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APPENDIX I

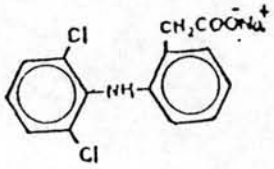
Details of Diclofenac Sodium and Enhancers Studied.

Diclofenac Sodium

(Adeyeye, 1990; Cedric and Reynard, 1992)

Diclofenac sodium is a synthetic, nonsteroid anti-inflammatory, and analgesic compound. It is a phenylacetic acid derivative that was first marketed in Japan in 1974 and enjoyed wide clinical usage worldwide with the exception of the United States, where more stringent Food and Drug Administration (FDA) criteria for acceptability precluded its introduction until 1988. The chemical structure includes a second aryl amino group and a phenyl ring with two choline atoms in the ortho position.

Structural Formula



Molecular formula $C_{14}H_{10}Cl_2No_2Na$

Molecular weight 318.13

Chemical names

1) 2-[(2, 6-dichlorophenyl) amino] benzene acetic acid monosodium salt
2) [0-(2, 6-dichloroanilino) phenyl] acetic acid sodium salt
3) sodium [0-[2, 6-dichlorophenyl) amino] phenyl] acetate

Appearance Diclofenac sodium is an odorless, white to off-white crystalline, slightly hygroscopic powder.

Solubility The equilibrium solubility performed in various solvents at the room temperature (RT) are shown in Table 10.

Table 13: Solubility of diclofenac sodium.

Solvent	Temperature	Solubility (mg/ml)
Deionized water (pH 5.2)	RT	>9
Methanol	RT	>24
Acetone	RT	6
Acetonitrile	RT	<1
Cyclohexane	RT	<1
pH 1.1 (HCl)	RT	<1
pH 7.2 phosphate buffer	RT	6

Dissociation constant and partition coefficient

The pKa of diclofenac sodium in water is 4 and the partition coefficient in n-octanol / pH 7.4 aqueous buffer is 13.4.

Stability

Diclofenac sodium tablets film coated with polymers like acrylate hydroxypropyl-cellulose were reported to be stable after storage for one week at 30^{0}C in 80% relative humidity. A suppository formulation was also analyzed for

stability using the thin layer chromatography and the ultraviolet spectroscopy. The formulation was stable for 24 months at room temperature. Stability in biological fluid (serum) was determined and the results demonstrated that diclofenac sodium can be frozen for at least two weeks without degradation.

Indications

Diclofenac sodium is effective as an anti-inflammatory agent in the treatment of rheumatoid arthritis, osteoarthritis, and ankylosing spondylitis. It is also effective in nonrheumatic conditions as an analgesic in dysmenorrhea, renal and biliary colic, oral surgery, and chronic musculoskeletal low back pain. It is a potent NSAIDS, approximately equal in potency to indomethacin.

Pharmacological actions

Although the mechanism of action of diclofenac is by PG synthesis inhibition, it also results in a decrease in lipoxygenase products by enhancing the uptake of arachidonic acid into triglycerides. The most important attribution of diclofenac, which differentiates it from many other NSAIDS, is its prolonged uptake into synovial fluid with concentrations persisting above plasma levels for 24 hours.

The pharmacological properties of diclofenac approach the ideal because high concentrations of the active drug are present where they are needed (e.g., joint synovial fluid) and in low concentrations where they produce side effects (e.g., plasma and nonsynovial organs and tissues).

Comparing favorably with other NSAIDS, diclofenac sodium is safer and better tolerated than the two most commonly used NSAIDS, aspirin and indomethacin. In particular, diclofenac had fewer GI side effects and markedly reduced CNS side effects that are common to aspirin (tinnitus and deafness) and indomethacin (headache and drowsiness).

Pharmacokinetics

Diclofenac is absorbed completely with a high rate of first-pass hepatic metabolism, so only 50-60% reaches the systemic circulation. Peak plasma concentrations occur in 2-3 hours, with a mean terminal half-life of 2 hours. Diclofenac is almost completely bound to plasma protein. Peak plasma concentrations are less than proportional to dose, with plasma concentrations ranging from 1 to 2 mcg/ml following ingestion of 25-50 mg. Repeated administration twice a day did not result in any drug accumulation in plasma level. A concomitant food intake may retard onset but not extent to absorption.

Diclofenac is distributed throughout all body tissues. It penetrates across synovial membrane to joint fluid within 4 hours which produces synovial fluid concentrations of higher than the plasma level and remain higher for up to 12 hours.

Diclofenac is metabolized extensively by the liver to at least four metabolites; the most prominent is the active 4-hydroxy-diclofenac. Conjugates of diclofenac and its three metabolites are eliminated mainly by the kidney (50%) and to a lesser extent in the bile (20%). Only a small amount of diclofenac is excreted unchanged.

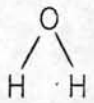
Availability and dosage

Diclofenac is available in 25, 50 and 75 mg enteric coated tablets. In rheumatoid arthritis, the recommended oral dosage is 150-200 mg/day in divided doses (50 mg three to four times per day or 75 mg two times per day). In osteoarthritis, the recommended dosage is 100-150 mg/day (50 mg two to three times per day or 75 mg two times per day).

In ankylosing spondylitis, the recommended dosage is 100-125 mg/day (25 mg four times per day with an additional bedtime of 25 mg dose if necessary).

Water

(Boylan, J.C., 1986)

Structural formula	
Empirical formula	H_2O
Molecular weight	18.02
Synonyms	Aqua
Appearance	Clear, colorless, odorless liquid.
Soivent properties	Miscible and soluble with most polar solvent and electrolytes.
Stability	Chemically stable in all physical states (ice, liquid water and steam).
Application	Solvent and vehicle for the manufacture of drug substance and excipients.
Safety	Water is the basis for many biological life forms, and its safety is unquestioned as long as it meets standard quality for portability and microbial content. Plain water is considered slightly more toxic upon injection to laboratory animals than physiological salt solutions (normal saline, Ringer's, etc.).

Brij 35

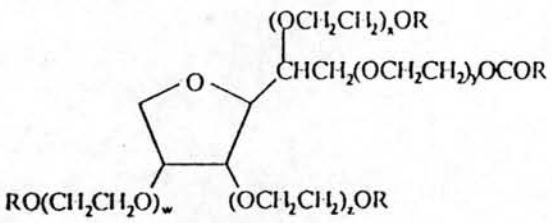
(Boylan, J.C., 1986)

Structural formula	$CH_3(CH_2)_{12}O(CH_2CH_2O)_{23}H$
Empirical formula	$C_{12}E_{23}$
Molecular weight	1856
Synonym	Polyoxyethylene dodecyl ether.
Chemical name	Polyoxyethylenelauryl ether.
Appearance	Paste or solid waxy substances, white or creamy with a slight odor.
Solubility	Soluble in water, ethanol and propylene glycol, insoluble in fixed oils.
Functional category	Nonionic emulsifying agent.
Stability	Stable in strong acidic and alkaline conditions. The surfactant can undergo autoxidation on storage, resulting in the formation of peroxides and a continual increase in acidity. Keep in airtight container.
Application	Used as emulsifying agent for w/o and o/w emulsions, solubilizing agents for essential oils, perfumery chemicals, vitamin oils and drugs of low water solubitity, gelling and foaming agent.
Safty	Minimally irritant.

Tween 20

(Boylan, J.C., 1986)

Structural formula



POLYOXYETHYLENE SORBITAN FATTY ESTER

w+x+y+z = 20 Polysorbate 20

Empirical formula	$C_{58}H_{114}O_{26}$
Molecular weight	1126
Synonyms	Polyoxyethylene 20 sorbitan monolaurate, polysorbate 20
Chemical name	Polysorbate 20-sorbitan, monododecanoate, polyoxyethylene 20 sorbitan monolaurate.
Appearance	Yellow oily liquid, characteristic odor and somewhat bitter taste.
Solubility	Soluble in water and ethanol, insoluble in vegetable oil and mineral oil.
Functional category	Wetting and/or solubilizing agent; emulsifying agent; non-ionic surface-active agents.

Stability Stable to electrolytes as well as to weak acid and base. There is gradual saponification by strong acid and base. Preserve in a tight containner protected from light, and store in a cool condition.

Application

Use	Concentration (%)
Emulsifiers	
Used alone in water-in-oil emulsion	1-15
Used in combination with hydrophilic emulsifiers in oil-in-water emulsions	1-10
Used to increase the water holding properties of ointments	1-10
Solubilizer	
For poorly soluble active constituents in lipophilic bases	1-10
Wetting Agents	
For insoluble active constituents in lipophilic bases	0.1-3

Safety Tween 20 is well tolerated, practically non-irritating,low toxicity.

Propylene Glycol

(Boyland, J.C., 1986)

Structural formula	$CH_3CH(OH)-CH_2OH$
Empirical formula	$C_3H_8O_2$
Molecular weight	76.09
Synonyms	1,2-Propanediol; propane-1,2-diol; methyl glycol; methyl ethylene glycol; 1,2-dihydroxypropane.
Appearance	Clear, colorless, viscous and practically odorless liquid, sweet, slightly acrid taste resembling glycerol.
Solubility	Miscible with water, acetone, alcohol, glycerine and chloroform; soluble in a ratio of 1:6 ether; immiscible with light mineral oil; immiscible with fixed oils, but dissolve some essential oils.
Functional category	Humectant; solvent; plasticizer; inhibitor of fermentation and mold growth; Hygroscopic agent; disinfectant; stabilizer for vitamin; water miscible cosolvent.
Stability	Under ordinary conditions, propylene glycol is stable in well-closed containners, but at high temperature in the open air, it tends to oxidize, giving rise to products such as propionaldehyde, lactic acid, pyruvic acid and acetic acid. Propylene glygol withstands autoclave sterilization in sealed

containers. Store in a well-closed container. Protect from light. Absorb moisture when exposed to moist air.

Application

Function	Dosage form	Concentration
Solvent or co-solvent	Oral solution	15-20%
	Parenterals	10-60%
	Topical preparations	5-80%
	Aerosol solutions	10-30%
Humectant	Topical	~15%
	Solution; semisolid	15-30%

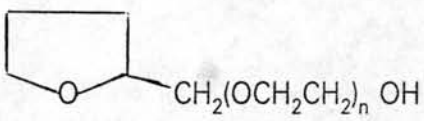
Safety

Propylene glycol is less toxic than other glycols. Some local irritation is produced upon application to mucous membranes or upon subcutaneous or intramuscular injection. Hypersensitivity to 38% propylene glycol applied topically has been reported.

Tetraglycol

(Boylan, J.C., 1986)

Structural formula



$CH_2(OCH_2CH_2)_n\ OH$

Glycofurol 75 : n = 1-2.

Empirical formula $C_9H_{18}O_4$

Molecular weight 190.24

Synonyms Tetraglycol (also used for tetrahydrofurfuryl alcohol); tetrahydrofurfuryl alcohol polyethylene glycol ether; Glycofurol 75.

Chemical name α-(tetrahydrofuranyl)-w-hydroxypoly (oxy-1,2-ethanediyl).

Appearance Clear, colorless, almost odorless liquid, with a bitter taste and production of a warm sensation on the tongue.

Solubility

Solvent	Miscibility (at 20 ^{0}C)
Water	Miscible in all proportions.*
Ethanol (96%)	Miscible in all proportions.
Propylene glycol	Miscible in all proportions.
Glycerol	Miscible in all proportions.

Propane-2-ol	Miscible in all proportions.
Castor oil	Miscible.*
Arachis oil	Immiscible.

* Cloudiness may occur.

Functional category Solvent.

Stability Stable if stored under nitrogen in a well-closed container protected from light.

Application Used as a solvent in parenteral product for intravenous or intramuscular injection, in concentration up to 50% v/v.

Safety When administered parenterally, quantities of tetraglycol should not exceed 0.07 ml per kg of body weight per day (man).

Ethanol

(Boyland, J.C., 1986)

Structural formula	C_2H_5OH
Empirical formula	C_2H_5OH
Molecular weight	46.07
Synonyms	Ethanol; ethyl alcohol; grain alcohol; methyl carbinol.
Appearance	Clean, colorless, mobile and volatile liquid with a slight, characteristic odor, burning taste.
Solubility	Completely miscible with water, with rise of temperature and contraction in volume. Completely miscible with chloroform, acetone, ether and glycerine.
Safety	Threshold limit value (TLV) in workroom air in the United Kingdom is 1,000 ppm (of vapor by volume). Exposure to concentration of 5,000-10,000 ppm results in irritation of the eyes and mucous membranes of the upper respiratory tract. If continued for an hour, stupor and drowsiness may occur. Preparations containing more than 50% ethanol may cause skin irritation when applied topically. Systemically, alcohol is a CNS depressant. Sufficient doses can lead to nausea, vomitting, flushing, mental excitemnt or

depression, drawsiness, impaired perception and incoordination. Severe overdosing can cause coma and death. Oral LD_{50} (rat): 13.7 g/kg of body weight.

Isopropyl Alcohol

(Boyland, J.C. 1986)

Structural formula	$CH_3CH(OH)CH_3$
Empirical formula	C_3H_8O
Molecular weight	60.1
Synonyms	Isopropanol; Isopropyl alcohol; alcohol isopropylicum; petrohol; dimethyl carbinol; 2-propanol; sec-propyl alcohol.
Appearance	Transparent, colorless, mobile, volatile, flamable liquid with a characteristic, spiritous odor resembling that of a mixture of ethanol and acetone, and a slightly bitter taste.
Solubility	Miscible with water, ethanol, benzene, chloroform, ether, and glycerine. Insoluble in salt solutions. Soluble in acetone.
Functional category	Solvent, local disinfectant.
Stability	Store in a tight container, remote from heat and protected from light.
Application	Used for pre-operative skin cleansing and as a disinfectant. Ingredient in lotions, but its marked degreasing properties may limit its usefulness in preparation used repeatedly. Solvent for film coating, cosmetics and perfume. Satisfactory non-aqueous moistening agent for tablet

granulation if the alcohol is subsequently evaporated.

Safety

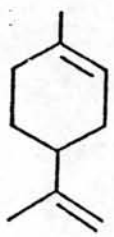
Isopropyl alcohol acts as a local irritant and, in high concentrations, as a narcotic. It is about twice as toxic as ethyl alcohol. It is slowly absorbed through the intact skin. Some isopropyl alcohol is converted in the body to acetone, which is slowly excreted in the breath and urine.

Orange Oil

(Smolinske, S.C., 1992; Reynold, 1993)

Orange oil is an essential oil that contains much of d-limonene which plays an important role in enhancement.

Structural formula



d-Limonene

Synonyms Essence of orange; essence of portugal; sweet orange oil.

Appearance A yellow, orange, or yellowish-brown volatile oil, containing not less than 1% w/w of aldehydes calculated as decanal ($C_{10}H_{20}O$). It has the characteristic odour and taste of orange.

Solubility Soluble in 1 in 7 of alcohol (90%) but rarely with the formation of bright solutions on account of the presence of waxy non-volatile substance.

Functional category	Used as flavouring agent and in perfumery.
Stability	Store at a temperature not exceeding 25 ^{O}C in airtight containers. Protect from light.
Safety	Associated with development of severe abdominal pain, nausea and vomitting. Orange oil contains more than 90% limonene, an essential oil that is a primary irritant and sensitizer.

APPENDIX II

Solubitity Data of Diclofenac Sodium in Donor Solutions.

Solubility of Diclofenac Sodium in Water at $33\pm1^{0}C$.

Calibration Curve Data

Concentration (mcg/ml)	4	8	12	24	32	40
Absorbance	0.148	0.267	0.397	0.789	1.038	1.292

$$Y = 0.016 + 0.032x$$

$$r^{2} = 0.9999$$

Sample No.	Diclofenac Sodium Conc. (mg/ml)
1	71.57
2	68.44
3	73.13
4	70.00
5	74.39
6	72.51
Mean	71.67
SD	6.918×10^{-3}
%CV	2.82

Solubility of Diclofenac Sodium in 0.01mg/ml Tween 20 in Water at $33\pm1^{0}C$.

Calibration Curve Data

Concentration (mcg/ml)	4	8	12	24	32	40
Absorbance	0.148	0.267	0.397	0.789	1.038	1.292

$$Y = 0.016 + 0.032x$$

$$r^{2} = 0.9999$$

Sample No.	Diclofenac Sodium Conc. (mg/ml)
1	94.42
2	98.86
3	93.49
4	93.49
5	90.67
6	91.92
Mean	92.78
SD	1.292
%CV	1.39

Solubility of Diclofenac Sodium in 0.05 mg/ml Tween 20 in Water at $33\pm1^{0}C$.

Calibration Curve Data

Concentration (mcg/ml)	4	8	12	24	32	40
Absorbance	0.148	0.267	0.397	0.789	1.038	1.292

$$Y = 0.016 + 0.032x$$

$$r^{2} = 0.9999$$

Sample No.	Diclofenac Sodium Conc. (mg/ml)
1	92.86
2	95.05
3	93.48
4	96.30
5	95.05
6	94.42
Mean	94.53
SD	1.231
%CV	1.30%

Solubility of Diclofenac Sodium in 0.4% w/v Brij 35 in Water at $33 \pm 1^{0}C$.

Calibration Curve Data

Concentration (mcg/ml)	4	8	12	24	32	40
Absorbance	0.148	0.267	0.397	0.789	1.038	1.292

$$Y = 0.016 + 0.032x$$

$$r^{2} = 0.9999$$

Sample No.	Diclofenac Sodium Conc. (mg/ml)
1	101.00
2	101.94
3	103.82
4	106.64
5	100.06
6	102.88
Mean	102.72
SD	7.449×10^{-3}
%CV	2.16

Solubility of Diclofenac Sodium in 1% w/v Brij 35 in Water at $33 \pm 1^{0}C$.

Calibration Curve Data

Concentration (mcg/ml)	4	8	12	24	32	40
Absorbance	0.148	0.267	0.397	0.789	1.038	1.292

$$Y = 0.016 + 0.032x$$

$$r^{2} = 0.9999$$

Sample No.	Diclofenac Sodium Conc. (mg/ml)
1	128.87
2	124.80
3	127.93
4	123.86
5	131.69
6	121.67
Mean	126.47
SD	0.0117
%CV	2.79

Solubility of Diclofenac Sodium in 10% w/v Propylene Glycol in Water at 33±1^{0}C.

Calibration Curve Data

Concentration (mcg/ml)	4	8	12	24	32	40
Absorbance	0.148	0.267	0.397	0.789	1.038	1.292

$$Y = 0.016 + 0.032x$$

$$r^{2} = 0.9999$$

Sample No.	Diclofenac Sodium Conc. (mg/ml)
1	269.77
2	272.27
3	285.74
4	272.27
5	276.84
6	270.39
Mean	274.10
SD	0.018
%CV	2.11

Solubility of Diclofenac Sodium in 10% w/v Tetraglycol in Water at 33 ± 1^{0}C.

Calibration Curve Data

Concentration (mcg/ml)	4	8	12	24	32	40
Absorbance	0.148	0.267	0.397	0.789	1.038	1.292

$$Y = 0.016 + 0.032x$$

$$r^2 = 0.9999$$

Sample No.	Diclofenac Sodium Conc. (mg/ml)
1	376.85
2	351.80
3	351.18
4	367.46
5	360.57
6	355.25
Mean	360.52
SD	0.0321
%CV	2.75

Solubility of Diclofenac Sodium in Ethanol at 33±1 ^{0}C.

Calibration Curve Data

Concentration (mcg/ml)	4	8	12	24	32	40
Absorbance	0.148	0.267	0.397	0.789	1.038	1.292

$$Y = 0.016 + 0.032x$$

$$r^2 = 0.9999$$

Sample No.	Diclofenac Sodium Conc. (mg/ml)
1	328.13
2	328.32
3	342.41
4	337.71
5	327.69
6	320.80
Mean	330.84
SD	0.0255
%CV	2.382

Solubility of Diclofenac Sodium in Isopropyl Alcohol at 33±1^{0}C.

Calibration Curve Data

Concentration (mcg/ml)	4	8	12	24	32	40
Absorbance	0.148	0.267	0.397	0.789	1.038	1.292

$Y = 0.016 + 0.032x$

$r^{2} = 0.9999$

Sample No.	Diclofenac Sodium Conc. (mg/ml)
1	39.63
2	39.94
3	40.57
4	41.20
5	38.38
6	41.82
Mean	40.26
SD	3.898×10^{-3}
%CV	2.68

Solubility of Diclofenac Sodium in 1% w/v Orange oil in Ethanol at $33 \pm 1^{0}C$.

Calibration Curve Data

Concentration (mcg/ml)	4	8	12	24	32	40
Absorbance	0.148	0.267	0.397	0.789	1.0380	1.292

$$Y = 0.016 + 0.032x$$

$$r^{2} = 0.9999$$

Sample No.	Diclofenac Sodium Conc. (mg/ml)
1	360.88
2	347.11
3	343.97
4	366.21
5	353.99
6	343.04
Mean	352.53
SD	0.0303
%CV	2.65

APPENDIX III

Fluxes of Diclofenac Sodium from Its Saturated Solution through Newborn Pig Skin.

Enhancer: Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.914	1.376	2.288	3.253	4.058	4.947

$$Y = 0.4887 + 3.588x$$

$$r^2 = 0.9994$$

Diffusion Run Data

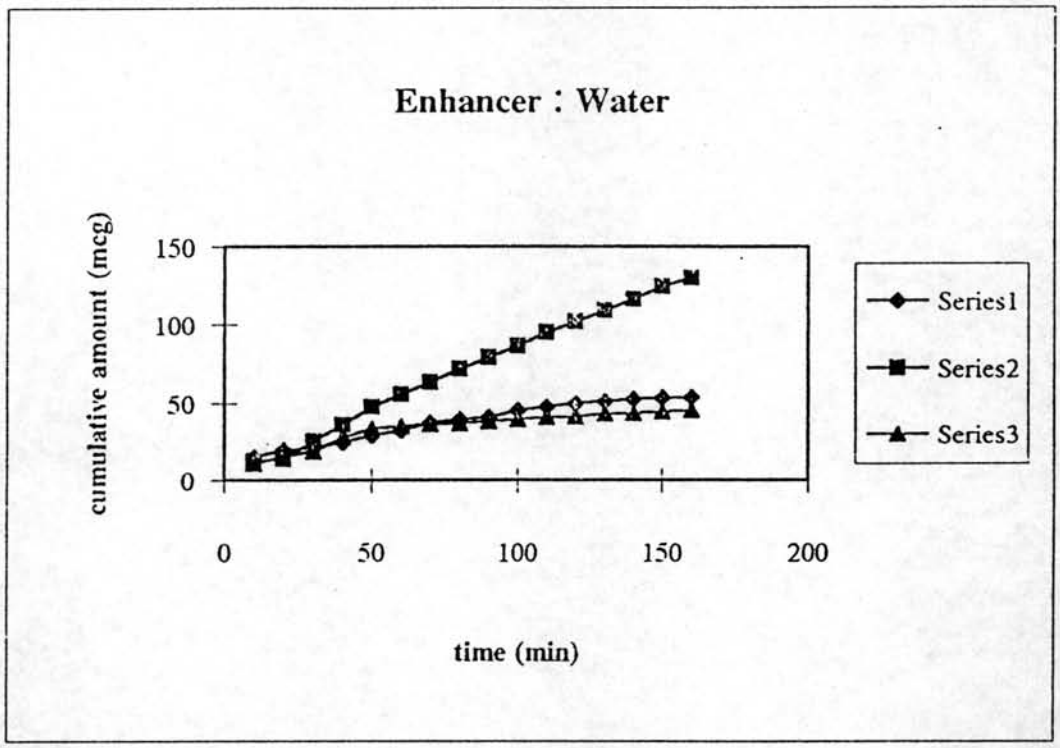
Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)
10	4.927	15.090	4.036	12.450	3.563	10.880
20	1.733	4.230	2.460	6.922	1.615	3.986
30	0.977	1.660	2.212	6.051	1.484	3.523
40	1.557	3.632	3.483	10.51	3.154	9.434
50	1.803	4.468	3.767	11.51	2.056	5.547
60	1.454	3.282	2.896	8.453	0.917	1.516
70	1.951	4.972	2.583	7.354	0.820	1.172
90	1.114	2.126	2.591	8.646	0.654	0.585
90	0.840	1.194	2.652	7.596	0.903	1.466
100	1.866	4.683	2.512	7.105	0.901	1.459
110	1.186	2.371	2.947	8.632	0.793	1.077
120	1.109	2.109	2.460	6.992	0.685	0.694
130	0.903	1.408	2.500	7.063	0.986	1.760
140	0.841	1.198	2.527	7.157	0.624	0.479
150	0.798	1.051	2.886	8.418	0.732	0.861
160	0.619	0.443	1.994	5.286	0.678	0.670
Receptor Volume (ml)	12.20		12.60		12.70	

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mcg)	Cumulative Amount (mcg)	Cumulative Amount (mcg)
10	15.09	12.45	10.88
20	19.32	19.37	14.86
30	20.98	25.43	18.39
40	24.61	35.94	27.82
50	29.08	47.45	33.37
60	32.36	55.91	34.88
70	37.33	63.26	36.05
80	39.46	71.91	36.64
90	40.65	79.50	38.11
100	45.33	86.61	39.56
110	47.70	95.24	40.64
120	49.81	102.10	41.34
130	51.22	109.20	43.10
140	52.42	116.30	43.57
150	53.47	124.80	44.44
160	53.91	130.00	45.11
Steady-state Slope (70-160 min)	0.1975	0.7451	0.1059
r^2	0.9509	0.9988	0.9875
Jss (mcg/min.cm^2)	0.1020	0.3659	0.0501
Membrane Thickness (mm.)	0.3380	0.3200	0.0750
Normalized Jss x10^3 (mcg/min.cm^2)	102.60	348.30	40.98

Jss = 163.96 ± 162.5

%cv = 99.16



Diclofenac Sodium Flux from Saturated Diclofenac Sodium Solution through Newborn Pig Skin.

Enhancer: 0.01 mg/ml Tween 20 in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.560	1.010	1.890	2.798	3.956	4.796

$$Y = 0.0399 + 3.811x$$

$$r^2 = 0.9980$$

Diffusion Run Data

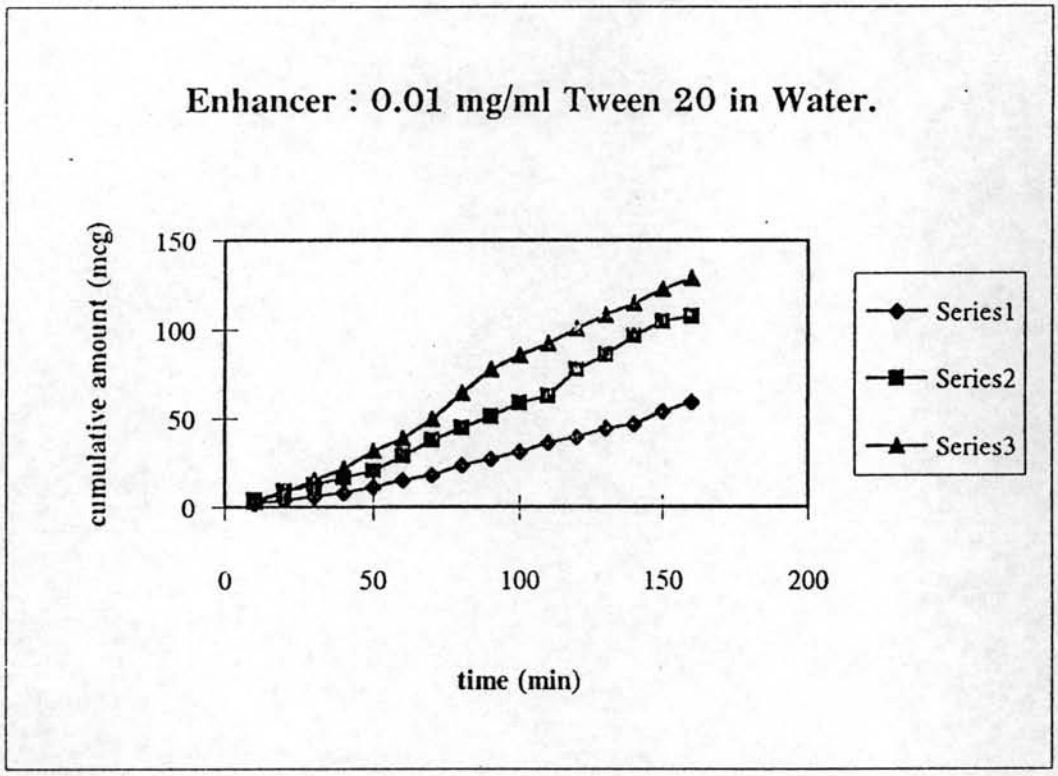
Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)
10	0.611	1.927	1.279	4.128	0.959	3.038
20	0.703	2.122	1.321	4.268	1.499	4.823
30	0.642	1.927	1.186	3.818	2.250	7.305
40	0.657	1.985	1.278	4.125	1.980	6.413
50	1.122	3.463	1.244	4.011	3.039	9.913
60	1.301	4.036	2.548	8.356	2.208	7.166
70	0.918	2.810	2.815	9.246	3.357	10.960
80	1.693	5.290	2.122	6.937	4.551	14.910
90	1.193	3.690	1.976	6.450	4.043	13.230
100	1.316	4.084	2.304	7.543	2.359	7.666
110	1.636	5.108	1.164	3.745	2.155	6.991
120	1.018	3.130	4.587	15.150	2.644	8.608
130	1.567	4.887	2.501	8.199	2.298	7.464
140	0.847	2.583	3.251	10.690	2.018	6.538
150	2.304	7.246	2.499	8.193	2.374	7.715
160	1.592	4.967	0.915	2.915	1.945	6.297
Receptor Volume (ml)	12.20		12.70		12.60	

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mcg)	Cumulative Amount (mcg)	Cumulative Amount (mcg)
10	1.82	4.12	3.03
20	3.94	8.39	7.86
30	5.87	12.21	15.16
40	7.85	16.33	21.57
50	11.31	20.35	31.49
60	15.34	28.70	38.65
70	18.15	37.95	49.62
80	23.44	44.88	64.53
90	27.13	51.33	77.76
100	31.21	58.88	85.43
110	36.31	62.62	92.42
120	39.44	77.77	101.00
130	44.32	85.97	108.50
140	46.90	96.67	115.00
150	54.14	104.86	122.70
160	59.10	107.78	129.00
Steady-state Slope (70-160 min)	0.4392	0.8304	0.8397
r^2	0.9948	0.9874	0.9822
Jss (mcg/min.cm^2)	0.2268	0.3931	0.4124
Membrane Thickness (mm.)	0.3080	0.2980	0.3600
Normalized Jss x10^3 (mcg/min.cm^2)	207.70	348.20	441.60

$$Jss = 332.50 \pm 177.10$$

$$\%cv = 35.40$$



Diclofenac Sodium Flux from Saturated Diclofenac Sodium Solution through Newborn Pig Skin.

Enhancer: 0.05 mg/ml Tween 20 in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.560	1.010	1.890	2.798	3.956	4.796

$$Y = 0.0399 + 3.811x$$

$$r^2 = 0.9980$$

Diffusion Run Data

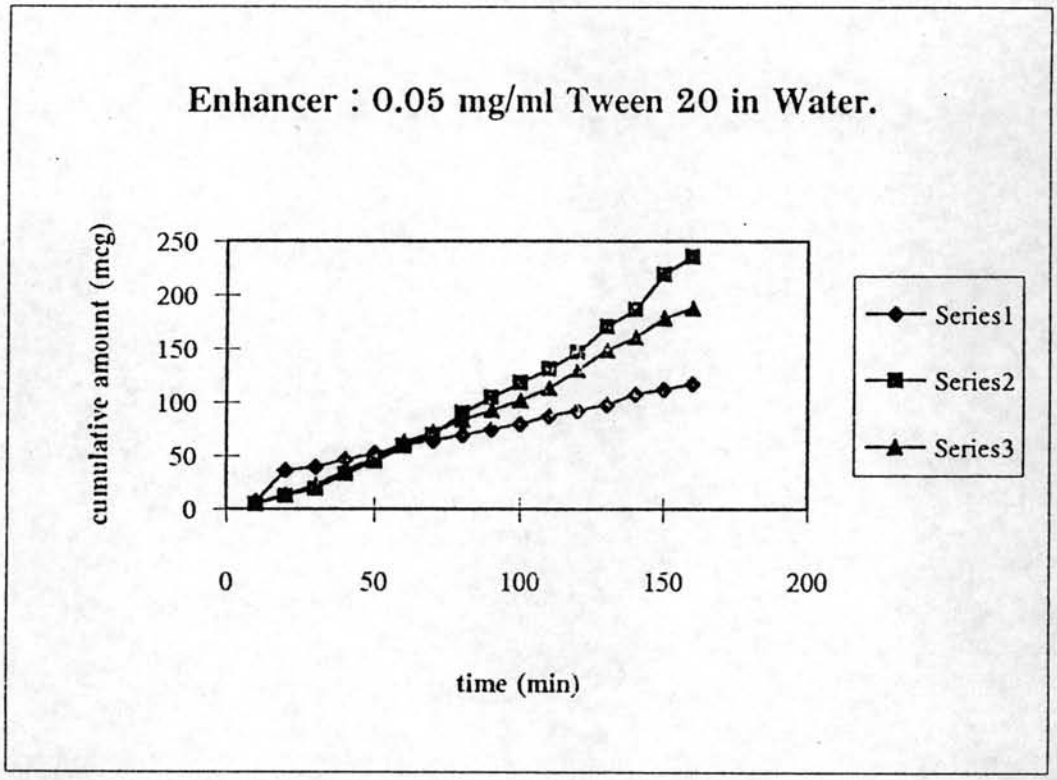
Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)
10	2.151	6.922	1.385	4.446	1.783	5.716
20	8.845	28.870	2.523	8.208	2.582	8.336
30	1.202	3.810	2.004	6.492	2.517	8.123
40	2.249	7.244	4.152	13.590	4.403	14.300
50	1.673	5.355	3.689	12.060	3.754	12.180
60	2.260	7.280	4.323	14.150	4.385	14.240
70	1.423	4.535	3.343	10.910	2.842	9.189
80	1.675	5.361	6.129	20.120	3.566	11.560
90	1.729	5.539	4.447	14.560	2.743	8.864
100	1.616	5.168	4.042	13.220	2.873	9.290
110	2.225	7.165	4.181	13.680	3.595	11.560
120	1.702	5.450	4.645	15.220	5.322	17.320
130	1.583	5.060	7.524	24.740	5.635	18.340
140	3.034	9.818	4.707	15.420	3.923	12.730
150	1.417	4.515	9.959	32.780	5.353	17.420
160	1.731	5.545	5.116	16.770	2.779	9.048
Receptor Volume (ml)	12.50		12.60		12.50	

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mcg)	Cumulative Amount (mcg)	Cumulative Amount (mcg)
10	6.92	4.44	5.71
20	35.79	12.65	14.05
30	39.60	19.14	22.17
40	46.84	32.73	36.48
50	52.19	44.80	48.66
60	59.47	58.95	62.91
70	64.00	69.87	72.10
80	69.36	90.00	83.66
90	74.89	104.50	92.52
100	80.05	117.80	101.80
110	87.21	131.40	113.30
120	92.66	146.70	130.60
130	97.72	171.40	149.00
140	107.50	186.80	161.70
150	112.00	219.60	179.20
160	117.50	236.40	188.30
Steady-state Slope (70-160 min)	0.6069	1.8140	1.3450
r^2	0.9966	0.9860	0.9893
Jss (mcg/min.cm^2)	0.2981	0.8910	0.6606
Membrane Thickness (mm.)	0.3660	0.4050	0.3570
Normalized Jss x10^3 (mcg/min.cm^2)	324.60	1073.60	701.50

Jss = 699.90 ± 374.50

%cv = 53.50



Diclofenac Sodium Flux from Saturated Diclofenac Sodium Solution through Newborn Pig Skin.

Enhancer: 0.4% w/v Brij 35 in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.615	1.069	2.042	2.971	3.796	4.905

$$Y = 0.1365 + 3.762x$$

$$r^2 = 0.9988$$

Diffusion Run Data

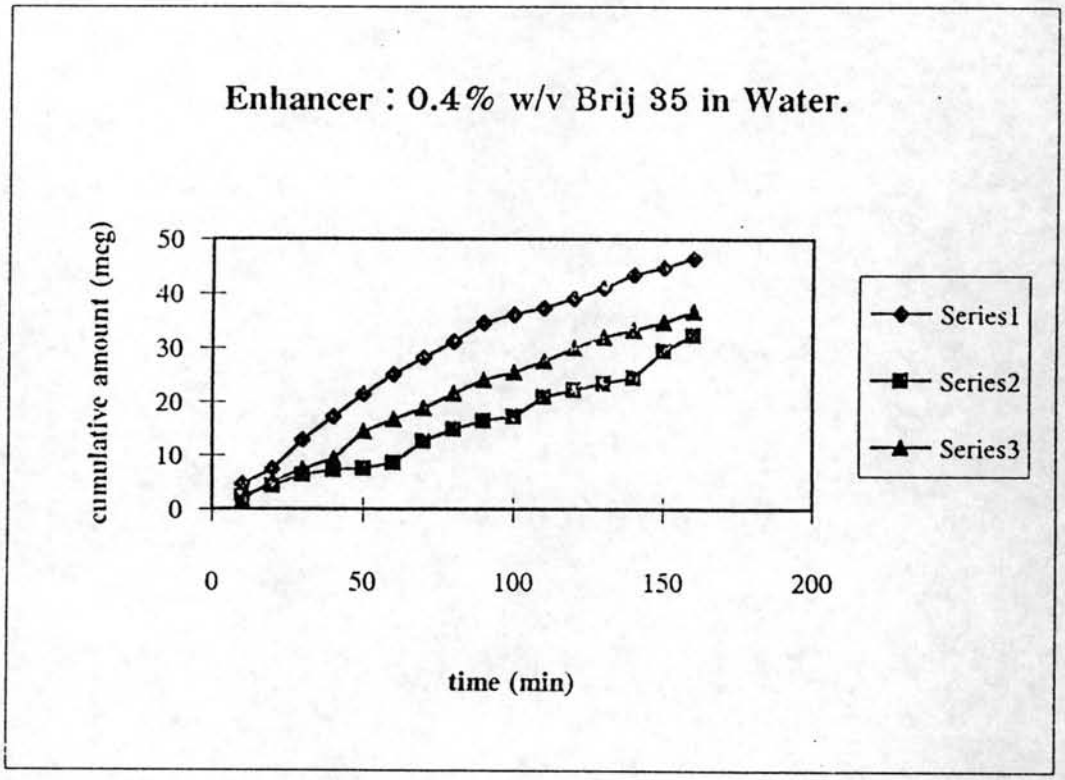
Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)
10	1.558	4.722	0.908	2.604	0.624	1.632
20	0.967	2.759	0.623	1.642	1.191	3.531
30	1.771	5.430	0.792	2.212	0.835	2.339
40	1.422	4.270	0.374	0.801	0.708	1.914
50	1.420	4.264	0.236	0.336	1.658	5.095
60	1.238	3.659	0.436	1.011	0.810	2.255
70	1.053	3.044	1.354	4.109	0.759	2.084
80	1.058	3.061	0.782	2.179	0.959	2.754
90	1.147	3.357	0.612	1.605	0.860	2.423
100	0.610	1.573	0.364	0.767	0.564	1.431
110	0.505	1.224	1.228	3.684	0.775	2.138
120	0.631	1.642	0.509	1.257	0.873	2.466
130	0.757	2.061	0.467	1.115	0.729	1.984
140	0.875	2.453	0.449	1.054	0.511	1.254
150	0.538	1.333	1.644	5.088	0.576	1.472
160	0.637	1.662	0.989	2.877	0.713	1.930
Receptor Volume (ml)	12.50		12.70		12.60	

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mcg)	Cumulative Amount (mcg)	Cumulative Amount (mcg)
10	4.72	2.60	1.63
20	7.48	4.24	5.16
30	12.91	6.45	7.50
40	17.18	7.25	9.41
50	21.44	7.59	14.51
60	25.10	8.60	16.76
70	28.14	12.71	18.85
80	31.20	14.89	21.60
90	34.55	16.49	24.02
100	36.12	17.26	25.45
110	37.34	20.95	27.59
120	38.98	22.20	30.06
130	41.04	23.32	32.04
140	43.49	24.37	33.30
150	44.82	29.46	34.77
160	46.48	32.34	36.70
Steady-state Slope (70-160 min)	0.1948	0.2045	0.1948
r^2	0.9861	0.9664	0.9927
Jss (mcg/min.cm^2)	0.0956	0.0968	0.0956
Membrane Thickness (mm.)	0.4080	0.3260	0.2970
Normalized Jss x10^3 (mcg/min.cm^2)	116.20	93.89	84.41

$$Jss = 98.16 \pm 16.32$$

$$\%cv = 16.62$$



Diclofenac Sodium Flux from Saturated Diclofenac Sodium Solution through Newborn Pig Skin.

Enhancer: 1% w/v Brij 35 in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.566	0.972	1.797	2.799	3.677	4.761

$$Y = 0.0311 + 3.712x$$

$$r^2 = 0.9980$$

Diffusion Run Data

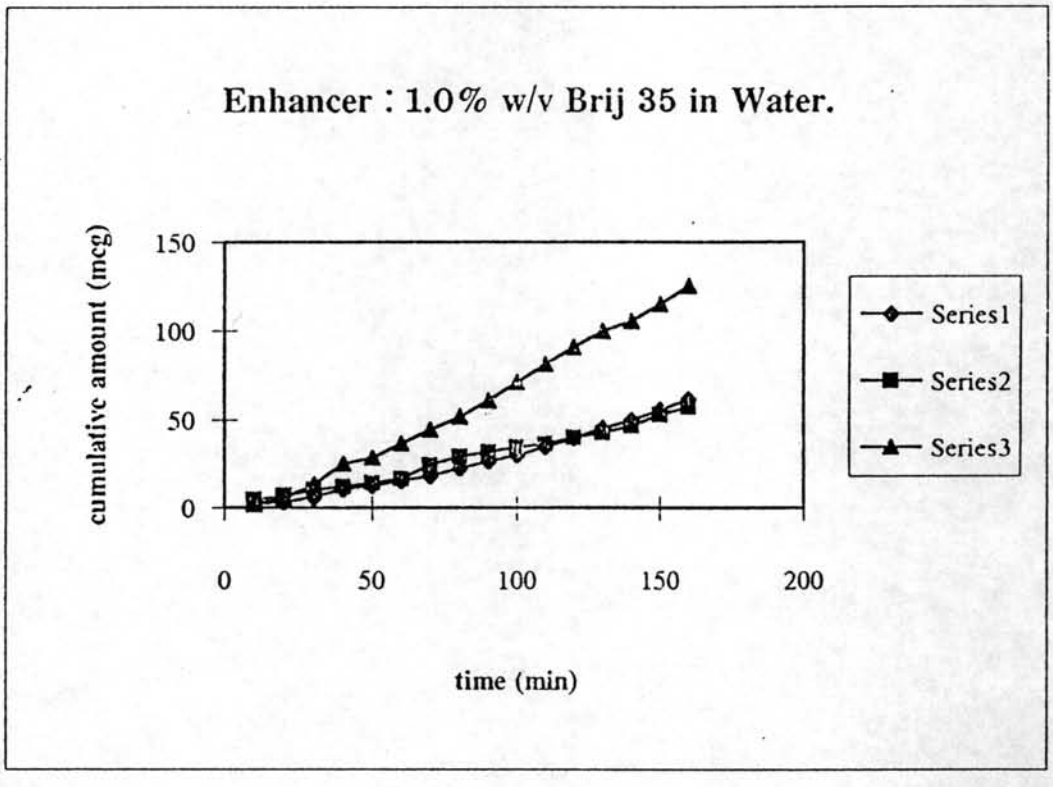
Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)
10	0.627	1.958	1.290	4.272	0.612	1.987
20	0.427	1.301	0.798	2.602	0.983	3.256
30	0.852	2.697	0.904	2.962	2.307	7.785
40	1.372	4.406	0.649	2.097	3.346	11.34
50	0.649	2.030	0.607	1.954	1.070	3.554
60	0.875	2.773	0.685	2.219	2.459	8.306
70	0.876	2.776	2.366	7.924	2.366	7.986
80	1.350	4.334	1.446	4.802	2.227	7.512
90	1.145	3.660	0.852	2.786	2.777	9.393
100	1.145	3.660	0.813	2.653	2.960	10.010
110	1.504	4.840	0.708	2.297	3.014	10.200
120	1.609	5.185	1.045	3.441	2.879	9.742
130	1.793	5.790	0.884	2.894	2.638	8.918
140	1.383	4.442	1.146	3.784	1.650	5.538
150	1.790	5.780	1.843	6.419	2.912	9.855
160	1.862	6.017	1.344	4.456	3.003	10.16
Receptor Volume (ml)	12.20		12.60		12.70	

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mcg)	Cumulative Amount (mcg)	Cumulative Amount (mcg)
10	1.95	4.27	1.98
20	3.25	6.87	5.24
30	5.95	9.83	13.02
40	10.36	11.93	24.36
50	12.39	13.88	27.92
60	15.16	16.09	36.22
70	17.94	24.01	44.21
80	22.27	28.81	51.72
90	25.93	31.59	61.12
100	29.59	34.24	71.13
110	34.43	36.53	81.34
120	39.62	39.97	91.08
130	45.41	42.86	100.00
140	49.85	46.64	105.50
150	55.63	53.05	115.30
160	61.64	57.50	125.50
Steady-state Slope (70-160 min)	0.4842	0.3488	0.9060
r^2	0.9942	0.9812	0.9978
Jss (mcg/min.cm^2)	0.2501	0.1671	0.4288
Membrane Thickness (mm.)	0.3100	0.3140	0.3070
Normalized Jss x10^3 (mcg/min.cm^2)	230.60	156.00	391.40

Jss = 259.33 ± 120.30

%cv = 46.38



Diclofenac Sodium Flux from Saturated Diclofenac Sodium Solution through Newborn Pig Skin.

Enhancer: 10% w/v Propylene Glycol in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.566	0.972	1.797	2.799	3.677	4.761

$$Y = 0.311 + 3.712x$$

$$r^2 = 0.9980$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)
10	1.110	36.620	1.026	33.490	0.816	26.430
20	1.116	36.820	0.828	26.830	0.563	17.910
30	1.083	35.700	1.175	38.510	0.382	11.810
40	1.112	36.680	1.127	36.900	0.816	26.430
50	1.067	35.160	1.504	49.590	0.409	12.720
60	1.181	39.030	1.244	40.840	0.987	32.180
70	0.941	30.880	1.388	45.680	0.694	22.320
80	1.120	36.960	1.240	40.700	0.518	16.390
90	0.895	29.320	1.164	38.140	0.363	11.170
100	1.417	47.040	1.830	60.570	0.450	14.100
110	1.261	41.740	1.577	52.050	0.699	22.490
120	1.038	34.170	2.006	66.490	0.890	28.920
130	0.999	32.850	1.742	57.600	0.396	12.290
140	1.103	36.380	2.199	72.990	1.923	63.700
150	1.234	40.830	1.496	49.320	0.899	29.220
160	1.093	36.040	1.213	39.790	0.538	17.060
Receptor Volume (ml)	12.60		12.50		12.500	

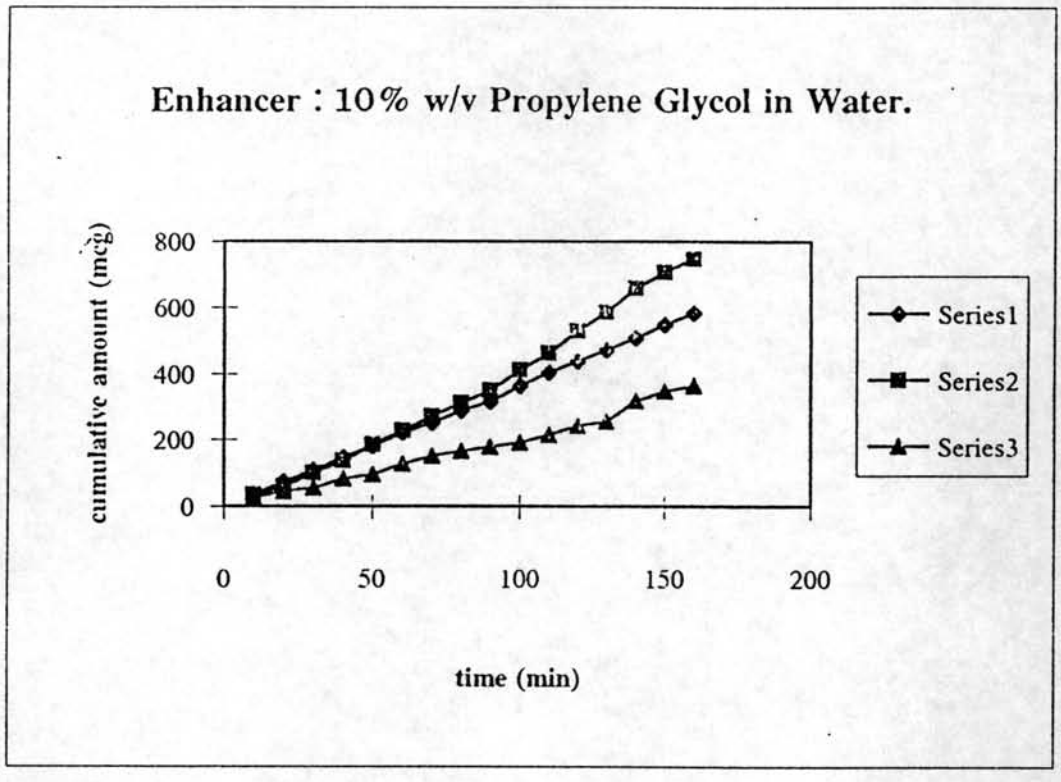
dilution factor: 10

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mcg)	Cumulative Amount (mcg)	Cumulative Amount (mcg)
10	36.62	33.49	26.43
20	73.44	60.32	44.34
30	109.10	98.83	56.15
40	145.80	135.70	82.58
50	180.90	185.30	95.30
60	220.00	226.10	127.40
70	250.80	271.70	149.80
80	287.80	312.40	166.20
90	317.10	350.50	177.30
100	364.20	411.10	191.40
110	405.90	463.10	213.40
120	440.10	529.60	242.20
130	472.90	587.20	255.10
140	509.30	660.20	318.80
150	550.10	709.50	348.00
160	586.20	749.20	365.10
Steady-state Slope (70-160 min)	3.743	5.588	2.507
r^2	0.9989	0.9952	0.9560
Jss (mcg/min.cm^2)	1.838	2.744	1.231
Membrane Thickness (mm.)	0.3140	0.3160	0.3570
Normalized Jss x10^3 (mcg/min.cm^2)	1716.60	2579.30	1307.30

Jss = 1867.73 ± 649.30

%cv = 34.76



Diclofenac Sodium Flux from Saturated Diclofenac Sodium Solution through Newborn Pig Skin.

Enhancer: 10% w/v Tetraglycol in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.566	1.273	2.011	3.071	3.874	4.853

$$Y = 2.081 + 3.715x$$

$$r^2 = 0.9968$$

Diffusion Run Data

Diffusion Run	Run I[a]		Run II[a]		Run III	
Time (min)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)
10	1.025	27.690	0.870	22.260	5.970	19.380
20	1.393	40.170	1.139	31.310	5.200	16.790
30	1.920	58.040	1.421	40.790	6.650	21.670
40	1.450	42.100	0.986	26.160	4.990	16.080
50	1.606	47.390	0.991	26.330	5.280	17.060
60	1.428	41.360	0.916	23.810	3.090	9.690
70	1.639	48.510	0.837	21.150	3.080	9.660
80	1.457	42.340	0.839	21.220	3.520	11.140
90	1.838	55.260	0.825	20.740	3.120	9.790
100	1.499	43.770	0.706	16.740	2.720	8.440
110	1.491	43.490	0.703	16.640	3.490	11.040
120	1.414	40.8880	0.728	17.480	1.880	5.620
130	1.563	45.940	0.584	12.640	2.100	6.360
140	1.502	43.870	0.708	16.810	3.250	10.230
150	1.288	36.610	0.632	14.250	1.900	5.690
160	1.251	35.360	0.658	15.130	2.440	7.500
Receptor Volume (ml)	12.60		12.50		12.50	

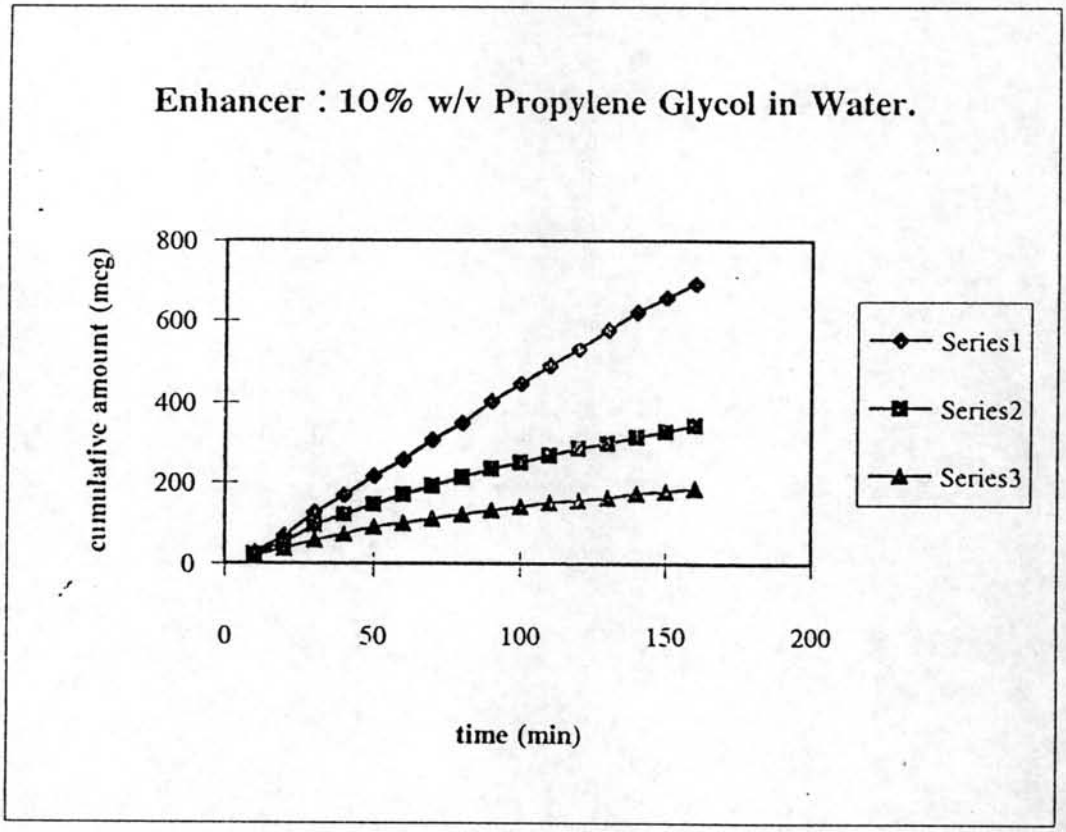
a: dilution factor = 10

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mcg)	Cumulative Amount (mcg)	Cumulative Amount (mcg)
10	27.69	22.26	19.38
20	67.87	53.57	36.17
30	125.90	94.36	57.84
40	168.00	120.50	73.92
50	215.40	146.80	90.99
60	256.70	170.60	100.90
70	305.30	191.70	110.60
80	347.60	212.90	121.70
90	402.90	233.60	131.50
100	446.60	250.30	139.90
110	490.10	266.90	151.00
120	531.00	284.30	156.60
130	577.00	296.90	163.00
140	620.80	313.70	173.20
150	657.40	327.90	178.90
160	692.80	343.00	186.40
Steady-state Slope (70-160 min)	4.350	1.651	0.8278
r^2	0.9980	0.9957	0.9932
Jss (mcg/min.cm^2)	2.136	0.8109	0.4066
Membrane Thickness (mm.)	0.0350	0.3180	0.3640
Normalized Jss x10^3 (mcg/min.cm^2)	1937.30	767.10	404.30

Jss = 1036.23 $\pm$ 801.10

%cv = 77.31



Diclofenac Sodium Flux from Saturated Diclofenac Sodium Solution through Newborn Pig Skin.

Enhancer: Ethanol.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.778	1.065	1.844	2.622	3.304	4.035

$$Y = 0.382 + 2.930x$$

$$r^2 = 0.9993$$

Diffusion Run Data

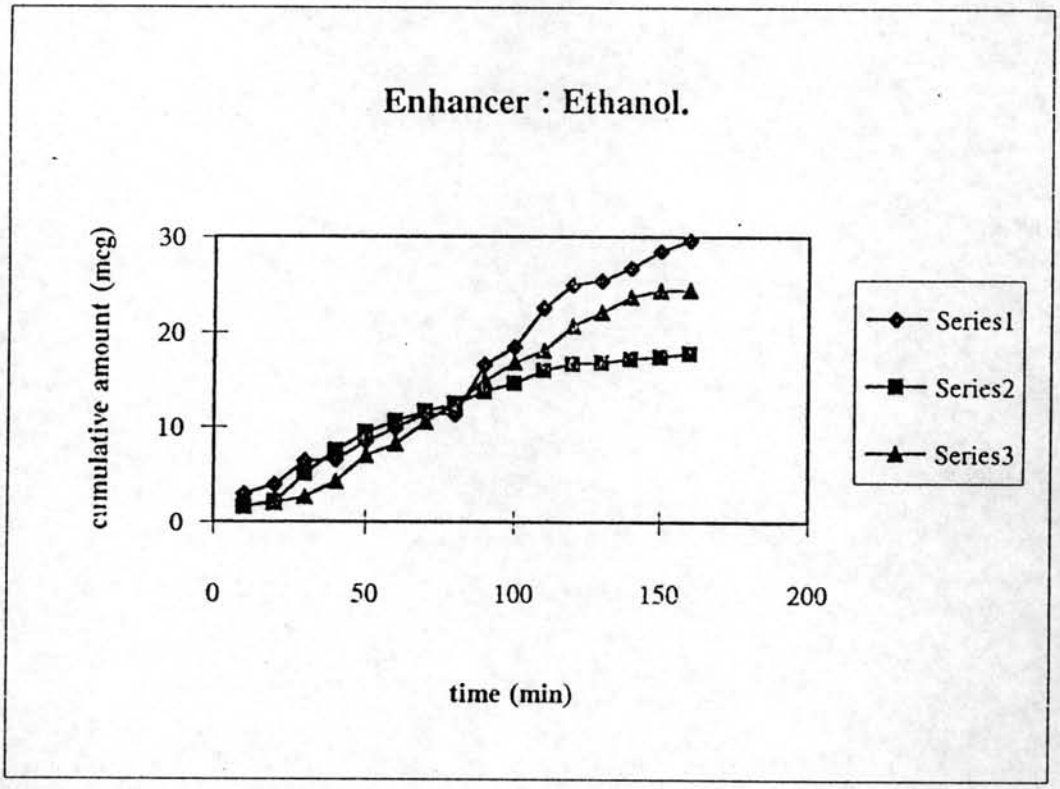
Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)
10	1.096	2.972	0.766	1.663	0.766	1.650
20	0.607	0.936	0.494	0.485	0.472	0.386
30	0.981	2.493	1.060	2.937	0.534	0.653
40	0.413	0.128	0.945	2.439	0.764	1.642
50	0.845	1.927	0.830	1.941	0.994	2.630
60	0.720	1.406	0.653	1.174	0.687	1.310
70	0.748	1.523	0.622	1.039	0.912	2.278
80	0.916	2.222	0.564	0.788	0.830	1.925
90	1.085	2.926	0.680	1.291	0.943	2.411
100	0.827	1.852	0.589	0.996	0.817	1.870
110	1.366	4.096	0.683	1.304	0.691	1.328
120	0.967	2.435	0.543	0.697	0.985	2.592
130	0.484	0.424	0.407	0.107	0.709	1.405
140	0.773	1.627	0.475	0.402	0.749	1.577
150	0.755	1.552	0.441	0.255	0.527	0.623
160	0.658	1.148	0.459	0.328	0.406	0.102
Receptor Volume (ml)	12.20		12.70		12.60	

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mcg)	Cumulative Amount (mcg)	Cumulative Amount (mcg)
10	2.97	1.66	1.65
20	3.90	2.14	2.03
30	6.40	5.08	2.68
40	6.52	7.52	4.33
50	8.45	9.46	6.96
60	9.86	10.63	8.27
70	11.38	11.67	10.54
80	13.60	12.46	12.47
90	16.53	13.75	14.88
100	18.38	14.65	16.75
110	22.48	15.95	18.08
120	24.91	16.65	20.67
130	25.34	16.76	22.08
140	26.67	17.16	23.65
150	28.51	17.41	24.28
160	29.66	17.74	24.38
Steady-state Slope (70-160 min)	0.2078	0.0687	0.1634
r^2	0.9670	0.9235	0.9693
Jss (mcg/min.cm^2)	0.1063	0.0325	0.0802
Membrane Thickness (mm.)	0.2350	0.3080	0.3210
Normalized Jss x10^3 (mcg/min.cm^2)	74.30	29.77	76.59

Jss = 60.22 ± 26.39

%cv = 43.83



Diclofenac Sodium Flux from Saturated Diclofenac Sodium Solution through Newborn Pig Skin.

Enhancer: Isopropyl Alcohol.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.369	0.894	1.715	2.632	3.595	4.447

$$Y = -0.0605 + 3.616X$$

$$r^2 = 0.9995$$

Diffusion Run Data

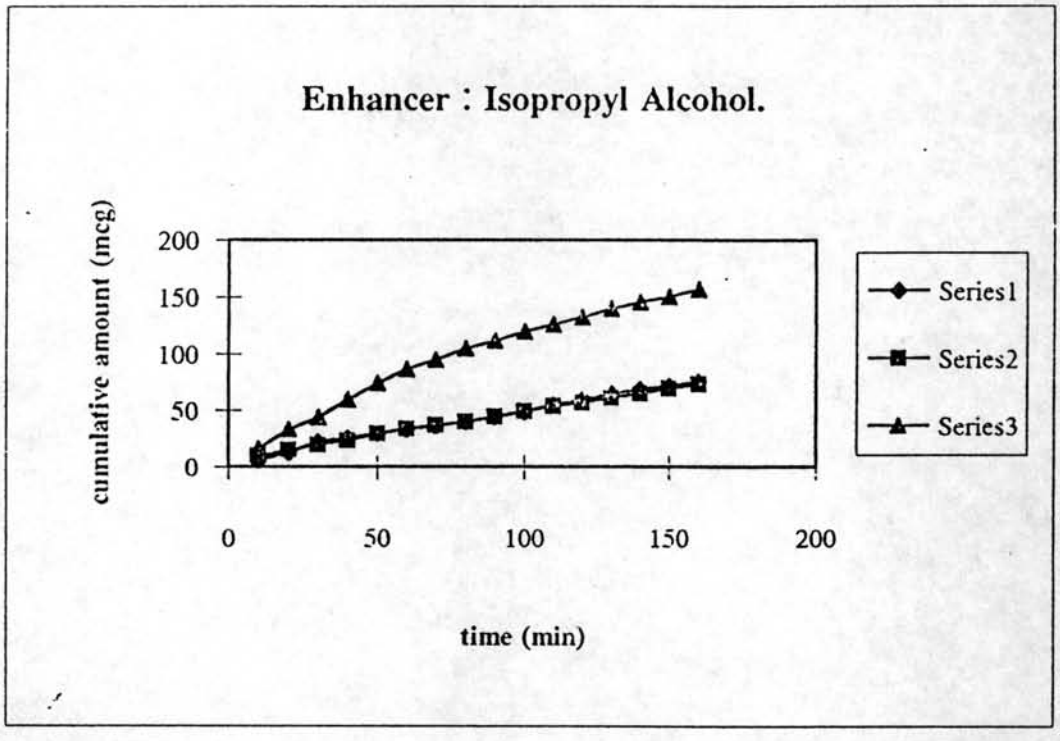
Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)
10	1.460	5.336	2.681	9.525	4.541	15.900
20	2.058	7.425	1.468	5.322	4.940	17.280
30	2.677	9.587	1.261	4.605	3.027	10.670
40	0.889	3.342	1.034	3.818	4.540	15.890
50	0.952	3.562	1.632	5.890	4.010	14.060
60	1.038	3.862	1.249	4.563	3.544	12.450
70	0.950	3.555	0.887	3.309	2.385	8.358
80	0.949	3.552	0.884	3.160	2.914	10.280
90	1.171	4.327	1.171	4.293	2.010	7.155
100	1.245	4.585	1.418	5.149	2.255	8.002
110	1.672	6.077	1.204	4.407	1.797	6.419
120	1.098	4.072	0.843	3.156	1.653	5.922
130	1.596	5.811	1.125	4.134	2.149	7.636
140	1.130	4.184	1.110	4.081	1.609	5.770
150	0.987	3.684	1.210	4.428	1.308	4.729
160	0.844	3.185	1.020	3.770	1.858	6.630
Receptor Volume (ml)	12.70		12.60		12.50	

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mcg)	Cumulative Amount (mcg)	Cumulative Amount (mcg)
10	5.33	9.52	15.90
20	12.76	14.84	33.18
30	22.34	19.45	43.85
40	25.69	23.27	59.74
50	29.25	29.16	73.80
60	33.11	33.72	86.25
70	36.66	37.03	94.60
80	40.22	40.19	104.80
90	44.54	44.48	111.90
100	49.13	49.63	119.90
110	55.21	54.04	126.30
120	59.28	57.19	132.20
130	65.09	61.33	139.80
140	69.27	65.41	145.50
150	72.16	69.84	150.20
160	76.14	73.61	156.80
Steady-state Slope (70-160 min)	0.4572	0.4119	0.6734
r^2	0.9956	0.9987	0.9934
Jss (mcg/min.cm^2)	0.2164	0.2023	0.3307
Membrane Thickness (mm.)	0.3700	0.3010	0.2660
Normalized Jss x10^3 (mcg/min.cm^2)	238.20	181.00	261.50

$Jss = 226.90 \pm 41.42$

%cv = 18.25



Diclofenac Sodium Flux from Saturated Diclofenac Sodium Solution through Newborn Pig Skin.

Enhancer: 1% w/v Orange oil in Ethanol.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.778	1.065	1.844	2.622	3.304	4.035

$$Y = 0.382 + 2.930x$$

$$r^2 = 0.9993$$

Diffusion Run Data

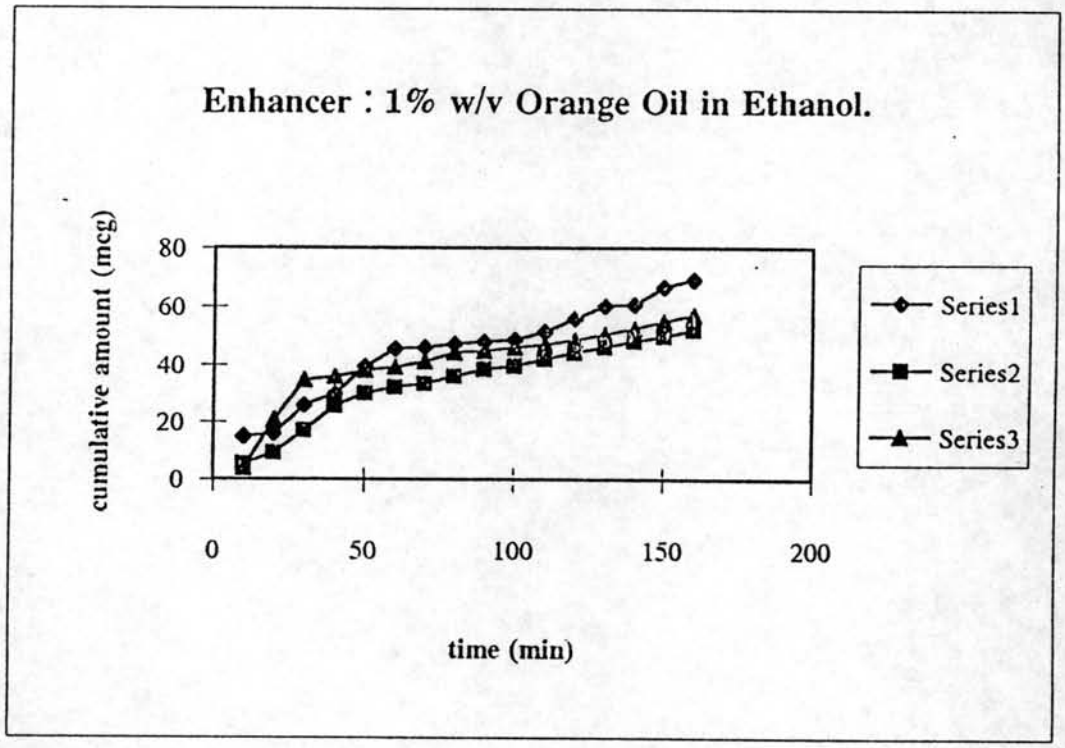
Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)
10	3.823	14.790	1.647	5.395	1.269	3.783
20	0.613	0.992	1.298	3.906	4.364	16.98
30	3.117	11.750	2.190	7.711	3.590	13.68
40	0.873	2.110	2.390	8.564	0.674	1.245
50	2.633	9.678	1.388	4.290	0.936	2.362
60	1.783	6.023	0.919	2.290	0.644	1.117
70	0.496	0.489	0.635	1.078	0.815	1.846
80	0.705	1.388	1.040	2.806	1.164	3.335
90	0.515	0.571	0.945	2.401	0.485	0.438
100	0.567	0.794	0.638	1.091	0.655	1.164
110	1.003	2.669	0.955	2.443	0.628	1.048
120	1.440	4.548	0.891	2.170	0.748	1.560
130	1.424	4.479	0.856	2.021	0.869	2.077
140	0.500	0.506	0.832	1.919	0.807	1.812
150	1.789	6.049	0.809	1.820	0.966	2.490
160	0.930	2.355	0.866	2.064	0.902	2.217
Receptor Volume (ml)	12.60		12.50		12.50	

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mcg)	Cumulative Amount (mcg)	Cumulative Amount (mcg)
10	14.79	5.39	3.78
20	15.78	9.30	20.76
30	27.54	17.01	34.45
40	29.65	25.57	35.69
50	39.33	29.86	38.05
60	45.35	32.15	39.17
70	45.84	33.23	41.02
80	47.23	36.04	44.35
90	47.80	38.44	44.79
100	48.59	39.53	45.95
110	51.26	41.97	47.00
120	55.81	44.14	48.56
130	60.29	46.16	50.64
140	60.80	48.05	52.45
150	66.85	49.90	54.94
160	69.20	51.96	57.16
Steady-state Slope (70-160 min)	0.2740	0.2034	0.1656
r^2	0.9473	0.9972	0.9757
Jss (mcg/min.cm^2)	0.1345	0.0991	0.0813
Membrane Thickness (mm.)	0.3550	0.3850	0.3920
Normalized Jss x10^3 (mcg/min.cm^2)	142.00	113.40	94.79

$$Jss = 116.73 \pm 23.78$$

$$\%cv = 20.37$$



Diclofenac Sodium Flux from Saturated Diclofenac Sodium Solution through Newborn Pig Skin.

APPENDIX IV

Fluxes of Diclofenac Sodium from Its Saturated Solution Through Human Amnion.

Enhancer: Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.219	0.992	1.975	3.426	3.860	4.815

$$Y = -0.060 + 4.038x$$

$$r^2 = 0.9906$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	3.217	1.980	1.786	1.472	1.871	1.205
10	2.291	1.420	2.249	1.841	2.101	1.348
15	1.218	0.772	1.312	1.094	1.266	0.827
20	3.027	1.865	2.784	2.267	1.379	0.898
25	2.274	1.410	2.748	2.239	1.322	0.862
30	1.575	0.988	1.389	1.155	1.836	1.183
35	1.044	0.667	1.440	1.196	1.579	1.022
40	1.254	0.794	1.566	1.296	1.218	0.797
45	1.377	0.868	2.658	2.167	2.877	1.832
50	2.578	1.594	3.278	2.661	2.526	1.613
55	3.779	2.319	3.898	3.156	2.176	1.395
60	1.969	1.226	5.525	4.453	2.573	1.643
65	4.531	2.774	3.710	3.006	2.779	1.771
70	2.763	1.705	3.129	2.543	3.752	2.378
75	2.404	1.488	3.655	2.962	2.732	1.742
80	2.988	1.841	3.402	2.760	1.997	1.283
Receptor Volume (ml)	12.20		16.10		12.60	

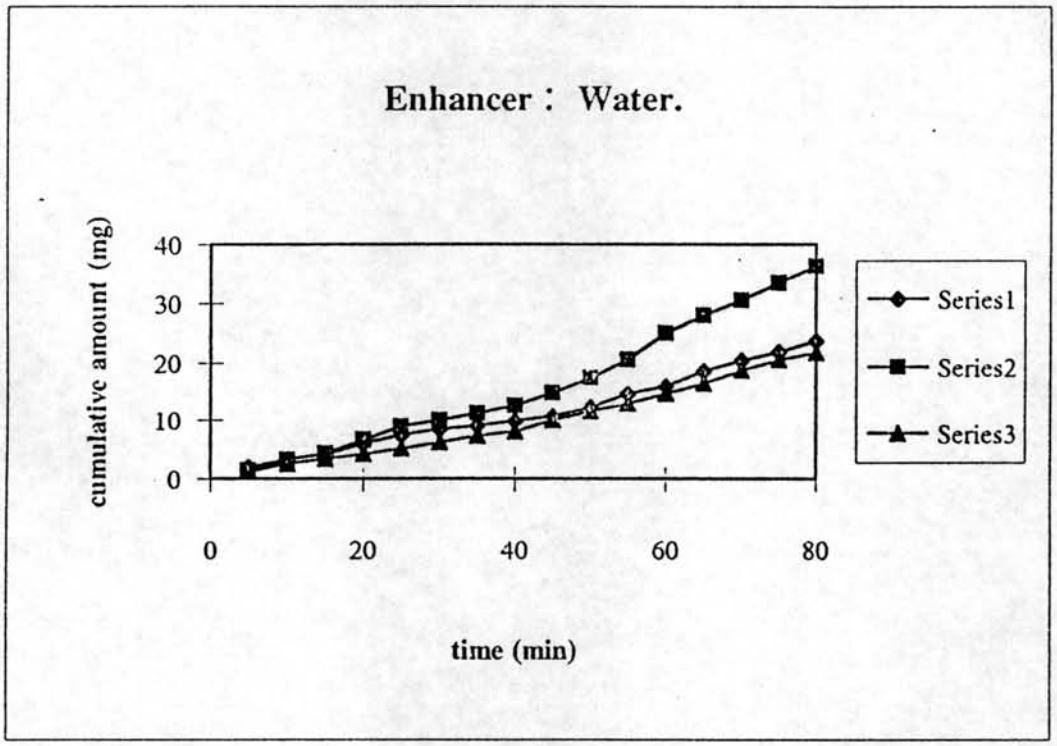
dilution factor: 200

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	1.98	1.47	1.20
10	3.40	3.31	2.55
15	4.17	4.40	3.38
20	6.03	6.67	4.27
25	7.44	8.91	5.14
30	8.43	10.07	6.32
35	9.10	11.27	7.34
40	9.89	12.56	8.14
45	10.76	14.73	9.97
50	12.35	17.39	11.58
55	14.67	20.55	12.98
60	15.90	25.01	14.62
65	18.67	28.01	16.39
70	20.38	30.56	18.77
75	21.87	33.52	20.51
80	23.71	36.28	21.79
Steady-state Slope (35-80 min)	0.3437	0.5906	0.3353
r^2	0.9870	0.9913	0.9944
Jss ($mg/min.cm^2$)	0.1775	0.2901	0.1606
Membrane Thickness (mm.)	0.0550	0.0550	0.0890
Normalized Jss $x10^3$ ($mg/min.cm^2$)	168.20	275.00	246.30

$$Jss = 229.83 \pm 55.24$$

$$\%cv = 24.03$$



Diclofenac Sodium Flux from Saturated Diclofenac Sodium Solution through Human Amnion.

Enhancer: 0.01 mg/ml Tween 20 in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.566	1.273	2.011	3.071	3.874	4.853

$$Y = 0.2081 + 3.715x$$

$$r^2 = 0.9968$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	3.034	1.855	3.163	2.020	2.557	1.593
10	3.106	1.903	2.704	1.706	3.669	2.347
15	3.122	1.913	1.955	1.194	3.651	2.335
20	3.106	1.903	2.238	1.387	3.781	2.423
25	3.466	2.139	2.675	1.686	2.985	1.883
30	2.975	1.817	2.064	1.268	3.201	2.029
35	2.928	1.786	2.202	1.362	2.991	1.887
40	2.951	1.801	1.815	1.098	3.427	2.183
45	2.996	1.830	2.124	1.309	3.067	1.938
50	2.319	1.386	1.949	1.190	2.594	1.618
55	2.540	1.531	1.685	1.009	2.291	1.412
60	1.978	1.162	1.964	1.200	2.319	1.431
65	2.417	1.450	1.617	0.963	2.347	1.450
70	2.476	1.489	1.431	0.836	2.260	1.391
75	2.952	1.801	1.771	1.068	2.352	1.453
80	2.394	1.435	1.678	1.004	1.869	1.126
Receptor Volume (ml)	12.20		12.70		12.60	

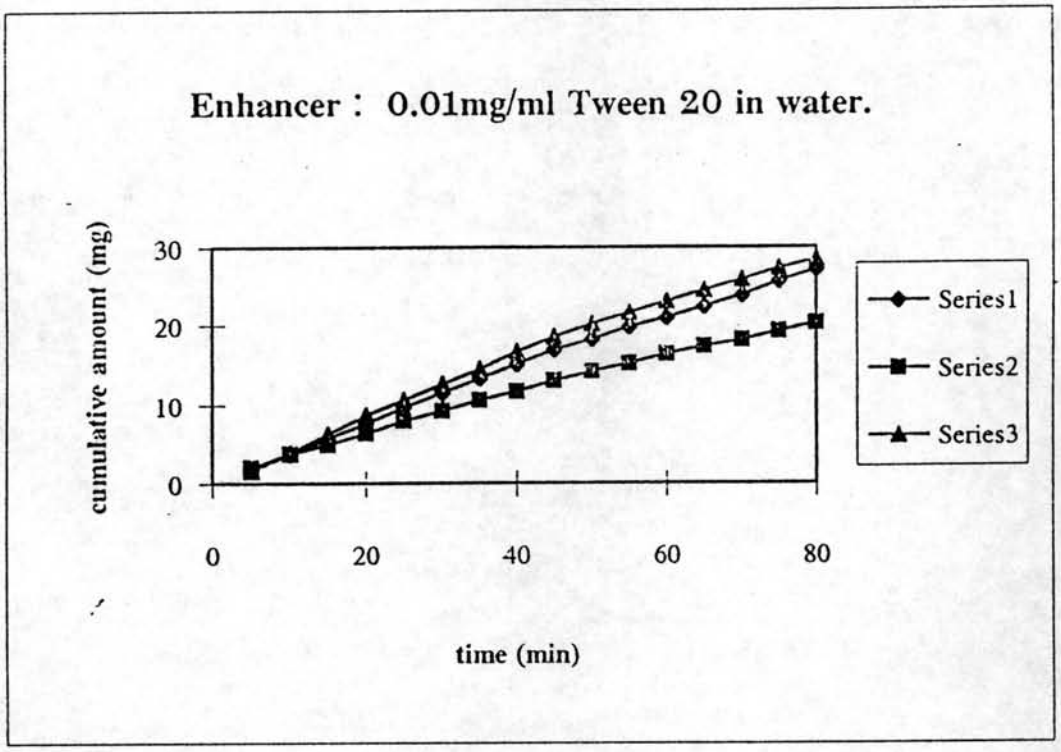
dilution factor: 200

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	1.85	2.02	1.59
10	3.75	3.72	3.94
15	5.67	4.92	6.27
20	7.57	6.30	8.69
25	9.71	7.99	10.58
30	11.53	9.26	12.61
35	13.31	10.62	14.49
40	15.11	11.72	16.68
45	16.94	13.03	18.61
50	18.33	14.22	20.23
55	19.86	15.22	21.64
60	21.02	16.42	23.07
65	22.47	17.39	24.52
70	23.96	18.22	25.92
75	25.76	19.29	27.37
80	27.20	20.30	28.49
Steady-state Slope (35-80 min)	0.3008	0.2142	0.3050
r^2	0.9979	0.9973	0.9936
Jss (mg/min.cm^2)	0.1553	0.1014	0.1498
Membrane Thickness (mm.)	0.1000	0.0920	0.1190
Normalized Jss x10^3 (mg/min.cm^2)	267.70	160.80	307.20

$$Jss = 245.23 \pm 75.74$$

$$\%cv = 30.88$$



Diclofenac Sodium Flux from Saturated Diclofenac Sodium Solution through Human Amnion.

Enhancer: 0.05 mg/ml Tween 20 in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.566	1.273	2.011	3.071	3.874	4.853

$$Y = 0.2081 + 3.715x$$

$$r^2 = 0.9968$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	3.634	2.304	3.078	1.946	2.767	1.721
10	4.436	2.844	3.380	2.151	3.591	3.997
15	4.393	2.815	4.086	2.630	3.089	5.935
20	2.911	1.818	3.167	2.006	2.593	7.539
25	3.924	2.499	3.732	2.389	2.672	9.196
30	3.563	2.257	3.829	2.455	3.042	11.100
35	3.980	2.537	3.453	2.200	2.372	12.550
40	3.330	2.100	3.345	2.127	2.788	14.990
45	3.400	2.147	3.358	2.136	2.915	16.110
50	2.951	1.845	2.546	1.585	2.521	17.660
55	2.834	1.766	2.718	1.702	3.147	19.640
60	2.921	1.825	2.667	1.667	2.192	20.980
65	2.617	1.620	3.082	1.949	2.669	22.630
70	3.273	2.061	2.597	1.620	2.558	24.210
75	2.586	1.599	2.344	1.448	2.360	25.660
80	2.887	1.802	1.835	1.103	2.143	26.960
Receptor Volume (ml)	12.50		12.60		12.50	

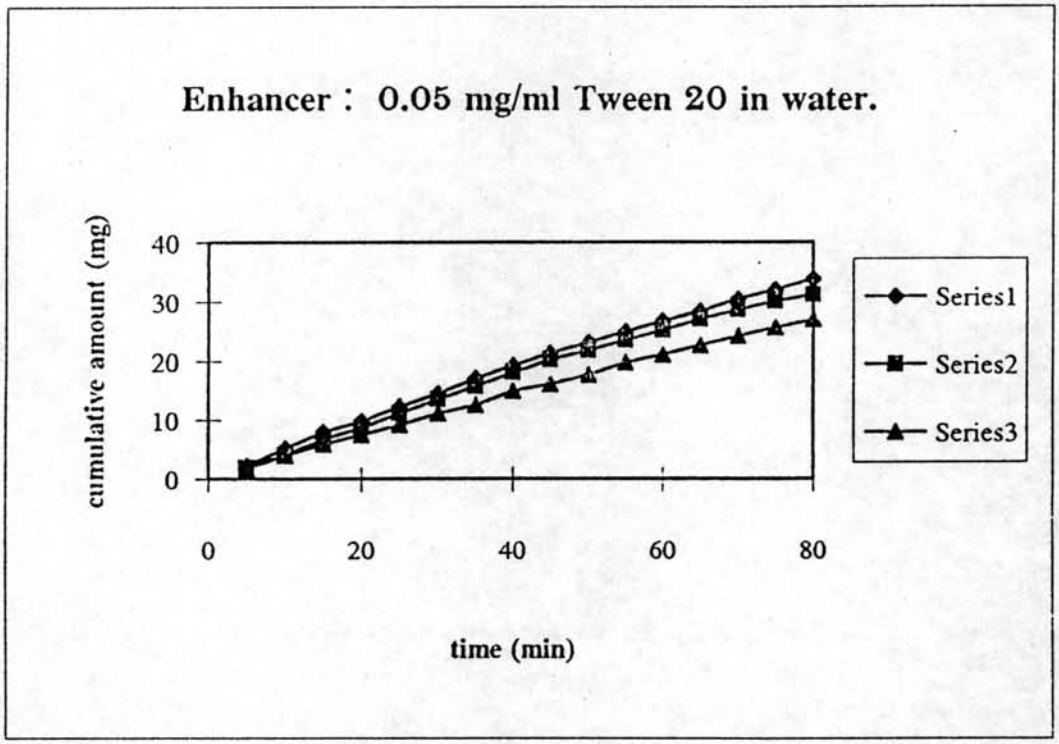
dilution factor: 200

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	2.30	1.94	1.72
10	5.14	4.09	3.99
15	7.96	6.72	5.93
20	9.78	8.73	7.53
25	12.28	11.12	9.19
30	14.53	13.57	11.10
35	17.06	15.77	12.55
40	19.16	17.99	14.99
45	21.30	20.13	16.11
50	23.14	21.71	17.66
55	24.90	23.41	19.64
60	26.72	25.08	20.98
65	28.34	27.03	22.63
70	30.40	28.65	24.21
75	31.99	30.10	25.66
80	33.79	31.20	26.96
Steady-state Slope (35-80 min)	0.3676	0.3440	0.3165
r^2	0.9988	0.9953	0.9971
Jss ($mg/min.cm^2$)	0.1805	0.1689	0.1554
Membrane Thickness (mm.)	0.0940	0.1000	0.1420
Normalized Jss $x10^3$ ($mg/min.cm^2$)	292.40	291.10	380.40

Jss = 321.30 + 51.18

%cv = 15.93



Diclofenac Sodium Flux from Saturated Diclofenac Sodium Solution through Human Amnion.

Enhancer: 0.4% w/v Brij 35 in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.497	0.963	1.900	2.766	3.832	4.685

$$Y = 0.225 + 3.743x$$

$$r^2 = 0.9993$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	0.697	1.373	1.252	2.586	1.054	2.186
10	1.065	2.123	1.242	2.565	0.949	1.964
15	1.150	2.296	0.907	1.860	0.941	1.947
20	1.335	2.672	0.996	2.047	1.174	2.441
25	1.025	2.041	0.946	1.942	1.159	2.409
30	0.879	1.744	0.846	1.732	0.796	1.639
35	1.195	2.387	1.422	2.943	0.900	1.860
40	0.869	1.723	0.785	1.477	0.817	1.684
45	0.842	1.668	0.657	1.334	0.940	1.945
50	0.595	1.165	0.979	2.011	1.110	2.307
55	0.775	1.532	0.882	1.807	0.994	2.059
60	0.625	1.226	0.546	1.101	0.812	1.673
65	0.552	1.078	0.536	1.080	0.730	1.499
70	0.883	1.752	0.898	1.841	1.255	2.612
75	0.774	1.530	0.547	1.103	0.733	1.506
80	0.664	1.306	0.641	1.300	0.518	1.050
Receptor Volume (ml)	12.20		12.60		12.70	

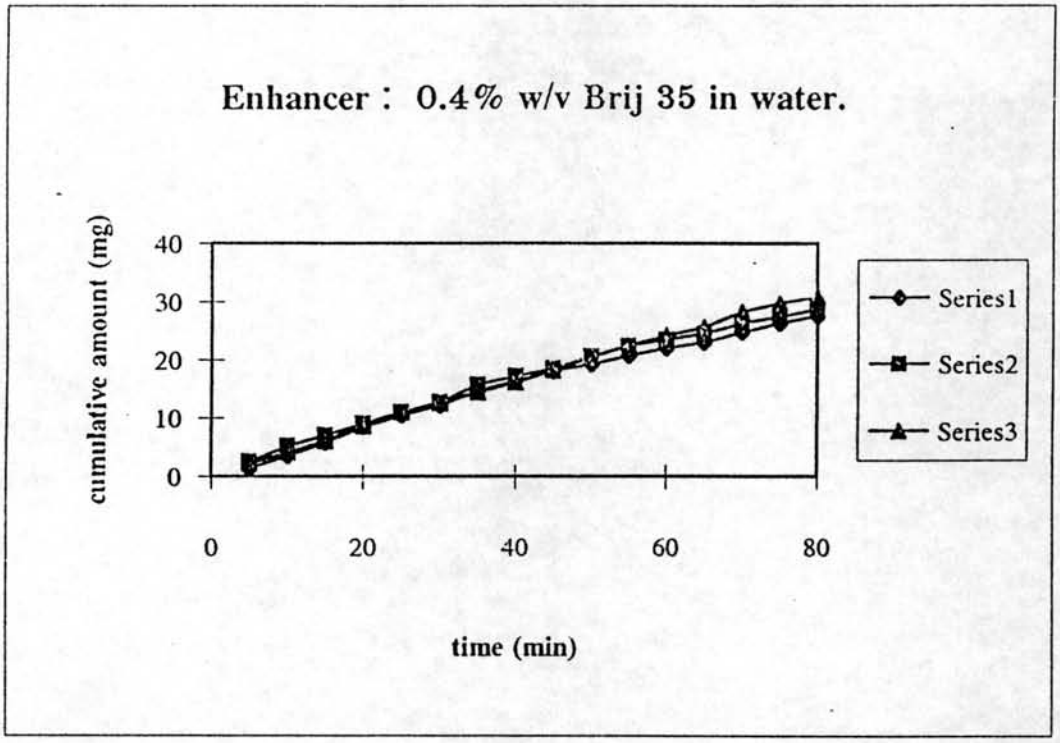
dilution factor: 625

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	1.37	2.58	2.18
10	3.49	5.15	4.15
15	5.79	7.01	6.09
20	8.46	9.05	8.53
25	10.50	11.00	10.94
30	12.24	12.73	12.58
35	14.63	15.67	14.44
40	16.35	17.15	16.13
45	18.02	18.48	18.07
50	19.19	20.49	20.38
55	20.72	22.30	22.44
60	21.95	23.40	24.11
65	23.02	24.48	25.61
70	24.78	26.32	28.22
75	26.31	27.42	29.73
80	27.61	28.72	30.78
Steady-state Slope (35-80 min)	0.2823	0.2929	0.3761
r^2	0.9980	0.9955	0.9960
Jss (mg/min.cm^2)	0.1458	0.1403	0.1780
Membrane Thickness (mm.)	0.0360	0.0390	0.0450
Normalized Jss x10^3 (mg/min.cm^2)	90.44	94.34	137.9

$$Jss = 107.56 \pm 26.34$$

$$\%cv = 24.53$$



Diclofenac Sodium Flux from Saturated Diclofenac Sodium Solution through Human Amnion.

Enhancer: 1% w/v Brij 35 in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.566	0.972	1.797	2.799	3.677	4.761

$$Y = 0.0311 + 3.712x$$

$$r^2 = 0.9980$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	2.419	1.569	3.177	2.135	3.015	1.987
10	2.476	1.606	3.139	2.109	3.465	2.219
15	2.684	1.743	3.816	2.569	3.451	2.210
20	2.215	1.435	3.499	2.354	3.342	2.140
25	3.151	2.050	3.145	2.133	3.655	2.342
30	2.584	1.677	3.922	2.641	3.338	2.137
35	2.295	1.487	3.597	2.413	3.421	2.191
40	2.383	1.545	3.830	2.578	3.632	2.327
45	2.374	1.534	3.846	2.589	2.571	1.642
50	2.064	1.336	2.912	1.955	3.243	2.076
55	2.790	1.813	3.090	2.076	3.248	2.079
60	2.508	1.627	2.320	1.553	3.179	2.035
65	2.179	1.411	2.036	1.360	2.326	1.438
70	1.948	1.259	2.027	1.354	2.737	1.749
75	1.946	1.258	1.626	1.082	2.910	1.861
80	2.049	1.326	2.246	1.571	2.973	1.901
Receptor Volume (ml)	12.20		12.60		12.70	

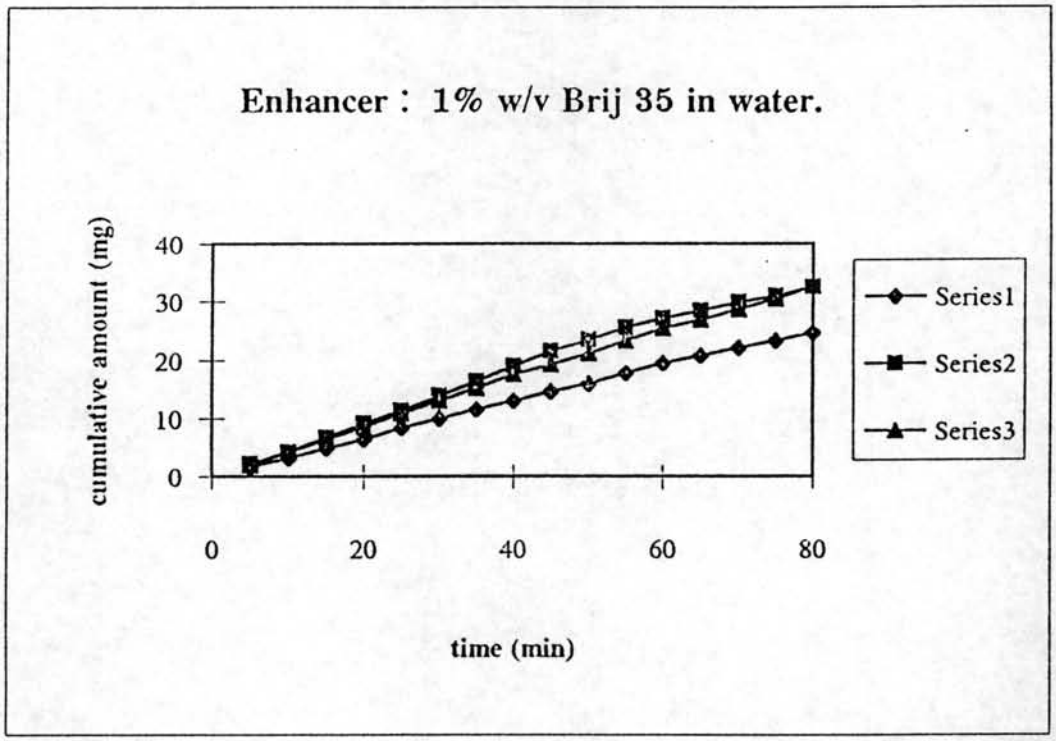
dilution factor: 200

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	1.56	2.35	1.98
10	3.17	4.24	4.20
15	4.92	6.81	6.41
20	6.35	9.16	8.55
25	8.40	11.30	10.90
30	10.08	13.94	13.03
35	11.57	16.35	15.23
40	13.11	18.92	17.55
45	14.65	21.51	19.20
50	15.99	23.46	21.20
55	17.80	25.54	23.35
60	19.43	27.09	25.39
65	20.84	28.45	26.87
70	22.10	29.80	28.62
75	23.36	30.88	30.48
80	24.69	32.45	32.68
Steady-state Slope (35-80 min)	0.2948	0.3473	0.3769
r^2	0.9978	0.9797	0.9985
Jss ($mg/min.cm^2$)	0.1522	0.1664	0.1784
Membrane Thickness (mm.)	0.0400	0.0720	0.0370
Normalized Jss $x10^3$ ($mg/min.cm^2$)	104.80	206.50	113.60

$Jss = 141.63 \pm 56.34$

$\%cv = 39.79$



Diclofenac Sodium Flux from Saturated Diclofenac Sodium Solution through Human Amnion.

Enhancer: 10% w/v Propylene Glycol in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.604	0.913	1.875	2.687	3.601	4.370

$$Y = 0.1361 + 3.415x$$

$$r^2 = 0.9988$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	2.452	5.170	2.452	5.382	2.543	5.532
10	1.553	3.163	2.140	4.657	2.537	5.518
15	2.211	4.632	2.469	5.422	1.990	4.261
20	1.638	3.353	1.900	4.099	2.347	5.082
25	1.701	3.494	2.047	4.441	1.886	4.022
30	1.852	3.831	2.508	5.512	2.291	4.953
35	1.995	4.150	2.841	6.286	2.216	4.780
40	1.827	3.775	1.605	3.414	2.377	5.151
45	1.785	3.681	1.892	4.080	2.809	6.144
50	1.404	2.830	2.258	4.931	2.227	4.806
55	1.462	2.960	1.561	3.311	1.721	3.643
60	1.618	3.308	1.689	3.609	1.590	3.341
65	1.686	3.460	1.328	2.770	1.833	3.900
70	1.449	2.931	1.636	3.486	2.077	4.461
75	1.939	4.025	1.300	2.705	1.380	2.859
80	1.201	2.377	1.192	2.454	1.535	3.215
Receptor Volume (ml)	12.20		12.70		12.50	

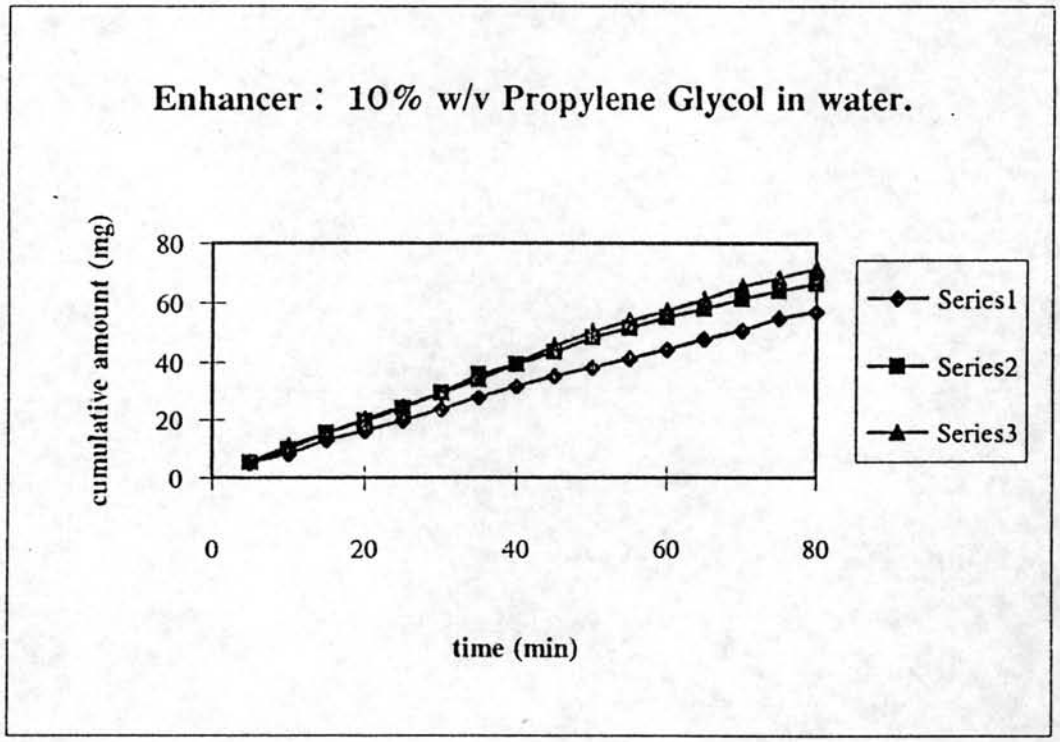
dilution factor: 625

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	5.17	5.38	5.53
10	8.33	10.03	11.05
15	12.96	15.46	15.31
20	16.31	19.56	20.39
25	19.81	24.00	24.41
30	23.64	29.51	29.36
35	27.79	35.79	34.14
40	31.56	39.21	39.29
45	35.24	43.29	45.44
50	38.07	48.22	50.24
55	41.03	51.51	53.89
60	44.34	55.14	57.23
65	47.80	57.91	61.13
70	50.73	61.40	65.59
75	54.76	64.10	68.45
80	57.14	66.56	71.66
Steady-state Slope (35-80 min)	0.6503	0.6962	0.8246
r^2	0.9988	0.9925	0.9895
Jss ($mg/min.cm^2$)	0.3359	0.3295	0.4050
Membrane Thickness (mm.)	0.0430	0.0350	0.0460
Normalized Jss $x10^3$ ($mg/min.cm^2$)	468.90	437.20	705.10

$$Jss = 537.06 \pm 146.3$$

$$\%cv = 27.25$$



Diclofenac Sodium Flux from Saturated Diclofenac Sodium Solution through Human Amnion.

Enhancer: 10% w/v Tetraglycol in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.566	1.273	2.011	3.071	3.874	4.853

$$Y = 0.2087 + 3.715x$$

$$r^2 = 0.9968$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	3.163	3.880	2.231	2.765	2.465	3.061
10	2.605	3.147	2.421	3.025	2.933	3.696
15	3.523	4.353	3.060	3.898	3.299	4.192
20	3.023	3.696	2.985	3.796	3.233	4.102
25	2.881	3.510	3.528	4.538	3.266	4.147
30	3.157	3.872	2.831	3.585	3.956	5.083
35	3.226	3.963	2.309	2.872	3.233	4.102
40	3.281	4.035	2.537	3.183	3.723	4.767
45	3.019	3.691	2.106	2.594	3.279	4.165
50	3.125	3.830	2.635	3.317	3.049	3.853
55	3.125	3.830	2.479	3.104	3.223	4.089
60	2.945	3.594	1.975	2.415	3.141	3.978
65	2.783	3.381	2.283	2.836	3.052	3.857
70	2.567	3.098	2.047	2.514	2.704	3.385
75	2.614	3.159	2.001	2.451	2.791	3.503
80	2.842	3.459	2.011	2.464	2.964	3.737
Receptor Volume (ml)	12.20		12.70		12.60	

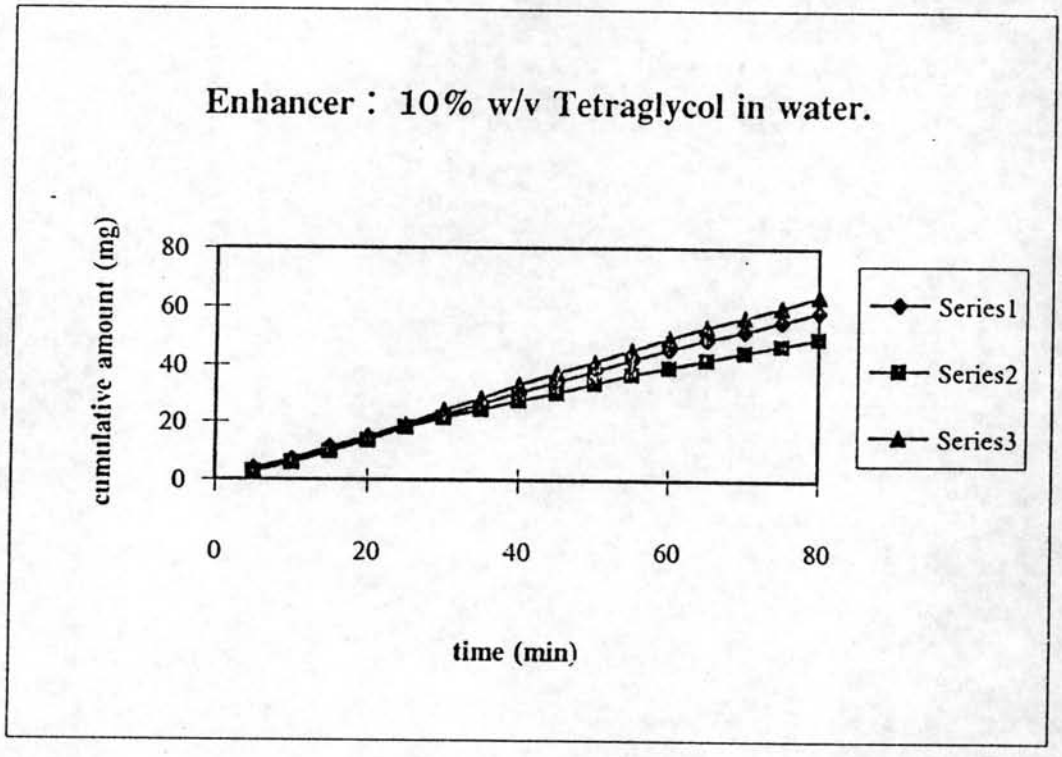
dilution factor: 400

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	3.88	2.76	3.06
10	7.02	5.79	6.75
15	11.38	9.68	10.94
20	15.07	13.48	15.05
25	18.58	18.02	19.19
30	22.45	21.60	24.28
35	26.42	24.47	28.38
40	30.45	27.66	33.15
45	34.14	30.25	37.31
50	37.97	33.57	41.16
55	41.80	36.67	45.25
60	45.40	39.09	49.23
65	48.78	41.92	53.09
70	51.80	44.44	56.47
75	55.03	46.89	59.98
80	58.49	49.35	63.71
Steady-state Slope (35-80 min)	0.7091	0.5538	0.7774
r^2	0.9982	0.9978	0.9983
Jss ($mg/min.cm^2$)	0.3662	0.2621	0.3818
Membrane Thickness (mm.)	0.0450	0.0610	0.0780
Normalized Jss $x10^3$ ($mg/min.cm^2$)	283.30	275.40	513.10

$Jss = 357.26 \pm 135.00$

$\%cv = 37.79$



Diclofenac Sodium Flux from Saturated Diclofenac Sodium Solution through Human Amnion.

Enhancer: Ethanol.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.644	1.043	1.965	2.787	3.951	4.623

$$Y = 0.1595 + 3.627x$$

$$r^2 = 0.9966$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	0.435	0.926	0.461	1.051	0.570	1.437
10	0.640	1.616	0.346	0.650	0.614	1.591
15	0.410	0.842	0.417	0.897	0.514	1.241
20	0.378	0.734	0.506	1.208	0.376	0.757
25	0.408	0.835	0.380	0.768	0.455	1.034
30	0.387	0.765	0.332	0.601	0.316	0.547
35	0.446	0.963	0.403	0.849	0.338	0.624
40	0.289	0.435	0.351	0.657	0.264	0.365
45	0.341	0.610	0.329	0.591	0.324	0.575
50	0.248	0.297	0.332	0.601	0.324	0.575
55	0.339	0.603	0.305	0.507	0.313	0.537
60	0.563	1.357	0.449	1.009	0.412	0.883
65	0.563	1.172	0.445	0.995	0.313	0.537
70	0.374	0.721	0.378	0.761	0.463	1.062
75	0.388	0.768	0.383	0.779	0.400	0.841
80	0.302	0.479	0.402	0.845	0.543	1.342
Receptor Volume (ml)	12.20		12.60		12.70	

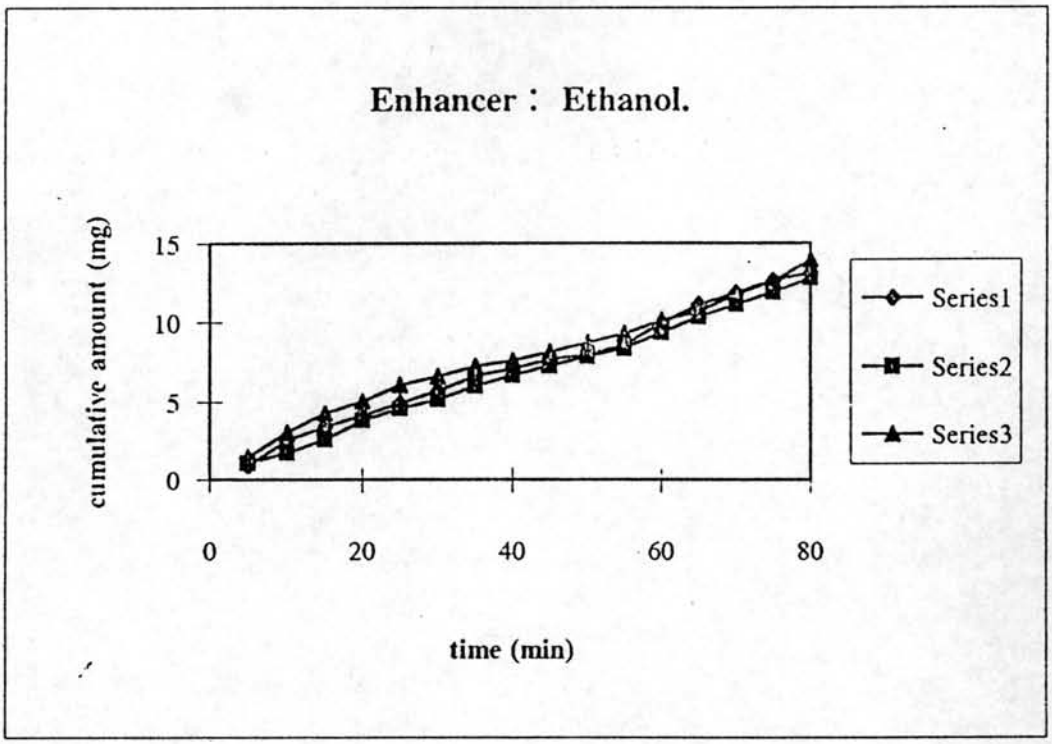
dilution factor: 1,000

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	0.92	1.05	1.43
10	2.54	1.70	3.02
15	3.38	2.59	4.26
20	4.11	3.80	5.02
25	4.95	4.57	6.06
30	5.71	5.17	6.60
35	6.68	6.02	7.23
40	7.11	6.69	7.59
45	7.72	7.28	8.17
50	8.02	7.88	8.74
55	8.62	8.39	9.28
60	9.98	9.39	10.16
65	11.15	10.39	10.70
70	11.87	11.15	11.76
75	12.64	11.93	12.60
80	13.12	12.79	13.94
Steady-state Slope (35-80 min)	0.1552	0.1522	0.1455
r^2	0.9768	0.9919	0.9761
Jss (mg/min.cm^2)	0.0802	0.0729	0.0688
Membrane Thickness (mm.)	0.0310	0.0320	0.0350
Normalized Jss x10^3 (mg/min.cm^2)	42.82	40.16	41.48

$$Jss = 41.65 \pm 1.08$$

$$\%cv = 2.60$$



Diclofenac Sodium Flux from Saturated Diclofenac Sodium Solution through Human Amnion.

Enhancer: Isopropyl Alcohol.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.547	1.169	2.029	2.875	3.768	4.680

$$Y = 0.1889 + 3.595x$$

$$r^2 = 0.9986$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	1.416	0.085	0.318	0.009	3.642	0.024
10	1.471	0.089	2.173	0.138	2.380	0.152
15	1.247	0.074	1.873	0.117	1.979	0.124
20	1.202	0.070	1.631	0.100	1.964	0.123
25	1.150	0.067	1.317	0.078	1.626	0.099
30	1.178	0.063	1.042	0.059	1.323	0.078
35	0.950	0.053	1.210	0.071	1.460	0.088
40	0.931	0.052	1.249	0.074	1.348	0.080
45	0.913	0.050	1.410	0.085	0.947	0.052
50	0.907	0.050	1.197	0.070	1.248	0.073
55	1.067	0.061	1.114	0.064	1.282	0.075
60	0.758	0.039	1.121	0.065	1.155	0.067
65	0.987	0.055	1.230	0.072	1.033	0.058
70	0.899	0.049	1.003	0.056	1.108	0.063
75	0.808	0.043	1.303	0.077	0.991	0.055
80	0.846	0.046	1.027	0.071	1.022	0.056
Receptor Volume (ml)	12.60		12.50		12.50	

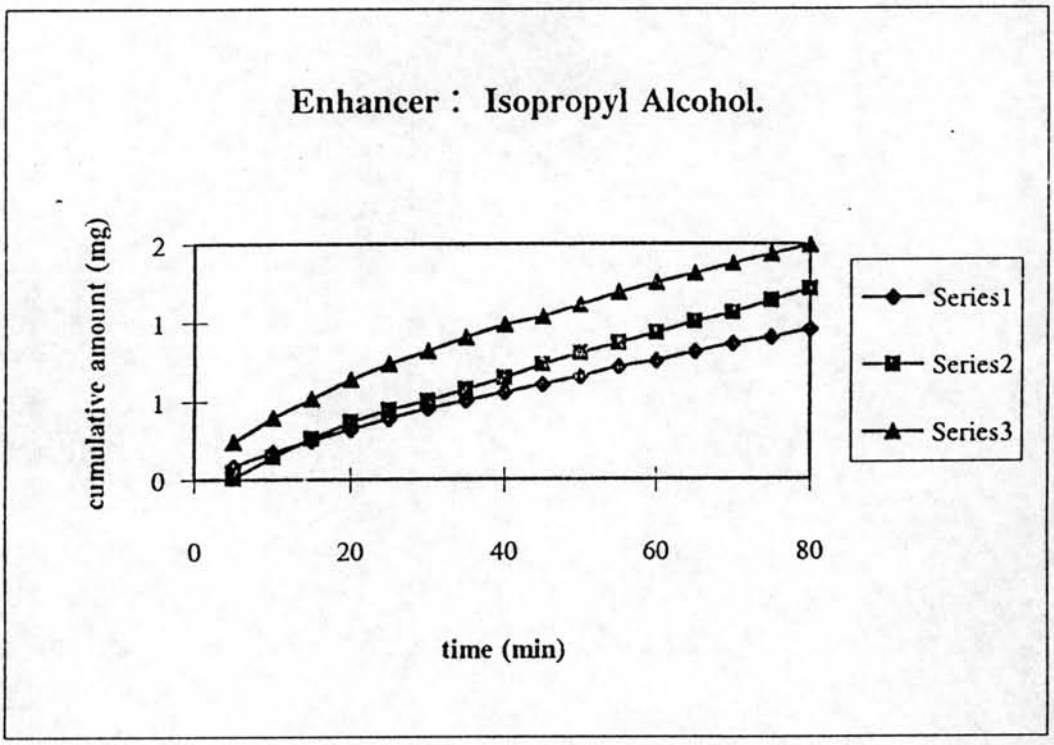
dilution factor: 20

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	0.085	0.009	0.240
10	0.175	0.147	0.392
15	0.249	0.265	0.516
20	0.320	0.365	0.640
25	0.388	0.444	0.740
30	0.451	0.504	0.818
35	0.505	0.575	0.907
40	0.556	0.649	0.987
45	0.607	0.735	1.040
50	0.658	0.805	1.114
55	0.719	0.870	1.190
60	0.759	0.935	1.257
65	0.815	1.007	1.316
70	0.865	1.064	1.379
75	0.908	1.142	1.435
80	0.954	1.213	1.492
Steady-state Slope (35-80 min)	0.0101	0.0139	0.0130
r^2	0.9989	0.9987	0.9978
Jss ($mg/min.cm^2$)	4.961×10^{-3}	6.827×10^{-3}	6.385×10^{-3}
Membrane Thickness (mm.)	0.0420	0.0210	0.0270
Normalized Jss $x10^3$ ($mg/min.cm^2$)	3.59	2.47	2.96

$$Jss = 3.01 \pm 0.56$$

$$\%cv = 18.64$$



Diclofenac Sodium Flux from Saturated Diclofenac Sodium Solution through Human Amnion.

Enhancer: 1% w/v Orange Oil in Ethanol.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	1.178	1.564	2.324	3.196	4.031	5.175

$$Y = 0.658 + 3.488x$$

$$r^2 = 0.9949$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	2.970	0.841	4.635	1.431	2.667	0.719
10	2.181	0.554	3.175	0.906	3.999	1.197
15	2.463	0.656	3.305	0.952	3.921	1.169
20	1.933	0.464	3.551	1.401	3.034	0.851
25	2.958	0.837	2.703	0.736	3.697	1.088
30	2.595	0.705	2.727	0.744	3.987	1.192
35	2.817	0.785	2.781	0.764	4.080	1.226
40	2.877	0.807	2.803	0.772	3.712	1.094
45	2.689	0.739	2.825	0.786	2.847	0.784
50	2.239	0.575	3.087	0.874	3.970	1.186
55	2.719	0.750	2.961	0.829	3.382	0.975
60	2.718	0.749	2.150	0.537	3.022	0.846
65	2.904	0.817	3.398	0.986	3.386	0.997
70	2.764	0.766	2.950	0.825	3.776	1.117
75	3.155	0.908	2.935	0.819	3.898	1.116
80	2.784	0.773	2.638	0.712	3.628	1.064
Receptor Volume (ml)	12.70		12.50		12.50	

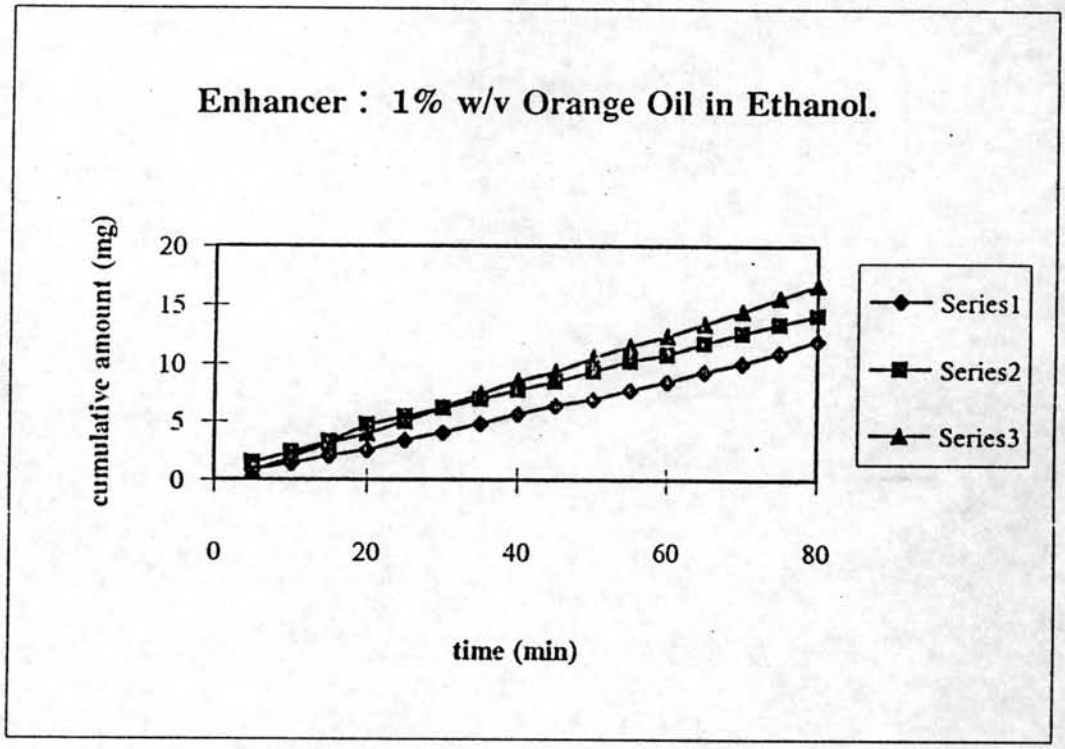
dilution factor: 100

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	0.84	1.43	0.719
10	1.39	2.33	1.91
15	2.05	3.29	3.08
20	2.51	4.69	3.93
25	3.35	5.42	5.02
30	4.05	6.17	6.21
35	4.84	6.93	7.44
40	5.65	7.70	8.53
45	6.39	8.48	9.32
50	6.96	9.36	10.50
55	7.71	10.19	11.48
60	8.46	10.73	12.33
65	9.28	11.71	13.33
70	10.05	12.54	14.44
75	10.96	13.36	15.60
80	11.69	14.07	16.67
Steady-state Slope (35-80 min)	0.1512	0.1595	0.2029
r^2	0.9983	0.9990	0.9987
Jss ($mg/min.cm^2$)	0.0715	0.0783	0.0996
Membrane Thickness (mm.)	0.0560	0.0320	0.0170
Normalized Jss $x10^3$ ($mg/min.cm^2$)	69.07	43.16	29.20

$$Jss = 47.14 \pm 20.23$$

$$\%cv = 42.90\%$$



Diclofenac Sodium Flux from Saturated Diclofenac Sodium Solution through Human Amnion.

APPENDIX V

Fluxes of Diclofenac Sodium from Its Saturated Solution Through Human Placental Membrane.

Enhancer: Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.615	1.069	2.042	2.971	3.796	4.905

$$Y = 0.1365 + 3.7622x$$

$$r^2 = 0.9988$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	2.897	0.447	2.642	0.422	1.103	0.161
10	4.408	0.692	3.349	0.542	2.469	0.390
15	4.954	0.722	4.745	0.777	3.255	0.522
20	4.467	0.702	5.067	0.832	3.386	0.544
25	4.646	0.731	4.938	0.810	3.177	0.509
30	4.666	0.734	4.751	0.778	3.397	0.545
35	4.558	0.716	4.228	0.690	3.196	0.510
40	4.519	0.710	4.376	0.714	2.947	0.470
45	5.284	0.834	4.473	0.731	3.218	0.515
50	4.492	0.706	4.084	0.666	2.588	0.410
55	4.132	0.647	4.454	0.728	3.144	0.503
60	4.415	0.693	4.625	0.757	3.016	0.482
65	4.592	0.722	3.988	0.650	2.771	0.441
70	4.498	0.707	4.134	0.674	3.138	0.502
75	3.989	0.624	3.852	0.627	2.652	0.421
80	3.918	0.613	3.761	0.611	2.937	0.468
Receptor Volume (ml)	12.20		12.70		12.60	

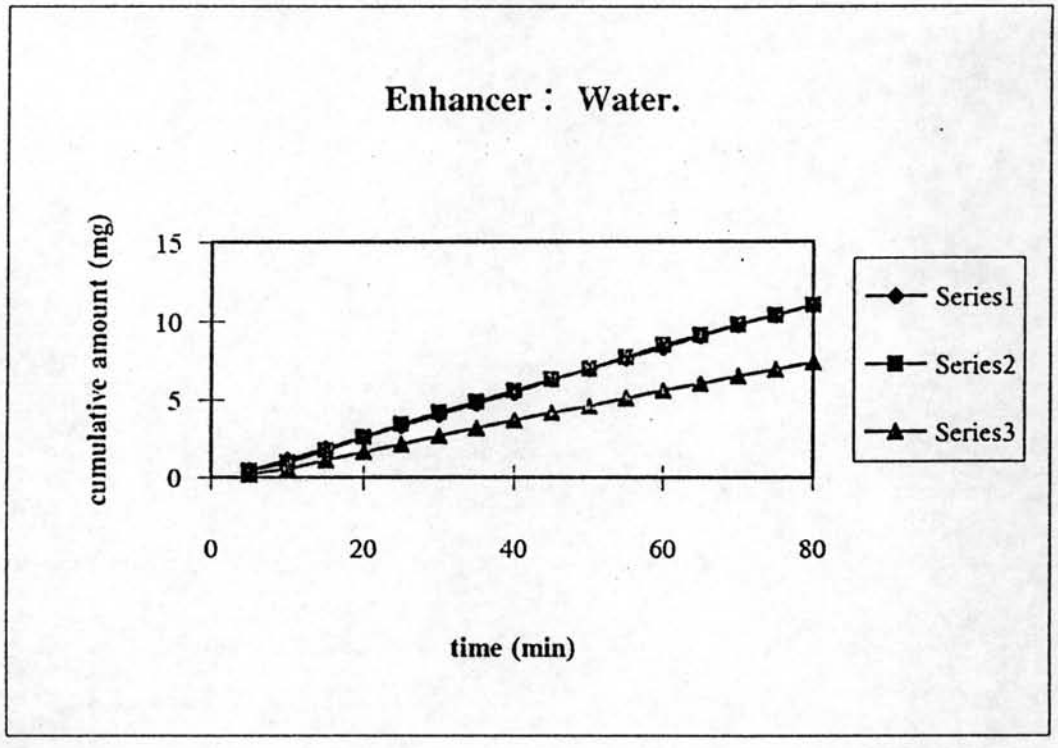
dilution factor: 50

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	0.44	0.422	0.16
10	1.14	0.965	0.55
15	1.86	1.74	1.07
20	2.56	2.57	1.61
25	3.29	3.38	2.12
30	4.03	4.16	2.67
35	4.74	4.85	3.18
40	5.45	5.56	3.65
45	6.29	6.30	4.17
50	6.99	6.96	4.58
55	7.64	7.69	5.08
60	8.34	8.45	5.56
65	9.06	9.10	6.00
70	9.77	9.77	6.51
75	10.39	10.40	6.93
80	11.00	11.01	7.40
Steady-state Slope (35-80 min)	0.1394	0.1378	0.0937
r^2	0.9989	0.9992	0.9997
Jss ($mg/min.cm^2$)	0.0720	0.0652	0.0460
Membrane Thickness (mm.)	0.1620	0.1730	0.1990
Normalized Jss $x10^3$ ($mg/min.cm^2$)	43.99	42.51	34.52

$Jss = 40.34 \pm 5.09$

$\%cv = 12.62$



Diclofenac Sodium Flux from Saturated Diclofenac Sodium through Human Placental Membrane.

Enhancer: 0.01 mg/ml Tween 20 in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.685	1.102	2.307	3.123	4.088	5.389

$$Y = 0.132 + 4.102x$$

$$r^2 = 0.9959$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	0.783	0.203	1.917	0.550	0.664	0.165
10	1.381	0.385	2.640	0.771	1.592	0.447
15	1.717	0.487	2.378	0.691	1.458	0.406
20	1.877	0.536	2.788	0.816	2.067	0.591
25	1.656	0.468	2.681	0.783	1.497	0.418
30	1.908	0.545	2.518	0.733	1.844	0.523
35	1.810	0.515	2.546	0.742	1.538	0.430
40	1.752	0.498	2.815	0.842	1.992	0.568
45	1.753	0.498	2.929	0.857	1.549	0.434
50	1.878	0.536	2.273	0.659	1.744	0.493
55	1.879	0.536	2.511	0.731	2.018	0.576
60	1.654	0.468	2.474	0.720	1.539	0.431
65	1.822	0.519	2.325	0.674	1.863	0.529
70	1.645	0.465	2.464	0.717	1.678	0.473
75	1.611	0.455	2.576	0.751	1.828	0.518
80	1.662	0.470	2.696	0.788	1.331	0.368
Receptor Volume (ml)	12.50		12.60		12.50	

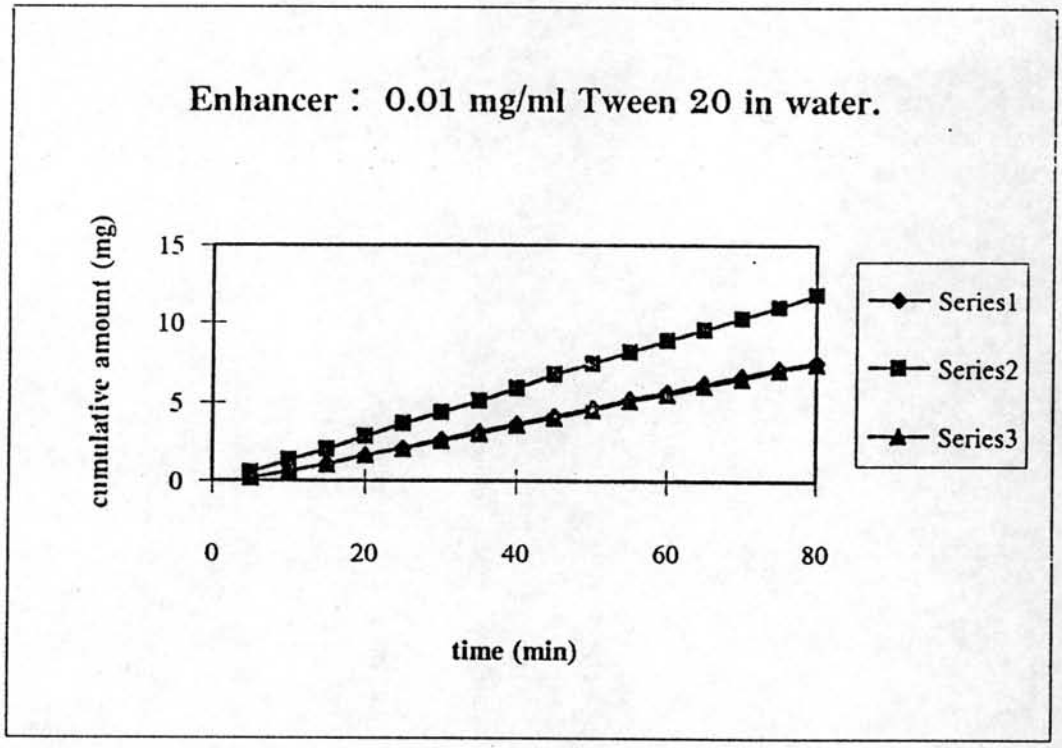
dilution factor: 100

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	0.20	0.55	0.16
10	0.58	1.32	0.61
15	1.07	2.01	1.02
20	1.61	2.82	1.61
25	2.08	3.61	2.02
30	2.62	4.34	2.55
35	3.14	5.08	2.98
40	3.64	5.91	3.55
45	4.13	6.77	3.98
50	4.67	7.43	4.48
55	5.21	8.16	5.05
60	5.68	8.88	5.48
65	6.20	9.55	6.01
70	6.66	10.27	6.49
75	7.12	11.02	7.01
80	7.52	11.81	7.37
Steady-state Slope (35-80 min)	0.0988	0.14614	0.0985
r^2	0.9989	0.9992	0.9991
Jss ($mg/min.cm^2$)	0.0485	0.0719	0.0483
Membrane Thickness (mm.)	0.1850	0.2340	0.3590
Normalized Jss $x10^3$ ($mg/min.cm^2$)	33.85	65.71	67.71

$$Jss = 55.75 \pm 18.99$$

$$\%cv = 34.07$$



Diclofenac Sodium Flux from Saturated Diclofenac Sodium through Human Placental Membrane.

Enhancer: 0.05 mg/ml Tween 20 in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.422	1.008	2.057	2.972	3.989	4.572

$$Y = 0.0805 + 3.751x$$

$$r^2 = 0.9928$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	0.894	0.272	0.276	0.077	0.933	0.294
10	1.813	0.567	1.011	0.323	1.894	0.612
15	2.163	0.679	1.367	0.441	2.496	0.811
20	2.180	0.684	1.718	0.558	2.207	0.719
25	2.190	0.688	1.685	0.547	1.923	0.622
30	2.204	0.692	1.737	0.565	2.054	0.665
35	1.817	0.568	1.868	0.608	2.213	0.718
40	1.812	0.566	1.625	0.527	2.125	0.689
45	1.843	0.576	1.622	0.526	2.315	0.751
50	1.984	0.622	1.624	0.527	2.246	0.729
55	1.775	0.535	1.516	0.491	2.210	0.717
60	1.835	0.574	1.688	0.548	2.186	0.709
65	1.819	0.569	1.655	0.537	1.718	0.554
70	1.569	0.489	1.541	0.499	2.249	0.730
75	1.646	0.513	1.535	0.497	2.202	0.714
80	1.844	0.577	1.717	0.558	1.818	0.581
Receptor Volume (ml)	12.20		12.70		12.60	

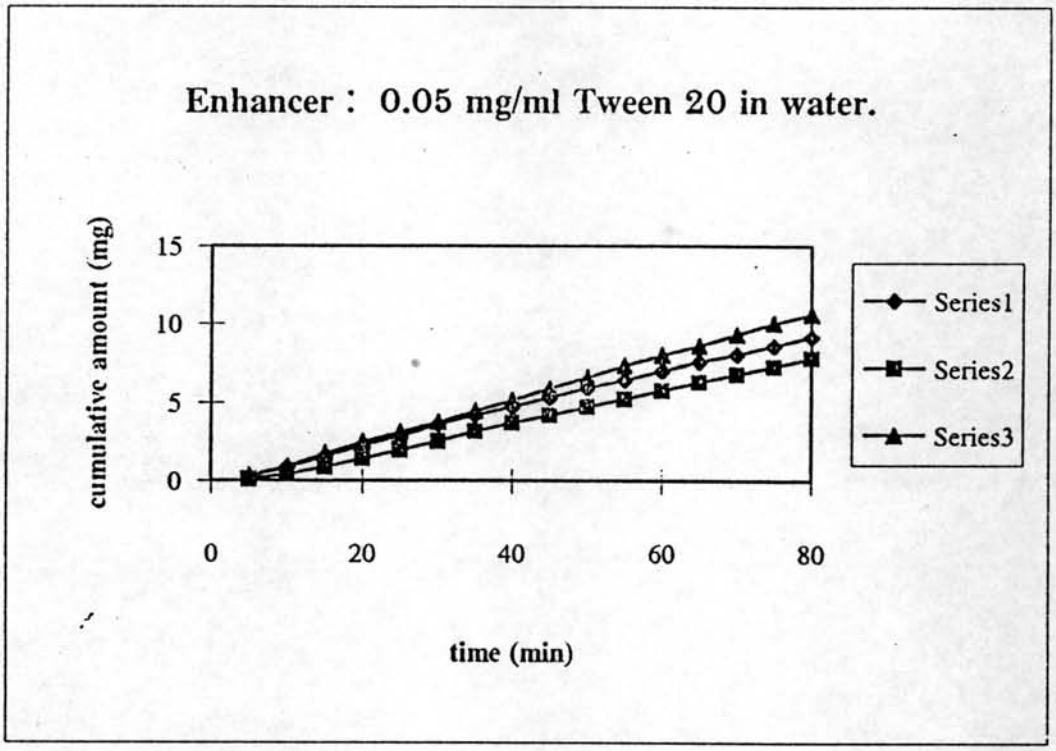
dilution factor: 100

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	0.27	0.07	0.29
10	0.84	0.40	0.90
15	1.51	0.84	1.71
20	2.20	1.40	2.43
25	2.82	1.94	3.06
30	3.58	2.51	3.72
35	4.15	3.12	4.44
40	4.72	3.65	5.13
45	5.29	4.17	5.88
50	5.91	4.70	6.61
55	6.45	5.19	7.33
60	7.02	5.74	8.04
65	7.59	6.28	8.59
70	8.08	6.78	9.32
75	8.60	7.28	10.04
80	9.17	7.83	10.62
Steady-state Slope (35-80 min)	0.1114	0.1044	0.139
r^2	0.9993	0.9999	0.9992
Jss ($mg/min.cm^2$)	0.0575	0.0494	0.0677
Membrane Thickness (mm.)	0.3210	0.2330	0.3570
Normalized Jss $x10^3$ ($mg/min.cm^2$)	69.63	43.42	91.19

$Jss = 68.08 \pm 23.92$

$\%cv = 35.13$



Diclofenac Sodium Flux from Saturated Diclofenac Sodium through Human Placental Membrane.

Enhancer: 0.4% w/v Brij 35 in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.615	1.069	2.042	2.971	3.796	4.905

$$Y = 0.1365 + 3.762x$$

$$r^2 = 0.9988$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	2.369	0.745	0.630	0.165	2.092	0.649
10	2.645	0.837	1.406	0.590	2.492	0.782
15	2.711	0.859	1.478	1.039	2.227	0.694
20	2.607	0.824	1.725	1.571	2.741	0.865
25	2.496	0.787	1.528	2.037	2.193	0.683
30	2.336	0.734	1.720	2.567	2.066	0.641
35	2.225	0.697	1.423	3.015	1.791	0.549
40	2.244	0.703	1.596	3.504	1.919	0.592
45	2.483	0.783	1.486	3.956	1.896	0.584
50	2.356	0.740	1.269	4.335	1.866	0.574
55	2.366	0.744	1.619	4.831	1.729	0.529
60	2.191	0.685	2.332	5.567	1.868	0.542
65	1.440	0.435	1.502	6.024	1.666	0.508
70	2.156	0.674	1.158	6.366	1.613	0.490
75	2.165	0.677	1.380	6.783	1.760	0.539
80	2.186	0.684	1.379	7.199	2.006	0.657
Receptor Volume (ml)	12.50		12.60		12.50	

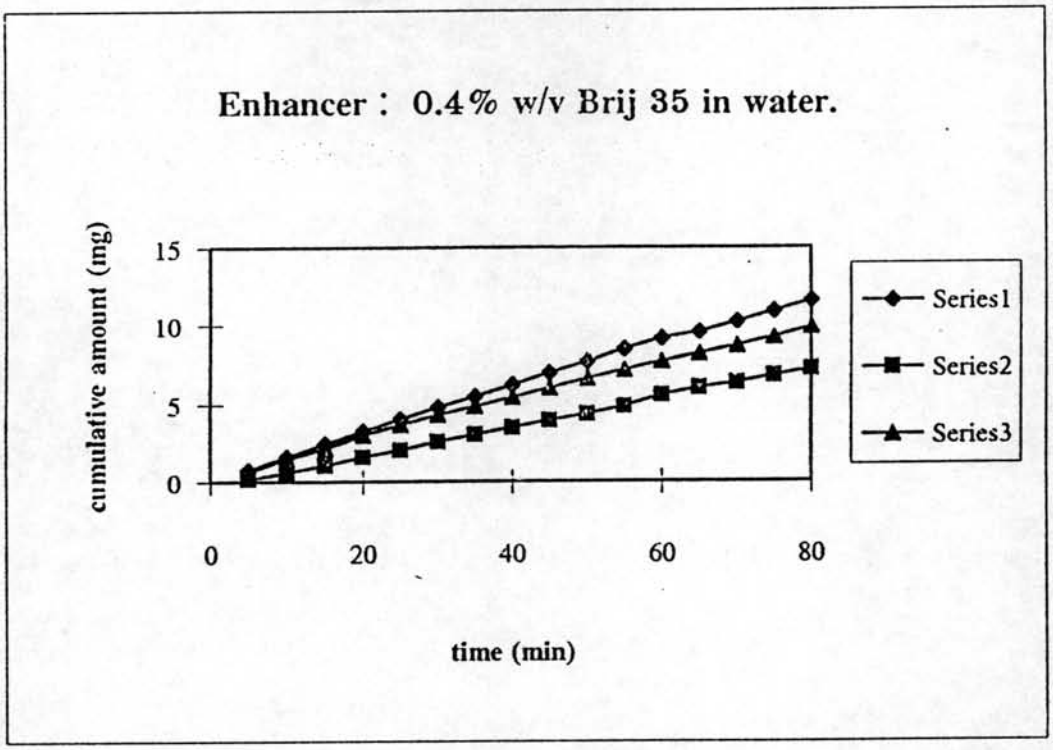
dilution factor: 100

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	0.74	0.16	0.64
10	1.58	0.59	1.43
15	2.44	1.03	2.12
20	3.26	1.57	2.99
25	4.05	2.03	3.67
30	4.78	2.56	4.31
35	5.48	3.01	4.86
40	6.18	3.50	5.45
45	6.97	3.95	6.04
50	7.71	4.33	6.61
55	8.45	4.83	7.14
60	9.14	5.56	7.68
65	9.57	6.02	8.19
70	10.25	6.36	8.68
75	10.93	6.78	9.22
80	11.61	7.19	9.88
Steady-state Slope (35-80 min)	0.1345	0.0951	0.1091
r^2	0.9972	0.9954	0.9991
Jss ($mg/min.cm^2$)	0.0660	0.0467	0.0536
Membrane Thickness (mm.)	0.2170	0.1530	0.1410
Normalized Jss $x10^3$ ($mg/min.cm^2$)	53.98	26.94	28.51

$Jss = 36.47 \pm 15.17$

$\%cv = 41.61$



Diclofenac Sodium Flux from Saturated Diclofenac Sodium through Human Placental Membrane.

Enhancer: 1.0% w/v Brij 35 in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.7780	1.065	1.844	2.622	3.304	4.035

$$Y = 0.322 + 2.930x$$

$$r^2 = 0.9993$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	2.245	0.500	2.890	0.672	3.079	0.719
10	3.334	0.793	4.633	1.138	4.701	1.151
15	2.771	0.642	4.417	1.080	3.850	0.924
20	3.372	0.803	4.996	1.236	3.995	0.963
25	3.313	0.787	5.396	1.343	3.565	0.848
30	3.254	0.771	4.823	1.189	5.120	1.263
35	2.752	0.637	4.649	1.143	3.659	0.873
40	4.080	0.993	5.645	1.409	4.144	1.002
45	2.820	0.655	3.950	0.955	3.943	0.949
50	3.036	0.713	4.132	1.004	3.566	0.848
55	2.939	0.687	5.260	1.306	3.286	0.769
60	2.673	0.615	5.947	1.490	3.919	0.942
65	3.020	0.708	3.838	0.925	3.498	0.830
70	3.288	0.780	3.793	0.913	3.641	0.868
75	2.706	0.624	3.470	0.827	3.399	0.804
80	2.701	0.623	3.543	0.846	3.158	0.740
Receptor Volume (ml)	12.60		12.50		12.50	

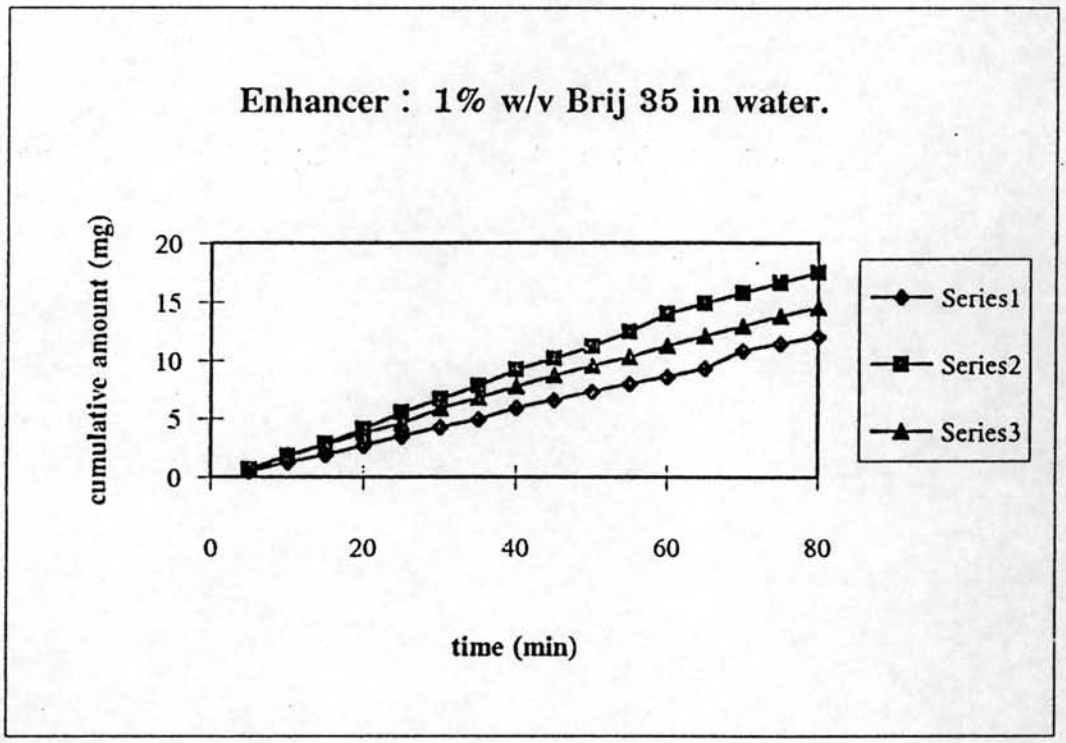
dilution factor: 62.5

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	0.50	0.67	0.71
10	1.29	1.81	2.87
15	1.93	2.81	9.79
20	2.73	4.12	3.75
25	3.52	5.46	4.60
30	4.29	6.65	5.86
35	4.93	7.80	6.74
40	5.92	9.21	7.74
45	6.58	10.16	8.69
50	7.29	11.16	9.54
55	7.98	12.47	10.30
60	8.59	13.96	11.25
65	9.30	14.89	12.08
70	10.80	15.80	12.94
75	11.42	16.63	13.75
80	12.04	17.47	14.49
Steady-state Slope (35-80 min)	0.1439	0.2179	0.1716
r^2	0.9863	0.9940	0.9990
Jss ($mg/min.cm^2$)	0.0706	0.1070	0.0842
Membrane Thickness (mm.)	0.2890	0.2040	0.2340
Normalized Jss $x10^3$ ($mg/min.cm^2$)	76.95	82.28	74.34

$Jss = 77.85 \pm 4.04$

$\%cv = 5.19$



Diclofenac Sodium Flux from Saturated Diclofenac Sodium through Human Placental Membrane.

Enhancer: 10% w/v Propylene Glycol in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.778	1.065	1.844	2.622	3.304	4.035

$$Y = 0.3821 + 2.930x$$

$$r^2 = 0.9993$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	0.169	0.043	1.610	0.332	0.533	0.040
10	1.974	0.414	3.479	0.838	1.730	0.362
15	2.241	0.483	3.714	0.902	1.894	0.406
20	2.536	0.560	4.560	1.131	3.334	0.793
25	1.825	0.375	4.522	1.121	2.494	0.567
30	2.607	0.578	4.529	1.123	2.822	0.655
35	2.258	0.488	4.732	1.178	2.759	0.638
40	2.852	0.620	4.697	1.168	2.721	0.628
45	2.189	0.470	4.519	1.120	2.631	0.604
50	2.610	0.579	4.455	1.103	3.370	0.802
55	2.214	0.476	4.339	1.071	2.890	0.674
60	2.350	0.512	3.062	0.725	2.910	0.679
65	2.397	0.524	4.714	1.173	3.272	0.776
70	1.976	0.414	4.935	1.233	3.289	0.781
75	1.900	0.394	4.513	1.118	2.308	0.517
80	2.186	0.469	3.443	0.829	2.693	0.621
Receptor Volume (ml)	12.20		12.70		12.60	

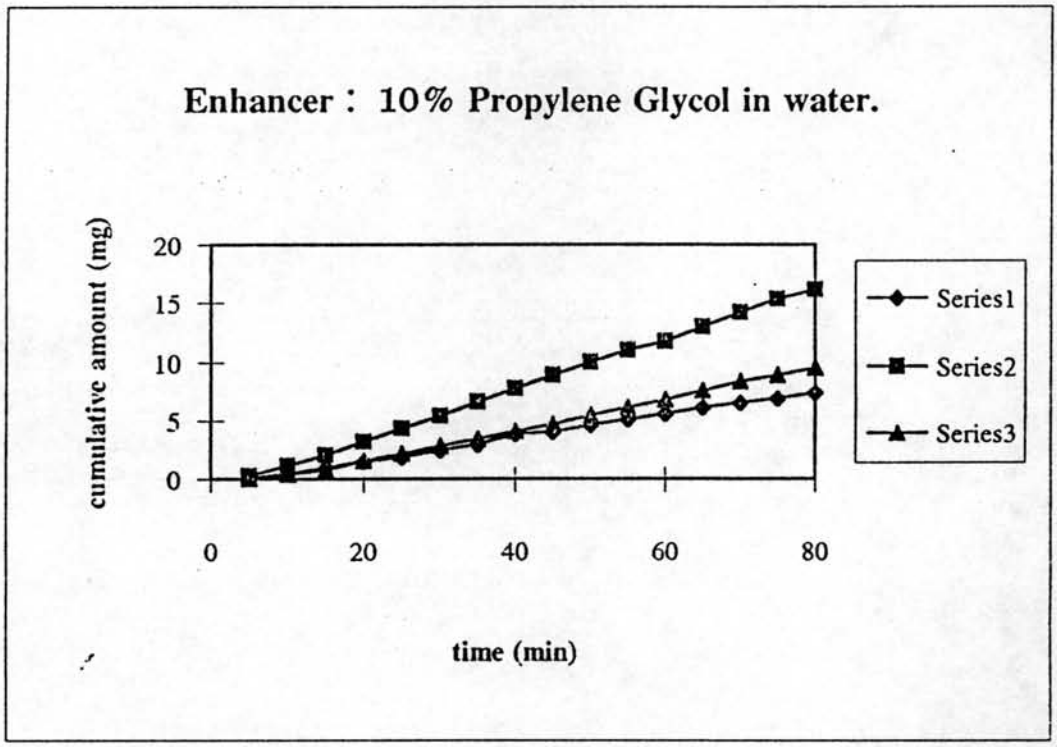
dilution factor: 62.5

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	0.04	0.33	0.04
10	0.45	1.17	0.40
15	0.94	2.07	0.80
20	1.50	3.20	1.60
25	1.87	4.32	2.16
30	2.45	5.44	2.82
35	2.94	6.62	3.46
40	3.85	7.79	4.08
45	4.05	8.91	4.69
50	4.63	10.01	5.49
55	5.10	11.08	6.16
60	5.62	11.81	6.84
65	6.14	12.98	7.62
70	6.55	14.21	8.40
75	6.95	15.33	8.92
80	7.42	16.16	9.54
Steady-state Slope (35-80 min)	0.0964	0.2117	0.1384
r^2	0.9937	0.9986	0.9987
Jss (mg/min.cm^2)	0.0498	0.1002	0.0679
Membrane Thickness (mm.)	0.3510	0.2660	0.4690
Normalized Jss x10^3 (mg/min.cm^2)	65.93	100.50	120.10

$Jss = 95.51 \pm 27.42$

$\%cv = 28.71$



Diclofenac Sodium Flux from Saturated Diclofenac Sodium through Human Placental Membrane.

Enhancer: 10% w/v Tetraglycol in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.422	1.008	2.057	2.972	3.989	4.572

$$Y = 0.0805 + 3.751x$$

$$r^2 = 0.9928$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	0.641	0.197	0.723	0.225	1.738	0.556
10	1.833	0.590	2.258	0.733	3.047	0.986
15	2.547	0.826	2.465	0.801	3.626	1.176
20	2.402	0.778	2.742	0.893	4.017	1.304
25	2.386	0.773	2.932	0.956	3.800	1.233
30	2.531	0.820	3.025	0.986	3.227	1.045
35	2.650	0.860	3.597	0.845	4.280	1.391
40	2.741	0.890	2.258	0.931	3.980	1.292
45	2.646	0.858	2.579	0.839	4.960	1.614
50	2.605	0.845	2.097	0.699	4.213	1.369
55	3.228	1.040	2.537	0.802	4.795	1.560
60	2.950	0.959	2.357	0.765	4.045	1.313
65	3.032	0.986	2.437	0.792	3.880	1.259
70	3.232	1.052	2.372	0.770	7.518	2.454
75	3.301	1.074	2.544	0.827	4.239	1.377
80	3.312	1.078	2.307	0.749	4.136	1.343
Receptor Volume (ml)	12.50		12.60		12.50	

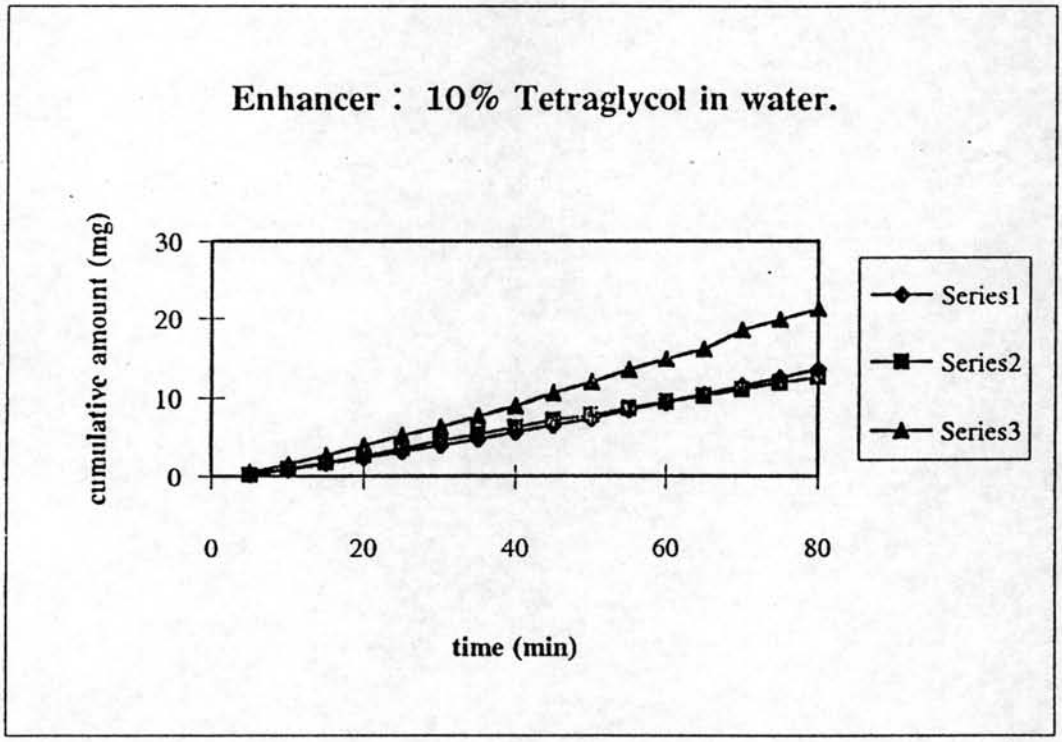
dilution factor: 100

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	0.19	0.22	0.55
10	0.78	0.95	1.54
15	1.61	1.75	2.71
20	2.39	2.65	4.02
25	3.16	3.60	5.25
30	3.98	4.59	6.30
35	4.84	5.44	7.69
40	5.73	6.37	8.98
45	6.59	7.21	10.60
50	7.44	7.89	11.96
55	8.48	8.71	13.53
60	9.44	9.48	14.84
65	10.42	10.27	16.10
70	11.47	11.04	18.55
75	12.55	11.87	19.93
80	13.63	12.62	21.27
Steady-state Slope (35-80 min)	0.1951	0.1577	0.3058
r^2	0.9983	0.9995	0.9967
Jss ($mg/min.cm^2$)	0.0958	0.0775	0.1502
Membrane Thickness (mm.)	0.2810	0.4160	0.3080
Normalized Jss $x10^3$ ($mg/min.cm^2$)	101.50	121.50	174.50

$Jss = 132.50 \pm 37.72$

$\%cv = 28.46$



Diclofenac Sodium Flux from Saturated Diclofenac Sodium through Human Placental Membrane.

Enhancer: Ethanol.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.566	1.273	2.011	3.071	3.874	4.853

$$Y = 0.2081 + 3.715x$$

$$r^2 = 0.9968$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	1.447	0.203	1.337	0.193	0.663	0.077
10	1.903	0.278	1.647	0.246	1.576	0.232
15	2.477	0.372	1.591	0.236	2.105	0.321
20	2.298	0.343	2.072	0.318	2.140	0.327
25	2.404	0.360	2.098	0.323	1.843	0.277
30	2.569	0.387	2.479	0.388	2.131	0.326
35	2.047	0.302	2.124	0.327	1.961	0.297
40	2.221	0.330	2.388	0.372	2.309	0.356
45	2.371	0.335	2.526	0.396	2.354	0.364
50	2.205	0.328	2.396	0.369	2.264	0.348
55	2.021	0.297	2.431	0.380	2.438	0.378
60	2.286	0.341	2.385	0.372	2.629	0.410
65	2.273	0.339	2.258	0.350	2.163	0.331
70	1.862	0.271	2.294	0.356	2.575	0.401
75	2.044	0.301	2.242	0.347	2.711	0.424
80	2.145	0.318	2.272	0.352	2.058	0.313
Receptor Volume (ml)	12.20		12.70		12.60	

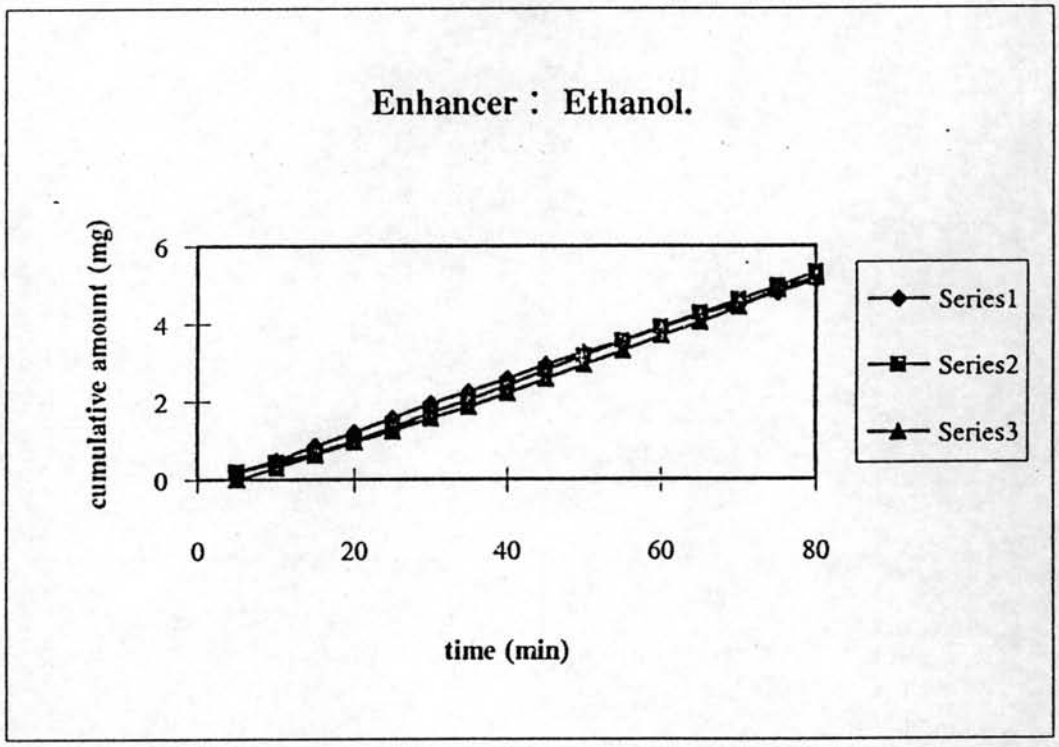
- dilution factor: 50

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	0.20	0.19	0.07
10	0.48	0.43	0.30
15	0.85	0.67	0.63
20	1.19	0.99	0.95
25	1.55	1.31	1.23
30	1.94	1.70	1.56
35	2.24	2.03	1.85
40	2.57	2.40	2.21
45	2.93	2.79	2.57
50	3.25	3.16	2.92
55	3.55	3.54	3.30
60	3.89	3.92	3.71
65	4.23	4.27	4.04
70	4.50	4.62	4.44
75	4.80	4.97	4.86
80	5.12	5.32	5.18
Steady-state Slope (35-80 min)	0.0638	0.0732	0.0745
r^2	0.9993	0.9996	0.9994
Jss ($mg/min.cm^2$)	0.0329	0.0346	0.0365
Membrane Thickness (mm.)	0.3100	0.2680	0.3230
Normalized Jss $x10^3$ ($mg/min.cm^2$)	38.46	34.98	44.45

$Jss = 39.29 \pm 4.79$

$\%cv = 12.18$



Diclofenac Sodium Flux from Saturated Diclofenac Sodium through Human Placental Membrane.

Enhancer: Isopropyl Alcohol.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.658	1.102	2.307	3.123	4.088	5.389

$$Y = 0.1186 + 4.1173x$$

$$r^2 = 0.9960$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	1.016	0.026	0.321	0.006	0.208	0.002
10	1.615	0.044	0.850	0.022	0.309	0.005
15	1.564	0.042	0.859	0.022	0.385	0.006
20	2.007	0.055	1.039	0.028	0.430	0.009
25	1.752	0.048	1.111	0.030	0.399	0.008
30	2.044	0.057	1.149	0.031	0.652	0.016
35	1.799	0.049	1.475	0.041	0.729	0.018
40	2.141	0.059	1.636	0.046	0.809	0.021
45	2.115	0.059	1.145	0.031	0.876	0.023
50	2.022	0.056	1 .410	0.039	0.799	0.020
55	1.821	0.050	1.360	0.038	0.823	0.021
60	1.890	0.052	1.500	0.042	0.944	0.025
65	1.965	0.054	1.402	0.039	1.005	0.027
70	1.685	0.046	1.611	0.046	1.003	0.028
75	1.803	0.049	1.474	0.041	1.060	0.028
80	1.939	0.053	1.396	0.039	1.164	0.032
Receptor Volume (ml)	12.20		12.70		12.60	

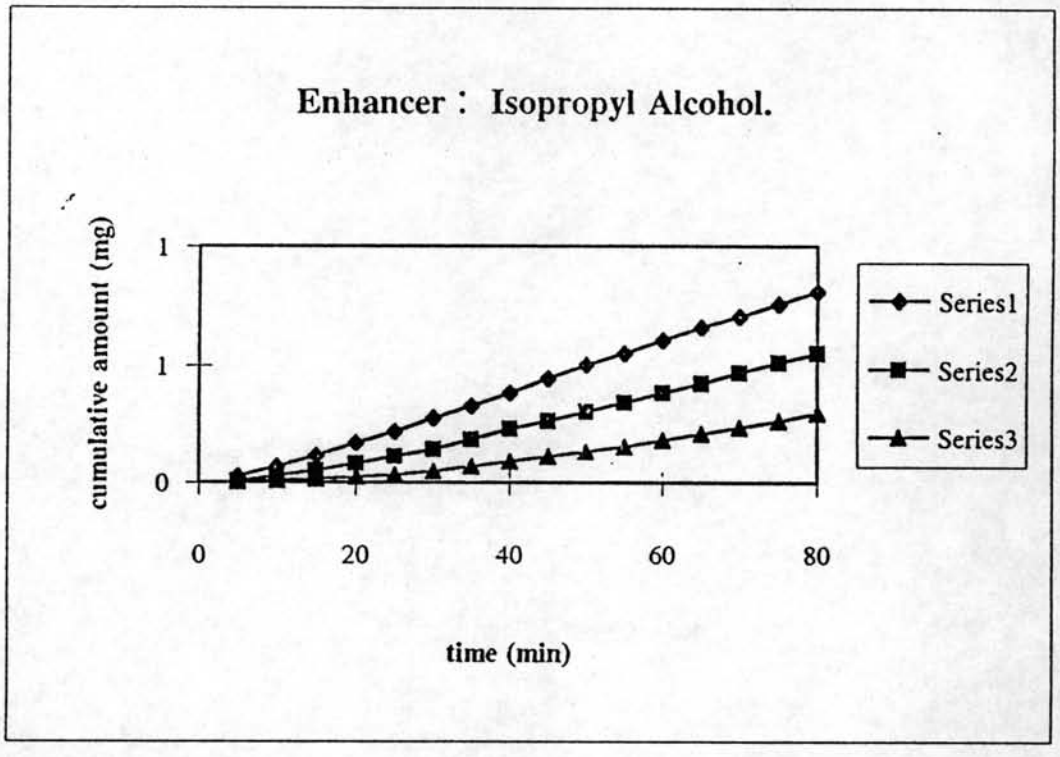
dilution factor: 10

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	0.026	0.006	0.002
10	0.070	0.028	0.008
15	0.113	0.051	0.015
20	0.169	0.080	0.024
25	0.218	0.110	0.033
30	0.275	0.142	0.049
35	0.324	0.184	0.068
40	0.384	0.231	0.089
45	0.443	0.262	0.112
50	0.500	0.302	0.133
55	0.550	0.340	0.155
60	0.603	0.383	0.180
65	0.657	0.422	0.207
70	0.704	0.468	0.235
75	0.754	0.510	0.264
80	0.808	0.549	0.296
Steady-state Slope (35-80 min)	0.0160	0.0081	0.0050
r^2	0.9989	0.9990	0.9949
Jss ($mg/min.cm^2$)	5.475x103	3.834x103	2.456x103
Membrane Thickness (mm.)	0.1360	0.4150	0.3250
Normalized Jss $x10^3$ ($mg/min.cm^2$)	2.80	6.00	3.02

$Jss = 3.94 \pm 1.786$

$\%cv = 45.30$



Diclofenac Sodium Flux from Saturated Diclofenac Sodium through Human Placental Membrane.

Enhancer: 1% w/v Orange Oil in Ethanol.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.778	1.065	1.844	2.622	3.304	4.035

$$Y = 0.382 + 2.930x$$

$$r^2 = 0.9993$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	0.621	0.062	0.841	0.124	0.486	0.027
10	1.629	0.324	2.108	0.467	1.611	0.330
15	1.565	0.307	2.029	0.446	1.385	0.269
20	1.599	0.316	1.964	0.428	1.699	0.353
25	1.714	0.346	2.374	0.539	1.664	0.344
30	1.629	0.342	2.269	0.311	1.228	0.227
35	1.654	0.331	1.837	0.394	1.878	0.402
40	1.710	0.345	2.294	0.517	1.649	0.340
45	1.677	0.337	1.840	0.394	1.648	0.340
50	1.449	0.277	1.755	0.371	1.680	0.348
55	1.626	0.323	1.823	0.390	1.672	0.346
60	1.671	0.335	1.919	0.416	1.751	0.367
65	1.726	0.349	1.480	0.297	1.778	0.358
70	1.566	0.308	1.724	0.363	1.837	0.390
75	1.604	0.318	1.696	0.355	1.466	0.291
80	2.045	0.432	1.478	0.296	1.663	0.336
Receptor Volume (ml)	12.20		12.70		12.60	

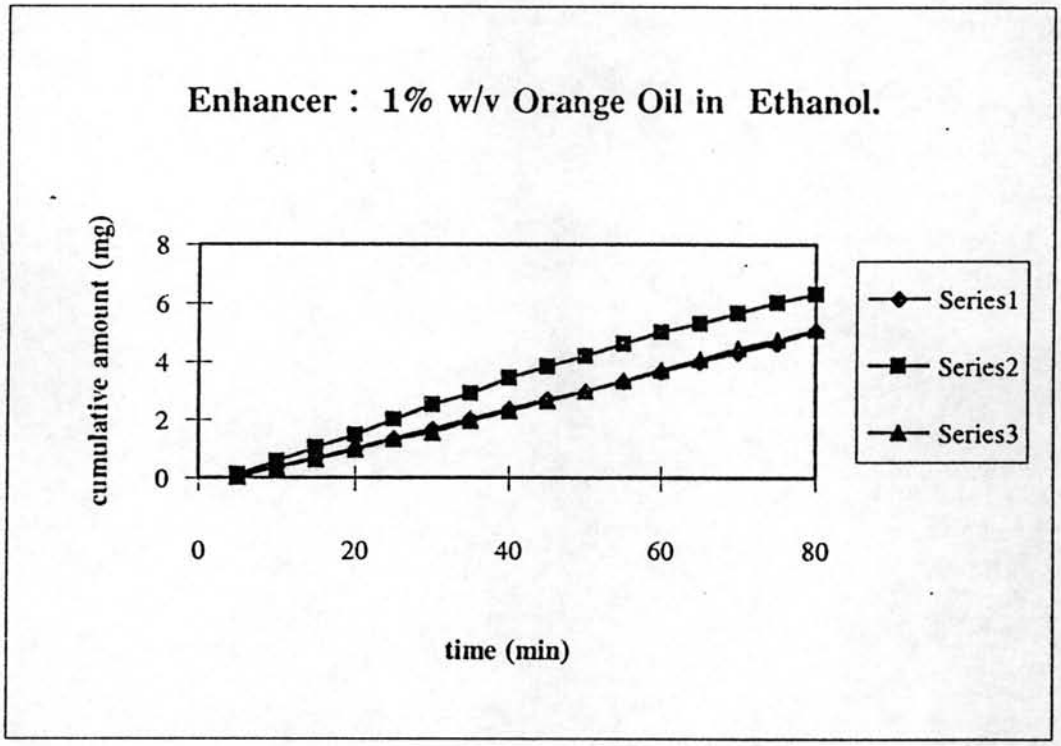
dilution factor: 62.5

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	0.06	0.12	0.02
10	0.38	0.59	0.35
15	0.69	1.03	0.62
20	1.00	1.46	0.97
25	1.35	2.00	1.32
30	1.69	2.51	1.55
35	2.02	2.90	1.95
40	2.37	3.42	2.29
45	2.71	3.82	2.63
50	2.98	4.19	2.98
55	3.31	4.58	3.32
60	3.64	4.99	3.69
65	3.99	5.29	4.05
70	4.30	5.65	4.44
75	4.62	6.01	4.73
80	5.05	6.30	5.06
Steady-state Slope (35-80 min)	0.0657	0.0746	0.0699
r^2	0.9989	0.9966	0.9996
Jss ($mg/min.cm^2$)	0.0339	0.0353	0.0343
Membrane Thickness (mm.)	0.2020	0.2540	0.3390
Normalized Jss $x10^3$ ($mg/min.cm^2$)	25.83	33.81	43.86

$Jss = 34.50 \pm 9.03$

$\%cv = 26.18$



Diclofenac Sodium Flux from Saturated Diclofenac Sodium through Human Placental Membrane.

APPENDIX VI

Fluxes of Diclofenac Sodium from 25 mg/ml Diclofenac Sodium Soluutions Through Newborn Pig Skin.

Enhancer: Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.504	0.911	1.796	2.630	3.557	4.392

$$Y = 0.0546 + 3.4741x$$

$$r^2 = 0.9998$$

Diffusion Run Data

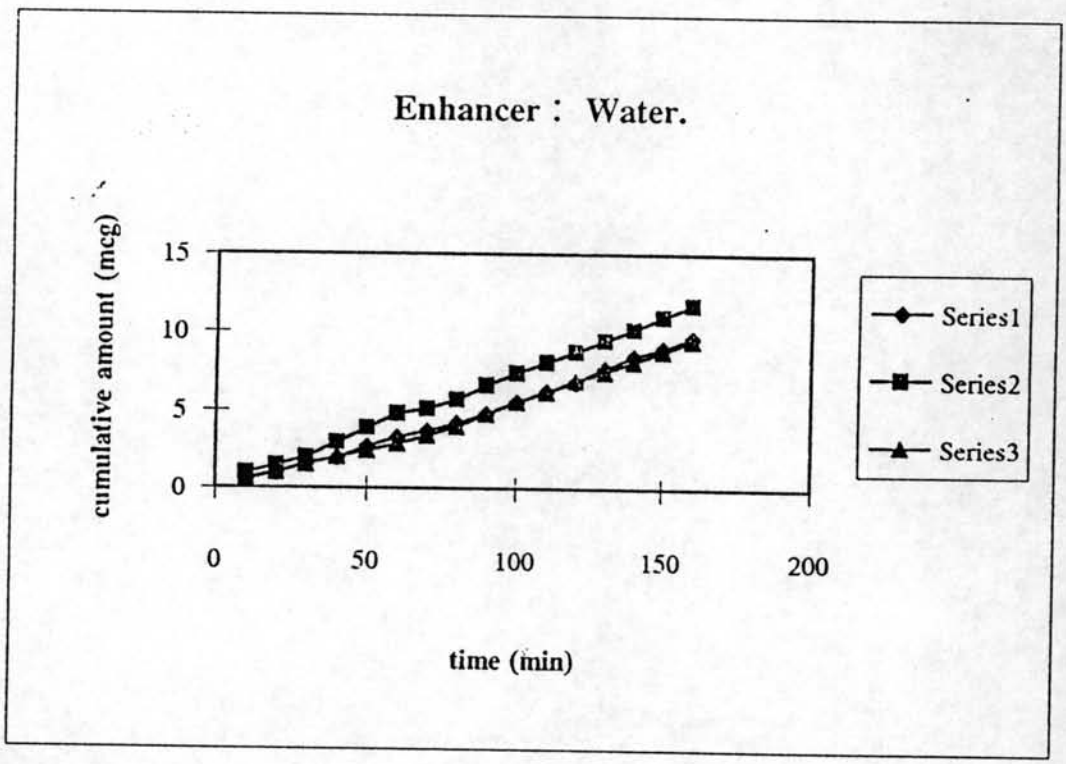
Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)
10	1.508	0.527	2.650	0.938	1.805	0.629
20	1.198	0.414	1.453	0.505	1.112	0.380
30	1.817	0.642	1.579	0.551	1.458	0.504
40	1.072	0.368	2.648	0.937	1.392	0.481
50	2.156	0.762	2.771	0.982	1.219	0.418
60	1.661	0.582	2.330	0.882	1.326	0.457
70	1.199	0.415	1.007	0.344	1.495	0.518
80	1.430	0.498	1.668	0.583	1.664	0.579
90	1.542	0.592	2.492	0.881	2.353	0.826
100	2.163	0.764	2.184	0.769	2.184	0.766
110	1.940	0.683	2.039	0.717	1.856	0.648
120	1.717	0.602	1.895	0.665	2.020	0.707
130	2.328	0.839	1.984	0.697	1.588	0.551
140	2.192	0.775	2.073	0.729	1.802	0.628
150	1.502	0.524	2.329	0.822	1.993	0.697
160	1.904	0.670	2.248	0.792	2.006	0.702
Receptor Volume (ml)	12.60		12.50		12.50	

Diffusion Run Data

Diffusion Run	Run I	-Run II	Run III
Time (min)	Cumulative Amount (mcg)	Cumulative Amount (mcg)	Cumulative Amount (mcg)
10	0.52	0.93	0.62
20	0.94	1.44	1.00
30	1.58	1.99	1.51
40	1.95	2.93	1.99
50	2.71	3.91	2.41
60	3.29	4.79	2.86
70	3.71	5.13	3.38
80	4.20	5.72	3.96
90	4.80	6.60	4.79
100	5.56	7.37	5.55
110	6.24	8.08	6.20
120	6.85	8.75	6.91
130	7.68	9.45	7.46
140	8.46	10.18	8.09
150	8.98	11.00	8.78
160	9.65	11.79	9.49
Steady-state Slope (70-160 min)	0.0680	0.0736	0.0676
r^2	0.9980	0.9991	0.9985
Jss (mcg/min.cm^2)	0.0334	0.0386	0.0332
Membrane Thickness (mm.)	0.4110	0.4020	0.4280
Normalized Jss x10^3 (mcg/min.cm^2)	40.84	43.17	42.26

Jss = 42.09 $\pm$ 1.174

%cv = 2.789



Diclofenac Sodium Flux from 25 mg/ml Diclofenac Sodium Solution Through Newborn Pig Skin.

Enhancer: 0.05 mg/ml Tween 20 in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.504	0.911	1.796	2.630	3.557	4.392

$$Y = 0.0546 + 3.474x$$

$$r^2 = 0.9998$$

Diffusion Run Data

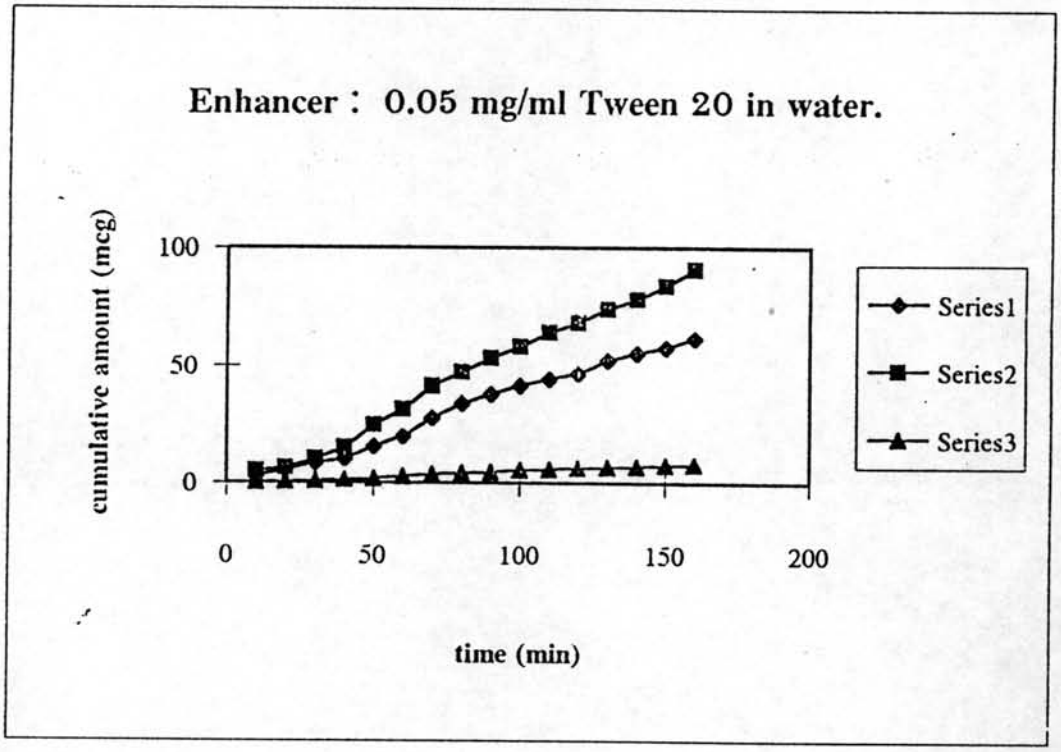
Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)
10	0.847	2.782	1.482	5.217	0.941	0.321
20	0.797	2.607	0.403	1.273	0.592	0.194
30	0.904	2.982	1.061	3.678	1.085	0.373
40	0.616	1.971	1.431	5.031	1.627	0.570
50	1.603	5.431	2.655	9.505	1.098	0.378
60	1.210	4.057	1.884	6.687	2.406	0.852
70	2.289	7.846	2.709	9.703	2.595	0.921
80	1.800	6.129	1.707	6.040	1.877	0.660
90	1.215	4.074	1.694	5.992	1.022	0.350
100	1.052	3.502	1.429	5.024	2.252	0.796
110	0.8380	2.751	1.703	6.025	1.116	0.384
120	0.6990	2.262	1.194	4.765	1.304	0.453
130	1.745	5.936	1.639	5.791	1.196	0.413
140	0.7870	2.571	1.184	4.128	0.826	0.279
150	0.7480	2.434	1.601	5.652	1.433	0.499
160	1.116	3.727	2.018	7.177	0.941	0.321
Receptor Volume (ml)	12.20		12.70		12.60	

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mcg)	Cumulative Amount (mcg)	Cumulative Amount (mcg)
10	2.78	5.21	0.32
20	5.38	6.49	0.51
30	8.37	10.16	0.88
40	10.34	15.19	1.45
50	15.77	24.70	1.83
60	19.83	31.39	2.68
70	27.67	41.09	3.60
80	33.80	47.13	4.26
90	37.87	53.12	4.61
100	41.38	58.15	5.41
110	44.13	64.17	5.79
120	46.39	68.30	6.25
130	52.33	74.13	6.66
140	55.20	78.25	6.94
150	57.63	83.91	7.44
160	61.36	91.08	7.76
Steady-state Slope (70-160 min)	0.3586	0.5353	0.0457
r^2	0.9905	0.9977	0.9885
Jss (mcg/min.cm^2)	0.1761	0.2629	0.0224
Membrane Thickness (mm.)	0.3500	0.3870	0.3950
Normalized Jss x10^3 (mcg/min.cm^2)	215.40	314.40	28.51

Jss = 186.10 ± 145.1

%cv = 78.01



Diclofenac Sodium Flux from 25 mg/ml Diclofenac Sodium Solution Through Newborn Pig Skin.

Enhancer: 1% w/v Brij 35 in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.451	0.920	1.678	2.499	3.391	4.339

$$Y = 0.0122 + 3.407x$$

$$r^2 = 0.9986$$

Diffusion Run Data

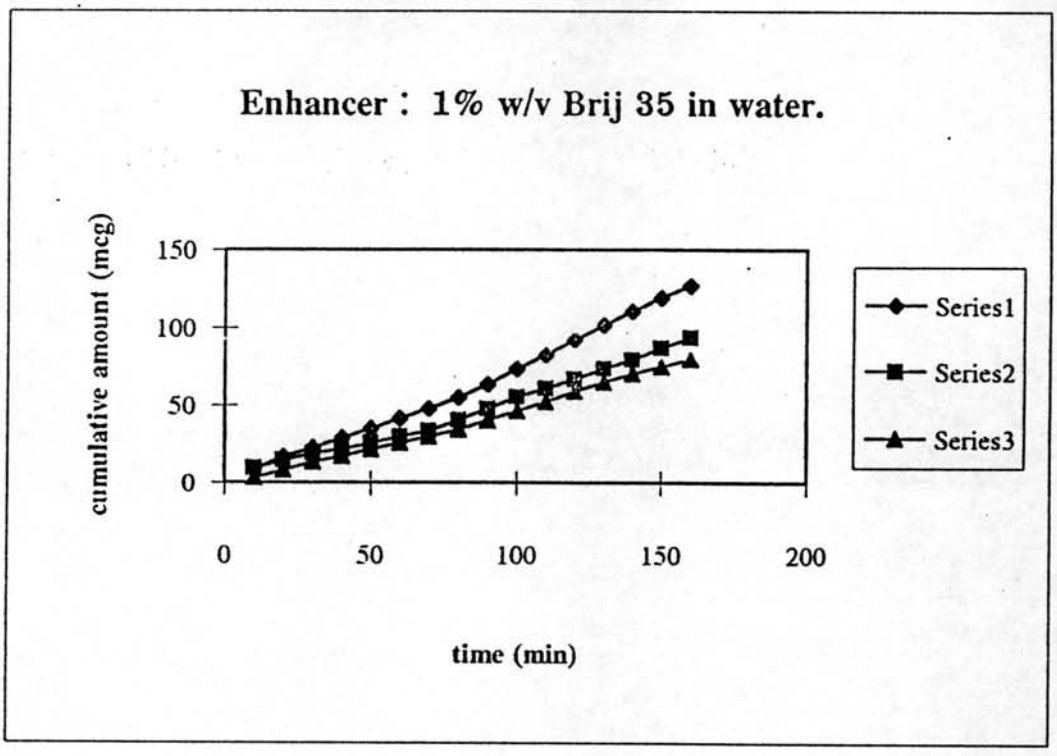
Diffusion Run	Run I		Run Ii		Run III	
Time (min)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)
10	2.486	9.219	2.579	9.460	0.844	3.051
20	2.065	7.650	1.436	5.247	1.408	5.119
30	1.602	5.924	1.221	4.455	1.456	5.296
40	1.649	6.100	0.758	2.748	1.020	3.696
50	1.641	6.070	1.053	3.836	1.252	4.547
60	1.670	6.178	1.137	4.415	1.172	4.254
70	1.785	6.606	1.050	3.824	1.093	3.964
80	1.900	7.035	1.837	6.725	1.272	4.621
90	2.324	8.615	1.906	6.980	1.555	5.659
100	2.749	10.19	2.088	7.650	1.595	5.805
110	2.417	8.960	1.500	5.483	1.659	6.040
120	2.702	10.02	1.655	6.054	1.830	6.667
130	2.518	9.338	1.810	6.626	1.724	6.729
140	2.426	8.995	1.671	6.114	1.478	5.376
150	2.334	8.653	2.090	7.658	1.250	4.540
160	2.111	7.821	1.880	6.844	1.369	4.976
Receptor Volume (ml)	12.70		12.50		12.50	

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mcg)	Cumulative Amount (mcg)	Cumulative Amount (mcg)
10	9.21	9.46	3.05
20	16.86	14.70	8.17
30	22.79	19.16	13.46
40	28.89	21.9	17.16
50	34.96	25.74	21.73
60	41.14	29.89	25.99
70	47.74	33.71	29.95
80	54.78	40.44	34.57
90	63.39	47.42	40.23
100	73.59	55.07	46.03
110	82.55	60.55	52.07
120	92.58	66.60	58.74
130	101.90	73.23	65.02
140	110.90	79.34	70.40
150	119.50	87.00	74.94
160	127.30	93.88	79.91
Steady-state Slope (70-160 min)	0.9100	0.6591	0.5737
r^2	0.9990	0.9991	0.9980
Jss (mcg/min.cm^2)	0.4307	0.3237	0.2818
Membrane Thickness (mm.)	0.2770	0.2200	0.2240
Normalized Jss x10^3 (mcg/min.cm^2)	425.50	310.10	224.50

Jss = 320.03 ± 100.8

%cv = 31.17



Diclofenac Sodium Flux from 25 mg/ml Diclofenac Sodium Solution Through Newborn Pig Skin.

Enhancer: 10% w/v Propylene Glycol in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.451	0.920	1.678	2.499	3.391	4.339

$$Y = 0.0122 + 3.407x$$

$$r^2 = 0.9986$$

Diffusion Run Data

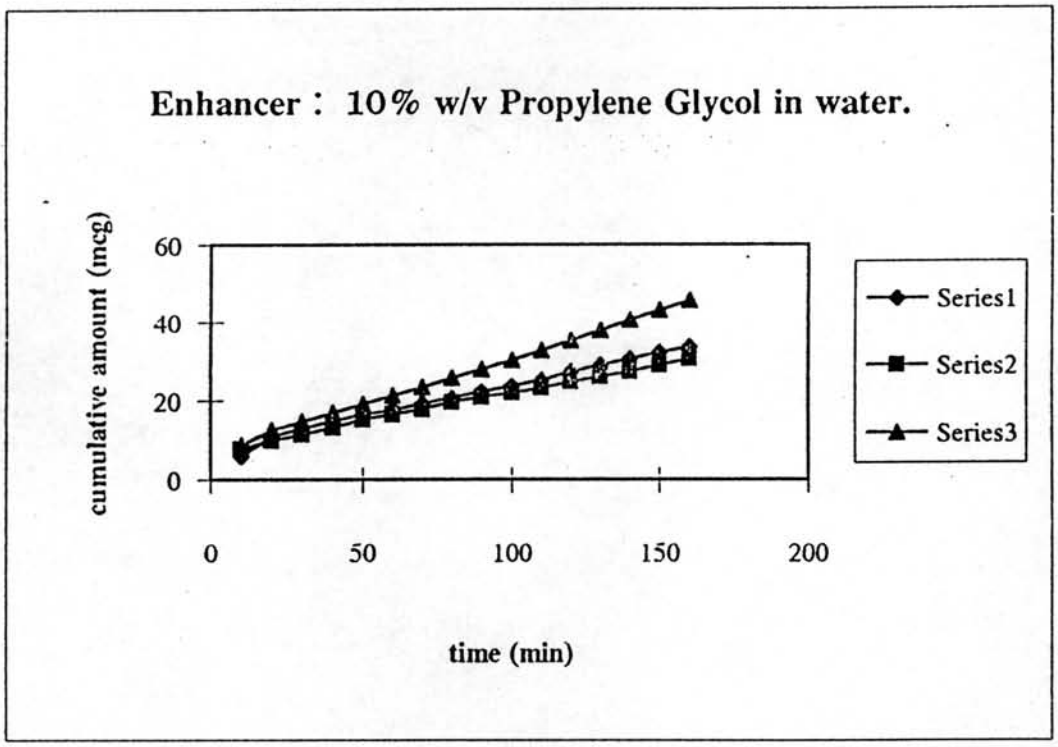
Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)
10	1.701	6.046	2.077	7.695	2.379	8.723
20	1.367	4.850	0.562	2.048	1.053	3.836
30	0.592	2.075	0.457	1.657	0.589	2.125
40	0.538	1.882	0.514	1.869	0.625	2.258
50	0.484	1.689	0.520	1.892	0.567	2.044
60	0.311	1.069	0.357	1.284	0.602	2.173
70	0.472	1.645	0.383	1.381	0.638	2.306
80	0.387	1.341	0.490	1.780	0.646	2.335
90	0.469	1.635	0.334	1.199	0.609	2.199
100	0.439	1.527	0.320	1.146	0.635	2.295
110	0.518	1.810	0.370	1.333	0.699	2.531
120	0.510	1.782	0.421	1.523	0.704	2.549
130	0.488	1.703	0.349	1.255	0.709	2.568
140	0.467	1.628	0.385	1.389	0.758	2.748
150	0.451	1.570	0.416	1.504	0.689	2.494
160	0.435	1.513	0.448	1.624	0.676	2.446
Receptor Volume (ml)	12.20		12.70		12.50	

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mcg)	Cumulative Amount (mcg)	Cumulative Amount (mcg)
10	6.04	7.69	8.72
20	10.89	9.74	12.55
30	12.97	11.40	14.68
40	14.85	13.26	16.94
50	16.54	15.16	18.98
60	17.61	16.44	21.15
70	19.25	17.82	23.46
80	20.59	19.60	25.80
90	22.23	20.80	27.99
100	23.75	21.95	30.29
110	25.56	23.28	32.82
120	27.35	24.80	35.37
130	29.05	26.06	37.94
140	30.68	27.45	40.69
150	32.25	28.95	43.18
160	33.76	30.57	45.63
Steady-state Slope (70-160 min)	0.1649	0.1377	0.2486
r^2	0.9992	0.9984	0.9991
Jss (mcg/min.cm^2)	0.0851	0.0651	0.1211
Membrane Thickness (mm.)	0.2770	0.4040	0.3790
Normalized Jss x10^3 (mcg/min.cm^2)	70.12	78.25	137.60

$Jss = 95.32 \pm 36.83$

$\%cv = 38.64$



Diclofenac Sodium Flux from 25 mg/ml Diclofenac Sodium Solution Through Newborn Pig Skin.

Enhancer: 10% w/v Tetraglycol in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.451	0.920	1.678	2.499	3.391	4.339

$$Y = 0.0122 + 3.407x$$

$$r^2 = 0.9986$$

Diffusion Run Data

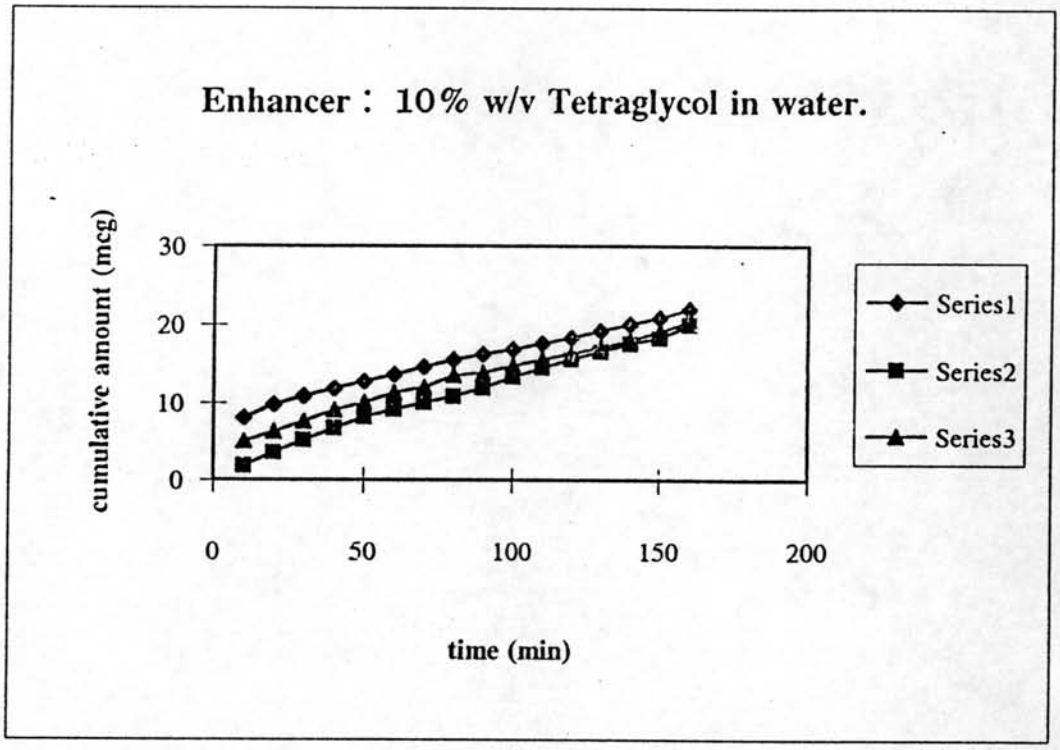
Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)	Peak Area Ratio	Amount (mcg)
10	2.170	8.041	0.515	1.853	1.372	4.987
20	0.484	1.758	0.463	1.661	0.367	1.301
30	0.302	1.079	0.450	1.613	0.381	1.352
40	0.282	1.005	0.437	1.565	0.396	1.407
50	0.264	0.938	0.411	1.469	0.302	1.062
60	0.246	0.871	0.276	0.972	0.345	1.220
70	0.290	1.035	0.256	0.898	0.218	0.754
80	0.247	0.874	0.237	0.828	0.281	0.985
90	0.196	0.684	0.317	1.123	0.265	0.927
100	0.198	0.692	0.397	1.418	0.249	0.868
110	0.192	0.669	0.348	1.237	0.233	0.809
120	0.219	0.770	0.300	1.060	0.225	0.780
130	0.247	0.874	0.286	1.008	0.217	0.751
140	0.241	0.852	0.268	0.942	0.277	0.791
150	0.835	0.830	0.212	0.736	0.307	1.081
160	0.290	1.035	0.177	0.607	0.338	1.194
Receptor Volume (ml)	12.7.		12.50		12.50	

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mcg)	Cumulative Amount (mcg)	Cumulative Amount (mcg)
10	8.04	1.85	4.98
20	9.79	3.51	6.28
30	10.87	5.12	7.64
40	11.88	6.69	9.04
50	12.82	8.16	10.10
60	13.69	9.13	11.32
70	14.72	10.03	12.08
80	15.60	10.85	13.62
90	16.28	11.98	13.99
100	16.97	13.40	14.86
110	17.64	14.63	15.67
120	18.41	15.69	16.45
130	19.29	16.70	17.20
140	20.14	17.64	18.17
150	20.97	18.38	19.25
160	22.00	19.99	20.44
Steady-state Slope (70-160 min)	0.0788	0.1046	0.0892
r^2	0.9967	0.9907	0.9965
Jss (mcg/min.cm^2)	0.0373	0.0513	0.0438
Membrane Thickness (mm.)	0.4170	0.3520	0.3350
Normalized Jss $x10^3$ (mcg/min.cm^2)	46.28	53.71	43.66

$Jss = 47.88 \pm 5.213$

$\%cv = 10.88$



Diclofenac Sodium Flux from 25 mg/ml Diclofenac Sodium Solution Through Newborn Pig Skin.

APPENDIX VII

Fluxes of Diclofenac Sodium from 25 mg/ml Diclofenac Sodium Solutions through Human Amnion.

Enhancer: Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.504	0.911	1.796	2.630	3.557	4.392

$$Y = 0.0546 + 3.474x$$

$$r^2 = 0.9988$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	2.243	4.803	3.557	8.002	3.985	0.809
10	2.808	6.043	2.714	6.076	4.582	10.260
15	3.453	7.458	2.078	4.622	4.283	9.584
20	2.262	4.844	2.383	5.319	4.086	9.138
25	2.115	4.522	2.374	5.299	5.180	11.610
30	2.348	5.033	1.811	4.012	2.328	5.243
35	2.433	5.220	1.610	3.553	0.759	6.130
40	3.290	7.100	3.120	4.003	2.954	6.504
45	2.479	5.321	3.152	7.076	2.090	6.880
50	1.274	2.676	1.944	4.316	3.106	6.916
55	2.417	5.184	2.227	4.963	2.614	5.801
60	2.320	4.972	2.736	6.126	2.871	6.384
65	2.311	4.952	2.940	6.952	3.249	7.240
70	2.302	4.932	2.507	5.603	3.060	6.812
75	2.175	4.653	2.290	6.107	2.292	5.071
80	2.708	5.981	2.074	4.613	2.676	5.942
Receptor Volume (ml)	12.20		12.70		12.60	

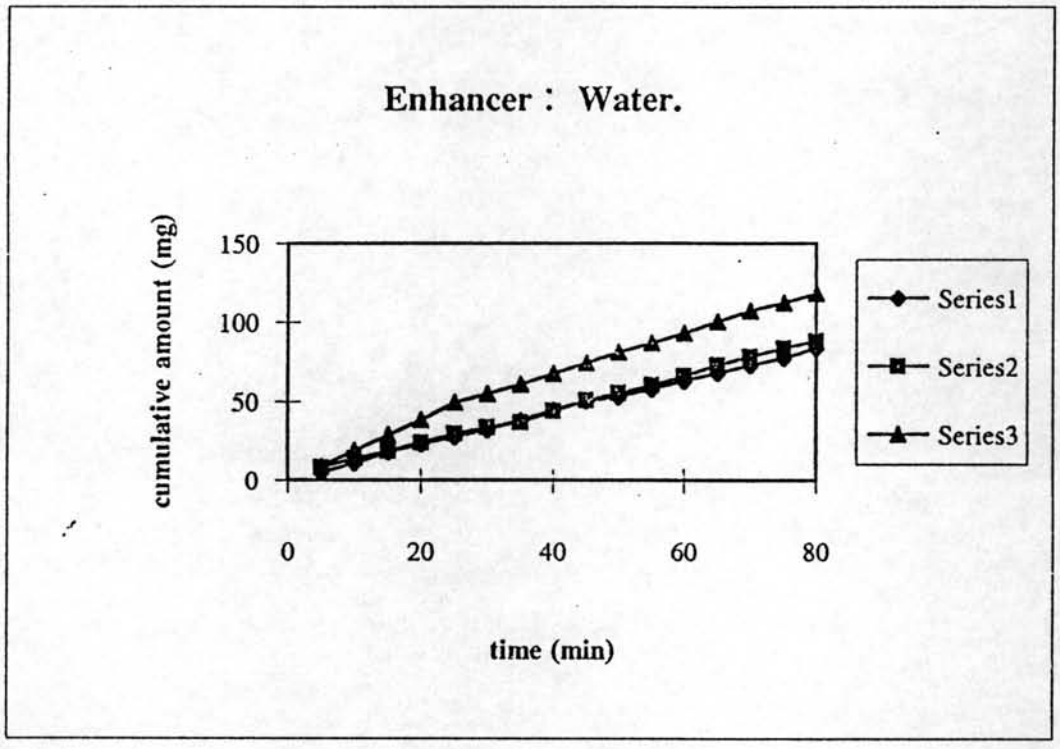
dilution factor: 625

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	4.80	8.00	8.90
10	10.84	14.07	19.17
15	18.30	18.70	28.75
20	23.14	24.01	37.89
25	27.67	29.31	49.51
30	32.07	33.33	54.75
35	37.92	36.88	60.88
40	45.02	43.88	67.38
45	50.34	50.96	74.26
50	53.02	55.27	81.18
55	58.20	60.24	86.98
60	63.17	66.36	93.36
65	68.12	72.95	100.6
70	73.06	78.56	107.4
75	77.71	83.66	112.4
80	83.69	88.28	118.4
Steady-state Slope (35-80 min)	0.9753	1.137	1.288
r^2	0.9968	0.9977	0.9991
Jss ($mg/min.cm^2$)	0.5037	0.5328	0.6326
Membrane Thickness (mm.)	0.0280	0.0420	0.0340
Normalized Jss $x10^3$ ($mg/min.cm^2$)	242.70	389.60	370.70

$Jss = 334.3 \pm 79.91$

$\%cv = 23.90$



Diclofenac Sodium Flux from 25 mg/ml Diclofenac Sodium Solution through Human Amnion.

Enhancer: 0.05 mg/ml Tween 20 in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.504	0.911	1.796	2.630	3.557	4.392

$$Y = 0.0546 + 3.474x$$

$$r^2 = 0.9988$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	5.593	4.049	3.132	2.225	2.724	1.920
10	5.077	3.672	2.583	1.795	2.741	1.932
15	6.152	4.457	3.648	2.598	4.074	2.892
20	5.047	3.650	3.281	2.332	3.031	2.141
25	5.710	4.134	3.094	2.197	4.456	3.167
30	5.570	4.032	3.621	2.578	4.753	2.661
35	5.614	4.064	3.509	2.497	4.163	2.956
40	4.991	3.069	2.360	1.666	3.089	2.183
45	4.431	3.199	3.265	2.321	3.023	2.136
50	5.020	3.630	2.758	1.954	3.089	2.183
55	5.389	3.900	3.488	2.482	3.105	2.195
60	5.293	3.829	3.291	2.340	3.698	2.621
65	4.702	3.397	3.627	2.583	3.545	2.511
70	5.341	8.864	3.459	2.461	3.621	2.566
75	5.021	3.631	3.375	2.400	3.659	2.593
80	5.181	3.748	3.501	2.491	3.602	2.552
Receptor Volume (ml)	12.70		12.50		12.50	

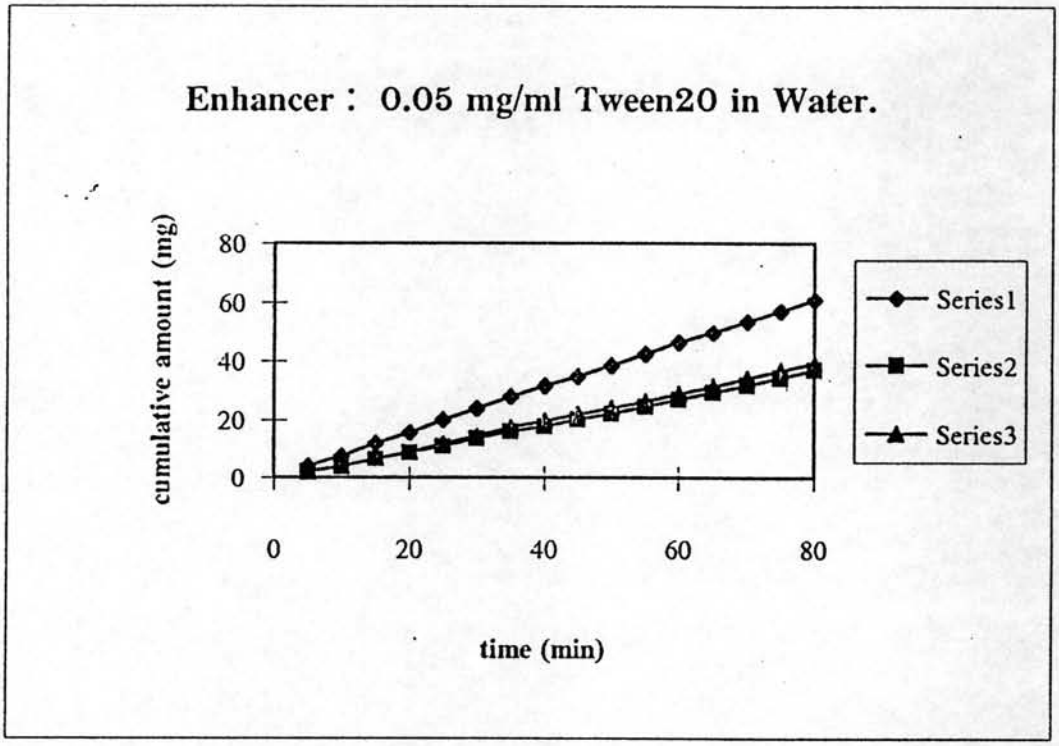
dilution factor: 200

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	4.04	2.22	1.92
10	7.72	4.02	3.85
15	12.17	6.61	6.74
20	15.82	8.95	8.88
25	19.96	11.14	12.05
30	23.99	13.72	14.71
35	28.05	16.22	17.67
40	31.66	17.88	19.85
45	34.86	20.20	21.98
50	38.49	22.16	24.17
55	42.39	24.64	26.36
60	46.22	26.98	28.98
65	49.62	29.56	31.49
70	53.48	32.02	34.06
75	57.11	34.42	36.65
80	60.86	36.92	39.18
Steady-state Slope (35-80 min)	0.7318	0.4675	0.4802
r^2	0.9997	0.9980	0.9983
Jss (mg/min.cm^2)	0.3594	0.2296	0.2358
Membrane Thickness (mm.)	0.0610	0.1020	0.1060
Normalized Jss x10^3 (mg/min.cm^2)	377.70	403.60	430.80

$Jss = 404.0 \pm 26.55$

$\%cv = 6.57$



Diclofenac Sodium Flux from 25 mg/ml Diclofenac Sodium Solution through Human Amnion.

Enhancer: 1% w/v Brij 35 in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.382	0.845	1.570	2.432	3.210	3.903

$$Y = 0.0122 + 3.407x$$

$$r^2 = 0.9986$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	1.021	2.508	1.211	2.955	1.163	2.822
10	1.719	4.272	2.044	5.037	1.039	2.513
15	1.950	4.855	1.108	2.698	1.144	2.774
20	1.259	3.109	1.475	3.615	1.084	2.625
25	1.644	4.082	1.049	2.550	1.245	3.026
30	1.637	4.065	2060	5.077	1.165	2.827
35	1.790	4.451	1.272	3.108	1.025	2.478
40	1.943	4.838	1.496	3.667	0.814	1.954
45	1.756	4.365	1.008	2.448	1.188	2.884
50	1.346	3.329	1.132	2.758	1.309	3.185
55	1.039	2.554	1.257	3.070	0.880	2.118
60	1.192	2.940	1.160	2.828	1.221	2.966
65	1.123	2.766	1.052	2.558	1.235	3.001
70	1.157	2.852	0.727	1.746	0.921	2.220
75	1.105	2.720	0.778	1.873	0.608	1.441
80	1.054	2.591	1.145	2.790	0.901	2.170
Receptor Volume (ml)	12.70		12.50		12.50	

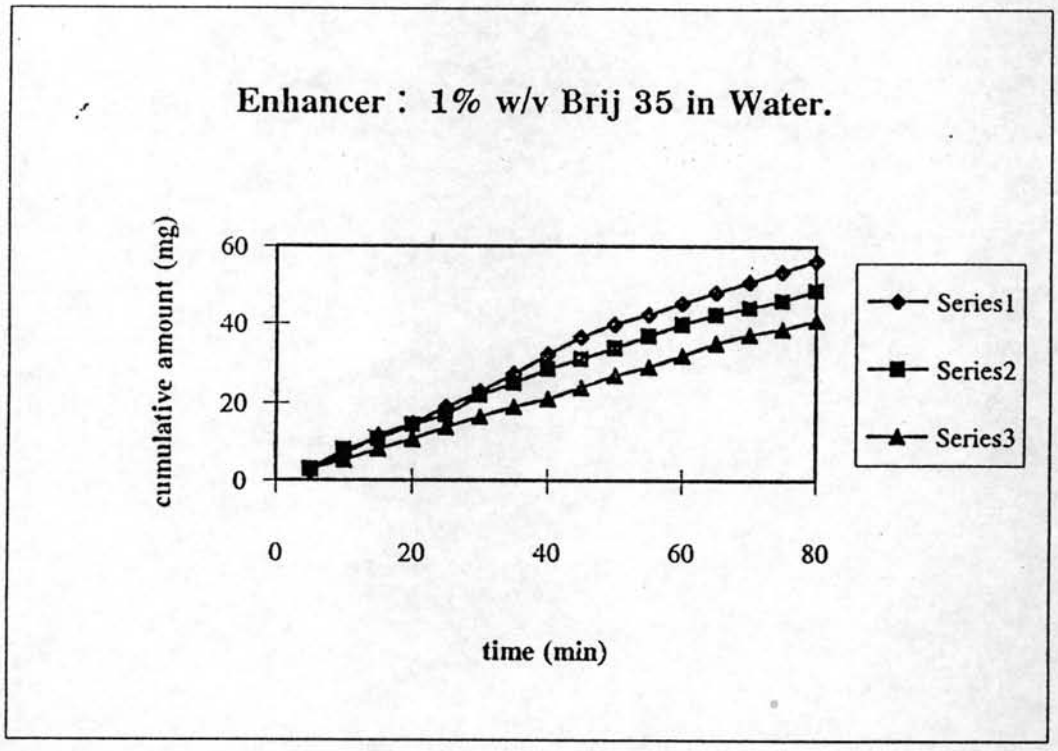
dilution factor: 625

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	2.50	2.95	2.82
10	6.78	7.99	5.33
15	11.63	10.69	8.10
20	14.74	14.30	10.73
25	18.82	16.85	13.76
30	22.89	21.93	16.58
35	27.34	25.04	19.08
40	32.18	28.70	21.01
45	36.54	31.15	23.90
50	39.87	33.91	27.08
55	42.42	36.98	29.20
60	45.36	39.81	32.17
65	48.13	42.39	35.17
70	50.98	44.14	37.39
75	53.70	46.01	38.83
80	56.29	48.80	41.00
Steady-state Slope (35-80 min)	0.6195	0.5244	0.5053
r^2	0.9894	0.9934	0.9944
Jss ($mg/min.cm^2$)	0.2933	0.2575	0.2482
Membrane Thickness (mm.)	0.0480	0.0510	0.0610
Normalized Jss $x10^3$ ($mg/min.cm^2$)	242.50	226.30	260.80

$Jss = 243.2 \pm 17.26$

$\%cv = 7.097$



Diclofenac Sodium Flux from 25 mg/ml Diclofenac Sodium Solution through Human Amnion.

Enhancer: 10% w/v Propylene Glycol in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.451	0.920	1.678	2.499	3.391	4.339

$$Y = 0.0122 + 3.407x$$

$$r^2 = 0.9986$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	1.987	4.418	1.343	3.099	0.610	1.377
10	1.742	3.870	0.936	2.151	0.886	2.012
15	1.498	3.324	1.506	3.479	1.162	2.648
20	1.248	2.765	2.077	4.809	2.141	4.903
25	1.162	2.572	1.678	3.880	2.242	5.136
30	1.076	2.380	1.280	2.953	0.733	1.660
35	1.688	3.749	1.803	4.171	0.761	1.724
40	1.398	3.100	1.684	3.894	0.815	1.849
45	1.109	2.454	1.565	3.616	0.869	1.973
50	1.138	2.519	1.344	3.102	0.990	2.252
55	1.167	2.583	1.103	2.540	1.005	2.286
60	0.745	1.639	1.322	3.050	1.021	2.323
65	1.020	3.254	1.261	2.908	1.138	2.593
70	0.874	1.928	1.542	3.563	1.553	3.549
75	0.947	2.091	1.982	4.588	1.027	2.337
80	0.983	2.172	1.200	2.766	0.917	2.084
Receptor Volume (ml)	12.20		12.70		12.50	

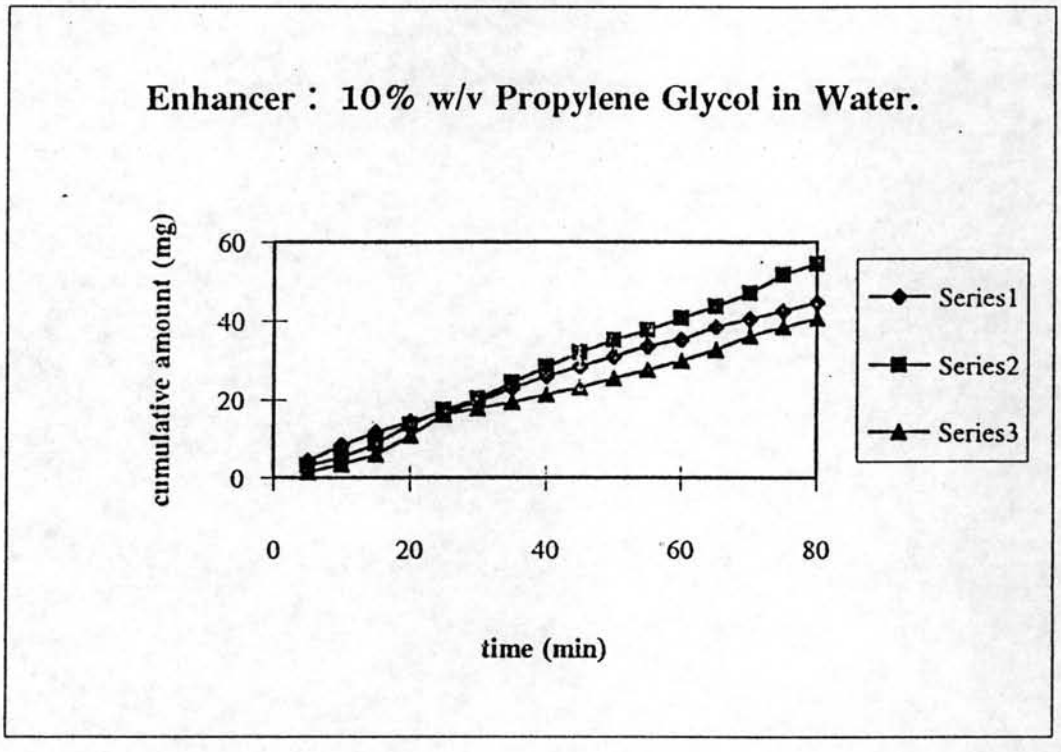
dilution factor: 625

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	4.41	3.09	1.37
10	8.28	5.25	3.38
15	11.61	8.72	6.03
20	14.37	13.53	10.94
25	16.94	17.41	16.07
30	19.32	20.37	17.73
35	23.07	24.54	19.46
40	26.17	28.43	21.30
45	28.63	32.05	23.28
50	31.15	35.15	25.53
55	33.73	37.69	27.82
60	35.37	40.74	30.14
65	38.62	43.65	32.73
70	40.55	47.21	36.28
75	42.64	51.80	38.62
80	44.81	54.56	40.70
Steady-state Slope (35-80 min)	0.4783	0.6525	0.4864
r^2	0.9971	0.9968	0.9946
Jss ($mg/min.cm^2$)	0.2470	0.3088	0.2389
Membrane Thickness (mm.)	0.0810	0.0770	0.1010
Normalized Jss $x10^3$ ($mg/min.cm^2$)	344.8	409.7	415.9

$Jss = 390.13 \pm 39.38$

$\%cv = 10.09$



Diclofenac Sodium Flux from 25 mg/ml Diclofenac Sodium Solution through Human Amnion.

Enhancer: 10% w/v Tetraglycol in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.451	0.920	1.678	2.499	3.391	4.339

$$Y = 0.0122 + 3.407x$$

$$r^2 = 0.9986$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	1.702	3.936	3.379	7.755	1.562	3.533
10	1.727	3.994	2.141	4.903	1.353	3.073
15	1.479	3.416	2.479	5.682	1.355	3.018
20	1.376	3.176	2.324	5.325	1.417	3.220
25	1.274	2.939	2.205	5.051	1.596	3.630
30	1.914	4.429	2.185	5.005	1.290	2.929
35	2.201	5.098	2.166	4.961	0.9840	2.227
40	2.063	4.776	2.538	5.818	1.775	4.041
45	2.438	5.650	2.333	5.346	1.393	3.165
50	2.401	5.564	1.791	4.097	1.290	2.929
55	2.357	5.461	1.900	4.348	1.699	3.867
60	2.314	5.361	1.876	4.293	1.750	3.984
65	2.227	5.158	1.853	4.240	1.700	3.869
70	2.140	4.956	1.784	4.081	1.801	4.100
75	2.020	4.676	1.715	3.922	1.902	4.332
80	1.878	4.345	1.699	3.885	1.799	4.096
Receptor Volume (ml)	12.70		12.50		12.50	

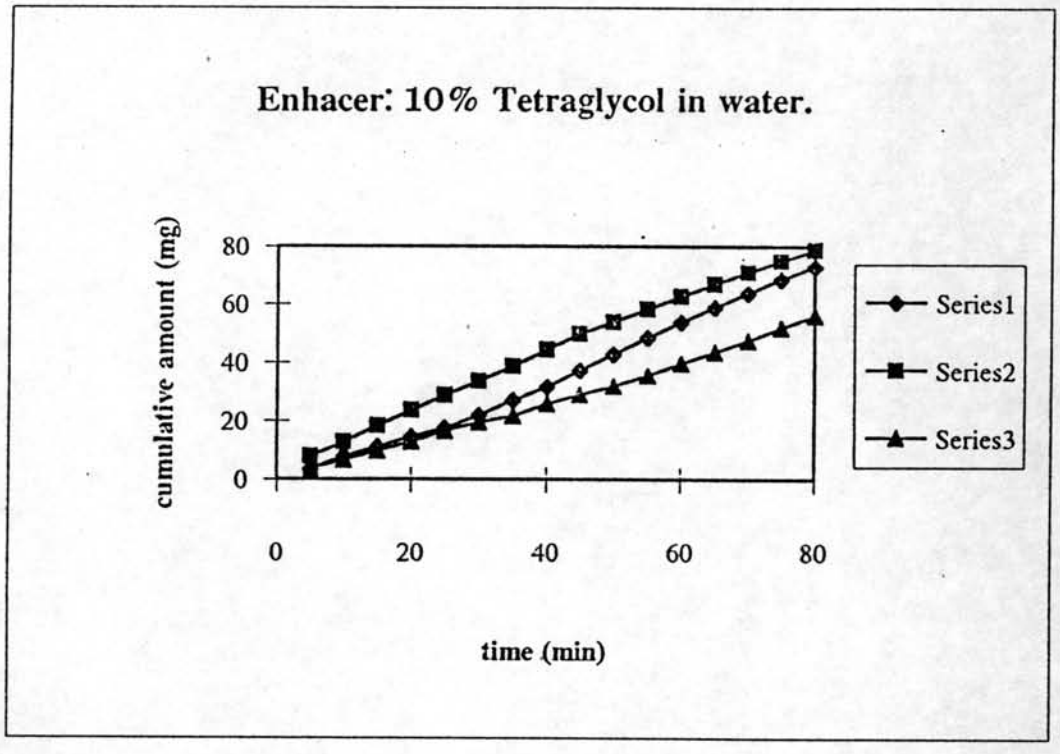
dilution factor: 625

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	3.39	7.75	3.55
10	7.93	12.68	6.62
15	11.34	18.34	9.70
20	14.52	23.66	12.92
25	17.46	28.71	16.55
30	21.89	33.72	19.48
35	26.98	38.68	21.71
40	31.76	44.50	25.75
45	37.41	49.84	28.91
50	42.97	53.94	31.84
55	48.43	58.29	35.71
60	53.80	62.58	39.69
65	58.95	66.82	43.56
70	63.91	70.90	47.66
75	68.59	74.82	51.99
80	72.93	78.71	96.09
Steady-state Slope (35-80 min)	1.038	0.8763	0..7587
r^2	0.9988	0.9967	0.9974
Jss ($mg/min.cm^2$)	0.4913	0.4291	0.3727
Membrane Thickness (mm.)	0.0620	0.0560	0.0770
Normalized Jss $x10^3$ ($mg/min.cm^2$)	524.70	414.08	494.50

$Jss = 477.76 \pm 57.22$

$\%cv = 11.97$



Diclofenac Sodium Flux from 25 mg/ml Diclofenac Sodium Solution through Human Amnion.

APPENDIX VIII

Fluxes of Diclofenac Sodium from 25 mg/ml Diclofenac Sodium Solutions through Human Placental Membrane.

Enhancer: Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.504	0.911	1.796	2.630	3.557	4.392

$$Y = 0.0546 + 3.474x$$

$$r^2 = 0.9998$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	4.304	1.492	3.814	1.374	0.781	0.263
10	3.574	1.235	4.224	1.524	1.327	0.461
15	3.045	1.050	3.851	1.387	1.805	0.634
20	3.245	1.120	3.965	1.429	1.999	0.705
25	3.384	1.169	4.022	1.450	1.761	0.618
30	3.713	1.284	4.442	1.630	1.355	0.471
35	2.549	0.886	3.422	1.230	1.465	0.511
40	2.736	0.941	3.625	1.305	1.619	0.567
45	2.441	0.838	2.520	0.901	1.625	0.569
50	2.438	0.836	3.117	1.119	1.239	0.429
55	2.471	0.848	3.476	1.250	1.197	0.414
60	2.818	0.970	3.246	1.166	1.562	0.546
65	2.173	0.743	3.633	1.308	1.024	0.351
70	2.811	0.976	3.826	1.378	1.880	0.662
75	2.825	0.972	4.020	1.449	1.423	0.496
80	1.729	0.587	3.988	1.437	1.465	0.511
Receptor Volume (ml)	12.20		12.70		12.60	

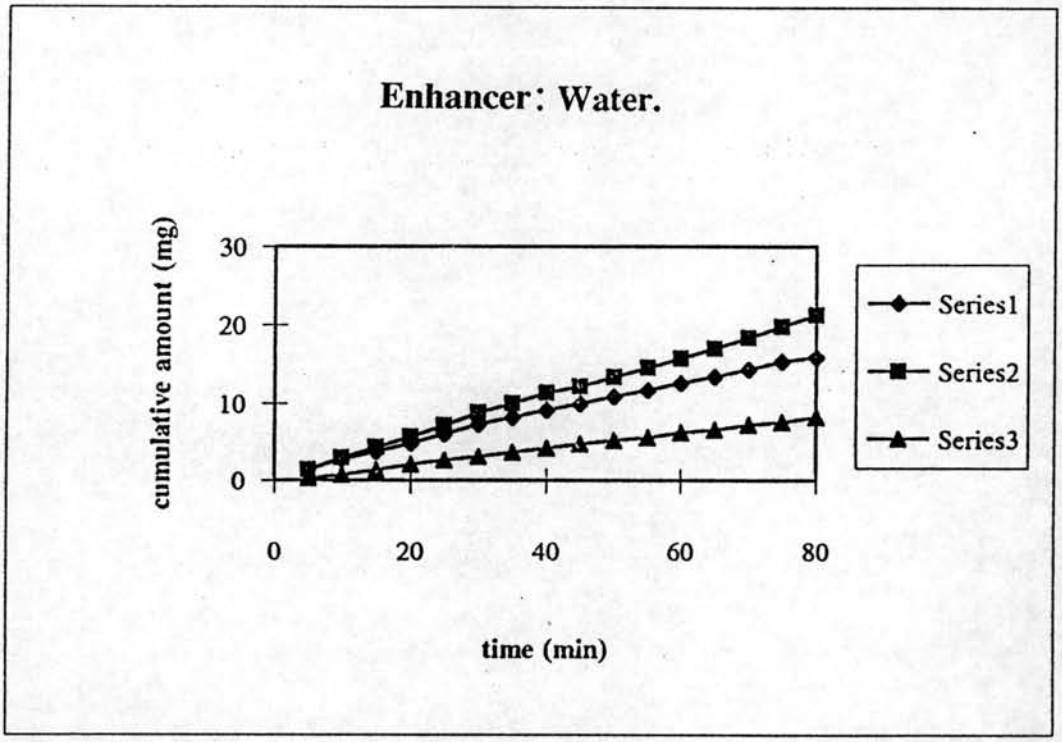
dilution factor: 100

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	1.49	1.37	0.26
10	2.72	2.89	0.72
15	3.77	4.28	1.35
20	4.87	5.71	2.06
25	6.06	7.16	2.68
30	7.35	8.76	3.15
35	8.23	9.99	3.66
40	9.17	11.30	4.23
45	10.01	12.20	4.79
50	10.85	13.32	5.22
55	11.69	14.57	5.64
60	12.66	15.73	6.18
65	13.41	17.04	6.53
70	14.37	18.42	7.20
75	15.35	19.87	7.60
80	15.93	21.31	8.20
Steady-state Slope (35-80 min)	0.1732	0.2487	0.0982
r^2	0.9991	0.9965	0.9979
Jss ($mg/min.cm^2$)	0.0894	0.1177	0.0482
Membrane Thickness (mm.)	0.1370	0.1450	0.2890
Normalized Jss $x10^3$ ($mg/min.cm^2$)	46.13	64.38	52.53

$Jss = 54.34 \pm 9.259$

$\%cv = 17.03$



Diclofenac Sodium Flux from 25 mg/ml Diclofenac Sodium Solution Through Human Placental membrane.

Enhancer: 0.05 mg/ml Tween 20 in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.504	0.911	1.796	2.630	3.557	4.392

$$Y = 0.0546 + 3.474x$$

$$r^2 = 0.9998$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	1.427	0.497	0.653	0.216	1.527	0.529
10	1.465	0.511	2.168	0.764	2.364	0.830
15	2.426	0.860	1.996	0.701	2.251	0.790
20	1.887	0.664	1.736	0.607	2.683	0.945
25	1.945	0.685	1.903	0.668	1.821	0.635
30	2.089	0.737	2.046	0.719	2.290	0.804
35	1.934	0.681	1.147	0.394	2.727	0.961
40	1.813	0.644	1.695	0.593	2.229	0.782
45	1.773	0.623	1.545	0.538	2.442	0.858
50	1.778	0.625	1.741	0.609	1.905	0.665
55	1.590	0.556	1.464	0.509	2.281	0.801
60	1.950	0.687	1.910	0.670	2.624	0.924
65	1.902	0.670	1.528	0.532	1.815	0.633
70	1.302	0.452	1.957	0.687	2.264	0.794
75	1.860	0.654	1.140	0.392	2.048	0.717
80	1.335	0.464	1.587	0.553	2.461	0.865
Receptor Volume (ml)	12.60		12.50		12.50	

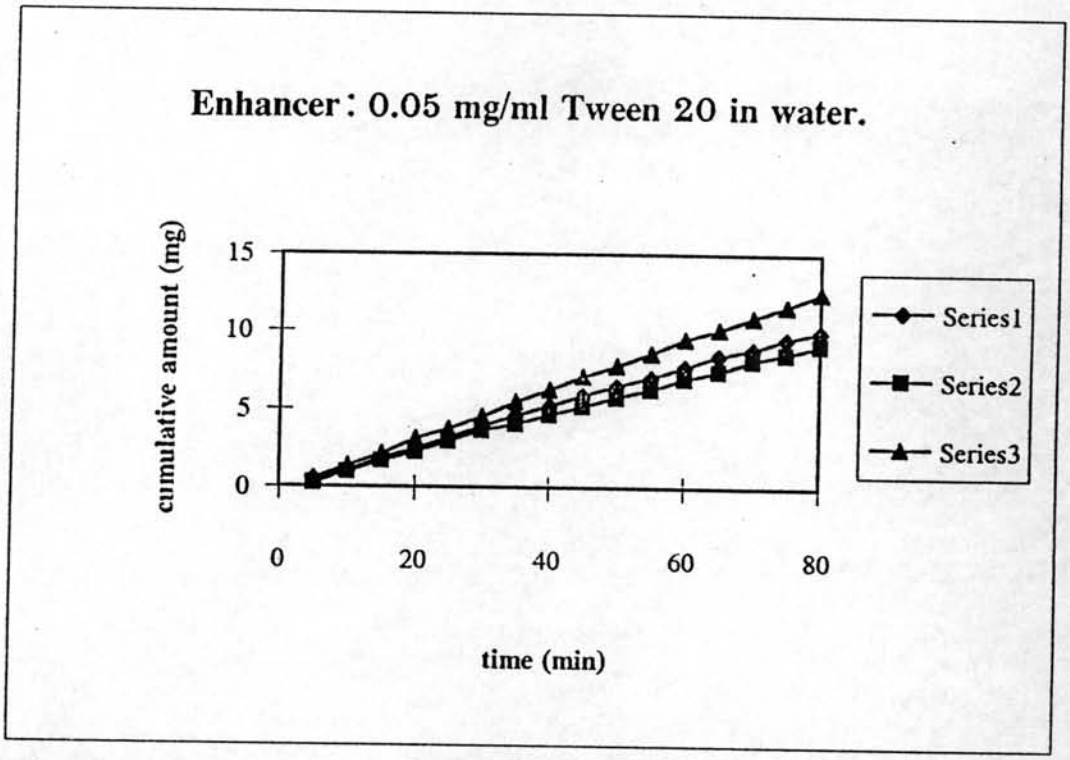
dilution factor: 100

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	0.49	0.21	0.52
10	1.00	0.98	1.35
15	1.86	1.68	2.14
20	2.53	2.28	3.09
25	3.21	2.98	3.72
30	3.95	3.67	4.53
35	4.63	4.06	5.49
40	5.27	4.66	6.27
45	5.90	5.2	7.13
50	6.52	5.809	7.79
55	7.08	6.31	8.60
60	7.77	6.98	9.52
65	8.44	7.52	10.15
70	8.89	8.20	10.95
75	9.54	8.59	11.66
80	10.01	9.15	12.53
Steady-state Slope (35-80 min)	0.1207	0.1141	0.1552
r^2	0.9987	0.9988	0.9994
Jss ($mg/min.cm^2$)	0.0592	0.0560	0.0762
Membrane Thickness (mm.)	0.1820	0.2170	0.2700
Normalized Jss $x10^3$ ($mg/min.cm^2$)	40.61	45.80	77.57

$Jss = 54.66 \pm 20.00$

$\%cv = 36.60$



Diclofenac Sodium Flux from 25 mg/ml Diclofenac Sodium Solution Through Human Placental membrane.

Enhancer: 1% w/v Brij 35 in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.451	0.920	1.678	2.499	3.391	4.339

$$Y = 0.0122 + 3.407$$

$$r^2 = 0.9986$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	0.744	0.261	0.6600	0.241	0.350	0.124
10	1.403	0.497	1.173	0.432	0.680	0.246
15	1.462	0.519	1.233	0.455	0.737	0.267
20	1.291	0.457	1.223	0.451	0.687	0.248
25	1.360	0.482	1.287	0.475	0.997	0.363
30	1.592	0.565	1.364	0.503	0.993	0.361
35	1.317	0.467	1.258	0.464	0.899	0.326
40	1.324	0.469	1.472	0.544	0.862	0.313
45	1.432	0.508	1.305	0.481	0.799	0.289
50	1.198	0.424	1.374	0.507	0.736	0.266
55	1.290	0.457	1.180	0.453	0.837	0.304
60	1.155	0.409	1.350	0.498	0.837	0.304
65	1.192	0.422	1.466	0.541	0.967	0.352
70	1.324	0.469	1.288	0.475	0.863	0.313
75	1.262	0.447	1.110	0.409	0.676	0.244
80	1.313	0.465	1.359	0.501	0.880	0.319
Receptor Volume (ml)	12.20		12.70		12.50	

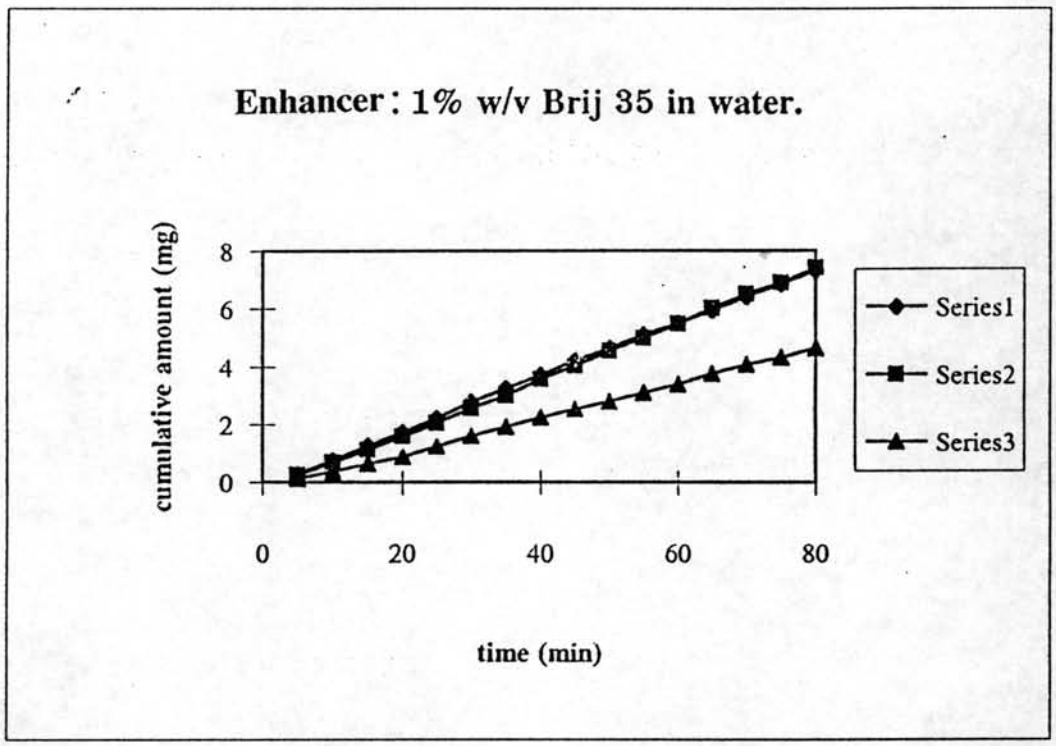
dilution factor: 100

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	0.26	0.24	0.12
10	0.75	0.67	0.37
15	1.27	1.12	0.63
20	1.73	1.57	0.88
25	2.21	2.05	1.24
30	2.78	2.55	1.60
35	3.24	3.02	1.93
40	3.71	3.56	2.24
45	4.22	4.04	2.53
50	4.64	4.55	2.80
55	5.10	4.98	3.10
60	5.51	5.48	3.41
65	5.93	6.02	3.76
70	6.40	6.50	4.07
75	6.85	6.91	4.32
80	7.31	7.41	4.63
Steady-state Slope (35-80 min)	0.0894	0.0971	0.0602
r^2	0.9996	0.9995	0.9993
Jss ($mg/min.cm^2$)	0.0461	0.0459	0.0295
Membrane Thickness (mm.)	0.2880	0.2720	0.3900
Normalized Jss $x10^3$ ($mg/min.cm^2$)	50.06	47.09	34.22

$Jss = 43.79 \pm 8.419$

$\%cv = 19.22$



Diclofenac Sodium Flux from 25 mg/ml Diclofenac Sodium Solution Through Human Placental membrane.

Enhancer: 10% w/v Propylene Glycol in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.382	0.845	1.570	2.432	3.210	3.903

$$Y = 0.0122 + 3.407x$$

$$r^2 = 0.9986$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	1.987	0.760	1.343	0.531	0.610	0.232
10	2.267	0.869	0.936	0.366	0.886	0.342
15	1.498	0.570	1.506	0.597	1.162	0.453
20	1.248	0.473	2.077	0.828	2.141	0.844
25	1.933	0.739	1.678	0.666	2.242	0.885
30	1.076	0.406	1.280	0.506	0.713	0.273
35	1.688	0.644	1.803	0.717	0.761	0.292
40	1.398	0.531	1.684	0.669	0.815	0.314
45	1.109	0.419	1.565	0.621	0.869	0.336
50	1.138	0.431	1.334	0.527	0.990	0.384
55	1.167	0.442	1.600	0.635	1.005	0.390
60	1.152	0.436	1.866	0.742	1.021	0.396
65	1.013	0.382	2.248	0.897	1.138	0.443
70	0.874	0.328	2.115	0.843	1.553	0.609
75	0.943	0.355	1.982	0.789	1.968	0.775
80	0.908	0.341	1.200	0.816	1.760	0.692
Receptor Volume (ml)	12.20		12.70		12.50	

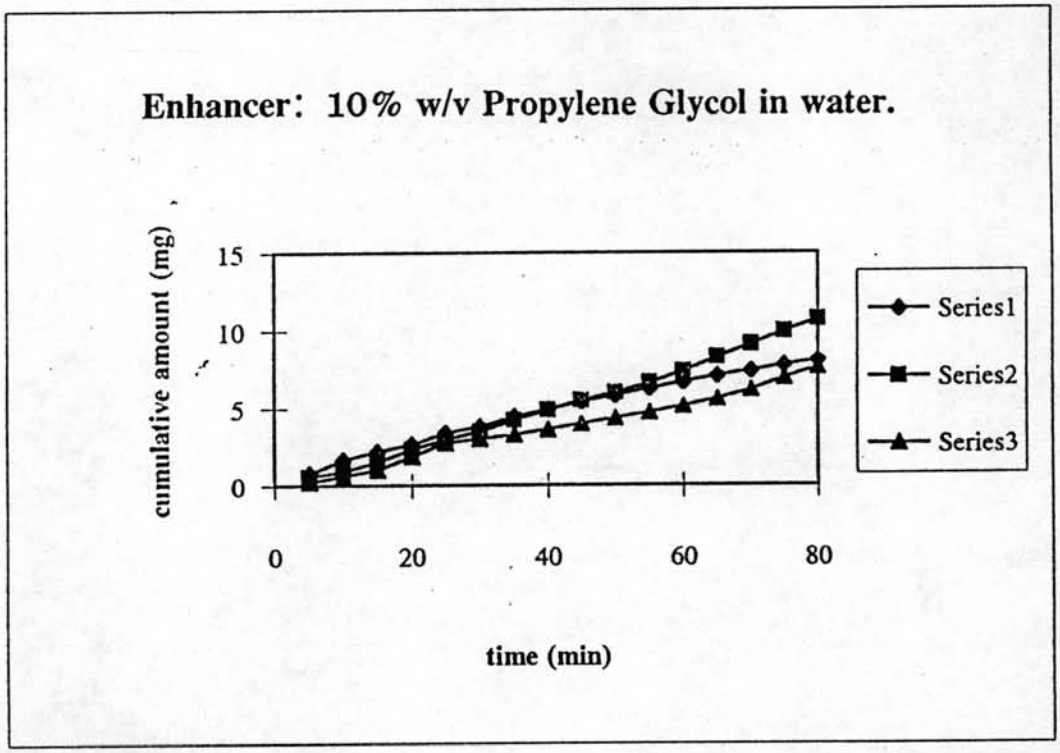
dilution factor: 100

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	0.76	0.53	0.23
10	1.62	0.89	0.57
15	2.19	1.49	1.02
20	2.67	2.32	1.87
25	3.41	2.98	2.75
30	3.81	3.49	3.02
35	4.46	4.21	3.32
40	4.99	4.88	3.63
45	5.41	5.50	3.97
50	5.84	6.02	4.35
55	6.28	6.66	4.74
60	6.72	7.40	5.14
65	7.10	8.30	5.58
70	7.43	9.14	6.19
75	7.78	9.93	6.96
80	8.12	10.75	7.66
Steady-state Slope (35-80 min)	0.0810	0.1454	0.0940
r^2	0.9959	0.9938	0.9747
Jss (mg/min.cm^2)	0.0418	0.0688	0.0461
Membrane Thickness (mm.)	0.1580	0.2990	0.2320
Normalized Jss x10^3 (mg/min.cm^2)	24.91	77.60	40.33

$Jss = 47.61 \pm 27.08$

%cv = 56.9



Diclofenac Sodium Flux from 25 mg/ml Diclofenac Sodium Solution Through Human Placental membrane.

Enhancer: 10% w/v Tetraglycol in Water.

Calibration Curve Data

Concentration (mcg/ml)	0.125	0.25	0.5	0.75	1.0	1.25
Peak Area Ratio	0.451	0.920	1.678	2.499	3.391	4.339

$$Y = 0.0122 + 3.407x$$

$$r^2 = 0.9986$$

Diffusion Run Data

Diffusion Run	Run I		Run II		Run III	
Time (min)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)	Peak Area Ratio	Amount (mg)
5	0.811	0.297	0.183	0.062	0.997	0.361
10	1.369	0.505	0.112	0.036	0.953	0.345
15	1.059	0.390	0.364	0.129	0.825	0.298
20	1.108	0.480	0.367	0.130	0.878	0.317
25	1.052	0.387	0.406	0.145	0.932	0.337
30	1.103	0.406	0.464	0.166	1.081	0.392
35	0.785	0.287	0.523	0.188	0.972	0.352
40	0.815	0.299	0.515	0.185	0.903	0.326
45	0.962	0.353	0.515	0.185	1.002	0.363
50	1.036	0.381	0.493	0.177	1.102	0.399
55	1.110	0.409	0.462	0.165	1.213	0.440
60	0.871	0.320	0.580	0.209	1.198	0.435
65	1.091	0.402	0.410	0.146	1.183	0.429
70	1.055	0.388	0.500	0.179	0.843	0.304
75	1.020	0.375	0.590	0.212	0.817	0.295
80	1.204	0.444	0.570	0.205	0.834	0.301
Receptor Volume (ml)	12.70		12.50		12.50	

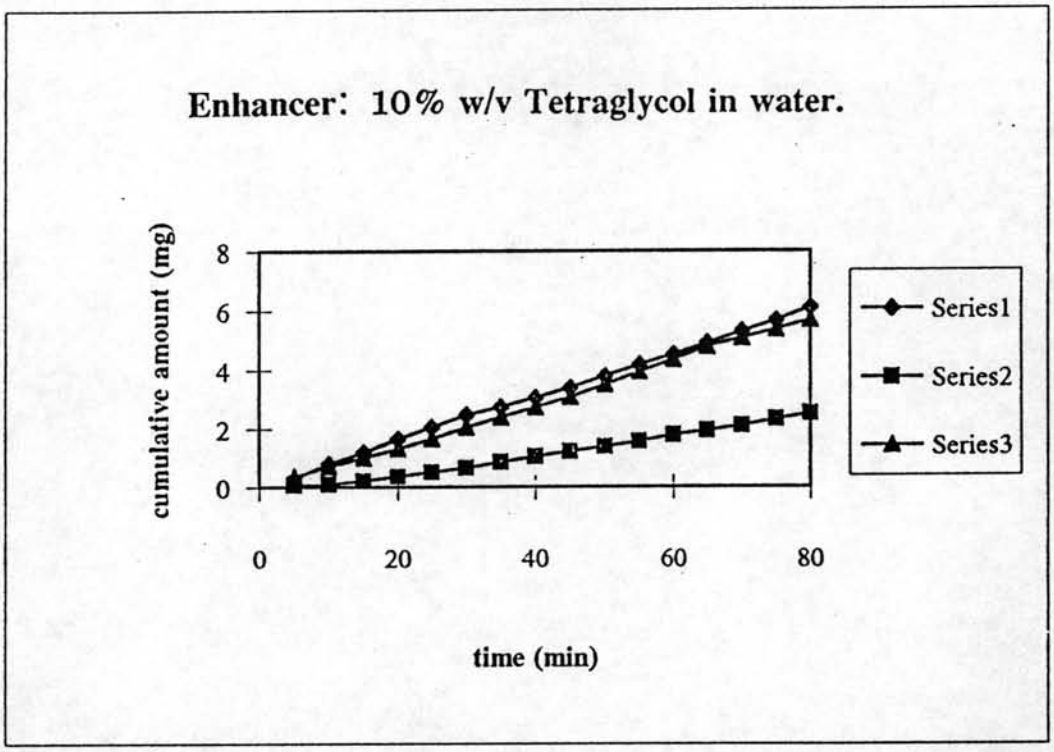
dilution factor: 10

Diffusion Run Data

Diffusion Run	Run I	Run II	Run III
Time (min)	Cumulative Amount (mg)	Cumulative Amount (mg)	Cumulative Amount (mg)
5	0.297	0.06	0.36
10	0.802	0.09	0.70
15	1.19	0.22	1.00
20	1.67	0.35	1.32
25	2.05	0.50	1.65
30	2.46	0.66	2.05
35	2.75	0.85	2.40
40	3.05	1.04	2.72
45	3.40	1.22	3.09
50	3.78	1.40	3.49
55	4.19	1.56	3.93
60	4.51	1.77	4.36
65	4.91	1.92	4.79
70	5.30	2.10	5.09
75	5.67	2.31	5.39
80	6.12	2.51	5.69
Steady-state Slope (35-80 min)	0.0750	0.0364	0.0759
r^2	0.9989	0.9991	0.9961
Jss ($mg/min.cm^2$)	0.0355	0.0179	0.0372
Membrane Thickness (mm.)	00.4170	0.3520	0.3350
Normalized Jss $x10^3$ ($mg/min.cm^2$)	25.60	28.90	31.84

$Jss = 32.11 \pm 3.36$

$\%cv = 10.45$



Diclofenac Sodium Flux from 25 mg/ml Diclofenac Sodium Solution Through Human Placental membrane.

APPENDIX IX

Partition Coefficient Data of Diclofenac Sodium.

Pig Skin: Donor Solution

Donor Solution	Initial conc. (mg/ml)	Final conc. (mg/ml)	Solution Volume (ml)	Membrane Volume (ml)	Partition Coefficient
Water	71.67	54.80	5	0.1644	9.36
Water	71.67	56.87	5	0.1608	8.09
Water	71.67	64.09	5	0.1712	3.45
(0.05 mg/ml) Tween 20 in Water	94.53	74.52	5	0.1400	9.59
(0.05 mg/ml) Tween 20 in Water	94.53	83.16	5	0.1548	4.42
(0.05 mg/ml) Tween 20 in Water	94.53	68.20	5	0.1580	12.21
(1% w/v) Brij 35 in Water	126.47	110.06	5	0.1108	6.73
(1% w/v) Brij 35 in Water	126.47	106.27	5	0.0880	10.80
(1% w/v) Brij 35 in Water	126.47	97.55	5	0.0896	16.50
(10% w/v) Propylene Glycol in Water	274.10	144.96	5	0.1668	26.72
(10% w/v) Propylene Glycol in Water	274.10	134.68	5	0.1408	36.80
(10% w/v) Propylene Glycol in Water	274.10	110.51	5	0.1340	55.24
(10% w/v) Tetraglycol in Water	360.52	231.95	5	0.1668	16.62
(10% w/v) Tetraglycol in Water	360.52	198.14	5	0.1408	29.11
(10% w/v) Tetraglycol in Water	360.52	203.69	5	0.1340	28.75

Water	=	6.97±3.11, %cv	= 44.62
Tween 20	=	8.74±3.97, %cv	= 45.38
Brij 35	=	11.34±4.91, %cv	= 43.28
Propylene glycol	=	39.58±14.46, %cv	= 36.53
Tetraglycol	=	24.82±7.11, %cv	= 28.63

Human Amnion: Donor Solution

Donor Solution	Initial conc. (mg/ml)	Final conc. (mg/ml)	Solution Volume (ml)	Membrane Volume (ml)	Partition Coefficient
Water	71.67	51.68	5	0.0110	175.87
Water	71.67	49.81	5	0.0168	130.60
Water	71.67	57.51	5	0.0136	90.52
(0.05 mg/ml) Tween 20 in Water	94.53	68.20	5	0.0610	31.64
(0.05 mg/ml) Tween 20 in Water	94.53	80.19	5	0.1020	8.76
(0.05 mg/ml) Tween 20 in Water	94.53	81.92	5	0.1060	7.26
(1% w/v) Brij 35 in Water	126.47	101.23	5	0.0192	64.84
(1% w/v) Brij 35 in Water	126.47	102.43	5	0.0204	57.44
(1% w/v) Brij 35 in Water	126.47	88.12	5	0.0244	89.01
(10% w/v) Propylene Glycol in Water	274.10	204.35	5	0.0810	21.09
(10% w/v) Propylene Glycol in Water	274.10	133.29	5	0.0770	68.68
(10% w/v) Propylene Glycol in Water	274.10	163.83	5	0.1010	33.33
(10% w/v) Tetraglycol in Water	360.52	159.06	5	0.0620	102.20
(10% w/v) Tetraglycol in Water	360.52	172.13	5	0.0560	97.75
(10% w/v) Tetraglycol in Water	360.52	171.68	5	0.0770	71.48

Water	=	132.32±42.66, %cv= 32.24
Tween 20	=	15.88±13.66, %cv = 85.98
Brij 35	=	70.43±16.51, %cv = 23.44
Propylene glycol	=	41.03±24.71, %cv = 60.22
Tetraglycol	=	90.47±16.59, %cv = 18.34

Human Placental Membrane: Donor Solution

Donor Solution	Initial conc. (mg/ml)	Final conc. (mg/ml)	Solution Volume (ml)	Membrane Volume (ml)	Partition Coefficient
Water	71.67	66.49	5	0.0548	7.108
Water	71.67	65.32	5	0.0580	8.380
Water	71.67	37.88	5	0.1150	38.78
(0.05 mg/ml) Tween 20 in Water	94.53	57.38	5	0.0728	44.46
(0.05 mg/ml) Tween 20 in Water	94.53	74.97	5	0.0868	15.02
(0.05 mg/ml) Tween 20 in Water	94.53	60.80	5	0.1080	25.68
(1% w/v) Brij 35 in Water	126.47	67.19	5	0.1152	38.24
(1% w/v) Brij 35 in Water	126.47	120.09	5	0.1088	2.450
(1% w/v) Brij 35 in Water	126.47	73.31	5	0.1560	23.21
(10% w/v) Propylene Glycol in Water	274.10	145.62	5	0.0632	69.82
(10% w/v) Propylene Glycol in Water	274.10	126.32	5	0.1196	48.92
(10% w/v) Propylene Glycol in Water	274.10	143.27	5	0.0928	49.25
(10% w/v) Tetraglycol in Water	360.5	195.73	5	0.1064	39.57
(10% w/v) Tetraglycol in Water	360.5	183.63	5	0.1712	28.13
(10% w/v) Tetraglycol in Water	360.5	171.53	5	0.0908	60.68

Water = 18.08±17.92, %cv = 99.11

Tween 20 = 28.383.14.90, %cv = 52.50

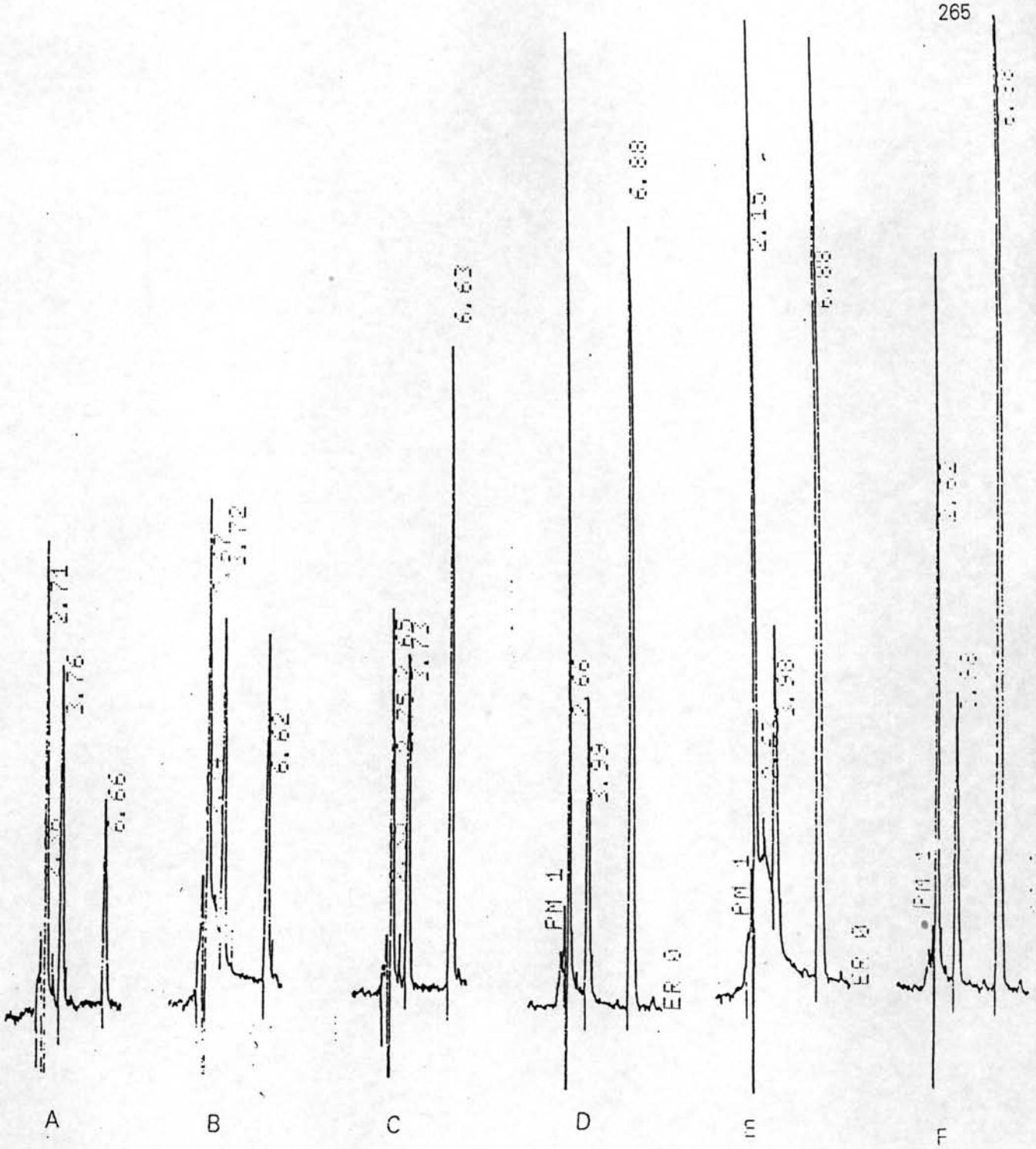
Brij 35 = 21.3±17.97, %cv = 84.37

Propylene glycol = 55.99±11.97, %cv = 21.38

Tetraglycol = 42.79±16.51, %cv = 38.58

APPENDIX X

HPLC Chromatogram of Diclofenac Sodium



High performance liquid chromatogram of diclofenac sodium (retention time ~ 6.62 - 6.88 min) and phenylbutazone (retention time ~ 3.72 - 3.98 min) at 280 nm.

Column : Spherisorb ODS 2, Injected volume : 20 µl.

Internal standard : 0.25 mcg/ml phenylbutazone.

Standard concentrations : A = 0.125 mcg/ml ; B = 0.25 mcg/ml.

C = 0.50 mcg/ml ; D = 0.75 mcg/ml.

E = 1.00 mcg/ml ; F = 1.25 mcg/ml.

VITA

Born on September 9, 1967, in Ayutthaya, Thailand, Miss. Jaratluck Akanimanee received a Bachelor of Science in Pharmacy in 1991 from the faculty of Pharmaceutical Science, Mahidol University, Bangkok, Thailand. She had been working as a pharmacist in the pharmacy department in Lopburi Hospital in 1991-1993.