1:1 Indomethacin:Single Carrier Systems

INDOMETHACIN TABLETS CONTAINING	AVERAGE DISINTEGRATION TIME* ± S.D. (MIN)
1:0 Indomethacin:carrier coprecipitate	5.07 ± 0.93
1:1 Indomethacin:dextrose coprecipitate	1.96 ± 0.90
1:1 Indomethacin:dextrose physical mixture	1.51 ± 0.73
1:1 Indomethacin:PEG 4000 coprecipitate	22.38 ± 2.92
1:1 Indomethacin:PEG 4000 physical mixture	12.84 ± 2.64
1:1 Indomethacin:SLS coprecipitate	20.73 ± 2.34
1:1 Indomethacin:SLS physical mixture	22.02 ± 2.03

* From 6 tablets

For 1:1 indomethacin:SLS ratio, comparable disintegration times were obtained from the tablets containing coprecipitate and the tablet containing physical mixture (α = 0.05). The indomethacin control tablets exhibited faster disintegration time than the tablets of coprecipitate or physical mixture.

Comparable disintegration times existed between the tablets of 1:1 indomethacin:PEG 4000 coprecipitate and the tablets of 1:1 indomethacin:SLS coprecipitate (α = 0.05), but both exhibited slower disintegration times than the tablets of 1:1 indomethacin: dextrose coprecipitate.

Among the tablets containing 1:1 indomethacin:single carrier physical mixtures, the tablets of 1:1 indomethacin:dextrose ratio produced fastest disintegration time and the tablets of 1:1 indomethacin:SLS produced the slowest disintegration time.

1.2 Tablet Dissolution Studies

The dissolution parameters and dissolution profiles of indomethacin tablets containing 1:1 indomethacin:single carriers were presented in Table 17 and Figures 31-35. The tablets containing 1:1 indomethacin:single carrier (dextrose or PEG 4000 or SLS) coprecipitate yielded faster dissolution rate than the tablets containing 1:1 indomethacin:single carrier (dextrose or PEG 4000 or SLS) physical mixture. Dissolution of all tablets containing drug:single carriers appeared to be faster than the dissolution of the control tablets.

Table 17. The Dissolution Parameters of Indomethacin Tablets Containing 1:1 Drug:Single Carrier Systems

INDOMETHACIN TABLETS CONTAINING	C_{20} [1]	C_{60} [2]	T_{80} [3] (MIN)
1:0 Indomethacin:carrier coprecipitate	35.8±2.13	70.2±1.55	>60
1:1 Indomethacin:dextrose coprecipitate	79.1±0.45	93.5±0.33	21.0
1:1 Indomethacin:dextrose physical mixture	67.3±0.00	86.3±0.74	40.5
1:1 Indomethacin:PEG 4000 coprecipitate	49.3±2.98	94.2±0.06	37.5
1:1 Indomethacin:PEG 4000 physical mixture	36.8±0.55	87.7±0.09	43.5
1:1 Indomethacin:SLS coprecipitate	42.4±0.85	98.4±0.42	37.0
1:1 Indomethacin:SLS physical mixture	24.4±0.60	85.5±0.06	55.5

[1] C_{20} = % Indomethacin dissolved obtained at the time of 20 minutes.

[2] C_{60} = % Indomethacin dissolved obtained at the time of 60 minutes.

[3] T_{80} = The time required for 80% indomethacin dissolution.

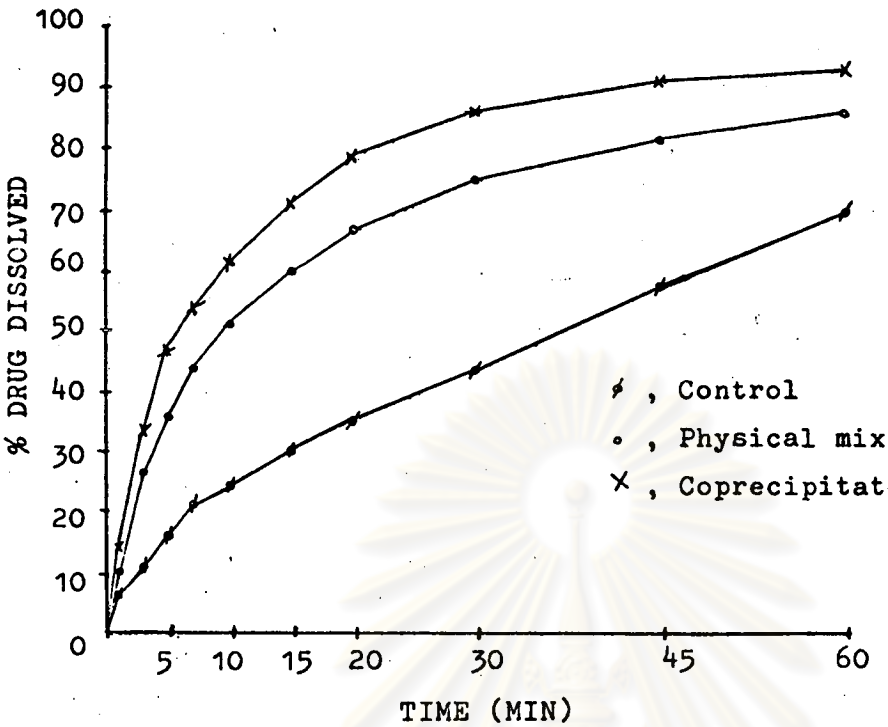

Figure 31. Dissolution profiles of tablets containing 1:1 indomethacin:dextrose.

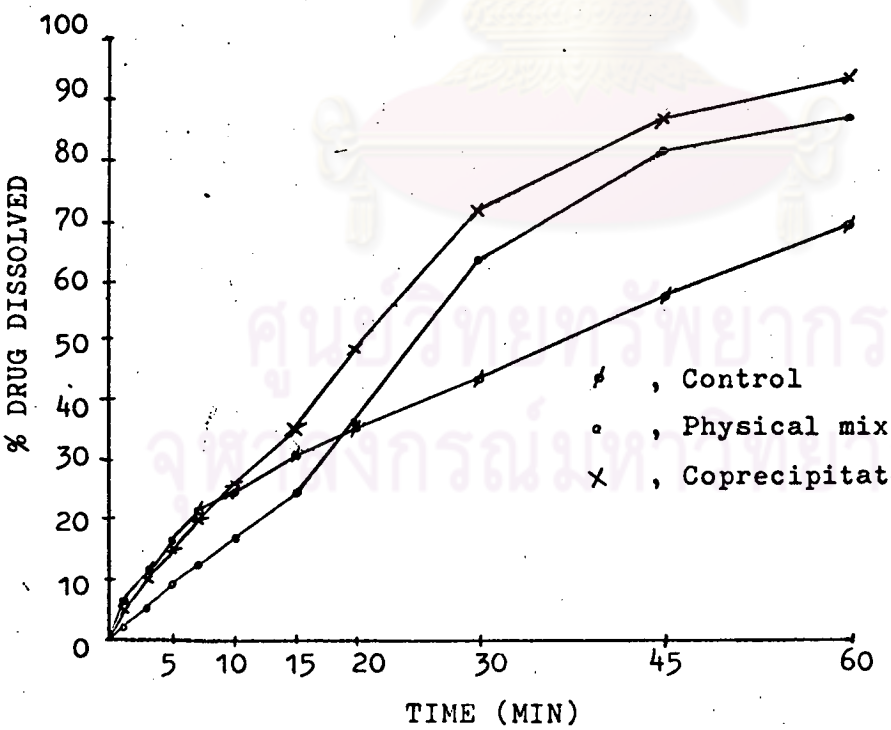

Figure 32. Dissolution profiles of tablets containing 1:1 indomethacin:PEG 4000.

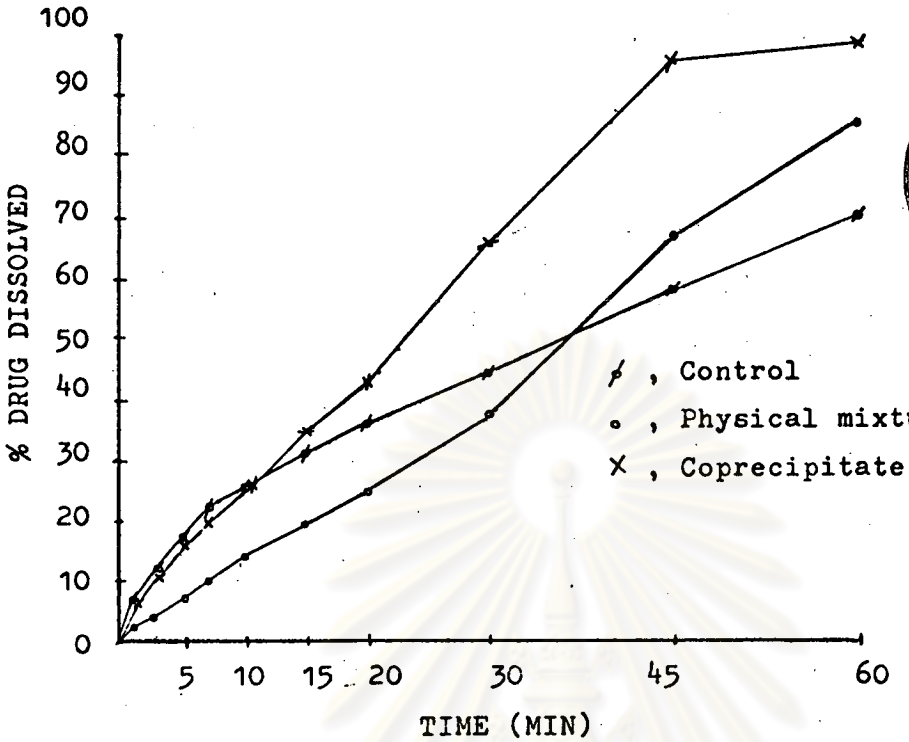

Figure 33. Dissolution profiles of tablets containing 1:1 indomethacin:SLS.

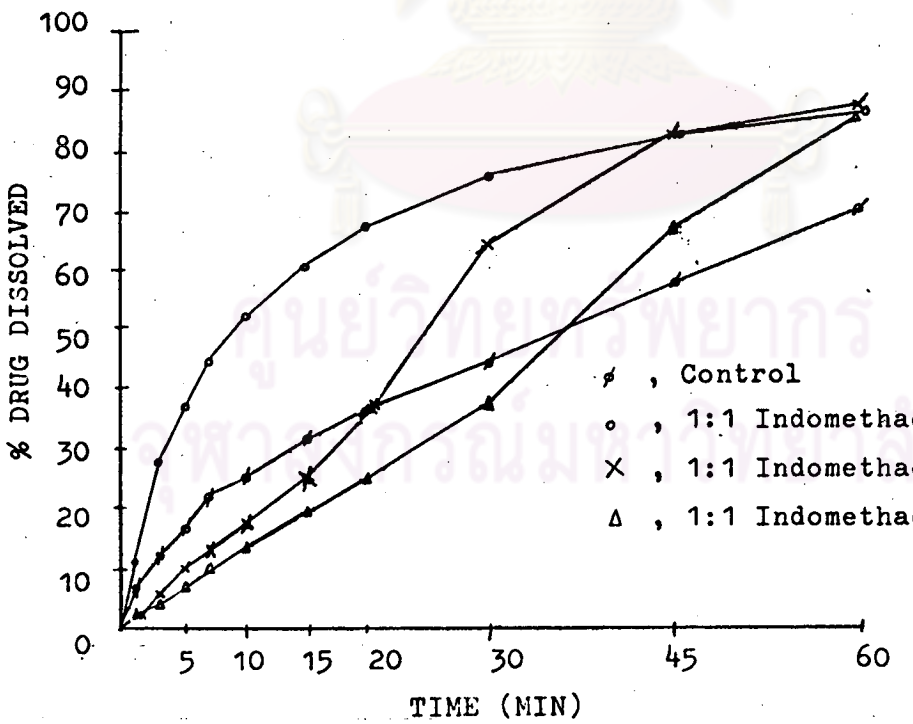

Figure 34. Dissolution profiles of tablets containing various systems of 1:1 indomethacin:single carrier physical mixtures.

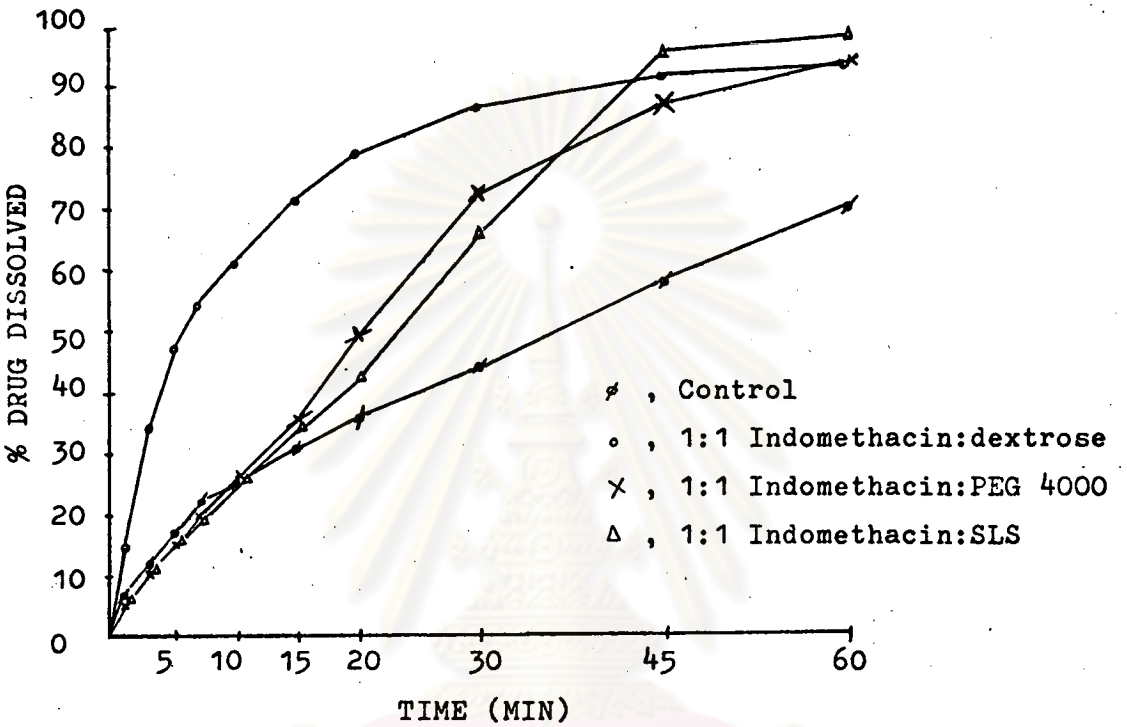

Figure 35. Dissolution profiles of tablets containing various systems of 1:1 indomethacin:single carrier coprecipitates.

Initially, the dissolution rates of the tablets containing 1:1 indomethacin:PEG 4000 physical mixture and the tablets containing 1:1 indomethacin:SLS physical mixture were slower than the dissolution rate of the indomethacin control tablets, but later on they became faster.

The fastest indomethacin dissolution rate was obtained from the tablets of 1:1 indomethacin:dextrose coprecipitate. The tablets of 1:1 indomethacin:PEG 4000 coprecipitate and the tablets of 1:1 indomethacin:SLS coprecipitate yielded similar dissolution profiles.

Among the tablets containing 1:1 indomethacin:single carrier physical mixture, the tablets of 1:1 indomethacin:dextrose produced the fastest dissolution rate, followed by the tablets of 1:1 indomethacin:PEG 4000 and the tablet of 1:1 indomethacin:SLS respectively.

Within 60 minutes the tablets containing 1:1 indomethacin: single carrier coprecipitates gave 93-98% indomethacin dissolutions while the indomethacin control tablets gave 70% indomethacin dissolution. The T_{80} of the tablets of 1:1 indomethacin:dextrose coprecipitate was 21 minutes comparing to more than 60 minutes in the indomethacin control tablets.

2. Indomethacin:(dextrose-PEG 4000) Systems

2.1 Tablet Disintegration Studies

The average disintegration times of the indomethacin tablets containing 1:1 drug:(dextrose-PEG 4000) were listed in Table 18.

Table 18. Average Disintegration Times of the Tablets Containing Various Systems of 1:1 Indomethacin:(dextrose-PEG 4000)

INDOMETHACIN TABLETS CONTAINING	AVERAGE DISINTEGRATION TIME* ± S.D. (MIN)
1:0 Indomethacin:carrier coprecipitate	5.07 ± 0.93
1:(0+1) Indomethacin:(dextrose+PEG 4000) coprecipitate	22.38 ± 2.92
1:(0+1) Indomethacin:(dextrose+PEG 4000) physical mixture	12.84 ± 2.64
1:(0.2+0.8) Indomethacin:(dextrose+PEG 4000) coprecipitate	13.39 ± 2.51
1:(0.2+0.8) Indomethacin:(dextrose+PEG 4000) physical mixture	3.75 ± 0.92
1:(0.4+0.6) Indomethacin:(dextrose+PEG 4000) coprecipitate	10.30 ± 1.07
1:(0.4+0.6) Indomethacin:(dextrose+PEG 4000) physical mixture	2.93 ± 0.82
1:(0.6+0.4) Indomethacin:(dextrose+PEG 4000) coprecipitate	7.06 ± 1.68
1:(0.6+0.4) Indomethacin:(dextrose+PEG 4000) physical mixture	3.72 ± 1.16
1:(0.8+0.2) Indomethacin:(dextrose+PEG 4000) coprecipitate	3.70 ± 1.04
1:(0.8+0.2) Indomethacin:(dextrose+PEG 4000) physical mixture	1.85 ± 0.86
1:(1+0) Indomethacin:(dextrose+PEG 4000) coprecipitate	1.96 ± 0.90
1:(1+0) Indomethacin:(dextrose+PEG 4000) physical mixture	1.51 ± 0.73

* From 6 tablets

Higher amount of dextrose and lower amount of PEG 4000 presented in indomethacin tablets caused decreasing in tablet disintegration time. Tablets containing coprecipitate showed slower disintegration time than tablets containing physical mixture having the same ratio of dextrose:PEG 4000. Comparing to indomethacin control tablets, faster disintegration times were observed from the tablets containing physical mixtures.

The tablets of coprecipitates showed slower disintegration times than the indomethacin control tablets, except the tablets of 1:(0.8+0.2) indomethacin:(dextrose+PEG 4000) coprecipitate which exhibited comparable disintegration time to the indomethacin control tablets ($\alpha = 0.05$).

2.2 Tablet Dissolution Studies

The dissolution parameters and dissolution profiles of the indomethacin tablets containing 1:1 drug:(dextrose-PEG 4000) were shown in Table 19 and Figures 36-41. The presence of dextrose in indomethacin tablets resulted in faster dissolution rate compared to the indomethacin control tablets. All the tablets of coprecipitates showed faster dissolution rates than the tablets of physical mixtures having the same ratio of dextrose:PEG 4000.

By comparing T_{80} of the indomethacin tablets containing 1:1 drug:(dextrose-PEG 4000), the best system for improving indomethacin dissolution was the system of 1:(0.6+0.4) indomethacin:(dextrose+PEG 4000) coprecipitate followed by the systems of 1:(0.4+0.6), 1:(0.2+0.8), 1:(0.8+0.2) indomethacin:(dextrose+PEG 4000)

Table 19. The Dissolution Parameters of Indomethacin Tablets Containing Various Systems of 1:1 Drug: (dextrose-PEG 4000)

INDOMETHACIN TABLETS CONTAINING	C_{20} [1]	C_{60} [2]	T_{80} [4] (MIN)
1:0 Indomethacin:carrier coprecipitate	35.8±2.13	70.2±1.55	>60
1:(0.2+0.8) Indomethacin:(dextrose+PEG 4000) coprecipitate	73.7±1.44	97.1±0.90	24.0
1:(0.2+0.8) Indomethacin:(dextrose+PEG 4000) physical mixture	64.3±0.90	85.0±1.10	44.5
1:(0.4+0.6) Indomethacin:(dextrose+PEG 4000) coprecipitate	88.9±0.44	97.2±1.17	15.0
1:(0.4+0.6) Indomethacin:(dextrose+PEG 4000) physical mixture	62.0±0.92	84.6±0.59	46.0
1:(0.6+0.4) Indomethacin:(dextrose+PEG 4000) coprecipitate	94.8±0.21	99.1±0.06	9.0
1:(0.6+0.4) Indomethacin:(dextrose+PEG 4000) physical mixture	61.5±1.67	86.6±1.03	42.5
1:(0.8+0.2) Indomethacin:(dextrose+PEG 4000) coprecipitate	76.6±0.51	90.0±1.04	25.5
1:(0.8+0.2) Indomethacin:(dextrose+PEG 4000) physical mixture	67.4±0.81	89.5±1.65	37.0

[1] C_{20} = % Indomethacin dissolved obtained at the time of 20 minutes.
[2] C_{60} = % Indomethacin dissolved obtained at the time of 60 minutes.
[3] T_{80} = The time required for 80% indomethacin dissolution.

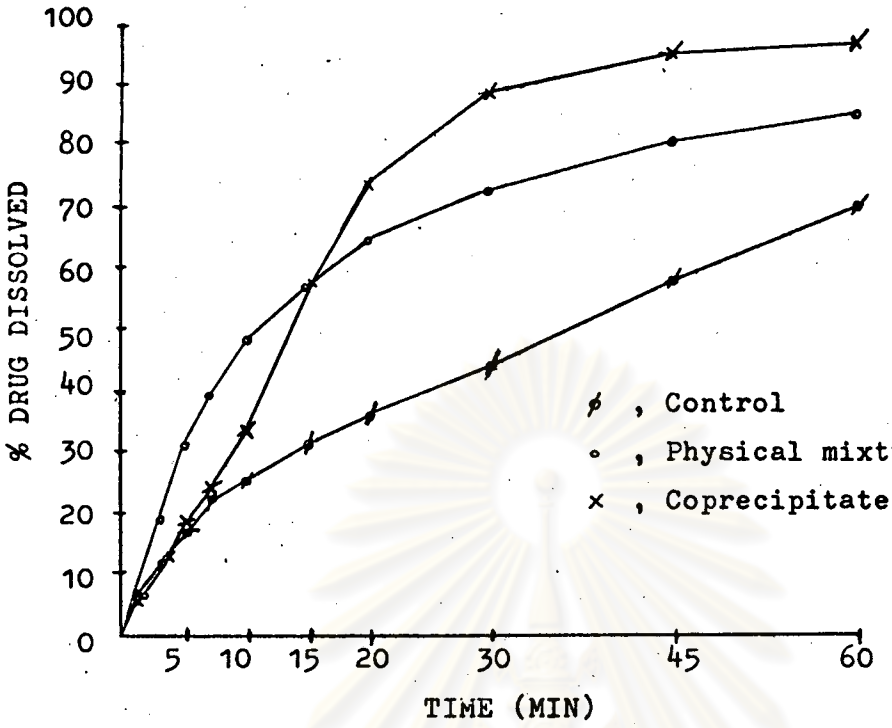

Figure 36. Dissolution profiles of tablets containing 1:(0.2+0.8) indomethacin:(dextrose+PEG 4000).

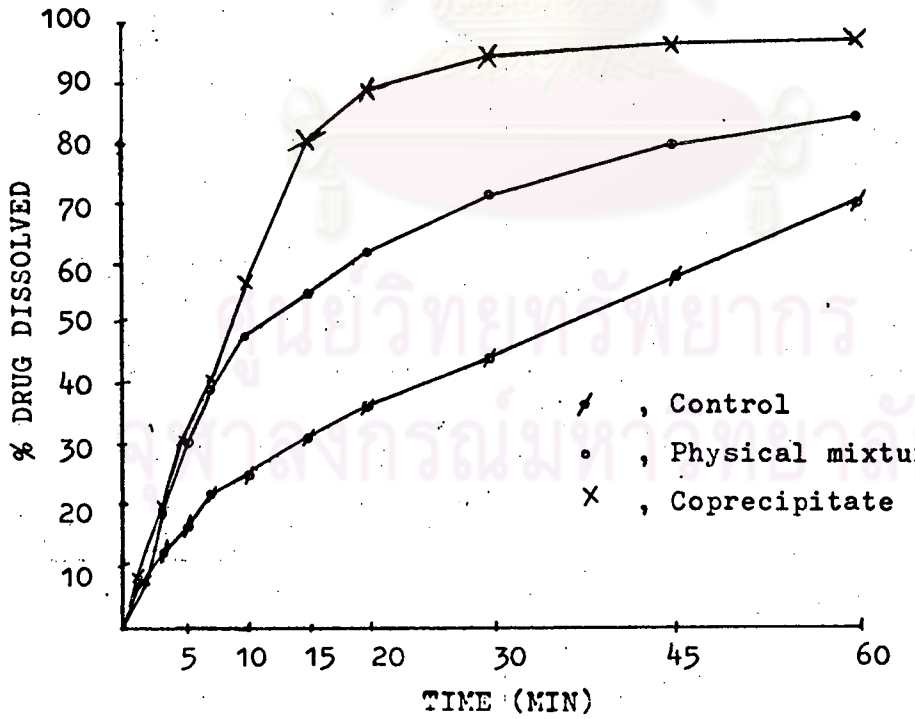

Figure 37. Dissolution profiles of tablets containing 1:(0.4+0.6) indomethacin:(dextrose+PEG 4000).

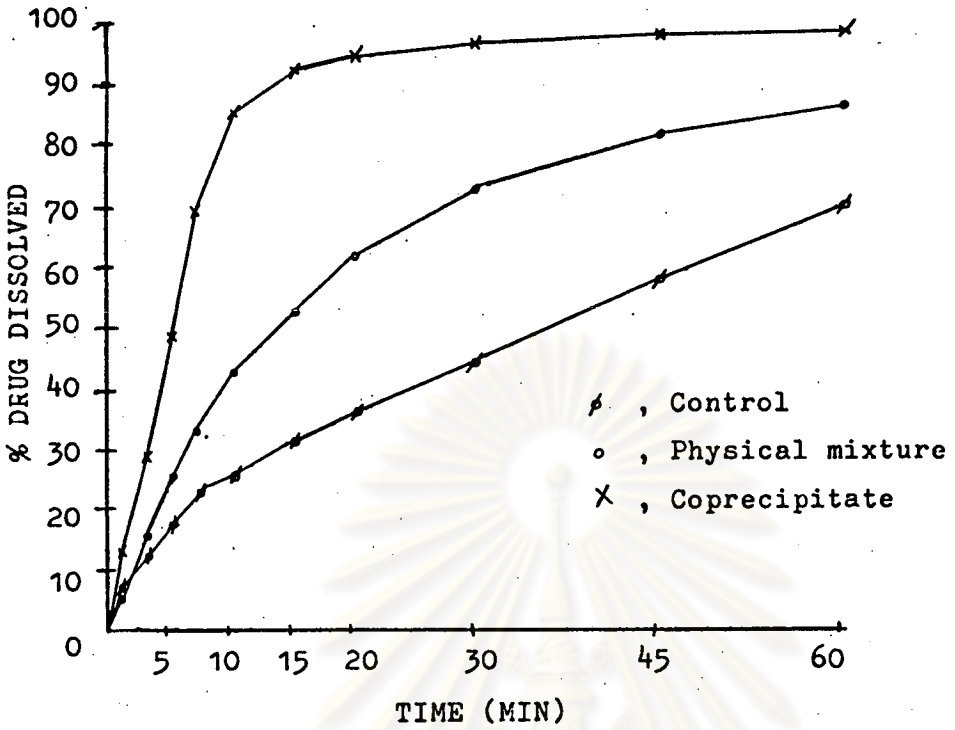

Figure 38. Dissolution profiles of tablets containing 1:(0.6+0.4) indomethacin:(dextrose+PEG 4000).

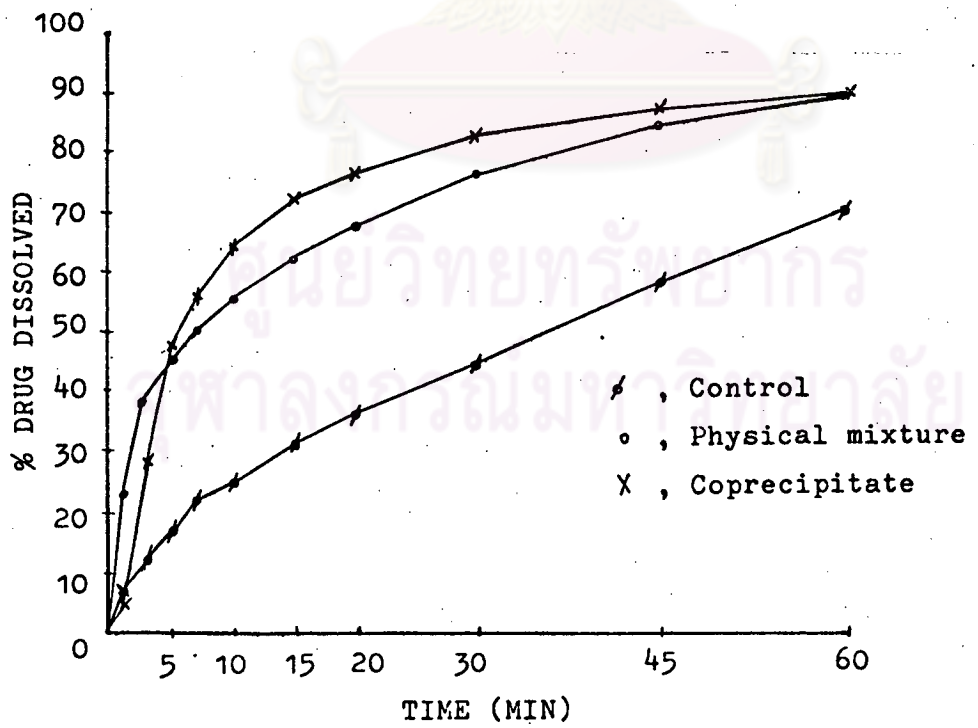

Figure 39. Dissolution profiles of tablets containing 1:(0.8+0.2) indomethacin:(dextrose+PEG 4000).

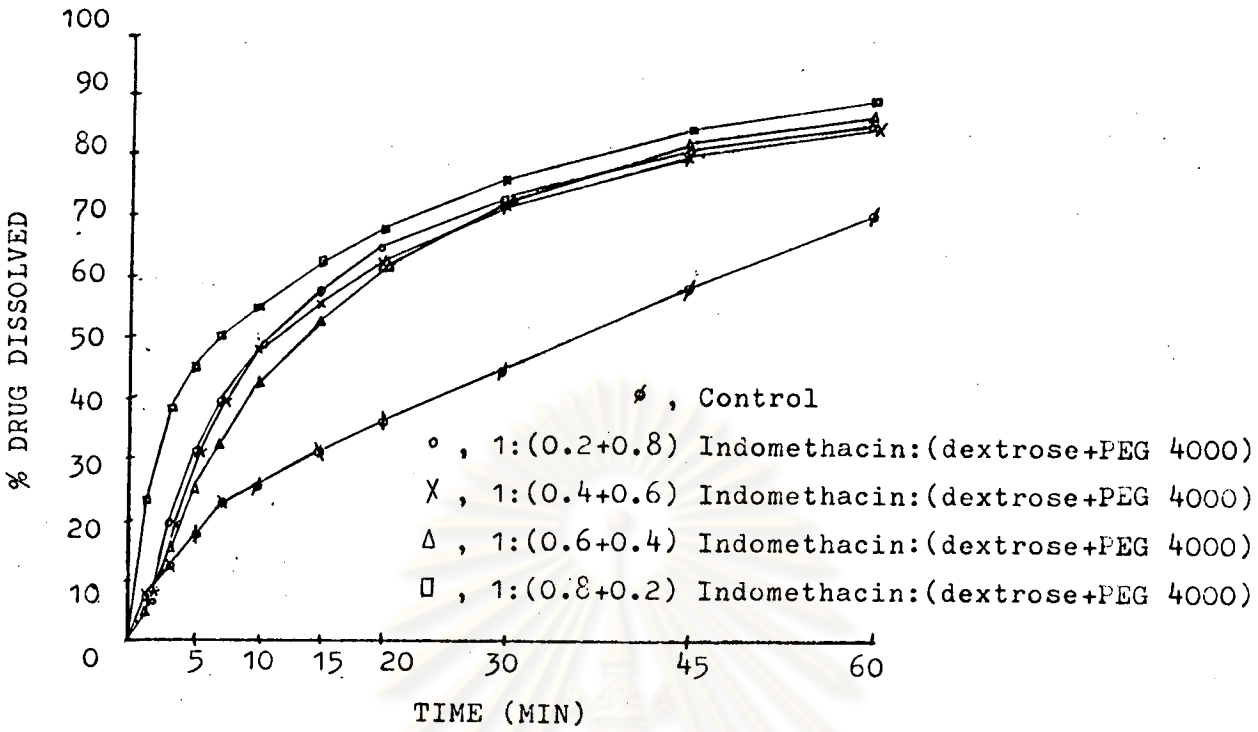

Figure 40. Dissolution profiles of tablets containing various systems of 1:1 indomethacin:(dextrose-PEG 4000) physical mixtures.

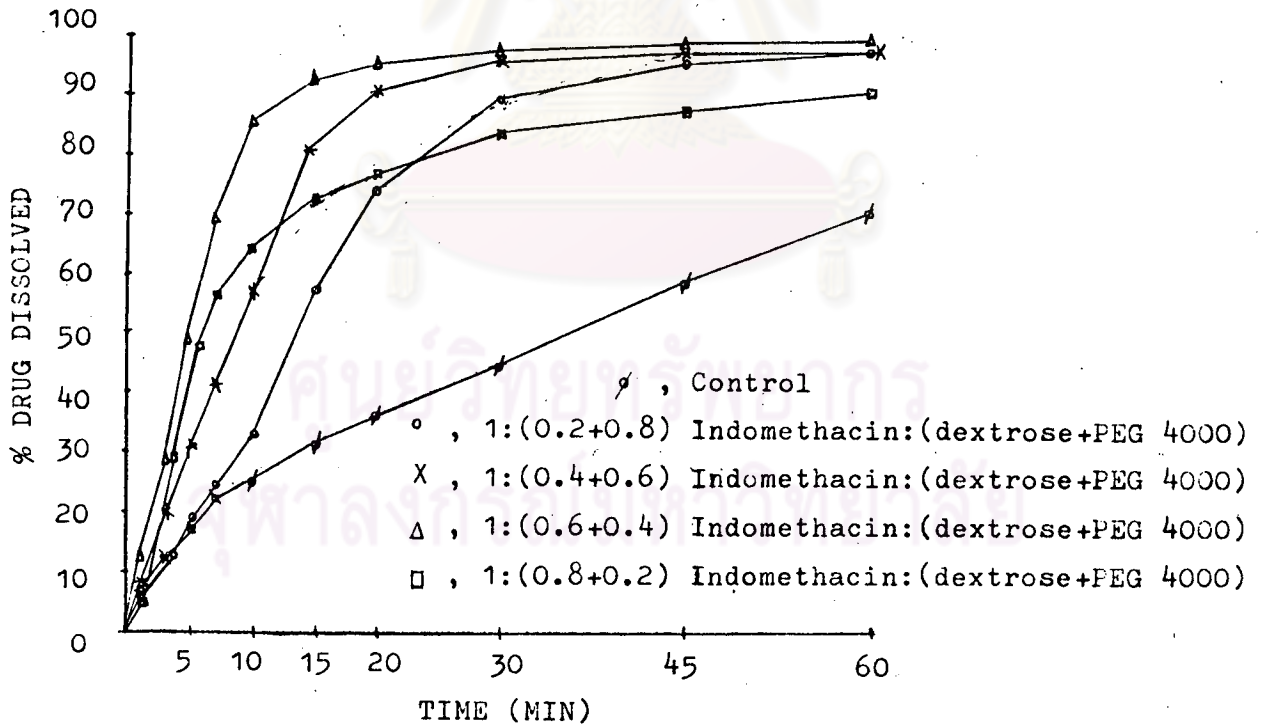

Figure 41. Dissolution profiles of tablets containing various systems of 1:1 indomethacin:(dextrose-PEG 4000) coprecipitates.

coprecipitates and the systems of physical mixtures respectively.

Among the tablets containing physical mixtures, the tablets of 1:(0.8+0.2) indomethacin:(dextrose+PEG 4000) ratio produced the fastest dissolution rate while the tablets of 1:(0.2+0.8), 1:(0.4 +0,6), and 1:(0.6+0.4) ratios exhibited comparable dissolution rates.

Within 20 minutes, the indomethacin control tablets yielded 36% indomethacin dissolution while the tablets containing physical mixtures yielded 61-68% indomethacin dissolutions and the tablets containing coprecipitates yielded 73-95% indomethacin dissolutions.

3. 1:1 Indomethacin:(dextrose-SLS) Systems

3.1 Tablet Disintegration Studies

The average disintegration times of the indomethacin tablets containing 1:1 indomethacin:(dextrose-SLS) were exhibited in Table 20. The increasing amount of SLS and decreasing amount of dextrose in indomethacin tablets retarded tablet disintegration time. No difference in disintegration time between the tablets containing coprecipitate and the tablets containing physical mixture having the same ratio of dextrose:SLS was observed (α = 0.05) except in the 0.4:0.6 dextrose:SLS ratio.

For 1:(0.4+0.6) indomethacin:(dextrose+SLS) ratio, the tablets of coprecipitate gave faster disintegration time than the tablets of physical mixture. The disintegration times of the tablets containing 1:1 indomethacin:(dextrose-SLS) were slower or equal to the disintegration time of the indomethacin control tablets.

Table 20. Average Disintegration Times of the Tablets Containing Various Systems of 1:1 Indomethacin:(dextrose-SLS)

INDOMETHACIN TABLETS CONTAINING	AVERAGE DISINTEGRATION TIME* ± S.D. (MIN)
1:0 Indomethacin:carrier coprecipitate	5.03 ± 0.93
1:(0+1) Indomethacin:(dextrose+SLS) coprecipitate	20.73 ± 2.34
1:(0+1) Indomethacin:(dextrose+SLS) physical mixture	22.02 ± 2.03
1:(0.2+0.8) Indomethacin:(dextrose+SLS) coprecipitate	20.51 ± 1.70
1:(0.2+0.8) Indomethacin:(dextrose+SLS) physical mixture	17.50 ± 2.54
1:(0.4+0.6) Indomethacin:(dextrose+SLS) coprecipitate	7.93 ± 1.25
1:(0.4+0.6) Indomethacin:(dextrose+SLS) physical mixture	14.92 ± 1.86
1:(0.6+0.4) Indomethacin:(dextrose+SLS) coprecipitate	7.82 ± 1.07
1:(0.6+0.4) Indomethacin:(dextrose+SLS) physical mixture	7.63 ± 0.86
1:(0.8+0.2) Indomethacin:(dextrose+SLS) coprecipitate	4.56 ± 0.58
1:(0.8+0.2) Indomethacin:(dextrose+SLS) physical mixture	5.03 ± 0.90
1:(1+0) Indomethacin:(dextrose+SLS) coprecipitate	1.96 ± 0.90
1:(1+0) Indomethacin:(dextrose+SLS) physical mixture	1.51 ± 0.73

* From 6 tablets

3.2 Tablet Dissolution Studies

The dissolution parameters and dissolution profiles of the indomethacin tablets containing 1:1 drug:(dextrose-SLS) were presented in Table 21 and Figures 42-47. The presence of dextrose and SLS in indomethacin tablets caused enhancement in indomethacin dissolution.

The tablets containing coprecipitate yielded faster dissolution rate than the tablets containing physical mixture having the same ratio of dextrose:SLS. The tablets of physical mixtures exhibited faster indomethacin dissolution rates then the indomethacin control tablets. However, the tablets of physical mixtures showed slower dissolution rates during the first part of their dissolution profiles than the indomethacin control tablets.

Within 20 minutes, the indomethacin control tablets gave 36% indomethacin dissolution while the tablets containing coprecipitates gave 91-96% indomethacin dissolutions.

For the tablets containing 1:1 indomethacin:(dextrose-SLS) the best system for enhancement in indomethacin dissolution was 1:(0.8+0.2) indomethacin:(dextrose+SLS) coprecipitate followed by the systems of 1:(0.6+0.4), 1:(0.4+0.6), 1:(0.2+0.8) indomethacin:(dextrose+SLS) coprecipitates and the systems of 1:(0.6+0.4), 1:(0.8+0.2), 1:(0.4+0.6), 1:(0.2+0.8) indomethacin:(dextrose+SLS) physical mixtures respectively.

Table 21. The Dissolution Parameters of Indomethacin Tablets Containing Various Systems of 1:1 Drug: (dextrose-SLS)

INDOMETHACIN TABLETS CONTAINING	C_{20} [1]	C_{60} [2]	T_{80} [3] (MIN)
1:0 Indomethacin:carrier coprecipitate	35.8 ± 2.13	70.2 ± 1.55	>60
1:(0.2+0.8) Indomethacin:(dextrose+SLS) coprecipitate	91.5 ± 3.08	100.7 ± 0.74	17.5
1:(0.2+0.8) Indomethacin:(dextrose+SLS) physical mixture	30.7 ± 0.24	87.4 ± 0.94	43.0
1:(0.4+0.6) Indomethacin:(dextrose+SLS) coprecipitate	93.2 ± 0.11	95.1 ± 0.26	14.0
1:(0.4+0.6) Indomethacin:(dextrose+SLS) physical mixture	38.7 ± 3.59	88.6 ± 0.21	42.0
1:(0.6+0.4) Indomethacin:(dextrose+SLS) coprecipitate	95.4 ± 1.70	101.0 ± 0.08	12.5
1:(0.6+0.4) Indomethacin:(dextrose+SLS) physical mixture	72.6 ± 4.96	89.6 ± 1.19	29.0
1:(0.8+0.2) Indomethacin:(dextrose+SLS) coprecipitate	95.0 ± 1.53	97.0 ± 0.48	10.0
1:(0.8+0.2) Indomethacin:(dextrose+SLS) physical mixture	65.2 ± 4.84	90.0 ± 1.65	33.5

[1] C_{20} = % Indomethacin dissolved obtained at the time of 20 minutes.
[2] C_{60} = % Indomethacin dissolved obtained at the time of 60 minutes.
[3] T_{80} = The time required for 80% indomethacin dissolution.

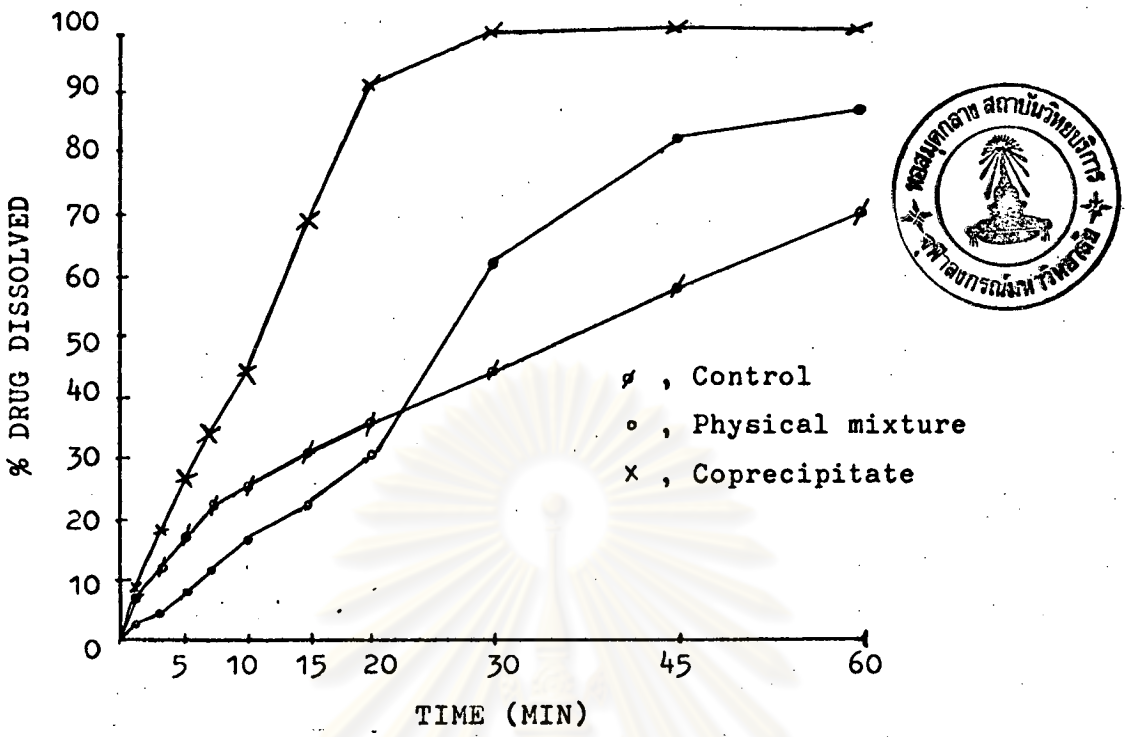

Figure 42. Dissolution profiles of tablets containing 1:(0.2+0.8) indomethacin:(dextrose+SLS).

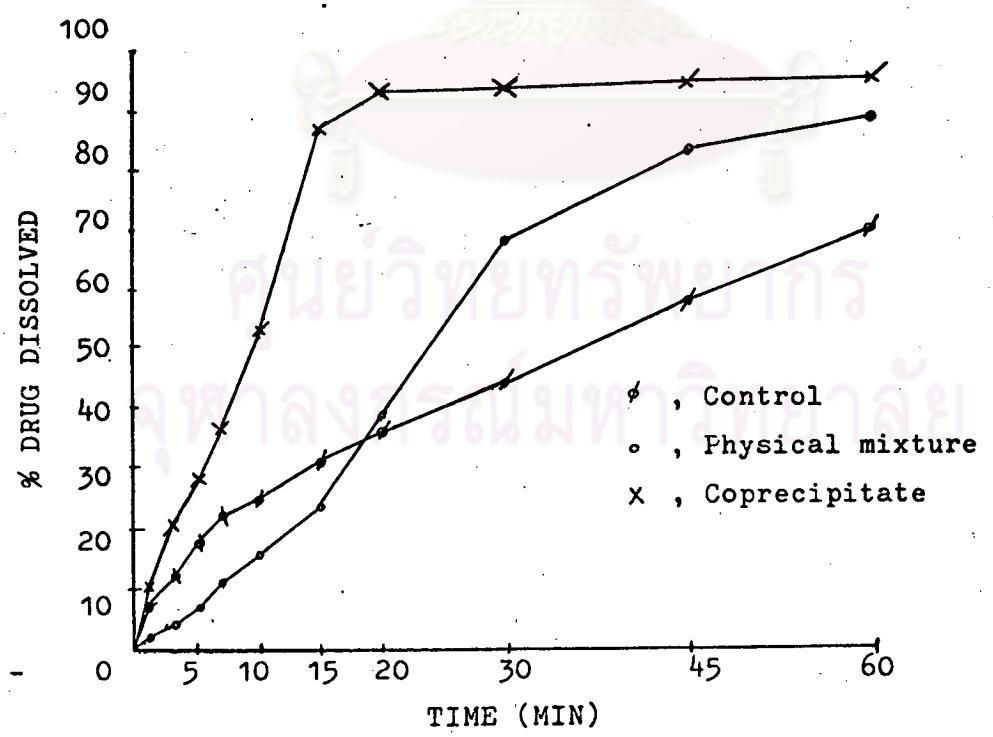

Figure 43. Dissolution profiles of tablets containing 1:(0.4+0.6) indomethacin:(dextrose+SLS).

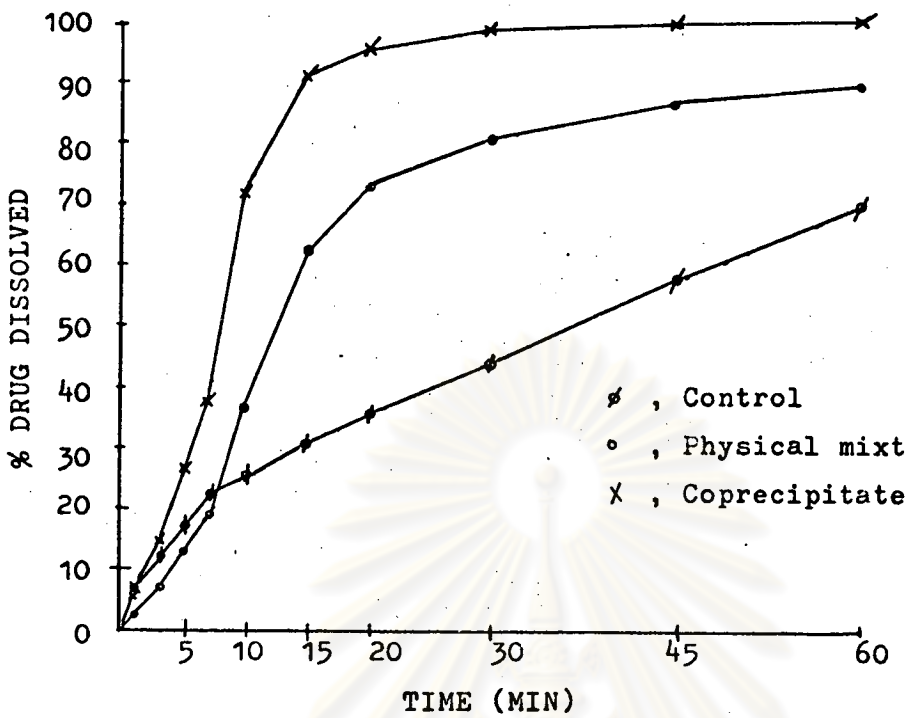

Figure 44. Dissolution profiles of tablets containing 1:(0.6+0.4) indomethacin:(dextrose+SLS).

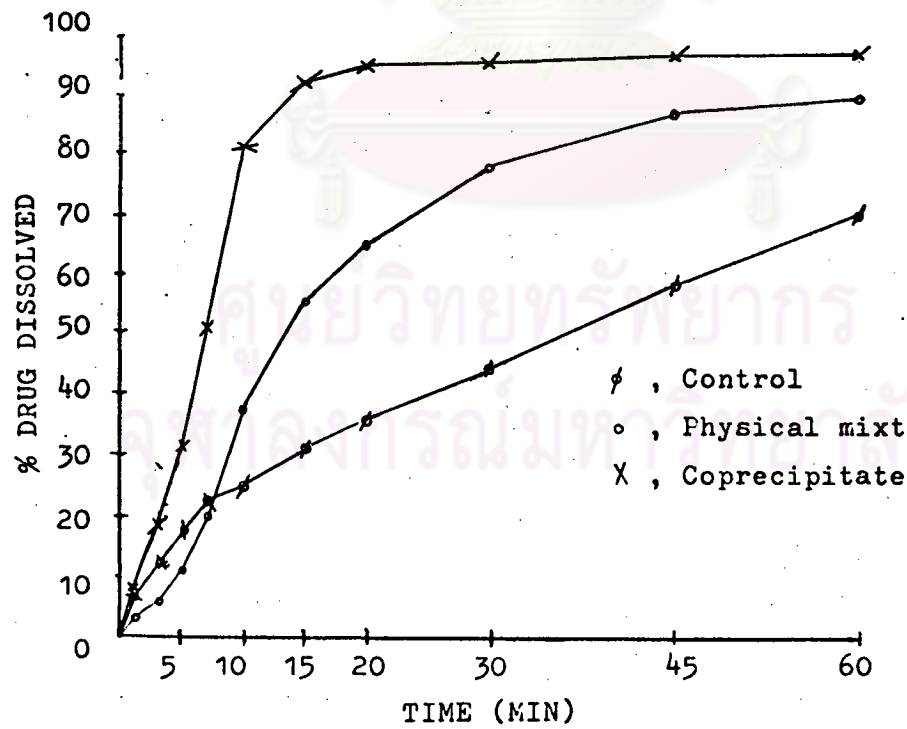

Figure 45. Dissolution profiles of tablets containing 1:(0.8+0.2) indomethacin:(dextrose+SLS).

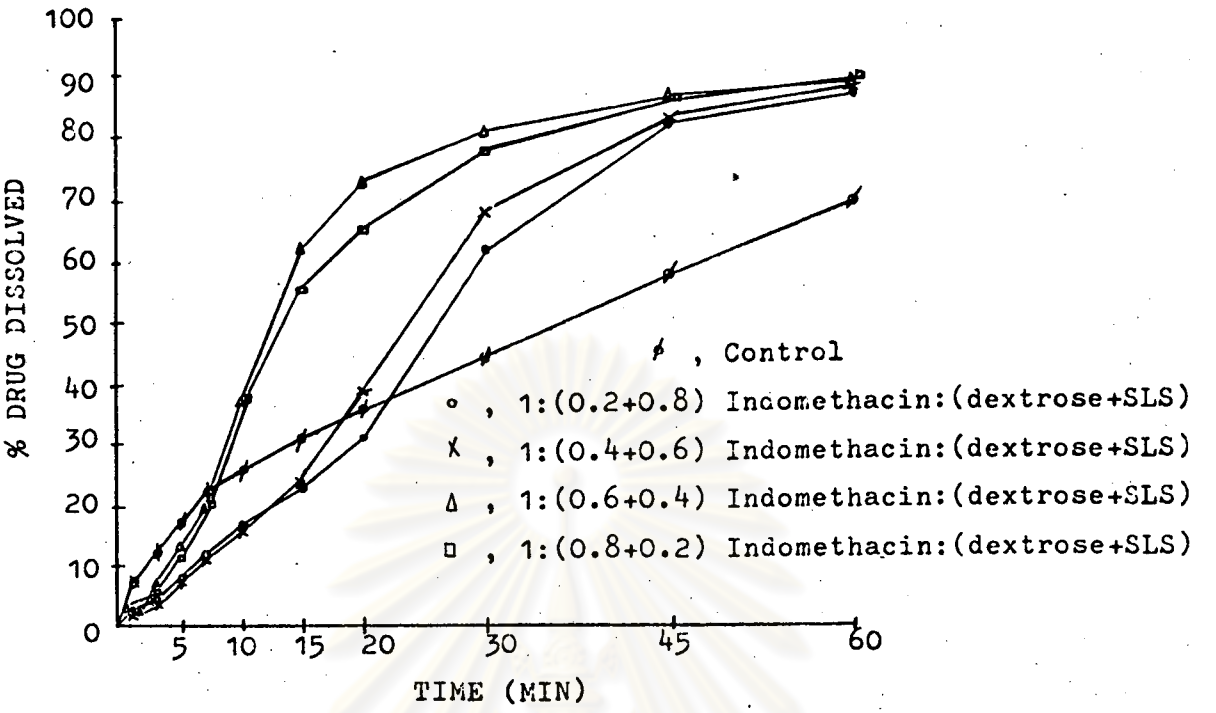

Figure 46. Dissolution profiles of tablets containing various systems of 1:1 indomethacin:(dextrose-SLS) physical mixtures.

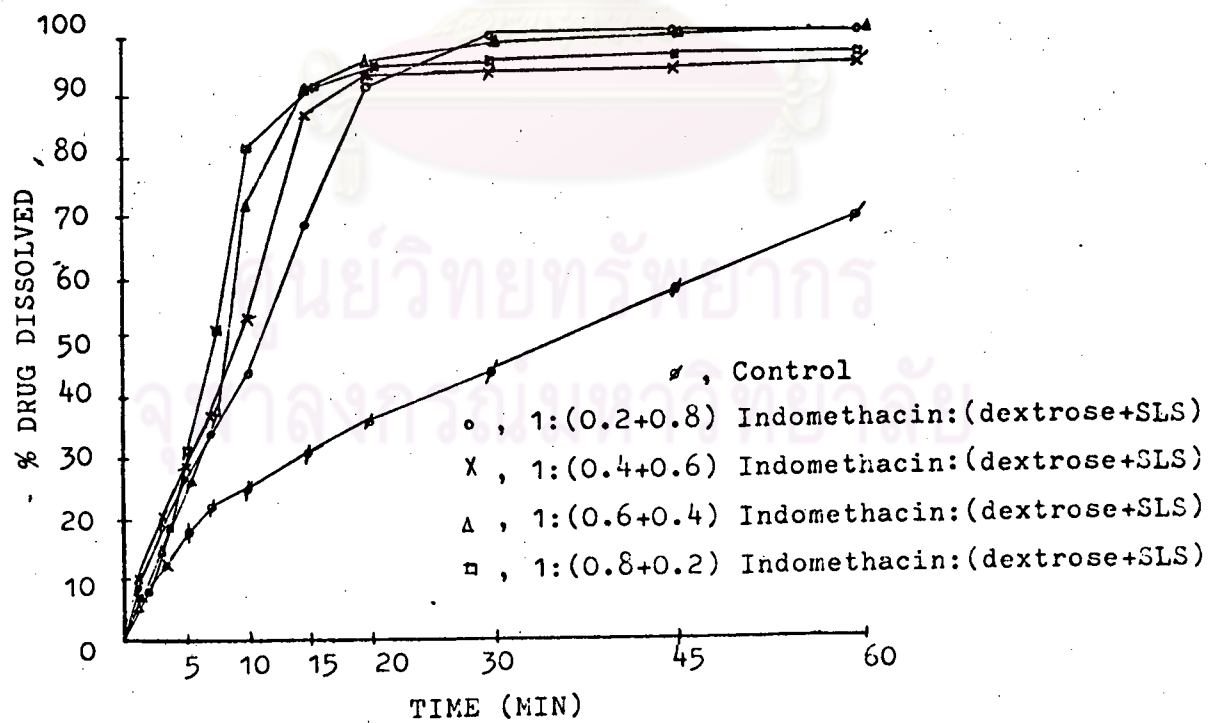

Figure 47. Dissolution profiles of tablets containing various systems of 1:1 indomethacin:(dextrose-SLS) coprecipitates.