CHAPTER III

RESULTS

1. Preliminary study

From the preliminary study, the suitable amount of cellulose acetate in coating solution for propranolol hydrochloride tablets should not be more than 1 % w/v because higher amount of cellulose acetate in coating solution resulted in a very viscous coating solution and possibly obstructed the spray nozzle. One percent w/v of coating solution was recommended because of no blockage at the spray nozzle and no agglomeration of the core tablets.

The suitable inlet air temperature suggested in the experiment is 40 °C because resulted in smooth surface of film deposited on tablets, no agglomeration of coated tablets and no blockage at spray nozzle was apparent. If inlet air temperature was increased from 40 °C to 45 °C and 50 °C, an orange peel surface and blockage at spray nozzle were evident. Reverse, if temperatures were decreased from 40 °C to 35 °C and 30 °C, overwetting of coated tablets and agglomeration of coated tablets were observed.

On the part of atomizing air pressure, the optimum atomizing air pressure is 1.0 kg/cm^2 owing to the smoothness surface of coated film and no blockage at the spray nozzle were apparent. At lower pressure of about 0.5 kg/cm^2, blockage at the spray nozzle was shown when the pressure was increased from 1.0 kg/cm^2 to 1.5 kg/cm^2, the result was similar to that obtained from pressure 1.0 kg/cm^2.

The suitable feed rate of coating solution was 9 ml/min. At this feed rate the process was still continuous. When feed rate was decreased from 9 ml/min to 6 ml/min and 3 ml/min, the process could not be continued and blockage of the spray nozzle was shown. If feed rate was increased from 9 ml/min to 12 ml/min, the delivery tube for the feed solution was swollen.

2. Evaluation of propranolol hydrochloride tablets

The propranolol hydrochloride tablets, propranolol hydrochloride-lactose tablets and propranolol hydrochloride-mannitol tablets were white, round shaped tablets with rather smooth surface. The propranolol hydrochloride-sucrose tablets and propranolol hydrochloride-sodium chloride tablets looked similar but the crystal of osmotic agents could be seem on face of the tablets. The physical properties of propranolol hydrochloride tablets and propranolol hydrochloride tablets containing different osmotic agents ; that is lactose, mannitol, sodium chloride and sucrose tablets are shown in Table 3. The diameter, hardness and weight of each tablet in each formula were in the controlled range values. Changing types of the osmotic agent in osmotic pump tablets affected the tablet thickness.

3. Evaluation of osmotic pump tablets

3.1 Film thickness

The results of film thickness of propranolol hydrochloride tablets coated with various cellulose acetate coating solutions and various level of coating solution were calculated and are shown in Table 75 - 82 (Appendix C).

Table 3. Physical properties of tablets prepared by direct compression technique.

Groups	Diameter (mm.) ± S.D.	Hardness (kg.) ± S.D.	Weight (mg.) ± S.D.
A	9.57 ± 0.004	4.94 ± 0.270	206 ± 0.006
B	9.56 ± 0.005	5.33 ± 0.800	254 ± 0.006
C	9.57 ± 0.006	5.50 ± 0.790	262 ± 0.110
D	9.56 ± 0.006	5.41 ± 0.650	268 ± 0.017
E	9.57 ± 0.007	5.41 ± 0.780	262 ± 0.011

A : propranolol hydrochloride tablets

B : propranolol hydrochloride-lactose tablets

C : propranolol hydrochloride-mannitol tablets

D : propranolol hydrochloride-sodium chloride tablets

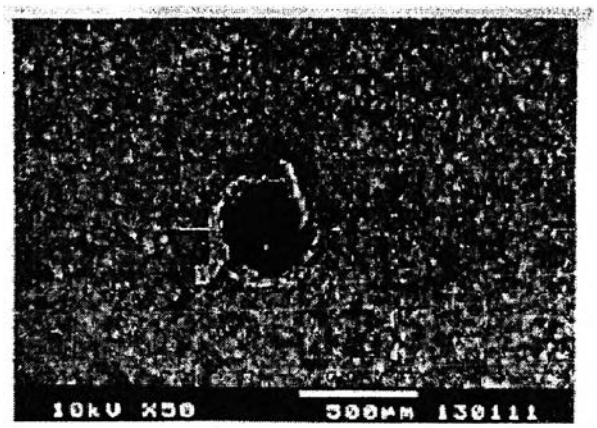
E : propranolol hydrochloride-sucrose tablets

Cellulose acetate coating solution, at coating level of 1 liter produced the film thickness of about 20 μm. At coating levels of 2 and 3 liters, the thickness were increased to about 65 μm and 95 μm, respectively. When plasticized with either PEG 400 or DBP the thickness was increased. The higher the amount of plasticizer the thickness the film could be obtained. With 20 % PEG 400, at coating solution level of 1, 2 and 3 liters, the thickness were increased to about 45 μm, 70 μm and 135 μm, respectively. When plasticized with 40% PEG 400, at coating solution of 1, 2 and 3 liters, the thickness of them were about 80 μm, 145 μm and 160 μm, respectively. When plasticized with 60% PEG 400, at coating solution of 1, 2 and 3 liters, the thickness about 80 μm, 160 μm and 230 μm, respectively, were obtained. When plasticized with 20% DBP, at coating level of 2 liters, the thickness was about 65 μm. When increasing the amount of DBP to 40 %, at the same coating level, the thickness was about 65 μm. In comparison of film thickness when plasticized with PEG 400 and DBP, the thickness from coating solution with PEG 400 was higher than the thickness from plasticized with DBP at same coating level.

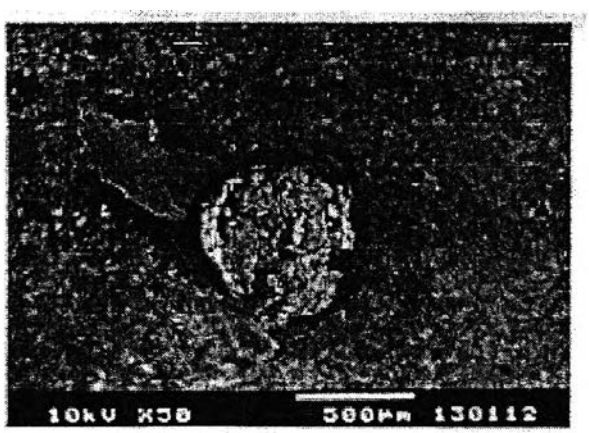
If 20 % PEG 4000 was added as flux enhancer to the formulation which plasticized with 20 % DBP, at coating level of 2 liters, the thickness was about 80 μm. If 40 and 60 % PEG 4000 was added, at the same coating level, the thickness was about 120 and 165 μm, respectively.

3.2 Shape and size of passageway morphology

SEM photomicrographs of the size of passageway of 400 and 700, 1000 and 1500 μm on the osmotic pump tablets are shown in Figures 18 and 19, respectively. The magnifications of 35 and 50 were used to investigate the shape and size of passageway on the osmotic pump tablets.

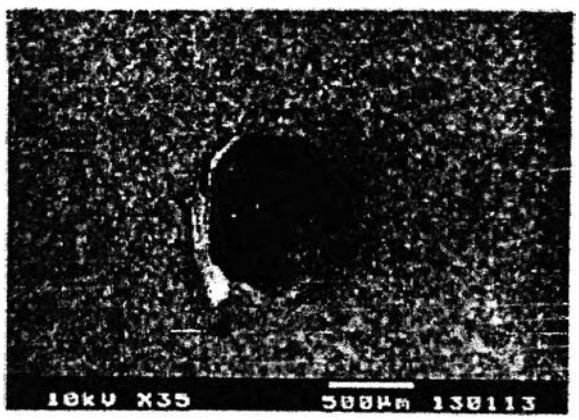


(A)



(B)

Figure 18 The photomicrographs of passageway (A : Passageway size 400µm x50, B : Passageway size 700µm x50).



(A)

(B)

Figure 19 The photomicrographs of passageway (A : Passageway size 1000µm x35, B : Passageway size 1500µm x35).

The round shape and dense passageway-edge were shown in Figure 18 (A). In consideration from Figure 18 (B) to Figure 19 (B), defect of passageway-edge and imperfect round shape of passageway were apparent. The diameter of the passageways observed from scanning electron photomicrographs in Figures 18 and 19 were approximately 400, 700, 1000 and 1500 μm, respectively.

3.3 The surface and cross-sectioned of deposited film of propranolol hydrochloride tablets

3.3.1 Cellulose acetate without plasticizer as film former

The surface and cross-sectioned morphology of propranolol hydrochloride tablets coated with cellulose acetate coating solution were displayed in Figures 20 and 21. Figure 20 illustrates the scanning electron photomicrograph of intact cellulose acetate whereas Figure 21 demonstrates cellulose acetate film after being exposed to dissolution medium.

A dense, homogeneous and non-defect cross-sectioned films were produced before exposure with water. The scanning electron photomicrograph of film after exposure to water showed rough surface cracks of cross-sectioned films.

3.3.2 Influence of plasticizer type on the surface and cross-sectioned of deposited film on propranolol hydrochloride tablets morphology

The microscopic images of cellulose acetate plasticized with various types of plasticizer film deposited onto propranolol hydrochloride tablets are shown in Figures 22- 23 and 26 - 27. Cellulose acetate plasticized with 20 % DBP films evaluated before

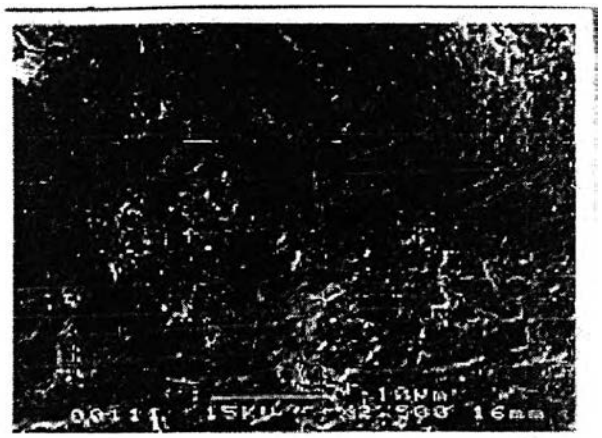
and after drug release are presented in Figures 22 - 23. Figures 26 - 27 illustrate the surface and cross-section of PEG 400 plasticized films.

On the part of DBP used as a plasticizer, a dense, non-porous and homogeneous structure, free of defect at cross-sectioned films was produced before and after films exposure with water. In addition, it was observed that osmotic pump tablets coated with cellulose acetate plasticized with 20 % DBP appeared to provide a smooth and continuous surface of the polymer after exposure with water as shown in Figure 23, as compared to a rough surface of osmotic pump tablet coated with cellulose acetate alone as shown in Figure 21.

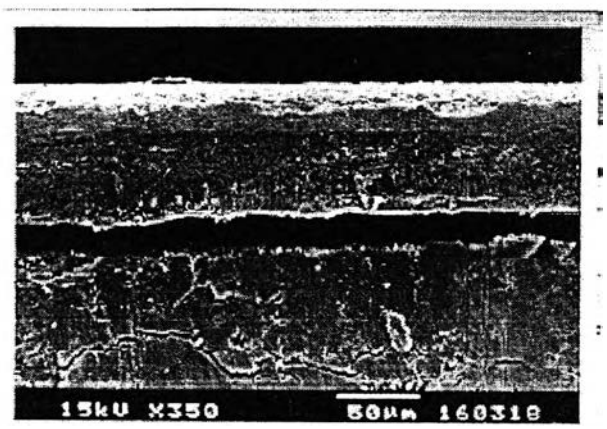
In the case of PEG 400 used as plasticizer, the results from Figure 26 was similar to that obtained from osmotic pump tablets coated with cellulose acetate or cellulose acetate plasticized with 20 % DBP before exposure to water as shown in Figures 20 and 22, respectively. However, cellulose acetate plasticized with 20 % PEG 400 films evaluated after drug release showed a highly porous structure by scanning electron microscope as shown in Figure 27.

3.3.3 Influence of various level of DBP on the surface and cross-sectioned of deposited film on propranolol hydrochloride tablets morphology

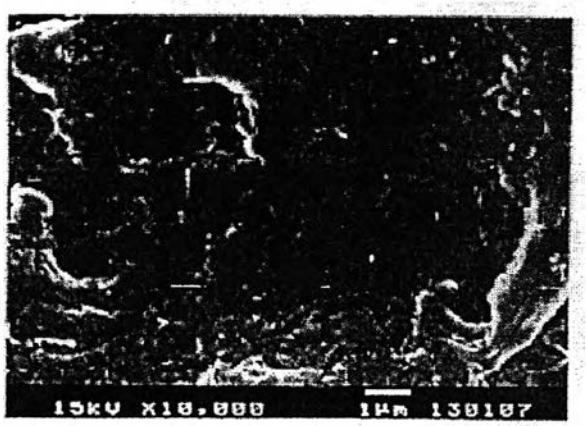
The microscopic views of the surface and cross-sectioned of cellulose acetate plasticized with various levels of DBP film are presented in Figures 22 - 25. Figures22 - 23 presented the surface and cross-sectioned of 20 % DBP plasticized film before and after exposure to the aqueous medium, respectively. The scanning electron micrographs of 40 % DBP plasticized films before and after exposure with water are shown in Figures 24 - 25.



(A)



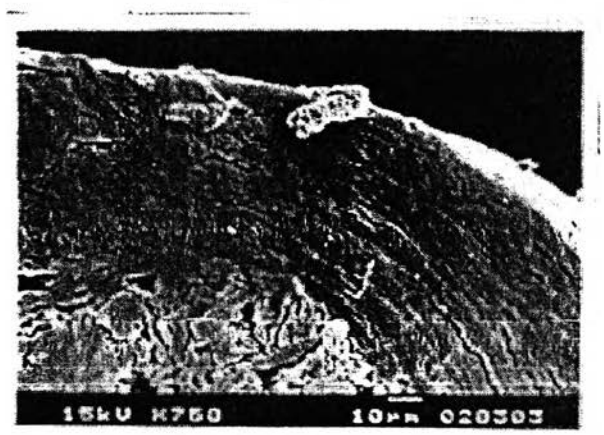
(B)



(C)

Figure 20 The photomicrographs of cellulose acetate without plasticizer film coated osmotic pump tablets before dissolution test (A : surface x2500, B : cross-section x350, C : surface x10000).

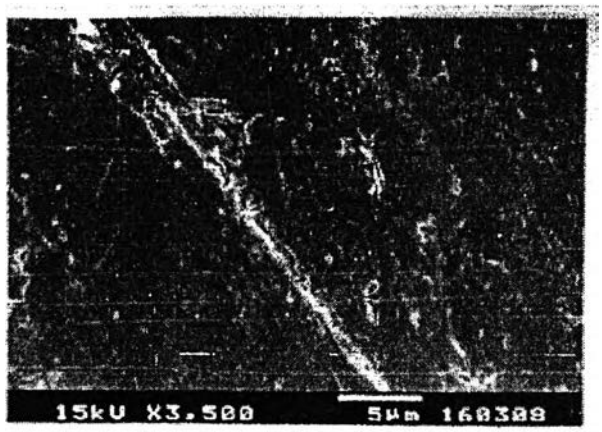
(A)



(B)

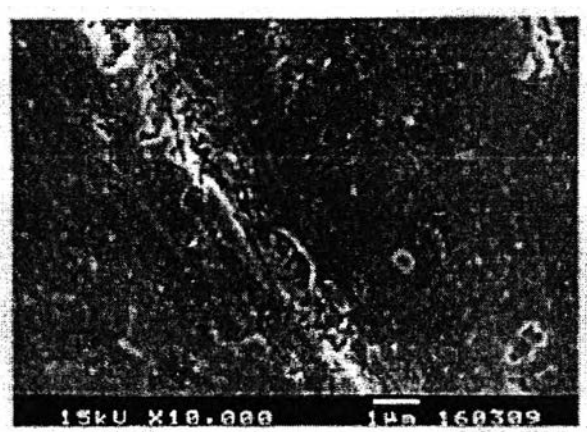
(C)

Figure 21 The photomicrographs of cellulose acetate without plasticizer film coated osmotic pump tablets after dissolution test (A : surface x2500, B : cross-section x750, C : surface x10000).



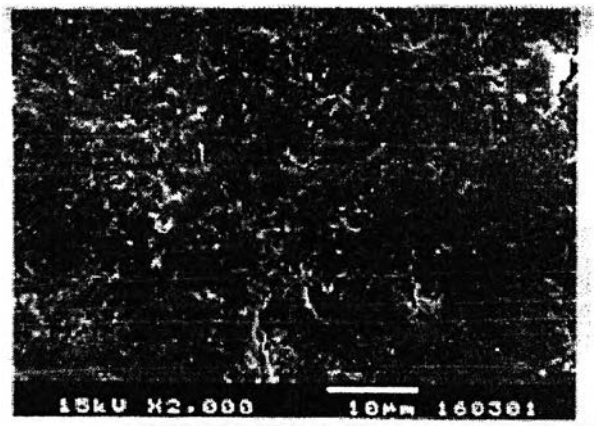
(A)

(B)

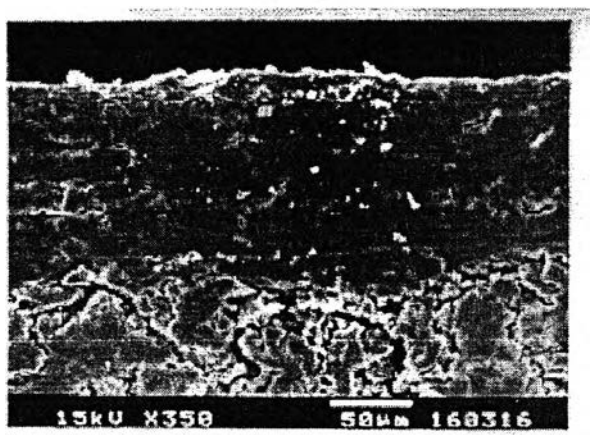


(C)

Figure 22 The photomicrographs of cellulose acetate plasticized with 20 % dibutyl phthalate film coated osmotic pump tablets before dissolution test (A : surface x3500, B : cross-section x350, C : surface x10000).



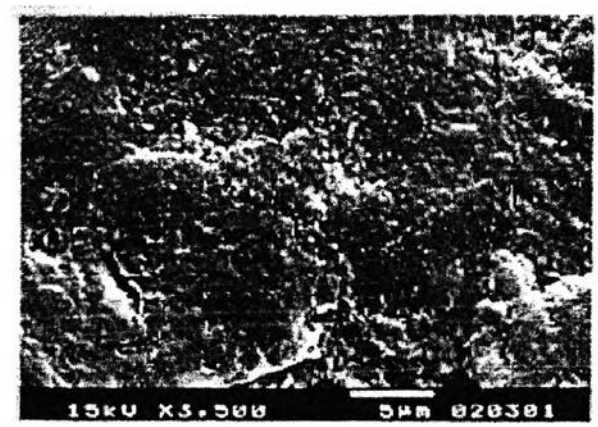
(A)



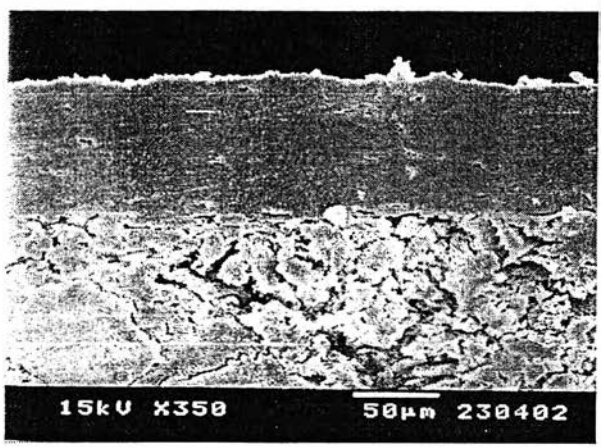
(B)

(C)

Figure 23 The microphotographs of cellulose acetate plasticized with 20 % dibutyl phthalate film coated osmotic pump tablets after dissolution test (A : surface x2000, B : cross-section x350, C : surface x10000).



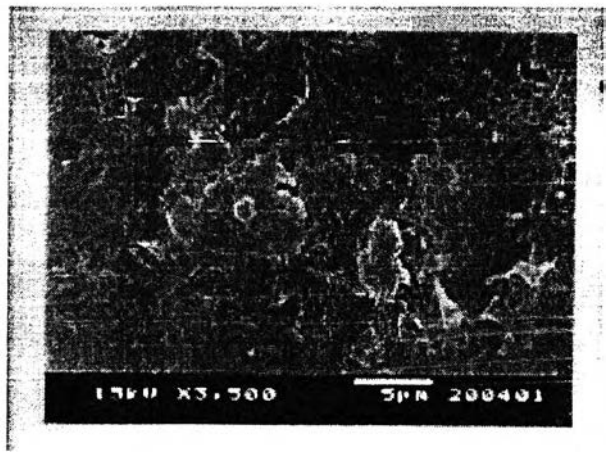
(A)



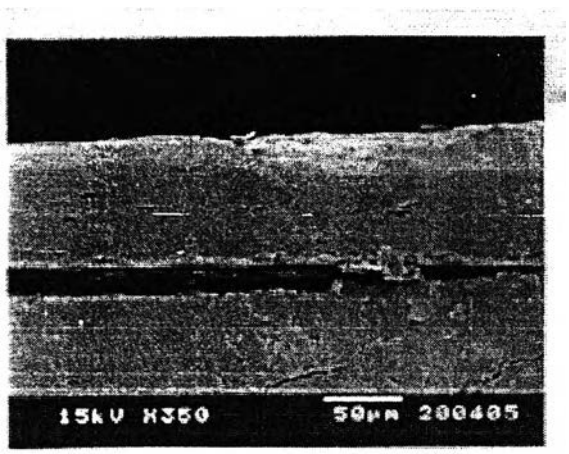
(B)

(C)

Figure 24 The photomicrographs of cellulose acetate plasticized with 40 % dibutyl phthalate film coated osmotic pump tablets before dissolution test (A : surface x3500, B : cross-section x350, C : surface x10000).



(A)



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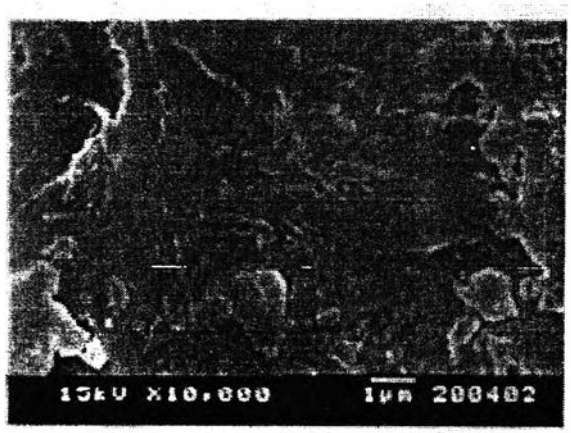
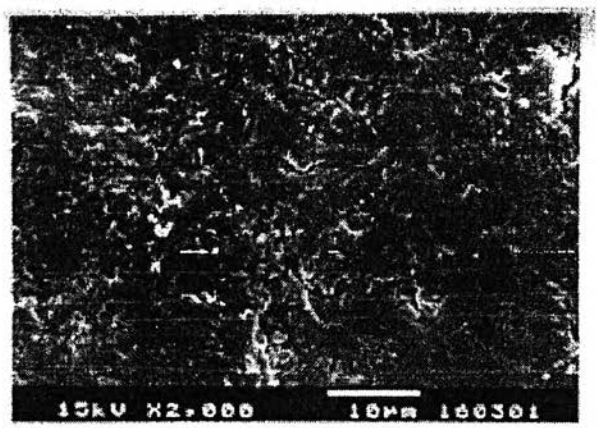


(C)

Figure 25 The microphotographs of cellulose acetate plasticized with 40 % dibutyl phthalate film coated osmotic pump tablets after dissolution test (A : surface x3500, B : cross-section x350, C : surface x10000).

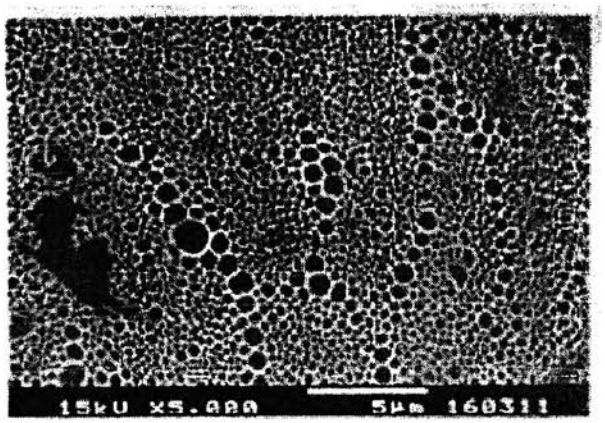


(A)

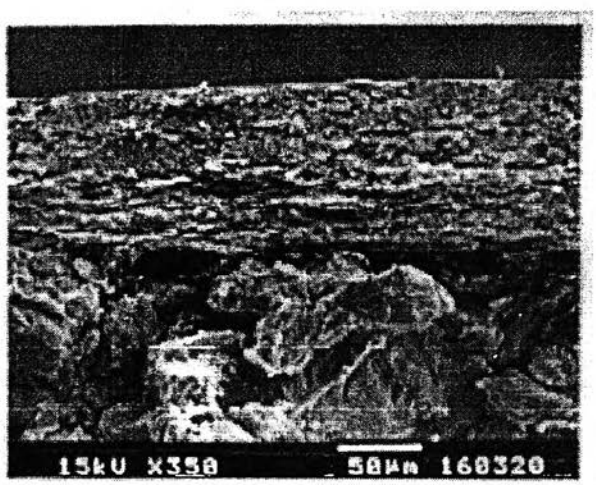
(B)

(C)

Figure 26 The photomicrographs of cellulose acetate plasticized with 20 % PEG 400 before dissolution test (A : surface x2000, B : cross-section x350, C : surface x10000).



(A)



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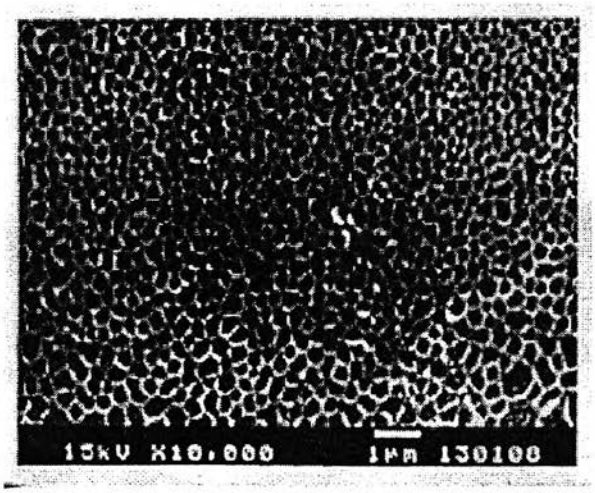
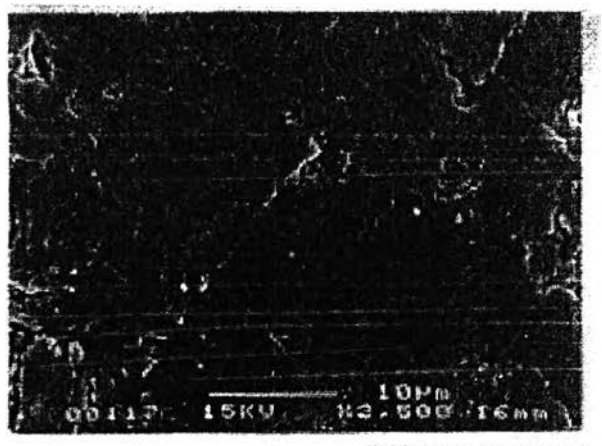
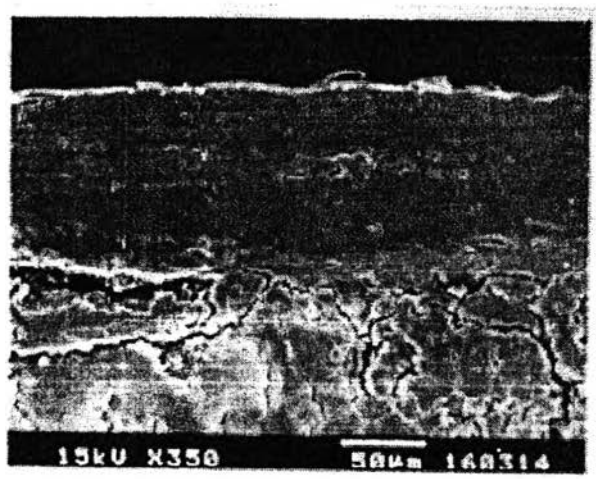


(C)

Figure 27 The photomicrographs of cellulose acetate plasticized with 20 % PEG 400 after dissolution test (A : surface x5000, B : cross-section x350, C : surface x10000).



(A)



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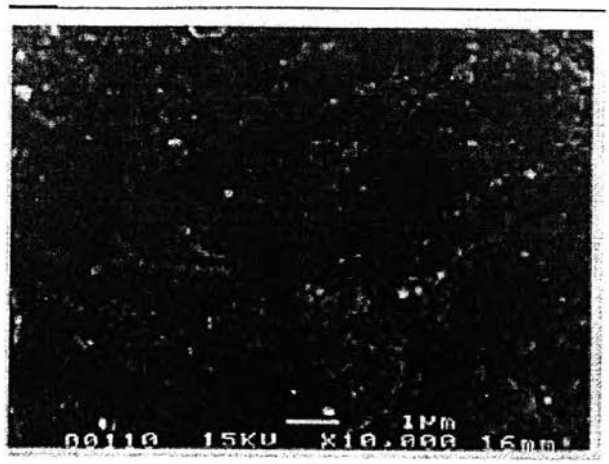
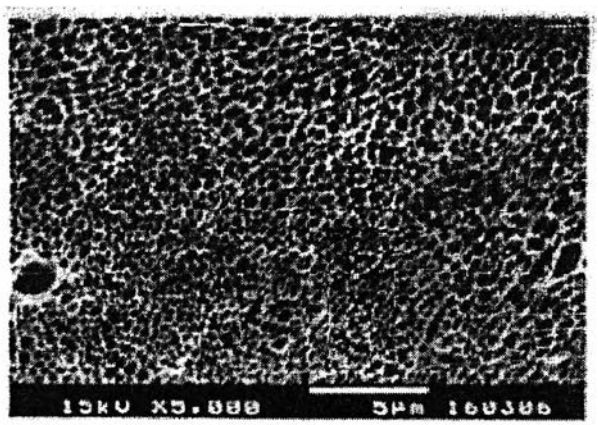
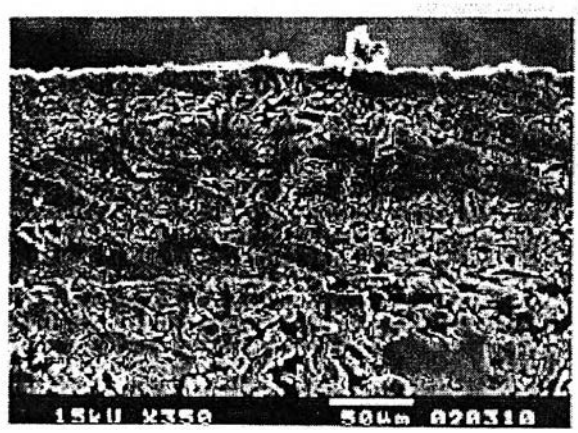


(C)

Figure 28 The photomicrographs of cellulose acetate plasticized with 40 % PEG 400 before dissolution test (A : surface x2500, B : cross-section x350, C : surface x10000).



(A)



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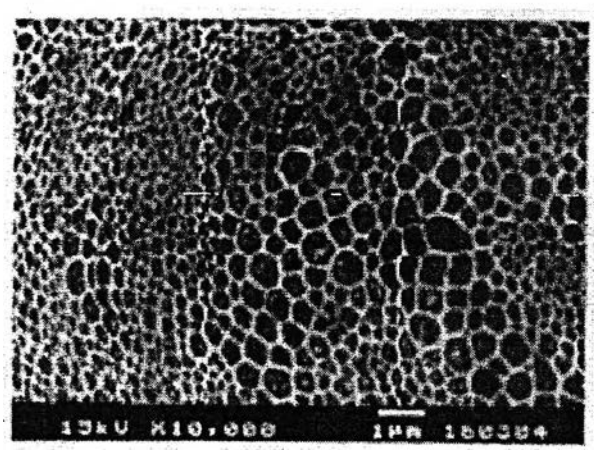
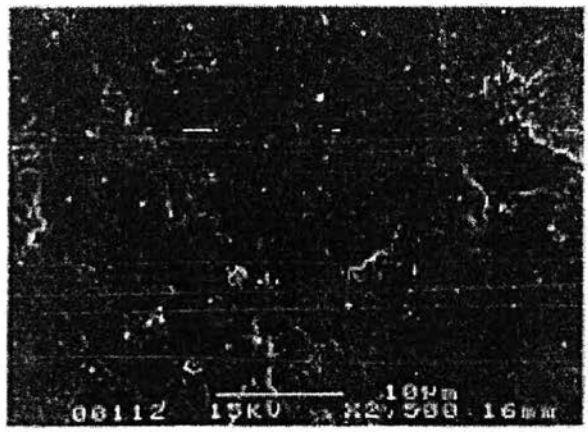
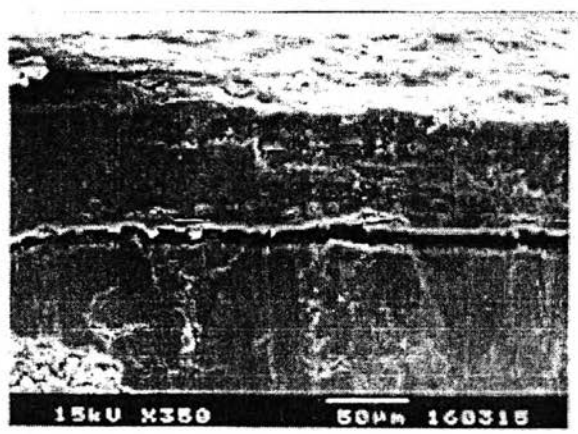


(C)

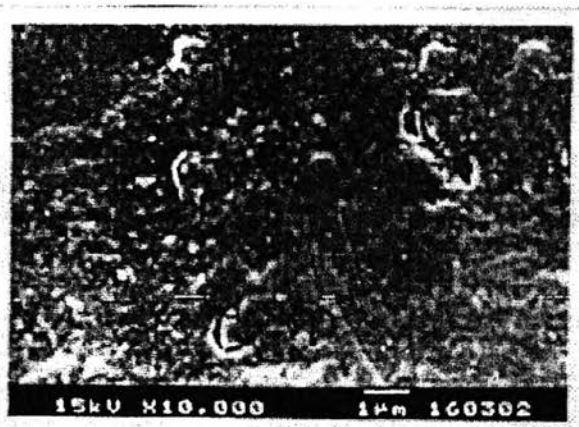
Figure 29 The photomicrographs of cellulose acetate plasticized with 40 % PEG 400 after dissolution test (A : surface x5000, B : cross-section x350, C : surface x10000).



(A)

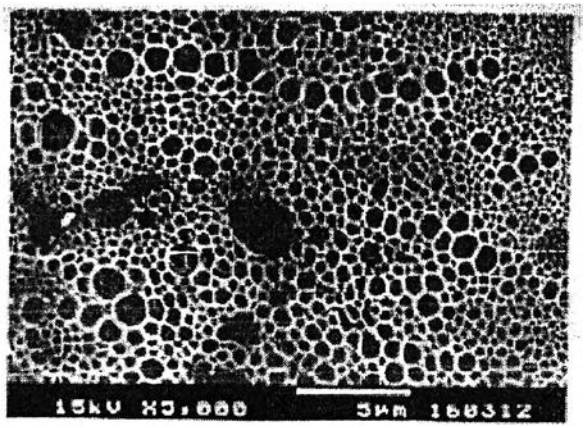


(B)



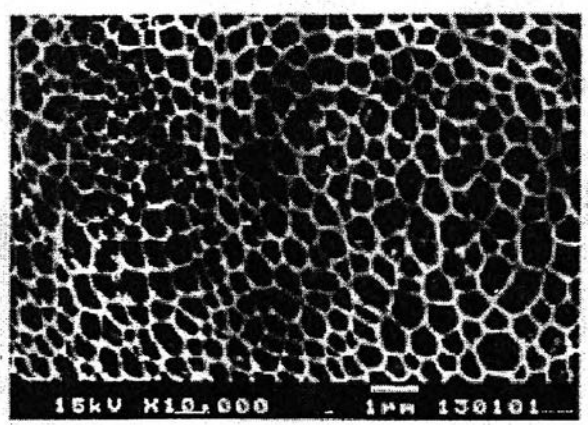
(C)

Figure 30 The photomicrographs of cellulose acetate plasticized with 60 % PEG 400 before dissolution test (A : surface x2500, B : cross-section x350, C : surface x10000).



(A)

(B)



(C)

Figure 31 The photomicrographs of cellulose acetate plasticized with 60 %PEG 400 after dissolution test (A : surface x5000, B : cross-section x350, C : surface x10000).

Before drug release was evaluated, the film containing 20 % DBP demonstrated rather smoother surface than 40 % DBP plasticized film. The same evaluation done after exposure to water demonstrated similar result.

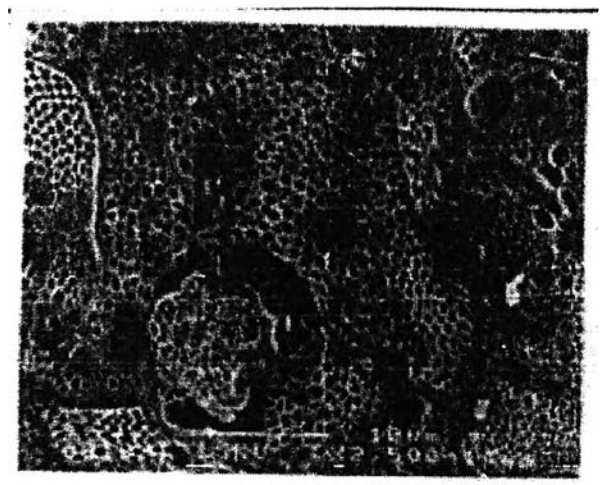
3.3.4 Influence of various level of PEG 400 on the surface and cross-sectioned of deposited film on propranolol hydrochloride tablets morphology

The microscopic images of cellulose acetate plasticized with various of PEG 400 levels films are demonstrated in Figures 26 - 31. Figures 26, 28 and 30 demonstrated the surface and cross-sectioned of cellulose acetate plasticized with 20, 40 and 60 % PEG 400 films, respectively, before exposure with water whereas Figures 27, 29 and 31 presented the films after exposure with water.

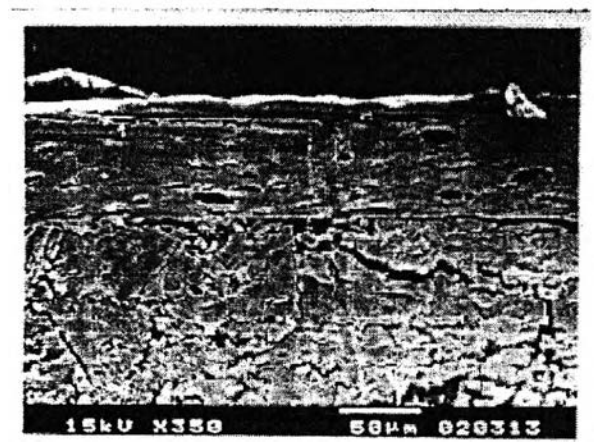
Cellulose acetate plasticized with PEG 400 films evaluated before drug release displayed the smooth, continuos surface and non-defect of cross-sectioned films. The same evaluation done after exposure to the aqueous medium displayed a highly porous structure and spongy films. In addition, the pore size on PEG 400 plasticized films after exposure with water was increased with increasing percent PEG 400 level.

3.3.5 Influence of various level of PEG 4000 on the surface and cross-sectioned of deposited film on propranolol hydrochloride tablets

The scanning electron photomicrographs of 20 % DBP plasticized films with PEG 4,000 at 20, 40 and 60 % levels are shown in Figures 32 - 37. Figures 32, 34 and 36 demonstrated the effect of PEG 4,000 on the surface and cross-sectioned of films before exposure with water whereas Figures 33, 35 and 37 presented the microscopic views of films after exposure with water.



(A)



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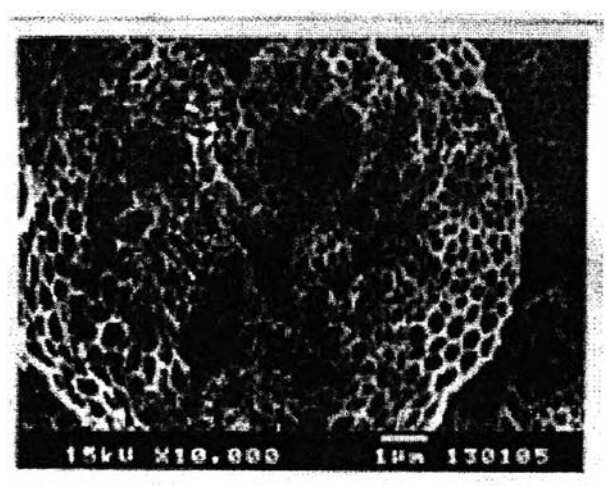
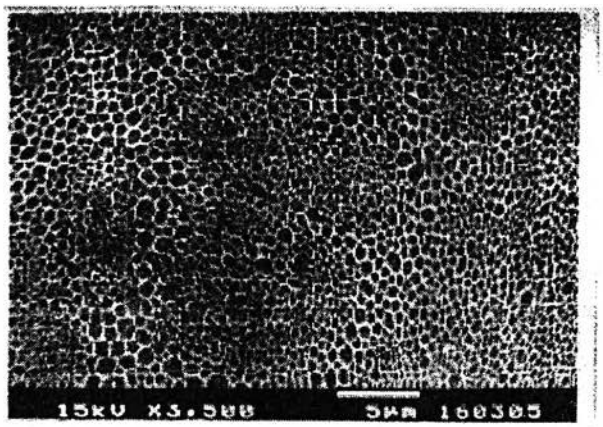
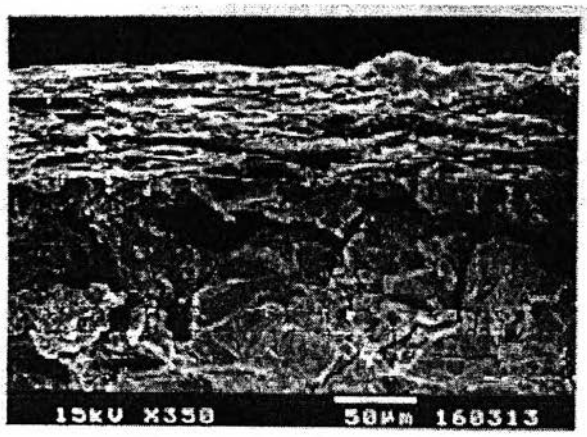


(C)

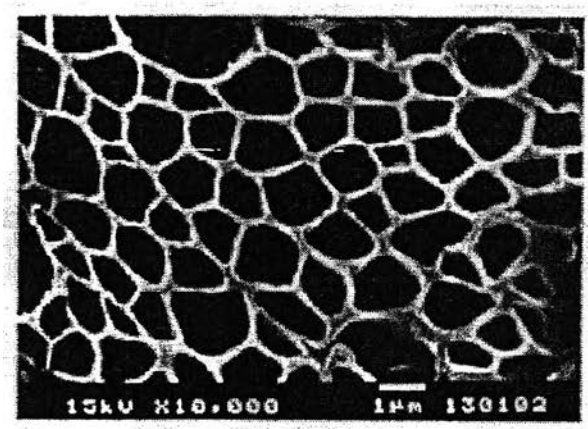
Figure 32 The photomicrographs of cellulose acetate plasticized with 20 % DBP and fluxed with 20 % PEG 4000 before dissolution test (A : surface x2500, B : cross-section x350, C : surface x10000).



(A)

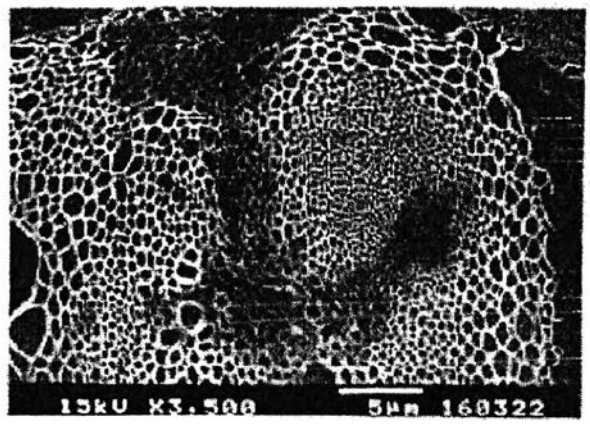


(B)

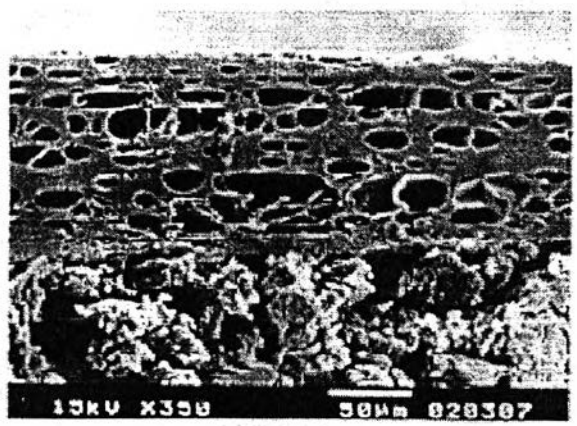


(C)

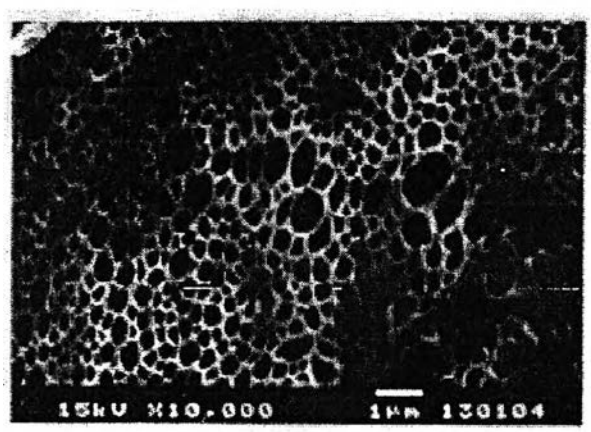
Figure 33 The photomicrographs of cellulose acetate plasticized with 20 % DBP and fluxed with 20 % PEG 4000 after dissolution test (A : surface x3500, B : cross-section x350, C : surface x10000).



(A)

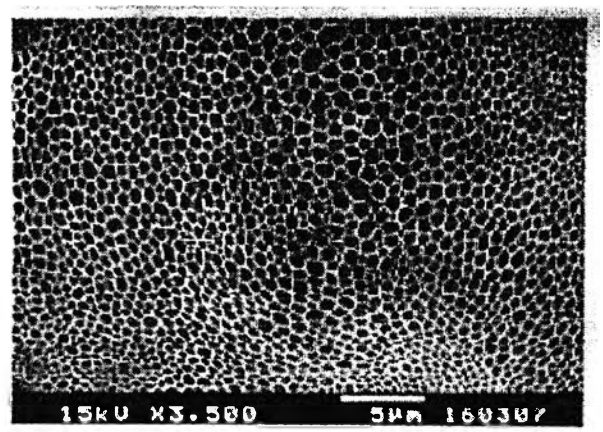


(B)

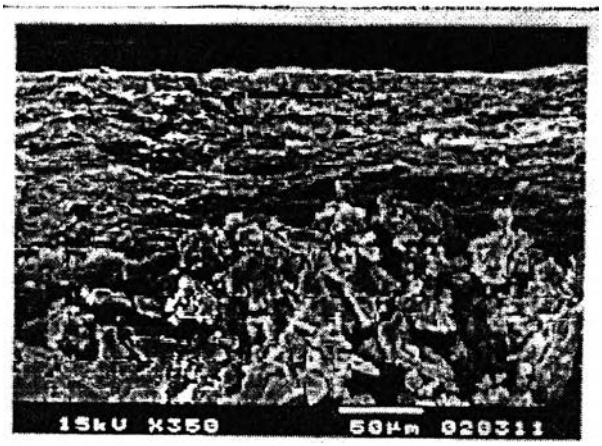


(C)

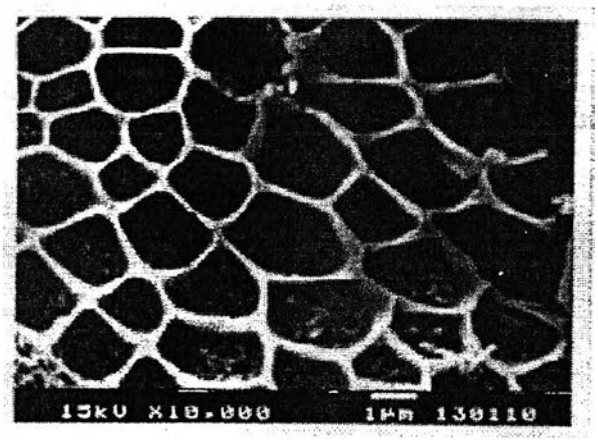
Figure 34 The photomicrographs of cellulose acetate plasticized with 20 % DBP and fluxed with 40 % PEG 4000 before dissolution test (A : surface x3500, B : cross-section x350, C : surface x10000).



(A)

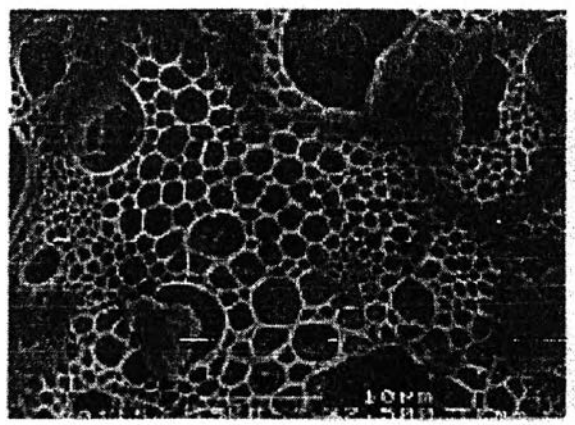


(B)

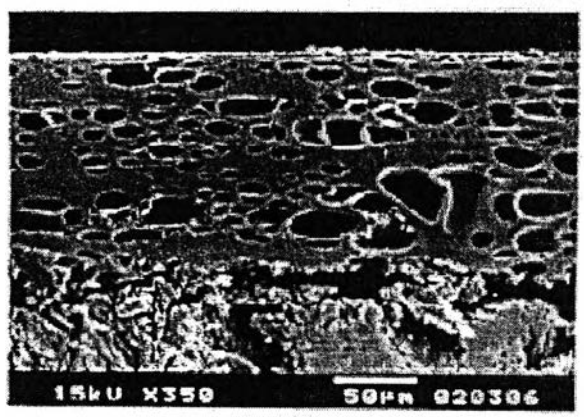


(C)

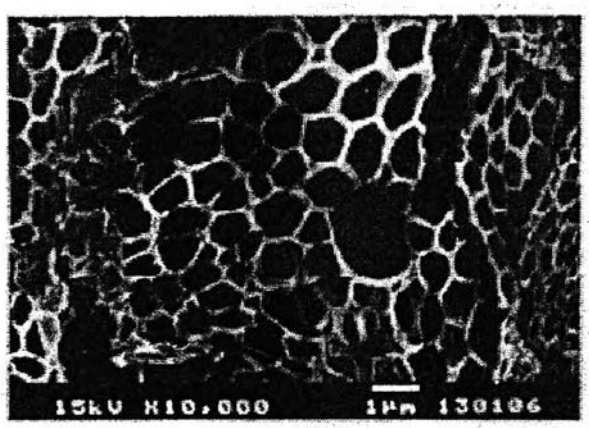
Figure 35 The photomicrographs of cellulose acetate plasticized with 20 % DBP and fluxed with 40 % PEG 4000 after dissolution test (A : surface x3500, B : cross-section x350, C : surface x10000).



(A)

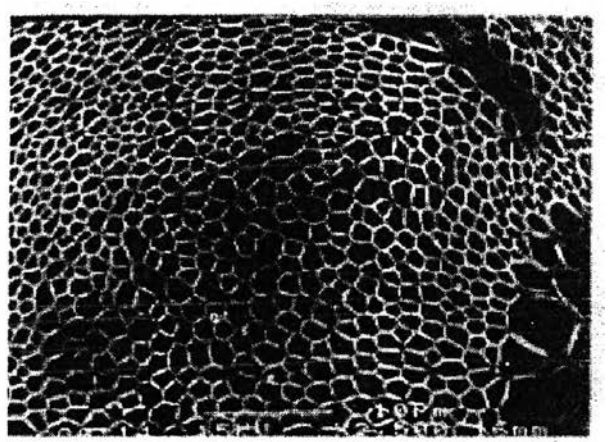


(B)

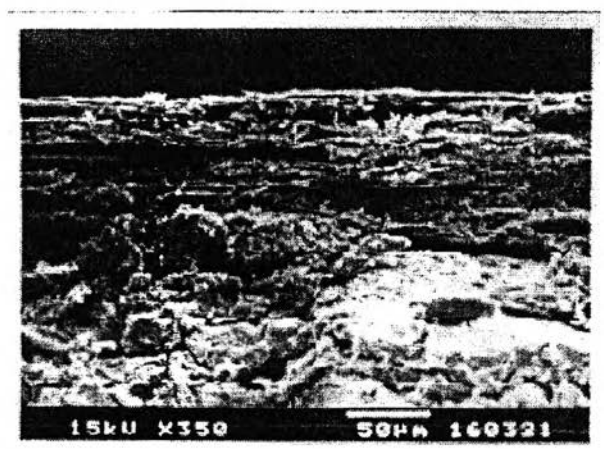


(C)

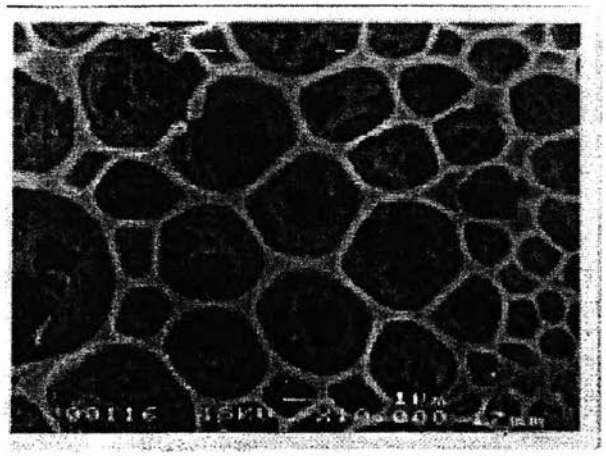
Figure 36 The photomicrographs of cellulose acetate plasticized with 20 % DBP and fluxed with 60 %PEG 4000 before dissolution test (A : surface x2500, B : cross-section x350, C : surface x10000).



(A)



(B)



(C)

Figure 37 The photomicrographs of cellulose acetate plasticized with 20 % DBP and fluxed with 60 % PEG 4000 after dissolution test (A : surface x2500, B : cross-section x350, C : surface x10000).

The macroporous, non-continuous surface and defection of cross-sectioned films were apparent before exposure to the aqueous medium. The pore size on films were increased with increasing amount of PEG 4,000. After drug release was evaluated, the films seems to be more porous and spongy films. Clearly, the pore size on PEG 400 plasticized films was observed to be smaller than that of films containing PEG 4,000.

4. Evaluation of osmotic pressure

The results of osmolarity were obtained from diluted lactose, sucrose, mannitol and sodium chloride solution. The results are 0.003, 0.012, 0.013 and 0.096 milliosmol/kilogram, respectively. These osmolality data, were used to calculate the osmotic pressure. And the results were 7.626, 30.504, 33.406 and 251.658 atm, respectively.

On the part of dissolution media, the result of osmolality which came from 0.1 N HCl and phosphate buffer pH 6.8 were 0.218 and 0.325 miliosmol/kilogram, respectively. The calculated osmotic pressure were 5.542 and 80.262 atm, respectively. The calculations are shown in Appendix D.

5. Dissolution study

All release data of propranolol hydrochloride from propranolol hydrochloride tablets, propranolol hydrochloride coated tablets, propranolol hydrochloride osmotic pump tablets and propranolol hydrochloride osmotic agents osmotic pump tablets are shown in Tables 8 - 69 (Appendix B). From these data, the release profiles could be plotted between the percentage of amount of drug release against time.

5.1 Propranolol hydrochloride tablets

The release data of propranolol hydrochloride from tablets are shown graphically in Figure 38. The average percentage of drug release was nearly 85 % within 15 minutes and was completely dissolved within 30 minutes.

5.2 Propranolol hydrochloride coated tablets

The release data of propranolol hydrochloride from coated tablets without passageway are shown in Tables 9 - 22 (Appendix B) and are shown graphically in Figures 39 - 43. Figure 39 illustrates the release profiles of tablets coated with different amount of cellulose acetate coating solution, 1, 2 and 3 liters, whereas Figures 40 - 42 are the release profiles of drug from tablets coated with different amount of cellulose acetate solution plasticized with 20, 40 and 60 % PEG 400. Figure 43 illustrates the release profiles of tablets coated with 2 liters of cellulose acetate solution plasticized with 20 and 40 % DBP.

At coating level of 3 liters, the percentage of drug released was less than 2 % after 6 hours in all cases. On the part of 2 liters of coating solution, the results were similar to those obtained from the coating level of 3 liters except the release profile of tablets coated with only cellulose acetate was found to be over than 50 % of drug on the 6^{th} hours of the experiment. In case of coating level of 1 liter, 56.24, 20.52, 61.59 and 42.84 % of drug were released from tablets coated with cellulose acetate, cellulose acetate plasticized with 20, 40 and 60 % PEG 400, respectively.

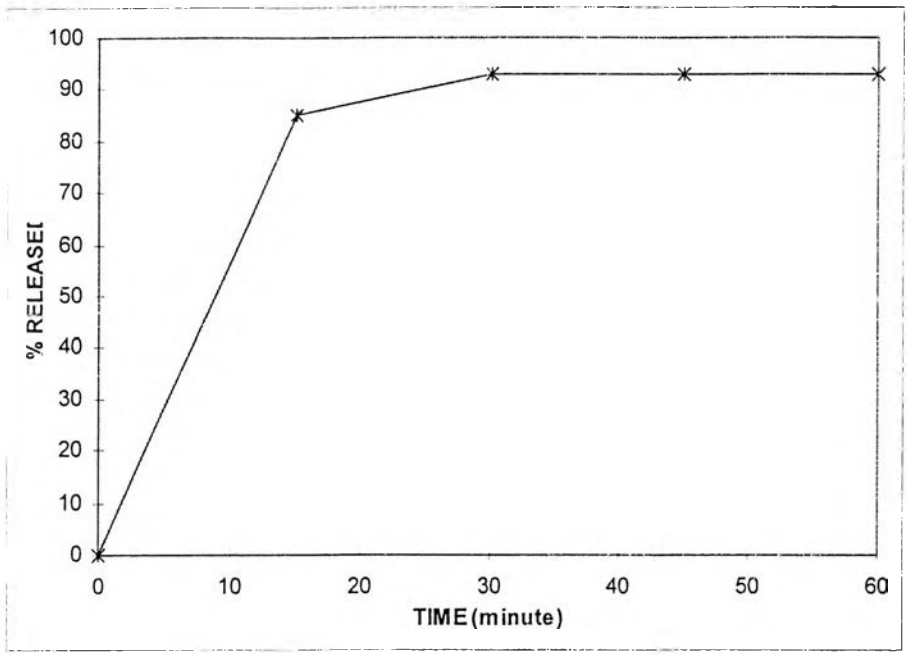


Figure 38 The release profile of propranolol hydrochloride from core tablets.

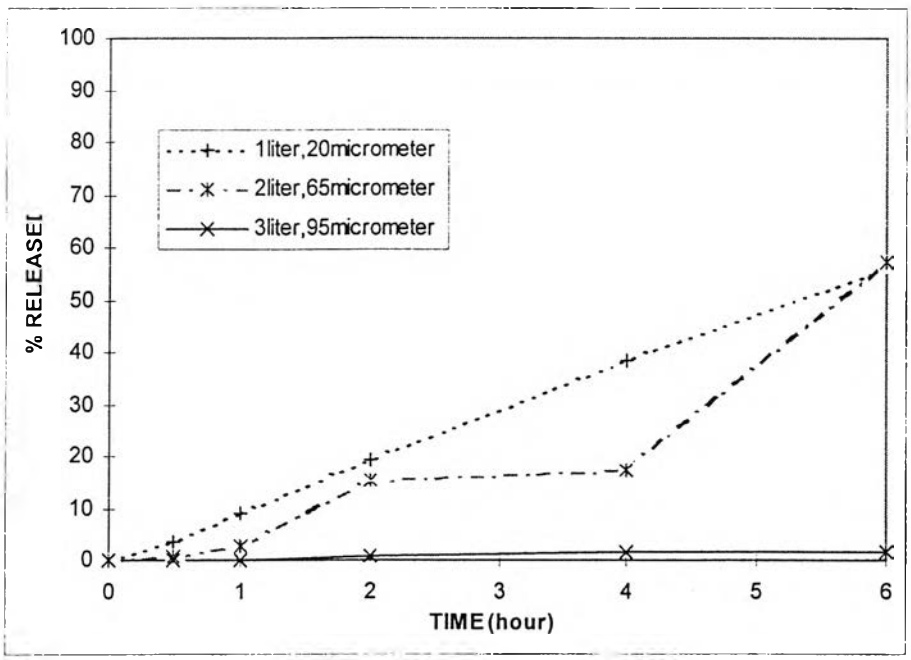


Figure 39 The release profile of propranolol hydrochloride from tablets coated with varying amount of cellulose acetate coating solution.

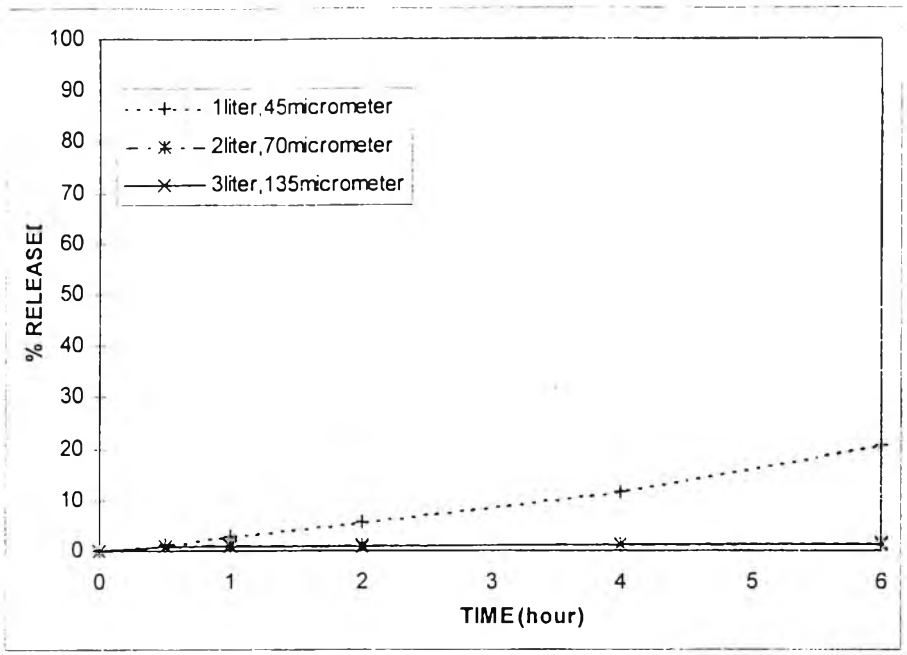


Figure 40 The release profile of propranolol hydrochloride from core tablets coated with varying amount of cellulose acetate plasticized with 20 % PEG 400 solution.

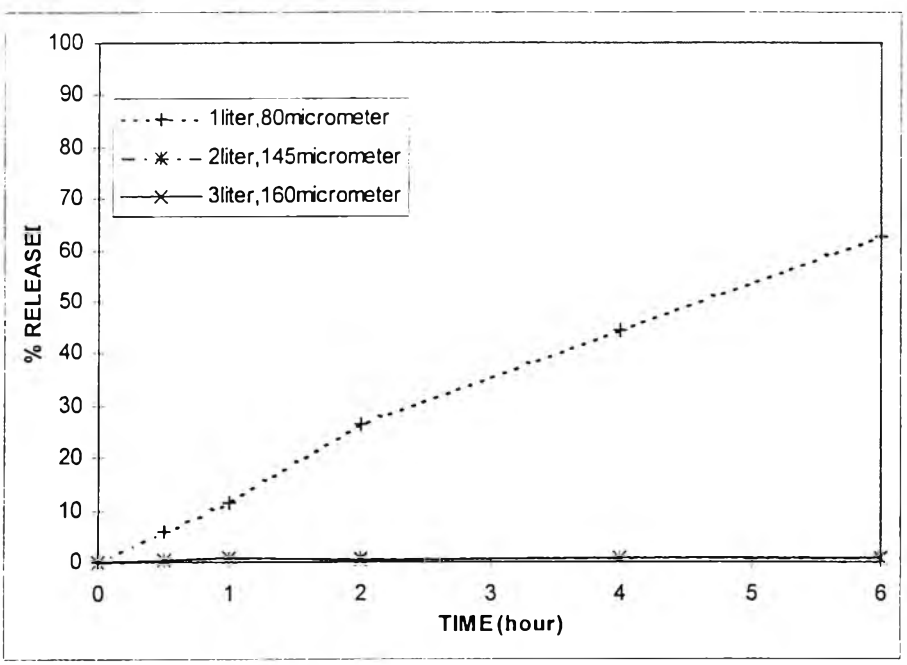


Figure 41 The release profile of propranolol hydrochloride from core tablets coated with varying amount of cellulose acetate plasticized with 40 % PEG 400 solution.

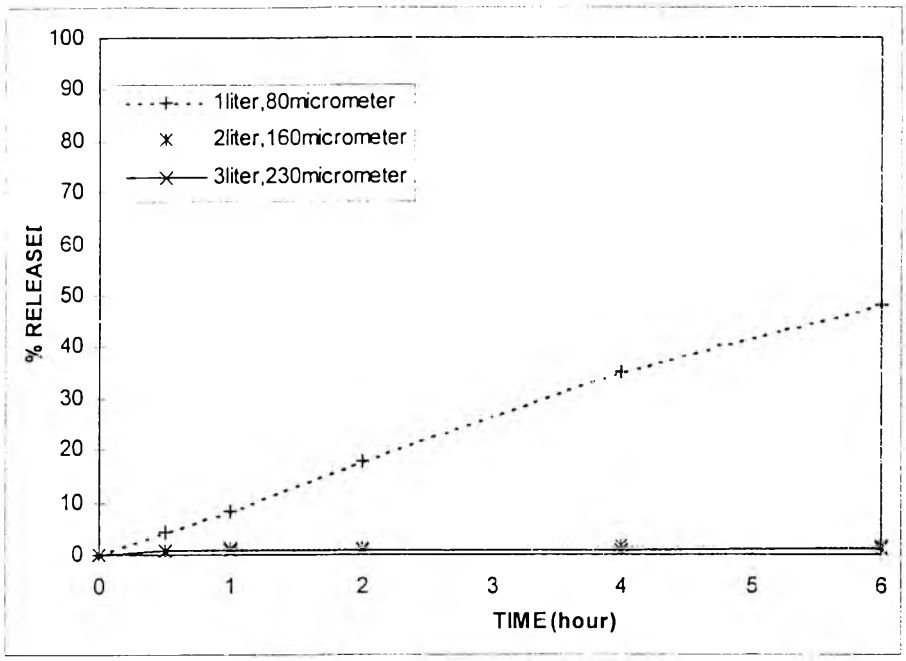


Figure 42 The release profile of propranolol hydrochloride from core tablets coated with varying amount of cellulose acetate plasticized with 60 % PEG 400 solution.

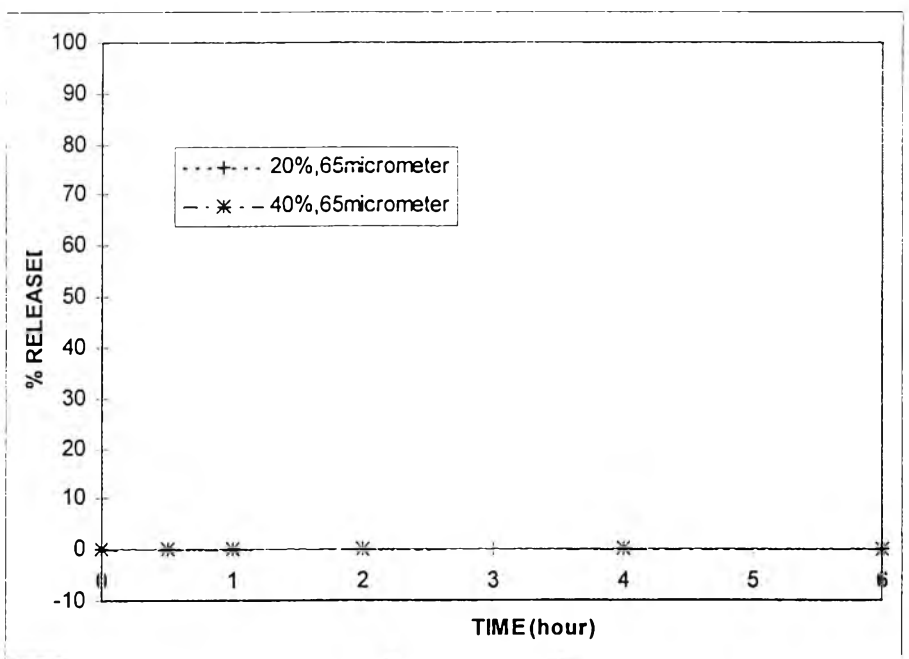


Figure 43 The release profile of propranolol hydrochloride from core tablets coated with cellulose acetate (2 liters) plasticized with 20 and 40 % DBP

No drug was released from osmotic pump tablets coated with cellulose acetate plasticized with 20 and 40 % DBP.

5.3 Propranolol hydrochloride osmotic pump tablets

A. Influence of plasticizer type on the release profiles

The comparative release profiles of osmotic pump tablets coated with cellulose acetate, cellulose acetate plasticized with 20 % PEG 400 and cellulose acetate plasticized with 20 % DBP are shown graphically in Figure 44. All release profiles were linear with different slopes. The release rate of osmotic pump devices coated with cellulose acetate, cellulose acetate plasticized with 20 % DBP and 20 % PEG 400 were 1.35, 0.38 and 2.38 % / hour with lag-time of 0.5, 1 and 0 hours respectively.

B. Influence of various levels of PEG 400 in coating film on the release profiles

The release profiles of osmotic pump tablets using cellulose acetate as film former and PEG 400 at 20, 40 and 60 % w/w of cellulose acetate are illustrated in Figure 45 (Tables 24-29, Appendix B). These three formulas showed a statistically significant difference between drug released pattern from osmotic pump tablets which the lowest drug released was from the plasticizer of 20 % followed by those of 40 % and 60 % respectively ($\alpha = 0.05$). The release profiles of osmotic pump tablets coated with 40 % and 60 % PEG 400 were curve whereas the release profile of osmotic pump tablets coated with 20 % PEG 400 was linear.

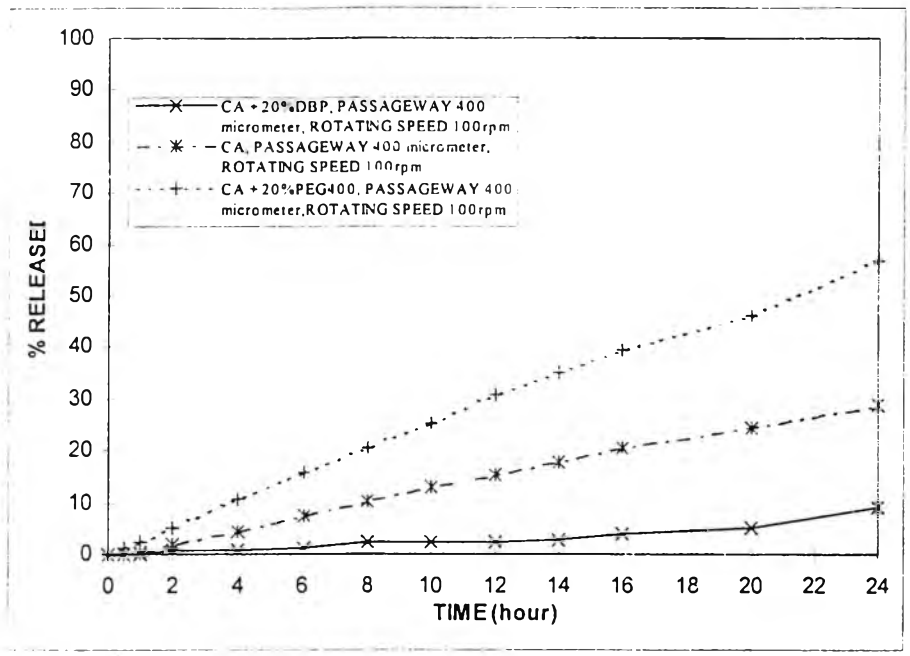


Figure 44 The influence of plasticizer type on the release profiles from osmotic pump tablets.

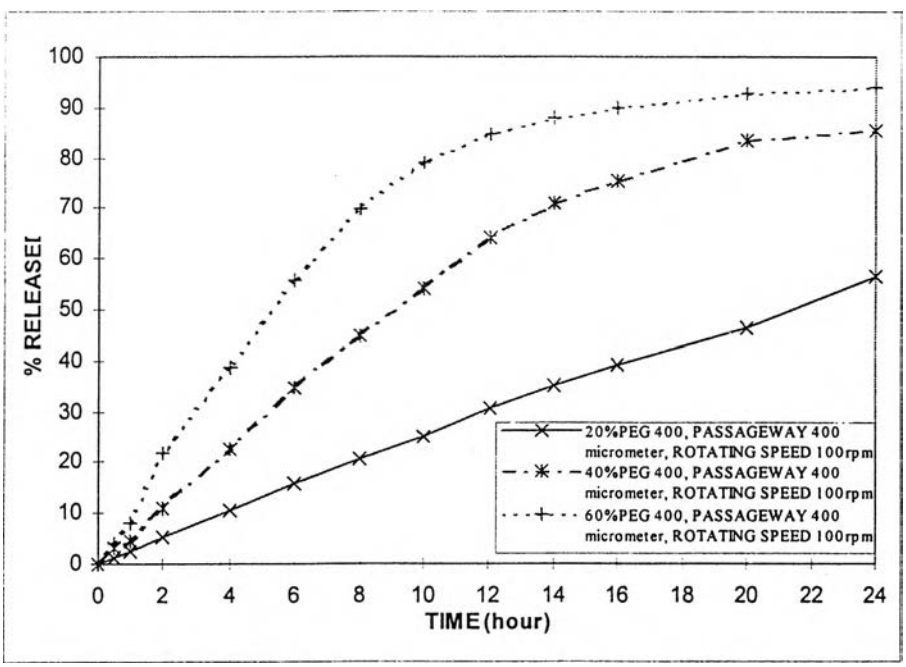


Figure 45 The effect of level of PEG 400 in coated film on the release profiles of osmotic pump tablets.

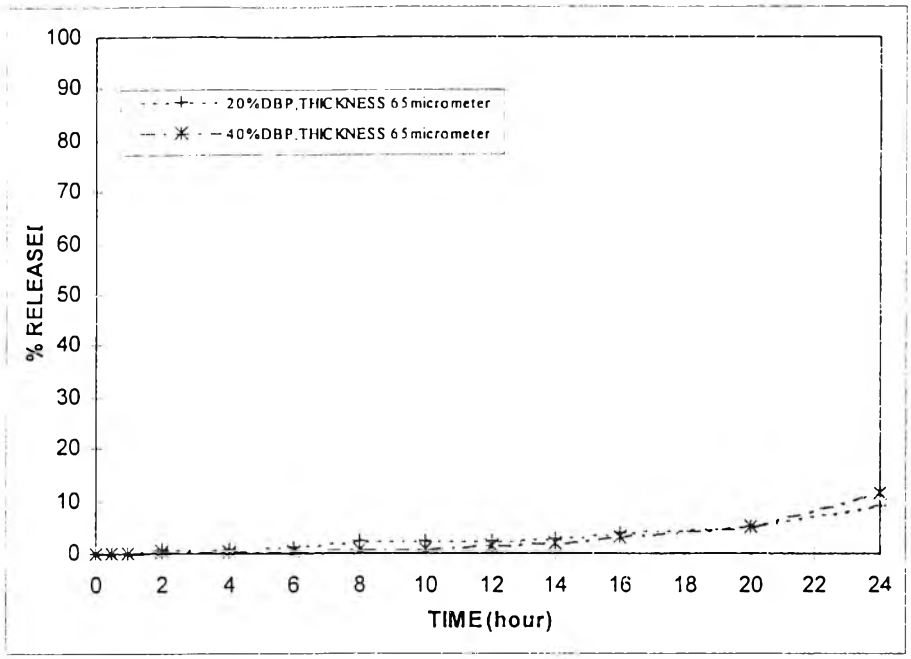


Figure 46 The effect of level of DBP in coated film on the release profiles of osmotic pump devices.

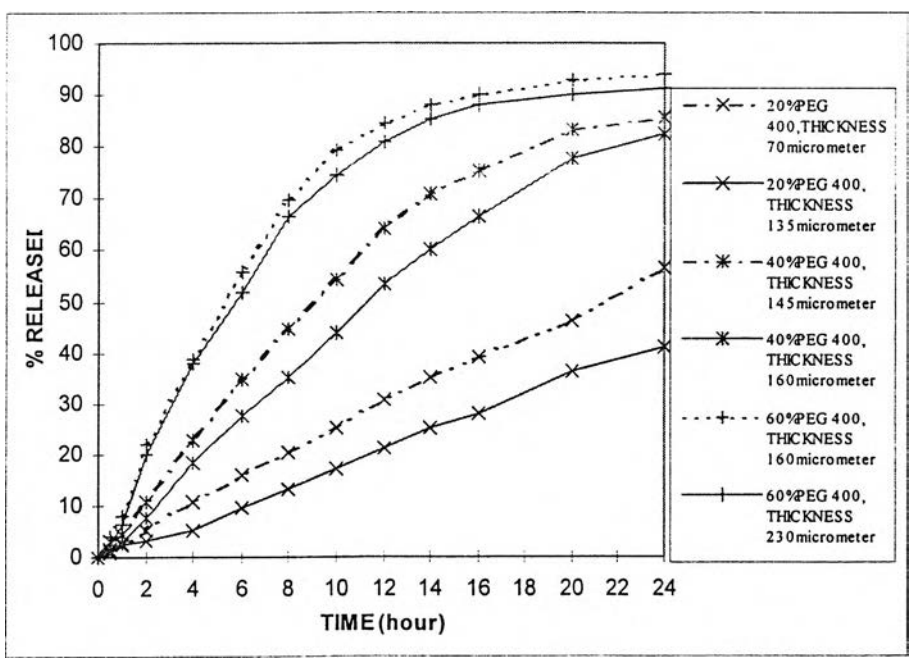


Figure 47 The effect of coating level on the release profiles of osmotic pump tablets.

C. Influence of various levels of DBP in coating film on the release profiles

Figure 46 demonstrates the release profiles of osmotic pump tablets coated with cellulose acetate plasticized with 20 and 40 % DBP. The release profiles of drug from both formulas were slightly different. The release of drug from both formulas after 24 hours was less than 10 %. The lag-time of the two formula that have different amount of DBP was 1 hour.

D. Influence of coating levels on the release profiles

The effect of coating levels on the release profiles of propranolol hydrochloride from osmotic pump devices coated with cellulose acetate plasticized with 20, 40 and 60% PEG 400 are presented in Figure 47. The set of profiles from 60 % PEG 400 plasticized film coated osmotic pump devices seem nearly superimposed. The set of profile of 40 % PEG 400 plasticized film coated osmotic devices was slightly different whereas the set of profile of 20 % PEG 400 plasticized film coated osmotic devices was very different. The interval between the release profiles of osmotic pump tablets coated with cellulose acetate plasticized with 60 % PEG 400 was less than the release profiles of osmotic pump tablets coated with cellulose acetate plasticized with 20 % PEG 400.

E. Influence of various levels of PEG 4,000 in coating film on the release profile

Figure 48 demonstrates the release profiles of drug from osmotic pump devices coated with cellulose acetate plasticized with 20 % DBP and containing PEG 4,000 at 20, 40 and 60 % levels, based on polymer weight. When the osmotic pump devices were coated with 20 % DBP plasticized film containing 60 % PEG 4000, the release of

drug was the highest followed by those of film containing 40 % and 20 % PEG 4000 respectively. The release profiles of osmotic devices coated with DBP plasticized film containing 60% and 40 % PEG 4000 were typically curve with plateau at the 8^{th} and 10^{th} hours respectively. In the case of DBP plasticized film containing 20 % PEG 4000 film, the release profile was also curvature.

F. Influence of passageway size on the release profile

The comparison of release profiles of osmotic pump tablets coated with cellulose acetate, cellulose acetate plasticized with 20 % and 60 % PEG 400 using four sizes (400, 700 1,000 and 1,500 μm) of passageway are represented in Figures 49-51. The set of drug release pattern from cellulose acetate coated osmotic devices was straight line and seemed to be a single line although the passageway size on the face of each osmotic pump tablet was different. The ANOVA (Appendix E) test method did not show a significant difference of drug release pattern. For the group of drug release pattern from 20 % PEG 400 plasticized film coated osmotic devices, the group was also straight line although the profiles were not superimposed. The ANOVA method also did not show a significant difference of the profiles but the paired t-test method showed a significant difference between the profiles of the osmotic devices with a passageway size of 400 μm and that the passageway size of 700 μm($\alpha = 0.05$). The set of release profile of 60 % PEG 400 plasticized film coated osmotic devices were curved and the profiles were not superimposed. In the test under the statistic ANOVA method, the results showed non-significant difference of the profiles. When all data were tested by using paired t-test method, the result showed a significant difference between the profile from osmotic devices with a passageway size of 400 μm and the profile from osmotic devices with a passageway size of 1500 μm.

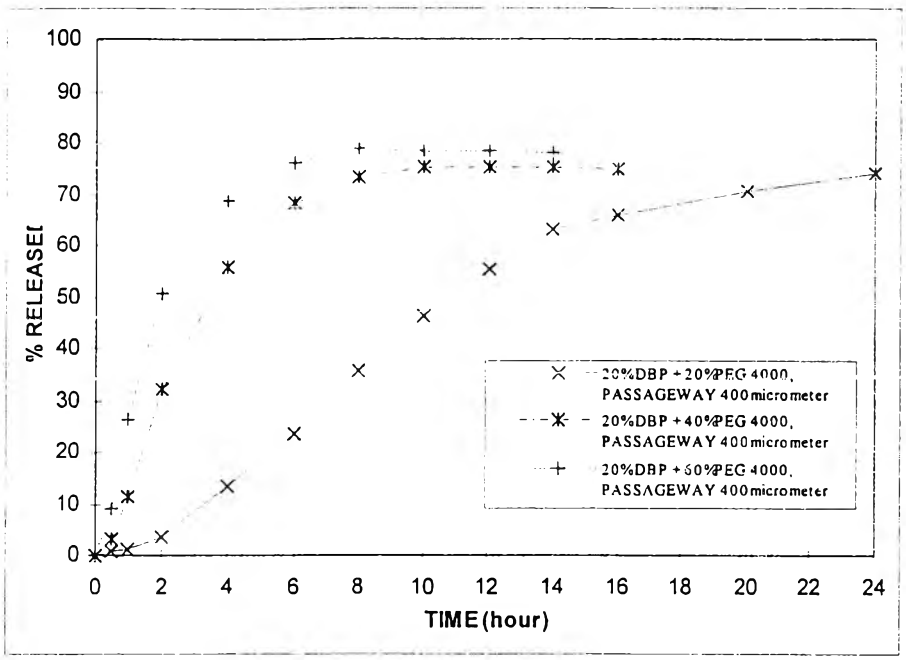


Figure 48 The effect of level of PEG 4000 in coated film on the release profiles.

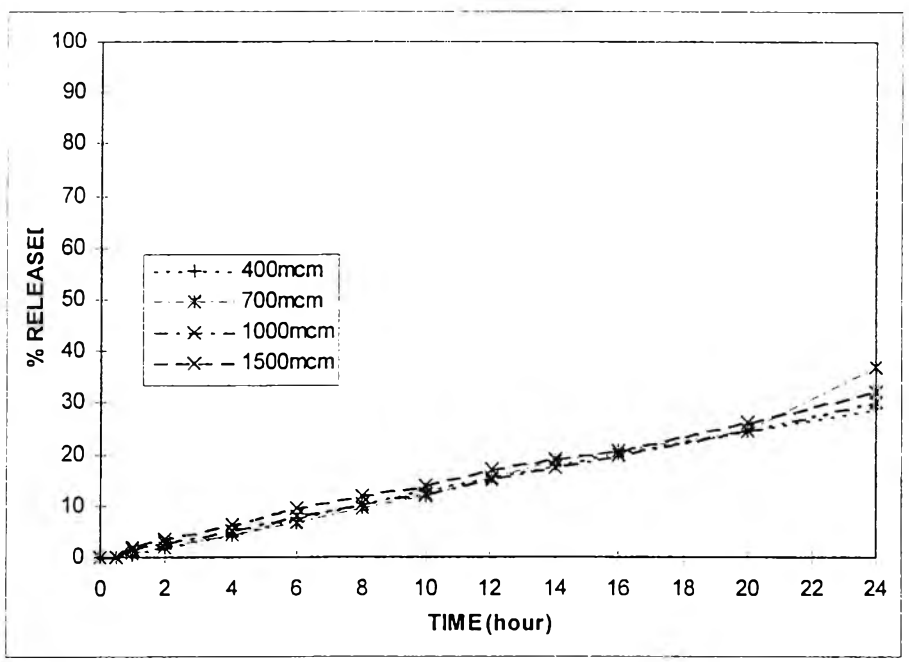


Figure 49 The effect of passageway size on the release profiles of osmotic pump devices coated with cellulose acetate .

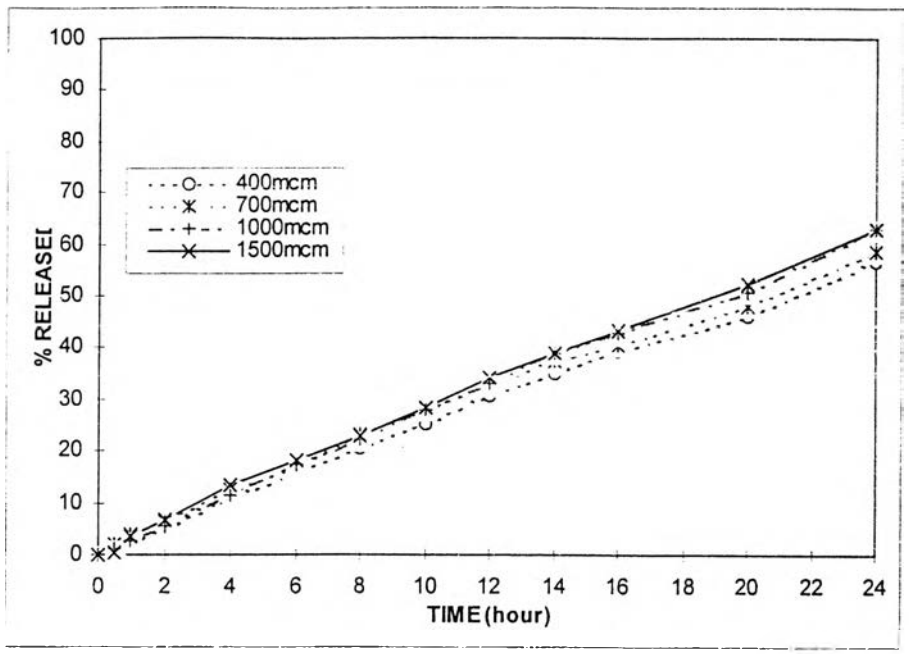


Figure 50 The effect of passageway size on the release profiles of osmotic devices coated with 20 % PEG 400 plasticized film.

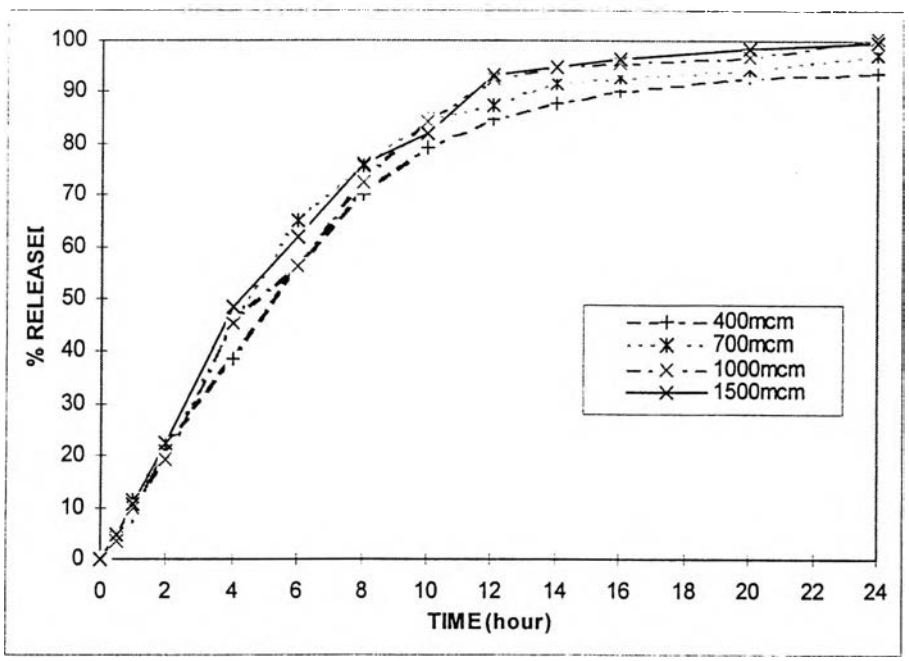


Figure 51 The effect of passageway size on the release profiles of osmotic pump devices coated with 60 % PEG 400 plasticized film.

G. Influence of rotating speed on the release profile

Figures 52-54 shows the release profiles of osmotic pump tablets coated with cellulose acetate, cellulose acetate plasticized with 20 % and 60 % using two sizes of passageway at 400 and 1500 μm under the rotating speed of basket type at 50, 100 and 150 rpm respectively. In Figure 52, the group of profile from cellulose acetate coated osmotic devices was linear with a lag-time of 0.5 hour. The ANOVA did not a significant different of the group of profile. For Figure 53, the group of profile from 20 % PEG 400 plasticized film coated osmotic devices was also linear without a lag-time. All release data were tested by ANOVA method. The result did not show significant differences. On the part of Figure 54, the group of profile from osmotic devices coated with 60 % PEG 400 plasticized film was curvature without plateau. By using paired t-test method, the result represented a significant difference between the profile of osmotic device with a passageway of 1500 μm under rotating speed of 50 rpm and 150 rpm.

H. Influence of rotating type on the release profiles

Figures 55 - 57 represents the release profiles of osmotic pump tablets coated with cellulose acetate, cellulose acetate plasticized with 20 % and 60 % PEG 400 using the basket and paddle as rotating type with two sizes (400 and 1500 μm) of passageway under the rotating speed at 100 rpm. The group of release profile from cellulose acetate coated osmotic devices followed a zero-order kinetic with a lag-time of 0.5 hour and all release profiles seemed to be superimposed. By using ANOVA test method, the result did not indicate significant difference if the rotating type was changed. The group of profile of osmotic pump devices coated with 20 % PEG 400 plasticized film were also followed a zero-order kinetic. When all release data were tested by using

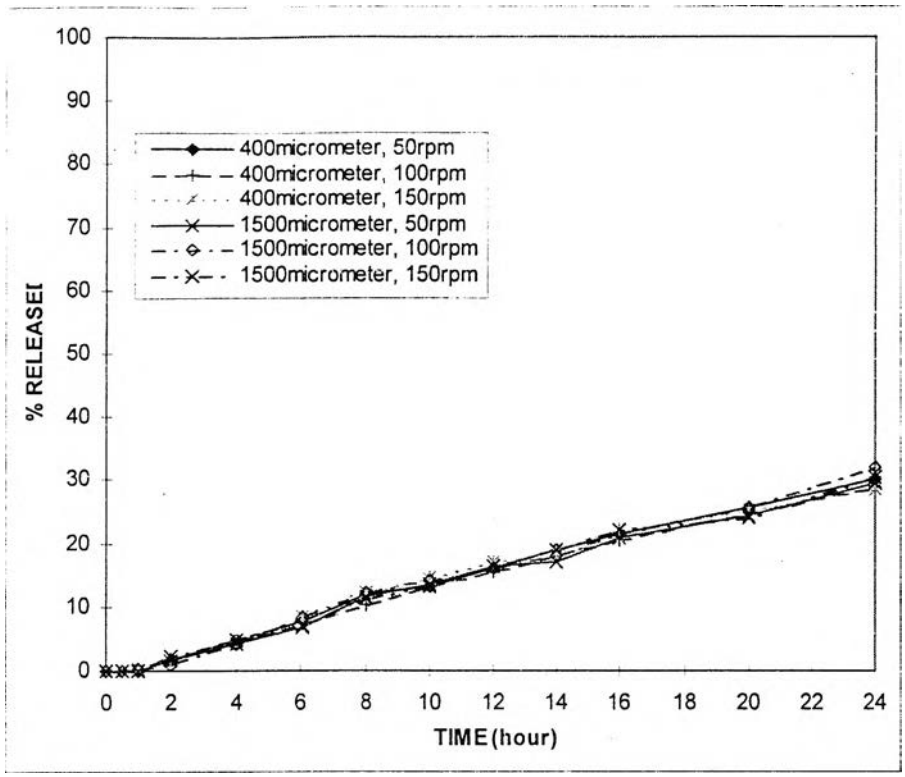


Figure 52 The effect of rotating speed on the release profiles of osmotic pump tablets coated with cellulose acetate.

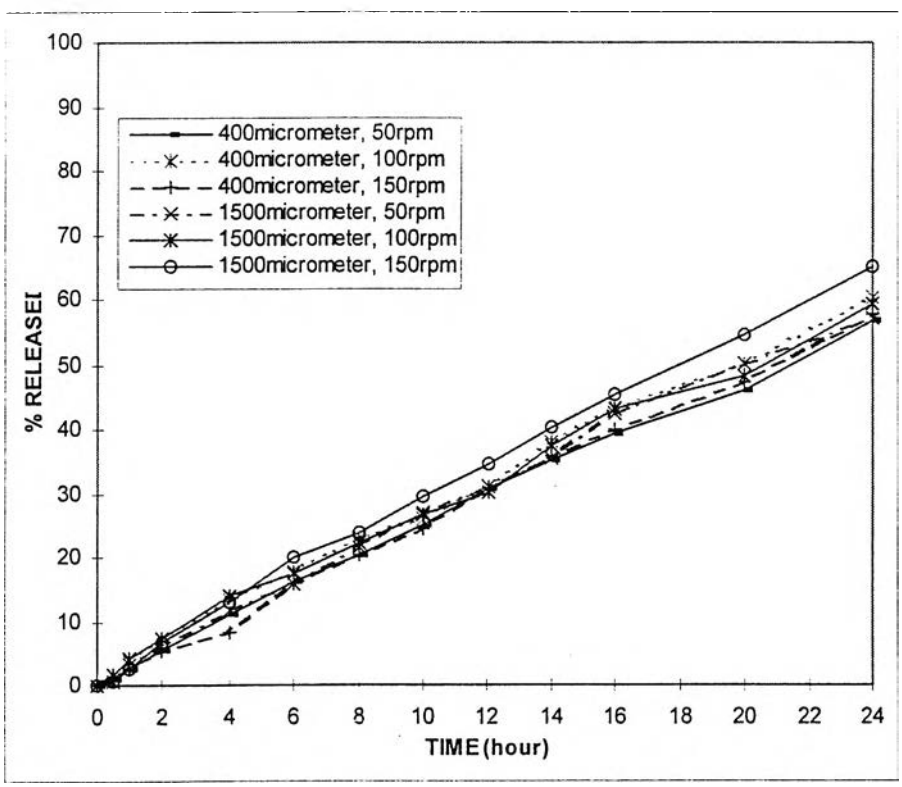


Figure 53 The effect of rotating speed on the release profiles of osmotic pump tablets coated with cellulose acetate plasticized with 20 % PEG 400.

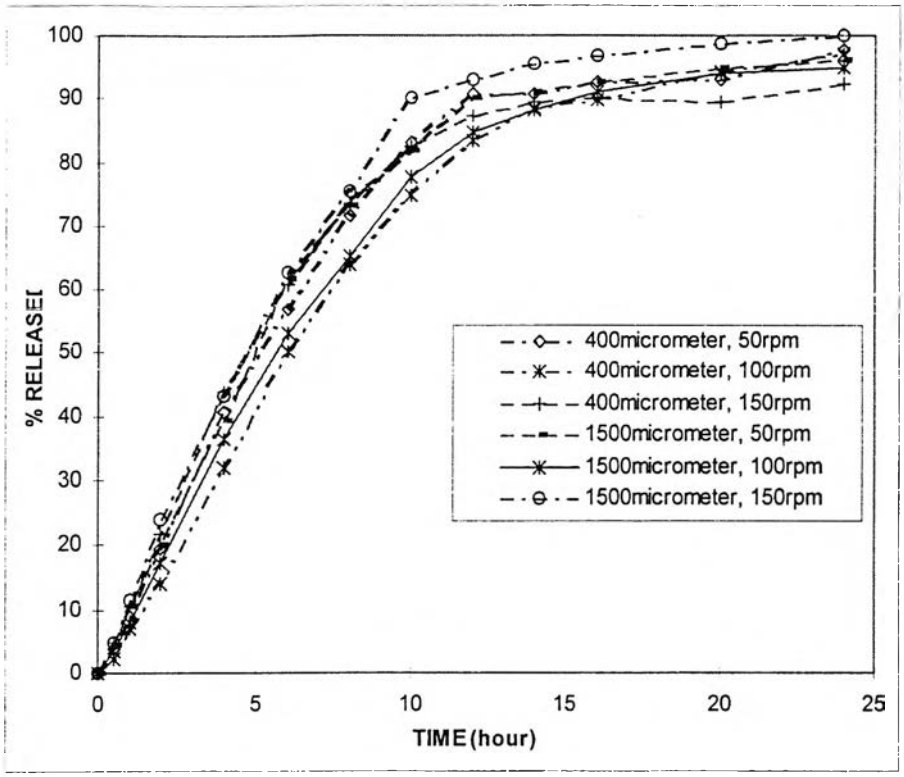


Figure 54 The effect of rotating speed on the release profiles of osmotic pump tablets coated cellulose acetate plasticized with 60 % PEG 400.

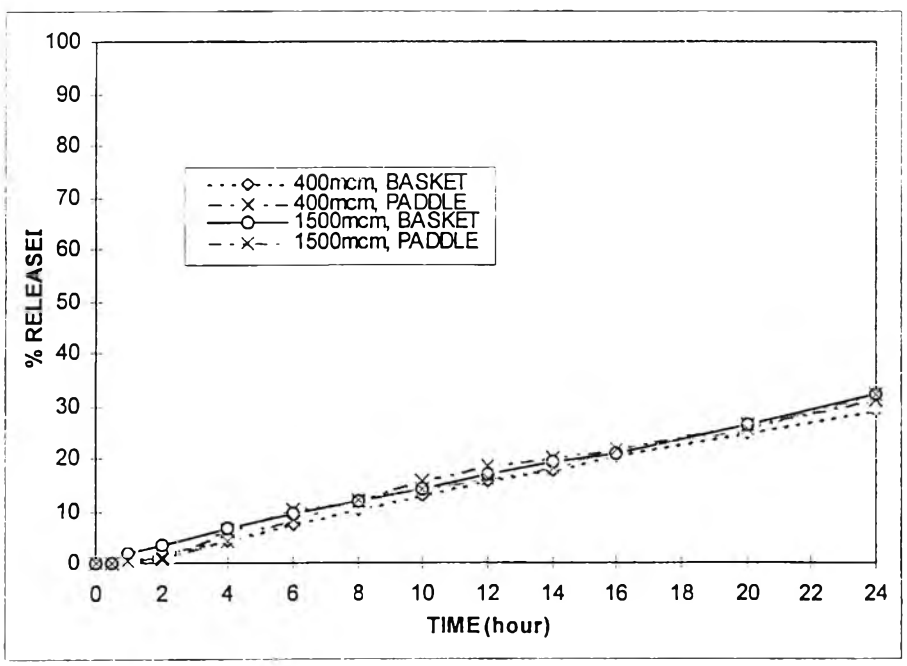


Figure 55 The effect of rotating type on the release profiles of cellulose acetate without plasticizer coated osmotic pump devices.

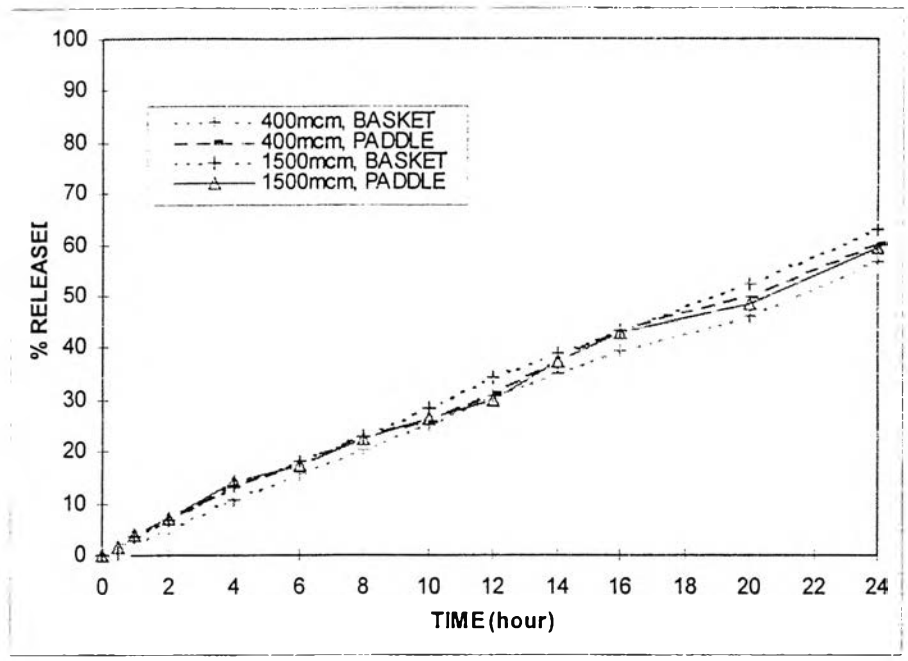


Figure 56 The effect of rotating type on the release profiles of 20 % PEG 400 plasticized film coated osmotic pump devices.

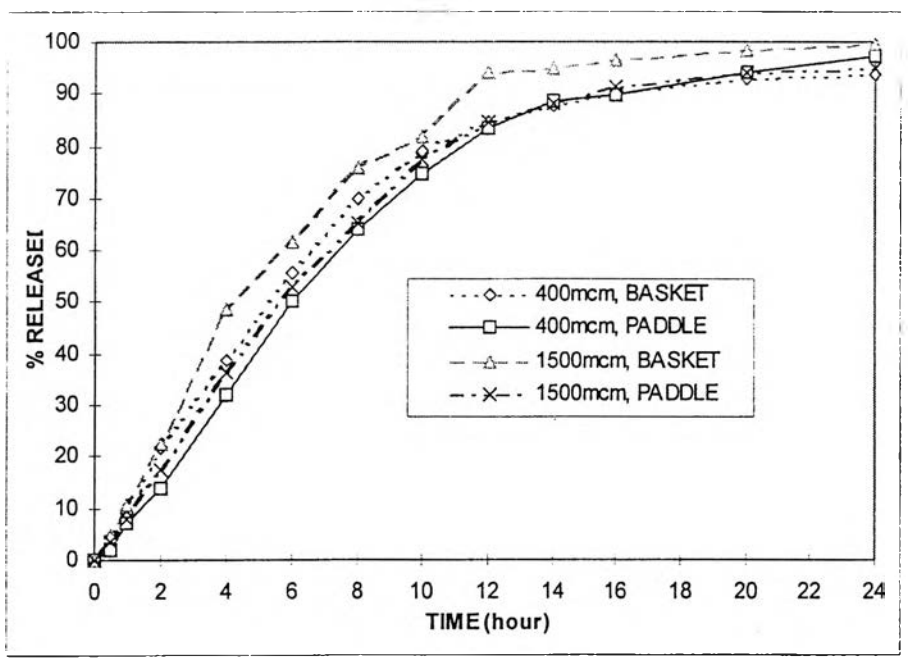


Figure 57 The effect of rotating type on the release profiles of 60 % PEG 400 plasticized film coated osmotic pump devices.

paired t-test method. The profiles of osmotic devices with a passageway size of 400 μm under basket and paddle were statistically different (α=0.05). When 60 % of PEG 400 plasticized film used as film former, the release profiles were curved. By using paired t-test method, the profiles of osmotic devices with a passageway size of 1500 μm under basket and paddle were different (α = 0.05).

I. Influence of dissolution medium on the release profile

The release profiles of osmotic pump devices coated with cellulose acetate, cellulose acetate plasticized with 20, 40 and 60 % PEG 400 in pH-change system compared to those in water are illustrated in Figure 58. The release of propranolol hydrochloride was affected by the type of dissolution medium. The release profile from the same formula in pH-change system was lower than that in water system. The interval of the release profile from the same formula was increased with increasing the amount of PEG 400 in coated film from 0 % to 20 % and 40 % PEG 400 respectively. When the amount of PEG 400 in coated film was increased from 40 % to 60 %, the interval was decreased.

J. Influence of osmotic agents on release profiles.

The release profiles of osmotic devices coated with cellulose acetate plasticized with 20 % PEG 400 using lactose, mannitol, sucrose and sodium chloride as osmotic agents are represented in Figure 59. When lactose was used within osmotic devices, the amount of drug released was the lowest followed by those of sucrose, mannitol and sodium chloride respectively. The final drug released from lactose-drug osmotic devices was 41.13 % whereas 55.28, 67.79 and 92.43 % of drug were released from drug-sucrose, drug-mannitol and drug-sodium chloride osmotic devices respectively. The

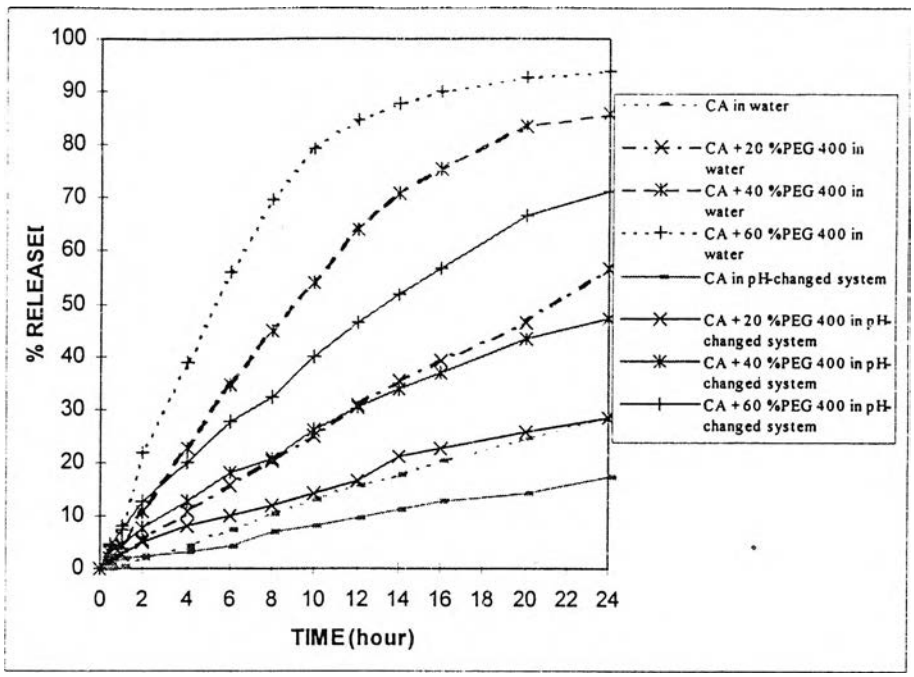


Figure 58 The effect of dissolution medium on the release profiles from osmotic pump devices.

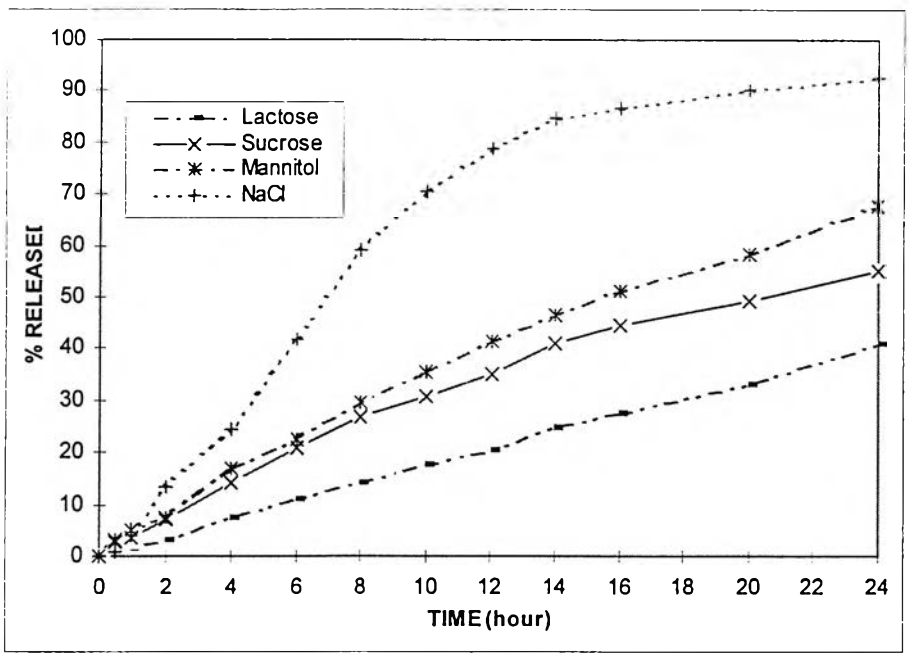


Figure 59 The effect of osmotic agent within osmotic pump devices on the release profiles.

release profiles of drug-mannitol, drug-sucrose and drug-lactose osmotic pump tablets were linear whereas the release profile of drug-sodium chloride osmotic pump tablets was curved.