Acta Pharmaceutica Turcica
XXXX (3) 103-119 (1998)

IN VITRO ADSORPTION STUDY OF DRUGS BY VARIOUS EXCIPIENTS

BAZI İLAÇ ETKEN MADDELERİNİN ÇEŞİTLİ YARDIMCI MADDELER TARAFINDAN SORPSİYONUNUN İN VİTRO İNCELENMESİ

KANDEMİR CANEFE, DEMET BAYEL, E. LEVENT ÜNVER

Department of Pharmaceutical Technology, Faculty of Pharmacy, Ankara University, 06100 Ankara, Turkey

The purpose of this study was to investigate by in vitro method whether a sorption phenomena took place and in which ratios it occurred when excipients talc, kaolin, microcrystalline cellulose, ethyl cellulose, Aerosil 200, Carbopol 934 having absorbent properties are present in the formulations of drugs containing procaine HCl, ephedrine HCl, caffeine and methylene blue or when excipients are taken concomitantly with these drug while they are present in different formulations. The adsoption of drugs was investigated both in distilled water and pH values where the drugs showed optimum stability. Among the drugs used, under the investigation conditions, ephedrine HCl and caffeine were found not to be adsorbed while procaine HCl and methylene blue were adsorbed to a significant extent. The fitness of results obtained to various adsorption isotherms were investigated and the type of the isotherms that the adsorption fitted was determined and was found that the adsorption of procaine HCl and methylene blue in all cases obeyed the Langmuir isotherm. In order to determine the dimensions of extent of adsorption and to make comparison between the excipients, the adsorption capacities of excipients were calculated and Aerosil 200 was found to possess the highest adsorptive capacity while ethyl cellulose possessed the lowest. In order to determine the relationship between the adsoption capacities and particle sizes of excipients, the particle sizes of excipients were analysed. Aerosil 200 was found to have the smallest particle size while ethyl cellulose was found to have the biggest. While for ethyl cellulose and Aerosil 200 there was a direct correlation between the particle sizes and adsorption capacities however, the same parallelism is not seeen at other excipients.

Çalışmamızda prokain HCl, efedrin HCl, kafein ve metilen mavisi olmak üzere dört farklı etken maddenin ilaç formülasyonlarında, adsorban özellik gösteren yardımcı maddelerden talk, kaolin, mikrokristal selüloz, etil selüloz, kolloidal silisyum dioksit (Aerosil 200) ve Carbopol 934 bulunması veya bu etken ve yardımcı maddelerin ayrı formülasyonlarda yer alıp, bir arada kullanımları halinde, bunlar arasında sorpsiyon olayının söz konusu olup olmadığının in vitro olarak incelenmesi amaçlandı.

Etken maddelerin adsorpsiyonları, distile su ile optimum dayanıklılık gösterdikleri pH ortamlarında incelendi ve kullanılan etken maddelerden efedrin HCl ve kafein inceleme şartları altında hiç adsorpsiyona uğramazken, prokain HCl ve metilen mavisinin yardımcı maddeler tarafından önemli miktarlarda adsorbe edildikleri görüldü. Elde edilen sonuçların çeşitli izotermlere uygunluğu araştırıldı ve ortaya çıkan adsorpsiyonun daha çok Langmuir adsorpsiyon izotermine uyum sağladığı görüldü.

Oluşan adsorpsiyon miktarının boyutlarını ortaya koymak ve kullanılan yardımcı maddeler arasında bir karşılaştırma yapmak amacıyla yardımcı maddelerin adsorpsiyon kapasiteleri hesaplandı ve Aerosil 200'ün en yüksek, etil selülozun ise en düşük adsorpsiyon kapasitesi gösteren madde oldukları bulundu.

Yardımcı maddelerin partikül büyüklükleri ile adsopsiyon özellikleri arasındaki ilişkiyi de ortaya koymak üzere yapılan partikül büyüklüğü analizlerinde Aerosil 200'ün en küçük, etil selülozun ise en büyük partikül çapına sahip yardımcı madde oldukları görüldü. Aerosil 200 ve etil selüloz için partikül büyüklükleri ile adsopsiyon kapasiteleri arasında bir korelasyon söz konusu iken, diğer yardımcı maddelerde aynı paralellik görülmemiştir.

Keywords : *Adsorption; Stability; Procaine HCl; Ephedrine HCl; Caffeine*

Anahtar kelimeler: *Adsorpsiyon; Stabilite; Prokain HCl; Efedrin HCl; Kafein*

Introduction

In pharmaceutical dosage formulations the problems related to drug-excipient interactions are frequently encountered and some changes may occur in the stability and therapeutic efficacy of drugs due to these interactions.

The purpose of this study was to investigate by in vitro method whether a sorption phenomena as a physico-chemical drug-excipient interaction takes place when excipients talc, kaolin, Aerosil 200, Carbopol 934, microcrystalline cellulose and ethyl cellulose having adsorbent properties are present in the formulations of drugs containing ephedrine HCl, procaine HCl, methylene blue and caffeine or when they are present in different formulations but are taken concomitantly.

Materials

Agents and excipients: Procaine HCl (Merck), ephedrine HCl (Sigma), caffeine (BDH), methylene blue (Hoechst), talc (BDH), kaolin (Sigma), ethyl cellulose (BDH), Aerosil 200 (Degussa), Carbopol 934 (Goodrich), microcrystalline cellulose (Baker).

Equipment: Mechanical shaker (Nüve, SL 3905), microscope (Nikon AFM), spectrophotometer (Pye-Unicam, SP8-100), pH meter (Beckman H4), centrifuge (Hettich, Rotofix), magnetic stirrer (Heidolph, MRO).

Methods

Certain amounts of excipients were added into the aqueous solutions of drugs prepared at different concentrations. The suspension and colloidal solution samples were placed in a mechanical shaker and agitated at room temperature for a time which was adequate to attain equilibrium. At the end of this period the suspension and isotherm samples were centrifuged at certain rotations for certain times determined beforehand. The supernatant solutions were analysed for residual drug concentrations. The adsorptions of drugs by excipients were investigated both in distilled water and various pH mediums where they showed the optimum stability. Langmuir and Freundlich isotherms were used for the kinetic evaluations in the systems where adsorption was observed. The best isotherms that the adsorption fitted were determined by regression analysis. To make comparison between the excipients used about their adsorption properties the adsorptive capacities were calculated in the systems that obeyed the Langmuir isotherm. To investigate the effect of pH on the extent of adsorption the pH of suspension and colloidal solution samples were analysed (1-86).

Results and Discussion

The centrifuge rotation, centrifuge and agitation times used in the experiments are seen in Tables 1 and 2. Ephedrine HCl and caffeine were found not to be adsorbed by excipients both in distilled water and in pH mediums where they showed optimum stability. As seen in Tables 3-6 the absorbancy values calculated at t=0 were constant at =24. Procaine HCl and methylene blue were found to be adsorbed to a significant extent. The adsorption of procaine HCl by various excipients in distilled water and in pH=4.0 phosphate buffer in most cases obeyed the Langmuir isotherm (Tables 7,8) while adsorption on Carbopol 934 in pH=4.0 medium obeyed Freundlich isotherm.

Langmuir and Freundlich adsorption isotherms for procaine HCl in distilled water and in pH=4.0 phosphate buffer are shown in figs. 1-22. Table 9 shows the adsorption of methylene blue on various excipients obeying the Langmuir isotherm. Figs. 23-32 represent the Langmuir isotherms for methylene blue. The adsorptive capacities of adsorbents were calculated from the slopes of Langmuir isotherms. As shown in Table 10 Aerosil 200 possessed the highest adsorptive capacity while ethyl cellulose possessed the lowest. The results of particle analysis indicated that Aerosil 200 had the smallest and ethyl cellulose had the largest particles sizes (Table 11). For ethyl cellulose and Aerosil 200 there was a direct correlation between the particle sizes and the adsorption capacities however, the same parallelism was not observed for the other excipients used.

The pH analysis of suspension and colloidal solution samples are shown in Table 12.

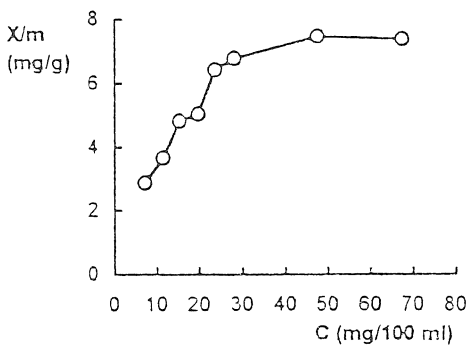

Fig.1. Langmuir adsorbtion isotherm for procaine HCl by talc in distilled water

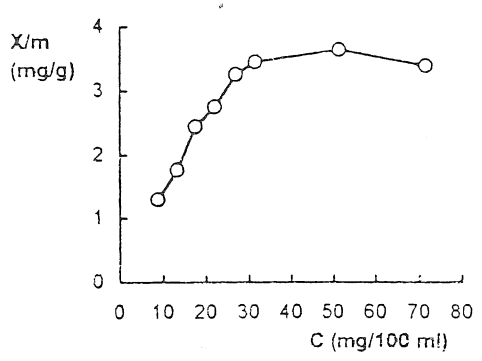

Fig.2. Langmuir adsorbtion isotherm for procaine HCl by kaolin in distilled water

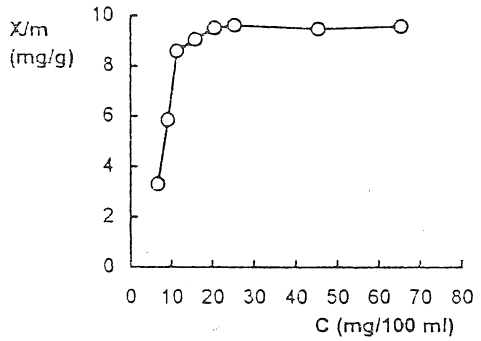

Fig.3. Langmuir adsorbtion isotherm for procaine HCl by Aerosil 200 in distilled water

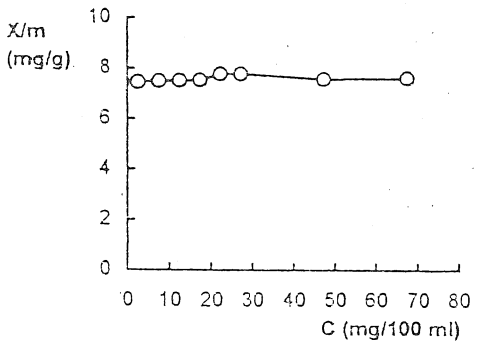

Fig.4. Langmuir adsorbtion isotherm for procaine HCl by microcrystalline cellulose in distilled water

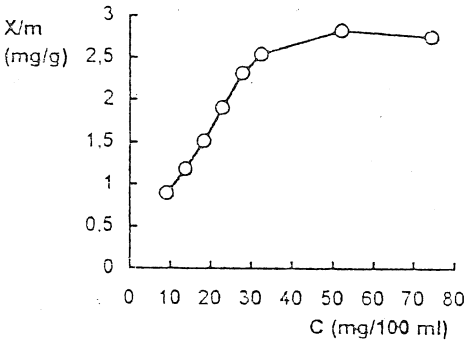

Fig.5. Langmuir adsorbtion isotherm for procaine HCl by ethyl cellulose in distilled water

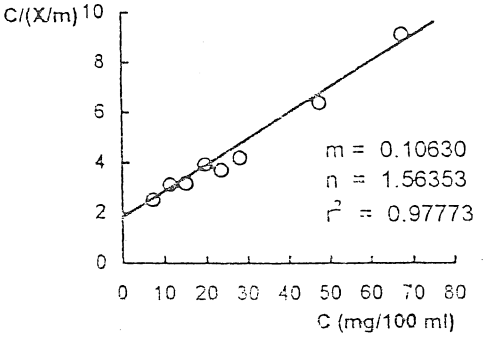

Fig.6. Langmuir adsorbtion isotherm for procaine HCl by talc in distilled water

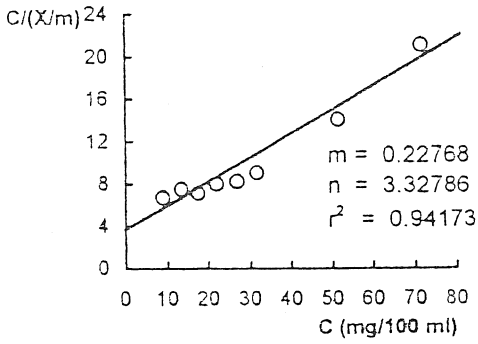

Fig.7. Linear Langmuir adsorbtion isotherm for procaine HCl by kaolin in distilled water

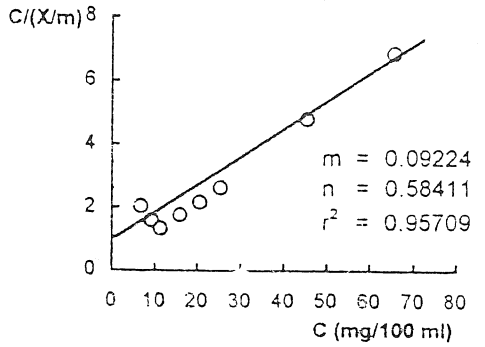

Fig.8. Linear Langmuir adsorbtion isotherm for procaine HCl by Aerosil 200 in distilled water

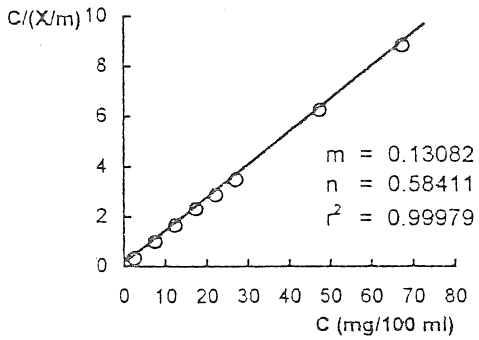

Fig.9. Linear Langmuir adsorbtion isotherm for procaine HCl by microcrystalline cellulose in distilled water

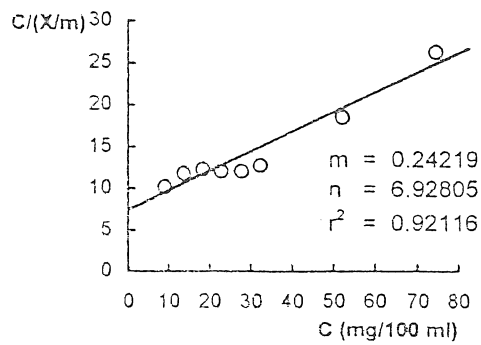

Fig.10. Linear Langmuir adsorbtion isotherm for procaine HCl by ethyl cellulose in distilled water

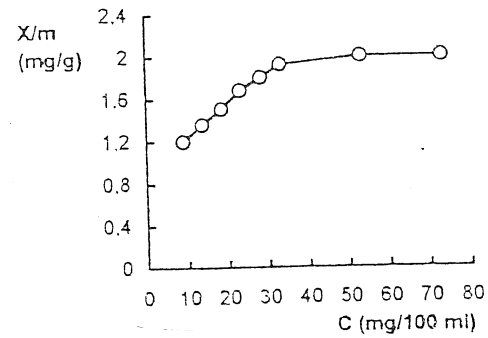

Fig.11. Langmuir adsorbtion isotherm for procaine HCl by talc in pH= 4.0 phosphate buffer

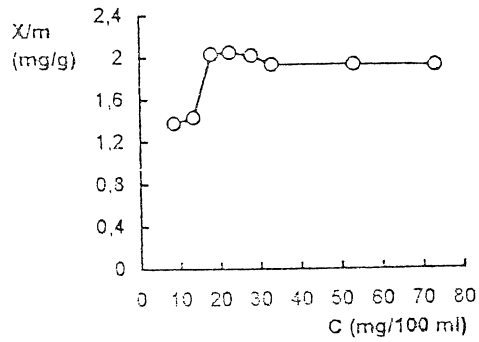

Fig.12. Langmuir adsorbtion isotherm for procaine HCl by kaolin in pH= 4.0 phosphate buffer

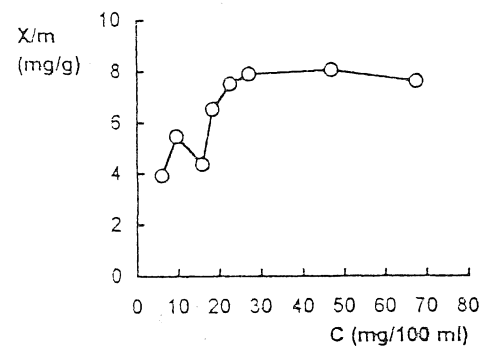

Fig.13. Langmuir adsorbtion isotherm for procaine HCl by Aerosil 200 in pH= 4.0 phosphate buffer

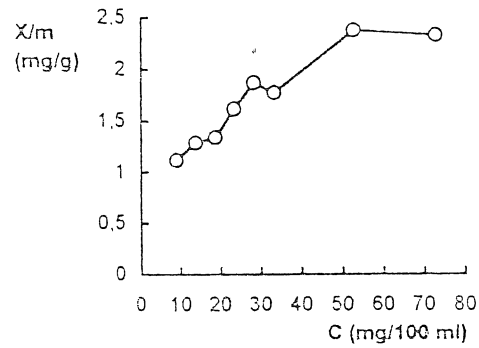

Fig.14. Langmuir adsorbtion isotherm for procaine HCl by microcrystalline cellulose in pH= 4.0 phosphate buffer

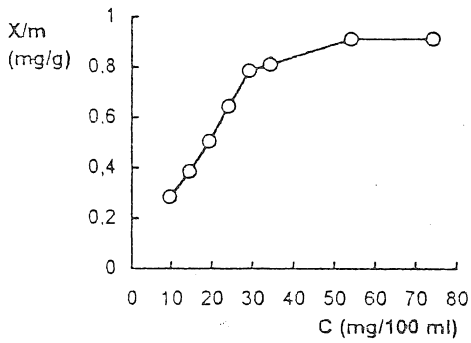

Fig.15. Langmuir adsorbtion isotherm for procaine HCl ethylene cellulose in pH= 4.0 phosphate buffer

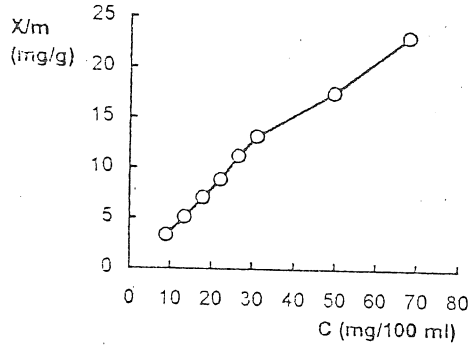

Fig.16. Freundlich adsorbtion isotherm for procaine HCl by Carbopol 934 in pH= 4.0 phosphate buffer

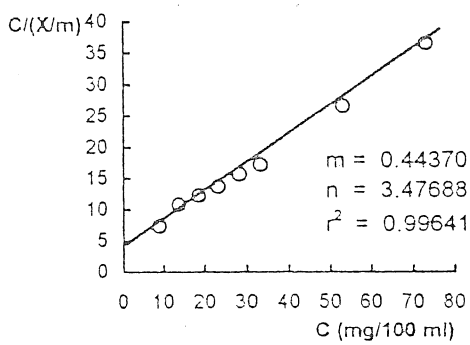

Fig.17. Linear Langmuir adsorbtion isotherm for procaine HCl by talc in pH= 4.0 phosphate buffer

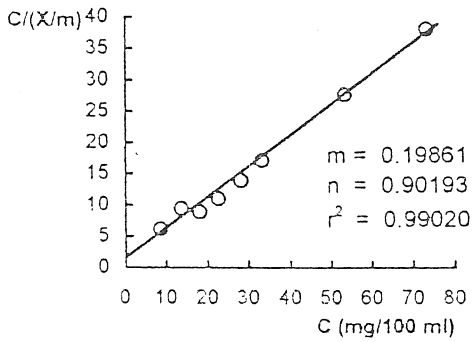

Fig.18. Linear Langmuir adsorbtion isotherm for procaine HCl by kaolin in pH= 4.0 phosphate buffer

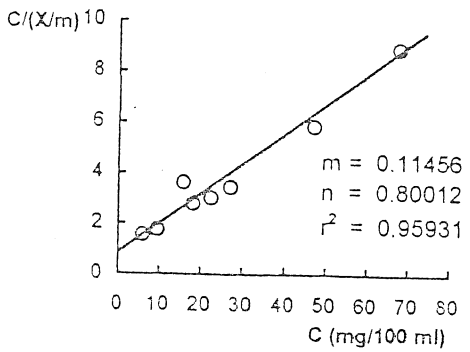

Fig.19. Linear Langmuir adsorbtion isotherm for procaine HCl by Aerosil 200 in pH= 4.0 phosphate buffer

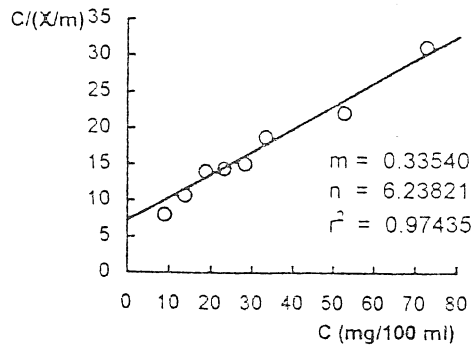

Fig.20. Linear Langmuir adsorbtion isotherm for procaine HCl by microcrystalline cellulose in pH= 4.0 phosphate buffer

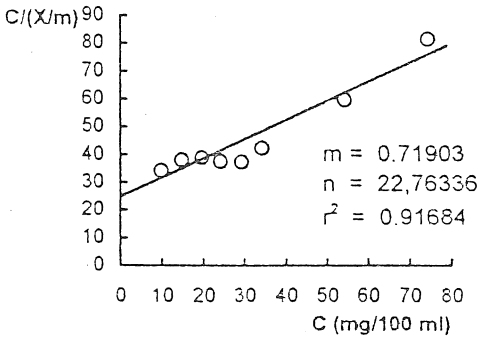

Fig.21. Linear Langmuir adsorbtion isotherm for procaine HCl ethylene cellulose in pH=4.0 phosphate buffer

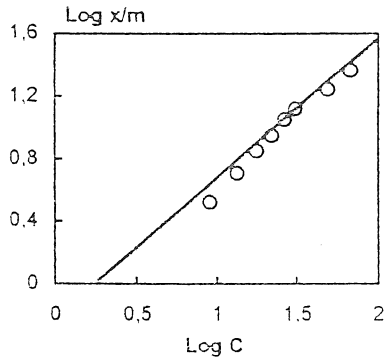

Fig.22. Linear Freundlich adsorbtion isotherm for procaine HCl by Carbopol 934 in pH=4.0 phosphate buffer

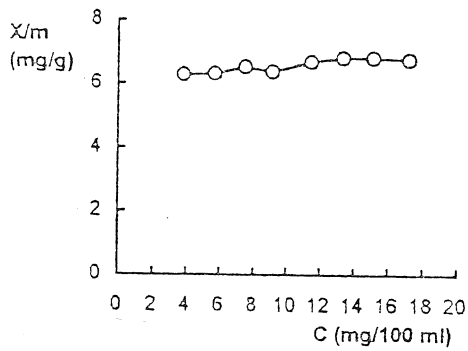

Fig.23. Langmuir adsorbtion isotherm for methylene blue by talc in distilled water

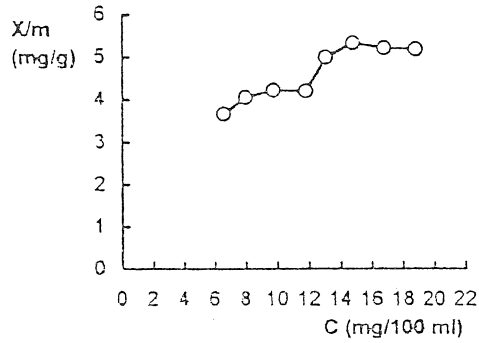

Fig.24. Langmuir adsorbtion isotherm for methylene blue by kaolin in distilled water

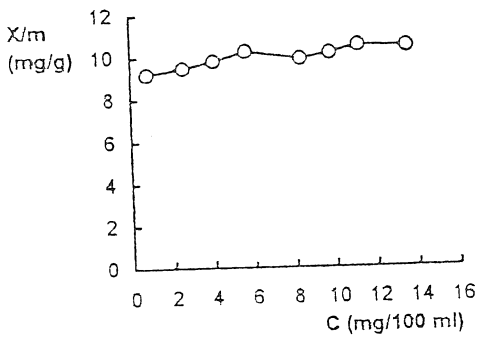

Fig.25. Langmuir adsorbtion isotherm for methylene blue by Aerosil 200 in distilled water

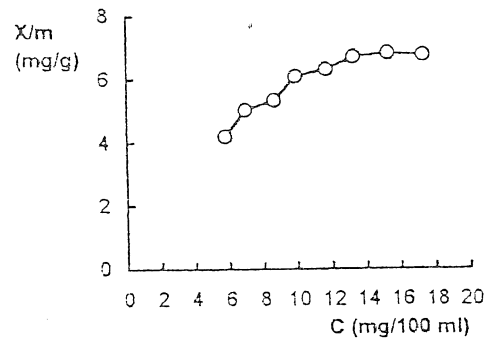

Fig.26. Langmuir adsorbtion isotherm for methylene blue by microcrystalline cellulose in distilled water

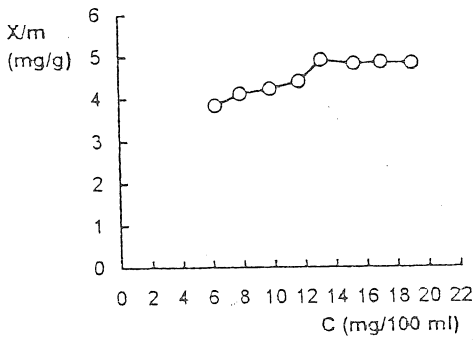

Fig.27. Langmuir adsorbtion isotherm for methylene blue by ethylene cellulose in distilled water

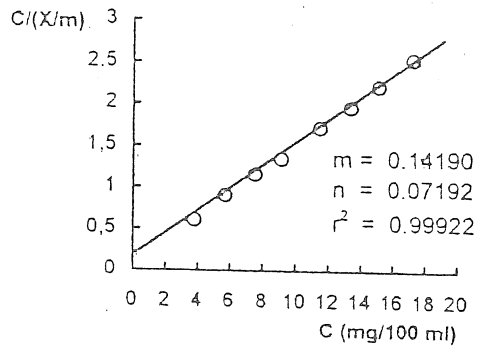

Fig.28. Linear Langmuir adsorbtion isotherm for methylene blue by talc in distilled water

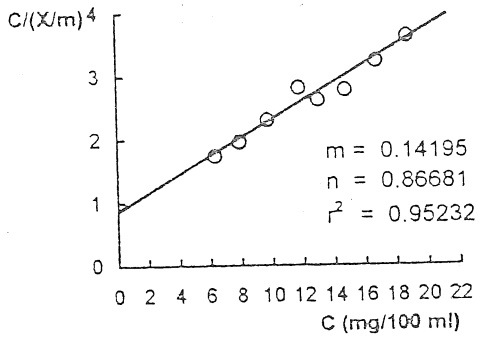

Fig.29. Linear Langmuir adsorbtion isotherm for methylene blue by kaolin in distilled water

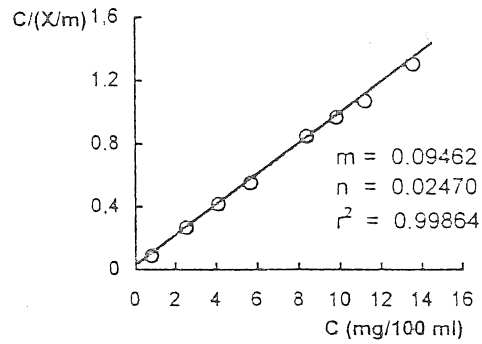

Fig.30. Linear Langmuir adsorbtion isotherm for methylene blue by Aerosil 200 in distilled water

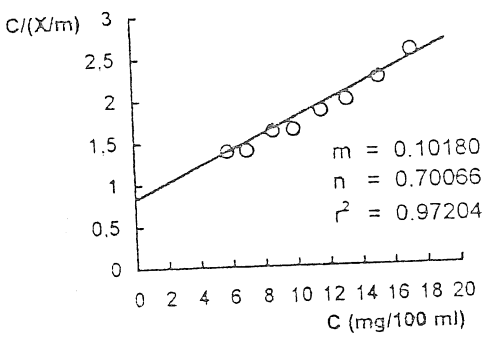

Fig.31. Linear Langmuir adsorbtion isotherm for methylene blue by microcystalline cellulose in distilled water

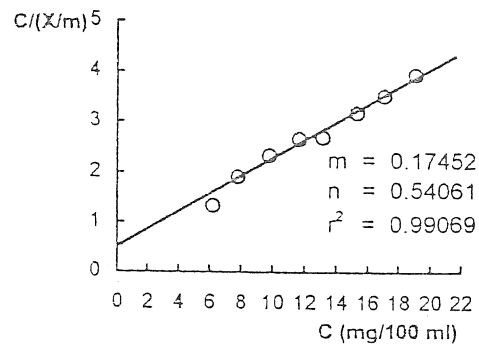

Fig.32. Linear Langmuir adsorbtion isotherm for methylene blue by ethylene cellulose in distilled water

Table 1. The amounts of excipients, the centrifuge rotations (rpm/min), centrifuge and agitation times used in investigation of adsorbtion of procaine HCl, methylene blue, ephedrine HCl and caffeine in distilled water

EXCIPIENTS	PROCAINE HCl				METHYLENE BLUE				EPHEDRINE HCl				CAFFEINE			
	The amount of excipients (g)	Agitation time (h)	Centrifuge rotation (rpm/min)	Centrifuge time (min)	The amount of excipients (g)	Agitation time (h)	Centrifuge rotation (rpm/min)	Centrifuge time (min)	The amount of excipients (g)	Agitation time (h)	Centrifuge rotation (rpm/min)	Centrifuge time (min)	The amount of excipients (g)	Agitation time (h)	Centrifuge rotation (rpm/min)	Centrifuge time (min)
Talc	0.50	1	2600	15	0.50	2	2600	15	0.50	24	2600	15	0.50	24	2600	15
Kaolin	0.50	1	2600	15	0.50	2	2600	15	0.50	24	2600	15	0.50	24	2600	15
Aerosil 200	0.50	2	3000	30	0.50	3	3000	30	0.50	24	3000	30	0.50	24	3000	30
Microcrystalline cellulose	0.50	2	2600	15	0.50	2	2600	15	0.50	24	2600	15	0.50	24	2600	15
Ethyl cellulose	0.50	2	2600	15	0.50	3	2600	15	0.50	24	2600	15	0.50	24	2600	15
Carbopol 934	0.15	3	3000	30	0.15	—	—	—	0.15	24	3000	30	0.15	24	3000	30

Table 2. The amounts of excipients, the centrifuge rotations (rpm/min), centrifuge and agitation times used in vestigation of adsorbtion of procaine HCl, methylene blue, ephedrine HCl and caffeine in pH mediums.

EXCIPIENTS	PROCAINE HCl pH=4.0				EPHEDRINE HCl pH=5.5				CAFFEINE pH=7.0			
	The amount of excipients (g)	Agitation time (h)	Centrifuge rotation (rpm/min)	Centrifuge time (min)	The amount of excipients (g)	Agitation time (h)	Centrifuge rotation (rpm/min)	Centrifuge time (min)	The amount of excipients (g)	Agitation time (h)	Centrifuge rotation (rpm/min)	Centrifuge time (min)
Talc	0.50	2	2600	15	0.50	24	2600	15	0.50	24	2600	15
Kaolin	0.50	2	2600	15	0.50	24	2600	15	0.50	24	2600	15
Aerosil 200	0.50	3	3000	30	0.50	24	3000	30	0.50	24	3000	30
Microcrystalline cellulose	0.50	3	2600	15	0.50	24	2600	15	0.50	24	2600	15
Ethyl cellulose	0.50	3	2600	15	0.50	24	2600	15	0.50	24	2600	15
Carbopol 934	0.15	4	3000	30	0.15	24	3000	30	0.15	24	3000	30

Table 3. In the presence of six various excipients the absorbance values obtained from the adsorbtion experiments of ephedrine HCl prepared at different eight concentrations in distilled water.

EXCIPIENTS	240 mg / 100 ml		270 mg / 100 ml		300 mg / 100 ml		330 mg / 100 ml		360 mg / 100 ml		390 mg / 100 ml		420 mg / 100 ml		450 mg / 100 ml	
	t=0	t=24	t=0	t=24	t=0	t=24	t=0	t=24	t=0	t=24	t=0	t=24	t=0	t=24	t=0	t=24
Talc	0.269	0.271	0.328	0.331	0.267	0.266	0.293	0.295	0.316	0.318	0.364	0.362	0.268	0.270	0.328	0.329
Kaolin	0.272	0.271	0.330	0.331	0.270	0.273	0.292	0.294	0.319	0.321	0.363	0.364	0.273	0.275	0.331	0.330
Aerosil 200	0.272	0.270	0.333	0.333	0.267	0.269	0.294	0.295	0.321	0.319	0.357	0.359	0.271	0.270	0.330	0.332
Microcrystalline cellulose	0.273	0.274	0.329	0.330	0.269	0.269	0.292	0.294	0.322	0.320	0.359	0.360	0.268	0.271	0.332	0.334
Ethyl cellulose	0.268	0.270	0.332	0.330	0.267	0.268	0.294	0.293	0.318	0.320	0.362	0.361	0.269	0.270	0.331	0.331
Carbopol 934	0.269	0.268	0.330	0.331	0.272	0.273	0.293	0.295	0.317	0.317	0.361	0.363	0.273	0.273	0.329	0.331

Table 4. In the presence of six various excipients the absorbance values obtained from the adsorbtion experiments of Caffeine prepared at different eight concentrations in distilled water.

EXCIPIENTS	10 mg / 100 ml		20 mg / 100 ml		30 mg / 100 ml		40 mg / 100 ml		50 mg / 100 ml		60 mg / 100 ml		80 mg / 100 ml		100 mg / 100 ml	
	t=0	t=24	t=0	t=24	t=0	t=24	t=0	t=24	t=0	t=24	t=0	t=24	t=0	t=24	t=0	t=24
Talc	0.301	0.302	0.400	0.398	0.297	0.299	0.402	0.404	0.503	0.501	0.598	0.600	0.400	0.404	0.501	0.503
Kaolin	0.299	0.300	0.404	0.403	0.298	0.300	0.401	0.402	0.504	0.503	0.602	0.604	0.402	0.404	0.503	0.500
Aerosil 200	0.302	0.302	0.402	0.405	0.301	0.300	0.399	0.401	0.502	0.503	0.604	0.602	0.404	0.402	0.502	0.503
Microcrystalline cellulose	0.300	0.301	0.400	0.399	0.299	0.302	0.399	0.400	0.499	0.502	0.602	0.604	0.404	0.403	0.504	0.505
Ethyl cellulose	0.303	0.305	0.399	0.401	0.302	0.303	0.397	0.398	0.497	0.500	0.600	0.599	0.400	0.399	0.499	0.499
Carbopol 934	0.303	0.306	0.401	0.399	0.300	0.303	0.399	0.404	0.500	0.499	0.601	0.599	0.399	0.401	0.499	0.500

Table 5. In the presence of six various excipients the absorbance values obtained from the adsorbtion experiments of ephedrine HCl prepared at different eight concentrations in distilled water.

EXCIPIENTS	240 mg / 100 ml		270 mg / 100 ml		300 mg / 100 ml		330 mg / 100 ml		360 mg / 100 ml		390 mg / 100 ml		420 mg / 100 ml		450 mg / 100 ml	
	t=0	t=24	t=0	t=24	t=0	t=24	t=0	t=24	t=0	t=24	t=0	t=24	t=0	t=24	t=0	t=24
Talc	0.273	0.274	0.332	0.330	0.272	0.270	0.296	0.297	0.320	0.319	0.360	0.362	0.268	0.273	0.332	0.323
Kaolin	0.274	0.270	0.328	0.329	0.268	0.269	0.298	0.296	0.317	0.319	0.358	0.360	0.274	0.275	0.334	0.329
Aerosil 200	0.270	0.272	0.333	0.331	0.269	0.271	0.297	0.299	0.318	0.321	0.365	0.364	0.276	0.275	0.328	0.333
Microcrystalline cellulose	0.267	0.271	0.333	0.334	0.273	0.273	0.300	0.300	0.322	0.323	0.366	0.366	0.271	0.268	0.327	0.329
Ethyl cellulose	0.268	0.270	0.334	0.336	0.274	0.273	0.301	0.298	0.324	0.325	0.361	0.359	0.272	0.268	0.334	0.333
Carbopol 934	0.268	0.268	0.336	0.334	0.271	0.272	0.298	0.300	0.323	0.323	0.362	0.359	0.273	0.274	0.335	0.335

Table 6. In the presence of six various excipients the absorbance values obtained from the experiments of caffeine prepared at different eight concentrations in pH=7.0 phosphate buffer.

EXCIPIENTS	10 mg / 100 ml		20 mg / 100 ml		30 mg / 100 ml		40 mg / 100 ml		50 mg / 100 ml		60 mg / 100 ml		80 mg / 100 ml		100 mg / 100 ml	
	t=0	t=24	t=0	t=24	t=0	t=24	t=0	t=24	t=0	t=24	t=0	t=24	t=0	t=24	t=0	t=24
Talc	0.303	0.305	0.401	0.400	0.299	0.302	0.405	0.404	0.505	0.507	0.598	0.661	0.798	0.801	0.504	0.505
Kaolin	0.298	0.298	0.400	0.400	0.297	0.298	0.399	0.400	0.502	0.500	0.599	0.597	0.803	0.802	0.505	0.504
Aerosil 200	0.300	0.300	0.404	0.405	0.304	0.301	0.404	0.404	0.502	0.500	0.599	0.596	0.804	0.802	0.500	0.502
Microcrystalline cellulose	0.304	0.303	0.399	0.402	0.301	0.305	0.400	0.402	0.499	0.498	0.606	0.606	0.799	0.799	0.499	0.500
Ethyl cellulose	0.302	0.299	0.405	0.407	0.301	0.306	0.398	0.397	0.497	0.499	0.605	0.605	0.800	0.804	0.498	0.499
Carbopol 934	0.299	0.302	0.403	0.404	0.300	0.302	0.397	0.399	0.506	0.505	0.605	0.604	0.800	0.801	0.503	0.501

Table 7. The regression parameters for Langmuir and Freundlich isotherms of procaine HCl in distilled water

EXCIPIENTS	LANGMUIR ISOTHERM				FREUNDLICH ISOTHERM			
	Linear Equation y= mx+n	Determination Coefficient (r^2)	Standart Error of Slope (Sm)	Standart Error of Intercept (Sn)	Linear Equation y= mx+n	Determination Coefficient (r^2)	Standart Error of Slope (Sm)	Standart Error of Intercept (Sn)
Talc	y= 0.106x + 1.564	0.978	0.006	0.190	y= 0.450x + 0.122	0.888	0.057	0.078
Kaolin	y= 0.228x + 3.328	0.942	0.020	0.726	y= 0.458x - 0.249	0.796	0.086	0.122
Aerosil 200	y= 0.092x + 0.584	0.957	0.007	0.218	y= 0.356x + 0.432	0.536	0.117	0.155
Microcrystalline celllulose	y= 0.131x + 0.001	0.999	0.001	0.022	y= 0.010x + 0.869	0.353	0.005	0.006
Ethyl cellulose	y= 0.242x + 6.928	0.921	0.025	0.927	y= 0.592x + 0.566	0.888	0.074	0.107
Carbopol 934	—	—	—	—	—	—	—	—

Table 8 The regression parameters for Langmuir and Freundlich isotherms of procaine HCl in pH=4.0 phosphate buffer

EXCIPIENTS	LANGMUIR ISOTHERM				FREUNDLICH ISOTHERM			
	Linear Equation y= mx+n	Determination Coefficient (r^2)	Standart Error of Slope (Sm)	Standart Error of Intercept (Sn)	Linear Equation y= mx+n	Determination Coefficient (r^2)	Standart Error of Slope (Sm)	Standart Error of Intercept (Sn)
Talc	y=0.444x + 3.475	0.996	0.010	0.0335	y=0.262x - 0.149	0.910	0.029	0.042
Kaolin	y=0.499x + 0.905	0.990	0.018	0.656	y=0.153x + 0.045	0.447	0.060	0.086
Aerosil 200	y=0.115x + 0.800	0.959	0.008	0.276	y=0.296x + 0.403	0.681	0.072	0.097
Microcrystalline celllulose	y=0.335x + 6.235	0.974	0.019	0.718	y=0.392x - 0.333	0.948	0.032	0.047
Ethyl cellulose	y=0.719x + 22.763	0.917	0.077	2.939	y=0.608x - 1.084	0.884	0.078	0.113
Carbopol 934	y=0.006x + 2.440	0.327	0.003	0.107	y=0.963x - 0.367	0.986	0.040	0.057

Table 9. The regression parameters for Langmuir and Freundlich isotherms of methylene blue in distilled water.

EXCIPIENTS	LANGMUIR ISOTHERM				FREUNDLICH ISOTHERM			
	Linear Equation y= mx+n	Determination Coefficient (r^2)	Standart Error of Slope (Sm)	Standart Error of Intercept (Sn)	Linear Equation y= mx+n	Determination Coefficient (r^2)	Standart Error of Slope (Sm)	Standart Error of Intercept (Sn)
Talc	y=0.142x + 0.072	0.999	0.001	0.016	y=0.063x + 0.761	0.820	0.010	0.010
Kaolin	y=0.142x + 0.867	0.952	0.112	0.147	y=0.354x + 0.282	0.877	0.047	0 051
Aerosil 200	y=0.095x + 0.025	0.999	0.001	0.010	y=0.046x + 0.965	0.857	0.007	0 006
Microcrystalline celllulose	y=0.102x + 0.701	0.972	0.006	0.072	y=0.436x + 0.321	0.916	0.047	0 048
Ethyl cellulose	y=0.175x + 0.541	0.991	0.006	0.079	y=0.229x + 0.407	0.899	0.027	0 029
Carbopol 934	—	—	—	—	—	—	—	—

Table 10 The "b" constant of Langmuir adsorbtion isotherms for adsorbtion of procaine HCl and methylene blue by excipients in distilled water and in buffer mediums.

DRUGS	EXCIPIENTS	y = mx + n	LANGMUIR CONSTANT (b)
PROCAINE HCl MEDIUM : DISTILLED WATER	Talc	y=0.106x + 1.564	9.434
	Kaolin	y=0.228x + 3.328	4.386
	Aerosil 200	y=0.092x + 0.584	10.870
	Microcrystalline cellulose	y=0.131x + 0.001	7.634
	Ethyl cellulose	y=0.292x + 6.928	4.132
PROCAINE HCl MEDIUM : pH= 4.0 PHOSPHATE BUFFER	Talc	y=0.444x + 3.475	2.252
	Kaolin	y=0.499x + 0.905	2.004
	Aerosil 200	y=0.115x + 0.800	8.696
	Microcrystalline cellulose	y=0.335x + 6.235	2.985
	Ethyl cellulose	y=0.719x + 22.763	1.391
	Carbopol 934	y=0.006x + 2.440	----
PROCAINE HCl MEDIUM : DISTILLED WATER	Talc	y=0.142x + 0.072	7.042
	Kaolin	y=0.142x + 0.867	7.042
	Aerosil 200	y=0.095x + 0.025	10.526
	Microcrystalline cellulose	y=0.102x + 0.701	9.804
	Ethyl cellulose	y=0.175x + 0.541	5.714

Table 11. The average arithmetic and geometric particle diameters of excipients

EXCIPIENTS	THE AVERAGE ARITHMETIC PARTICLE DIAMETER (μm)	THE AVERAGE GEOMETRIC PARTICLE DIAMETER (μm)	THE GEOMETRIC STANDART DEVIATION OF DISTRIBUTION
TALC	22.14	19.00	1.84
KAOLIN	10.26	9.50	1.58
MICROCRYSTALLINE CELLULOSE	27.02	24.00	1.80
ETHYL CELLULOSE	47.74	36.00	1.90
AEROSİL 200	8.57	7.75	1.74

Table 12. The results of pH analyses of suspension and colloidal solutions containing drugs and excipients at the begining of the adsorbtion experiments (t=0).

EXCIPIENTS	Procaine HCl 20 mg/100 ml			Methylene blue 10 mg/100 ml			Ephedrine HCl 250 mg/100 ml			Caffeine 20 mg/100 ml		
	pH	Standart Deviation (S.D.)	% 95 Probability Level Range	pH	Standart Deviation (S.D.)	% 95 Probability Level Range	pH	Standart Deviation (S.D.)	% 95 Probability Level Range	pH	Standart Deviation (S.D)	% 95 Probability Level Range
TALC 1 g/100 ml	7.61	0.19	± 0.33	8.30	0.46	± 0.77	7.75	0.11	± 0.18	7.65	0.08	± 0.14
KAOLIN 1 g/100 ml	7.91	0.27	± 0.46	8.50	0.70	± 1.19	8.01	0.14	± 0.24	7.90	0.13	± 0.22
Aerosil 200 1 g/100 ml	4.48	0.33	± 0.56	5.06	0.12	± 0.20	4.32	0.12	± 0.20	4.38	0.07	± 0.12
MICROCRYSTALLINE CELLULOSE 1 g/100 ml	5.73	0.37	± 0.62	5.91	0.11	± 0.19	5.66	0.06	± 0.10	5.50	0.18	± 0.30
ETHYL CELLULOSE 1 g/100 ml	5.51	0.11	± 0.19	5.78	0.30	± 0.50	5.49	0.06	± 0.10	5.31	0.07	± 0.12
CARBOPOL 934 0.3 g/100 ml	3.11	0.02	± 0.05	3.22	0.21	± 0.36	3.03	0.11	± 0.19	3.26	0.06	± 0.10

References

1. Abe, I., Kamaya, H., Ueda, I.:J. Pharm. Sci. 79, 354 (1990)
2. Akers, M.J., Lach, J.L., Fischer, L.J.: J. Pharm. Sci. 62, 391 (1973)
3 AlGohary, O., Lyal, J., Murray, J.B.: Pharm. Acta. Helv. 63, 13 (1988)
4. AlGohary, O.MN.: Int. J. Pharm. 67, 89 (1991)
5. Al Shora, H.I., Moustafa, M.A.:Int. J. Pharm. 47, 209 (1988)
6. Armstrong, N.A., Clarke, C.D.: J. Pharm. Pharmac. 23, 95 (1971)
7. Armstrong, N.A., Clarke, C.D.: J. Pharm. Sci. 65, 373 (1976)
8. Aulton, M.E.: The Science of Dosage From Design In. Pharmaceutics, ELBS Publiched, Edingburg, 1990
9. Batuyios, N.H., Brecht, E.A.: J. Am. Pharm. 56, 524 (1957)
10. Bean, H.S., Dempsey, G.: J. Pharm. Pharmac. 23, 699 (1971)
11. Berkem, A.R., Baykut, S.: Fizikokimya, pp. 787-816, Şirketi Mürettibiye Basımevi, İstanbul, 1975
12. Beveridge, E.G., Tood, K.: J. Pharm. Pharmac. 25, 741 (1973)
13. Blaug, S.M., Gross, M.R.: J. Pharm. Sci. 54, 289 (1965)
14. Boman, G., Lundgren, P., Stjernström, G.: Europ. J. Clin. Pharmacol. 8, 293 (1975)
15. Bondy, S.C., Harrington, M.E.: Science 206, 483 (1979)
16.Bornstein, M., Lach, J.L.: J. Pharm. Sci. 55, 1033 (1966)
17. Canefe, K., İzgü, E.: A.Ü. Ecz. Fak. Mec. 11(1) 53 (1981)
18. Carstensen, J.T.: Theory of Pharmaceutical Systems, Vol 2, Academic Press Inc., New York 1973
19. Castellan, G.W.: Physical Chemistry, pp. 548-550, Addison-Wesley Publishing Company Inc., USA 1964
20. Chang, K., Chiou, W.L.: J.Pharm. Sci. 65, 56 (1976)
21. Chien, Y.W., Van Nostrand, P., Shami, E.G.: J. Pharm. Sci. 70, 709 (1981)
22. Clark, C.D., Armstrong, N.A.: Pharm. J. 209, 44 (1972)
21. Çalış, S., Şumnu, M., Hıncal, A.A.: Drug Dev. Ind. Pharm. 12, 1833 (1986)
22. Clark, C.D., Armstrong, N.A.: Pharm. J. 209, 44 (1972)
23. Çalış, S., Şumnu, M., Hıncal, A.A.: Drug Dev. Ind. Pharm. 12, 1833 (1986)
24. Çelebi, N.: Türkiye'nin Doğal Anorganik Hidrokolloidlerinin Adsorbsiyon Özelliklerinin İncelenmesi, Doktora Tezi, Ankara, 1980
25. Dittert, L.W.: Sprowis' American Pharmacy, pp. 127-132, 7th Ed., J.B. Lippincott Company, Phiadelphia, 1974
26. El Gamal, S.S., Boraje, N.A., Naggar, V.F.: Pharm. Ind. 48, 1207 (1986)
27. El Masry, S., Khalil, S.A.: J. Pharm. Pharmac. 26, 243 (1974)
28. El Samaligy, M.S., El Mahrouk, G.M., El Kirsh, T.A.: Int. J. Pharm. 31, 137 (1986)
29. El Sayed, Y.M., Al Meshal, M.A., Al Angary, A.A., Lutfi, K.M.: Int. J. Pharm. 64, 109 (1990)
30. Farrington, R.A., Daniels, A.: Physical Chemistry, pp. 230-236, 5th Ed., John Wiley and Sons, New York 1979
31. Florence, A.T., Attwood, D.: Physicochemical Principles of Pharmacy, Macmillan Publishers Ltd. London 1981
32. Franz, R.M., Peck, G.E.: J. Pharm. Sci. 71, 1193 (1982)
33. Gessner, P.K., Hasan, M.M.: J.Pharm. Sci. 76, 319 (1987)
34. Giles , C.H., Mac Ewan, T.H., Nakhwa, S.N., Smith, D.: J. Chem. Soc. 3973 (1960)
35. Gregg, S.J.: The Surface Chemistry of Solids, 2nd Ed. Chapman and Hall Ltd., London, 1965
36. Hıncal, A., Sheth, B.: J. Pharm. Sci. 68, 472 (1979)
37. Hiemenz, P.C.: Principles of Colloid and Surface Chemistry, pp. 306-320, Marcel Dekker Inc., New York, 1977
38. İsmail, F.A., Khalafallah, N., Khalil, S.A.: Int. J. Pharm. 34, 189 (1987)
39. İzgü, A., Canefe, K.: Doğa 1, 82 (1977)
40. Judis, J.: J.Pharm. Sci. 74, 479 (1985)
41. Khalil, S.A.H.: J. Pharm. Pharmac. 26, 961(1974)
42. Khalil, S.A.H., Mortada, L.M., El Khawas, M.E.: Int. J. Pharm. 18, 157 (1984)
43. Khalil, S.A.H., Mortada, L.M., El Khawas, M.E.: Int. J. Pharm. 19, 233 (1984)
44. Khalil, S.A.H., Mortada, L.M., Shams-Eldeen, M.A., El Khawas, M.M.: Drug Dev. Ind. Pharm. 13, 369 (1987)
45. Khalil, S.A.H., Mortada, L.M., El Khawas, M.E.: Drug Dev. Ind. Pharm. 13, 547 (1987)
46. Koeleman, H.A., Zyl, R., Steyn, N. Bone-schans, B., Steyn, H.S.: Drug Dev. Ind. Pharm. 16, 791 (1990)
47. Kryt, H.R.: Colloid Science, Elsevier Publishing Inc., New York 1949
48. Lachman, L., Lieberman, H.A., Kanig, J.L.: The Theory and Practice of Industrial Pharmacy, Lea and Febiger, Philadelphia 1970
49. Mantel, C.L.: Chemical Engineering Series, Adsorbtion, 2nd Ed., Mc Graw Hill Book Company Inc., New York 1951
50. Martin, C.L., Swarbrick, J., Cammarata, A.: Physical Pharmacy, 2nd Ed. Lea and Febiger,Philadelphia 1970
51. Mc Callister, J.D., Chin, T., Lach, J.L.: J. Pharm. Sci. 59, 1286 (1970)
52. Mc Ginity, J.W., Hill, J.A.: Ibid. 64, 1566 (1975)
53. Mc Ginity, J.W., Lach, S.L.: J. Ibid. 65, 896 (1976)
54. Monthouse, D.C., Lach, J.L.: Ibid. 61, 1435 (1972)

55. Morefield, E.M., Peck, G.E., Hem, S.L., Feldkamp, J.R.: Ibid. 74, 1019 (1985)
56. Moriguchi, I., Kaneniwa, N.: Chem. Pharm. Bull. 17, 394 (1969)
57. Moriguchi, I., Kaneniwa, N.: Ibid.17, 961 (1969)
58. Moustafa, M.A., Babhair, S.A., Kouta, H.I.: Int. J. Pharm. 36, 185 (1987)
59. Nada, A.H., Etman, M.A., Ebian, A.R.: Ibid. 53, 175 (1989)
60. Nikolakakis, I., Newton, J.M.: J. Pharm. Pharmacol. 41, 145 (1989)
61. Okada, S., Nakahara, H., Isaka, H.: Chem. Pharm. Bull. 35, 761 (1987)
62. Othman, S., Muti, H., Shaheen, O., Awidi, A., Al Turk, W.A.: Int. J. Pharm. 41, 197 (1988)
63. Othmer, D.: Encyclopedia of Chemical Technology, Vol 1, 2nd Ed., John Wiley and Sons Inc., New York 1970
64. Özdemir, O., Baktır, G., Ekinci, A.C.: Acta Pharm. Turc. 18, 83 (1986)
65. Parrot, E.L.: Pharmaceutical Technology, pp. 20-27, Fundemmental Pharmaceutics, Burgess Pub. Co. Minneapolis 1971
66. Naggar, V.F.B., Boraje, N.A., Shams Eldeen, M.A.: Int. J. Pharm. 28, 239 (1986)
67. Porubucan, L.S., Serna, C.J., White, J.L., Hem, S.L.: J. Pharm. Sci. 67, 1081 (1978)
68. Rawlins, E.A.: Bentley's Textbook of Pharmaceutics, pp. 101-106, 8th Ed., Bailliere and Tindall, London 1977
69. Ridout, C.W.: Pharm. Acta Helv. 43, 177 (1968)
70. Rupprecht, H.H.: J. Pharm. Sci. 61, 700 (1972)
71. Rybolt, T.R., Burrell, D.E., Shults, J.M., Kelley, A.K.: Ibid. 75, 904 (1986)
72. Sepelyak, R.J., Feldkamp, J.R., Moody, T.E., White, J.L., Hem, S.L.: Ibid. 73, 1514 (1984)
73. Sepelyak, R.J., Feldkamp, J.R., Moody, T.E., White, J.L., Hem, S.L.: Ibid. 73, 1517 (1984)
74. Shotton, E., Ridgway, K.: Physical Pharmaceutics, Clarendon Press, Oxford 1974
75. Singh, A., Mital, H.C.: Acta. Pharm. Technol. 25, 217 (1979)
76. Sorby, D.L.: J. Pharm. Sci. 54, 677 (1965)
77. Sorby, D.L., Liu, G.: J. Pharm. Sci. 55, 504 (1965)
78. Sorby, D.L., Plein, E.M., Benmaman, J.D.: Ibid. 55, 785 (1966)
79. Stotzky, G., Rem, L.T.: Can. J. Microbiol. 12, 547 (1966)
80. Sunam, G., Güven, K.C., Hıncal, A.: İst. Ecz. Fak. Mec. 3, 155 (1967)
81. Swarbrick, J., Boylan, J. : Encyclopedia of Pharmaceutical Technology, pp 73-114, Vol. 2, Marcel Dekker Inc., New York 1990
82. Takahashi, H., Watanabe, Y., Shimamura, H., Sugito, K.: J. Pharm. Sci. 74, 862 (1985)
83. Tsuchiya, T., Levy, G.: Ibid. 61, 586 (1972)
84. Tsuchiya, T., Levy, G.: Ibid. 61, 624 (1972)
85. Wai, K., Banker, G.S.:Ibid. 55, 1215 (1966)
86. Yousef, R.T., El Nakeeb, M.A., Labib, S.: Acta. Pharm. Suecica 8, 303 (1971)

Accepted : 25.12.1997