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APPENDICES

APPENDIX A

Calibration curve

The amount of diltiazem hydrochloride was determined by the UV-visible spectrophotometer. The relationship between diltiazem hydrochloride concentration versus absorbance in various media was presented in Table 1A-5A. The calibration curve of diltiazem hydrochloride and the linear relationship with the correlation of determination in each medium were also depicted in Figure 1A-21A.

Table 1(A) The absorbance of diltiazem hydrochloride in water at 237 nm

Concentration (µg/ml)	Absorbance
4	0.2114
6	0.3277
8	0.4250
10	0.5333
12	0.6397
16	0.8543

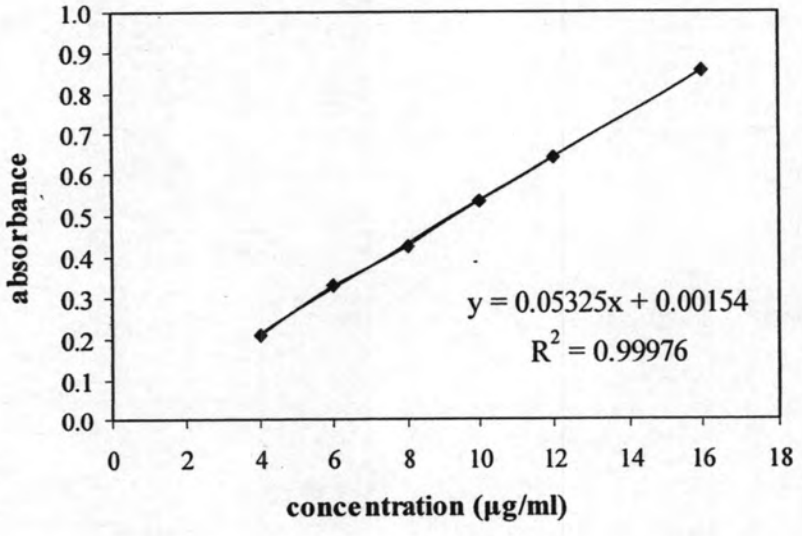

Figure 1(A) Calibration curve of diltiazem hydrochloride in water at 237 nm.

Table 2(A) The absorbance of diltiazem hydrochloride in 0.1 M hydrochloric acid, phosphate buffer pH 6.8, phosphate buffer pH 6.8 (ionic strength=0.1), phosphate buffer pH 7.2 and phosphate buffer pH 7.2 (ionic strength = 0.1) at 237 nm

Concentration (µg/ml)	Absorbance				
	0.1 M HCl	phosphate buffer pH 6.8	phosphate buffer pH 6.8 (ionic strength=0.1)	phosphate buffer pH 7.2	phosphate buffer pH 6.8 (ionic strength=0.1)
4	0.2110	0.2151	0.2185	0.2166	0.2016
6	0.3177	0.3208	0.3239	0.3131	0.3220
8	0.4223	0.4265	0.4292	0.4225	0.4311
10	0.5310	0.5346	0.5346	0.5260	0.5264
12	0.6366	0.6378	0.6338	0.6325	0.6363
16	0.8509	0.8492	0.8507	0.8504	0.8496

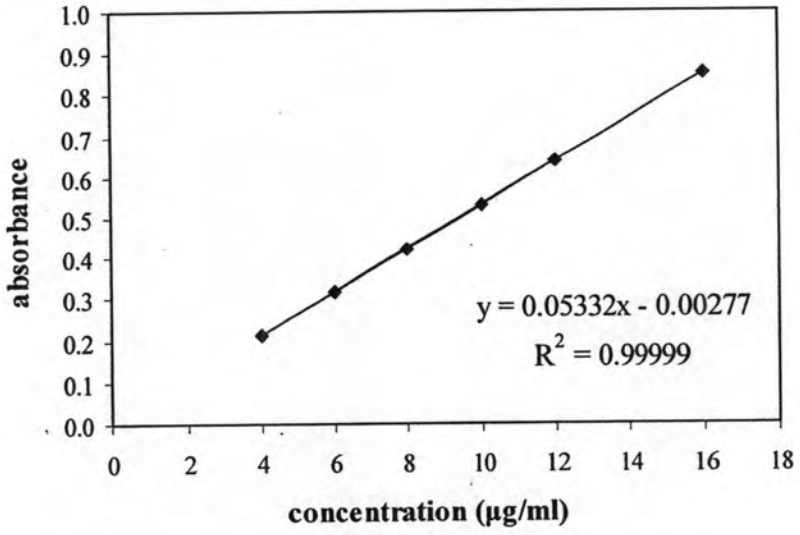

Figure 2(A) Calibration curve of diltiazem hydrochloride in 0.1 M hydrochloric acid at 237 nm.

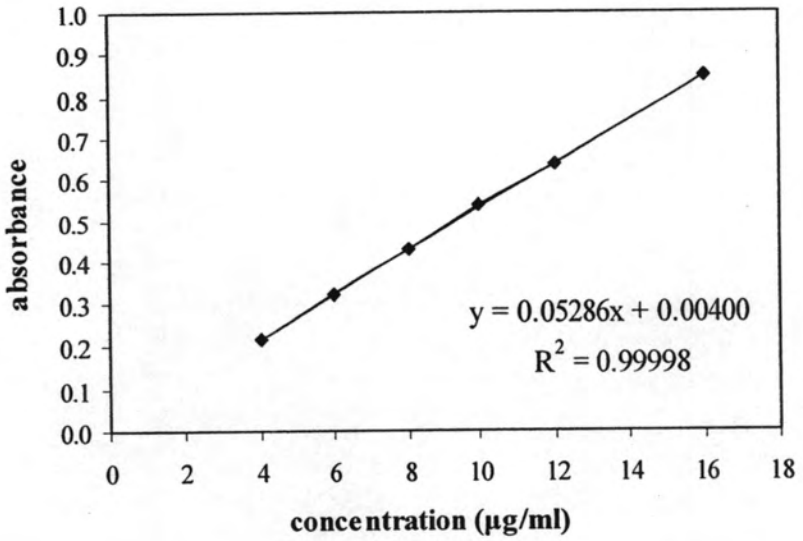

Figure 3(A) Calibration curve of diltiazem hydrochloride in 0.1 M phosphate buffer pH 6.8 at 237 nm.

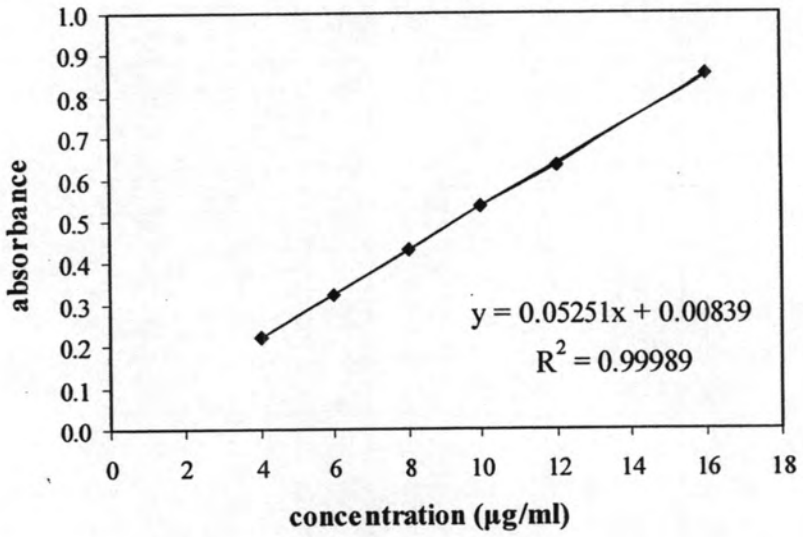

Figure 4(A) Calibration curve of diltiazem hydrochloride in phosphate buffer pH 6.8 adjusted ionic strength = 0.1 at 237 nm.

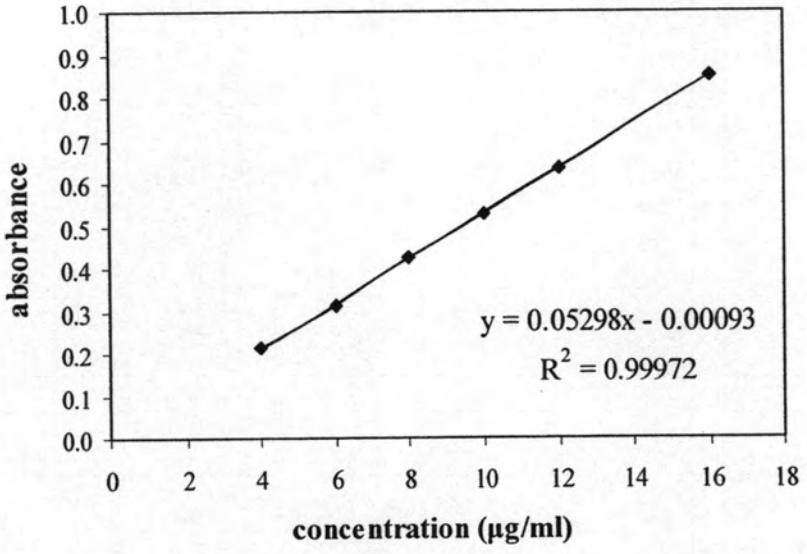

Figure 5(A) Calibration curve of diltiazem hydrochloride in phosphate buffer pH 7.2 at 237 nm.

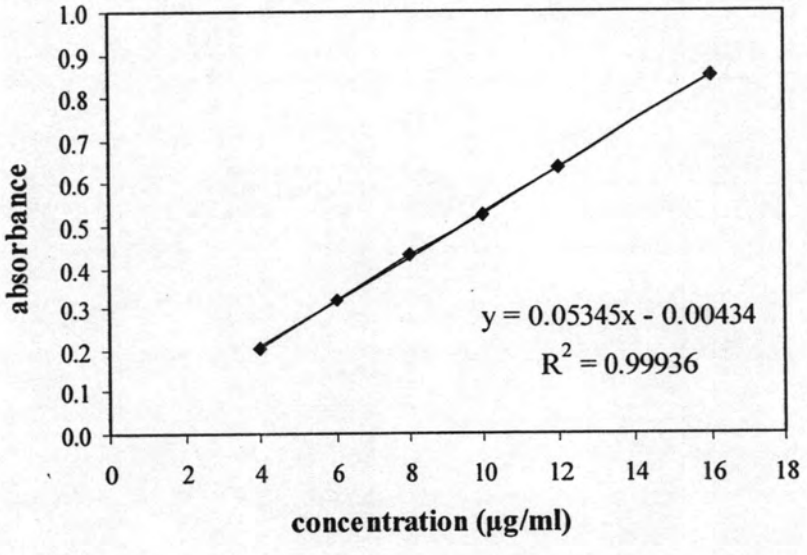

Figure 6(A) Calibration curve of diltiazem hydrochloride in phosphate buffer pH 7.2 adjusted ionic strength = 0.1 at 237 nm.

Table 3(A) The absorbance of diltiazem hydrochloride in potassium chloride at 237 nm

Concentration (µg/ml)	Absorbance						
	0.01 M	0.05 M	0.1 M	0.2 M	0.3 M	0.4 M	0.5 M
4	0.2151	0.2152	0.2154	0.2218	0.2207	0.2140	0.2095
6	0.3228	0.3209	0.3214	0.3290	0.3264	0.3200	0.3259
8	0.4265	0.4227	0.4275	0.4362	0.4381	0.4291	0.4373
10	0.5321	0.5324	0.5355	0.5433	0.5358	0.5302	0.5387
12	0.6308	0.6382	0.6396	0.6405	0.6345	0.6382	0.6451
16	0.8491	0.8447	0.8569	0.8658	0.8550	0.8503	0.8579

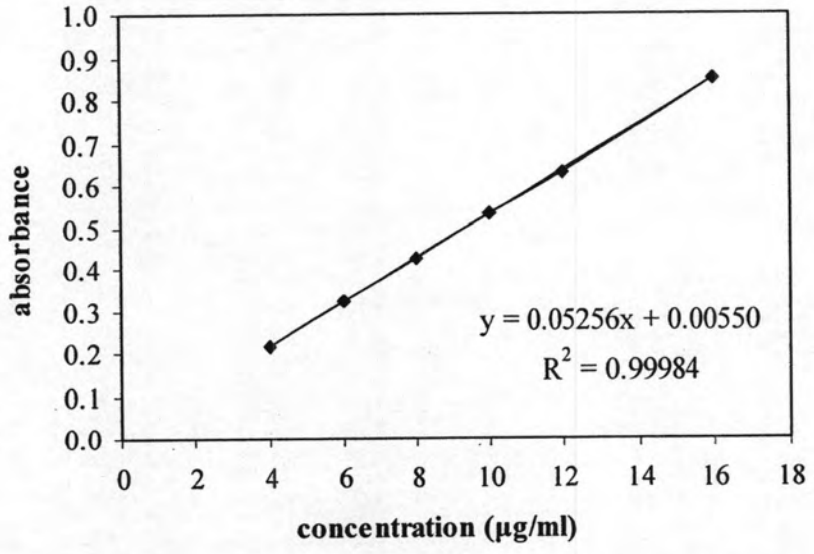

Figure 7(A) Calibration curve of diltiazem hydrochloride in 0.01 M potassium chloride at 237 nm.

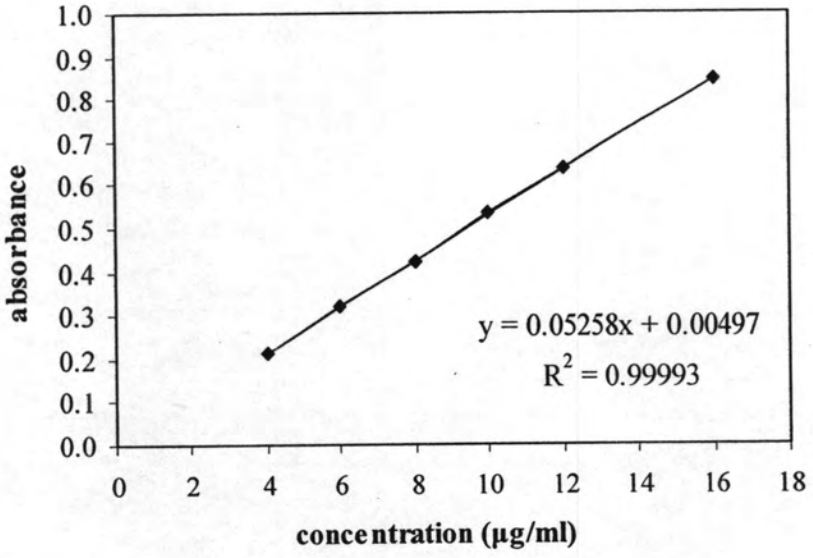

Figure 8(A) Calibration curve of diltiazem hydrochloride in 0.05 M potassium chloride at 237 nm.

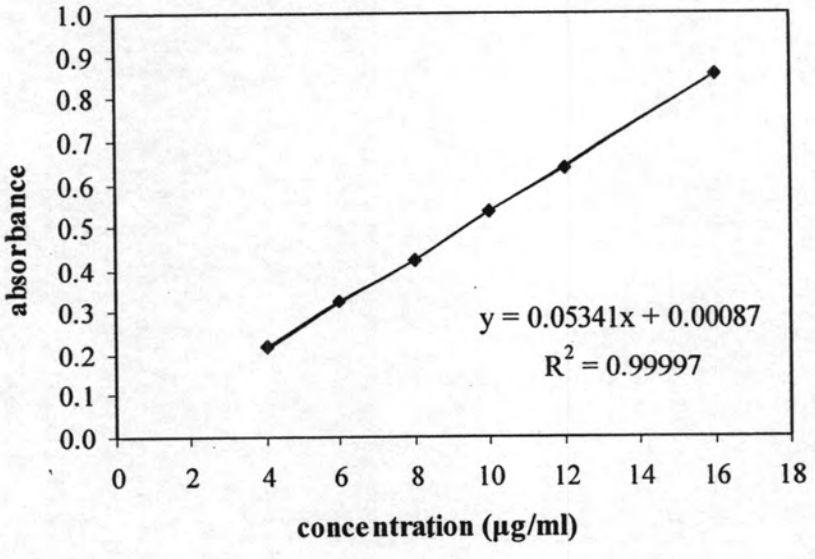

Figure 9(A) Calibration curve of diltiazem hydrochloride in 0.1 M potassium chloride at 237 nm.

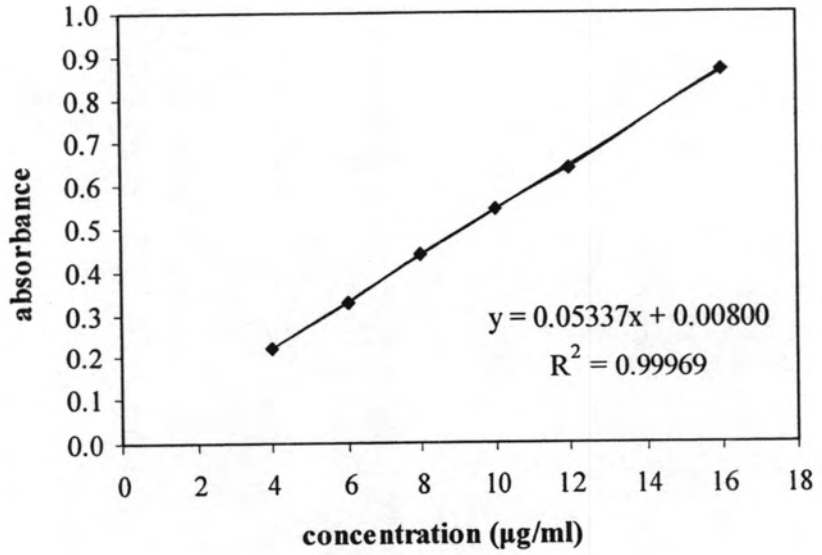

Figure 10(A) Calibration curve of diltiazem hydrochloride in 0.2 M potassium chloride at 237 nm.

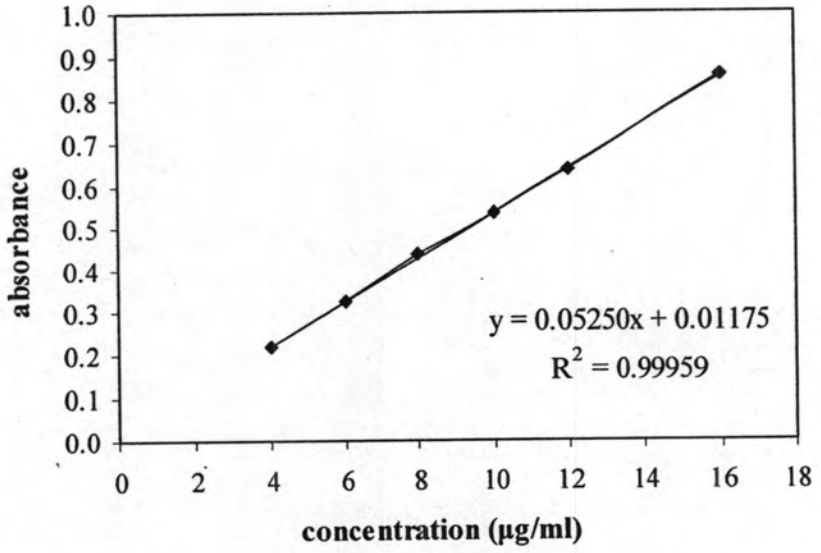

Figure 11(A) Calibration curve of diltiazem hydrochloride in 0.3 M potassium chloride at 237 nm.

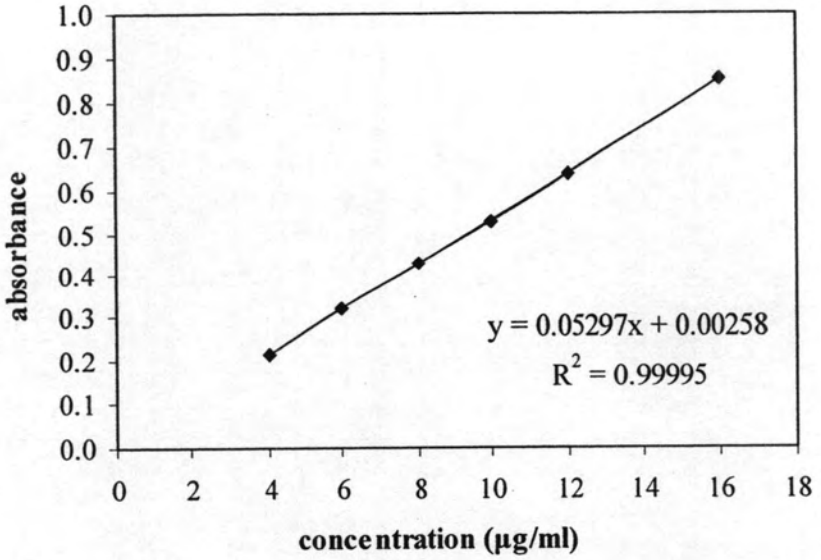

Figure 12(A) Calibration curve of diltiazem hydrochloride in 0.4 M potassium chloride at 237 nm.

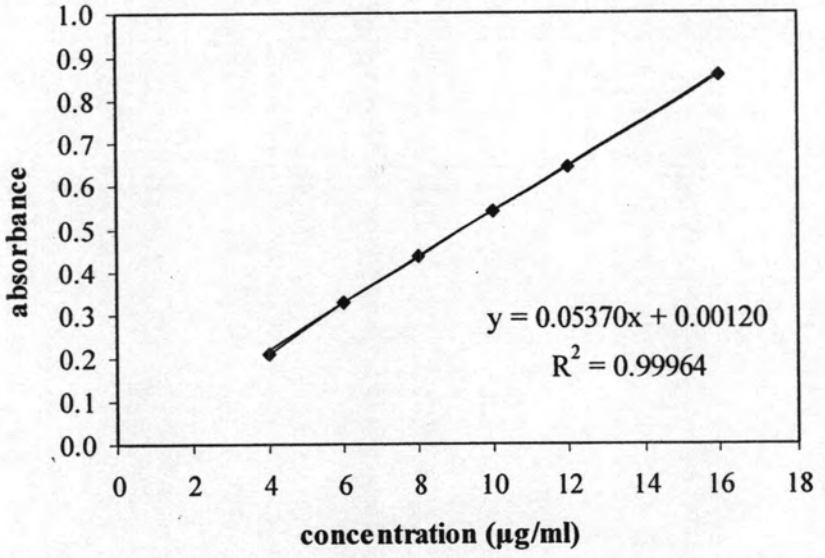

Figure 13(A) Calibration curve of diltiazem hydrochloride in 0.5 M potassium chloride at 237 nm.

Table 4(A) The absorbance of diltiazem hydrochloride in sodium chloride at 237 nm

Concentration (µg/ml)	Absorbance						
	0.01 M	0.05 M	0.1 M	0.2 M	0.3 M	0.4 M	0.5 M
4	0.2145	0.2143	0.2125	0.2169	0.2174	0.2197	0.2209
6	0.3250	0.3216	0.3193	0.3295	0.3239	0.3235	0.3286
8	0.4296	0.4232	0.4341	0.4260	0.4305	0.4243	0.4243
10	0.5371	0.5332	0.5359	0.5326	0.5391	0.5370	0.5351
12	0.6407	0.6435	0.6396	0.6392	0.6407	0.6438	0.6398
16	0.8598	0.8581	0.8560	0.8523	0.8568	0.8574	0.8483

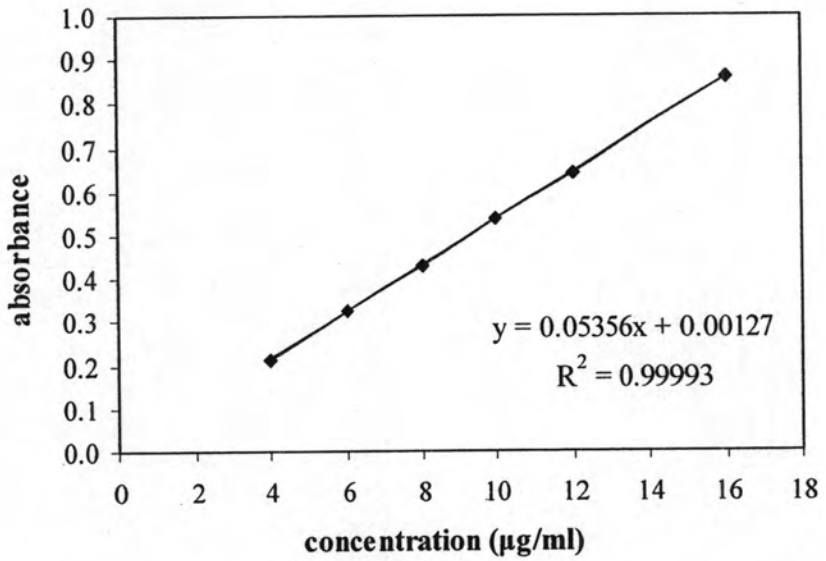

Figure 14(A) Calibration curve of diltiazem hydrochloride in 0.01 M sodium chloride at 237 nm.

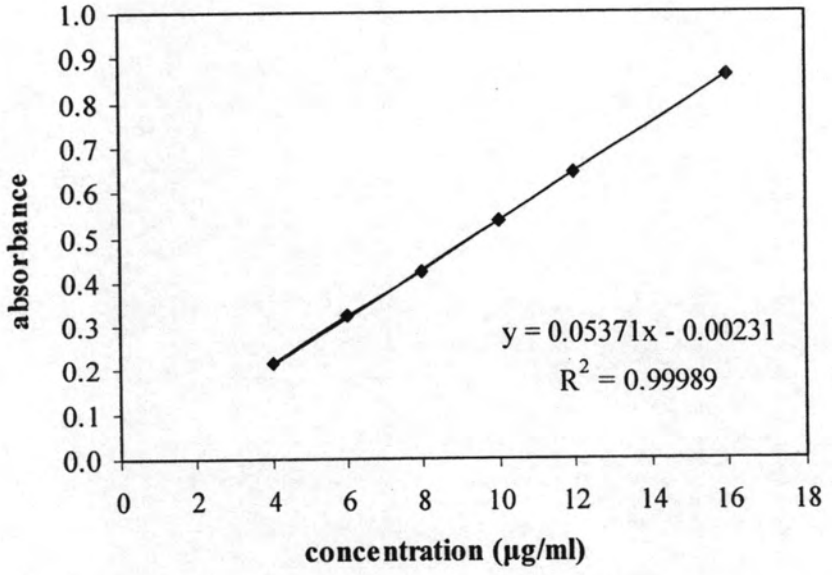

Figure 15(A) Calibration curve of diltiazem hydrochloride in 0.05 M sodium chloride at 237 nm.

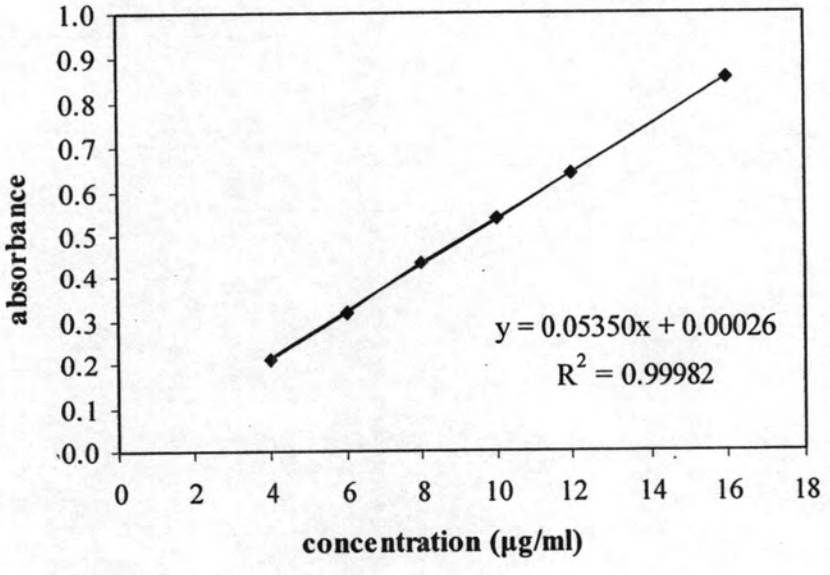

Figure 16(A) Calibration curve of diltiazem hydrochloride in 0.1 M sodium chloride at 237 nm.

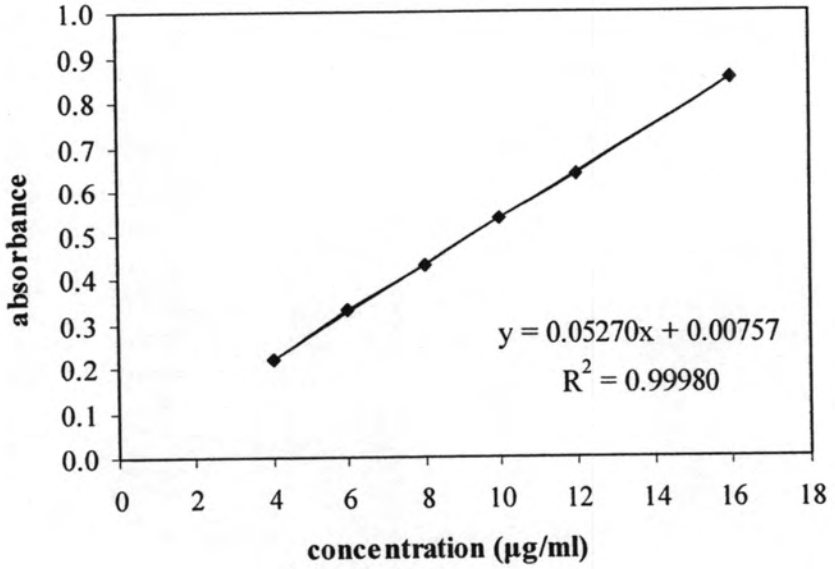

Figure 17(A) Calibration curve of diltiazem hydrochloride in 0.2 M sodium chloride at 237 nm.

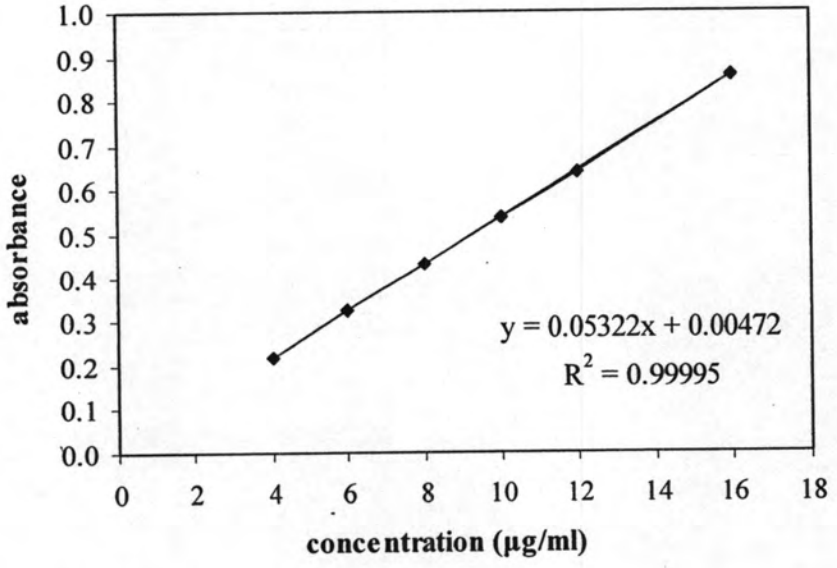

Figure 18(A) Calibration curve of diltiazem hydrochloride in 0.3 M sodium chloride at 237 nm.

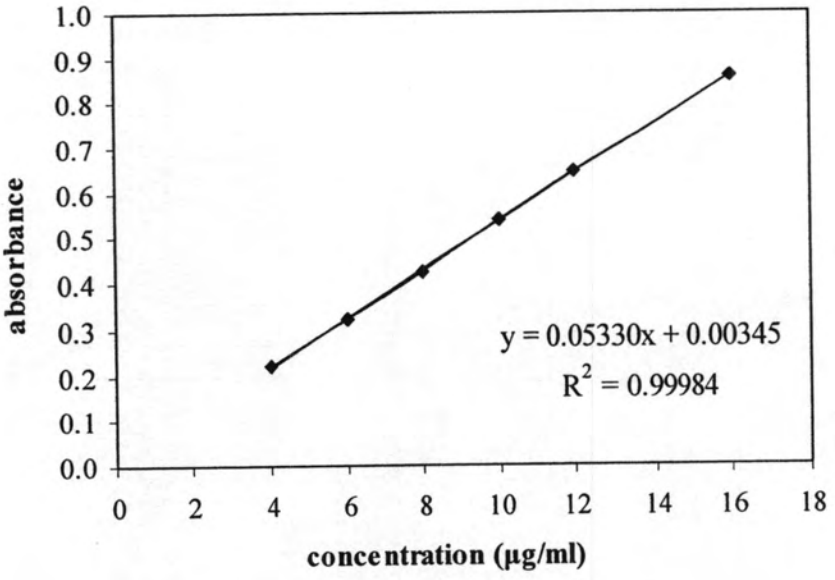

Figure 19(A) Calibration curve of diltiazem hydrochloride in 0.4 M sodium chloride at 237 nm.

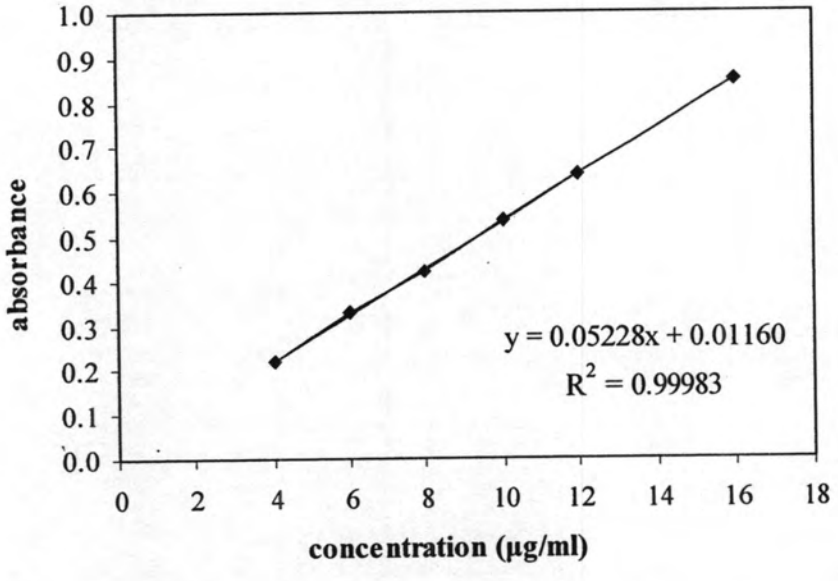

Figure 20(A) Calibration curve of diltiazem hydrochloride in 0.5 M sodium chloride at 237 nm.

Table 5(A) The absorbance of diltiazem hydrochloride in 0.04 M calcium chloride (ionic strength = 0.1) at 237 nm

Concentration (µg/ml)	Absorbance
4	0.2109
6	0.3206
8	0.4293
10	0.5381
12	0.6428
16	0.8497

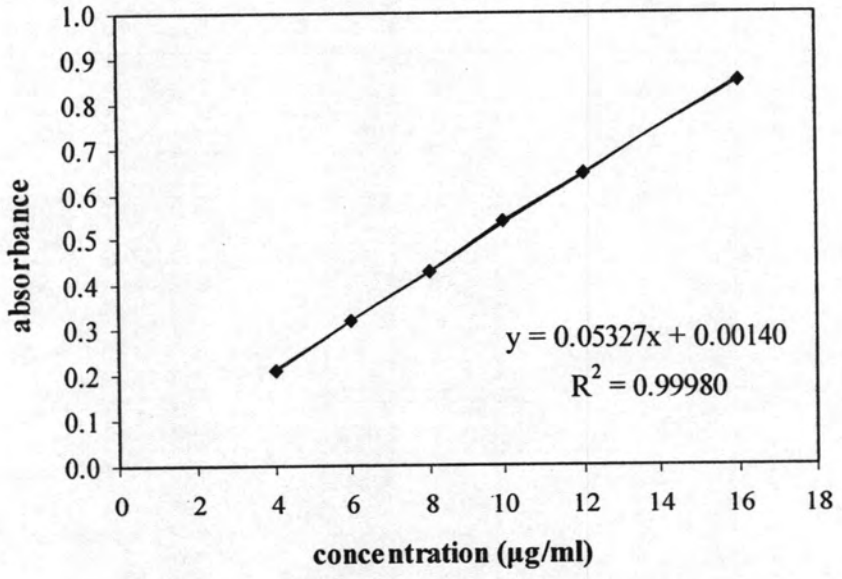

Figure 21(A) Calibration curve of diltiazem hydrochloride in 0.04 M calcium chloride (ionic strength = 0.1) at 237 nm.

APPENDIX B

Validation of UV-visible spectrophotometry

The parameters evaluated to ensure the acceptability of the performance of the selected analytical method were accuracy, precision, specificity and linearity (USPXXI).

1. Accuracy

The accuracy was performed by analyzing placebos spiked with known quantities of active ingredients and evaluated as the percentage of recovery. The final concentration of the diltiazem hydrochloride was 4, 6, 8, 10, 12 and 16 µg/ml. Each sample was analyzed from triplicate. The percentage of the analytical recovery of each sample was calculated.

Table 1(B) Accuracy data of percentage of analytical recovery of diltiazem hydrochloride

Actual concentration (µg/ml)	Absorbance			Analytical concentration (µg/ml)		
	n1	n2	n3	n1	n2	n3
4.00	0.2139	0.2177	0.2136	3.9880	4.0593	3.9823
6.00	0.3257	0.3264	0.3269	6.0875	6.1007	6.1100
8.00	0.4307	0.4272	0.4303	8.0593	7.9936	8.0518
10.00	0.5420	0.5413	0.5472	10.1495	10.1363	10.2471
12.00	0.6562	0.6527	0.6549	12.2941	12.2284	12.2697
16.00	0.8590	0.8591	0.8502	16.1025	16.1044	15.9373

Actual concentration (µg/ml)	%Recovery					
	n1	n2	n3	Mean	SD	%CV
4.00	99.70	101.48	99.56	100.25	1.073	1.070
6.00	101.46	101.68	101.83	101.66	0.189	0.186
8.00	100.74	99.92	100.65	100.44	0.450	0.448
10.00	101.49	101.36	102.47	101.78	0.605	0.595
12.00	102.45	101.90	102.25	102.20	0.277	0.271
16.00	100.64	100.65	99.61	100.30	0.600	0.598

2. Precision

2.1 Within run precision

The within run precision was determined by analyzing the calibration curve in the same day. The percentage of coefficient of variation (%CV) of concentration of diltiazem hydrochloride from six replicated calibration curves was determined.

2.2 Between run precision

The between run precision was determined by comparing each concentration of calibration curves prepared and analyzed on different day for six days. The percentage of coefficient of variation (%CV) of concentration of diltiazem hydrochloride from three sets of the calibration curves was determined.

Table 2(B) Within run precision data of diltiazem hydrochloride

Actual concentration (µg/ml)	Absorbance					
	n1	n2	n3	n4	n5	n6
4.00	0.2137	0.2136	0.2136	0.2138	0.2136	0.2137
6.00	0.3218	0.3222	0.3219	0.3217	0.3219	0.3219
8.00	0.4303	0.4301	0.4301	0.4302	0.4301	0.4302
10.00	0.5390	0.5392	0.5391	0.5391	0.5392	0.5391
12.00	0.6509	0.6510	0.6508	0.6509	0.6509	0.6511
16.00	0.8586	0.8589	0.8586	0.8587	0.8587	0.8586

Actual concentration (µg/ml)	Analytical concentration (µg/ml)								
	n1	n2	n3	n4	n5	n6	Mean	SD	%CV
4.00	3.984	3.982	3.982	3.986	3.982	3.984	3.984	0.002	0.038
6.00	6.014	6.022	6.016	6.012	6.016	6.016	6.016	0.003	0.052
8.00	8.052	8.048	8.048	8.050	8.048	8.050	8.049	0.002	0.019
10.00	10.093	10.097	10.095	10.095	10.097	10.095	10.095	0.001	0.014
12.00	12.195	12.196	12.193	12.195	12.195	12.198	12.195	0.002	0.016
16.00	16.095	16.101	16.095	16.097	16.097	16.095	16.097	0.002	0.014

Table 3(B) Between run precision data of diltiazem hydrochloride

Actual concentration (µg/ml)	Absorbance								
	Day 1			Day 2			Day 3		
	n1	n2	n3	n1	n2	n3	n1	n2	n3
4.00	0.2137	0.2136	0.2136	0.2138	0.2136	0.2137	0.2170	0.2162	0.2172
6.00	0.3218	0.3222	0.3219	0.3217	0.3219	0.3219	0.3230	0.3224	0.3220
8.00	0.4303	0.4301	0.4301	0.4302	0.4301	0.4302	0.4253	0.4255	0.4248
10.00	0.5390	0.5392	0.5391	0.5391	0.5392	0.5391	0.5338	0.5339	0.5333
12.00	0.6509	0.6510	0.6508	0.6509	0.6509	0.6511	0.6464	0.6454	0.6455
16.00	0.8586	0.8589	0.8586	0.8587	0.8587	0.8586	0.8564	0.8559	0.8552

Actual concentration (µg/ml)	Absorbance								
	Day 4			Day 5			Day 6		
	n1	n2	n3	n1	n2	n3	n1	n2	n3
4.00	0.2178	0.2175	0.2170	0.2165	0.2172	0.2165	0.2130	0.2133	0.2137
6.00	0.3252	0.3248	0.3249	0.3239	0.3230	0.3233	0.3205	0.3209	0.3204
8.00	0.4293	0.4286	0.4290	0.4246	0.4246	0.4245	0.4226	0.4230	0.4225
10.00	0.5319	0.5319	0.5329	0.5234	0.5228	0.5224	0.5220	0.5227	0.5221
12.00	0.6510	0.6514	0.6519	0.6455	0.6452	0.6458	0.6518	0.6519	0.6518
16.00	0.8505	0.8501	0.8493	0.8548	0.8537	0.8554	0.8517	0.8521	0.8518

Table 3(B) Between run precision data of diltiazem hydrochloride (continue)

Actual concentration (µg/ml)	Analytical concentration (µg/ml)								
	Day 1			Day 2			Day 3		
	n1	n2	n3	n1	n2	n3	n1	n2	n3
4.00	3.984	3.982	3.982	3.986	3.982	3.984	4.046	4.031	4.050
6.00	6.014	6.022	6.016	6.012	6.016	6.016	6.037	6.026	6.018
8.00	8.052	8.048	8.048	8.050	8.048	8.050	7.958	7.962	7.949
10.00	10.093	10.097	10.095	10.095	10.097	10.095	9.995	9.997	9.986
12.00	12.195	12.196	12.193	12.195	12.195	12.198	12.110	12.091	12.093
16.00	16.095	16.101	16.095	16.097	16.097	16.095	16.054	16.044	16.031

Actual concentration (µg/ml)	Analytical concentration (µg/ml)								
	Day 4			Day 5			Day 6		
	n1	n2	n3	n1	n2	n3	n1	n2	n3
4.00	4.061	4.056	4.046	4.037	4.050	4.037	3.971	3.977	3.984
6.00	6.078	6.071	6.072	6.054	6.037	6.042	5.990	5.997	5.988
8.00	8.033	8.020	8.027	7.945	7.945	7.943	7.907	7.915	7.905
10.00	9.960	9.960	9.979	9.800	9.789	9.781	9.774	9.787	9.776
12.00	12.196	12.204	12.213	12.093	12.088	12.099	12.211	12.213	12.211
16.00	15.943	15.935	15.920	16.024	16.003	16.035	15.965	15.973	15.967

Actual concentration (µg/ml)	Mean	SD	%CV
4.00	4.014	0.034	0.847
6.00	6.028	0.027	0.447
8.00	7.989	0.057	0.711
10.00	9.953	0.132	1.330
12.00	12.166	0.052	0.428
16.00	16.026	0.063	0.394

3. Specificity

The specificity of the method was determined by comparing the chromatograms from UV-visible spectrophotometer between non-active ingredients and diltiazem hydrochloride. Specificity is established by showing that the active ingredient should have no interference from non-active ingredients. This validation was made by comparing the peak scan between the dissolution medium taken from the placebo system without drug with the drug containing system of the similar composition.

The absorbance of the dissolution medium taken from non-drug containing (placebo) at 237 nm was shown in Table 4(B)-5(B).

Table 4(B) The absorbance of hard gelatin capsule shell in 0.1 M KCl

Time (hr)	Absorbance			Mean	SD	%CV
1	0.0889	0.0884	0.0880	0.0884	0.0005	0.510%
4	0.0953	0.0948	0.0951	0.0951	0.0003	0.265%
8	0.0910	0.0914	0.0911	0.0912	0.0002	0.228%
12	0.0910	0.0911	0.0913	0.0911	0.0002	0.168%

Table 5(B) The absorbance of placebo tablet (tablet formulation F11) in 0.1 M KCl

Time (hr)	Absorbance			Mean	SD	%CV
1	0.0012	0.0015	0.0013	0.0013	0.0002	11.456%
4	0.0048	0.0049	0.0046	0.0048	0.0002	3.158%
8	0.0069	0.0074	0.0076	0.0073	0.0004	4.939%
12	0.0080	0.0080	0.0084	0.0081	0.0002	2.839%

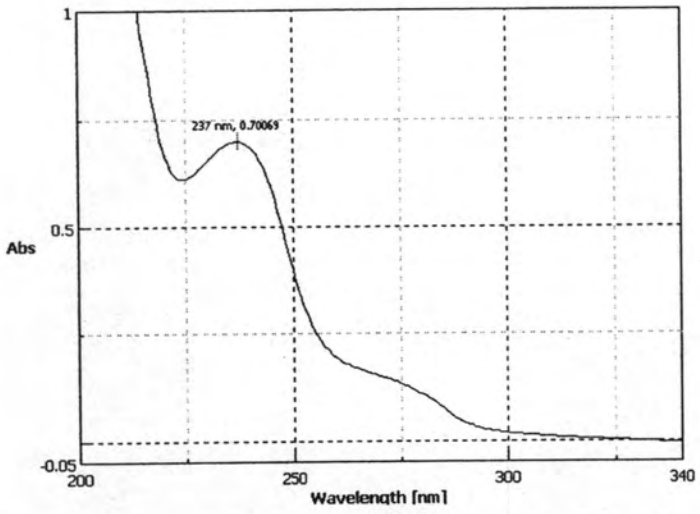

Figure 1(B) The chromatogram of diltiazem hydrochloride in water.

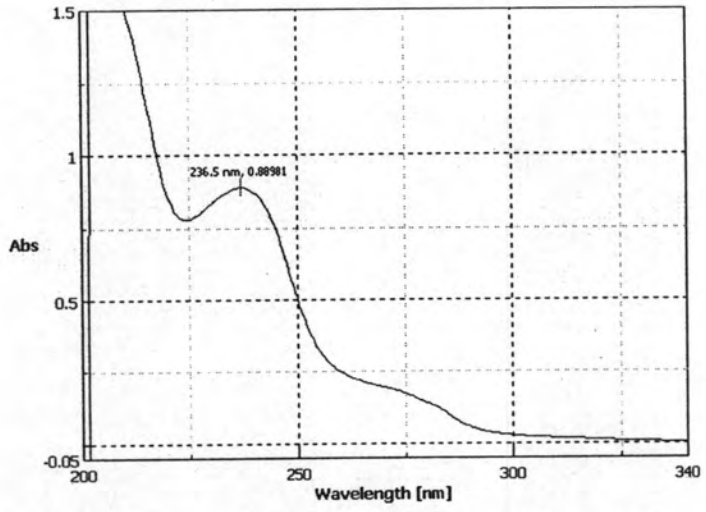

Figure 2(B) The chromatogram of diltiazem hydrochloride in 0.1 M HCl.

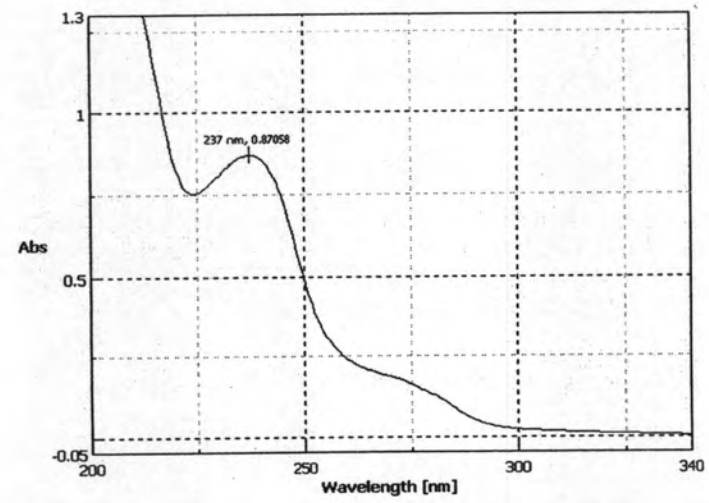

Figure 3(B) The chromatogram of diltiazem hydrochloride in phosphate buffer pH 6.8.

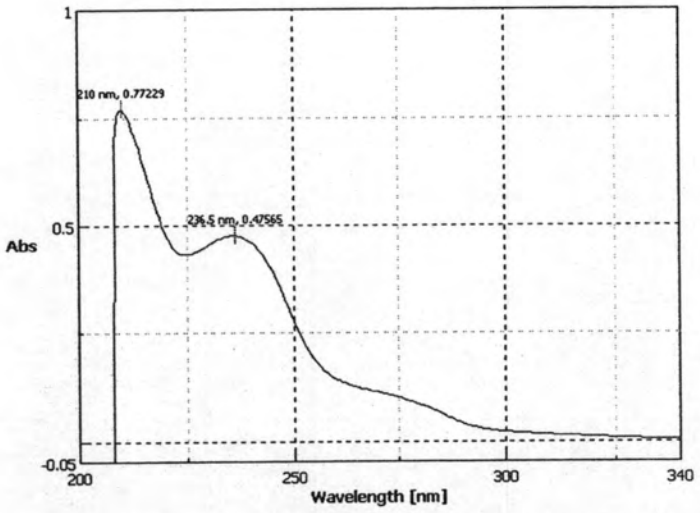

Figure 4(B) The chromatogram of diltiazem hydrochloride in 0.1 M KCl.

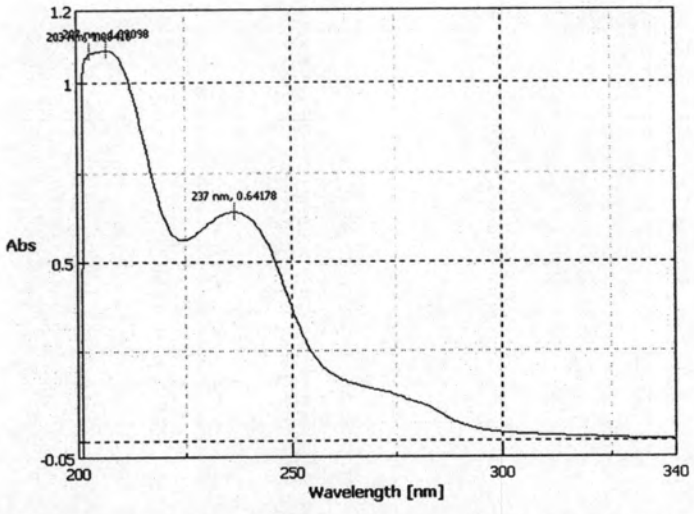

Figure 5(B) The chromatogram of diltiazem hydrochloride in 0.1 M NaCl.

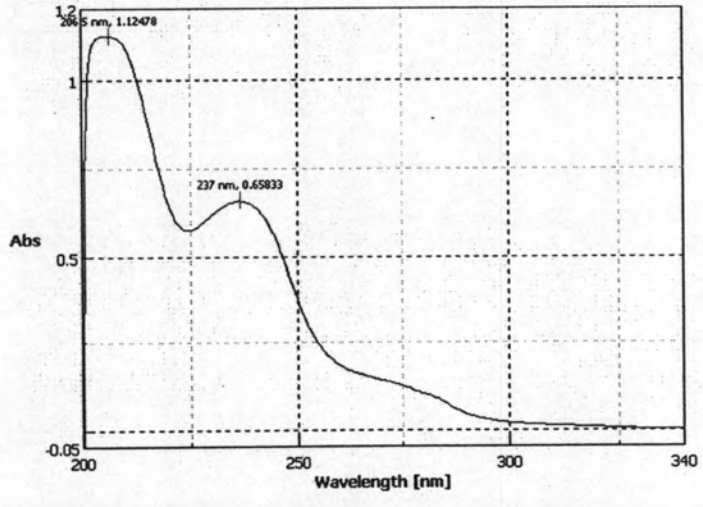

Figure 6(B) The chromatogram of diltiazem hydrochloride in 0.04 M $CaCl_2$.

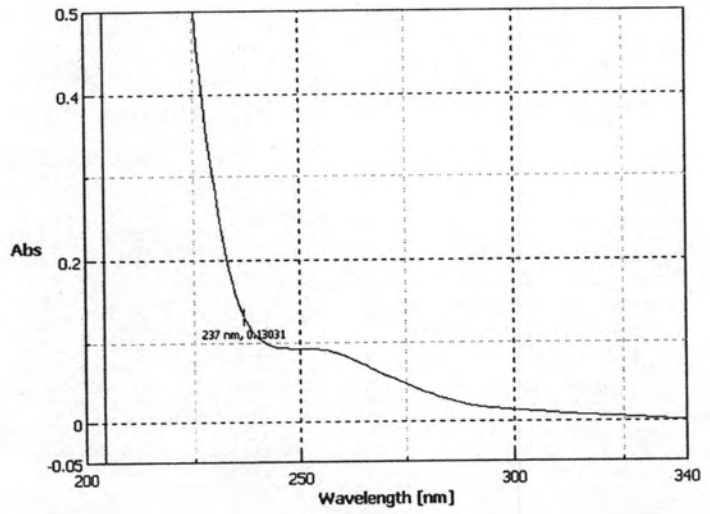

Figure 7(B) The chromatogram of hard gelatin capsule shell in 0.1 M KCl.

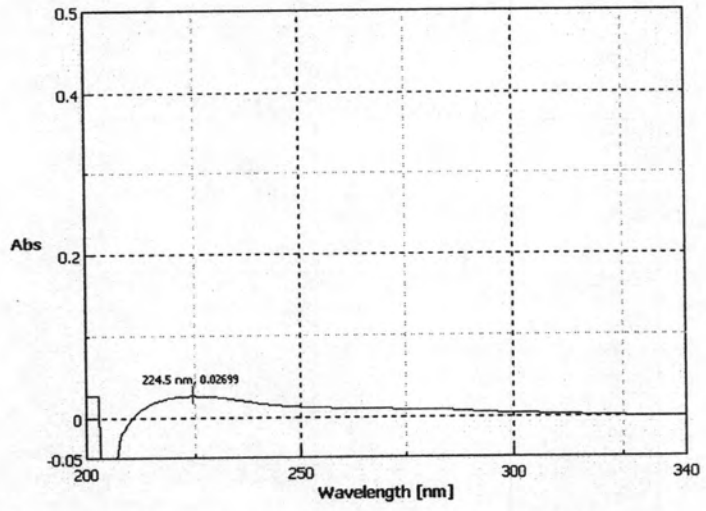

Figure 8(B) The chromatogram of placebo tablet in 0.1 M KCl.

4. linearity

Triplicate of diltiazem hydrochloride solutions containing drug in various concentrations ranging from 4-16 µg/ml were prepared and analyzed. The linear equation of the curve obtained by plotting the absorbance versus the concentrations was calculated.

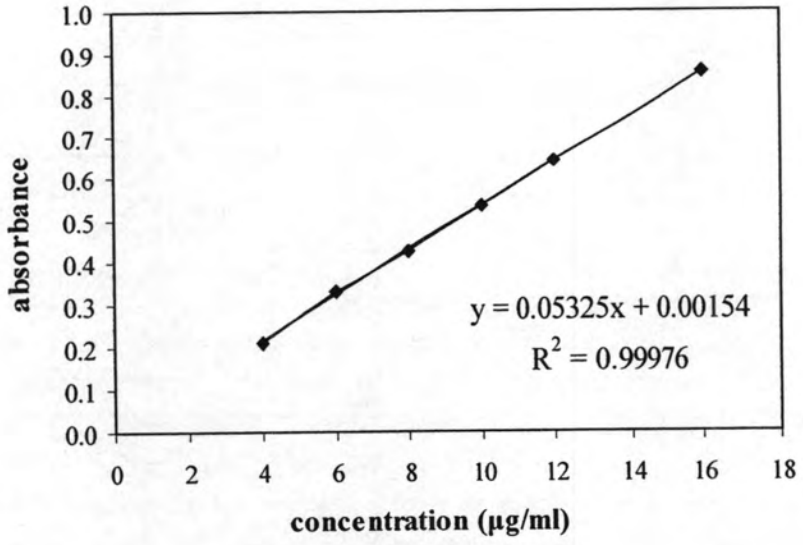

Figure 9(B) Calibration curve of diltiazem hydrochloride in water analyzed by UV-visible spectrophotometer at 237 nm.

Table 6(B) The analytical method validation parameter of UV-visible spectrophotometry for diltiazem hydrochloride

Parameter	Limited of acceptability (USP 27, 2004)	Result value
1. Accuracy - %Recovery - SD	95.0-105.0%	100.25-102.20% 0.189-1.073
2. Precision (%CV) - Within run precision - Between run precision	not more than 2	0.014-0.052 0.394-1.330
3. Specificity	No other peak interfere drug peak	Some placebo peak interfere drug peak
4. Linearity - Correlation coefficient (R^2)	more than 0.999	0.99976

APPENDIX C

Solubility of drug

The solubility of diltiazem hydrochloride was determined by continuous shaking of excess amount of drugs for 168 hours in various medium at 37°C.

Table 1(C) Solubility of diltiazem hydrochloride in 0.1 M KCl at 37°C

Time (hr)	pH (initial)	pH (filtrate)	Solubility (mg/ml)			Mean	SD	%CV
			n1	n2	n3			
24	5.40	-	417.647	414.932	423.170	418.583	4.198	1.003
96	-	-	559.474	558.725	560.504	559.567	0.893	0.160
168	-	2.36	579.601	577.542	578.291	578.478	1.042	0.180

Table 2(C) Solubility of diltiazem hydrochloride in 0.1 M NaCl at 37°C

Time (hr)	pH (initial)	pH (filtrate)	Solubility (mg/ml)			Mean	SD	%CV
			n1	n2	n3			
24	5.76	-	382.093	380.692	380.131	380.972	1.011	0.265
96	-	-	540.879	540.318	541.626	540.941	0.656	0.121
168	-	2.48	564.991	564.710	563.308	564.336	0.901	0.160

Table 3(C) Solubility of diltiazem hydrochloride in 0.04 M $CaCl_2$ at 37°C

Time (hr)	pH (initial)	pH (filtrate)	Solubility (mg/ml)			Mean	SD	%CV
			n1	n2	n3			
24	5.69	-	410.175	406.045	409.518	408.579	2.219	0.543
96	-	-	559.227	558.288	557.255	558.257	0.986	0.177
168	-	2.31	606.908	606.814	605.313	606.345	0.895	0.148

APPENDIX D

Study of drug stability

The preliminary study of the stability of diltiazem hydrochloride solution at different temperatures was determined in the conditions same as during drug loading process. The drug solutions in deionized water were shaken in temperature-controlled shaking bath at 30, 40, and 50°C. After 24 hr, the amount of drug in solution was analyzed by UV-visible spectrophotometer.

Table 1(D) The stability data of 4 % w/v diltiazem hydrochloride in water (n=3)

Temperature (°C)	%Remaining drugs compared with Initial amount	
	Mean	SD
30	100.116	0.158
40	98.438	0.332
50	102.404	0.112

APPENDIX E

Data of in vitro dissolution study

Table 1(E) The diltiazem hydrochloride release from resinates in 0.01 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	0.50	1.52	1.79	1.27	0.68	53.30
0.25	3.95	4.96	4.69	4.53	0.52	11.52
0.50	7.38	9.01	7.86	8.08	0.84	10.37
1	12.51	14.99	12.79	13.43	1.36	10.10
2	20.99	23.66	21.27	21.98	1.47	6.67
4	32.36	34.88	32.86	33.36	1.34	4.00
6	40.26	42.51	40.71	41.16	1.19	2.89
8	44.93	47.11	46.03	46.02	1.09	2.37
10	49.39	51.21	49.63	50.08	0.99	1.98
12	52.43	54.61	53.34	53.46	1.10	2.05

Table 2(E) The diltiazem hydrochloride release from resinates in 0.05 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	3.44	2.86	2.43	2.91	0.50	17.35
0.25	10.15	7.85	8.31	8.77	1.22	13.92
0.50	19.03	14.28	14.51	15.94	2.68	16.79
1	27.27	24.64	22.77	24.89	2.26	9.07
2	40.85	38.69	36.96	38.83	1.95	5.02
4	55.45	53.76	52.91	54.04	1.29	2.39
6	63.95	62.75	62.36	63.02	0.83	1.31
8	69.96	68.28	67.83	68.69	1.13	1.64
10	73.34	72.62	71.96	72.64	0.69	0.95
12	76.21	75.13	74.93	75.42	0.69	0.91

Table 3(E) The diltiazem hydrochloride release from resinates in 0.1 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	5.73	5.06	4.86	5.22	0.46	8.77
0.25	13.29	11.15	10.63	11.69	1.41	12.07
0.50	20.96	17.93	19.35	19.41	1.52	7.83
1	33.17	29.25	32.03	31.48	2.02	6.41
2	48.30	45.40	46.02	46.57	1.53	3.28
4	62.97	61.43	61.68	62.03	0.83	1.33
6	70.76	69.53	70.78	70.36	0.71	1.01
8	77.19	78.04	77.61	77.61	0.42	0.54
10	80.77	80.94	80.22	80.64	0.37	0.46
12	83.88	84.47	84.24	84.20	0.30	0.36

Table 4(E) The diltiazem hydrochloride release from resinates in 0.2 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	6.59	7.28	6.18	6.69	0.56	8.34
0.25	18.53	17.38	13.64	16.52	2.56	15.47
0.50	30.13	28.45	21.63	26.74	4.50	16.84
1	45.74	44.65	34.51	41.63	6.19	14.87
2	61.04	60.60	50.98	57.54	5.69	9.89
4	74.33	74.34	70.59	73.09	2.16	2.96
6	81.75	81.26	77.97	80.33	2.05	2.56
8	85.27	86.18	83.26	84.90	1.50	1.76
10	88.45	88.54	87.59	88.19	0.52	0.59
12	88.89	88.94	89.26	89.03	0.20	0.22

Table 5(E) The diltiazem hydrochloride release from resinates in 0.3 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	8.21	6.77	6.42	7.13	0.95	13.28
0.25	20.18	20.59	20.06	20.28	0.28	1.37
0.50	32.94	33.47	32.30	32.90	0.59	1.78
1	49.22	49.73	50.36	49.77	0.57	1.15
2	65.97	66.63	66.07	66.23	0.35	0.54
4	78.95	79.86	79.04	79.28	0.50	0.63
6	84.46	84.17	83.84	84.16	0.31	0.37
8	87.73	87.11	86.70	87.18	0.52	0.59
10	89.71	89.74	90.44	89.96	0.41	0.46
12	89.84	89.48	89.89	89.74	0.22	0.25

Table 6(E) The diltiazem hydrochloride release from resinates in 0.4 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	5.84	8.93	8.66	7.81	1.71	21.89
0.25	20.44	22.06	21.03	21.18	0.82	3.87
0.50	29.72	32.51	30.29	30.84	1.47	4.78
1	45.29	49.90	47.88	47.69	2.31	4.85
2	65.32	67.97	66.49	66.59	1.32	1.99
4	80.78	81.40	81.02	81.07	0.31	0.38
6	87.74	88.13	88.65	88.17	0.46	0.52
8	91.68	90.46	91.82	91.32	0.75	0.82
10	93.12	93.08	93.27	93.15	0.10	0.11
12	93.63	93.63	94.55	93.94	0.54	0.57

Table 7(E) The diltiazem hydrochloride release from resinates in 0.5 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	8.98	10.15	10.09	9.74	0.66	6.76
0.25	19.36	23.26	23.38	22.00	2.28	10.38
0.50	30.18	38.72	36.41	35.11	4.42	12.58
1	44.90	54.93	53.14	50.99	5.35	10.49
2	62.18	68.66	68.39	66.41	3.67	5.52
4	78.50	82.14	80.37	80.34	1.82	2.27
6	86.04	87.82	86.93	86.93	0.89	1.02
8	92.51	91.87	90.87	91.75	0.83	0.91
10	93.69	95.19	93.75	94.21	0.85	0.90
12	93.80	95.81	94.53	94.71	1.01	1.07

Table 8(E) The diltiazem hydrochloride release from resinates in 0.01 M NaCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	1.82	1.72%	1.70	1.75	0.07	3.94
0.25	4.48	3.92	3.77	4.06	0.37	9.18
0.50	8.38	7.50	7.21	7.70	0.61	7.91
1	16.43	16.10	15.64	16.06	0.40	2.46
2	21.64	20.59	20.52	20.92	0.63	3.01
4	31.31	30.46	30.35	30.71	0.53	1.72
6	40.78	37.11	36.85	38.25	2.20	5.74
8	42.94	42.10	41.71	42.25	0.63	1.48
10	47.38	45.89	46.56	46.61	0.75	1.60
12	48.61	47.89	48.05	48.18	0.38	0.79

Table 9(E) The diltiazem hydrochloride release from resinates in 0.05 M NaCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	2.74	2.99	3.22	2.99	0.24	8.11
0.25	5.97	7.33	6.97	6.76	0.71	10.46
0.50	10.80	12.81	12.18	11.93	1.03	8.61
1	18.83	21.59	20.58	20.34	1.40	6.86
2	30.52	34.34	32.51	32.45	1.91	5.89
4	44.70	47.76	45.98	46.15	1.54	3.33
6	53.80	56.11	54.65	54.85	1.17	2.13
8	58.75	63.11	62.03	61.29	2.27	3.70
10	64.63	66.43	65.65	65.57	0.90	1.38
12	67.80	69.45	68.18	68.47	0.86	1.26

Table 10(E) The diltiazem hydrochloride release from resinates in 0.1 M NaCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	5.59	5.14	4.09	4.94	0.77	15.59
0.25	11.69	11.79	9.60	11.03	1.24	11.20
0.50	19.90	19.70	15.77	18.45	2.33	12.63
1	29.62	30.25	24.95	28.27	2.89	10.23
2	43.41	43.77	37.59	41.59	3.47	8.34
4	58.47	58.55	55.47	57.49	1.76	3.06
6	67.05	67.00	64.95	66.33	1.20	1.81
8	71.79	72.62	71.20	71.87	0.71	0.99
10	76.09	77.19	75.50	76.26	0.86	1.12
12	79.67	80.57	79.22	79.82	0.69	0.86

Table 11(E) The diltiazem hydrochloride release from resinates in 0.2 M NaCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	4.65	3.63	6.98	5.09	1.72	33.80
0.25	13.06	12.25	15.10	13.47	1.47	10.89
0.50	21.49	19.58	22.46	21.17	1.46	6.91
1	34.63	31.81	33.75	33.40	1.44	4.32
2	51.31	48.29	49.71	49.77	1.51	3.04
4	63.50	63.80	61.54	62.95	1.23	1.95
6	74.54	73.49	74.92	74.32	0.74	1.00
8	79.35	78.55	79.07	78.99	0.40	0.51
10	81.75	81.37	81.89	81.67	0.27	0.33
12	85.35	84.03	84.09	84.49	0.74	0.88

Table 12(E) The diltiazem hydrochloride release from resinates in 0.3 M NaCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	6.00	7.66	3.89	5.85	1.89	32.26
0.25	16.23	17.23	11.14	14.87	3.26	21.95
0.50	26.62	26.73	19.66	24.34	4.05	16.64
1	42.04	42.30	32.55	38.96	5.56	14.26
2	57.12	58.73	48.25	54.70	5.64	10.32
4	70.39	71.46	66.13	69.33	2.82	4.07
6	77.07	78.26	75.45	76.93	1.41	1.83
8	82.73	83.39	82.08	82.73	0.66	0.79
10	84.89	85.71	82.73	84.44	1.54	1.82
12	87.05	87.23	85.39	86.56	1.01	1.17

Table 13(E) The diltiazem hydrochloride release from resinates in 0.4 M NaCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	5.44	5.54	7.22	6.07	1.00	16.49
0.25	15.64	14.56	17.30	15.83	1.38	8.71
0.50	26.75	23.93	28.48	26.39	2.29	8.69
1	42.02	38.94	42.59	41.18	1.96	4.76
2	59.32	55.50	59.39	58.07	2.23	3.84
4	73.99	72.77	73.90	73.55	0.68	0.93
6	79.77	81.08	80.15	80.33	0.68	0.84
8	83.93	83.68	84.16	83.93	0.24	0.28
10	86.53	86.53	87.33	86.80	0.46	0.53
12	87.82	88.21	88.23	88.09	0.23	0.26

Table 14(E) The diltiazem hydrochloride release from resinates in 0.5 M NaCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	6.09	8.38	8.62	7.70	1.40	18.15
0.25	19.54	18.35	20.04	19.31	0.87	4.49
0.50	33.04	27.88	32.39	31.11	2.81	9.04
1	50.19	42.47	49.30	47.32	4.23	8.93
2	65.00	60.16	64.31	63.15	2.62	4.14
4	78.98	77.10	78.97	78.35	1.09	1.39
6	84.14	82.98	84.11	83.74	0.66	0.79
8	86.86	86.15	86.54	86.52	0.36	0.41
10	89.58	88.68	89.47	89.25	0.49	0.55
12	93.40	92.37	92.86	92.88	0.51	0.55

Table 15(E) The diltiazem hydrochloride release from resinates in 0.04 M $CaCl_2$ (ionic strength = 0.1)

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	4.09	3.77	4.17	4.01	0.21	5.22
0.25	10.23	9.93	9.97	10.04	0.16	1.64
0.50	17.31	18.19	16.51	17.34	0.84	4.86
1	25.27	26.87	26.38	26.17	0.82	3.13
2	39.53	37.02	37.47	38.01	1.34	3.53
4	52.19	52.00	51.23	51.81	0.51	0.98
6	60.46	61.20	59.11	60.26	1.06	1.76
8	69.00	67.31	64.45	66.92	2.30	3.44
10	72.37	69.16	70.58	70.70	1.61	2.28
12	76.70	75.33	74.34	75.46	1.19	1.58

Table 16(E) The diltiazem hydrochloride release from resinates in 0.1 M HCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	4.47	4.41	4.89	4.59	0.26	5.67
0.25	9.92	9.32	8.29	9.17	0.82	8.98
0.50	16.97	15.99	16.72	16.56	0.51	3.05
1	22.59	22.42	23.03	22.68	0.31	1.39
2	36.25	36.14	36.57	36.32	0.22	0.61
4	51.43	41.38	53.19	48.67	6.37	13.09
6	57.28	58.97	58.87	58.37	0.95	1.62
8	65.19	64.11	65.90	65.07	0.90	1.39
10	68.29	67.91	68.80	68.33	0.45	0.65
12	71.74	71.00	71.82	71.52	0.45	0.64

Table 17(E) The diltiazem hydrochloride release from resinates in phosphate buffer pH 6.8

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	4.15	2.43	3.04	3.21	0.87	27.20
0.25	9.64	8.35	9.63	9.21	0.74	8.08
0.50	15.87	15.78	16.16	15.94	0.20	1.24
1	26.20	25.30	26.29	25.93	0.55	2.10
2	38.59	37.79	39.34	38.58	0.77	2.01
4	56.56	55.56	57.17	56.43	0.81	1.44
6	64.03	63.48	65.10	64.20	0.82	1.28
8	71.65	69.44	70.47	70.52	1.10	1.56
10	73.82	75.35	74.56	74.58	0.77	1.03
12	77.65	76.10	77.62	77.12	0.89	1.15

Table 18(E) The diltiazem hydrochloride release from resinates in phosphate buffer pH 6.8 adjusted ionic strength = 0.1

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	4.45	5.46	3.17	4.36	1.15	26.34
0.25	8.72	12.63	8.54	9.96	2.31	23.20
0.50	14.06	20.79	14.59	16.48	3.74	22.69
1	24.11	33.13	24.75	27.33	5.03	18.42
2	38.18	46.82	39.48	41.49	4.66	11.22
4	56.88	61.99	57.85	58.91	2.72	4.61
6	66.45	69.48	67.35	67.76	1.55	2.29
8	72.55	75.66	72.43	73.54	1.83	2.49
10	76.60	79.38	78.35	78.11	1.40	1.80
12	78.22	80.20	79.09	79.17	0.99	1.26

Table 19(E) The diltiazem hydrochloride release from resinates in phosphate buffer pH 7.2

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	4.66	3.57	3.85	4.03	0.57	14.12
0.25	9.04	9.94	10.02	9.67	0.54	5.62
0.50	14.26	17.17	17.04	16.16	1.64	10.16
1	23.12	25.96	25.40	24.83	1.51	6.07
2	35.26	39.57	37.05	37.30	2.16	5.80
4	50.31	52.25	52.04	51.53	1.07	2.07
6	59.32	61.46	60.22	60.33	1.08	1.78
8	66.63	67.84	67.53	67.33	0.63	0.93
10	71.90	72.74	72.43	72.36	0.42	0.59
12	75.79	77.29	76.98	76.68	0.79	1.03

Table 20(E) The diltiazem hydrochloride release from resinates in phosphate buffer pH 7.2 adjusted ionic strength = 0.1

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	4.81	4.78	4.44	4.68	0.21	4.41
0.25	10.88	10.28	10.75	10.64	0.32	2.96
0.50	16.57	17.19	16.76	16.84	0.32	1.89
1	24.83	26.58	28.14	26.52	1.65	6.23
2	40.75	42.19	39.96	40.97	1.13	2.77
4	54.63	55.46	53.21	54.44	1.14	2.09
6	65.57	63.82	63.42	64.27	1.14	1.78
8	70.89	71.28	70.23	70.80	0.53	0.75
10	74.55	74.47	74.26	74.43	0.15	0.20
12	77.01	77.12	77.28	77.14	0.13	0.17

Table 21(E) The diltiazem hydrochloride release from coated resinate formulation C1 in 0.1 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	0.23	0.30	0.09	0.21	0.11	52.65
0.25	2.12	2.32	1.86	2.10	0.23	10.82
0.50	6.77	7.01	6.51	6.76	0.25	3.68
1	14.42	14.39	13.61	14.14	0.46	3.24
2	25.28	25.39	24.40	25.02	0.54	2.18
4	38.20	38.41	38.05	38.22	0.18	0.46
6	48.10	48.63	47.43	48.05	0.60	1.25
8	55.19	55.79	54.81	55.26	0.49	0.89
10	61.68	61.83	61.17	61.56	0.34	0.56
12	66.74	67.25	66.15	66.71	0.55	0.82

Table 22(E) The diltiazem hydrochloride release from coated resinate formulation C2 in 0.1 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	0.03	0.12	0.02	0.06	0.05	93.28
0.25	1.49	1.92	1.31	1.57	0.31	19.92
0.50	6.25	6.19	5.99	6.14	0.14	2.24
1	13.22	13.07	13.26	13.18	0.10	0.74
2	24.10	23.80	23.91	23.94	0.15	0.62
4	37.42	36.91	37.24	37.19	0.26	0.70
6	46.73	46.77	46.37	46.62	0.22	0.47
8	53.38	53.60	53.39	53.46	0.13	0.24
10	59.39	59.76	59.67	59.61	0.20	0.33
12	64.12	63.77	63.91	63.93	0.18	0.28

Table 23(E) The diltiazem hydrochloride release from coated resinate formulation C3 in 0.1 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	0.05	0.13	0.16	0.11	0.06	50.57
0.25	1.01	0.95	0.95	0.97	0.03	3.29
0.50	4.19	4.25	4.21	4.21	0.03	0.73
1	10.67	10.67	10.53	10.63	0.08	0.75
2	19.42	19.52	19.84	19.59	0.22	1.12
4	32.83	33.18	32.84	32.95	0.20	0.60
6	42.10	41.87	40.48	41.48	0.88	2.12
8	49.91	49.87	48.23	49.34	0.96	1.94
10	54.08	54.45	54.57	54.37	0.25	0.46
12	59.23	59.32	58.54	59.03	0.42	0.72

Table 24(E) The diltiazem hydrochloride release from coated resinate formulation C4 in 0.1 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	0.07	0.31	0.19	0.19	0.12	62.97
0.25	0.51	0.56	0.41	0.49	0.08	15.99
0.50	2.45	2.64	2.42	2.50	0.12	4.93
1	7.26	7.55	7.41	7.41	0.14	1.95
2	15.19	15.61	15.26	15.35	0.22	1.45
4	26.58	27.02	27.04	26.88	0.26	0.96
6	34.59	35.02	35.03	34.88	0.25	0.72
8	40.30	40.59	40.67	40.52	0.19	0.48
10	45.39	45.67	45.73	45.60	0.18	0.39
12	49.67	49.99	50.07	49.91	0.21	0.43

Table 25(E) The diltiazem hydrochloride release from coated resinate formulation C5 in 0.1 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	0.01	0.02	0.02	0.02	0.01	47.95
0.25	0.30	0.33	0.34	0.32	0.02	6.94
0.50	0.83	0.80	0.91	0.84	0.05	6.45
1	3.64	3.64	3.89	3.73	0.14	3.88
2	9.76	9.80	10.04	9.87	0.15	1.57
4	18.55	18.44	19.02	18.67	0.31	1.65
6	25.24	25.21	25.90	25.45	0.39	1.53
8	29.91	30.78	30.41	30.37	0.44	1.44
10	34.36	34.43	35.30	34.69	0.52	1.50
12	38.51	38.56	39.35	38.80	0.47	1.21

Table 26(E) The diltiazem hydrochloride release from coated resinate formulation C6 in 0.1 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	0.08	0.05	0.11	0.08	0.03	37.59
0.25	0.25	0.29	0.38	0.31	0.06	21.05
0.50	0.30	0.27	0.22	0.26	0.04	14.65
1	2.39	2.16	2.51	2.36	0.18	7.57
2	7.16	7.29	7.32	7.26	0.09	1.20
4	15.34	15.22	15.38	15.31	0.08	0.52
6	20.85	20.78	20.88	20.84	0.05	0.25
8	25.51	25.79	25.82	25.71	0.17	0.67
10	29.67	30.02	30.15	29.95	0.25	0.82
12	33.03	33.16	33.64	33.27	0.32	0.97

Table 27(E) The diltiazem hydrochloride release from uncoated resinates, compressed with compression pressure 3,000 psi in 0.1 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	8.70	8.92	9.16	8.93	0.23	2.57
0.25	17.22	16.30	16.97	16.83	0.48	2.83
0.50	24.67	23.61	23.69	23.99	0.59	2.45
1	34.49	33.86	33.61	33.98	0.45	1.33
2	45.77	47.09	46.07	46.31	0.69	1.50
4	59.18	61.43	62.11	60.91	1.53	2.52
6	74.26	70.92	71.49	72.22	1.79	2.47
8	77.25	76.14	76.24	76.55	0.61	0.80
10	80.25	79.86	79.79	79.97	0.25	0.31
12	84.58	82.91	83.07	83.52	0.92	1.10

Table 28(E) The diltiazem hydrochloride release from coated resinate formulation C3, compressed with compression pressure 3,000 psi in 0.1 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	2.37	2.09	2.23	2.23	0.14	6.16
0.25	6.77	6.52	6.89	6.73	0.19	2.80
0.50	11.56	11.25	11.63	11.48	0.20	1.74
1	19.12	18.62	18.94	18.89	0.25	1.33
2	28.73	28.17	28.64	28.51	0.30	1.04
4	41.16	40.45	41.08	40.90	0.39	0.96
6	49.91	49.40	49.69	49.67	0.26	0.52
8	56.35	55.50	56.26	56.04	0.47	0.83
10	60.61	60.90	60.96	60.82	0.19	0.31
12	66.21	65.89	66.00	66.04	0.16	0.25

Table 29(E) The diltiazem hydrochloride release from tablet formulation F10 in 0.1 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	0.09	0.20	0.17	0.15	0.06	36.59
0.25	0.61	0.68	0.67	0.66	0.04	5.55
0.50	2.13	2.43	2.55	2.37	0.22	9.10
1	6.32	7.82	7.09	7.08	0.75	10.58
2	13.61	15.72	14.74	14.69	1.05	7.17
4	23.95	27.76	26.21	25.97	1.92	7.37
6	33.21	39.25	36.60	36.35	3.03	8.33
8	41.79	47.71	45.02	44.84	2.96	6.61
10	47.16	52.83	49.87	49.95	2.84	5.68
12	53.08	58.68	56.13	55.96	2.81	5.01

Table 30(E) The diltiazem hydrochloride release from tablet formulation F11 in 0.1 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	0.21	0.23	0.25	0.23	0.02	7.85
0.25	0.78	0.83	0.84	0.82	0.03	3.88
0.50	2.57	2.62	2.80	2.66	0.12	4.62
1	6.69	7.16	7.47	7.11	0.40	5.58
2	13.86	14.84	15.23	14.64	0.71	4.83
4	24.61	25.29	28.01	25.97	1.80	6.93
6	32.98	36.03	37.11	35.37	2.14	6.05
8	39.57	42.77	44.67	42.34	2.58	6.09
10	44.65	48.00	51.16	47.94	3.25	6.78
12	49.13	54.66	56.28	53.36	3.75	7.02

Table 31(E) The diltiazem hydrochloride release from tablet formulation F12 in 0.1 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	0.06	0.02	0.07	0.05	0.03	52.83
0.25	0.13	0.12	0.18	0.14	0.03	23.57
0.50	0.70	0.65	0.80	0.72	0.08	10.78
1	2.49	2.51	2.66	2.55	0.10	3.73
2	7.26	7.81	6.93	7.34	0.45	6.08
4	17.65	18.83	16.71	17.73	1.06	5.98
6	26.67	28.45	24.87	26.66	1.79	6.71
8	33.79	36.00	31.83	33.87	2.09	6.16
10	40.46	42.09	37.32	39.96	2.42	6.06
12	46.20	46.91	42.57	45.23	2.33	5.15

Table 32(E) The diltiazem hydrochloride release from tablet formulation F14 in 0.1 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	5.02	6.87	5.63	5.84	0.94	16.14
0.25	12.45	15.47	14.00	13.97	1.51	10.79
0.50	17.05	17.70	17.39	17.38	0.33	1.89
1	22.78	26.71	25.07	24.85	1.98	7.96
2	30.59	36.58	32.59	33.26	3.05	9.16
4	40.34	48.82	44.20	44.45	4.25	9.55
6	48.57	57.08	52.25	52.63	4.27	8.11
8	55.01	64.25	59.23	59.50	4.63	7.78
10	60.39	69.34	65.87	65.20	4.51	6.92
12	63.28	72.68	69.05	68.34	4.74	6.94

Table 33(E) The diltiazem hydrochloride release from tablet formulation F15 in 0.1 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	0.53	0.43	0.79	0.59	0.18	31.45
0.25	1.63	1.21	1.85	1.56	0.32	20.64
0.50	4.47	3.94	5.63	4.68	0.87	18.55
1	8.84	8.78	9.19	8.94	0.22	2.44
2	16.22	15.64	17.49	16.45	0.94	5.73
4	29.29	28.33	33.17	30.26	2.56	8.47
6	39.41	38.79	39.95	39.38	0.58	1.47
8	47.12	46.75	47.26	47.04	0.26	0.55
10	53.16	51.32	53.88	52.79	1.32	2.50
12	58.29	58.17	58.47	58.31	0.15	0.26

Table 34(E) The diltiazem hydrochloride release from tablet formulation F16 in 0.1 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	0.31	0.35	0.32	0.33	0.02	6.78
0.25	1.14	1.09	1.11	1.11	0.03	2.43
0.50	3.12	3.16	3.16	3.15	0.02	0.69
1	8.37	7.65	7.84	7.95	0.38	4.72
2	15.60	16.35	15.72	15.89	0.40	2.53
4	27.00	28.67	28.42	28.03	0.90	3.22
6	36.13	38.00	38.18	37.44	1.14	3.04
8	44.05	46.23	45.92	45.40	1.18	2.59
10	50.20	51.84	51.35	51.13	0.84	1.65
12	55.37	57.28	57.02	56.56	1.03	1.83

Table 35(E) The diltiazem hydrochloride release from tablet formulation F17 (without PEG 4000) in 0.1 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	0.64	0.56	0.35	0.52	0.15	29.80
0.25	1.62	1.43	1.22	1.42	0.20	14.12
0.50	3.67	3.33	3.35	3.45	0.19	5.61
1	7.47	7.18	6.85	7.17	0.31	4.32
2	14.07	13.40	12.63	13.37	0.72	5.38
4	25.09	23.47	23.24	23.93	1.01	4.21
6	33.45	31.64	31.99	32.36	0.96	2.96
8	41.69	39.50	40.17	40.45	1.12	2.77
10	49.19	44.95	45.93	46.69	2.22	4.75
12	54.89	50.25	52.28	52.47	2.32	4.43

Table 36(E) The diltiazem hydrochloride release from separated uncoated resinates of tablet formulation F14 in 0.1 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	7.38	7.59	6.72	7.23	0.45	6.27
0.25	13.23	13.23	11.85	12.77	0.80	6.24
0.50	19.04	17.73	17.10	17.96	0.99	5.51
1	26.83	25.98	25.91	26.24	0.51	1.94
2	37.66	36.27	37.16	37.03	0.70	1.90
4	54.58	49.46	48.31	50.78	3.34	6.57
6	64.26	59.70	59.04	61.00	2.84	4.66
8	72.10	67.95	65.05	68.37	3.55	5.19
10	79.52	72.02	71.01	74.18	4.65	6.27
12	81.25	76.27	74.70	77.41	3.42	4.42

Table 37(E) The diltiazem hydrochloride release from separated coated resinates of tablet formulation F11 in 0.1 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	0.58	0.60	0.71	0.63	0.07	10.89
0.25	2.09	1.83	2.09	2.00	0.15	7.30
0.50	4.81	4.05	4.62	4.50	0.40	8.79
1	9.36	8.28	9.15	8.93	0.57	6.42
2	17.38	15.56	16.82	16.59	0.93	5.61
4	28.67	26.22	28.59	27.83	1.39	5.00
6	37.74	34.37	37.16	36.42	1.80	4.94
8	46.17	42.06	45.81	44.68	2.28	5.10
10	51.78	48.08	51.90	50.59	2.18	4.30
12	56.30	51.56	55.96	54.61	2.64	4.84

Table 38(E) The diltiazem hydrochloride release from tablet formulation F11 with compression pressure 1,500 psi (340 pound) in 0.1 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	0.29	0.28	0.29	0.29	0.01	2.00
0.25	0.90	0.79	0.81	0.84	0.06	7.29
0.50	2.21	2.13	2.18	2.17	0.04	1.99
1	6.19	5.86	6.01	6.02	0.17	2.74
2	13.09	13.13	13.16	13.13	0.03	0.25
4	24.27	24.91	25.01	24.73	0.40	1.62
6	34.58	35.54	35.12	35.08	0.48	1.38
8	41.64	44.09	43.44	43.06	1.27	2.94
10	48.63	51.47	48.76	49.62	1.60	3.23
12	54.06	57.67	55.32	55.68	1.83	3.29

Table 39(E) The diltiazem hydrochloride release from tablet formulation F11 with compression pressure 4,500 psi (1,022 pound) in 0.1 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	0.21	0.18	0.21	0.20	0.02	8.37
0.25	0.58	0.58	0.72	0.62	0.08	12.75
0.50	1.42	1.48	1.47	1.46	0.03	2.14
1	3.85	4.26	3.97	4.03	0.21	5.26
2	9.42	10.44	10.04	9.97	0.52	5.18
4	18.79	21.43	19.41	19.88	1.38	6.95
6	28.01	31.76	34.11	31.29	3.08	9.84
8	35.97	40.04	38.15	38.05	2.03	5.35
10	42.49	46.72	45.08	44.76	2.13	4.77
12	48.06	52.99	52.03	51.03	2.62	5.13

Table 40(E) The diltiazem hydrochloride release from tablet formulation F14 with compression pressure 1,500 psi (340 pound) in 0.1 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	5.95	4.98	5.61	5.52	0.49	8.91
0.25	11.33	11.44	11.43	11.40	0.06	0.53
0.50	16.97	15.69	15.07	15.91	0.97	6.08
1	23.35	22.85	23.18	23.13	0.26	1.10
2	32.92	31.19	30.00	31.37	1.47	4.68
4	46.70	46.57	46.81	46.69	0.12	0.26
6	58.04	55.71	57.63	57.13	1.24	2.17
8	66.62	64.74	66.05	65.80	0.96	1.46
10	73.74	71.71	74.14	73.20	1.30	1.78
12	78.79	79.14	79.05	79.00	0.18	0.23

Table 41(E) The diltiazem hydrochloride release from tablet formulation F14 with compression pressure 4,500 psi (1,022 pound) in 0.1 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	3.20	4.51	3.91	3.88	0.66	16.91
0.25	7.56	11.94	10.84	10.11	2.28	22.50
0.50	11.68	15.38	14.27	13.78	1.90	13.80
1	18.94	20.42	19.88	19.75	0.75	3.79
2	26.30	29.02	28.14	27.82	1.39	4.98
4	36.62	42.00	40.34	39.65	2.76	6.95
6	45.92	52.81	48.11	48.95	3.52	7.19
8	53.07	61.37	58.75	57.73	4.24	7.34
10	59.60	69.52	64.75	64.62	4.96	7.68
12	64.81	71.39	64.96	67.05	3.76	5.60

Table 42(E) The diltiazem hydrochloride release from tablet formulation F11, compressed by single punch tableting machine, in 0.1 M KCl

Time (hr)	% Diltiazem release			Mean	SD	%CV
	n1	n2	n3			
0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.083	0.18	0.18	0.18	0.18	0.00	1.03
0.25	0.57	0.72	0.89	0.73	0.16	22.00
0.50	1.95	2.18	2.52	2.22	0.29	12.91
1	5.26	6.04	6.31	5.87	0.55	9.33
2	11.80	11.86	11.12	11.59	0.41	3.57
4	23.51	21.79	23.33	22.88	0.94	4.13
6	31.15	30.22	32.24	31.20	1.01	3.24
8	39.44	37.89	39.46	38.93	0.90	2.32
10	45.05	44.27	45.63	44.98	0.68	1.52
12	50.09	49.66	50.65	50.13	0.50	0.99

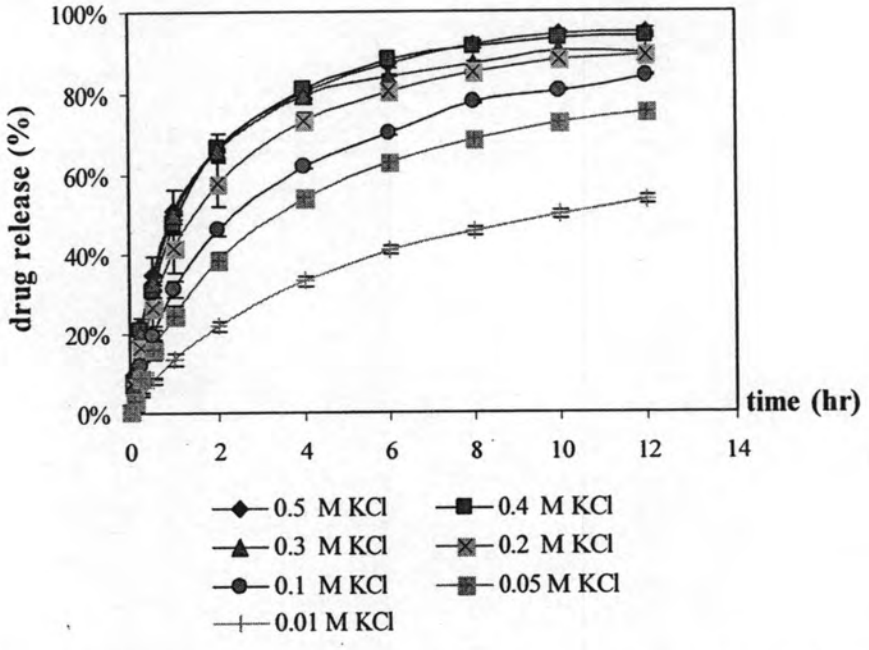

Figure 1(E) The diltiazem hydrochloride release from resinates in potassium chloride

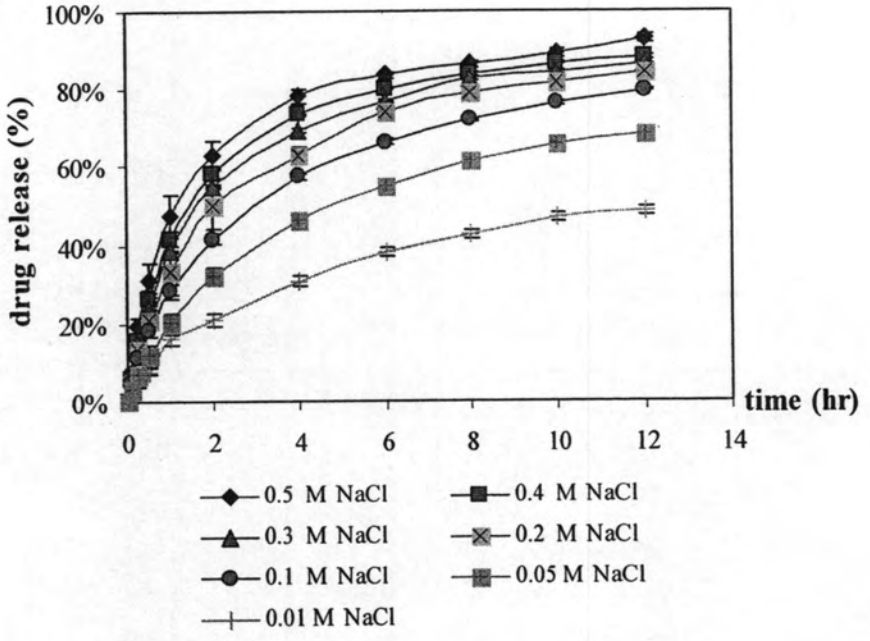

Figure 2(E) The diltiazem hydrochloride release from resinates in sodium chloride

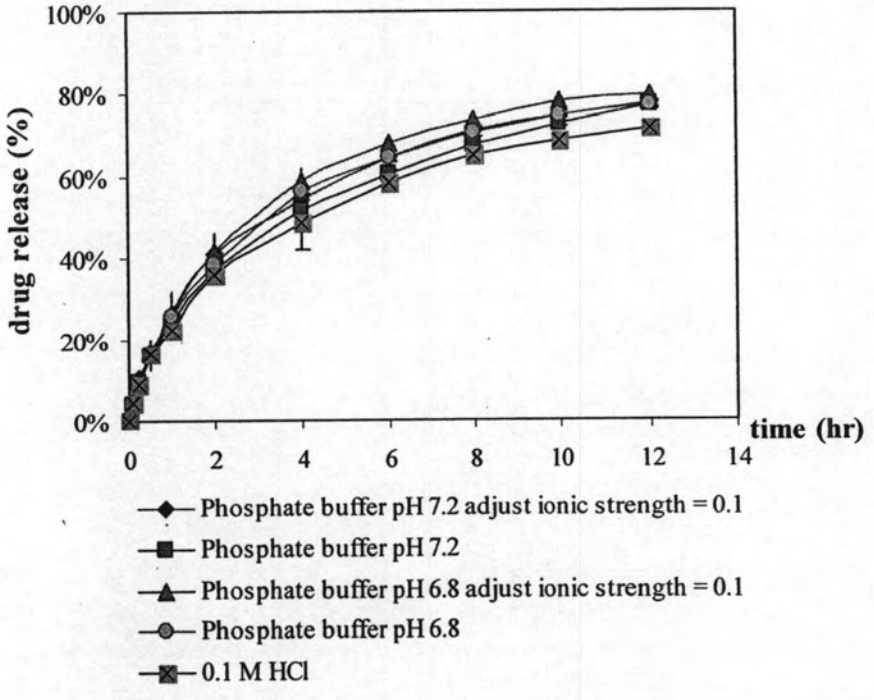

Figure 3(E) The diltiazem hydrochloride release from resinates in various pH

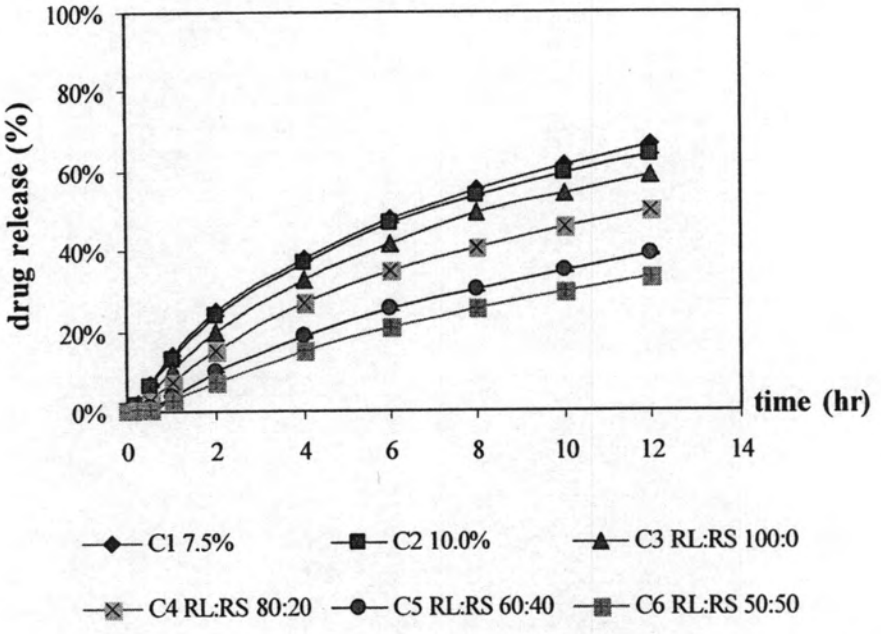

Figure 4(E) The diltiazem hydrochloride release from coated resinates in 0.1 M potassium chloride

Table 43(E) Kinetic analysis of diltiazem hydrochloride released from uncoated resinates in various dissolution mediums

Dissolution medium	Ionic strength	Zero order		First order		Higuchi	
		R^2	K_0	R^2	K_1	R^2	K
KCl 0.01 M	0.01	0.9222	0.9222	0.6423	0.2267	0.9930	0.1678
KCl 0.05 M	0.05	0.9167	0.9167	0.6621	0.5843	0.9921	0.2765
KCl 0.1 M	0.1	0.9113	0.9113	0.6968	0.5166	0.9918	0.3289
KCl 0.2 M	0.2	0.9288	0.9288	0.7428	0.9426	0.9902	0.4273
KCl 0.3 M	0.3	0.9079	0.9079	0.6952	0.9470	0.9876	0.4979
KCl 0.4 M	0.4	0.9256	0.9256	0.7283	0.9173	0.9924	0.4905
KCl 0.5 M	0.5	0.8912	0.8912	0.7244	0.8363	0.9909	0.4938
NaCl 0.01 M	0.01	0.9066	0.9066	0.6482	0.2104	0.9899	0.1516
NaCl 0.05 M	0.05	0.9235	0.9235	0.6896	0.3038	0.9930	0.2329
NaCl 0.1 M	0.1	0.9210	0.9210	0.7043	0.5094	0.9951	0.3006
NaCl 0.2 M	0.2	0.8883	0.8883	0.6573	0.5057	0.9881	0.3374
NaCl 0.3 M	0.3	0.9384	0.9384	0.6466	0.4960	0.9878	0.4065
NaCl 0.4 M	0.4	0.9365	0.9365	0.7382	0.9850	0.9882	0.4316
NaCl 0.5 M	0.5	0.9111	0.9111	0.7223	0.9122	0.9900	0.4717
$CaCl_2$ 0.04 M	0.1	0.9019	0.9019	0.6588	0.3522	0.9932	0.2601
Buffer 7.2	0.085	0.9138	0.0976	0.6812	0.3590	0.9947	0.2606
Buffer 7.2	0.1	0.9095	0.1035	0.6914	0.3521	0.9935	0.2769
Buffer 6.8	0.072	0.9419	0.1372	0.6585	0.3899	0.9910	0.2957
Buffer 6.8	0.1	0.9388	0.1431	0.6943	0.3729	0.9917	0.3090
HCl 0.1 M	0.1	0.9175	0.0933	0.7074	0.3473	0.9951	0.2487

Table 44(E) Kinetic analysis of diltiazem hydrochloride released from coated resinates in 0.1 M KCl

Sample formulation	Zero order		First order		Higuchi	
	R^2	K_0	R^2	K_1	R^2	K
Coated resinates						
C1	0.9457	0.0624	0.5475	0.3793	0.9973	0.2232
C2	0.9451	0.0608	0.4902	0.4287	0.9967	0.2177
C3	0.9485	0.0511	0.5559	0.3536	0.9961	0.1980
C4	0.9552	0.0436	0.6208	0.3600	0.9944	0.1682
C5	0.9725	0.0343	0.5906	0.4420	0.9894	0.1307
C6	0.9798	0.0297	0.6932	0.4313	0.9831	0.1126
Tablets Formulation F11 (coated resinate C3)	0.9716	0.0463	0.6520	0.3488	0.9934	0.1772

Determination of the release kinetic was preliminary calculated the first 60 % of dissolution profiles following mathematical kinetic model such as the zero order model, the first order model and the square-root-of-time release model (Higuchi model). The kinetic analysis of diltiazem hydrochloride released from the uncoated resinates in various dissolution mediums was shown in Table 44(E). The results showed that the release of drug from resinates in all dissolution medium were best described by the Higuchi model, which provided the highest values of the determination coefficient (R^2). The release kinetic of drug from coated resinates and tablet formulation F11 which formulated from coated resinate formulation C3 was also described by the Higuchi model (Table 45(E)). In conclusion, the release kinetic of diltiazem from uncoated resinates, coated resinates and disintegrating tablets were best described by the Higuchi model.

VITA

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