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APPENDICES

APPENDIX A

UV-Vis Spectrum and Calibration Curve of Sodium Diclofenac

UV-Vis Spectrum of Sodium Diclofenac

UV-Vis spectrophotometer was used to determine the amount of sodium diclofenac. The λ_{max} of drug absorbance in 0.1 N HCl (pH 1.2), phosphate buffer saline pH 6.6 and pH 7.4, NaOH solutions (2.5-7.5% (w/v)) and 5.0% (w/v) NaOH/KCl (0.1-0.5M) was identical (276 nm). The absorbance spectra in these dissolution media were illustrated in Figures A1-A9.

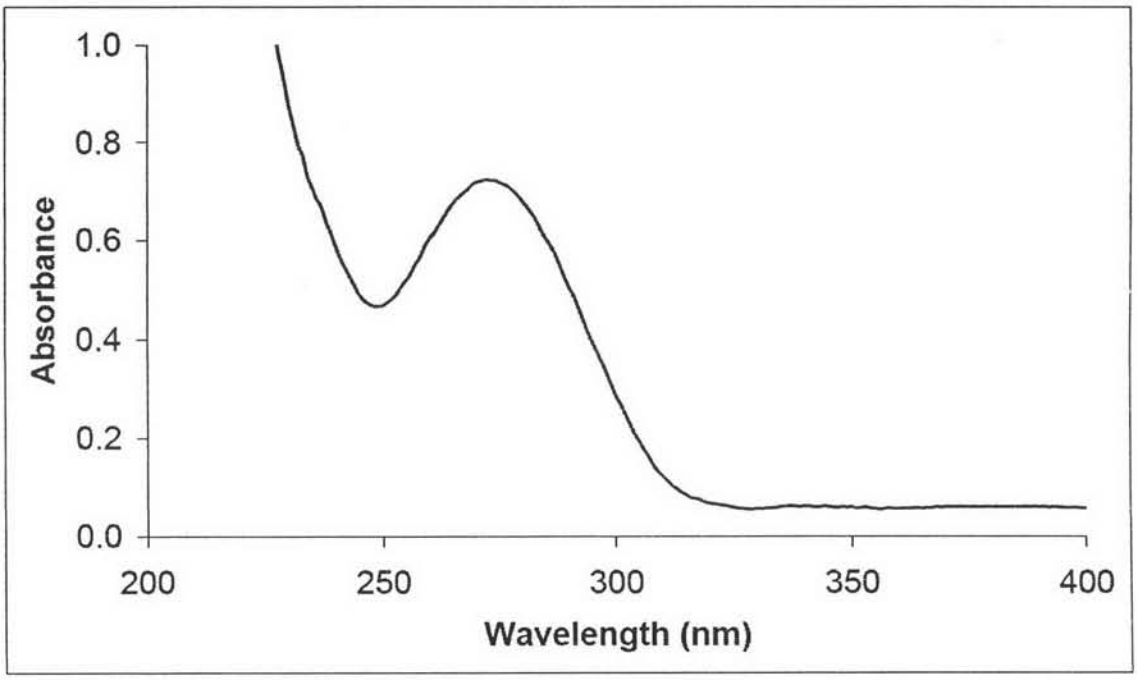

Figure A1 UV-Vis spectrum of sodium diclofenac in 0.1N HCl.

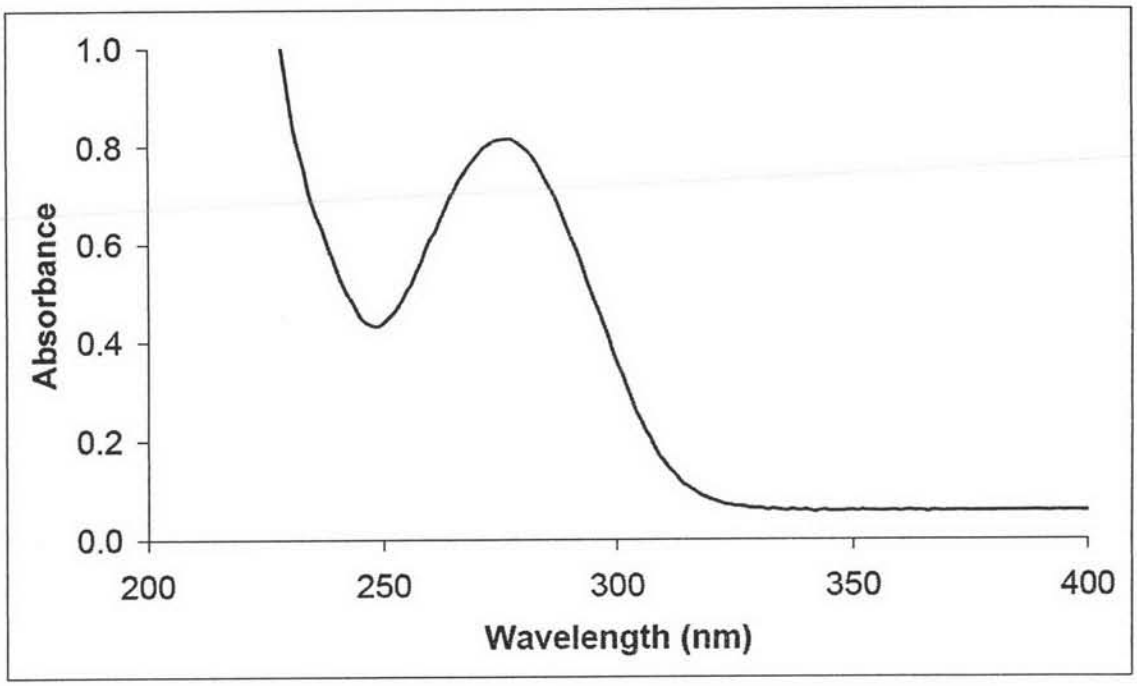

Figure A2 UV-Vis spectrum of sodium diclofenac in phosphate buffer saline pH 6.6.

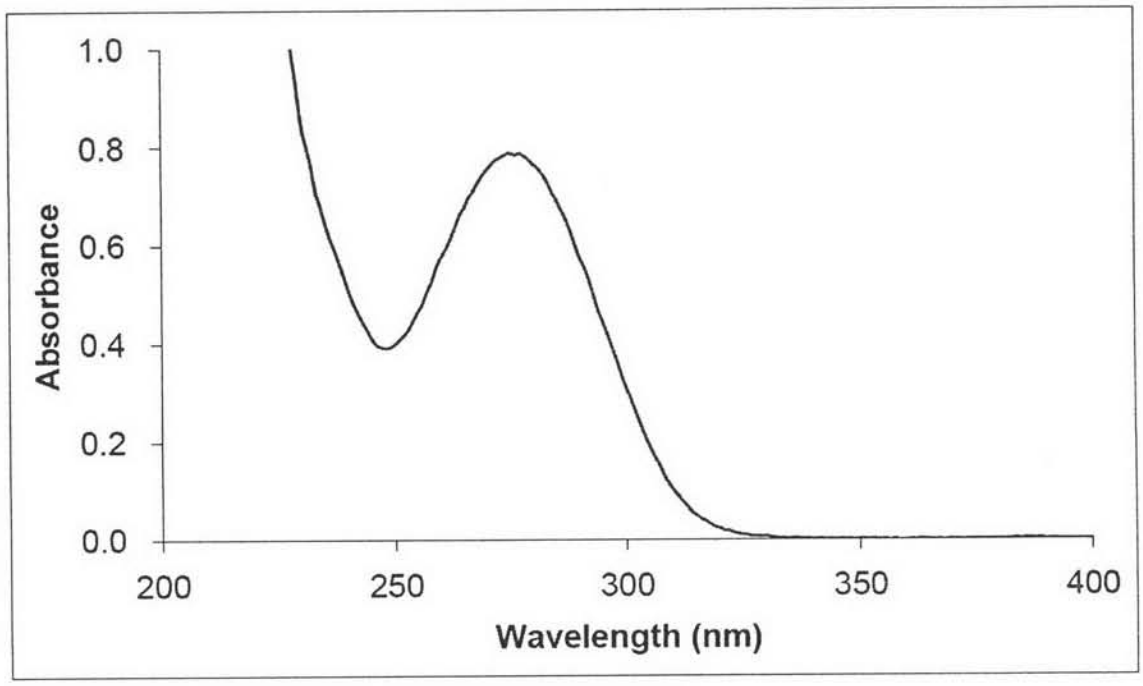

Figure A3 UV-Vis spectrum of sodium diclofenac in phosphate buffer saline pH 7.4.

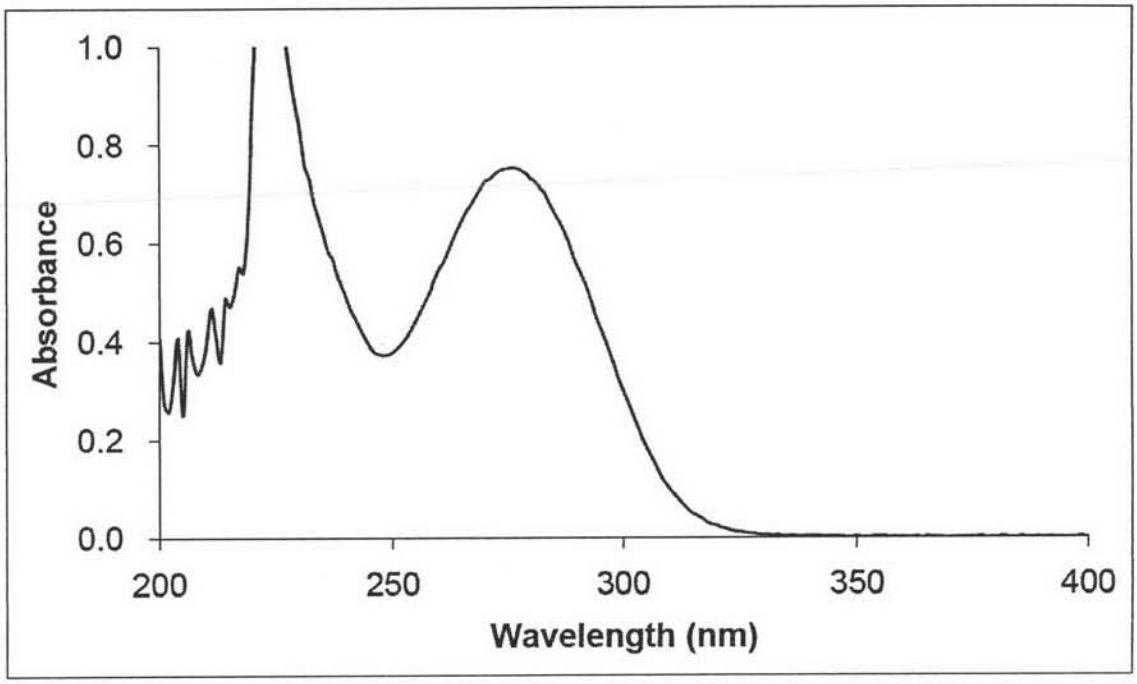

Figure A4 UV-Vis spectrum of sodium diclofenac in 2.5% (w/v) NaOH solution.

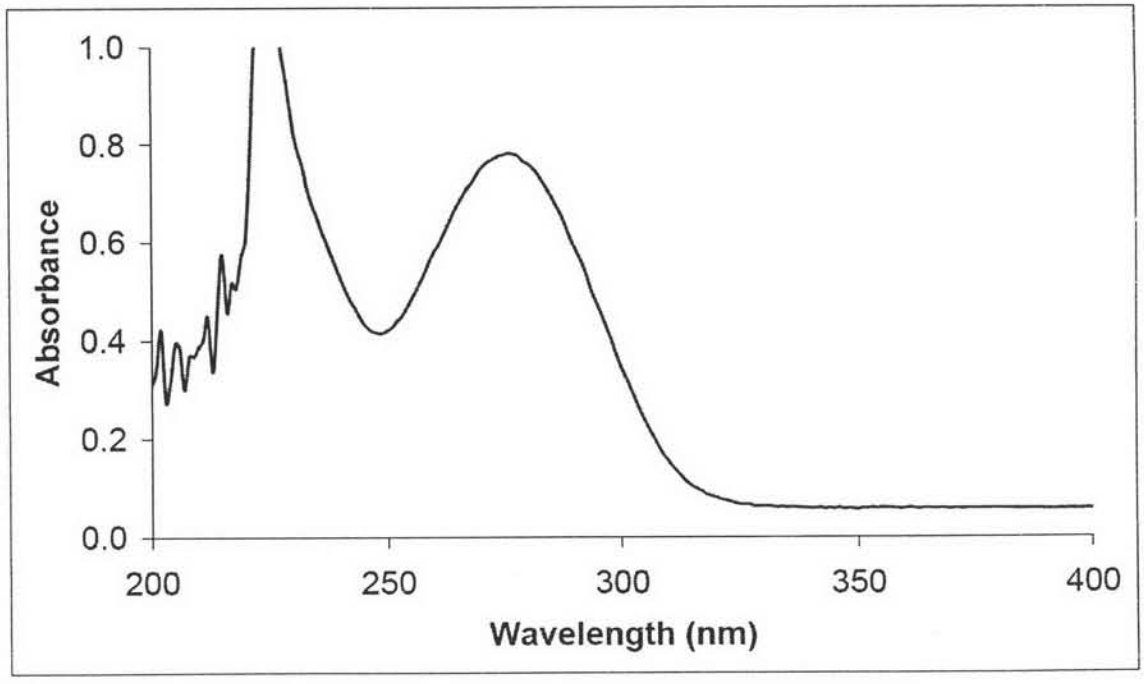

Figure A5 UV-Vis spectrum of sodium diclofenac in 5.0% (w/v) NaOH solution.

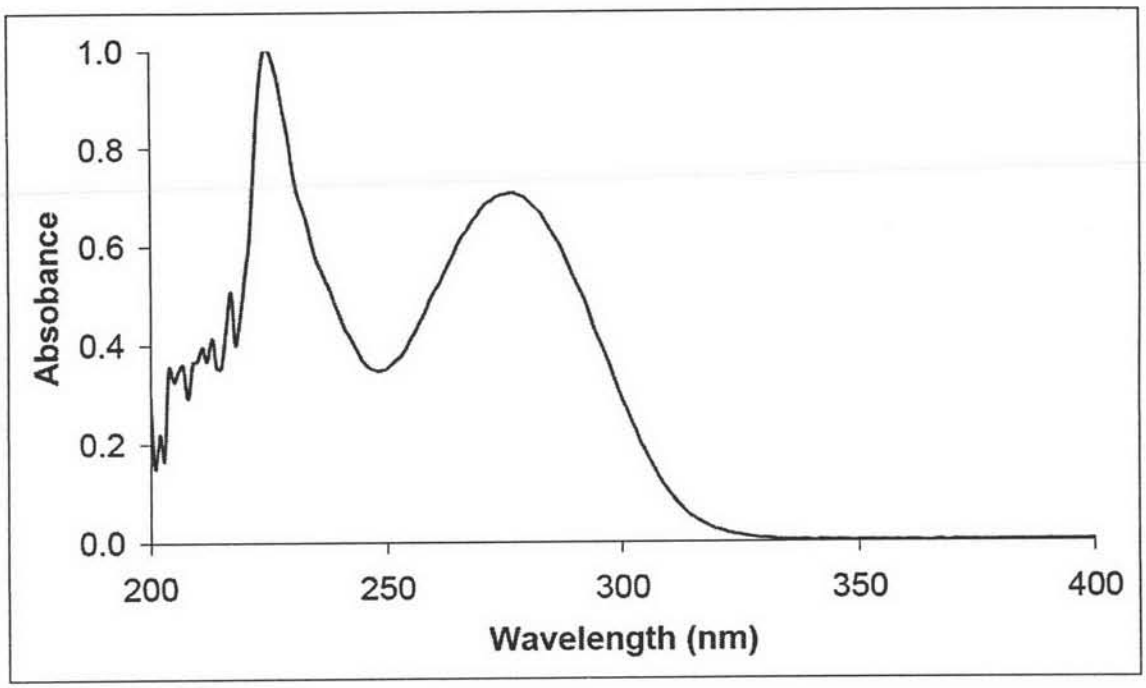

Figure A6 UV-Vis spectrum of sodium diclofenac in 7.5% (w/v) NaOH solution.

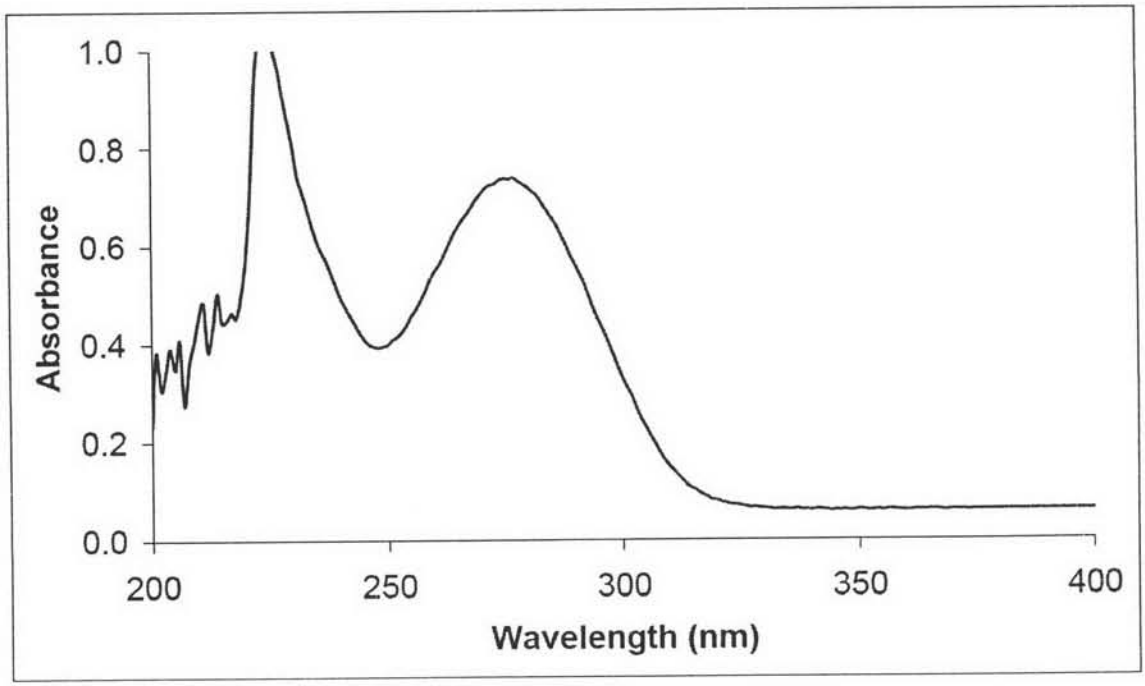

Figure A7 UV-Vis spectrum of sodium diclofenac in 5.0% (w/v) NaOH/0.1M KCl solution.

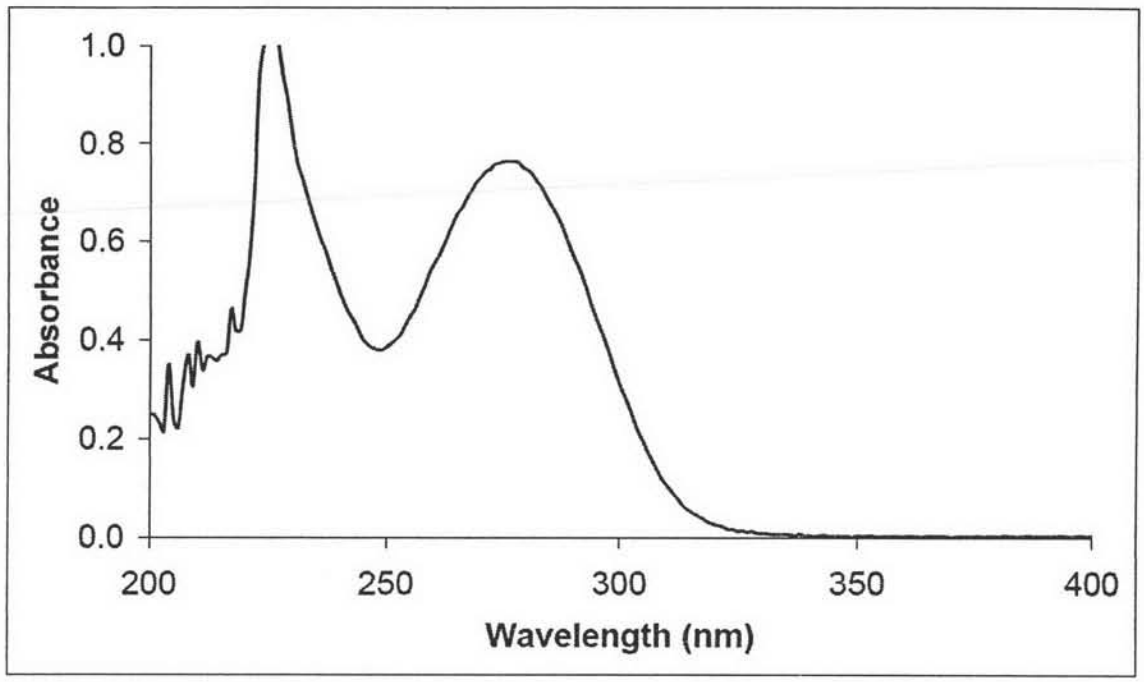

Figure A8 UV-Vis spectrum of sodium diclofenac in 5.0% (w/v) NaOH/0.3M KCl solution.

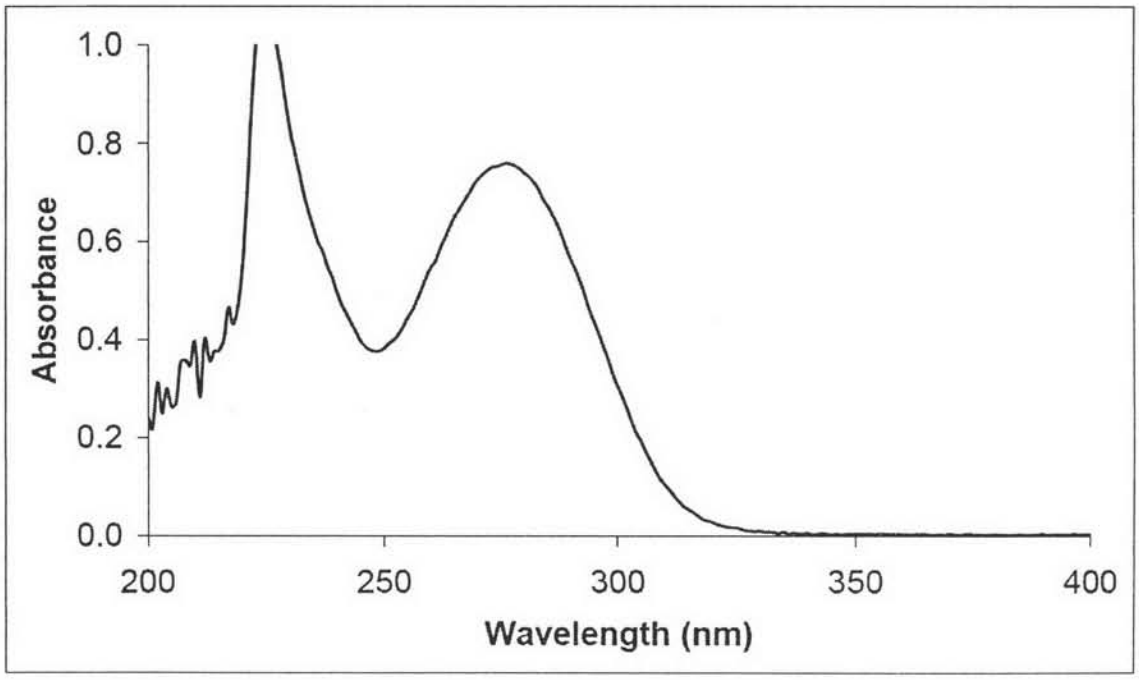

Figure A9 UV-Vis spectrum of sodium diclofenac in 5.0% (w/v) NaOH/0.5M KCl solution.

Calibration Curve of Sodium Diclofenac

The concentration versus absorbance of sodium diclofenac in 0.1 N HCl (pH 1.2), phosphate buffer saline pH 6.6 and pH 7.4, NaOH solutions (2.5-7.5% (w/v)) and 5.0% (w/v) NaOH/KCl (0.1-0.5M) at 276 nm are presented in Tables A1-A9. The standard curves of sodium diclofenac in these dissolution media are illustrated in Figures A10-A18.

Table A1 Absorbance of sodium diclofenac in 0.1N HCl determined at 276 nm

Concentration (ppm)	Absorbance
2	0.060
4	0.112
6	0.163
8	0.220
10	0.273

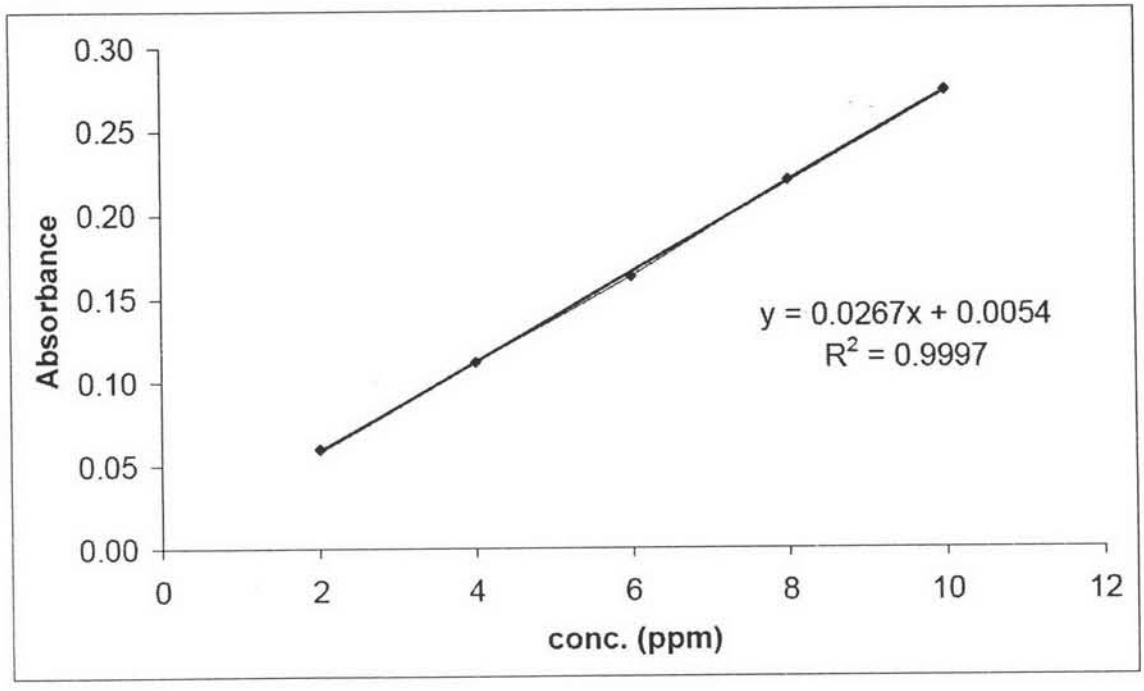

Figure A10 Calibration curve of sodium diclofenac in 0.1N HCl at 276 nm.

Table A2 Absorbance of sodium diclofenac in phosphate buffer saline pH 6.6 determined at 276 nm

Concentration (ppm)	Absorbance
2	0.066
4	0.131
6	0.193
8	0.257
10	0.318

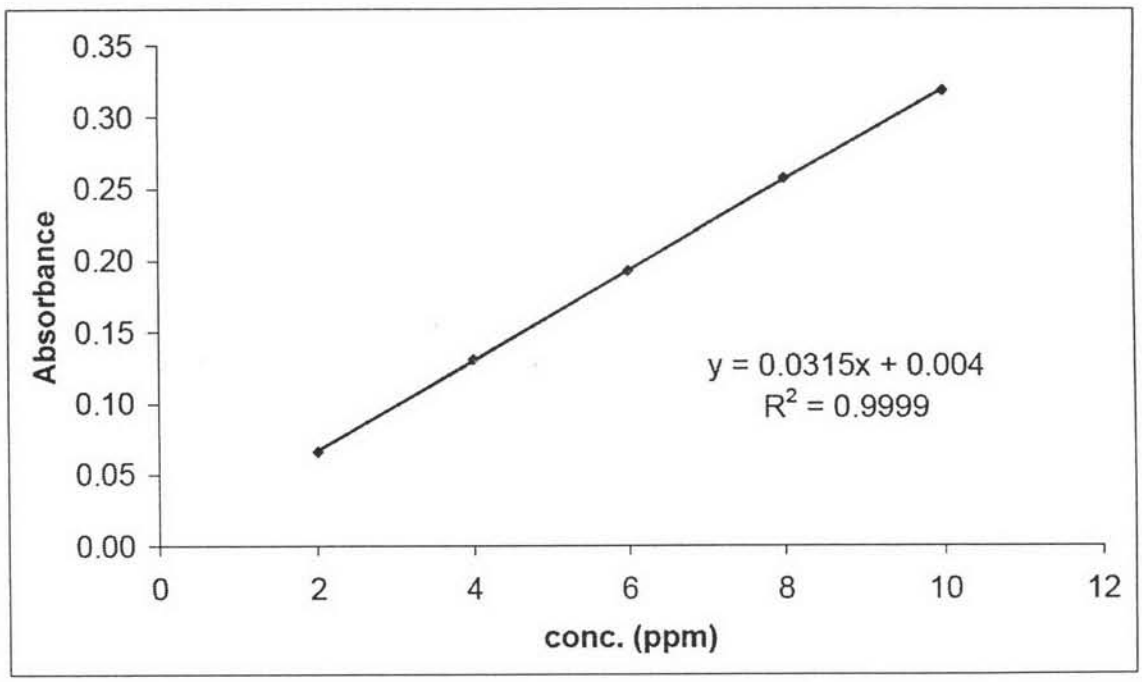

Figure A11 Calibration curve of sodium diclofenac in phosphate buffer saline pH 6.6 at 276 nm.

Table A3 Absorbance of sodium diclofenac in phosphate buffer saline pH 7.4 determined at 276 nm

Concentration (ppm)	Absorbance
5	0.169
10	0.335
15	0.496
20	0.656
25	0.816
30	0.990
35	1.149

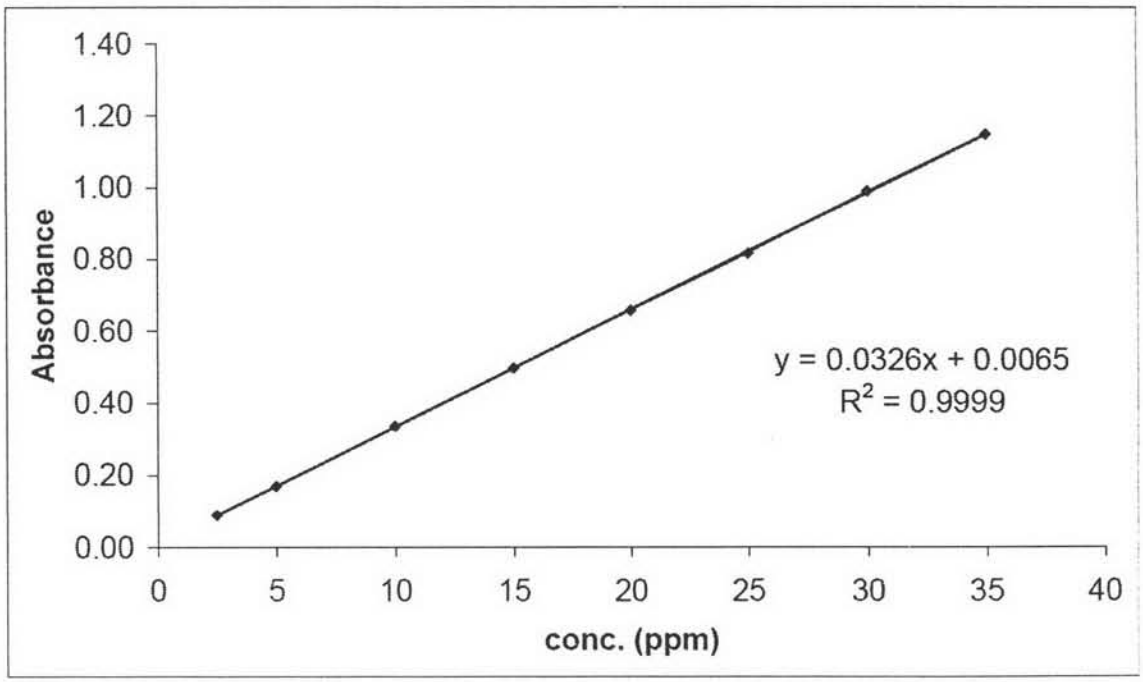

Figure A12 Calibration curve of sodium diclofenac in phosphate buffer saline pH 7.4 at 276 nm.

Table A4 Absorbance of sodium diclofenac in 2.5% (w/v) NaOH solution determined at 276 nm

Concentration (ppm)	Absorbance
5	0.165
10	0.326
20	0.642
30	0.944
40	1.257

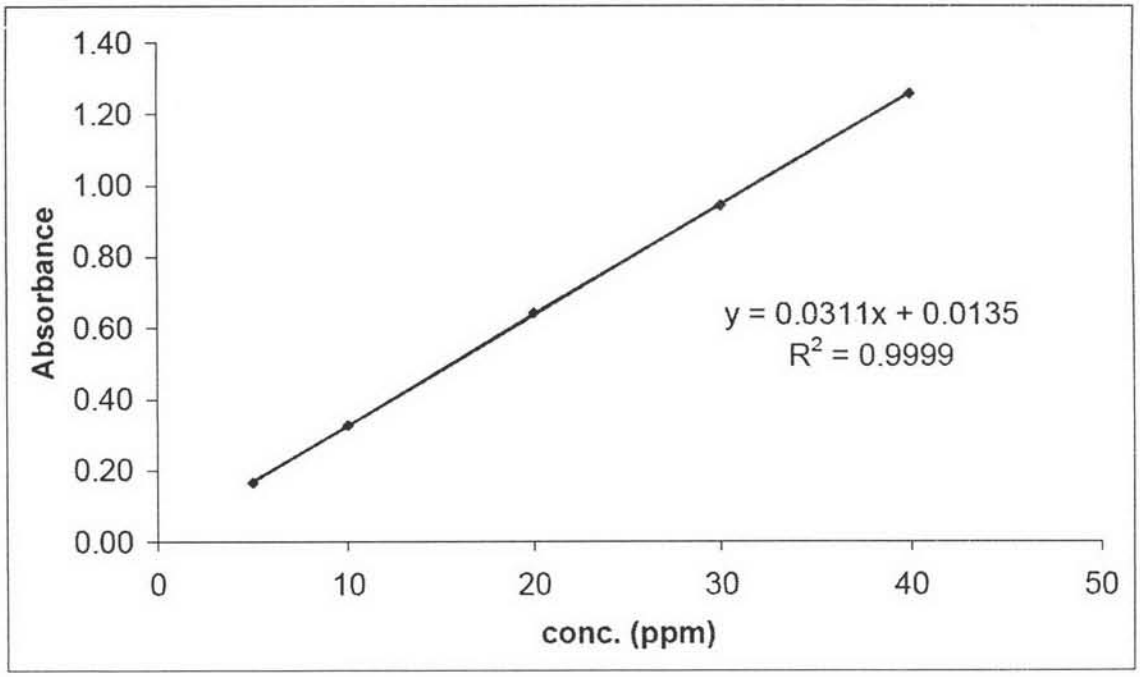

Figure A13 Calibration curve of sodium diclofenac in 2.5% (w/v) NaOH solution at 276 nm.

Table A5 Absorbance of sodium diclofenac in 5.0% (w/v) NaOH solution determined at 276 nm

Concentration (ppm)	Absorbance
5	0.165
10	0.343
20	0.677
30	1.010
40	1.347

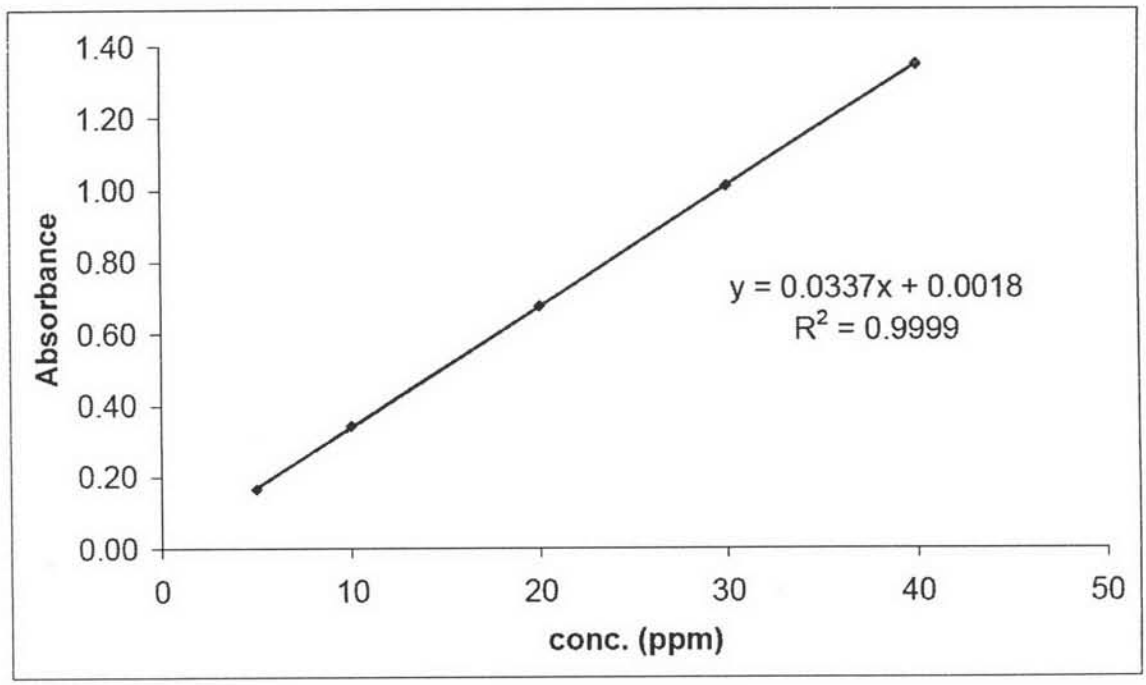

Figure A14 Calibration curve of sodium diclofenac in 5.0% (w/v) NaOH solution at 276 nm.

Table A6 Absorbance of sodium diclofenac in 7.5% (w/v) NaOH solution determined at 276 nm

Concentration (ppm)	Absorbance
5	0.178
10	0.344
20	0.667
30	0.990
40	1.301

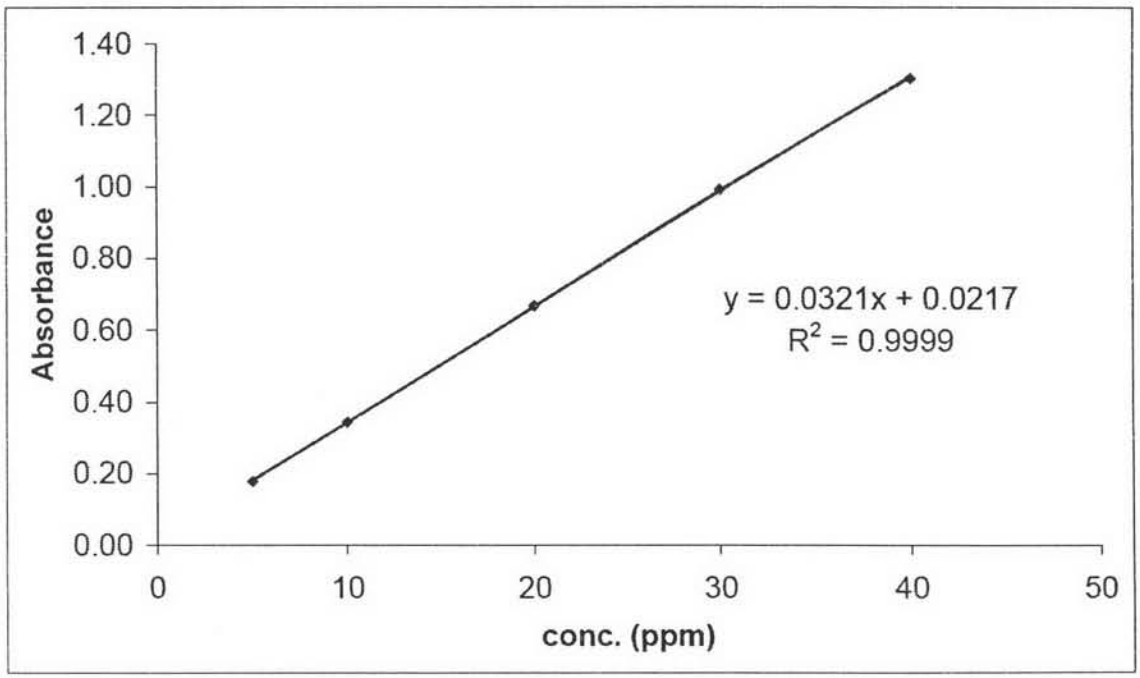

Figure A15 Calibration curve of sodium diclofenac in 7.5% (w/v) NaOH solution at 276 nm.

Table A7 Absorbance of sodium diclofenac in 5.0% (w/v) NaOH/0.1M KCl solution determined at 276 nm

Concentration (ppm)	Absorbance
5	0.174
10	0.334
20	0.676
30	1.001
40	1.369

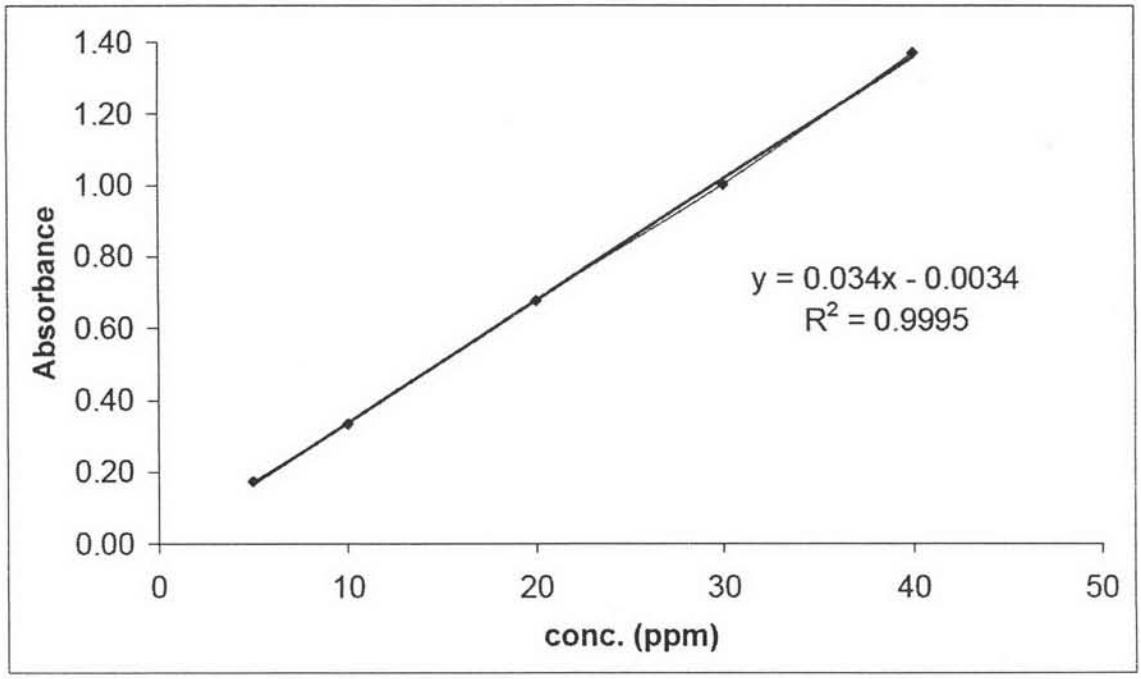

Figure A16 Calibration curve of sodium diclofenac in 5.0% (w/v) NaOH/0.1M KCl solution at 276 nm.

Table A8 Absorbance of sodium diclofenac in 5.0% (w/v) NaOH/0.3M KCl solution determined at 276 nm

Concentration (ppm)	Absorbance
5	0.181
10	0.345
20	0.658
30	0.998
40	1.342

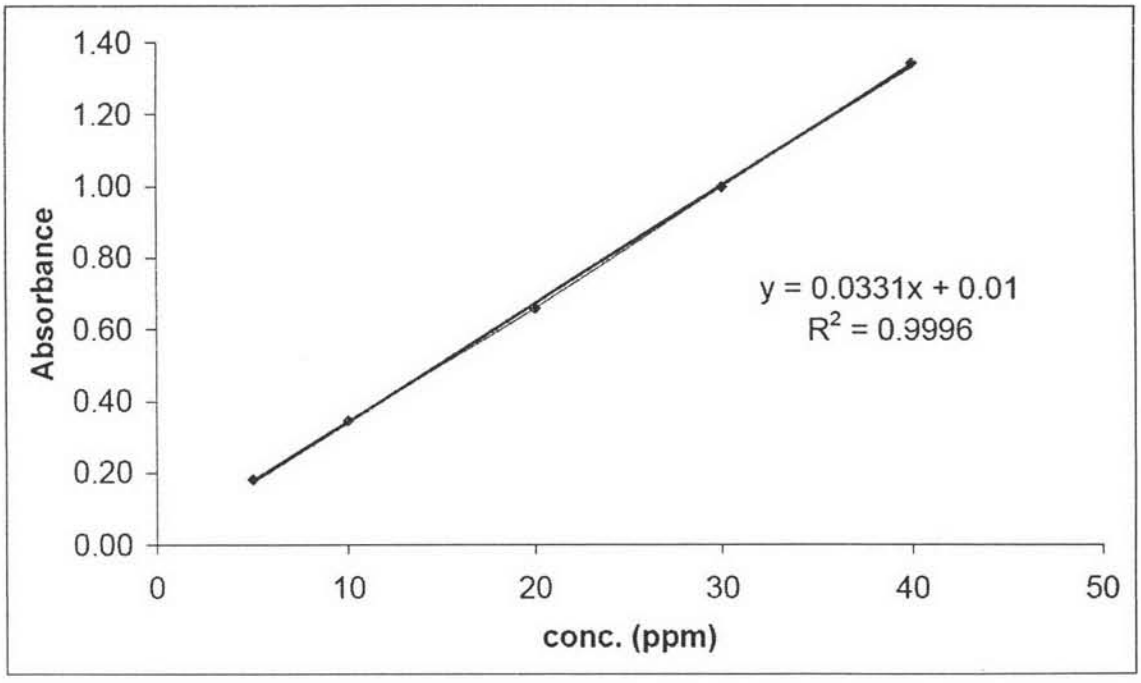

Figure A17 Calibration curve of sodium diclofenac in 5.0% (w/v) NaOH/0.3M KCl solution at 276 nm.

Table A9 Absorbance of sodium diclofenac in 5.0% (w/v) NaOH/0.5M KCl solution determined at 276 nm

Concentration (ppm)	Absorbance
5	0.182
10	0.337
20	0.652
30	1.002
40	1.297

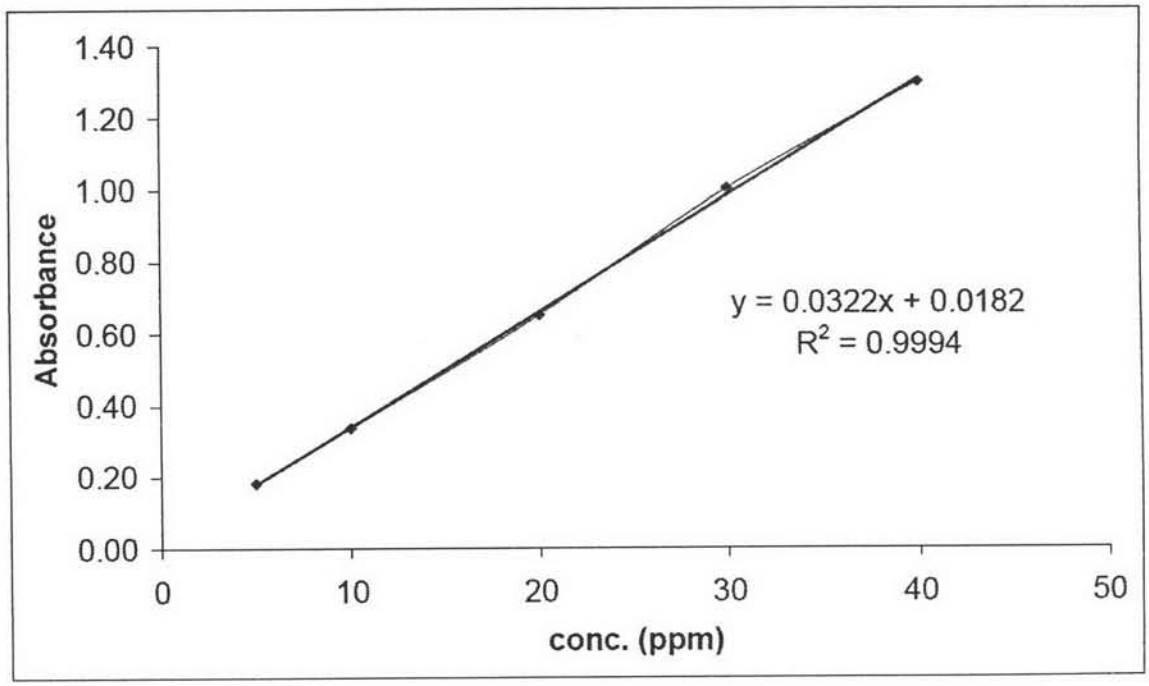

Figure A18 Calibration curve of sodium diclofenac in 5.0% (w/v) NaOH/0.5M KCl solution at 276 nm.

APPENDIX B

Swelling Ratio

Table B1 The swelling ratio of the chitosan/carrageenan (CS/CR : 2/1) bead with 5% (w/v) DFNa content in three dissolution systems

Time (hr:min)	pH 1.2 system		pH 7.4 system		pH-alternating system	
	Swelling ratio	S.D.	Swelling ratio	S.D.	Swelling ratio	S.D.
0:00	1.00	0.00	1.00	0.00	1.00	0.00
0:05	0.97	0.12	1.03	0.10	1.01	0.02
0:10	1.01	0.10	1.06	0.06	1.01	0.02
0:15	1.00	0.08	1.19	0.02	1.05	0.00
0:20	1.01	0.10	1.19	0.02	1.05	0.00
0:30	0.95	0.10	1.22	0.07	1.06	0.01
0:45	0.94	0.08	1.21	0.05	1.10	0.04
1:00	0.95	0.07	1.18	0.03	1.10	0.01
1:15	0.96	0.06	1.19	0.05	1.08	0.02
1:30	0.97	0.07	1.16	0.02	1.06	0.01
2:00	0.95	0.10	1.14	0.01	1.05	0.00
2:30	0.94	0.08	1.16	0.02	0.93	0.06
3:00	0.94	0.08	1.16	0.02	0.93	0.06
4:00	0.94	0.08	1.16	0.02	0.96	0.01
5:00	0.95	0.07	1.16	0.02	0.96	0.01

APPENDIX C

Percentage of Drug Release and Release Rate

Table C1 Percentage of DFNa release from commercial products and the beads from formulation A-S in pH-alternating method

Time (hr:min)	Voltaren® SR tablet		Subsyde® CR capsule		Formulation A		Formulation B		Formulation C	
	%drug release	S.D.	%drug release	S.D.	%drug release	S.D.	%drug release	S.D.	%drug release	S.D.
0:00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0:40	0.49	0.19	1.29	0.34	14.33	1.19	14.36	1.41	13.98	0.30
1:20	0.42	0.12	1.54	0.30	13.14	0.82	13.17	1.01	14.16	0.39
2:00	0.36	0.12	1.61	0.06	13.08	0.57	13.10	0.77	13.81	0.33
2:15	0.42	0.06	2.03	0.25	15.01	0.92	15.04	1.14	16.36	0.49
2:30	0.42	0.06	6.08	0.52	15.45	1.04	15.48	1.26	16.71	0.20
2:45	0.42	0.06	11.90	0.56	15.95	1.06	15.98	1.29	17.05	0.16
3:00	0.42	0.06	16.54	0.75	16.32	0.95	16.35	1.18	17.52	0.25
3:15	0.42	0.06	22.28	0.84	33.99	0.20	33.93	0.79	35.88	0.82
3:30	43.20	6.60	30.17	0.61	43.22	0.49	43.14	0.27	43.74	1.01
3:45	110.85	6.74	39.25	0.72	45.27	0.66	45.19	0.14	49.01	1.11
4:00	120.61	6.31	48.40	0.91	46.89	1.11	46.80	0.28	52.13	1.88
4:30	110.03	0.96	67.19	1.68	50.19	2.41	50.09	1.53	57.18	2.92
5:00	113.37	2.58	83.51	1.44	51.42	2.50	51.32	1.59	60.50	1.42
5:30	112.59	0.45	90.13	0.88	51.67	2.57	51.56	1.66	62.87	1.71
6:00	114.71	0.61	91.41	1.35	52.44	2.71	52.33	1.79	64.67	1.82
6:30	110.69	2.02	92.24	1.19	52.29	2.78	52.19	1.86	66.01	1.86
7:00	110.88	1.27	93.36	1.71	52.34	2.71	52.23	1.79	66.53	2.36
7:30	114.65	1.46	93.88	1.46	52.48	2.78	52.37	1.86	67.14	2.41
8:00	114.65	1.46	94.34	1.11	52.48	2.52	52.37	1.60	67.48	2.47
24:00	114.65	1.46	98.13	1.03	52.98	3.35	52.86	2.42	68.07	1.97

Table C1 (continued) Percentage of DFNa release from commercial products and the beads from formulation A-S in pH-alternating method

Time (hr:min)	Formulation D		Formulation I		Formulation J		Formulation K		Formulation L	
	%drug release	S.D.	%drug release	S.D.	%drug release	S.D.	%drug release	S.D.	%drug release	S.D.
0:00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0:40	15.18	1.64	7.24	0.37	5.89	0.29	5.69	0.34	5.29	0.42
1:20	12.99	0.96	7.08	0.33	5.95	0.48	5.71	0.20	5.07	0.48
2:00	13.24	1.37	6.75	0.15	5.98	0.59	5.79	0.25	4.78	0.46
2:15	15.52	1.30	7.56	0.18	6.95	0.54	6.62	0.26	5.94	0.67
2:30	16.25	1.32	8.08	0.21	7.44	0.65	7.08	0.41	6.19	0.62
2:45	16.83	1.40	8.44	0.32	7.57	0.56	7.31	0.35	6.37	0.58
3:00	17.27	1.38	8.61	0.22	7.69	0.64	7.43	0.33	6.39	0.58
3:15	29.95	2.74	16.18	0.96	23.07	2.73	19.60	2.88	16.30	0.69
3:30	38.26	2.58	22.07	1.57	29.13	3.45	25.26	2.74	22.74	1.61
3:45	44.95	1.97	26.44	2.60	33.01	3.41	34.64	2.41	26.95	2.03
4:00	48.10	1.69	30.16	2.98	35.99	3.30	38.45	1.31	31.09	2.06
4:30	52.02	1.64	36.49	3.22	40.21	3.15	41.23	3.12	43.17	2.87
5:00	56.18	2.37	42.28	3.80	43.63	3.18	45.14	2.81	51.69	1.05
5:30	56.78	2.17	46.23	3.94	46.10	3.22	49.28	2.68	57.18	0.64
6:00	58.04	2.48	50.79	3.73	48.65	3.23	49.92	1.32	61.45	0.01
6:30	57.25	1.09	54.43	4.20	50.31	3.14	52.10	2.70	64.87	0.92
7:00	57.74	0.77	57.61	3.39	51.81	3.27	58.49	3.42	66.93	1.46
7:30	58.96	0.02	65.42	3.67	53.50	3.50	63.78	3.37	68.67	1.73
8:00	58.66	0.33	67.65	2.45	54.90	3.63	64.30	1.89	69.74	1.57
24:00	58.16	0.10	87.39	0.17	77.33	0.28	75.27	0.85	89.78	4.42

Table C1 (continued) Percentage of DFNa release from commercial products and the beads from formulation A-S in pH-alternating method

Time (hr:min)	Formulation O		Formulation P		Formulation Q		Formulation R		Formulation S	
	%drug release	S.D.	%drug release	S.D.	%drug release	S.D.	%drug release	S.D.	%drug release	S.D.
0:00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0:40	4.31	0.30	4.90	0.25	3.78	0.18	4.02	0.13	0.95	0.07
1:20	4.33	0.12	4.84	0.12	3.76	0.10	3.71	0.08	1.40	0.10
2:00	4.47	0.38	5.13	0.33	3.82	0.14	3.66	0.03	1.87	0.07
2:15	5.78	0.70	7.28	0.47	4.76	0.14	9.51	1.51	1.34	0.08
2:30	6.22	0.61	7.93	0.85	5.19	0.09	11.83	1.69	1.42	0.08
2:45	6.40	0.66	8.46	0.88	5.33	0.16	12.97	2.18	1.47	0.07
3:00	6.47	0.66	8.61	0.97	5.70	0.27	13.94	2.72	1.53	0.06
3:15	20.25	1.64	21.68	0.43	17.26	2.43	25.54	1.61	2.59	0.20
3:30	27.48	1.80	26.85	0.25	22.29	2.74	30.52	1.69	5.30	0.20
3:45	31.66	1.30	30.57	0.73	27.00	1.15	33.73	1.67	8.43	0.31
4:00	34.00	1.32	32.85	0.56	29.90	1.03	36.43	1.44	11.59	0.27
4:30	37.06	1.26	36.09	0.63	34.13	1.38	39.59	1.31	17.14	0.17
5:00	39.50	1.31	38.45	0.52	38.66	1.44	42.59	1.22	21.86	0.50
5:30	41.33	1.34	40.20	0.33	40.52	1.49	44.64	1.25	26.54	0.55
6:00	42.40	1.39	41.88	0.21	42.56	1.61	46.42	1.21	30.58	0.69
6:30	44.21	1.46	42.96	0.22	44.57	1.80	47.92	1.02	34.26	0.52
7:00	45.08	1.58	44.64	0.28	46.06	1.92	49.53	1.39	38.28	0.62
7:30	45.90	1.63	45.62	0.39	47.54	2.16	50.54	1.18	41.71	0.73
8:00	46.74	1.77	46.44	0.62	49.17	2.26	51.60	1.14	44.89	0.50
24:00	50.11	3.01	52.45	1.65	57.53	3.30	56.43	2.02	69.93	2.82

Table C2 The release rate of commercial products and the beads from formulation A-S in pH-alternating method

Mean Time (hr:min)	Release Rate (%/hour)				
	Voltaren® SR	**Subsyde® CR**	**Formulation A**	**Formulation B**	**Formulation C**
0:00	0.00	0.00	0.00	0.00	0.00
0:20	0.74	1.94	21.50	21.54	20.67
1:00	-0.11	0.37	-1.78	-1.79	0.00
1:40	-0.10	0.11	-0.09	-0.09	0.54
2:30	0.07	14.92	3.24	3.25	3.10
3:15	85.89	27.28	53.80	53.59	50.89
3:45	154.82	36.45	7.34	7.32	11.44
4:15	-21.17	37.59	6.60	6.57	8.49
4:45	6.67	32.63	2.47	2.46	10.58
5:15	-1.56	13.24	0.49	0.49	3.12
5:45	4.25	2.03	1.54	1.53	4.33
6:15	-8.04	2.19	-0.28	-0.28	3.45
6:45	0.38	2.23	0.09	0.09	2.60
7:15	7.53	1.04	0.28	0.28	0.35
7:45	0.00	0.92	0.00	0.00	1.13
16:00	0.00	0.24	0.03	0.03	0.02

Table C2 (continued) The release rate of commercial products and the beads from formulation A-S in pH-alternating method

Mean Time (hr:min)	Release Rate (%/hour)				
	Formulation D	**Formulation I**	**Formulation J**	**Formulation K**	**Formulation L**
0:00	0.00	0.00	0.00	0.00	0.00
0:20	22.77	10.86	8.84	8.54	7.93
1:00	-3.27	-0.24	0.09	0.03	-0.33
1:40	0.36	-0.50	0.05	0.11	-0.43
2:30	4.04	1.86	1.71	1.64	1.62
3:15	41.98	33.48	42.87	39.96	32.69
3:45	19.67	17.20	13.72	17.38	16.70
4:15	7.84	12.79	8.45	10.26	24.17
4:45	8.34	11.37	6.83	7.81	17.04
5:15	1.18	7.43	4.95	8.28	10.98
5:45	2.54	8.83	5.10	6.23	8.54
6:15	-1.58	6.63	3.31	3.82	6.83
6:45	0.97	6.20	3.00	3.10	4.12
7:15	2.44	4.27	3.38	8.17	3.49
7:45	-0.60	5.55	2.82	0.90	2.14
16:00	-0.03	1.24	0.88	0.54	0.89

Table C2 (continued) The release rate of commercial products and the beads from formulation A-S in pH-alternating method

Mean Time (hr:min)	Release Rate (%/hour)				
	Formulation O	**Formulation P**	**Formulation Q**	**Formulation R**	**Formulation S**
0:00	0.00	0.00	0.00	0.00	0.00
0:20	6.47	7.35	5.68	6.03	1.43
1:00	0.02	-0.08	-0.03	-0.47	0.67
1:40	0.21	0.43	0.08	-0.08	0.70
2:30	2.01	3.48	1.88	10.28	-0.34
3:15	42.00	36.48	33.19	33.15	7.54
3:45	13.05	12.00	15.22	11.82	12.59
4:15	6.12	6.49	8.45	6.33	11.09
4:45	4.89	4.72	9.06	6.00	9.44
5:15	3.65	3.49	3.73	4.10	9.36
5:45	2.15	3.37	4.09	3.55	8.08
6:15	3.61	2.16	4.02	3.01	7.37
6:45	1.75	3.34	2.97	3.22	8.02
7:15	1.62	1.98	2.97	2.02	6.87
7:45	1.69	1.63	3.24	2.11	6.36
16:00	0.21	0.38	0.52	0.30	1.57

VITA

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