

REFERENCES

- (1) Gupta, K. C. and Ravi K. Drug release behavior of beads and microgranules of chitosan. Biomaterials 21 (2000): 1115-1119.
- (2) González-Rodríguez, M. L., Holgado, M. A., Sánchez-Lafuente, C., Rabasco, A. M. and Fini, A. et al. Alginate/chitosan particulate systems for sodium diclofenac release. International Journal of Pharmaceutics 232 (2002): 225-234.
- (3) Remuñán-López, C., Lorenzo-Lamosa, M. L., Vila-Jato, J. L. and Alonso, M. J. Development of new chitosan-cellulose multicore microparticles for controlled drug delivery. European Journal of Pharmaceutics and Biopharmaceutics 45 (1998): 49-56.
- (4) Kim, T. K., Park, Y. H., Kim, K. J. and Cho, C. S. Release of albumin from chitosan-coated pectin beads in vitro. International Journal of Pharmaceutics 250 (2003): 371-383.
- (5) Torre, P. M., Enobakhare, Y., Torrado, G., and Torrado, S. Release of amoxicillin from polyionic complexes of chitosan and poly(acrylic acid). study of polymer/polymer and polymer/drug interactions within the network structure. Biomaterials 24 (2003): 1499-1506.
- (6) Wang, Q., Dong, Z., Yumin, D., and Kennedy, J. F. Controlled release of ciprofloxacin hydrochloride from chitosan/polyethylene glycol blended films. Carbohydrate Polymers (2007):
Doi:10.1016/j.carbopol 2006.10.014].
- (7) Zhong, M. L., Gong, X. H., Zhao, Y. D., and Zhang, N. M. Properties and biocompatibility of chitosan films modified by blending with PEG. Biomaterials 23 (2002): 2614-1648.
- (8) Lin, W.C., Yu, D.G., and Yang, M.C. pH-sensitive polyelectrolyte complex gel microspheres composed of chitosan/sodium tripolyphosphate/dextran sulfate: swelling kinetics and drug delivery properties. Colloids and Surfaces B: Biointerfaces 44 (2005) 143-151.

- (9) Ida, G., Monica, C., Annalia, A., Bice, C., and Luisa, M. Influence of glutaraldehyde on drug release and mucoadhesive properties of chitosan microspheres. Carbohydrate Polymers 36 (1998): 81-88.
- (10) Gupta, V. K., Hariharan, M., Wheatley, T. A., and Price, J. C. Controlled-release tablets from carrageenans: effect of formulation, storage and dissolution factors. European Journal of Pharmaceutics and Biopharmaceutics 51 (2001): 241-248.
- (11) Gillman, A. G., Nies, T. W., and Taylor, P. The pharmacological basis of therapeutics. 8th ed. New York: Pergamon Press, 1991.
- (12) O' Brien, W. M. Adverse reactions to nonsteroidal anti-inflammatory drugs: diclofenac compared with other nonsteroidal anti-inflammatory drugs. The American Journal of Medicine 80 (1986): 70-80.
- (13) Berger, J., Reist, M., Mayer, J. M., Felt, O., Peppas, N. A., and Gurny, R. Structure and interactions in covalently and ionically crosslinked chitosan hydrogels for biomedical applications. European Journal of Pharmaceutics and Biopharmaceutics 57 (2004): 19-34.
- (14) Çetinus, S. A., and Öztop, H. N. Immobilization of catalase into chemically crosslinked chitosan beads. Enzyme and Microbial Technology 32 (2003): 889-894.
- (15) Hoffman, A. S. Hydrogels for biomedical applications. Advanced Drug Delivery Reviews 54 (2002): 3-12.
- (16) Sriamornsak, P. Effect of calcium concentration, hardening agent and drying condition on release characteristics of oral proteins from calcium pectinate gel beads. European Journal of Pharmaceutics Sciences 8 (1999): 221-227.
- (17) Roy, I., and Gupta, M. N. κ -Carrageenan as a new smart macroaffinity ligand for the purification of pullulanase. Journal of Chromatography A 998 (2003): 103-108.
- (18) Kim, C. Controlled release dosage form design. Pennsylvania: Technology Publishing Company Book, 2000.

- (19) Baker, R. Controlled release of biologically active agents. California: John Wiley & Sons. Inc., 1987.
- (20) Shalaby, S. W., Ikada, Y., Langer, R., and Williams, J. Polymers of biological and biomedical significance. Washington D. C.: American Chemical Society, 1994.
- (21) Banker, G. S., and Rhodes, C. T. Drug and the pharmaceutical sciences. 3rd ed. New York: Marcel Dekker, 1996.
- (22) Paul, W., and Sharma, C. P. Chitosan, a drug carrier for the 21st century: a review. *S.T.P. Pharmasciences* 10 (2000): 5-22.
- (23) Sinha, V. R., Singla, A. K., Wadhawan, S., Kumria, R., Bonsal, K., and Dhawan, S. Chitosan microspheres as a potential carrier for drugs. *International Journal of Pharmaceutics* 274 (2004): 1-33.
- (24) Patel, V. R. and Amiji, M. M. Preparation and characterization of freeze-dried chitosan-poly(ethylene oxide) hydrogels for site-specific antibiotic delivery in the stomach. *Pharmaceutical Research* 13 (1996): 588-593.
- (25) Ueno, H., Mori, T. and Fujinaga, T. Topical formulations and wound healing applications of chitosan. *Advanced drug delivery reviews* 52 (2001): 105-115.
- (26) Munjeri, O., Collett, J. H., and Fell, J. T. Hydrogel beads based on amidated pectins for colon-specific drug delivery: the role of chitosan in modifying drug release. *Journal of Controlled Release* 46 (1997): 273-278.
- (27) Stanley, P. H., Davis, S., and Illum, L. In vitro evaluation of the mucoadhesive properties of chitosan microspheres. *International Journal of Pharmaceutics* 166 (1998): 75-88.
- (28) Muzzarelli, R. A. Chitosan-based dietary foods. *Carbohydrate Polymers* 29 (1996): 306-316.

- (29) Zhu, Z., Xiong, C., Zhang, L., Yuan, M., Deng, X. Preparation of biodegradable polylactide-co-poly(ethylene glycol) copolymer by lactide reacted poly(ethylene glycol). European Polymer Journal 35, 10 (1999) 1821-1828.
- (30) Sallmann, A. R. The history of diclofenac. The American Journal of Medicine 80 (1986): 29-33.
- (31) Lund, W. The pharmaceutical codex priciples and pratice of pharmaceutics. 12th ed. London: The pharmaceutical press, 1994.
- (32) Samani, S.M., Montaseri, H., and Kazemi, A. The effect of polymer blends on release profiles of diclofenac sodium from matrics. European Journal of Pharmaceutics and Biopharmaceutics 55 (2003) : 351-355.
- (33) Shu, X. Z., and Zhu, K. J. A novel approach to prepare tripolyphosphate/chitosan complex beads for controlled release drug delivery. International Journal of Pharmaceutics 201 (2000): 51-58.
- (34) Shu, X. Z., and Zhu, K. J. Controlled drug release properties of ionically cross-linked chitosan beads: influence of anion structure International Journal of Pharmaceutics 233 (2002): 217-225.
- (35) Shu, X. Z., and Zhu, K. J. The influence of multivalent phosphate structure on the properties of ionically cross-linked chitosan films for controlled drug release. European Journal of Pharmaceutics and Biopharmaceutics 54 (2002): 235–243.
- (36) Bhumkar, D.R., and Pokharkar, V.B. Studies on effect of pH on cross-linking of chitosan with sodium tripolyphosphate : A technical note. American Association of Pharmaceutical Scientists 7 (2) (2006) Article 50.
- (37) Alsarra, I.A., Neau, S.H., and Howard, M.A. Effect of preparative parameters on the properties of chitosan hydrogel beads containing *Candida rugosa* lipase. Biomaterials 25 (2004): 2645-2655.

- (38) Ko, J.A.; Park, H.J., Hwang, S.J., Park, J.B., and Lee, J.S. Preparation and characterization of chitosan microparticles intended for controlled drug delivery. International Journal of Pharmaceutics 249 (2002) : 165-174.

APPENDICES

APPENDIX A

Calibration Curve of Sodium Diclofenac

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 7.4, NaOH solution 5% (w/v), sodium tripolyphosphate 1-10% (w/v) at 276 nm. are presented in tables xxx. The standard curves of sodium diclofenac in these solution media are illustrated in Figure xxxx

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

Concentration (ppm)	Absorbance
2	0.050
4	0.108
6	0.163
8	0.214
10	0.266

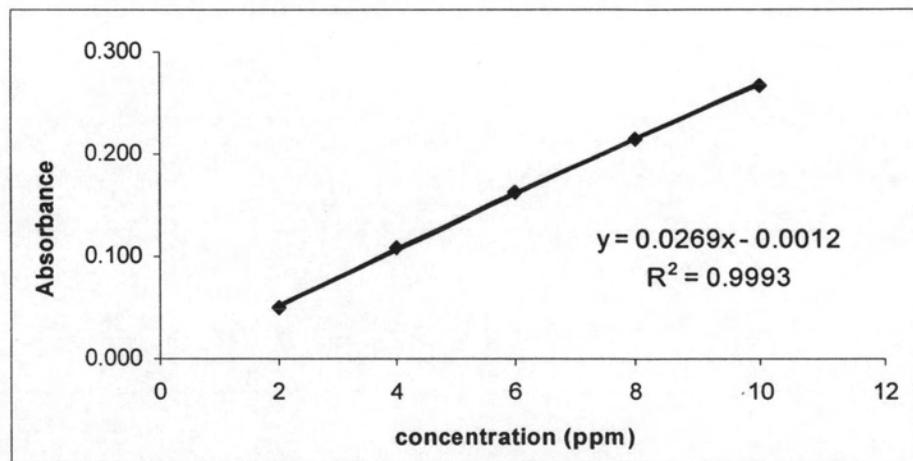


Figure A10 Calibration curve of sodium diclofenac drug in 0.1 N of HCl at 276 nm.

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

Concentration (ppm)	Absorbance
5	0.159
10	0.314
25	0.763
50	1.528
100	3.110

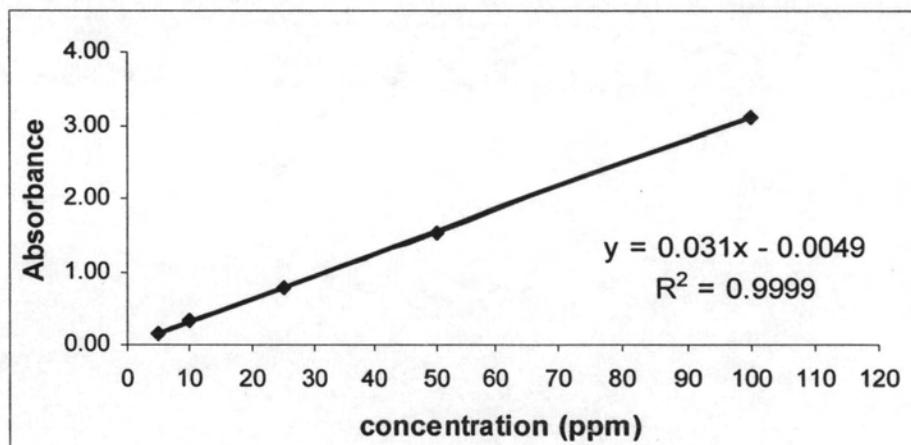


Figure A11 Calibration curve of Sodium diclofenac drug in phosphate buffer saline pH 6.6 at 276 nm.

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

Concentration (ppm)	Absorbance
5	0.165
10	0.329
15	0.487
20	0.638
25	0.793
30	0.958

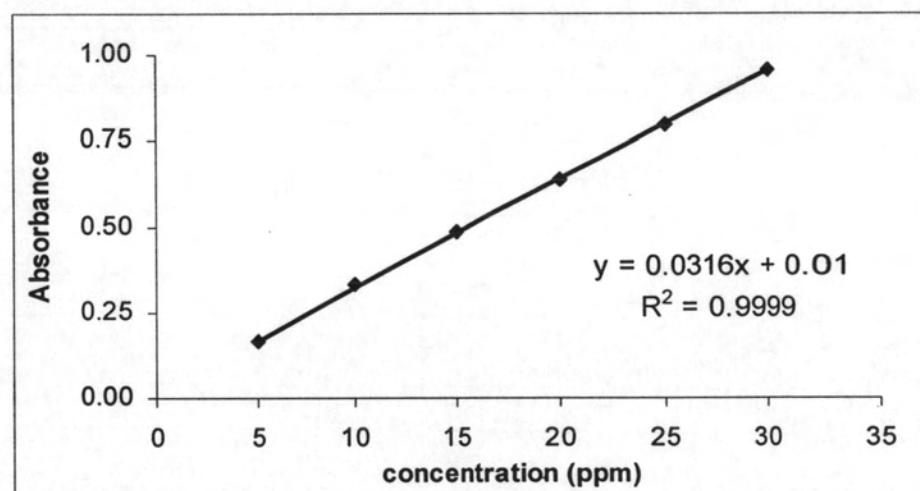


Figure A12 Calibration curve of Sodium diclofenac drug in phosphate buffer saline pH 7.4 at 276 nm.

Table A4 Absorbance of sodium diclofenac drug in 1.0% sodium tripolyphosphate solution determined at 276 nm.

Concentration (ppm)	Absorbance
2.5	0.088
5	0.166
10	0.324
15	0.481
20	0.638
25	0.791
50	1.582

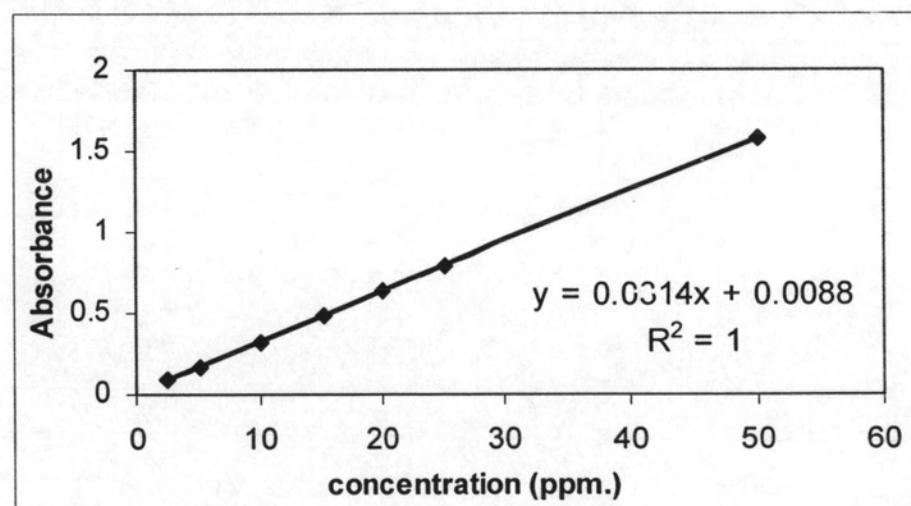


Figure A13 Calibration curve of Sodium diclofenac drug in 1.0% (w/v) sodium tripolyphosphate solution at 276 nm.

Table A5 Absorbance of sodium diclofenac drug in 5.0% sodium tripolyphosphate solution determined at 276 nm.

Concentration (ppm)	Absorbance
2.5	0.1
5	0.163
10	0.321
15	0.48
20	0.636
25	0.791
50	1.571

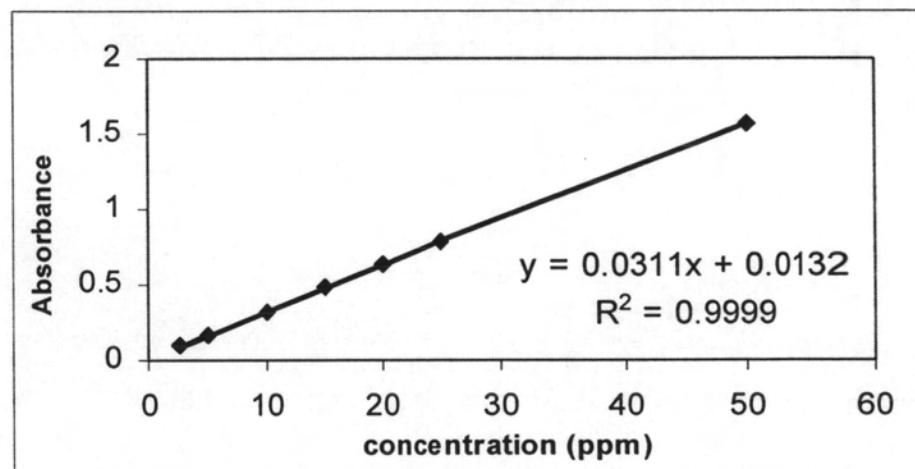


Figure A14 Calibration curve of Sodium diclofenac drug in 5.0% (w/v) sodium tripolyphosphate solution at 276 nm.

Table A6 Absorbance of sodium diclofenac drug in 10.0% sodium tripolyphosphate solution determined at 276 nm.

Concentration (ppm)	Absorbance
2.5	0.077
5	0.15
10	0.307
15	0.455
20	0.609
25	0.767
50	1.547

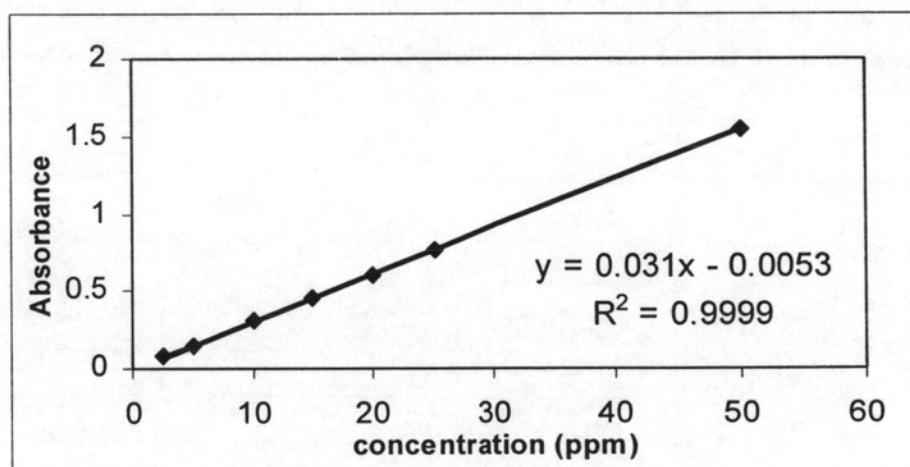
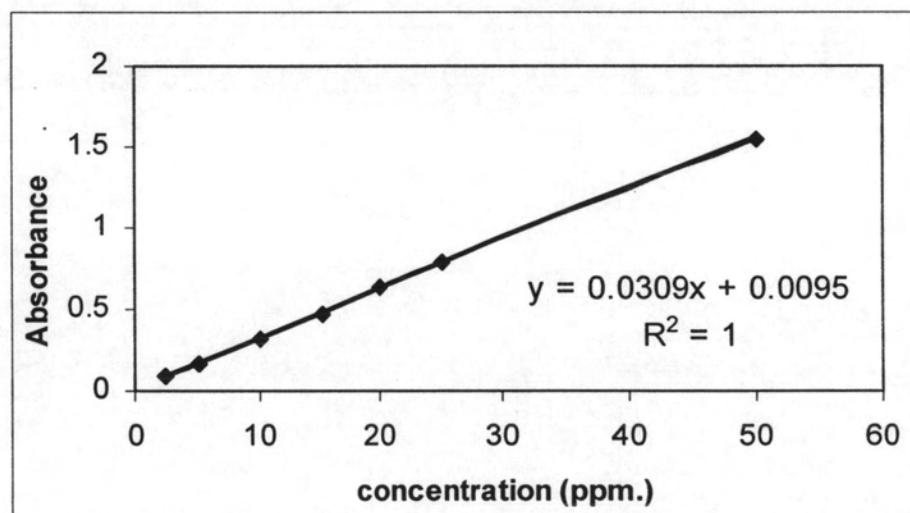


Figure A15 Calibration curve of Sodium diclofenac drug in 10.0% (w/v) sodium tripolyphosphate solution at 276 nm.

Table A7 Absorbance of sodium diclofenac drug in D.I. water determined at 276 nm.

Concentration (ppm)	Absorbance
2.5	0.084
5	0.163
10	0.317
15	0.477
20	0.63
25	0.782
50	1.552

**Figure A16** Calibration curve of Sodium diclofenac drug in D.I. water at 276 nm.

APPENDIX B

Swelling Ratio

Table B1 The swelling percent of chitosan bead in 0.1 N HCl (pH 1.2)

Time (hour)	Subsyde CR	Formulation A0	Formulation A1	Formulation B	Formulation C
	Swelling ratio ± S.D.				
0	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00
1	1.13 ± 0.02	*0.79 ± 0.05	1.20 ± 0.12	1.03 ± 0.05	1.38 ± 0.05
2	1.15 ± 0.02	-	1.23 ± 0.09	1.02 ± 0.08	1.60 ± 0.08
3	1.15 ± 0.02	-	-	0.99 ± 0.07	1.65 ± 0.07
4	1.17 ± 0.02	-	-	-	1.83 ± 0.08
5	1.18 ± 0.02	-	-	-	1.94 ± 0.11
6	1.18 ± 0.01	-	-	-	2.04 ± 0.08
24	1.28 ± 0.04	-	-	-	2.11 ± 0.07

* detected at 30 minute before beads erosions.

- The erosion of beads was happened.

Table B1 (continued) The swelling percent of chitosan bead in 0.1 N HCl (pH 1.2)

Time (hour)	Formulation D	Formulation E	Formulation F	Formulation G	Formulation H
	Swelling ratio ± S.D.				
0	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00
1	1.94 ± 0.12	1.35 ± 0.13	1.67 ± 0.08	1.33 ± 0.04	1.22 ± 0.12
2	2.07 ± 0.15	1.53 ± 0.12	2.03 ± 0.29	1.49 ± 0.07	1.29 ± 0.13
3	2.19 ± 0.15	1.67 ± 0.19	2.02 ± 0.05	1.64 ± 0.11	1.42 ± 0.16
4	2.23 ± 0.16	1.90 ± 0.22	2.12 ± 0.05	1.84 ± 0.09	1.56 ± 0.19
5	2.14 ± 0.17	2.04 ± 0.22	2.33 ± 0.08	2.03 ± 0.10	1.62 ± 0.21
6	2.13 ± 0.27	2.12 ± 0.21	2.41 ± 0.03	2.14 ± 0.04	1.68 ± 0.13
24	2.21 ± 0.30	2.17 ± 0.22	2.72 ± 0.27	2.18 ± 0.03	1.72 ± 0.07

* Detected at 30 minute before beads erosions.

- The erosion of beads was happened.

Table B1 (continued) The swelling percent of chitosan bead in 0.1 N HCl (pH 1.2)

Time (hour)	Formulation J	Formulation K	Formulation L	Formulation M
	Swelling ratio ± S.D.			
0	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00
1	1.19 ± 0.10	1.18 ± 0.07	1.23 ± 0.02	1.07 ± 0.03
2	1.27 ± 0.08	1.23 ± 0.06	1.25 ± 0.04	1.11 ± 0.04
3	1.29 ± 0.08	1.28 ± 0.04	1.23 ± 0.04	1.16 ± 0.06
4	1.38 ± 0.12	1.35 ± 0.04	1.25 ± 0.03	1.21 ± 0.03
5	1.42 ± 0.13	1.39 ± 0.05	1.2 ± 0.21	1.23 ± 0.03
6	1.47 ± 0.15	1.49 ± 0.01	1.35 ± 0.09	1.34 ± 0.08
24	2.00 ± 0.14	1.92 ± 0.12	1.74 ± 0.07	1.8 ± 0.10

Table B1 (continued) The swelling percent of chitosan bead in 0.1 N HCl (pH 1.2)

Time (hour)	Formulation N	Formulation O	Formulation P	Formulation Q
	Swelling ratio ± S.D.			
0	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00
1	1.23 ± 0.07	1.23 ± 0.03	1.23 ± 0.02	1.07 ± 0.03
2	1.31 ± 0.07	1.30 ± 0.02	1.25 ± 0.04	1.11 ± 0.04
3	1.35 ± 0.09	1.37 ± 0.01	1.23 ± 0.04	1.16 ± 0.06
4	1.40 ± 0.09	1.40 ± 0.03	1.25 ± 0.03	1.21 ± 0.03
5	1.48 ± 0.11	1.48 ± 0.02	1.20 ± 0.21	1.23 ± 0.03
6	1.63 ± 0.24	1.65 ± 0.12	1.35 ± 0.09	1.34 ± 0.08
24	2.30 ± 0.24	2.29 ± 0.16	1.74 ± 0.07	1.80 ± 0.10

Table B1 (continued) The swelling percent of chitosan bead in 0.1 N HCl (pH 1.2)

Time (hour)	Formulation PEG2	Formulation PEG3	Formulation PEG4	Formulation PEG6	Formulation PEG7
	Swelling ratio ± S.D.				
0	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00
1	1.29 ± 0.01	1.36 ± 0.11	1.41 ± 0.01	1.19 ± 0.04	1.05 ± 0.02
2	1.49 ± 0.02	1.50 ± 0.11	1.51 ± 0.05	1.29 ± 0.04	1.13 ± 0.04
3	1.69 ± 0.07	1.60 ± 0.16	1.62 ± 0.06	1.36 ± 0.04	1.26 ± 0.05
4	1.92 ± 0.09	1.69 ± 0.13	1.77 ± 0.09	1.44 ± 0.05	1.34 ± 0.03
5	1.90 ± 0.12	1.77 ± 0.14	1.94 ± 0.11	1.49 ± 0.04	1.40 ± 0.05
6	1.87 ± 0.15	1.80 ± 0.17	2.13 ± 0.14	1.36 ± 0.30	1.12 ± 0.08
24	-	-	-	-	-

Table B2 The swelling ratios of chitosan bead in Phosphate buffer saline (pH 7.4)

Time (hour)	Subsyde CR	Formulation A0	Formulation A1	Formulation B	Formulation C
	Swelling ratio ± S.D.				
0	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00
1	1.13 ± 0.02	1.03 ± 0.05	1.03 ± 0.07	1.08 ± 0.03	1.08 ± 0.05
2	1.15 ± 0.02	1.03 ± 0.02	1.02 ± 0.04	1.03 ± 0.04	1.08 ± 0.08
3	1.15 ± 0.02	1.06 ± 0.01	0.99 ± 0.06	1.01 ± 0.02	1.09 ± 0.07
4	1.17 ± 0.02	1.07 ± 0.03	1.00 ± 0.04	1.01 ± 0.04	1.07 ± 0.08
5	1.18 ± 0.02	1.07 ± 0.03	1.00 ± 0.06	0.90 ± 0.03	1.08 ± 0.28
6	1.18 ± 0.01	1.08 ± 0.01	1.00 ± 0.05	0.94 ± 0.04	1.09 ± 0.05
24	1.28 ± 0.04	1.08 ± 0.04	1.01 ± 0.04	0.94 ± 0.02	1.07 ± 0.03

Table B2 (continued) The swelling ratios of chitosan bead in Phosphate buffer saline (pH 7.4)

Time (hour)	Formulation D	Formulation E	Formulation F	Formulation G	Formulation H
	Swelling ratio ± S.D.				
0	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00
1	1.08 ± 0.06	1.02 ± 0.01	1.07 ± 0.07	1.10 ± 4.36	1.03 ± 0.02
2	1.06 ± 0.03	1.04 ± 0.04	1.07 ± 0.05	1.10 ± 5.79	1.02 ± 0.02
3	1.08 ± 0.04	1.06 ± 0.04	1.08 ± 0.07	1.10 ± 5.43	1.02 ± 0.02
4	1.06 ± 0.04	1.05 ± 0.02	1.08 ± 0.06	1.10 ± 7.44	1.03 ± 0.02
5	1.07 ± 0.03	1.06 ± 0.02	1.07 ± 0.06	1.11 ± 7.57	1.02 ± 0.03
6	1.08 ± 0.02	1.06 ± 0.04	1.08 ± 0.06	1.11 ± 7.06	1.04 ± 0.03
24	1.06 ± 0.03	1.05 ± 0.06	1.05 ± 0.04	1.09 ± 7.38	1.03 ± 0.03

Table B2 (continued) The swelling ratios of chitosan bead in Phosphate buffer saline (pH 7.4)

Time (hour)	Formulation J	Formulation K	Formulation L	Formulation M
	Swelling ratio ± S.D.			
0	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00
1	0.97 ± 0.01	0.85 ± 0.05	1.02 ± 0.02	0.88 ± 0.03
2	0.96 ± 0.04	0.85 ± 0.06	1.00 ± 0.04	0.88 ± 0.04
3	0.91 ± 0.04	0.84 ± 0.04	1.00 ± 0.04	0.89 ± 0.03
4	0.94 ± 0.06	0.79 ± 0.04	0.99 ± 0.03	0.90 ± 0.03
5	0.94 ± 0.01	0.79 ± 0.05	1.02 ± 0.02	0.90 ± 0.03
6	0.94 ± 0.01	0.79 ± 0.02	1.00 ± 0.05	0.90 ± 0.04
24	0.94 ± 0.03	0.79 ± 0.02	0.96 ± 0.06	0.88 ± 0.03

Table B2 (continued) The swelling ratios of chitosan bead in Phosphate buffer saline (pH 7.4)

Time (hour)	Formulation N	Formulation O	Formulation P	Formulation Q
	Swelling ratio ± S.D.			
0	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00
1	1.01 ± 0.03	1.01 ± 0.03	1.00 ± 0.02	1.04 ± 0.02
2	1.01 ± 0.04	1.02 ± 0.04	1.01 ± 0.03	1.04 ± 0.03
3	1.00 ± 0.03	1.02 ± 0.01	1.01 ± 0.02	1.03 ± 0.02
4	0.99 ± 0.01	0.99 ± 0.02	1.01 ± 0.03	1.03 ± 0.03
5	0.99 ± 0.02	0.99 ± 0.01	1.01 ± 0.02	1.02 ± 0.02
6	0.99 ± 0.03	0.97 ± 0.02	1.01 ± 0.03	1.02 ± 0.03
24	0.98 ± 0.04	0.96 ± 0.04	1.01 ± 0.03	1.03 ± 0.04

Table B2 (continued) The swelling ratios of chitosan bead in Phosphate buffer saline (pH 7.4)

Time (hour)	Formulation PEG2	Formulation PEG3	Formulation PEG4	Formulation PEG6	Formulation PEG7
	Swelling ratio ± S.D.				
0	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00
1	1.01 ± 0.01	1.01 ± 0.03	1.01 ± 0.02	1.01 ± 0.02	1.03 ± 0.02
2	1.01 ± 0.02	0.99 ± 0.01	1.01 ± 0.01	1.02 ± 0.03	1.04 ± 0.01
3	0.99 ± 0.01	0.99 ± 0.02	0.99 ± 0.01	1.01 ± 0.03	1.02 ± 0.02
4	0.99 ± 0.01	0.99 ± 0.02	0.99 ± 0.03	0.99 ± 0.02	1.02 ± 0.03
5	0.98 ± 0.02	0.98 ± 0.04	0.97 ± 0.01	0.98 ± 0.02	1.01 ± 0.01
6	0.98 ± 0.02	0.97 ± 0.02	0.96 ± 0.01	0.97 ± 0.03	1.03 ± 0.04
24	0.98 ± 0.02	0.96 ± 0.02	0.97 ± 0.03	0.97 ± 0.03	1.01 ± 0.02

APPENDIX C

Percentage of Drug release

Table C1 Percentage of DFNa release from commercial products and the beads from formulation A-GD7.5 in pH-alternating method

Time (hr:min)	Subsyde® CR capsule	Voltaren tablet	Voltaren SR tablet
	% 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
0:40	0.55 ± 0.34	0.16 ± 0.13	0.18 ± 0.02
1:20	0.69 ± 0.30	0.16 ± 0.15	0.19 ± 0.02
2:00	0.75 ± 0.06	0.08 ± 0.06	0.25 ± 0.06
2:15	1.78 ± 0.25	0.27 ± 0.11	0.99 ± 0.11
2:30	4.75 ± 0.52	0.31 ± 0.36	1.03 ± 0.16
2:45	11.05 ± 0.56	0.34 ± 0.23	1.10 ± 0.13
3:00	15.20 ± 0.75	0.38 ± 0.34	1.61 ± 0.15
3:15	23.60 ± 0.84	5.22 ± 0.81	6.91 ± 0.22
3:30	32.84 ± 0.61	39.09 ± 0.53	7.72 ± 0.45
3:45	40.98 ± 0.72	97.32 ± 0.88	8.97 ± 0.11
4:00	47.69 ± 0.91	93.63 ± 0.62	10.69 ± 0.42
4:30	67.31 ± 1.68	94.96 ± 1.33	22.41 ± 0.76
5:00	77.55 ± 1.44	97.26 ± 1.12	28.54 ± 1.02
5:30	85.89 ± 0.88	97.80 ± 0.55	35.30 ± 0.76
6:00	89.36 ± 1.35	98.51 ± 1.41	45.33 ± 0.37
6:30	91.06 ± 1.19	99.37 ± 1.21	52.68 ± 1.58
7:00	92.14 ± 1.71	99.44 ± 1.44	61.21 ± 2.14
7:30	95.52 ± 1.46	98.54 ± 1.51	62.57 ± 1.33
8:00	93.40 ± 1.11	98.92 ± 1.11	62.81 ± 1.79
24:00	94.97 ± 1.03	98.98 ± 1.25	85.56 ± 1.36

Table C1 Percentage of DFNa release from commercial products and the beads from formulation A-GD7.5 in pH-alternating method

Time (hr:min)	Formulation A1		Formulation C		Formulation D	
	% drug release ± S.D.					
0:00	0.00 ± 0.00		0.00 ± 0.00		0.00 ± 0.00	
0:40	5.03 ± 0.49		3.31 ± 0.48		1.63 ± 0.17	
1:20	5.49 ± 0.52		3.70 ± 0.58		1.60 ± 0.31	
2:00	5.45 ± 0.69		4.56 ± 0.69		2.28 ± 0.15	
2:15	18.04 ± 4.73		7.51 ± 1.06		4.18 ± 0.11	
2:30	18.52 ± 7.67		7.91 ± 1.12		4.26 ± 0.18	
2:45	20.81 ± 7.66		7.91 ± 1.20		4.33 ± 0.19	
3:00	22.05 ± 7.18		8.12 ± 1.26		4.45 ± 0.12	
3:15	33.55 ± 5.13		25.01 ± 2.78		17.56 ± 0.31	
3:30	34.42 ± 4.03		33.54 ± 2.54		26.80 ± 0.58	
3:45	34.67 ± 3.98		37.20 ± 1.05		33.01 ± 1.90	
4:00	35.14 ± 4.01		40.83 ± 2.87		36.41 ± 0.75	
4:30	35.40 ± 4.18		42.64 ± 4.84		40.55 ± 0.47	
5:00	36.40 ± 3.34		44.02 ± 5.93		43.01 ± 0.07	
5:30	37.16 ± 4.30		44.30 ± 6.26		44.74 ± 0.01	
6:00	36.78 ± 3.08		45.02 ± 6.59		46.09 ± 1.43	
6:30	35.25 ± 3.29		45.33 ± 6.61		47.73 ± 2.26	
7:00	35.32 ± 3.39		45.77 ± 6.85		48.50 ± 2.30	
7:30	35.51 ± 3.67		46.00 ± 7.37		49.20 ± 3.17	
8:00	35.86 ± 4.18		46.77 ± 7.47		49.97 ± 3.14	
24:00	34.93 ± 3.24		46.83 ± 7.74		50.72 ± 4.23	

Table C1 (continued) Percentage of DFNa release from commercial products and the beads from formulation A-GD7.5 in pH-alternating method

Time (hr:min)	Formulation E		Formulation F		Formulation G		Formulation H	
	% drug release ± S.D.							
0:00	0.00 ± 0.00		0.00 ± 0.00		0.00 ± 0.00		0.00 ± 0.00	
0:40	2.51 ± 0.49		1.60 ± 0.46		1.58 ± 0.13		1.27 ± 0.00	
1:20	2.71 ± 0.53		1.66 ± 0.63		1.88 ± 0.10		1.13 ± 0.22	
2:00	3.14 ± 0.60		2.11 ± 0.46		2.09 ± 0.17		1.60 ± 0.03	
2:15	5.13 ± 0.98		3.48 ± 0.44		3.51 ± 0.27		2.97 ± 0.16	
2:30	5.25 ± 0.99		3.53 ± 0.51		3.51 ± 0.19		3.12 ± 0.32	
2:45	5.35 ± 1.07		3.56 ± 0.54		3.56 ± 0.18		3.17 ± 0.32	
3:00	5.40 ± 1.12		3.65 ± 0.62		3.63 ± 0.15		3.27 ± 0.30	
3:15	18.62 ± 7.18		15.21 ± 0.87		11.19 ± 2.94		11.36 ± 2.20	
3:30	27.80 ± 6.94		21.52 ± 1.38		15.89 ± 3.96		14.80 ± 1.84	
3:45	32.25 ± 8.41		24.54 ± 4.03		19.97 ± 4.30		17.82 ± 1.29	
4:00	34.56 ± 8.56		27.18 ± 5.03		22.53 ± 4.42		19.48 ± 1.71	
4:30	38.79 ± 10.37		29.75 ± 2.72		26.30 ± 5.06		23.04 ± 0.90	
5:00	41.06 ± 11.65		30.82 ± 7.19		29.31 ± 5.45		25.51 ± 0.08	
5:30	42.62 ± 12.27		31.46 ± 7.56		30.99 ± 5.88		27.24 ± 0.70	
6:00	43.53 ± 12.87		31.89 ± 7.87		33.33 ± 6.70		28.85 ± 0.32	
6:30	43.87 ± 13.19		32.38 ± 7.92		34.45 ± 6.67		29.95 ± 0.11	
7:00	44.54 ± 13.47		31.97 ± 7.02		35.29 ± 6.91		31.28 ± 0.11	
7:30	45.02 ± 13.75		32.94 ± 8.56		36.35 ± 7.41		32.25 ± 0.45	
8:00	45.34 ± 14.02		33.15 ± 8.68		37.31 ± 7.75		32.70 ± 0.69	
24:00	45.48 ± 13.69		32.80 ± 8.58		42.12 ± 10.54		36.51 ± 2.66	

Table C1 (continued) Percentage of DFNa release from commercial products and the beads from formulation A-GD7.5 in pH-alternating method

Time (hr:min)	Formulation J	Formulation K	Formulation L	Formulation M
	% drug release ± S.D.			
0:00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
0:40	2.64 ± 0.51	4.12 ± 0.59	1.30 ± 0.75	2.49 ± 1.04
1:20	3.28 ± 0.67	4.27 ± 0.62	2.41 ± 1.09	3.00 ± 1.29
2:00	4.67 ± 1.17	4.98 ± 0.26	3.30 ± 1.30	3.80 ± 0.97
2:15	6.94 ± 1.38	8.16 ± 0.30	5.09 ± 1.75	4.49 ± 1.10
2:30	7.21 ± 1.36	8.54 ± 0.33	6.15 ± 1.57	4.77 ± 1.09
2:45	7.31 ± 1.12	9.03 ± 0.44	6.41 ± 1.76	5.04 ± 1.10
3:00	7.29 ± 1.29	9.57 ± 0.63	7.18 ± 1.89	5.14 ± 1.08
3:15	45.52 ± 8.54	41.08 ± 9.56	36.91 ± 4.92	5.22 ± 1.16
3:30	58.23 ± 5.45	65.86 ± 10.54	49.97 ± 5.47	7.72 ± 1.59
3:45	65.75 ± 2.33	75.00 ± 3.97	60.82 ± 2.69	10.79 ± 2.30
4:00	69.81 ± 4.32	81.62 ± 1.88	65.15 ± 5.78	13.70 ± 3.16
4:30	72.86 ± 3.12	86.26 ± 4.87	71.11 ± 4.81	18.13 ± 5.42
5:00	72.97 ± 2.69	91.10 ± 4.20	80.27 ± 3.58	24.11 ± 6.19
5:30	73.98 ± 3.35	92.49 ± 3.84	81.94 ± 3.05	30.05 ± 6.86
6:00	74.79 ± 3.38	94.87 ± 4.29	85.12 ± 2.08	34.85 ± 8.30
6:30	74.89 ± 3.24	94.82 ± 4.36	86.57 ± 1.88	39.38 ± 10.42
7:00	75.85 ± 2.99	96.02 ± 4.31	87.86 ± 1.12	42.37 ± 10.70
7:30	75.99 ± 2.98	96.27 ± 4.44	90.38 ± 0.94	45.75 ± 10.95
8:00	76.48 ± 3.76	96.89 ± 5.19	91.69 ± 1.13	50.38 ± 11.89
24:00	76.40 ± 3.49	97.08 ± 4.52	95.52 ± 3.23	73.28 ± 10.40

Table C1 (continued) Percentage of DFNa release from commercial products and the beads from formulation A-GD7.5 in pH-alternating method

Time (hr:min)	Formulation N	Formulation O	Formulation P	Formulation Q
	% drug release ± S.D.			
0:00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
0:40	1.14 ± 0.28	1.49 ± 0.57	0.75 ± 0.14	2.35 ± 0.36
1:20	1.47 ± 0.55	1.88 ± 0.58	1.32 ± 0.33	2.51 ± 0.36
2:00	2.16 ± 0.16	3.14 ± 0.57	1.85 ± 0.45	2.75 ± 0.24
2:15	3.25 ± 0.37	4.15 ± 0.69	3.16 ± 1.39	3.69 ± 0.46
2:30	4.00 ± 0.43	4.68 ± 0.60	3.24 ± 1.27	4.01 ± 0.34
2:45	4.40 ± 0.37	5.00 ± 0.63	3.61 ± 1.25	4.31 ± 0.41
3:00	4.83 ± 0.25	5.51 ± 0.60	3.82 ± 1.29	4.51 ± 0.41
3:15	49.61 ± 12.06	37.49 ± 15.74	29.68 ± 6.64	36.63 ± 5.08
3:30	59.91 ± 11.94	45.95 ± 11.45	46.07 ± 6.18	38.28 ± 1.95
3:45	67.17 ± 13.11	55.38 ± 12.73	55.74 ± 4.98	42.42 ± 0.72
4:00	72.95 ± 10.17	66.48 ± 13.77	61.90 ± 6.44	44.15 ± 0.38
4:30	76.38 ± 7.76	75.10 ± 10.40	69.99 ± 5.96	44.94 ± 0.90
5:00	81.58 ± 5.25	80.40 ± 9.20	75.80 ± 6.14	46.27 ± 1.71
5:30	83.46 ± 5.09	84.84 ± 9.00	79.21 ± 4.45	46.17 ± 1.27
6:00	85.47 ± 4.71	87.08 ± 8.86	80.94 ± 4.25	45.80 ± 1.49
6:30	87.85 ± 4.41	89.61 ± 8.01	83.66 ± 3.66	46.23 ± 1.04
7:00	90.01 ± 5.03	91.93 ± 7.93	84.89 ± 4.43	45.54 ± 1.56
7:30	89.77 ± 3.30	95.02 ± 6.13	83.60 ± 5.14	45.37 ± 1.64
8:00	91.53 ± 2.07	96.62 ± 7.55	85.34 ± 6.13	46.26 ± 2.31
24:00	93.41 ± 0.79	99.79 ± 6.05	88.39 ± 8.26	45.40 ± 1.12

Table C1 (continued) Percentage of DFNa release from commercial products and the beads from formulation A-GD7.5 in pH-alternating method

Time (hr:min)	Formulation PEG1	Formulation PEG2	Formulation PEG3	Formulation PEG4
	% drug release ± S.D.			
0:00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
0:40	1.42 ± 0.21	0.04 ± 0.08	0.43 ± 0.28	2.44 ± 1.38
1:20	2.40 ± 0.38	0.13 ± 0.23	1.21 ± 0.36	3.69 ± 2.05
2:00	2.22 ± 0.11	0.45 ± 0.28	1.11 ± 0.46	3.97 ± 2.74
2:15	3.35 ± 0.11	0.03 ± 0.10	1.85 ± 0.68	6.08 ± 3.18
2:30	3.69 ± 0.17	0.29 ± 0.12	2.22 ± 0.81	6.54 ± 3.19
2:45	3.82 ± 0.12	0.60 ± 0.08	2.62 ± 0.65	6.65 ± 3.15
3:00	3.94 ± 0.14	1.46 ± 0.08	2.99 ± 0.91	7.01 ± 3.20
3:15	14.58 ± 3.04	21.96 ± 4.88	18.91 ± 7.67	29.88 ± 8.17
3:30	20.64 ± 2.22	37.67 ± 7.29	31.68 ± 9.73	31.08 ± 9.23
3:45	31.38 ± 4.75	46.15 ± 9.48	42.13 ± 8.89	34.17 ± 9.15
4:00	38.21 ± 2.73	50.96 ± 8.25	48.32 ± 10.67	35.82 ± 9.89
4:30	42.25 ± 1.13	59.56 ± 5.46	51.95 ± 6.72	35.21 ± 11.66
5:00	50.92 ± 1.83	66.56 ± 4.19	57.22 ± 8.31	35.63 ± 11.61
5:30	55.58 ± 0.90	73.08 ± 2.57	61.38 ± 7.37	36.01 ± 11.25
6:00	61.48 ± 2.17	75.20 ± 2.71	64.69 ± 4.46	36.67 ± 11.56
6:30	60.38 ± 2.47	78.12 ± 5.40	73.25 ± 3.83	35.72 ± 11.72
7:00	63.22 ± 2.27	80.07 ± 3.94	77.14 ± 3.55	35.60 ± 12.15
7:30	64.74 ± 1.85	80.68 ± 3.40	77.86 ± 3.28	35.56 ± 11.91
8:00	66.66 ± 2.21	84.57 ± 7.19	79.64 ± 2.74	35.10 ± 12.05
24:00	74.19 ± 10.87	92.66 ± 0.62	83.35 ± 5.36	35.10 ± 12.39

Table C1 (continued) Percentage of DFNa release from commercial products and the beads from formulation A-GD7.5in pH-alternating method

Time (hr:min)	Formulation PEG5	Formulation PEG6	Formulation PEG7
	% 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
0:40	2.61 ± 0.47	0.26 ± 0.54	1.25 ± 0.21
1:20	4.35 ± 0.26	0.70 ± 0.40	1.51 ± 0.20
2:00	3.10 ± 0.22	0.83 ± 0.43	1.24 ± 0.30
2:15	7.64 ± 0.96	1.17 ± 0.77	2.29 ± 0.37
2:30	7.73 ± 0.97	1.37 ± 0.79	2.46 ± 0.34
2:45	8.08 ± 0.52	1.55 ± 0.78	2.55 ± 0.33
3:00	8.31 ± 0.55	1.99 ± 0.78	2.54 ± 0.32
3:15	28.30 ± 4.77	25.11 ± 5.74	20.99 ± 3.78
3:30	45.40 ± 4.34	32.61 ± 3.80	31.58 ± 3.79
3:45	50.01 ± 3.17	40.39 ± 3.71	36.22 ± 4.38
4:00	55.99 ± 9.61	44.71 ± 1.83	42.78 ± 3.81
4:30	58.12 ± 5.90	51.46 ± 4.60	49.64 ± 4.14
5:00	62.11 ± 2.40	58.54 ± 2.02	57.10 ± 3.11
5:30	63.33 ± 3.01	60.82 ± 2.93	59.67 ± 2.96
6:00	65.91 ± 2.51	64.26 ± 3.57	61.90 ± 2.98
6:30	64.79 ± 3.46	66.70 ± 3.22	63.91 ± 3.30
7:00	64.17 ± 3.23	69.15 ± 3.85	66.26 ± 2.03
7:30	66.07 ± 6.92	68.28 ± 7.04	68.08 ± 2.20
8:00	62.42 ± 3.83	69.97 ± 7.97	68.10 ± 2.18
24:00	63.30 ± 4.49	80.79 ± 4.38	75.45 ± 3.26

Table C1 (continued) Percentage of DFNa release from commercial products and the beads from formulation A-GD7.5 in pH-alternating method

Time (hr:min)	Formulation GD2.5%		Formulation GD5		Formulation GD7.5	
	% 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
0:40	4.10	± 1.49	4.71	± 0.46	3.49	± 0.66
1:20	5.15	± 1.45	6.03	± 1.09	4.49	± 0.61
2:00	5.57	± 1.40	6.61	± 0.30	4.67	± 0.60
2:15	6.78	± 1.66	7.90	± 0.15	5.72	± 0.76
2:30	7.01	± 1.80	8.30	± 0.60	9.47	± 3.39
2:45	7.32	± 1.94	8.43	± 0.55	6.33	± 1.07
3:00	7.63	± 1.90	8.73	± 0.45	6.68	± 0.93
3:15	16.38	± 3.96	13.21	± 0.73	12.72	± 0.17
3:30	29.67	± 3.04	24.75	± 1.93	26.17	± 2.08
3:45	38.82	± 2.52	32.36	± 2.01	32.85	± 3.48
4:00	46.67	± 2.90	41.04	± 2.80	39.77	± 3.89
4:30	55.69	± 2.27	48.92	± 1.75	47.26	± 3.62
5:00	60.28	± 1.17	50.76	± 2.65	51.97	± 1.76
5:30	68.59	± 2.27	61.61	± 2.07	61.02	± 2.83
6:00	76.75	± 1.03	69.57	± 2.68	69.46	± 2.33
6:30	83.42	± 1.05	73.68	± 1.36	74.69	± 1.43
7:00	86.29	± 1.17	78.76	± 2.86	77.77	± 1.61
7:30	89.27	± 1.42	81.75	± 1.32	81.94	± 1.62
8:00	91.31	± 0.33	83.61	± 1.47	82.78	± 0.37
24:00	99.83	± 1.10	99.61	± 0.60	97.14	± 0.97

VITA

Name : Miss Thawachinee Buranachai
Date of Birth : March 16, 1982
Nationality : Thai
Address : 59/253, Rama VI Rd., Samsein nai, Payatai,
Bangkok, Thailand 10400
University Education : Bachelor's Degree from Department of Chemistry,
Faculty of Science, Chulalongkorn University in year
2000-2004
Master's Degree from Science Program in
Petrochemistry and Polymer Science, Chulalongkorn
University in year 2004-2007
Conference attendance : Poster presentation at 10th International Conference
on Chitin and Chitosan (10th I.C.C.C.) and 7th
International Conference of the European Chitin
Society EUCHIS'06 in Montpellier, France in year
2006