CHAPTER III

RESULTS

Preparation of dispersion systems of ergoloid mesylate and treated ergoloid mesylate

Ergoloid mesylate solid dispersions from PVP K-30, PVP K-90, and mixture of poloxamer 188 in PVP K-30 were glass-like, transparent, and brittle, easily pulverized, and free-flowing powder. For PEG 4000, PEG 6000 and poloxamer 188 systems, the products were white stable masses which could be manipulated to powder forms.

Both physical mixtures and treated ergoloid mesylate were relatively easy to be prepared. In PEG 4000 and PEG 6000 systems, the products were somewhat sticky but when dried they were white stable powders which could be pulverized to yield dry nonsticky white powders.

Assay for content of ergoloid mesylate in dispersion systems

Typical calibration curves of ergoloid mesylate in 0.1 N. HCl as determined using linear regression was presented in Appendices 2 and 3. The sensitivity of spectrofluorophotometer could not be equally adjusted every preparation so the calibration curves should be freshly prepared before the samples were measured.

The percentage content of ergoloid mesylate in each dispersion systems obtained are shown in Table 3. The ergoloid mesylate content was between 97.05-104.93%.

Dissolution studies of ergoloid mesylate in dispersion systems

The dissolution profile and data of all forty-eight preparations --- twenty-three solid dispersions, twenty-three physical mixtures, treated drug, and pure drug --- were presented in Figures 11-45, experimental data in Appendices 4-16, respectively. The results from the solid dispersions and physical mixture dissolution determinations revealed that the poloxamer 188 system had the fastest dissolution profile, followed by the mixture of 3% poloxamer 188 in PVP K-30, PVP K-30, PVP K-90, PEG 4000, and, finally, PEG 6000.

1. Ergoloid mesylate-PVP K-30 systems

The dissolution parameters and dissolution profile of ergoloid mesylate systems containing drug and PVP K-30 were demonstrated in Appendices 5-6 and Figures 11-16. The pure drug exhibited the slowest dissolution profile while the dissolution profile of the treated drug slightly different from its pure drug. The solid dispersions gave markedly higher ergoloid mesylate dissolution than the physical mixtures at all drug: PVP K-30 ratio within 15 minutes. The dissolution of drug increased as the content of PVP K-30 increased in both solid dispersions and physical mixture.

Table 3 The percentage content of ergoloid mesylate in each dispersion system

System	Percentage content	
	Solid dispersion	Physical mixture
1:1 Ergoloid mesylate-PVP K 30	98.15	103.00
1:3 Ergoloid mesylate-PVP K 30	100.23	100.77
1:5 Ergoloid mesylate-PVP K 30	102.14	104.93
1:7 Ergoloid mesylate-PVP K 30	99.43	99.10
1:1 Ergoloid mesylate-PVP K 90	103.21	98.81
1:3 Ergoloid mesylate-PVP K 90	97.05	97.99
1:5 Ergoloid mesylate-PVP K 90	98.83	100.11
1:7 Ergoloid mesylate-PVP K 90	99.01	101.43
1:1 Ergoloid mesylate-PEG 4000	100.58	102.37
1:3 Ergoloid mesylate-PEG 4000	102.24	99.57
1:5 Ergoloid mesylate-PEG 4000	98.09	102.34
1:7 Ergoloid mesylate-PEG 4000	99.92	99.87
1:1 Ergoloid mesylate-PEG 6000	101.15	104.12
1:3 Ergoloid mesylate-PEG 6000	102.43	101.32
1:5 Ergoloid mesylate-PEG 6000	97.98	99.02
1:7 Ergoloid mesylate-PEG 6000	99.17	103.67
1:1 Ergoloid mesylate-poloxamer 188	101.67	100.80
1:3 Ergoloid mesylate-poloxamer 188	104.53	98.31
1:5 Ergoloid mesylate-poloxamer 188	99.17	97.78
1:7 Ergoloid mesylate-poloxamer 188	100.39	102.95
1:1 Ergoloid mesylate-3% poloxamer 188 in PVP K 30	101.93	102.05
1:4 Ergoloid mesylate-3% poloxamer 188 in PVP K 30	98.67	103.86
1:6 Ergoloid mesylate-3% poloxamer 188 in PVP K 30	99.88	101.29

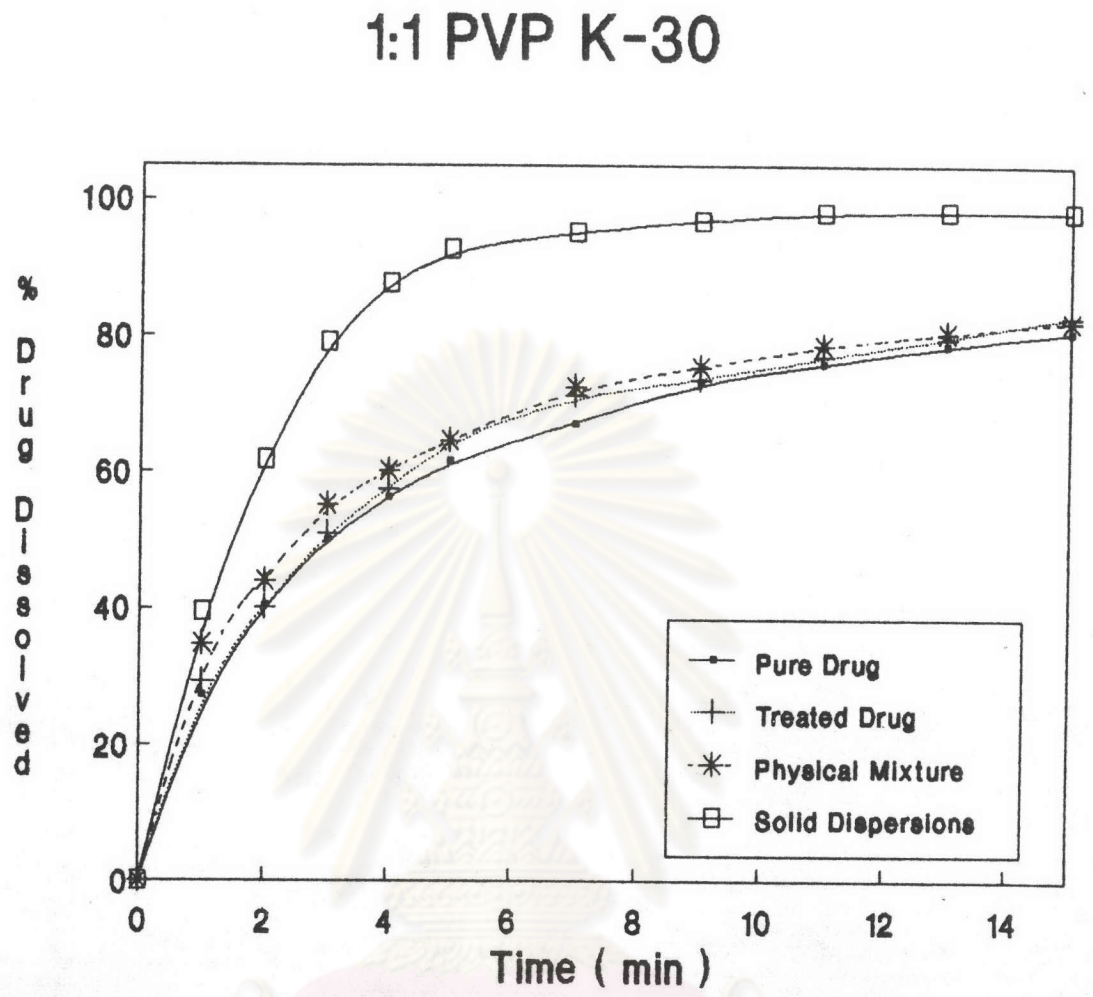


Figure 11 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and 1 : 1 ergoloid mesylate - PVP K-30 physical mixture and solid dispersion systems in 0.1 N. HCl at 37 ^{o} C

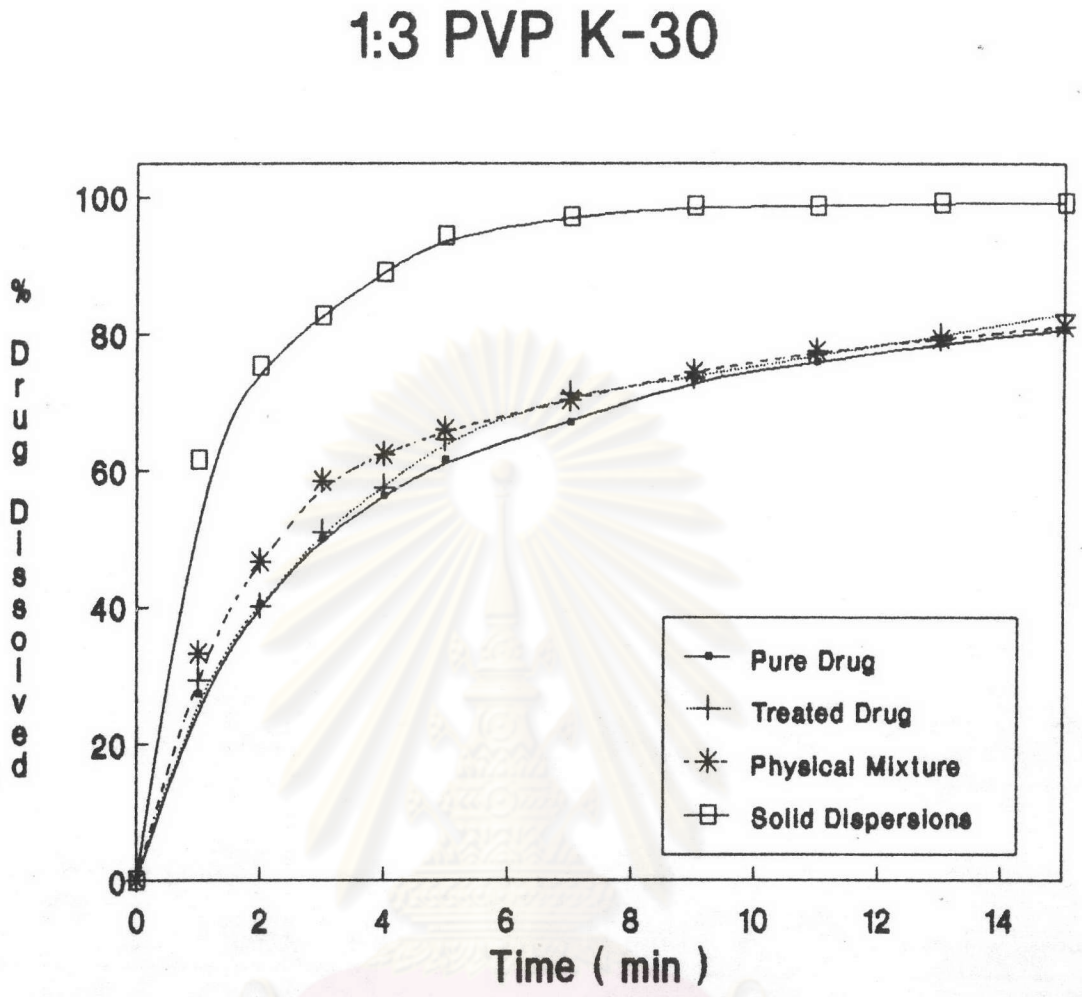


Figure 12 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and 1 : 3 ergoloid mesylate - PVP K-30 physical mixture and solid dispersion systems in 0.1 N. HCl at 37 ^{o} C

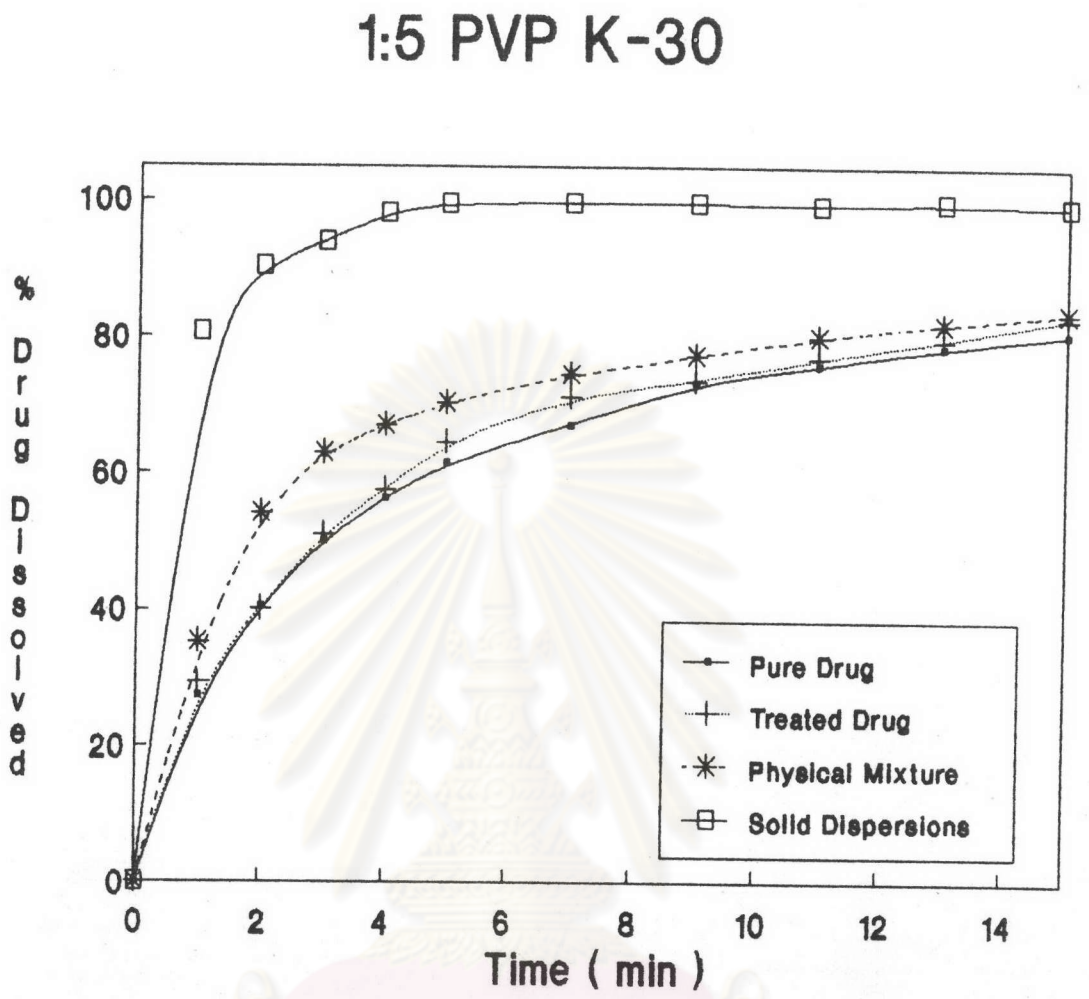


Figure 13 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and 1 : 5 ergoloid mesylate - PVP K-30 physical mixture and solid dispersion systems in 0.1 N. HCl at 37 ^{o} C

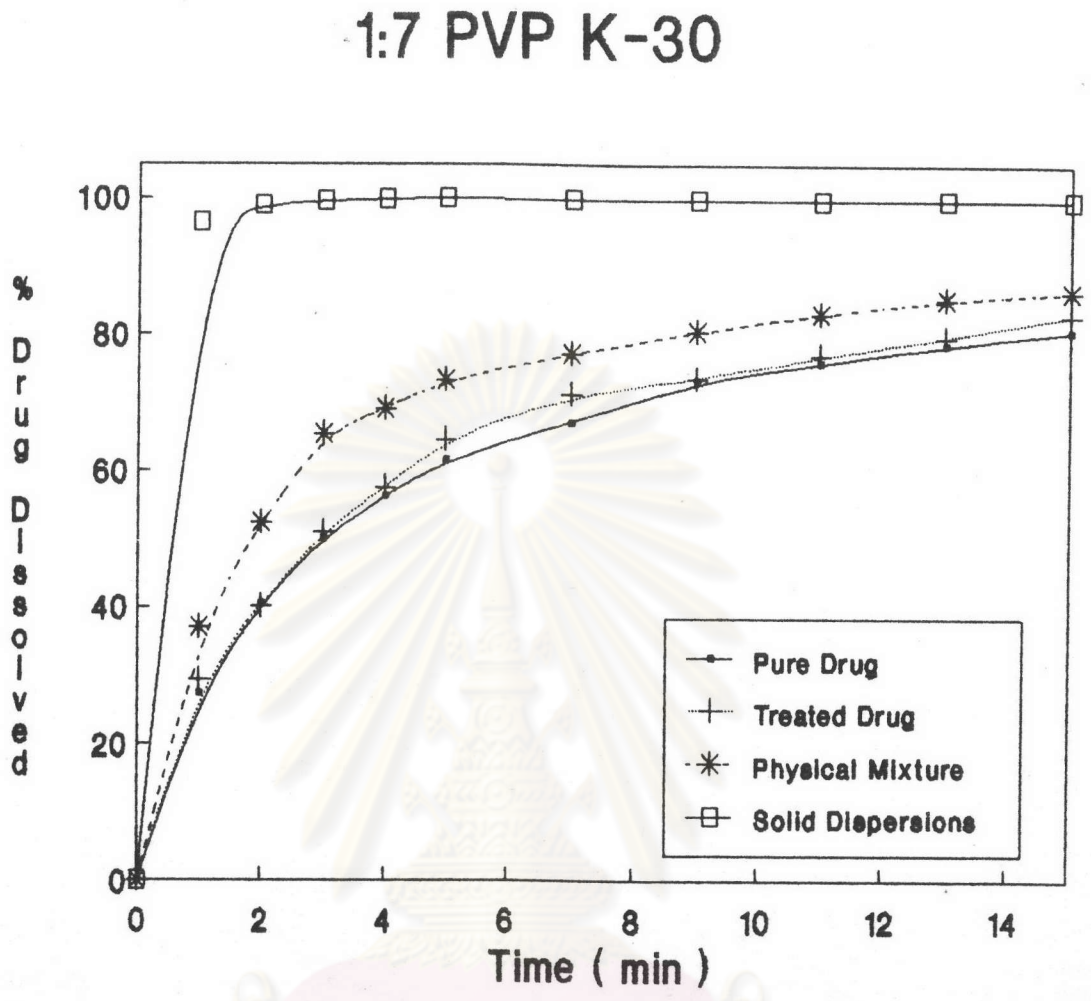


Figure 14 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and 1 : 7 ergoloid mesylate - PVP K-30 physical mixture and solid dispersion systems in 0.1 N. HCl at 37 ^{o} C

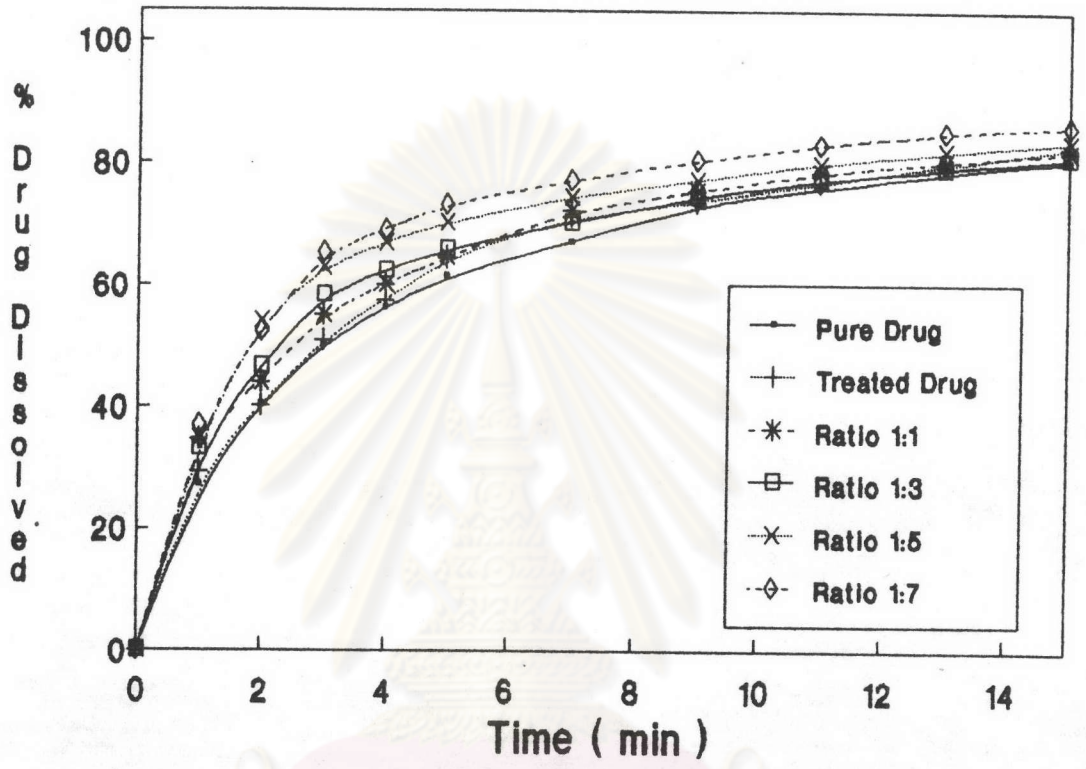


Figure 15 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and ergoloid mesylate physical mixture systems , using different ratio of PVP K-30 as the carriers , in 0.1 N. HCl at 37 ^{o} C

SOLID DISPERSIONS
PVP K-30

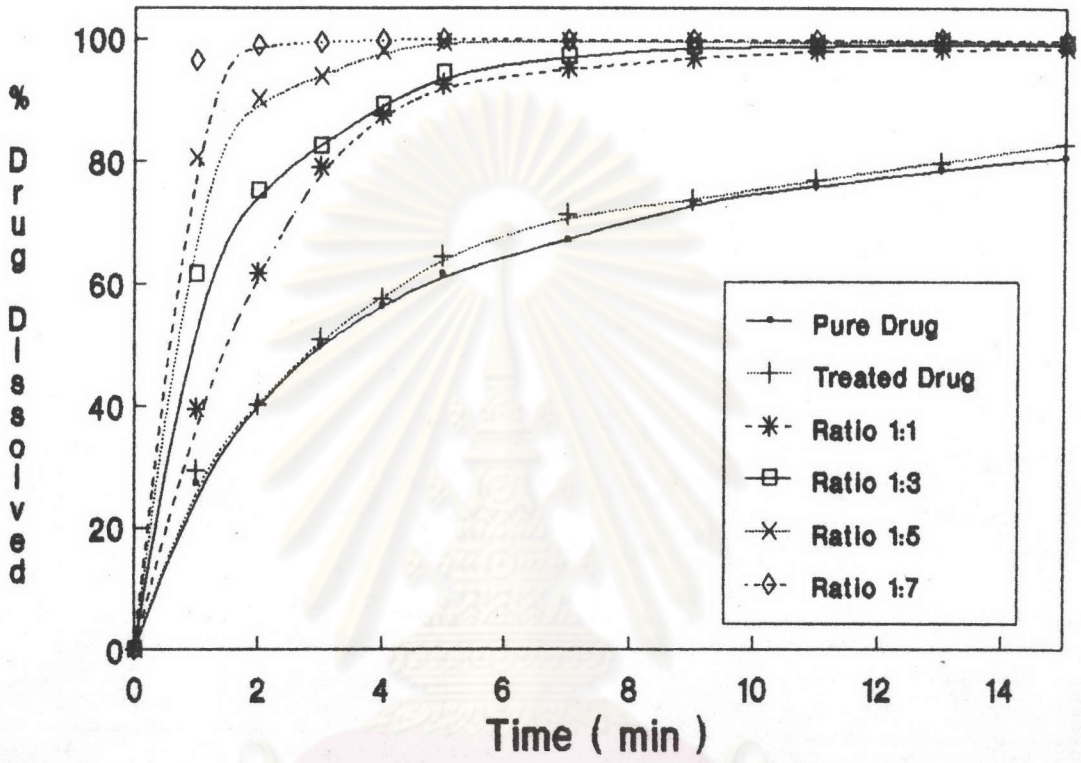


Figure 16 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and ergoloid mesylate solid dispersion systems , using different ratio of PVP K-30 as the carriers , in 0.1 N. HCl at 37 ^{o} C

2. Ergoloid mesylate-PVP K-90 systems

The ergoloid mesylate dissolution data and their dissolution profiles were presented in Appendices 7-8 and Figures 17-22, respectively. No marked enhancement in ergoloid mesylate dissolution was observed in physical mixtures compared to pure drug and treated drug, except 1:7 ergoloid mesylate:PVP K-90. The physical mixture of 1:7 ergoloid mesylate:PVP K-90 seemed to exhibit higher dissolution than pure and treated drug. However, the dissolution profiles from physical mixtures tended to increase with increasing concentration of PVP K-90. All ratios of solid dispersion preparations showed marked faster dissolution rate of ergoloid mesylate than their ratios of physical mixture preparations. Among the solid dispersions, the preparation of 1:7 ergoloid mesylate:PVP K-90 yielded the fastest dissolution rate, followed by the 1:5, 1:3, and 1:1 ratio, respectively.

3. Ergoloid mesylate-PEG 4000 systems

The dissolution parameters and dissolution profiles of ergoloid mesylate dispersion systems were shown in Appendices 9-10 and Figures 23-28. No difference in dissolution profile was observed between the all preparations of physical mixtures and the pure drug but the tendency of the dissolution declined as the weight fraction of PEG 4000 decreased. In solid dispersions, the dissolution of drug increased as the content of PEG 4000 increased. However, all proportions of solid dispersions gave markedly higher dissolution rate than their physical mixtures.

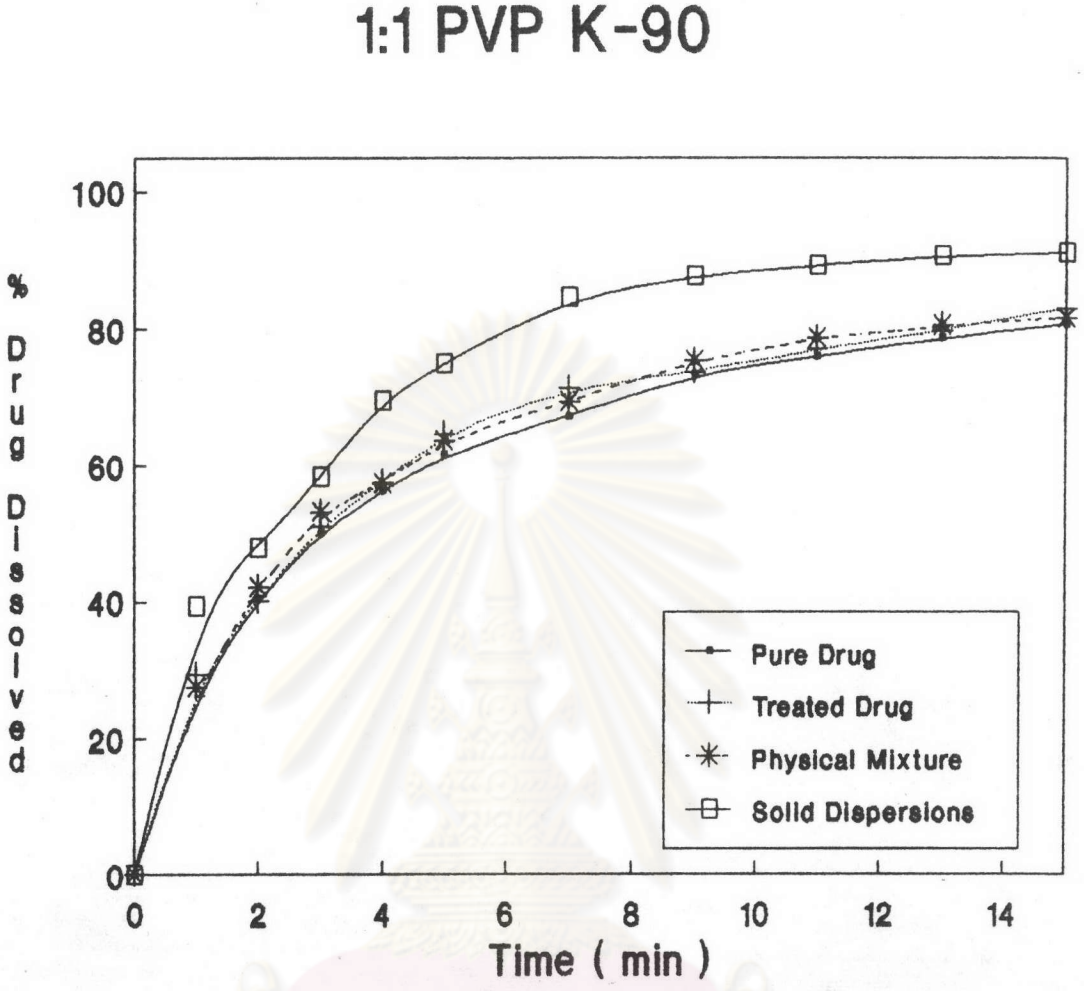


Figure 17 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and 1 : 1 ergoloid mesylate - PVP K-90 physical mixture and solid dispersion systems in 0.1 N. HCl at 37 ^{o} C

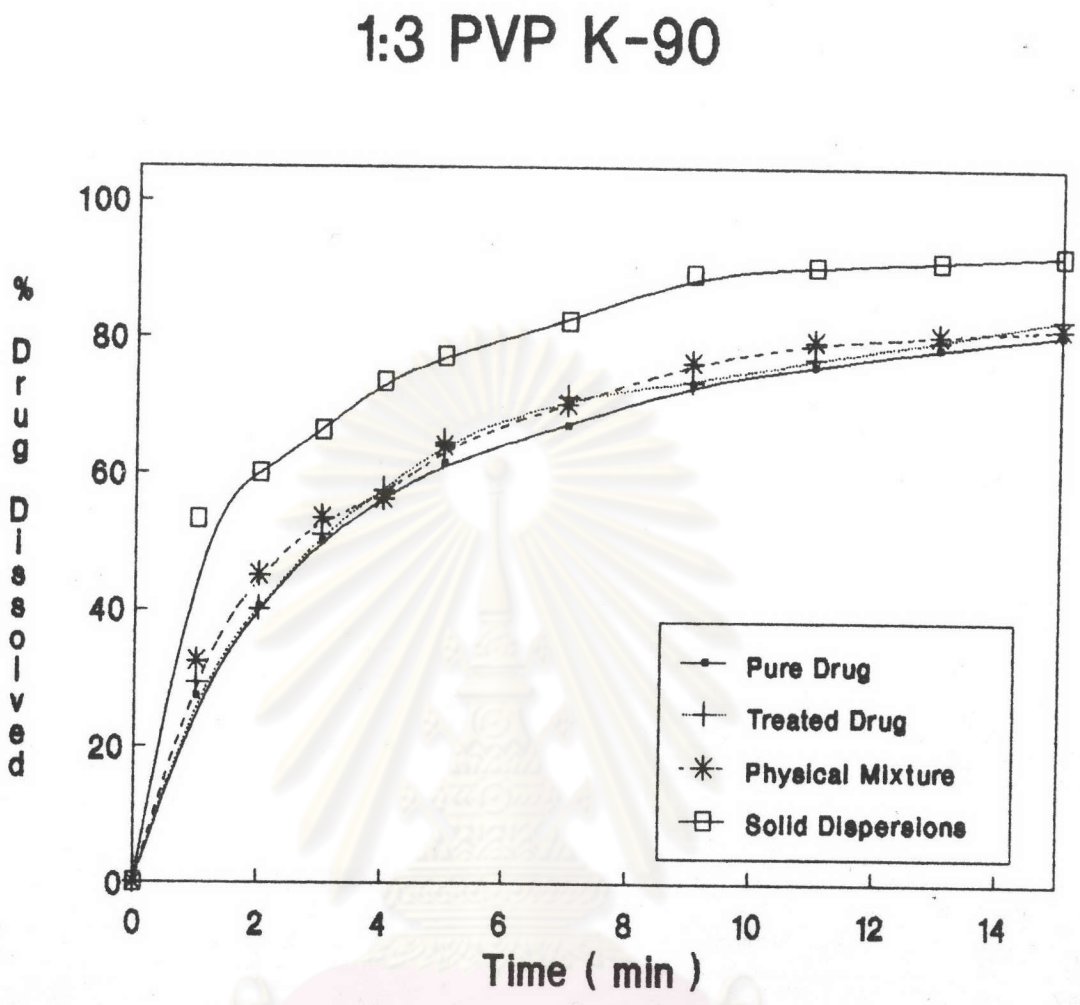


Figure 18 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and 1 : 3 ergoloid mesylate - PVP K-90 physical mixture and solid dispersion systems in 0.1 N. HCl at 37 ^{o} C

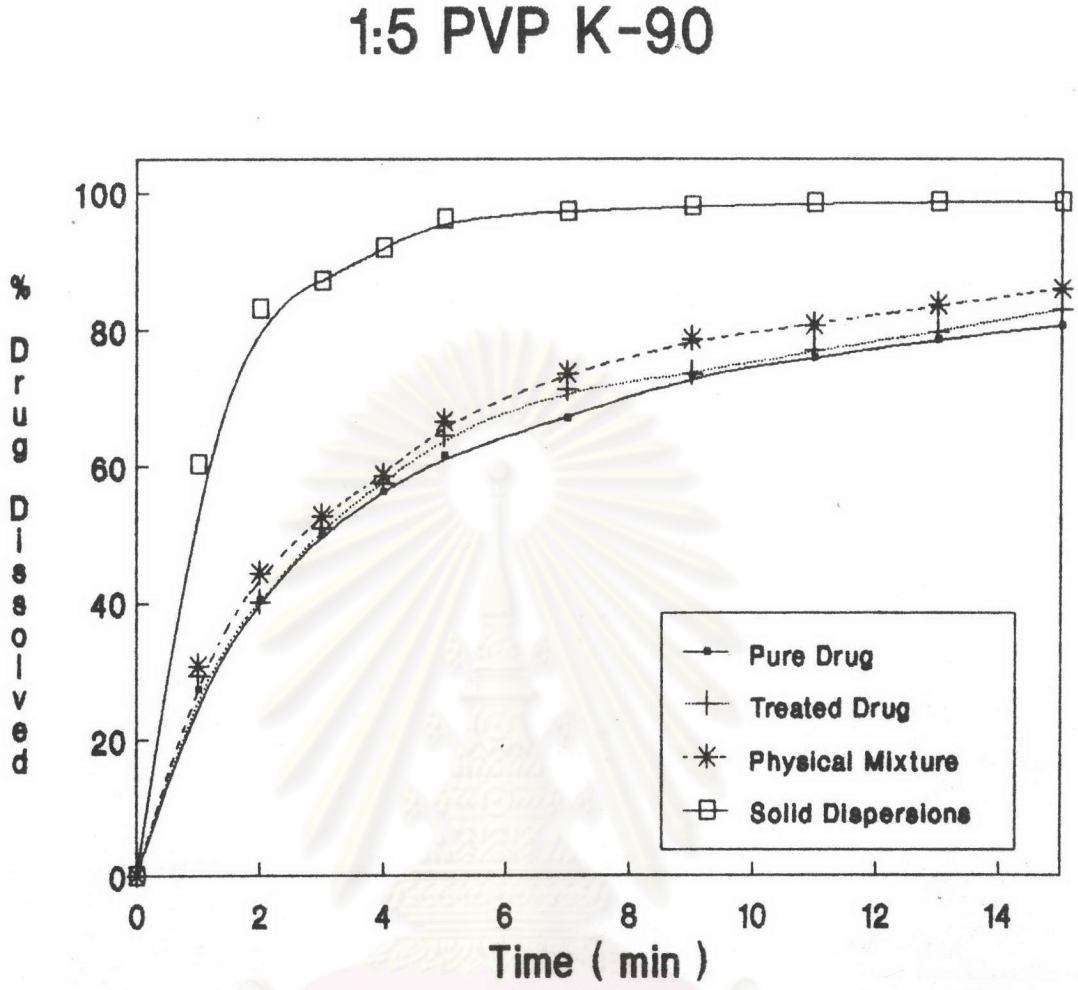


Figure 19 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and 1 : 5 ergoloid mesylate - PVP K-90 physical mixture and solid dispersion systems in 0.1 N. HCl at 37 ^{o} C

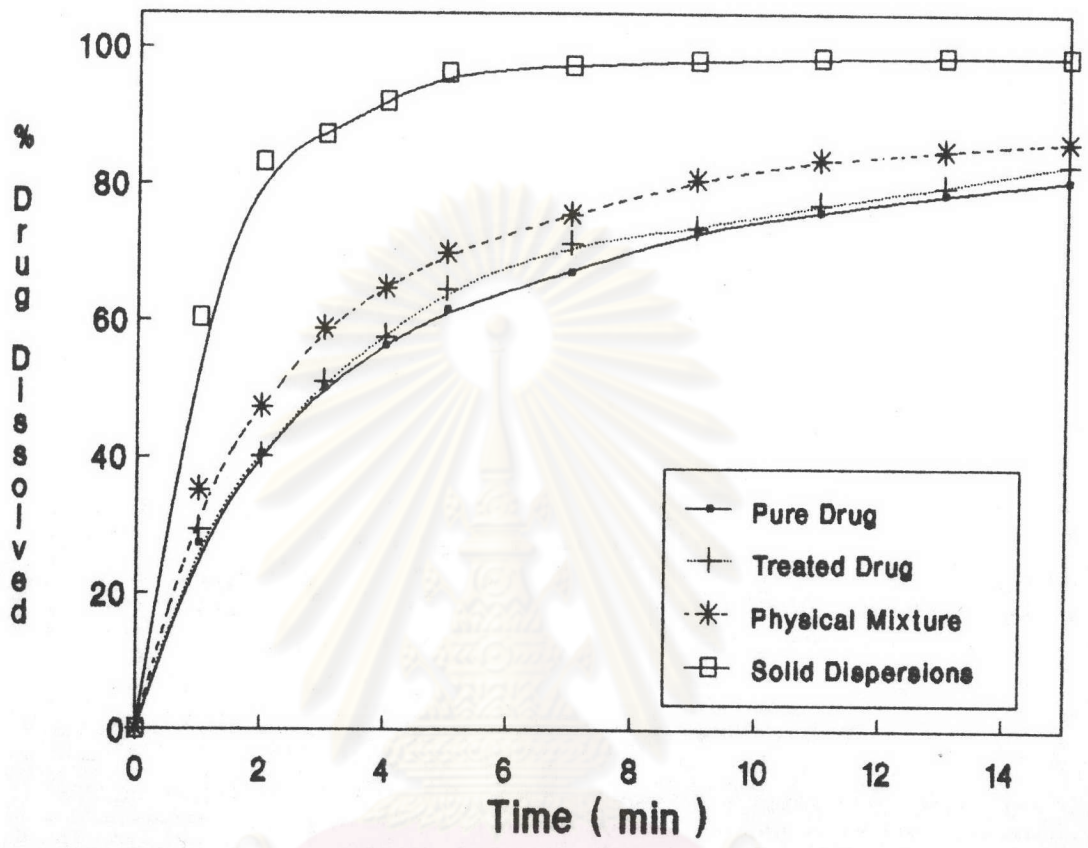


Figure 20 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and 1 : 7 ergoloid mesylate - PVP K-90 physical mixture and solid dispersion systems in 0.1 N. HCl at 37 ^{o} C

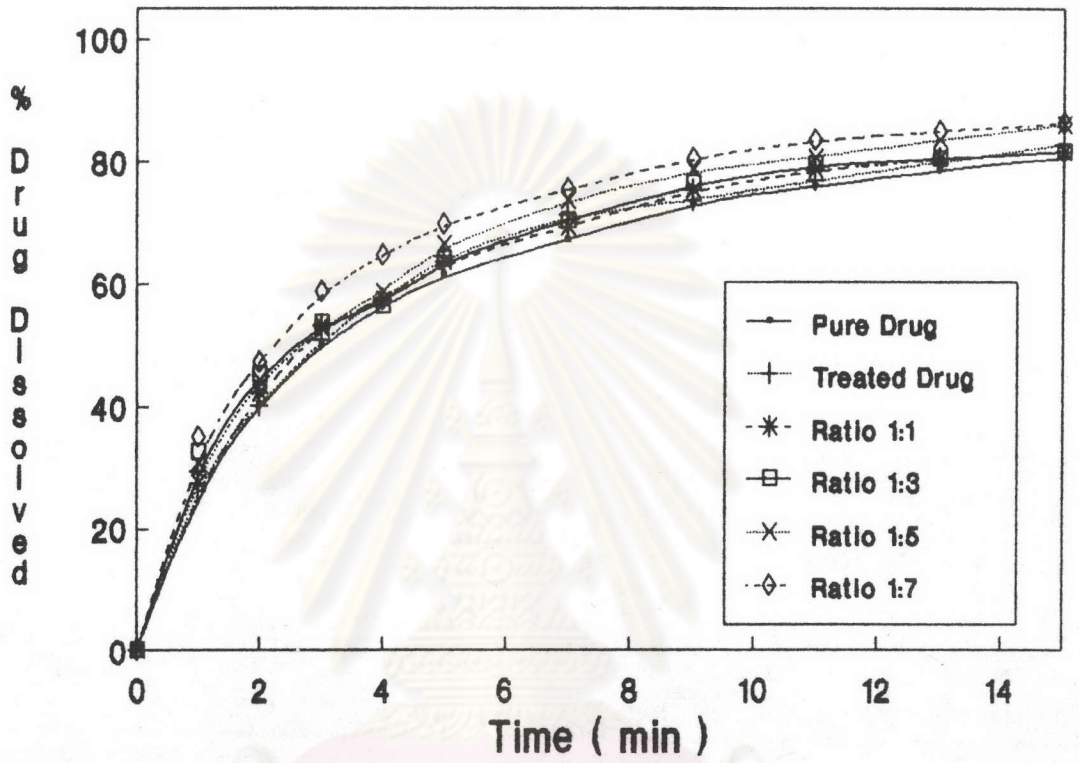


Figure 21 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and ergoloid mesylate physical mixture systems , using different ratio of PVP K-90 as the carriers , in 0.1 N. HCl at 37 ^{O} C

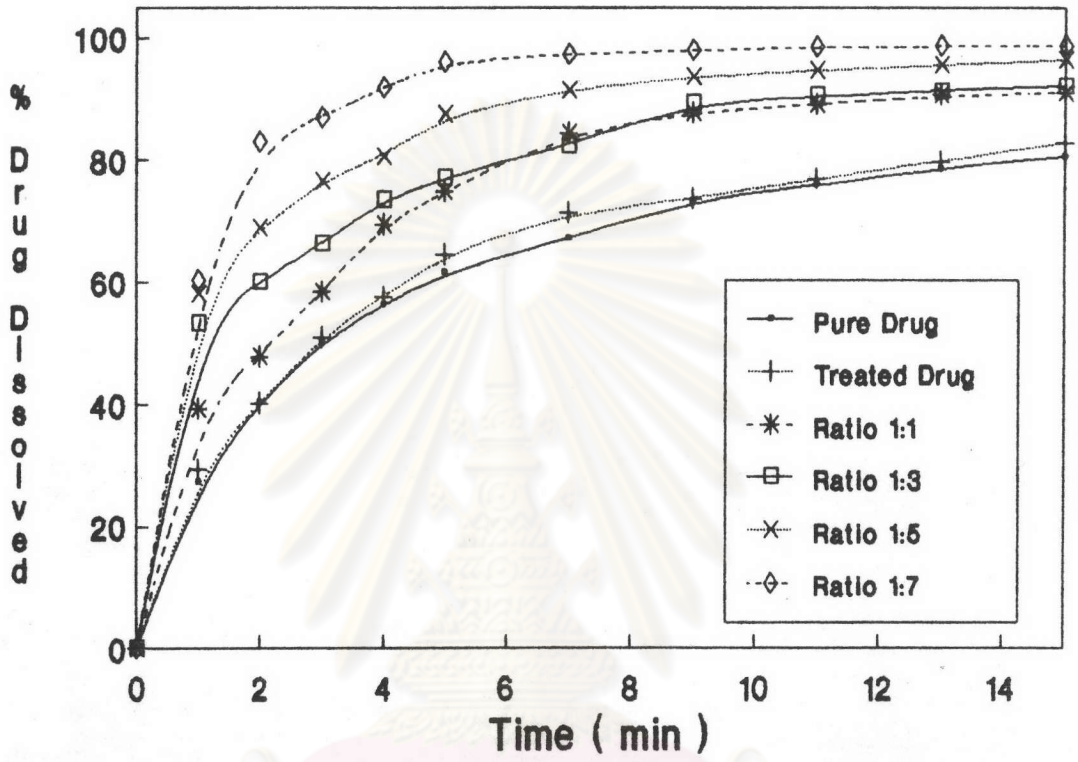


Figure 22 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and ergoloid mesylate solid dispersion systems , using different ratio of PVP K-90 as the carriers , in 0.1 N. HCl at 37 ^{o} C

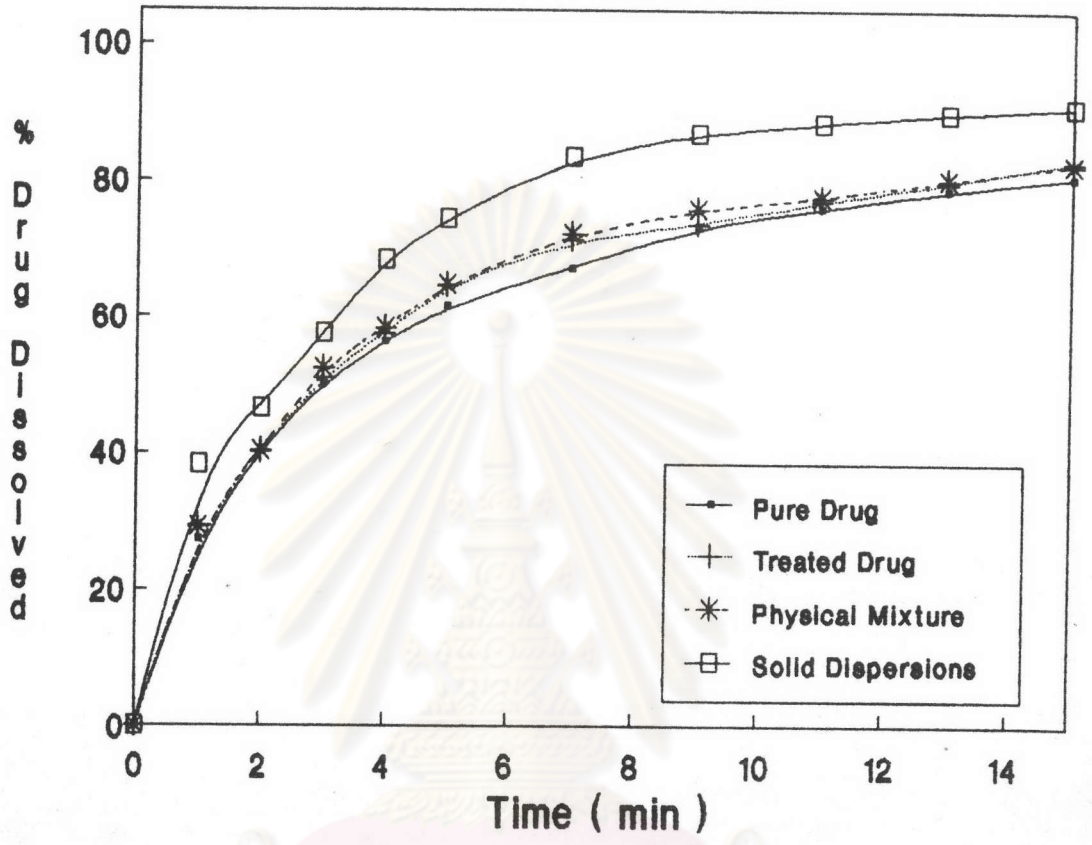


Figure 23 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and 1 : 1 ergoloid mesylate - PEG 4000 physical mixture and solid dispersion systems in 0.1 N. HCl at 37 ^{o} C

1:3 PEG 4000

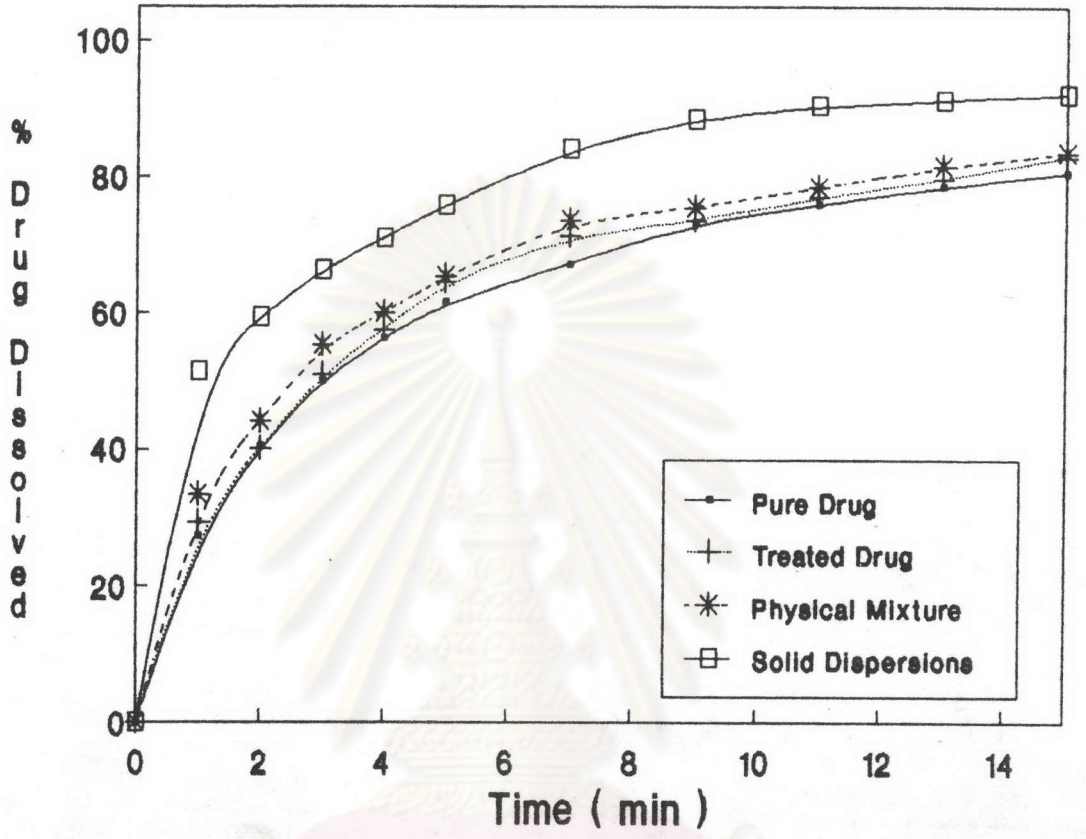


Figure 24 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and 1 : 3 ergoloid mesylate - PEG 4000 physical mixture and solid dispersion systems in 0.1 N. HCl at 37 ^{o} C

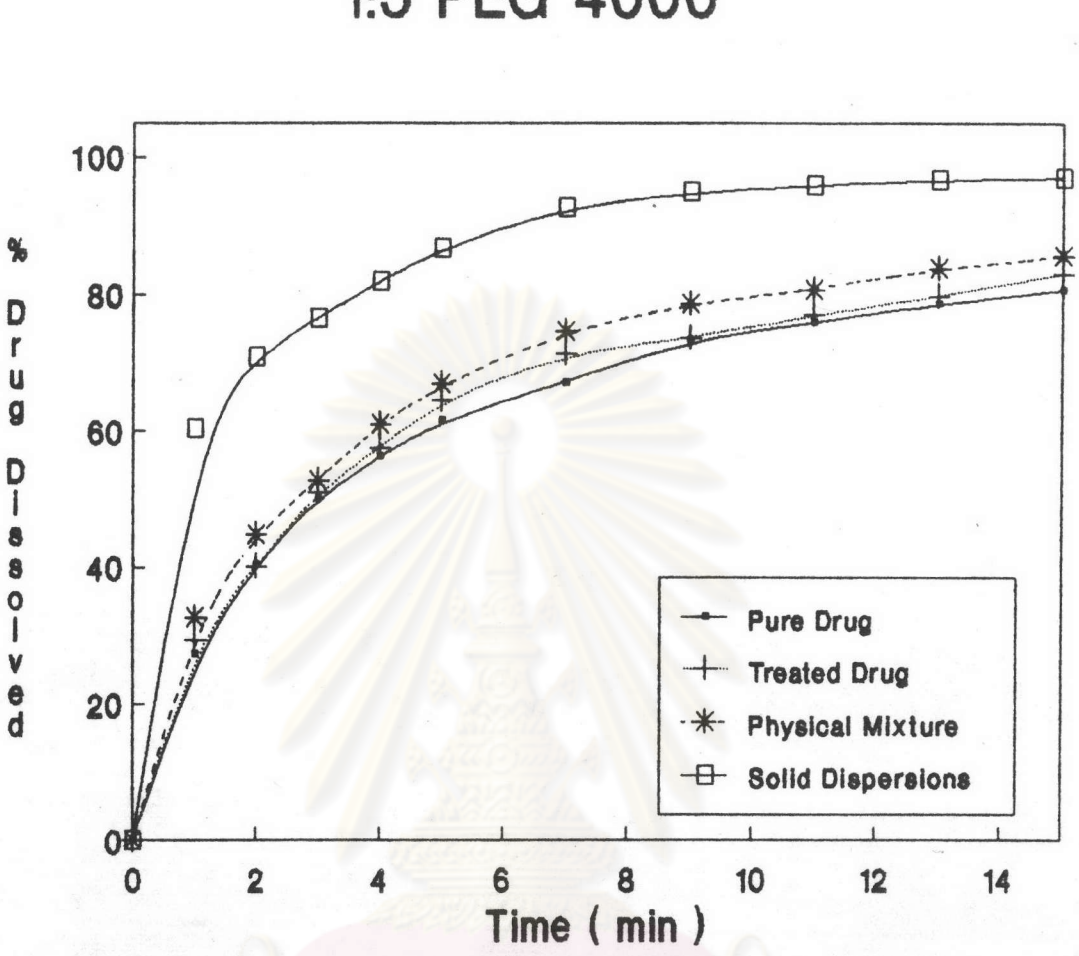


Figure 25 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and 1 : 5 ergoloid mesylate - PEG 4000 physical mixture and solid dispersion systems in 0.1 N. HCl at 37 ^{o} C

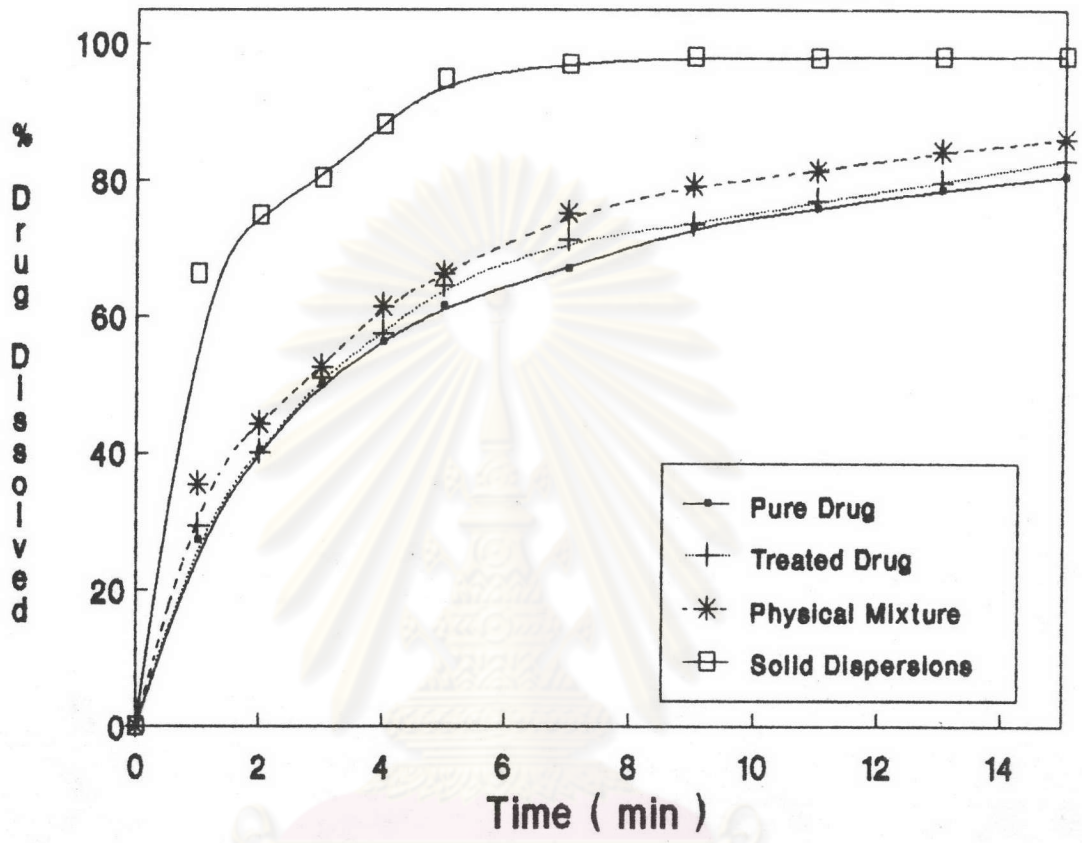


Figure 26 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and 1 : 7 ergoloid mesylate - PEG 4000 physical mixture and solid dispersion systems in 0.1 N. HCl at 37 ^{o} C

PHYSICAL MIXTURE
PEG 4000

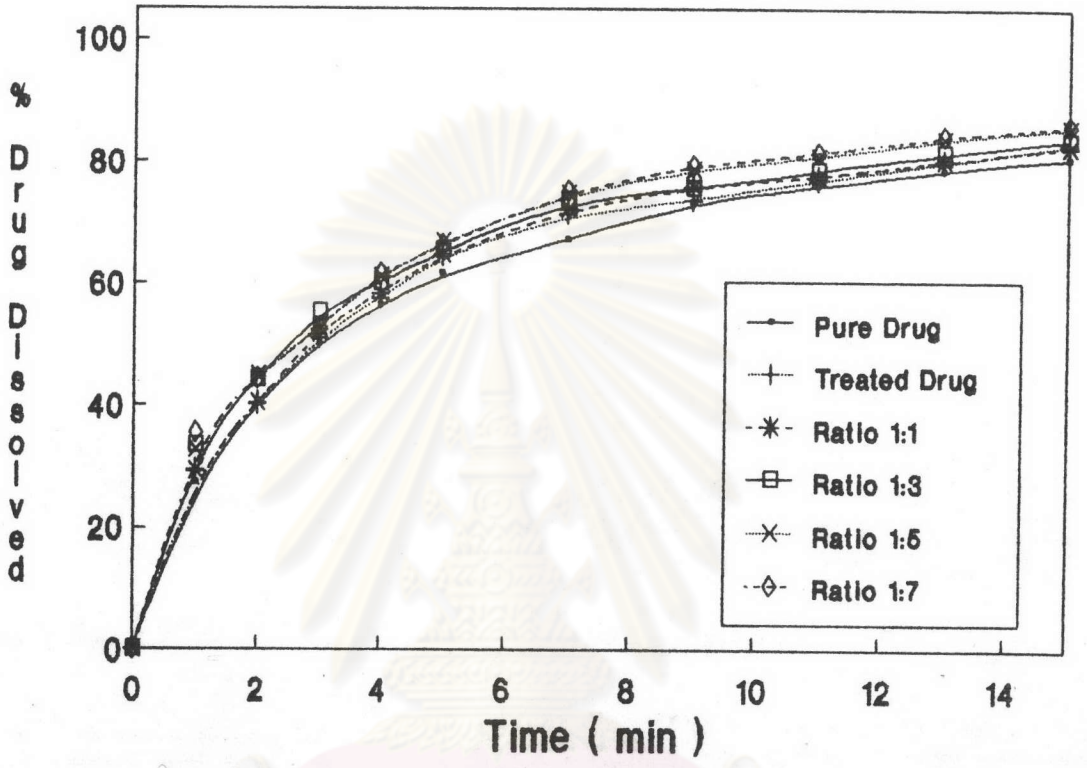


Figure 27 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and ergoloid mesylate physical mixture systems , using different ratio of PEG 4000 as the carriers , in 0.1 N. HCl at 37 ^{o} C

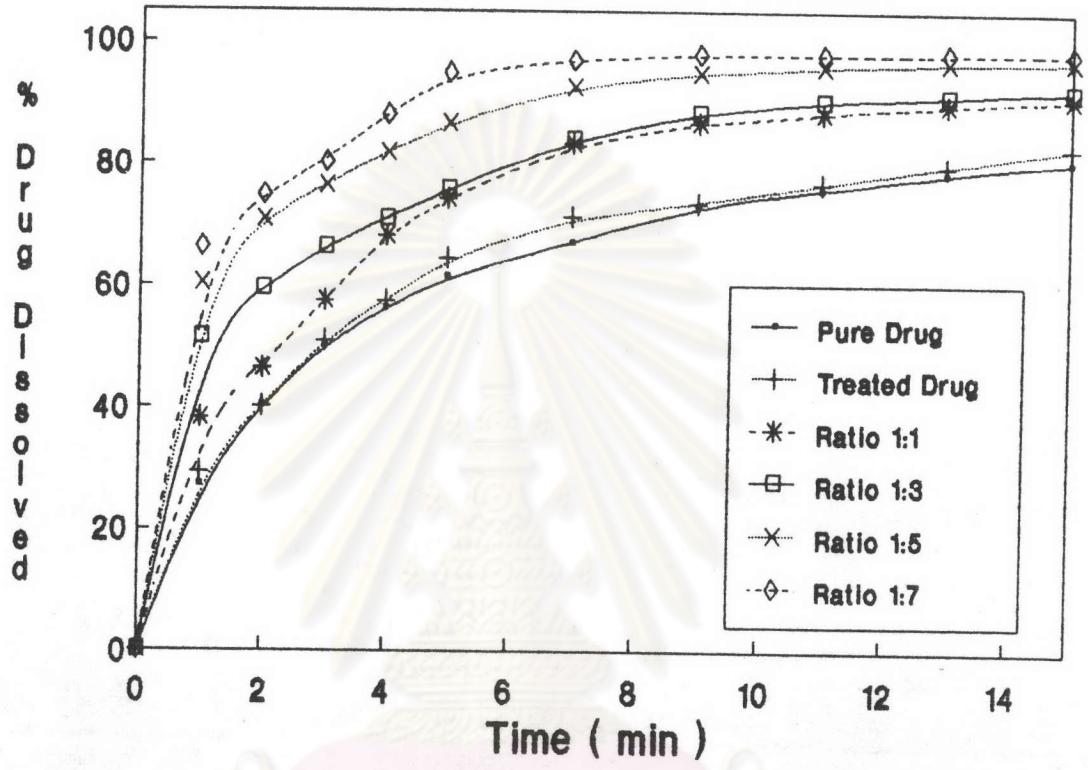


Figure 28 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and ergoloid mesylate solid dispersion systems , using different ratio of PEG 4000 as the carriers , in 0.1 N. HCl at 37 ^{o} C

4. Ergoloid mesylate-PEG 6000 system

The dissolution parameters and dissolution profiles of ergoloid mesylate powders containing ergoloid mesylate:PEG 6000 were respectively shown in Appendices 11-12 and Figure 29-34.

Among these types of solid dispersions, the fastest ergoloid mesylate dissolution rate was obtained from 1:7 ergoloid mesylate:PEG 6000 solid dispersions, followed by 1:5, 1:3, and 1:1 ergoloid mesylate:PEG 6000, respectively. However, the dissolution rate of 1:3 ergoloid mesylate:PEG 6000 solid dispersions was slower than the dissolution rate of 1:5 ergoloid mesylate:PEG 6000 solid dispersions, but later (at 11 minutes) on they yielded similar dissolution rate. All cases of ergoloid mesylate-PEG 6000 physical mixture yielded the same dissolution profiles as pure and treated drug, nevertheless the inclination of their dissolution increased with increasing PEG 6000 weight fraction. The dissolution profiles of the solid dispersions shown higher than the physical mixtures at every drug:PEG 6000 proportion.

5. Ergoloid mesylate-poloxamer 188 system

The dissolution data and dissolution profiles of ergoloid mesylate were shown in Appendices 13-14 and Figures 35-40. The presence of poloxamer 188 in ergoloid mesylate powder resulted in faster dissolution rate compared to the pure and treated drug powder. All the preparations of solid dispersions shown markedly faster dissolution rates than the preparations of physical mixture having the same ratio of ergoloid mesylate:poloxamer 188.

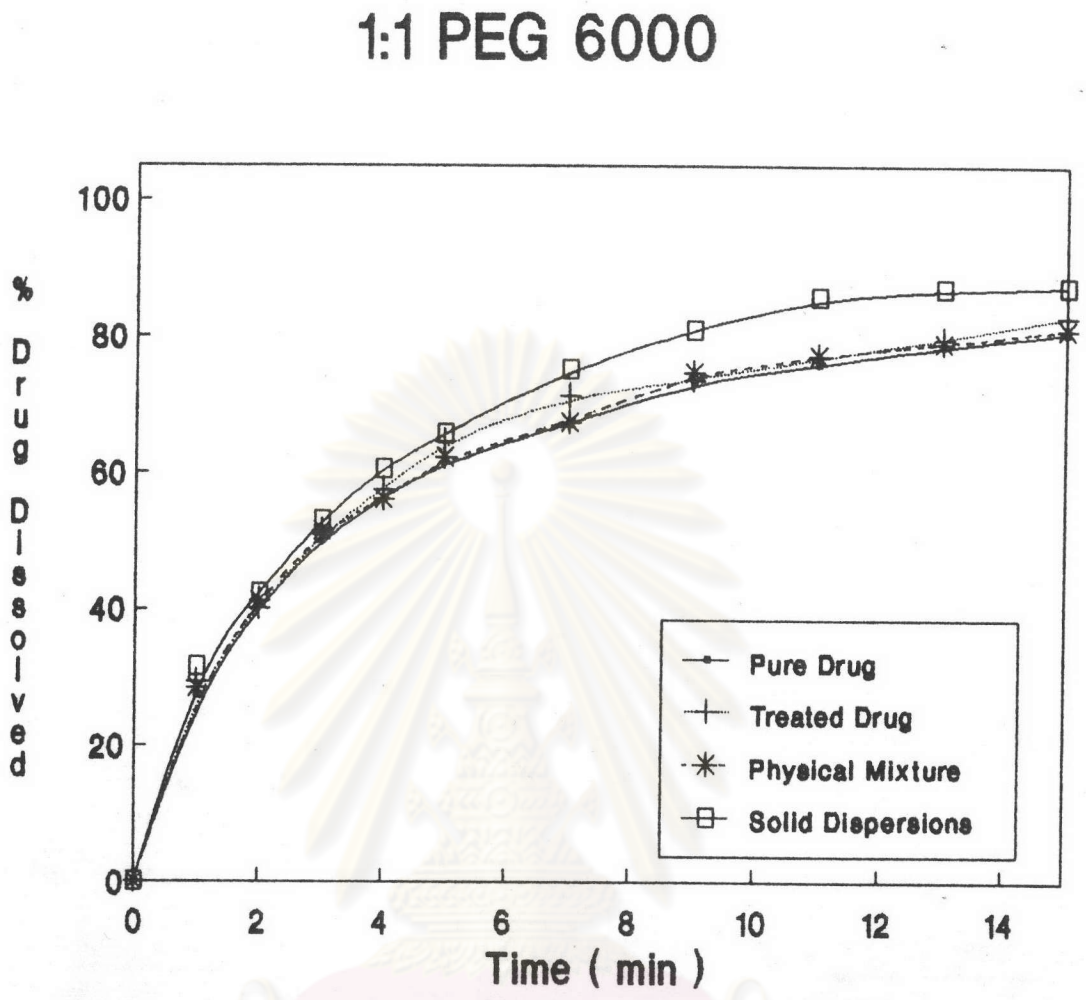


Figure 29 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and 1 : 1 ergoloid mesylate - PEG 6000 physical mixture and solid dispersion systems in 0.1 N. HCl at 37 ^{o} C

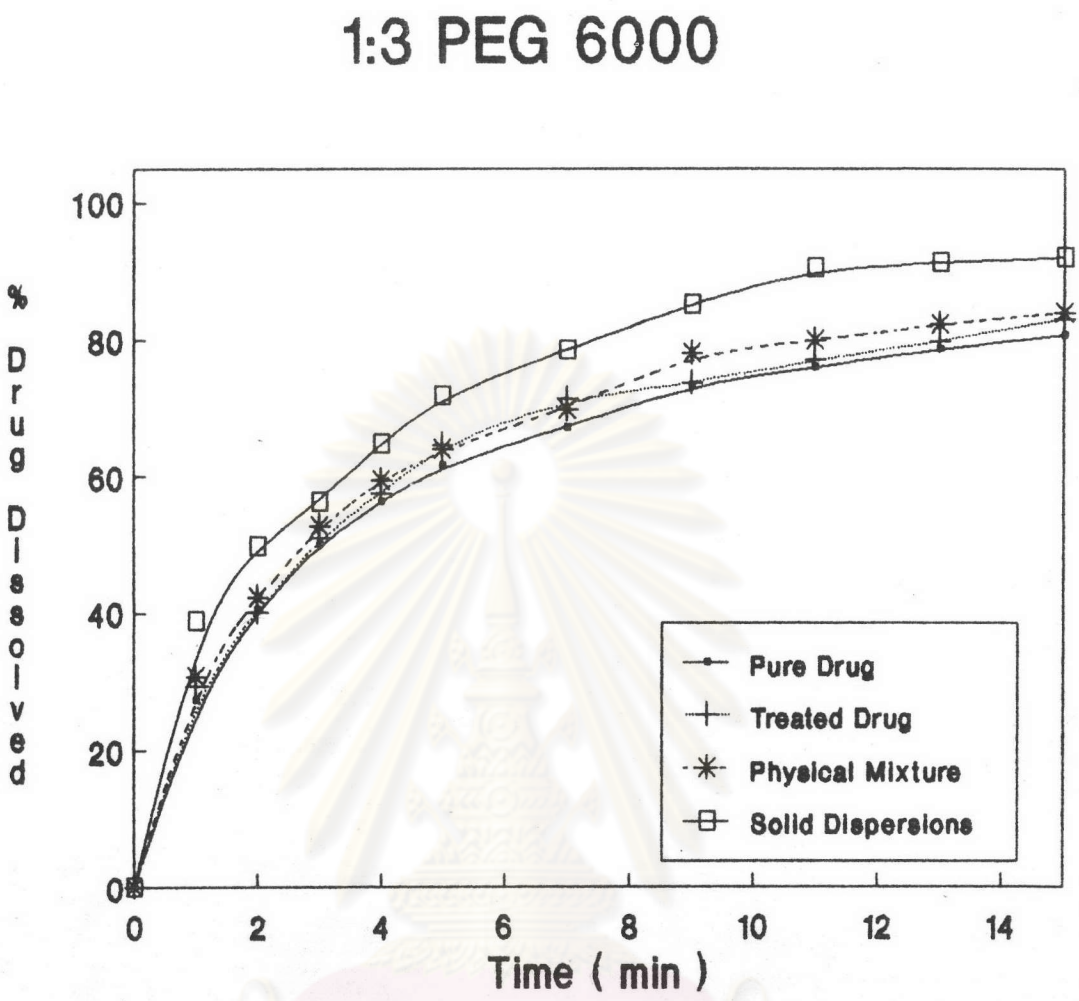


Figure 30 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and 1 : 3 ergoloid mesylate - PEG 6000 physical mixture and solid dispersion systems in 0.1 N. HCl at 37 ^{o} C

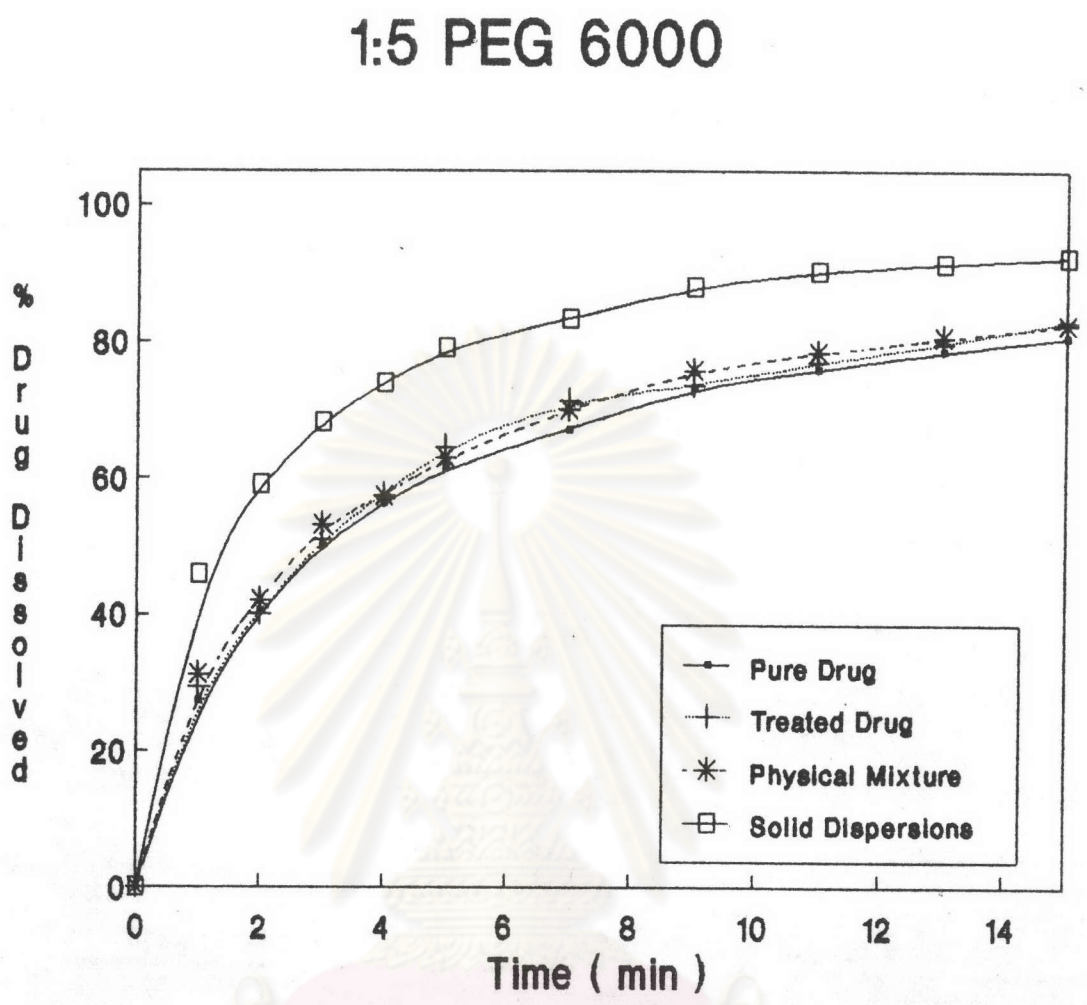


Figure 31 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and 1 : 5 ergoloid mesylate - PEG 6000 physical mixture and solid dispersion systems in 0.1 N. HCl at 37 ^{o} C

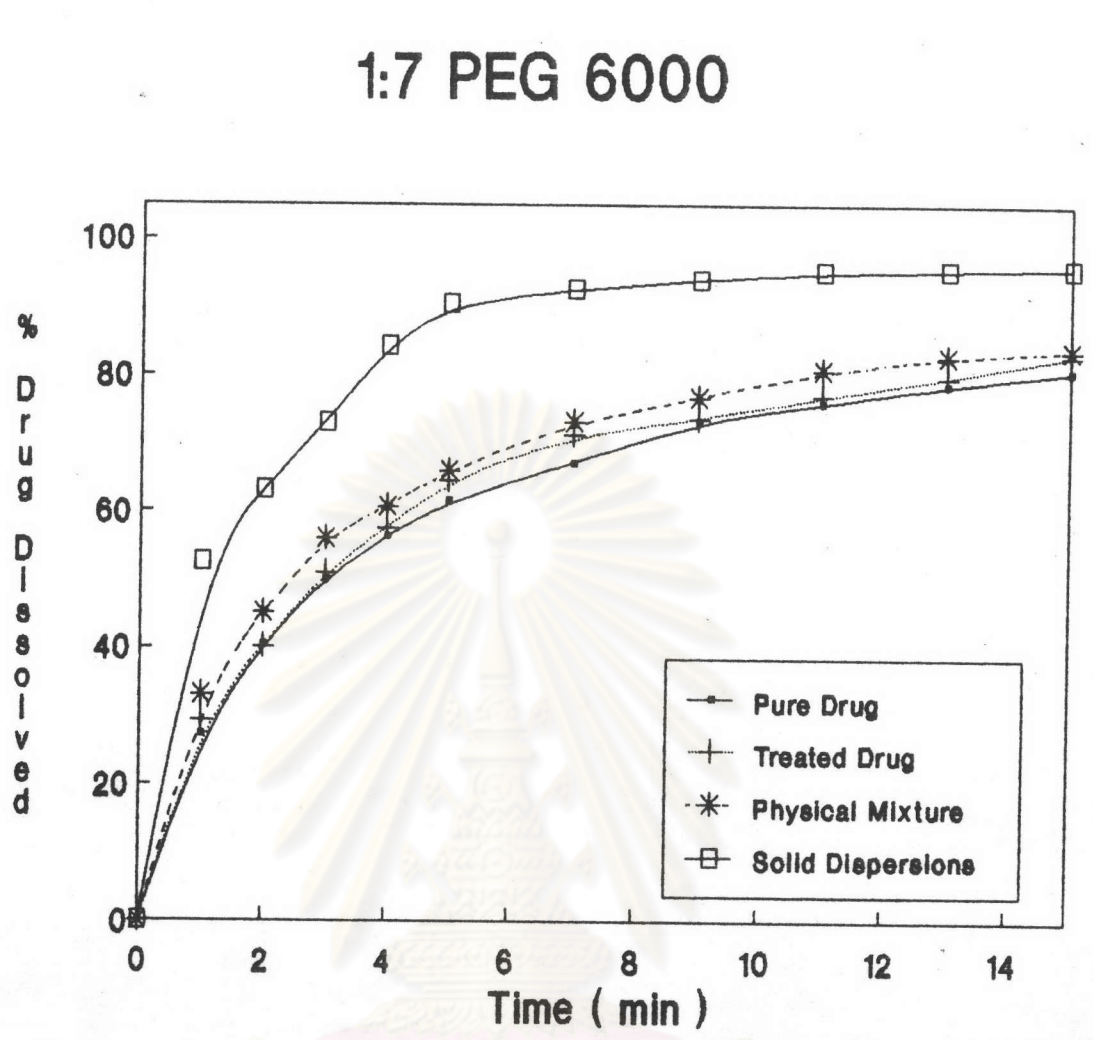


Figure 32 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and 1 : 7 ergoloid mesylate - PEG 6000 physical mixture and solid dispersion systems in 0.1 N. HCl at 37 ^{o} C

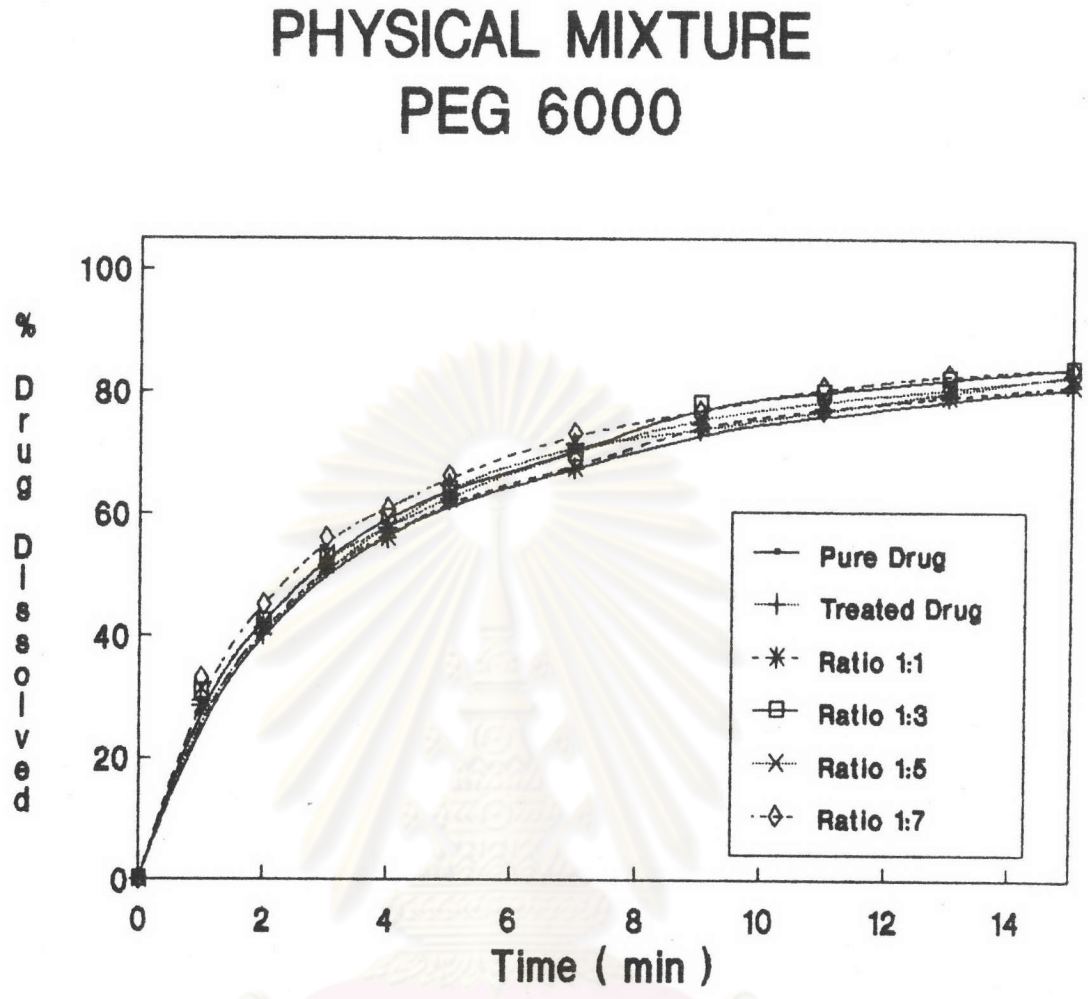


Figure 33 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and ergoloid mesylate physical mixture systems , using different ratio of PEG 6000 as the carriers , in 0.1 N. HCl at 37 ^{O} C

SOLID DISPERSIONS
PEG 6000

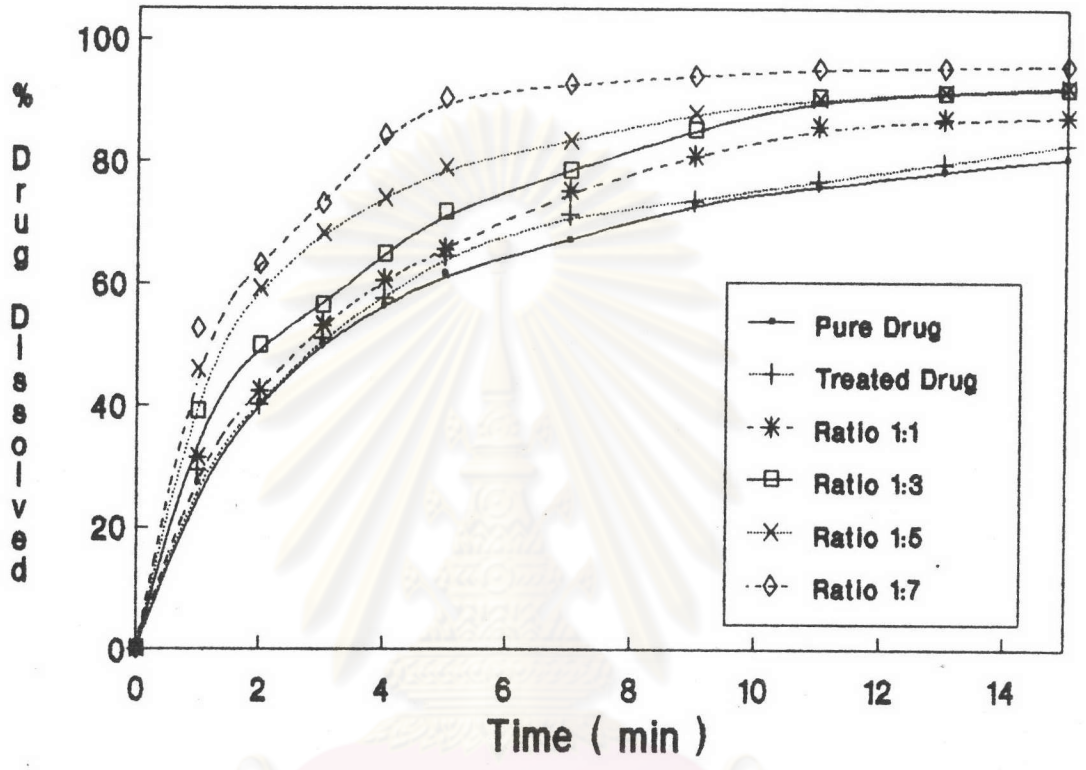


Figure 34 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and ergoloid mesylate solid dispersion systems , using different ratio of PEG 6000 as the carriers , in 0.1 N. HCl at 37 ^{o} C

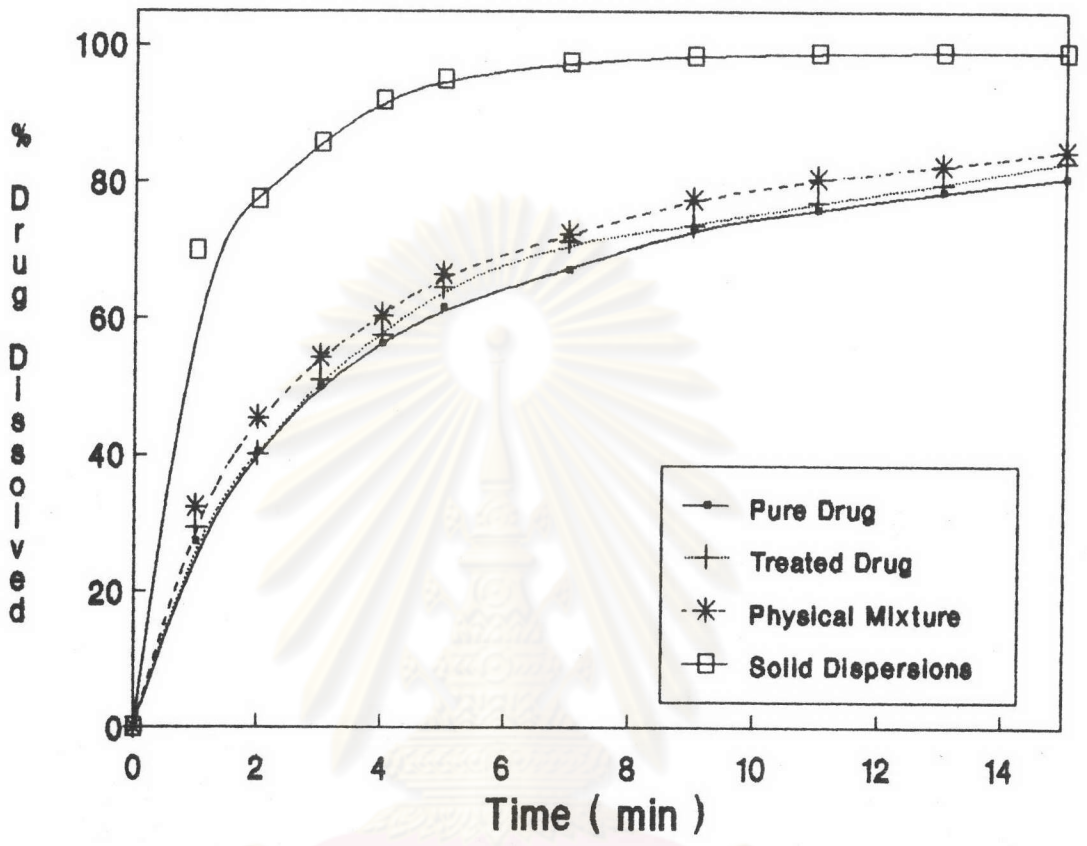


Figure 35 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and 1 : 1 ergoloid mesylate - poloxamer 188 physical mixture and solid dispersion systems in 0.1 N. HCl at 37 ^{o} C

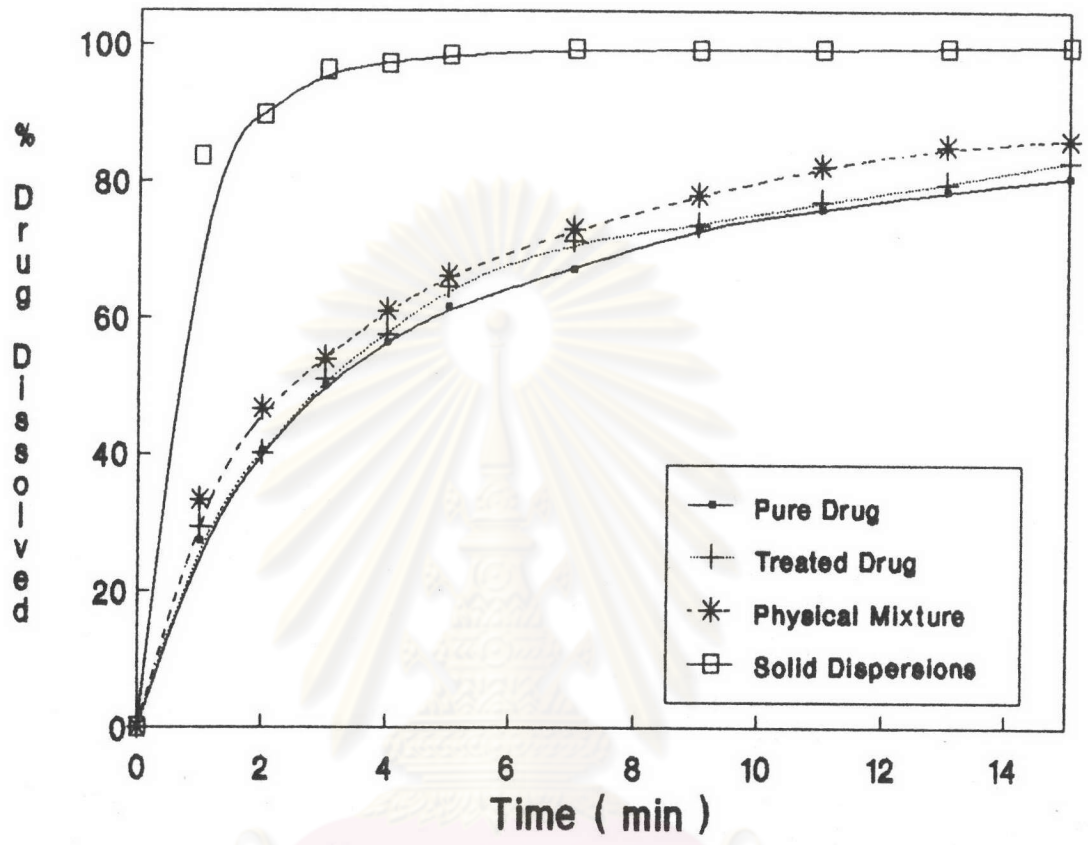


Figure 36 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and 1 : 3 ergoloid mesylate - poloxamer 188 physical mixture and solid dispersion systems in 0.1 N. HCl at 37 ^{o} C

1:5 POLOXAMER 188

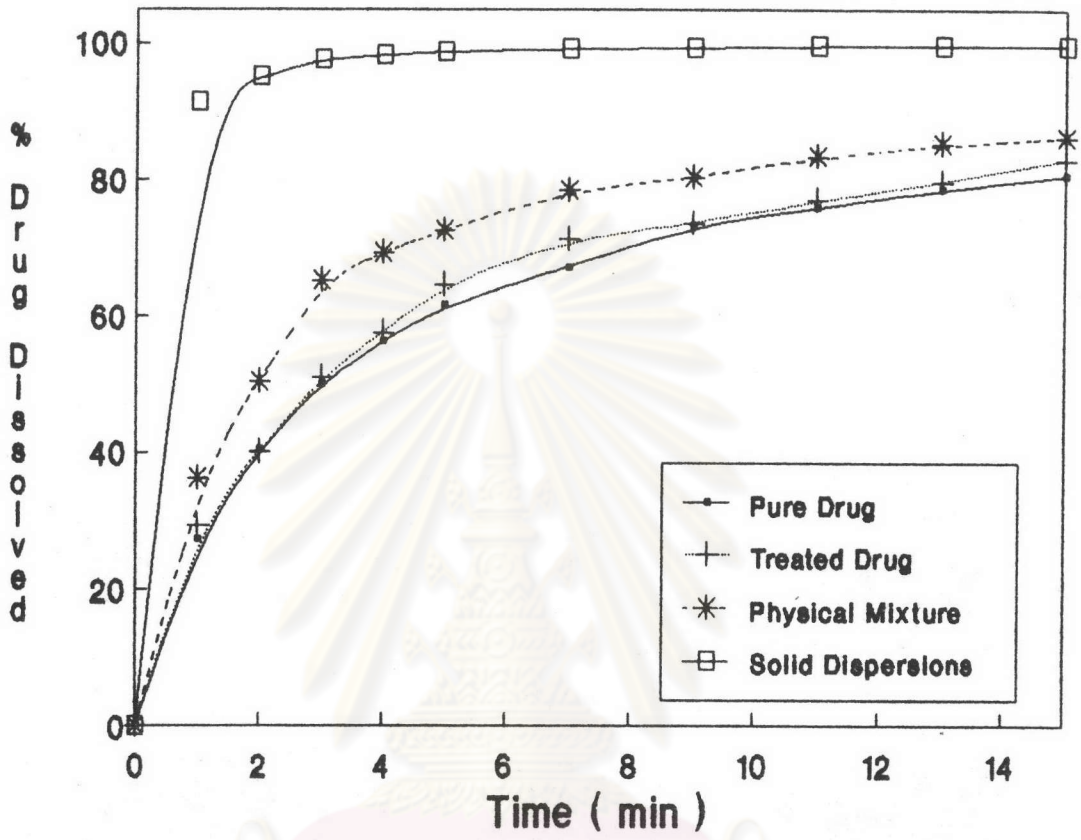


Figure 37 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and 1 : 5 ergoloid mesylate - poloxamer 188 physical mixture and solid dispersion systems in 0.1 N. HCl at 37 ^{o} C

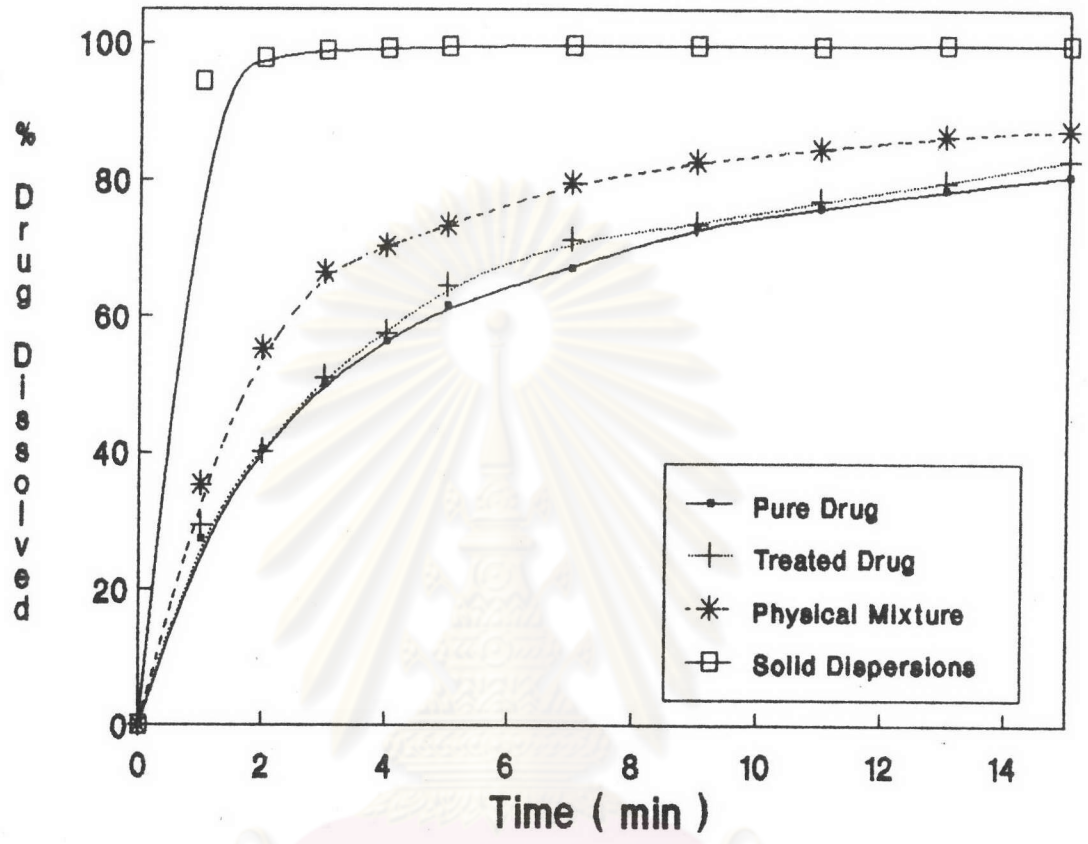


Figure 38 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and 1 : 7 ergoloid mesylate - poloxamer 188 physical mixture and solid dispersion systems in 0.1 N. HCl at 37 ^{o} C

SOLID DISPERSIONS
POLOXAMER 188

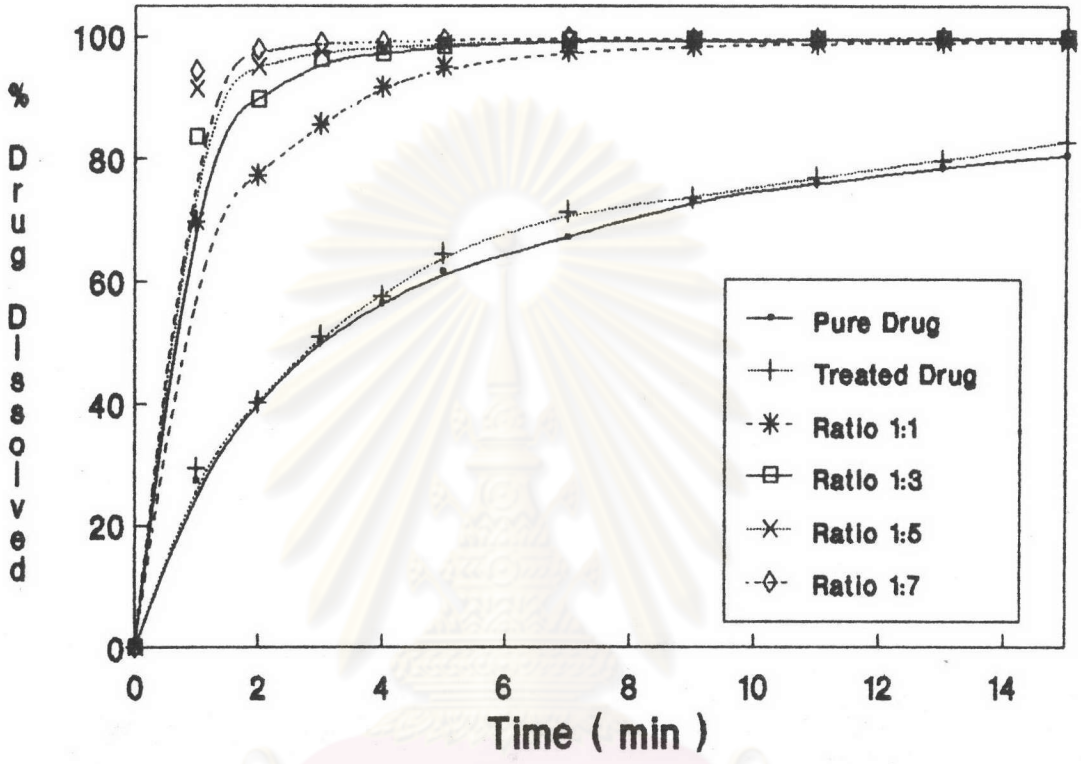


Figure 40 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and ergoloid mesylate solid dispersion systems , using different ratio of poloxamer 188 as the carriers , in 0.1 N. HCl at 37 ^{o} C

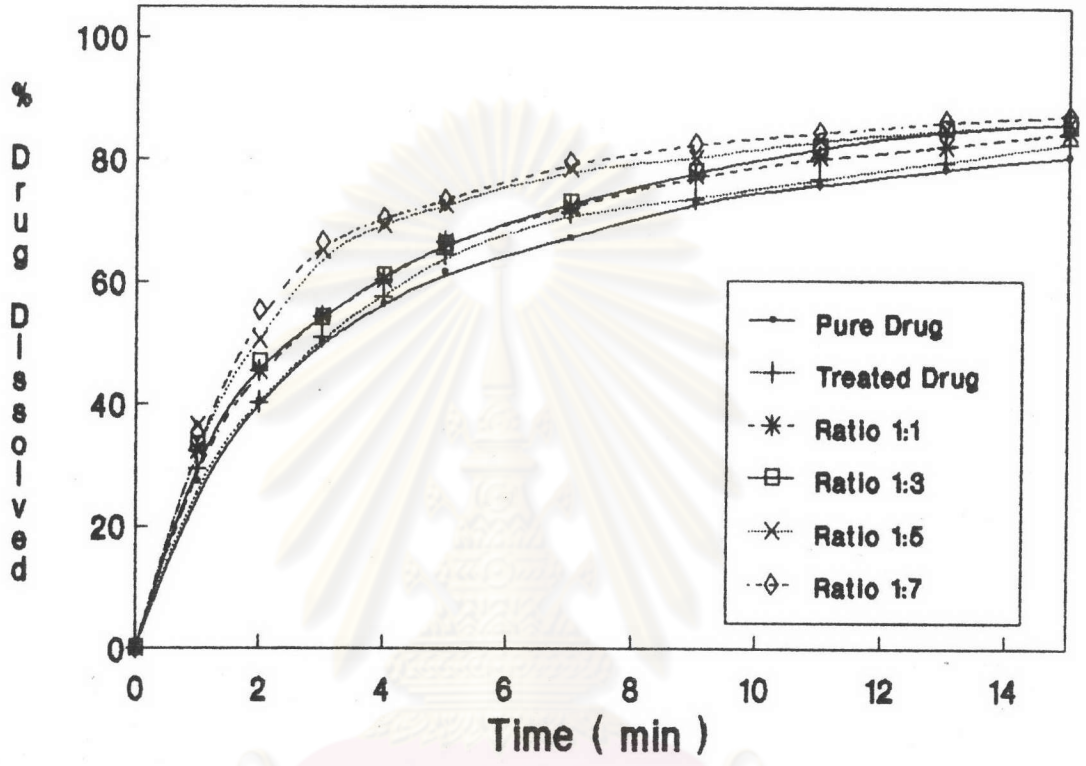


Figure 39 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and ergoloid mesylate physical mixture systems , using different ratio of poloxamer 188 as the carriers , in 0.1 N. HCl at 37 ^{o} C

By comparing dissolution data, the best system for improving ergoloid mesylate dissolution was the system of 1:7 ergoloid mesylate:poloxamer 188 solid dispersion followed by the solid dispersions of 1:5, 1:3, and 1:1 ergoloid mesylate:carrier, respectively. All four formulations of ergoloid mesylate:poloxamer 188 solid dispersions nearly gave 100% ergoloid mesylate dissolution within 15 minutes, while the physical mixtures and pure drug gave ergoloid mesylate dissolutions of 75-85%.

The similar dissolution profiles were obtained between the 1:1 and 1:3 ergoloid mesylate:poloxamer 188 physical mixture, but the dissolution profiles of them were lower than 1:5, and 1:7 ergoloid mesylate:poloxamer 188 physical mixture, respectively.

6. Ergoloid mesylate-mixture of 3% poloxamer 188 in PVP K-30

The dissolution parameters and dissolution profiles of ergoloid mesylate solid dispersions and physical mixture were demonstrated in Appendices 15-16 and Figures 41-45. All six preparations containing drug:carriers gave higher ergoloid mesylate dissolution than the treated and pure drug. Comparing with the physical mixtures, the solid dispersions of the same ratio drug:carrier gave markedly faster ergoloid mesylate dissolution rate. The complete ergoloid mesylate dissolution were obtained from the all ratios of solid dispersions while 80-85% ergoloid mesylate dissolutions were obtained from the physical

1:1 3 % POLOXAMER 188 IN PVP K-30

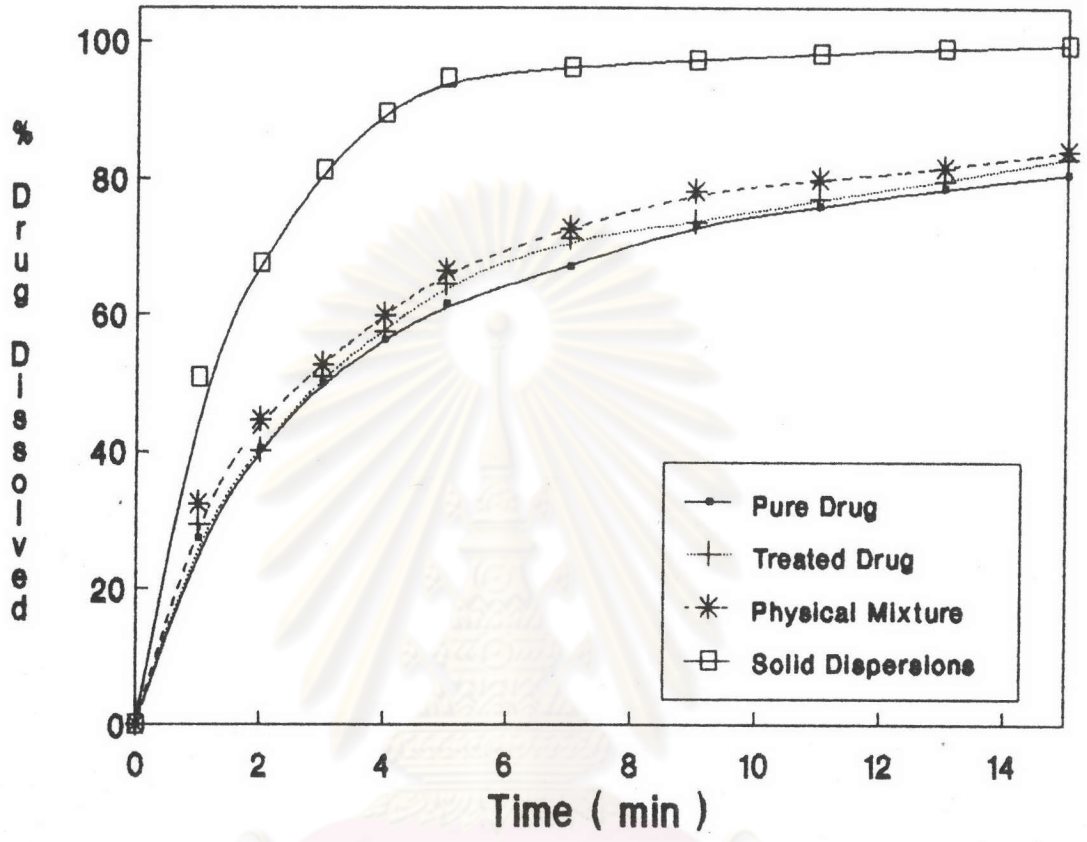


Figure 41 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and 1 : 1 ergoloid mesylate - mixture of 3 % poloxamer 188 in PVP K-30 physical mixture and solid dispersion systems in 0.1 N. HCl at 37 ^{o} C

1:4 3 % POLOXAMER 188 IN PVP K-30

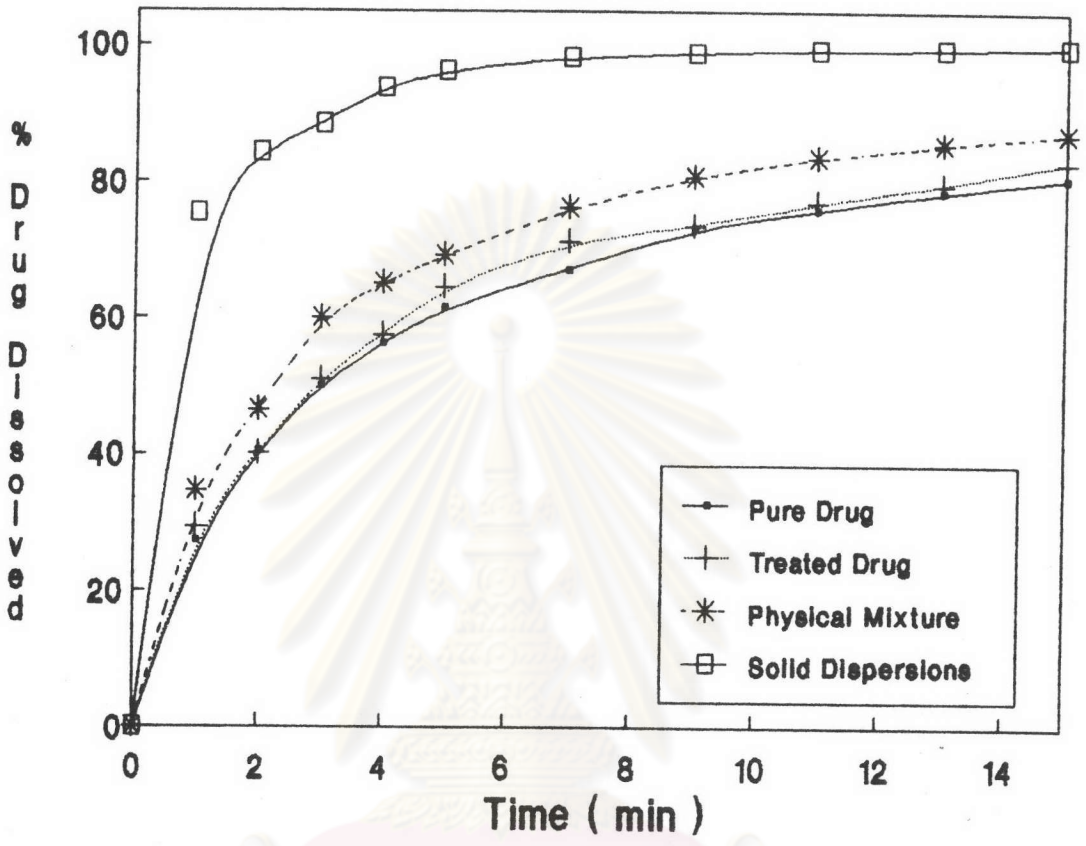


Figure 42 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and 1 : 4 ergoloid mesylate - mixture of 3 % poloxamer 188 in PVP K-30 physical mixture and solid dispersion systems in 0.1 N. HCl at 37 ^{o} C

1:6 3 % POLOXAMER 188 IN PVP K-30

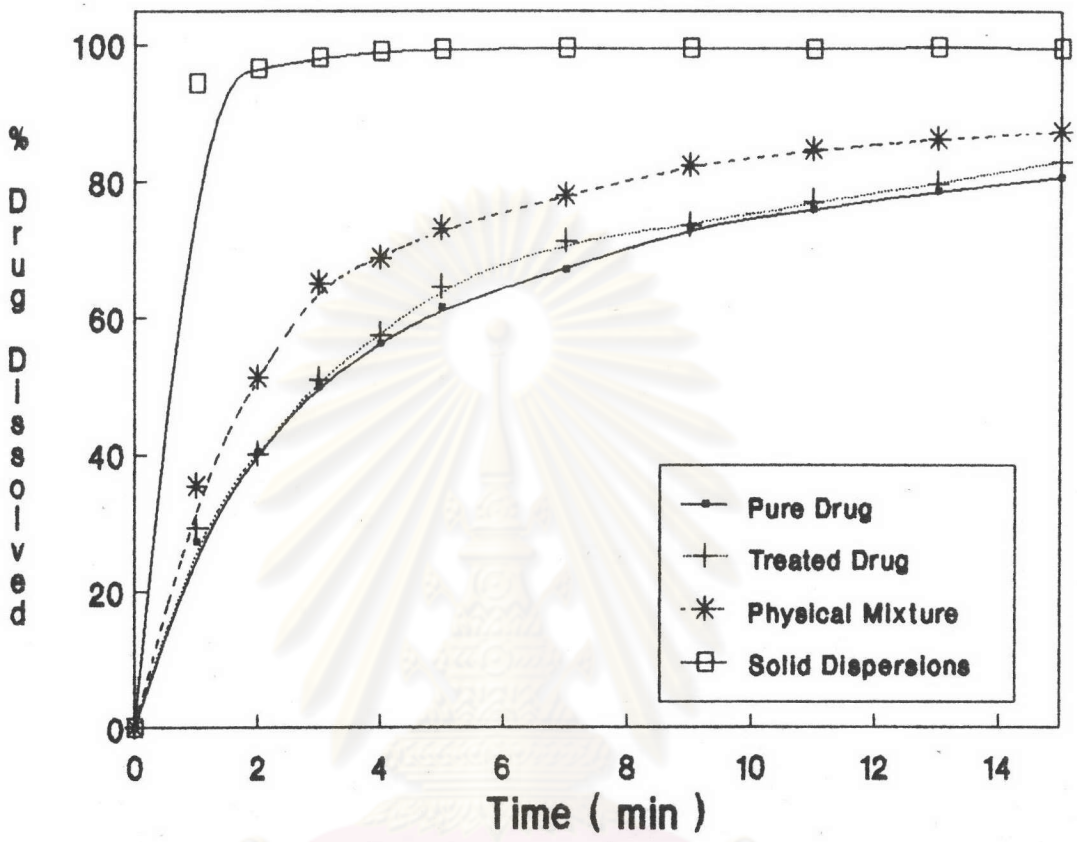


Figure 43 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and 1 : 6 ergoloid mesylate - mixture of 3 % poloxamer 188 in PVP K-30 physical mixture and solid dispersion systems in 0.1 N. HCl at 37 ^{o} C

PHYSICAL MIXTURE
3 % POLOXAMER 188 IN PVP K-30

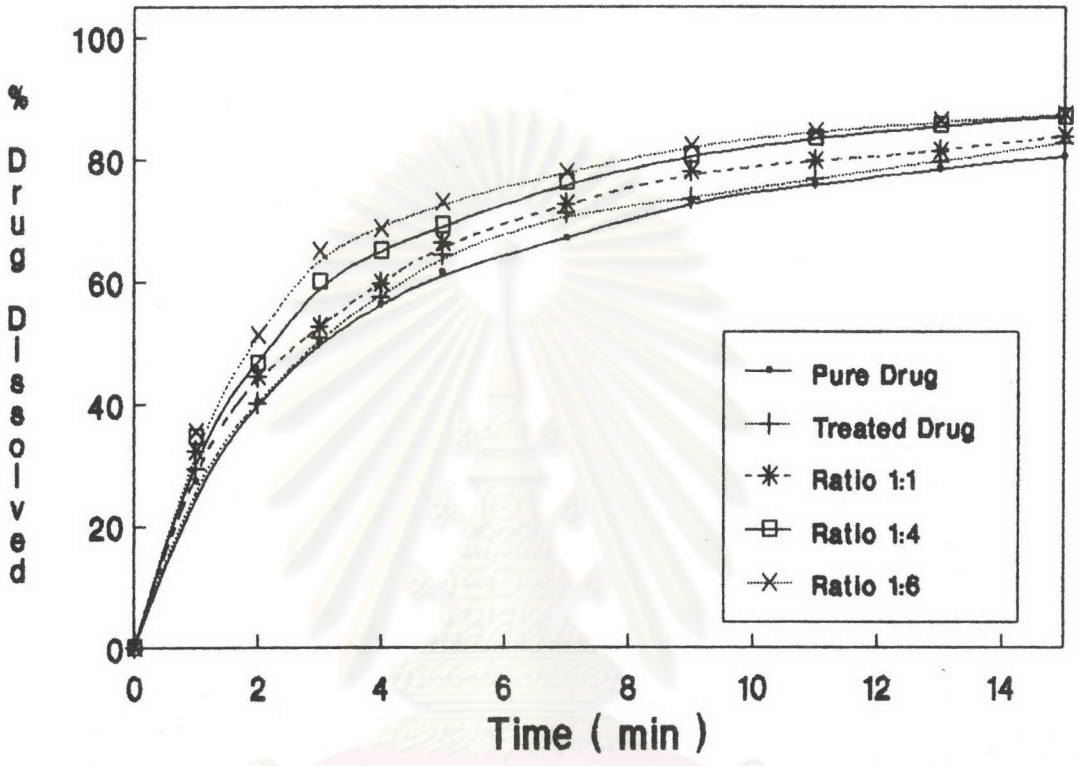


Figure 44 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and ergoloid mesylate physical mixture systems , using different ratio of mixture of 3 % poloxamer 188 in PVP K-30 as the carriers , in 0.1 N. HCl at 37 ^{o} C

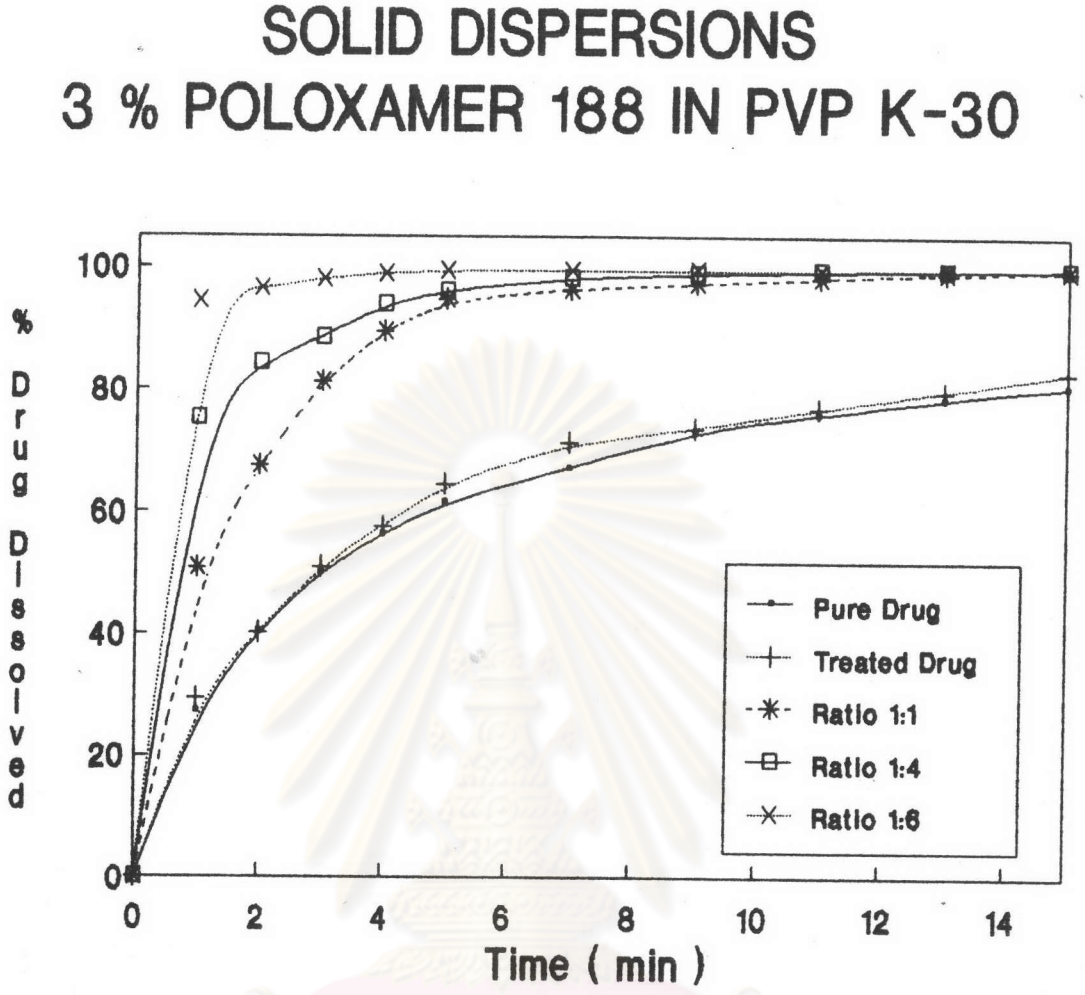


Figure 45 Dissolution profile of ergoloid mesylate from pure and treated ergoloid mesylate powder and ergoloid mesylate solid dispersion systems , using different ratio of mixture of 3 % poloxamer 188 in PVP K-30 as the carriers , in 0.1 N. HCl at 37 ^{o} C

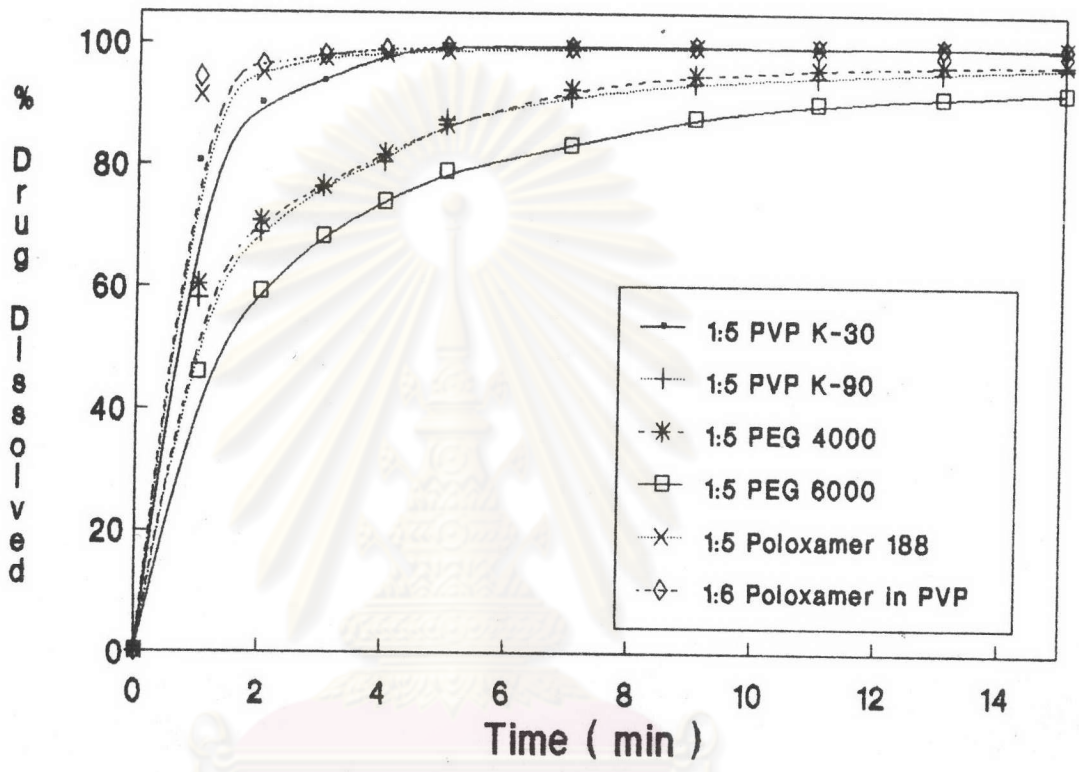


Figure 46 Dissolution profile of ergoloid mesylate from solid dispersion systems, using different carriers, in 0.1 N. HCl at 37 ^{O} C

mixtures and pure and treated drug after 15 minutes. Both solid dispersion and physical mixture, the dissolution of drug increased as the content of carriers increased.

Physicochemical properties of ergoloid mesylate powders

1. Morphology of Powders

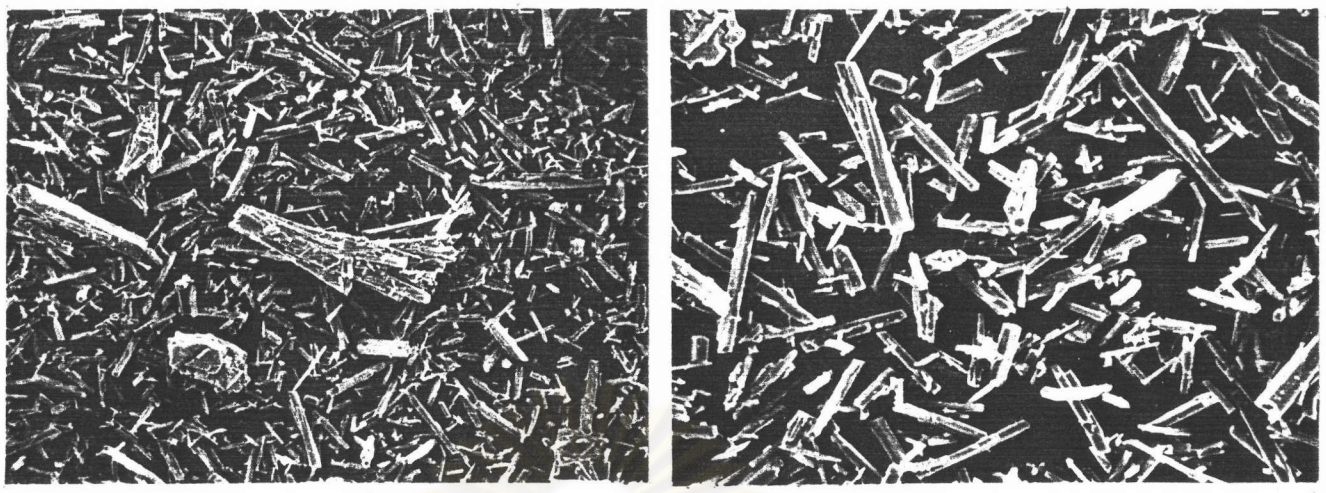
Photomicrographs of pure drug, treated drug, carriers and all types of 1:5 dispersion systems (Physical mixture and solid dispersions), except mixture of 3% Poloxamer 188 in PVP K-30 dispersion systems-the 1:4 drug:carrier, were presented in Figures 47-65 with different magnifications. The general shape and surface topography could be observed.

1.1 Pure ergoloid mesylate and treated ergoloid mesylate

The microscopic appearances of pure ergoloid mesylate and treated ergoloid mesylate powder were shown in Figures 47 and 48, respectively. Pure ergoloid mesylate powder composed of needle shape in various length, and the surface of powder was smooth. While most particle of treated ergoloid mesylate were irregular shape and different size with the irregular surface.

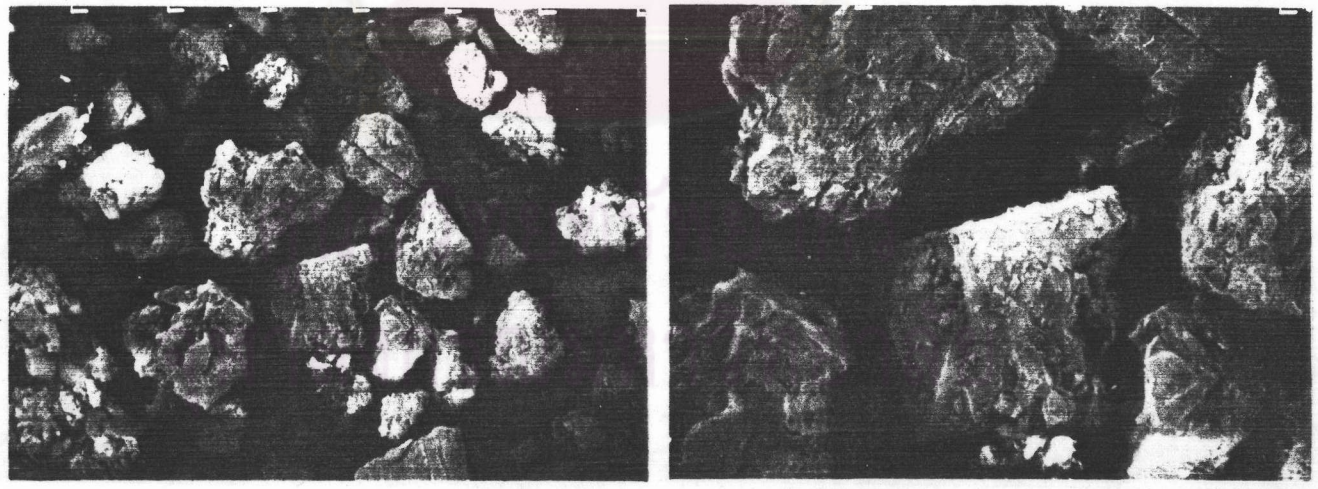
1.2 Ergoloid Mesylate - PVP K-30 Systems

The SEM photomicrographs of PVP K-30 and 1:5 drug:carrier ratio of physical mixture and solid dispersions in different magnification were displayed in Figures 49-51. Particles of PVP K-30 possessed round shape with the basin-like



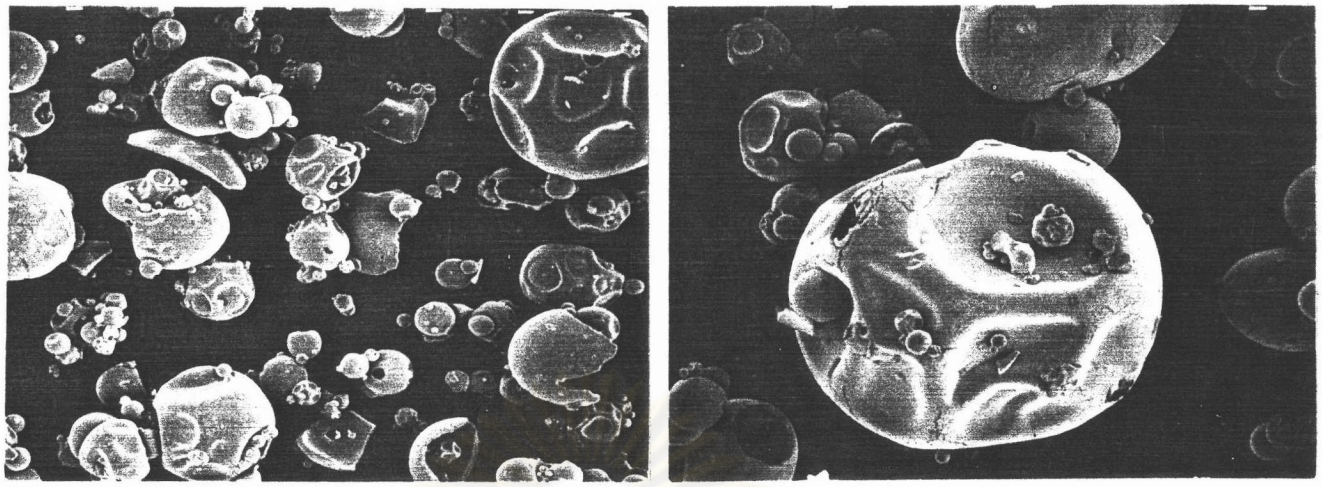
A B

Figure 47 SEM photomicrographs of pure ergoloid mesylate in magnifications X150 (A) and X350 (B)



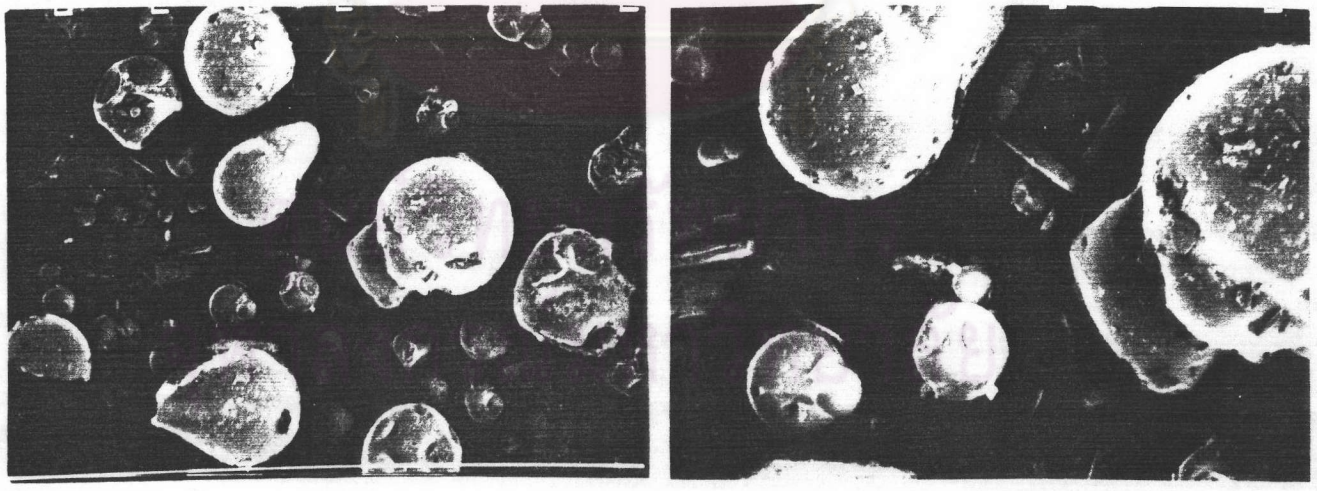
A B

Figure 48 SEM photomicrographs of treated ergoloid mesylate in magnifications X150 (A) and X350 (B)



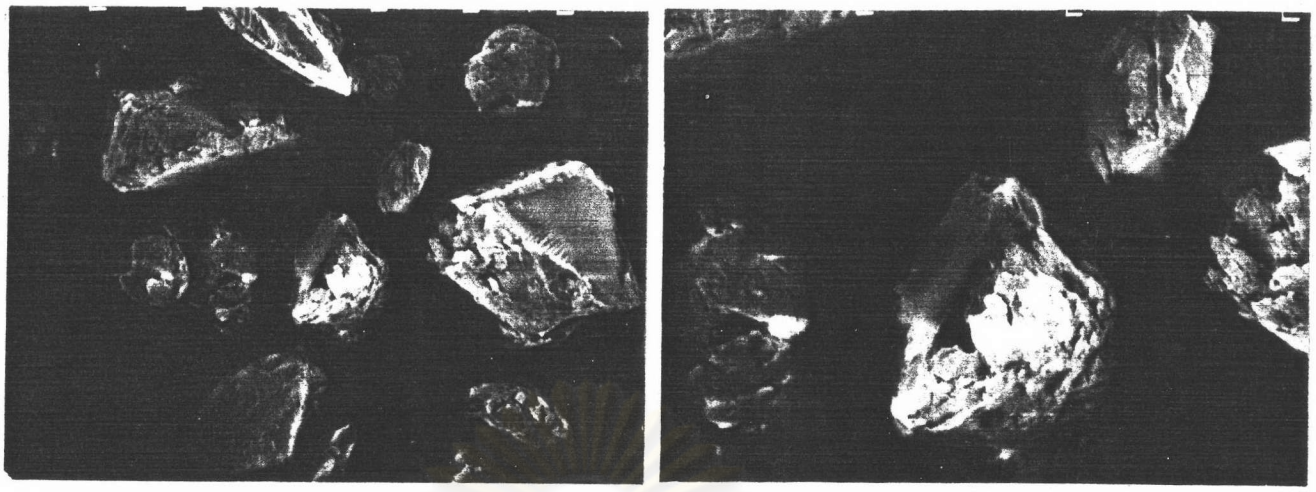
A B

Figure 49 SEM photomicrographs of PVP K-30 in magnifications X150 (A) and X350 (B)



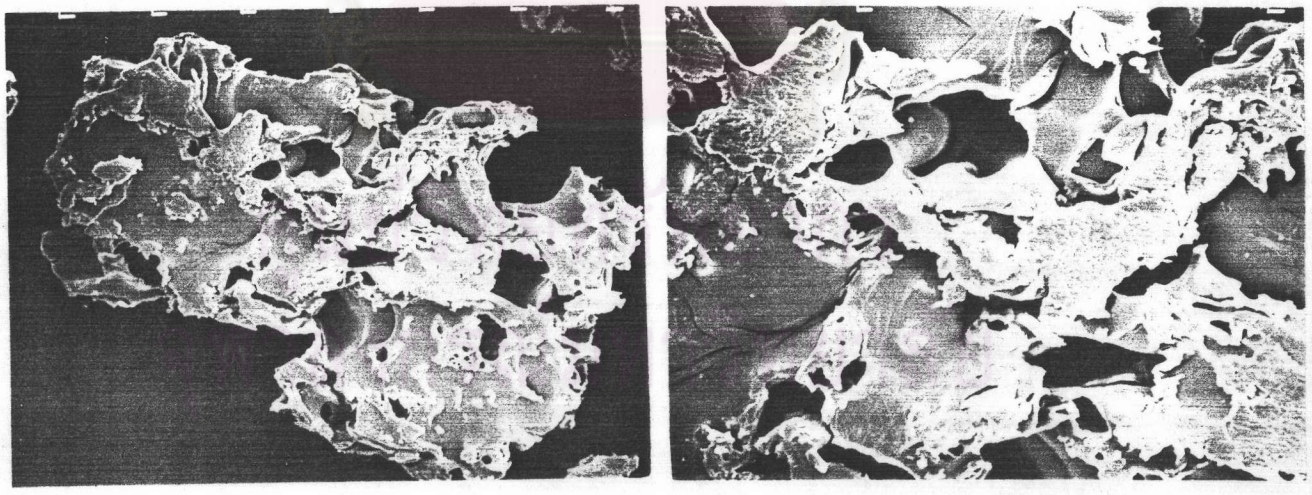
A B

Figure 50 SEM photomicrographs of 1 : 5 ergoloid mesylate - PVP K-30 physical mixture systems in magnifications X150 (A) and X350 (B)



A B

Figure 51 SEM photomicrographs of 1 : 5 ergoloid mesylate - PVP K-30 solid dispersions systems in magnifications X150 (A) and X350 (B)



A B

Figure 52 SEM photomicrographs of PVP K-90 in magnifications X150 (A) and X350 (B)

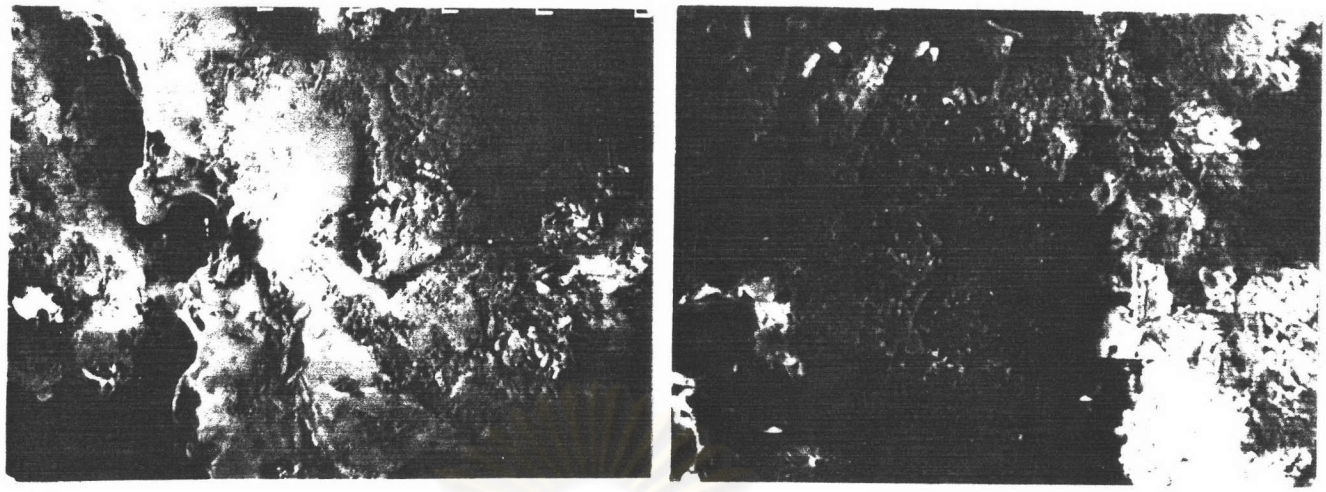
on the surface. Some microspherical particles of PVP K-30 agglomerated together. In physical mixture, the ergoloid mesylate particles were found in two sizes, one as thick needle shape, sepatated from PVP K-30 particles, the other as fine needle shape, adhered on the PVP K-30 particles. While the solid dispersions, the shape of particles was irregular with different size. The surface topography of solid dispersions particle were not smooth.

1.3 Ergoloid mesylate-PVP K-90 system

The microscopic image of these system were depicted in Figures 52-54. Big flakes with rugged surface topograghy like dense sponge were observed in the PVP K-90 particle. In physical mixture, most needle particles of ergoloid mesylate mostly adhered on the surface of PVP K-90 particle. The particles of PVP K-90 solid dispersions were similar to PVP K-30 solid dispersions system but the particle size was relatively bigger than PVP K-30 solid dispersions particles.

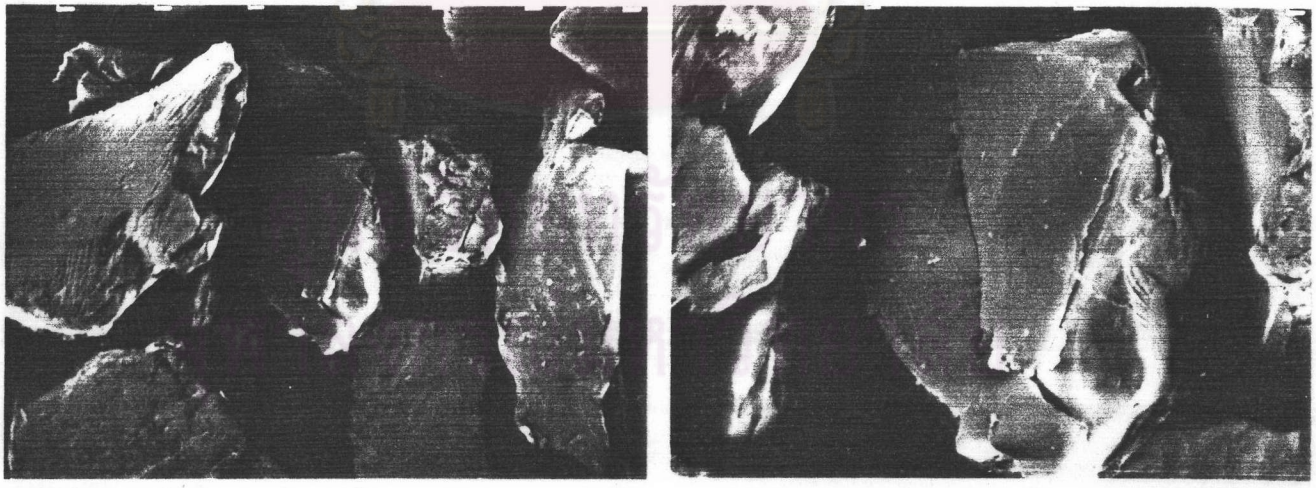
1.4 Ergoloid mesylate-PEG 4000 system

The microsopic appearances of PEG 4000 dispersion systems were introduced in Figures 55-57. PEG 4000 powder composed of irregular shaped particles in various big size with rough surface. In physical mixture, was shown in Figure 56, the surface of PEG 4000 was covered with ergoloid mesylate particle. Solid dispersion particles (Figure 57) constituted of irregular shapes and size, like the PEG 4000 particle, but the size was smaller than PEG 4000 particle.



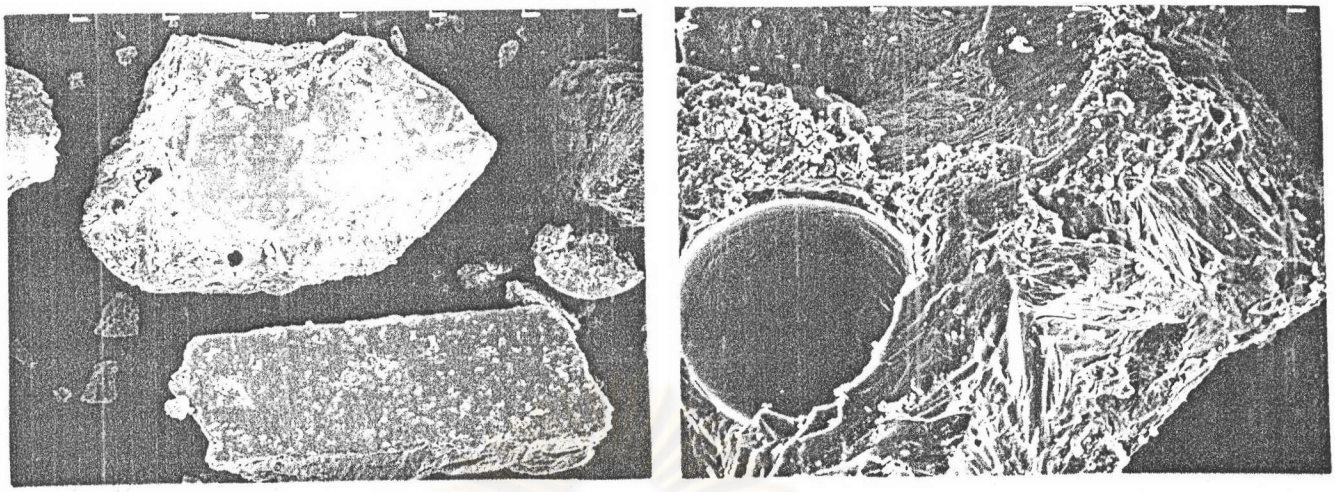
A B

Figure 53 SEM photomicrographs of 1 : 5 ergoloid mesylate - PVP K-90 physical mixture systems in magnifications X150 (A) and X350 (B)



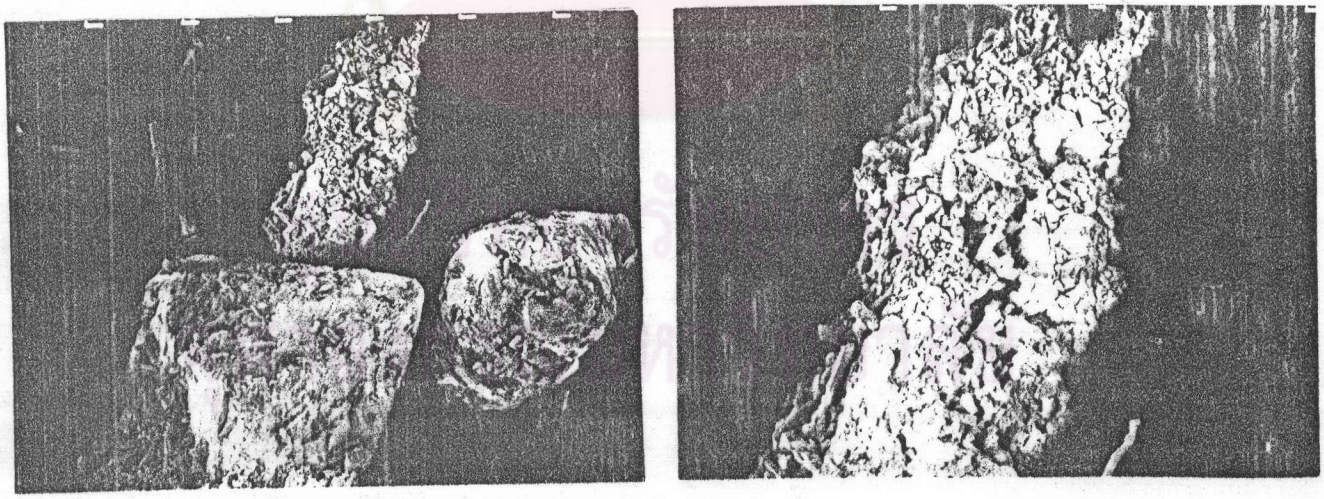
A B

Figure 54 SEM photomicrographs of 1 : 5 ergoloid mesylate - PVP K-90 solid dispersions systems in magnifications X150 (A) and X350 (B)



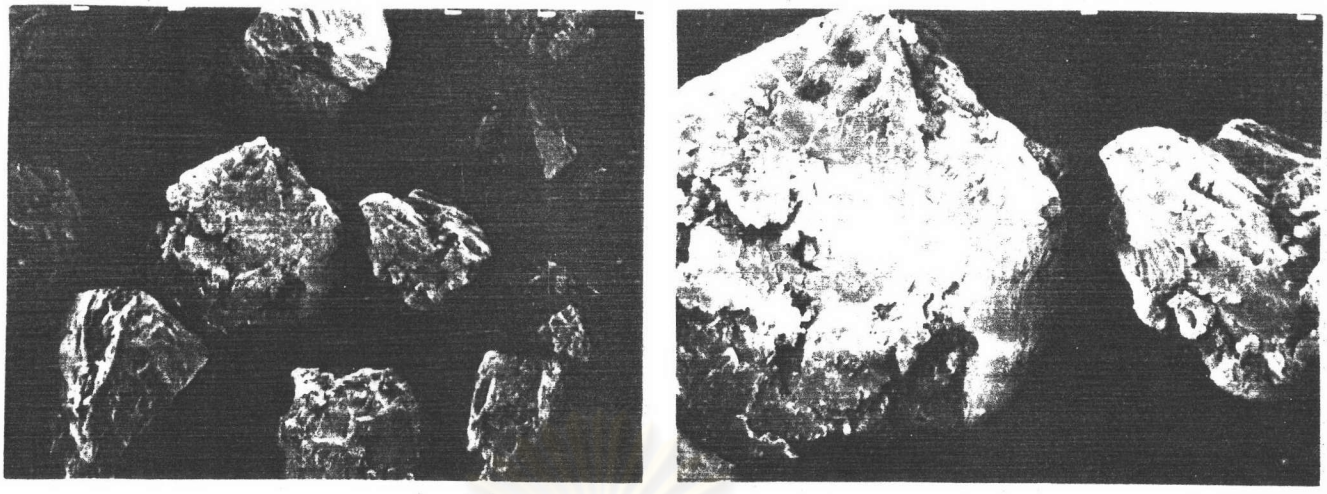
A B

Figure 55 SEM photomicrographs of PEG 4000 in magnifications X150 (A) and X350 (B)



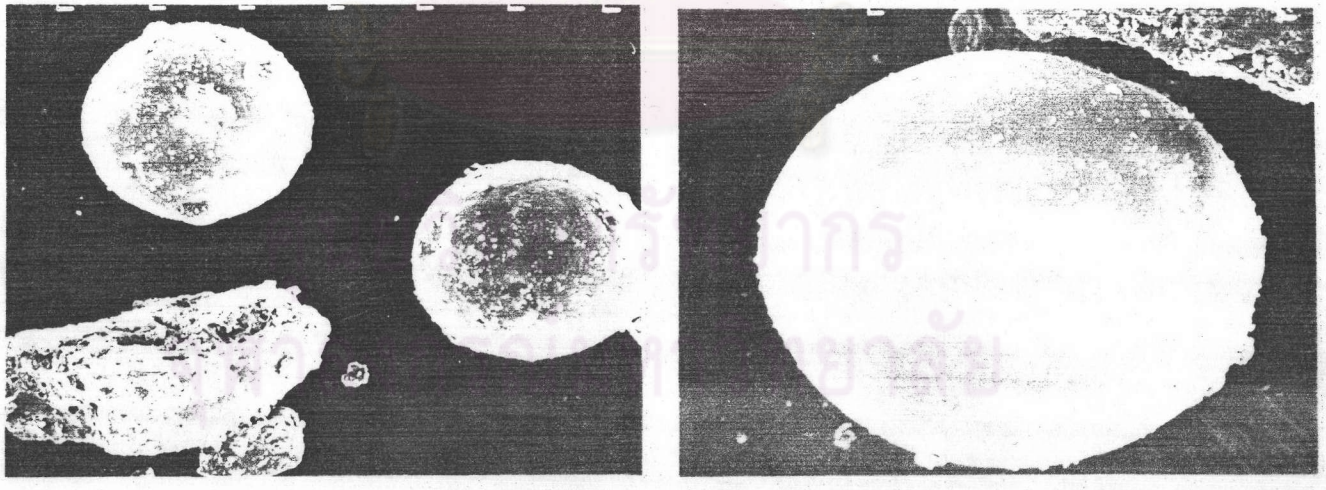
A B

Figure 56 SEM photomicrographs of 1 : 5 ergoloid mesylate - PEG 4000 physical mixture systems in magnifications X150 (A) and X350 (B)



A B

Figure 57 SEM photomicrographs of 1 : 5 ergoloid mesylate - PEG 4000 solid dispersions systems in magnifications X150 (A) and X350 (B)



A B

Figure 58 SEM photomicrographs of PEG 6000 in magnifications X150 (A) and X350 (B)

1.5 Ergoloid mesylate-PEG 6000 system

PEG 6000 powders (Figure 58) consisted of particles in two types of shapes; sphere and irregular. The smooth surface was found on the sphere shape particles while the rough surface was found on the irregular one. In physical mixture (Figure 59), some ergoloid mesylate particles bound to the surface of PEG 6000 and others was in free form. Figure 60 showed the PEG 6000 solid dispersions system. It was similar to other solid dispersions systems.

1.6 Ergoloid mesylate-poloxamer 188 system

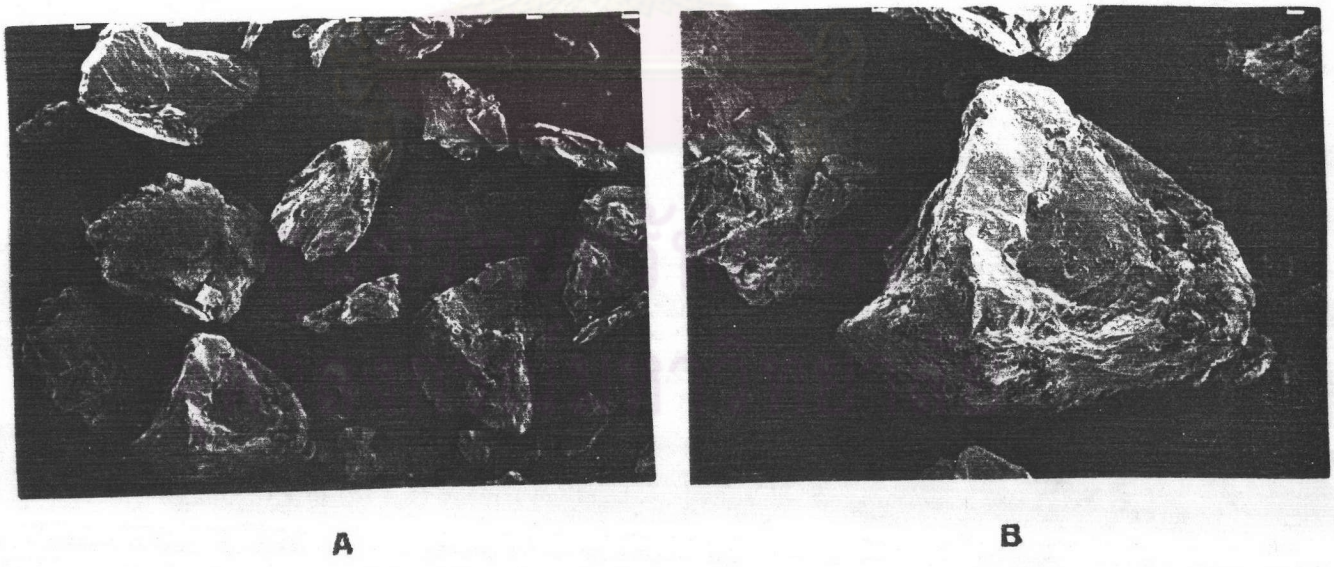
Photomicrograph of pure poloxamer 188 was exhibited in Figure 61. It showed rugged surface, like lichen coated rock and the shape as well as size were irregular. Figure 62 presented the physical mixture,of which the surface topography aws similar to PEG 6000 physical mixture system. While in the solid dispersions, most particles were in irregular shape and size, like a broken brick, with rough surface.

1.7 Ergoloid mesylate mixture of 3 % poloxamer 188 in PVP K-30 system

The microscopic images of 1:4 drug:carrier physical mixture and solid dispersion systems were depicted in Figures 64 and 65. The physical mixture of these system resembled to the physical mixture system of PVP K-30 and poloxamer 188. In the same way, the solid dispersion system was similar to solid

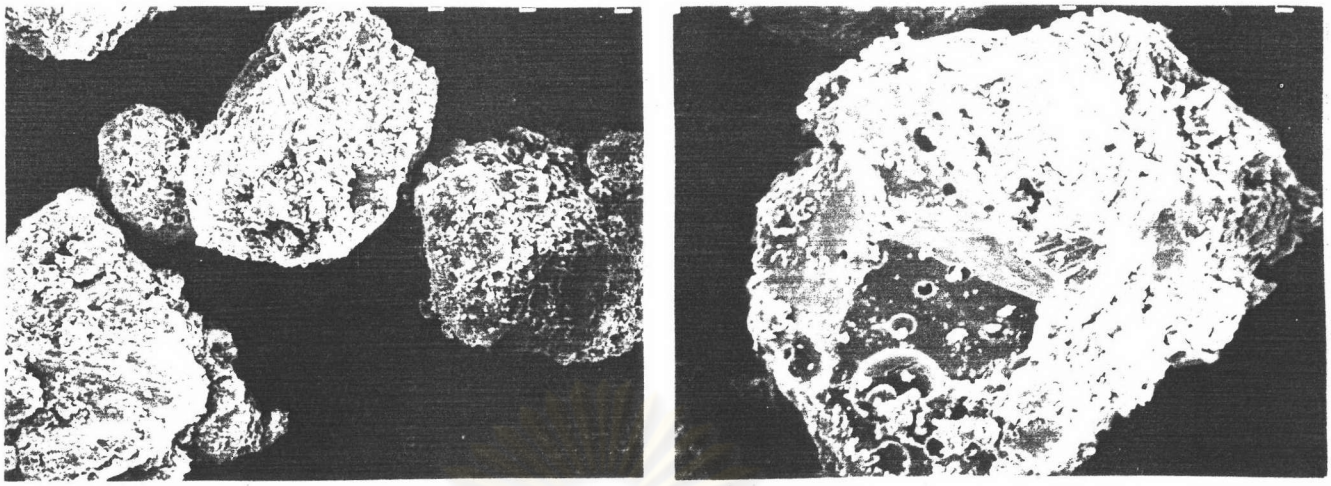
A B

Figure 59 SEM photomicrographs of 1 : 5 ergoloid mesylate - PEG 6000 physical mixture systems in magnifications X150 (A) and X350 (B)



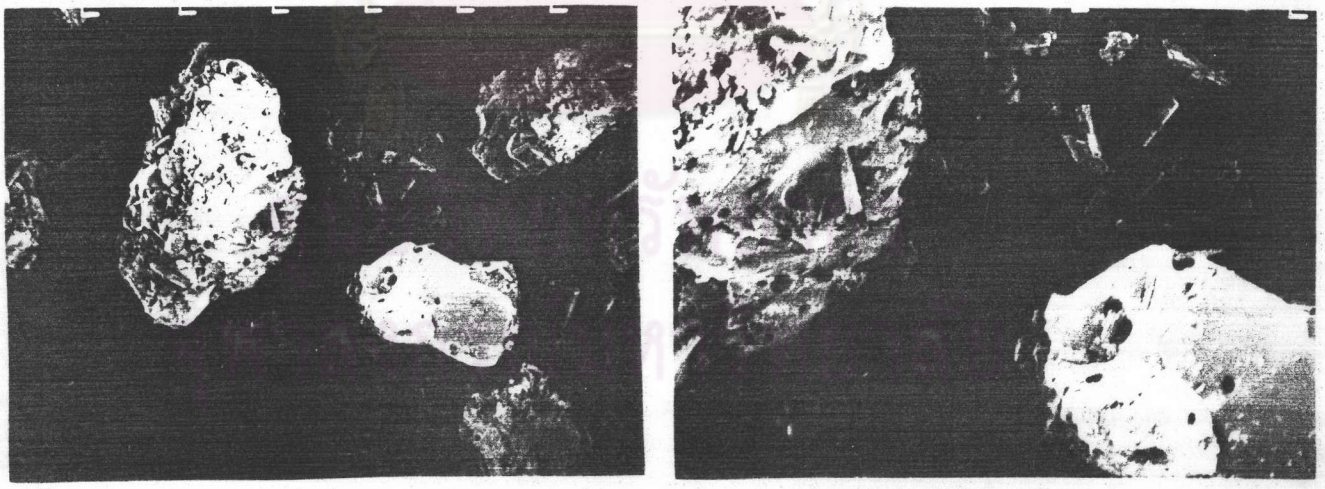
A B

Figure 60 SEM photomicrographs of 1 : 5 ergoloid mesylate - PEG 6000 solid dispersions systems in magnifications X150 (A) and X350 (B)



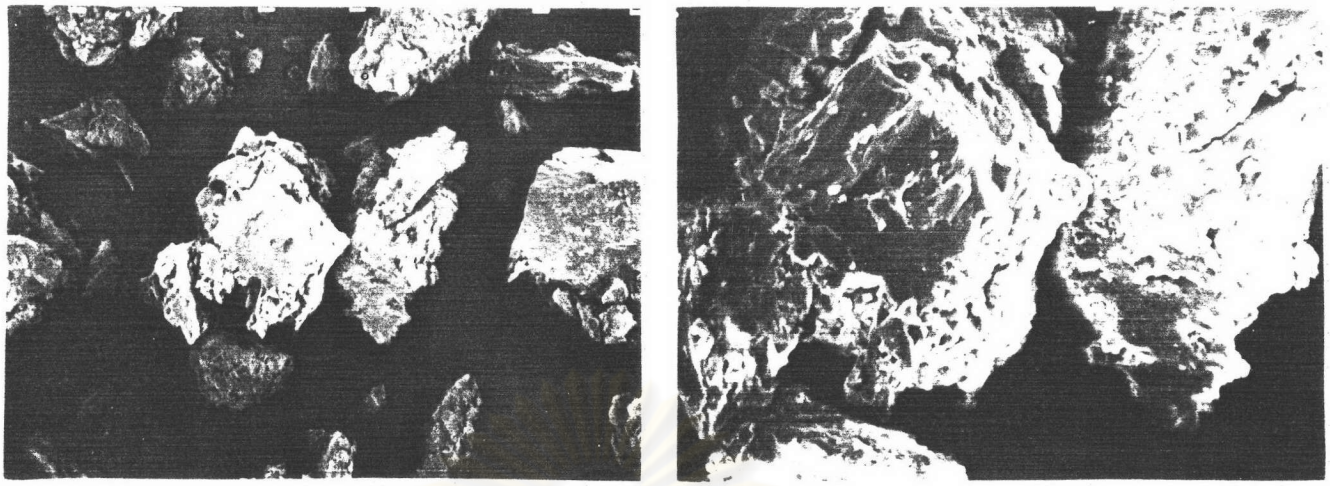
A B

Figure 61 SEM photomicrographs of poloxamer 188 in magnifications X150 (A) and X350 (B)



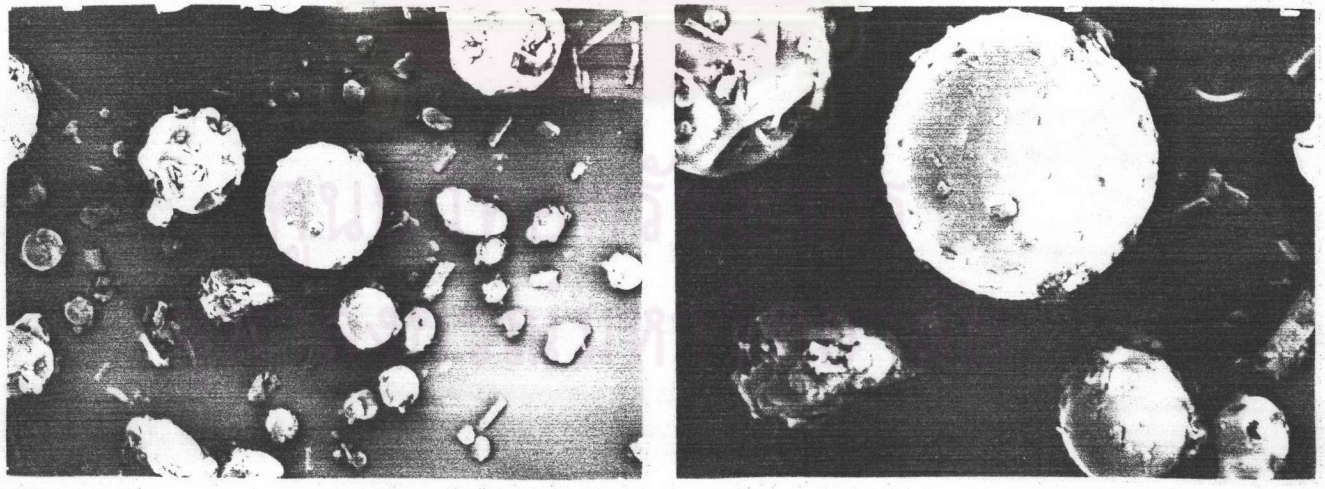
A B

Figure 62 SEM photomicrographs of 1 : 5 ergoloid mesylate - poloxamer 188 physical mixture systems in magnifications X150 (A) and X350 (B)



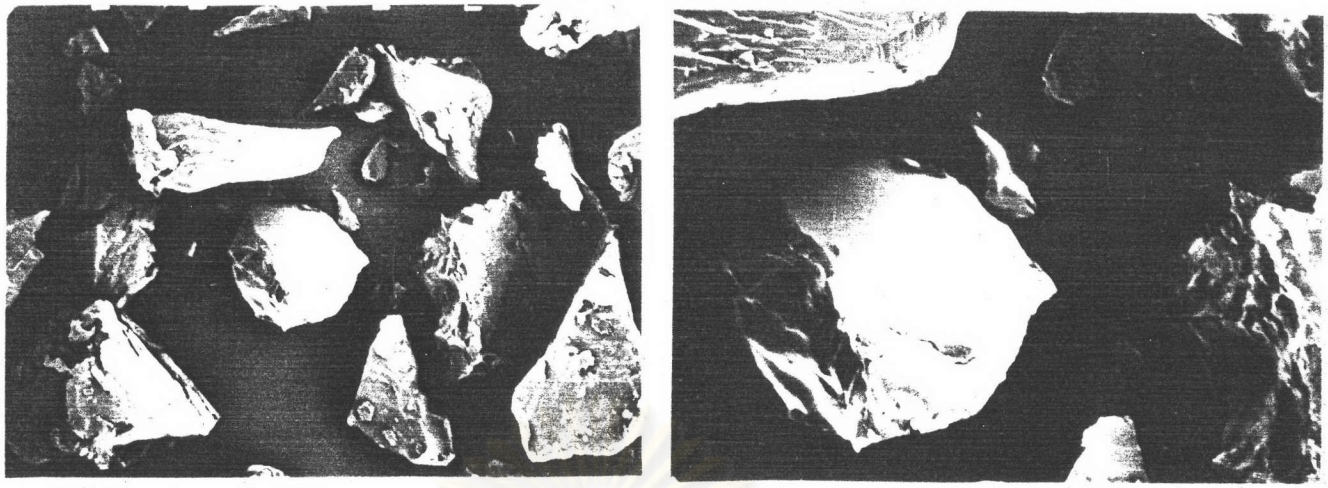
A B

Figure 63 SEM photomicrographs of 1 : 5 ergoloid mesylate - poloxamer 188 solid dispersions systems in magnifications X150 (A) and X350 (B)



A B

Figure 64 SEM photomicrographs of 1 : 5 ergoloid mesylate - mixture of 3 % poloxamer 188 in PVP K-30 physical mixture systems in magnifications X150 (A) and X350 (B)



A B

Figure 65 SEM photomicrographs of 1 : 5 ergoloid mesylate - mixture of 3 % poloxamer 188 in PVP K-30 solid dispersions systems in magnifications X150 (A) and X350 (B)

dispersion system of PVP K-30 and poloxamer 188.

2. Infrared spectra

The IR spectra of pure ergoloid mesylate, carriers, physical mixtures and solid dispersions, using various carriers, were presented in Figures 66-71. At the bottom of every IR spectra system, it showed the peak of ergoloid mesylate -- at 3400 $cm.^{-1}$ resulted from O-H and N-H stretching, at 1750 $cm.^{-1}$ resulted from C=O stretching of five member ring, peak between 1700-1600 $cm.^{-1}$ resulted from C=O stretching of six member ring and amide group, respectively, at 1550 $cm.^{-1}$ resulted from C-H bending, and at 1200 $cm.^{-1}$ resulted from C-O stretching. The absorption band characteristic of ergoloid mesylate was almost unaffected in every dispersion system except little scattering peak in solid dispersion systems.

3. DTA thermograms

Thermograms of pure ergoloid mesylate, carriers, solid dispersions, and physical mixtures of ergoloid mesylate and various carriers were shown in Figures 72-77. The thermogram of pure drug gave the characteristic melting endotherm at 160^{o}, 196^{o}, and 203^{o} while PVP and PEG showed the melting endotherm at 65^{o} and $75^{o}C$, respectively. Poloxamer 188 showed melting endotherm at $58^{o}C$. Ergoloid mesylate-PVP (1:5) solid dispersion system exhibited the characteristic melting endotherm of PVP but not that of ergoloid mesylate (Figures 72-73). In physical mixture systems the thermograms combined the features of the thermograms of each component. But ergoloid mesylate showed only

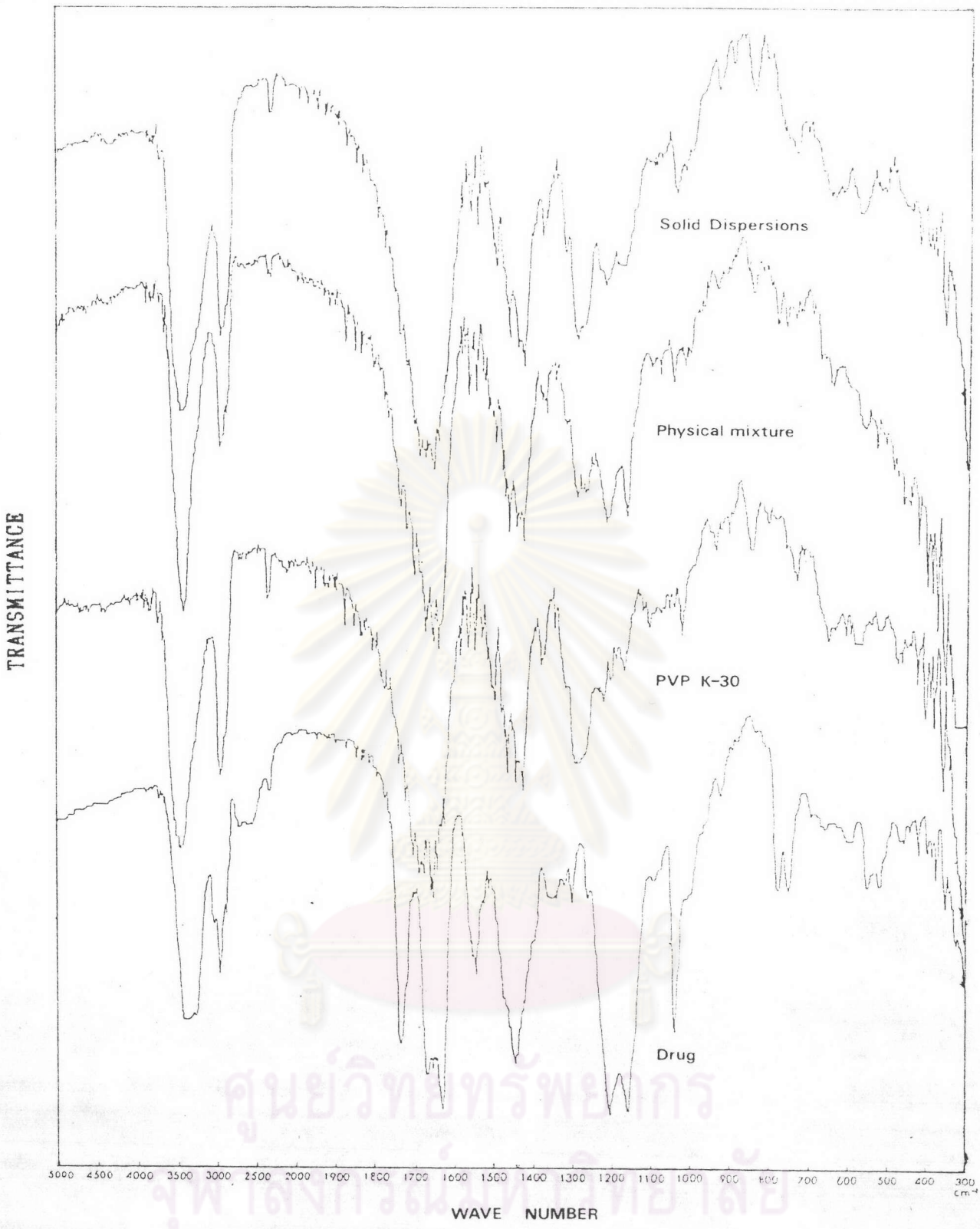


Figure 66 IR spectra of pure ergoloid mesylate , PVP K-30 and 1:5 ergoloid mesylate - PVP K-30 physical mixture and solid dispersions in KBr disks

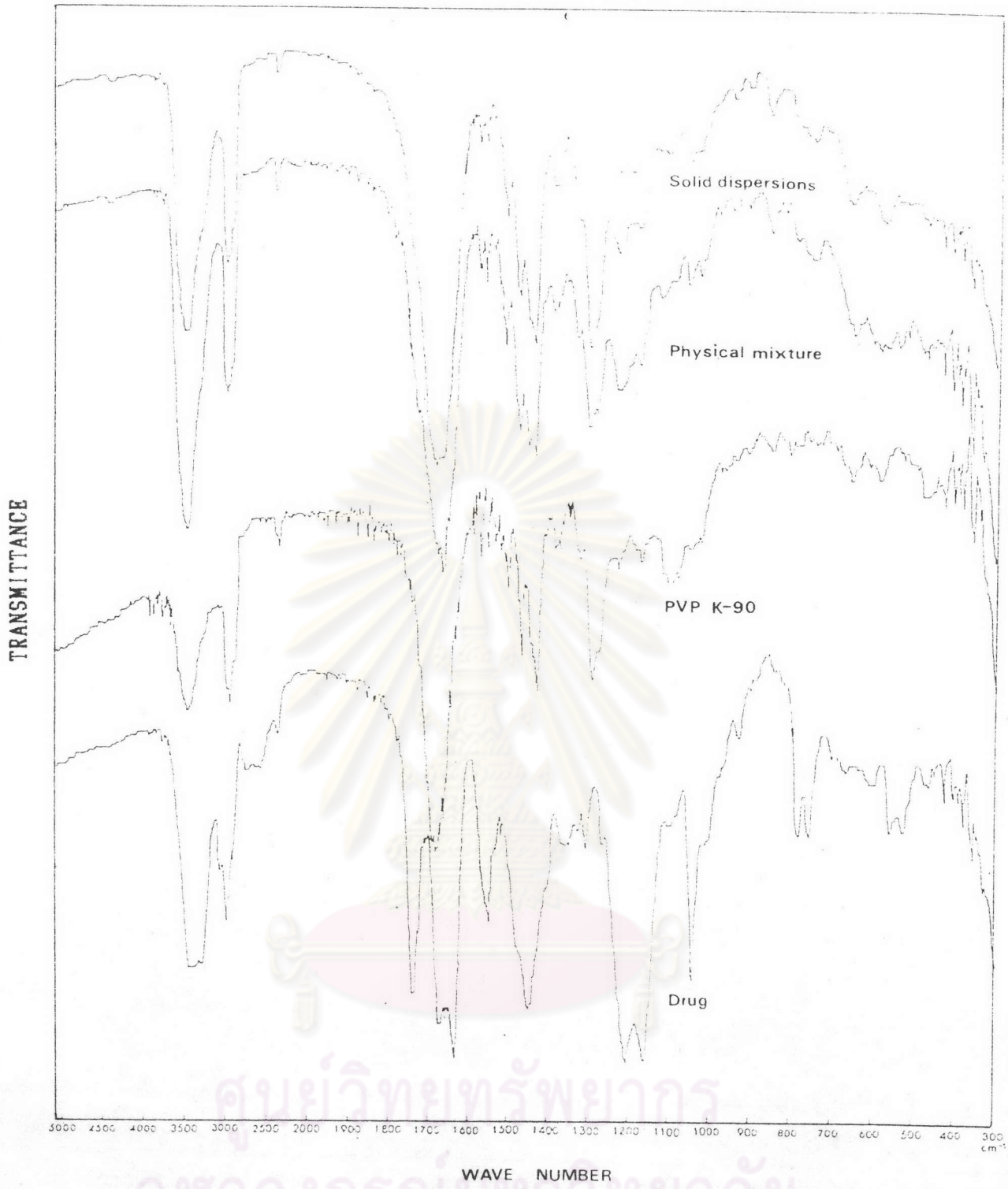


Figure 67 IR spectra of pure ergoloid mesylate , PVP K-90 and 1:5 ergoloid mesylate - PVP K-90 physical mixture and solid dispersions in KBr disks

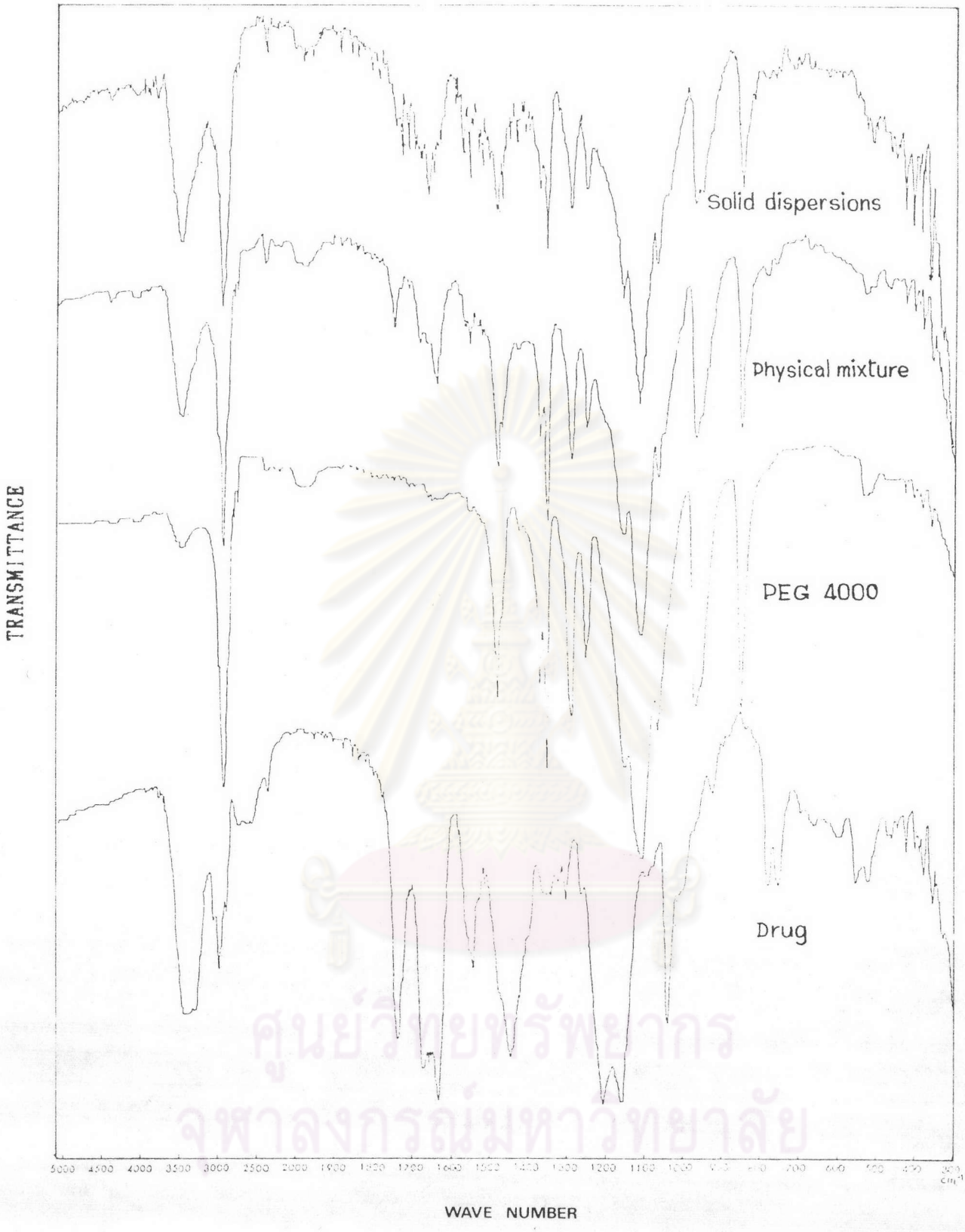


Figure 68 IR spectra of pure ergoloid mesylate , PEG 4000 and 1:5 ergoloid mesylate - PEG 4000 physical mixture and solid dispersions in KBr disks

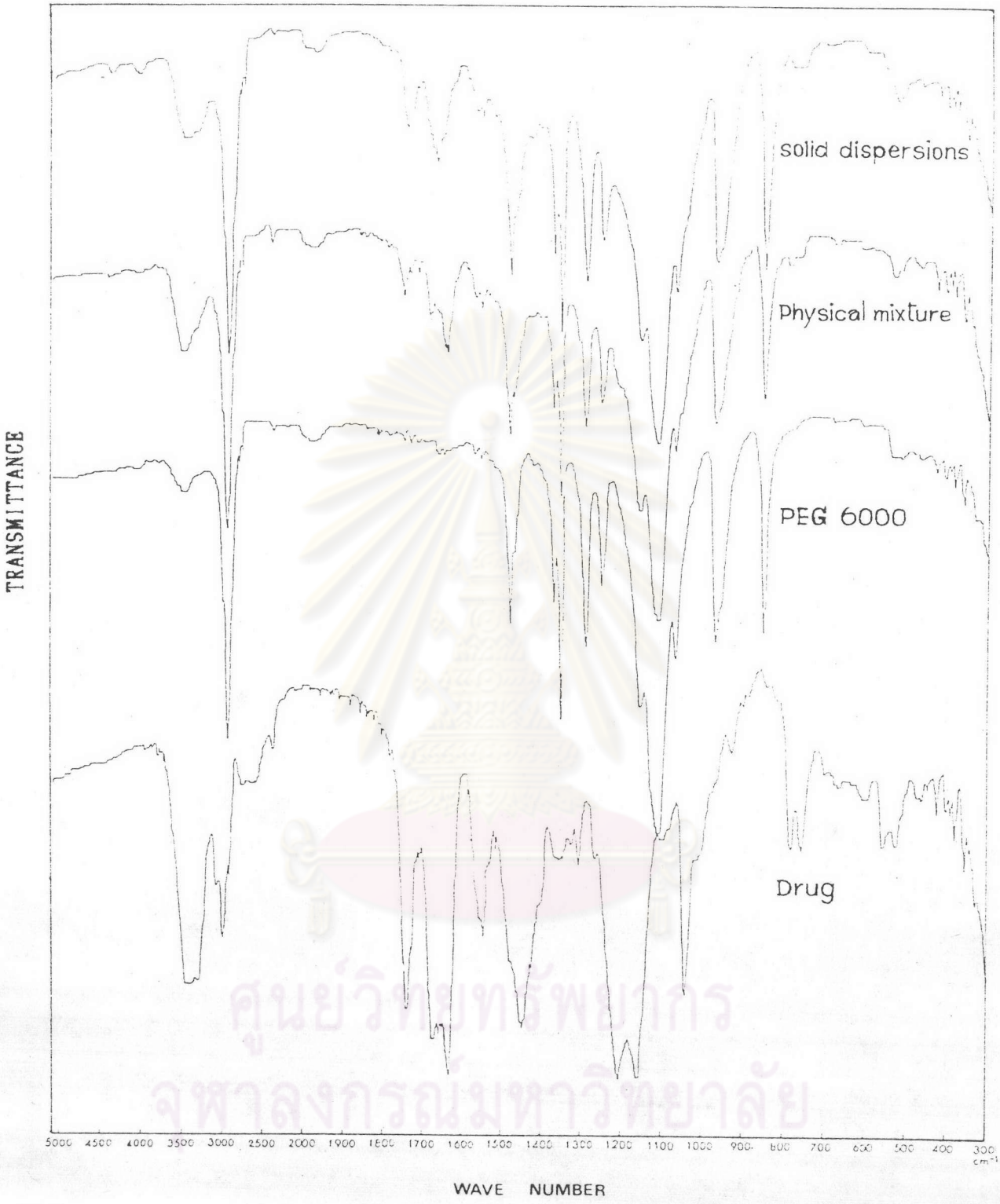


Figure 69 IR spectra of pure ergoloid mesylate , PEG 6000 and 1:5 ergoloid mesylate - PEG 6000 physical mixture and solid dispersions in KBr disks

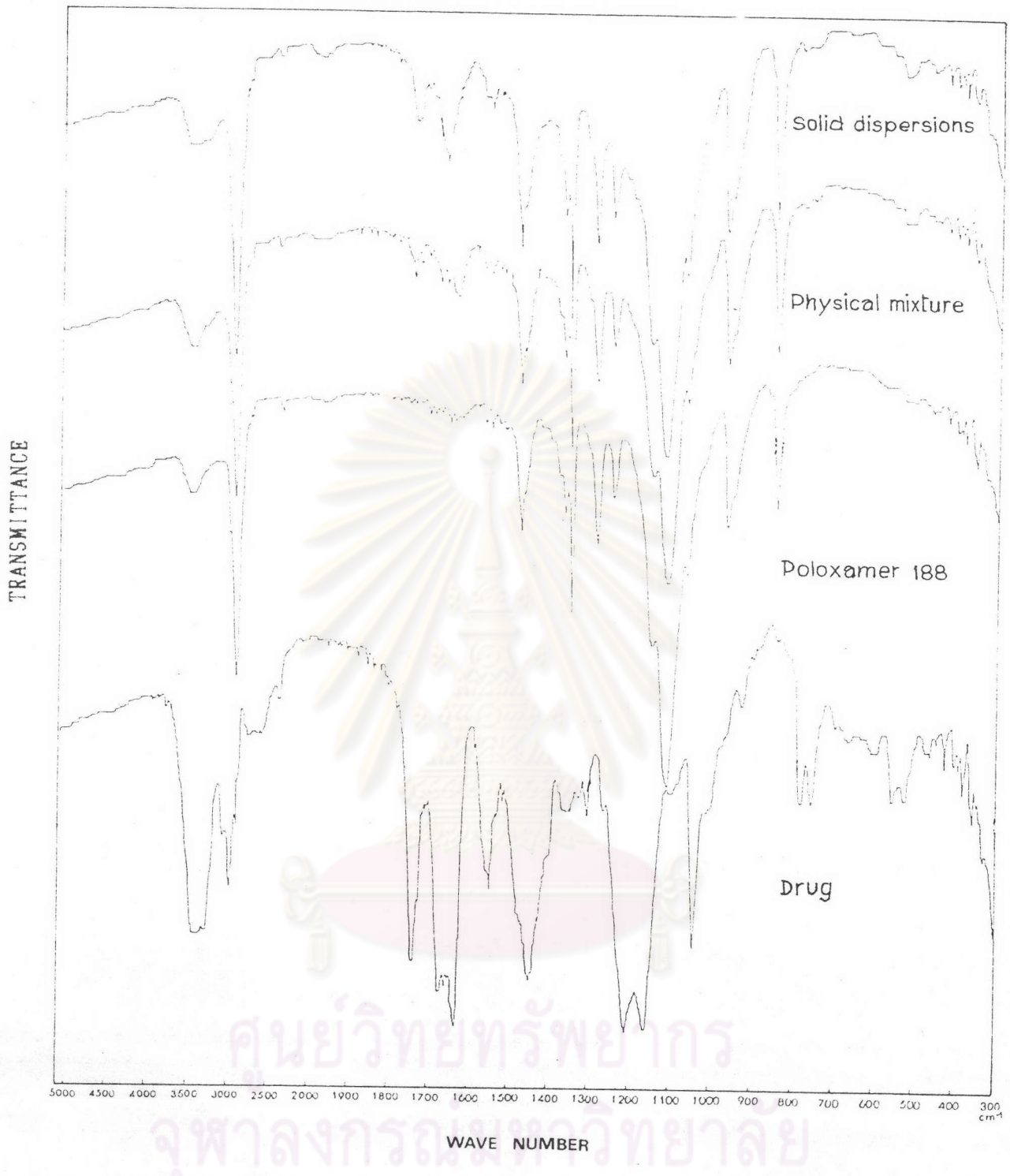


Figure 70 IR spectra of pure ergoloid mesylate , poloxamer 188 and 1:5 ergoloid mesylate - poloxamer 188 physical mixture and solid dispersions in KBr disks

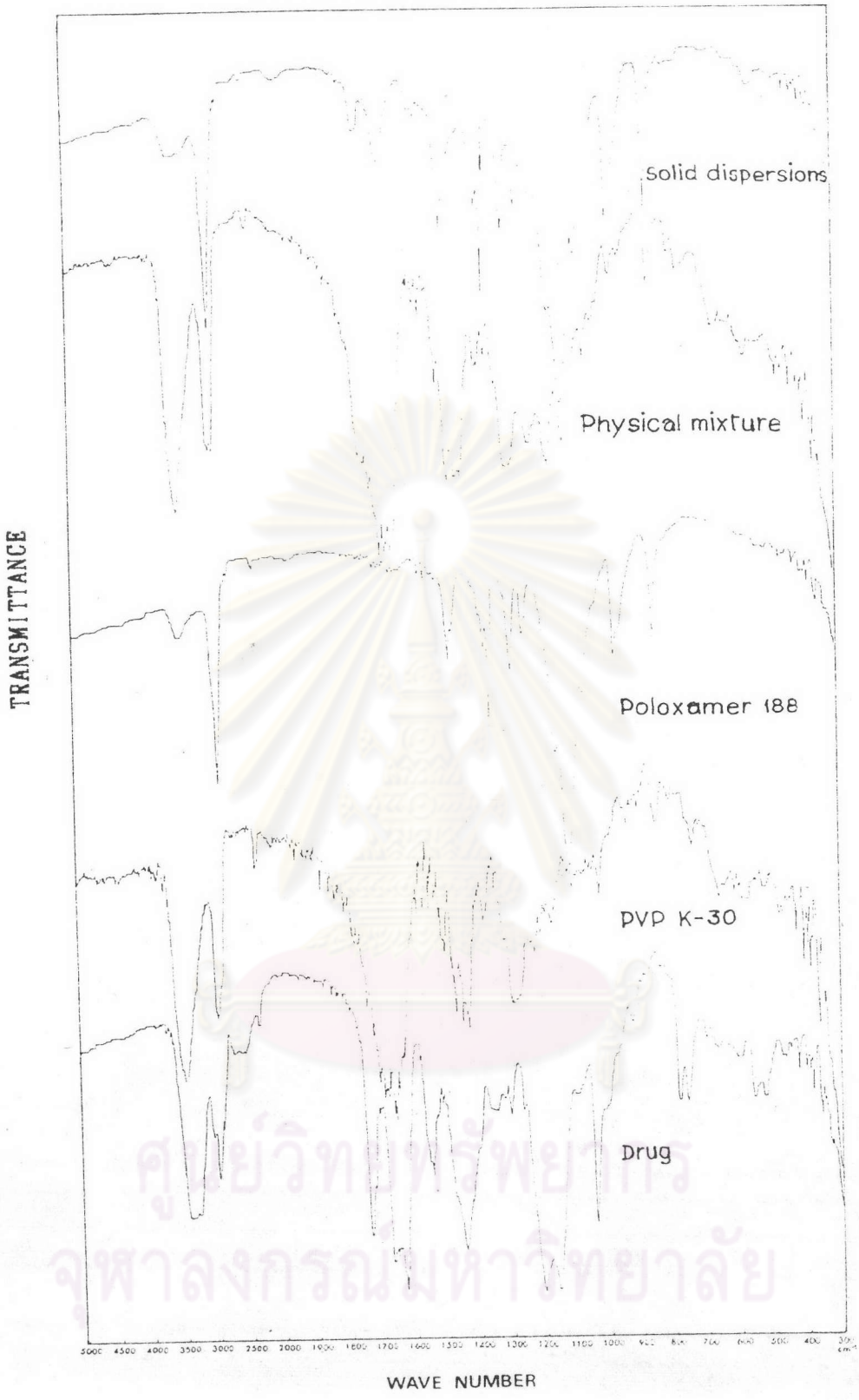


Figure 71 IR spectra of pure ergoloid mesylate , PVP K-30 , poloxamer 188 and 1:5 ergoloid mesylate - mixture of 3 % poloxamer 188 in PVP K-30 physical mixture and solid dispersions in KBr disks

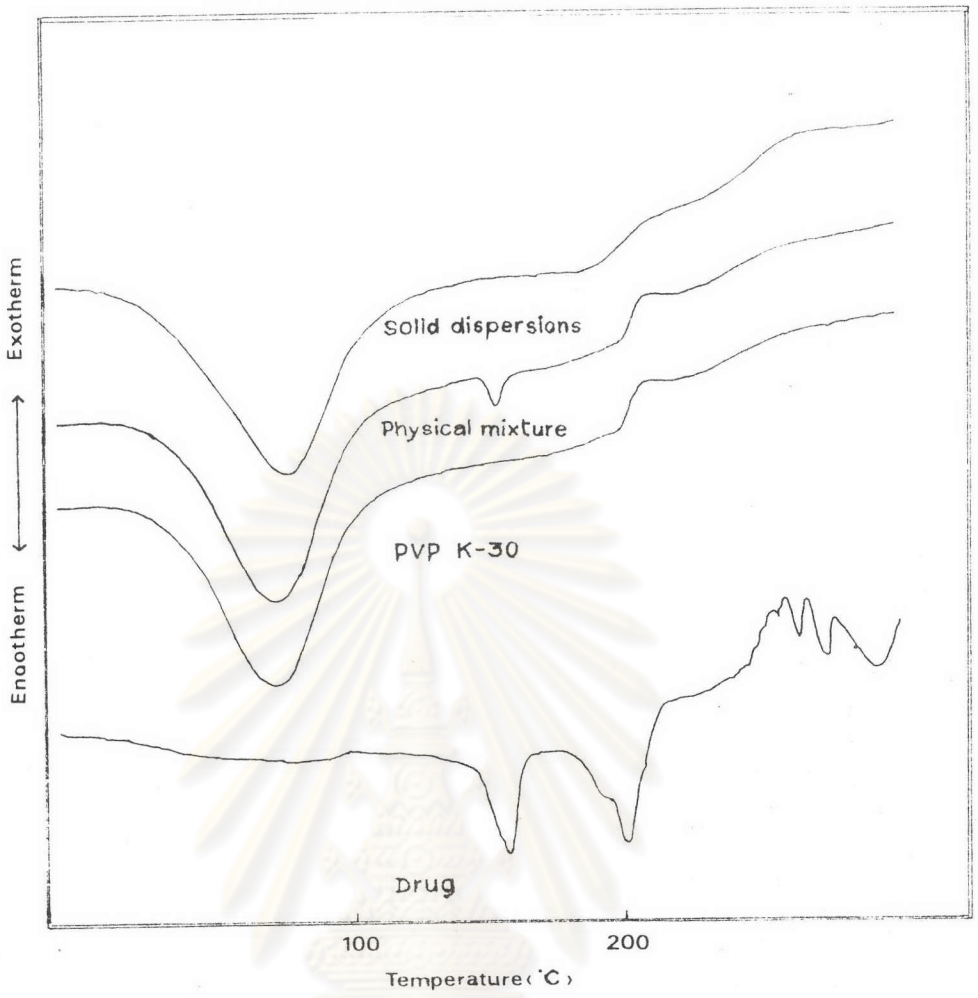


Figure 72 DTA thermograms of pure ergoloid mesylate , PVP K-30 and 1 : 5 ergoloid mesylate - PVP K-30 physical mixture and solid dispersions

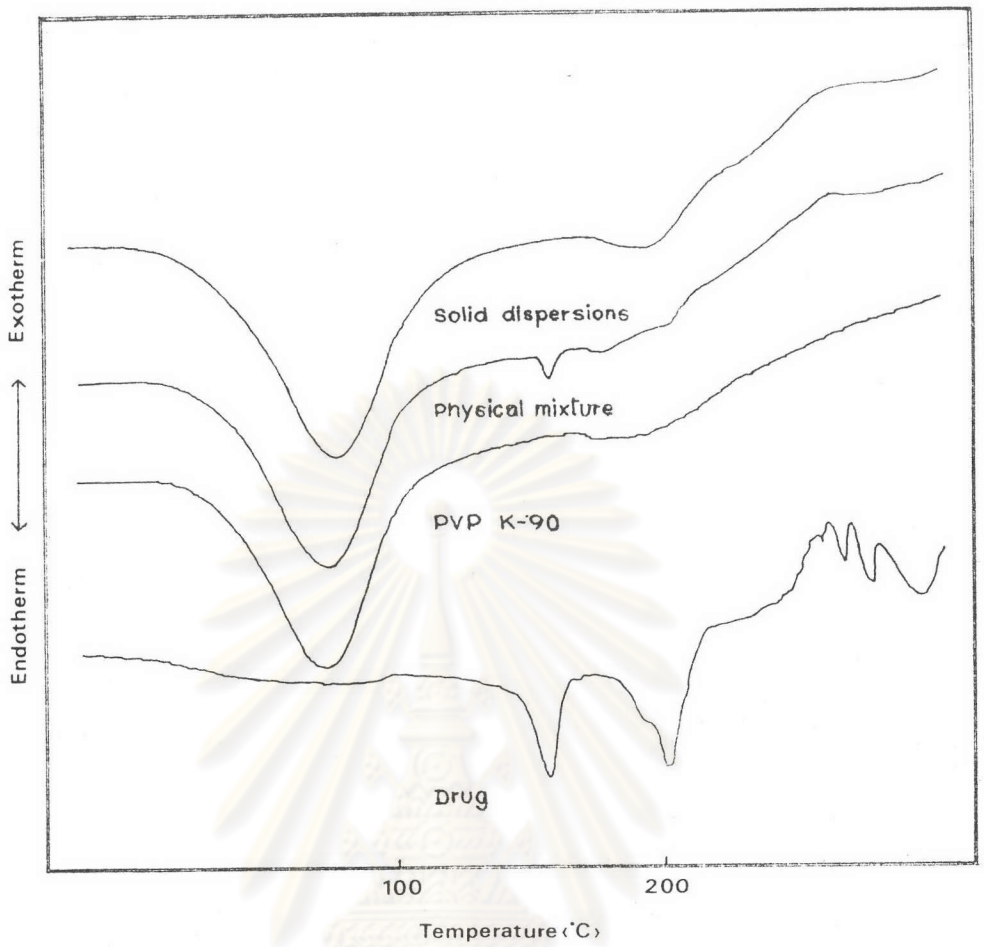


Figure 73 DTA thermograms of pure ergoloid mesylate , PVP K-90 and 1 : 5 ergoloid mesylate - PVP K-90 physical mixture and solid dispersions

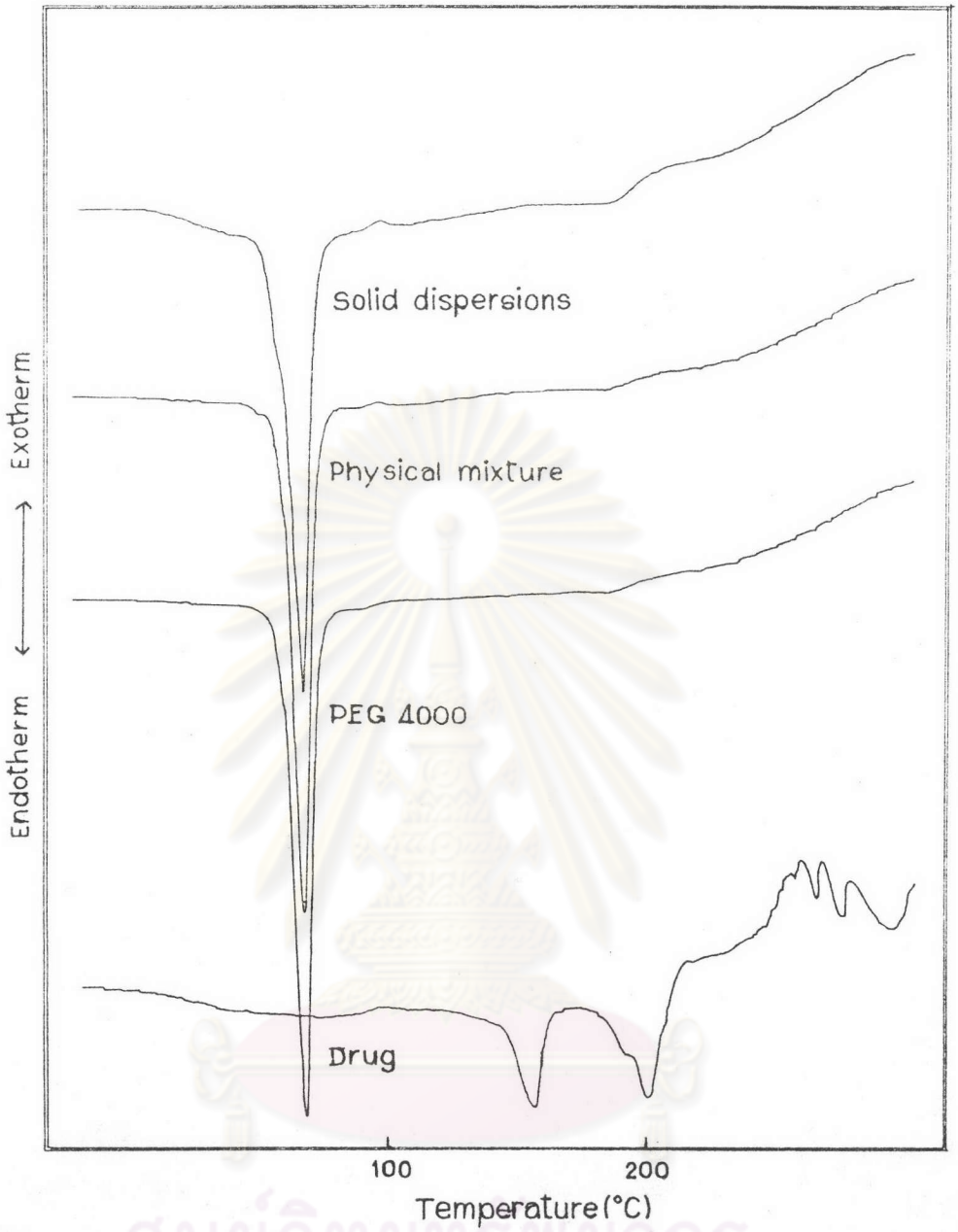


Figure 74 DTA thermograms of pure ergoloid mesylate , PEG 4000 and 1 : 5 ergoloid mesylate - PEG 4000 physical mixture and solid dispersions

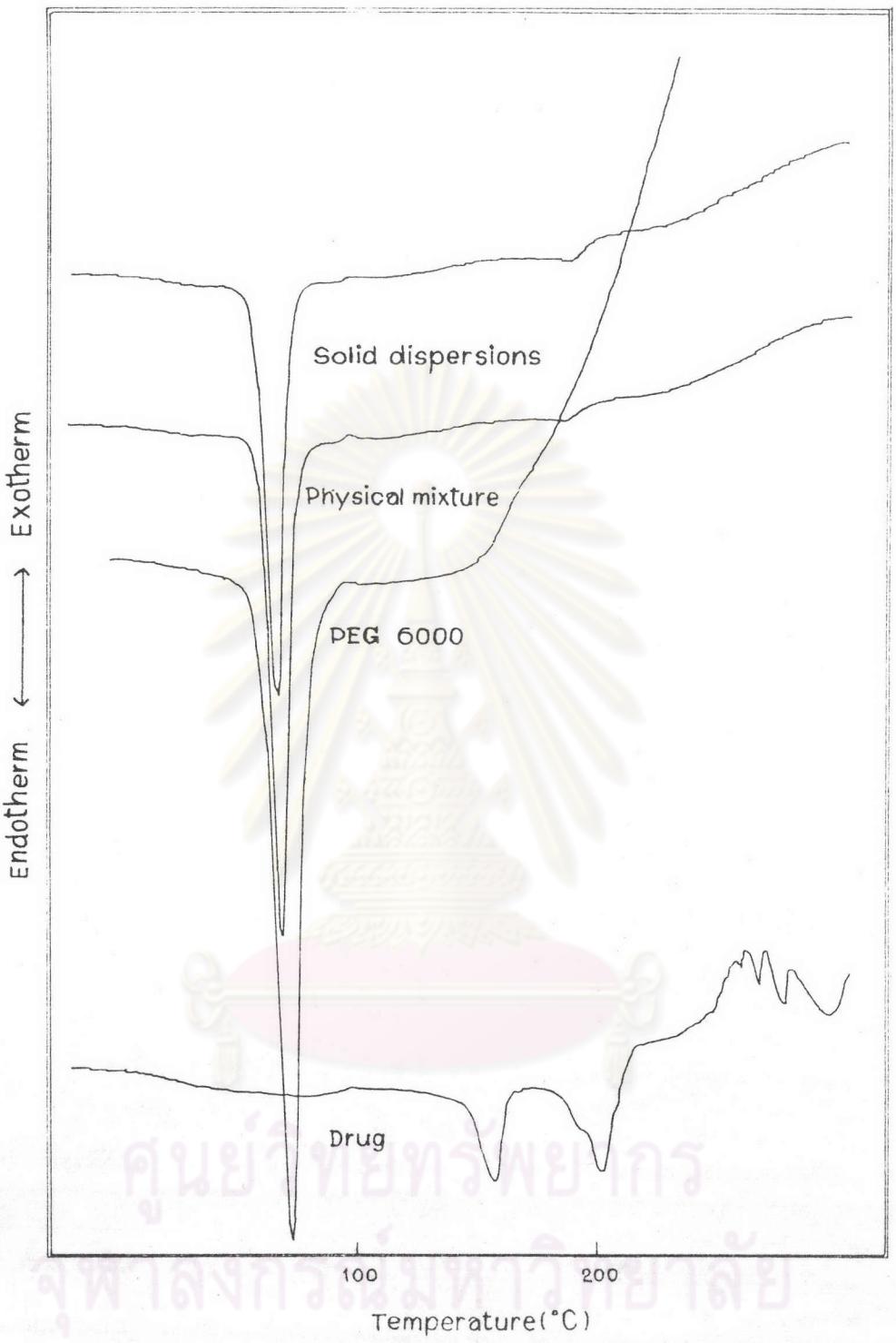


Figure 75 DTA thermograms of pure ergoloid mesylate , PEG 6000 and 1 : 5 ergoloid mesylate - PEG 6000 physical mixture and solid dispersions

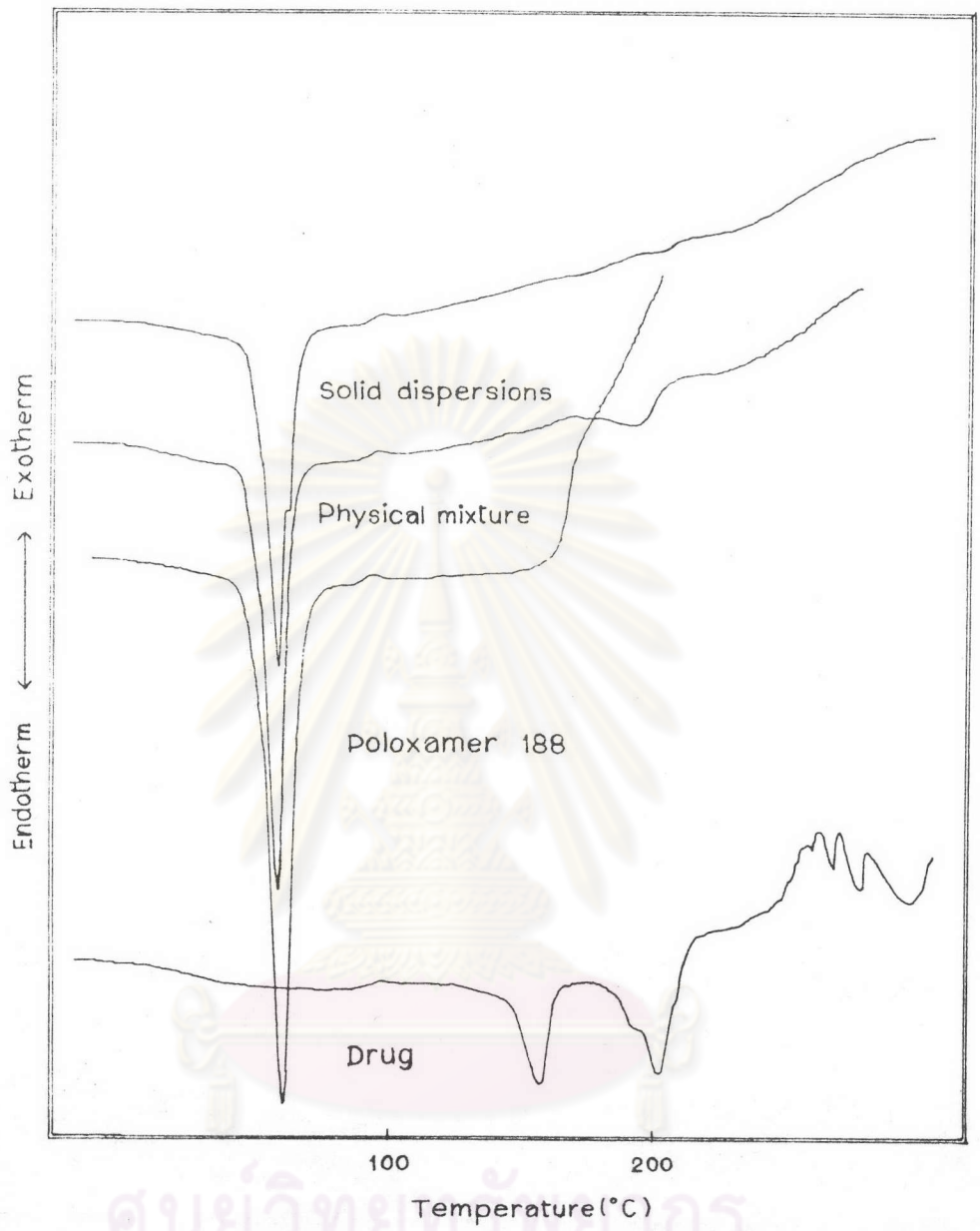


Figure 76 DTA thermograms of pure ergoloid mesylate , poloxamer 188 and 1 : 5 ergoloid mesylate - poloxamer 188 physical mixture and solid dispersions

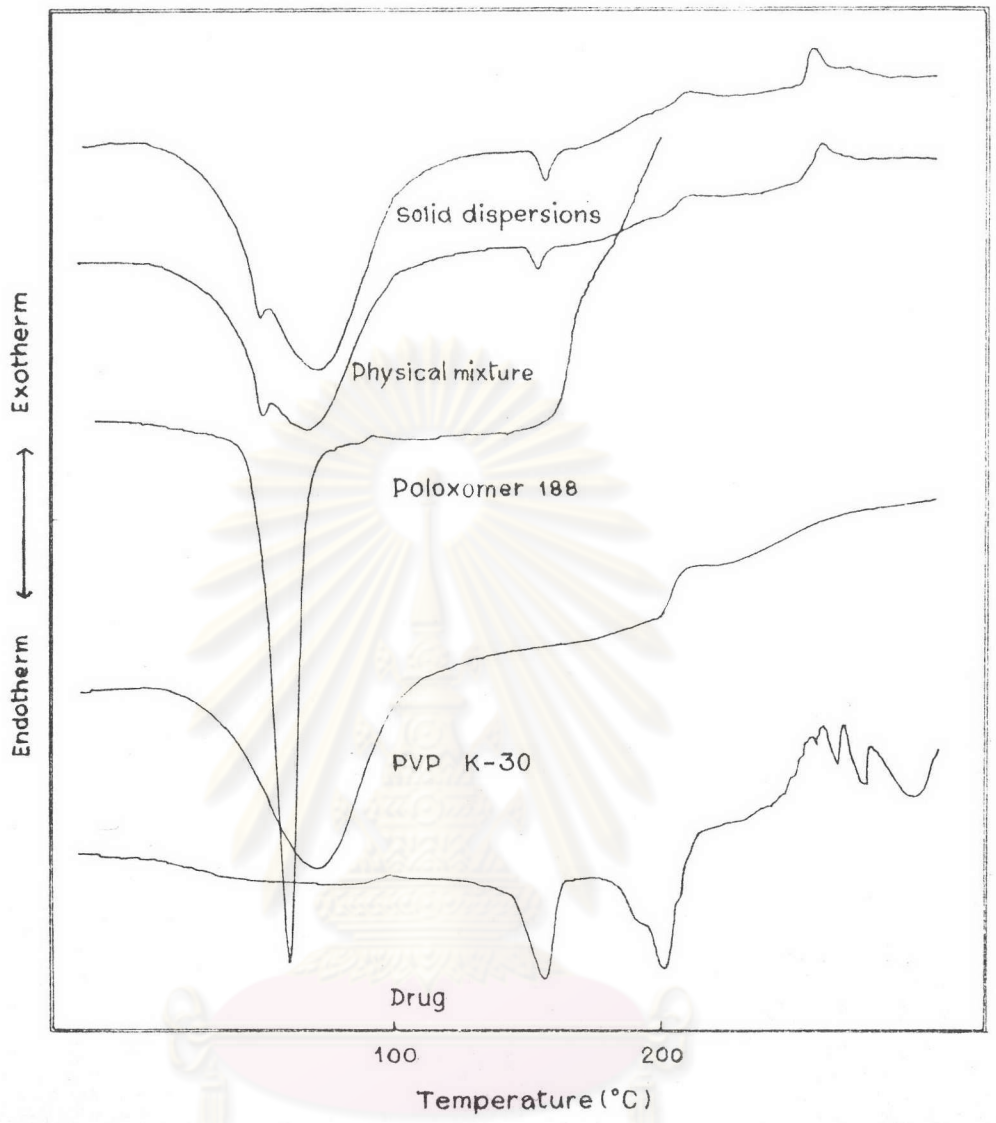


Figure 77 DTA thermograms of pure ergoloid mesylate , PVP K-30 , poloxamer 188 and 1 : 4 ergoloid mesylate - PVP K-30 physical mixture and solid dispersions

a small endotherm near 160°C. Furthermore, poloxamer 188 and mixture of 3% poloxamer 188 in PVP K-30 (Figures 76-77) exhibited the characteristic melting endotherm as same as PVP dispersion systems. Both physical mixture and solid dispersion of ergoloid mesylate and PEG (1:5) showed the melting endotherms of PEG but did not show the melting endotherm of ergoloid mesylate (Figures 74-75).

4. X-ray diffraction spectra

X-ray diffraction patterns for pure ergoloid mesylate and ergoloid mesylate-PVP K-30 (1:5) solid dispersion were shown in Figure 78. Major x-ray diffraction peaks of ergoloid mesylate, particularly at 7-10 and 19° were present in pure ergoloid mesylate. The x-ray diffraction spectrum of ergoloid mesylate-PVP K-30 (1:5) exhibited absence of crystalline ergoloid mesylate peaks.

All of the x-ray diffraction patterns of other solid dispersion systems were similar to the patterns of PVP K-30 systems, the peaks of ergoloid mesylate did not occur.

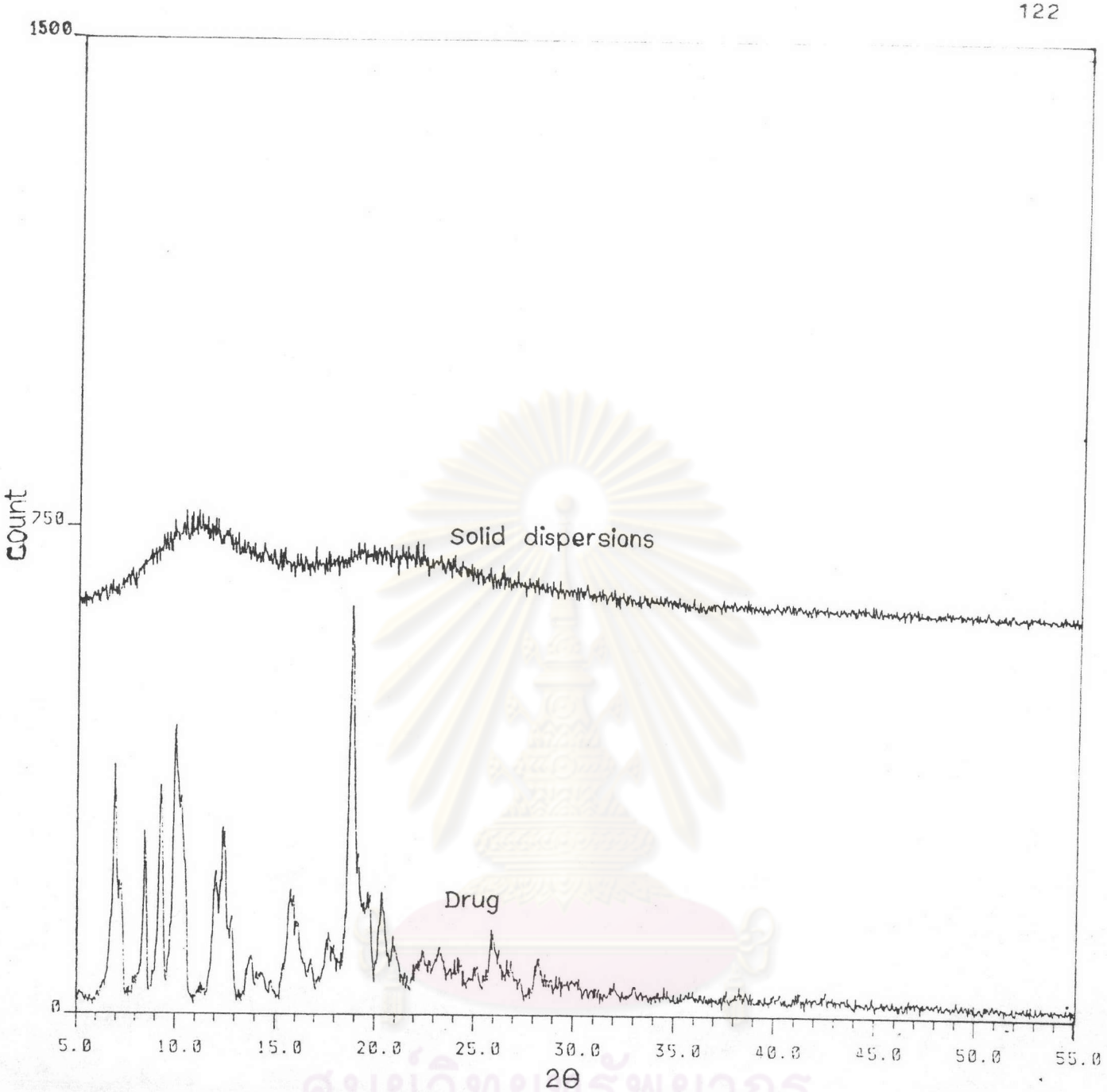


Figure 78 Powder X - ray diffraction patterns of ergoloid mesylate and 1 : 5 ergoloid mesylate - PVP K-30 solid dispersions

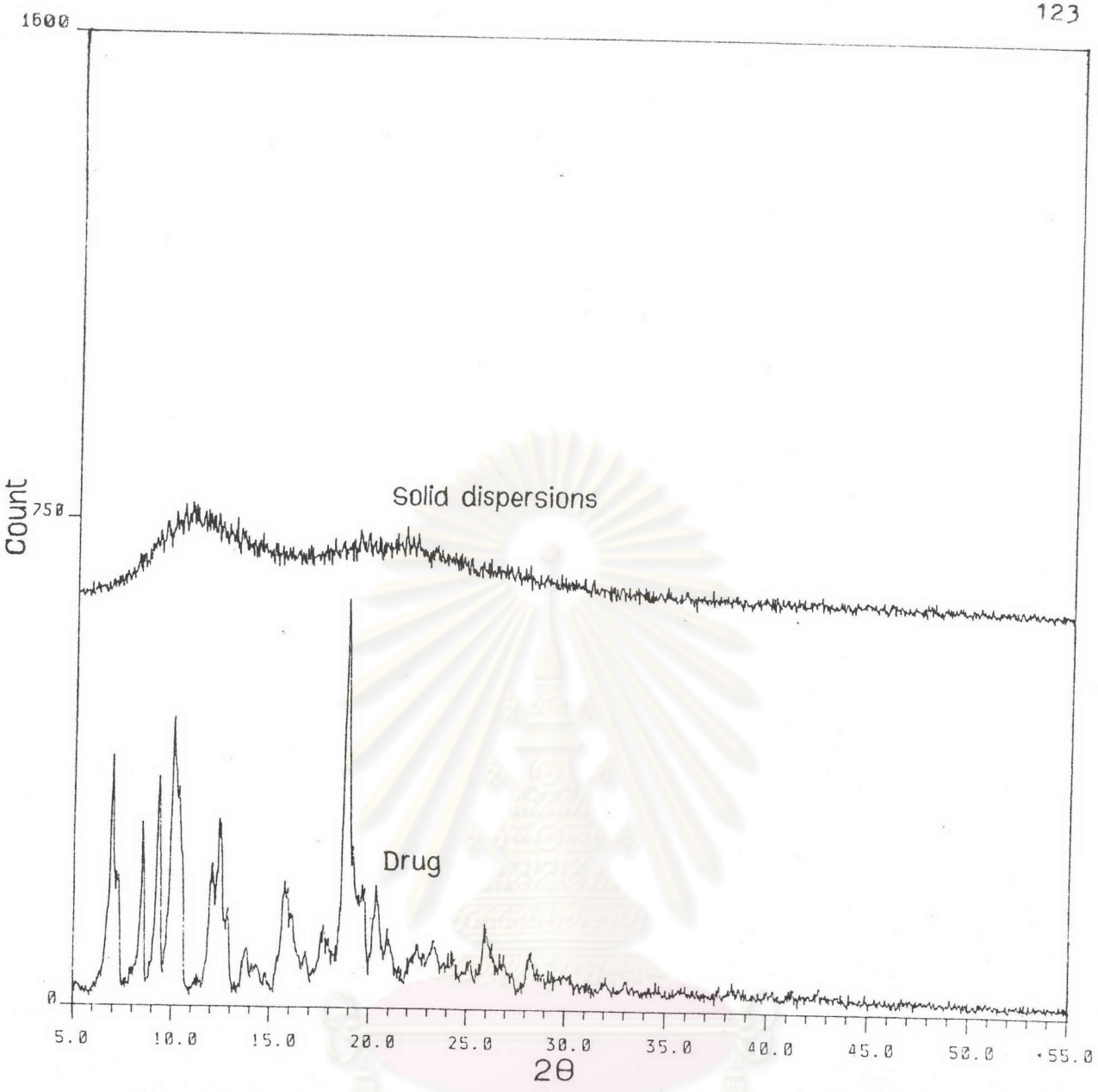


Figure 79 Powder X - ray diffraction patterns of ergoloid mesylate and 1 : 5 ergoloid mesylate - PVP K-90 solid dispersions

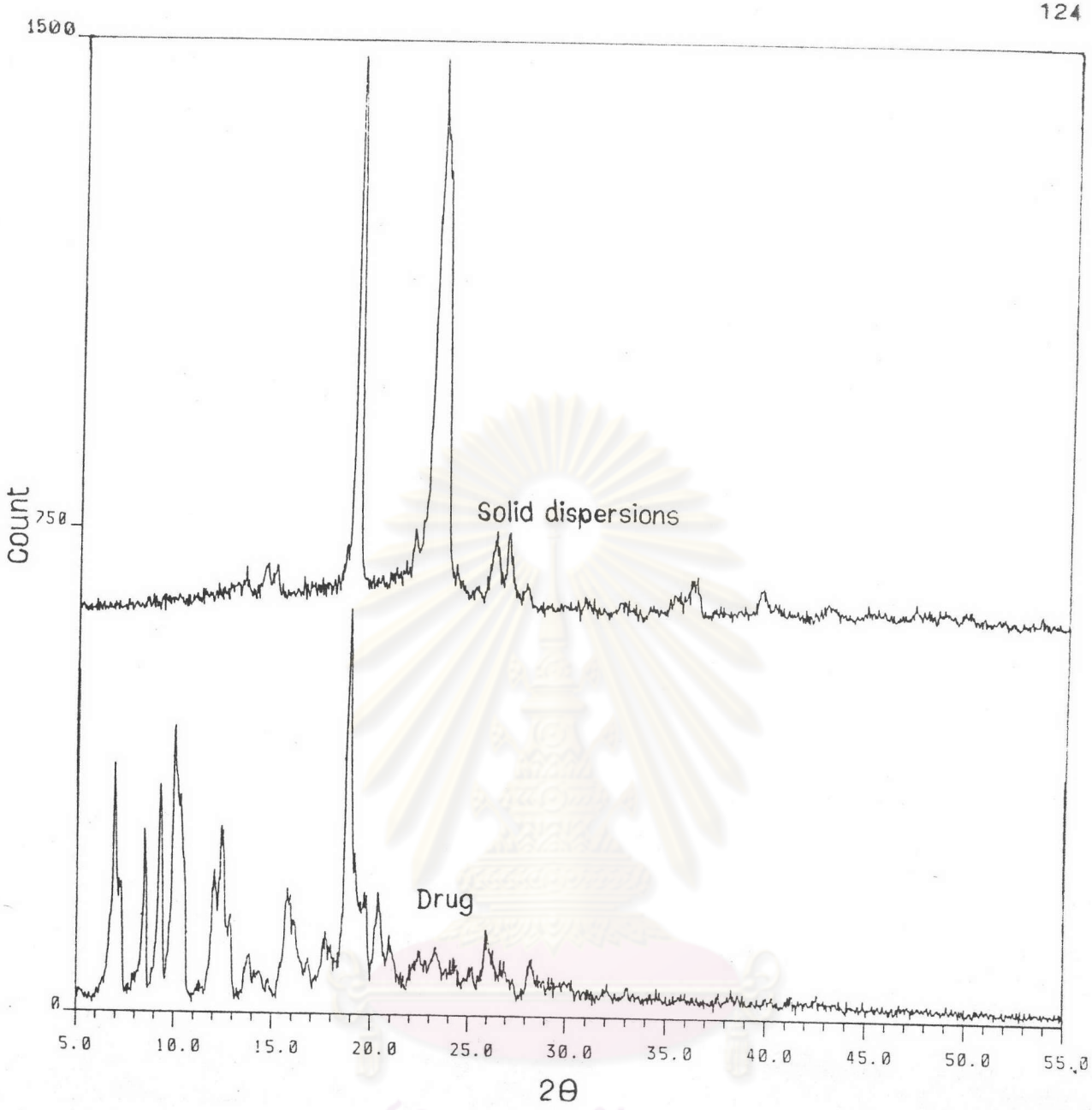


Figure 80 Powder X - ray diffraction patterns of ergoloid mesylate and 1 : 5 ergoloid mesylate - PEG 4000 solid dispersions

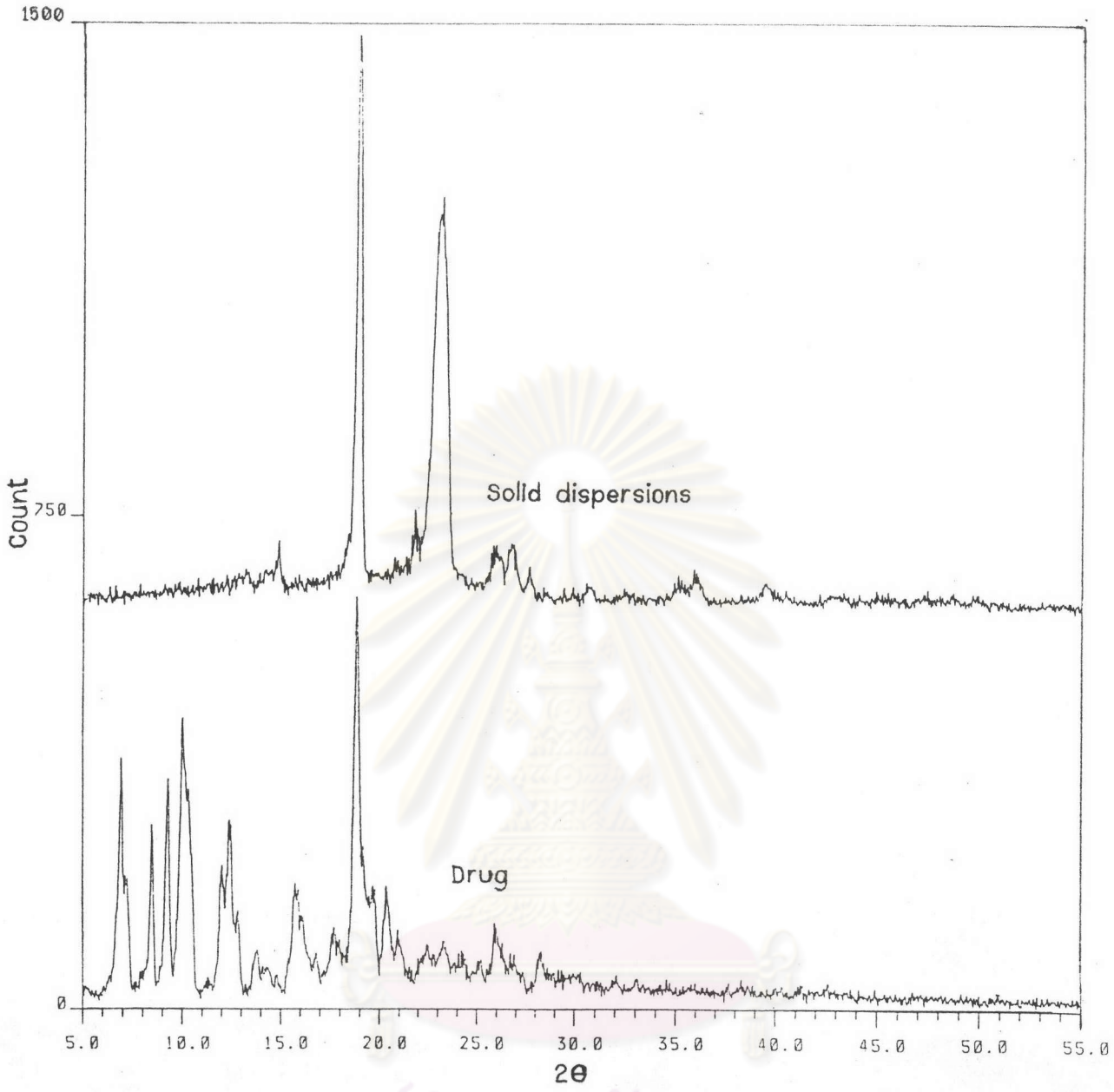


Figure 81 Powder X - ray diffraction patterns of ergoloid mesylate and 1 : 5 ergoloid mesylate - PEG 6000 solid dispersions

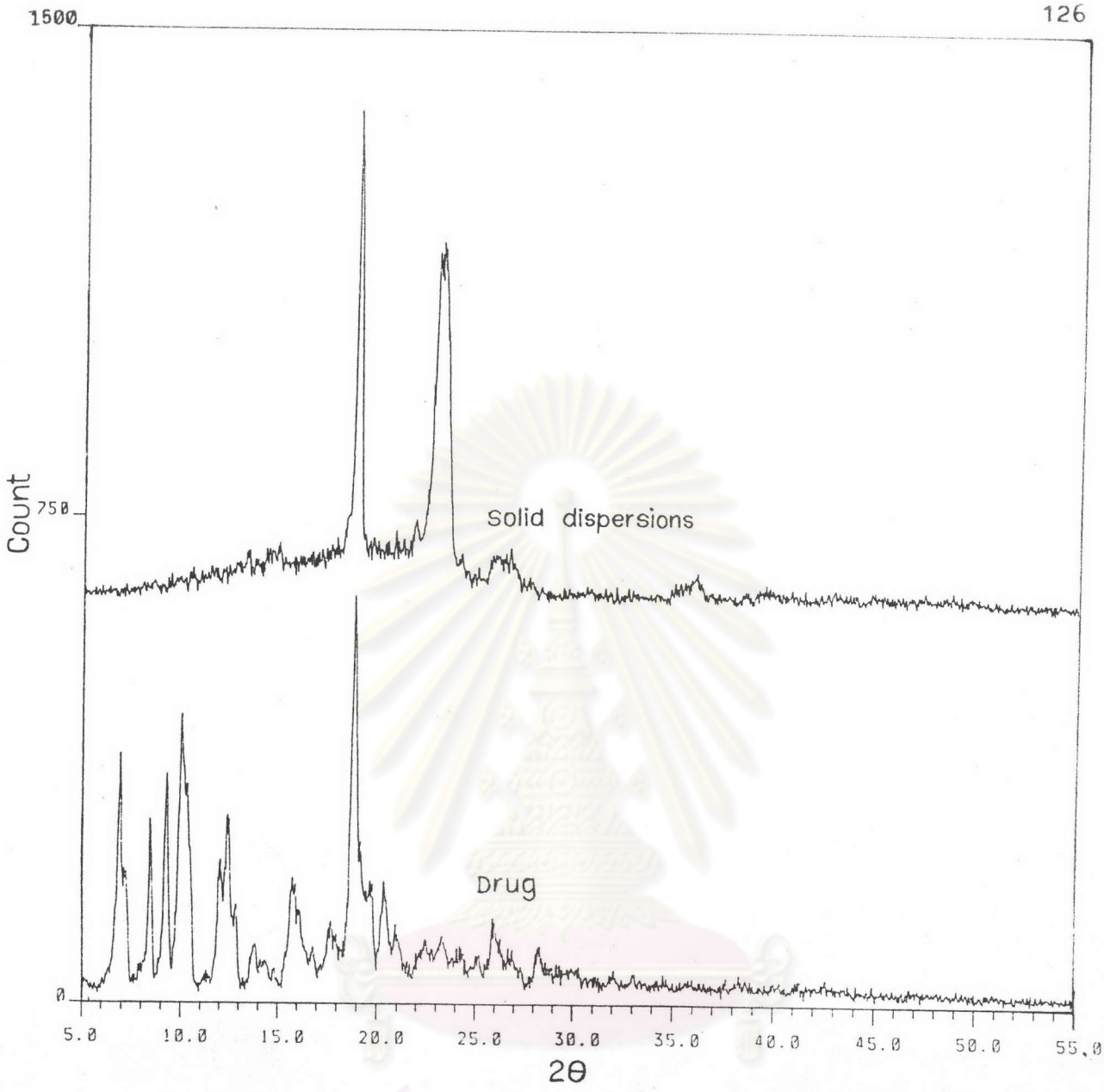


Figure 82 Powder X - ray diffraction patterns of ergoloid mesylate and 1 : 5 ergoloid mesylate - poloxamer 188 solid dispersions

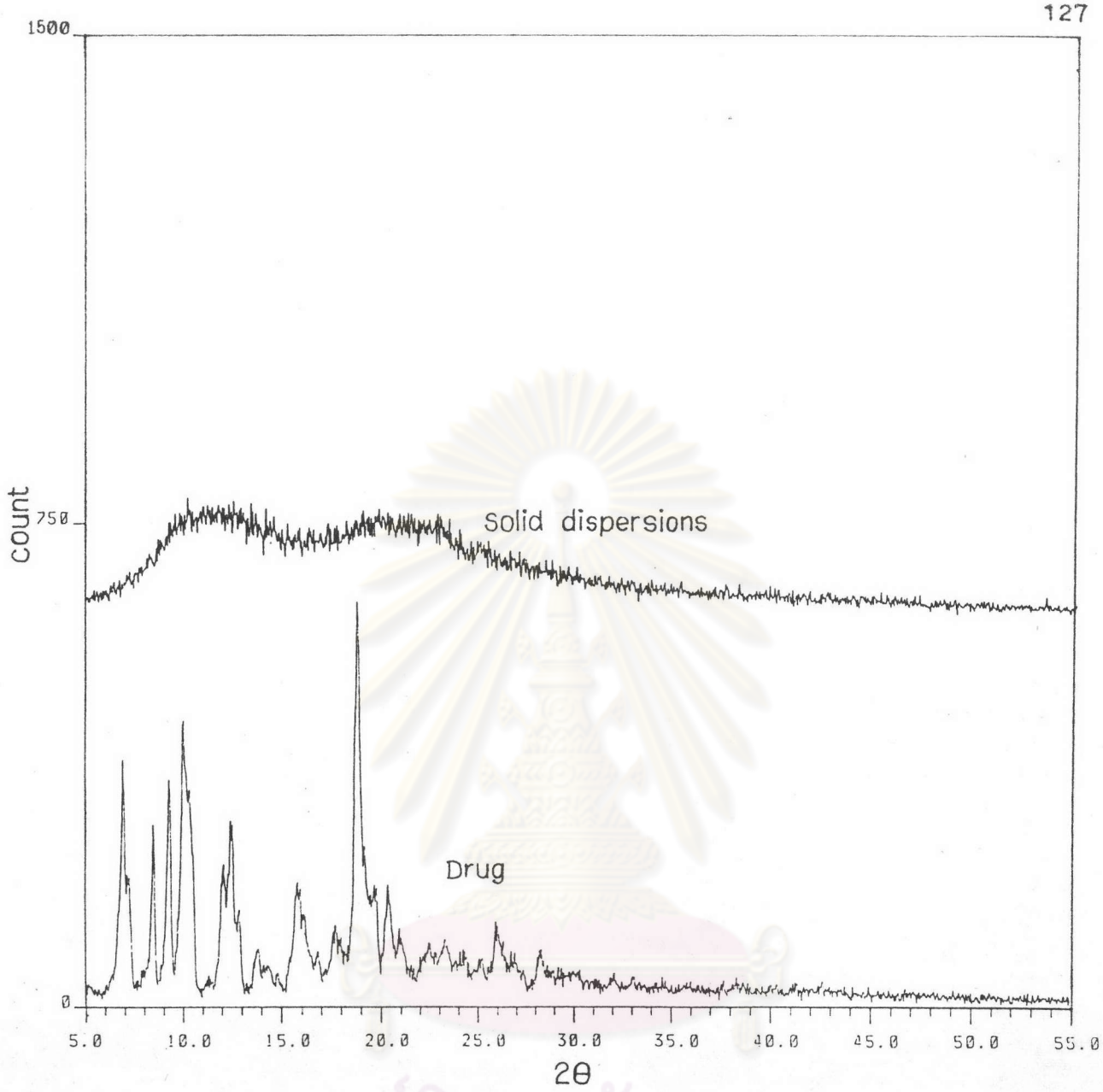


Figure 83 Powder X - ray diffraction patterns of ergoloid mesylate and 1 : 4 ergoloid mesylate - mixture of 3 % poloxamer 188 in PVP K-30 solid dispersions

Tablet Evalutions

Five procedures of prepared ergoloid mesylate tablets were relatively easy to be manufactured. Prepared tablets as well as five commercial ergoloid mesylate tablet products were observed for their physical properties as follows:

1. Weight variation

The average values and standard deviations of weight for prepared tablets and commercial products were presented in Tables 4 and 5, respectively. In all cases, weight variation of tablets were complied with USP. requirement.

2. Hardness

The data of average hardness and standard deviations of ergoloid mesylate tablets were shown in Tables 4 and 5. In prepared tablets, the hardness was in the range of 4 $\pm$0.5 Kp.

3. Thickness

The results of average thickness and standard deviations were displayed in Tables 4 and 5. The thicknesses of commercial products was found to be in the range of 2.3-3.0 mm., nevertheless the prepared tablet thickness was found to be 3.2 mm.

4. Disintegration time of tablet

The average disintegration times of ergoloid mesylate tablets were presented in Tables 4 and 5. In all cases,

Table 4 Physical properties of the prepared ergoloid mesylate tablets

Physical Properties of tablets	Type of ergoloid mesylate tablet products				
	A	B	C	D	E
Weight (mg.)	163.39	163.13	163.32	163.22	163.25
Standard deviation	1.66	1.09	0.89	1.30	0.99
Relative Standard deviation	1.02	0.67	0.55	0.80	0.61
Maximun deviation (%)	1.96	1.21	1.09	1.77	0.92
Minimum deviation (%)	1.71	1.30	0.93	1.54	1.23
Hardness (Kp.)	4.40	4.20	3.92	3.99	3.97
Standard deviation	0.30	0.27	0.35	0.22	0.21
Thickness (mm.)	3.236	3.256	3.239	3.244	3.240
Standard deviation	0.052	0.022	0.011	0.017	0.020
Disintegration time (sec.)	314.17	312.50	232.50	223.83	225.71
Standard deviation	17.65	24.62	28.98	23.70	20.53

Table 5 Physical properties of the commercial ergoloid mesylate tablet products

Physical Properties of tablets	Type of commercial ergoloid mesylate tablet				
	Brand A	Brand B	Brand C	Brand D	Brand E
Weight (mg.)	188.48	167.36	156.61	158.68	162.98
Standard deviation	3.01	2.69	3.34	2.43	4.30
Relative Standard deviation	1.60	1.61	2.13	1.53	2.64
Maximun deviation (%)	2.16	3.13	4.78	2.22	5.84
Minimum deviation (%)	3.81	4.45	3.97	3.58	4.59
Hardness (Kp.)	3.79	5.10	4.42	4.53	4.38
Standard deviation	0.27	2.31	0.97	0.92	0.29
Thickness (mm.)	2.981	2.710	2.305	2.471	2.447
Standard deviation	0.059	0.080	0.055	0.037	0.041
Disintegration time (sec.)	687.33	146.00	102.50	120.67	312.50
Standard deviation	48.48	7.23	21.21	20.82	44.93

disintegration times were well within the limit of USP. standard (< 15 minutes). Disintegration time of prepared tablets might be ranked as follows: formula A = formula B > formula C > formula D = formula E. In commercial products, the highest disintegration time was brand A followed by brand E, brand B, brand D, respectively, and the shortest disintegration time was brand C.

5. Content Uniformity of tablet

The data of content uniformity of the prepared and commercial ergoloid mesylate tablets were given in Tables 6 and 7, respectively. It was found that in all cases the content uniformity met USP requirement except the formulae D and E. The calibration concentration fluorescence intensity curve of ergoloid mesylate in water was shown in Appendices 17 and 18.

6. Dissolution of tablet

The dissolution profiles and data of five procedure prepared ergoloid mesylate tablets were displayed in Figure 84. and Appendix 19. Formula A showed the slowest dissolution profile, followed by formula B and C, respectively. Formula D seemed to produced nearly the same average concentration of dissolved ergoloid mesylate as formula E. In addition both of them produced the quickest dissolution rate and the highest amount of ergoloid mesylate dissolved. Finally, formula B shown faster dissolution rate than the formula A in the initial part of dissolution profile, followed by subsequent slower dissolution rate in the latter part of dissolution profile.

Table 6 Content uniformity of the prepared ergoloid mesylate tablets

Sample number	% Drug in tablets				
	Type of ergoloid mesylate tablet procedure				
	A	B	C	D	E
1	100.46	103.46	98.16	107.42	105.22
2	99.76	102.35	97.53	105.72	86.38
3	101.99	99.82	100.64	91.32	92.66
4	101.32	100.11	103.21	88.12	103.51
5	98.66	101.90	97.96	96.23	91.45
6	99.64	102.47	96.21	102.61	96.45
7	101.56	100.46	98.47	95.32	102.55
8	98.83	102.00	99.81	89.12	93.02
9	100.21	101.33	100.45	98.37	110.12
10	100.56	100.98	101.33	106.31	99.43
Mean	100.30	101.49	99.38	98.05	98.08
S.D.	1.1137	1.1571	2.0868	7.2277	7.3463
R.S.D.	1.1104	1.1401	2.0999	7.3711	7.4902

Sample number	% Drug in tablets					
	Type of ergoloid mesylate tablet procedure					
	D			E		
1	107.42	87.11	110.11	105.22	90.26	90.55
2	105.72	100.37	109.00	86.38	112.71	98.63
3	91.32	90.41	91.08	92.66	100.34	92.41
4	88.12	110.34	100.67	103.51	98.1	95.28
5	96.23	93.55	112.02	91.45	92.39	87.35
6	102.61	99.71	105.09	96.45	107.43	110.35
7	95.32	91.82	91.22	102.55	112.26	96.68
8	89.12	90.13	99.34	93.02	92.21	110.72
9	98.37	107.05	91.56	110.12	89.51	100.01
10	106.31	90.98	107.89	99.43	99.66	108.63
Mean		98.67			98.88	
S.D.		7.8818			7.9171	
R.S.D.		7.9883			8.0071	

Table 7 Content uniformity of the commercial ergoloid mesylate tablets

Sample number	% Drug in tablets				
	Type of commercial ergoloid mesylate tablet products				
	Brand B	Brand E	Brand D	Brand C	Brand A
1	100.34	99.82	98.33	100.55	95.39
2	102.98	101.32	96.54	105.45	97.07
3	104.54	100.98	97.71	100.97	100.72
4	100.46	98.92	99.14	102.65	101.05
5	97.76	99.71	95.89	101.66	96.73
6	99.05	99.54	100.37	106.06	98.01
7	98.88	100.31	94.01	99.98	99.69
8	99.15	100.03	97.50	103.45	97.22
9	100.61	99.21	98.00	103.29	94.53
10	101.17	100.59	95.24	100.81	100.88
Mean	100.49	100.04	97.27	102.49	98.13
S.D.	2.0280	0.7636	1.8914	2.0811	2.3482
R.S.D.	2.0181	0.7633	1.9444	2.0306	2.3929

PREPARED TABLETS

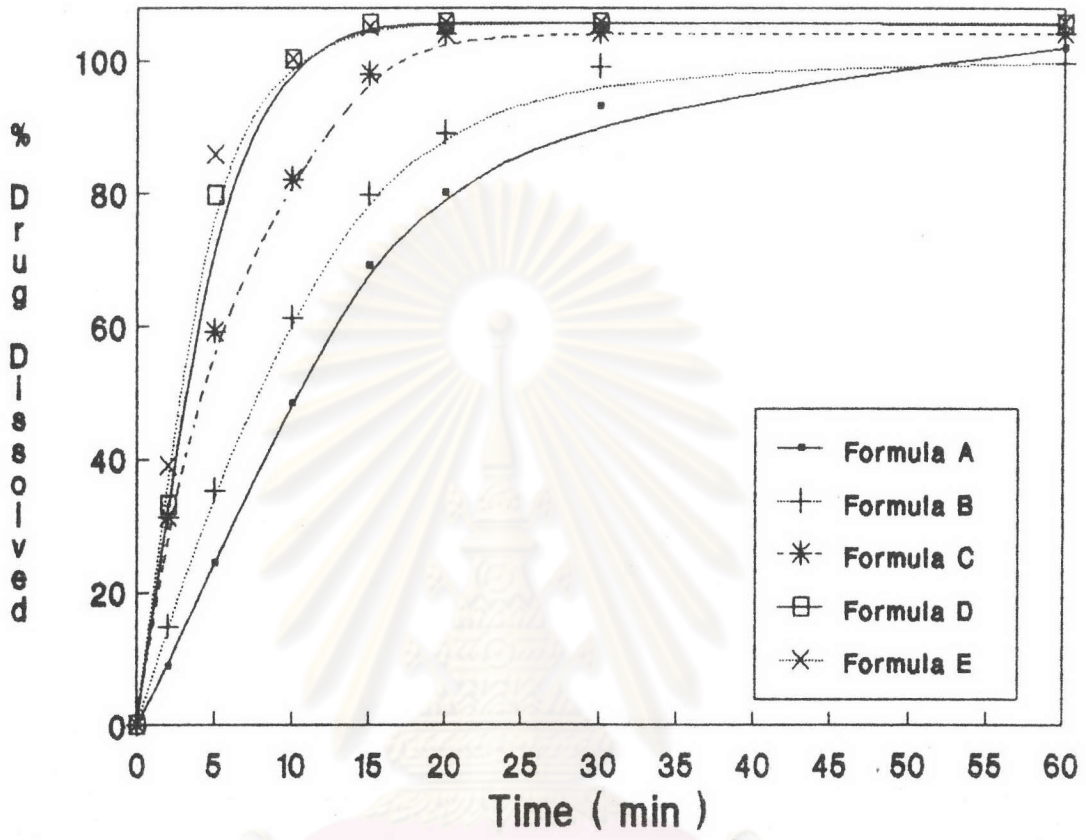


Figure 84 Dissolution profile of ergoloid mesylate from the prepared tablet with various procedures in water

Each formula of ergoloid mesylate prepared tablets possessed the dissolution studies in the limit of USP. standard, the time requires for 75% of ergoloid mesylate to dissolve was 30 minutes.

Among the commercial ergoloid mesylate tablets, the dissolution profiles of the ergoloid mesylate with various sources of manufacture were illustrated in Figure 85 and the dissolution data for each brand were also listed in Appendix 20. All tablet products exhibited within the USP. requirement, except the brand A, which gave markedly lower dissolution than the USP. requirement. Brand A showed the slowest dissolution rate and the lowest amount of ergoloid mesylate dissolved. However, the initial ergoloid mesylate dissolution rates of the brand B, brand C, and brand D were higher than the brand E, followed by the subsequent slower ergoloid mesylate dissolution rates. Brand E exhibited the highest amount of ergoloid mesylate dissolved.

COMMERCIAL TABLETS

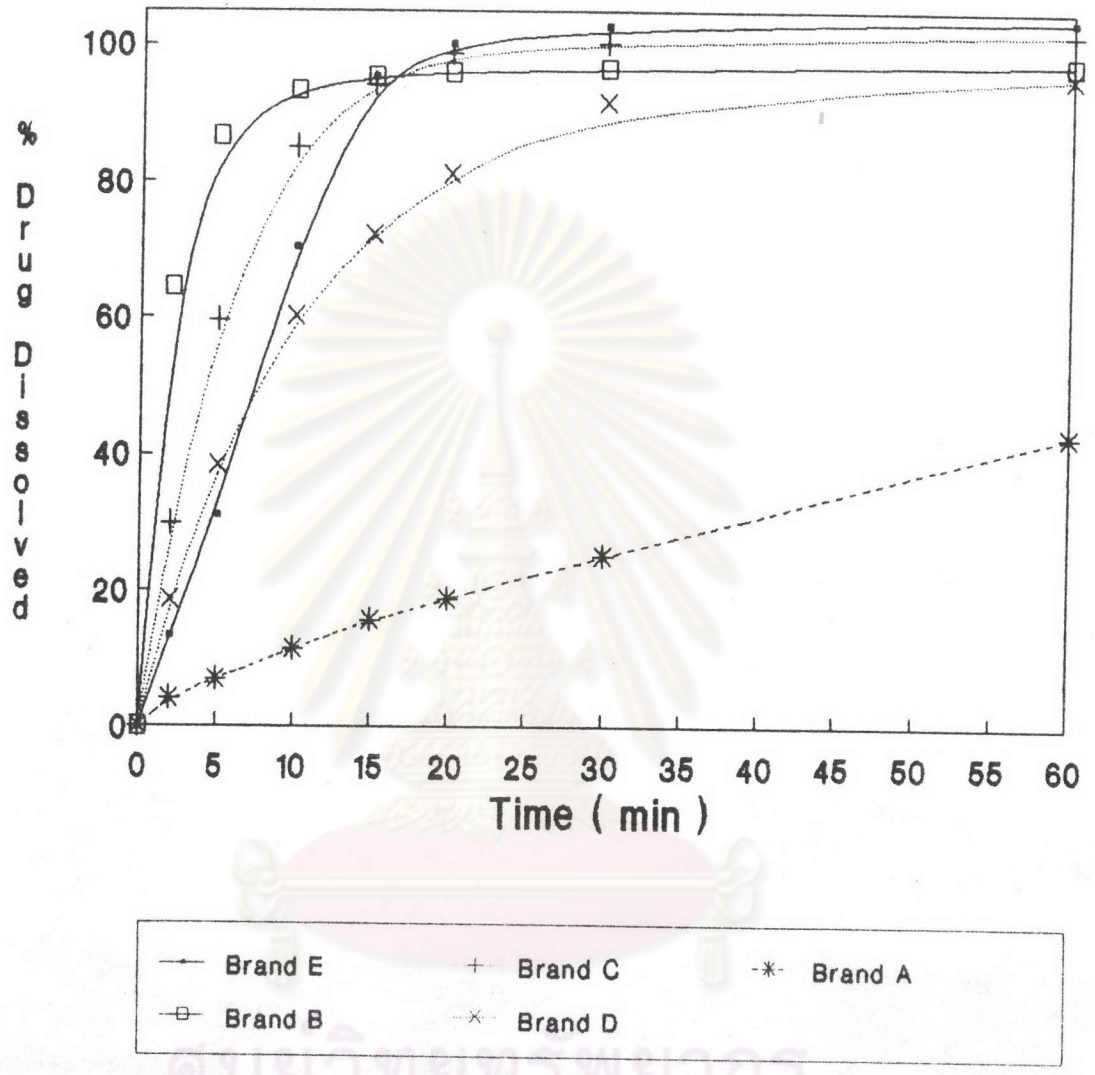


Figure 85 Dissolution profile of ergoloid mesylate from the commercial ergoloid mesylate tablet products in water