REFERENCES

Addicks, W.J. and Weiner, N.D. 1987. Drug delivery from topical Formulations: Theoretical prediction and experimental assessment. Topical Drug Delivery Formulations, Vol. 42; pp. 221-244. New York: Marcel Dekker.

Al-Khamis, K., Davis, S.S. and Hadgraft, J. 1987. *In vitro-in vivo* correlations for the percutaneous absorption of salicylates. Int. J. Pharm. 40: 111-118.

Barry, B.W. 1983. Percutaneous absorption: methods for studying percutaneous absorption. Dermatological Formulations, pp. 234-293. New York: Macel Dekker.

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

Bonaccorsi, A. and West, G.B. 1963. Absence of capillary permeability response in rats to dextran and egg-white. Pharm. Pharmacol. 15: 372-379.

Bouclier, M. Chatelus, A. and Hensby, C.N. 1989. *In vivo* animal models for the evaluation of anti-inflammatory drug action in the skin. In Hensby, C.N. and Lowe, N.J. (eds.), Nonsteroidal Anti-inflammatory Drugs., Vol. 2; pp. 118-135. Switzerland: Karger Basel.

Boudinot, F.D. and Ibrahim, S.S. 1988. High-performance liquid chromatographic assay for piroxicam in human plasma. J. Chromatogr. 430: 424-428.

Brittain, H.G. 1993. Tenoxicam. Analytical Profiles of Drug Substances and Excipients, Vol. 22; pp. 431-435. California: Academic Press.

Brogden, R.N., Heel, R.C., Speight, T.M. and Avery, G.S. 1981. Piroxicam: A review of its pharmacological properties and therapeutic efficacy. Drug 22: 165-187.

Cerretani, D., Micheli, L., Fiaschi, A.I. and Giorgi, G. 1993. Rapid and sensitive determination of piroxicam in rat plasma, muscle and skin by high-performance liquid chromatography. J. Chromatogr. 614: 103-108.

Chambin-Remoussenard, O., Treffel, P., Bechtel, Y. and Agache, P. 1993. Surface recovery and stripping methods to quantity percutaneous absorption of caffeine in humans. J. Pharm. Sci. 82(11): 1099-1101.

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.

Dipasquale, G. Rassaert, C.L. and Mc Dougall, E. 1970. Modified granuloma pouch procedure for the evaluation of topically applied anti-inflamatory steroids. J. Pharm. Sci. 59: 267-270.

Elmquist, W.F., Chan, K.K.H. and Sawchuk, R.J. 1994. Transsynovial drug distribution : Synovial. mean transit time of diclofenac and other nonsteroidal anti-inflammatory drugs. Pharm. Res. 11(12): 1689-1697.

Evans, D.P., Hossacks, M. and Thomson, D.S. 1971. Inhibition of contact sensitivity in the mouse by topical application of corticosteroids. Br. J. Pharmac. 43: 403-408.

Flynn, G.L., and Smith, E.W. 1971. Membrane diffusion I : Design and testing of new multifeatured diffusion cell. J. Pharm. Sci. 60: 1713-1717.

Friend, D.R., 1992. *In vitro* skin permeation technique. J. Control. Rel. 18: 235-248.

Fourtillan, J.B. and Girault, J. 1992. Piroxicam plasma concentrations following repeated topical application of a piroxicam 0.5% gel. Drug Invest. 4(5): 435-440.

Glikfeld, P., Cullander.C., Hinz, R.S. and Guy, R.H. 1988. New systems for *in vitro* studies of iontophoresis. Pharm. Res. 5: 443-447.

Gummer, C.L., Hinz, R.S. and Maibach, H.I. 1987. The skin penetration cell: A design update. Int. J. Pharm. 40: 101-104.

Gupta, N. and Levy, L. 1973. Delayed manifestation of ultraviolet reaction in the guinea-pig caused by anti-inflammatory drugs. Br. J. Pharm. 47: 240-248.

Hadgraft, J. 1989. Formulation of anti-inflammatory agents. In Hensby, C.N. and Lowe, N.J. (eds.), Nonsteroidal Anti-inflammatory Drugs. Vol. 2; pp. 21-43. Switzerland: Karger Basel.

_____ and Guy, R.H. 1992. Synthetic membranes as biological models. Advances in Pharmaceutical Sciences. Vol. 6; pp.43-64. London: David Garderton Trevor Jones Academie Press.

Hawkins G.S. and Reifenrath, W.G. 1986. Influence of skin source, penetration cell fluid, and partition coefficient on *in vitro* skin penetration. J Pharm. Sci. 75(4): 378-381.

Herzfeldt, C.D. and Kummel, R. 1983. Piroxicam. Drug Dev. Ind. Pharm. 9(5): 767-793.

Hiramatsu, Y., Akita, S., Salamin, P.A. and Maier, R. 1990. Assessment of topical nonsteroidal anti-inflammatory drugs in animal models Arzeim.-Forsch./Drug Res. 40(II): 1117-1124.

Huang, Y-C. 1987. *In vitro* evaluations of transdermal drug delivery. Transdermal Controlled Systemic Medications, Vol. 31; pp.159-178. New York; Marcel Dekker.

Issekutz, A.C. and Issekutz, T.B. 1989. Quantitation of blood cell accumulation and vascular responses in inflammatory reactions. In Chang, J.Y. and Lewis, A.J. (eds.), Pharmacological Methods in the Control of Inflammation, Vol. 2, pp. 129-150. New york: Alan R. Liss.

Kroll, M.P., Wiseman, R.L. and Guttadauria, M. 1989. A clinical evaluation of piroxicam gel: An open comparative trial with diclofenae gel in the treatment of acute musculoskeletal disorders. Clin. Ther. 11(3): 382-391.

Law, E. and Lewis, A.J. 1977. The effect of systemically and topically applied drugs on ultraviolet-induced erythema in the rat. Br. J. Pharmac. 59: 591-597.

Liu, P., Higuchi, W.I., Ghanem, A-H. and Good W.R. 1994. Transport of β-estradial in freshly excised human skin *in vitro*: diffusion and metabolism in each skin layer. Pharm. Res. 11(12); 1777-1784.

Logan, G. and Wilhelm, D.L. 1960. Vascular permeability changes in inflammation I.: The role of endogenous permeability factors in ultraviolet injury. Br. J. Exp. Path. 41: 300-314.

Lowe, N.J., Virgadamo, F. and Stoughton, R.B. 1977. Anti-inflammatory properties of a prostaglandin antagonist, a corticosteroid and indomethacin in experimental contact dermatitis. Br. J. Dermatol. 96: 433-438.

Macek, J. and Vacha, J. 1987. Rapid and sensitive method for determination of piroxicam in human plasma by high-performance liquid chromatography. J. Chromatogr. 420: 445-449.

Martin, A., Bustamante, P. and Chun, A.H.C. 1993. Diffusion and dissolution. Physical Pharmacy, pp. 324-361. London: Lea & Fediger.

Milligan, P.A. 1992. Determination of piroxicam and its major metabolites in the plasma, urine and bile of humans by high-performance liquid chromatography. J. Chromatogr. 576: 121-128.

Monteiro-Riviere, N.A., Inman, A.O., Riviere, J.E., McNeill, S.C. and Francoeur, M.L. 1993. Topical penetration of piroxicam is dependent on the distribution of the local cutaneous vasculature. Pharm. Res. 10(9): 1326-1331.

Otterness, I.G. and Bliven, M. 1985. Laboratory models for testing non-steroidal anti-inflammatory drug. In Lombardino, J.G. (ed.), Non-Steroidal Anti-Inflammatory Drugs, pp. 113-252. Canada: John Wiley & Sons.

Pershing, L.K., Silver, B.S., Krueger, G.G. Shah, V.P. and Skelley, J.P. 1992. Feasibility of Measuring the bioavailability of topical betamethasone dipropionate in commercial formulations using drug content in skin and a skin blanching bioassay. Pharm. Res. 9(1): 45-51.

Poelman, M.C., Plot, B., Guyon, F., Deroni, M. and Leveque, J.L. 1989. Assessment of topical nonsteroidal anti-inflammatory drugs. J. Pharm. Pharmacol. 41: 720-722.

Radermacher, J., Jentsch, D. and Scholl, M.A. 1991. Diclofenac concentrations in synovial fluid and plasma after cutaneous application in inflammatory and degenerative joint disease. Br. J. Clin. Pharm. 31: 537-541.

Reynolds, J.E.F. 1989a. Essential oils. Martindale. The Extra Pharmacopoeia. 29th ed., pp. 1064. London: The Pharmaceutical Press.

_____ 1989b. Piroxicam. Martindale. The Extra Pharmacopoeia. 29th ed., pp. 37. London: The Pharmaceutical Press.

Riviere, J.E. and Williams, P.L. 1992. Pharmacokinetic implications of changing blood flow in skin. J. Pharm. Sci. 81: 601-602.

Rongone, E.L. 1981. Skin struture, function and biochemistry. In Marzulliz, F.N. and Maibach, H.I. (eds.), Dermatotoxiccology, 3th ed., pp. 1-46. Washington: Hemisphere Publishing Corporation.

Rougier, A., Dupuis, D., Lotte, C., Roguet, R. and Schaefer, H. 1983. *In vivo* correlation between stratum corneum reservoir function and percutaneous absorption. J. Invest. Dermatol. 81: 275-278.

Samitamarn, W. 1995. Evaluation of diclofenac diethylammonium gel products by *in vitro* permeation and *in vivo* bioavailability studies. Master's Thesis, Chulalongkorn University.

Scheuplein, R.J. 1967. Mechanism of percutaneous absorption II. transient diffusion and the relative importance of various routes of skin penetration. J. Invest. Dermatol. 48: 79-88.

Schiantarelli, P., Acerbi, D. and Bovis, G. 1981. Some pharmacokinetic properties and bioavailability by oral and rectal route of piroxicam in rodents and in man. Arzeim.-Forsch. 31: 92-97.

Sondergaard, J. and Greaves, W.M. 1971. Prostaglandin E: Effect on human cutaneous vasculature and skin histamine. Br. J. Dermatol. 84: 424-428.

Steele, R.H. and Wilhelm, D.L. 1966. The inflammatory reaction in chemical injury I. Increased vascular permeability and erythema induced by various chemicals. Br. J. Exp. Pathol. 47: 612-623.

Tengamnuay, P. and Samitamarn, W. 1996. Development of skin stripping technique to evaluate *in vivo* percutaneous absorption of diclofenac II : Correlation with *in vitro* drug release and application to topical bioavailability determination. Thai J. Pharm. Sci. 20(4): 211-223.

_____ , Janthasoot, W and Sithichai, N. 1995. Evaluation of anti-inflammatory activities of diclofenac diethylammonium gels using mouse-ear edema model. J. Gov. Pharm. Organiz. 21(2) : 9-15.

_____ , Samitamarn, W. and Suvanakoot, U. 1996. Development of skin stripping technique to evaluate *in vivo* percutaneous absorption of diclofenac I : Effects of skin stripping sequence, occlusion time, and sites of application. Thai J. Pharm. Sci. 20(3): 159-169.

Tyle, P., and Agarwala, P. 1989. Drug delivery by iontophoresis. Pharm. Res. 6: 355-361.

Walkow J.E, Mc Ginity J.W. 1987. The effect of physiochemical properties on the *in vitro* diffusion of drug through synthetic membranes and pig skin. I.: Methyl salicylate. Int. J. Pharm. 35: 91-102.

Washitake M., Takachima Y., Tanak, S., Anmo, T., and Tanaka, I. 1980. Drug permeation through egg shell membranes. Chem. Pharm. Bull. 28: 2855-2861.

Wilhelm, D.L. and Mason, B. 1960. Vascular permeability changes in inflammation: The role of endogenous permeability factors in mild thermal injury. Br. J. Exp. Path. 41: 487-506.

Williams, T.J. and Jose, P.J. 1981. Mediation of increased vascular permeability after complement activation J. Exp. Med. 153(Jan): 136-153.

Wurster, D.E., Ostrenga, J.A. and Matheson, Jr., L.E. 1979. Sarin transport across excised human skin I.: Permeability and absorption characteristics. J. Pharm. Sci. 68: 1406-1409.

Young, J.M. and De Young, L.M. 1989. Cutaneous models of inflammation for the evaluation of topical and systemic pharmacological agents, In Chang, J.Y. and Lewis, A.J. (eds.), Pharmacological Methods in the Control of Inflammation, Vol. 2, pp. 215-231. New york: Alan R. Liss.

Zesch, A. 1982. Methods for evaluation of drug concentration in human skin, In Brandau, R. and Lippold, B. (eds.), Dermal and Transdermal Absorption, Vol. 2; pp 116-129. New York: Marcel Dekker.

Appendix I

Details of Piroxicam and Tenoxicam

Piroxicam

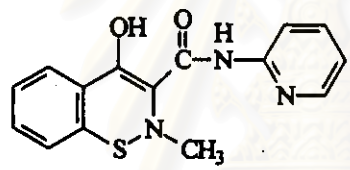
(Reynolds, 1989b and Brogden et al, 1981)

Trade name Feldene gel (Pfizer, UK)

Chemical name

4-Hydroxy-2-methyl-N-(2-pyridyl)-2H-1,2-benzothiazine-3-carboxamide 1,1-dioxide

Formula



Molecular formula $C_{15}H_{13}N_3O_4S$

Molecular weight 331.4

Appearance

An off-white to light tan or light yellow, odorless powder. It forms a monohydrate that is yellow.

Solubility

It is very slightly soluble in water, diluted acids, and most organic solvents; slightly soluble in alcohol and aqueous alkaline solutions.

Pharmacological actions

It is a nonsteroidal anti-inflammatory (NSAID) agent which also possesses analgesic properties. Edema, erythema, tissue proliferation, fever and pain can all be inhibited in laboratory animals by the administration of Feldene gel.

The anti-inflammatory and analgesic effects of Feldene gel were studied in rats and guinea pigs using such standard models of pain and inflammation as carageenan-induced rat paw edema, ultraviolet erythema in guinea pigs, traumatic edema in rats, yeast-induced pain in rats, croton oil-induced erythema in guinea pigs' abdomens, cotton pellet-induced granuloma formation in rats and adjuvant-induced arthritis in rats.

Pharmacokinetics

On the basis of various pharmacokinetic and tissue distribution studies in rats and dogs, piroxicam 0.5% gel is continuously and gradually released from the skin to underlying muscle or synovial fluid. In addition, equilibrium between skin and muscle or synovial fluid appears to be reached rapidly, within a few hours after application. A multiple-dose study of twice-daily application of piroxicam 0.5% gel (total daily dose equivalent to 20 mg/day) for 14 days found that plasma levels rose slowly over the course of the treatment period and reach a value of over 200 ng/ml on the 4th day. On average, steady-state plasma levels were between 300 and 400 ng/ml even on the 14th day of treatment. These piroxicam observed at equilibrium

were approximately 5% of those observed in subjects receiving similar oral dosing (20 mg daily). Elimination half-life in this study was calculated to be approximately 79 hr. In humans, the gel was well tolerated in skin sensitive volunteers.

Indications

For a variety of conditions characterized by pain and inflammation, e.g. osteoarthritis, post-traumatic or acute musculoskeletal disorders in including tendinitis, tenosynovitis, periarthritis, sprains, strains and low back pain.

Dosage and administration

A dosage of 1 g (corresponding to 5 mg of piroxicam) should be applied to the affected site 3 or 4 times/day.

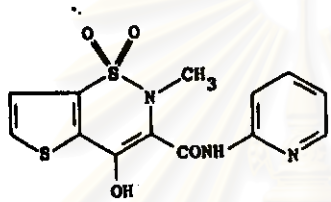
Tenoxicam

(Brittain, 1993)

Chemical name

4-Hydroxy-2-methyl-N-(2-pyridyl)-2H-thieno[2,3-e][1,2] thiazine-3-carboxamide 1,1-dioxide

Formula



Molecular formula $C_{13}H_{11}N_3O_4S_2$

Molecular weight 337.4

Appearance It is a yellow crystalline powder, almost odorless

Melting point 209-213 °C

Dissociation constant It is a weak acid with pKa values of 5.3 and 1.1

Stability Sensitive to light

Solubility Approximate solubility data obtained at room temperature are given in Table

Solvent	mg/ml
Water	0.045
Ethanol	<1
Methanol	<1
Acetone	2
Dichloromethane	10
Chloroform	8
DMSO	63

Appendix II

Data on the Release of Six Piroxicam Gel Products through Cellulose acetate membrane

Product A : release through cellulose acetate

Calibration Curve Data

Conc (μg/ml)	4.32	8.64	12.96	17.28	21.60	43.20	64.80
PAR	0.284	0.643	1.088	1.418	1.807	3.550	5.534

$$Y = -0.074 + 0.172\ X$$

$$r^2 = 0.9994$$

Diffusion Run Data :

Diffusion Run Time (hr)	Run I		Run II		Run III	
	PAR	Amount (μg)	PAR	Amount (μg)	PAR	Amount (μg)
0.50	0.878	135.413	0.865	137.414	0.706	113.603
1.00	1.412	211.333	0.869	137.999	0.748	119.716
1.50	0.920	141.384	0.938	148.092	1.373	210.691
2.00	0.846	130.863	0.490	82.562	0.400	69.061
2.50	0.675	106.552	0.348	61.792	0.311	56.106
3.00	0.687	108.258	0.333	59.598	0.382	66.441
3.50	0.625	99.443	0.311	56.380	0.449	76.194
4.00	0.606	96.742	0.269	50.237	0.558	92.060
5.00	0.958	146.787	0.250	91.339	0.638	103.705
6.00	0.988	151.0520	0.580	95.727	0.553	91.332
Receptor Volume (ml)	12.214		12.566		12.505	
Diffusion area (cm^2)	1.92		1.65		1.67	

PAR = Peak Area Ratio

Product A :

Diffusion Run		Run I	Run II	Run III
Time (hr)	Square root of time ($min^{1/2}$)	Cumulative Amount ($\mu g/cm^2$)	Cumulative Amount ($\mu g/cm^2$)	Cumulative Amount ($\mu g/cm^2$)
0.50	5.48	70.528	83.281	68.026
1.00	7.74	180.597	166.917	139.712
1.50	9.49	254.234	256.670	265.874
2.00	10.95	322.392	306.707	307.228
2.50	12.25	377.888	344.157	340.824
3.00	13.42	434.272	380.277	380.610
3.50	14.49	486.066	414.447	426.235
4.00	15.49	536.452	444.893	481.360
5.00	17.32	612. 904	500.250	543.459
6.00	18.97	691.576	558.267	598.149
Release Rate ($\mu g/min^{1/2} . cm^2$)		45.895	34.559	39.501
r^2		0.9997	0.9932	0.9911
Membrane Thickness (cm)		0.0135	0.0136	0.0136
Normalized Rate ($\mu g/min^{1/2} . cm^3$)		3399.630	2541.103	2904.485

Average release rate = $39.985 \pm 4.640\ \mu g/cm^2 .min^{1/2}$

Average cumulative amount = $615.997 \pm 55.867\ \mu g/cm^2$

Average normalized release rate = $2948.406 \pm 351.865\ \mu g/cm^3 .min^{1/2}$

Product B : release through cellulose acetate

Calibration Curve Data

Conc (μg/ml)	4.32	8.64	12.96	17.28	21.60	43.20	64.80
PAR	0.284	0.643	1.088	1.418	1.807	3.550	5.534

$$Y = -0.074 + 0.172\ X$$

$$r^2 = 0.9994$$

Diffusion Run Data :

Diffusion Run	Run I		Run II		Run III	
Time (hr)	PAR	Amount (μg)	PAR	Amount (μg)	PAR	Amount (μg)
0.50	2.494	365.164	2.759	420.353	3.015	449.701
1.00	1.472	219.863	1.804	278.675	1.767	268.042
1.50	1.486	221.854	1.409	220.076	1.504	229.468
2.00	1.152	174.368	1.103	174.679	1.072	166.878
2.50	1.181	178.491	1.109	175.570	1.034	161.346
3.00	0.974	148.777	0.860	138.629	0.924	145.335
3.50	0.991	151.478	0.884	142.190	0.934	146.790
4.00	0.856	132.285	1.744	269.774	0.872	137.766
5.00	1.770	262.231	0.803	130.173	1.747	265.131
6.00	1.489	222.280	1.348	211.026	1.505	229.905
Receptor Volume (ml)	12.214		12.745		12.505	
Diffusion area (cm^2)	1.92		1.70		1.67	

PAR = Peak Area Ratio

Product B :

Diffusion Run		Run I	Run II	Run III
Time (hr)	Square root of time ($min^{1/2}$)	Cumulative Amount ($\mu g/cm^2$)	Cumulative Amount ($\mu g/cm^2$)	Cumulative Amount ($\mu g/cm^2$)
0.50	5.48	190.190	247.266	269.282
1.00	7.74	304.702	411.193	429.786
1.50	9.49	420.250	540.649	567.192
2.00	10.95	511.067	643.402	667.119
2.50	12.25	604.031	746.678	763.734
3.00	13.42	681.519	828.188	850.760
3.50	14.49	760.414	911.866	938.659
4.00	15.49	829.312	1070.556	1021.153
5.00	17.32	965.891	1147.129	1179.914
6.00	18.97	1081.662	1271.262	1317.582
Release Rate ($\mu g/min^{1/2} . cm^2$)		67.168	77.392	77.447
r^2		0.9973	0.9947	0.9984
Membrane Thickness (cm.)		0.0136	0.0138	0.0135
Normalized Rate ($\mu g/min^{1/2} . cm^3$)		4938.824	5608.116	5736.815

Average release rate = 74.002 ± 4.833 $\mu g/cm^2 .min^{1/2}$

Average cumulative amount = 1223.502 ± 102.063 $\mu g/cm^2$

Average normalized release rate = 5427.918 ± 349.810 $\mu g/cm^3 .min^{1/2}$

Product C : release through cellulose acetate

Calibration Curve Data

Conc (μg/ml)	4.32	8.64	12.96	17.28	21.60	43.20	64.80
PAR	0.284	0.643	1.088	1.418	1.807	3.550	5.534

$$Y = -0.074 + 0.172\ X$$

$$r^2 = 0.9994$$

Diffusion Run Data :

Diffusion Run	Run I		Run II		Run III	
Time (hr)	PAR	Amount (μg)	PAR	Amount (μg)	PAR	Amount (μg)
0.50	2.542	371.988	2.164	332.083	1.054	311.329
1.00	1.467	219.153	1.144	180.762	0.991	155.844
1.50	1.196	180.624	0.916	146.937	0.664	108.014
2.00	0.980	149.914	0.612	101.839	0.584	96.312
2.50	0.985	150.625	1.002	159.696	0.583	96.166
3.00	0.626	99.585	0.774	125.871	0.775	124.250
3.50	0.644	102.144	0.703	115.338	0.751	120.740
4.00	0.747	116.788	0.749	122.162	0.758	121.763
5.00	1.234	186.026	1.106	175.124	1.272	196.946
6.00	1.261	189.865	1.254	197.081	1.463	224.883
Receptor Volume (ml)	12.214		12.745		12.566	
Diffusion area (cm^2)	1.92		1.70		1.65	

PAR = Peak Area Ratio

Product C :

Diffusion Run		Run I	Run II	Run III
Time (hr)	Square root of Time ($min^{1/2}$)	Cumulative Amount ($\mu g/cm^2$)	Cumulative Amount ($\mu g/cm^2$)	Cumulative Amount ($\mu g/cm^2$)
0.50	5.48	193.744	195.343	188.684
1.00	7.74	307.886	301.674	283.135
1.50	9.49	401.961	388.107	348.598
2.00	10.95	480.041	448.012	406.969
2.50	12.25	558.492	541.951	465.252
3.00	13.42	610.359	615.993	540.554
3.50	14.49	663.559	683.839	613.730
4.00	15.49	724.386	755.699	687.526
5.00	17.32	821.274	858.713	806.887
6.00	18.97	920.162	974.643	943.180
Release Rate ($\mu g/min^{1/2}.cm^2$)		53.614	58.427	55.342
r^2		0.9995	0.9939	0.9764
Membrane Thickness (cm.)		0.0136	0.0132	0.0136
Normalized Rate ($\mu g/min^{1/2}.cm^3$)		3942.206	4426.288	4069.265

Average release rate = 55.794 ± 1.991 $\mu g/cm^2.min^{1/2}$

Average cumulative amount = 945.995 ± 22.331 $\mu g/cm^2$

Average normalized release rate = 4145.920 ± 204.924 $\mu g/cm^3.min^{1/2}$

Product D : release through cellulose acetate

Calibration Curve Data

Conc (μg/ml)	4.32	8.64	12.96	17.28	21.60	43.20	64.80
PAR	0.284	0.643	1.088	1.418	1.807	3.550	5.534

$$Y = -0.074 + 0.172\ X$$

$$r^2 = 0.9994$$

Diffusion Run Data :

Diffusion Run	Run I		Run II		Run III	
Time (hr)	PAR	Amount (μg)	PAR	Amount (μg)	PAR	Amount (μg)
0.50	1.098	166.691	1.116	176.608	0.957	150.138
1.00	0.948	145.365	0.939	150.349	0.940	147.664
1.50	0.825	127.877	0.849	136.998	0.779	124.229
2.00	0.691	108.826	0.701	115.041	0.602	98.464
2.50	0.632	100.438	0.677	111.481	0.486	81.580
3.00	0.393	66.459	0.559	93.975	0.595	97.446
3.50	0.542	87.226	0.556	93.530	0.603	98.610
4.00	0.525	85.226	0.524	88.783	0.600	98.173
5.00	0.935	143.517	0.988	157.619	0.921	144.898
6.00	0.800	124.323	0.734	119.940	1.077	167.606
Receptor Volume (ml)	12.214		12.745		12.505	
Diffusion area (cm^2)	1.92		1.70		1.67	

PAR = Peak Area Ratio

Product D :

Diffusion Run		Run I	Run II	Run III
Time (hr)	Square root of Time ($min^{1/2}$)	Cumulative Amount ($\mu g/cm^2$)	Cumulative Amount ($\mu g/cm^2$)	Cumulative Amount ($\mu g/cm^2$)
0.50	5.48	86.818	103.887	89.903
1.00	7.74	162.529	192.328	178.324
1.50	9.49	229.132	272.915	252.713
2.00	10.95	285.812	340.586	311.674
2.50	12.25	338.123	406.163	360.524
3.00	13.42	372.738	461.442	418.875
3.50	14.49	418.385	516.460	477.923
4.00	15.49	462.773	568.685	536.709
5.00	17.32	537.522	661.402	623.474
6.00	18.97	602.273	731.955	723.837
Release Rate ($\mu g/min^{1/2}.cm^2$)		38.434	47.609	46.696
r^2		0.9988	0.9986	0.9933
Membrane Thickness (cm)		0.0130	0.0136	0.0135
Normalized Rate ($\mu g/min^{1/2}.cm^3$)		2956.462	3500.662	3458.963

Average release rate = 44.246 ± 4.127 $\mu g/cm^2.min^{1/2}$

Average cumulative amount = 686.022 ± 59.312 $\mu g/cm^2$

Average normalized release rate = 3305.362 ± 247.296 $\mu g/cm^3.min^{1/2}$

Product E : release through cellulose acetate

Calibration Curve Data

Conc (μg/ml)	4.32	8.64	12.96	17.28	21.60	43.20	64.80
PAR	0.284	0.643	1.088	1.418	1.807	3.550	5.534

$$Y = -0.074 + 0.172\ X$$

$$r^2 = 0.9994$$

Diffusion Run Data :

Diffusion Run	Run I		Run II		Run III	
Time (hr)	PAR	Amount (μg)	PAR	Amount (μg)	PAR	Amount (μg)
0.50	1.646	255.236	1.500	230.295	0.750	120.007
1.00	1.080	171.267	1.032	161.841	1.209	186.819
1.50	0.591	98.722	0.648	105.673	0.544	90.022
2.00	0.671	110.591	0.707	114.303	0.703	113.166
2.50	0.592	98.871	0.662	107.710	0.750	120.007
3.00	0.546	92.046	0.607	99.676	0.683	110.255
3.50	0.478	81.958	0.532	88.706	0.473	79.687
4.00	0.350	62.969	0.523	87.389	0.486	81.580
5.00	0.832	134.476	1.025	160.812	1.090	169.498
6.00	0.781	126.910	0.923	145.898	0.981	153.632
Receptor Volume (ml)	12.745		12.566		12.505	
Diffusion area (cm^2)	1.70		1.65		1.67	

PAR = Peak Area Ratio

Product E :

Diffusion Run		Run I	Run II	Run III
Time (hr)	Square root of Time ($min^{1/2}$)	Cumulative Amount ($\mu g/cm^2$)	Cumulative Amount ($\mu g/cm^2$)	Cumulative Amount ($\mu g/cm^2$)
0.50	5.48	150.139	139.573	71.860
1.00	7.74	250.884	237.658	183.728
1.50	9.49	308.956	301.702	237.634
2.00	10.95	374.009	370.977	305.398
2.50	12.25	432.169	436.256	377.258
3.00	13.42	486.314	496.665	443.279
3.50	14.49	534.524	550.427	490.996
4.00	15.49	571.565	603.390	539.846
5.00	17.32	650.668	700.852	641.342
6.00	18.97	725.321	789.274	733.337
Release Rate ($\mu g/min^{1/2} . cm^2$)		42.610	48.440	48.880
r^2		0.9992	0.9965	0.9959
Membrane Thickness (cm)		0.0132	0.0132	0.0133
Normalized Rate ($\mu g/min^{1/2} . cm^3$)		3228.030	3669.697	3675.188

Average release rate = 46.643 ± 2.858 $\mu g/cm^2 .min^{1/2}$

Average cumulative amount = 749.311 ± 28.447 $\mu g/cm^2$

Average normalized release rate = 3524.305 ± 209.510 $\mu g/cm^3 .min^{1/2}$

Product F : release through cellulose acetate

Calibration Curve Data

Conc (μg/ml)	4.32	8.64	12.96	17.28	21.60	43.20	64.80
PAR	0.284	0.643	1.088	1.418	1.807	3.550	5.534

$$Y = -0.074 + 0.172\ X$$

$$r^2 = 0.9994$$

Diffusion Run Data :

Diffusion Run	Run I		Run II		Run III	
Time (hr.)	PAR	Amount (μg)	PAR	Amount (μg)	PAR	Amount (μg)
0.50	2.204	323.934	2.214	334.732	2.384	357.852
1.00	1.186	179.202	1.208	187.584	1.169	181.997
1.50	1.184	178.918	1.135	176.907	0.827	131.216
2.00	1.077	163.705	0.731	117.814	0.866	136.892
2.50	0.700	110.106	0.856	136.097	0.732	117.387
3.00	1.004	153.327	0.850	135.220	0.703	113.166
3.50	0.970	148.493	0.683	110.793	0.815	129.469
4.00	0.615	98.021	0.574	94.849	0.558	92.060
5.00	1.515	225.977	0.992	155.990	1.336	205.306
6.00	1.344	201.665	0.902	142.826	1.095	170.226
Receptor Volume (ml)	12.214		12.566		12.505	
Diffusion area (cm^2)	1.92		1.65		1.67	

PAR = Peak Area Ratio

Product F :

Diffusion Run		Run I	Run II	Run III
Time (hr)	Square root of Time ($min^{1/2}$)	Cumulative Amount ($\mu g/cm^2$)	Cumulative Amount ($\mu g/cm^2$)	Cumulative Amount ($\mu g/cm^2$)
0.50	5.48	168.716	202.868	214.283
1.00	7.74	262.050	316.555	323.263
1.50	9.49	355.236	423.772	401.835
2.00	10.95	440.499	495.174	483.806
2.50	12.25	497.846	577.657	554.098
3.00	13.42	577.704	659.608	621.862
3.50	14.49	655.044	726.756	699.389
4.00	15.49	706.097	784.240	754.514
5.00	17.32	823.793	878.779	877.452
6.00	18.97	928.827	965.341	979.384
Release Rate ($\mu g/min^{1/2} . cm^2$)		57.271	57.924	57.253
r^2		0.9992	0.9965	0.9959
Membrane Thickness (cm)		0.0132	0.0135	0.0130
Normalized Rate ($\mu g/min^{1/2} . cm^3$)		4338.712	4290.667	4404.077

Average release rate = 57.483 ± 0.312 $\mu g/cm^2 .min^{1/2}$

Average cumulative amount = 957.851 ± 21.308 $\mu g/cm^2$

Average normalized release rate = 4344.485 ± 46.479 $\mu g/cm^3 .min^{1/2}$

Appendix III

Statistical Analyses of the Release Rate and Cumulative Amount Released of Four Piroxicam Gel Products through Cellulose acetate Membrane

Release rate comparison of six piroxicam gel products through cellulose acetate membrane

One way ANOVA

Means		Product
Mean # 1 =	39.985	A
Mean # 2 =	74.002	B
Mean # 3 =	55.794	C
Mean # 4 =	44.246	D
Mean # 5 =	46.643	E
Mean # 6 =	57.483	F

Source	df	SS	MS	F	Prob.
Between	5	2266.262	453.2524	24.45151	.0001
Within	12	222.4414	18.53678		
Total	17	2488.703			

Duncan's new multiple range test

MS Error = 18.53678 , df Error = 12

Significant level = .05

Least Significant Ranges

LSR where p = 2 ----	7.6561
LSR where p = 3 ----	8.0290
LSR where p = 4 ----	8.2775
LSR where p = 5 ----	8.3521
LSR where p = 6 ----	8.4515

Means		Product
Mean # 1 =	74.023	B
Mean # 2 =	57.483	F
Mean # 3 =	55.794	C
Mean # 4 =	46.643	E
Mean # 5 =	44.246	D
Mean # 6 =	39.985	A

Result : A < D < E < C < F < B

Comparison of cumulative amount of six piroxicam gel products released through cellulose acetate membrane at 6 hr

One way ANOVA

Means		Product
Mean # 1 =	615.997	A
Mean # 2 =	1223.502	B
Mean # 3 =	945.995	C
Mean # 4 =	686.022	D
Mean # 5 =	749.311	E
Mean # 6 =	957.851	F

Source	df	SS	MS	F	Prob.
Between	5	753311	150662.2	32.02456	.0001
Within	12	56455	4704.584		
Total	17	809766			

Duncan's new multiple range test

MS Error = 4704.584 , df Error = 12

Significant level = .05

Least Significant Ranges

LSR where p = 2 ----	121.9693
LSR where p = 3 ----	127.9094
LSR where p = 4 ----	131.8695
LSR where p = 5 ----	133.0575
LSR where p = 6 ----	134.6415

Means		Product
Mean # 1 =	615.997	A
Mean # 2 =	686.022	D
Mean # 3 =	749.311	E
Mean # 4 =	945.995	C
Mean # 5 =	957.851	F
Mean # 6 =	1223.502	B

Result : A < D < E < C < F < B

Appendix IV

Data on the Permeation of the Four Piroxicam Gel Products through New Born Pig Skin

Product A : permeate through new born pig skin

Calibration Curve Data

Conc (ng/ml)	5.225	10.45	20.9	41.80	62.70	83.60
PAR	0.176	0.425	0.772	1.584	2.254	3.299

$$Y = -0.026 + 0.038X$$

$$r^2 = 0.9956$$

Diffusion Run Data :

Diffusion Run	Run I		Run II		Run III	
Time (hr)	PAR	Amount (ng/cm^2)	PAR	Amount (ng/cm^2)	PAR	Amount (ng/cm^2)
3.0	-	-	0.136	24.758	0.395	63.658
6.0	0.327	39.978	0.533	85.451	0.462	73.797
9.0	0.472	56.366	0.687	109.033	0.659	103.609
12.0	0.496	59.083	0.838	132.190	0.768	120.104
15.0	0.556	65.839	0.947	148.924	0.856	133.421
18.0	0.802	93.733	1.188	185.759	0.807	126.006
21.0	0.885	103.133	1.338	208.693	0.979	152.035
24.0	0.991	115.139	1.326	206.810	1.084	167.925
Receptor Volume (ml)	12.62		12.63		12.78	
Diffusion area (cm^2)	2.89		2.14		2.19	

Product A :

Diffusion Run	Run I	Run II	Run III
Time (hr)	Cumulative Amount (ng/cm^2)	Cumulative Amount (ng/cm^2)	Cumulative Amount (ng/cm^2)
3.0	-	24.758	63.658
6.0	39.978	110.209	137.455
9.0	96.344	219.242	241.064
12.0	155.427	351.432	361.168
15.0	221.266	500.356	494.589
18.0	314.999	686.115	620.595
21.0	418.132	894.808	772.630
24.0	533.271	1101.618	940.555
J_{ss}* ($ng/hr.cm^2$)	29.20	59.31	46.26
r^2	0.9837	0.9917	0.9962
Membrane thickness (cm)	0.023 ± 0.001	0.024 ± 0.002	0.027 ± 0.001
Normalized J_{ss} ($ng/hr.cm^3$)	1269.76	2471.34	1713.53

* time 9.0 - 24.0 hr

Average normalized flux = 1818.21 ± 496.10 $ng/hr.cm^3$

Average flux = 44.92 ± 12.33 $ng/hr.cm^2$

Product D : permeate through new born pig skin

Calibration Curve Data

Conc (ng/ml)	10.20	20.40	40.80	61.20	81.60	102.00	204.00	306.00
PAR	0.108	0.180	0.394	0.506	0.713	1.010	1.991	3.082

$$Y = -0.0468 + 0.01X$$

$$r^2 = 0.9980$$

Diffusion Run Data :

Diffusion Run	Run I		Run II		Run III	
Time (hr)	PAR	Amount (ng/cm^2)	PAR	Amount (ng/cm^2)	PAR	Amount (ng/cm^2)
3.0	0.654	302.500	0.366	234.051	0.252	174.330
6.0	1.114	501.048	0.795	477.265	0.441	284.584
9.0	1.184	531.078	0.905	539.861	0.607	381.282
12.0	1.366	610.001	0.995	590.430	0.712	442.820
15.0	1.490	663.339	1.067	631.471	0.847	521.428
18.0	1.712	759.160	1.316	772.637	0.916	561.680
21.0	1.596	709.092	1.302	764.700	1.084	659.684
24.0	1.789	792.396	1.479	865.047	1.214	735.521
Receptor Volume (ml)	12.62		13.02		12.63	
Diffusion area (cm^2)	2.89		2.27		2.14	

Product D ;

Diffusion Run	Run I	Run II	Run III
Time (hr)	Cumulative Amount (ng/cm^2)	Cumulative Amount (ng/cm^2)	Cumulative Amount (ng/cm^2)
3.0	302.500	234.051	174.330
6.0	803.548	711.316	458.914
9.0	1334.626	1251.177	840.196
12.0	1944.627	1841.607	1283.016
15.0	2607.966	2473.078	1804.444
18.0	3367.126	3245.715	2366.124
21.0	4076.218	4010.415	3025.808
24.0	4868.614	4875.462	3761.329
J_{ss}** ($ng/hr.cm^2$)	227.39	231.13	182.88
r^2	0.9962	0.9931	0.9879
Membrane thickness (cm)	0.025 ± 0.001	0.024 ± 0.001	0.030 ± 0.001
Normalized J_{ss} ($ng/hr.cm^3$)	9095.66	9630.47	6095.86

** time 6.0 - 24.0 hr

Average normalized flux = 8274.00 ± 1555.57 $ng/hr.cm^3$

Average flux = 213.80 ± 21.92 $ng/hr.cm^2$

Product B : permeate through new born pig skin

Calibration Curve Data

Conc (ng/ml)	10.00	20.00	40.00	80.00	200.00	400.00
PAR	0.059	0.193	0.324	0.656	1.954	3.962

$$Y = -0.063 + 0.010X$$

$$r^2 = 0.9990$$

Diffusion Run Data :

Diffusion Run	Run I		Run II		Run III	
Time (hr)	PAR	Amount (ng/cm^2)	PAR	Amount (ng/cm^2)	PAR	Amount (ng/cm^2)
3.0	0.047	48.090	0.052	66.022	0.133	114.257
6.0	0.179	105.507	0.278	195.143	0.286	203.194
9.0	0.220	123.341	0.325	221.996	0.543	352.584
12.0	0.236	130.300	0.307	211.712	0.506	331.077
15.0	0.265	142.915	0.297	205.998	0.533	346.771
18.0	0.224	125.081	0.260	184.859	0.499	327.008
21.0	0.144	90.283	0.303	209.426	0.423	282.830
24.0	0.197	113.336	0.238	172.290	0.505	330.495
Receptor Volume (ml)	12.62		13.02		12.78	
Diffusion area (cm^2)	2.89		2.27		2.19	

Product B :

Diffusion Run	Run I	Run II	Run III
Time (hr)	Cumulative Amount (ng/cm^2)	Cumulative Amount (ng/cm^2)	Cumulative Amount (ng/cm^2)
3.0	48.090	66.022	114.257
6.0	153.597	261.135	317.451
9.0	276.938	483.161	670.035
12.0	407.238	694.873	1001.112
15.0	550.153	900.871	1347.883
18.0	675.234	1085.730	1674.891
21.0	765.517	1295.156	1957.721
24.0	878.853	1467.446	2288.216
J_{ss}** ($ng/hr.cm^2$)	40.72	67.07	109.06
r^2	0.9964	0.9989	0.9992
Membrane thickness (cm)	0.027 ± 0.002	0.024 ± 0.001	0.026 ± 0.001
Normalized J_{ss} ($ng/hr.cm^3$)	1508.34	2794.49	4194.80

** time 6.0 - 24.0 hr

Average normalized flux = 2832.54 ± 1097.07 $ng/hr.cm^3$

Average flux = 72.28 ± 28.14 $ng/hr.cm^2$

Product C : permeate through new born pig skin

Calibration Curve Data

Conc (ng/ml)	10.20	20.40	40.80	61.20	81.60	102.00	204.00	306.00
PAR	0.108	0.180	0.394	0.506	0.713	1.010	1.991	3.082

$$Y = -0.0468 + 0.01X$$

$$r^2 = 0.9980$$

Diffusion Run Data :

Diffusion Run	RunI		Run II		Run III	
Time (hr)	PAR	Amount (ng/cm^2)	PAR	Amount (ng/cm^2)	PAR	Amount (ng/cm^2)
3.0	0.146	109.326	0.120	97.326	0.193	138.341
6.0	0.264	176.460	0.129	102.292	0.010	32.620
9.0	0.313	203.972	0.143	111.22	0.099	83.885
12.0	0.320	207.767	0.241	167.904	0.049	55.102
15.0	0.474	295.280	0.334	222.165	0.041	50.666
18.0	0.571	350.272	0.378	247.833	0.054	58.164
21.0	0.645	392.226	0.285	193.581	0.059	61.048
24.0	0.706	426.808	0.376	246.666	0.069	66.816
Receptor Volume (ml)	13.02		12.63		12.78	
Diffusion area (cm^2)	2.27		2.14		2.19	

Product C :

Diffusion Run	Run I	Run II	Run III
Time (hr)	Cumulative Amount (ng/cm^2)	Cumulative Amount (ng/cm^2)	Cumulative Amount (ng/cm^2)
3.0	109.326	97.326	138.341
6.0	285.786	199.618	170.961
9.0	489.758	310.640	254.846
12.0	697.525	478.544	309.948
15.0	992.805	700.709	360.614
18.0	1343.077	948.542	418.778
21.0	1735.303	1142.123	479.826
24.0	2162.111	1388.789	546.642
J_{ss}*($ng/hr.cm^2$)	112.62	72.66	19.30
r^2	0.9868	0.9974	0.9978
Membrane thickness (cm)	0.029 ± 0.001	0.027 ± 0.002	0.026 ± 0.002
Normalized J_{ss} ($ng/hr.cm^3$)	3883.54	2691.12	742.41

* time 9.0 - 24.0 hr

Average normalized flux = 2439.02 ± 1294.69 $ng/hr.cm^3$

Average flux = 68.19 ± 38.23 $ng/hr.cm^2$

Appendix V

Statistical Analyses of Permeation Flux of Four Piroxicam Gel Products through New Born Pig Skin

Flux comparison of four piroxicam gel products permeate through new born pig skin after 24 hr

One way ANOVA

Means		Product
Mean # 1 =	44.923	A
Mean # 2 =	72.283	B
Mean # 3 =	68.193	C
Mean # 4 =	213.800	D

Source	df	SS	MS	F	Prob.
Between	3	53290.78	17763.59	16.41506	.0013
Within	8	8657.219	1082.152		
Total	11	61948			

Duncan's new multiple range test

MS Error = 1082.152 , df Error = 8

Significant level = .05

Least Significant Ranges

LSR where p = 2 ----	61.9158
LSR where p = 3 ----	64.3848
LSR where p = 4 ----	65.9042

Means		Product
Mean # 1 =	44.923	A
Mean # 2 =	68.193	C
Mean # 3 =	72.283	B
Mean # 4 =	213.800	D

Result : A < C < B < D

Comparison of cumulative amount of four piroxicam gel products diffused through new born pig skin after 24 hr

One way ANOVA

Means		Product
Mean # 1 =	858.481	A
Mean # 2 =	1544.838	B
Mean # 3 =	1365.847	C
Mean # 4 =	4501.802	D

Source	df	SS	MS	F	Prob.
Between	3	2.446E+07	8153044	19.75375	.0009
Within	8	3301872	412734		
Total	11	2.7761E+07			

Duncan's new multiple range test

MS Error = 412734 , df Error = 8

Significant level = .05

Least Significant Ranges

LSR where p = 2 ----	1209.1830
LSR where p = 3 ----	1257.4020
LSR where p = 4 ----	1287.0760

Means		Product
Mean # 1 =	858.481	A
Mean # 2 =	1365.847	C
Mean # 3 =	1544.838	B
Mean # 4 =	4501.802	D

Result : A < C < B < D

Appendix VI

Data on Oxazolone-induced Ear Edema and Statistical Analyses

Product A : ear weight differance, induced by oxazolone

Subject No.	Right ear (mg)	Left ear (mg)	Weight difference (mg)
1	20.1	11.2	8.9
2	22.0	10.2	11.8
3	18.1	9.4	8.7
4	16.2	10.4	5.8
5	22.3	10.8	11.5
6	28.0	9.3	18.7
7	18.5	14.0	4.5
8	23.6	9.2	14.4
9	19.0	9.6	9.4
10	20.5	10.2	10.3
11	25.8	11.2	14.6
12	11.7	9.7	2.0

Average ear weight differance = 10.05 ± 4.64 mg

Product B : ear weight differance, induced by oxazolone

Subject No.	Right ear (mg)	Left ear (mg)	Weight difference (mg)
1	18.0	10.8	7.2
2	26.8	14.3	12.5
3	28.4	10.3	18.1
4	13.4	9.5	3.9
5	20.4	10.6	9.8
6	21.3	11.9	9.4
7	14.7	10.1	4.6
8	23.0	11.8	11.2
9	20.4	10.1	10.3
10	28.9	10.4	18.5
11	15.0	9.8	5.2
12	24.3	10.4	13.9

Average ear weight differance = 10.38 ± 4.83 mg

Product C : ear weight differance, induced by oxazolone

Subject No.	Right ear (mg)	Left ear (mg)	Weight difference (mg)
1	23.0	10.6	12.4
2	28.3	10.8	17.5
3	18.0	10.4	7.6
4	31.5	10.9	20.6
5	13.1	9.9	3.2
6	19.8	10.3	9.5
7	24.1	9.6	14.5
8	13.8	12.8	1.0
9	23.8	10.2	13.6
10	14.5	10.5	4.0
11	12.0	9.9	2.1
12	14.4	10.5	3.9

Average ear weight differance = 9.16 ± 6.52 mg

Product D : ear weight differance, induced by oxazolone

Subject No.	Right ear (mg)	Left ear (mg)	Weight difference (mg)
1	28.5	11.0	17.5
2	18.6	9.7	8.9
3	28.2	12.4	15.8
4	13.4	9.5	3.9
5	16.0	9.7	6.3
6	21.7	9.6	12.1
7	18.7	9.9	8.8
8	14.8	10.5	4.3
9	15.5	9.2	6.3
10	13.0	9.8	3.2
11	22.5	10.7	11.8
12	16.2	10.0	6.1

Average ear weight differance = 8.75 ± 4.67 mg

Control group : ear weight differance, induced by oxazolone

Subject No.	Right ear (mg)	Left ear (mg)	Weight difference (mg)
1	35.4	10.4	25.0
2	28.0	10.0	18.0
3	33.6	10.6	23.0
4	30.3	8.1	22.2
5	29.8	7.2	22.6
6	26.5	9.8	16.7
7	25.0	9.6	15.4
8	27.9	8.6	19.3
9	29.9	10.3	19.6
10	30.7	9.0	21.7
11	33.3	17.2	16.1
12	36.7	9.3	27.4

Average ear weight differance = 20.58 ± 3.70 mg

Comparison of ear weight differance of four piroxicam gel products and control group

One way ANOVA

Means		Product
Mean # 1 =	10.05	A
Mean # 2 =	10.38	B
Mean # 3 =	9.16	C
Mean # 4 =	8.75	D
Mean # 5 =	20.58	Control

Source	df	SS	MS	F	Prob.
Between	4	1181.955	295.4888	12.0149	.0001
Within	55	1352.642	24.59348		
Total	59	2534.597			

Duncan's new multiple range test

MS Error = 24.59348 , df Error = 55

Significant level = .05

Least Significant Ranges

LSR where p = 2 ----	4.0514
LSR where p = 3 ----	4.2661
LSR where p = 4 ----	4.4093
LSR where p = 5 ----	4.4952

Means		Product
Mean # 1 =	8.75	D
Mean # 2 =	9.16	C
Mean # 3 =	10.05	A
Mean # 4 =	10.38	B
Mean # 5 =	20.58	Control

Result : D < C < A < B < Control

Appendix VII

Data on Histamine-induced Vascular Permeability and Statistical Analyses

Product A : size of blue spot, induced by histamine

Subject No.	Longest (mm)	Shortest (mm)	Area (mm^2)	Average area (mm^2)
1	19.1	15.9	303.69	
	17.5	16.3	285.25	271.75
	16.4	13.8	226.32	
2	20.8	12.2	253.76	
	15.9	11.2	178.08	216.11
	16.4	13.2	216.48	
3	15.2	12.1	183.92	
	12.7	12.5	158.75	192.94
	16.4	14.4	236.16	
4	13.1	13.0	170.30	
	14.7	12.8	188.16	189.76
	16.6	12.7	210.82	
5	19.6	13.2	258.72	
	18.5	13.9	257.15	267.37
	20.3	14.1	286.23	
6	18.4	14.6	268.64	
	15.4	14.1	217.14	223.32
	16.3	11.3	184.19	

Product A ;

Subject No.	Longest (mm)	Shortest (mm)	Area (mm^2)	Average area (mm^2)
7	12.8	12.5	160.00	
	13.6	13.0	176.80	177.52
	14.5	13.5	195.75	
8	13.5	10.9	147.15	
	13.2	12.2	161.04	177.36
	16.1	13.9	223.79	
9	16.1	12.9	207.69	
	13.8	11.7	161.46	205.21
	15.7	15.7	246.49	
10	15.6	10.2	159.12	
	14.4	13.4	192.96	199.81
	16.6	14.9	247.34	

Average size of blue spot = 212.12 ± 31.97

Product B : size of blue spot, induced by histamine

Subject No.	Longest (mm)	Shortest (mm)	Area (mm^2)	Average area (mm^2)
1	17.4	13.6	236.64	
	15.0	11.1	166.50	201.89
	15.7	12.9	202.53	
2	18.4	12.4	228.16	
	16.0	13.5	216.00	237.81
	18.7	14.4	269.28	
3	16.6	12.4	205.84	
	13.0	9.6	124.80	169.49
	15.2	11.7	177.84	
4	15.0	14.0	210.00	
	15.6	13.7	213.72	212.08
	16.1	13.2	212.52	
5	15.1	12.5	188.75	
	12.9	12.1	156.09	188.65
	16.5	13.4	221.10	
6	14.6	14.0	204.40	
	14.5	13.5	195.75	189.55
	13.7	12.3	168.51	

Product B :

Subject No.	Longest (mm)	Shortest (mm)	Area (mm^2)	Average area (mm^2)
7	17.3	12.3	212.79	
	13.5	12.3	166.05	195.27
	15.8	13.1	206.98	
8	17.5	13.3	232.75	
	14.5	14.5	210.25	220.60
	15.3	14.3	218.79	
9	16.0	10.7	171.20	
	14.8	9.2	136.16	174.84
	16.4	13.1	214.84	
10	16.3	12.3	200.49	
	16.9	14.4	243.36	210.02
	14.0	13.3	186.20	

Average size of blue spot = 200.02 ± 19.82

Product C : size of blue spot, induced by histamine

Subject No.	Longest (mm)	Shortest (mm)	Area (mm^2)	Average area (mm^2)
1	16.6	13.0	215.80	
	15.7	14.2	222.94	249.43
	20.5	15.1	309.55	
2	15.1	15.0	226.50	
	17.6	14.8	260.48	244.99
	15.5	16.0	248.00	
3	20.3	13.9	282.17	
	16.3	13.3	216.79	250.11
	17.1	14.7	251.37	
4	19.2	14.0	268.80	
	15.8	15.4	243.32	261.34
	17.1	15.9	271.89	
5	17.3	13.0	224.90	
	14.4	13.8	198.72	218.54
	16.0	14.5	232.00	
6	18.5	16.0	296.00	
	14.6	13.4	195.64	226.20
	16.4	11.4	186.96	

Product C :

Subject No.	Longest (mm)	Shortest (mm)	Area (mm^2)	Average area (mm^2)
7	16.9	12.5	211.25	
	14.6	12.6	183.96	194.38
	16.2	11.6	187.92	
8	13.5	11.4	153.90	
	17.6	13.3	234.08	204.76
	15.5	14.6	226.30	
9	14.5	13.8	200.10	
	15.3	12.6	192.78	235.12
	18.6	16.8	312.48	
10	15.1	13.7	206.87	
	14.7	16.2	238.14	219.96
	13.6	15.8	214.88	

Average size of blue spot = 230.48 ± 20.41

Product D : size of blue spot, induced by histamine

Subject No.	Longest (mm)	Shortest (mm)	Area (mm^2)	Average area (mm^2)
1	14.1	12.6	177.66	
	16.8	15.3	257.04	208.37
	16.0	11.9	190.40	
2	18.2	14.3	260.26	
	19.0	13.3	252.70	256.79
	15.6	16.5	257.40	
3	15.0	14.3	214.50	
	14.1	14.1	198.81	201.37
	15.9	12.0	190.80	
4	15.7	11.8	185.26	
	12.1	11.3	136.73	185.90
	16.6	14.2	235.72	
5	17.6	13.3	234.08	
	14.7	13.6	199.92	199.62
	15.7	10.5	164.85	
6	14.9	14.7	219.03	
	14.6	14.3	208.78	198.37
	14.3	11.7	167.31	

Product D :

Subject No.	Longest (mm)	Shortest (mm)	Area (mm^2)	Average area (mm^2)
7	16.6	11.4	189.24	
	14.3	12.1	173.03	174.52
	12.7	12.7	161.29	
8	14.3	11.1	158.73	
	12.6	12.4	156.24	168.31
	15.7	12.1	189.97	
9	15.6	13.0	202.80	
	14.0	12.5	175.00	207.98
	16.3	15.1	246.13	
10	17.5	15.0	262.50	
	16.5	14.9	245.85	249.20
	16.5	14.5	239.25	

Average size of blue spot = 205.04 ± 27.17

Control : size of blue spot, induced by histamine

Subject No.	Longest (mm)	Shortest (mm)	Area (mm^2)	Average area (mm^2)
1	17.9	14.4	257.76	
	16.3	16.0	260.80	260.94
	18.1	14.6	264.26	
2	19.1	12.0	229.20	
	17.4	17.4	302.76	273.65
	16.9	17.1	288.99	
3	19.3	17.9	345.47	
	16.8	15.9	267.12	280.46
	17.6	13.0	228.80	
4	17.3	11.8	204.14	
	15.1	12.3	185.73	214.74
	16.2	15.7	254.34	
5	16.7	12.8	213.76	
	15.5	13.4	207.70	222.33
	18.6	13.2	245.52	
6	16.2	16.2	262.44	
	17.9	14.4	257.76	250.12
	16.8	13.7	230.16	

Control :

Subject No.	Longest (mm)	Shortest (mm)	Area (mm^2)	Average area (mm^2)
7	18.0	13.4	241.20	
	14.5	13.2	191.40	208.60
	16.1	12.0	193.20	
8	17.3	14.9	257.77	
	17.7	15.7	277.89	286.45
	19.5	16.6	323.70	
9	16.6	13.3	220.78	
	13.9	13.8	191.82	213.01
	14.8	15.3	226.44	
10	16.0	15.6	249.60	
	15.5	14.6	226.30	251.57
	17.0	16.4	278.80	

Average size of blue spot = 246.19 ± 28.08

Comparison of sizes of blue spot of four piroxicam gel products and control group

Means		Product
Mean # 1 =	212.115	A
Mean # 2 =	200.02	B
Mean # 3 =	230.483	C
Mean # 5 =	205.043	D
Mean # 4 =	246.187	Control

Source	df	SS	MS	F	Prob.
Between	4	14731.5	3682.875	4.935176	.0026
Within	45	33581.25	746.25		
Total	49	48312.75			

Duncan's new multiple range test

MS Error = 746.25 , df Error = 45

Significant level = .05

Least Significant Ranges

LSR where p = 2 ----	24.7063
LSR where p = 3 ----	26.0021
LSR where p = 4 ----	26.7796
LSR where p = 5 ----	27.3843

Means		Product
Mean # 1 =	200.02	B
Mean # 2 =	205.043	D
Mean # 3 =	212.115	A
Mean # 4 =	230.483	C
Mean # 5 =	246.187	Control

Result : B < D < A < C < Control

Appendix VIII

Data on *In vivo* Percutaneous Absorption of four Piroxicam Gel Products Using Skin Stripping technique

Calibration Curve Data :

1.

Conc.(μg/ml)	0.2475	0.4950	0.9900	1.4850	1.9800	2.9700
PAR	0.131	0.221	0.424	0.731	0.961	1.400

$Y = -0.00539 + 0.4775X$, $r^2 = 0.9969$

2.

Conc.(μg/ml)	0.2010	0.5025	1.0050	2.0100	3.0150	4.0200
PAR	0.143	0.424	0.773	1.958	3.144	4.279

$Y = -0.1795 + 1.097X$, $r^2 = 0.9969$

3.

Conc.(μg/ml)	0.1990	0.4975	0.9950	1.9900	2.9850	3.9800
PAR	0.166	0.448	0.832	1.739	2.741	3.594

$Y = -0.0345 + 0.00091X$, $r^2 = 0.9992$

4.

Conc.(μg/ml)	0.2190	0.5475	1.0950	2.1900	3.2850	4.3800
PAR	0.176	0.499	0.843	1.803	3.032	3.933

$Y = -0.07059 + 0.9141X$, $r^2 = 0.9964$

Product A: percutaneous absorption through stratum corneum of eight subjects at various times

Subject No.	Time (hr)	PAR	Conc. (μg/ml)	Amount (μg)	stratum corneum weight (mg)	Amount in stratum corneum (μg/mg)
1(2)	0	1.153	1.214	3.644	3.90	0.934
	1	0.869	0.955	2.866	3.16	0.907
	3	0.752	0.849	2.548	2.97	0.858
	6	0.811	0.902	2.707	3.38	0.801
2(3)	0	0.966	1.095	3.285	2.41	1.363
	1	0.403	0.479	1.436	2.20	0.653
	3	0.142	0.193	0.579	1.71	0.339
	6	0.148	0.200	0.599	1.88	0.319
3(1)	0	0.806	1.699	6.796	4.41	1.541
	1	0.321	0.683	2.734	2.84	0.963
	3	0.289	0.616	2.465	2.77	0.890
	6	0.315	0.672	2.686	3.81	0.705
4(1)	0	0.955	2.012	8.048	3.89	2.069
	1	0.727	1.533	6.133	3.25	1.887
	3	0.254	0.543	2.172	1.43	1.519
	6	0.510	1.079	4.316	3.43	1.258

( ) = Calibrationcurve number

Product A:

Subject No.	Time (hr)	PAR	Conc. (μg/ml)	Amount (μg)	stratum corneum weight (mg)	Amount in stratum corneum (μg/mg)
5(1(	0	0.617	1.303	5.213	2.59	2.013
	1	0.452	0.958	3.833	2.46	1.558
	3	0.273	0.583	2.330	2.16	1.079
	6	0.209	0.449	1.795	1.79	1.003
6(3)	0	1.435	1.609	4.826	2.57	1.878
	1	0.905	1.028	3.085	2.74	1.126
	3	0.606	0.701	2.103	2.47	0.851
	6	0.327	0.396	1.187	2.45	0.484
7(3)	0	1.228	1.382	4.146	2.66	1.558
	1	0.541	0.630	1.889	2.22	0.851
	3	0.474	0.557	1.670	2.23	0.749
	6	0.336	0.406	1.217	1.97	0.618
8(1)	0	0.330	0.703	2.811	2.56	1.098
	1	0.235	0.504	2.018	2.87	0.703
	3	0.158	0.342	1.368	2.21	0.619
	6	0.189	0.406	1.625	2.95	0.551

( ) = Calibrationcurve number

Product B: percutaneous absorption through stratum corneum of eight subjects at various times

Subject No.	Time (hr)	PAR	Conc. (μg/ml)	Amount (μg)	stratum corneum weight (mg)	Amount in stratum corneum (μg/mg)
1(1)	0	0.828	1.745	6.980	2.76	2.529
	1	0.607	1.282	5.128	2.07	2.477
	3	0.276	0.589	2.356	1.76	1.339
	6	0.376	0.799	3.196	2.44	1.310
2(1)	0	0.568	1.201	4.804	3.48	1.380
	1	0.345	0.734	2.936	2.57	1.142
	3	0.120	0.262	1.048	2.10	0.499
	6	0.070	0.158	0.632	2.52	0.251
3(4)	0	0.831	0.987	2.961	3.45	0.858
	1	0.175	0.269	0.807	2.38	0.339
	3	0.139	0.230	0.689	2.69	0.256
	6	0.145	0.236	0.708	3.32	0.213
4(3)	0	1.050	1.187	3.561	3.68	0.968
	1	0.220	0.278	0.836	3.25	0.257
	3	0.067	0.111	0.333	2.57	0.130
	6	0.069	0.113	0.340	3.07	0.111

( ) = Calibrationcurve number

Product B:

Subject No.	Time (hr)	PAR	Conc. (μg/ml)	Amount (μg)	stratum corneum weight (mg)	Amount in stratum corneum (μg/mg)
5(4)	0	1.563	1.787	5.362	2.26	2.372
	1	0.183	0.278	0.833	1.73	0.482
	3	0.084	0.169	0.506	1.82	0.278
	6	0.039	0.120	0.360	1.65	0.218
6(1)	0	0.930	1.959	7.836	3.23	2.426
	1	0.235	0.503	2.012	2.59	0.777
	3	0.140	0.304	1.216	2.17	0.560
	6	0.112	0.246	0.984	2.04	0.482
7(3)	0	0.927	1.052	3.157	2.99	1.056
	1	0.502	0.587	1.761	2.56	0.688
	3	0.307	0.373	1.120	2.68	0.418
	6	0.084	0.129	0.388	3.08	0.126
8(2)	0	0.995	1.070	3.212	2.66	1.207
	1	0.253	0.394	1.183	1.70	0.696
	3	0.178	0.326	0.978	1.98	0.494
	6	0.129	0.281	0.844	2.05	0.411

( ) = Calibrationcurve number

Product C: percutaneous absorption through stratum corneum of eight subjects at various times

Subject No.	Time (hr)	PAR	Conc. (μg/ml)	Amount (μg)	stratum corneum weight (mg)	Amount in stratum corneum (μg/mg)
1[3]	0	1.617	1.808	5.423	3.29	1.648
	1	1.068	1.206	3.619	3.43	1.055
	3	0.676	0.777	2.332	2.46	0.948
	6	0.423	0.500	1.501	2.78	0.540
2[4]	0	0.508	0.633	1.899	2.69	0.706
	1	0.274	0.377	1.132	1.88	0.602
	3	0.268	0.371	1.113	2.12	0.525
	6	0.138	0.228	0.684	1.56	0.439
3[3]	0	0.420	0.497	1.492	2.71	0.550
	1	0.357	0.429	1.287	2.86	0.450
	3	0.249	0.310	0.931	2.12	0.439
	6	0.171	0.225	0.676	3.03	0.223
4[4]	0	0.451	0.571	1.712	3.20	0.535
	1	0.134	0.224	0.671	1.79	0.375
	3	0.113	0.201	0.602	1.94	0.311
	6	0.122	0.211	0.632	1.45	0.436

( ) = Calibrationcurve number

Product C:

Subject No.	Time (hr)	PAR	Conc. (μg/ml)	Amount (μg)	stratum corneum weight (mg)	Amount in stratum corneum (μg/mg)
5(3)	0	0.762	0.872	2.615	2.32	1.127
	1	0.539	0.628	1.883	1.93	0.976
	3	0.358	0.430	1.289	1.47	0.877
	6	0.449	0.529	1.587	2.00	0.794
6(4)	0	1.065	1.242	3.727	2.77	1.346
	1	0.297	0.402	1.206	1.97	0.612
	3	0.276	0.379	1.167	2.54	0.447
	6	0.193	0.288	0.864	2.42	0.357
7(2)	0	1.049	1.120	3.359	3.47	0.968
	1	0.607	0.717	2.151	2.40	0.896
	3	0.722	0.822	2.465	2.79	0.884
	6	0.617	0.726	2.178	2.68	0.813
8(2)	0	0.806	0.899	2.696	2.68	1.006
	1	0.361	0.493	1.478	1.60	0.924
	3	0.405	0.533	1.598	1.79	0.893
	6	0.309	0.446	1.337	1.96	0.682

( ) = Calibrationcurve number

Product D: percutaneous absorption through stratum corneum of eight subjects at various times

Subject No.	Time (hr)	PAR	Conc. (μg/ml)	Amount (μg)	stratum corneum weight (mg)	Amount in stratum corneum (μg/mg)
1[4]	0	1.146	1.330	3.992	4.32	0.924
	1	0.542	0.670	2.010	4.07	0.494
	3	0.199	0.295	0.886	2.53	0.350
	6	0.325	0.433	1.299	4.23	0.307
2[2]	0	1.940	1.932	5.796	3.66	1.583
	1	0.267	0.407	1.221	2.64	0.462
	3	0.050	0.209	0.628	1.88	0.334
	6	0.046	0.206	0.617	2.07	0.298
3[2]	0	1.038	1.110	3.329	3.45	0.965
	1	0.332	0.466	1.399	2.31	0.605
	3	0.209	0.354	1.062	2.50	0.425
	6	0.077	0.234	0.701	1.81	0.387
4[2]	0	0.507	0.626	1.877	2.56	0.733
	1	0.420	0.547	1.641	2.69	0.610
	3	0.112	0.266	0.797	1.81	0.440
	6	0.035	0.196	0.586	1.96	0.299

( ) = Calibrationcurve number

Product D:

Subject No.	Time (hr)	PAR	Conc. (μg/ml)	Amount (μg)	stratum corneum weight (mg)	Amount in stratum corneum (μg/mg)
5(4)	0	0.324	0.432	1.295	1.80	0.719
	1	0.176	0.27.	0.810	1.61	0.503
	3	0.056	0.138	0.415	1.54	0.270
	6	0.030	0.110	0.330	1.91	0.173
6(4)	0	1.133	1.317	3.951	3.49	1.132
	1	0.657	0.796	2.388	2.88	0.829
	3	0.241	0.340	1.022	1.72	0.594
	6	0.194	0.289	0.868	2.73	0.318
7(2)	0	1.520	1.549	4.647	3.27	1.421
	1	1.510	1.540	4.620	3.85	1.200
	3	0.768	0.863	2.590	2.93	0.884
	6	0.260	0.400	1.202	2.09	0.575
8(1)	0	0.355	0.755	3.020	2.41	1.253
	1	0.151	0.327	1.309	1.98	0.661
	3	0.111	0.245	0.981	2.22	0.442
	6	0.109	0.239	0.956	2.53	0.378

( ) = Calibrationcurve number

The amount of piroxicam in stratum corneum of four gel products at 0 hr

Subject No.	Amount of piroxicam in stratum corneum (μg/mg)			
	A	B	C	D
1	0.934	2.529	1.648	0.924
2	1.363	1.380	0.706	1.583
3	1.541	0.858	0.550	0.965
4	2.069	0.968	0.535	0.733
5	2.013	2.372	1.127	0.719
6	1.878	2.426	1.346	1.132
7	1.558	1.056	0.968	1.421
8	1.098	1.207	1.006	1.253
mean ± SD	1.557 ± 0.389	1.600 ± 0.700	0.986 ± 0.364	1.091 ± 0.294

The amount of piroxicam in stratum corneum of four gel products at 1 hr

Subject No.	Amount of piroxicam in stratum corneum (μg/mg)			
	A	B	C	D
1	0.907	2.477	1.055	0.494
2	0.653	1.142	0.602	0.462
3	0.963	0.339	0.450	0.605
4	1.887	0.257	0.375	0.610
5	1.558	0.482	0.976	0.503
6	1.126	0.777	0.612	0.829
7	0.851	0.688	0.896	1.200
8	0.703	0.696	0.924	0.661
mean ± SD	1.081 ± 0.403	0.857 ± 0.665	0.736 ± 0.241	0.670 ± 0.228

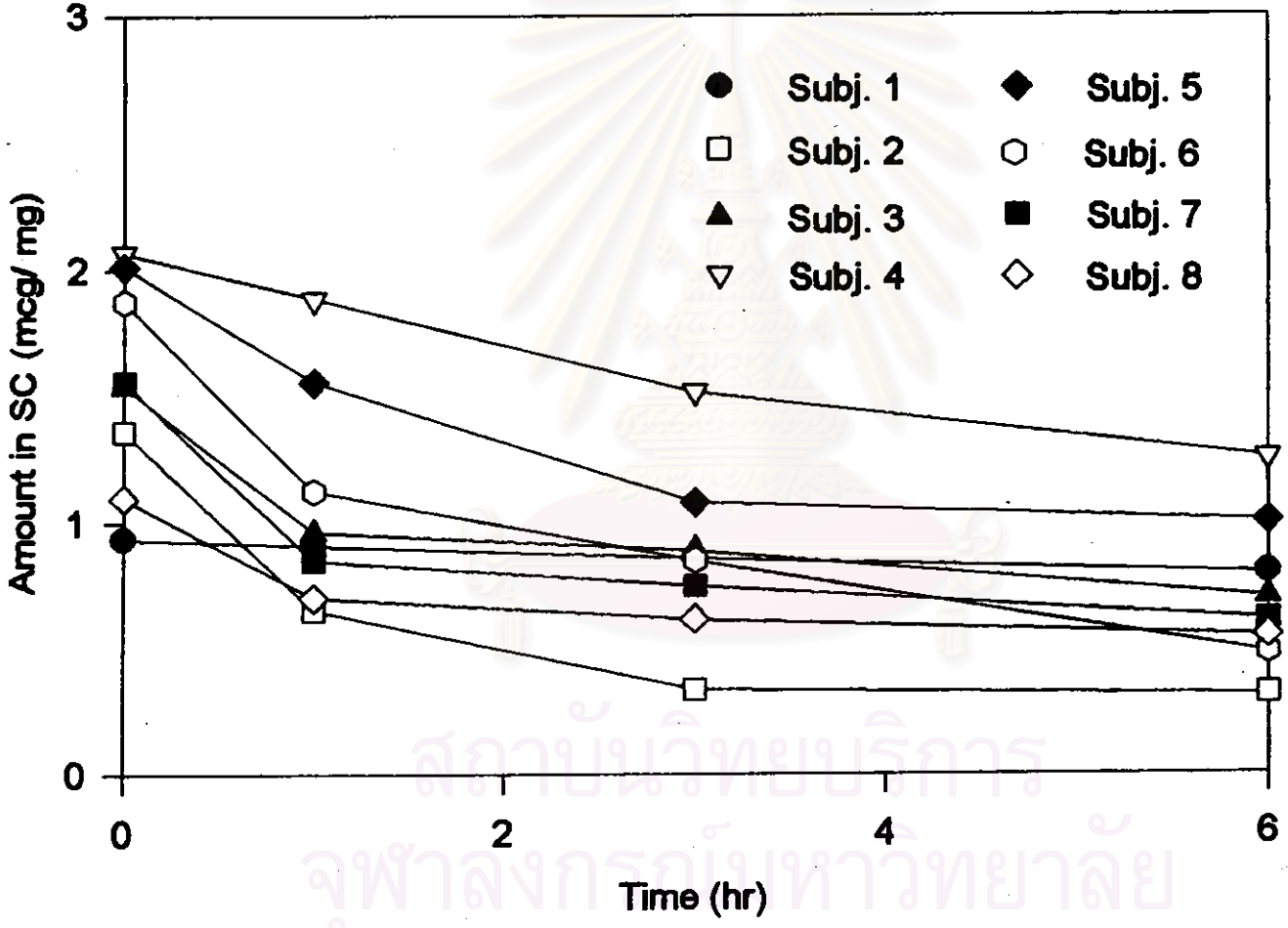
The amount of piroxicam in stratum corneum of four gel products at 3 hr

Subject No.	Amount of piroxicam in stratum corneum (μg/mg)			
	A	B	C	D
1	0.858	1.339	0.948	0.350
2	0.339	0.499	0.525	0.334
3	0.890	0.256	0.439	0.425
4	1.519	0.130	0.311	0.440
5	1.079	0.278	0.877	0.270
6	0.851	0.560	0.447	0.594
7	0.749	0.418	0.884	0.884
8	0.619	0.494	0.893	0.442
mean ± SD	0.863 ± 0.321	0.497 ± 0.346	0.666 ± 0.242	0.467 ± 0.181

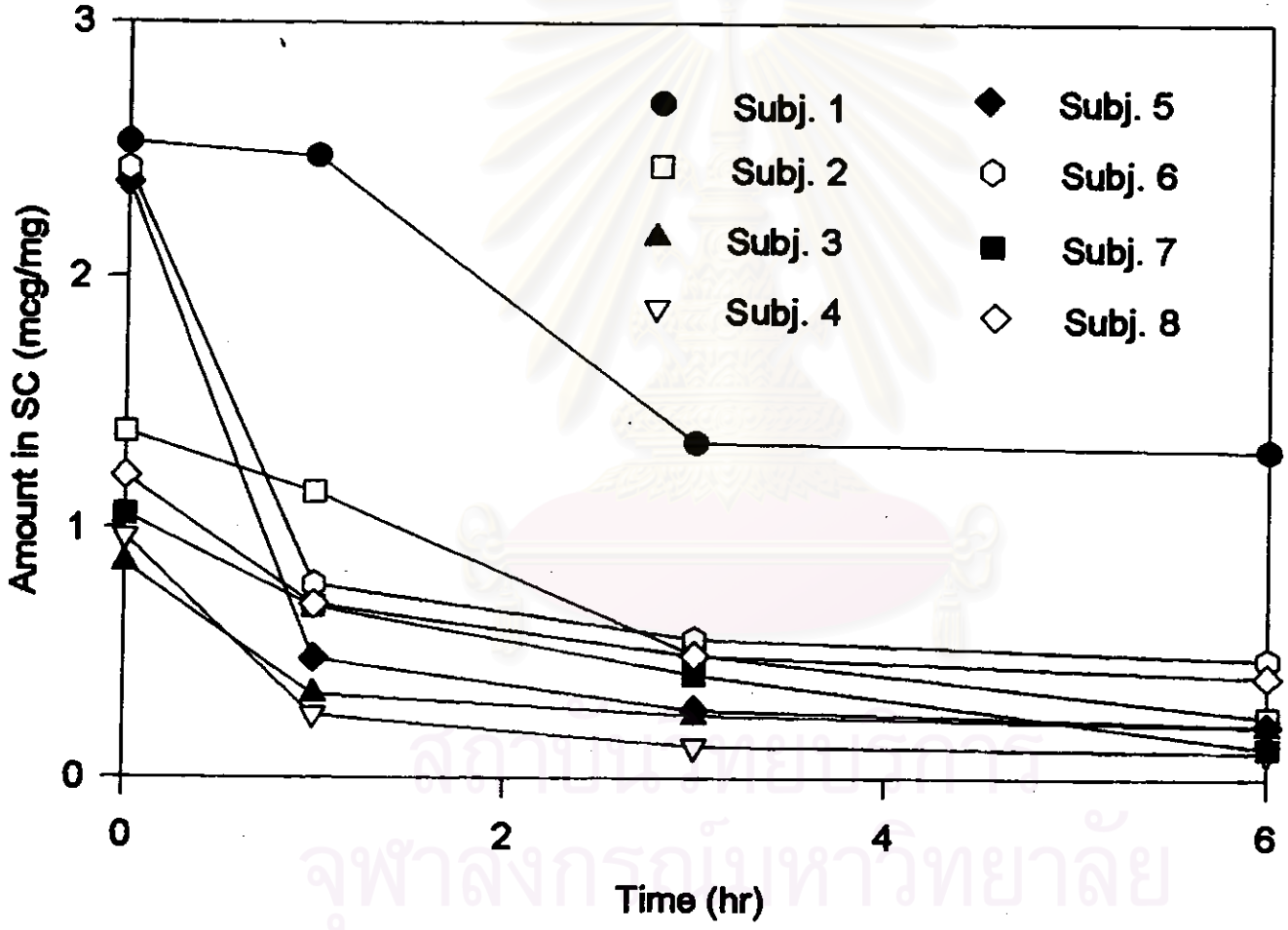
The amount of piroxicam in stratum corneum of four gel products at 6 hr

Subject No.	Amount of piroxicam in stratum corneum (μg/mg)			
	A	B	C	D
1	0.801	1.310	0.540	0.307
2	0.319	0.251	0.439	0.298
3	0.705	0.213	0.223	0.387
4	1.258	0.111	0.436	0.299
5	1.003	0.218	0.794	0.173
6	0.484	0.482	0.357	0.318
7	0.618	0.126	0.813	0.575
8	0.551	0.411	0.682	0.378
mean ± SD	0.717 ± 0.281	0.390 ± 0.368	0.536 ± 0.198	0.342 ± 0.107

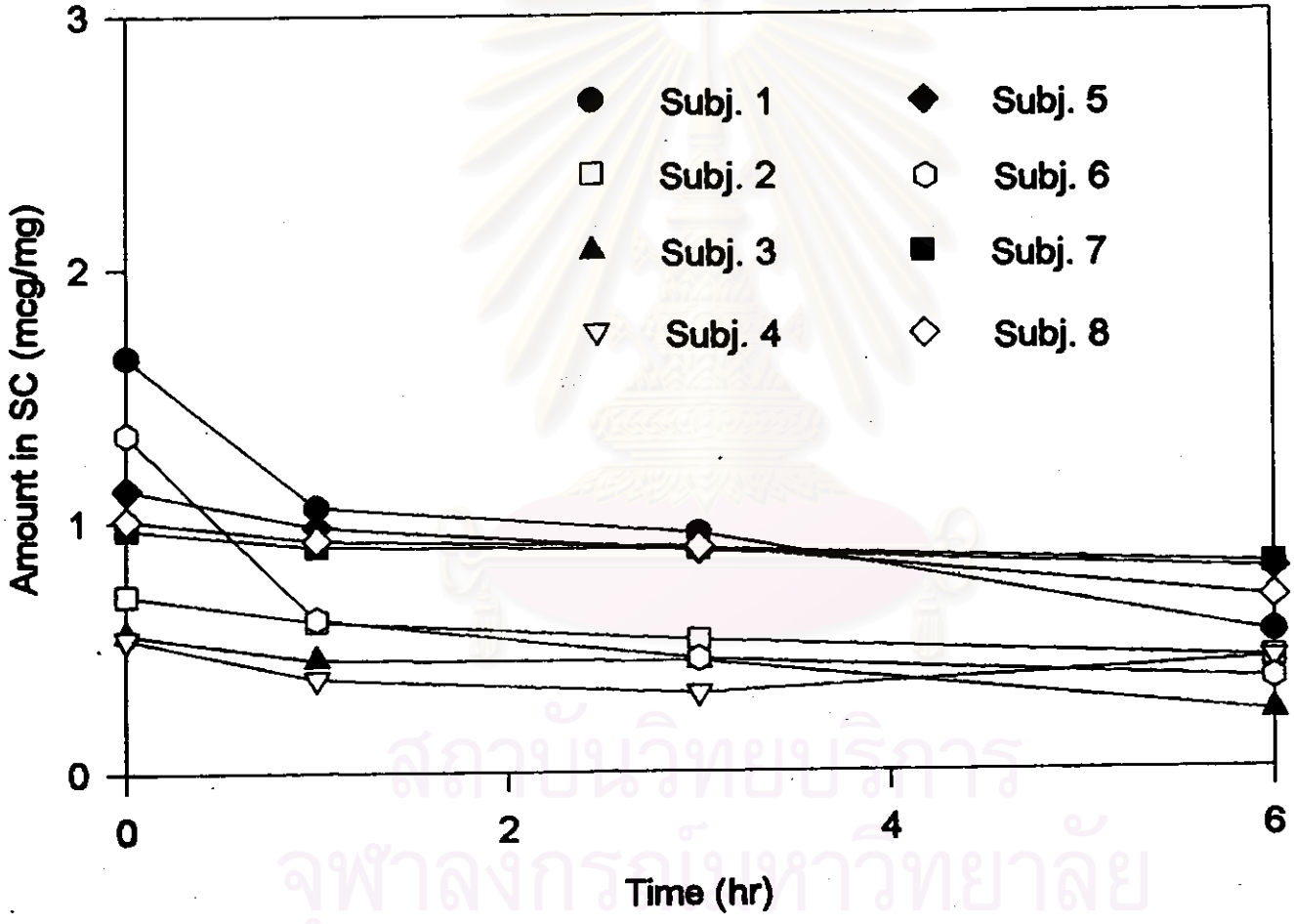
Percutaneous absorption profiles of piroxicam through stratum corneum of 8 subject from product A



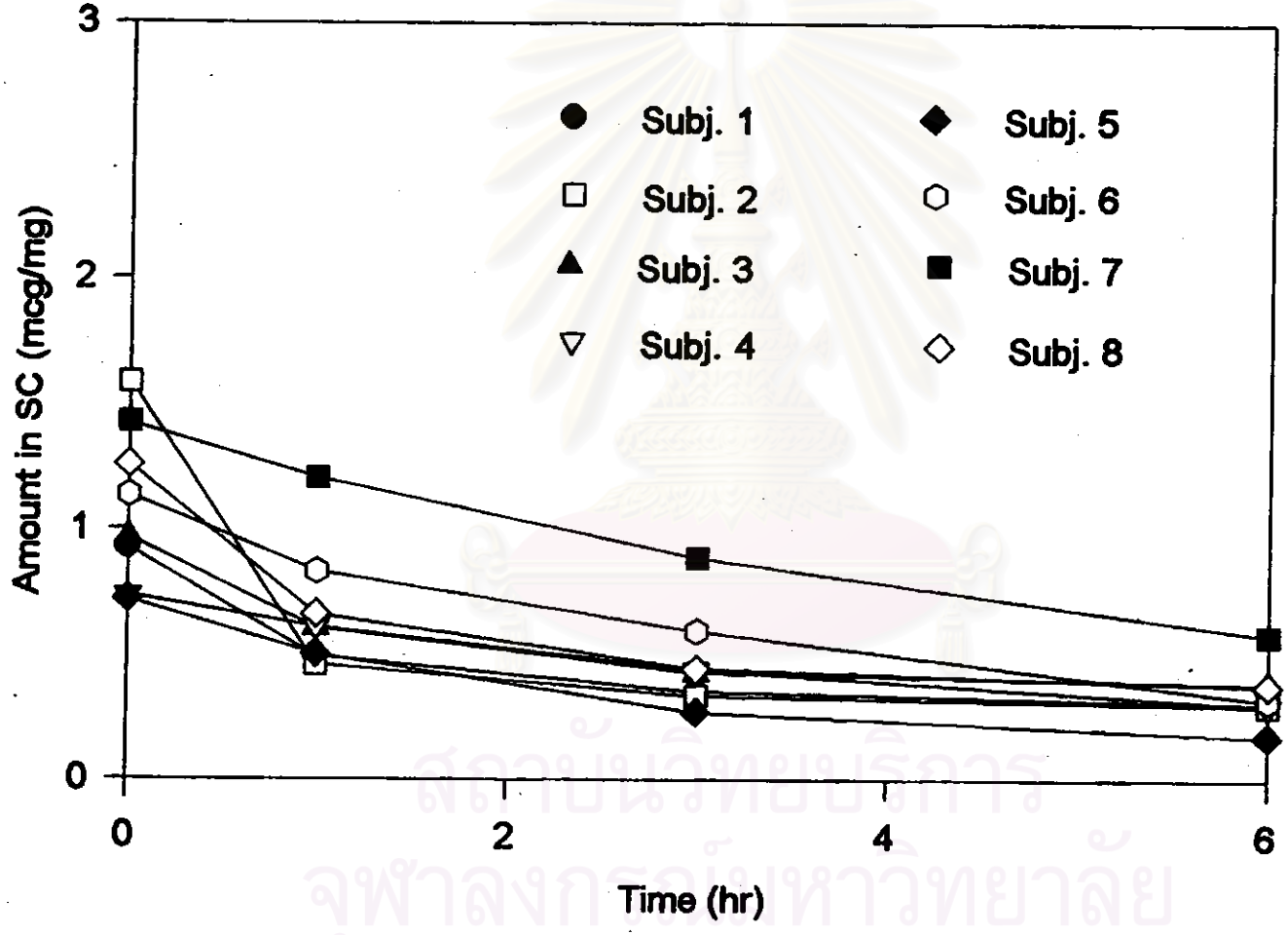
Percutaneous absorption profiles of piroxicam through stratum corneum of 8 subject from product B



Percutaneous absorption profiles of piroxicam through stratum corneum of 8 subject from product C



Percutaneous absorption profiles of piroxicam through stratum corneum of 8 subject from product D



Comparison of amount in stratum corneum of four piroxicam gel products at 0 hr

Randomized Blocks ANOVA

Grand mean = 1.308313 Total of observations = 32

Product means

A = 1.5567 B = 1.5995 C = 0.9857 D = 1.0912

Subject means

1 = 1.5088 2 = 1.2580 3 = 0.9785 4 = 1.0762

5 = 1.5578 6 = 1.6955 7 = 1.2508 8 = 1.1410

Source	df	SS	MS	F	Prob.
Subject (Bl)	7	1.79509	0.25644	1.132702	0.3807
Product (A)	3	2.38137	0.79379	3.506173	0.0328*
Error	21	4.75436	0.22639		
Total	31	8.930817			

* = significant among four products

Duncan's new multiple range test

MS Error = 0.2263979 , df Error = 21

Significant level = .05

Least Significant Ranges

LSR where p = 2 ----	0.4963
LSR where p = 3 ----	0.5215
LSR where p = 4 ----	0.5350

Means		Product
Mean # 1 =	0.9857	C
Mean # 2 =	1.0912	D
Mean # 3 =	1.5568	A
Mean # 4 =	1.5995	B

Result : C < D < A < B

Comparison of amount in stratum corneum of four piroxicam gel products at 1 hr

Randomized Blocks ANOVA

Grand mean = 0.83625 Total of observations = 32

Product means

A = 1.081 B = 0.8572 C = 0.7362 D = 0.6705

Subject means

1 = 1.2332 2 = 0.7147 3 = 0.5892 4 = 0.7822

5 = 0.8798 6 = 0.8360 7 = 0.9088 8 = 0.7460

Source	df	SS	MS	F	Prob.
Subject (Bl)	7	1.006361	0.14376	0.640529	0.7191
Product (A)	3	0.782534	0.26084	1.162157	0.3480^{NS}
Error	21	4.75436	0.22639		
Total	31	6.502318			

^{NS} = non-significant among four products

Comparison of amount in stratum corneum of four piroxicam gel products at 3 hr

Randomized Blocks ANOVA

Grand mean = 0.6231563 Total of observations = 32

Product means

A = 0.8630 B = 0.4968 C = 0.6655 D = 0.4674

Subject means

1 = 0.8738 2 = 0.4242 3 = 0.5025 4 = 0.6000

5 = 0.6260 6 = 0.6130 7 = 0.7338 8 = 0.6120

Source	df	SS	MS	F	Prob.
Subject (Bl)	7	0.51968	7.4240E-02	0.78068	0.6116
Product (A)	3	0.79651	0.2655	2.79193	0.0648^{NS}
Error	21	1.99704	9.5097E-02		
Total	31	3.31324			

^{NS} = non-significant among four products

Comparison of amount in stratum corneum of four piroxicam gel products at 6 hr

Randomized Blocks ANOVA

Grand mean = 0.49625 Total of observations = 32

Product means

A = 0.7174 B = 0.3902 C = 0.5355 D = 0.3419

Subject means

1 = 0.7395 2 = 0.3268 3 = 0.3820 4 = 0.5260

5 = 0.5470 6 = 0.4102 7 = 0.5330 8 = 0.5055

Source	df	SS	MS	F	Prob.
Subject (Bl)	7	0.45298	6.4712E-02	0.814909	0.5861
Product (A)	3	0.68404	0.22801	2.871317	0.0599 NS
Error	21	1.66761	7.9410E-02		
Total	31	2.80463			

NS = non-significant among four products

Appendix IX

Data on Percent Absorbed of Piroxicam from Four Gel Products at Various Time and Statistical Analysis

Percent absorbed of piroxicam from 4 gel products at 1 hr

Subject No.	Percent absorbed of piroxicam			
	A	B	C	D
1	2.89	2.06	35.98	46.54
2	52.09	17.25	14.73	70.81
3	37.51	60.49	18.18	37.30
4	8.80	73.45	29.91	16.78
5	22.60	79.68	13.40	30.04
6	40.04	69.52	54.53	26.77
7	45.38	15.51	7.44	15.55
8	35.97	42.34	8.15	47.25
mean ± SD	30.66 ± 16.40	45.04 ± 28.16	22.79 ± 15.23	36.38 ± 17.17

Percent absorbed of piroxicam from 4 gel products at 3 hr

Subject No.	Percent absorbed of piroxicam			
	A	B	C	D
1	8.14	47.05	42.48	62.12
2	75.13	63.84	25.64	78.90
3	42.24	70.16	20.18	55.96
4	26.58	86.57	41.87	39.97
5	46.40	88.28	22.18	71.21
6	54.68	76.39	66.79	47.53
7	51.92	82.38	8.68	37.79
8	43.62	59.07	11.23	64.72
mean ± SD	43.59 ± 18.52	71.72 ± 13.52	29.88 ± 18.14	57.28 ± 13.77

Percent absorbed of piroxicam from 4 gel products at 6 hr

Subject No.	Percent absorbed of piroxicam			
	A	B	C	D
1	14.24	48.20	67.23	66.77
2	76.60	81.81	37.82	81.17
3	54.25	75.17	59.45	59.90
4	39.20	88.53	18.50	59.21
5	50.17	90.81	29.55	75.94
6	74.23	79.68	73.48	71.91
7	60.33	94.69	16.01	59.54
8	49.82	65.95	32.21	69.83
mean ± SD	52.36 ± 18.61	78.10 ± 14.20	41.78 ± 20.70	68.03 ± 7.67

Comparison of percent absorbed of piroxicam from four gel products at 1 hr

Randomized Blocks ANOVA

Grand mean = 34.24938 Total of observations = 32

Product means

A = 30.66 B = 45.04 C = 22.79 D = 36.38

Subject means

1 = 21.87 2 = 38.72 3 = 38.37 4 = 32.24

5 = 36.43 6 = 47.72 7 = 20.97 8 = 33.43

Source	df	SS	MS	F	Prob.
Subject (Bl)	7	2220.649	317.236	0.6350	0.7233
Product (A)	3	2111.922	703.974	1.4092	0.2674^{NS}
Error	21	10490.97	499.570		
Total	31	14823.54			

^{NS} = non-significant among four products

Comparison of percent absorbed of piroxicam from four gel products at 3 hr

Randomized Blocks ANOVA

Grand mean = 50.61563 Total of observations = 32

Product means

A = 43.59 B = 71.72 C = 29.88 D = 57.28

Subject means

1 = 39.95 2 = 60.88 3 = 47.14 4 = 48.75

5 = 57.02 6 = 61.35 7 = 45.19 8 = 44.66

Source	df	SS	MS	F	Prob.
Subject (Bl)	7	1823.016	260.4308	0.8371	0.5698
Product (A)	3	7751.414	2583.805	8.3051	0.0011*
Error	21	6533.305	311.1098		
Total	31	16107.74			

* = significant among four products

Percent absorbed at 3 hr

Duncan's new multiple range test

MS Error = 311.1098 , df Error = 21

Significant level = .05

Least Significant Ranges

LSR where p = 2 ----	18.3964
LSR where p = 3 ----	19.3319
LSR where p = 4 ----	19.8307

Means		Product
Mean # 1 =	29.8812	C
Mean # 2 =	43.5888	A
Mean # 3 =	57.2750	D
Mean # 4 =	71.7175	B

Result : C < A < D < B

Comparison of percent absorbed of piroxicam from four gel products at 6 hr

Randomized Blocks ANOVA

Grand mean = 60.06875 Total of observations = 32

Product means

A = 52.36 B = 78.10 C = 41.78 D = 68.03

Subject means

1 = 49.11 2 = 69.35 3 = 62.19 4 = 51.36

5 = 61.62 6 = 74.82 7 = 57.64 8 = 54.45

Source	df	SS	MS	F	Prob.
Subject (Bl)	7	2176.672	310.9531	1.0697	0.4167
Product (A)	3	6261.469	2087.156	7.1798	0.0020*
Error	21	6104.68	290.699		
Total	31	14542.82			

* = significant among four products

Percent absorbed at 6 hr

Duncan's new multiple range test

MS Error = 290.699 , df Error = 21

Significant level = .05

Least Significant Ranges

LSR where p = 2 ----	17.7827
LSR where p = 3 ----	18.6870
LSR where p = 4 ----	19.1692

Means		Product
Mean # 1 =	41.7812	C
Mean # 2 =	52.3550	A
Mean # 3 =	68.0338	D
Mean # 4 =	78.1050	B

Result : C < A < D < B

Appendix X

Data on Rate Constants of Percutaneous Absorption of Four Piroxicam Gel Products over 6 hr and Statistical Analysis

Product A : Rate constant of percutaneous absorption over 6 hr

Subject No.	ln of amount in stratum corneum (μg/mg)				Rate constants over 6 hr	
	0 hr	1hr	3 hr	6 hr	k	r^2
1	-0.068	-0.098	-0.153	-0.222	-0.0255	0.9968
2	0.310	-0.426	-1.082	-1.142	-0.2225	0.7520
3	0.432	-0.038	-0.116	-0.350	-0.1098	0.7843
4	0.727	0.635	0.418	0.230	-0.0837	0.9833
5	0.700	0.443	0.076	0.003	-0.1126	0.8367
6	0.630	0.119	-0.161	-0.726	-0.2083	0.9499
7	0.443	-0.161	-0.289	-0.481	-0.1284	0.7235
8	0.094	-0.352	-0.480	-0.596	-0.0967	0.7196
mean	0.443	0.078	-0.147	-0.333	-0.1172	0.8638
mean ± SD					-0.1234 ± 0.0604	

Product B : Rate constant of percutaneous absorption over 6 hr

Subject No.	ln of amount in stratum corneum (μg/mg)				Rate constants over 6 hr	
	0 hr	1hr	3 hr	6 hr	k	r^2
1	0.928	0.907	0.292	0.270	-0.1233	0.7873
2	0.322	0.133	-0.695	-1.382	-0.2948	0.9824
3	-0.153	-1.082	-1.363	-1.547	-0.1948	0.6929
4	-0.032	-1.359	-2.040	-2.198	-0.3140	0.7096
5	0.864	-0.730	-1.280	-1.523	-0.3350	0.6821
6	0.886	-0.252	-0.580	-0.730	-0.2229	0.6507
7	0.054	-0.374	-0.872	-2.072	-0.3458	0.9915
8	0.188	-0.362	-0.705	-0.889	-0.1615	0.8142
mean	0.470	-0.154	-0.699	-0.942	-0.2140	0.8274
mean ± SD					-0.2490 ± 0.0792	

Product C : Rate constant of percutaneous absorption over 6 hr

Subject No.	ln of amount in stratum corneum (μg/mg)				Rate constants over 6 hr	
	0 hr	1hr	3 hr	6 hr	k	r^2
1	0.500	0.054	-0.053	-0.616	-0.1673	0.9303
2	-0.348	-0.508	-0.644	-0.823	-0.0748	0.9619
3	-0.598	-0.798	-0.823	-1.501	-0.2781	0.7333
4	-0.626	-0.981	-1.168	-0.830	-0.0216	0.0620
5	0.120	-0.024	-0.131	-0.231	-0.0541	0.9089
6	0.297	-0.491	-0.805	-1.030	-0.1911	0.7601
7	-0.032	-0.110	-0.123	-0.207	-0.0257	0.9067
8	0.006	-0.079	-0.113	-0.383	-0.0615	0.9399
mean	-0.014	-0.306	-0.406	-0.624	-0.0900	0.8860
mean ± SD					-0.1093 ± 0.0864	

Product D : Rate constant of percutaneous absorption over 6 hr

Subject No.	ln of amount in stratum corneum (μg/mg)				Rate constants over 6 hr	
	0 hr	1hr	3 hr	6 hr	k	r^2
1	-0.079	-0.705	-1.050	-1.181	-0.1621	0.7576
2	0.459	-0.772	-1.097	-1.211	-0.2274	0.6173
3	-0.036	-0.502	-0.856	-0.949	-0.1384	0.7823
4	-0.311	-0.494	-0.821	-1.207	-0.1484	0.9942
5	-0.330	-0.687	-1.309	-1.754	-0.2351	0.9602
6	0.124	-0.188	-0.521	-1.146	-0.2047	0.8832
7	0.351	0.182	-0.123	-0.553	-0.1499	0.9991
8	0.226	-0.414	-0.816	-0.973	-0.1789	0.7835
mean	0.087	-0.400	-0.761	-1.073	0.1790	0.8994
mean ± SD					-0.1805 ± 0.0351	

Comparison of the rate constants of four piroxicam gel products over 6 hr

Randomized Blocks ANOVA

Grand mean = 0.165162 Total of observations = 32

Product means

A = 0.1234 B = 0.2490 C = 0.1093 D = 0.1806

Subject means

1 = 0.1195 2 = 0.2048 3 = 0.1802 4 = 0.1418

5 = 0.1842 6 = 0.2068 7 = 0.1624 8 = 0.1247

Source	df	SS	MS	F	Prob.
Subject (Bl)	7	3.2657E-02	4.6653E-03	0.8420	0.5662
Product (A)	3	9.7038E-02	3.2346E-02	5.8378	0.0049*
Error	21	0.1164	5.5408E-03		
Total	31	0.2460			

* = significant among four products

Rate constants over 6 hr

Duncan's new multiple range test

MS Error = 0.0055408 , df Error = 21

Significant level = .05

Least Significant Ranges

LSR where p = 2 ----	0.0776
LSR where p = 3 ----	0.0816
LSR where p = 4 ----	0.0837

Means		Product
Mean # 1 =	0.1093	C
Mean # 2 =	0.1234	A
Mean # 3 =	0.1806	D
Mean # 4 =	0.2490	B

Result C < A < D < B

Appendix XI

Data of the Area Under the Content of Piroxicam in Stratum Corneum-time curve of the four piroxicam gel products at 0-6 hr and Statistical Analysis

Area under the Concentration-time Curve of piroxicam gel products in the stratum corneam at 0-6 hr

Subject No.	$AUC_{(0-6)}$			
	A	B	C	D
1	5.174	10.292	5.587	2.538
2	2.987	4.027	3.227	2.368
3	5.498	1.897	2.382	3.033
4	9.550	1.361	2.262	2.830
5	7.546	2.931	5.411	2.048
6	5.482	4.502	3.244	3.772
7	4.855	2.794	5.258	5.583
8	2.656	3.499	5.144	3.290
Mean ± SD	5.468 ± 2.107	3.913 ± 2.599	4.064 ± 1.331	3.183 ± 1.039

Comparison of the area under the concentration-time curve of the four piroxicam gel products at 0-6 hr

Randomized Blocks ANOVA

Grand mean = 4.1571 Total of observations = 32

Product means

A = 5.468 B = 3.913 C = 4.064 D = 3.183

Subject means

1 = 5.898 2 = 3.152 3 = 3.202 4 = 4.001

5 = 4.484 6 = 4.250 7 = 4.622 8 = 3.647

Source	df	SS	MS	F	Prob.
Subject (Bl)	7	22.2694	3.1813	0.7418	0.6411
Product (A)	3	21.8989	7.2996	1.7020	0.1963^{NS}
Error	21	90.0630	4.0887		
Total	31	134.2313			

NS = No significant among four products

Appendix XII

Correlation Results between In Vitro Release/Permeation and In Vivo Studies

Correlation data of release rate through cellulose acetate membrane at 6 hr of six piroxicam gel products and amount remaining in stratum corneum at 0 hr

Product	Release rate, X ($\mu g/cm^2.min^{1/2}$)	Amount in SC, Y ($\mu g/mg$)
A	39.985	1.56
B	74.002	1.60
C	55.794	0.99
D	44.246	1.09

Test of Zero correlation

$$Ho : \rho = 0 \qquad Ha : \rho \neq 0$$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.2693

$$\therefore t_{n-2} = \left| \frac{0.2693\sqrt{4-2}}{\sqrt{1-(0.2693)^2}} \right|$$

$$= 0.3954$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of release rate through cellulose acetate membrane at 6 hr and amount remaining in stratum corneum at 0 hr ($p > 0.05$).

Correlation data of cumulative amount through cellulose acetate membrane at 6 hr of six piroxicam gel products and amount remaining in stratum corneum at 0 hr

Product	Cumulative amount, X ($\mu g/cm^2$)	Amount in SC, Y ($\mu g/mg$)
A	615.997	1.56
B	1223.502	1.60
C	945.995	0.99
D	686.022	1.09

Test of Zero correlation

$Ho : \rho = 0 \qquad Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.2114

$$\therefore t_{n-2} = \left| \frac{0.2114\sqrt{4-2}}{\sqrt{1-(0.2114)^2}} \right|$$

$$= 0.3059$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of cumulative amount through cellulose acetate membrane at 6 hr and amount remaining in stratum corneum at 0 hr ($p > 0.05$).

Correlation data of flux through new born pig skin at 24 hr of six piroxicam gel products and amount remaining in stratum corneum at 0 hr

Product	Flux, X ($ng/cm^2.hr$)	Amount in SC, Y ($\mu g/mg$)
A	44.923	1.56
B	72.283	1.60
C	68.193	0.99
D	213.800	1.09

Test of Zero correlation

$Ho : \rho = 0$ $\quad$ $Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.5044

$$\therefore t_{n-2} = \left| \frac{0.5044\sqrt{4-2}}{\sqrt{1-(0.5044)^2}} \right|$$

$$= 0.8261$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of flux through new born pig skin at 24 hr and amount remaining in stratum corneum at 0 hr ($p > 0.05$).

Correlation data of cumulative amount through new born pig skin at 24 hr of six piroxicam gel products and amount remaining in stratum corneum at 0 hr

Product	Cumulative amount, X (ng/cm^2)	Amount in SC, Y ($\mu g/mg$)
A	858.481	1.56
B	1544.838	1.60
C	1365.847	0.99
D	4501.802	1.09

Test of Zero correlation

$$Ho : \rho = 0 \qquad Ha : \rho \neq 0$$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.4912

$$\therefore t_{n-2} = \left| \frac{0.4912\sqrt{4-2}}{\sqrt{1-(0.4912)^2}} \right|$$

$$= 0.7975$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of cumulative amount through new born pig skin at 24 hr and amount remaining in stratum corneum at 0 hr ($p > 0.05$).

Correlation data of release rate through cellulose acetate membrane at 6 hr of six piroxicam gel products and amount remaining in stratum corneum at 1 hr

Product	Release rate, X ($\mu g/cm^2.min^{1/2}$)	Amount in SC, Y ($\mu g/mg$)
A	39.985	1.08
B	74.002	0.86
C	55.794	0.74
D	44.246	0.67

Test of Zero correlation

$$Ho : \rho = 0 \qquad Ha : \rho \neq 0$$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.1817

$$\therefore t_{n-2} = \left| \frac{0.1817\sqrt{4-2}}{\sqrt{1-(0.1817)^2}} \right|$$

$$= 0.2613$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of release rate through cellulose acetate membrane at 6 hr and amount remaining in stratum corneum at 1 hr ($p > 0.05$).

Correlation data of cumulative amount through cellulose acetate membrane at 6 hr of six piroxicam gel products and amount remaining in stratum corneum at 1 hr

Product	Cumulative amount, X ($\mu g/cm^2$)	Amount in SC, Y ($\mu g/mg$)
A	615.997	1.08
B	1223.502	0.86
C	945.995	0.74
D	686.022	0.67

Test of Zero correlation

$Ho : \rho = 0 \qquad Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.2029

$$\therefore t_{n-2} = \left| \frac{0.2029\sqrt{4-2}}{\sqrt{1-(0.2029)^2}} \right|$$

$$= 0.2930$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of cumulative amount through cellulose acetate membrane at 6 hr and amount remaining in stratum corneum at 1 hr ($p > 0.05$).

Correlation data of flux throug new born pig skin at 24 hr of six piroxicam gel products and amount remaining in stratum corneum at 1 hr

Product	Flux, X ($ng/cm^2.hr$)	Amount in SC, Y ($\mu g/mg$)
A	44.923	1.08
B	72.283	0.86
C	68.193	0.74
D	213.800	0.67

Test of Zero correlation

$Ho : \rho = 0$ $\quad$ $Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.7217

$$\therefore t_{n-2} = \left| \frac{0.7217\sqrt{4-2}}{\sqrt{1-(0.7217)^2}} \right|$$

$$= 1.4746$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of flux through new born pig skin at 24 hr and amount remaining in stratum corneum at 1 hr ($p > 0.05$).

Correlation data of cumulative amount through new born pig skin at 24 hr of six piroxicam gel products and amount remaining in stratum corneum at 1 hr

Product	Cumulative amount, X (ng/cm^2)	Amount in SC, Y ($\mu g/mg$)
A	858.481	1.08
B	1544.838	0.86
C	1365.847	0.74
D	4501.802	0.67

Test of Zero correlation

$Ho : \rho = 0$ $\quad$ $Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.7250

$$\therefore t_{n-2} = \left| \frac{0.7250\sqrt{4-2}}{\sqrt{1-(0.7250)^2}} \right|$$

$$= 1.4886$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of cumulative amount through new born pig skin at 24 hr and amount remaining in stratum corneum at 1 hr ($p > 0.05$).

Correlation data of release rate through cellulose acetate membrane at 6 hr of six piroxicam gel products and amount remaining in stratum corneum at 3 hr

Product	Release rate, X ($\mu g/cm^2.min^{1/2}$)	Amount in SC, Y ($\mu g/mg$)
A	39.985	0.86
B	74.002	0.50
C	55.794	0.67
D	44.246	0.47

Test of Zero correlation

$Ho : \rho = 0 \qquad Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.5123

$$\therefore t_{n-2} = \left| \frac{0.5123\sqrt{4-2}}{\sqrt{1-(0.5123)^2}} \right|$$

$$= 0.8436$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of release rate through cellulose acetate membrane at 6 hr and amount remaining in stratum corneum at 3 hr ($p > 0.05$).

Correlation data of cumulative amount through cellulose acetate membrane at 6 hr of six piroxicam gel products and amount remaining in stratum corneum at 3 hr

Product	Cumulative amount, X ($\mu g/cm^2$)	Amount in SC, Y ($\mu g/mg$)
A	615.997	0.86
B	1223.502	0.50
C	945.995	0.67
D	686.022	0.47

Test of Zero correlation

$Ho : \rho = 0 \qquad Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.4829

$$\therefore t_{n-2} = \left| \frac{0.4829\sqrt{4-2}}{\sqrt{1-(0.4829)^2}} \right|$$

$$= 0.7799$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of cumulative amount through cellulose acetate membrane at 6 hr and amount remaining in stratum corneum at 3 hr ($p > 0.05$).

Correlation data of flux through new born pig skin at 24 hr of six piroxicam gel products and amount remaining in stratum corneum at 3 hr

Product	Flux, X ($ng/cm^2.hr$)	Amount in SC, Y ($\mu g/mg$)
A	44.923	0.86
B	72.283	0.50
C	68.193	0.67
D	213.800	0.47

Test of Zero correlation

$Ho : \rho = 0 \qquad Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.6881

$$\therefore t_{n-2} = \left| \frac{0.6881\sqrt{4-2}}{\sqrt{1-(0.6881)^2}} \right|$$

$$= 1.3411$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of flux through new born pig skin at 24 hr and amount remaining in stratum corneum at 3 hr ($p > 0.05$).

Correlation data of cumulative amount through new born pig skin at 24 hr of six piroxicam gel products and amount remaining in stratum corneum at 3 hr

Product	Cumulative amount, X (ng/cm^2)	Amount in SC, Y ($\mu g/mg$)
A	858.481	0.86
B	1544.838	0.50
C	1365.847	0.67
D	4501.802	0.47

Test of Zero correlation

$Ho : \rho = 0$ $\quad$ $Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.7062

$$\therefore t_{n-2} = \left| \frac{0.7062\sqrt{4-2}}{\sqrt{1-(0.7062)^2}} \right|$$

$$= 1.4106$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of cumulative amount through new born pig skin at 24 hr and amount remaining in stratum corneum at 3 hr ($p > 0.05$).

Correlation data of release rate through cellulose acetate membrane at 6 hr of six piroxicam gel products and amount remaining in stratum corneum at 6 hr

Product	Release rate, X ($\mu g/cm^2.min^{1/2}$)	Amount in SC, Y ($\mu g/mg$)
A	39.985	0.72
B	74.002	0.39
C	55.794	0.54
D	44.246	0.32

Test of Zero correlation

$$Ho : \rho = 0 \qquad Ha : \rho \neq 0$$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.4291

$$\therefore t_{n-2} = \left| \frac{0.4291\sqrt{4-2}}{\sqrt{1-(0.4291)^2}} \right|$$

$$= 0.6719$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of release rate through cellulose acetate membrane at 6 hr and amount remaining in stratum corneum at 6 hr ($p > 0.05$).

Correlation data of cumulative amount through cellulose acetate membrane at 6 hr of six piroxicam gel products and amount remaining in stratum corneum at 6 hr

Product	Cumulative amount, X ($\mu g/cm^2$)	Amount in SC, Y ($\mu g/mg$)
A	615.997	0.72
B	1223.502	0.39
C	945.995	0.54
D	686.022	0.32

Test of Zero correlation

$$Ho : \rho = 0 \qquad Ha : \rho \neq 0$$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.3992

$$\therefore t_{n-2} = \left| \frac{0.3992\sqrt{4-2}}{\sqrt{1-(0.3992)^2}} \right|$$

$$= 0.6158$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of cumulative amount through cellulose acetate membrane at 6 hr and amount remaining in stratum corneum at 6 hr ($p > 0.05$).

Correlation data of flux through new born pig skin at 24 hr of six piroxicam gel products and amount remaining in stratum corneum at 6 hr

Product	Flux, X ($ng/cm^2.hr$)	Amount in SC, Y ($\mu g/mg$)
A	44.923	0.72
B	72.283	0.39
C	68.193	0.54
D	213.800	0.32

Test of Zero correlation

$Ho : \rho = 0$ $\quad$ $Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.7534

$$\therefore t_{n-2} = \left| \frac{0.7534\sqrt{4-2}}{\sqrt{1-(0.7534)^2}} \right|$$

$$= 1.6203$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of flux through new born pig skin at 24 hr and amount remaining in stratum corneum at 6 hr ($p > 0.05$).

Correlation data of cumulative amount through new born pig skin at 24 hr of six piroxicam gel products and amount remaining in stratum corneum at 6 hr

Product	Cumulative amount, X (ng/cm^2)	Amount in SC, Y ($\mu g/mg$)
A	858.481	0.72
B	1544.838	0.39
C	1365.847	0.54
D	4501.802	0.32

Test of Zero correlation

$Ho : \rho = 0 \qquad Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.7696

$$\therefore t_{n-2} = \left| \frac{0.7696\sqrt{4-2}}{\sqrt{1-(0.7696)^2}} \right|$$

$$= 1.7045$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of cumulative amount through new born pig skin at 24 hr and amount remaining in stratum corneum at 6 hr ($p > 0.05$).

Correlation data of release rate through cellulose acetate membrane at 6 hr of six piroxicam gel products and rate constant over 6 hr

Product	Release rate, X ($\mu g/cm^2.min^{1/2}$)	Rate constant , Y ($\mu g/mg.hr$)
A	39.985	0.1234
B	74.002	0.2490
C	55.794	0.1093
D	44.246	0.1805

Test of Zero correlation

$Ho : \rho = 0 \qquad Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.6940

$$\therefore t_{n-2} = \left| \frac{0.6940\sqrt{4-2}}{\sqrt{1-(0.6940)^2}} \right|$$

$$= 1.3631$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of release rate through cellulose acetate membrane at 6 hr and rate constant over 6 hr ($p > 0.05$).

Correlation data of cumulative amount through cellulose acetate membrane at 6 hr of six piroxicam gel products and rate constant over 6 hr

Product	Cumulative amount, X ($\mu g/cm^2$)	Rate constant , Y ($\mu g/mg.hr$)
A	615.997	0.1234
B	1223.502	0.2490
C	945.995	0.1093
D	686.022	0.1805

Test of Zero correlation

$Ho : \rho = 0$ $\quad$ $Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.6295

$$\therefore t_{n-2} = \left| \frac{0.6295\sqrt{4-2}}{\sqrt{1-(0.6295)^2}} \right|$$

$$= 1.1458$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of cumulative amount through cellulose acetate membrane at 6 hr and rate constant over 6 hr ($p > 0.05$).

Correlation data of flux through new born pig skin at 24 hr of six piroxicam gel products and rate constant over 6 hr

Product	Flux, X ($ng/cm^2.hr$)	Rate constant , Y ($\mu g/mg.hr$)
A	44.923	0.1234
B	72.283	0.2490
C	68.193	0.1093
D	213.800	0.1805

Test of Zero correlation

$Ho : \rho = 0$ $\quad$ $Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.2384

$$\therefore t_{n-2} = \left| \frac{0.2384\sqrt{4-2}}{\sqrt{1-(0.2384)^2}} \right|$$

$$= 0.3471$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of flux through new born pig skin at 24 hr and rate constant over 6 hr ($p > 0.05$).

Correlation data of cumulative amount through new born pig skin at 24 hr of six piroxicam gel products and rate constant over 6 hr

Product	Cumulative amount, X (ng/cm^2)	Rate constant , Y ($\mu g/mg.hr$)
A	858.481	0.1234
B	1544.838	0.2490
C	1365.847	0.1093
D	4501.802	0.1805

Test of Zero correlation

$Ho: \rho = 0$ $\quad$ $Ha: \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When $r = 0.2646$

$$\therefore t_{n-2} = \left| \frac{0.2646\sqrt{4-2}}{\sqrt{1-(0.2646)^2}} \right|$$

$$= 0.3880$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of cumulative amount through new born pig skin at 24 hr and rate constant over 6 hr ($p > 0.05$).

Correlation data of release rate through cellulose acetate membrane at 6 hr of six piroxicam gel products and percent absorbed at 1 hr

Product	Release rate, X ($\mu g/cm^2.min^{1/2}$)	% Absorbed, Y
A	39.985	30.60
B	74.002	45.04
C	55.794	22.79
D	44.246	36.38

Test of Zero correlation

Ho : $\rho = 0$ Ha : $\rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.5242

$$\therefore t_{n-2} = \left| \frac{0.5242\sqrt{4-2}}{\sqrt{1-(0.5242)^2}} \right|$$

$$= 0.8706$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of release rate through cellulose acetate membrane at 6 hr and percent absorbed at 1 hr ($p > 0.05$).

Correlation data of cumulative amount through cellulose acetate membrane at 6 hr of six piroxicam gel products and percent absorbed at 1 hr

Product	Cumulative amount, X ($\mu g/cm^2$)	% Absorbed, Y
A	615.997	30.60
B	1223.502	45.04
C	945.995	22.79
D	686.022	36.38

Test of Zero correlation

Ho : $\rho = 0$ Ha : $\rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.4464

$$\therefore t_{n-2} = \left| \frac{0.4464\sqrt{4-2}}{\sqrt{1-(0.4464)^2}} \right|$$

$$= 0.7054$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of cumulative amount through cellulose acetate membrane at 6 hr and percent absorbed at 1 hr ($p > 0.05$).

Correlation data of flux through new born pig skin at 24 hr of six piroxicam gel products and percent absorbed at 1 hr

Product	Flux, X ($ng/cm^2.hr$)	% Absorbed, Y
A	44.923	30.60
B	72.283	45.04
C	68.193	22.79
D	213.800	36.38

Test of Zero correlation

$Ho : \rho = 0$ $\quad$ $Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When $r = 0.2346$

$$\therefore t_{n-2} = \left| \frac{0.2346\sqrt{4-2}}{\sqrt{1-(0.2346)^2}} \right|$$

$$= 0.3413$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of flux through new born pig skin at 24 hr and percent absorbed at 1 hr ($p > 0.05$).

Correlation data of cumulative amount through new born pig skin at 24 hr of six piroxicam gel products and percent absorbed at 1 hr

Product	Cumulative amount, X (ng/cm^2)	% Absorbed, Y
A	858.481	30.60
B	1544.838	45.04
C	1365.847	22.79
D	4501.802	36.38

Test of Zero correlation

$Ho : \rho = 0 \qquad Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When $r = 0.2584$

$$\therefore t_{n-2} = \left| \frac{0.2584\sqrt{4-2}}{\sqrt{1-(0.2584)^2}} \right|$$

$$= 0.3784$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of cumulative amount through new born pig skin at 24 hr and percent absorbed at 1 hr ($p > 0.05$).

Correlation data of release rate through cellulose acetate membrane at 6 hr of six piroxicam gel products and percent absorbed at 3 hr

Product	Release rate, X ($\mu g/cm^2.min^{1/2}$)	% Absorbed, Y
A	39.985	43.59
B	74.002	71.72
C	55.794	29.88
D	44.246	57.28

Test of Zero correlation

Ho : $\rho = 0$ Ha : $\rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.5102

$$\therefore t_{n-2} = \left| \frac{0.5102\sqrt{4-2}}{\sqrt{1-(0.5102)^2}} \right|$$

$$= 0.8389$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of release rate through cellulose acetate membrane at 6 hr and percent absorbed at 3 hr ($p > 0.05$).

Correlation data of cumulative amount through cellulose acetate membrane at 6 hr of six piroxicam gel products and percent absorbed at 3 hr

Product	Cumulative amount, X ($\mu g/cm^2$)	% Absorbed, Y
A	615.997	43.59
B	1223.502	71.72
C	945.995	29.88
D	686.022	57.28

Test of Zero correlation

$$Ho : \rho = 0 \quad \therefore \quad Ha : \rho \neq 0$$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.4323

$$\therefore t_{n-2} = \left| \frac{0.4324\sqrt{4-2}}{\sqrt{1-(0.4324)^2}} \right|$$

$$= 0.6782$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of cumulative amount through cellulose acetate membrane at 6 hr and percent absorbed at 3 hr ($p > 0.05$).

Correlation data of flux through new born pig skin at 24 hr of six piroxicam gel products and percent absorbed at 3 hr

Product	Flux, X ($ng/cm^2.hr$)	% Absorbed, Y
A	44.923	43.59
B	72.283	71.72
C	68.193	29.88
D	213.800	57.28

Test of Zero correlation

$Ho : \rho = 0 \qquad Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When $r = 0.2940$

$$\therefore t_{n-2} = \left| \frac{0.2940\sqrt{4-2}}{\sqrt{1-(0.2940)^2}} \right|$$

$$= 0.4350$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of flux through new born pig skin at 24 hr and percent absorbed at 3 hr ($p > 0.05$).

Correlation data of cumulative amount through new born pig skin at 24 hr of six piroxicam gel products and percent absorbed at 3 hr

Product	Cumulative amount, X (ng/cm^2)	% Absorbed, Y
A	858.481	43.59
B	1544.838	71.72
C	1365.847	29.88
D	4501.802	57.28

Test of Zero correlation

$Ho : \rho = 0$ $Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.3177

$$\therefore t_{n-2} = \left| \frac{0.3177\sqrt{4-2}}{\sqrt{1-(0.3177)^2}} \right|$$

$$= 0.4738$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of cumulative amount through new born pig skin at 24 hr and percent absorbed at 3 hr ($p > 0.05$).

Correlation data of release rate through cellulose acetate membrane at 6 hr of six piroxicam gel products and percent absorbed at 6 hr

Product	Release rate, X ($\mu g/cm^2.min^{1/2}$)	% Absorbed, Y
A	39.985	52.36
B	74.002	78.10
C	55.794	41.78
D	44.246	68.03

Test of Zero correlation

$Ho : \rho = 0 \qquad Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.4862

$$\therefore t_{n-2} = \left| \frac{0.4862\sqrt{4-2}}{\sqrt{1-(0.4862)^2}} \right|$$

$$= 0.7868$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of release rate through cellulose acetate membrane at 6 hr and percent absorbed at 6 hr ($p > 0.05$).

Correlation data of cumulative amount through cellulose acetate membrane at 6 hr of six piroxicam gel products and percent absorbed at 6 hr

Product	Cumulative amount, X ($\mu g/cm^2$)	% Absorbed, Y
A	615.997	52.36
B	1223.502	78.10
C	945.995	41.78
D	686.022	68.03

Test of Zero correlation

$Ho : \rho = 0 \qquad Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.4091

$$\therefore t_{n-2} = \left| \frac{0.4091\sqrt{4-2}}{\sqrt{1-(0.4091)^2}} \right|$$

$$= 0.6340$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of cumulative amount through cellulose acetate membrane at 6 hr and percent absorbed at 6 hr ($p > 0.05$).

Correlation data of flux through new born pig skin at 24 hr of six piroxicam gel products and percent absorbed at 6 hr

Product	Flux, X ($ng/cm^2.hr$)	% Absorbed, Y
A	44.923	52.36
B	72.283	78.10
C	68.193	41.78
D	213.800	68.03

Test of Zero correlation

$Ho : \rho = 0 \qquad Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.3789

$$\therefore t_{n-2} = \left| \frac{0.3789\sqrt{4-2}}{\sqrt{1-(0.3789)^2}} \right|$$

$$= 0.5790$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of flux through new born pig skin at 24 hr and percent absorbed at 6 hr ($p > 0.05$).

Correlation data of cumulative amount through new born pig skin at 24 hr of six piroxicam gel products and percent absorbed at 6 hr

Product	Cumulative amount, X (ng/cm^2)	% Absorbed, Y
A	858.481	52.36
B	1544.838	78.10
C	1365.847	41.78
D	4501.802	68.03

Test of Zero correlation

$Ho : \rho = 0$ $\quad$ $Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When $r = 0.4020$

$$\therefore t_{n-2} = \left| \frac{0.4020\sqrt{4-2}}{\sqrt{1-(0.4020)^2}} \right|$$

$$= 0.6209$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of cumulative amount through new born pig skin at 24 hr and percent absorbed at 6 hr ($p > 0.05$).

Correlation data of release rate through cellulose acetate membrane at 6 hr of six piroxicam gel products and area under the piroxicam content in stratum corneum versus time curve

Product	Release rate, X ($\mu g/cm^2.min^{1/2}$)	$AUC_{(0\text{-}6\ hr)}$, Y ($\mu g/mg$)
A	39.985	5.468
B	74.002	3.913
C	55.794	4.064
D	44.246	3.183

Test of Zero correlation

$$Ho : \rho = 0 \qquad Ha : \rho \neq 0$$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.3185

$$\therefore t_{n-2} = \left| \frac{0.3185\sqrt{4-2}}{\sqrt{1-(0.3185)^2}} \right|$$

$$= 0.4752$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of release rate through cellulose acetate membrane at 6 hr and area under the piroxicam content in stratum corneum versus time curve ($p > 0.05$).

Correlation data of cumulative amount through cellulose acetate membrane at 6 hr of six piroxicam gel products and area under the piroxicam content in stratum corneum versus time curve

Product	Cumulative amount, X ($\mu g/cm^2$)	$AUC_{(0\text{-}6\ hr)}$, Y ($\mu g/mg$)
A	615.997	5.468
B	1223.502	3.913
C	945.995	4.064
D	686.022	3.183

Test of Zero correlation

$Ho : \rho = 0 \qquad Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.3122

$$\therefore t_{n-2} = \left| \frac{0.3122\sqrt{4-2}}{\sqrt{1-(0.3122)^2}} \right|$$

$$= 0.4647$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of cumulative amount through cellulose acetate membrane at 6 hr and area under the piroxicam content in stratum corneum versus time curve ($p > 0.05$).

Correlation data of flux through new born pig skin at 24 hr of six piroxicam gel products and area under the piroxicam content in stratum corneum versus time curve

Product	Flux, X ($ng/cm^2.hr$)	$AUC_{(0\text{-}6\ hr)}$, Y ($\mu g/mg$)
A	44.923	5.468
B	72.283	3.913
C	68.193	4.064
D	213.800	3.183

Test of Zero correlation

$Ho : \rho = 0 \qquad Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.7863

$$\therefore t_{n-2} = \left| \frac{0.7863\sqrt{4-2}}{\sqrt{1-(0.7863)^2}} \right|$$

$$= 1.7998$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of flux through new born pig skin at 24 hr and area under the piroxicam content in stratum corneum versus time curve ($p > 0.05$).

Correlation data of cumulative amount through new born pig skin at 24 hr of six piroxicam gel products and area under the piroxicam content in stratum corneum versus time curve

Product	Cumulative amount, X (ng/cm^2)	$AUC_{(0\text{-}6\ hr)}$, Y ($\mu g/mg$)
A	858.481	5.468
B	1544.838	3.913
C	1365.847	4.064
D	4501.802	3.183

Test of Zero correlation

$$Ho : \rho = 0 \qquad Ha : \rho \neq 0$$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.7968

$$\therefore t_{n-2} = \left| \frac{0.7968\sqrt{4-2}}{\sqrt{1-(0.7968)^2}} \right|$$

$$= 1.8649$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of cumulative amount through new born pig skin at 24 hr and area under the piroxicam content in stratum corneum versus time curve ($p > 0.05$).

Correlation data of release rate through cellulose acetate membrane at 6 hr of six piroxicam gel products and ear weight difference

Product	Release rate, X ($\mu g/cm^2.min^{1/2}$)	Ear weight difference, Y (mg)
A	39.985	10.05
B	74.002	10.38
C	55.794	9.16
D	44.246	8.75

Test of Zero correlation

$Ho : \rho = 0 \qquad Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.4845

$$\therefore t_{n-2} = \left| \frac{0.4845\sqrt{4-2}}{\sqrt{1-(0.4845)^2}} \right|$$

$$= 0.7832$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of release rate through cellulose acetate membrane at 6 hr and ear weight difference ($p > 0.05$).

Correlation data of cumulative amount through cellulose acetate membrane at 6 hr of six piroxicam gel products and ear weight difference

Product	Cumulative amount, X ($\mu g/cm^2$)	Ear weight difference, Y (mg)
A	615.997	10.05
B	1223.502	10.38
C	945.995	9.16
D	686.022	8.75

Test of Zero correlation

$Ho : \rho = 0$ $\quad$ $Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When $r = 0.4520$

$$\therefore t_{n-2} = \left| \frac{0.4520\sqrt{4-2}}{\sqrt{1-(0.4520)^2}} \right|$$

$$= 0.7166$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of cumulative amount through cellulose acetate membrane at 6 hr and ear weight difference ($p > 0.05$).

Correlation data of flux through new born pig skin at 24 hr of six piroxicam gel products and ear weight difference

Product	Flux, X ($ng/cm^2.hr$)	Ear weight difference, Y (mg)
A	44.923	10.05
B	72.283	10.38
C	68.193	9.16
D	213.800	8.75

Test of Zero correlation

$Ho : \rho = 0$ $\quad$ $Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When $r = 0.7376$

$$\therefore t_{n-2} = \left| \frac{0.7376\sqrt{4-2}}{\sqrt{1-(0.7376)^2}} \right|$$

$$= 1.5448$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of flux through new born pig skin at 24 hr and ear weight difference ($p > 0.05$).

Correlation data of cumulative amount through new born pig skin at 24 hr of six piroxicam gel products and ear weight difference

Product	Cumulative amount, X (ng/cm^2)	Ear weight difference, Y (mg)
A	858.481	10.05
B	1544.838	10.38
C	1365.847	9.16
D	4501.802	8.75

Test of Zero correlation

$Ho : \rho = 0$ $\quad$ $Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.7230

$$\therefore t_{n-2} = \left| \frac{0.7230\sqrt{4-2}}{\sqrt{1-(0.7230)^2}} \right|$$

$$= 1.4800$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of cumulative amount through new born pig skin at 24 hr and ear weight difference ($p > 0.05$).

Correlation data of release rate through cellulose acetate membrane at 6 hr of six piroxicam gel products and size of blue spot

Product	Release rate, X ($\mu g/cm^2.min^{1/2}$)	Size of blue spot, Y (mm^2)
A	39.985	212.115
B	74.002	200.020
C	55.794	230.483
D	44.246	205.043

Test of Zero correlation

$Ho : \rho = 0$ $\quad$ $Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.2307

$$\therefore t_{n-2} = \left| \frac{0.2307\sqrt{4-2}}{\sqrt{1-(0.2307)^2}} \right|$$

$$= 0.3353$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of release rate through cellulose acetate membrane at 6 hr and size of blue spot ($p > 0.05$).

Correlation data of cumulative amount through cellulose acetate membrane at 6 hr of six piroxicam gel products and size of blue spot

Product	Cumulative amount, X ($\mu g/cm^2$)	Size of blue spot, Y (mm^2)
A	615.997	212.115
B	1223.502	200.020
C	945.995	230.483
D	686.022	205.043

Test of Zero correlation

$$Ho : \rho = 0 \qquad Ha : \rho \neq 0$$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.1429

$$\therefore t_{n-2} = \left| \frac{0.1429\sqrt{4-2}}{\sqrt{1-(0.1429)^2}} \right|$$

$$= 0.2042$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of cumulative amount through cellulose acetate membrane at 6 hr and size of blue spot ($p > 0.05$).

Correlation data of flux through new born pig skin at 24 hr of six piroxicam gel products and size of blue spot

Product	Flux, X ($ng/cm^2.hr$)	Size of blue spot, Y (mm^2)
A	44.923	212.115
B	72.283	200.020
C	68.193	230.483
D	213.800	205.043

Test of Zero correlation

$$Ho : \rho = 0 \qquad Ha : \rho \neq 0$$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.3424

$$\therefore t_{n-2} = \left| \frac{0.3424\sqrt{4-2}}{\sqrt{1-(0.3424)^2}} \right|$$

$$= 0.5154$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of flux through new born pig skin at 24 hr and size of blue spot ($p > 0.05$).

Correlation data of cumulative amount through new born pig skin at 24 hr of six piroxicam gel products and size of blue spot

Product	Cumulative amount, X (ng/cm^2)	Size of blue spot, Y (mm^2)
A	858.481	212.115
B	1544.838	200.020
C	1365.847	230.483
D	4501.802	205.043

Test of Zero correlation

$$Ho : \rho = 0 \qquad Ha : \rho \neq 0$$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.3606

$$\therefore t_{n-2} = \left| \frac{0.3606\sqrt{4-2}}{\sqrt{1-(0.3606)^2}} \right|$$

$$= 0.5468$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of cumulative amount through new born pig skin at 24 hr and size of blue spot ($p > 0.05$).

Appendix XIII

Correlation results between *In Vivo* Pharmacological Studies and *In Vivo* Skin Stripping Technique

Correlation data of ear weight difference of four gel products and amount remaining in stratum corneum at 0 hr

Product	Ear weight difference, X (mg)	Amount in SC, Y (μg/mg)
A	10.05	1.56
B	10.38	1.60
C	9.16	0.99
D	8.75	1.09

Test of Zero correlation

Ho : $\rho = 0$ Ha : $\rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.9285

$$\therefore t_{n-2} = \left| \frac{0.9285\sqrt{4-2}}{\sqrt{1-(0.9285)^2}} \right|$$

$$= 3.5361$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of ear weight difference of four gel products and amount remaining in stratum corneum at 0 hr ($p > 0.05$).

Correlation data of size of blue spot of four gel products and amount remaining in stratum corneum at 0 hr

Product	Size of blue spot, X (mm^2)	Amount in SC, Y (μg/mg)
A	212.115	1.56
B	200.020	1.60
C	230.483	0.99
D	205.043	1.09

Test of Zero correlation

$Ho : \rho = 0$ $\quad$ $Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.6274

$$\therefore t_{n-2} = \left| \frac{0.6274\sqrt{4-2}}{\sqrt{1-(0.6274)^2}} \right|$$

$$= 1.1394$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of size of blue spot of four gel products and amount remaining in stratum corneum at 0 hr ($p > 0.05$).

Correlation data of ear weight difference of four gel products and amount remaining in stratum corneum at 1 hr

Product	Ear weight difference, X (mg)	Amount in SC, Y (μg/mg)
A	10.05	1.08
B	10.38	0.86
C	9.16	0.74
D	8.75	0.67

Test of Zero correlation

Ho : $\rho = 0$ Ha : $\rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.7578

$$\therefore t_{n-2} = \left| \frac{0.7578\sqrt{4-2}}{\sqrt{1-(0.7578)^2}} \right|$$

$$= 1.6425$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of ear weight difference of four gel products and amount remaining in stratum corneum at 1 hr ($p > 0.05$).

Correlation data of size of blue spot of four gel products and amount remaining in stratum corneum at 1 hr

Product	Size of blue spot, X (mm^2)	Amount in SC, Y (μg/mg)
A	212.115	1.08
B	200.020	0.86
C	230.483	0.74
D	205.043	0.67

Test of Zero correlation

$Ho : \rho = 0$ $\quad$ $Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When $r = 0.1269$

$$\therefore t_{n-2} = \left| \frac{0.1269\sqrt{4-2}}{\sqrt{1-(0.1269)^2}} \right|$$

$$= 0.1809$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ ($df = 2$) is 4.30. Therefore, there is no correlation of size of blue spot of four gel products and amount remaining in stratum corneum at 1 hr ($p > 0.05$).

. Correlation data of ear weight difference of four gel products and amount remaining in stratum corneum at 3 hr

Product	Ear weight difference, X (mg)	Amount in SC, Y (μg/mg)
A	10.05	0.86
B	10.38	0.50
C	9.16	0.67
D	8.75	0.47

Test of Zero correlation

$Ho : \rho = 0$ $\quad$ $Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.2975

$$\therefore t_{n-2} = \left| \frac{0.2975\sqrt{4-2}}{\sqrt{1-(0.2975)^2}} \right|$$

$$= 0.4407$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of ear weight difference of four gel products and amount remaining in stratum corneum at 3 hr ($p > 0.05$).

Correlation data of size of blue spot of four gel products and amount remaining in stratum corneum at 3 hr

Product	Size of blue spot, X (mm^2)	Amount in SC, Y (μg/mg)
A	212.115	0.86
B	200.020	0.50
C	230.483	0.67
D	205.043	0.47

Test of Zero correlation

$Ho : \rho = 0$ $\quad$ $Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.4686

$$\therefore t_{n-2} = \left| \frac{0.4686\sqrt{4-2}}{\sqrt{1-(0.4686)^2}} \right|$$

$$= 0.7502$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of size of blue spot of four gel products and amount remaining in stratum corneum at 3 hr ($p > 0.05$).

Correlation data of ear weight difference of four gel products and amount remaining in stratum corneum at 6 hr

Product	Ear weight difference, X (mg)	Amount in SC, Y (μg/mg)
A	10.05	0.72
B	10.38	0.39
C	9.16	0.54
D	8.75	0.32

Test of Zero correlation

Ho : $\rho = 0$ Ha : $\rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.5360

$$\therefore t_{n-2} = \left| \frac{0.5360\sqrt{4-2}}{\sqrt{1-(0.5360)^2}} \right|$$

$$= 0.8979$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of ear weight difference of four gel products and amount remaining in stratum corneum at 6 hr ($p > 0.05$).

Correlation data of size of blue spot of four gel products and amount remaining in stratum corneum at 6 hr

Product	Size of blue spot, X (mm^2)	Amount in SC, Y (μg/mg)
A	212.115	0.72
B	200.020	0.39
C	230.483	0.54
D	205.043	0.32

Test of Zero correlation

Ho : $\rho = 0$ Ha : $\rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.4602

$$\therefore t_{n-2} = \left| \frac{0.4602\sqrt{4-2}}{\sqrt{1-(0.4602)^2}} \right|$$

$$= 0.7330$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of size of blue spot of four gel products and amount remaining in stratum corneum at 6 hr ($p > 0.05$).

Correlation data of ear weight difference of four gel products and rate constant over 6 hr

Product	Ear weight difference, X (mg)	Rate constant, Y (μg/mg.hr)
A	10.05	0.1234
B	10.38	0.2490
C	9.16	0.1093
D	8.75	0.1806

Test of Zero correlation

$Ho : \rho = 0$ $\quad$ $Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.4014

$$\therefore t_{n-2} = \left| \frac{0.4014\sqrt{4-2}}{\sqrt{1-(0.4014)^2}} \right|$$

$$= 0.6198$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of ear weight difference of four gel products and rate constant over 6 hr ($p > 0.05$).

Correlation data of size of blue spot of four gel products and rate constant over 6 hr

Product	Size of blue spot, X (mm^2)	Rate constant, Y (μg/mg.hr)
A	212.115	0.1234
B	200.020	0.2490
C	230.483	0.1093
D	205.043	0.1806

Test of Zero correlation

Ho : $\rho = 0$ Ha : $\rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.8447

$$\therefore t_{n-2} = \left| \frac{0.8447\sqrt{4-2}}{\sqrt{1-(0.8447)^2}} \right|$$

$$= 2.2317$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of size of blue spot of four gel products and rate constant over 6 hr ($p > 0.05$).

Correlation data of ear weight difference of four gel products and percent absorbed at 1 hr

Product	Ear weight difference, X (mg)	% Absorbed, Y
A	10.05	30.60
B	10.38	45.04
C	9.16	22.79
D	8.75	36.38

Test of Zero correlation

Ho : $\rho = 0$ Ha : $\rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.4668

$$\therefore t_{n-2} = \left| \frac{0.4668\sqrt{4-2}}{\sqrt{1-(0.4668)^2}} \right|$$

$$= 0.7465$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of ear weight difference of four gel products and percent absorbed at 1 hr ($p > 0.05$).

Correlation data of size of blue spot of four gel products and percent absorbed at 1 hr

Product	Size of blue spot, X (mm^2)	% Absorbed, Y
A	212.115	30.60
B	200.020	45.04
C	230.483	22.79
D	205.043	36.38

Test of Zero correlation

Ho : $\rho = 0$ Ha : $\rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.9940

$$\therefore t_{n-2} = \left| \frac{0.9940\sqrt{4-2}}{\sqrt{1-(0.9940)^2}} \right|$$

$$= 12.852$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is significant correlation of size of blue spot of four gel products and percent absorbed at 1 hr ($p < 0.05$).

Correlation data of ear weight difference of four gel products and percent absorbed at 3 hr

Product	Ear weight difference, X (mg)	% Absorbed, Y
A	10.05	43.59
B	10.38	71.72
C	9.16	29.88
D	8.75	57.28

Test of Zero correlation

$Ho : \rho = 0$ $\quad$ $Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.6844

$$\therefore t_{n-2} = \left| \frac{0.6844\sqrt{4-2}}{\sqrt{1-(0.6844)^2}} \right|$$

$$= 1.3275$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of ear weight difference of four gel products and percent absorbed at 3 hr ($p > 0.05$).

Correlation data of size of blue spot of four gel products and percent absorbed at 3 hr

Product	Size of blue spot, X (mm^2)	% Absorbed, Y
A	212.115	43.59
B	200.020	71.72
C	230.483	29.88
D	205.043	57.28

Test of Zero correlation

Ho : $\rho = 0$ Ha : $\rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.9502

$$\therefore t_{n-2} = \left| \frac{0.9502\sqrt{4-2}}{\sqrt{1-(0.9502)^2}} \right|$$

$$= 4.3120$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is significant correlation of size of blue spot of four gel products and percent absorbed at 3 hr ($p < 0.05$).

Correlation data of ear weight difference of four gel products and percent absorbed at 6 hr

Product	Ear weight difference, X (mg)	% Absorbed, Y
A	10.05	52.36
B	10.38	78.10
C	9.16	41.78
D	8.75	68.03

Test of Zero correlation

$Ho : \rho = 0$ $\quad$ $Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.6160

$$\therefore t_{n-2} = \left| \frac{0.6160\sqrt{4-2}}{\sqrt{1-(0.6160)^2}} \right|$$

$$= 1.1059$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of ear weight difference of four gel products and percent absorbed at 6 hr ($p > 0.05$).

Correlation data of size of blue spot of four gel products and percent absorbed at 6 hr

Product	Size of blue spot, X (mm^2)	% Absorbed, Y
A	212.115	52.36
B	200.020	78.10
C	230.483	41.78
D	205.043	68.03

Test of Zero correlation

Ho : $\rho = 0$ Ha : $\rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.9446

$$\therefore t_{n-2} = \left| \frac{0.9446\sqrt{4-2}}{\sqrt{1-(0.9446)^2}} \right|$$

$$= 4.0700$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of size of blue spot of four gel products and percent absorbed at 6 hr ($p > 0.05$).

Correlation data of ear weight difference of four gel products and area under the piroxicam content in stratum corneum versus time curve

Product	Ear weight difference, X (mg)	$AUC_{(0\text{-}6\ hr)}$, Y (μg/mg)
A	10.05	5.468
B	10.38	3.913
C	9.16	4.064
D	8.75	3.183

Test of Zero correlation

$Ho : \rho = 0 \qquad Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.5837

$$\therefore t_{n-2} = \left| \frac{0.5837\sqrt{4-2}}{\sqrt{1-(0.5837)^2}} \right|$$

$$= 1.0166$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of ear weight difference of four gel products and area under the piroxicam content in stratum corneum versus time curve ($p > 0.05$).

Correlation data of size of blue spot of four gel products and area under the piroxicam content in stratum corneum versus time curve

Product	Size of blue spot, X (mm^2)	$AUC_{(0\text{-}6\ hr)}$, Y (μg/mg)
A	212.115	5.468
B	200.020	3.913
C	230.483	4.064
D	205.043	3.183

Test of Zero correlation

$Ho : \rho = 0$ $\quad$ $Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When r = 0.5894

$$\therefore t_{n-2} = \left| \frac{0.5894\sqrt{4-2}}{\sqrt{1-(0.5894)^2}} \right|$$

$$= 1.0266$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ (df = 2) is 4.30. Therefore, there is no correlation of size of blue spot of four gel products and area under the piroxicam content in stratum corneum versus time curve ($p > 0.05$).

Correlation data of size of blue spot of four gel products and ear weight difference

Product	Size of blue spot, X (mm^2)	Ear weight difference, Y (mg)
A	212.115	10.05
B	200.020	10.38
C	230.483	9.16
D	205.043	8.75

Test of Zero correlation

$Ho : \rho = 0$ $\quad$ $Ha : \rho \neq 0$

Where ρ is the true correlation coefficient, estimate by r

$$t_{n-2} = \left| \frac{r\sqrt{n-2}}{\sqrt{1-r^2}} \right|$$

When $r = 0.3795$

$$\therefore t_{n-2} = \left| \frac{0.3795\sqrt{4-2}}{\sqrt{1-(0.3795)^2}} \right|$$

$$= 0.5801$$

From the correlation coefficient at 5% level of significance, $t_{0.025}$ ($df = 2$) is 4.30. Therefore, there is no correlation of size of blue spot of four gel products and ear weight difference ($p > 0.05$).

VITA

Miss Maytinee Limsiriwong was borned on 25th July 1969 in Bangkok, Thailand. She has graduated Bachelor of Science in Pharmacy from Faculty of Pharmacy, Chiangmai University, Chiangmai, Thailand since 1992. She works at Department of Medical Science, Nonthaburi, Thailand.