REFERENCES

Adam, S. J., Cooke, E. M., and Cunliffe, W. J. The use of oral and topical antibiotics in acne. J. Antimicrob. Chemother., 7 (1981) (Suppl A) : 75

Adams, I., and Davis, S. S.The formulation and sterilization of a surgical lubricant gel based on carboxypolymethylene. J. Pharm. Pharmcol., 25 (1973) : 640-646.

Algra, R.J., Rosen, T., and Waisman, M. Topical clindamycin in acne vulgaris. Arch. Dermatol. 113 (1977) : 1390-1391.

Babar, A., Bhandari, R. D., and Plakogiannis, F.M. In-vitro release studies of chlorpheniramine maleate from topical bases using cellulose membrane and hairless mouse skin. Drug Dev. Ind. Pharm. 17 (160) (1991) : 2145-2156.

_____. Solanki, U. D., Cutie, A. J., and Plakogiannis. Piroxicam release from dermatological bases : In-vitro studies using cellulose membrane and hairless mouse skin. Drug Dev. Ind. Pharm. 16 (3) (1990) : 523-540.

Barry, B. W., ed. Dermatological Formulation. New York and Basel : Mercel Dekker, Inc.,1983,49-94.

Beatrice, H.,Spang-Brunner, and Speiser, P. P. Release of a drug from Homogeneous ointments containing the drug in solution. J. Pharm.Pharmacol. 28 (1976) : 23-28.

Becker, L. E., Bergstresser, D. R., Whiling, D. A., Clendenning, W. E., Dobson, R. L., Jordan, W. P. ,Abell, E., Le Zotte, L.A., Pochi, P. E., Shipack, J. L., Sigafoe, R. B., Stoughton, R. B., and Voorhees, J. J. Topical clindamycin therapy for acne vulgaris. Arch. Dermatol. 117 (August 1981) : 482-485,

Bevan, J. A., and Thompson, J. H.,eds. Essential of Pharmacology. 3 rd ed. Philadelphia : Harper & Row, 1983, 633-634.

Billmeyer, F. W., ed. Textbook of Polymer Science. New York and London : John Wiley & Sons, 1962.

Borglund, E., Hagermark, O., Nord, C. E. Impact of topical clindamycin and systemic tetracycline on the skin and colon microflora in patient with acne vulgaris. Scand. J. Infect. Dis. Suppl 43 (1984) : 76-81.

Bottri, F., DiColo, G., Nannipier, E., Saettone, M., and Serafini. Influence of drug concentration on *in vitro* release of salicylic acid from ointment beses . J. Pharm. Sci. 63 (1974) : 1779-1881.

_____ . Release of drugs from ointment base II : *In Vitro* release of benzocaine from suspension-type aqueous gels. J. Pharm. Sci. 66 (7) (1977) : 926-931.

Braathen, L. R. Topical clindamycin versus oral tetracycline and placebo in acne vulgalis. Scand. J. Infect. Dis. Suppl. 43 (1984) : 71-75.

Brian, W. B., ed. Dermatological Formulations. New York and Bassel : Marcel Dekker, Inc., 1989, 296-354.

Bronaugh, R. L., Stewart, R. F. Method for in vitro percutaneous absorption study III : hydrophobic compound. J. Pharm. Sci. 73 (9) (1984).

Cartensen, J. T. Stability of solids and disperse systems. Drug Dev. Ind. Pharm. 10 (1984) : 1277-1296.

_____ . Drug Stability. New York : Mercel Dekker Inc., 1990.

Chen-Chow, P. C., and Frank, S. G. Comparison of lidocaine release from pluronic F-127 gels and other formulations. Acta. Pharm. Suec. 18 (1981) : 239-244.

_____ . The determination of lidocaine and benzocaine in isopropyl myristate. Int. J. Pharm. 8 (1981) : 81-87.

Chi, S. C., and Jun, H. W. Release rates of ketoprofen from poloxamer gels in a membraneless diffusion cell. J. Pharm. Sci. 80 (3) (1991) : 280-283.

Collett, D. M., and Aulton, M. E., eds. Pharmaceutical Practice. Edinburgh, London, Melbourne and New York : Churchill Livingstone, 1990.

Colo, G. D., CArelli, V., Giannaccini, B., Serafini, M.F. and Bottari, F. Vehicle effects in percutaneous absorption : In vitro study of Influence of solvent power and microscopic viscosity on benzocaine release from suspension hydrogel. J. Pharm. Sci. 69 (4) (1980) : 387-391.

Connors, K. A., Amidon, G. L., and Stella, V. J., eds. Chemical Stability of Pharmaceuticals. A Handbook for Pharmacists 2 nd ed. New York : John Wiley & Sons, 1986.

DiPiro, J. T., Talbert, R. L., Hayes, P. E., Yee, G. C.,and Posey, L. M., eds. Pharmacotherapy. A Pathophysiologic Approach. Elsevier Science Publishing : New York, Amssterdam, London, 1989, 956-961.

Fisher, A. The safety of topically applied clindamycin of acne. Cutis. 23 (1979) : 406-418.

Florey, K., ed. Analytical Profiles of Drug Substances. New York : Academic Press, 10 (1981), 75-91.

Flynn, G. L., and Yalkowsky, S.H. Correlation and prediction of mass transport across membrane. I : Influence of alkyl chain length of flux-determinaing properties of barrier and diffusant. J. pharm. Sci. 61 (1972) : 838-841.

Gilbert, J. C., Hadgraft, J., Bye, A., and Brookes, L. G. Drug release from pluronic F-127 gels. Int. J. Pharm. 40 (1986) : 101-104.

Gratton, D.,et al. Topical clindamycin versus system tetracycline in the treatment of acne. Result of multiclinic trial. J. Am. Acad. Dermatol. 7 (1) (July 1982) : 50-53.

Grayson, M., ed. Chemotherapeutics & Antibacterial Agent for Disease Control. New York : John Wiley & Sons, 1982, 149-155.

Greer, K. E., ed. Common Problems in Dermatology. Chicago and London : Year Book Medical, 1988, 1-7.

Grimm, W., ed. Stability testing of Drug Products. WissenschafHiche Verlagsgesellshaft mbH Sttugart, 1987.

Harper, C.A., ed. Handbook of Plastics and Elastomers. New York : McGraw-Hill Book Company, 1975.

Herfinaldal, E. T., Gourkey, D. R., Hart, L. L.,eds. Clinical Pharmacy and Therapeutics. 4th ed. Balltimore, Hong Kong,London and Sydney : Willians & Wilkins, 1988, 506-512.

Kabara, J. J., ed. Cosmetic and Preservation Principles and Practice. New York and Basel : Marcel Dekker, Inc, 1984, 31-62.

Katsambas, A., Towarky, A. A., and Stratigos, J. Topical clindamycin phosphate compared with oral tetracycline in the treatment of acne vulgaris. Br. J. Dermatol. 116 (3) (March 1987) :387-391.

Kostenbander, H. B., Boxenbaum, H. G., and Deluca, P.P. Nylon as a dialysis membrane. J. Pharm. Sci. 58 (6) (1969) : 753-757.

Kucers, A., ed. The Use of Antibiotics. London : William Heinemann Medical Books Ltd., 1972.

_____. and Bennett, N. Mck, eds. The Use of Antibiotics : A Comprehensive Review with Clinical Emphasis. 4 th ed. London :

William Heinemann Medical Books, 1987, 810-850

Kuhlman, D. S., and Callen, J. P. A comparison of clindamycin phosphate 1 percent topical lotion and placebo in the treatment of acne vulgaris. Cutis. 38 (3) (1986) : 203-206.

Lacina,N.C., Orr, R.J., Peters, L.S., and Flynn, G. L. Topical clindamycin for acne : art 1 : current prescribing practices. Am. Pharm. 18 (10) (1979) : 30-33.

Landis, J. B. Grant, M. E., and Nelson, S. A., Determination of clindamycin in pharmaceutical by High Performance Liquid Chromatography using Ion-pair formation. J. Chromato. 202 (1980) : 99-106.

Levy, M. Y., and Benita, S. Drug release from submicronized o/w emulsion : a new in vitro kinetic evaluation model. Int. J. Pharm. 66 (1990) : 29-37.

Leyden, J. J., Shalita, A. R., Saatjian, G. D., Sefton, J. Erythromycin 2 % gel in comparison with clindamycin phosphate 1 % solution in acne vulgaris. J Am. Acad. Dermatol. 16 (4) (1987) :822-827.

Lieberman, H. A., Rieger, M. M.,and Banker, G. S., eds. Pharmaceutical Dosage Forms. Vol. 2 : disperse Systems. New York : Marcel Dekker, 1988.

Linter, C. J., ed. Pharmaceutical Product Stability in Quality Control in Pharmaceutical Industry. Vol 2. New York and London : Academic Press, 1973.

Macedo, T., Block, L. H., and Shukla, A. J. Release of Tolmetin from Carbomer gel systems. Drug Dev. Ind. Pharm. 19 (8) (1993) : 887-902.

Martin, A., ed. Physical Pharmacy. 4 th ed. Philadephia, London : Lea & Feibiger, 1993.

Migton, J. M., Kennon, L., Sideman, M., and Plakogiannis, F. M. A stability study of clindamycin hydrochloride and phosphate salts in topical

formulations. Drug Dev. Ind. Pharm. 10 (4) (1984) : 563-573.

Millipore Coorperation. Membrane Filtration Technology. Millipore Coorperation Massachusetts, USA, 1987.

Milston, E. B., McDonald, A. J. and Schollhamer C. F. Pseudomembranous Colitis after topical application of clindamycin. Arch Dermatol. 117 (1981) : 154.

Miyazaki, S., takeuchi, S., Yokouchi, C., and Takeda, M. Pluronic F-127 gels as a vehicle for topical administration of anticancer agents. Chem. Pharm. Bull. 32 (10) (1984) : 4205-4208.

_____. Yokouchi, C., Nakamura, T., Hashiguchi, N., and Hou, W. N. Pluronic F-127 gels as a Novel vehicle for rectal administration of indomethacin. Chem. Pharm. Bull. 34 (4) (1986) : 1801-1808.

Norwood, T. E. Stability analysis of pharmaceutical stability data. Drug Dev. Ind. Pharm. 12 (4) (1986) : 553-560.

Oesterling, T. O. Aqueous stability of clindamycin. J. Pharm. Sci. 59 (1970) : 63-67.

_____. and Rowe, E. L. Hydrolysis of Lincomycin-2-phosphate and Clindamycin-2-phosphate. J. Pharm. Sci. 59 (2) (1970) : 175-179.

Osborne, D. W., and Amann, A. H., eds. Topical Drug Delivery Formulations. New York and Bassel : Marcel Dekker, 1990.

Parikh, N. H., Babar, A., and Plakogiannis, F. M. Medicament release from ointment bases : II. Testosterone : in vitro release and effects of addition on its release . Drug Dev. Ind. Pharm. 12 (14) (1986) : 2493-2509.

Parker, F.A. comparison of clindamycin 1% solution versus clindamycin 1% gel in treatment of acne vulgaris. Int. J. Dermatol. 26 (2) (1987):121-122.

Parry, M. F., and Rha, C. K. Pseudomembranous colitis caused by topical clindamycin phosphate Arch. Dermatol. 122 (1986) : 583-584.

Poulos, E. T., Tedesco, F. J. Acne vulgaris : Double-blind trial comparing tetracycline and clindamycin. Arch. Dermatol. 112 (1976) : 974-976.

Poulsen, B. J., Young. E., Coquilla, V., and Katz, M., Effect of topical vehicle composition on the in vitro release of fluocinolone acetonide and its acetate ester. J. Pharm. Sci. 57 (1968) : 928-933.

Resh, W., and Stoughton, R.B. Topical clindamycin in the control of acne vulgais. Cutis 17 (1976) : 551-554 .

Shar, V.P., Elkins, J. Lam, S.Y., and Skelly, J.P. Determination of in vitro drug release from hydrocortisone creams. Int. J. Pharm. 53 (1989) : 53-59.

Sheehan-Dare, R.A., Parworth-Smith, J. Cumliffe, W.J. A double-blind comparison of topical clindamycin and oral minocycline in the treatment of acne vulgaris. Acta. Derm. Venereol. 70 (6) (1990) : 534-537.

Shahlita, A.R., Smith, E.B.,and Bauer, E. Topical erythromycin vs clindamycin therapy for acne. A multicenter, double-blind comparison. Arch. Dermatol. 120 (3) (1984) :351-355.

Siegle, R.J., Fekety, R., Sarbone, P.D., Finch, R.N.,Deery, H.G., and Voorhees, J.J. Effects of topical clindamycin and intestinal microflora in patients with acne. J. Am. Acad. Dermatol. 15 (1986) : 180-185.

Smolinske, S.C., ed. Handbook of Food, Drug and Cosmetic Excipients. Denver and Corolado : Micromedex Inc., 1992, 55-57.

Somrutai Jitpukdeebodindra. Evaluation of Various Ointment Preparation of Clindamycin. Master's Thesis, Chulalongkorn University 1985.

Stoughton, R.B., and Resh, W. Topical clindamycin in the control of acne vulgaris. Cuitis. 17 (1976) : 551-554.

Su Wu, H.L., and Miller, S.C. In vitro release of nicotinic acid alkyl esters from poloxamer vehicle. Int. J. Pharm. 66 (1990) : 213-221.

Swarbrick, J., Boylan, J.C. , eds. Encyclopedia of Pharmaceutical Technology. Vol. 6. New York, Bassel and Hong Kong : Marcel Dekker, Inc.,1988.

Thomas, D.R., Raimer, S., and Smith, E.B. Comparison of topical erythromycin 1.5 percent solution versus topical clindamycin phosphate 1.0 percent solution in the treatment of acne vulgaris. Cutis. 29 (6) (1992) : 624-625, 628-632.

Thomsen, R.J., Stranieri, A., Knutson, D., and Strauss, J.S. Topical clindamycin treatment of acne. Arch. Dermatol. 116 (1980) : 1031-1034.

Tomida, H. Shinohara, M. Kuuada, N. and Kiryn, S. In-vitro release characteristics of diclofenac and hydrocortisone from pluronic F-127 gels. Acta. Pharm. Suec. 24 (1987) :263-272 .

Umprayn, K., and Mendes, R.W. Hygroscopicity and moisture absorption kinetics of pharmaceutical solids : A Reveiw. Drug Dev. Ind. Pharm. 13 (1987) : 653-693.

Vandenbosshe, G.M.R., Vanhaecke, E. Muynck, C.D., and Remon, J.P. Stability of topical erythromycin formulation. Int. J. Pharm. 67 (1991) : 195-199.

Vermorken, A.J.M., and Goos, C.M.A. A acne and antibiotic. Drug Intel. Clin. Pharm. 14 (1980) : 498-506.

Walkow, J.C., and McGinity, J.W. The effect of physicochemical properties on the in vitro diffusion of drug through synthetic membranes and pigskin. I : Methyl salicylate.Int. J. Pharm. 35 (1987) : 91-102.

_____. The effect of physicochemical properties on the in vitro diffusion of drug through synthetic membranes and pigskin. II : Salicylic acid. Int. J. Pharm. 35 (1987) : 103-109.

Yalkawsky, S.H., and Swabrick, J., eds. Modern Pharmaceutics. New York and Bassel : Marcel Dekker, Inc., 1979, : 298-237.

Appendix I

Composition and Preparation of Acetate Buffer pH 4.5 ± 0.1

pH 4.5 ± 0.1

Sodium acetate 0.1 N	33.5 ml
Acetic acid 0.1 N	66.5 ml

Mix the required amount of these solution together.

Sodium acetate 0.1 N
($C_2H_3O_2Na$)

Dissolve sodium acetate powder 8.204 g in purified water then adjust to the final volume of 1000 ml.

Acetic acid 0.1 N

Disperse glacial acetic acid 6.005 g in purified water, adjust to the final volume of 1000 ml.

Appendix II

Preparation of Gel Bases

Poloxamer 407 Gel

A weighed amount of poloxamer 407 was slowly added to cold mixture (~ 5°C) of glycerin and bronopol® in acetate buffer about 2/3 of the formula. This dispersion was then placed in a refrigerator to ensure complete dissolution. Eventually, a clear and viscous solution was formed and transformed to gel state when the solutions was later stored at room temperature.

Hydroxyethyl Cellulose Gel

The hydroxyethyl cellulose gel was prepared by scattering hydroxyethyl cellulose powder in hot mixture (~ 80-90°C) of glycerine and bronopol® in acetate buffer about 2/3 of the formula with gentle stirring using a stirring rod until they were clear and uniform.

Hydroxypropyl Methylcellulose Gel

The hydroxypropyl methylcellulose gel was prepared by dispersing hydroxypropyl methylcellulose powder in hot buffer (~80°C) in small increments with continuous stirring until a white smooth paste was formed. Cold mixture (~ 4°C) of glycerin and bronopol® in acetate buffer about 2/3 of the formula was added to the paste immediately to form a clear gel.

Appendix III

Stability Data of Clindamycin Hydrochloride Gel.

Stability Data of Clindamycin Hydrochloride in Poloxamer 407 Gel at Joel-Davis Condition.

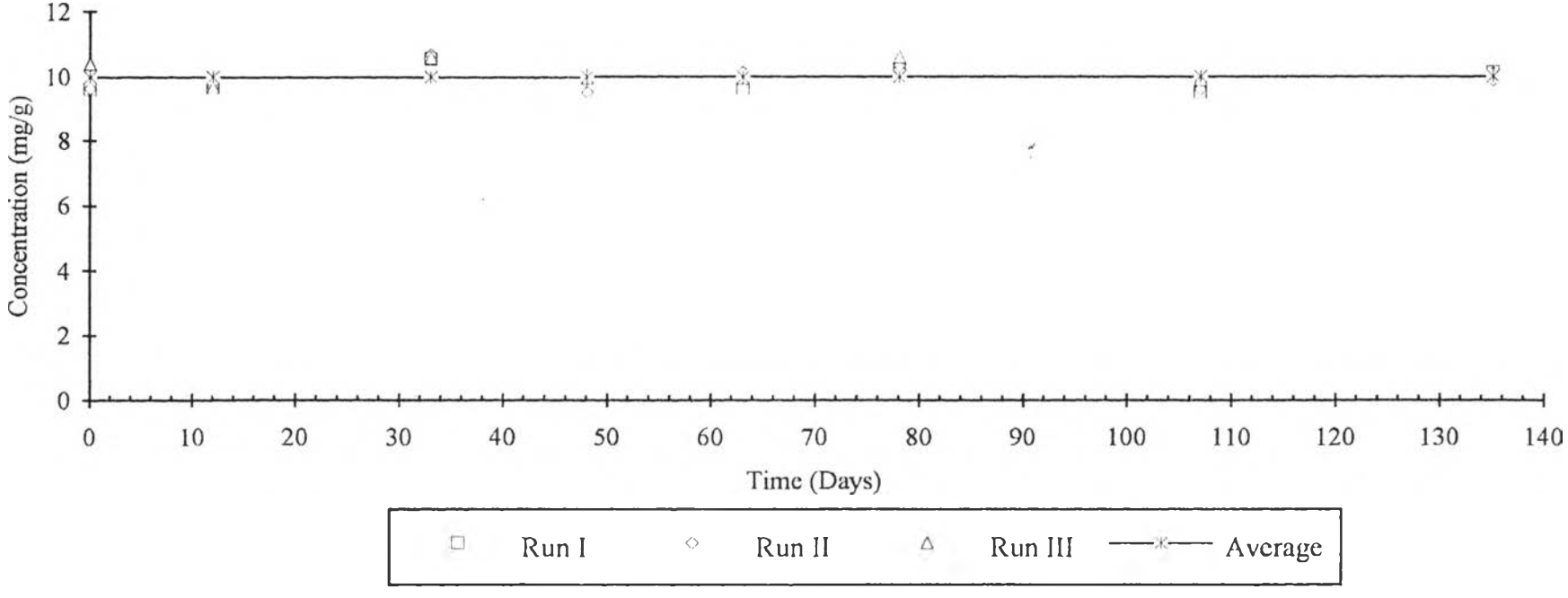
Time (Days)	Concentration[a] (mg/g)
0	9.8922 ± 0.4452
12	10.6044 ± 0.0562
48	9.8527 ± 0.2800
63	9.9260 ± 0.2484
78	10.3622 ± 0.2609
107	9.6965 ± 0.2057
135	10.0661 ± 0.1342

a: Mean ± SD, (n = 3)

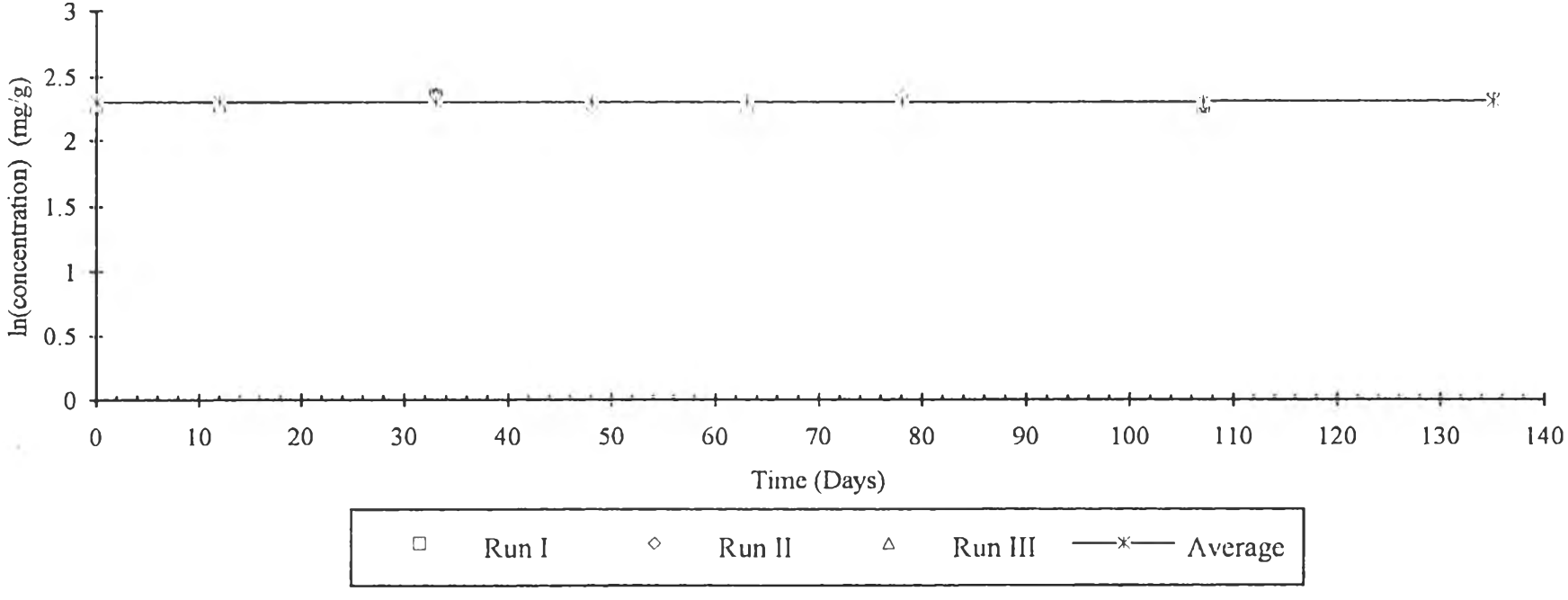
Concentration = $9.9957+2.5903 \times 10^{-4}$ time ; r^2 = 0.0014

ln(concentration) = $2.3015+2.8979 \times 10^{-5}$ time ; r^2 = 0.0018

The Concentration vs Time Plots of Clindamycin Hydrochloride in Poloxamer 407 Gel at Joel-Davis Condition.



The ln(concentration) vs Time Plots of Clindamycin Hydrochloride in Poloxamer 407 Gel at Joel-Davis Condition.



Stability Data of Clindamycin Hydrochloride in Hydroxyethyl Cellulose Gel at Joel-Davis Condition.

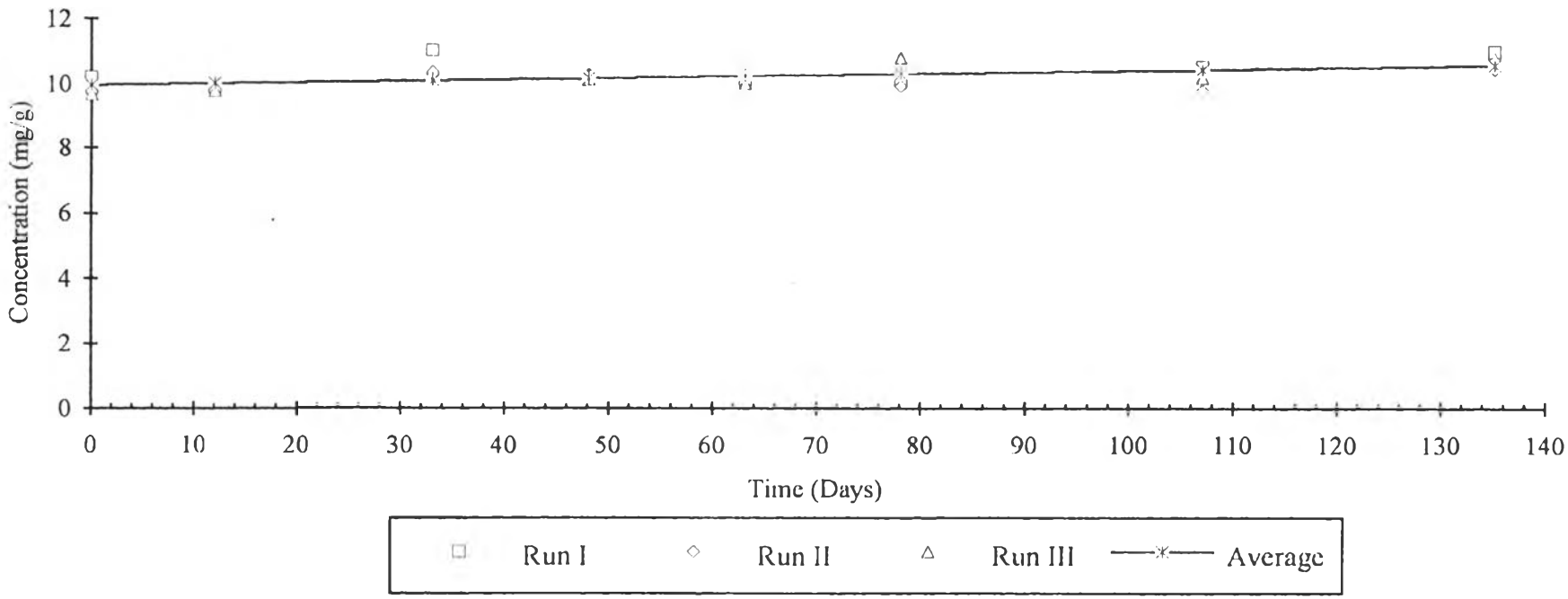
Time (Days)	Concentration[a] (mg/g)
0	9.8806 ± 0.2812
12	9.8697 ± 0.0571
33	10.5310 ± 0.4463
48	10.2415 ± 0.0947
63	10.1535 ± 0.1377
78	10.2985 ± 0.4619
107	10.1864 ± 0.3646
135	10.7477 ± 0.2657

a : Mean ± SD, (n = 3)

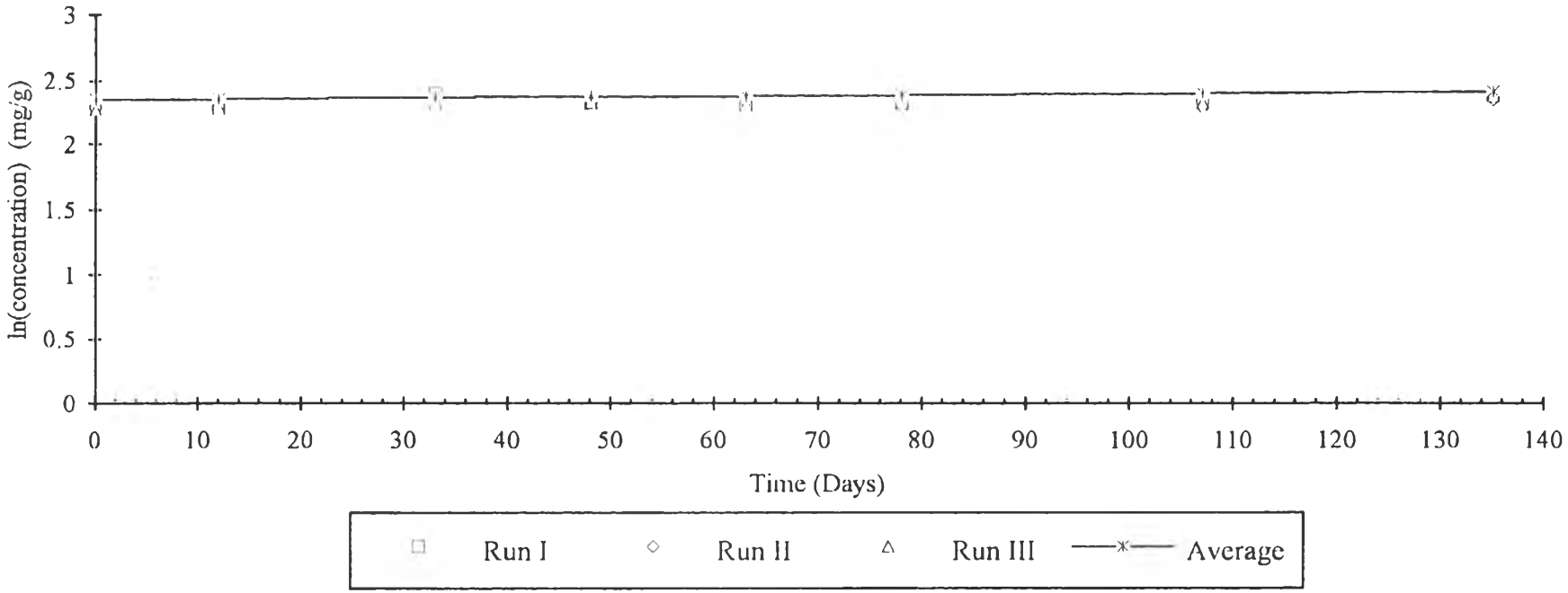
Concentration = $9.9686 + 4.5382 \times 10^{-3}$ time ; $r^2 = 0.4943$

ln(concentration) = $2.2995 + 4.4219 \times 10^{-4}$ time ; $r^2 = 0.4964$

The Concentration vs Time Plots of Clindamycin Hydrochloride in Hydroxyethyl Cellulose Gel at Joel-Davis Condition.



The ln(concentration) vs Time Plots of Clindamycin Hydrochloride in Hydroxyethyl Cellulose Gel at 40 Joel-Davis Condition.



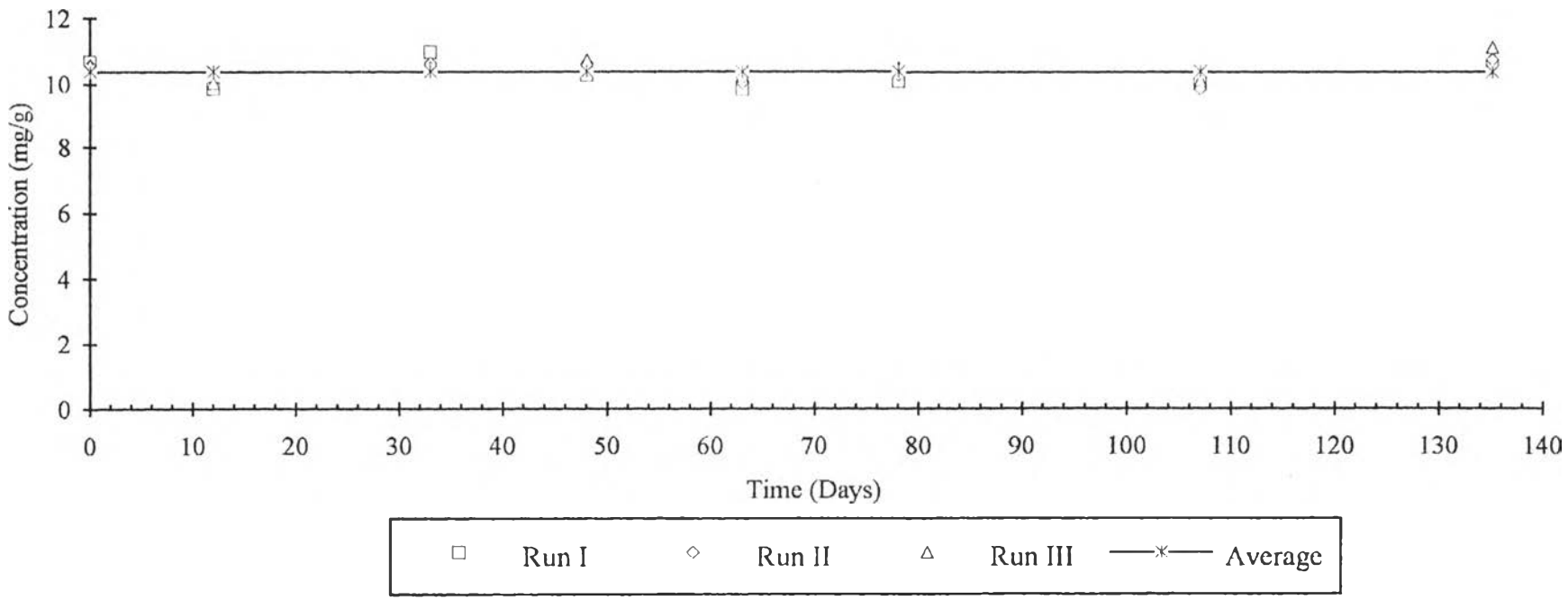
Stability Data of Clindamycin Hydrochloride in Hydroxypropyl Methylcellulose Gel at Joel-Davis Condition.

Time (Days)	Concentration[a] (mg/g)
0	10.6102 ± 0.0598
12	10.0952 ± 0.2705
33	10.6988 ± 0.2311
48	10.5310 ± 0.2550
63	10.0213 ± 0.2165
78	10.2634 ± 0.2041
107	9.9617 ± 0.1345
135	10.7566 ± 0.3016

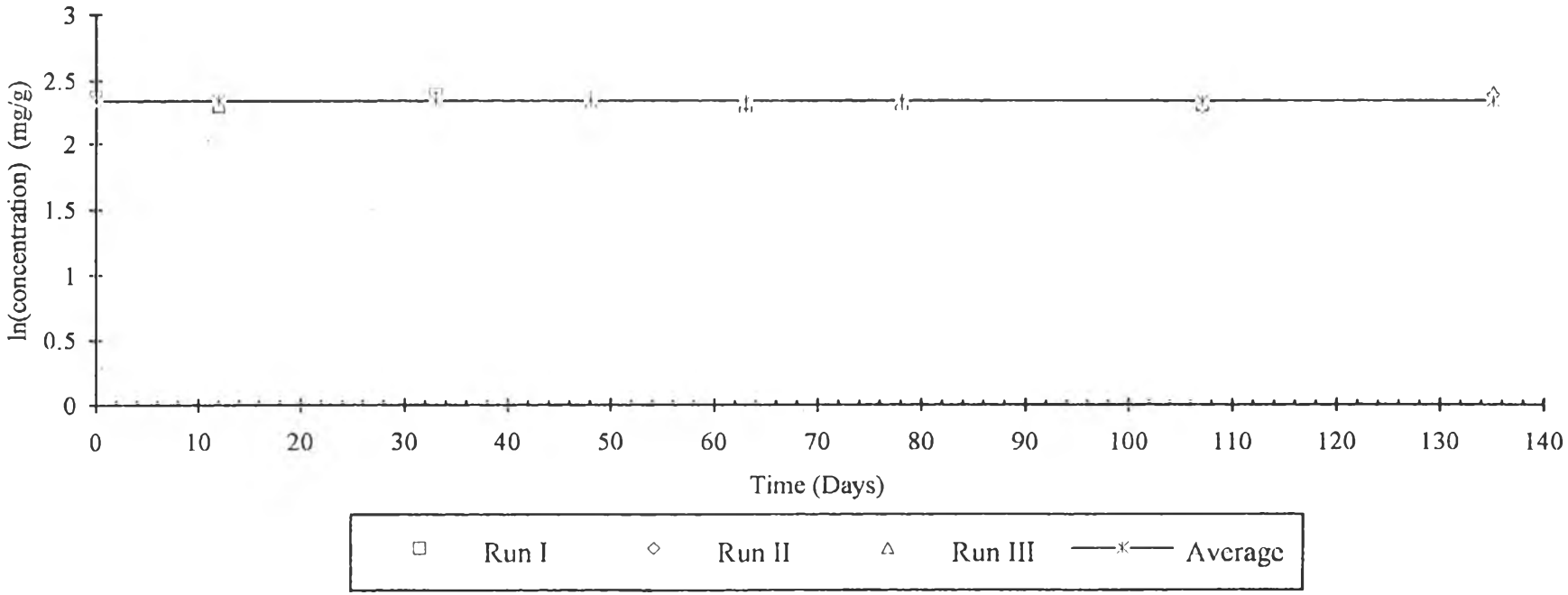
a : Mean ± SD, (n = 3)

Concentration = 10.3880-3.4815 x 10^{-4} time ; r^2 = 0.0025
ln(concentration) = 2.3404-3.6802 x 10^{-5} time ; r^2 = 0.0030

The Concentration vs Time Plots of Clindamycin Hydrochloride in Hydroxypropyl Methylcellulose Gel at Joel-Davis Condition.



The ln(concentration) vs Time Plots of Clindamycin Hydrochloride in Hydroxypropyl Methylcellulose Gel at Joel-Davis Condition.



Stability Data of Clindamycin Hydrochloride in Poloxamer 407 Gel at Ambient Temperature.

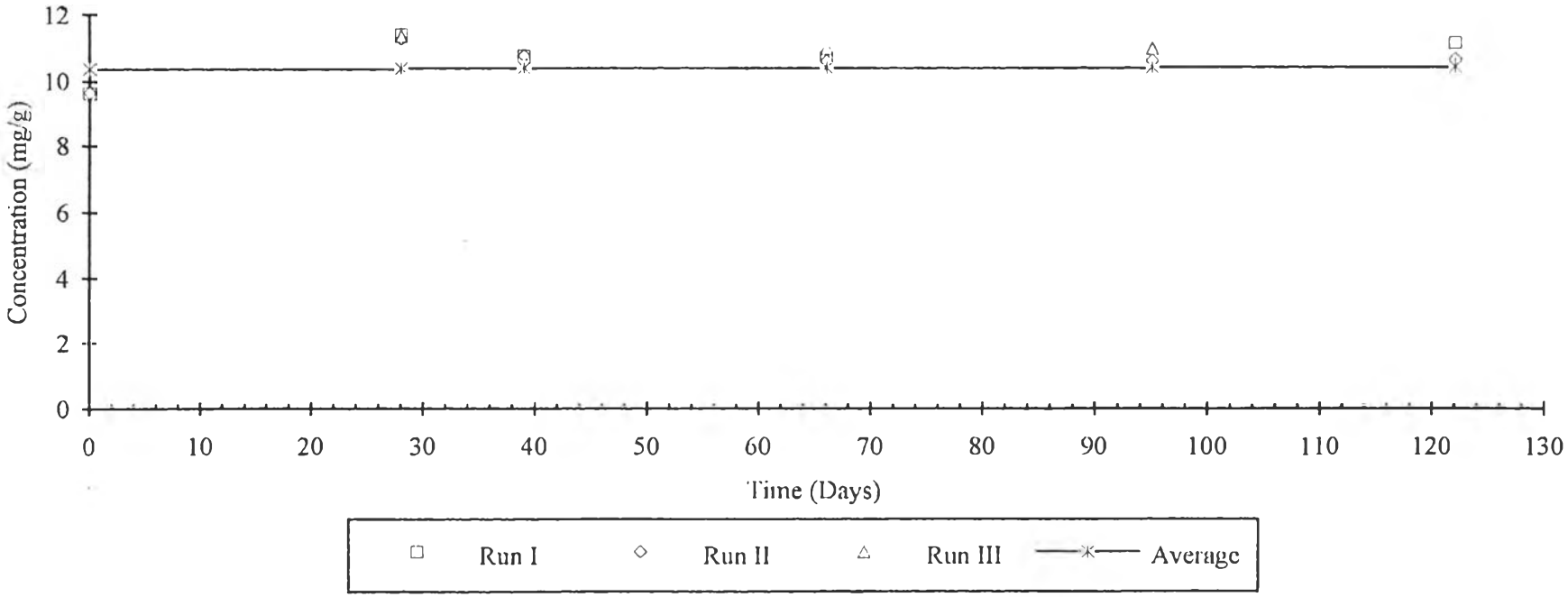
Time (Days)	Concentration[a] (mg/g)
0	9.6350 ± 0.4452
28	11.3339 ± 0.0593
39	10.6990 ± 0.1156
66	10.7629 ± 0.2019
95	10.6892 ± 0.2620
122	10.7618 ± 0.3361

a :Mean ± SD, (n = 3)

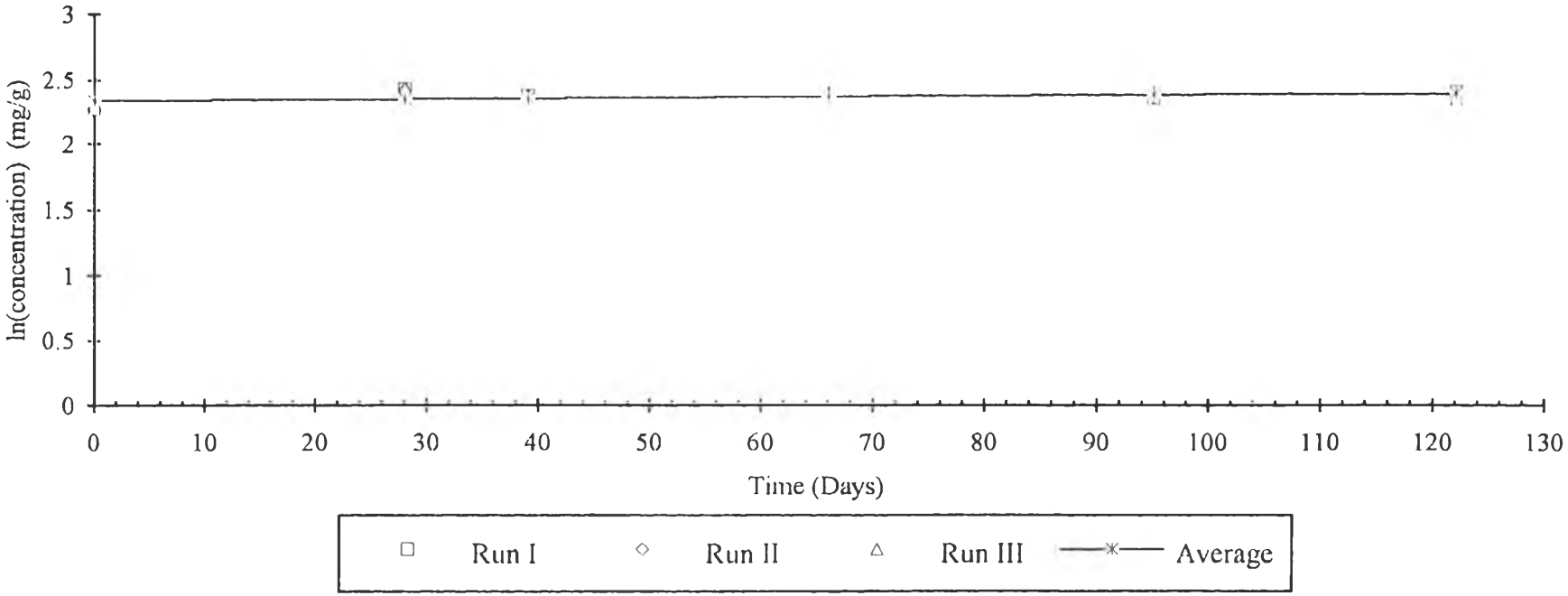
Concentration = $10.3770 + 4.6231 \times 10^{-3}$ time ; $r^2 = 0.1421$

ln(concentration) = $2.3368 + 4.6742 \times 10^{-4}$ time ; $r^2 = 0.1568$

The Concentration vs Time Plots of Clindamycin Hydrochloride in Poloxamer 407 Gel at Ambient Temperature.



The ln(concentration) vs Time Plots of Clindamycin Hydrochloride in Poloxamer 407 Gel at Ambient Temperature.



Stability Data of Clindamycin Hydrochloride in Hydroxyethyl Cellulose Gel at Ambient Temperature.

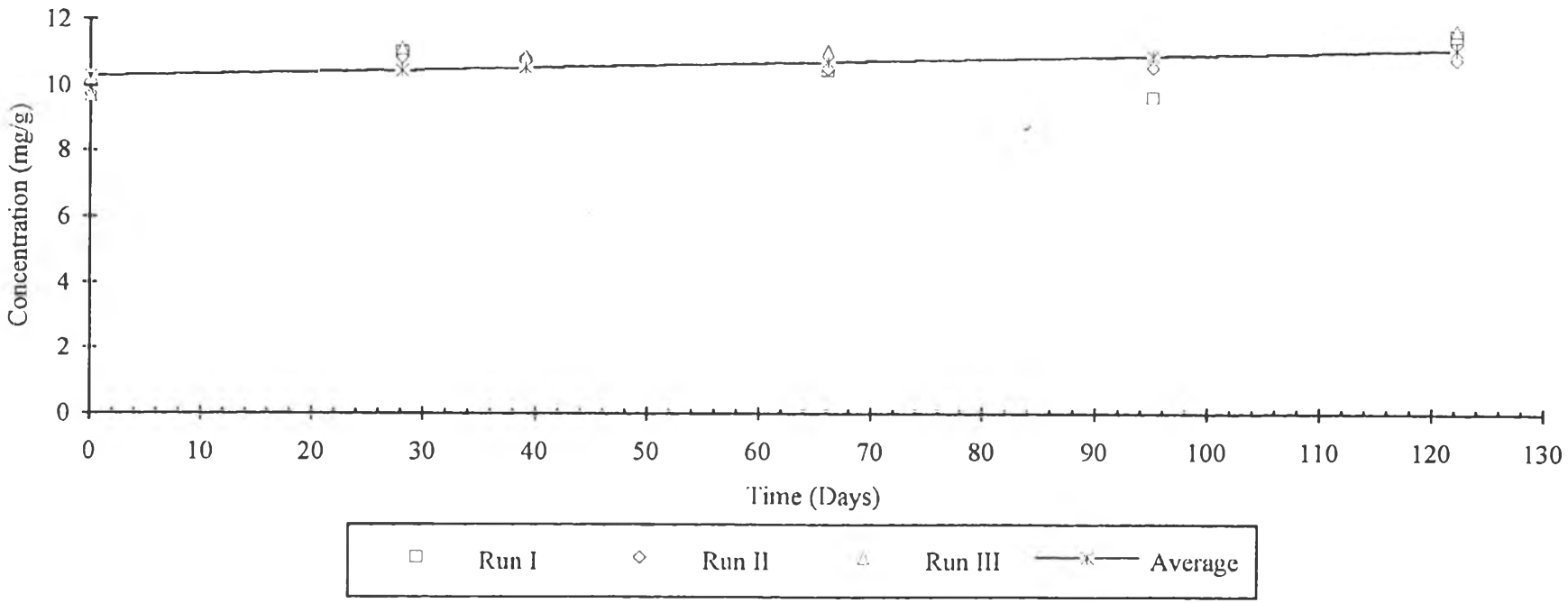
Time (Days)	Concentration[a] (mg/g)
0	9.8806 ± 0.2812
28	11.0109 ± 0.1300
39	10.7929 ± 0.1583
66	10.6849 ± 0.3266
95	10.3928 ± 0.6506
122	11.3317 ± 0.4684

a : Mean ± SD, (n = 3)

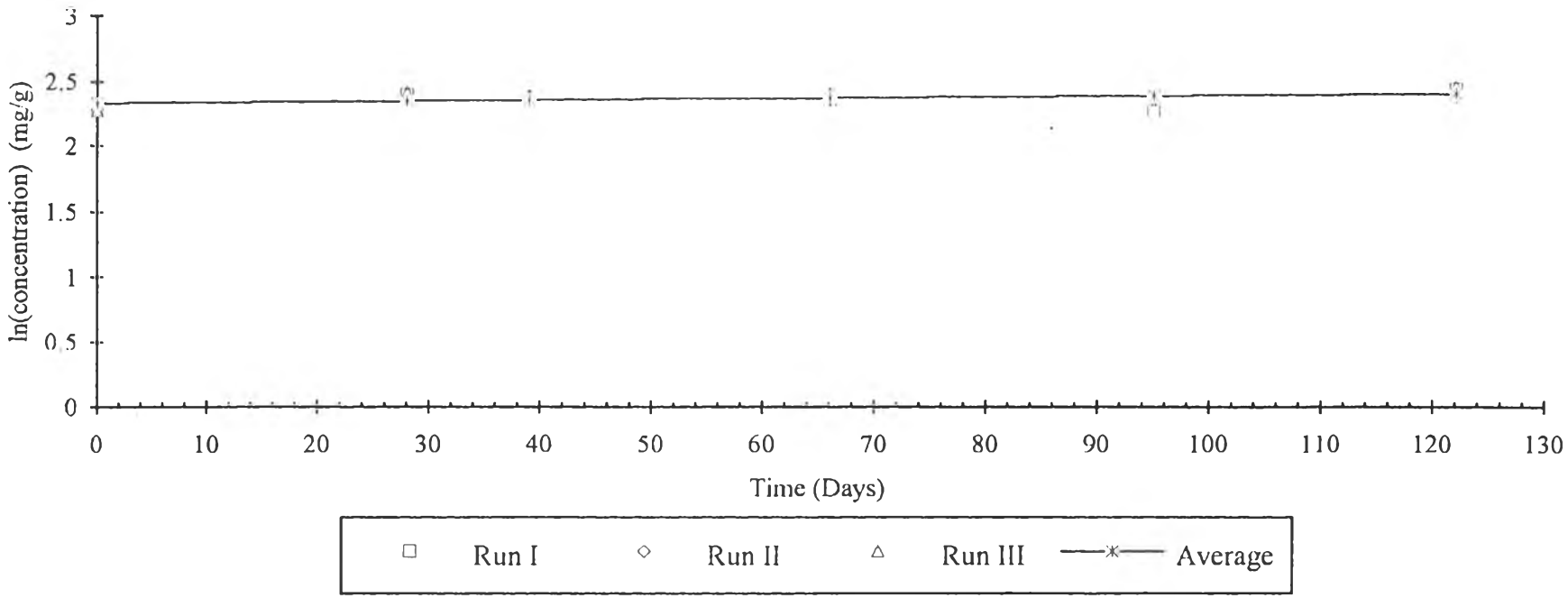
Concentration = $10.3065 + 6.4422 \times 10^{-3}$ time ; $r^2 = 0.3322$

ln(concentration) = $2.3322 + 6.0830 \times 10^{-4}$ time ; $r^2 = 0.3310$

The Concentration vs Time Plots of Clindamycin Hydrochloride in Hydroxyethyl Cellulose Gel at Ambient Temperature.



The ln(concentration) vs Time Plots of Clindamycin Hydrochloride in Hydroxyethyl Cellulose Gel at Ambient Temperature.



Stability Data of Clindamycin Hydrochloride in Hydroxypropyl Methylcellulose Gel at Ambient Temperature.

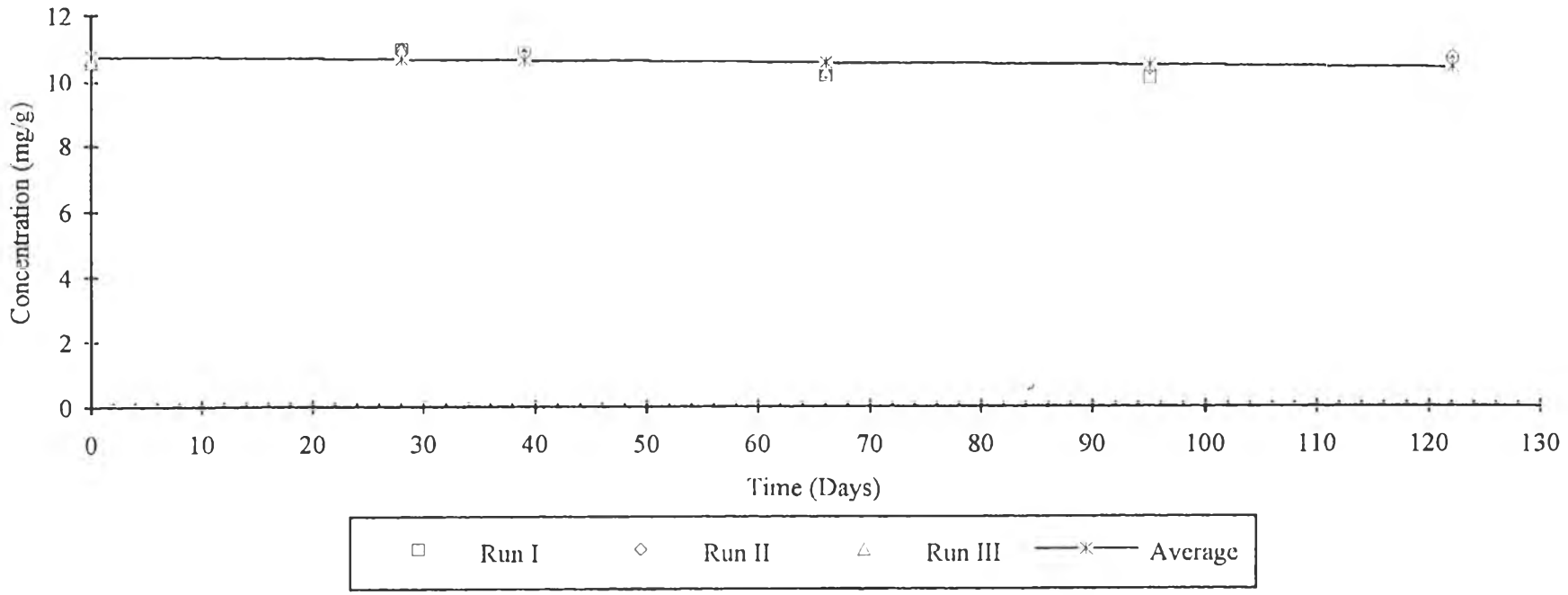
Time (Days)	Concentration[a] (mg/g)
0	10.6102 ± 0.0597
28	10.9722 ± 0.0087
39	10.8012 ± 0.0423
66	10.2363 ± 0.0656
95	10.3049 ± 0.1947
122	10.6020 ± 0.1036

a : Mean ± SD, (n = 3)

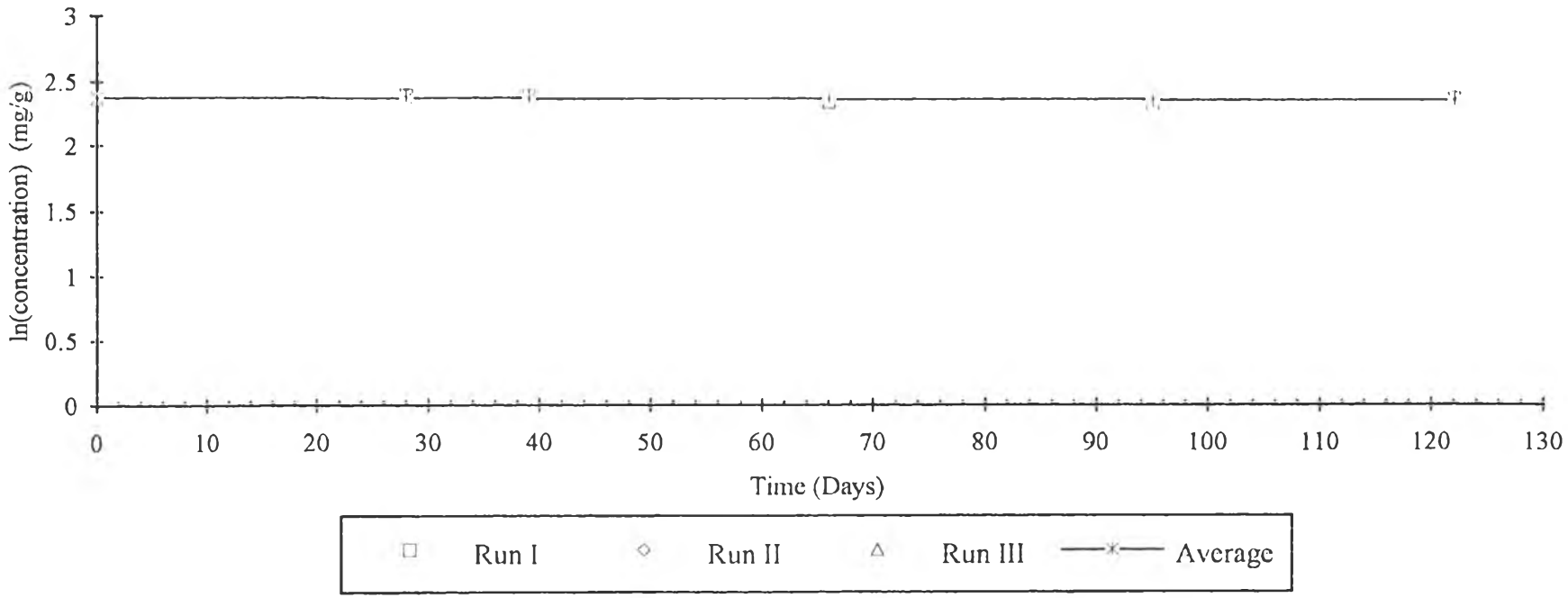
$$\text{Concentration} = 10.7559 - 2.8814 \times 10^{-3} \text{ time} ; r^2 = 0.2120$$

$$\ln(\text{concentration}) = 2.3752 - 2.7185 \times 10^{-4} \text{ time} ; r^2 = 0.2112$$

The Concentration vs Time Plots of Clindamycin Hydrochloride in Hydroxypropyl Methylcellulose Gel at Ambient Temperature.



The ln(concentration) vs Time Plots of Clindamycin Hydrochloride in Hydroxypropyl Methylcellulose Gel at Ambient Temperature.



APPENDIX IV

In Vitro Release Data of Clindamycin Hydrochloride Gel.

Gelling Agent: Poloxamer 407, 18% w/w

Membrane: Durapore(R); Thickness: 0.132 mm.; Pore size: 0.45 micron

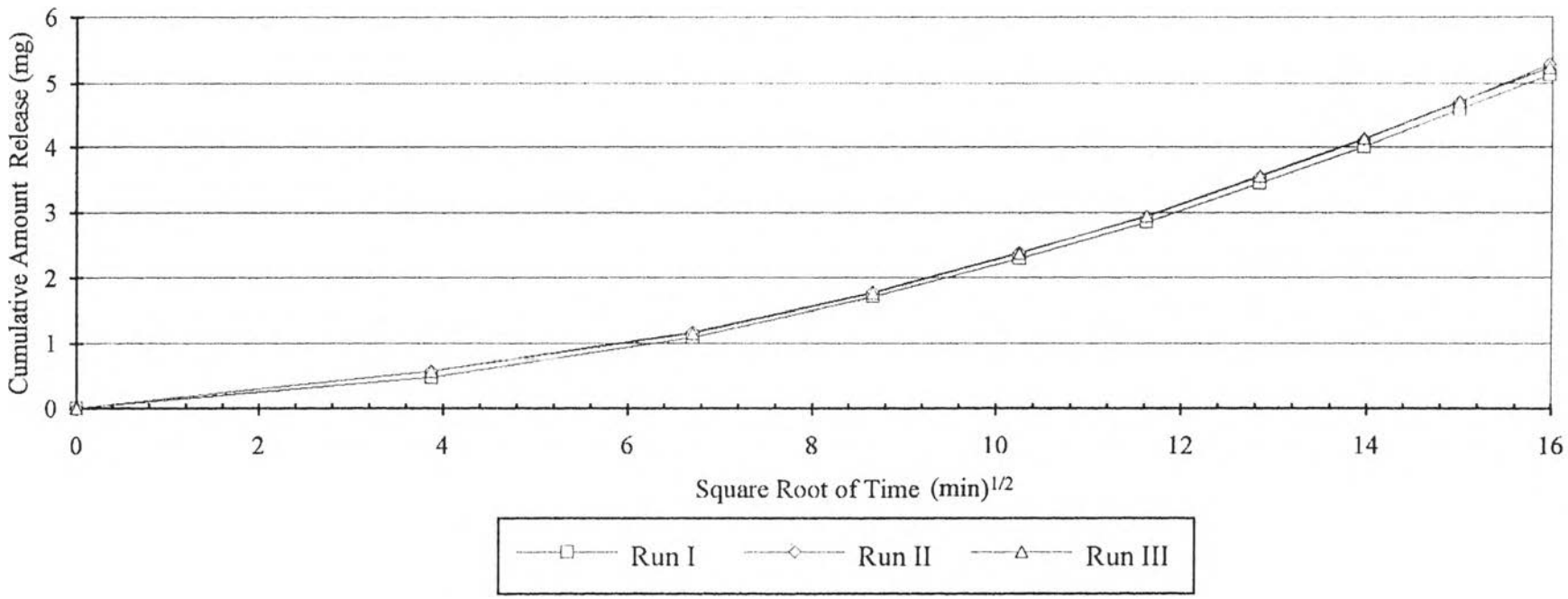
Receiving Medium: Acetate Buffer

Release Run Data

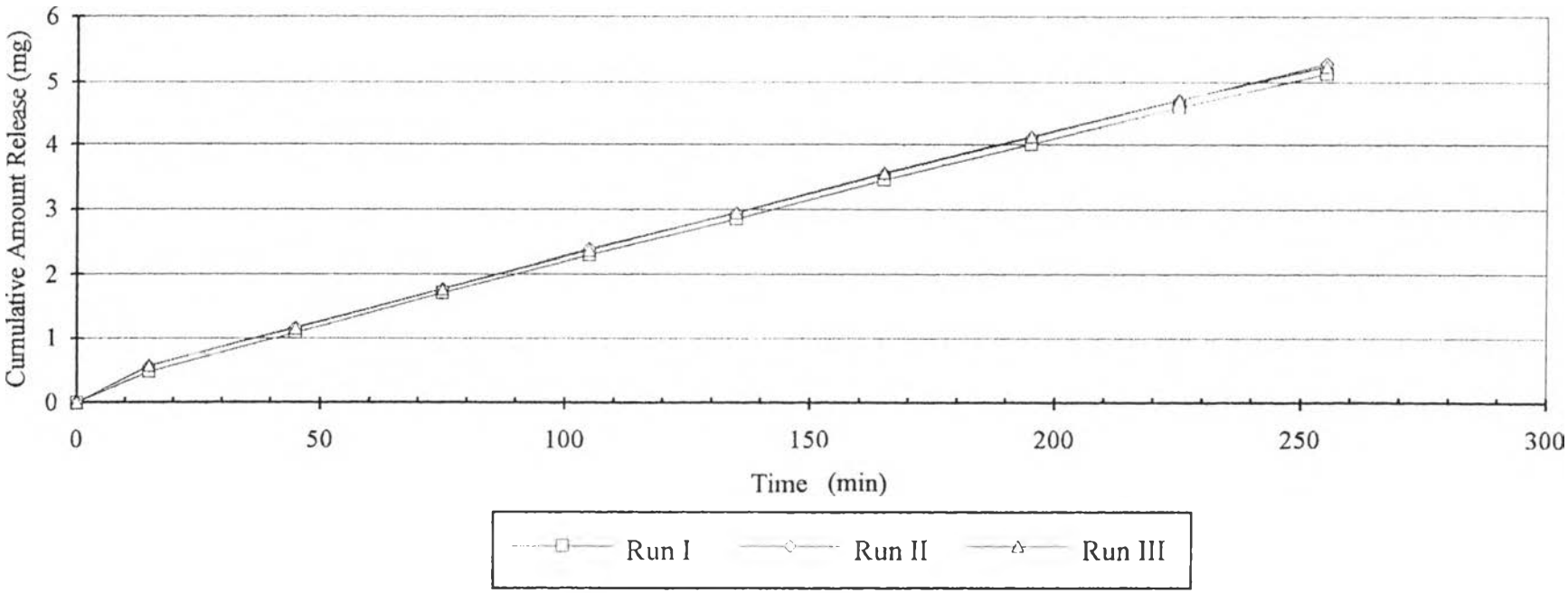
Time (min)		Run I		Run II		Run III	
T	$T^{1/2}$	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)
15	3.875	0.4703	0.4703	0.5656	0.5656	0.5690	0.5690
45	6.708	0.6124	1.0827	0.6034	1.1690	0.5823	1.1513
75	8.660	0.6255	1.7081	0.6110	1.7800	0.6152	1.7665
105	10.247	0.5833	2.2915	0.6082	2.3882	0.6033	2.3698
135	11.619	0.5511	2.8427	0.5471	2.9253	0.5701	2.9439
165	12.845	0.6028	3.4465	0.6112	3.5464	0.6157	3.5596
195	13.965	0.5603	4.0068	0.5730	4.1195	0.5746	4.1342
225	15.000	0.5856	4.5924	0.5851	4.7046	0.5803	4.7415
255	15.969	0.5406	5.1330	0.5835	5.2881	0.5292	5.2437
Steady -state slope Cumulative Amount vs $T^{1/2} \times 10^{-2}$ ($mcg/min^{-1/2}$)		5.0012		5.0090		5.0642	
Diffusion Coefficient x 10^4 (cm^2/min)		8.2832		8.5766		8.4940	
r^2		0.9964		0.9952		0.9974	

$D = 8.4513 \pm 0.1513$ %CV = 1.7902

Clindamycin Hydrochloride Release from Poloxamer 407 Gel by Using Durapore(R) and Acetate Buffer.



Clindamycin Hydrochloride Release from Poloxamer 407 Gel by Using Durapore(R) and Acetate Buffer.



Gelling Agent: Hydroxyethyl Celulose; 2% w/w

Membrane: Durapore(R); Thickness: 0.132 mm.; Pore size: 0.45 micron

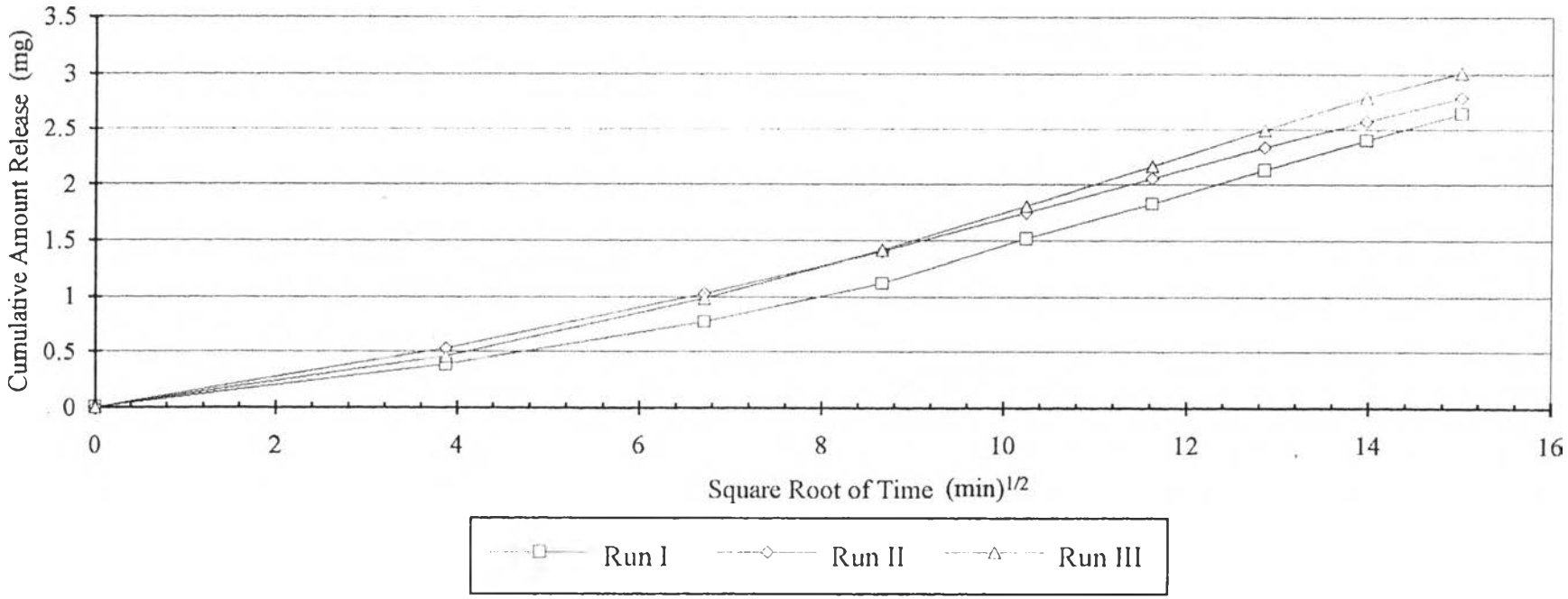
Receiving Medium : Acetate Buffer

Release Run Data

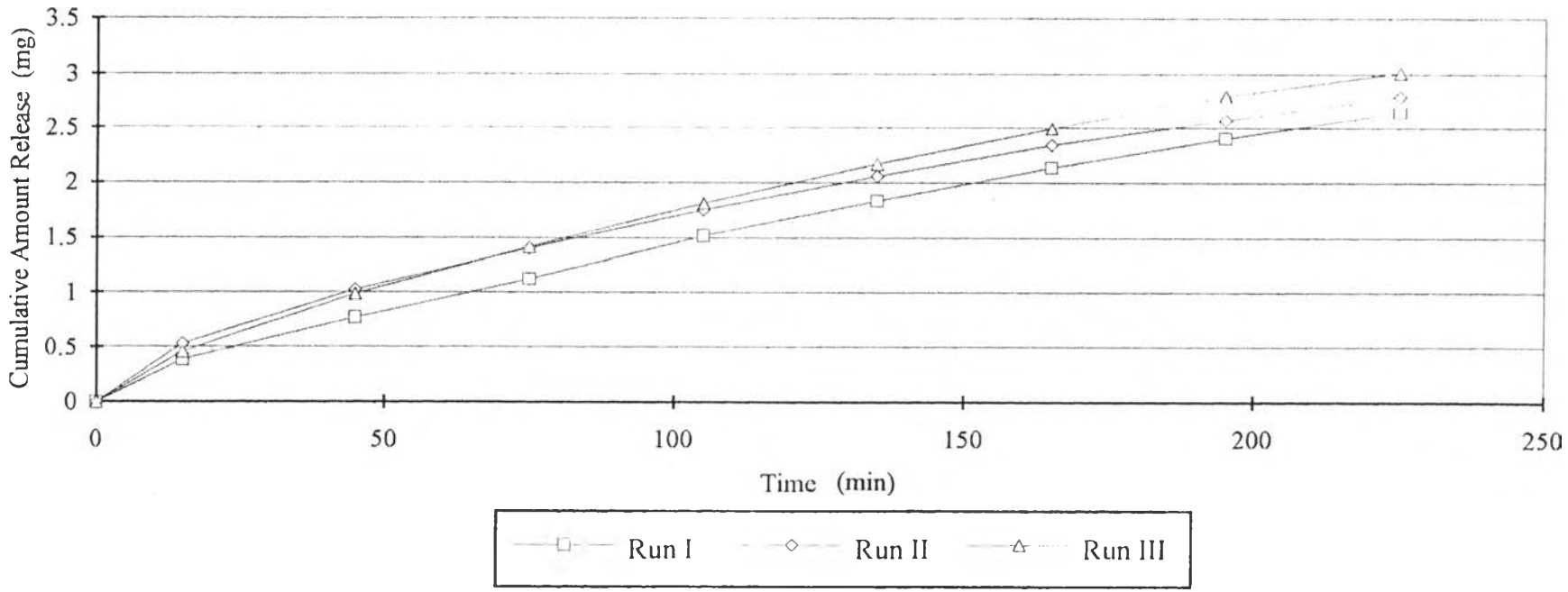
Time (min)		Run I		Run II		Run III	
T	$T^{1/2}$	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)
15	3.875	0.3857	0.3857	0.5325	0.5325	0.4586	0.4586
45	6.708	0.3875	0.7714	0.4948	1.0273	0.5290	0.9876
75	8.660	0.3512	1.1226	0.3748	1.4021	0.4294	1.4171
105	10.247	0.3909	1.5175	0.3480	1.7502	0.3925	1.8496
135	11.619	0.3120	1.8295	0.3053	2.0555	0.3586	2.1682
165	12.845	0.3040	2.1335	0.2828	2.3384	0.3255	2.4937
195	13.965	0.2654	2.3989	0.2318	2.5702	0.2996	2.7932
225	15.000	0.2444	2.6433	0.2192	2.7894	0.2189	3.0122
Steady -state slope Cumulative Amount vs $T^{1/2} \times 10^{-2}$ (mcg/min $^{-1/2}$)		2.3945		2.1975		2.5545	
Diffusion Coefficient x 10^4 (cm ^{2}/min)		1.8990		1.5994		2.1612	
r^2		0.9999		0.9998		0.9993	

D = 1.8865 $\pm$ 0.2811 %CV = 14.9007

Clindamycin Hydrochloride Release from Hydroxyethyl Cellulose Gel by Using Durapore (R) and Acetate Buffer.



Clindamycin Hydrochloride Release from Hydroxyethyl Cellulose Gel by Using Durapore(R) and Acetate Buffer.



Gelling Agent: Hydroxypropyl Methylcellulose, 3% w/w

Membrane: Durapore(R); Thickness: 0.132 mm.; Pore size: 0.45 micron

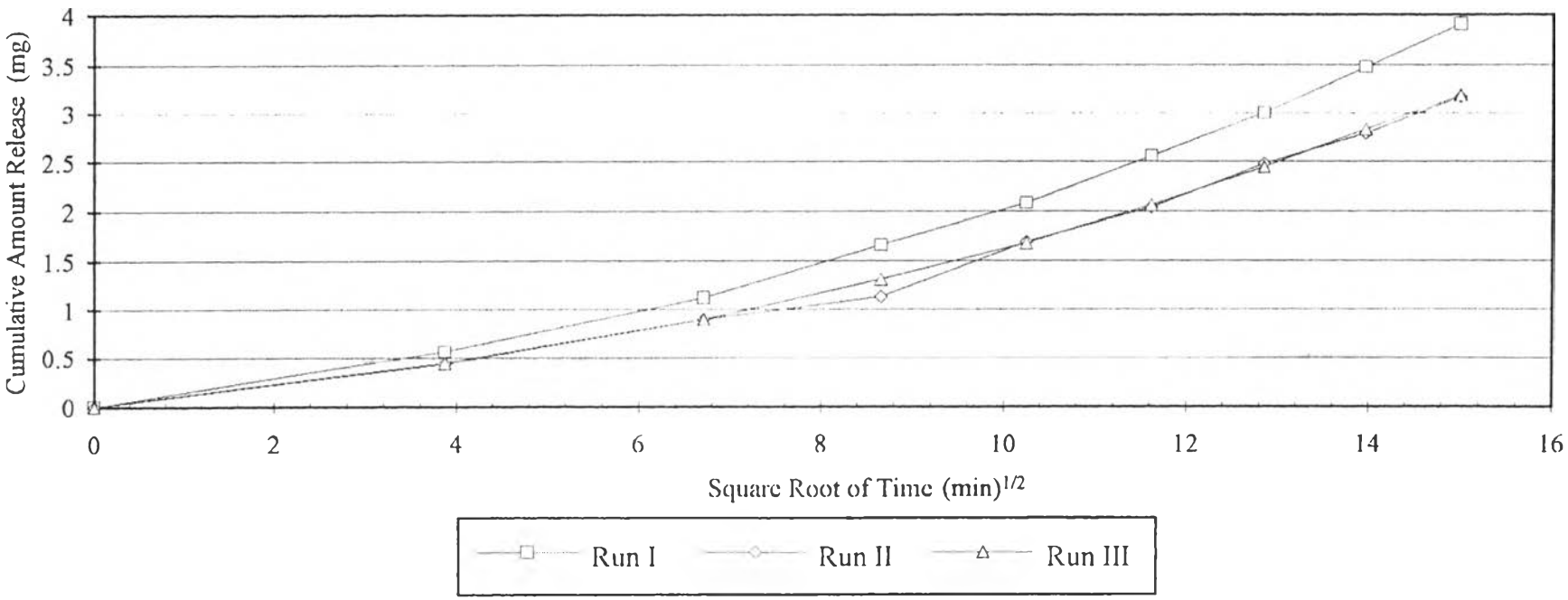
Receiving Medium: Acetate Buffer

Release Run Data

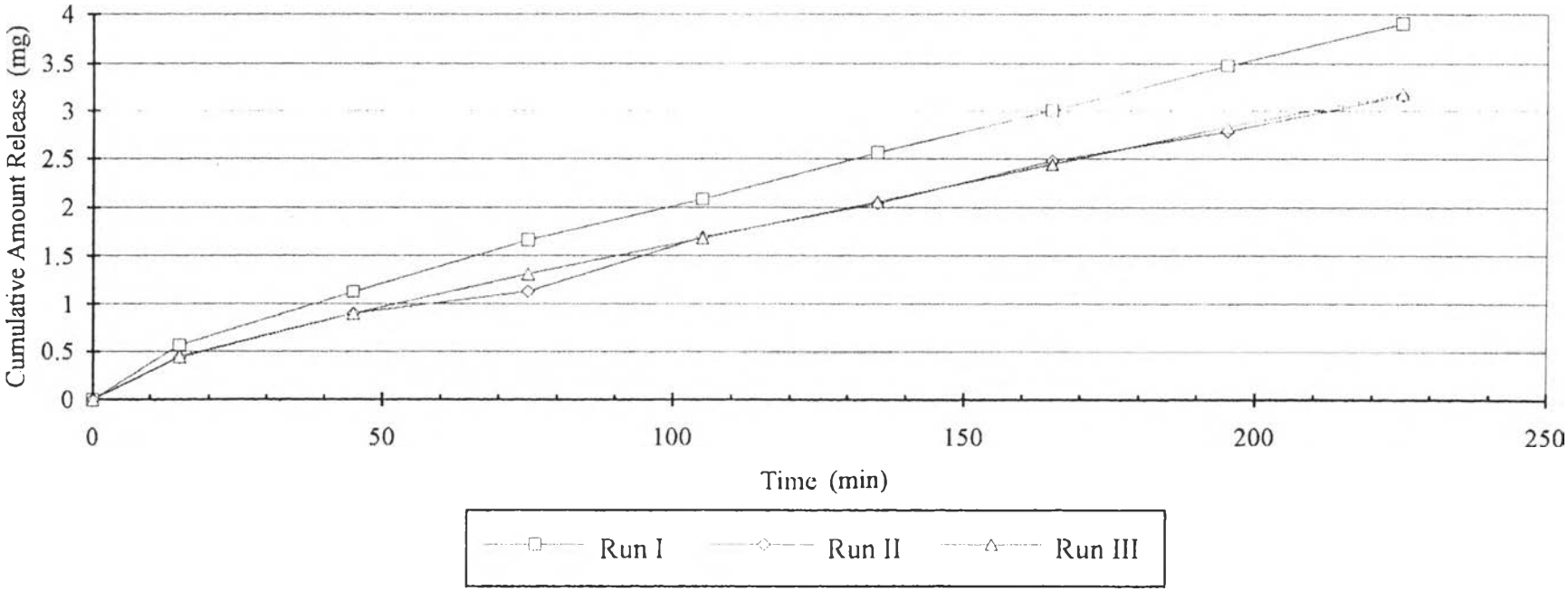
Time (min)		Run I		Run II		Run III	
T	$T^{1/2}$	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)
15	3.875	0.5648	0.5648	0.4344	0.4344	0.4450	0.4450
45	6.708	0.5580	1.1229	0.4651	0.8995	0.4531	0.8981
75	8.660	0.5420	1.6648	0.4164	1.3159	0.4124	1.3105
105	10.247	0.4177	2.0825	0.3774	1.6933	0.3738	1.6843
135	11.619	0.4776	2.5601	0.3457	2.0390	0.3760	2.0604
165	12.845	0.4436	3.0038	0.4398	2.4788	0.3821	2.4425
195	13.965	0.4716	3.4754	0.3069	2.7857	0.3910	2.8335
225	15.000	0.4304	3.9058	0.3799	3.1655	0.3540	3.1875
Steady -state slope Cumulative Amount vs $T^{1/2} \times 10^{-2}$ (mcg/min $^{-1/2}$)		3.9984		3.2735		3.3468	
Diffusion Coefficient x 10^{4} (cm ^{2}/min)		5.2950		3.5491		3.7098	
r^2		0.9988		0.9972		0.9994	

D = 4.1846 ± 0.9649 %CV = 23.0595

Clindamycin Hydrochloride Release from Hydroxypropyl Methylcellulose Gel by Using Durapore(R) and Acetate Buffer.



Clindamycin Hydrochloride Release from Hydroxypropyl Methylcellulose Gel by Using Durapore(R) and Acetate Buffer.



Gelling Agent: Poloxamer 407, 18% w/w

Membrane: Durapore(R); Thickness: 0.132 mm.; Pore size: 0.45 micron

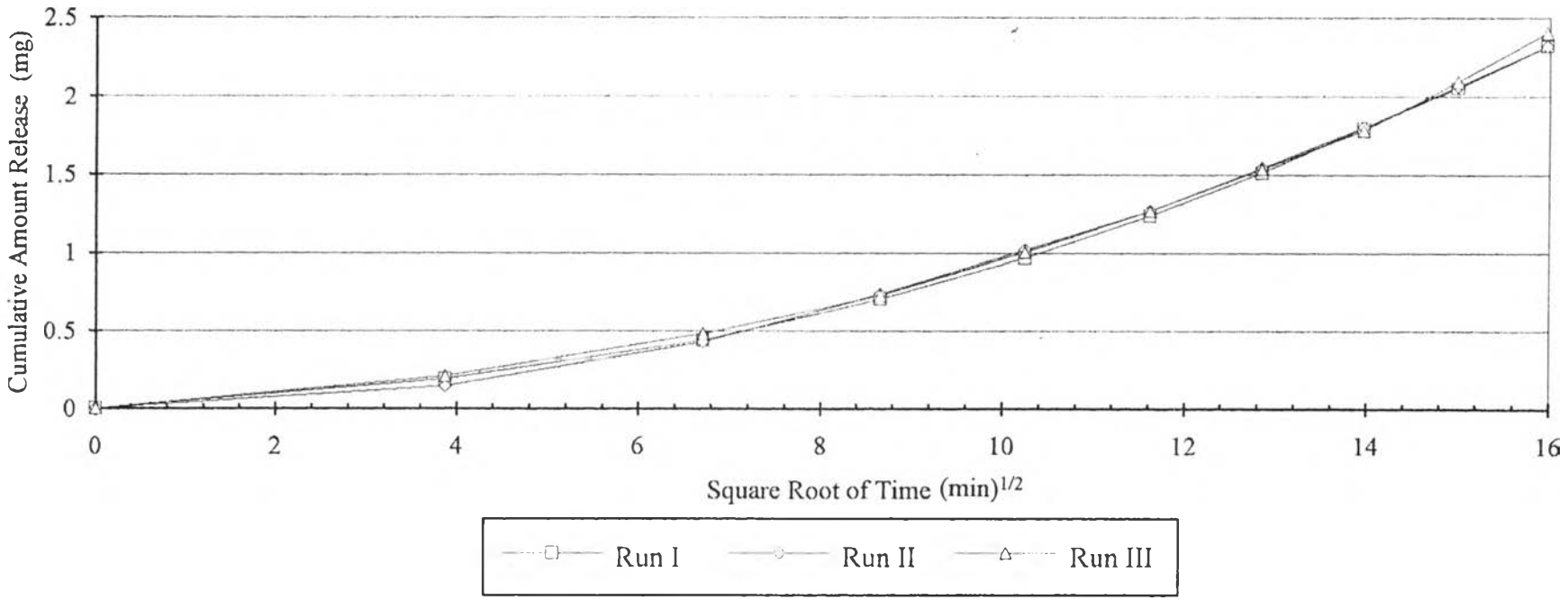
Receiving Medium: Chloroform

Release Run Data

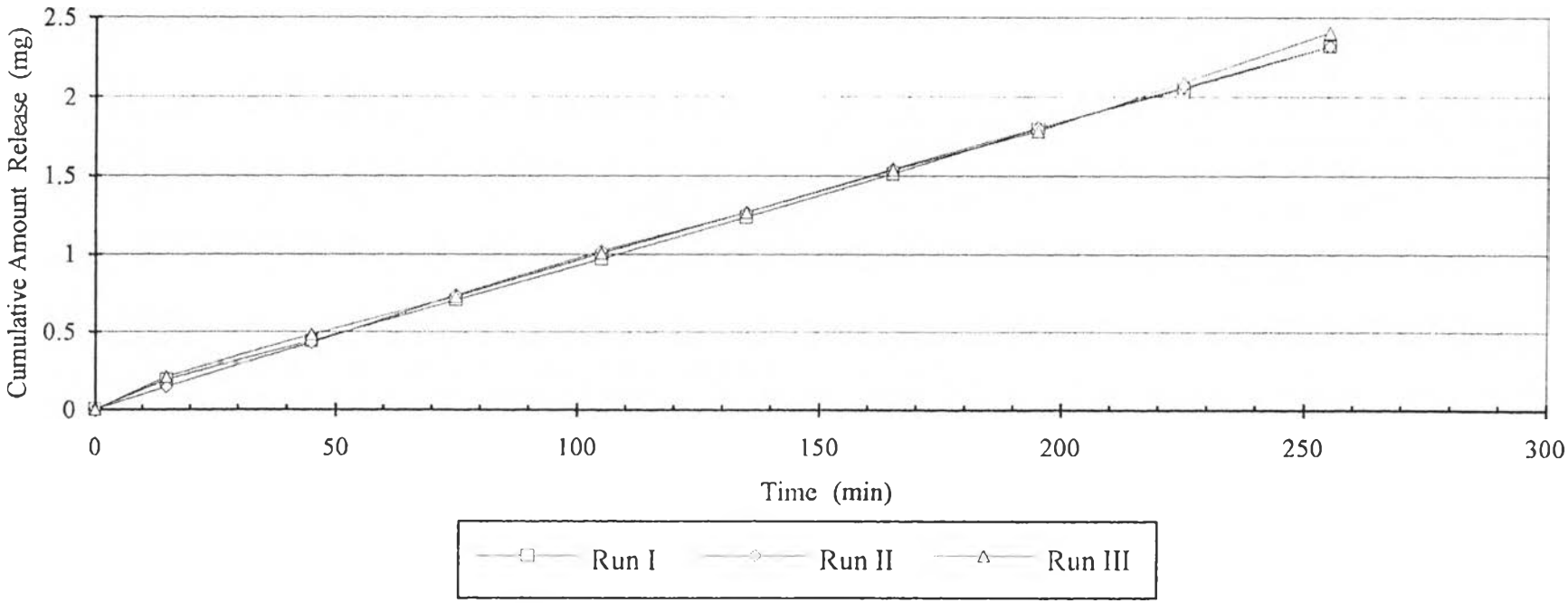
Time (min)		Run I		Run II		Run III	
T	$T^{1/2}$	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)
15	3.875	0.1913	0.1913	0.1460	0.1460	0.2094	0.2094
45	6.708	0.2486	0.4399	0.2819	0.4279	0.2740	0.4834
75	8.660	0.2658	0.7057	0.3091	0.7371	0.2453	0.7287
105	10.247	0.2636	0.9693	0.2834	1.0205	0.2762	1.0049
135	11.619	0.2686	1.2379	0.2466	1.2671	0.2619	1.2668
165	12.845	0.2729	1.5108	0.2736	1.5407	0.2694	1.5363
195	13.965	0.2897	1.8005	0.2636	1.8043	0.2469	1.7832
225	15.000	0.2559	2.0564	0.2644	2.0687	0.3139	2.0971
255	15.969	0.2659	2.3223	0.2533	2.3221	0.3130	2.4101
Steady -state slope Cumulative Amount vs $T^{1/2} \times 10^{-2}$ (mcg/min $^{-1/2}$)		2.4350		2.3666		2.4242	
Diffusion Coefficient x 10^4 (cm ^{2}/min)		1.9638		1.8553		1.9464	
r^2		0.9990		0.9990		0.9910	

$D = 1.9217 \pm 0.0584$ %CV = 3.0412

Clindamycin Hydrochloride Release from Poloxamer 407 Gel by Using Durapore$^{(R)}$ and Chloroform.



Clindamycin Hydrochloride Release from Poloxamer 407 Gel by Using Durapore(R) and Chloroform.



Gelling Agent: Hydroxyethyl Cellulose, 2% w/w

Membrane: Durapore(R); Thickness: 0.132 mm.; Pore size: 0.45 micron

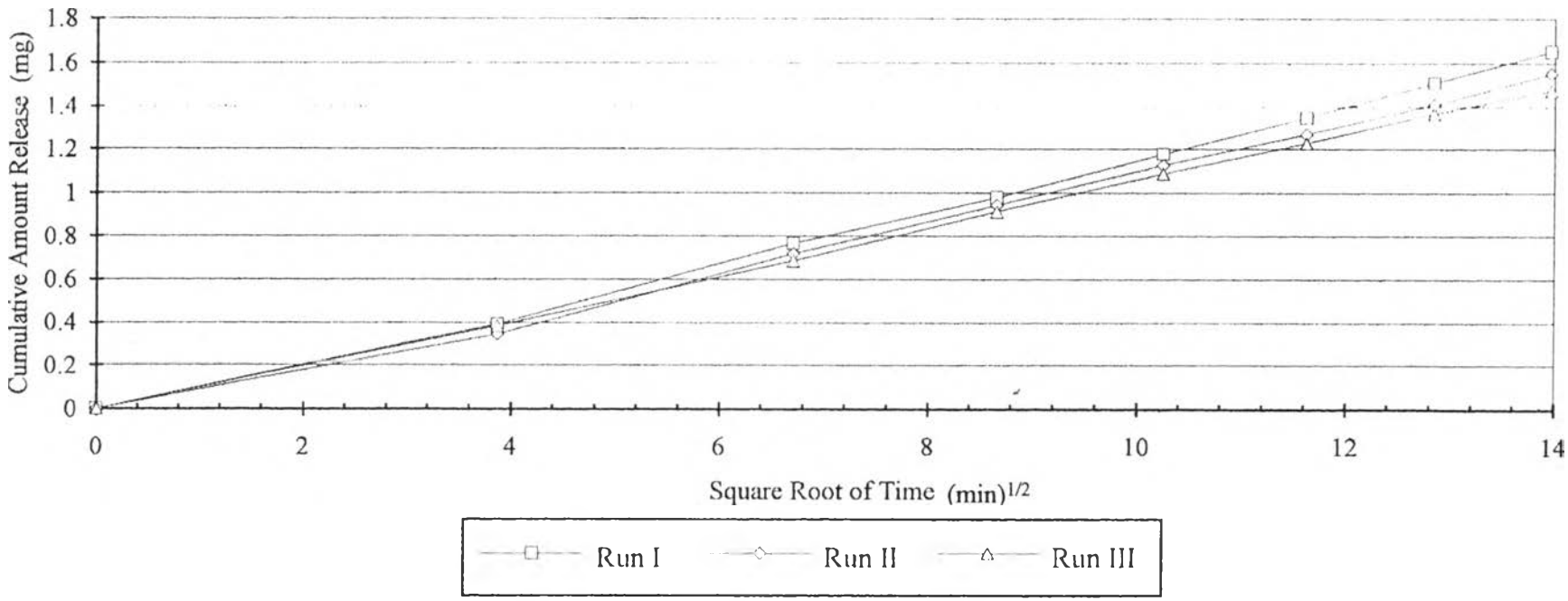
Receiving Medium: Chloroform

Release Run Data

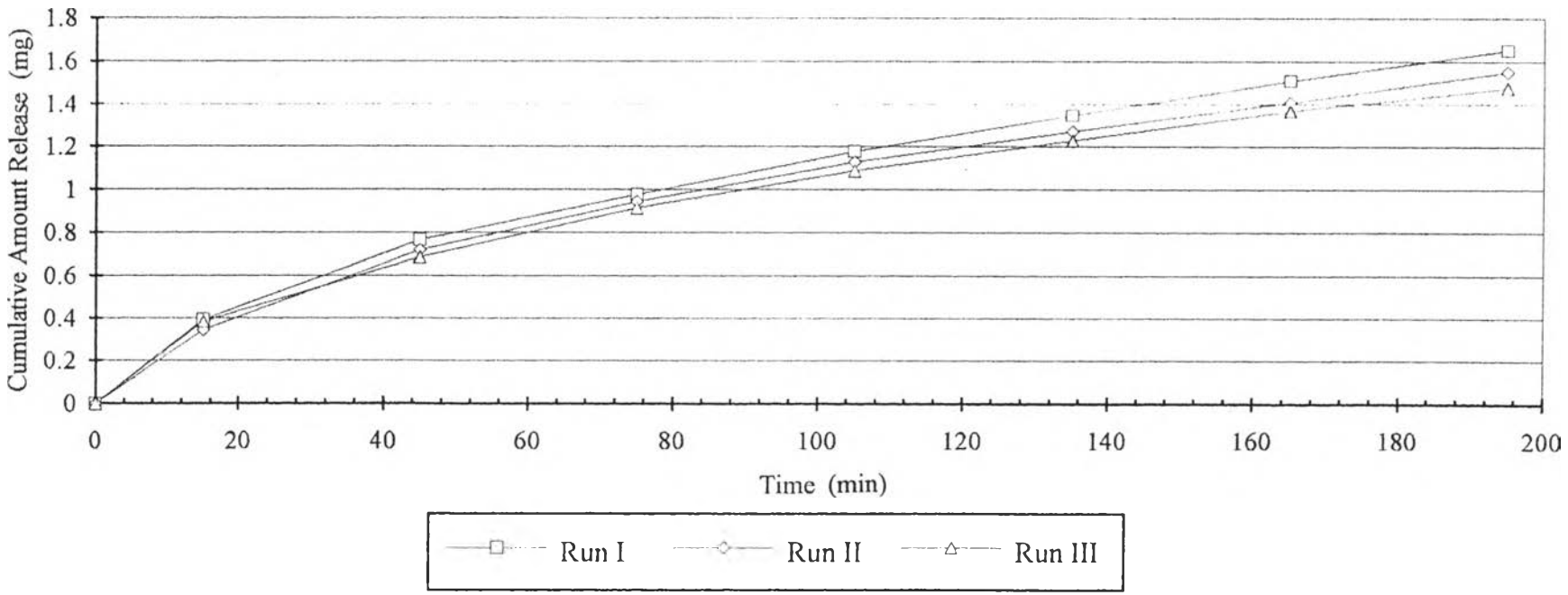
Time (min)		Run I		Run II		Run III	
T	$T^{1/2}$	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)
15	3.875	0.3936	0.3936	0.3446	0.3446	0.3847	0.3847
45	6.708	0.3736	0.7372	0.3746	0.7192	0.3019	0.6866
75	8.660	0.2100	0.9773	0.2236	0.9428	0.2281	0.9147
105	10.247	0.1996	1.1769	0.1844	1.1272	0.1727	1.0874
135	11.619	0.1685	1.3454	0.1431	1.2703	0.1403	1.2277
165	12.845	0.1651	1.5105	0.1372	1.4075	0.1385	1.3663
195	13.965	0.1424	1.6529	0.1448	1.5523	0.1096	1.4759
Steady -state slope Cumulative Amount vs $T^{1/2} \times 10^{-2}$ (mcg/min $^{-1/2}$)		1.2528		1.1762		1.0887	
Diffusion Coefficient x 10^{4} (cm ^{2}/min)		0.5198		0.4582		0.3926	
r^2		0.9990		0.9986		0.9997	

$D = 0.4569 \pm 0.0636$ %CV = 13.9232

Clindamycin Hydrochloride Release from Hydroxyethyl Cellulose Gel by Using Durapore(R) and Chloroform



Clindamycin Hydrochloride Release from Hydroxyethyl Cellulose Gel by Using Durapore(R) and Chloroform.



Gelling Agent: Hydroxypropyl Methylcellulose, 3% w/w

Membrane: Durapore(R); Thickness: 0.132 mm.; Pore size: 0.45 micron

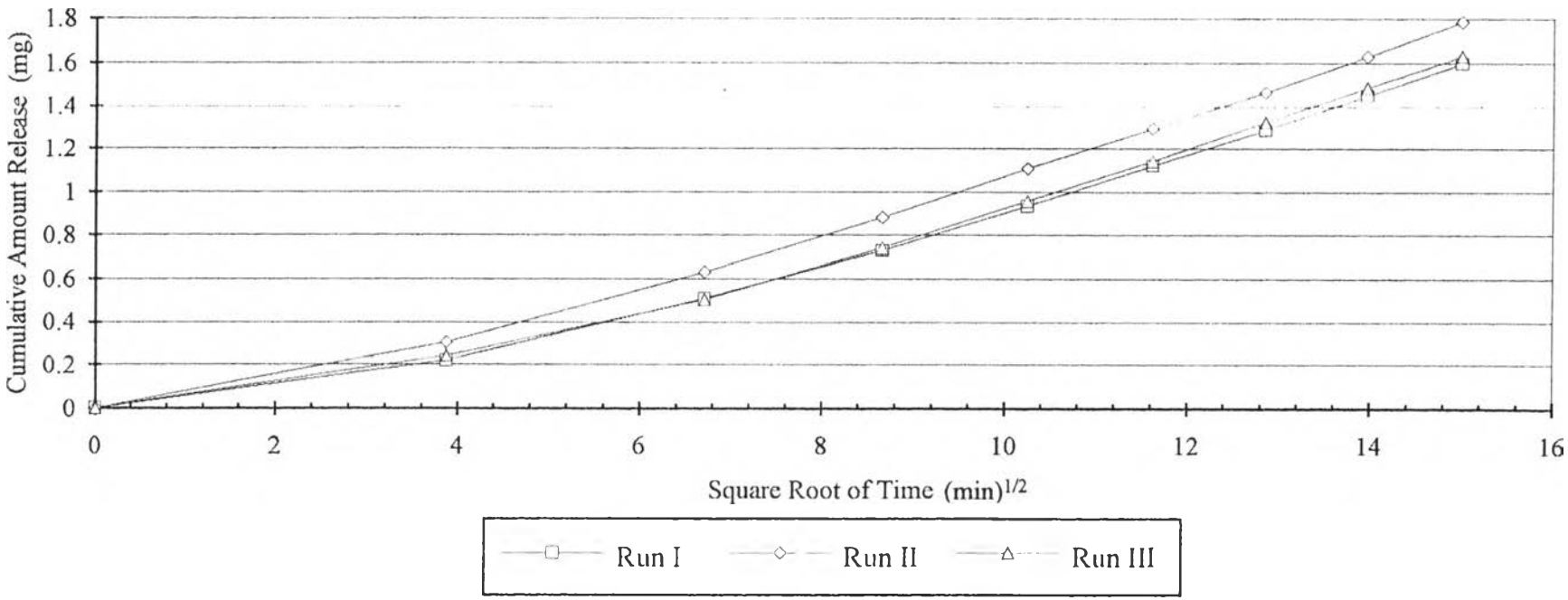
Receiving Medium: Chloroform

Release Run Data

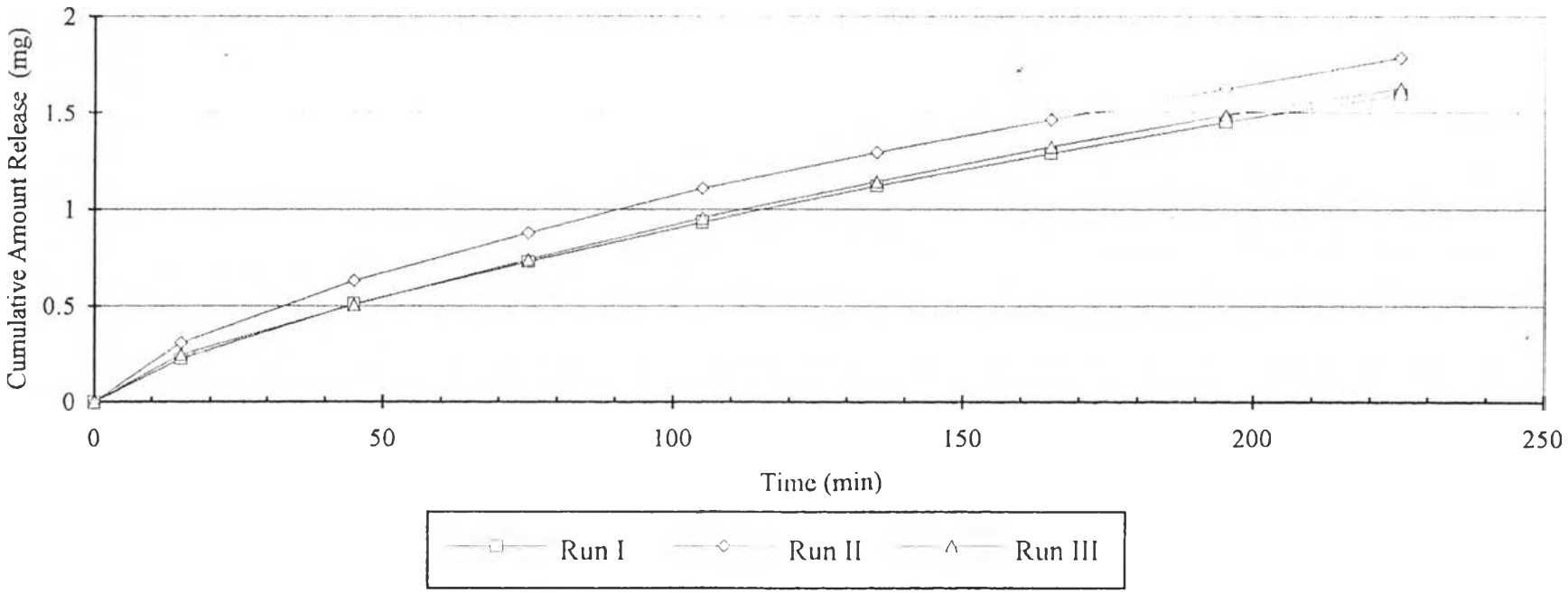
Time (min)		Run I		Run II		Run III	
T	$T^{1/2}$	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)
15	3.875	0.2211	0.2211	0.3061	0.3061	0.2431	0.2431
45	6.708	0.2904	0.5115	0.3260	0.6321	0.2625	0.5056
75	8.660	0.2187	0.7302	0.3495	0.8817	0.2378	0.7435
105	10.247	0.2042	0.9345	0.2266	1.1083	0.2141	0.9576
135	11.619	0.1867	1.1211	0.1854	1.2938	0.1866	1.1442
165	12.845	0.1660	1.2872	0.1702	1.4640	0.1797	1.3239
195	13.965	0.1629	1.4501	0.1653	1.6293	0.1637	1.4876
225	15.000	0.1491	1.5992	0.1586	1.7879	0.1441	1.6317
Steady -state slope Cumulative Amount vs $T^{1/2} \times 10^{-2}$ (mcg/min $^{-1/2}$)		1.3983		1.4278		1.4268	
Diffusion Coefficient x 10^{4} (cm ^{2}/min)		0.6476		0.6752		0.6742	
r^2		0.9997		0.9993		0.9998	

D = 0.6657 ± 0.0156 %CV = 2.3516

Clindamycin Hydrochloride Release from Hydroxypropyl Methylcellulose Gel by Using Durapore$^{(R)}$ and Chloroform.



Clindamycin Hydrochloride Release from Hydroxypropyl Methylcellulose Gel by Using Durapore(R) and Chloroform.



Gelling Agent: Poloxamer 407, 18% w/w

Membrane: Fluoropore(R); Thickness: 0.066 mm.; Pore size: 0.5 micron

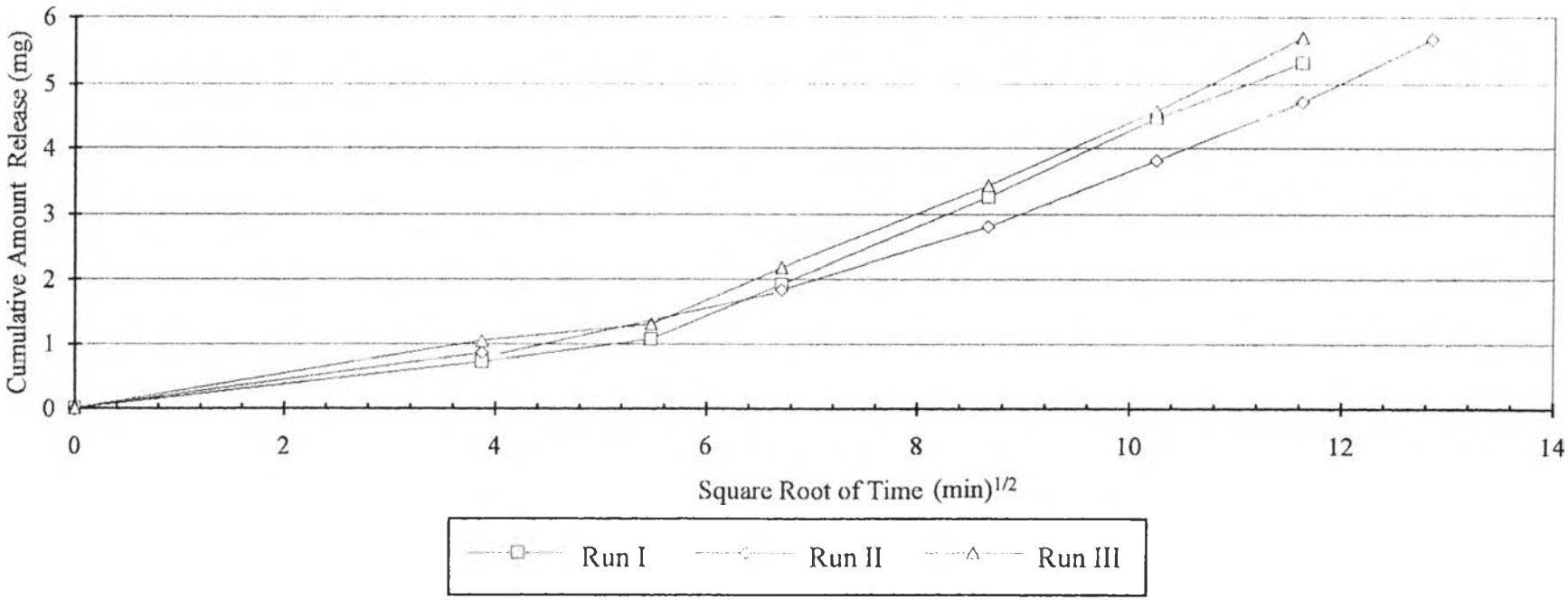
Receiving Medium: Acetate Buffer

Release Run Data

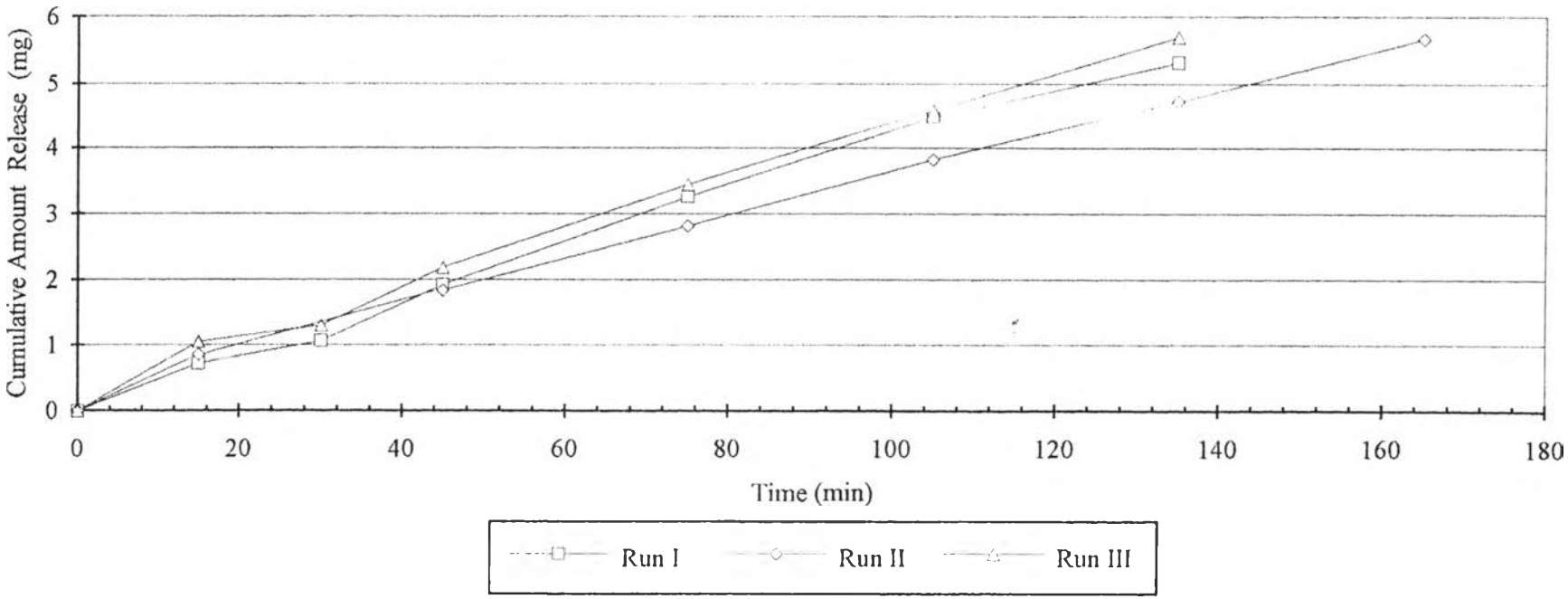
Time (min)		Run I		Run II		Run III	
T	$T^{1.2}$	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)
15	3.875	0.7164	0.7164	0.8562	0.8562	1.0458	1.0458
30	5.477	0.3499	1.063	0.2751	1.1363	0.2581	1.3039
45	6.708	0.8596	1.9259	0.7058	1.8371	0.8794	2.1833
75	8.660	1.3315	3.2574	0.9739	2.8110	1.1735	3.3568
105	10.247	1.2119	4.4693	1.0084	3.8194	1.1453	4.5020
135	11.619	0.8491	5.3184	0.9016	4.7210	1.1165	5.6185
165	12.845	-	-	0.9490	5.6700	-	-
Steady -state slope Cumulative Amount vs $T^{1/2} \times 10^{-2}$ (mcg/min $^{-1/2}$)		6.9854		6.7891		6.9780	
Diffusion Coefficient x 10^{-4} (cm ^{2}/min)		16.1612		15.2656		16.1270	
r^2		0.9988		0.9979		0.9953	

D = 15.8513 $\pm$ 0.5075 %CV = 3.2016

Clindamycin Hydrochloride Release from Poloxamer 407 Gel by Using Fluoropore(R) and Acetate Buffer.



Clindamycin Hydrochloride Release from Poloxamer 407 Gel by Using Fluoropore(R) and Acetate Buffer.



Gelling Agent: Hydroxyethyl Celulose, 2% w/w

Membrane: Fluoropore(R); Thickness: 0.066 mm.; Pore size: 0.5 micron

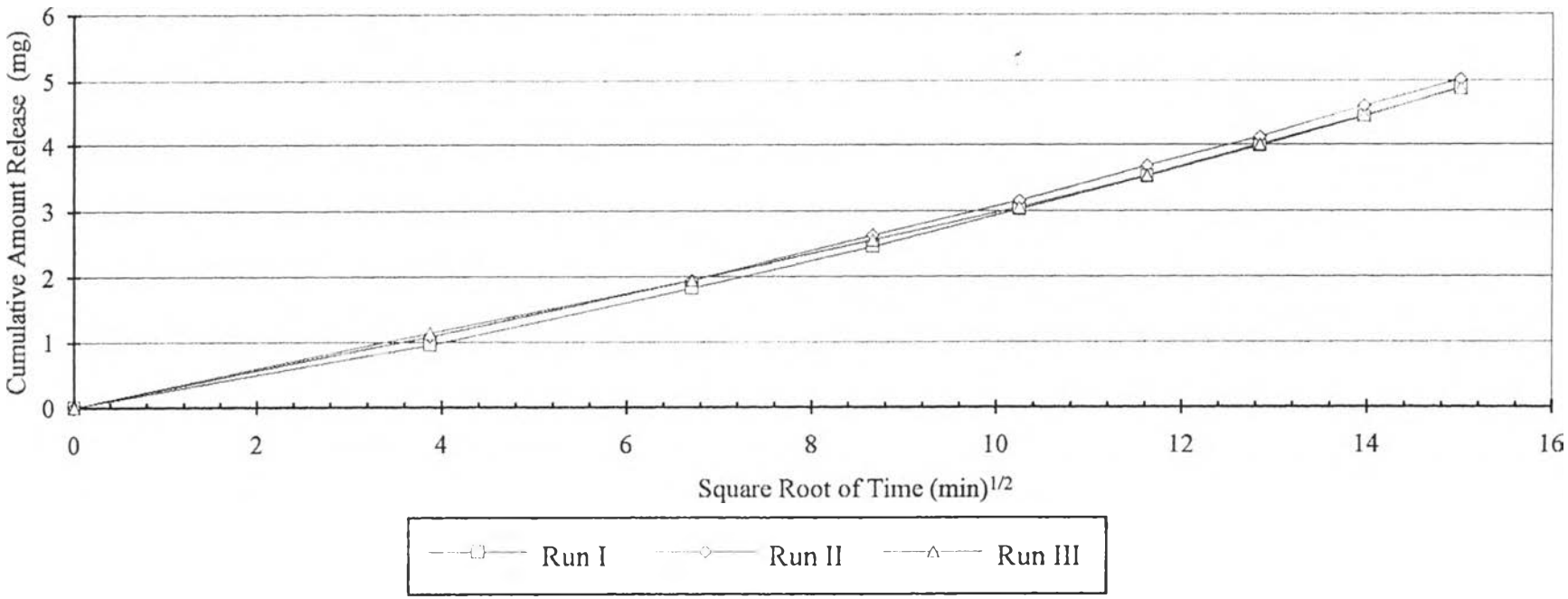
Receiving Medium: Acetate Buffer

Release Run Data

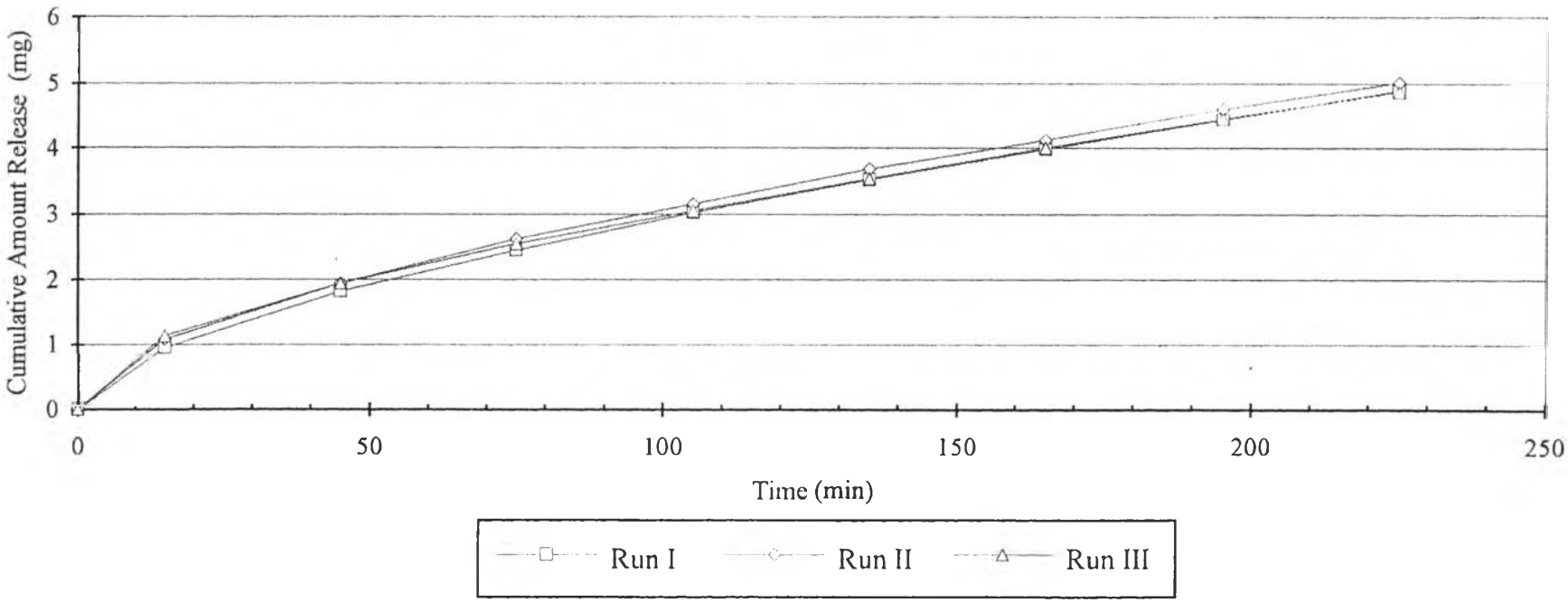
Time (min)		Run I		Run II		Run III	
T	$T^{1/2}$	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)
15	3.875	0.9466	0.9466	1.0784	1.0784	1.1348	1.1348
45	6.708	0.8745	1.8211	0.8692	1.9476	0.8136	1.9484
75	8.660	0.6308	2.4520	0.6758	2.6234	0.6063	2.5547
105	10.247	0.5647	3.0166	0.5280	3.1514	0.4952	3.0500
135	11.619	0.5060	3.5227	0.5314	3.6828	0.4870	3.5369
165	12.845	0.4612	3.9839	0.4422	4.1250	0.4648	4.0018
195	13.965	0.4513	4.4351	0.4470	4.6020	0.4479	4.4496
225	15.000	0.4523	4.8874	0.4094	5.0115	0.4255	4.8752
Steady-state slope Cumulative Amount vs $T^{1/2} \times 10^{-2}$ (mcg/min $^{-1/2}$)		3.8221		3.6666		3.4837	
Diffusion Coefficient x 10^{4} (cm ^{2}/min)		4.8383		4.4526		4.8932	
r^2		0.9987		0.9996		0.9992	

$D = 4.7280 \pm 0.2401$ %CV = 5.0783

Clindamycin Hydrochloride Release from Hydroxyethyl Cellulose Gel by Using Fluoropore(R) and Acetate Buffer.



Clindamycin Hydrochloride Release from Hydroxyethyl Cellulose Gel by Using Fluoropore(R) and Acetate Buffer.



Gelling Agent: Hydroxyethyl Methylcellulose, 3% w/w

Membrane: Fluoropore(R); Thickness: 0.066 mm.; Pore size: 0.5 micron

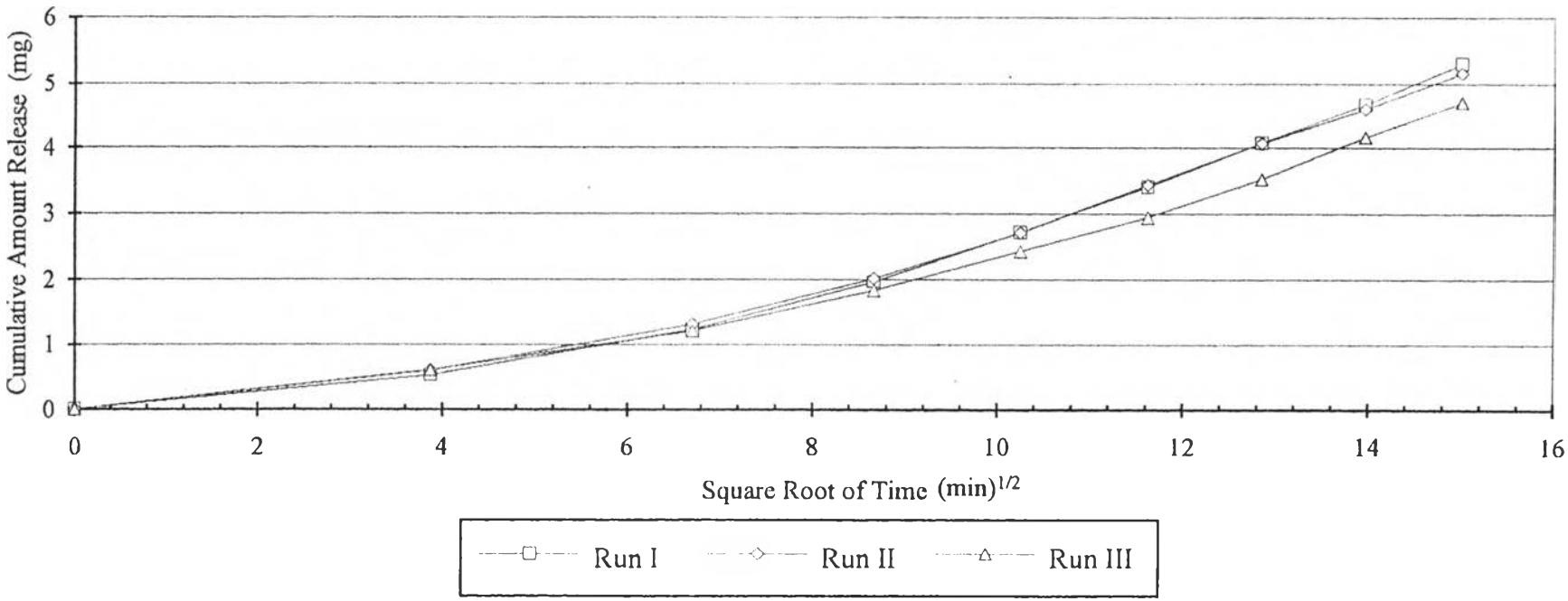
Receiving Medium : Acetate Buffer

Release Run Data

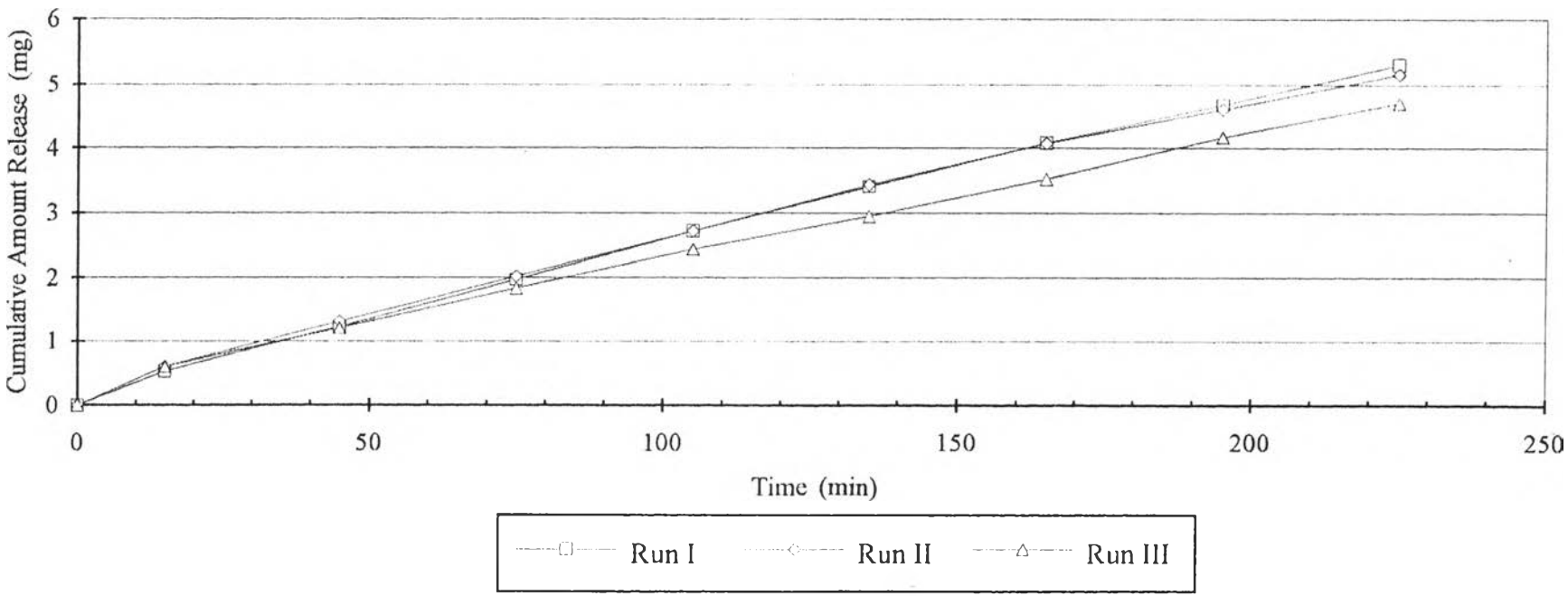
Time (min)		Run I		Run II		Run III	
T	$T^{1/2}$	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)
15	3.875	0.5220	0.5220	0.5931	0.5931	0.6025	0.6025
45	6.708	0.7085	1.2305	0.7174	1.3105	0.6057	1.2082
75	8.660	0.7407	1.9712	0.7081	2.0186	0.6258	1.8340
105	10.247	0.7466	2.7178	0.6973	2.7159	0.6009	2.4349
135	11.619	0.6870	3.4048	0.7171	3.4330	0.5094	2.9443
165	12.845	0.6738	4.0786	0.6421	4.0751	0.5779	3.5222
195	13.965	0.6007	4.6793	0.5284	4.6035	0.6441	4.1663
225	15.000	0.6300	5.3093	0.5571	5.1606	0.5407	4.7070
Steady -state slope Cumulative Amount vs $T^{1/2} \times 10^{-2}$ (mcg/min $^{-1/2}$)		5.2570		4.9869		5.2620	
Diffusion Coefficient x 10^{4} (cm ^{2}/min)		9.1531		8.2368		9.1705	
r^2		0.9982		0.9992		0.9984	

D = 8.8533 $\pm$ 0.5344 %CV = 6.0363

Clindamycin Hydrochloride Release from Hydroxypropyl Methylcellulose Gel by Using Fluoropore(R) and Acetate Buffer.



Clindamycin Hydrochloride Release from Hydroxypropyl Methylcellulose Gel by Using Fluoropore(R) and Acetate Buffer.



Gelling Agent: Poloxamer 407, 18% w/w

Membrane: Fluoropore (R) ; Thickness: 0.066 mm.; Pore size: 0.5 micron

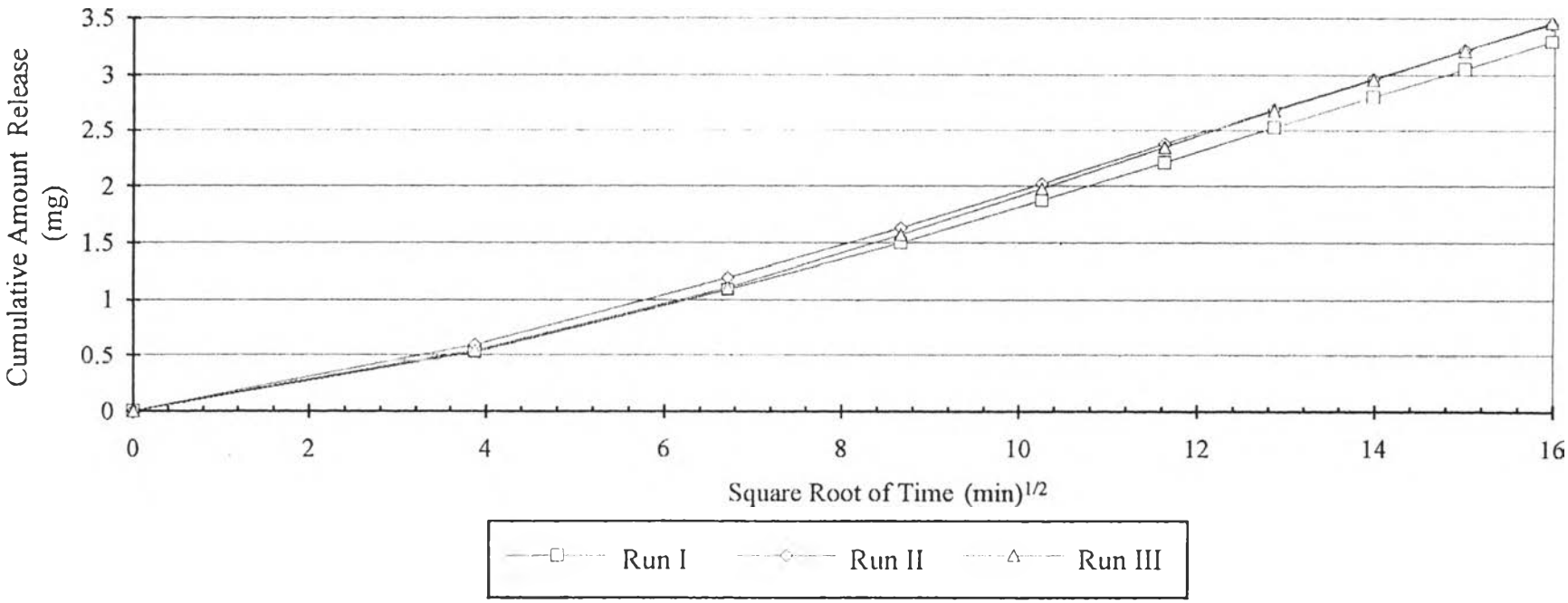
Receiving Medium: Chloroform

Release Run Data

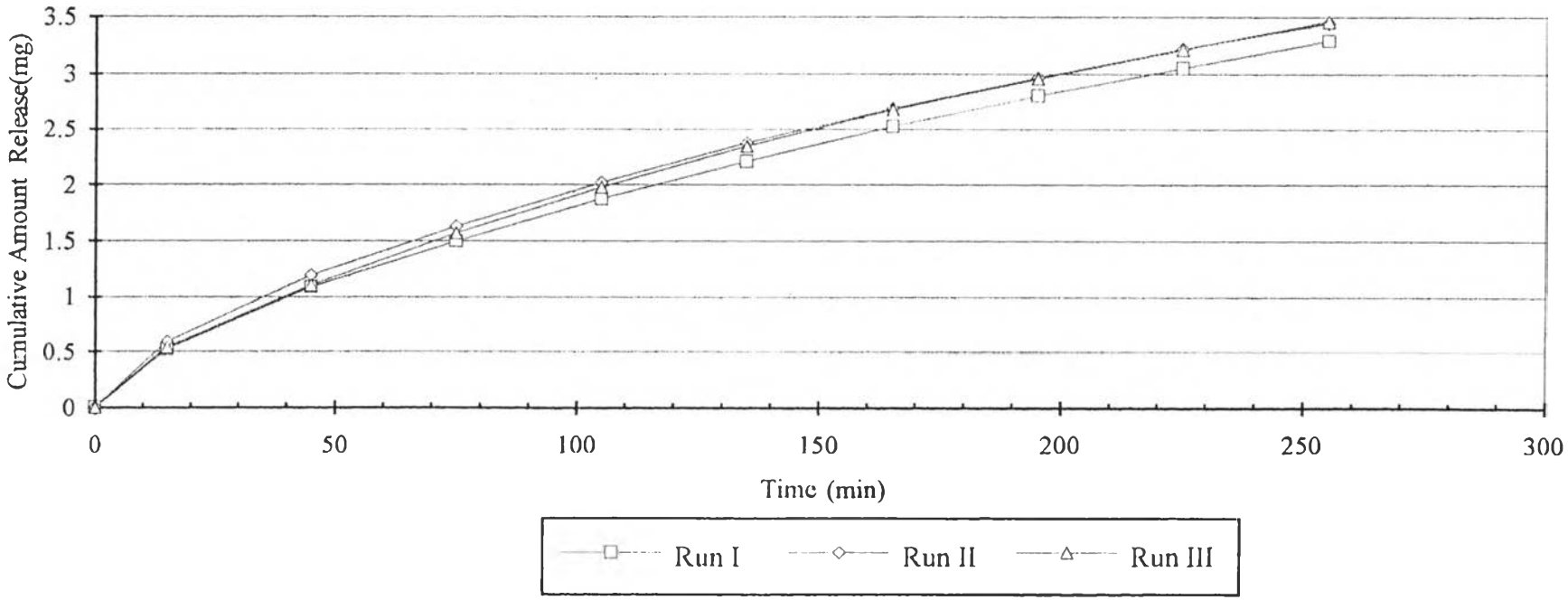
Time (min)		Run I		Run II		Run III	
T	$T^{1/2}$	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)
15	3.875	0.5282	0.5282	0.5934	0.5934	0.5453	0.5453
45	6.708	0.5588	1.0870	0.6000	1.1934	0.5607	1.1060
75	8.660	0.4117	1.4987	0.4363	1.6297	0.4629	1.5689
105	10.247	0.3794	1.8781	0.3935	1.9932	0.4097	1.9786
135	11.619	0.3322	2.2103	0.3510	2.3442	0.3687	2.3473
165	12.845	0.3148	2.5251	0.3145	2.6587	0.3293	2.6766
195	13.965	0.2816	2.8067	0.2789	2.9376	0.2823	2.9585
225	15.000	0.2436	3.0503	0.2561	3.1937	0.2599	3.2188
255	15.969	0.2450	3.2953	0.2257	3.4194	0.2468	3.4656
Steady -state slope Cumulative Amount vs $T^{1/2} \times 10^{-2}$ (mcg/min $^{-1/2}$)		2.468		2.5042		2.6021	
Diffusion Coefficient x 10^{4} (cm ^{2}/min)		2.0154		2.0770		2.2425	
r^2		0.9999		0.9999		0.9998	

$D = 2.1116 \pm 0.1174$ %CV = 5.5618

Clindamycin Hydrochloride Release from Poloxamer 407 Gel by Using Fluoropore(R) and Chloroform.



Clindamycin Hydrochloride Release from Poloxamer 407 Gel by Using Fluoropore$^{(R)}$ and Chloroform.



Gelling Agent: Hydroxyethyl Cellulose, 2% w/w

Membrane: Fluoropore(R); Thickness: 0.066 mm.; Pore size: 0.5 micron

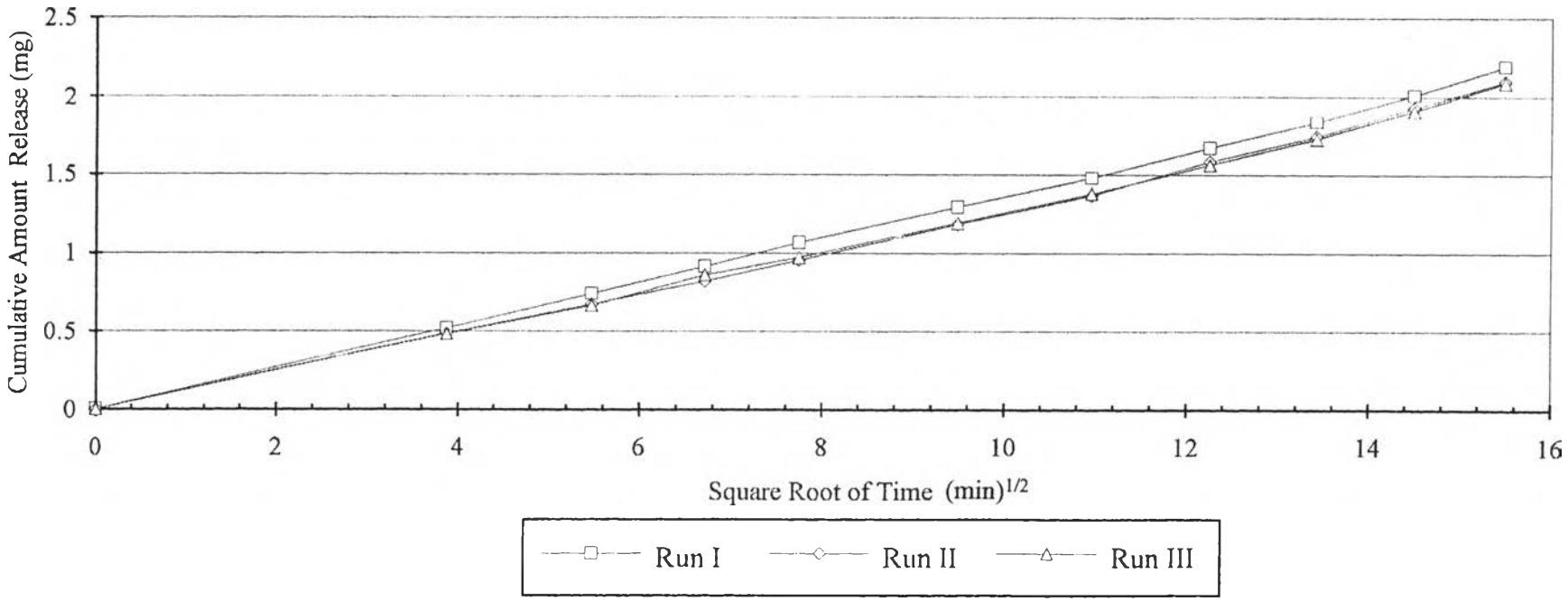
Receiving Medium: Chloroform

Release Run Data

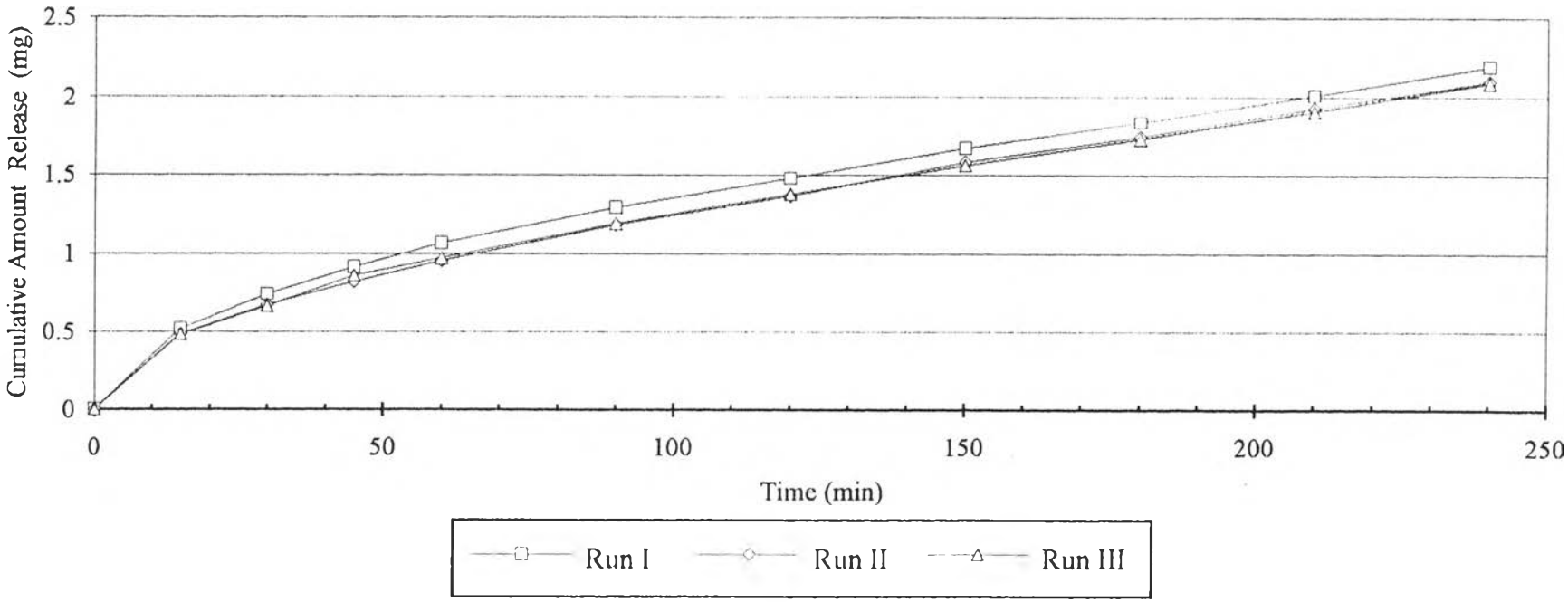
Time (min)		Run I		Run II		Run III	
T	$T^{1/2}$	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)
15	3.875	0.5197	0.1597	0.4851	0.4851	0.4823	0.4823
30	5.477	0.2212	0.7409	0.1893	0.6744	0.1814	0.6637
45	6.708	0.1737	0.9146	0.1463	0.8207	0.1947	0.8584
60	7.746	0.1512	1.0658	0.1327	0.9534	0.1126	0.9710
90	9.489	0.2247	1.2905	0.2396	1.1830	0.2199	1.1909
120	10.954	0.1867	1.4772	0.1825	1.3655	0.1856	1.3765
150	12.247	0.1928	1.6700	0.2147	1.5802	0.1818	1.5583
180	13.416	0.1652	1.8352	0.1624	1.7426	0.1675	1.7258
210	14.491	0.1774	2.0126	0.1897	1.9323	0.1842	1.9000
240	15.492	0.1840	2.1966	0.1699	2.1022	0.1832	2.0932
Steady -state slope Cumulative Amount vs $T^{1/2} \times 10^{-2}$ (mcg/min $^{-1/2}$)		1.5015		1.5399		1.4952	
Diffusion Coefficient x 10^4 (cm ^{2}/min)		0.7467		0.7854		0.7404	
r^2		0.9964		0.9970		0.9952	

$D = 0.7575 \pm 0.0244$ %CV = 3.2167

Clindamycin Hydrochloride Release from Hydroxyethyl Cellulose Gel by Using Fluoropore(R) and Chloroform.



Clindamycin Hydrochloride Release from Hydroxyethyl Cellulose Gel by Using Fluoropore(R) and Chloroform.



Gelling Agent: Hydroxypropyl Methylcellulose, 3% w/w

Membrane: Fluoropore(R); Thickness: 0.066 mm.; Pore size: 0.5 micron

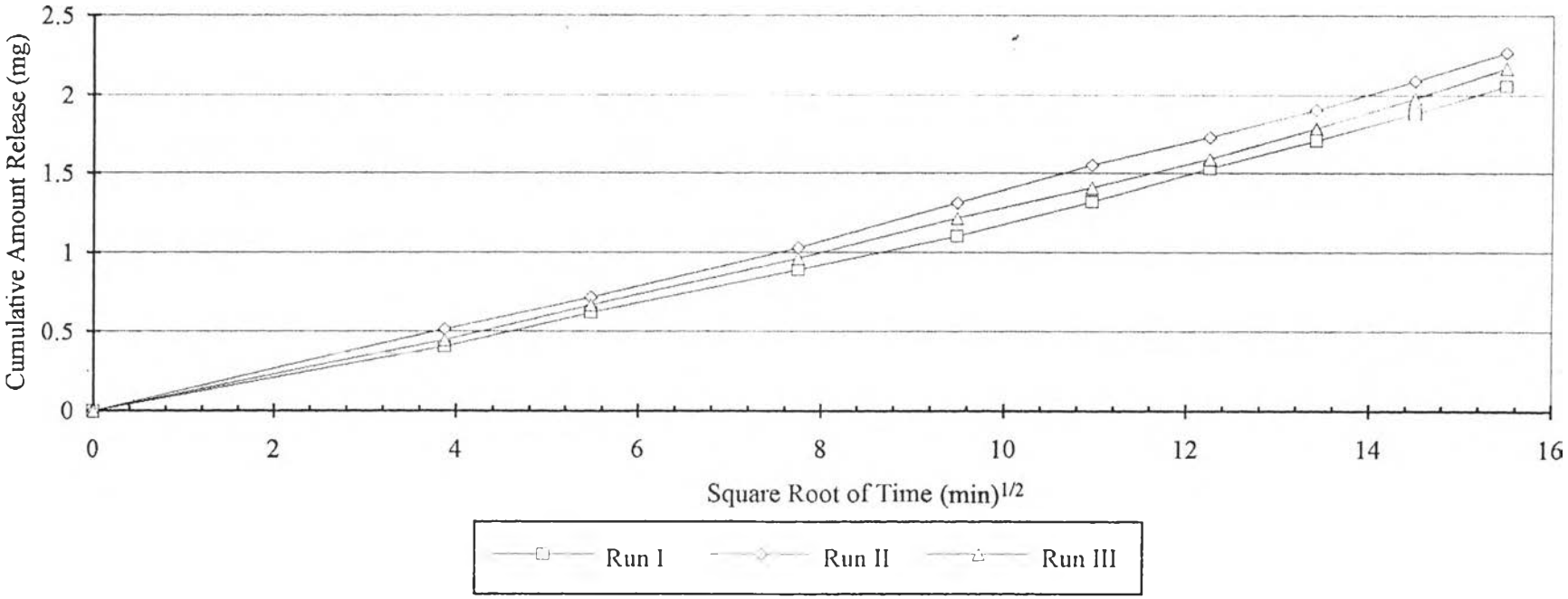
Receiving Medium: Chloroform

Release Run Data

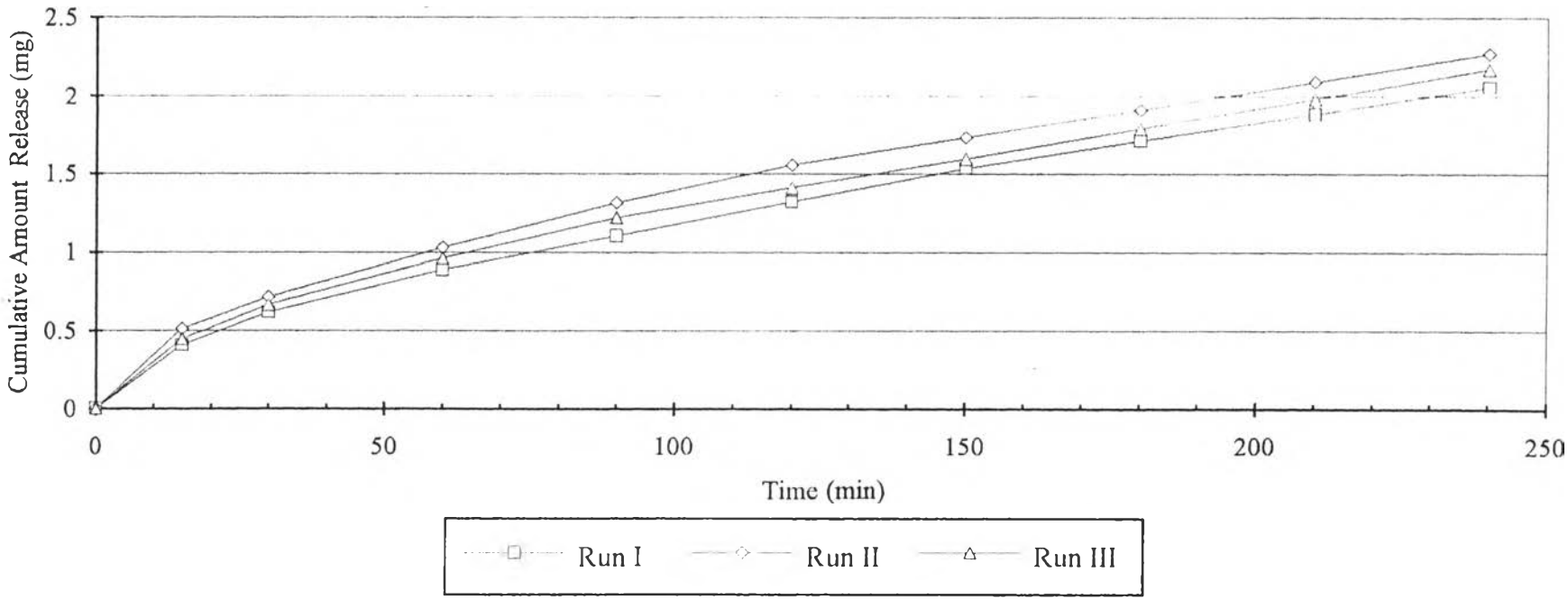
Time (min)		Run I		Run II		Run III	
T	$T^{1/2}$	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)
15	3.875	0.4052	0.4052	0.5140	0.5140	0.4450	0.4450
30	5.477	0.2151	0.6203	0.2034	0.7174	0.2243	0.6693
60	7.746	0.2762	0.8915	0.3139	1.0313	0.2939	0.9632
90	9.487	0.2105	1.1020	0.2812	1.3125	0.2551	1.2183
120	10.954	0.2179	1.3199	0.2408	1.5533	0.1933	1.4116
150	12.247	0.2124	1.5323	0.1764	1.7297	0.1804	1.5920
180	13.416	0.1763	1.7086	0.1789	1.9486	0.1962	1.7882
210	14.491	0.1745	1.8831	0.1873	2.0959	0.1929	1.9811
240	15.492	0.1789	2.0620	0.1777	2.2736	0.1947	2.1758
Steady -state slope Cumulative Amount vs $T^{1/2} \times 10^{-2}$ (mcg/min $^{-1/2}$)		1.5922		1.5806		1.5923	
Diffusion Coefficient x 10^4 (cm ^{2}/min)		0.8396		0.8274		0.8397	
r^2		0.9994		0.9990		0.9938	

$D = 0.8356 \pm 0.0071$ %CV = 0.8464

Clindamycin Hydrochloride Release from Hydroxypropyl Methylcellulose Gel by Using Fluoropore(R) and Chloroform.



Clindamycin Hydrochloride Release from Hydroxypropyl Methylcellulose Gel by Using Fluoropore(R) and Chloroform.



Gelling Agent: Poloxamer 407, 18% w/w

Membrane: Nylon 66; Thickness: 0.149 mm.; Pore size: 0.45 micron

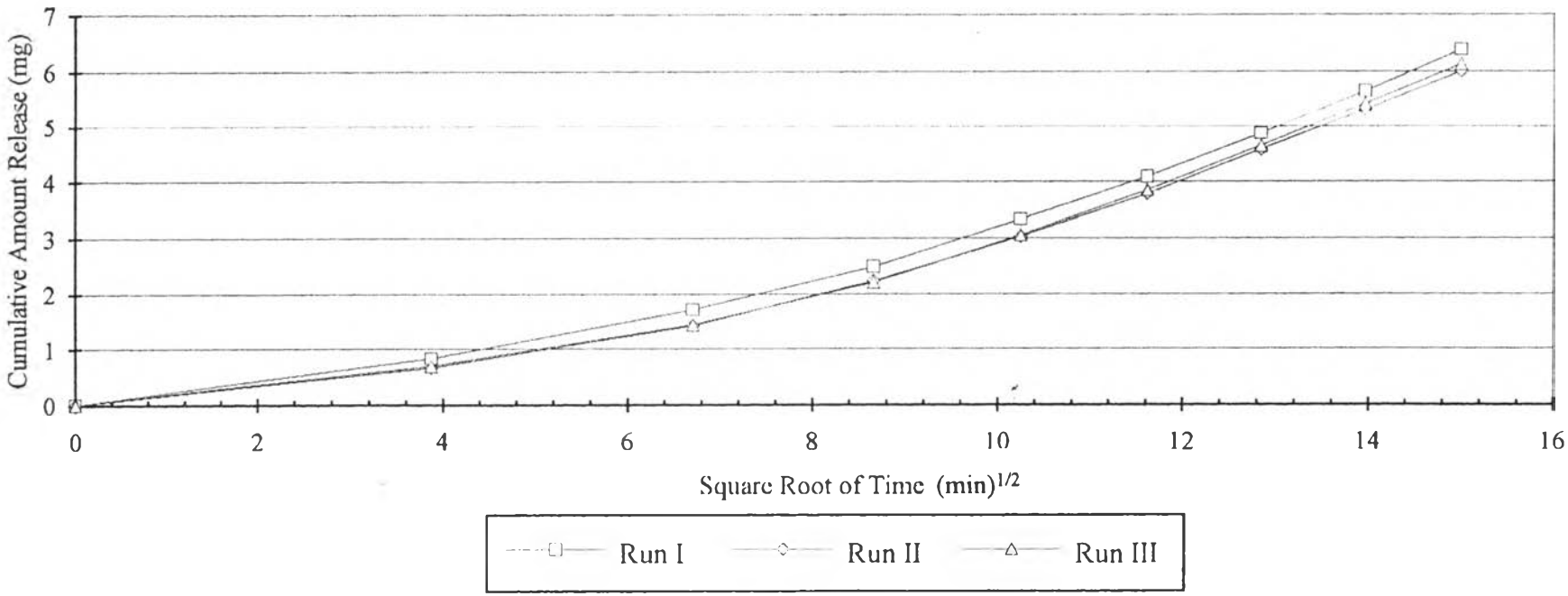
Receiving Medium: Acetate Buffer

Release Run Data

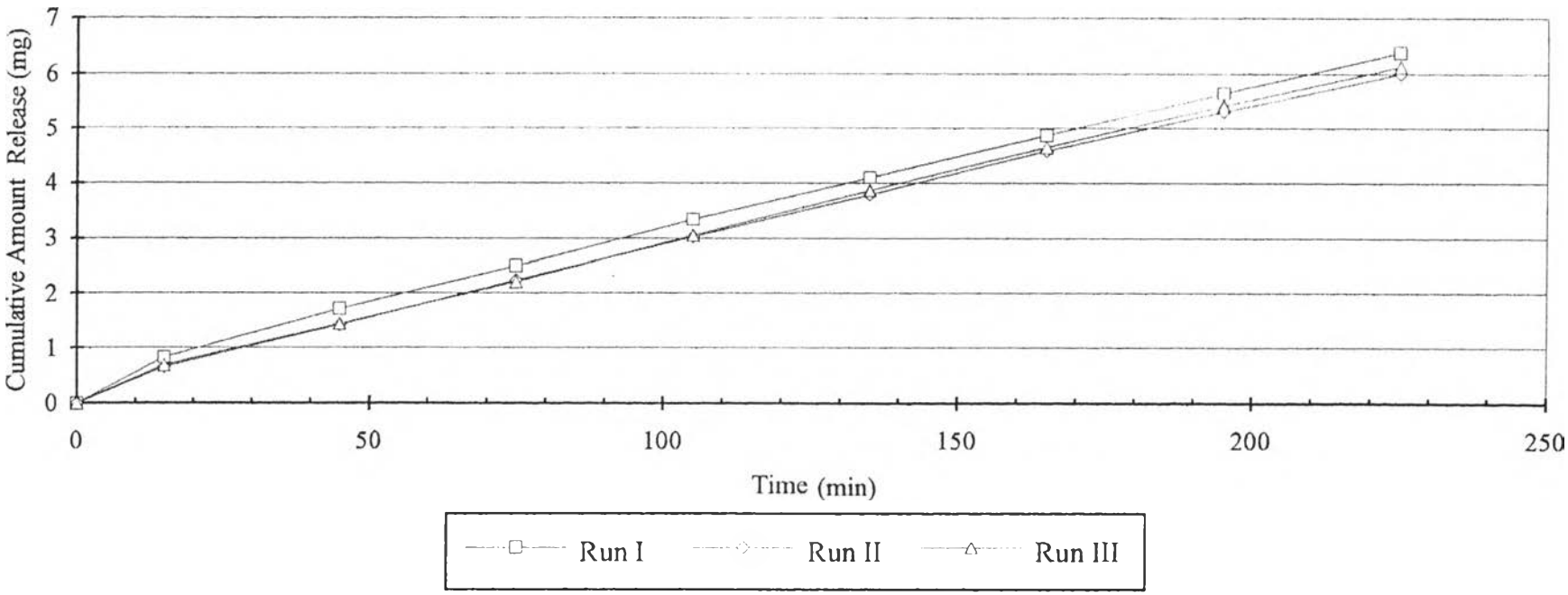
Time (min)		Run I		Run II		Run III	
T	$T^{1/2}$	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)
15	3.875	0.8309	0.8309	0.6596	0.6596	0.6919	0.6919
45	6.708	0.8841	1.7150	0.7671	1.4267	0.7496	1.4415
75	8.660	0.7777	2.4927	0.9102	2.2369	0.7721	2.6125
105	10.247	0.8428	3.3355	0.7883	3.0252	0.8376	3.0001
135	11.619	0.7619	4.0974	0.7601	3.7853	0.8069	3.8070
165	12.845	0.7683	4.8657	0.7919	4.5772	0.7893	4.5963
195	13.965	0.7798	5.6455	0.7299	5.3071	0.7658	5.3621
225	15.000	0.7396	6.3851	0.6965	6.0036	0.7215	6.0836
Steady -state slope Cumulative Amount vs $T^{1/2} \times 10^{-2}$ (mcg/min $^{-1/2}$)		6.7780		6.5543		6.7400	
Diffusion Coefficient x 10^4 (cm ^{2}/min)		15.2158		14.2280		15.0456	
r^2		0.9990		0.9999		0.9996	

$D = 14.8298 \pm 0.5281$ %CV = 3.5609

Clindamycin Hydrochloride Release from Poloxamer 407 Gel by Using Nylon 66 and Acetate Buffer.



Clindamycin Hydrochloride Release from Poloxamer 407 Gel by Using Nylon 66 and Acetate Buffer.



Gelling Agent: Hydroxyethyl Cellulose, 2% w/w

Membrane: Nylon 66; Thickness: 0.149 mm.; Pore size: 0.45 micron

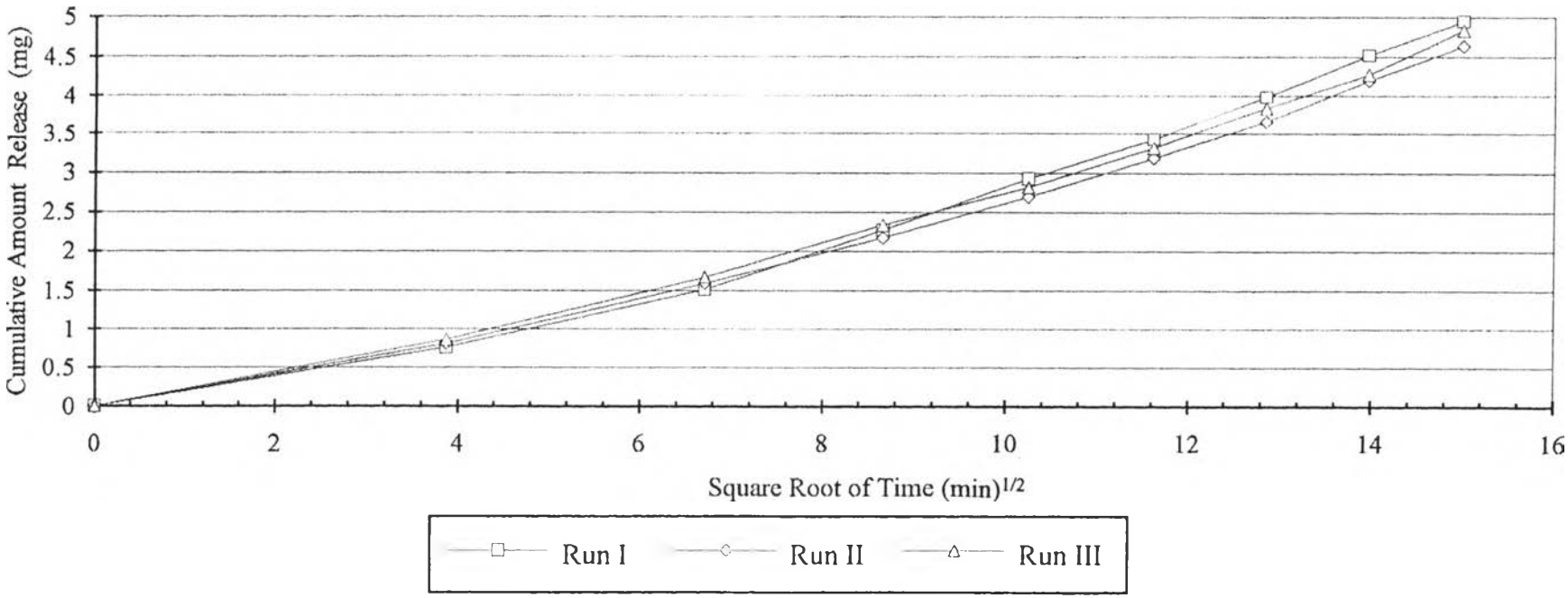
Receiving Medium: Acetate Buffer

Release Run Data

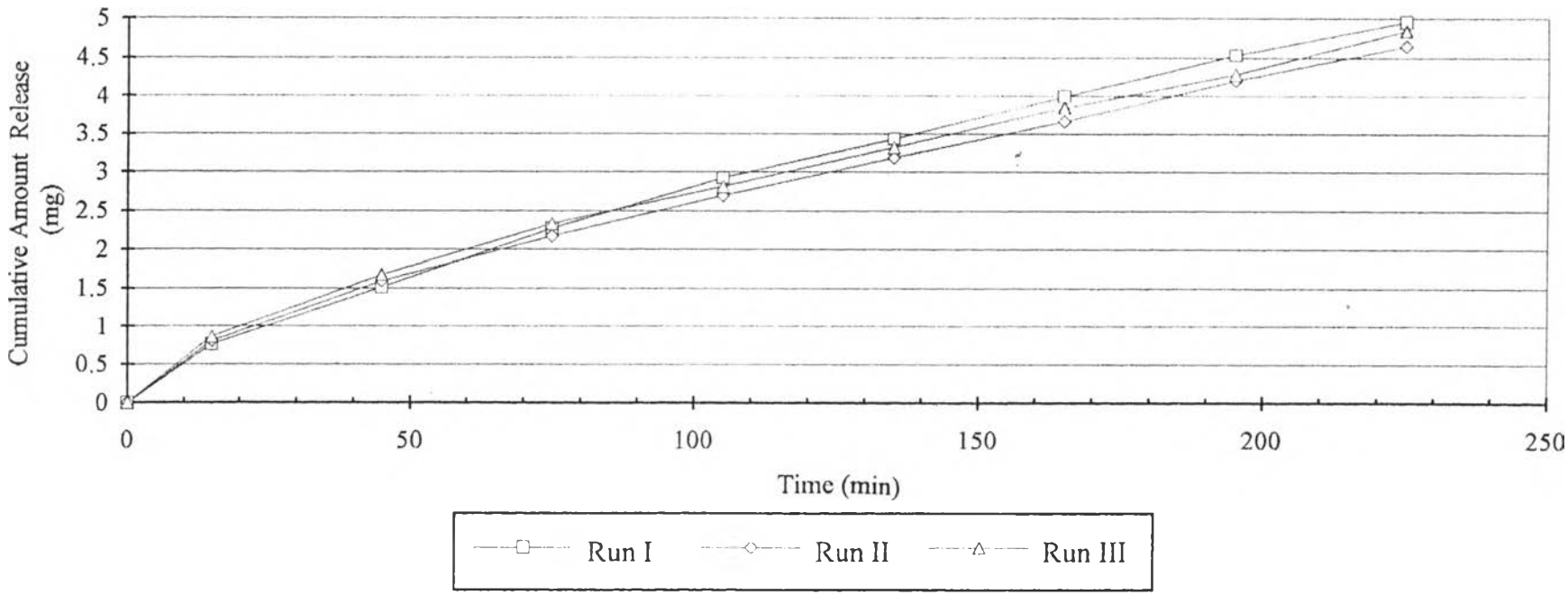
Time (min)		Run I		Run II		Run III	
T	$T^{1/2}$	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)
15	3.873	0.7589	0.7589	0.8039	0.8039	0.8637	0.8637
45	6.708	0.7539	1.5128	0.7896	1.5935	0.8063	1.6700
75	8.660	0.7546	2.2674	0.5787	2.1722	0.6527	2.3227
105	10.247	0.6548	2.9222	0.5235	2.6957	0.4893	2.8120
135	11.619	0.5075	3.4297	0.4895	3.1852	0.5093	3.3213
165	12.845	0.5626	3.9923	0.4759	3.6611	0.5233	3.8446
195	13.964	0.5336	4.5259	0.5413	4.2024	0.4398	4.2844
225	15.000	0.4259	4.9518	0.4401	4.6425	0.5595	4.8439
Steady -state slope Cumulative Amount vs $T^{1/2} \times 10^{-2}$ (mcg/min $^{-1/2}$)		4.1615		4.3591		4.2283	
Diffusion Coefficient x 10^4 (cm ^{2}/min)		5.7357		6.2934		5.9214	
r^2		0.9991		0.9982		0.9958	

$D = 5.9835 \pm 0.2840$ %CV = 4.4762

Clindamycin Hydrochloride Release from Hydroxyethyl Cellulose Gel by Using Nylon 66 and Acetate Buffer.



Clindamycin Hydrochloride Release from Hydroxyethyl Cellulose Gel by Using Nylon 66 and Acetate Buffer.



Gelling Agent: Hydroxypropyl Methylcellulose, 3% w/w

Membrane: Nylon 66; Thickness: 0.149 mm.; Pore size: 0.45 micron

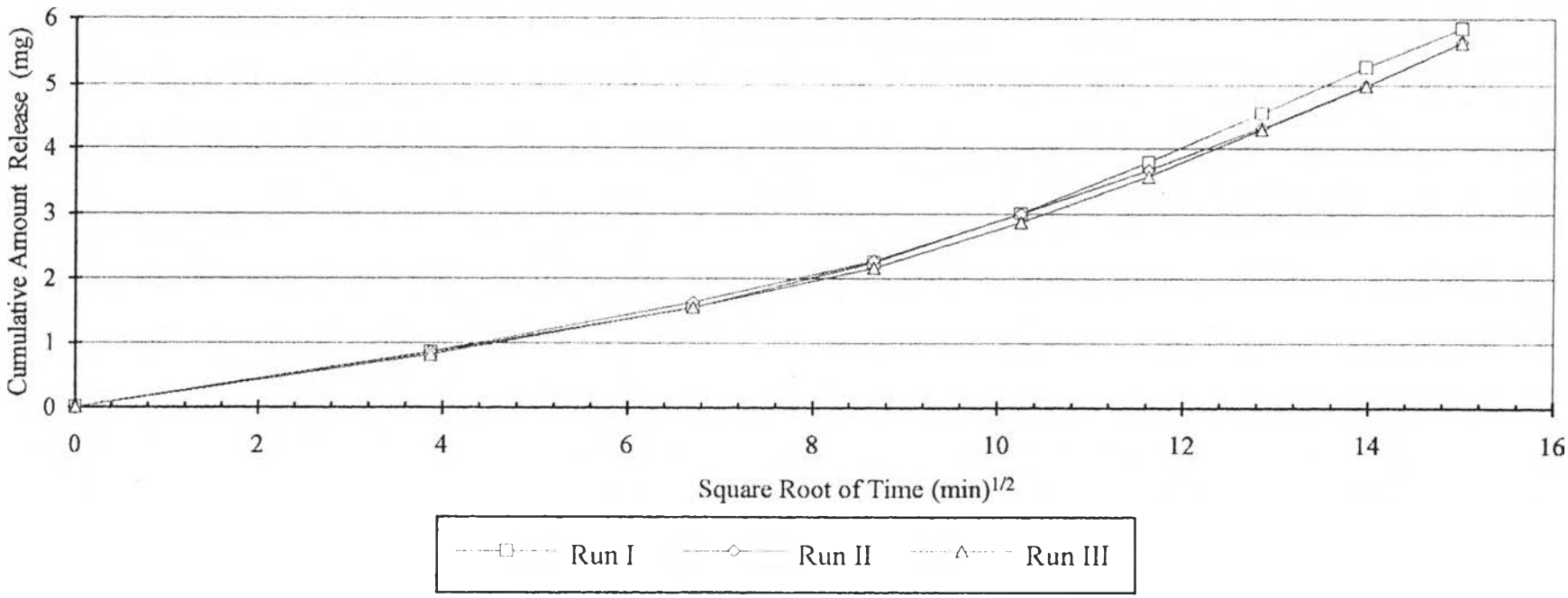
Receiving Medium: Acetate Buffer

Release Run Data

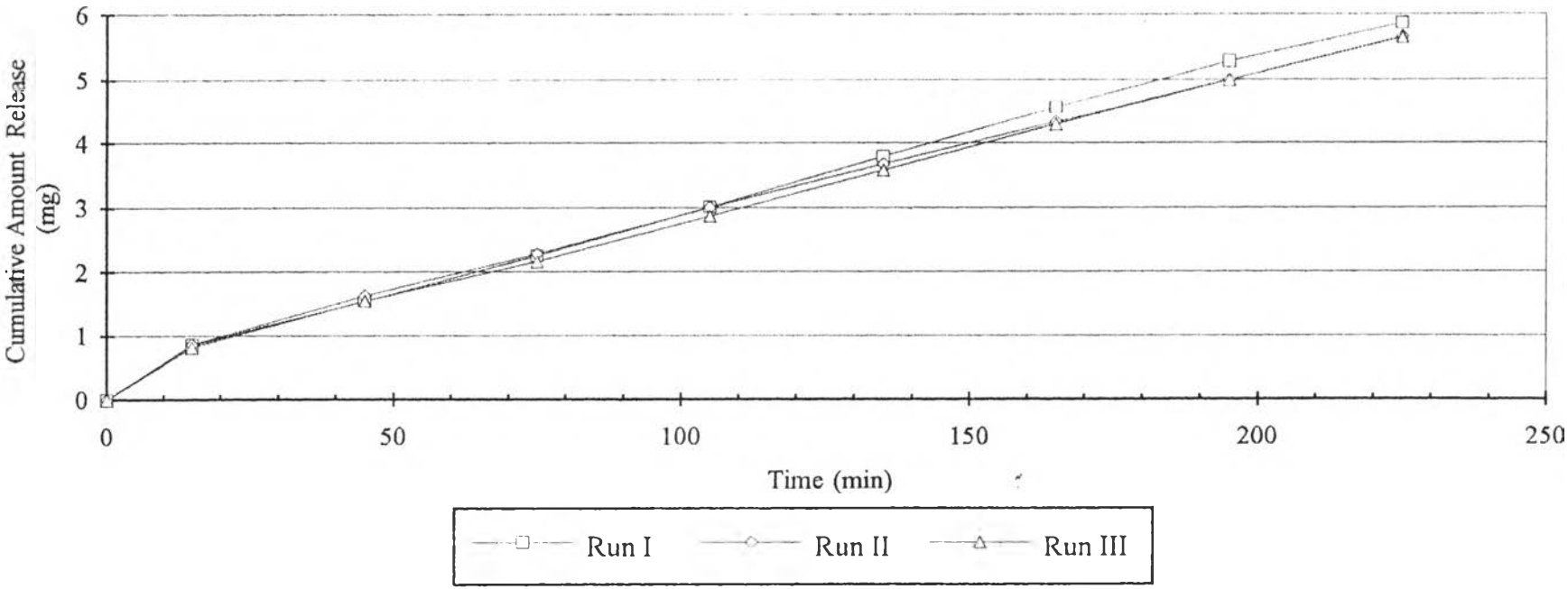
Time (min)		Run I		Run II		Run III	
T	$T^{1/2}$	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)
15	3.873	0.8525	0.8525	0.8595	0.8595	0.8131	0.8131
45	6.708	0.6888	1.5413	0.7700	1.6292	0.7373	1.5504
75	8.660	0.7096	2.2509	0.6489	2.2784	0.6128	2.1632
105	10.247	0.7521	3.0030	0.7201	2.9985	0.7009	2.8641
135	11.619	0.7883	3.7913	0.6717	3.6702	0.7103	3.5744
165	12.845	0.7714	4.5627	0.6583	4.3285	0.7211	4.2955
195	13.964	0.7141	5.2768	0.6634	4.9919	0.6925	4.9880
225	15.000	0.5834	5.8602	0.6658	5.6577	0.6634	5.6514
Steady -state slope Cumulative Amount vs $T^{1/2} \times 10^{-2}$ (mcg/min $^{-1/2}$)		6.0746		5.8740		5.8830	
Diffusion Coefficient x 10^4 (cm ^{2}/min)		12.2215		11.4277		11.4627	
r^2		0.9996		0.9984		0.9982	

$D = 11.7040 \pm 0.4485$ %CV = 3.8324

Clindamycin Hydrochloride Release from Hydroxypropyl Methylcellulose Gel by Using Nylon 66 and Acetate Buffer.



Clindamycin Hydrochloride Release from Hydroxypropyl Methylcellulose Gel by Using Nylon 66 and Acetate Buffer.



Gelling Agent: Poloxamer 407, 18% w/w

Membrane: Nylon 66; Thickness: 0.149 mm.; Pore size: 0.45 micron

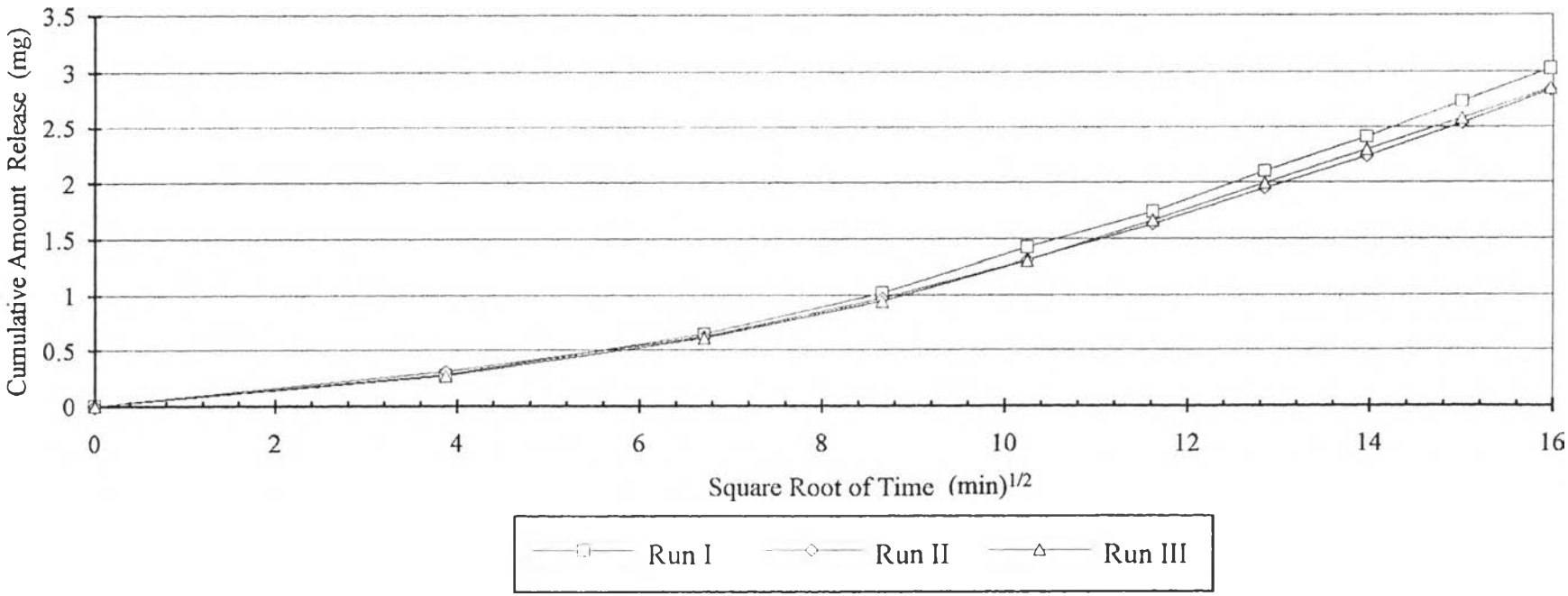
Receiving Medium: Chloroform

Release Run Data

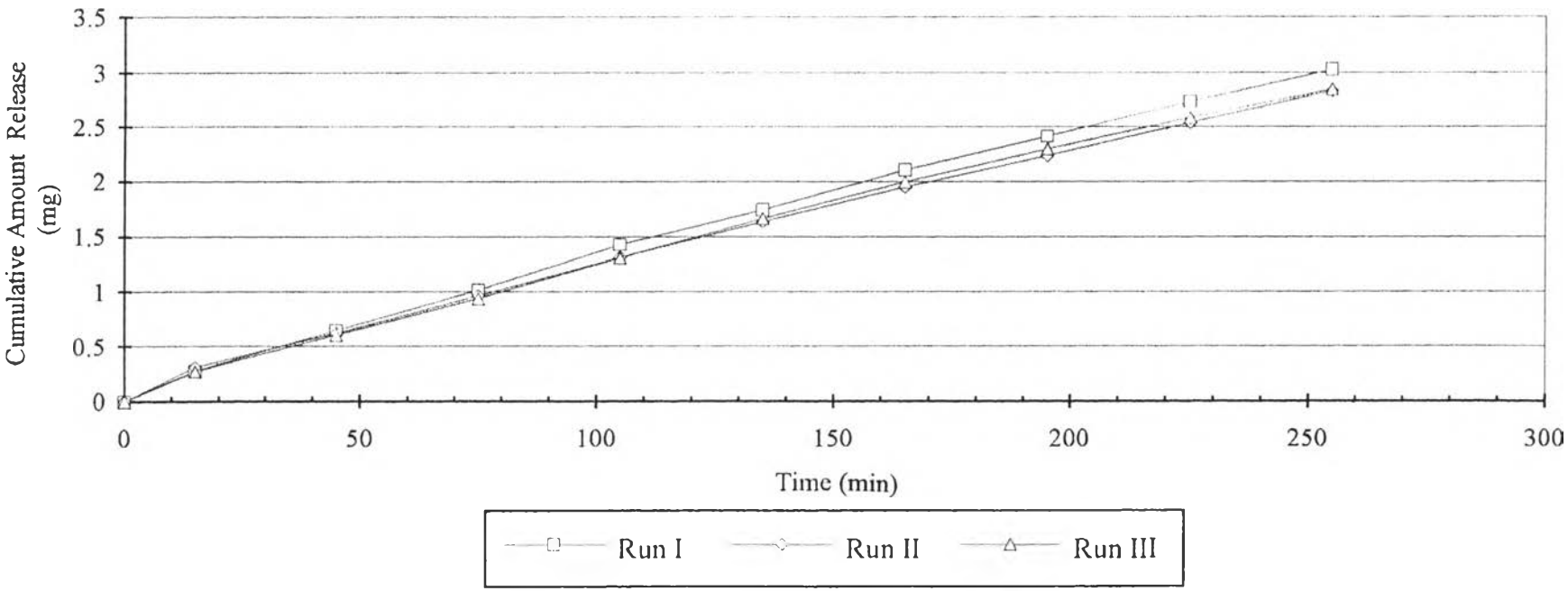
Time (min)		Run I		Run II		Run III	
T	$T^{1/2}$	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)
15	3.873	0.2784	0.2784	0.3109	0.3109	0.2724	0.2724
45	6.708	0.3680	0.6464	0.3109	0.6218	0.3340	0.6064
75	8.660	0.3710	1.0174	0.3467	0.9685	0.3353	0.9417
105	10.247	0.4090	1.4264	0.3433	1.3118	0.3660	1.3077
135	11.619	0.3146	1.7416	0.3185	1.6303	0.3545	1.6622
165	12.845	0.3627	2.1037	0.3176	1.9479	0.3319	1.9941
195	13.865	0.3070	2.4107	0.2858	2.2337	0.2992	2.2933
225	15.000	0.3235	2.7342	0.3002	2.5339	0.2875	2.5848
255	15.965	0.2909	3.0251	0.3002	2.8341	0.2696	2.8544
Steady -state slope Cumulative Amount vs $T^{1/2} \times 10^{-2}$ (mcg/min $^{-1/2}$)		2.7453		2.5459		2.6291	
Diffusion Coefficient x 10^4 (cm ^{2}/min)		2.4961		2.1467		2.2893	
r^2		0.9976		0.9962		0.9990	

$D = 2.3107 \pm 0.1757$ %CV = 7.6029

Clindamycin Hydrochloride Release from Poloxamer 407 Gel by Using Nylon 66 and Chloroform.



Clindamycin Hydrochloride Release from Poloxamer 407 Gel by Using Nylon 66 and Chloroform.



Gelling Agent: Hydroxyethyl Cellulose, 2% w/w

Membrane: Nylon 66; Thickness: 0.149 mm.; Pore size: 0.45 micron

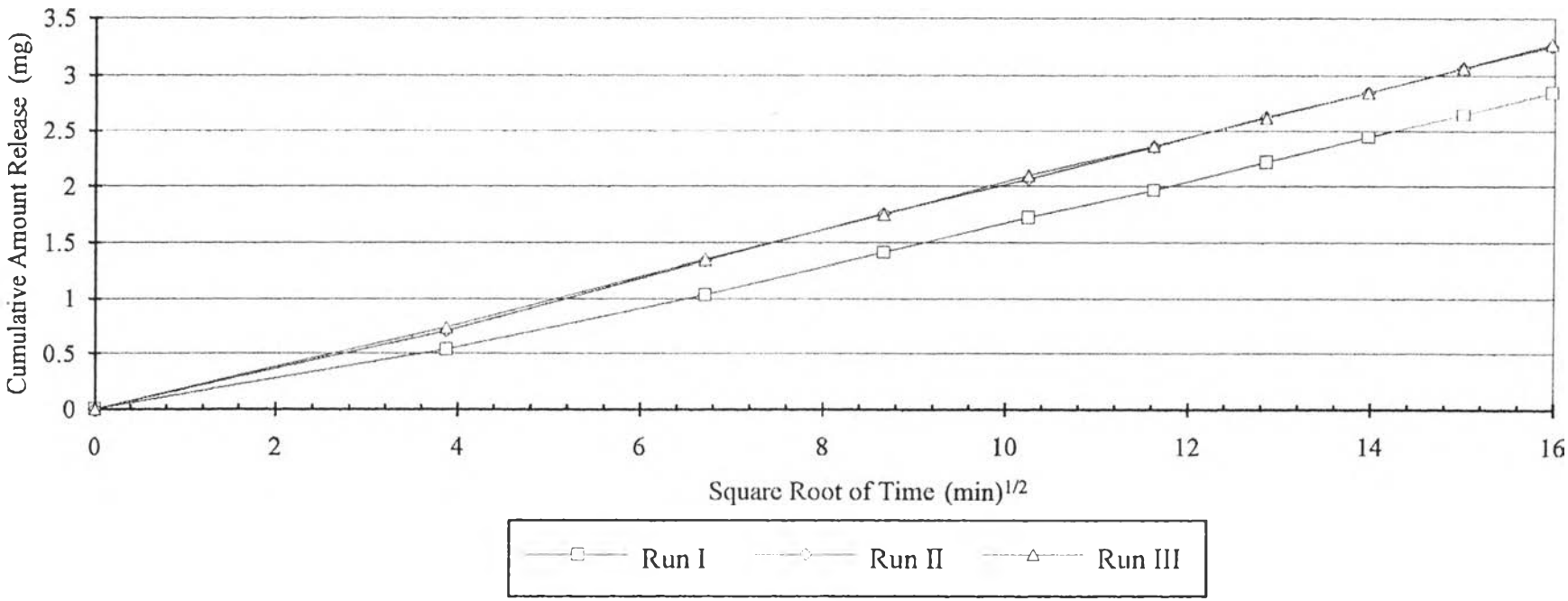
Receiving Medium: Chloroform

Release Run Data

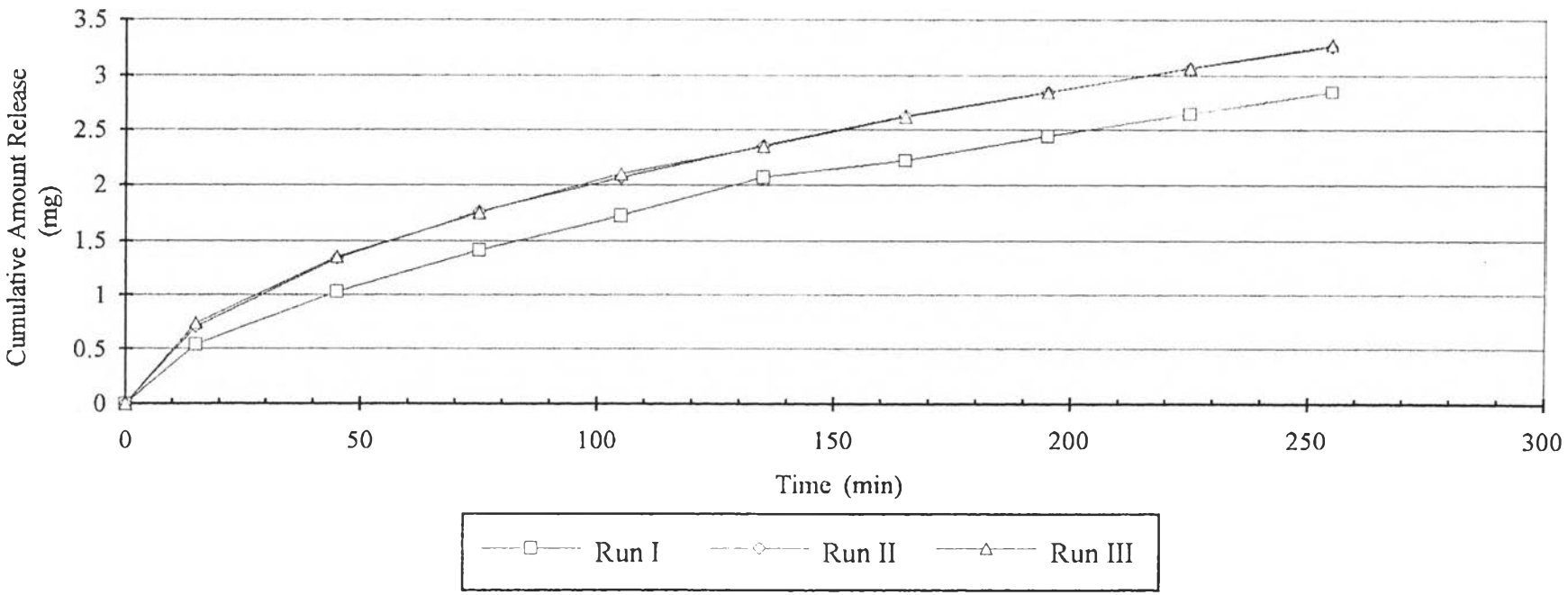
Time (min)		Run I		Run II		Run III	
T	$T^{1/2}$	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)
15	3.875	0.5396	0.5396	0.7054	0.7054	0.7391	0.7391
45	6.708	0.4927	1.0323	0.6351	1.3405	0.6118	1.3509
75	8.660	0.3805	1.4128	0.4159	1.7564	0.3983	1.7492
105	10.247	0.3098	1.7226	0.3084	2.0648	0.3485	2.0977
135	11.619	0.2443	1.9669	0.2891	2.3539	0.2666	2.3643
165	12.845	0.2528	2.2197	0.2759	2.9698	0.2540	2.6183
195	13.965	0.2216	2.4413	0.2201	2.8499	0.2283	2.8466
225	15.000	0.2047	2.6460	0.2146	3.0645	0.2220	3.0686
255	15.969	0.2040	2.8500	0.1947	3.2592	0.2089	3.2775
Steady -state slope Cumulative Amount vs $T^{1/2} \times 10^{-2}$ (mcg/min $^{-1/2}$)		1.9532		2.0755		2.0732	
Diffusion Coefficient x 10^{4} (cm^{2}/min)		1.2635		1.4267		1.4236	
r^2		0.9999		0.9999		0.9999	

$D = 1.3713 \pm 0.0933$ %CV = 6.8069

Clindamycin Hydrochloride Release from Hydroxyethyl Cellulose Gel by Using Nylon 66 and Chloroform,



Clindamycin Hydrochloride Release from Hydroxyethyl Cellulose Gel by Using Nylon 66 and Chloroform.



Gelling Agent: Hydroxypropyl Methylcellulose, 3% w/w

Membrane: Nylon 66; Thickness: 0.149 mm.; Pore size: 0.45 micron

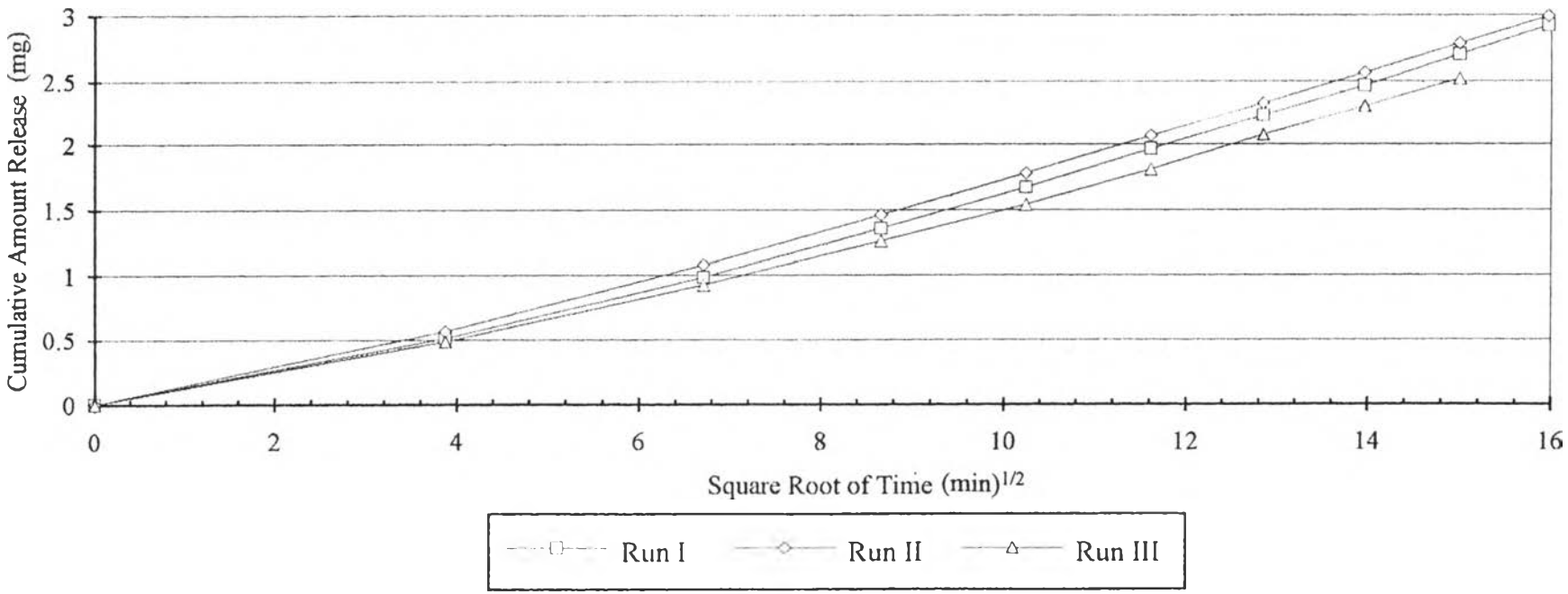
Receiving Medium : Chloroform

Release Run Data

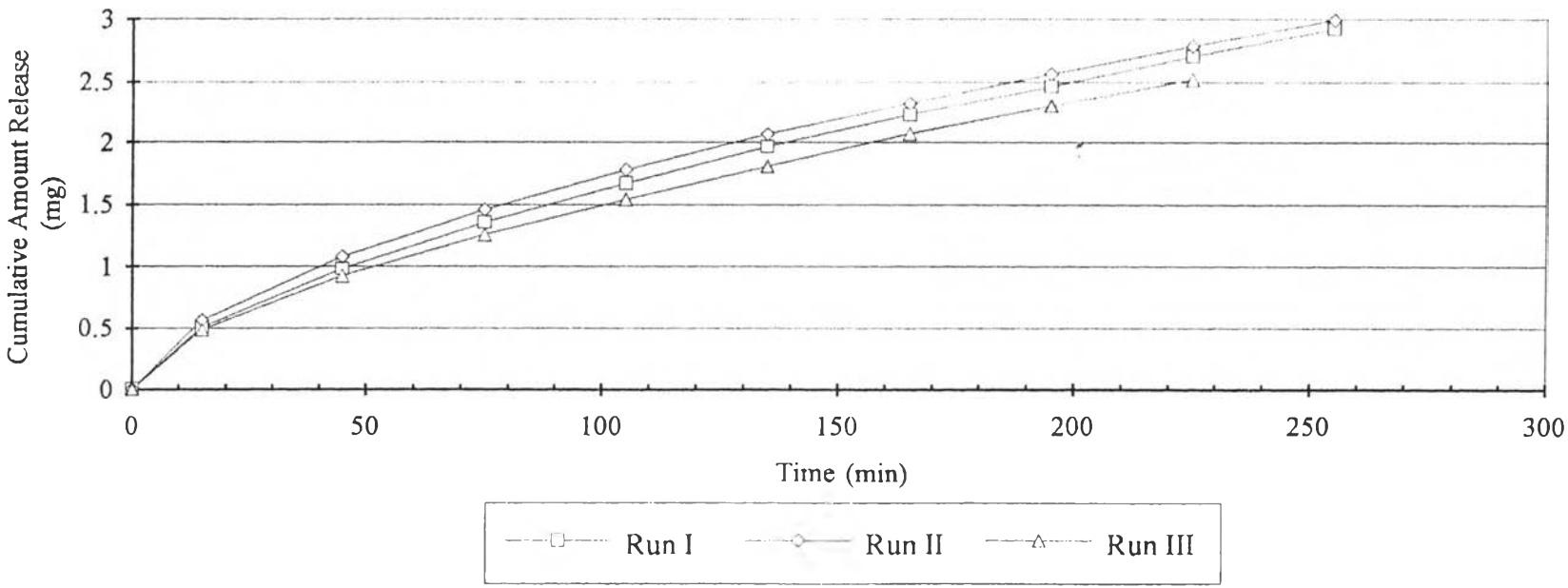
Time (min)		Run I		Run II		Run III	
T	$T^{1/2}$	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)	Amount (mg)	Cumulative Amount (mg)
15	3.875	0.5077	0.5077	0.5645	0.5645	0.4843	0.4843
45	6.708	0.4763	0.9840	0.5154	1.0799	0.4402	0.9245
75	8.660	0.3721	1.3561	0.3798	1.4597	0.3362	1.2607
105	10.247	0.3132	1.6693	0.3214	1.7811	0.2773	1.5380
135	11.619	0.2968	1.9661	0.2881	2.0692	0.2720	1.8100
165	12.845	0.2630	2.2291	0.2539	2.3231	0.2644	2.0744
195	13.965	0.2344	2.4635	0.2410	2.5641	0.2291	2.3035
225	15.000	0.2416	2.7051	0.2254	2.7895	0.2162	2.5197
255	15.969	0.2199	2.9250	0.2047	2.9942	-	-
Steady -state slope Cumulative Amount vs $T^{1/2} \times 10^{-2}$ (mcg/min $^{-1/2}$)		2.1500		2.1045		2.0725	
Diffusion Coefficient x 10^4 (cm ^{2}/min)		1.5310		1.4668		1.4226	
r^2		0.9994		0.9999		0.9999	

$D = 1.4735 \pm 0.0545$ %CV = 3.6992

Clindamycin Hydrochloride Release from Hydroxypropyl Methylcellulose Gel by Using Nylon 66 and Chloroform.



Clindamycin Hydrochloride Release from Hydroxypropyl Methylcellulose Gel by Using Nylon 66 and Chloroform.

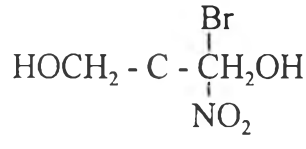


Appendix V

Details of Some Excipients

Bronopol(R)

Bronopol(R) is a water-soluble antimicrobial preservative that is especially effective against Pseudomonas species. Activity can be demonstrated against Gram-negative bacteria, Gram-positive bacteria, yeasts, and fungi. Bronopol(R) is considered a formaldehyde-releasing antimicrobial agent. It has been used as an effective preservative at concentration of 0.01-0.02% in various cosmetic, toiletry, household, and pharmaceutical formulations over the past 16 years because of its high activity.



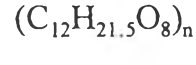
Molecular weight : 200

Synonyms : BNPD, 2-Bromo-2-nitro-1, 3-propanediol,2-Bromo-2-nitropropane-1,3-diol, Myacide BT(R) Onyxide 500(R)

Bronopol(R) is a white or almost white crystalline powder with a faint characteristic odor. Its melting point is approximately 130°C. Bronopol(R) is readily soluble in water and polar organic solvents. It is effective over a wide pH range.

Hydroxyethyl Cellulose 4000 (HEC)

Hydroxyethyl cellulose is a partially substituted 2-hydroxyethyl ether of cellulose.



Cellosize and Natrosol are two trade names for hydroxyethyl cellulose. It is a light tan, white, yellow-white powder, practically odourless, hygoscopic

agent. It is soluble in cold or hot water, forming colloidal solution. Variation in pH between about 2 and 12 have little effect on the viscosity of the solutions. It can be used with a wide variety of water-soluble preservatives. Hydroxyethyl cellulose solutions tolerate salts except sulfates and especially aluminium salts. Strong acids and alkalies are undesirable. Hydroxyethyl cellulose is an effective film former, binder, thickener, stabilizer and dispersant in shampoo, hair sprays, neutralizers, creams, gel and lotion. The concentration to be used is dependent on the solvent and molecular weight of the grade used.

To prepare solution of hydroxyethyl cellulose, the dry loose material is sifted into water at 65°C, agitating continuously. Allow to set overnight in a refrigerator.

Hydroxypropyl Methylcellulose 4000 (HPMC)

Hydroxypropyl methylcellulose is a cellulose hydroxypropyl methylether.

$$C_8H_{15}O_6\text{-}(C_{10}H_8O_6)_n\text{-}C_8H_{15}O_5$$

Hydroxypropyl methylcellulose is an odorless, tasteless white or creamy-white fibrous or granular powder. It is soluble in cold water, forming a viscous colloidal solution, insoluble in alcohol, ether and chloroform but soluble in mixtures of methylalcohol and methylene chloride. The solution of HPMC is stable at pH 3.0-11.0. It is incompatible in the extreme pH conditions and with oxidizing materials. HPMC can be used as a film-former, thickening agent, protective colloid, emulsifying agent, suspending agent and stabilizer.

Aqueous gels are formed on heating, the gel point ranges from 50 to 90°C, depending on the grade. Addition of small amounts of water-immisible solvent, such as ethanol and the glycols, raises that gel point (Swarbrick, 1988).

Poloxamer 407

Poloxamer is a series of nonionic polyoxyethylene polyoxypropylene copolymers (A-B-A block copolymers) with the following chemical structure.

$$HO\text{-}(CH_2\text{-}CH_2\text{-}O)_a\text{-}(CH_2\text{-}\underset{\displaystyle CH_3}{\underset{|}{C}}H\text{-}O)_b\text{-}(CH_2\text{-}CH_2\text{-}O)_a\text{-}H$$

The other name is Pluronic(R) F-127 is one of the Pluronic series that have average molecular weight of 12500. The composition of this copolymer is 70% w/w polyoxyethylene and 30% w/w polyoxypropylene. It is the most efficient gelling agent in the series. A distinguishing property of poloxamer is that it can be liquified by merely lowering their temperature without concomitant loss of product integrity. Also, it can be reversed to their original consistency. Therefore it is called as "thermoreversible gel" that is, they gel with heating and melt with cooling. One of the advantages of a reversible gel product is that it can eliminate any air bubbles which may have been accidentally incorporated during the processing.

Poloxamer gels have many characteristics favorable for use as artificial skin, which is helpful in treating third-degree burns. These gels mimic mucous and are optically clear, which make them suitable for opthalmic drug delivery (Swarbrick, 1988).

Physicochemical Characteristic of Poloxamer Series

Poloxamer	Trade Name	Physical Characteristics			
		Molecular Weight	POE/kg	POP/kg	HLB at 25°C
188	F-68	8350	17.96	3.59	29.0
238	F-88	10800	17.86	3.61	28.0
288	F-98	13000	18.77	3.62	27.5
333	P-103	4950	8.08	10.91	9.0
334	P-104	5850	10.60	9.23	13.0
335	P-105	6500	11.69	8.31	15.0
338	F-108	14000	18.29	3.86	27.0
407	F-127	12500	15.68	5.36	22.0

Appendix VI

Physicochemical Properties of Synthetic Membrane

Durapore(R)
Polyvinylidene Difluoride

These polymers are consisted of saturated hydrocarbons in which hydrogen atoms have been replaced with fluorine. Polyvinylidene difluoride is resistant to most inorganic acids and bases. Among the organics, nearly complete resistance is shown to aliphatic and aromatic hydrocarbons, alcohol, acids and chlorinated solvents. Strongly polar solvent such as ketones amines and esters cause partial solvation. They exhibit good resistance to oxidizing agent and the halogens.

Durapare(R) membrane (HVLP04700) is a hydrophilic membrane with 0.45 micron pore size, 47 mm diameter. Water flow rates, which are milliliters per minutes per cm^2 of filtration area at 20°C with a differential pressure of 0.7 kg/cm^2, are 35. Typical porosity is 75%. Bubble point pressure is 1.45 kg/cm^2. Bubble point pressure is the pressure required to force air through the pores of a water-wet membrane.

Fluoropore(R)

Polytetrafluoroethylene (PTFE)

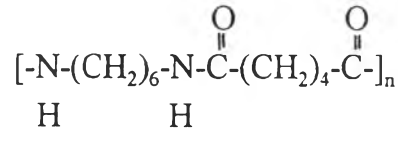
Polytetrafluoroethylene is a highly crystalline, orientable polymer. The PTFE consists of linear $-CF_2-CF_2-$ chains. It is extremely resistant to attack by corrosive reagents or solvents. Only alkali metals, either molten or dissolved in liquid ammonia, attack the polymer, presumably by removing fluorine atoms from the chain. The polymer is completely unaffected by water. Water absorption is zero. Its electrical and mechanical properties do not change for long internal (months) at temperature as high as 250°C. The polymer is not hard but slippery and waxy to the touch, and has a very low coefficient of friction on most substances.

Fluoropore(R) membrane are polytetrafluoroethylene bonded to high-density polyethylene to improve handling. These membrane are hydrophobic and can only be used with gases or nonaqueous fluids unless prewet with a low-surface-tension fluid such as methanol.

Fluoropore(R) membrane (FHUP04700) is 0.5 micron, pore size, 47 mm diameter. Methanol flow rate is forty milliters per minutes per cm^2 of filtration area at 20°C with a differential pressure of 0.7 kg/cm^2. The 85% typical porosity and 0.49 kg/cm^2 bubble point pressure.

Nylon 66

Nylon has been accepted as a generic term for synthetic polyamides. The nylons are described by a numbering system which indicates the number of carbon atoms in the monomer chains. Amino acid polymers are designated by a single number, as Nylon 6 for polycarprolactam. Nylons from diamines and dibasic acids are designated by two numbers, as Nylon 66 for the polymer of hexamethylenediamine and adipic acid.



Nylon 66 (polyhexamethylene adipamide) is characterized by a combination of high strength, elasticity, toughness and abrasion resistance. The solvent resistant is good; only phenol, cresol and formic acid dissolve the polymer at room temperature. They are essentially unaffected by lubricants,oils, fuel.

The permeability of nylon membrane to drug is not that exhibited by a porous membrane, nor that of many polymeric membranes. Nylon is relatively impermeable to small molecules and ions, such as water, urea and sodium chloride, but many less polar, higher molecular weight, unionized species, as well as such ionic compounds as cetyl-, dodecyl-, and ethylpyridinium bromides and sodium napthalene sulfonate diffuse readily through Nylon membrane.

VITA

Miss Pavena Wongtrakul was born on 18th June 1967, in Bangkok, Thailand. She got Bachelor of Science in Pharmacy in 1989 from Faculty of Pharmaceutical Science, Chulalongkorn University, Bangkok, Thailand. She had worked as a teacher at Vithayarai Satharanasuk, Chonburi after graduation for two years. At the present, she has studied for the Master Degree in Pharmaceutical Sciences at Chulalongkorn University from 1992.