

References

- Adeyeye, C.M. and Li, P. 1990. Diclofenac sodium. In Flory, K. (ed.), Analytical profiles of drug substances, Vol. 19, pp. 123-144. USA: Florida Academic Press.
- American Pharmaceutical Association Staff. 1994. Handbook of Pharmaceutical Excipients. Washington : The American Pharmaceutical Association.
- Bhatt, P.P., Rytting, J.H., and Topp E.M. 1991. Influence of Azone[®] and lauryl alcohol on the transport of acetaminophen and ibuprofen through shed snake skin. Int. J. Pharm. 72: 219-226.
- Bhattachar, S.N., Rytting, J.H., Itoh, T., and Nishihata, T. 1992. The effects of complexation with hydrogenated phospholipid on the transport of salicylic acid, diclofenac and indomethacin across snake stratum corneum. Int. J. Pharm. 79: 263-271.
- Blagbrough, I.S., Daykin, M.M., and Doherty, M. 1992. High performance liquid chromatographic determination of naproxen, ibuprofen and diclofenac in plasma and synovial fluid in man. J. Chromato. Biomed. Appl.: 251-257.
- Bronaugh, R.L., and Stewart, R.F. 1986. Method for in vitro percutaneous absorption study VI: preparation of the barrier layer. J. Pharm. Sci. 75: 487-491.

- Chen-Chow, P.C., and Frank, S.G. 1981. In vitro release of lidocaine from pluronic F-127 gels. Int. J. Pharm. 8: 89-99.
- Chowdary K.P.R. and Naidu, R.P.S. 1993. Design of transdermal drug delivery systems : effect of semisolid formulations of transdermal diffusion of diclofenac sodium. Indian Drugs 31(1): 36-40.
- Chien, Y.W. 1987. Drug delivery systems of tomorrow. Drugs of Today 23: 31-45.
- Chien, Y.W., and Valia, K.H. 1984. Development of a dynamic skin permeation system for long-term permeation studies. Drug. Dev. Ind. Pharm. 10: 575-599.
- Connors, K.A. 1981. Long-acting parenteral drug formulations. J. Parent. Sci. Tech. 35(3): 106-138.
- Dawid, A.W., "Polymeric Materials Used in Drug Delivery Systems," Material Used in Pharmaceutical Formulation, (Florence, A.T. ed.), Butler & Tanner Ltd., Frome and London, 1984.
- Dehghan, M.H.G., Parakh, S.R., and Deshpande S.G. 1993. Studies on polymeric systems for transdermal drug delivery. Indian Drugs 30(12): 616-621.

- Downie, W.W. 1993. Diclofenac/Misoprostol A review of the major clinical trials evaluation its clinical efficacy and upper gastrointestinal tolerability in rheumatoid arthritis and osteoarthritis. Drugs 45(Supp. I): 1-6.
- Flynn, B.L. 1994. Rheumatoid arthritis and osteoarthritis: current and future therapies. American Pharmacy NS.34(11): 31-42.
- Flynn, G.L., Yalkowsky, S.H., and Roseman, T.J. 1974. Mass Transport Phenomena and Models: Theoretical Concepts. J. Pharm. Sci. 63(4): 479-510.
- Franz, T.J. 1975. Percutaneous absorption on the relevance of in-vitro data. J. Invest. Dermatol. T4: 190-193.
- Geis, S. 1993. Efficacy and upper GI safety of diclofenac/misoprostol, piroxicam and naproxen in patients with osteoarthritis: Drugs 45(Supp. I): 15-16.
- Gummer, C.L., Hinz, R.S., and Maibach, H.I. 1987. The skin penetration cell: a design update. Int. J. Pharm. 40: 101-104.
- Hadgraft, J., and Howard, J.R. 1982. Drug release from pluronic gels. J. Pharm. Pharmacol. 34: 30-32.
- Harada, K., and others 1992. In-vitro permeability to salicylic acid of human, rodent, and shed snake skin. J. Pharm. Pharmacol. 45: 414-418.

- Ho H., Huang F, Sokoloski T.D., and Sheu M. 1993. The influence of cosolvents on the in-vitro percutaneous penetratuon of diclofenac sodium from a gel system. J. Pharm. Pharmacol. 46: 636-642.
- Itoh, T., Xia, J., Magavi, R., Nishihata, T., and Rytting, J.H. 1990. Use of shed snake skin as a model membrane for in-vitro percutaneous penetration studies: comparison with human skin. Pharm. Res. 7(10): 1042-1047.
- Itoh, T., Wasinger, L., Turunen, T.M., and Rytting, J.H. 1992. Effects of transdermal penetration enhancers on the permeability of shed snakeskin. Pharm. Res. 9(9): 1168-1172.
- Jayanthi, C. and Udupa, N. 1992. Screening of diclofenac topical preparations to optimize permeation across excised mouse skin. Indian Drugs 29(11): 511-513.
- Jayanthi, C. and Udupa, N. 1993. Pharmacodynamic and pharmacokinetic profiles of diclofenac topical preparations. Indian Drugs 30(12): 606-610.
- Jayanthi, C. and Udupa, N. 1994. Anti-inflammatory activity and skin retention profiles of topically applied diclofenac gels. Indian. J. Pharm. Sci. 56(1): 22-24.
- Karim, A. 1993. Pharmacokinetics of diclofenac and misoprostol when administered alone or as a combination product. Drugs 45(Supp. I): 7-14.

- Kennedy, K., and Krawczeniuk, M. 1993. Topical analgesics: concepts and counseling strategies for pharmacists. American Druggist (6): 50-58.
- Keshary, P.R., and Chien, Y.W. 1984. Mechanisms of transdermal controlled nitroglycerin administration (I) : development of a finite-dosing skin permeation system. Drug. Dev. Ind. Pharm. 10: 883-913.
- Kroll M.P., Wiseman, R.L., and Guttadauria, M. 1989. A clinical evaluation of piroxicam gel: an open comparative trial with diclofenac gel in the treatment of acute musculoskeletal disorders. Clin. Ther. 11(3): 382-391.
- Madhavan, M. and Hwang, G. C. 1992. Design and evaluation of transdermal flufenamic acid delivery system. Drug. Dev. Ind. Pharm. 18(5): 617-626.
- McKenna, F. 1993. Efficacy of diclofenac/misoprostol vs diclofenac in the treatment of ankylosing spondylitis. Drugs 45(Supp. I): 24-30.
- Mueller, K.R., Robert, M.E., and Scott, L.A. 1990. Automated in vitro method for evaluating diffusion characteristics of transdermal nitroglycerin delivery systems with or without skin. Drug. Dev. Ind. Pharm. 16: 1857-1880.
- Nelson, L.A., and Lawson, L.A. 1983. Rheumatoid arthritis and osteoarthritis. American Druggist (11): 47-68.
- Nishihata, T., Kotera K., Nakano. Y., and Yamazak, M. 1987. Rat percutaneous transport of diclofenac and influence of hydrogenated soya phospholipids. Chem. Pharm. Bull. 35(9): 3807-3812.

- Nishihata, T., and others 1988. Percutaneous absorption of diclofenac in rats and humans: aqueous gel formulation. Int. J. Pharm. 46: 1-7.
- Nishihata, T., and others 1988. Clinical investigation of sodium diclofenac sustained-release suppositories. Int. J. Pharm. 42: 251-256.
- Nishihata, T., Tsutsumi, A., Ikawa, C., and Sakai, K. 1988. Sustained release suppository of sodium diclofenac: use of water absorbable polymer. Drug. Dev. Ind. Pharm. 16(10): 1675-1686.
- Nishihata, T., Rytting, J.H., Tsutsumi, A., and Sakai, K. 1991. Aqueous-lipid transdermal formulation of anti-inflammatory agents, prepared with hydrogenated soya phospholipid. Drug. Dev. Ind. Pharm. 17(16): 2157-2172.
- Nozawa, I., Suzuki, Y., Sato, S., Sugibayashi, K., and Morimoto, Y. 1989. Application of a thermo-responsive membrane to the transdermal delivery of non-steroidal anti-inflammatory drugs and antipyretic drugs. J. Controlled Release 15: 29-37.
- Obata, Y., Takayama, K., Maitani, Y., Machida, Y., and Nagai, T. 1993. Effect of ethanol on skin permeation of nonionized and ionized diclofenac. Int. J. Pharm. 89: 191-198.
- Ogiso, T., Iwaki, M., Tanino, T., Yatomi, M., and Tsujimoto, C., 1993. Percutaneous absorption of terodiline and the membrane-controlled transdermal therapeutic system. Int. J. Pharm. 98: 113-120.

- Pugh, M.C. 1989. Treatment of rheumatic diseases. American Druggist : 61-68.
- Reiss, W., and others 1986. Percutaneous absorption of diclofenac. Arzneim.-Forsch. 36(II): 1092-1096.
- Reynold, A. 1993. Martindale the Extra Pharmacopoeia. 30th ed. London: The Pharmaceutical Press.
- Schapira, D., Linn, S., and Scharf, Y. 1991. A placebo-controlled evaluation of diclofenac diethylamine salt in the treatment of lateral epicondylitis of the elbow. Current Therapeutic Research 49(2): 162-168.
- Shah, Y., Joshi, S., Jindal, K.C., and Khanna, S. 1994. High performance liquid chromatographic determination of diclofenac diethylammonium in gels. Drug. Dev. Ind. Pharm. 20(7): 1303-1307.
- Singh, U.V., Pandey, S., and Udupa, N. 1992. Preparation and evaluation of flurbiprofen and diclofenac sodium transdermal films. Indian. J. Pharm. Sci. 55(7): 145-147.
- Sugibayashi, K., and Morimoto, Y. 1994. Polymer for transdermal drug delivery systems. J. Controlled Release. 29: 177-185.
- Tomida, H., Shinohar, M., Kuwada, N., and Kiryu, S. 1987. In vitro release characteristics of diclofenac and hydrocortisone from pluronic F-127 gels. Acta Pharm. Sued. 24: 263-272.

- Urban, M., Aunaud, P., Zuber, M., and Chaumeil, J.C. 1991. Influence of enhancers on the physicochemical properties and on the release of suppositories of clomipramine hydrochloride. Drug. Dev. Ind. Pharm. 17: 1325-1342.
- Vyas, S.P., Gogoi, P.J., and Jain, S.K. 1991. Development and characterization of pseudolatex based transdermal drug delivery system of diclofenac. Drug. Dev. Ind. Pharm. 17(8): 1041-1058.
- Wan, L.S.C., Heng, P.W.S., and Wong, L.F. 1990. Effect of hydroxypropyl methylcellulose on drug release from a matrix system. NUS-JSPS Seminar: 35-56.
- Zatz, J.L. 1990. Scratching the surface: skin permeation. Cosm.&Toilet. 105: 229-241.
- Zuinen, C. 1993. Diclofenac/misoprostol vs diclofenac/placebo in treating acute episodes of tendinitis/bursitis of the shoulder. Drugs 45(Supp. I): 17-23.

สถาบันวิทยบริการ
จุฬาลงกรณ์มหาวิทยาลัย

APPENDIX

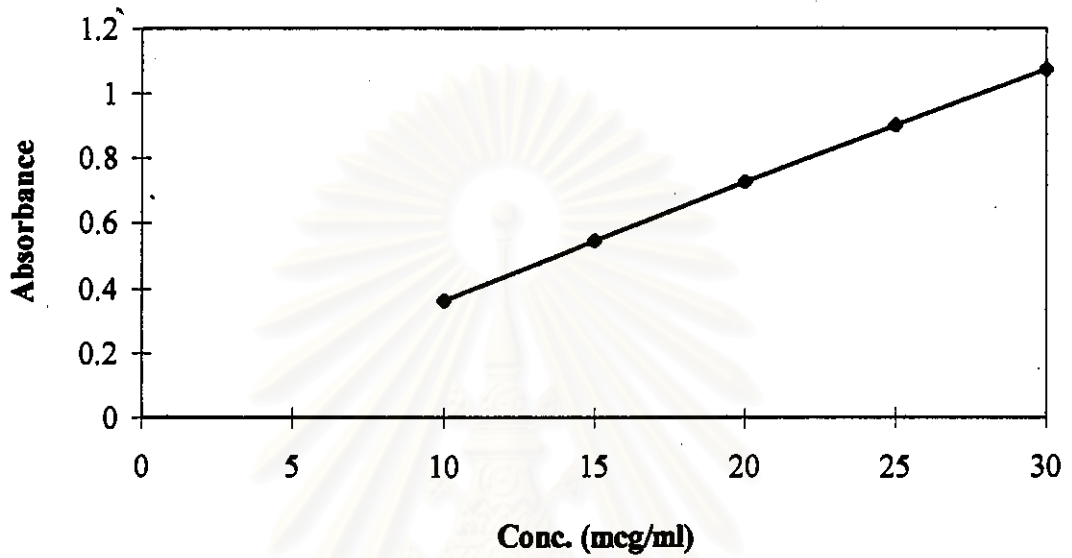


Figure 39 Calibration curve of diclofenac diethylamine in ethyl alcohol.

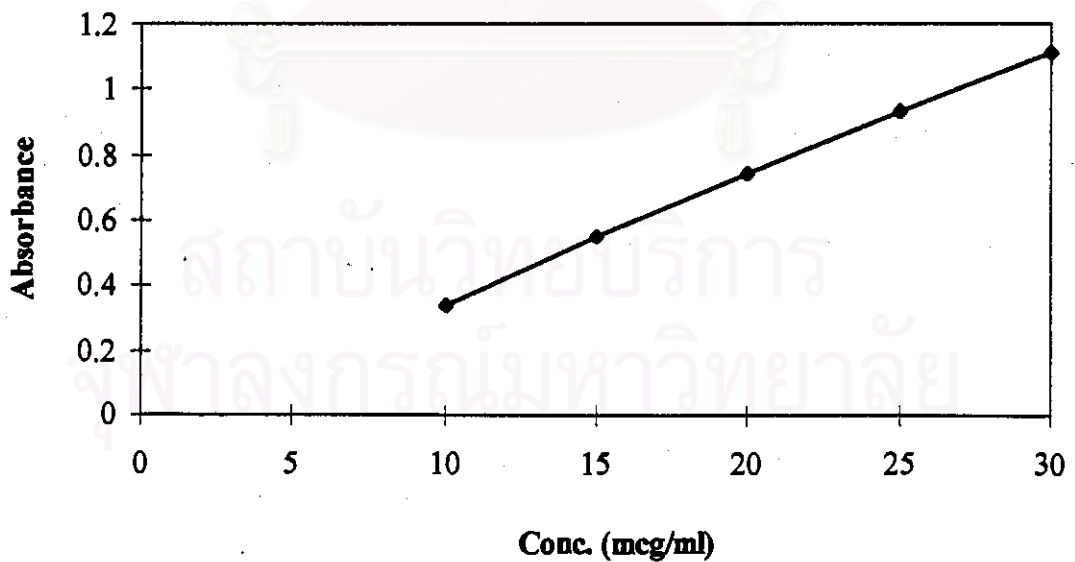


Figure 40 Calibration curve of diclofenac diethylamine in isopropyl alcohol.

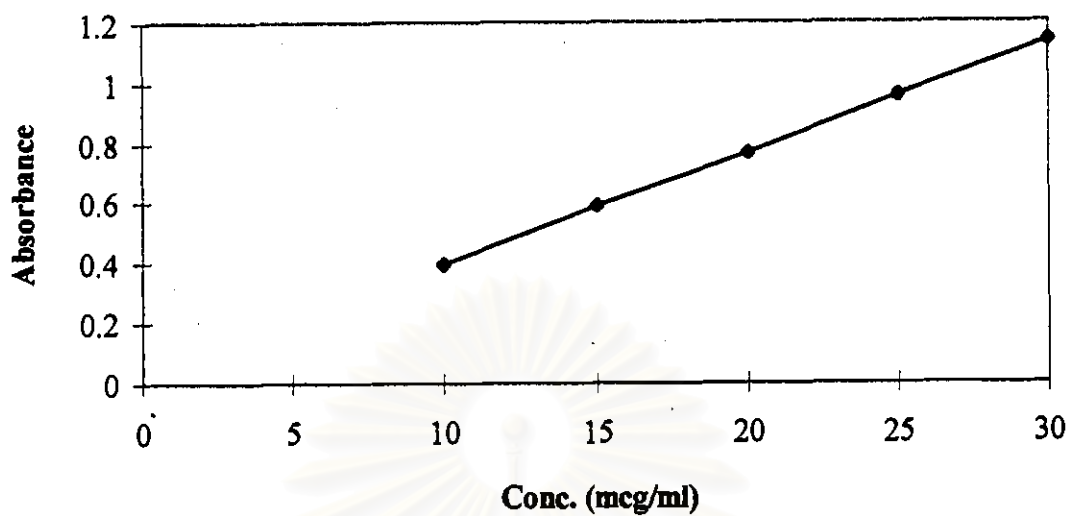


Figure 41 Calibration curve of diclofenac diethylamine in propylene glycol.

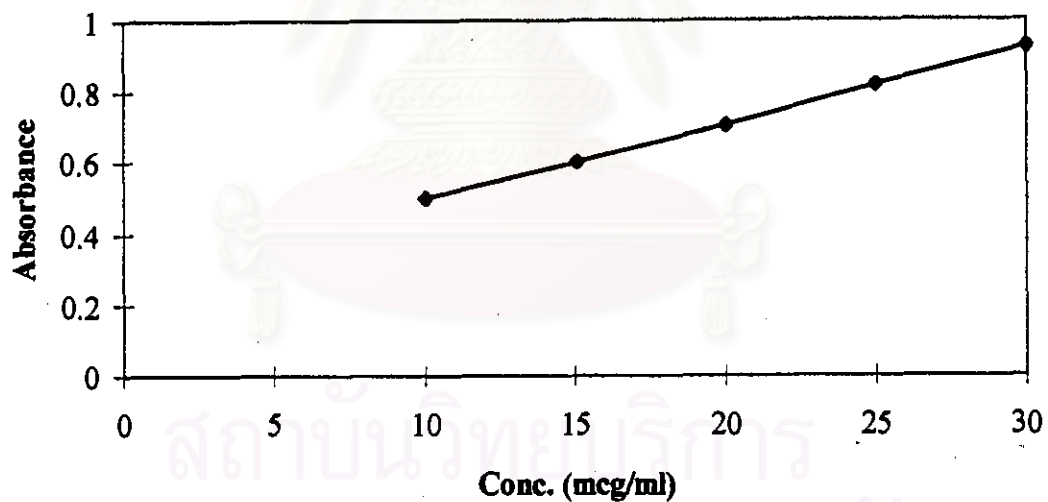


Figure 42 Calibration curve of diclofenac diethylamine in polyethylene glycol 400.

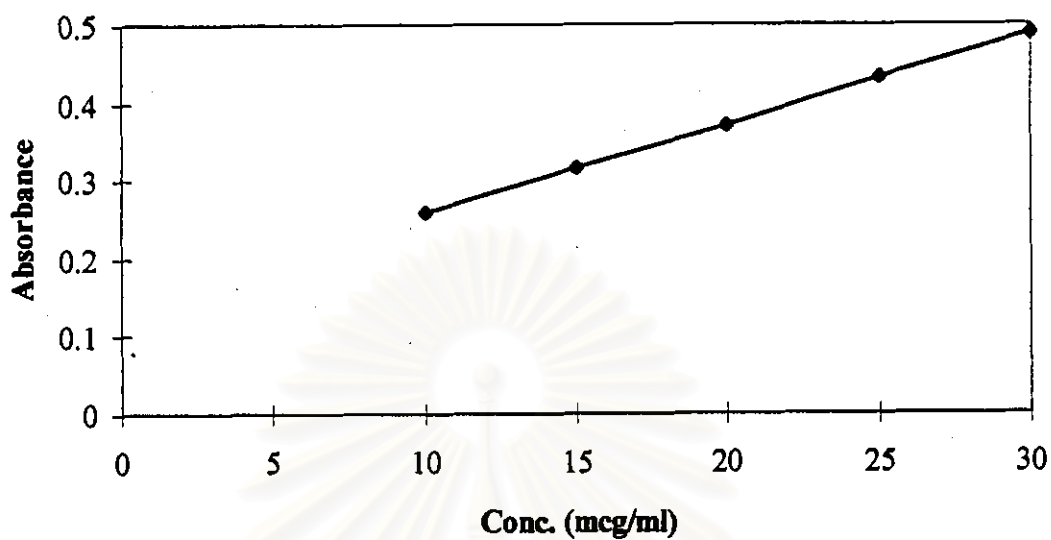


Figure 43 Calibration curve of diclofenac diethylamine in benzyl alcohol.

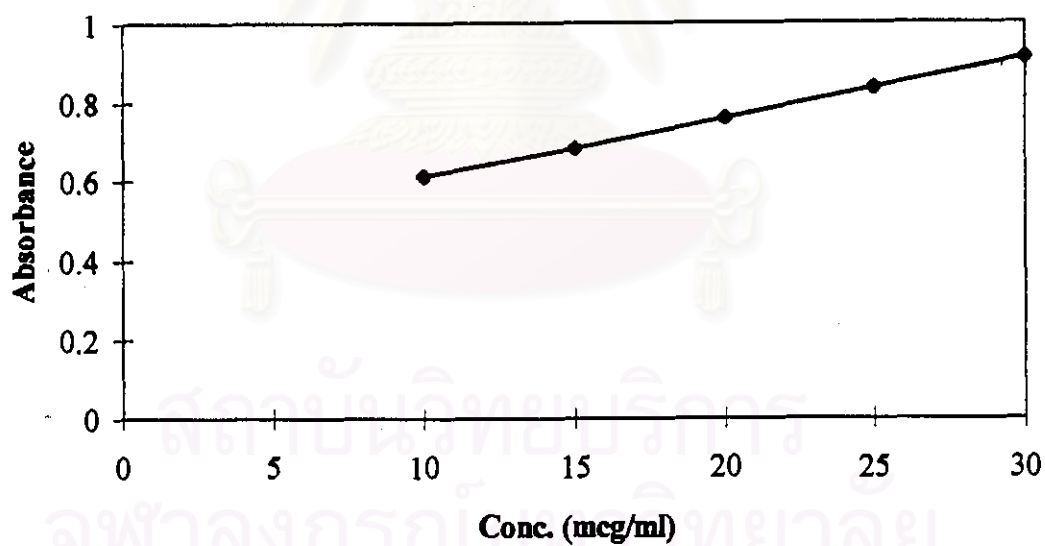


Figure 44 Calibration curve of diclofenac diethylamine in N,N-dimethyl acetamide.

Table 15 Ratio between peak area of internal standard and diclofenac diethylamine with HPLC method at 282 nm.

Conc. (mcg/ml)	Ratio	Conc. (mcg/ml)	Ratio
0	0	0	0
2	0.987	10	0.851
4	1.953	20	1.722
6	2.917	30	2.616
8	3.883	40	3.467
10	4.849	50	4.299
r^2	0.999	r^2	0.999
intercept	-0.021	intercept	0.011
slope	2.065	slope	11.527

Table 16 Cumulative release of diclofenac diethylamine per surface area (mg/cm^2) from Voltaren[®] emulgel patch.

Time	A	B	C	D	E	F	G	H	I	J	Mean	SD
0.5	0.551	0.516	0.438	0.385	0.475	0.415	0.388	0.219	0.066	0.065	0.352	0.175
1	0.637	0.710	0.557	0.584	0.514	0.548	0.482	0.473	0.106	0.107	0.472	0.205
2	0.828	0.850	0.750	0.792	0.858	0.736	0.659	0.820	0.251	0.409	0.695	0.205
3	1.020	1.012	0.895	0.869	0.894	0.901	0.823	1.211	0.426	0.772	0.882	0.202
4	1.121	1.195	0.941	0.980	1.049	1.013	0.974	1.378	0.670	1.085	1.040	0.183
5	1.266	1.378	1.052	1.060	1.128	1.081	1.049	1.543	0.974	1.331	1.186	0.184
6	1.324	1.384	1.165	1.144	1.270	1.152	1.121	1.560	1.072	1.315	1.251	0.149
8	1.323	1.395	1.318	1.311	1.398	1.309	1.288	1.496	1.243	1.464	1.354	0.081
10	1.323	1.571	1.471	1.478	1.526	1.494	1.403	1.525	1.194	1.620	1.460	0.125
12	1.839	1.913	1.435	1.420	1.606	1.418	1.409	1.667	1.175	1.565	1.545	0.221

Table 17 Cumulative skin permeation of diclofenac diethylamine per surface area (mg/cm^2) from Voltaren[®] emulgel patch.

Time	A	B	C	D	E	F	G	H	I	J	K	Mean	SD
0.5	0.000	0.003	0.000	0.004	0.002	0.002	0.004	0.002	0.009	0.008	0.015	0.005	0.005
1	0.014	0.002	0.000	0.005	0.004	0.002	0.002	0.003	0.012	0.011	0.012	0.006	0.005
2	0.004	0.007	0.007	0.008	0.008	0.004	0.002	0.004	0.015	0.011	0.013	0.007	0.004
3	0.008	0.013	0.009	0.003	0.004	0.002	0.001	0.009	0.013	0.012	0.012	0.008	0.004
4	0.013	0.011	0.005	0.006	0.009	0.006	0.003	0.003	0.013	0.011	0.012	0.008	0.004
5	0.007	0.015	0.009	0.006	0.011	0.003	0.002	0.003	0.013	0.013	0.010	0.008	0.004
6	0.010	0.016	0.009	0.005	0.012	0.003	0.002	0.002	0.014	0.013	0.011	0.009	0.005
8	0.012	0.026	0.013	0.005	0.019	0.004	0.003	0.001	0.011	0.014	0.012	0.011	0.007
10	0.018	0.030	0.013	0.010	0.029	0.004	0.003	0.004	0.011	0.016	0.012	0.014	0.009
12	0.019	0.047	0.014	0.011	0.032	0.005	0.003	0.006	0.012	0.016	0.012	0.016	0.013

Table 18 Cumulative skin permeation of diclofenac diethylamine per surface area (mg/cm^2) from Voltaren[®] emulgel.

Time	A	B	C	D	E	F	Mean	SD
0.5	0.001	0.000	0.000	0.009	0.000	0.010	0.003	0.005
1.0	0.001	0.004	0.005	0.014	0.000	0.012	0.006	0.006
2.0	0.002	0.000	0.002	0.043	0.007	0.011	0.011	0.016
3.0	0.004	0.003	0.003	0.062	0.010	0.014	0.016	0.023
4.0	0.005	0.007	0.015	0.074	0.010	0.019	0.022	0.026
5.0	0.011	0.008	0.009	0.076	0.012	0.024	0.023	0.026
6.0	0.010	0.014	0.008	0.085	0.015	0.028	0.026	0.029
8.0	0.020	0.023	0.017	0.091	0.021	0.034	0.034	0.028
10.0	0.028	0.033	0.023	0.104	0.027	0.046	0.043	0.031
12.0	0.040	0.045	0.034	0.115	0.036	0.061	0.055	0.031

Table 19 Cumulative release of diclofenac diethylamine per surface area (mg/cm^2) from diclofenac diethylamine-TDS in propylene glycol and various gelling agents.

R ₁ #	Time (hr)	Cumulative release			Mean	SD	R ₂ #	Time (hr)	Cumulative release			Mean	SD
		A	B	C					A	B	C		
1	0	0	0	0	0	0	4	0	0	0	0	0	
	0.5	1.540	1.334	0.574	1.150	0.509		0.5	0.494	0.533	0.554	0.527	0.030
	1	1.682	1.614	0.990	1.429	0.382		1	0.778	0.833	0.867	0.826	0.045
	2	1.707	1.678	1.186	1.523	0.293		2	1.154	1.219	1.284	1.219	0.065
	3	1.763	1.681	1.429	1.625	0.174		3	1.306	1.381	1.442	1.376	0.068
	4	1.766	1.694	1.445	1.635	0.168		4	1.382	1.460	1.526	1.456	0.072
	5	1.774	1.695	1.550	1.673	0.113		5	1.413	1.481	1.559	1.485	0.073
	6	1.777	1.711	1.556	1.681	0.114		6	1.439	1.508	1.571	1.506	0.066
	8	1.778	1.738	1.578	1.698	0.106		8	1.478	1.532	1.586	1.532	0.054
	10	1.798	1.765	1.592	1.718	0.111		10	1.515	1.570	1.611	1.565	0.048
12	1.838	1.770	1.605	1.738	0.120	12	1.531	1.570	1.616	1.572	0.042		
2	0	0	0	0	0	0	5	0	0	0	0	0	
	0.5	1.137	0.681	0.200	0.672	0.468		0.5	0.400	0.440	0.469	0.436	0.035
	1	1.825	1.182	0.639	1.215	0.594		1	0.637	0.685	0.734	0.685	0.048
	2	2.028	1.682	1.395	1.702	0.317		2	0.968	1.047	1.116	1.044	0.074
	3	2.203	1.990	1.774	1.989	0.214		3	1.181	1.267	1.338	1.262	0.079
	4	2.421	2.210	2.016	2.216	0.203		4	1.324	1.405	1.480	1.403	0.078
	5	2.560	2.350	2.154	2.355	0.203		5	1.469	1.552	1.638	1.553	0.085
	6	2.589	2.380	2.192	2.387	0.199		6	1.582	1.667	1.748	1.666	0.083
	8	2.634	2.420	2.236	2.430	0.199		8	1.770	1.853	1.943	1.855	0.087
	10	2.649	2.433	2.259	2.447	0.196		10	1.951	2.031	2.080	2.021	0.066
12	2.659	2.441	2.267	2.456	0.196	12	1.974	2.053	2.104	2.044	0.065		
3	0	0	0	0	0	0	6	0	0	0	0	0	
	0.5	1.180	0.723	0.230	0.711	0.475		0.5	1.152	1.271	1.388	1.270	0.118
	1	1.825	1.184	0.599	1.203	0.613		1	1.620	1.781	1.936	1.779	0.158
	2	2.368	1.976	1.619	1.988	0.374		2	2.109	2.281	2.489	2.293	0.190
	3	2.875	2.457	2.113	2.482	0.382		3	2.492	2.716	2.930	2.712	0.219
	4	3.105	2.841	2.499	2.815	0.304		4	2.635	2.835	3.051	2.841	0.208
	5	3.245	2.936	2.657	2.946	0.294		5	2.770	2.975	3.190	2.979	0.210
	6	3.280	2.970	2.701	2.984	0.290		6	2.843	3.076	3.270	3.063	0.214
	8	3.416	3.106	2.883	3.135	0.268		8	3.082	3.321	3.506	3.303	0.212
	10	3.465	3.153	2.940	3.186	0.264		10	3.349	3.571	3.727	3.549	0.190
12	3.488	3.176	2.967	3.210	0.262	12	3.375	3.581	3.732	3.563	0.179		

Table 19 Cumulative release of diclofenac diethylamine per surface area (mg/cm^2) from diclofenac diethylamine-TDS in propylene glycol and various gelling agents. (continue)

R _z #	Time (hr)	Cumulative release			Mean	SD	R _z #	Time (hr)	Cumulative release (mg/cm^2)			Mean	SD
		A	B	C					A	B	C		
7	0	0	0	0	0	0	10	0	0	0	0	0	
	0.5	0.616	0.652	0.725	0.664	0.055		0.5	0.550	0.589	0.641	0.593	0.046
	1	0.861	0.920	1.011	0.931	0.076		1	0.983	1.025	1.115	1.041	0.067
	2	1.273	1.355	1.466	1.365	0.097		2	1.566	1.629	1.702	1.632	0.068
	3	1.480	1.573	1.697	1.583	0.109		3	1.880	1.826	1.964	1.890	0.069
	4	1.695	1.785	1.914	1.798	0.110		4	2.118	2.176	2.261	2.185	0.072
	5	1.878	1.967	2.117	1.987	0.121		5	2.177	2.231	2.318	2.242	0.071
	6	2.044	2.133	2.274	2.151	0.116		6	2.256	2.347	2.399	2.334	0.072
	8	2.462	2.552	2.696	2.570	0.118		8	2.385	2.473	2.524	2.461	0.070
	10	2.781	2.860	3.009	2.883	0.115		10	2.481	2.439	2.563	2.494	0.063
12	2.799	2.868	3.009	2.892	0.107	12	2.459	2.505	2.579	2.514	0.061		
8	0	0	0	0	0	0	11	0	0	0	0	0	
	0.5	0.459	0.502	0.523	0.494	0.033		0.5	1.729	1.832	1.965	1.842	0.119
	1	0.621	0.662	0.677	0.654	0.029		1	2.322	2.422	2.565	2.436	0.122
	2	0.990	1.041	1.064	1.032	0.038		2	2.879	2.946	3.139	2.988	0.135
	3	1.277	1.323	1.358	1.319	0.040		3	3.138	3.044	3.308	3.163	0.134
	4	1.471	1.511	1.554	1.512	0.042		4	3.186	3.269	3.454	3.303	0.137
	5	1.660	1.711	1.739	1.703	0.040		5	3.270	3.320	3.533	3.374	0.139
	6	1.838	1.922	1.937	1.899	0.053		6	3.281	3.368	3.538	3.395	0.131
	8	2.002	2.088	2.108	2.066	0.056		8	3.326	3.368	3.535	3.409	0.111
	10	2.180	2.261	2.279	2.240	0.053		10	3.356	3.390	3.553	3.433	0.105
12	2.241	2.321	2.359	2.307	0.060	12	3.368	3.400	3.560	3.442	0.103		
9	0	0	0	0	0	0	12	0	0	0	0	0	
	0.5	0.025	0.028	0.031	0.028	0.003		0.5	1.012	1.046	1.116	1.058	0.053
	1	0.121	0.124	0.141	0.129	0.011		1	1.719	1.756	1.851	1.775	0.068
	2	0.291	0.288	0.328	0.302	0.023		2	2.321	2.470	2.329	2.374	0.084
	3	0.431	0.445	0.496	0.457	0.034		3	2.860	2.906	3.031	2.932	0.088
	4	0.516	0.527	0.581	0.541	0.035		4	3.019	3.115	3.193	3.109	0.087
	5	0.647	0.656	0.716	0.673	0.037		5	3.127	3.111	3.250	3.163	0.076
	6	0.725	0.730	0.794	0.750	0.038		6	3.130	3.117	3.249	3.165	0.073
	8	0.965	0.979	1.049	0.997	0.045		8	3.144	3.145	3.268	3.186	0.071
	10	1.101	1.195	1.125	1.140	0.049		10	3.152	3.154	3.276	3.194	0.071
12	1.217	1.221	1.301	1.246	0.047	12	3.171	3.156	3.285	3.204	0.071		

Table 19 Cumulative release of diclofenac diethylamine per surface area (mg/cm^2) from diclofenac diethylamine-TDS in propylene glycol and various gelling agents. (continue)

R ₁ #	Time (hr)	Cumulative release			Mean	SD	R ₂ #	Time (hr)	Cumulative release (mg/cm^2)			Mean	SD
		A	B	C					A	B	C		
13	0	0	0	0	0	0	16	0	0	0	0	0	
	0.5	0.856	0.869	0.934	0.886	0.042		0.5	1.403	1.634	1.985	1.674	0.293
	1	1.493	1.505	1.585	1.528	0.050		1	2.105	2.416	2.845	2.455	0.372
	2	2.119	2.116	2.233	2.156	0.067		2	2.739	3.024	3.418	3.060	0.341
	3	2.348	2.355	2.471	2.391	0.069		3	2.925	3.246	3.629	3.267	0.353
	4	2.569	2.590	2.695	2.618	0.067		4	2.992	3.327	3.637	3.318	0.323
	5	2.647	2.669	2.762	2.693	0.061		5	3.096	3.402	3.696	3.398	0.300
	6	2.703	2.728	2.802	2.744	0.052		6	3.160	3.412	3.699	3.424	0.270
	8	2.748	2.765	2.843	2.785	0.051		8	3.247	3.439	3.719	3.468	0.238
	10	2.788	2.787	2.870	2.815	0.047		10	3.312	3.447	3.723	3.494	0.209
12	2.834	2.831	2.911	2.859	0.045	12	3.318	3.451	3.723	3.498	0.206		
14	0	0	0	0	0	0	17	0	0	0	0	0	
	0.5	0.036	0.043	0.054	0.044	0.009		0.5	1.289	1.498	1.727	1.504	0.219
	1	0.127	0.156	0.183	0.155	0.028		1	1.839	1.984	2.346	2.056	0.261
	2	0.351	0.412	0.486	0.416	0.067		2	2.526	2.626	3.049	2.734	0.278
	3	0.502	0.576	0.656	0.578	0.077		3	2.804	2.875	3.282	2.987	0.258
	4	0.639	0.713	0.801	0.717	0.081		4	2.880	2.956	3.304	3.047	0.226
	5	0.731	0.813	0.899	0.815	0.084		5	2.948	2.982	3.309	3.080	0.199
	6	0.842	0.923	1.013	0.926	0.086		6	3.003	3.012	3.314	3.109	0.177
	8	0.923	0.987	1.066	0.992	0.071		8	3.014	3.016	3.317	3.116	0.175
	10	1.002	1.061	1.142	1.068	0.071		10	3.024	3.028	3.326	3.126	0.173
12	1.085	1.150	1.227	1.154	0.071	12	3.035	3.032	3.333	3.133	0.173		
15	0	0	0	0	0	0	18	0	0	0	0	0	
	0.5	0.211	0.246	0.290	0.249	0.039		0.5	1.002	1.136	1.303	1.147	0.151
	1	0.412	0.473	0.535	0.473	0.062		1	1.607	1.755	2.005	1.789	0.201
	2	0.832	0.937	1.047	0.939	0.108		2	2.366	2.508	2.803	2.559	0.223
	3	1.111	1.231	1.349	1.230	0.119		3	2.623	2.716	3.024	2.788	0.210
	4	1.363	1.477	1.599	1.479	0.118		4	2.736	2.856	3.116	2.903	0.194
	5	1.590	1.696	1.819	1.702	0.115		5	2.792	2.932	3.142	2.955	0.176
	6	1.690	1.769	1.905	1.788	0.109		6	2.865	2.969	3.163	2.999	0.151
	8	1.895	1.922	2.110	1.976	0.117		8	2.892	3.003	3.181	3.026	0.146
	10	2.041	2.065	2.253	2.119	0.116		10	2.965	3.036	3.208	3.070	0.125
12	2.042	2.079	2.257	2.126	0.115	12	2.975	3.043	3.216	3.078	0.124		

Table 19 Cumulative release of diclofenac diethylamine per surface area (mg/cm^2) from diclofenac diethylamine-TDS in propylene glycol and various gelling agents. (continue)

R _x	Time	Cumulative release			Mean	SD	R _x	Time	Cumulative release			Mean	SD
#	(hr)	A	B	C			#	(hr)	(mg/cm ²)				
									A	B	C		
19	0	0	0	0	0	0	22	0	0	0	0	0	0
	0.5	0.261	0.273	0.337	0.290	0.041		0.5	0.911	1.021	1.120	1.017	0.104
	1	0.526	0.554	0.644	0.575	0.062		1	1.858	2.187	2.202	2.082	0.194
	2	1.041	1.085	1.201	1.109	0.082		2	2.615	2.922	3.016	2.851	0.210
	3	1.301	1.313	1.455	1.356	0.086		3	2.900	3.115	3.294	3.103	0.197
	4	1.512	1.554	1.651	1.572	0.072		4	3.057	3.201	3.386	3.215	0.165
	5	1.685	1.706	1.800	1.731	0.061		5	3.129	3.251	3.436	3.272	0.154
	6	1.692	1.739	1.812	1.748	0.060		6	3.169	3.298	3.455	3.307	0.144
	8	1.761	1.777	1.844	1.794	0.044		8	3.249	3.322	3.487	3.352	0.122
	10	1.786	1.786	1.840	1.804	0.031		10	3.297	3.371	3.515	3.394	0.111
	12	1.793	1.797	1.840	1.810	0.026		12	3.319	3.396	3.521	3.412	0.102
20	0	0	0	0	0	0	23	0	0	0	0	0	0
	0.5	1.142	1.241	1.480	1.288	0.174		0.5	0.326	0.369	0.409	0.368	0.042
	1	1.702	1.825	2.093	1.873	0.200		1	0.688	0.775	0.828	0.763	0.071
	2	2.106	2.252	2.472	2.277	0.184		2	1.288	1.376	1.489	1.384	0.101
	3	2.245	2.423	2.566	2.411	0.161		3	1.809	1.927	2.049	1.928	0.120
	4	2.257	2.429	2.573	2.419	0.158		4	2.283	2.376	2.537	2.399	0.129
	5	2.286	2.450	2.573	2.436	0.144		5	2.549	2.646	2.778	2.657	0.115
	6	2.296	2.452	2.574	2.441	0.139		6	2.742	2.853	2.959	2.851	0.108
	8	2.304	2.497	2.576	2.459	0.140		8	2.960	3.036	3.160	3.052	0.101
	10	2.318	2.500	2.579	2.466	0.133		10	2.977	3.049	3.175	3.067	0.100
	12	2.343	2.511	2.577	2.477	0.121		12	2.994	3.052	3.176	3.074	0.093
21	0	0	0	0	0	0							
	0.5	1.305	1.562	1.716	1.528	0.208							
	1	2.451	2.764	3.055	2.757	0.302							
	2	3.286	3.634	3.933	3.617	0.324							
	3	3.472	3.876	4.063	3.803	0.302							
	4	3.546	3.905	4.116	3.855	0.288							
	5	3.597	3.947	4.140	3.895	0.275							
	6	3.631	3.974	4.152	3.919	0.265							
	8	3.640	3.977	4.158	3.925	0.263							
	10	3.655	3.982	4.166	3.934	0.259							
	12	3.686	4.013	4.189	3.963	0.255							

Table 20 Cumulative skin permeation of diclofenac diethylamine per surface area (mg/cm^2) from diclofenac diethylamine-TDS in poloxamer F-127.

R _x #	Time (hr)	Cumulative skin permeation						Mean	SD
		A	B	C	D	E	F		
6	0	0	0	0	0	0	0	0	0
	0.5	0.005	0.006	0.009	0.009	0.009	0.011	0.008	0.002
	1	0.005	0.007	0.009	0.009	0.009	0.011	0.008	0.002
	2	0.006	0.008	0.010	0.010	0.010	0.013	0.009	0.002
	3	0.006	0.008	0.010	0.010	0.010	0.013	0.010	0.002
	4	0.006	0.008	0.010	0.011	0.010	0.013	0.010	0.003
	5	0.006	0.008	0.011	0.011	0.011	0.013	0.010	0.002
	6	0.007	0.009	0.011	0.011	0.011	0.015	0.011	0.002
	8	0.011	0.012	0.013	0.014	0.014	0.017	0.013	0.002
	10	0.013	0.016	0.016	0.017	0.017	0.021	0.017	0.003
12	0.014	0.019	0.020	0.020	0.021	0.023	0.019	0.003	
7	0	0	0	0	0	0	0	0	0
	0.5	0.006	0.006	0.008	0.008	0.009	0.012	0.008	0.002
	1	0.006	0.006	0.008	0.008	0.009	0.012	0.008	0.002
	2	0.006	0.006	0.008	0.009	0.010	0.012	0.008	0.002
	3	0.007	0.007	0.009	0.009	0.010	0.012	0.009	0.002
	4	0.007	0.007	0.009	0.009	0.010	0.013	0.009	0.002
	5	0.007	0.007	0.009	0.010	0.011	0.013	0.009	0.002
	6	0.007	0.008	0.009	0.010	0.012	0.014	0.010	0.002
	8	0.009	0.010	0.011	0.011	0.013	0.018	0.012	0.003
	10	0.009	0.012	0.014	0.016	0.016	0.019	0.014	0.003
12	0.011	0.014	0.015	0.017	0.018	0.022	0.016	0.004	
8	0	0	0	0	0	0	0	0	0
	0.5	0.004	0.007	0.009	0.009	0.009	0.010	0.008	0.002
	1	0.004	0.006	0.009	0.009	0.010	0.012	0.008	0.003
	2	0.004	0.006	0.008	0.009	0.010	0.012	0.008	0.003
	3	0.003	0.007	0.009	0.009	0.012	0.013	0.009	0.004
	4	0.003	0.007	0.009	0.009	0.011	0.014	0.009	0.004
	5	0.006	0.007	0.008	0.008	0.010	0.013	0.009	0.003
	6	0.005	0.008	0.009	0.010	0.011	0.012	0.009	0.003
	8	0.006	0.008	0.011	0.012	0.012	0.014	0.010	0.003
	10	0.005	0.011	0.013	0.014	0.014	0.016	0.012	0.004
12	0.011	0.011	0.014	0.014	0.014	0.017	0.014	0.002	

Table 21 Cumulative skin permeation of diclofenac diethylamine per surface area (mg/cm^2) from diclofenac diethylamine-TDS in hydroxypropyl methylcellulose.

R _r #	Time (hr)	Cumulative skin permeation						Mean	SD
		A	B	C	D	E	F		
11	0	0	0	0	0	0	0	0	0
	0.5	0.008	0.010	0.012	0.012	0.013	0.015	0.012	0.002
	1	0.010	0.011	0.012	0.014	0.014	0.019	0.013	0.003
	2	0.011	0.011	0.013	0.014	0.015	0.020	0.014	0.003
	3	0.012	0.012	0.014	0.014	0.015	0.020	0.014	0.003
	4	0.012	0.013	0.015	0.014	0.016	0.020	0.015	0.003
	5	0.012	0.013	0.015	0.014	0.016	0.020	0.015	0.003
	6	0.014	0.013	0.015	0.014	0.017	0.021	0.016	0.003
	8	0.015	0.015	0.016	0.016	0.017	0.024	0.017	0.003
	10	0.016	0.017	0.018	0.019	0.020	0.026	0.019	0.004
	12	0.018	0.018	0.020	0.021	0.021	0.028	0.021	0.004
12	0	0	0	0	0	0	0	0	0
	0.5	0.007	0.007	0.011	0.013	0.014	0.016	0.011	0.004
	1	0.007	0.008	0.011	0.013	0.014	0.016	0.012	0.004
	2	0.007	0.009	0.011	0.013	0.014	0.016	0.012	0.003
	3	0.007	0.009	0.011	0.013	0.014	0.017	0.012	0.003
	4	0.008	0.010	0.011	0.013	0.015	0.017	0.012	0.003
	5	0.008	0.009	0.011	0.013	0.015	0.017	0.012	0.004
	6	0.008	0.009	0.013	0.013	0.015	0.018	0.013	0.004
	8	0.009	0.012	0.013	0.015	0.017	0.019	0.014	0.004
	10	0.011	0.012	0.013	0.015	0.017	0.021	0.015	0.004
	12	0.011	0.013	0.015	0.016	0.018	0.024	0.016	0.004
13	0	0	0	0	0	0	0	0	0
	0.5	0.006	0.009	0.010	0.011	0.013	0.015	0.011	0.003
	1	0.007	0.009	0.010	0.011	0.014	0.016	0.011	0.003
	2	0.007	0.009	0.010	0.011	0.014	0.016	0.011	0.003
	3	0.007	0.009	0.010	0.011	0.014	0.016	0.011	0.003
	4	0.007	0.009	0.010	0.011	0.014	0.016	0.011	0.003
	5	0.007	0.009	0.010	0.011	0.014	0.016	0.011	0.003
	6	0.007	0.010	0.010	0.012	0.014	0.017	0.012	0.003
	8	0.008	0.010	0.011	0.013	0.015	0.017	0.012	0.003
	10	0.008	0.010	0.012	0.014	0.016	0.017	0.013	0.003
	12	0.009	0.010	0.012	0.015	0.016	0.018	0.013	0.003

Table 22 Paw edema volume (ml) after applied with Voltaren[®] emulgel and formulated patch for 3 and 12 hours induced by carrageenan in Wistar rat.

	No.	T ₀	T ₃	Edema	Mean	SD	
		C	C	Volume			
Control group	1	1.10	1.44	0.34	0.51	0.10	
	2	1.15	1.76	0.61			
	3	1.19	1.62	0.43			
	4	1.15	1.74	0.59			
	5	1.09	1.71	0.62			
	6	1.11	1.71	0.60			
	7	1.15	1.62	0.47			
	8	1.26	1.76	0.50			
	9	1.18	1.57	0.39			
	10	1.22	1.81	0.59			
		time of application = 3 hrs					
		T ₀	T ₃	Edema			
	No.	C	C	Volume	Mean	SD	%inhibition
Voltaren ^(R) emulgel group	1	1.23	1.69	0.46	0.34	0.15	34.82
	2	1.32	1.23	-0.09			
	3	1.12	1.12	0.00			
	4	0.91	1.38	0.47			
	5	1.08	1.27	0.19			
	6	1.17	1.39	0.22			
		time of application = 3 hrs					
		T ₀	T ₃	Edema			
	No.	C	C	Volume	Mean	SD	%inhibition
Patch group	1	1.02	1.01	-0.01	0.20	0.14	61.09
	2	1.04	1.21	0.17			
	3	1.01	1.40	0.39			
	4	1.15	1.23	0.08			
	5	1.13	1.43	0.30			
	6	1.14	1.20	0.06			

Table 22 Paw edema volume (ml) after applied with Voltaren[®] emulgel and formulated patch for 3 and 12 hours induced by carrageenan in Wistar rat (continue).

	No.	time of application = 12 hrs			Edema Volume	Mean	SD	%inhibition
		T ₀	T ₃					
		C	C					
Voltaren ^(R) emulgel group	1	1.03	1.08	0.05	0.44	0.29	14.72	
	2	1.10	1.24	0.14				
	3	1.23	1.68	0.45				
	4	1.19	1.75	0.56				
	5	1.15	1.82	0.67				
	6	1.13	1.89	0.76				
	No.	time of application = 12 hrs			Edema Volume	Mean	SD	
		T ₀	T ₃					
		C	C					
Patch group	1	1.21	1.34	0.13	0.13	0.07	74.32	
	2	1.20	1.28	0.08				
	3	1.09	1.33	0.24				
	4	1.01	1.09	0.08				
	5	1.18	1.08	-0.10				
	6	1.11	1.24	0.13				

Remark : C = carrageenan injected, T₀ = before injection, T₃ = 3 hours after injection .

VITAE

Mr. Ekapol Limpongsa was born on January 3, 1972 in Nakornratchasima. He got his degree in Bachelor of Pharmacy in 1993 from Faculty of Pharmacy, Chiangmai University, Chiangmai, Thailand.



สถาบันวิทยบริการ
จุฬาลงกรณ์มหาวิทยาลัย