CHAPTER IV
RESULTS AND DISCUSSION

4.1 Preparation of Chitin

Shrimp shells compose of three major components, which are chitin, calcium carbonate, and protein. Calcium carbonate and protein can be removed by solvent extraction and chitin will be obtained as the remaining substance.

In this research, chitin was prepared from shells of *Penaeus merguiensis* shrimp by demineralization with hydrochloric acid solution and deproteinization with sodium hydroxide solution in order to remove the calcium carbonate and the protein, respectively. The yield obtained during chitin production is shown in Table 4.1.

Table 4.1 Yield of chitin production from shrimp shell

Materials	Yield* (%)
Shrimp shell	100
Product after demineralization	48.67
Product after deproteinization (chitin)	31.30

*dry weight basis

FTIR spectrum of chitin is showed in Figure 4.1. Chitin has some extent of amino groups other than acetamide groups at C2 position of N-acetyl glucosamine repeating units. The degree of deacetylation of chitin depends on the nature of chitin resources and the conditions used during deproteinization. The chitin used in this study was inevitably subjected to N-deacetylation during deproteinization process under alkalline condition and heating. The degree of deacetylation of chitin was 24.14 %.
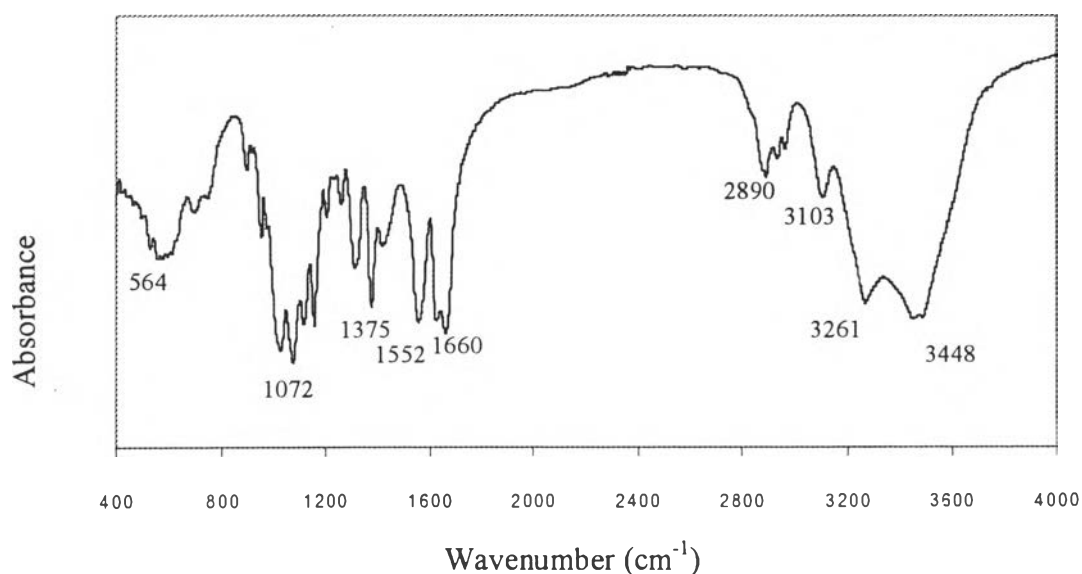
Figure 4.1 FTIR spectrum of chitin powder.

Figure 4.1 shows an IR spectrum of chitin. The characteristic absorption bands at 1660, 1552 and 1310 cm^{-1} due to the amide I, II and III bands which assigned to C=O, N-H and C-N stretching of acetamide groups, respectively. The sharp band at 1375 cm^{-1} has been assigned to the CH_3 symmetrical deformation mode. The absorptions at 2890 and 3448 cm^{-1} assigned to C-H and O-H stretching bands, respectively. The characteristic absorption bands of this study are similar to that of chitin which was reported by Sannan *et al.*, (1978). The molecular weight of chitin was determined by viscometric method. The intrinsic viscosity was 14.54 (100 ml/g). The viscosity-average molecular weight of chitin obtained from the calculation was 8.68×10^5 g/ mol.

4.2 Preparation of CM-Chitin

Chitin is insoluble in common solvents. However, the dissolubility of chitin can be improved by chemical modification. Chitin was modified to be CM-chitin, a water-soluble derivative, by carboxymethylation with monochloroacetic acid.
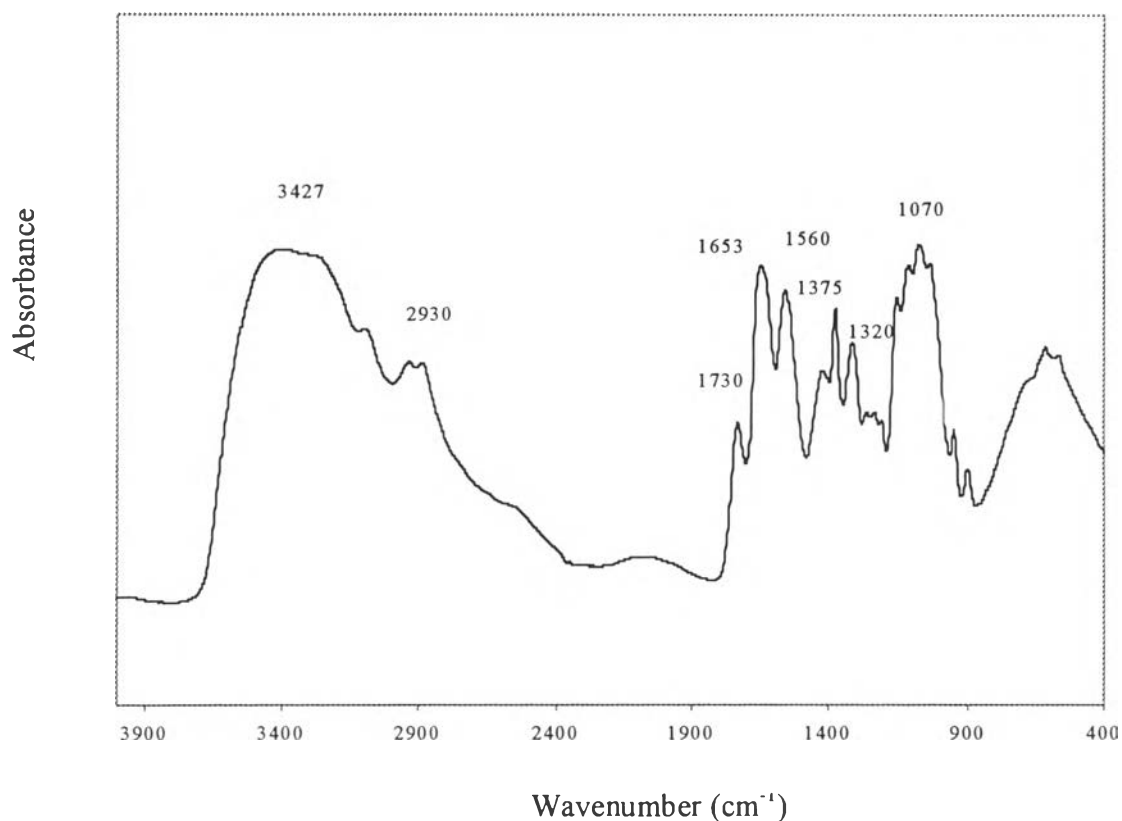
Figure 4.2 FTIR spectrum of CM-chitin.

Figure 4.2 shows an IR spectrum of CM-chitin. The characteristic absorption band at 1730 cm^{-1}, attributed to carbonyl stretching of carboxyl group, was increased by carboxymethylation procedure. The absorption due to primary hydroxyl group appears at 1070 cm^{-1} that assigned to C-O stretching band. The characteristic absorption band appear at 1423, 1625, 1560,1320 and 1375 cm^{-1} due to symmetric stretching vibration of COO$^-$ which it indicate a successful substitution of carboxymethyl groups, amide I, II, III and CH$_3$ vibration bands, respectively. The strong, broad band of spectrum at 3427 and 3292 cm^{-1} are assigned to the hydrogen-bonded –OH and –NH bands. The secondary amide vibration band at 1560 cm^{-1} appears in the spectrum, conforming the NH deformation.

The molecular weight of CM-chitin was determined by viscometric method. According to the method of Kaneko (1982), the molecular weight of CM-chitin was derived from its intrinsic viscosity. The intrinsic viscosity was 5.32 (100 ml/g). The viscosity-average molecular weight of CM-chitin obtained from the calculation was 6.72 x 10^4 g/ mol. The degree of substitution of CM-chitin was 0.64. The weight

averaged molecular weight and molecular weight distribution of the obtained CM-chitin was 1.45×10^5 and 4.038, respectively, as determined by gel permeation chromatography (GPC).

4.3 Characterization of CM-Chitin/Silk Fibroin Blend Films

4.3.1 FTIR Analysis of Blend Films

Silk fibroin has two conformations, random coil and β-sheet structures. The characteristic peaks appeared at 1660 cm^{-1} (amide I), 1540 cm^{-1} (amide II), 1275 cm^{-1} (amide III), and 650 cm^{-1} (amide V) are assigned to the random coil conformation (Chen *et al.*, 1997). In case of β-sheet structure, the characteristic peaks appear at 1630 cm^{-1} (amide I), 1530 cm^{-1} (amide II), 1265 cm^{-1} (amide III) and 700 cm^{-1} (amide V) (Park *et al.*, 1999). The structural characterizations of CM-chitin, silk fibroin and the blend films, as well as the determination of specific interactions between CM-chitin and silk fibroin were carried out by using FTIR spectrometer.

The FTIR spectrum of silk fibroin [Figure 4.3(a)] shows the characteristic absorption bands at 1660 cm^{-1} (amide I), 1540 cm^{-1} (amide II), and 1275 cm^{-1} (amide III), assigned to random coil conformation (Liang and Hirabayashi, 1992; Freddi *et al.*, 1999; Park *et al.*, 1999; Kweon *et al.*, 2001). The FTIR spectrum of CM-chitin [Figure 4.3(k)] shows the characteristic absorption bands at 1653 cm^{-1} (amide I) and 1560 cm^{-1} (amide II). However, the peak at 1732 cm^{-1} attributed to carbonyl stretching of carboxyl group which was formed by carboxymethylation procedure (Tokura *et al.*, 1983a; Uraki *et al.*, 1988) could not be seen for CM-chitin in the form of sodium salt that was used in this study. The FTIR spectra of CM-chitin/silk fibroin blend films [Figure 4.3(b-j)] are characterized by the presence of absorption bands of the pure components, of which intensities are roughly related to the blending ratio. Moreover, it was found that the conformation transition of silk fibroin from random coil to β-sheet structure did not occur by blending silk fibroin with CM-chitin. Kweon *et al.* (2001) studied on physical properties of silk fibroin/chitosan blend films and reported that the chitosan film

showed absorption bands at 1154 cm^{-1} and 900 cm^{-1}, which are attributed to the saccharide structure, and the bands at 1598 cm^{-1} and 1651 cm^{-1}, which are attributed to amino and acetamide groups of chitosan, respectively. The absorption bands at 1660 cm^{-1} (amide I), 1540 cm^{-1} (amide II) and 1235 cm^{-1} (amide III), which are assigned to the random coil conformation of silk fibroin, shifted to 1630 cm^{-1}, 1530 cm^{-1} and 1265 cm^{-1}, in accordance with the β-sheet structure.
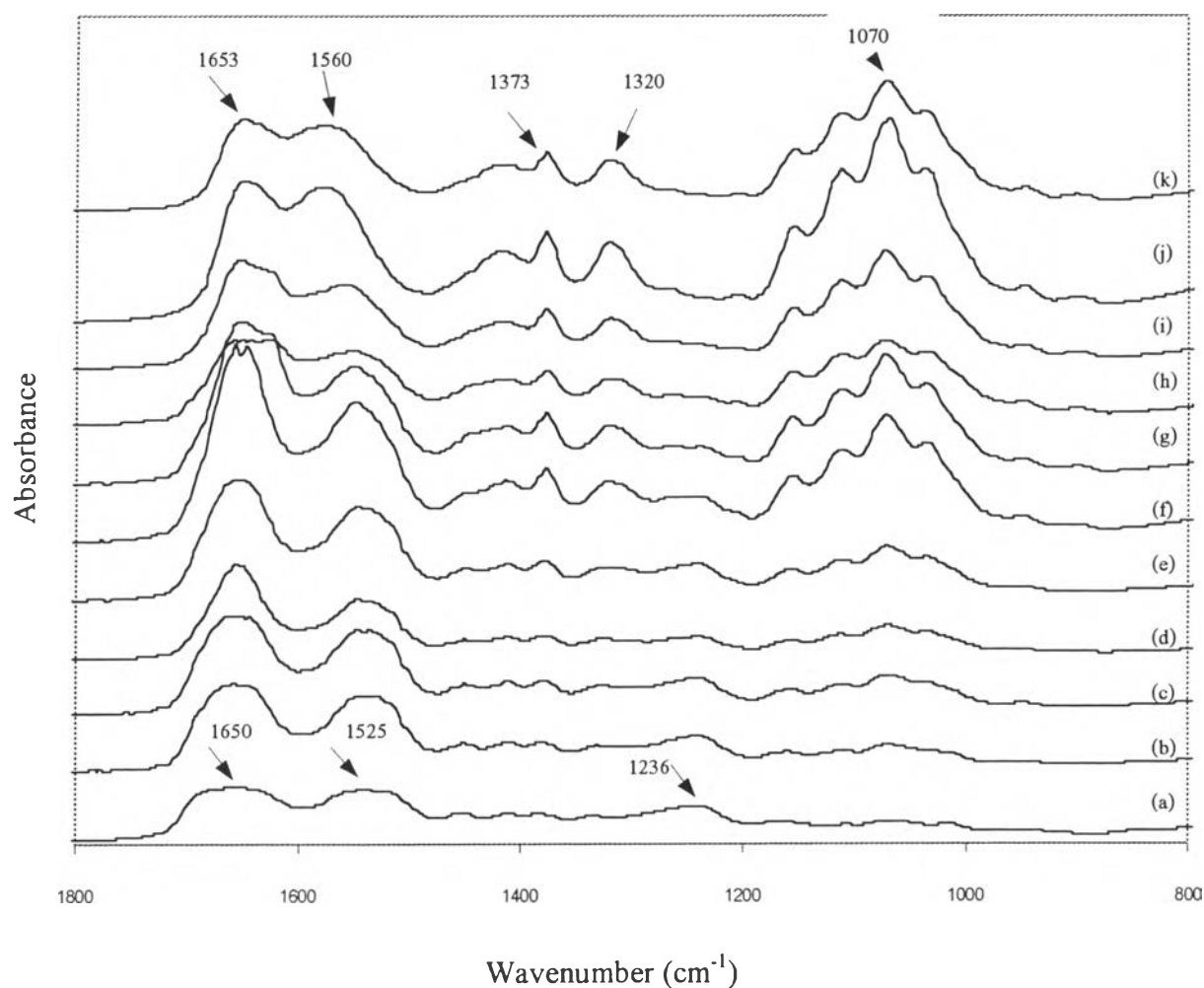

Figure 4.3 FTIR spectra of pure CM-chitin and blend films with various blend compositions of CM-chitin and silk fibroin: CM-chitin/silk fibroin composition: (a) 0/100 (silk fibroin); (b) 10/90; (c) 20/80; (d) 30/70; (e) 40/60; (f) 50/50; (g) 60/40; (h) 70/30; (i) 80/20; (j) 90/10 and (k) 100/0 (CM-chitin).

In this study, the conformation transition of silk fibroin in the blend films from random coil to β-sheet structure could not be observed. Moreover, it is difficult to observe the interaction between silk fibroin and CM-chitin by using FTIR technique. However, from our results, it seems that there was no interaction between silk fibroin and CM-chitin under our condition.

4.4 Effect of pH on Degree of Swelling

It is well-known that swelling and shrinking responding to changes of pH is a typical phenomenon of polyelectrolyte gels. CM-chitin, a hydrophilic polymer having gel-forming ability, contains both carboxyl and amino groups within its polymer chain. Tokura *et al.* (1983a) reported that the pK_a values of the carboxyl group and amino group of CM-chitin are 3.40 and 6.40, respectively. Moreover, it has been reported that CM-chitin forms a hydrogel with pH-sensitive character in their swelling behavior (Zhao *et al.*, 2003). In case of silk fibroin which composed mainly of non-polar amino acids, it has been reported that the swell ratio of silk fibroin were small for the pH range from pH 2 to pH 11 (Chen *et al.*, 1997). Figure 4.4 shows the degree of swelling of CM-chitin and the blend films of CM-chitin and silk fibroin as a function of pH. It was found that the minimum degrees of swelling of CM-chitin and the blend films were observed at pH 4. It may be explained that at pH 4 the number of ionized functional groups along the polymer chain might be less than at the other pHs, resulting in the lowest swelling ability of the films. At pH higher than 4, the swelling of the films resulted mainly from ionization of carboxyl groups of CM-chitin, whereas at pH less than 4 the protonization of amino groups of CM-chitin led to the swelling of the films. Both the ionization of carboxyl groups and protonation of amino groups of CM-chitin resulted in increasing of the hydrophilicity and osmotic pressure of network. Therefore, when the number of ionized functional groups increased, the degree of swelling increased. The degrees of swelling of CM-chitin and the blend films at alkaline pH were higher than at acidic pH, indicating that swelling of the films mainly resulted from ionization of carbonyl groups of CM-chitin.
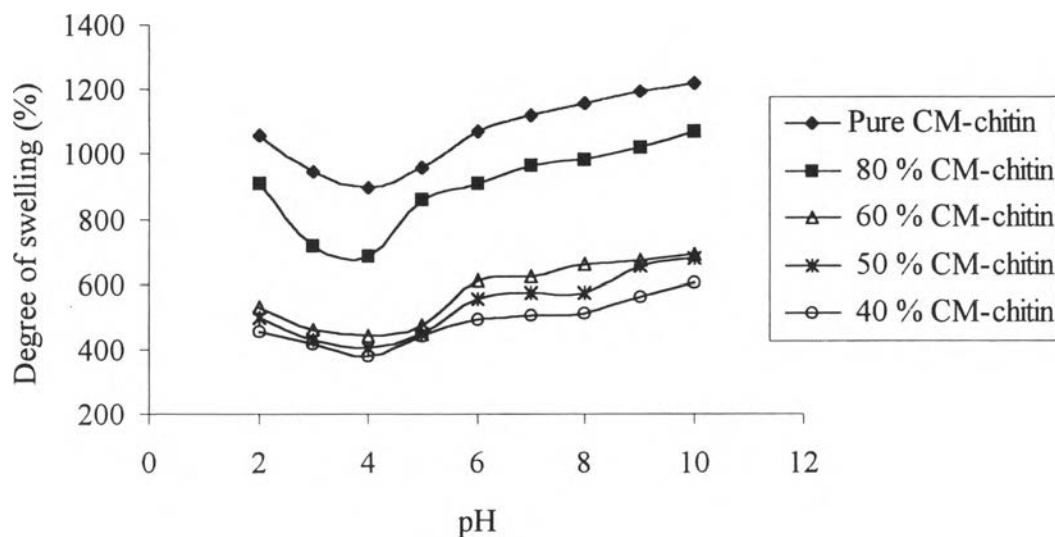
Figure 4.4 Effect of blend composition on degree of swelling as a function of pH.
CM-chitin/silk fibroin: ◆ 100/0 (CM-chitin); ■ 80/20; △ 60/40; ＊ 50/50; ○ 40/60.

4.5 Effect of Blend Composition on Degree of Swelling

The effect of blend compositions on the degree of swelling as a function of immersion time at pH 2.0, pH 5.5 and pH 7.2 are shown in Figures 4.5-4.7. The blend films of CM-chitin and silk fibroin were prepared at five different blend compositions, i.e. 100%, 80 %, 60%, 50% and 40 % CM-chitin contents. The results for the blend films with CM-chitin contents less than 40% were not reported because the films were brittle and difficult to handle without cracking. The degrees of swelling of the blend films increase with increasing CM-chitin content. Since, highly repetitive sections of silk fibroin are composed of glycine, alanine, and serine which have short side chains and permit close packing of crystals through the stacking of hydrogen bond, the water molecules are difficult to penetrate into structure of silk fibroin (Shen *et al.*, 1998). Ayub *et al.* (1994) reported that the swelling properties of silk fibroin showed only a little swelling and at the final (equilibrium) water content level, silk fibroin absorbed about 20% water with a little swelling. According to low swelling ratio of silk fibroin, the absorption of water into the blend films occurred

mainly by CM-chitin. Therefore, the swelling ability of the blend films depends on the CM-chitin content in the blend film.
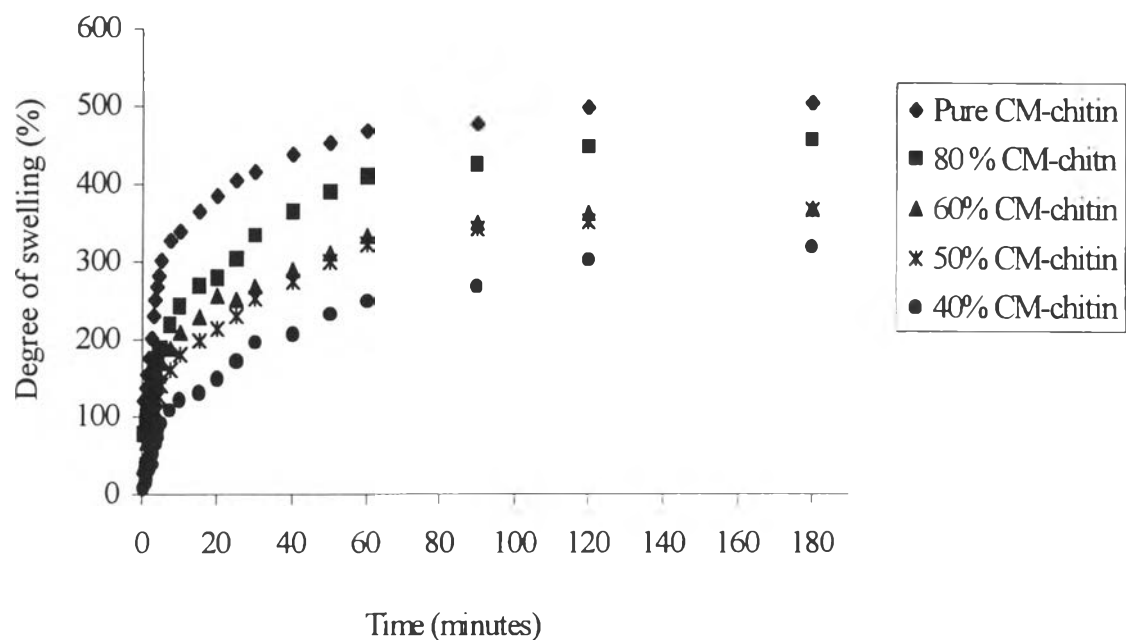

Figure 4.5 Degree of swelling of CM-chitin/silk fibroin blend films at pH 2.0. CM-chitin/silk fibroin: ◆ 100/0 (CM-chitin) ; ■ 80/20 ; ▲ 60/40 ;* 50/50; ● 40/60.
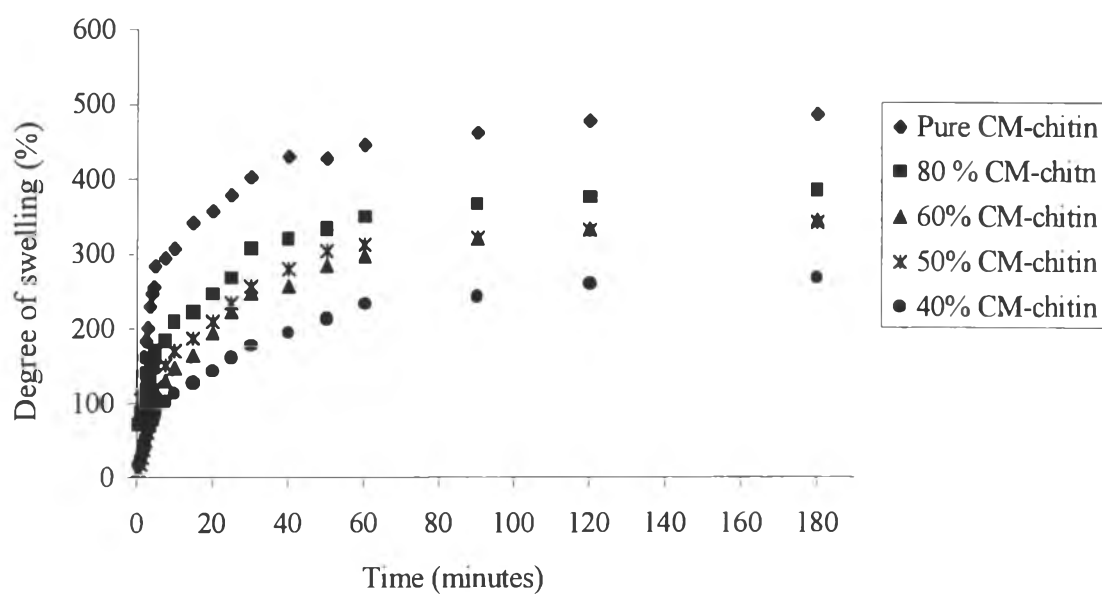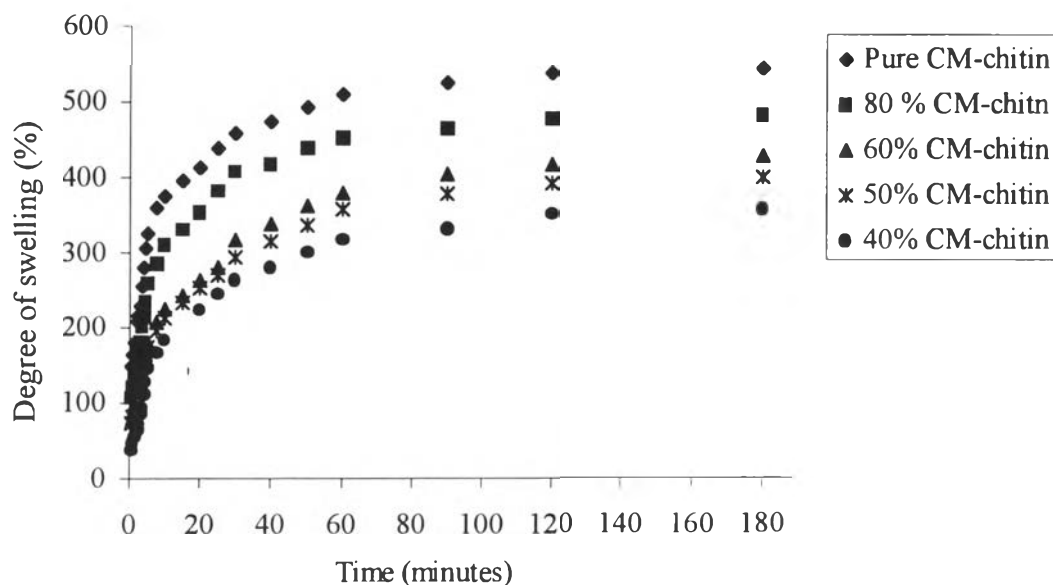

Figure 4.6 Degree of swelling of CM-chitin/silk fibroin blend at pH 5.5. CM-chitin/silk fibroin: ◆ 100/0 (CM-chitin) ; ■ 80/20 ; ▲ 60/40 ;* 50/50; ● 40/60.

Figure 4.7 Degree of swelling of CM-chitin/silk fibroin blend films at pH 7.2. CM chitin/silk fibroin: ◆ 100/0 (CM-chitin) ; ■ 80/20 ; ▲ 60/40 ;* 50/50; ● 40/60.

4.6 Effect of Blend composition on Drug Release

The drug-loaded blend films with CM-chitin contents of 100, 80, 60, 50 and 40% were used in this study. The concentration of drug in the blend films was 0.1 % w/w. The drug release study was carried out at simulated physiological pH, i.e. pH 2.0, pH 5.5 and pH 7.2.

The effect of blend ratios on drug release at pH 2.0, pH 5.5 and pH 7.2 is shown in Table 4.2. It was found that the maximum releases of drugs were observed for pure CM-chitin film for all model drugs and the amounts of released drugs decreased as CM-chitin content decreased. This could be explained in term of swelling behavior of the films. It was found that pure CM-chitin film showed the maximum degree of swelling and swelling ability of the blend films depended on CM-chitin content in the blend films as shown in Table 4.3.

Peppas *et al.* (1983) suggested that drug release from hydrogel delivery system is controlled by swelling behavior of hydrogel. Hydrogels are initially dry and, when they are placed in aqueous systems, the hydrogels will absorb and swell. The swelling results in the increasing of the aqueous solvent content within the

formulation as well as the polymer mesh size, enabling the drug to diffuse through the swollen network into the external environment. Several researchers reported the effect of swelling behavior on drug release property. Yao *et al.* (1933 and 1994) studied the release of cimetidine and chlorhexidini acetas from crosslinked-chitosan/polyether semi-interpenetrating polymer network and reported that the higher degrees of swelling, the higher amounts of drug released. Gupta and Ravi Kumar, (2000) studied drug release behavior of beads and microgranules of chitosan by using diclofenac sodium as a model drug and reported that the release of the drug depended greatly on the swelling behavior.

In this study, the amounts of drug released from the blend films increased with increasing degree of swelling. It can be concluded that the drug release from the blend films was controlled by the swelling behavior of the blend films.

Besides the release of drug is controlled by swelling behavior of the carrier, drug release may be concerned with erosion process. This process is associated with macroscopic changes in the appearance of the device, changes in the physicomechanical properties of the polymeric material, deformation or structural disintegration, weight loss, and the eventual loss of functions. Table 4.4 shows the weight loss of drug-loaded CM-chitin and the blend films after immersion in buffer solution for 2 h. It was found that the weight loss of the films at pH 2 was higher than pH 5.5 and pH 7.2 (pH 2 > pH 5.5 > pH 7.2). This indicated that drug released by erosion process could be occurred in this system.

Table 4.2 Effect of blend composition on drug release at pH 2.0, pH 5.5 and pH 7.2

Drug	Weight Ratio of CM-chitin to Silk Fibroin	Drug release (%)[a]		
		pH 2	pH5.5	pH 7.2
Salicylic acid	100:00	84.01±0.18	76.92±0.11	87.20±3.00
	80:20	77.37±0.12	74.61±0.18	84.38±0.68
	60:40	76.74±0.26	63.18±0.39	76.54±0.40
	50:50	65.98±0.18	61.88±0.45	74.30±0.18
	40:60	63.19±0.16	58.62±0.15	64.14±0.33
Theophylline	100:00	54.41±0.05	54.37±0.24	65.26±0.52
	80:20	56.14±0.49	54.24±0.22	57.07±1.07
	60:40	55.65±0.57	53.58±0.51	55.27±0.52
	50:50	54.60±0.12	52.90±0.13	55.68±0.15
	40:60	49.78±0.02	48.43±0.12	50.44±0.56
Diclofenac sodium	100:00	53.64±1.20	50.61±0.74	60.21±1.03
	80:20	50.53±0.30	48.97±0.24	54.41±0.52
	60:40	49.26±0.37	47.28±1.35	50.11±0.48
	50:50	48.75±1.54	37.85±0.40	50.14±0.07
	40:60	40.27±0.64	29.56±0.17	48.53±0.89
Amoxcillin trihydrate	100:00	18.21±0.80	13.26±0.62	19.10±0.53
	80:20	14.40±0.19	13.39±0.18	14.24±0.18
	60:40	11.77±0.17	11.29±0.15	12.96±0.20
	50:50	10.28±0.60	10.39±0.53	11.48±0.30
	40:60	7.92±0.38	6.28±0.33	8.98±0.21

a   the average value from three experiments

Table 4.3 Equilibrium degree of swelling of drug-loaded CM-chitin and blend films after releasing of time of 2 h

Drug	Weight Ratio of CM-chitin to Silk Fibroin	Degree of Swelling (%)[a]		
		pH 2	pH5.5	pH 7.2
Salicylic acid	100:00	442.47±20.09	408.41±22.96	459.88±12.35
	80:20	419.08±7.14	389.08±7.84	422.59±19.65
	60:40	417.54±33.05	385.48±22.48	419.55±31.41
	50:50	411.64±40.34	381.62±24.35	413.81±26.42
	40:60	377.08±12.20	369.00±34.49	408.41±14.90
Theophylline	100:00	420.25±23.93	410.8±17.73	504.92±16.22
	80:20	412.22±46.44	402.83±40.13	444.74±29.94
	60:40	401.01±37.72	383.56±32.61	428.79±23.02
	50:50	383.92±21.56	381.74±23.21	411.11±17.54
	40:60	348.42±18.32	347.72±12.67	407.55±25.59
Diclofenac sodium	100:00	470.37±31.42	454.97±24.56	480.31±27.11
	80:20	414.95±19.36	363.76±28.63	432.25±31.02
	60:40	383.31±33.21	357.26±38.72	428.18±28.56
	50:50	379.44±33.12	351.47±26.45	412.94±22.47
	40:60	360.33±21.21	345.78±24.56	391.09±20.32
Amoxcillin trihydrate	100:00	424.64±27.36	373.53±21.24	448.90±18.76
	80:20	396.27±23.14	349.08±29.30	422.50±32.46
	60:40	383.32±31.26	357.26±26.54	428.18±19.21
	50:50	379.91±19.24	341.17±16.73	411.60±21.34
	40:60	362.66±23.21	337.09±34.16	337.09±21.34

a   the average value from three experiments

Table 4.4 Weight loss of drug-loaded CM-chitin and blend films after releasing time of 2 h

Drug	Weight Ratio of CM-chitin to Silk Fibroin	Weight Loss (%)[a]		
		pH 2	PH5.5	pH 7.2
Salicylic acid	100:00	24.05±1.34	22.69±0.67	19.24±2.93
	80:20	22.38±0.94	21.08±0.60	16.03±2.34
	60:40	23.78±0.79	19.72±1.40	15.30±3.35
	50:50	33.19±5.72	23.31±4.31	19.40±2.77
	40:60	12.25±4.05	11.70±3.10	12.20±5.30
Theophylline	100:00	16.91±0.92	14.52±0.85	11.40±1.51
	80:20	29.74±3.16	24.49±1.72	15.81±4.20
	60:40	29.38±2.14	27.32±0.81	25.18±0.66
	50:50	27.44±0.97	25.22±1.21	24.68±1.03
	40:60	18.76±1.67	17.88±1.23	15.46±1.52
Diclofenac sodium	100:00	21.15±1.13	19.68±2.04	12.89±1.76
	80:20	22.37±2.21	14.25±0.78	13.24±1.59
	60:40	18.70±2.42	17.68±1.23	15.63±0.81
	50:50	16.44±1.02	15.68±0.82	14.29±0.62
	40:60	16.59±0.36	13.08±0.52	13.10±0.26
Amoxcillin trihydrate	100:00	19.42±1.17	14.42±2.78	8.94±1.59
	80:20	22.55±0.84	19.65±0.61	12.41±1.43
	60:40	18.70±1.72	17.68±1.81	15.63±0.39
	50:50	18.49±1.12	15.79±0.74	13.06±0.46
	40:60	17.84±0.63	12.99±0.74	12.03±1.12

a   the average value from three experiments

4.7 Effect of pH on Drug Release

The effect of pH on drug released from CM-chitin and the blend films is shown in Table 4.2. The amounts of drug released from the drug-loaded blend films were measured at pH 2.0, pH 5.5 and pH 7.2 for the releasing time of 1 h. It was found that the amounts of released drugs depend on the pH of the solutions. The percentages of the drug released at pH 7.2 were higher than those at pH 2.0 and pH 5.5, respectively, for all model drugs. This is in good agreement with swelling behavior of the films at these pHs as shown in Table 4.3. The differences in the percentages of released drugs due to the effect of pH were high for the blend films with high CM-chitin contents. It is because CM-chitin has ionizable functional groups more than silk fibroin and the change in pH can effect on the ionization of these functional groups of CM-chitin. CM-chitin has two ionizable formational groups, carboxyl group and amino group, with pK_a of 3.40 and 6.40, respectively. In acidic medium, the network is dissociated due to protonation of amino group leading to swelling stage of hydrogel. On the other hand, in alkaline medium, swelling stage occurred due to ionization of carboxyl groups of the adjacent chains of CM-chitin. Therefore, it can be concluded that the release of drug from the blend films was affected by pH of the releasing solution.

4.8 Effect of Drug Nature on Drug Release

The percentages of model drugs, salicylic acid, theophylline, diclofenac sodium and amoxycillin, released from CM-chitin and the blend films with various blend compositions were determined at pH 2.0, pH 5.5 and pH 7.2 for the releasing time of 1 h (see Table 1).

For all blend compositions and at all pH studied, the amounts of drug released from the films from the highest to the lowest were in the order as follows: salicylic acid > theophylline > diclofenac sodium > amoxycillin. The chemical structures of the model drugs are shown in the Figure 4.8-4.11. The molecular weight of salicylic acid, theophylline, diclofenac sodium, and amoxycillin were 138.12, 180.16, 318.13 and 381.15, respectively. One factor that can affect the penetration of

a drug from a polymer matrix is the molecular weight of the drug. The molecule of salicylic acid is smaller than theophylline. Thus, the penetration of salicylic acid from the matrix was easier than theophylline. The releasing amount of diclofenac sodium was found to be less than those of theophylline and salicylic acid which have lower molecular weight than diclofenac sodium. Among the model drugs investigated in this study, amoxycillin has the highest molecular weight and it was found that the amounts of amoxycillin released from the films were the lowest values at all pH studied. From these results, it seems that molecular weight of drug is a factor that had a great effect on drug release from CM-chitin and the blend films.

In addition to molecular weight of drug, there are other factors that can affect the penetration of a drug from a polymer matrix, such as drug-polymer interaction and solubility of drug in the blend solution. The solubilities of salicylic acid, theophylline, diclofenac sodium and amoxycillin in water are 2.17 mg/ml, 8.3 mg/ml, 21 mg/ml and 1-10 mg/ml, respectively (Brittain, 1994; Florey, 1975). In this study, all model drugs completely dissolved in the blend solutions without any remaining insoluble residues. In case of drug-polymer interaction, there might be interaction between the amino group in CM-chitin and salicylic acid by salicylate formation. Since theophylline is a neutral drug, there should be no drug-polymer interaction between theophylline and the polymer matrix. Puttipipatkhlachorn *et al.* (2001) studied on drug release from chitosan films by using salicylic acid and theophylline as model drugs. The drug-polymer interaction was investigated by Fourier transform infrared and solid-state ^{13}C NMR spectroscopy. They reported that there was the drug-polymer interaction between salicylic acid and chitosan, resulting in salicylate formation, whereas no drug-polymer interaction was observed for theophylline-loaded chitosan films. For diclofenac sodium and amoxicillin trihydrate, there might be interaction between the polymer matrix and model drugs. However, the interaction might be very little due to the stearic effect of bulky group of the drug molecules.
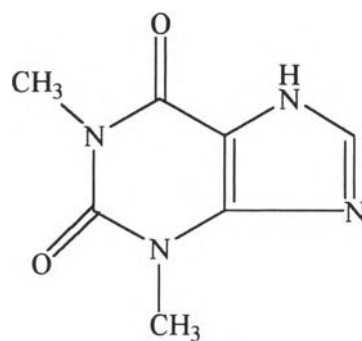
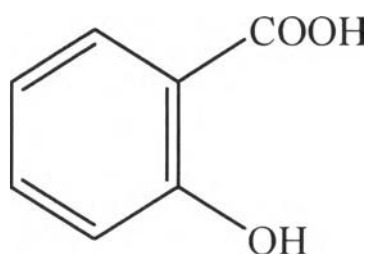**Figure 4.8** Chemical structure of anhydrous theophylline.

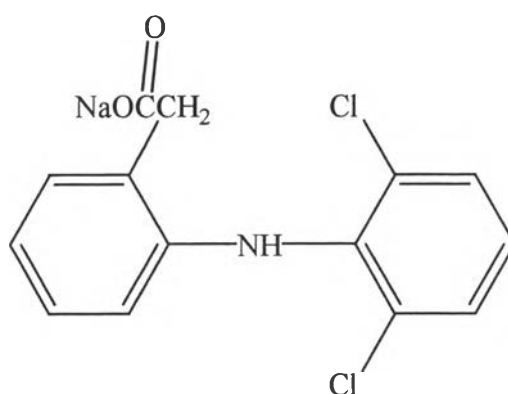**Figure 4.9** Chemical structure of salicylic acid.

Figure 4.10 Chemical structure of diclofenac sodium.
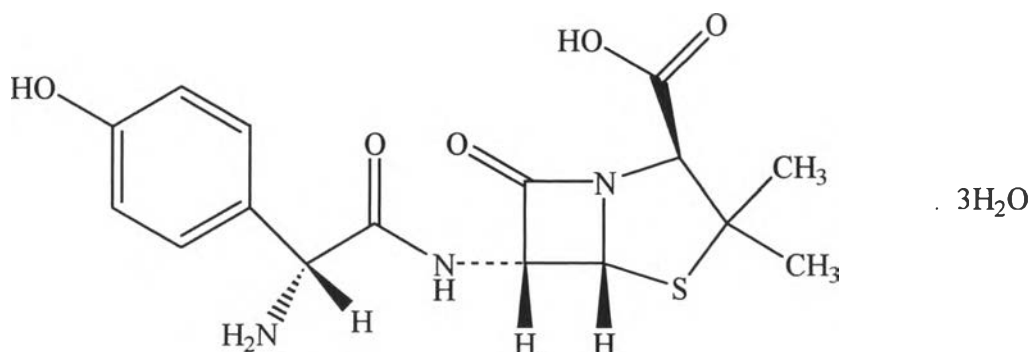
. $3H_2O$

Figure 4.11 Chemical structure of amoxycillin trihydrate.

4.9 Effect of Immersion Time on Drug Release

The release profiles of each model drug in buffer solutions at pH 2.0, 5.5, and 7.2 for CM-chitin and the blend films are illustrated in Figures 4.12-4.26. The releases of the model drugs from CM-chitin and the blend films were fast. In most case of drug release reached the equilibrium within 10 minutes, expect for diclofenac sodium that took longer time than the other model drugs to reach the plateau. The releases of all model drugs from the films were fast at the initial state due to the burst effect. It is known that the burst release in hydrogel systems is a common problem that leads to short, high drug releasing rate at the beginning of swelling. When the film was immersed in buffer solution, a large amount of water was absorbed in the film, leading to swollen state of hydrogel, according to this, the size of hydrogel increased remarkably resulting in cracking of hydrogel. After that the model drug in the hydrogel could diffuse through this cracking into the buffer solution. Gupta and Ravi Kumar, (2000) studied drug release behavior of beads and microgranules of chitosan by using diclofenac sodium as a model drug and reported that a significant burst effect occurred in the first hour of drug release.
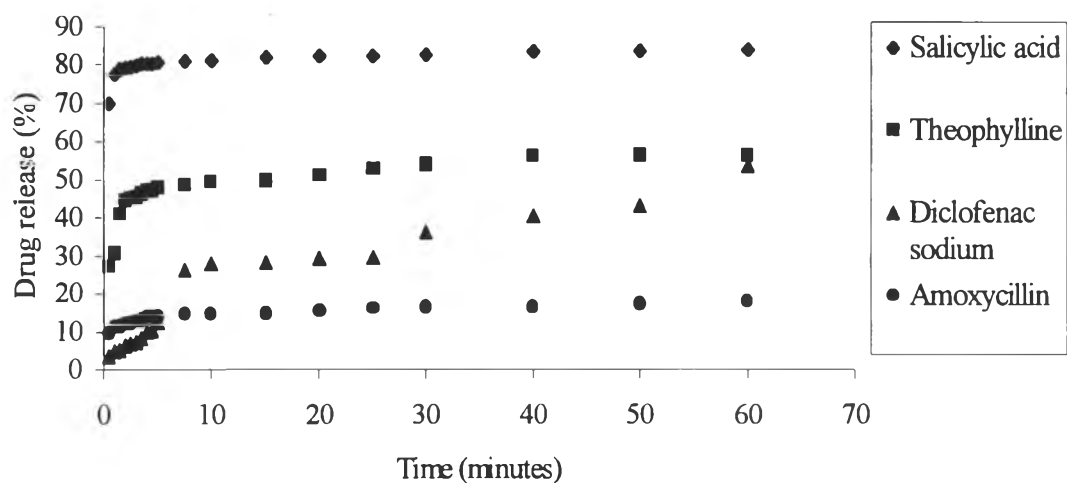
Figure 4.12 Drug release profiles for pure CM-chitin film at pH 2.0. ◆ salicylic acid; ■ theophylline; ▲ diclofenac sodium; ● amoxycilin trihydrate.
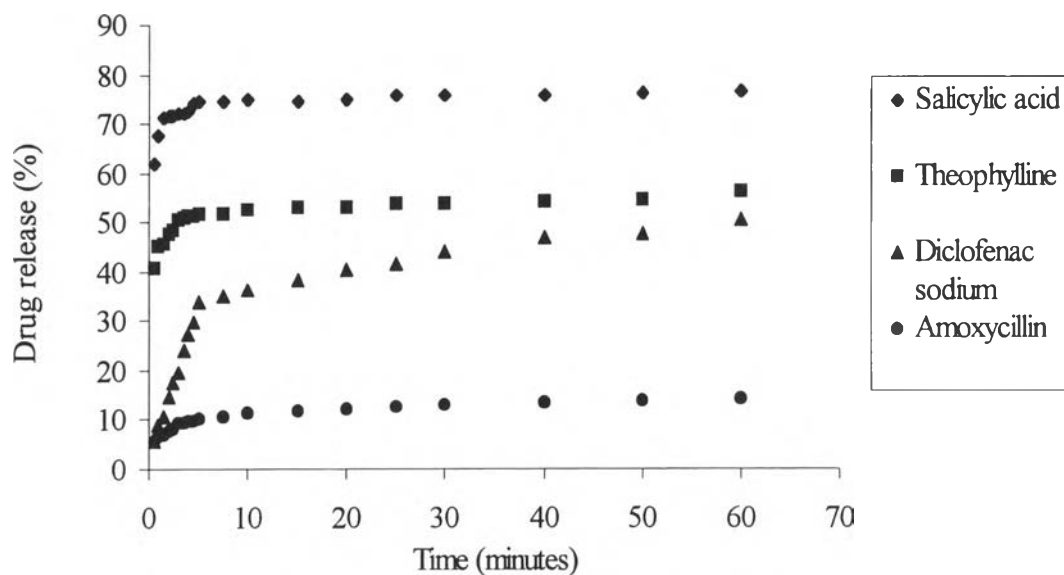

Figure 4.13 Drug release profiles for the blend films with 80 % CM-chitin content at pH 2.0. ◆ salicylic acid; ■ theophylline; ▲ diclofenac sodium; ● amoxycilin trihydrate.
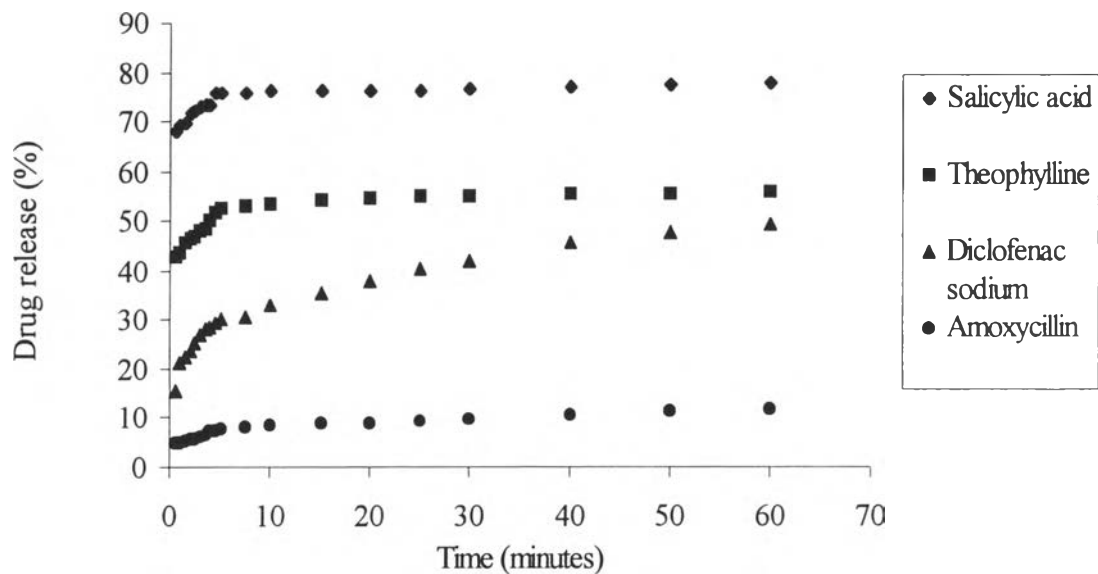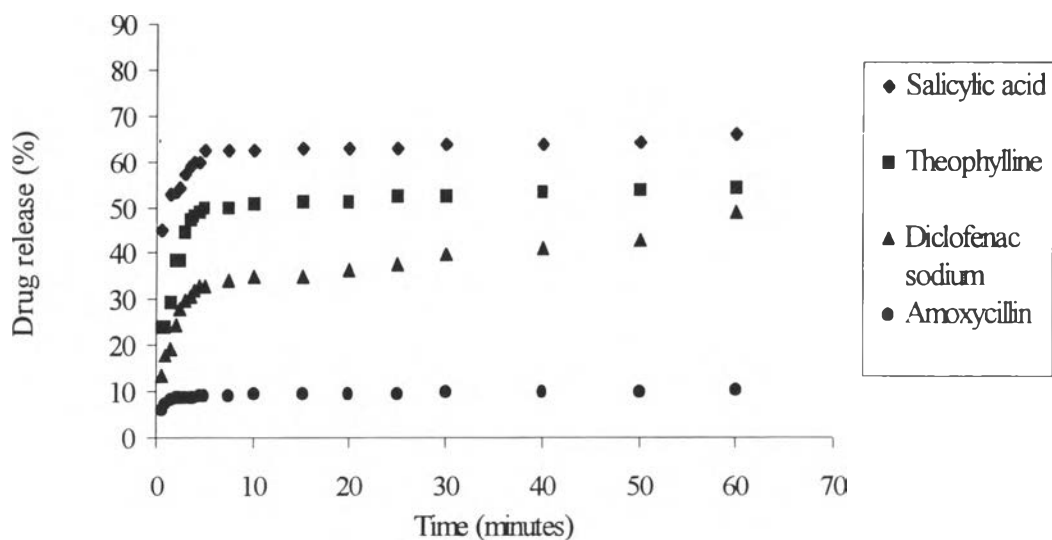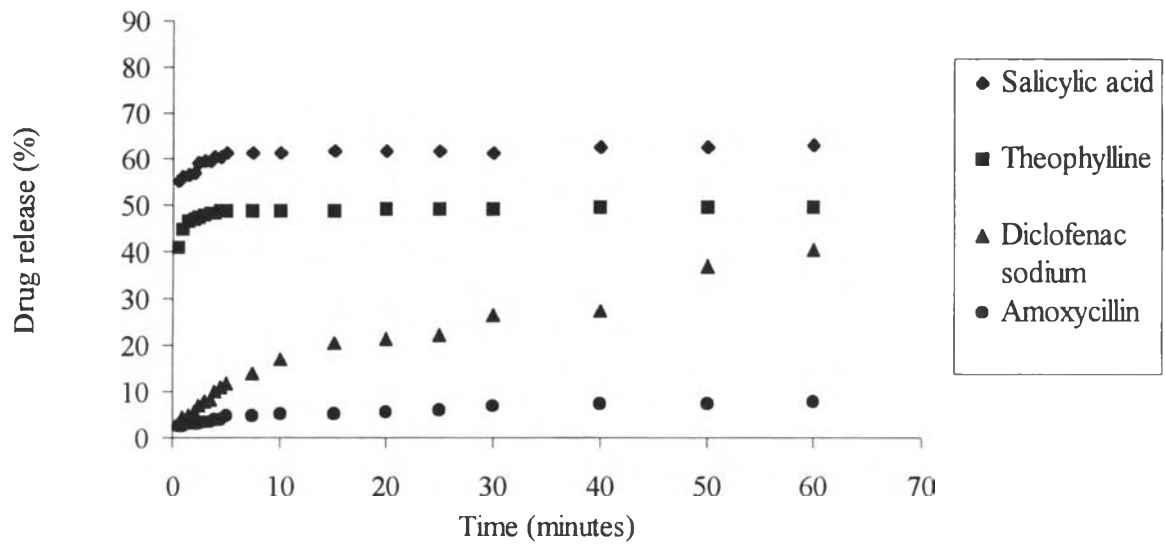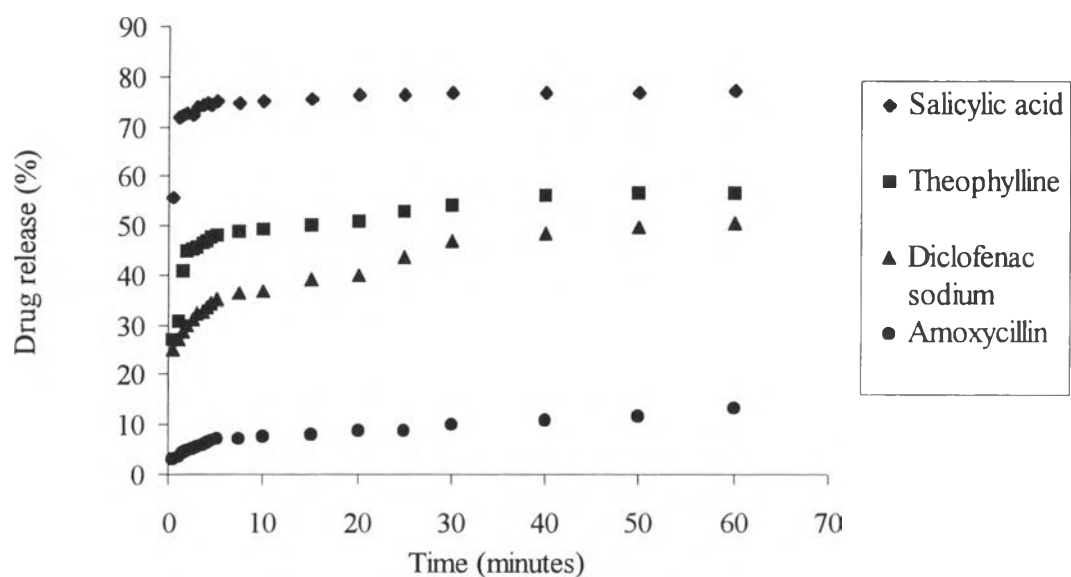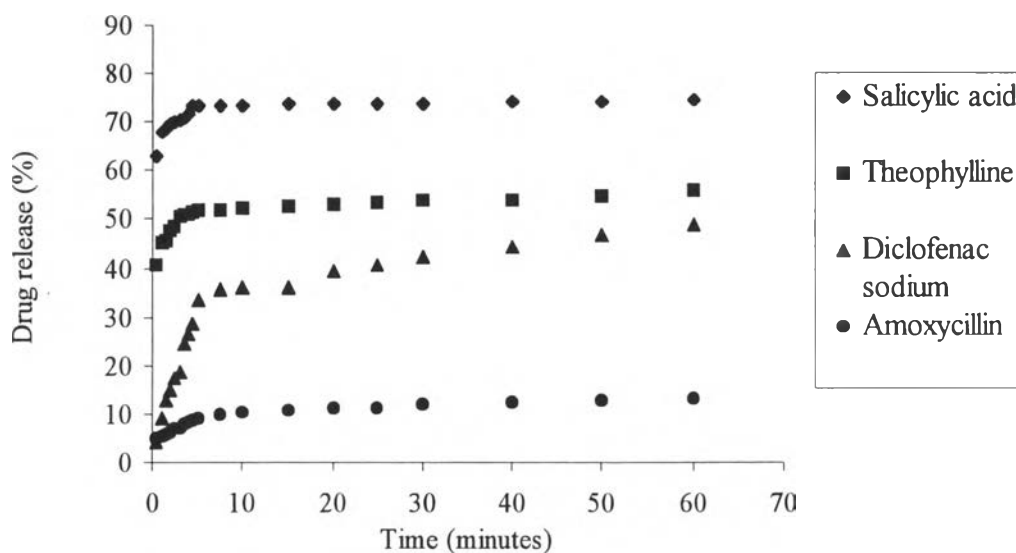
Figure 4.14 Drug release profiles for the blend films with 60 % CM-chitin content at pH 2.0. ◆ salicylic acid; ■ theophylline; ▲ diclofenac sodium; ● amoxycilin trihydrate.

Figure 4.15 Drug release profiles from the blend films with 50 % CM-chitin content at H 2.0. ◆ salicylic acid; ■ theophylline; ▲ diclofenac sodium; ● amoxycilin trihydrate.

Figure 4.16 Drug release profiles for the blend films with 40 % CM-chitin content at pH 2.0. ◆ salicylic acid; ■ theophylline; ▲ diclofenac sodium; ● amoxycilin trihydrate.
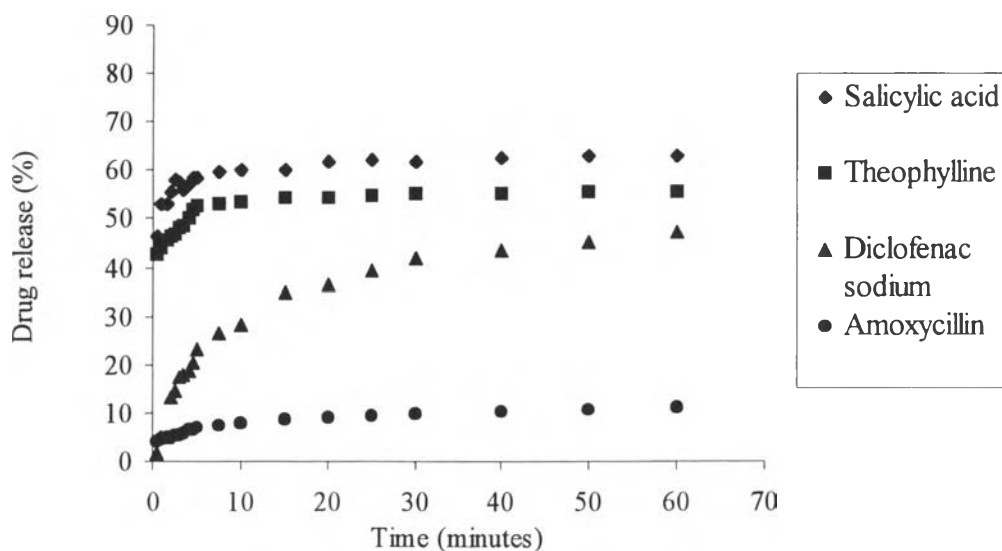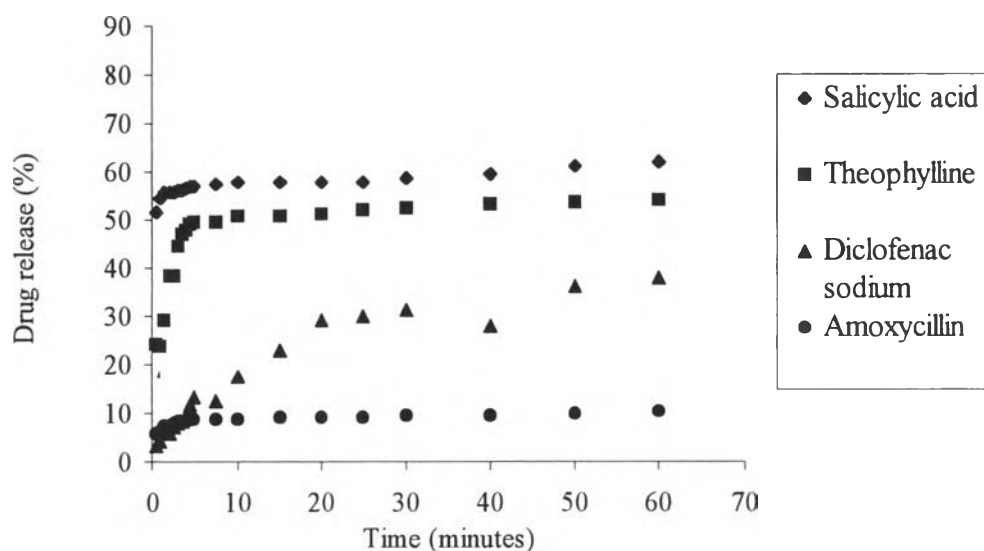

Figure 4.17 Drug release profiles for pure CM-chitin film at pH 5.5. ◆ salicylic acid; ■ theophylline; ▲ diclofenac sodium; ● amoxycilin trihydrate.

Figure 4.18 Drug release profiles for the blend films with 80 % CM-chitin content at pH 5.5. ◆ salicylic acid; ■ theophylline; ▲ diclofenac sodium; ● amoxycilin trihydrate.
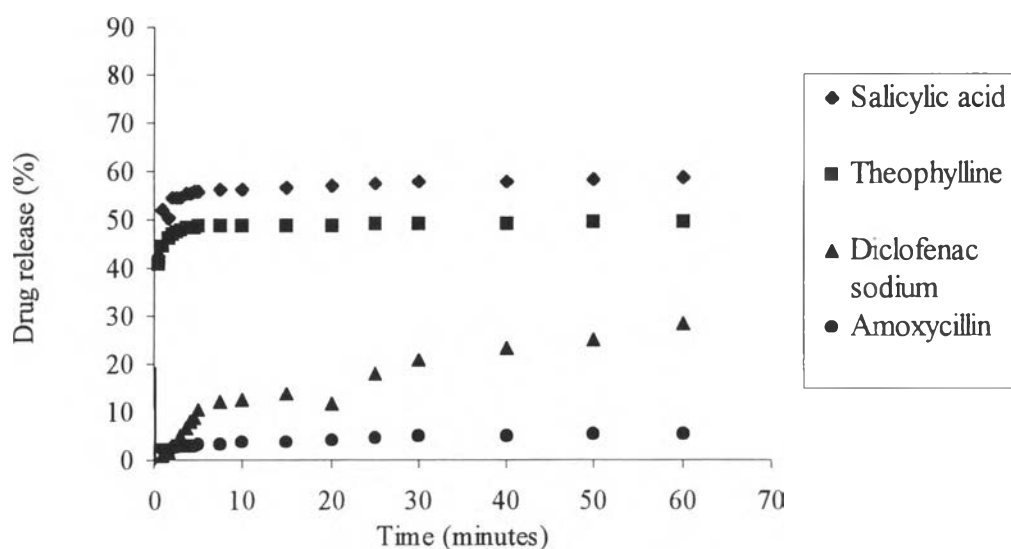

Figure 4.19 Drug release profiles for the blend films with 60 % CM-chitin content at pH 5.5. ◆ salicylic acid; ■ theophylline; ▲ diclofenac sodium; ● amoxycilin trihydrate.

Figure 4.20 Drug release profiles from the blend films with 50 % CM-chitin content at pH 5.5. ◆ salicylic acid; ■ theophylline; ▲ diclofenac sodium; ● amoxycilin trihydrate.

Figure 4.21 Drug release profiles for the blend films with 40 % CM-chitin content at pH 5.5. ◆ salicylic acid; ■ theophylline; ▲ diclofenac sodium; ● amoxycilin trihydrate.
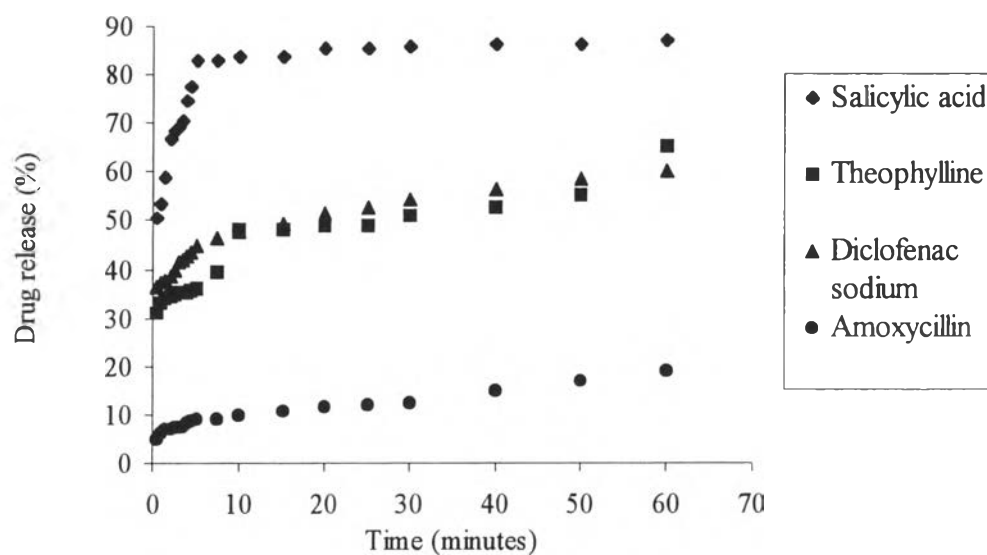
Figure 4.22 Drug release profiles for pure CM-chitin film at pH 7.2. ◆ salicylic acid; ■ theophylline; ▲ diclofenac sodium; ● amoxycilin trihydrate.
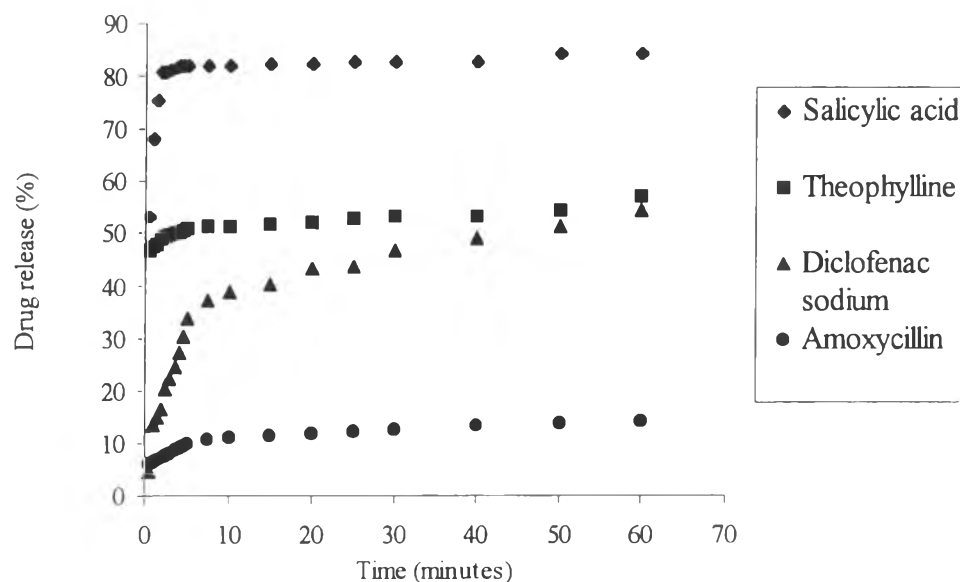

Figure 4.23 Drug release profiles for the blend films with 80 % CM-chitin content at pH 7.2. ◆ salicylic acid; ■ theophylline; ▲ diclofenac sodium; ● amoxycilin trihydrate.
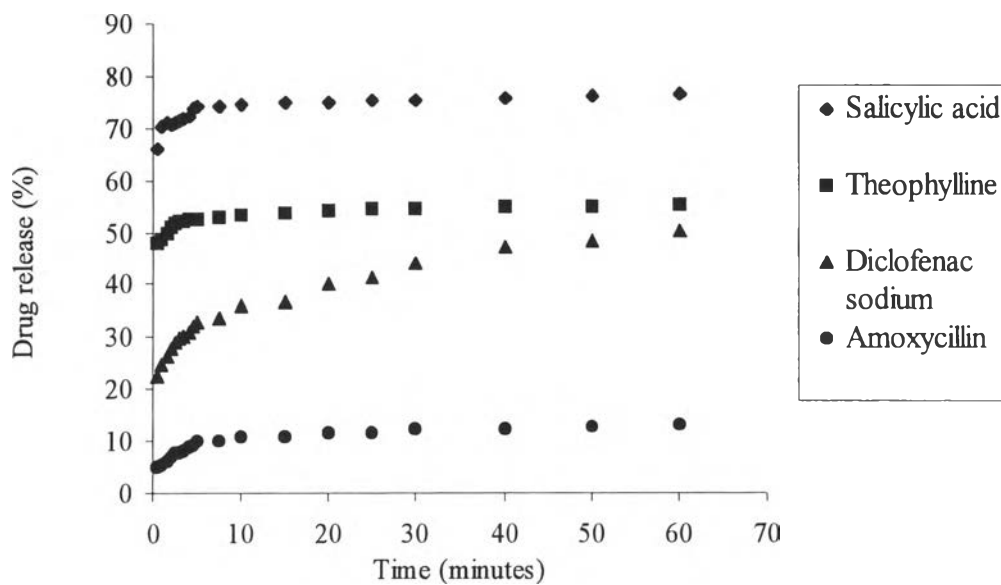
Figure 4.24 Drug release profiles for the blend films with 60 % CM-chitin content at pH 7.2. ◆ salicylic acid; ■ theophylline; ▲ diclofenac sodium; ● amoxycilin trihydrate.

Figure 4.25 Drug release profiles from the blend films with 50 % CM-chitin content at pH 7.2. ◆ salicylic acid; ■ theophylline; ▲ diclofenac sodium; ● amoxycilin trihydrate.
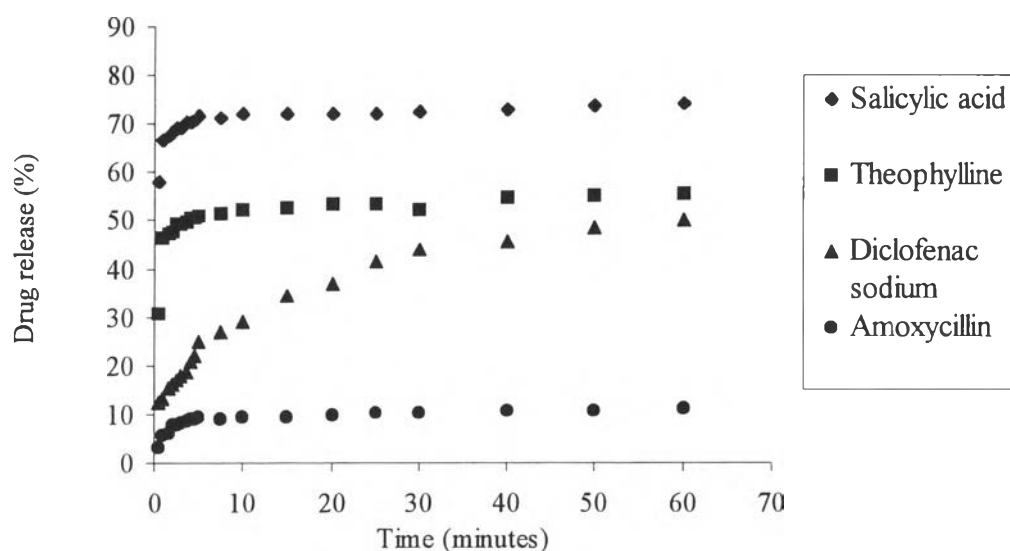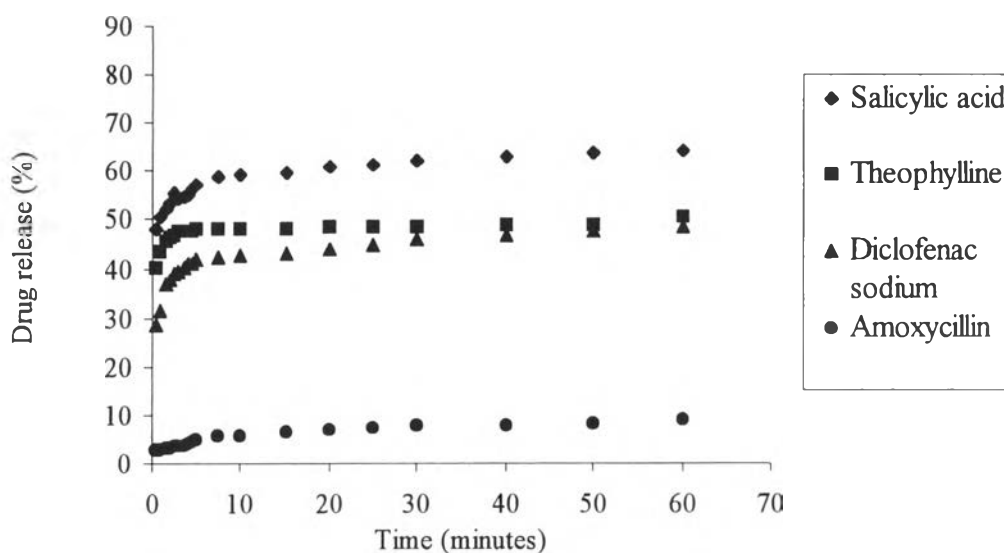
Figure 4.26 Drug release profiles from the blend films with 40 % CM-chitin content at pH 7.2. ◆ salicylic acid; ■ theophylline; ▲ diclofenac sodium; ● amoxycilin trihydrate.

4.10 Effect of PVA on the Blend Films

PVA is a synthetic polymer that can form a hydrogel which is widely used in biomedical applications (Liu *et al.*, 1996). Similar to silk fibroin, degree of swelling of pure PVA film was constant for a wide pH range due to pH stability of PVA (Gudeman *at al.*, 1995). A comparison of drug releases from CM-chitin/silk fibroin blend films and CM-chitin/PVA blend films using salicylic acid as a model drug is shown in Table 4.5. It was found that the releases of salicylic acid from CM-chitin/PVA blend films were similar to those released from CM-chitin/silk fibroin blend films. The amounts of drug released from CM-chitin/PVA blend films were a little bit higher than those released from CM-chitin/silk fibroin blend films. This may be due to the difference in swelling ability of PVA and silk fibroin. The degrees of swelling of silk fibroin and PVA which were 20 % (Ayub *et al.*, 1994) and 120 % (Peesan *et al.*, 2003), respectively. In addition, it was found that the releasing amounts of drug decreased as the increasing of PVA content in the blend films which is similar to the results of CM-chitin and silk fibroin blend films. The drug released

from both CM-chitin/silk fibroin and CM-chitin/PVA blend films depended on CM-chitin content in the blend films, indicating that CM-chitin had a dominant effect on drug release as compared to silk fibroin and PVA. This may be explained that CM-chitin, the component with more ionizable functional groups, played an important role in swelling behavior and consequently affected the drug release characteristics of the blend films.

Table 4.5 Effect of blend components and compositions on the release of salicylic acid at pH 2.0, pH 5.5 and pH 7.2 for the releasing time of 1 h

Weigh ratio of CM-chitin to silk fibroin or PVA	Drug release (%)[a]					
	CM-chitin/silk fibroin			CM-chitin/PVA		
	pH 2	pH 5.5	pH 7.2	pH 2	pH 5.5	pH 7.2
100:0	84.0±0.18	76.9±0.11	87.2±3.00	84.1±0.18	76.9±0.11	87.2±3.00
80:20	76.3±0.12	74.6±0.18	84.3±0.68	83.1±0.89	76.6±0.81	87.7±1.34
60:40	77.6±0.26	63.1±0.39	76.5±0.40	82.9±0.22	68.7±0.88	82.5±0.48
50:50	65.5±0.18	61.8±0.46	73.4±0.18	75.1±0.72	65.3±0.88	80.6±0.28
40:60	63.1±0.16	58.6±0.15	64.1±0.33	72.6±0.63	64.8±1.08	72.8±2.24

a   the average value from three experiments