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APPENDICES

Appendix A Preparation of Natural Rubber Film

Natural rubber film was prepared by using UV irradiation method (UV-curing). TMPTMP as a photoinitiator and MMMP as a crosslinking agent were added into a plasticizer. Then, indomethacin (IN) as a drug was added into the solution and stirred at 70 °C for 30 min. The solution would be a yellow homogeneous solution. The yellow solution was added in the natural rubber latex which was continuously stirred, and stirring was continued for 1 min to obtain a homogeneous rubber. The natural rubber films were prepared at various crosslinking agent concentrations of 0, 0.5, and 0.83 %v/v of dry rubber content (DRC) (60 %v/v of latex and density of rubber = 0.94 g/cm^3) by fixing the photoinitiator at 1.67 %wt of DRC. Then samples were inserted in the UV-curing machine for 10 min.

Effect of amount of crosslinking agent

Table A1 Natural rubber film preparation at various amounts of crosslinking agent with ethylene glycol (EG) 10 mL using initially 5 mL of DCNR

Photo-initiator		Crosslinking agent		Film characteristic	Film preparation	Sample name
%wt (DRC)	Content (g)	%v/v (DRC)	Content (mL)			
0	0	0	0		Separation of plasticizer and rubber	EG-DCNR1_0
1.67	0.047	0.5	0.015		Yes	EG-DCNR1_0.5
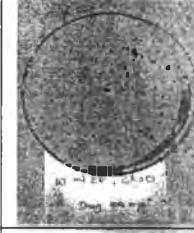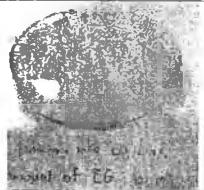
| 1.67	0.047	0.83	0.025		Yes	EG-DCNR1_0.83

The natural rubber films were successfully prepared at the amount of crosslinking agent of 0.5 and 0.83 %v/v of DRC. In this work, the lowest amount of crosslinking agent (0.5 %v/v of DRC) was chosen and used to prepare the natural rubber films at various amounts of plasticizer.

Effect of types of plasticizer

There were many types of plasticizers to prepare the natural rubber film. Difference in plasticizers affected the quality of the film when mixed with the natural rubber latex.

Table A2 Effect of types of plasticizer (10 mL) to prepare natural rubber film by using crosslinking agent (CR) at 0.5 %v/v and photoinitiator (PhI) at 1.67 %wt of DRC using initially 5 mL of DCNR

Types of plasticizer	Amount of PhI (g)	Amount of CR (mL)	Film characteristic	Film preparation	Sample name
Propanol (PR)	0.047	0.015		Rubber agglomeration	10PR_DCNR1
Tween20 (TW)	0.047	0.015		Rubber agglomeration	10TW_DCNR1

Dibuthyl phthalate (DBP)	0.047	0.015		Rubber agglomeration	10DBP_ DCNR1
Ethylene glycol (EG)	0.047	0.015		Yes	10EG_ DCNR1
Propylene glycol (PG)	0.047	0.015		Yes	10PG_ DCNR1
Glycerol (GLY)	0.047	0.015		Yes	10GLY_ DCNR1
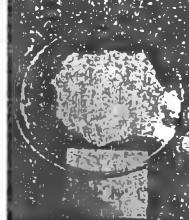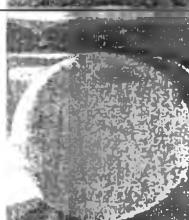
The plasticizers namely EG, PG, and GLY could be used to prepare the natural rubber film but the plasticizers namely propanol, tween80, and DBP could not be used to prepare the film because of the aggregation of the rubber.

Effect of amounts of plasticizer (EG)

Table A3 Natural rubber film preparation by using crosslinking agent (CR) at 0.5 %v/v and photoinitiator (PhI) 1.67 %wt of DRC with various amounts of EG using initially 5 mL of DCNR

Amount of EG (mL)	Amount of PhI (g)	Amount of CR (mL)	Film characteristic	Film preparation	Sample name
10	0.047	0.015		Yes	100IN-10EG_DCNR1
20	0.047	0.015		Separation of plasticizer and rubber	100IN-20EG_DCNR1
30	0.047	0.015		Separation of plasticizer and rubber	100IN-30EG_DCNR1
50	0.047	0.015		Separation of plasticizer and rubber	100IN-50EG_DCNR1
70	0.047	0.015		Separation of plasticizer and rubber	100IN-70EG_DCNR1
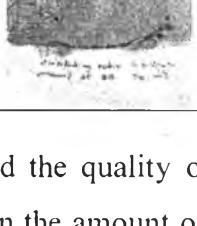
The amount of plasticizer affected the quality of natural rubber film. The natural rubber could not be prepared when the amount of ethylene glycol was more than 20 ml due to the separation between the plasticizer and the rubber.

Conditions of natural rubber patches for testing

The conditions of natural rubber patch are shown in Table A4. The samples were prepared for the permeation study of IN through pig skin membrane under the effects of plasticizer type, amount of plasticizer, and electrical potential.

Table A4 Information of IN-loaded plastiizers_DCNR using crosslinking agent (CR) at 0.5 %v/v and photoinitiator (PhI) at 1.67 %wt of DRC using initially 5 mL of DCNR

Amount of CR (mL)	Amount of PhI (g)	Amount of IN (mg)	Type of plasticizer	Amount of plasticizer (mL)	Sample name
0.015	0.047	100	GLY	10	100IN-10GLY_DCNR1
			PG	10	100IN-10PG_DCNR1
			EG	5	100IN-5EG_DCNR1
				10	100IN-10EG_DCNR1
				15	100IN-15EG_DCNR1
		200		10	200IN-10EG_DCCNR1
		300 (maximum)		10	300IN-10EG_DCNR1

The initial amounts of IN in IN-GLY_NR2, IN-PG_NR2, IN-EG_NR1, IN-EG_NR2, IN-EG_NR3, and mIN-EG_NR2 (area 3.14 cm^2) were 2.66, 3.88, 3.29, 3.24, 2.58, and 7.25 mg, respectively. IN-GLY_NR2, IN-PG_NR2, and IN-EG_NR2 were used for the permeation study of IN under the effect of plasticizer type. IN-EG_NR1, IN-EG_NR2, IN-EG_NR3 were used for the permeation study of IN under the effect of plasticizer amount and mIN-EG_NR2 was used for the permeation study of IN under the effect of electrical potential.

Preparation of deproteinized natural rubber patch

The deproteinized natural rubber latex (DPNR) was used to prepare the DPNR patch by using 0.5 %v/v crosslinking agent and 1.67 %wt of DRC and using EG as the plasticizer. The crosslinking agent and photoinitiator were dissolved in 10 mL of EG. Then, IN was added in the solution and stirring was kept at 70 °C for an hour to obtain a yellow homogeneous solution. Ammonia (NH_3) was added in the DPNR at various amounts of NH_3 of 1.0, 1.5, and 2.0 mL per 5 mL DPNR. The yellow homogeneous solution was then added into DPNR with and without NH_3. Then, the mixture solution was poured in a petri dish and inserted in the UV-curing machine for 10 min.

Effect of amounts of ammonia (NH_3)

Table A5 Deproteinized natural rubber film preparation by using crosslinking agent at 0.5 %v/v and photoinitiator at 1.67 %wt of DRC at various amounts of NH_3 using initially 5 mL of DPNR

Amount of IN (mg)	Amount of EG (mL)	Amount of NH_3 (mL)	Film characteristic	Film preparation	Sample name
100	10	-		Rubber agglomeration	100IN-EG_DPNR2
200	10	-		Rubber agglomeration	200IN-EG_DPNR2
300	10	-		Rubber agglomeration	300IN-EG_DPNR2

100	10	1.0		Rubber agglomeration	100IN-1AEG_DPNR
100	10	1.5		Rubber agglomeration	100IN-1.5AEG_DPNR
100	10	2.0		Yes	100IN-2AEG_DPNR
300	10	2.0		Yes	300IN-2AEG_DPNR

The DPNR was successfully used to prepare the DPNR film by adding NH_3 into the DPNR at 2.0 mL per 5 mL DPNR before pouring the yellow homogeneous solution into the DPNR. The DPNR film with the amount of NH_3 less than 2.0 mL could not be used to prepare the film because of the agglomeration of the rubber.

Effect of plasticizer

Table A6 Deproteinized natural rubber film preparation by using crosslinking agent at 0.5 %v/v and photoinitiator at 1.67 %wt of DRC using various of plasticizers using initially 5 mL of DPNR

Types of plasticizer	Amounts of plasticizer (mL)	Amount of IN (mg)	Film characteristic	Film preparation	Sample name
EG	5			Rubber agglomeration	100IN-EG_DPNR1
PG	5	100		Rubber agglomeration	100IN-PG_DPNR1
GLY	5			Rubber agglomeration	100IN-GLY_DPNR1
DBP	5			Rubber agglomeration	100IN-DBP_DPNR1

The DPNR film could not be prepared by using four types of plasticizer namely EG, PG, GLY, and DBP due to the aggregation of the rubber when adding a mixture of plasticizer and IN into the DPNR. The amounts of EG, PG, GLY, and DBP that caused the agglomeration of rubber were 5mL.

Effect of amounts of surfactant

- **Ethylene glycol (EG)**

Table A7 Deproteinized natural rubber film preparation by using crosslinking agent at 0.5 %v/v and photoinitiator at 1.67 %wt of DRC using various types and amounts of surfactant using initially amount of EG 10 mL per 5 mL of DPNR

Types of surfactant	Amount surfactant (mg)	Amount of IN (mg)	Film characteristic	Film preparation	Sample name
SDS	2.5			Rubber agglomeration	100IN-2.5SEG_DPNR
	25	100		Rubber agglomeration	100IN-25SEG_DPNR
	250	.		Rubber agglomeration	100IN-250SEG_DPNR
TWEEN20	2.5			Rubber agglomeration	100IN-2.5TEG_DPNR
	25	100		Rubber agglomeration	100IN-25TEG_DPNR
	250			Yes	100IN-250TEG_DPNR

TWEEN20	250	200		Rubber agglomeration	200IN-250TEG_DPNR
		300		Rubber agglomeration	300IN-250TEG_DPNR
	500	200		Yes	200IN-10EG_DPNR
		300		Rubber agglomeration	300IN-500TEG_DPNR
	700			Rubber agglomeration	300IN-700TEG_DPNR
	800	300		Rubber agglomeration	300IN-800TEG_DPNR
	900			Rubber agglomeration	300IN-900TEG_DPNR
	1000			Separation of plasticizer and rubber	300IN-1000TEG_DPNR
CTAB	2.5	100		Rubber agglomeration	100IN-2.5CEG_DPNR
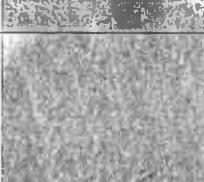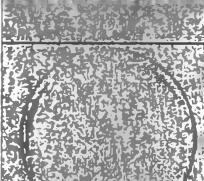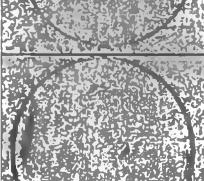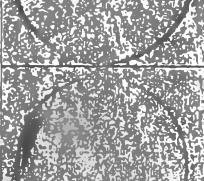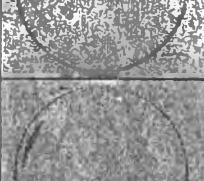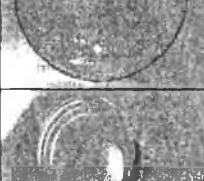
o

CTAB	25	100		Rubber agglomeration	100IN-25CEG_DPNR
				Yes	100IN-250CEG_DPNR
	250	200		Rubber agglomeration	200IN-250CEG_DPNR
		300		Rubber agglomeration	300IN-250CEG_DPNR
	500	200		Rubber agglomeration	200IN-500CEG_DPNR
	700	300		Rubber agglomeration	300IN-700CEG_DPNR
	800			Rubber agglomeration	300IN-800CEG_DPNR
	900			Rubber agglomeration	300IN-900CEG_DPNR
	1000			Rubber agglomeration	300IN-1000CEG_DPNR
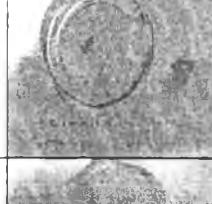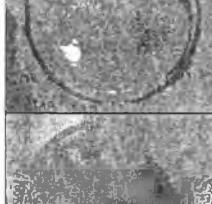
The DNR film using EG as the plasticizer was successfully prepared by using TWEEN20 or CTAB as surfactants at 500 mg and 250 mg, respectively using initially 5 mL of DPNR. The maximum amounts of IN loaded in system of TWEEN20 and CTAB were 200 and 100 mg, respectively.

- **Propylene glycol (PG)**

Table A8 Deproteinized natural rubber film preparation by using crosslinking agent at 0.5 %v/v and photoinitiator at 1.67 %wt of DRC using various types and amounts of surfactant using initially amount of PG 10 mL per 5 mL of DPNR

Types of surfactant	Amount surfactant (mg)	Amount of IN (mg)	Film characteristic	Film preparation	Sample name
SDS	2.5			Rubber agglomeration	100IN-2.5SPG_DPNR
	25	100		Rubber agglomeration	100IN-25SPG_DPNR
	250			Rubber agglomeration	100IN-250SPG_DPNR
TWEEN20	2.5	100		Rubber agglomeration	100IN-2.5TPG_DPNR
	25			Rubber agglomeration	100IN-25TPG_DPNR

TWEEN20	250	100		Rubber agglomeration	100IN-250TPG_DPNR
CTAB	2.5	100		Rubber agglomeration	100IN-2.5CPG_DPNR
	25			Rubber agglomeration	100IN-25CPG_DPNR
	250			Rubber agglomeration	100IN-250CPG_DPNR

The DPNR film could not be prepared in all of surfactant conditions by using PG as the plasticizer due to the agglomeration of DPNR.

- **Glycerol (GLY)**

Table A9 Deproteinized natural rubber film preparation by using crosslinking agent at 0.5 %v/v and photoinitiator at 1.67 %wt of DRC using various types and amounts of surfactant using initially amount of GLY 10 mL per 5 mL of DPNR

Types of surfactant	Amount surfactant (mg)	Amount of IN (mg)	Film characteristic	Film preparation	Sample name
SDS	2.5	100		Rubber agglomeration	100IN-2.5SGLY_DPNR

SDS	25	100		Rubber agglomeration	100IN-25SGLY_DPNR
	250			Rubber agglomeration	100IN-250SGLY_DPNR
TWEEN20	2.5	100		Rubber agglomeration	100IN-2.5TGLY_DPNR
	25			Rubber agglomeration	100IN-25TGLY_DPNR
	250			Rubber agglomeration	100IN-250TGLY_DPNR
CTAB	2.5	100		Rubber agglomeration	100IN-2.5CGLY_DPNR
	25			Rubber agglomeration	100IN-25CGLY_DPNR
	250			Rubber agglomeration	100IN-250CGLY_DPNR
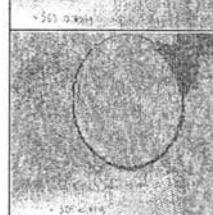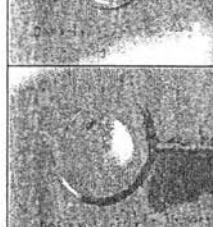
The DPNR film could not be prepared in all surfactant conditions by using GLY as the plasticizer due to the agglomeration of DPNR.

- **Dibutyl phthalate (DBP)**

Table A10   Deproteinized natural rubber film preparation by using crosslinking agent at 0.5 %v/v and photoinitiator at 1.67 %wt of DRC using various types and amounts of surfactant using initially amount of DBP 10 mL per 5 mL of DPNR
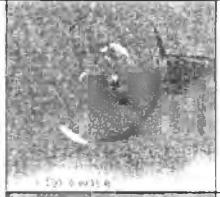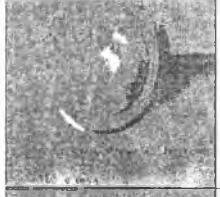
Types of surfactant	Amount surfactant (mg)	Amount of IN (mg)	Film characteristic	Film preparation	Sample name
SDS	2.5			Separation of plasticizer and rubber	100IN-2.5SDBP_DPNR
	25	100		Separation of plasticizer and rubber	100IN-25SDBP_DPNR
	250			Separation of plasticizer and rubber	100IN-250SDBP_DPNR
TWEEN20	2.5			Separation of plasticizer and rubber	100IN-2.5TDBP_DPNR
	25	100		Separation of plasticizer and rubber	100IN-25TDBP_DPNR
	250			Separation of plasticizer and rubber	100IN-250TDBP_DPNR
CTAB	2.5	100		Separation of plasticizer and rubber	100IN-2.5CDBP_DPNR
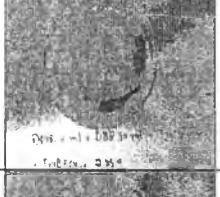
				Separation of plasticizer and rubber	100IN-25CDBP_DPNR
CTAB	25	100			
	250			Separation of plasticizer and rubber	100IN-250CDBP_DPNR

The DPNR film could not be prepared in all of surfactant condition by using DBP as the plasticizer due to the separation of DBP and DPNR.

- **Polydimethylsiloxane (PDMS)**

Table A11 Dissolution of IN in PDMS by various types of surfactant using initially amount of PDMS at 10 mL

Types of surfactant	Amount surfactant (mg)	Amount of IN (mg)	Film characteristic	Film preparation	Sample name
-	-			IN cannot dissolve in PDMS	100IN-PDMS
SDS	250			IN cannot dissolve in PDMS	100IN-250SPDMS
TWEEN20	250	100		IN cannot dissolve in PDMS	100IN-250TPDMS
CTAB	250			IN cannot dissolve in PDMS	100IN-250CPDMS
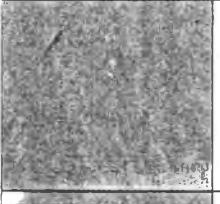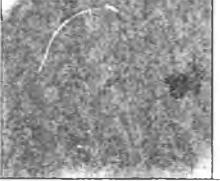
IN did not dissolve in PDMS even if the surfactants were added into the PDMS. Hence, PDMS could not be used as a plasticizer to prepare DPNR film.

Appendix B Preparation of Deproteinized Natural Rubber via Saponification Method

```
┌─────────────────────────────┐
│   Double centrifuge natural │
│         rubber latex        │
└─────────────────────────────┘
               │
               ▼
┌─────────────────────────────┐
│   Alkaline base + Surfactant│
└─────────────────────────────┘
               │      Stirred at 60 °C for 3 h
               ▼
┌─────────────────────────────┐
│  Washing with deionized water│
│ (ratio of rubber:water (v:v) = 1:5)│
│          for 30 min         │
└─────────────────────────────┘
               │
               ▼
┌─────────────────────────────┐        ┌──────────────────────┐
│   Centrifugation for 60 min │ ────▶  │   Measuring with CHNS │
│          at 25 °C           │        │        analyzer       │
└─────────────────────────────┘        └──────────────────────┘
```
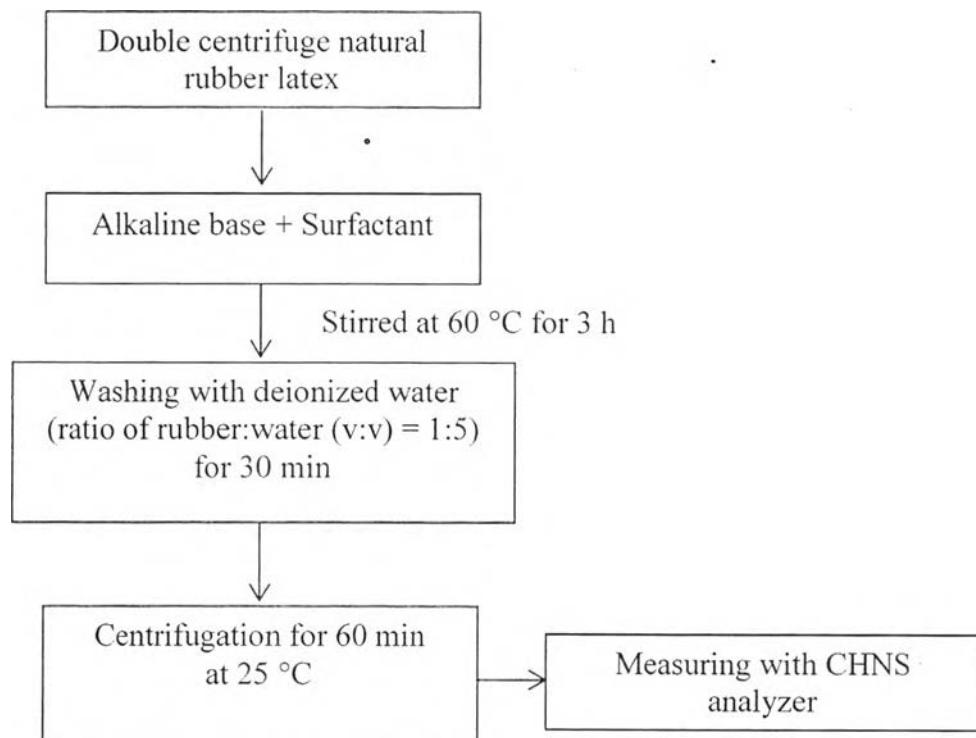
Figure B1 Deproteinized natural rubber method via saponification method.

The solution was prepared by mixing between sodium hydroxide (NaOH) or potassium hydroxide (KOH) (1.5, 3.0, 5.0, and 7.5 g per 100 ml DCNR) and surfactants namely SDS, DBSA, or CTAB (2 g per 100 ml DCNR). Furthermore, the amount of surfactant was varied between 1.5, 2.0, 2.5, and 3.0 g per 100 ml DCNR. The solution was continuously stirred at 60 °C for 3 h. Then, the distilled water was added into the solution at volume ratio of DCNR: water of 1:5 and stirred at room temperature for 30 min. Then, this solution was centrifuged at 8000 rpm for 60 min to separate rubber layer and water layer from each other. The rubber layer, namely deproteinized rubber (DPNR), was further investigated the nitrogen content by using a CHNS analyzer.

Table B1 Condition of deproteinized natural rubber via saponification method

Types of surfactant	Amount of surfactant (g) per 100 ml DCNR	Amount of NaOH (g) per 100 ml DCNR	Amount of KOH (g) per 100 ml DCNR
SDS	2.0	1.5	-
		3.0	
		5.0	
		7.5	
		-	1.5
			3.0
			5.0
			7.5
DBSA	2.0	1.5	-
		3.0	
		5.0	
		7.5	
		-	1.5
			3.0
			5.0
			7.5
CTAB	2.0	1.5	-
		3.0	
		5.0	
		7.5	
		-	1.5
			3.0
			5.0
			7.5

Appendix C Nitrogen Content of Deproteinized Natural Rubber

Amount of nitrogen (% wt of nitrogen) in the deproteinized natural rubber (DCNR) was analyzed by a CHN analyzer (TruSpec Micro model of LECO company). The calibration curve was created by using ethylenediaminetetraacetic acid (EDTA) which had a certain amount of nitrogen. The calibration curve for determining amount of nitrogen in DPNR was considered and used at the least amount of nitrogen on the curve (at % nitrogen near zero) to receive the highest accuracy of the analysis because the DPNR had quite a low nitrogen content. Before analyzing the samples, the CHN analyzer was operated in air to eliminate air background (repeating no less than 10 times). The samples were wrapped with a foil cup before inserted into the analyzer. The samples were completely oxidized under oxygen atmosphere at 950 °C. The results were reported in % nitrogen by weight of the sample.

Table C1 Amounts of nitrogen in deproteinized natural rubber latex

Types of surfactant	Amount of surfactant (g) per 100 ml DCNR	Amount of NaOH (g) per 100 ml DCNR	Amount of KOH (g) per 100 ml DCNR	Amount of nitrogen (% wt)
SDS	2.0	1.5		0.01431
		3.0		0.01662
		5.0		0.03995
		7.5		0.03452
			1.5	0.06144
			3.0	0.08259
			5.0	0.06395
			7.5	0.05084

DBSA	2.0	1.5		0.04139
		3.0	-	0.03911
		5.0		0.03338
		7.5		0.03444
			1.5	0.06109
		-	3.0	0.08170
			5.0	0.05316
			7.5	0.08167
CTAB	2.0	1.5		0.09233
		3.0	-	0.07225
		5.0		0.02639
		7.5		0.03545
			1.5	0.08550
		-	3.0	0.09215
			5.0	0.05764
			7.5	0.03830

Table C1 shows the amounts of nitrogen of DPNR via saponification method by fixing the amount of surfactant at 2 g per 100 ml DCNR and at various amounts of NaOH and KOH from 1.5 to 7.5 g per 100 ml DCNR. NaOH has a higher efficiency to reduce the nitrogen content than KOH in all conditions of the saponification method. The lowest nitrogen content as measured by CHN analyzer is shown to be at 0.0131 %wt by using the condition of 2 g SDS and 1.5 g NaOH per 100 mL DCNR. Hence, this condition was used further to study the amounts of nitrogen by varying the amount of surfactant (SDS) from 1.5 to 3.0 g per 100 mL DCNR.

Table C2 Amounts of nitrogen in deproteinized natural rubber latex (various amount of SDS)

Amount of NaOH (g) per 100 ml DCNR	Amount of SDS (g) per 100 ml DCNR	Amount of nitrogen (% wt)
1.5	1.5	0.01686
	2.0	0.01531
	2.5	0.02835
	3.0	0.02942

Table C2 shows the amounts of nitrogen in DPNR by various amounts of surfactant (SDS) from 1.5 to 3.0 g by fixing the amount of NaOH at 1.5 g per 100 mL DCNR (the condition in Table C1 has the nitrogen content at 0.01031 %). The amount of nitrogen decreases with increasing amount of SDS from 1.5 to 2.0 g per 100 mL DCNR. However, the amount of nitrogen increases when increasing amount of SDS from 2.5 to 3.0 g per 100 mL DCNR.

Table C3 Amounts of nitrogen in DCNR before and after curing

Materials	Amount of nitrogen (% wt)
Virgin DCNR	0.21748
UV cured DCNR	0.20573
10EG_DCNR	0.22036
10PG_DCNR	0.22056
10GLY_DCNR	0.21853
100IN-10EG_DCNR	0.23598
100IN-10PG_DCNR	0.24359
100IN-10GLY_DCNR	0.24853

Table C3 shows the amounts of nitrogen in virgin natural rubber (DCNR) before and after curing by UV radiation for studying the effect of UV radiation on

the nitrogen content in the rubber without the photoinitiator and crosslinking agents added. The results show no difference in the amounts of nitrogen before and after curing.

Table C4 Amount of nitrogen in deproteinized natural rubber film

Materials	%wt of Nitrogen
10EG_DPNR (10 mL EG per 5 mL DPNR)	0.01492
200IN-10EG_DPNR (200 mg IN, 500 mg TWEEN20 and 10 mL EG per 5 mL DPNR)	0.02547
100IN-0.25CEG_DPNR (100 mg IN, 250 mg CTAB and 10 mL EG per 5 mL DPNR)	0.02138
2AEG_DPNR2 (2 ml NH$_3$ and 10 mL EG per 5 mL DPNR)	0.15138
IN3-2AEG_DPNR2 (300 mg IN, 2 mL NH$_3$ and 10 mL EG per 5 mL DPNR)	0.18520

Table C4 shows the amount of nitrogen in 2AEG-DPNR2 (5mL DPNR + 2mL ammonia + 10 mL EG) and IN3-2AEG-DPNR2 (5mL DPNR + 2mL ammonia + 10 mL EG + 300 mg IN). The result shows the increasing of nitrogen content from pure DPNR due to the nitrogen from ammonia and IN inside the DPNR film.

Appendix D Cytotoxicity Testing

Reference: Biological *In vitro* Testing for Biomaterial Service. MTEC, Thailand

Cell suspension of 1×10^5 cells/ml L929 (Mouse Fibroblast Cells, ATCC CCL1, NCTC 929, of Strain L) in MEM completed medium was seeded into the 96-well plate. It was incubated at 37 ± 1 °C, $5 \pm 0.1\%$ CO_2 and $95 \pm 5\%$ relative humidity for 24 ± 2 h to obtain confluent monolayers of cells prior to testing. The MEM completed medium was replaced with the extracts of:

- The blank (The media without test specimen)

- The negative control ('Thermanox' (Nunc) coverslip was used as a negative control material. The surface-are-to-volume extraction ratio of 6 cm^2/ml was used)

- The positive control ('Polyurethane film containing 0.1% Zinc diethyldithiocarbamate (ZDEC): RM-A' was used as a positive control material. The surface-area-to-volume extraction ratio of 3 cm^2/ml was used)

- The M1 100 tested specimen (The surface-area-to-volume extraction ratio of 3 cm^2/ml was used)

*All of them were extracted at 37 ± 1 °C for 24 ± 2 h. All of the extracts were used without any manipulation.

The cells were incubated further for 24 ± 2 h. After incubation, the viable cells were stained with MTT (3-(4,5-dimethylthiosol-2-yl)-2,5-diphenyltetrazolium bromide) and incubated for further 2 h. Then MTT was removed and DMSO was added in each well. The absorbance was measured using Microplate reader at 570 nm. The %viability of cells was determined follow by:

$$\%viability = 100 \times OD_{570c}/OD_{570b}$$

where OD_{570c} is the mean value of the measured optical density of the 100% extracted of the test samples.

OD_{570b} is the mean value of the measured optical density of the 100% extracted of the blank.

*If viability was less than 70% of the blank, it had a cytotoxic potential.

Table D1 Percentages of cell viability of the samples (1ˢᵗ test)

Samples	The average of	
	OD 570 nm	% Viability
• Blank	1.032	100
Negative control	0.933	90
Positive control	0.008	1
Ibuprofen/NR	0.134	13
IN-NR/PEG	0.019	2
IN-Doped PCz/DCNR	0.662	64

Table D1 shows the percentages of cell viability of L929 cells from cytotoxicity test of Ibuprofen/NR, IN-NR/PEG, and IN-Doped PCz/DCNR. All of samples show the percent viability values less than 70% of the blank which can be referred to as cytotoxic samples.

Table D2 Percentages of cell viability of the samples (2ⁿᵈ test)

Samples	The average of	
	OD 570 nm	% Viability
Blank	0.859	100
Negative control	0.856	99
Positive control	0.001	0
NR/PCZ	0.475	55
NR/EG300	0.004	0
10%wt CaCl₂ from eggshell (compliant electrode)	0.746	86
30 phr Ag (compliant electrode)	0.001	0
35% GP/NR (compliant electrode)	0.510	59
PW (PPV) dope Ibuprofen	0.237	27

Table D2 shows the percent viability values of L929 cells from cytotoxicity test of NR/PCZ, NR/EG300, PW dope ibuprofen, and compliant electrodes (10 wt % $CaCl_2$ from eggshell, 30 phr. Ag, and 35% GP/NR). All of samples show the percent viability values less than 70% of the blank except 10%wt $CaCl_2$ from eggshell (compliant electrode). Thus, $CaCl_2$ from eggshell (compliant electrode) has no cytotoxic potential.

Table D3 Percentages of cell viability of the samples (3rd test)

Samples	The average of	
	OD 570 nm	**% Viability**
Blank	0.902	100
Negative control	0.837	93
Positive control	0.003	0
DCNR+SDS+NaOH (DPNR1_1) (2 g SDS and 1.5 g NaOH per 100 mL DCNR)	1.043	116
DCNR+SDS+KOH (DPNR1_2) (2 g SDS and 7.5 g KOH per 100 mL DCNR)	1.068	118
DCNR+DBSA+NaOH (DPNR1_3) (2 g DBSA and 5 g NaOH per 100 mL DCNR)	1.027	114
DCNR+DBSA+KOH (DPNR1_4) (2 g DBSA and 5 g KOH per 100 mL DCNR)	0.997	111

Table D3 shows percent viability values of L929 cells from cytotoxicity test of deproteinized natural rubber via saponification method at various conditions. From the results, all of the deproteinized natural rubbers show the percent viability values higher than 70% of the blank. Hence, they confirm that the deproteinized natural rubbers via saponification method have no cytotoxic potential.

The cytotoxicity of the natural rubber or the other samples is the most important problem in contact with the human skin which causes the skin allergenic response. The cytotoxicity was successfully passed in all of the deproteinized natural

rubber via saponification method which yielded the percent viability values of L929 cells higher than 70% of the blank due to the reduction of protein in the natural rubber. Furthermore, CaCl2 from eggshell which was used to prepare the compliant electrode showed the percent viability of L929 cells higher than 70% of the blank.

Table D4 Percentages of cell viability of the samples (4th test)

Samples	The average of	
	OD 570 nm	% Viability
Blank	0.468	100
Negative control	0.469	100
Positive control	0.000	0
10EG_DPNR1 (10 ml EG per 5 ml DPNR1)	0.001	0
0.5TEG_DPNR1 (500 mg TWEEN20 and 10 ml EG per 5 ml DPNR1)	0.000	0
0.25CEG_DPNR1 (250 mg CTAB and 10 ml EG per 5 ml DPNR1)	0.001	0
200IN-10EG_DPNR1 (200 mg IN, 500 mg TWEEN20 and 10 ml EG per 5 ml DPNR1)	0.000	0
100IN-0.25CEG_DPNR1 (100 mg IN, 250 mg CTAB and 10 ml EG per 5 ml DPNR1)	0.001	0

Appendix E Functional Groups of Transdermal Natural Rubber Patch

Transdermal natural rubber patch was prepared by mixing the natural rubber latex with a photoinitiator and a crosslinking agent and dissolved in ethylene glycol acting as a plasticizer, with indomethacin (IN) as a drug. The natural rubber latex solution was poured into the petri dish and inserted in the UV-curing machine for 10 min. The indomethacin, double-centrifuge natural rubber (DCNR1) with and without adding drug, deproteinized natural rubber (DPNR1) with and without adding drug, and IN were investigated for the functional groups using the FTIR spectrometer (Thermo Nicolet, Nexus 670) at 64 scans and resolution of 4 cm^{-1}.
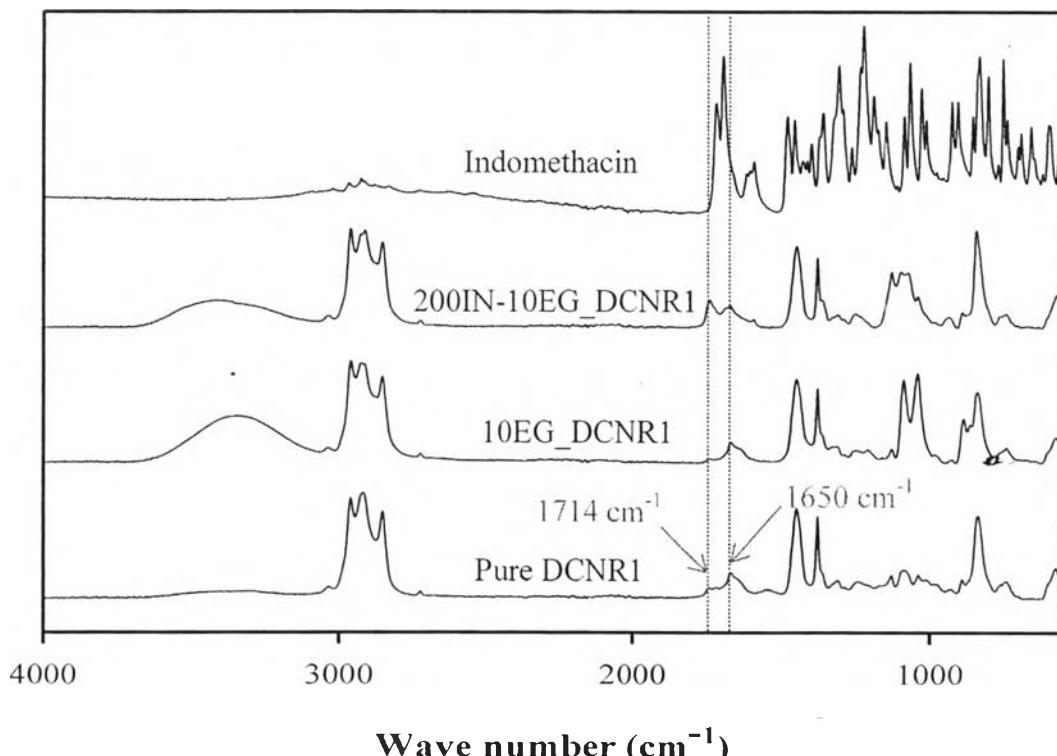
Figure E1 FT-IR spectra of DCNR1 patches.
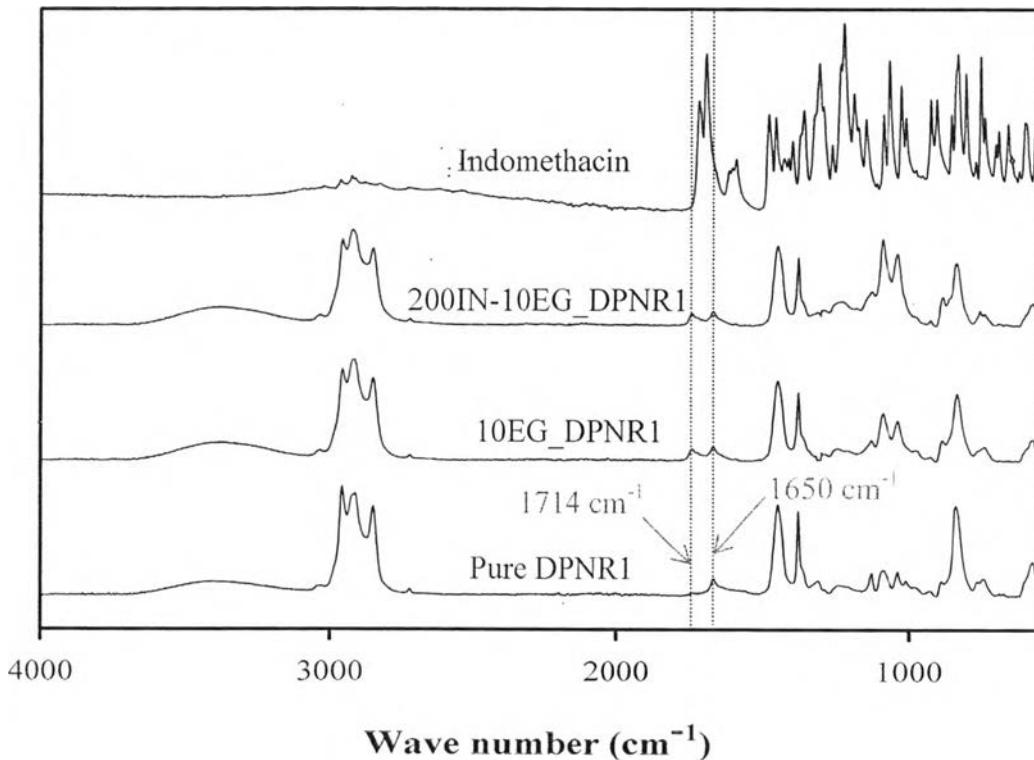
Figure E2 FT-IR spectra of DPNR1 patches.

The FT-IR spectrum of DCNR1 and DPNR1 with and without adding the drug show peaks of the aromatic ring at 754-840 and 1011-1014 cm^{-1}; the C-H stretching, C-H vibration and C_{sp3}-H vibration can be assigned to the peaks at 926-929 cm^{-1}, 1401 cm^{-1} and 2919-2926 cm^{-1}, respectively. The other peaks can be observed at 1087-1089 cm^{-1} (O-H stretching), 1222-1224 cm^{-1} (C-CO-O vibration), 1310 cm^{-1} (C-O vibration), 1375 cm^{-1} (C-N vibration), 1650-1658 cm^{-1} (N-H vibration), 1714 cm^{-1} (C=O vibration), 1655 cm^{-1} (C=C stretching) and 3356 cm^{-1} (O-H vibration).

Table E1 The characteristic peaks of natural rubber film

Wavenumber (cm^{-1})	Assignment	Reference
926-929	C-H stretching	Herculano et al., 2010;
1087-1089	O-H stretching	Pichayakorn et al., 2012;
1222-1224	C-CO-O vibration	Taoudi et al., 2000;
1310	C-O vibration	Dupeyron et al., 2013
1375	C-N vibration	Kong and Yu, 2007
1401	C-H vibration	Junoi et al., 2014
1650-1658	N-H vibration	
1655	C=C stretching	
1714-1737	C=O stretching	
2919-2926	C_{sp3}-H stretching	
3295-3320	N-H stretching	
3356	O-H stretching	

Table E2 Assignments of bands of indomethacin (Dupeyron et al., 2013)

Wavenumber (cm^{-1})	Assignment
839, 832, 803, 752, 702 (s-m)	Aromatic ring
926, 905 (s)	γ CH
1086, 1067	γ O-H
1189, 1148, 1028, 1012 (s)	Aromatic ring
1,233, 1,222 (s-m)	ν C-CO-O
1,306, 1,291 (s)	ν C-O
1,372, 1,358 (m-w)	ν C-N
1,428, 1,411, 1,396 (m-w)	ν C-H
1,712, 1,690 (s)	ν C=O
2,967, 2,928 (w)	ν C_{sp3}-H
3,370 (w)	ν O-H
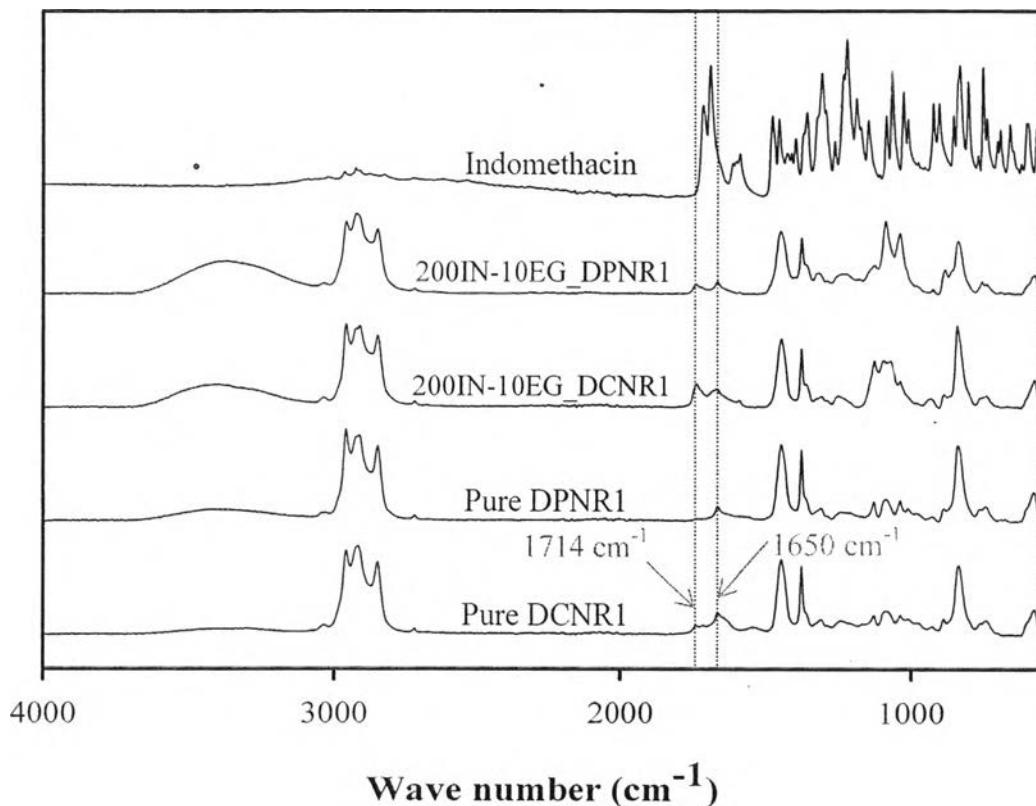
Figure E3 FT-IR spectra of DCNR1 and DPNR1 patches.

Figure E3 shows the FT-IR spectra of DCNR1 and DPNR1 patches with and without adding the drug. The FT-IR spectra of DPNR1 with and without adding drug show the decreases of the N-H vibration peak at 1650-1658 cm^{-1} relative to the DCNR1; the peak can be assigned to the α-helix of protein (Kong and Yu, 2007). Hence, this result could confirm the decreases of protein amount present in DPNR1 and interaction between the drug and the protein in the natural rubber DPNR1 patch (Nowak et al., 1992). In addition, the disappearance of the C=O stretching peak in pure DPNR1 at 1714-1737 cm^{-1}, relative to pure DCNR1, can be referred to the removal of phospholipid in rubber (Sansatsadeekul et al., 2011 and Nawamawat et al., 2010).

Appendix F Thermal Properties of Transdermal Natural Rubber Patch

The thermal behavior of transdermal natural rubber patch was determined by the thermogravimetric analyzer (Thermo, TGA Q 50). The sample was weighed in a range 4-10 mg and placed it in a ceramic pan, and then weighed sample was heated from 30 to 550 °C under nitrogen atmosphere with the heating rate 10 °C/min.
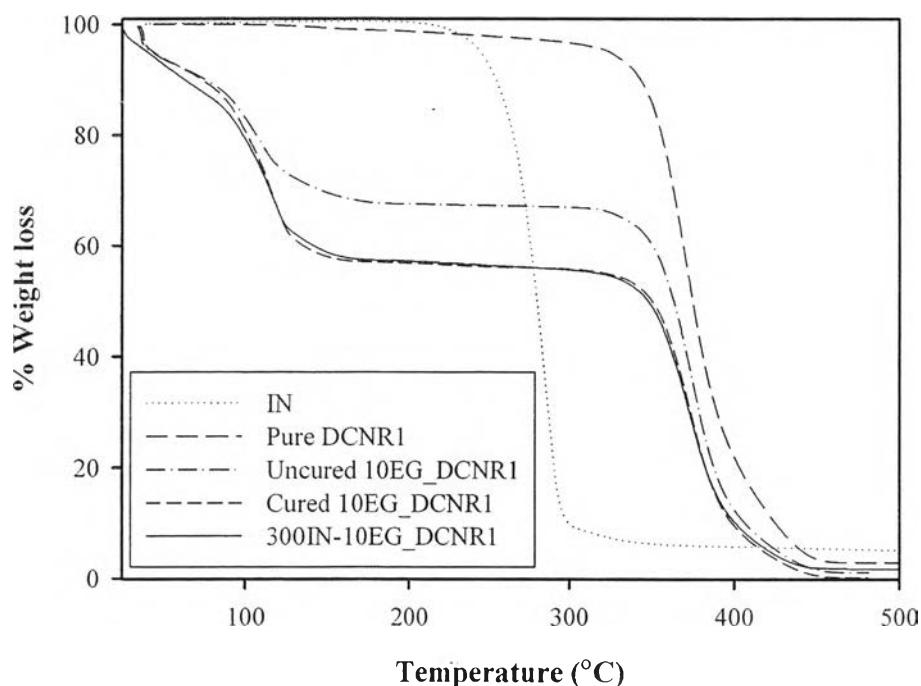
Figure F1 TGA thermograms of transdermal natural rubber patch.

The TGA thermogram of natural rubber patch shows two degradation steps at 104.86 and 370.51 °C for the degradation of moisture and the degradation of natural rubber backbone with the pyrolysis of plasticizer, respectively. The percent weight loss of the uncured 10EG_DCNR1 is less than the cured 10EG_DCNR1 and 300IN-10EG_DCNR1 at first degradation step because curing natural rubber may induce the higher amount of plasticizer inside the natural rubber patch as the plasticizer has a greater ability to exist inside the cured rubber patch.

Table F1 The decomposition temperature and weight loss (%) in TGA thermograms of natural rubber patch and indomethacin

Sample	T_d (°C)	Weight loss (%)
Indomethacin	286.36	95.06
Pure natural rubber	375.98	97.52
Uncuring 10EG_DCNR1	107.82	31.69
	374.25	66.14
Curing 10EG_DCNR1	115.33	69.82
	374.36	29.28
300IN-10EG_DCNR1	104.86	42.12
	370.51	55.87

Appendix G Scanning Electron Microscope (SEM) Images
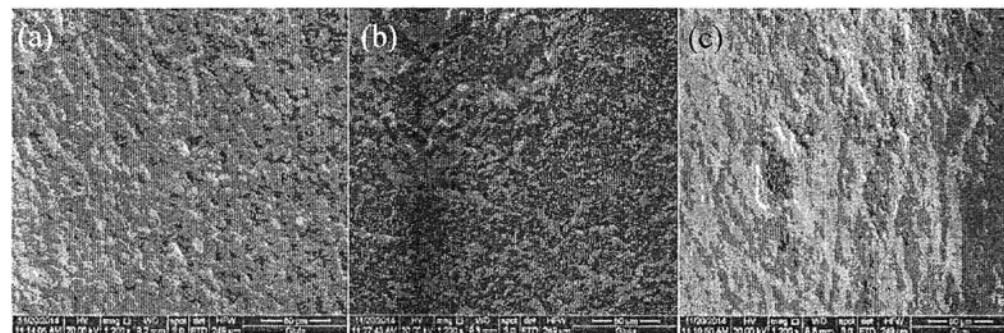
Figure G1 SEM micrographs of: (a) 100IN-10EG_DCNR1 after the release study in PBS buffer pH 7.4 for 48 h; (b) 100IN-10PG_DCNR1 after the release study in PBS buffer pH 7.4 for 48 h; and (c) 100IN-10GLY_DCNR1 after the release study in PBS buffer pH 7.4 for 48 h at magnification of 1200x.

The surface morphology of 100IN-10EG_DCNR1, 100IN-10PG_DCNR1, and 100IN-10GLY_DCNR1 show roughness of surface because of the matrices erosion after the release study in PBS buffer pH 7.4 for 48 h.
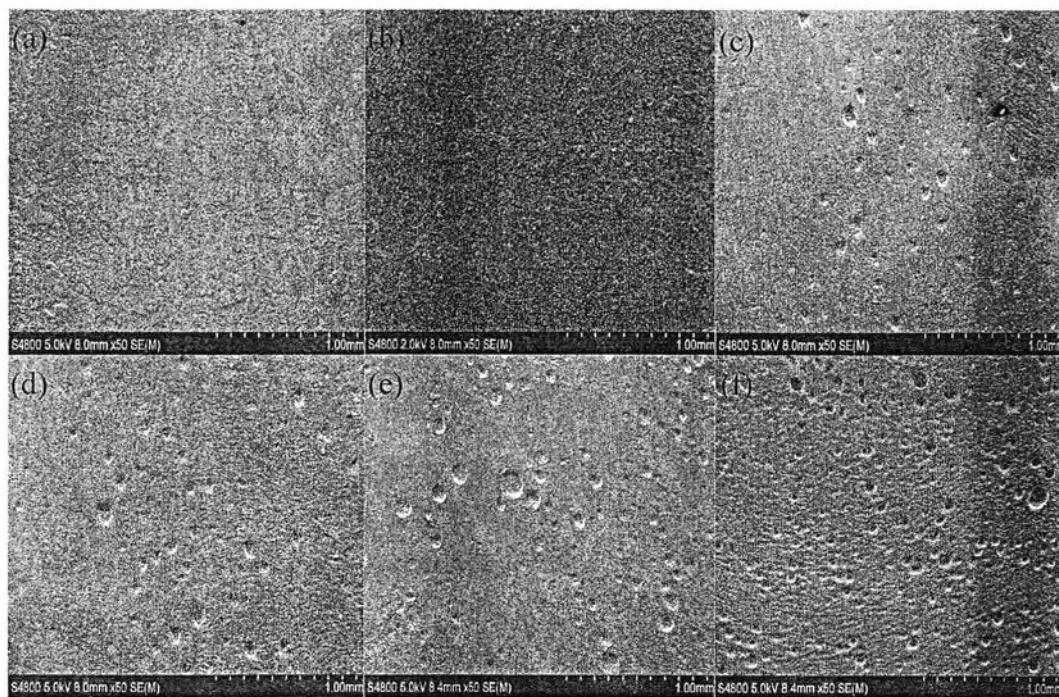
Figure G2 SEM micrographs of: (a) 300IN-10EG_DCNR1 before the permeation study; (b) 300IN-10EG_DCNR1 under an absence of electrical potential (E = 0 V); under electrical potential at (c) E = 3 V; (d) E = 5 V; (e) E = 7 V; and (f) E = 9 V at magnification of 50.
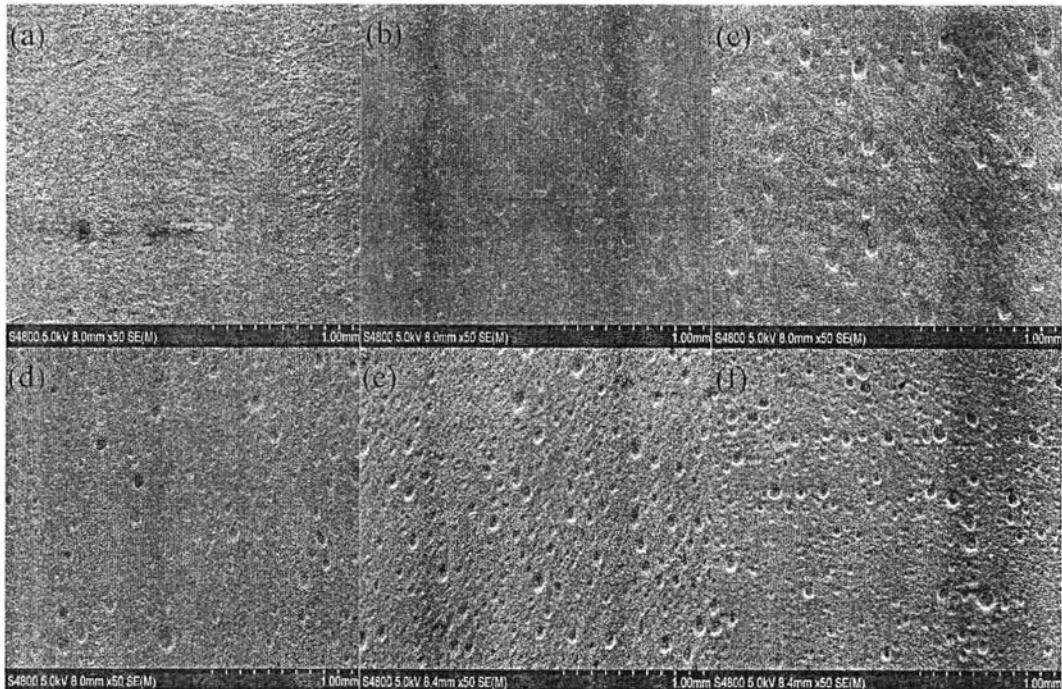
Figure G3 SEM micrographs of: (a) 200IN-10EG_DPNR1 before the permeation study; (b) 200IN-10EG_DPNR1 under an absence of electrical potential (E = 0 V); under electrical potential at (c) E = 3 V; (d) E = 5 V; (e) E = 7 V; and (f) E = 9 V at magnification of 50.

The surface morphology of 300IN-10EG_DCNR1 (Figure G2) and 200IN-10EG_DPNR1 (Figure G3) after permeation study under various electrical potentials (0-9 V) shows roughness of surface because of the matrices erosion. The electrical potential generates the driving force of drug via electro-repulsive force. Hence, the roughness of surface increases with increasing the electrical potential.
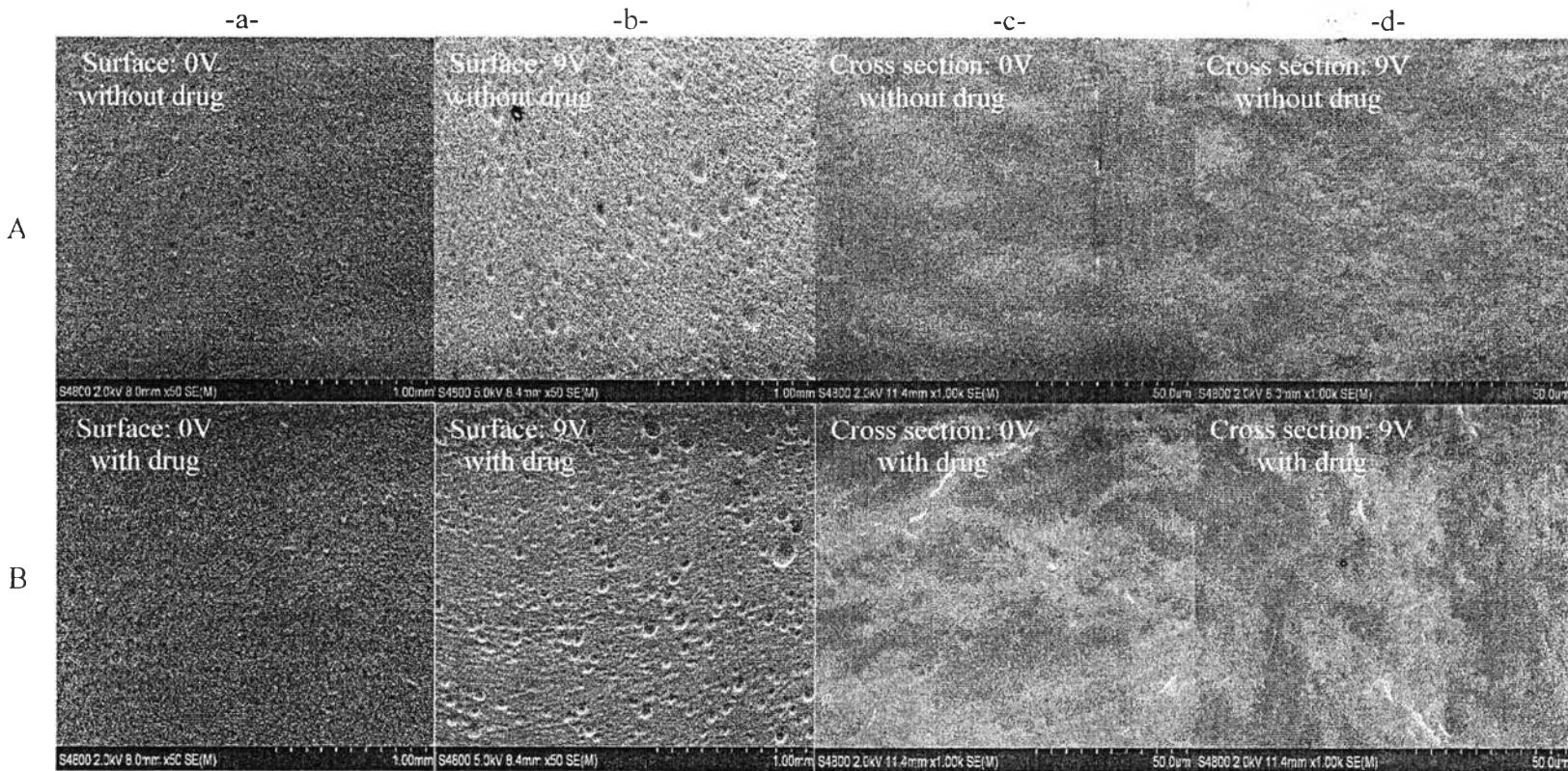
Figure G4 SEM micrograph of: (A) 10EG_DCNR1 and (B) 300IN-10EG_DCNR1(a and b: surface of rubber patch after permeation test without and with apply electrical potential (9 V), respectively, c and d: cross section of rubber patch after permeation·test without and with apply electrical potential (9 V), respectively).

Appendix H Indomethacin Characteristics

IN was investigated for the maximum wavelength (nm) using the UV-visible spectrometer (TECAN, Infinite M200) in the scanning mode. The indomethacin (0.0045 mg) was dissolved in MeOH (5 mL) followed with an addition of PBS buffer until a volume was 100 ml. The IN solution has the characteristic peaks at 266 nm and 324 nm
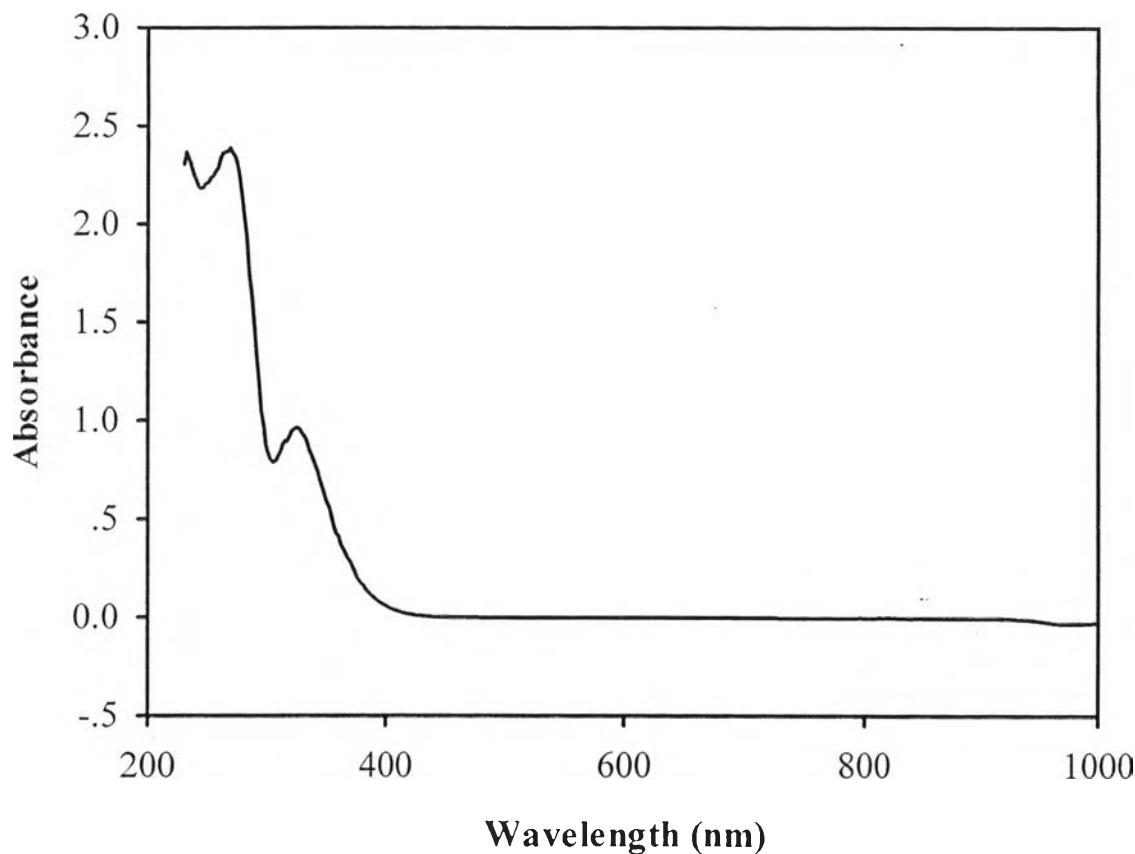
Figure H1 The UV-visible spectrum of IN.

The calibration curve of indomethacin was prepared by plotting the absorbance at 324 nm versus the concentration of IN (ppm). Preparation of IN solution, the IN was dissolved at certain weight of 45 mg (450 ppm) in 100 ml of PBS buffer at pH 7.4. The solution was diluted with the PBS buffer to produce the solutions at 15-150 ppm of IN.
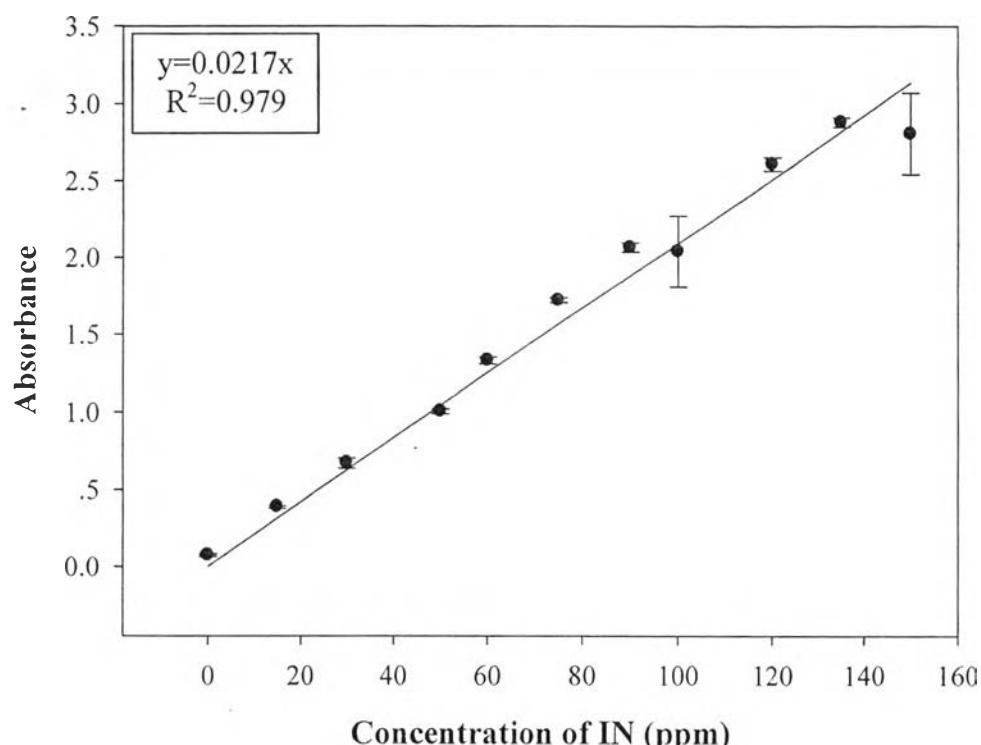
Figure H2 The calibration curve of indomethacin dissolved in PBS buffer at 324 nm.

Table H1 The absorbance of indomethacin at various concentrations at 324 nm

Concentration of IN (ppm)	Absorbance	Avg	SD
0	0.0000 0.0000 0.0000	0.0000	0.0000
15	0.3909 0.3778 0.3936	0.3874	0.0085
30	0.6373 0.7038 0.6748	0.6720	0.0333
50	1.0109 0.9891 1.0157	1.0052	0.0142
60	1.3307 1.3084 1.3530	1.3307	0.0223
75	1.7312 1.7032 1.7312	1.7219	0.0162
90	2.0331 2.0944 2.0673	2.0649	0.0307
100	2.1380 1.7768 2.2060	2.0403	0.2307
120	2.5584 2.6226 2.6402	2.6071	0.0431
135	2.8492 2.8840 2.9076	2.8803	0.0294
150	3.0850 2.5632 2.7703	2.8062	0.2627

Appendix I Determination of Actual Drug Content

The actual amounts of indomethacin in natural rubber films were measured by dissolving a piece of film (area of 3.14 cm^2 of DCNR film and 12.56 cm^2 of DPNR film) in 100 mL of hexane. The 0.3 mL solution was quantified by using the UV-visible spectrophotometer at a wavelength of 324 nm. Then, the absorbance amount of the solution was determined by the calibration curve of indomethacin. The initial drug concentration in the film, C_0, was calculated from an actual amount of IN in the film (g) divided by a volume of the film (cm^3) in which the thickness (cm) of natural rubber films was 0.25 cm.

Table I1 The raw data of the determination of actual amount of IN in the IN-loaded natural rubber films

Sample	Actual amount of IN in the film area 3.14 cm^2		Volume ($\pi r^2 h$, cm^3)	C_0 (mg/cm^3)
	ppm	mg		
100IN-10GLY_DCNR1_1	26.86	2.27		2.89
100IN10-GLY_DCNR1_2	26.72	2.67		3.40
100IN10-GLY_DCNR1_3	26.15	2.61		3.32
Avg	**26.57**	**2.66**		**3.21**
SD	**0.37**	**0.04**		**0.27**
100IN-10PG_DCNR1_1	38.91	3.89		4.96
100IN-10PG_DCNR1_2	38.87	3.89		4.96
100IN-10PG_DCNR1_3	38.49	3.85	0.785	4.90
Avg	**38.76**	**3.88**		**4.94**
SD	**0.23**	**0.02**		**0.03**
100IN-5EG_DCNR1_1	32.59	3.26		4.15
100IN-5EG_DCNR1_2	32.34	3.23		4.11
100IN-5EG_DCNR1_3	33.75	3.38		4.31
Avg	**32.90**	**3.29**		**4.19**
SD	**0.75**	**0.08**		**0.10**

Sample	Actual amount of IN in the film area 3.14 cm²		Volume ($\pi r^2 h$, cm³)	C_0 (mg/cm³)
	ppm	mg		
100IN-10EG_DCNR1_1	33.16	3.32		4.23
100IN-10EG_DCNR1_2	31.10	3.11		3.96
100IN-10EG_DCNR1_3	33.20	3.23		4.11
Avg	32.49	3.24		4.14
SD	1.20	0.12		0.13
100IN-15EG_DCNR1_1	26.68	2.67		3.40
100IN-15EG_DCNR1_2	24.80	2.48		3.16
100IN-15EG_DCNR1_3	26.02	2.60		3.31
Avg	25.83	2.58		3.29
SD	0.96	0.10		0.12
200IN-10EG_DCNR1_1	40.53	4.05		5.16
200IN-10EG_DCNR1_2	43.71	4.37		5.57
200IN-10EG_DCNR1_3	42.87	4.29	0.785	5.46
Avg	42.37	4.23		5.40
SD	1.65	0.16		0.21
300IN-10EG_DCNR1_1	75.52	7.55		9.62
300IN-10EG_DCNR1_2	79.81	7.98		10.17
300IN-10EG_DCNR1_3	61.98	6.20		7.90
Avg	72.44	7.24		9.22
SD	9.31	0.93		1.18
200IN-10EG_DPNR1_1	35.32	3.53		4.50
200IN-10EG_DPNR1_2	32.71	3.27		4.17
200IN-10EG_DPNR1_3	36.34	3.63		4.63
Avg	34.79	3.48		4.43
SD	1.87	0.19		0.24

Sample	Actual amount of IN in the film area 12.56 cm^2		Volume ($\pi r^2 h$, cm^3)	C_0 (mg/cm^3)
	ppm	mg		
IN3-2AEG_2DPNR1_1	157.74	15.17		. 4.83
IN3-2AEG_2DPNR1_2	151.65	15.17		4.83
IN3-2AEG_2DPNR1_3	150.96	15.10		4.80
Avg	151.45	15.11		4.82
SD	0.43	0.043		0.01
200IN-10EG_DPNR1_1	142.30	14.23		4.53
200IN-10EG_DPNR1_2	139.98	14.00		4.45
200IN-10EG_DPNR1_3	140.65	14.07	3.143	4.48
Avg	140.98	14.10		4.49
SD	1.20	0.12		0.04
IN1-3CEG_2DPNR1_1	126.14	12.61		4.01
IN1-3CEG_2DPNR1_2	127.81	12.78		4.07
IN1-3CEG_2DPNR1_3	123.67	12.37		3.94
Avg	125.87	12.6		4.00
SD	2.08	0.21		0.07

Appendix J   Determination of the Crosslink Density of Transdermal Natural Rubber Patch

The crosslink density of films was calculated following a procedure of ATSM6814-02. The films (1 cm^2) were weighed in air and methanol (MeOH) before and after leaving them to obtain the equilibrium swelling state in toluene for 5 days. A crosslink density was calculated using Eq. (J1) (Flory-Rehner equation).

$$v_e = \frac{-[\ln(1-V_r)+V_r+\chi_1 V_r^2]}{[V_1(V_r^{1/3}-V_r)/2]} \quad\text{... (J1)}$$

where: v_e = the number of chains in a real network per unit volume,

V_1 = the molar volume of tolune (106.29 mL/mol),

V_r = the crosslinked DCNR volume fraction in swollen state,

χ = the Flory interaction parameter of cis-1,4-polyisoprene in toluene (0.391).

V_r can be calculated following Eq. (J2);

$$V_r = \frac{\text{Weight of dry rubber} / \text{Density of dry rubber}}{\left(\dfrac{\text{Weight of dry rubber}}{\text{Density of dry rubber}}\right) + \left(\dfrac{\text{Weight of toluene absorbed by sample}}{\text{Density of toluene}}\right)} \quad\text{.... (J2)}$$

in which the density of the dry rubber can be computed by using the Eq. (J3)

$$\text{Density at } 23 \pm 2\,°C \text{ (g/mL)} = 0.7913 \times \frac{A}{A\text{-}B} \quad\text{.............................(J3)}$$

where: A = the weight of dried film measured in air (g),

B = the weight of dried film measured in MeOH (g),

0.7913 = the density of MeOH at $23 \pm 2\,°C$ (g/mL).

Table J1   The crosslink density of natural rubber film with various types of plasticizer after immersion in toluene for 5 days

Sample	Wi		Ws		Wd		v_e	Swelling ratio (%)
	Air	MeOH	Air	MeOH	Air	MeOH		
DCNR1_1	0.063	0.060	0.998	0.982	0.055	0.054	5.37E-06	1594.1
DCNR1_2	0.072	0.071	0.936	0.892	0.055	0.053	7.29E-06	1296.4
DCNR1_3	0.071	0.069	0.982	0.953	0.049	0.047	7.61E-06	1386.7
Avg							**6.75E-06**	**1425.7**
SD							**1.21E-06**	**152.6**
PG_DCNR1_1	0.045	0.043	0.429	0.417	0.035	0.033	1.82E-05	961.0
PG_DCNR1_2	0.047	0.045	0.437	0.426	0.035	0.035	3.36E-06	931.1
PG_DCNR1_3	0.042	0.040	0.418	0.407	0.033	0.032	7.02E-06	995.2
Avg							**9.52E-06**	**962.5**
SD							**7.71E-06**	**32.1**
EG_DCNR1_1	0.037	0.035	0.442	0.421	0.023	0.020	2.45E-05	1194.9
EG_DCNR1_2	0.037	0.035	0.407	0.398	0.023	0.022	1.06E-05	1111.4
EG_DCNR1_3	0.035	0.034	0.406	0.397	0.020	0.019	7.89E-06	1146.3
Avg							**1.43E-05**	**1150.9**
SD							**8.89E-06**	**41.9**
GLY_DCNR1_1	0.047	0.046	0.436	0.419	0.037	0.035	1.62E-05	922.9
GLY_DCNR1_2	0.047	0.045	0.450	0.440	0.035	0.034	8.15E-06	961.8
GLY_DCNR1_3	0.047	0.046	0.424	0.411	0.036	0.035	9.59E-06	894.7
Avg							**1.13E-05**	**926.5**
SD							**4.29E-06**	**33.7**
DPNR1_1	0.084	0.079	1.068	0.995	0.075	0.073	6.80E-06	1271.4
DPNR1_2	0.087	0.084	1.101	1.035	0.079	0.076	9.94E-06	1265.5
DPNR1_3	0.078	0.076	1.083	1.016	0.073	0.069	1.34E-05	1388.5
Avg							**1.01E-05**	**1308.5**
SD							**3.32E-06**	**69.3**
EG_DPNR1_1	0.042	0.040	0.492	0.487	0.035	0.033	1.49E-05	1171.4
EG_DPNR1_2	0.044	0.039	0.471	0.468	0.038	0.034	3.17E-05	1070.5
EG_DPNR1_3	0.043	0.040	0.453	0.450	0.039	0.036	2.48E-05	1053.5
Avg							**2.38E-05**	**1098.5**
SD							**8.46E-06**	**63.8**

Appendix K Pig Skin Preparation

A pig skin (abdominal part) was washed with normal saline. Then, the hair and subcutaneous fat on the pig skin surface were removed by using a sharp razor blade until the thickness of the skin was 0.2 cm. The prepared pig skin was cut to circle shape (diameter of 2 cm) and immersed in a PBS buffer at pH of 7.4 at room temperature for 24 h before using it as a membrane in the permeation testing.
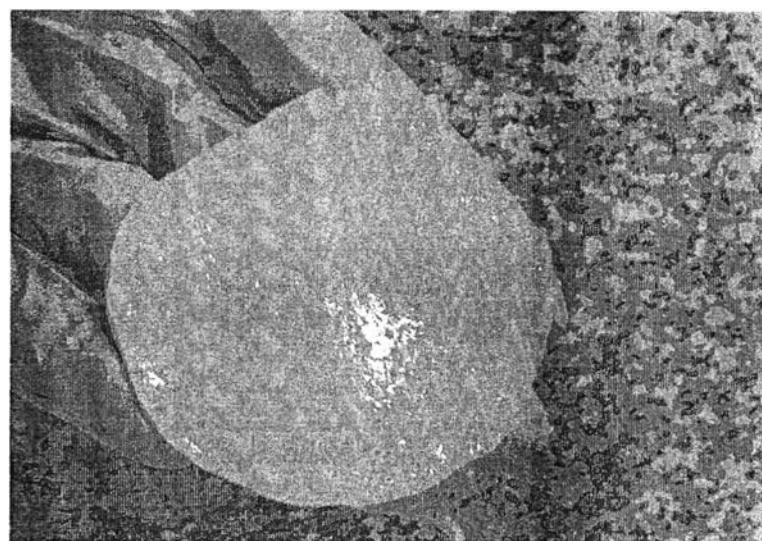
Figure K1 A pigskin membrane.

Appendix L Release Kinetics of Model Drug from Natural Rubber Patch

The one step IN permeation from all natural rubber patches was investigated to determine the transport behavior using the Korsmeyer-Peppas equation:

$$\frac{M_t}{M_\infty} = kt^n \tag{L1}$$

where M_t and M_∞ = the amount of drug released from DCNR film at time t and the total amount of drug release, respectively (mg),

k = the kinetic constant (h^{-n}),

t = time (h),

n = the diffusion scaling exponent.

Then, the log value of M_t/M_∞ was plotted against log time to calculate the release exponent n according to Eq. (L2)

$$\log\left(\frac{M_t}{M_\infty}\right) = \log k + n \log t \tag{L2}$$

The data were then force-fitted to the Higuchi equation (n = 0.5) and then the diffusion coefficient of IN from a natural rubber patch was calculated by Eq. (L3), Eq. (L4), and Eq. (L5):

$$\frac{M_t}{M_\infty} = kt^{1/2} \tag{L3}$$

$$Q = \frac{M_t}{A} = 2C_0\left(\frac{Dt}{\pi}\right)^{1/2} \tag{L4}$$

$$M_t = k_H M_\infty t^{1/2} = 2C_0\left(\frac{D^{1/2}}{\pi^{1/2}}\right) A t^{1/2} \tag{L5}$$

where M_t/M_∞ =   the fractional drug release

   k_H =   the Higuchi kinetic constant (with the unit of t^{-n})

   t =   the release time

   Q =   the amount of material flowing through a unit cross section of barrier (g/cm^2) in unit time, t (s)

   C_0 =   the initial drug concentration in the film (g/cm^3)

   D =   the diffusion coefficient of a drug (cm^2/s)

The diffusion coefficient was calculated from the slope of the plot of the amounts of IN permeated from IN-loaded DCNR at time t versus square root of time.

Appendix M   Determination of Amounts and Diffusion Coefficient of IN Permeated from Natural Rubber Patch with Various Types of Plasticizer in an Absence of Electrical Potential
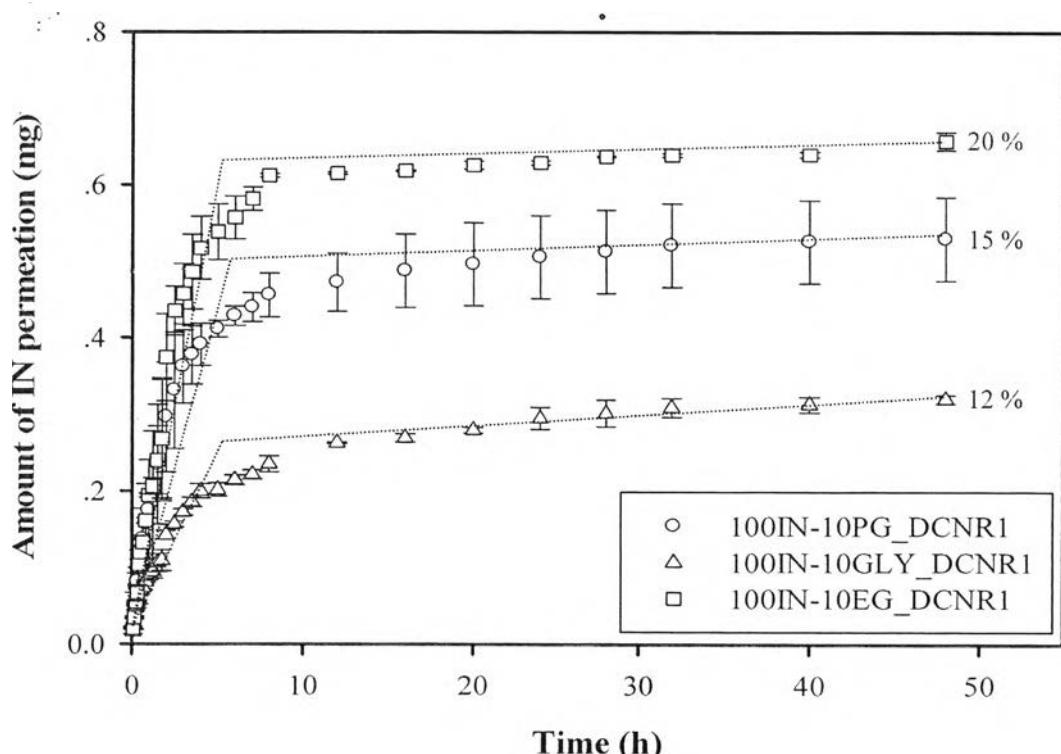
Figure M1   Amount of IN permeated from 100IN-10PG_DCNR1, 100IN-10GLY_DCNR1, and 100IN-10EG_DCNR1 at the crosslink ratio at 0.3 %v/v of DCNR versus time t under an absence of electrical potential, pH 7.4, 37 °C.

The total amounts of IN permeated from 3.14 cm^2 of 100IN-10PG_DCNR1, 100IN-10GLY_DCNR1, and 100IN-10EG_DCNR1 are 15 % (0.52 mg), 12% (0.31 mg), and 20 % (0.65 mg), respectively. The amount of IN permeation depends on the plasticizer type which is ranked as follow: EG > PG > GLY. The time to obtain permeation equilibrium of 100IN-10PG_DCNR1, 100IN-10GLY_DCNR1, and 100IN-10EG_DCNR1 were 7.5, 6, and 6 hours, respectively.

The diffusion from each plasticizer had one diffusion stage. The diffusion scaling exponents (n) were equal to 0.66, 0.78, and 0.90 for 100IN-10GLY_DCNR1, 100IN-10PG_DCNR1, and 100IN-10EG_DCNR1, respectively. The result indicates

that the drug transport behavior of all plasticizer systems can be considered as the anomalous transport resulting from the pure Fickian diffusion and the matrix swelling.
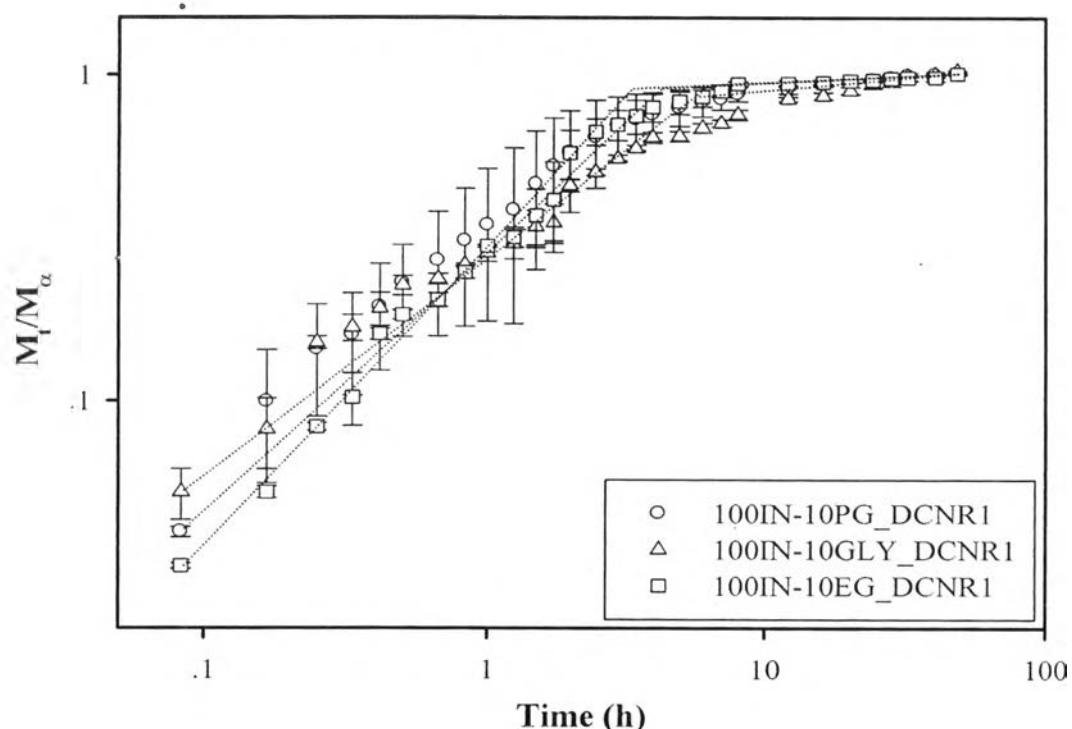
Figure M2 Plot of log M_t/M_∞ versus log time from 100IN-10PG_DCNR1, 100IN-10GLY_DCNR1, and 100IN-10EG_DCNR1 at the crosslink ratio of 0.3 %v/v of DCNR under an absence of electrical potential, pH 7.4, 37 °C.
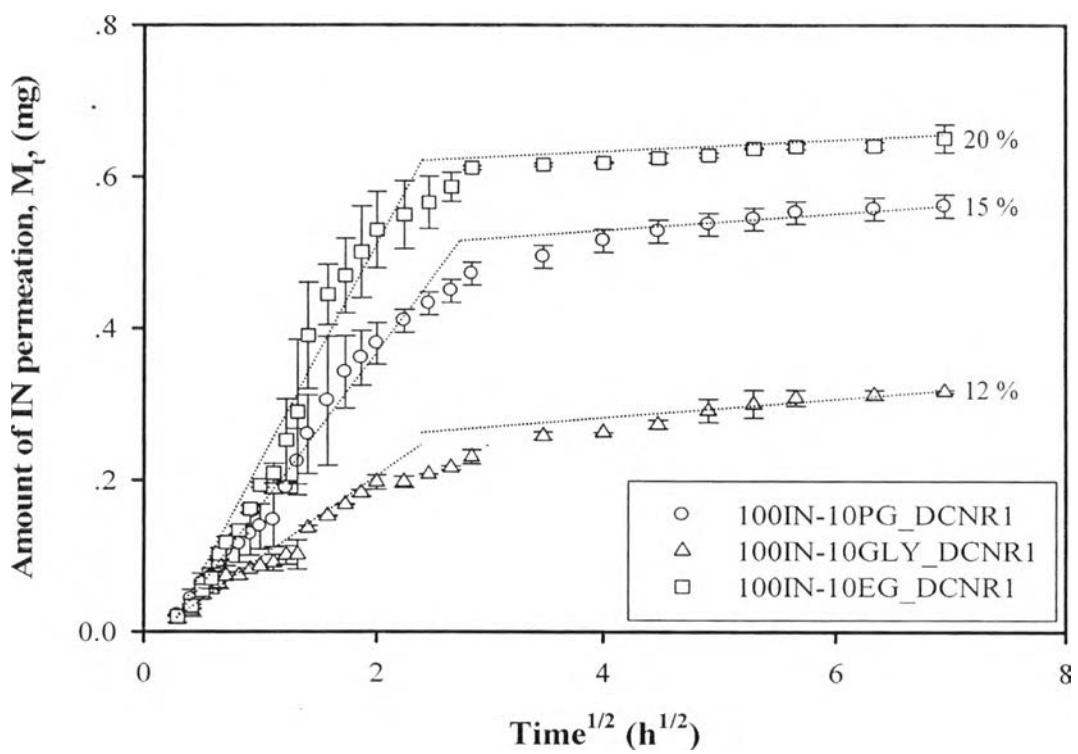
Figure M3 Amounts of IN permeated from 100IN-10PG_DCNR1, 100IN-10GLY_DCNR1, and 100IN-10EG_DCNR1 at the crosslink ratio of 0.5 %v/v of DCNR versus time $t^{1/2}$ under an absence of electrical potential, pH 7.4, 37 °C.

Table M1   The diffusion coefficients (D) of IN permeated from 100IN-10PG_DCNR1, 100IN-10GLY_DCNR1, and 100IN-10EG_DCNR1, pH 7.4 at 37 °C, E = 0 V

Sample	slope	M_∞ (mg)	C_0 (mg/cm^3)	D (cm^2/s)
100IN-10GLY_DCNR1	0.381	0.309	3.21	9.54058E-08
	0.304	0.317	3.21	6.39254E-08
	0.359	0.310	3.21	8.52551E-08
Avg	**0.348**			**8.15288E-08**
SD	**0.040**			**1.60676E-08**
100IN-10PG_DCNR1	0.470	0.461	4.94	2.09983E-07
	0.362	0.567	4.94	1.88438E-07
	0.370	0.546	4.94	1.82547E-07
Avg	**0.401**			**1.93656E-07**
SD	**0.060**			**1.44429E-08**
100IN-10EG_DCNR1	0.340	0.638	4.14	2.51138E-07
	0.452	0.654	4.14	4.66385E-07
	0.421	0.663	4.14	4.15818E-07
Avg	**0.404**			**3.7778E-07**
SD	**0.058**			**1.12553E-07**

Table M2 The absorbance intensity and amount of IN permeated from 100IN-10EG_DCNR1 without electrical potential

Time (h)	Absorbance			Amount of drug permeated (mg)				
	1	2	3	1	2	3	Avg	SD
0.0833	0.0348	0.0353	0.0344	0.0201	0.0205	0.0199	0.0202	0.0003
0.1667	0.0200	0.0256	0.0264	0.0318	0.0353	0.0352	0.0341	0.0020
0.25	0.0340	0.0357	0.0348	0.0515	0.0560	0.0554	0.0543	0.0024
0.3333	0.0478	0.0077	0.0088	0.0792	0.0605	0.0605	0.0667	0.0108
0.4167	0.0313	0.0820	0.0811	0.0974	0.1080	0.1075	0.1043	0.0060
0.5	0.0264	0.0256	0.0271	0.1127	0.1228	0.1232	0.1196	0.0060
0.6667	0.0420	0.0126	0.0119	0.1370	0.1301	0.1301	0.1324	0.0040
0.8333	0.0483	0.0486	0.0501	0.1650	0.1583	0.1592	0.1608	0.0036
1	0.0448	0.0642	0.0633	0.1910	0.1955	0.1959	0.1941	0.0027
1.25	0.0473	0.0074	0.0081	0.2184	0.1998	0.2006	0.2063	0.0105
1.5	0.1256	0.0254	0.0242	0.2913	0.2146	0.2146	0.2402	0.0443
1.75	0.1137	0.0141	0.0148	0.3572	0.2227	0.2232	0.2677	0.0775
2	0.1431	0.2043	0.2035	0.4401	0.3412	0.3412	0.3741	0.0571
2.5	0.0557	0.1295	0.1310	0.4724	0.4162	0.4171	0.4353	0.0322
3	0.0538	0.0318	0.0307	0.5036	0.4347	0.4349	0.4577	0.0397
3.5	0.0680	0.0396	0.0409	0.5430	0.4576	0.4586	0.4864	0.0490
4	0.0379	0.0625	0.0616	0.5650	0.4939	0.4943	0.5177	0.0409
5	0.0277	0.0408	0.0419	0.5811	0.5175	0.5186	0.5391	0.0364
6	0.0154	0.0409	0.0401	0.5900	0.5412	0.5419	0.5577	0.0280
7	0.0165	0.0541	0.0550	0.5996	0.5726	0.5738	0.5820	0.0153
8	0.0168	0.0702	0.0694	0.6093	0.6133	0.6140	0.6122	0.0025
12	0.0131	0.0009	0.0016	0.6169	0.6138	0.6149	0.6152	0.0016
16	0.0008	0.0085	0.0077	0.6173	0.6187	0.6194	0.6185	0.0011
20	0.0044	0.0169	0.0180	0.6199	0.6285	0.6298	0.6261	0.0054
24	0.0099	0.0030	0.0020	0.6256	0.6303	0.6310	0.6289	0.0029
28	0.0205	0.0106	0.0118	0.6375	0.6364	0.6378	0.6372	0.0007
32	0.0073	0.0010	0.0009	0.6418	0.6370	0.6383	0.6390	0.0025
40	0.0036	0.0006	0.0004	0.6438	0.6373	0.6386	0.6399	0.0034
48	0.0002	0.0456	0.0449	0.6440	0.6638	0.6646	0.6575	0.0117

Table M3 The absorbance intensity and amount of IN permeated from 100IN-10GLY_DCNR1 without electrical potential

Time (h)	Absorbance			Amount of drug permeated (mg)				
	1	2	3	1	2	3	Avg	SD
0.0833	0.0297	0.0223	0.0325	0.0172	0.0129	0.0188	0.0163	0.0031
0.1667	0.0069	0.0160	0.0248	0.0212	0.0222	0.0332	0.0255	0.0067
0.25	0.0428	0.0393	0.0290	0.0460	0.0450	0.0500	0.0470	0.0026
0.3333	0.0003	0.0163	0.0109	0.0462	0.0544	0.0563	0.0523	0.0054
0.4167	0.0120	0.0062	0.0207	0.0532	0.0580	0.0683	0.0598	0.0077
0.5	0.0203	0.0201	0.0141	0.0649	0.0697	0.0765	0.0704	0.0058
0.6667	0.0154	0.0007	0.0005	0.0739	0.0701	0.0768	0.0736	0.0034
0.8333	0.0118	0.0175	0.0109	0.0807	0.0802	0.0831	0.0813	0.0016
1	0.0205	0.0133	0.0024	0.0926	0.0879	0.0845	0.0883	0.0041
1.25	0.0130	0.0175	0.0002	0.1001	0.0981	0.0831	0.0938	0.0093
1.5	0.0278	0.0196	0.0150	0.1162	0.1095	0.0918	0.1058	0.0126
1.75	0.0060	0.0096	0.0006	0.1197	0.1150	0.0878	0.1075	0.0172
2	0.0505	0.0410	0.0804	0.1489	0.1388	0.1344	0.1407	0.0074
2.5	0.0165	0.0229	0.0330	0.1585	0.1521	0.1535	0.1547	0.0034
3	0.0289	0.0266	0.0255	0.1752	0.1675	0.1683	0.1703	0.0042
3.5	0.0161	0.0212	0.0304	0.1846	0.1798	0.1859	0.1834	0.0032
4	0.0253	0.0193	0.0309	0.1992	0.1910	0.2038	0.1980	0.0065
5	0.0066	0.0025	0.0002	0.2030	0.1924	0.2027	0.1994	0.0060
6	0.0297	0.0259	0.0086	0.2202	0.2074	0.2077	0.2118	0.0073
7	0.0069	0.0119	0.0179	0.2242	0.2143	0.2181	0.2189	0.0050
8	0.0216	0.0166	0.0333	0.2368	0.2239	0.2374	0.2327	0.0076
12	0.0468	0.0660	0.0299	0.2639	0.2622	0.2547	0.2603	0.0049
16	0.0170	0.0015	0.0145	0.2738	0.2631	0.2631	0.2667	0.0062
20	0.0167	0.0253	0.0111	0.2834	0.2777	0.2696	0.2769	0.0069
24	0.0167	0.0058	0.0571	0.2931	0.2811	0.3027	0.2923	0.0108
28	0.0053	0.0110	0.0188	0.2962	0.2875	0.3136	0.2991	0.0133
32	0.0109	0.0237	0.0044	0.3025	0.3012	0.3161	0.3066	0.0083
40	0.0063	0.0121	0.0021	0.3062	0.3082	0.3173	0.3106	0.0059
48	0.0204	0.0129	0.0029	0.3180	0.3157	0.3190	0.3176	0.0017

Table M4 The absorbance intensity and amount of IN permeated from 100IN-10PG_DCNR1 without electrical potential

Time (h)	Absorbance			Amount of drug permeated (mg)				
	1	2	3	1	2	3	Avg	SD
0.0833	0.0316	0.0382	0.0370	0.0183	0.0221	0.0214	0.0206	0.0020
0.1667	0.0838	0.0505	0.0203	0.0669	0.0514	0.0332	0.0505	0.0169
0.25	0.0448	0.0371	0.0359	0.0929	0.0729	0.0540	0.0733	0.0194
0.3333	0.0134	0.0123	0.0155	0.1006	0.0801	0.0630	0.0812	0.0188
0.4167	0.0426	0.0190	0.0291	0.1253	0.0911	0.0799	0.0988	0.0237
0.5	0.0261	0.0495	0.0211	0.1405	0.1198	0.0921	0.1175	0.0243
0.6667	0.0676	0.0213	0.0104	0.1797	0.1321	0.0981	0.1366	0.0409
0.8333	0.0576	0.0273	0.0182	0.2130	0.1479	0.1087	0.1566	0.0527
1	0.0578	0.0205	0.0152	0.2466	0.1598	0.1175	0.1746	0.0658
1.25	0.0685	0.0207	0.0073	0.2863	0.1718	0.1217	0.1933	0.0843
1.5	0.0659	0.0226	0.1247	0.3245	0.1849	0.1940	0.2345	0.0781
1.75	0.0482	0.0143	0.1061	0.3524	0.1932	0.2555	0.2671	0.0802
2	0.0253	0.0524	0.0724	0.3671	0.2236	0.2975	0.2961	0.0718
2.5	0.0301	0.0358	0.1158	0.3845	0.2444	0.3646	0.3312	0.0758
3	0.0288	0.1112	0.0199	0.4012	0.3088	0.3762	0.3621	0.0478
3.5	0.0154	0.0462	0.0176	0.4102	0.3356	0.3864	0.3774	0.0381
4	0.0063	0.0433	0.0220	0.4138	0.3607	0.3991	0.3912	0.0274
5	0.0031	0.0660	0.0364	0.4156	0.3990	0.4202	0.4116	0.0112
6	0.0093	0.0392	0.0392	0.4210	0.4217	0.4430	0.4286	0.0125
7	0.0011	0.0286	0.0286	0.4216	0.4383	0.4595	0.4398	0.0190
8	0.0064	0.0388	0.0388	0.4253	0.4608	0.4820	0.4560	0.0286
12	0.0082	0.0385	0.0385	0.4301	0.4831	0.5044	0.4725	0.0382
16	0.0066	0.0365	0.0365	0.4339	0.5042	0.5255	0.4879	0.0479
20	0.0013	0.0214	0.0214	0.4347	0.5166	0.5379	0.4964	0.0545
24	0.0160	0.0160	0.0160	0.4440	0.5259	0.5472	0.5057	0.0545
28	0.0123	0.0123	0.0123	0.4511	0.5331	0.5543	0.5128	0.0545
32	0.0145	0.0145	0.0145	0.4595	0.5415	0.5627	0.5212	0.0545
40	0.0085	0.0085	0.0085	0.4644	0.5464	0.5677	0.5262	0.0545
48	0.0065	0.0065	0.0065	0.4682	0.5502	0.5714	0.5299	0.0545

**Appendix N Determination of Amounts and Diffusion Coefficient of IN
Permeated from Natural Rubber Patch with Various Amount of Plasticizer in
an Absence of Electrical Potential**
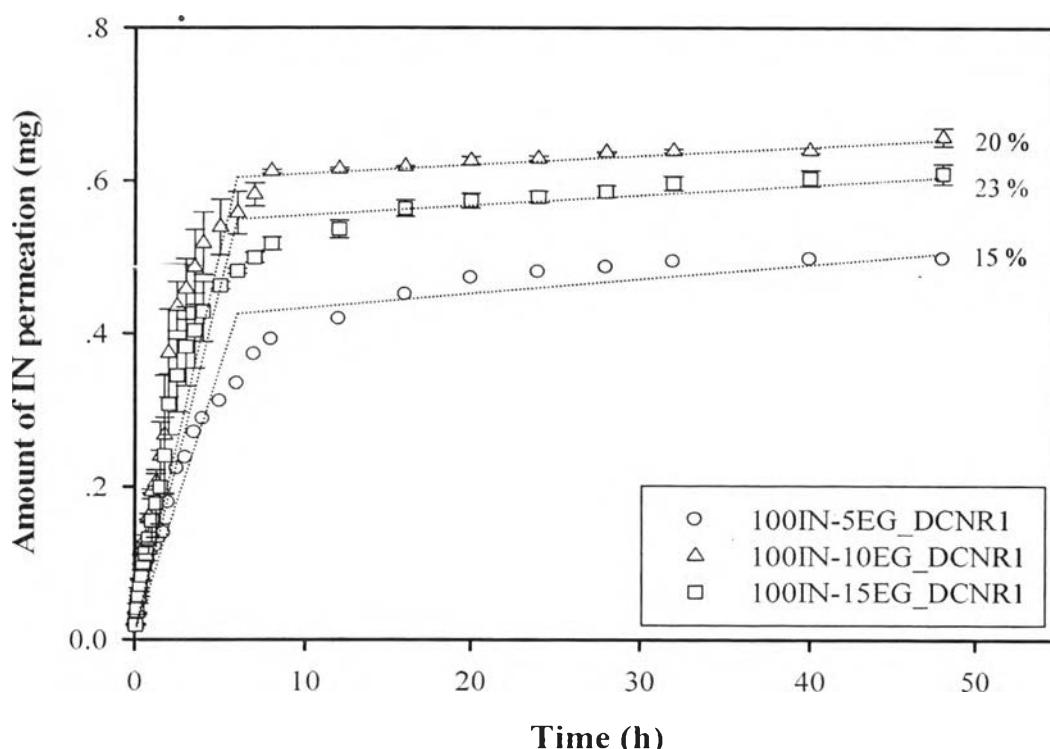
Figure N1 Amounts of IN permeated from natural rubber patches of various
plasticizer amounts versus time t under an absence of electrical potential, pH 7.4, 37
°C.

The total amounts of IN permeated from 3.14 cm^2 of 100IN-5EG_DCNR1,
100IN-10EG_DCNR1, and 100IN-15EG_DCNR1 having the amounts of EG at 5,
10, and 15 mL using initially 5 mL of DCNR are 15 % (0.49 mg), 23 % (0.65 mg),
and 20 % (0.60 mg), respectively. The amount of IN permeation is affected by the
amount of plasticizer and initial amount of drug in the samples. The plasticizer in the
natural rubber patch acts as the drug carrier pathway which increases the amount of
IN permeation with increasing the amount of plasticizer in the cases of 100IN-
5EG_DCNR1 and 100IN-10EG_DCNR1. The times to permeation equilibrium of
100IN-5EG_DCNR1, 100IN-10EG_DCNR1, and 100IN-15EG_DCNR1 were 10. 6,

and 7.5 hours, respectively.

The diffusion from each plasticizer has one diffusion stage. The n values were equal to 0.60, 0.90, and 0.85 for 100IN-5EG_DCNR1, 100IN-10EG_DCNR1, and 100IN-15EG_DCNR1, respectively. The result indicates that the drug transport behavior can be considered to be the anomalous transport which results from the pure diffusion and the matrix swelling.
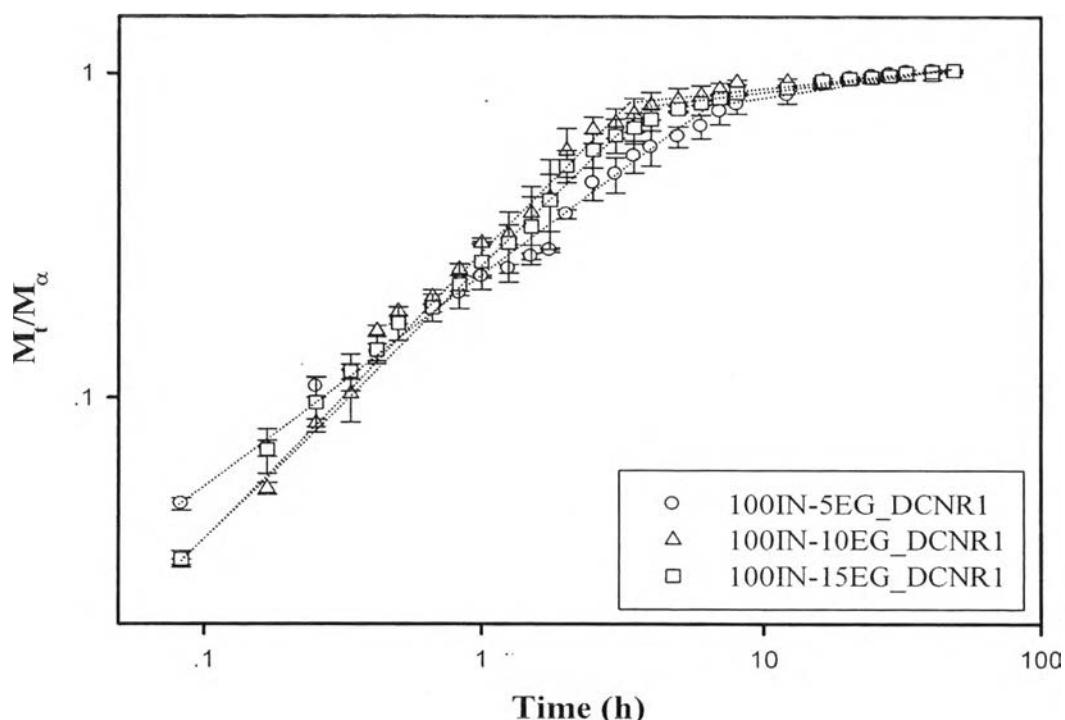

Figure N2 Plot of log M_t/M_∞ versus log time from 100IN-5EG_DCNR1, 100IN-10EG_DCNR1, and 100IN-15EG_DCNR1 at the crosslink ratio of 0.3 %v/v of DCNR under an absence of electrical potential, pH 7.4, 37 °C.
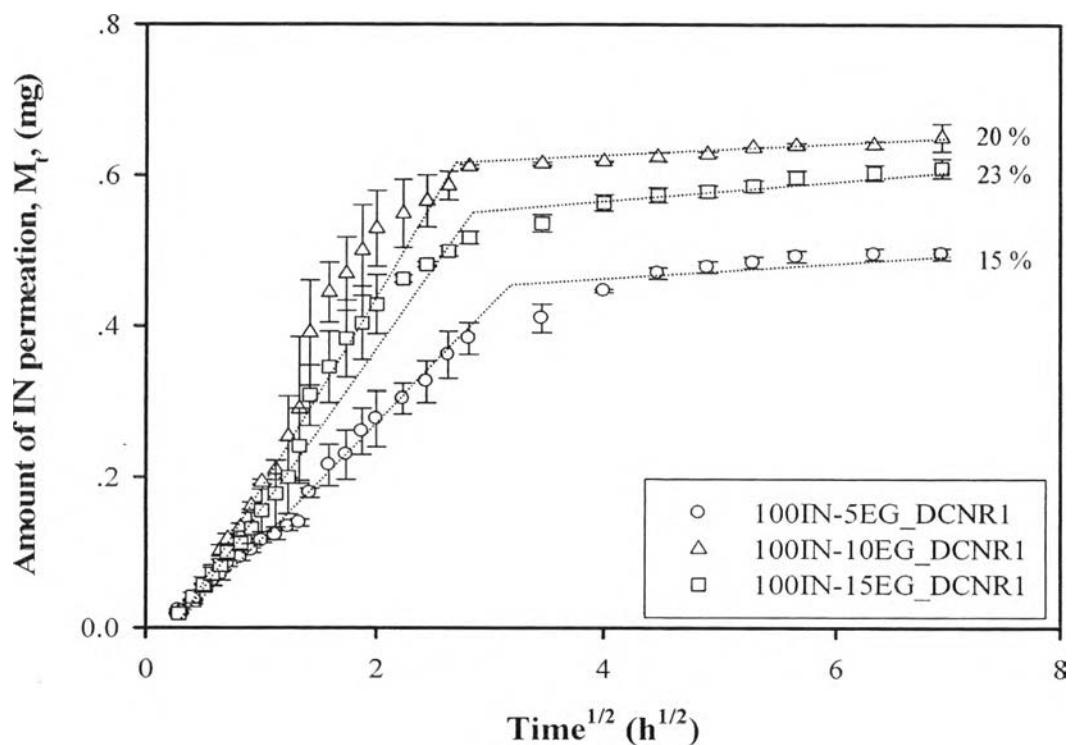
Figure N3   Amount of IN permeated from 100IN-5EG_DCNR1, 100IN-10EG_DCNR1, and 100IN-15EG_DCNR1 at the crosslink ratio of 0.5 %v/v of DCNR versus time $t^{1/2}$ under an absence of electrical potential, pH 7.4, 37 °C.
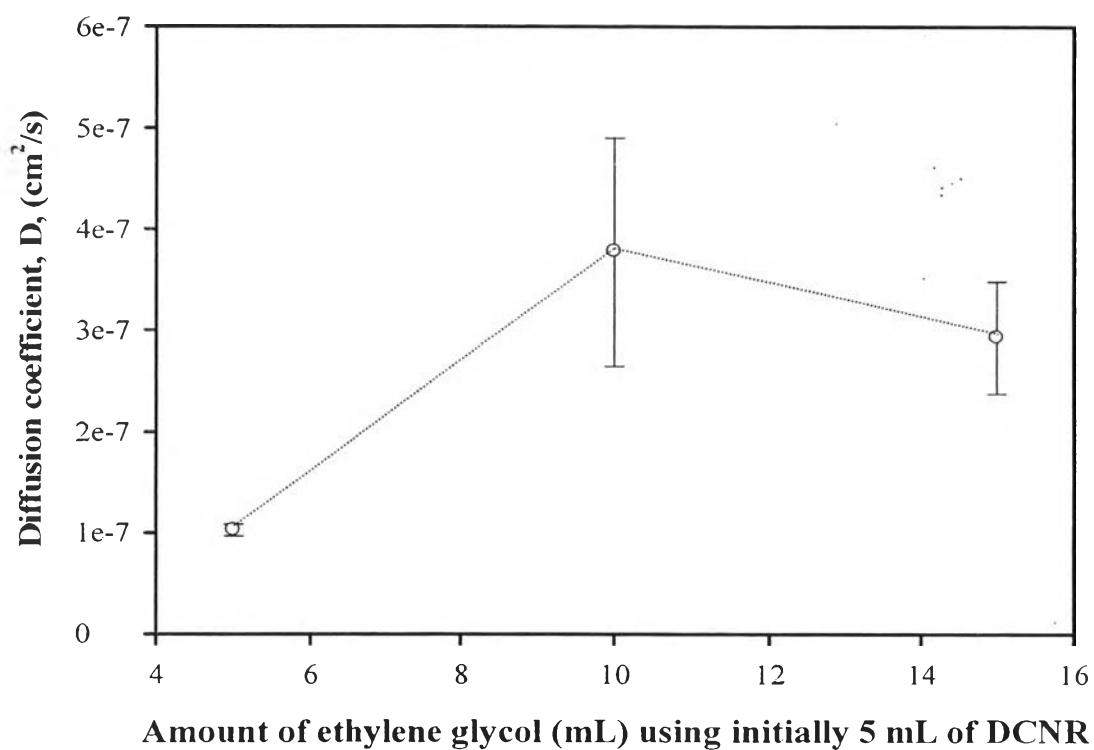
Figure N4 Diffusion coefficients (D) of IN permeated from 100IN-5EG_DCNR1, 100IN-10EG_DCNR1, and 100IN-15EG_DCNR1 without electrical potential, pH 7.4, 37 °C.

Table N1 The diffusion coefficients (D) of IN permeated from 100IN-5EG_DCNR1, 100IN-10EG_DCNR1, and 100IN-15EG_DCNR1 without electrical potential, pH 7.4 at 37 °C

Sample	slope	M_o (mg)	C_0 (mg/cm^3)	D (cm^2/s)
100IN-5EG_DCNR1	0.277	0.495	4.19	9.91445E-08
	0.284	0.484	4.19	9.96383E-08
	0.298	0.484	4.19	1.09704E-07
Avg	**0.286**			**1.02829E-07**
SD	**0.011**			**5.95904E-09**
100IN-10EG_DCNR1	0.340	0.638	4.14	2.51138E-07
	0.452	0.654	4.14	4.66385E-07
	0.421	0.663	4.14	4.15818E-07
Avg	**0.404**			**3.7778E-07**
SD	**0.058**			**1.12553E-07**
100IN-15EG_DCNR1	0.321	0.585	3.29	2.36831E-07
	0.348	0.604	3.29	2.96722E-07
	0.381	0.596	3.29	3.46306E-07
Avg	**0.350**			**2.93286E-07**
SD	**0.030**			**5.4818E-08**

Table N2 The absorbance intensity and amount of IN permeated from 100IN-5EG_DCNR1 without electrical potential

Time (h)	Absorbance			Amount of drug permeated (mg)				
	1	2	3	1	2	3	Avg	SD
0.0833	0.0420	0.0388	0.0378	0.0243	0.0225	0.0219	0.0229	0.0013
0.1667	0.0213	0.0176	0.0186	0.0367	0.0327	0.0327	0.0340	0.0023
0.25	0.0364	0.0311	0.0293	0.0578	0.0507	0.0497	0.0527	0.0044
0.3333	0.0089	0.0102	0.0113	0.0630	0.0566	0.0562	0.0586	0.0038
0.4167	0.0167	0.0144	0.0135	0.0726	0.0650	0.0641	0.0672	0.0047
0.5	0.0272	0.0305	0.0317	0.0884	0.0827	0.0824	0.0845	0.0034
0.6667	0.0123	0.0129	0.0118	0.0955	0.0901	0.0893	0.0917	0.0034
0.8333	0.0161	0.0176	0.0191	0.1049	0.1004	0.1004	0.1019	0.0026
1	0.0212	0.0228	0.0219	0.1172	0.1136	0.1130	0.1146	0.0022
1.25	0.0170	0.0083	0.0092	0.1270	0.1184	0.1184	0.1213	0.0050
1.5	0.0178	0.0202	0.0193	0.1373	0.1301	0.1296	0.1323	0.0043
1.75	0.0090	0.0102	0.0125	0.1426	0.1360	0.1368	0.1385	0.0036
2	0.0548	0.0812	0.0722	0.1743	0.1831	0.1787	0.1787	0.0044
2.5	0.0370	0.0893	0.1023	0.1958	0.2348	0.2380	0.2229	0.0235
3	0.0174	0.0297	0.0290	0.2059	0.2521	0.2548	0.2376	0.0275
3.5	0.0562	0.0511	0.0631	0.2384	0.2817	0.2914	0.2705	0.0282
4	0.0205	0.0360	0.0351	0.2503	0.3026	0.3117	0.2882	0.0331
5	0.0667	0.0257	0.0264	0.2890	0.3175	0.3270	0.3112	0.0198
6	0.0295	0.0477	0.0429	0.3061	0.3451	0.3519	0.3344	0.0247
7	0.0569	0.0661	0.0731	0.3391	0.3834	0.3942	0.3723	0.0292
8	0.0502	0.0252	0.0245	0.3682	0.3980	0.4084	0.3916	0.0209
12	0.0487	0.0440	0.0452	0.3964	0.4235	0.4346	0.4182	0.0197
16	0.0836	0.0421	0.0408	0.4449	0.4480	0.4583	0.4504	0.0070
20	0.0528	0.0288	0.0300	0.4755	0.4646	0.4757	0.4719	0.0063
24	0.0140	0.0140	0.0128	0.4836	0.4728	0.4831	0.4798	0.0061
28	0.0106	0.0106	0.0121	0.4898	0.4789	0.4901	0.4863	0.0064
32	0.0136	0.0136	0.0126	0.4976	0.4868	0.4974	0.4940	0.0062
40	0.0052	0.0052	0.0058	0.5006	0.4898	0.5008	0.4971	0.0063
48	0.0010	0.0010	0.0014	0.5012	0.4904	0.5016	0.4977	0.0064

Table N3 The absorbance intensity and amount of IN permeated from 100IN-10EG_DCNR1 without electrical potential

Time (h)	Absorbance			Amount of drug permeated (mg)				
	1	2	3	1	2	3	Avg	SD
0.0833	0.0348	0.0353	0.0344	0.0201	0.0205	0.0199	0.0202	0.0003
0.1667	0.0200	0.0256	0.0264	0.0318	0.0353	0.0352	0.0341	0.0020
0.25	0.0340	0.0357	0.0348	0.0515	0.0560	0.0554	0.0543	0.0024
0.3333	0.0478	0.0077	0.0088	0.0792	0.0605	0.0605	0.0667	0.0108
0.4167	0.0313	0.0820	0.0811	0.0974	0.1080	0.1075	0.1043	0.0060
0.5	0.0264	0.0256	0.0271	0.1127	0.1228	0.1232	0.1196	0.0060
0.6667	0.0420	0.0126	0.0119	0.1370	0.1301	0.1301	0.1324	0.0040
0.8333	0.0483	0.0486	0.0501	0.1650	0.1583	0.1592	0.1608	0.0036
1	0.0448	0.0642	0.0633	0.1910	0.1955	0.1959	0.1941	0.0027
1.25	0.0473	0.0074	0.0081	0.2184	0.1998	0.2006	0.2063	0.0105
1.5	0.1256	0.0254	0.0242	0.2913	0.2146	0.2146	0.2402	0.0443
1.75	0.1137	0.0141	0.0148	0.3572	0.2227	0.2232	0.2677	0.0775
2	0.1431	0.2043	0.2035	0.4401	0.3412	0.3412	0.3741	0.0571
2.5	0.0557	0.1295	0.1310	0.4724	0.4162	0.4171	0.4353	0.0322
3	0.0538	0.0318	0.0307	0.5036	0.4347	0.4349	0.4577	0.0397
3.5	0.0680	0.0396	0.0409	0.5430	0.4576	0.4586	0.4864	0.0490
4	0.0379	0.0625	0.0616	0.5650	0.4939	0.4943	0.5177	0.0409
5	0.0277	0.0408	0.0419	0.5811	0.5175	0.5186	0.5391	0.0364
6	0.0154	0.0409	0.0401	0.5900	0.5412	0.5419	0.5577	0.0280
7	0.0165	0.0541	0.0550	0.5996	0.5726	0.5738	0.5820	0.0153
8	0.0168	0.0702	0.0694	0.6093	0.6133	0.6140	0.6122	0.0025
12	0.0131	0.0009	0.0016	0.6169	0.6138	0.6149	0.6152	0.0016
16	0.0008	0.0085	0.0077	0.6173	0.6187	0.6194	0.6185	0.0011
20	0.0044	0.0169	0.0180	0.6199	0.6285	0.6298	0.6261	0.0054
24	0.0099	0.0030	0.0020	0.6256	0.6303	0.6310	0.6289	0.0029
28	0.0205	0.0106	0.0118	0.6375	0.6364	0.6378	0.6372	0.0007
32	0.0073	0.0010	0.0009	0.6418	0.6370	0.6383	0.6390	0.0025
40	0.0036	0.0006	0.0004	0.6438	0.6373	0.6386	0.6399	0.0034
48	0.0002	0.0456	0.0449	0.6440	0.6638	0.6646	0.6575	0.0117

Table N4 The absorbance intensity and amount of IN permeated from 100IN-15EG_DCNR1 without electrical potential

Time (h)	Absorbance			Amount of drug permeated (mg)				
	1	2	3	1	2	3	Avg	SD
0.0833	0.0341	0.0320	0.0313	0.0198	0.0186	0.0181	0.0188	0.0008
0.1667	0.0429	0.0269	0.0450	0.0446	0.0341	0.0442	0.0410	0.0059
0.25	0.0360	0.0203	0.0280	0.0655	0.0459	0.0605	0.0573	0.0102
0.3333	0.0124	0.0280	0.0325	0.0727	0.0621	0.0793	0.0714	0.0087
0.4167	0.0177	0.0238	0.0198	0.0830	0.0759	0.0908	0.0832	0.0074
0.5	0.0356	0.0214	0.0322	0.1036	0.0883	0.1095	0.1005	0.0109
0.6667	0.0139	0.0243	0.0231	0.1117	0.1024	0.1228	0.1123	0.0102
0.8333	0.0187	0.0268	0.0565	0.1225	0.1180	0.1556	0.1320	0.0205
1	0.0230	0.0423	0.0559	0.1358	0.1425	0.1880	0.1554	0.0284
1.25	0.0090	0.0390	0.0668	0.1410	0.1651	0.2267	0.1776	0.0442
1.5	0.0215	0.0510	0.0401	0.1535	0.1947	0.2500	0.1994	0.0484
1.75	0.0705	0.0696	0.0745	0.1944	0.2350	0.2932	0.2409	0.0497
2	0.1178	0.1779	0.0506	0.2627	0.3382	0.3225	0.3078	0.0398
2.5	0.0528	0.0823	0.0578	0.2933	0.3859	0.3560	0.3451	0.0473
3	0.0524	0.0462	0.0971	0.3237	0.4126	0.4123	0.3829	0.0513
3.5	0.0411	0.0259	0.0403	0.3475	0.4277	0.4357	0.4036	0.0488
4	0.0625	0.0275	0.0381	0.3837	0.4436	0.4577	0.4284	0.0393
5	0.1294	0.0300	0.0178	0.4587	0.4610	0.4681	0.4626	0.0049
6	0.0401	0.0406	0.0172	0.4820	0.4845	0.4780	0.4815	0.0033
7	0.0363	0.0329	0.0233	0.5030	0.5036	0.4915	0.4994	0.0068
8	0.0125	0.0399	0.0404	0.5103	0.5267	0.5150	0.5173	0.0085
12	0.0431	0.0373	0.0181	0.5353	0.5484	0.5255	0.5364	0.0115
16	0.0285	0.0418	0.0712	0.5518	0.5726	0.5667	0.5637	0.0107
20	0.0207	0.0178	0.0138	0.5638	0.5829	0.5747	0.5738	0.0096
24	0.0130	0.0061	0.0061	0.5713	0.5864	0.5783	0.5787	0.0076
28	0.0122	0.0125	0.0125	0.5784	0.5937	0.5855	0.5859	0.0077
32	0.0158	0.0209	0.0209	0.5875	0.6058	0.5976	0.5970	0.0091
40	0.0083	0.0123	0.0123	0.5924	0.6129	0.6048	0.6034	0.0104
48	0.0046	0.0130	0.0130	0.5950	0.6205	0.6123	0.6093	0.0130

Appendix O **Determination of Amounts and Diffusion Coefficient of IN Permeated from 300IN-10EG_DCNR1 with Various Electrical Potentials**
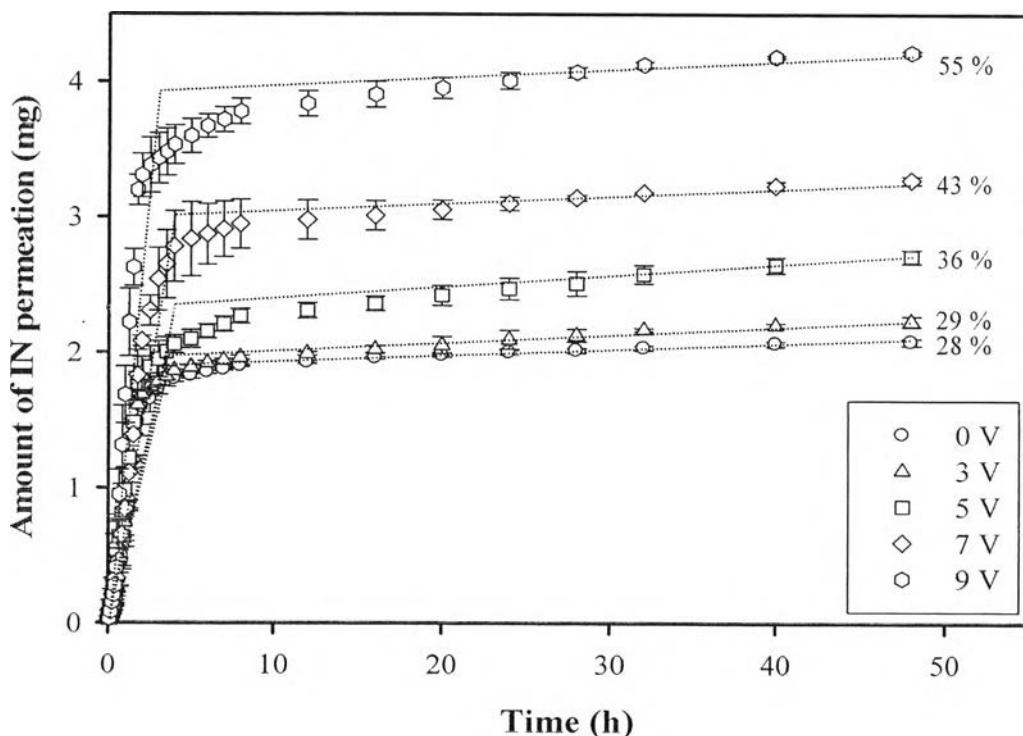
Figure O1 Amount of IN permeated from 300IN-10EG_DCNR1 with various electrical potentials, pH 7.4, 37 °C.

The total amounts of IN permeated from 3.14 cm^2 of 300IN-10EG_DCNR1 at E = 0, 0.1, 1, 3, 5, 7, and 9 V are 28 % (2.03 mg), 29 % (2.10 mg), 36 % (2.59 mg), 43 % (3.11 mg), and 55 % (3.97 mg), respectively. The amount of IN permeation depends on electrical potential. The driving force of the drug transportation is generated by the electro-repulsive force between a negatively charge of the anionic drug and the negatively charged cathode. Thus, the increase in electric field strength influences the driving force which promotes the diffusion of IN from the 300IN-10EG_DCNR1. The times to permeation equilibrium of 300IN-10EG_DCNR1 under applied electrical potential at 0, 3, 5, 7, and 9 were equal to 2.8, 2.8, 2.4, 2.4, and 2.2 hours, respectively.

The diffusion from each plasticizer has one diffusion stage. The n values

were equal to 1.42, 1.35, 1.27, 1.43, and 1.59 for 300IN-10EG_DCNR1 at E = 0, 3, 5, 7, and 9 V, respectively. The result indicates that the drug transport behavior can be considered as the Super Case II transport which results from the relaxation of polymer and the erosion mechanism (Sriamornsak *et al.*, 2007).
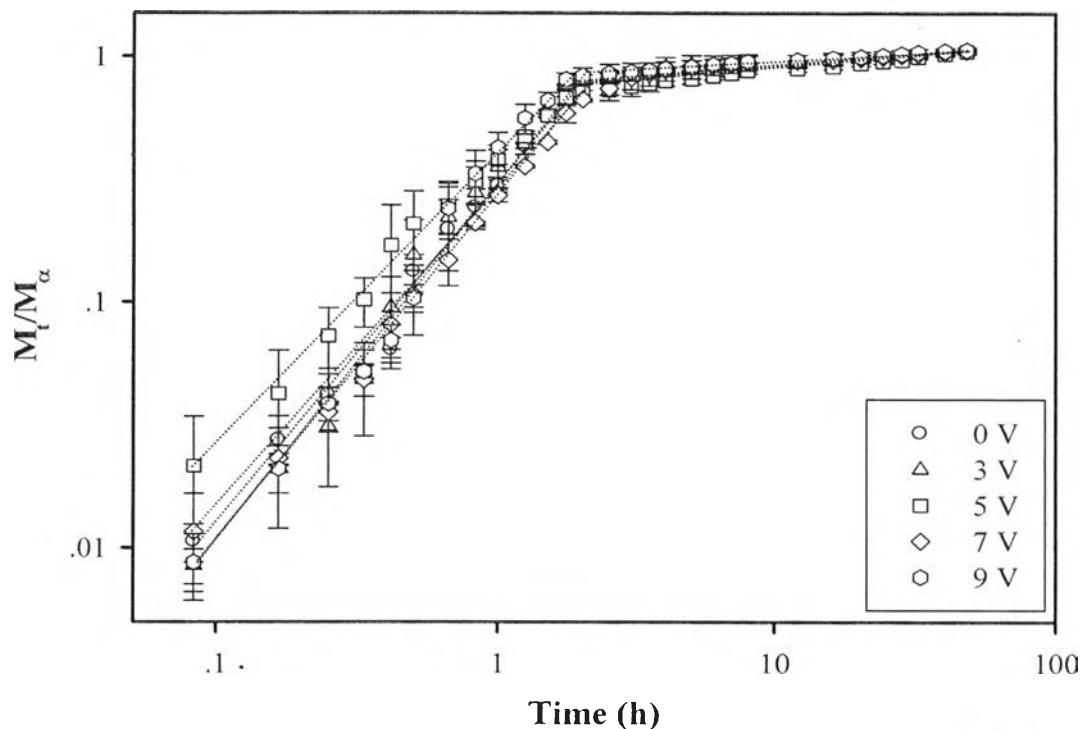
Figure O2 Plot of log M_t/M_∞ versus log time from 300IN-10EG_DCNR1 at various electrical potentials (0-9 V) at the crosslink ratio of 0.3 %v/v of, pH 7.4, 37 °C.
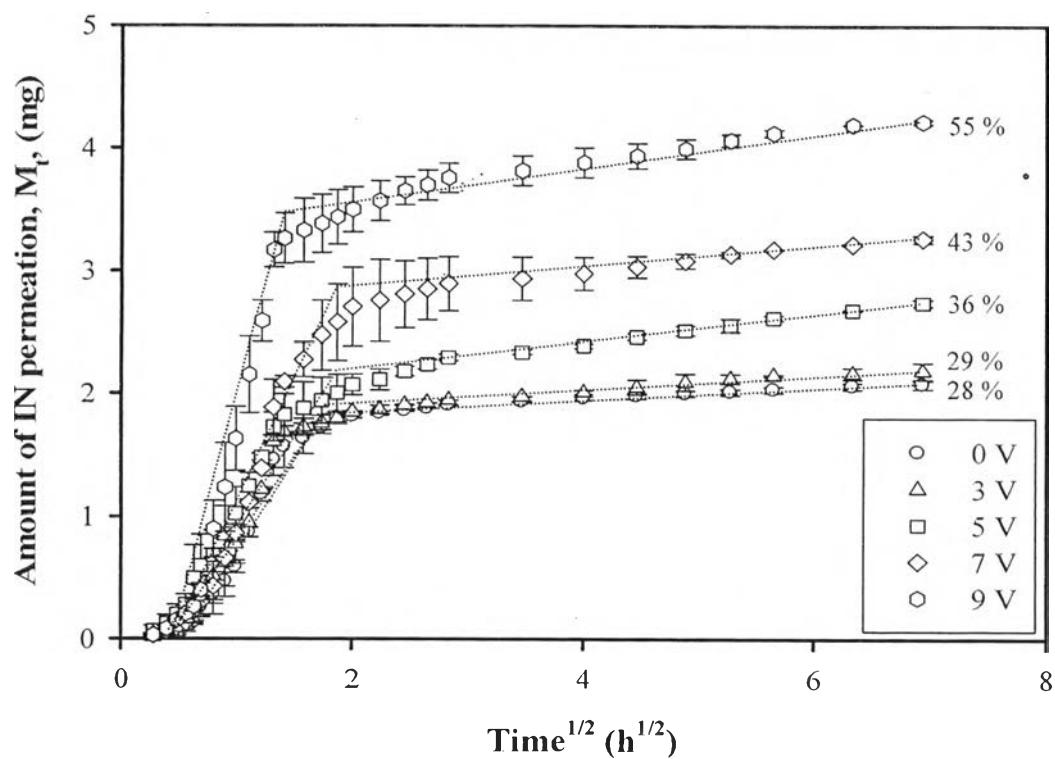
Figure O3 Amount of IN permeated from 300IN-10EG_DCNR1 at the crosslink ratio of 0.5 %v/v of DCNR versus time $t^{1/2}$ at various electrical potentials (0-9 V).
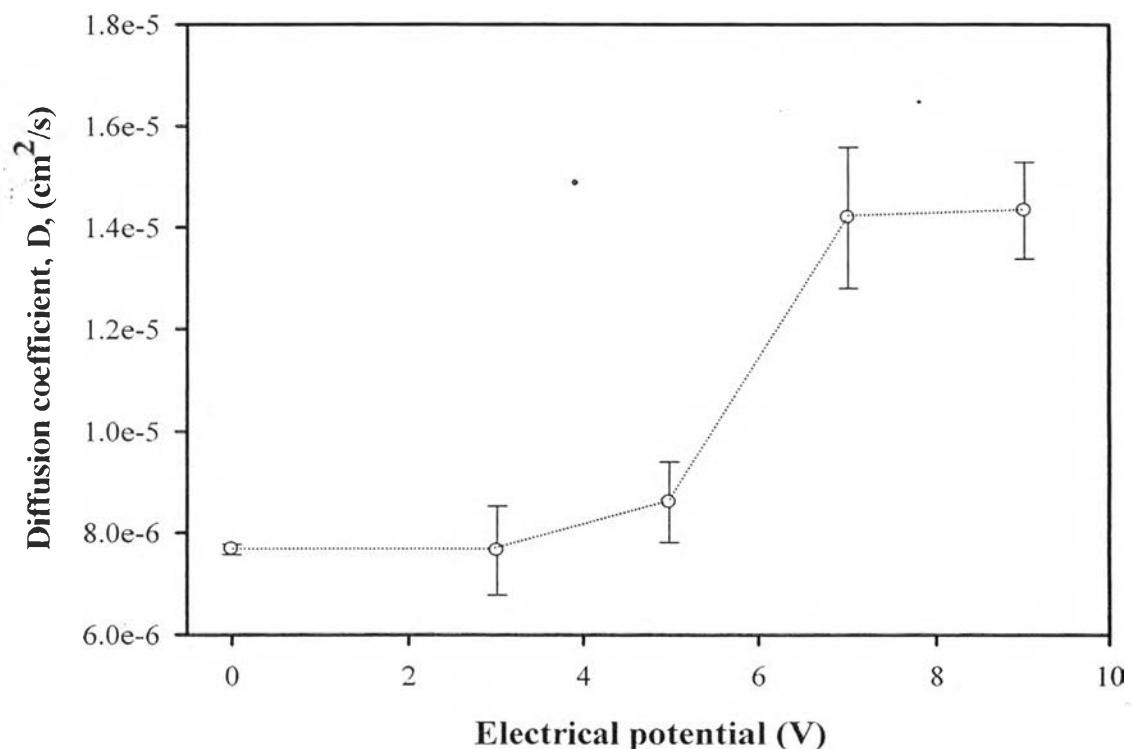
Figure O4 Diffusion coefficient, D, of IN permeated from 300IN-10EG_DCNR1 versus electrical potentials.

Table O1   The diffusion coefficients (D) of IN permeated from 300IN-10EG_DCNR1 with various electrical potentials, pH 7.4 at 37 °C

Sample	slope	M_{∞} (mg)	C_0 (mg/cm^3)	D (cm^2/s)
0° V	0.871	2.045	9.22	7.60335E-06
	0.883	2.036	9.22	7.74567E-06
	0.794	2.007	9.22	6.0858E-06
Avg	**0.849**			**7.14494E-06**
SD	**0.048**			**9.19997E-07**
3 V	0.820	2.089	9.22	7.03212E-06
	0.871	2.133	9.22	8.2718E-06
	0.813	2.091	9.22	6.92582E-06
Avg	**0.835**			**7.40991E-06**
SD	**0.032**			**7.48304E-07**
5 V	0.763	2.563	9.22	9.16491E-06
	0.717	2.555	9.22	8.0427E-06
	0.718	2.649	9.22	8.66951E-06
Avg	**0.733**			**8.62571E-06**
SD	**0.026**			**5.62384E-07**
7 V	0.763	3.077	9.22	1.32095E-05
	0.813	3.095	9.22	1.51735E-05
	0.813	3.163	9.22	1.58475E-05
Avg	**0.796**			**1.47435E-05**
SD	**0.029**			**1.37057E-06**
9 V	0.642	3.898	9.22	1.50084E-05
	0.610	3.914	9.22	1.3661E-05
	0.677	4.105	9.22	1.85091E-05
Avg	**0.643**			**1.57262E-05**
SD	**0.034**			**2.50247E-06**

Table O2 The absorbance intensity and amount of IN permeated from 300IN-10EG_DCNR1 under an absence of electrical potential (E = 0 V)

Time (h)	Absorbance			Amount of drug permeated (mg)				
	1	2	3	1	2	3	Avg	SD
0.0833	0.0300	0.0422	0.0394	0.0174	0.0245	0.0228	0.0216	0.0037
0.1667	0.0592	0.0664	0.0525	0.0517	0.0630	0.0533	0.0560	0.0061
0.25	0.0483	0.0479	0.0547	0.0797	0.0907	0.0850	0.0851	0.0055
0.3333	0.0324	0.0390	0.0270	0.0985	0.1133	0.1006	0.1042	0.0080
0.4167	0.0360	0.0554	0.0425	0.1194	0.1455	0.1253	0.1300	0.0137
0.5	0.3147	0.1162	0.2930	0.3018	0.2128	0.2951	0.2699	0.0496
0.6667	0.2985	0.0614	0.3174	0.4749	0.2484	0.4791	0.4008	0.1320
0.8333	0.1418	0.2296	0.1081	0.5571	0.3815	0.5418	0.4935	0.0972
1	0.1210	0.2991	0.1459	0.6272	0.5549	0.6264	0.6028	0.0415
1.25	0.4693	0.4971	0.4429	0.8993	0.8431	0.8832	0.8752	0.0289
1.5	0.5560	0.5095	0.5577	1.2216	1.1385	1.2065	1.1888	0.0443
1.75	0.5696	0.3950	0.5515	1.5518	1.3675	1.5262	1.4818	0.0999
2	0.2280	0.1311	0.2399	1.6840	1.4435	1.6653	1.5976	0.1338
2.5	0.0591	0.1750	0.0481	1.7182	1.5449	1.6931	1.6521	0.0937
3	0.0618	0.2428	0.0668	1.7541	1.6857	1.7319	1.7239	0.0349
3.5	0.0422	0.2301	0.0330	1.7785	1.8191	1.7510	1.7829	0.0342
4	0.0398	0.0091	0.0569	1.8016	1.8243	1.7840	1.8033	0.0202
5	0.0424	0.0440	0.0410	1.8262	1.8498	1.8078	1.8279	0.0211
6	0.0484	0.0264	0.0574	1.8542	1.8651	1.8410	1.8535	0.0121
7	0.0433	0.0250	0.0411	1.8793	1.8796	1.8649	1.8746	0.0085
8	0.0471	0.0368	0.0492	1.9067	1.9010	1.8934	1.9003	0.0067
12	0.0384	0.0591	0.0365	1.9289	1.9352	1.9145	1.9262	0.0106
16	0.0703	0.0240	0.0756	1.9697	1.9491	1.9584	1.9591	0.0103
20	0.0452	0.0246	0.0383	1.9959	1.9634	1.9806	1.9799	0.0162
24	0.0351	0.0313	0.0379	2.0162	1.9816	2.0025	2.0001	0.0175
28	0.0223	0.0212	0.0261	2.0291	1.9938	2.0177	2.0136	0.0180
32	0.0343	0.0352	0.0244	2.0490	2.0142	2.0318	2.0317	0.0174
40	0.0562	0.0478	0.0663	2.0816	2.0420	2.0703	2.0646	0.0204
48	0.0333	0.0162	0.0303	2.1009	2.0514	2.0878	2.0800	0.0257

Table O3 The absorbance intensity and amount of IN permeated from 300IN-10EG_DCNR1 under an electrical potential (E = 3 V)

Time (h)	Absorbance			Amount of drug permeated (mg)				
	1	2	3	1	2	3	Avg	SD
0.0833	0.0325	0.0255	0.0345	0.0188	0.0148	0.0200	0.0179	0.0027
0.1667	0.0350	0.0732	0.0332	0.0391	0.0572	0.0392	0.0452	0.0104
0.25	0.0477	0.0096	0.0500	0.0668	0.0628	0.0682	0.0659	0.0028
0.3333	0.0506	0.1325	0.0488	0.0961	0.1396	0.0965	0.1107	0.0250
0.4167	0.1096	0.2408	0.1146	0.1597	0.2792	0.1630	0.2006	0.0681
0.5	0.1541	0.3467	0.1580	0.2490	0.4802	0.2546	0.3279	0.1319
0.6667	0.1846	0.3636	0.1767	0.3560	0.6910	0.3570	0.4680	0.1931
0.8333	0.2285	0.1575	0.2330	0.4885	0.7823	0.4921	0.5876	0.1686
1	0.3035	0.2215	0.3014	0.6644	0.9107	0.6668	0.7473	0.1415
1.25	0.3513	0.2401	0.3591	0.8681	1.0499	0.8750	0.9310	0.1030
1.5	0.6001	0.3294	0.5933	1.2160	1.2408	1.2189	1.2252	0.0136
1.75	0.6695	0.6661	0.6754	1.6041	1.6270	1.6105	1.6139	0.0118
2	0.1314	0.1303	0.1284	1.6803	1.7025	1.6849	1.6892	0.0117
2.5	0.1616	0.0042	0.1662	1.7740	1.7050	1.7813	1.7534	0.0421
3	0.0498	0.0749	0.0456	1.8028	1.7484	1.8077	1.7863	0.0329
3.5	0.0473	0.0802	0.0547	1.8302	1.7949	1.8394	1.8215	0.0235
4	0.0373	0.1335	0.0458	1.8519	1.8723	1.8660	1.8634	0.0104
5	0.0692	0.0012	0.0628	1.8920	1.8730	1.9024	1.8891	0.0149
6	0.0272	0.1016	0.0436	1.9078	1.9319	1.9276	1.9224	0.0129
7	0.0322	0.0330	0.0285	1.9264	1.9510	1.9442	1.9405	0.0127
8	0.0340	0.0435	0.0356	1.9461	1.9762	1.9648	1.9624	0.0152
12	0.0547	0.0442	0.0507	1.9778	2.0018	1.9942	1.9913	0.0123
16	0.0345	0.0850	0.0370	1.9978	2.0511	2.0156	2.0215	0.0271
20	0.0176	0.1258	0.0155	2.0080	2.1240	2.0246	2.0522	0.0627
24	0.0668	0.0853	0.0687	2.0468	2.1735	2.0645	2.0949	0.0686
28	0.0820	0.0071	0.0700	2.0943	2.1776	2.1050	2.1257	0.0453
32	0.1022	0.0005	0.1162	2.1536	2.1779	2.1724	2.1680	0.0128
40	0.0788	0.0099	0.0768	2.1992	2.1836	2.2169	2.1999	0.0166
48	0.0618	0.0103	0.0868	2.2351	2.1896	2.2672	2.2306	0.0390

Table O4 The absorbance intensity and amount of IN permeated from 300IN-10EG_DCNR1 under an electrical potential (E = 5 V)

Time (h)	Absorbance			Amount of drug permeated (mg)				
	1	2	3	1	2	3	Avg	SD
0.0833	0.0597	0.1664	0.0656	0.0346	0.0965	0.0380	0.0564	0.0348
0.1667	0.0741	0.1387	0.0696	0.0776	0.1769	0.0784	0.1109	0.0571
0.25	0.1143	0.1406	0.1513	0.1438	0.2584	0.1661	0.1894	0.0607
0.3333	0.1329	0.1423	0.1159	0.2209	0.3409	0.2333	0.2650	0.0660
0.4167	0.1505	0.6012	0.1635	0.3081	0.6894	0.3281	0.4419	0.2146
0.5	0.1949	0.1563	0.1669	0.4211	0.7800	0.4248	0.5420	0.2062
0.6667	0.2031	0.0830	0.2231	0.5389	0.8281	0.5542	0.6404	0.1628
0.8333	0.2751	0.3278	0.2601	0.6983	1.0182	0.7049	0.8071	0.1828
1	0.3024	0.2740	0.3234	0.8736	1.1770	0.8924	0.9810	0.1700
1.25	0.5116	0.2515	0.4876	1.1702	1.3228	1.1751	1.2227	0.0867
1.5	0.5034	0.3105	0.5424	1.4621	1.5028	1.4895	1.4848	0.0208
1.75	0.5997	0.2457	0.5667	1.8097	1.6453	1.8181	1.7577	0.0975
2	0.2330	0.1121	0.1080	1.9448	1.7102	1.8807	1.8452	0.1212
2.5	0.1435	0.0305	0.0624	2.0280	1.7279	1.9169	1.8909	0.1517
3	0.0781	0.1385	0.0911	2.0733	1.8082	1.9697	1.9504	0.1336
3.5	0.0609	0.1485	0.0578	2.1086	1.8943	2.0032	2.0020	0.1071
4	0.0428	0.2028	0.0442	2.1334	2.0119	2.0288	2.0580	0.0658
5	0.0703	0.0693	0.0655	2.1741	2.0520	2.0668	2.0977	0.0666
6	0.0599	0.1738	0.0636	2.2089	2.1528	2.1037	2.1551	0.0526
7	0.0930	0.1003	0.0837	2.2628	2.2109	2.1522	2.2086	0.0553
8	0.0867	0.1145	0.0954	2.3130	2.2773	2.2075	2.2660	0.0537
12	0.0682	0.0798	0.0630	2.3526	2.3236	2.2440	2.3067	0.0562
16	0.0828	0.0883	0.0952	2.4006	2.3748	2.2992	2.3582	0.0527
20	0.0704	0.1841	0.0638	2.4414	2.4815	2.3362	2.4197	0.0751
24	0.0755	0.1000	0.0799	2.4852	2.5395	2.3825	2.4690	0.0797
28	0.0542	0.0936	0.0529	2.5166	2.5937	2.4132	2.5078	0.0906
32	0.1420	0.0602	0.1474	2.5989	2.6286	2.4986	2.5754	0.0681
40	0.1437	0.0793	0.1376	2.6822	2.6746	2.5784	2.6451	0.0579
48	0.1315	0.0787	0.1343	2.7584	2.7202	2.6562	2.7116	0.0516

Table O5 The absorbance intensity and amount of IN permeated from 300IN-10EG_DCNR1 under an electrical potential (E = 7 V)

Time	Absorbance			Amount of drug permeated (mg)				
(h)	1	2	3	1	2	3	Avg	SD
0.0833	0.0755	0.0319	0.0794	0.0438	0.0185	0.0460	0.0361	0.0153
0.1667	0.0848	0.0242	0.0770	0.0929	0.0325	0.0907	0.0720	0.0342
0.25	0.0860	0.0255	0.0883	0.1428	0.0473	0.1419	0.1106	0.0549
0.3333	0.0791	0.0581	0.0662	0.1886	0.0810	0.1802	0.1500	0.0599
0.4167	0.1934	0.1291	0.2005	0.3008	0.1558	0.2965	0.2510	0.0825
0.5	0.1661	0.1027	0.1479	0.3971	0.2154	0.3822	0.3315	0.1009
0.6667	0.2004	0.2372	0.2224	0.5132	0.3529	0.5111	0.4591	0.0920
0.8333	0.2316	0.5524	0.2226	0.6475	0.6731	0.6402	0.6536	0.0173
1	0.2863	0.4133	0.2874	0.8135	0.9127	0.8068	0.8443	0.0593
1.25	0.5206	0.3385	0.5170	1.1153	1.1090	1.1065	1.1102	0.0045
1.5	0.4892	0.4747	0.4962	1.3989	1.3841	1.3942	1.3924	0.0075
1.75	0.5640	1.1429	0.5594	1.7258	2.0467	1.7185	1.8303	0.1874
2	0.5795	0.1428	0.5874	2.0618	2.1295	2.0590	2.0834	0.0399
2.5	0.5387	0.0815	0.5315	2.3741	2.1767	2.3671	2.3060	0.1120
3	0.5201	0.1639	0.5261	2.6756	2.2718	2.6721	2.5398	0.2322
3.5	0.2117	0.1491	0.2059	2.7983	2.3582	2.7915	2.6493	0.2522
4	0.2293	0.2075	0.2408	2.9313	2.4785	2.9311	2.7803	0.2614
5	0.1088	0.0695	0.1046	2.9943	2.5188	2.9917	2.8349	0.2738
6	0.0105	0.1642	0.0184	3.0004	2.6140	3.0024	2.8723	0.2237
7	0.0498	0.1018	0.0405	3.0293	2.6730	3.0259	2.9094	0.2047
8	0.0381	0.1120	0.0429	3.0514	2.7379	3.0507	2.9467	0.1808
12	0.0178	0.1239	0.0167	3.0617	2.8097	3.0604	2.9773	0.1451
16	0.0179	0.1264	0.0229	3.0721	2.8830	3.0737	3.0096	0.1096
20	0.0386	0.1480	0.0367	3.0944	2.9688	3.0950	3.0527	0.0727
24	0.0501	0.1240	0.0605	3.1235	3.0407	3.1300	3.0981	0.0498
28	0.0507	0.1343	0.0431	3.1529	3.1186	3.1550	3.1422	0.0205
32	0.0473	0.0925	0.0529	3.1803	3.1722	3.1857	3.1794	0.0068
40	0.0499	0.0880	0.1409	3.2092	3.2232	3.2674	3.2333	0.0304
48	0.0562	0.1059	0.0628	3.2418	3.2846	3.3038	3.2767	0.0317

Table O6 The absorbance intensity and amount of IN permeated from 300IN-10EG_DCNR1 under an electrical potential (E = 9 V)

Time	Absorbance			Amount of drug permeated (mg)				
(h)	1	2	3	1	2	3	Avg	SD
0.0833	0.0688	0.0403	0.0697	0.0399	0.0234	0.0404	0.0346	0.0097
0.1667	0.0764	0.1020	0.0755	0.0842	0.0825	0.0842	0.0836	0.0010
0.25	0.1108	0.1326	0.1207	0.1484	0.1594	0.1541	0.1540	0.0055
0.3333	0.1095	0.0708	0.0951	0.2119	0.2004	0.2093	0.2072	0.0060
0.4167	0.1440	0.0611	0.1538	0.2954	0.2358	0.2984	0.2765	0.0353
0.5	0.2478	0.2199	0.2257	0.4390	0.3633	0.4293	0.4105	0.0412
0.6667	1.0738	0.6456	1.0768	1.0615	0.7376	1.0535	0.9509	0.1848
0.8333	0.7441	0.4213	0.7282	1.4929	0.9818	1.4757	1.3168	0.2902
1	0.5547	0.8048	0.5652	1.8145	1.4484	1.8033	1.6887	0.2082
1.25	0.9613	0.8356	0.9504	2.3718	1.9328	2.3543	2.2196	0.2486
1.5	0.5833	0.9246	0.5887	2.7099	2.4688	2.6956	2.6248	0.1353
1.75	0.9698	1.0359	0.9645	3.2721	3.0693	3.2547	3.1987	0.1124
2	0.2369	0.0885	0.2373	3.4095	3.1207	3.3923	3.3075	0.1620
2.5	0.1793	0.0428	0.1646	3.5134	3.1455	3.4877	3.3822	0.2054
3	0.0688	0.1246	0.0724	3.5533	3.2177	3.5297	3.4336	0.1873
3.5	0.0707	0.1078	0.0660	3.5943	3.2802	3.5680	3.4808	0.1742
4	0.0612	0.1547	0.0649	3.6298	3.3699	3.6056	3.5351	0.1436
5	0.0974	0.1470	0.0898	3.6862	3.4551	3.6576	3.5997	0.1260
6	0.0798	0.2058	0.0916	3.7325	3.5744	3.7108	3.6725	0.0857
7	0.0907	0.0665	0.0867	3.7851	3.6130	3.7610	3.7197	0.0932
8	0.1007	0.1023	0.1146	3.8435	3.6723	3.8275	3.7811	0.0946
12	0.1003	0.1031	0.0901	3.9016	3.7320	3.8797	3.8378	0.0922
16	0.1128	0.1121	0.1294	3.9670	3.7970	3.9547	3.9062	0.0948
20	0.0716	0.1183	0.0615	4.0085	3.8656	3.9904	3.9548	0.0778
24	0.0728	0.1248	0.0790	4.0507	3.9379	4.0362	4.0083	0.0613
28	0.0849	0.1566	0.0824	4.0999	4.0287	4.0839	4.0709	0.0373
32	0.0749	0.1290	0.0798	4.1433	4.1035	4.1302	4.1257	0.0203
40	0.0818	0.1493	0.0755	4.1908	4.1901	4.1740	4.1849	0.0095
48	0.0664	0.0222	0.0788	4.2293	4.2029	4.2196	4.2173	0.0133

Appendix P Determination of Amounts and Diffusion Coefficient of IN Permeated from 200IN-10EG_DCNR1 and 200IN-10EG_DPNR1 under an Electrical Potential (9 V)
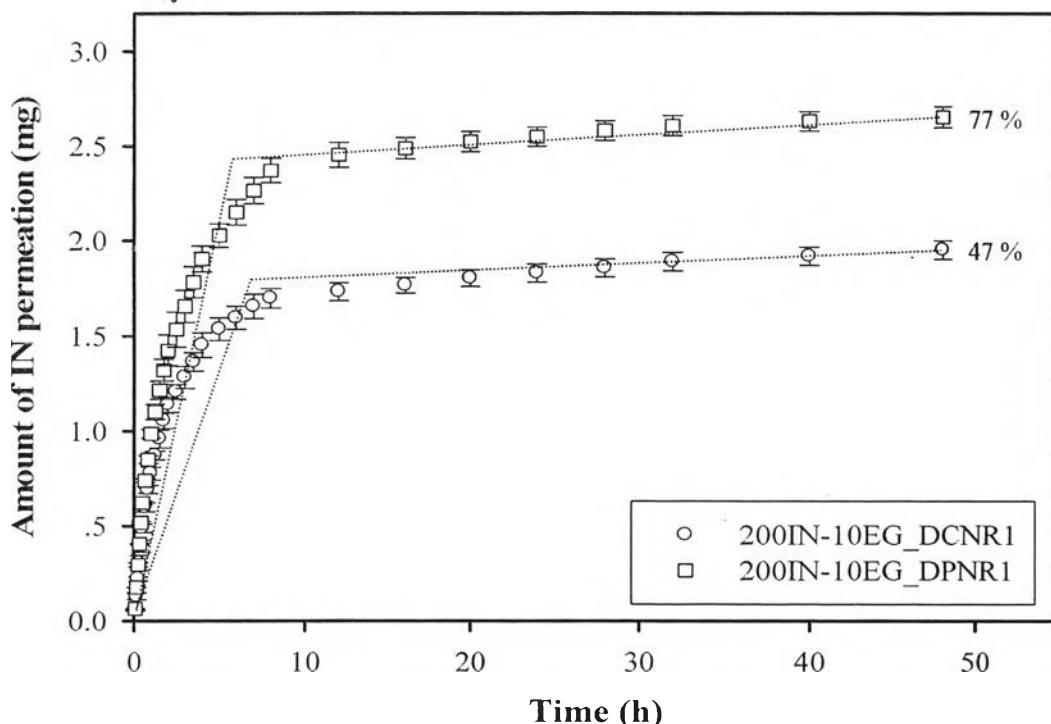
Figure P1   Amount of IN permeated from 200IN-10EG_DCNR1 and 200IN-10EG_DPNR1 under electrical potentials at 9 V (sample area 3.14 cm^2), pH 7.4, 37 °C.

The total amounts of IN permeated from 3.14 cm^2 of 200IN-10EG_DCNR1 and 200IN-10EG_DPNR1 at E = 9 V are 47 % (1.98 mg) and 77 % (2.69 mg), respectively. The amount of IN permeation depends on types of rubber matrix. The driving force of the drug transportation is generated by the electro-repulsive force between a negatively charge of the anionic drug and the negatively charged cathode. The times to permeation equilibrium of 200IN-10EG_DCNR1 and 200IN-10EG_DPNR1 under applied electrical potential at 9 V were equal to 6 and 8.5 hour, respectively.

The diffusion has one diffusion stage. The n values were equal to 1.32 and 0.68 for 200IN-10EG_DCNR1 and 200IN-10EG_DPNR1, respectively at E = V.

The result indicates that the drug transport behavior of 200IN-10EG_DCNR1 and 200IN-10EG_DPNR1 can be considered as the Super Case II transport which results from the relaxation of polymer and the erosion mechanism (Sriamornsak *et al.*, 2007) and the anomalous transport resulting from the pure Fickian diffusion and the matrix swelling.
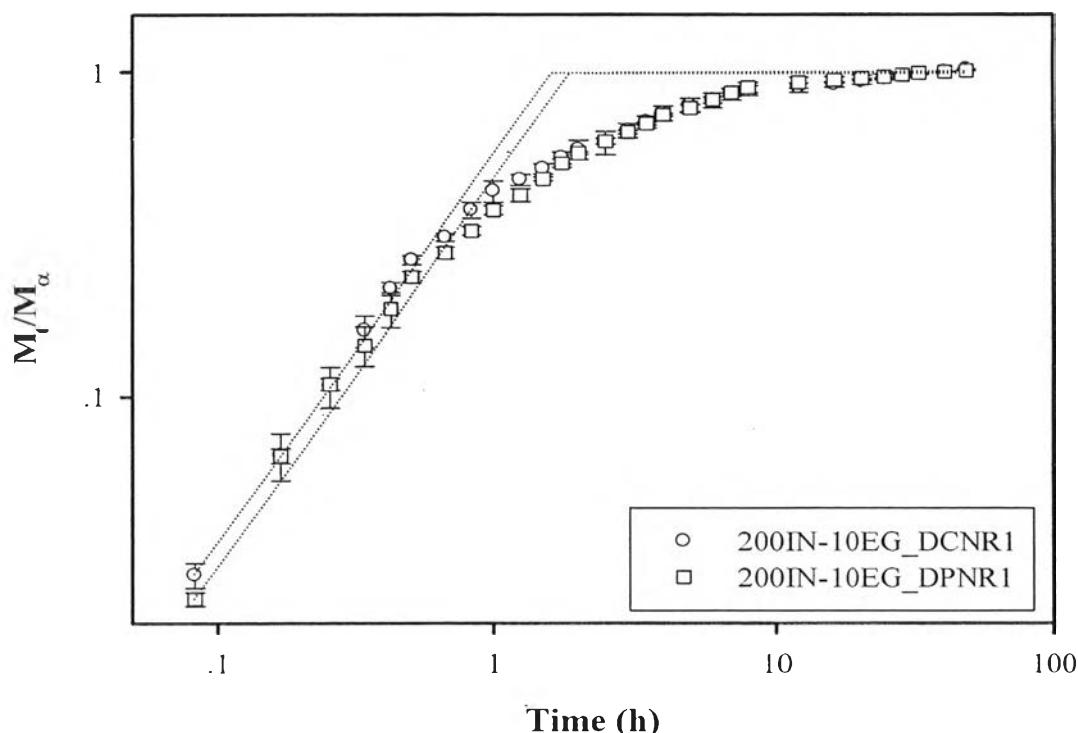
Figure P2   Plot of log M_t/M_∞ versus log time from 200IN-10EG_DCNR1 and 200IN-10EG_DPNR1 under electrical potentials at 9 V (sample area 3.14 cm^2), pH 7.4, 37 °C.
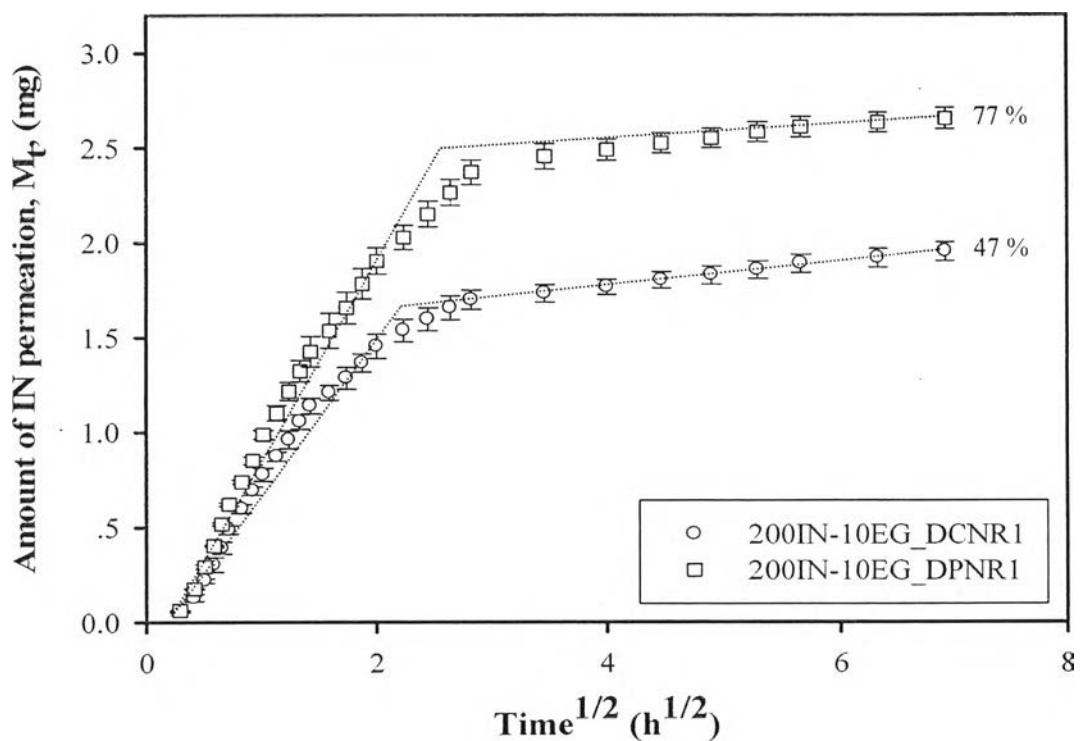
Figure P3 Amount of IN permeated from 200IN-10EG_DCNR1 and 200IN-10EG_DPNR1 under electrical potentials at 9 V (sample area 3.14 cm^2), pH 7.4, 37 °C.

Table P1   The diffusion coefficients (D) of IN permeated from 200IN-10EG_DCNR1 and 200IN-10EG_DPNR1 under electrical potentials at 9 V (sample area 3.14 cm^2), pH 7.4, 37 °C

Sample	slope	M_∞(mg)	C_0(mg/cm^3)	D(cm^2/s)
200IN-10EG_DCNR1	0.436	1.910	5.40	2.83765E-06
	0.452	1.911	5.40	3.05293E-06
	0.469	1.974	5.40	3.50719E-06
Avg	**0.452**			**3.13259E-06**
SD	**0.017**			**3.41803E-07**
200IN-10EG_DPNR1	0.530	2.822	4.33	1.11591E-05
	0.508	2.681	4.33	9.25093E-06
	0.488	2.575	4.33	7.87778E-06
Avg	**0.509**			**9.42926E-06**
SD	**0.021**			**1.64791E-06**

Table P2 The absorbance intensity and amount of IN permeated from 200IN-10EG_DCNR1 under electrical potentials at 9 V

Time (h)	Absorbance			Amount of drug permeated (mg)				
	1	2	3	1	2	3	Avg	SD
0.0833	0.0950	0.1044	0.0941	0.0538	0.0592	0.0533	0.0555	0.0032
0.1667	0.0978	0.1462	0.1506	0.1093	0.1420	0.1387	0.1300	0.0180
0.25	0.1337	0.1564	0.1439	0.1851	0.2307	0.2203	0.2120	0.0239
0.3333	0.1830	0.1874	0.1669	0.2888	0.3369	0.3149	0.3135	0.0241
0.4167	0.1717	0.1482	0.1493	0.3861	0.4209	0.3995	0.4022	0.0176
0.5	0.1852	0.1352	0.1815	0.4911	0.4976	0.5024	0.4970	0.0057
0.6667	0.1006	0.1712	0.2116	0.5481	0.5946	0.6223	0.5883	0.0375
0.8333	0.1609	0.1858	0.1517	0.6393	0.6999	0.7083	0.6825	0.0376
1	0.2367	0.1463	0.1769	0.7735	0.7828	0.8086	0.7883	0.0182
1.25	0.1848	0.1818	0.1314	0.8782	0.8859	0.8830	0.8824	0.0039
1.5	0.1053	0.2033	0.1516	0.9379	1.0011	0.9690	0.9693	0.0316
1.75	0.1782	0.1466	0.1756	1.0389	1.0842	1.0685	1.0639	0.0230
2	0.1223	0.1360	0.1652	1.1082	1.1613	1.1622	1.1439	0.0309
2.5	0.0637	0.1300	0.1115	1.1444	1.2350	1.2254	1.2016	0.0498
3	0.0786	0.1571	0.1488	1.1889	1.3240	1.3097	1.2742	0.0742
3.5	0.1613	0.1216	0.1447	1.2803	1.3930	1.3917	1.3550	0.0647
4	0.1223	0.1747	0.1692	1.3497	1.4920	1.4876	1.4431	0.0809
5	0.1602	0.1574	0.1281	1.4405	1.5812	1.5602	1.5273	0.0759
6	0.1067	0.1114	0.0951	1.5009	1.6443	1.6141	1.5865	0.0756
7	0.1570	0.1054	0.1161	1.5899	1.7041	1.6799	1.6580	0.0602
8	0.1003	0.0597	0.0659	1.6468	1.7379	1.7173	1.7007	0.0478
12	0.0678	0.0502	0.0603	1.6852	1.7664	1.7515	1.7344	0.0432
16	0.0702	0.0363	0.0704	1.7250	1.7870	1.7914	1.7678	0.0371
20	0.0606	0.0641	0.0737	1.7594	1.8233	1.8331	1.8053	0.0401
24	0.0674	0.0206	0.0735	1.7976	1.8350	1.8748	1.8358	0.0386
28	0.0593	0.0285	0.0578	1.8312	1.8511	1.9076	1.8633	0.0396
32	0.0590	0.0537	0.0623	1.8646	1.8816	1.9429	1.8964	0.0412
40	0.0898	0.0531	0.0523	1.9155	1.9117	1.9725	1.9332	0.0341
48	0.0622	0.0509	0.0610	1.9508	1.9405	2.0071	1.9661	0.0359

Table P3 The absorbance intensity and amount of IN permeated from 200IN-10EG_DPNR1 under electrical potentials at 9 V

Time (h)	Absorbance			Amount of drug permeated (mg)				
	1	2	3	.1	2	3	Avg	SD
0.0833	0.0957	0.0986	0.0955	0.0631	0.0650	0.0629	0.0637	0.0011
0.1667	0.1724	0.1673	0.1757	0.1767	0.1752	0.1787	0.1769	0.0018
0.25	0.1945	0.1636	0.1759	0.3048	0.2830	0.2946	0.2942	0.0109
0.3333	0.0570	0.1826	0.1743	0.3424	0.4033	0.4095	0.3851	0.0371
0.4167	0.1622	0.1817	0.1663	0.4493	0.5231	0.5191	0.4972	0.0415
0.5	0.2683	0.1653	0.1501	0.6261	0.6320	0.6180	0.6254	0.0070
0.6667	0.1809	0.1808	0.1785	0.7453	0.7512	0.7356	0.7440	0.0078
0.8333	0.2130	0.1721	0.1877	0.8857	0.8646	0.8593	0.8699	0.0140
1	0.2041	0.2126	0.2044	1.0202	1.0047	0.9940	1.0063	0.0132
1.25	0.1453	0.1967	0.1760	1.1159	1.1343	1.1100	1.1201	0.0127
1.5	0.2777	0.1945	0.1620	1.2989	1.2625	1.2168	1.2594	0.0412
1.75	0.3459	0.1733	0.1670	1.5269	1.3767	1.3268	1.4101	0.1041
2	0.1100	0.1772	0.1807	1.5994	1.4934	1.4459	1.5129	0.0786
2.5	0.2574	0.1821	0.1728	1.7690	1.6134	1.5598	1.6474	0.1087
3	0.1513	0.1780	0.1740	1.8687	1.7307	1.6744	1.7579	0.1000
3.5	0.1050	0.1827	0.1988	1.9379	1.8511	1.8054	1.8648	0.0673
4	0.2080	0.1741	0.1727	2.0749	1.9659	1.9192	1.9867	0.0799
5	0.0766	0.1837	0.1780	2.1254	2.0869	2.0365	2.0830	0.0446
6	0.1923	0.2054	0.1624	2.2522	2.2223	2.1436	2.2060	0.0561
7	0.1688	0.1709	0.1798	2.3634	2.3349	2.2620	2.3201	0.0523
8	0.0852	0.1551	0.1614	2.4195	2.4371	2.3684	2.4083	0.0357
12	0.1198	0.1248	0.1337	2.4985	2.5193	2.4565	2.4914	0.0320
16	0.1424	0.0471	0.0287	2.5923	2.5504	2.4754	2.5394	0.0592
20	0.0720	0.0535	0.0358	2.6398	2.5856	2.4990	2.5748	0.0710
24	0.0511	0.0349	0.0271	2.6734	2.6086	2.5169	2.5996	0.0787
28	0.0658	0.0485	0.0366	2.7168	2.6406	2.5410	2.6328	0.0882
32	0.1126	0.0339	0.0238	2.7910	2.6629	2.5567	2.6702	0.1173
40	0.0483	0.0261	0.0323	2.8228	2.6801	2.5780	2.6936	0.1230
48	0.0453	0.0294	0.0202	2.8527	2.6995	2.5913	2.7145	0.1314

Appendix Q   Determination of Amounts and Diffusion Coefficient of IN Permeated from 200IN-10EG_DPNR1 with Various Electrical Potentials
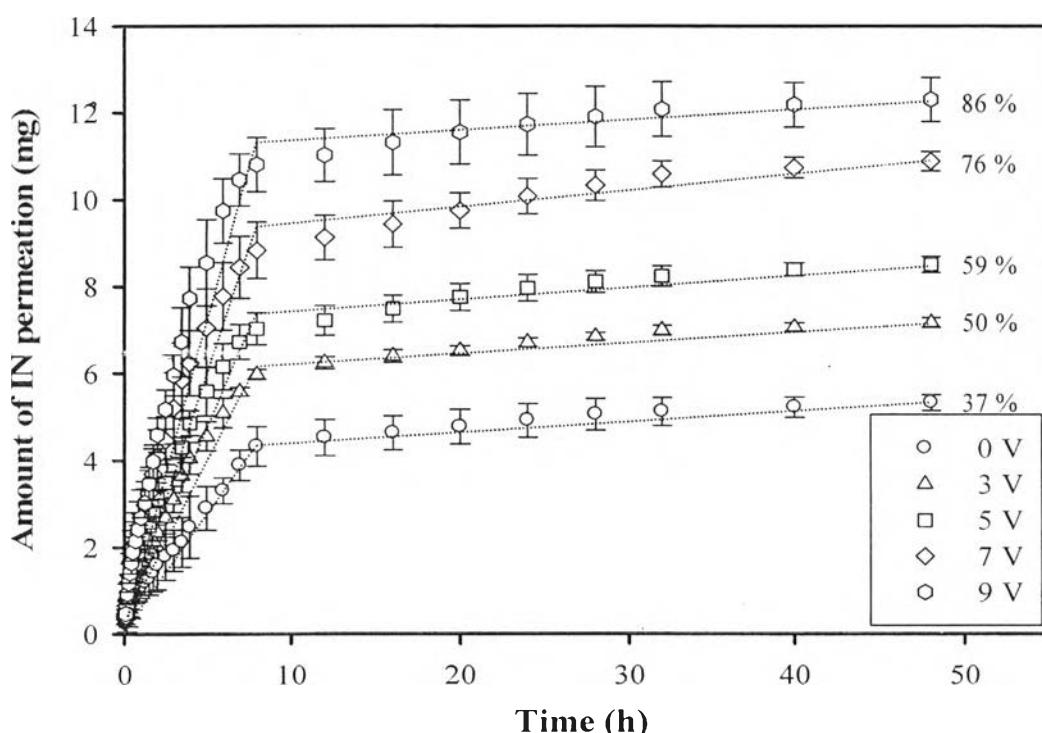
Figure Q1   Amount of IN permeated from 200IN-10EG_DPNR1 with various electrical potentials, pH 7.4, 37 °C.

The total amounts of IN permeated from 12.56 cm^2 of 200IN-10EG_DPNR1 at E = 0, 3, 5, 7, and 9 V are 37 % (5.22 mg), 50 % (7.07 mg), 59 % (8.38 mg), 76 % (10.73 mg), and 86 % (12.19 mg), respectively. The amount of IN permeation depends on electrical potential. The driving force of the drug transportation is generated by the electro-repulsive force between a negatively charge of the anionic drug and the negatively charged cathode. Thus, the increase in electric field strength influences the driving force which promotes the diffusion of IN from the 200IN-10EG_DPNR1. The times to permeation equilibrium of 200IN-10EG_DPNR1 at all applied electrical potential conditions were equal to 10 hours.

The diffusion has one diffusion stage. The n values were equal to 0.62, 0.54, 0.65, 0.67, and 0.70 for 200IN-10EG_DPNR1 at E = 0, 3, 5, 7, and 9 V, respectively. The result indicates that the drug transport behavior of all plasticizer systems can be

considered as the anomalous transport resulting from the pure Fickian diffusion and the matrix swelling.
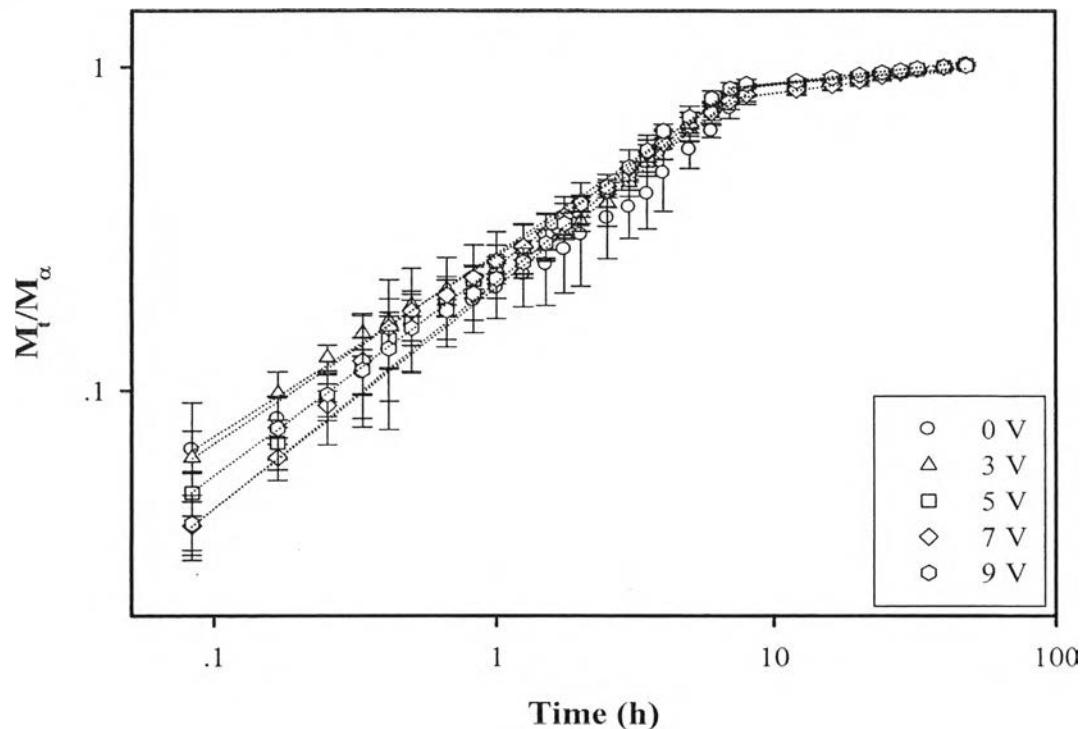
Figure Q2 Plot of log M_t/M_∞ versus log time from 200IN-10EG_DPNR1 at various electrical potentials (0-9 V) at the crosslink ratio of 0.3 %v/v, pH 7.4, 37 °C.
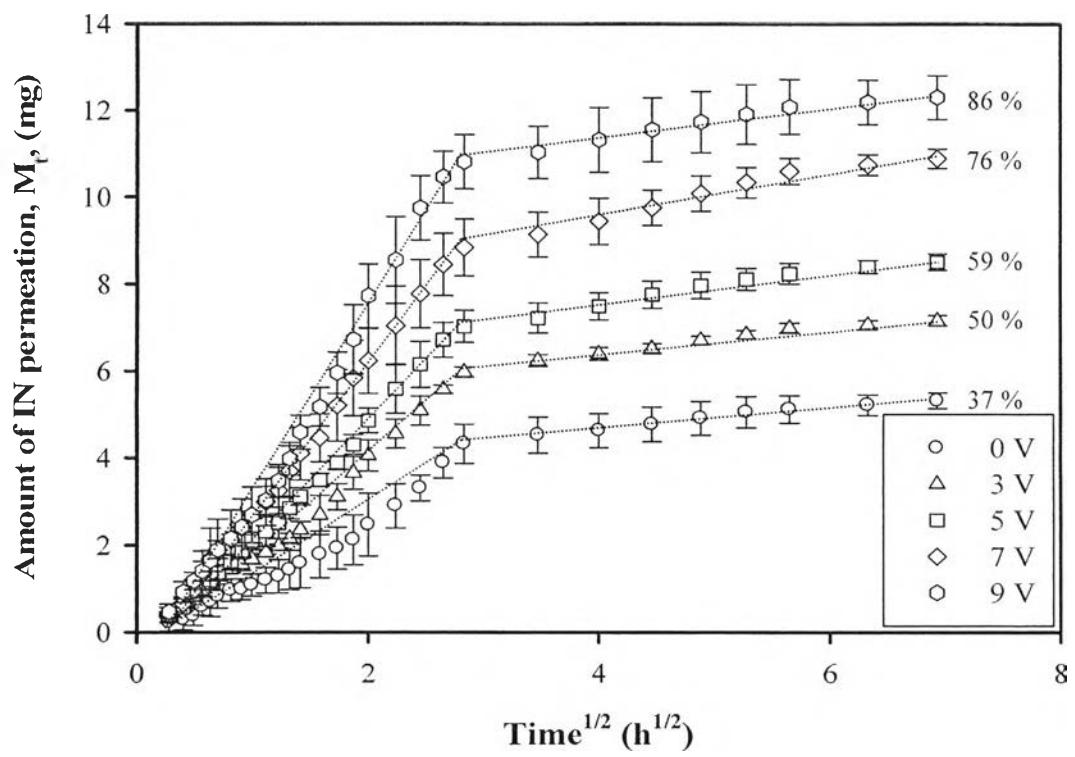
Figure Q3 Amount of IN permeated from 200IN-10EG_DPNR1 at the crosslink ratio of 0.5 %v/v of DPNR1 versus time $t^{1/2}$ at various electrical potentials (0-9 V).
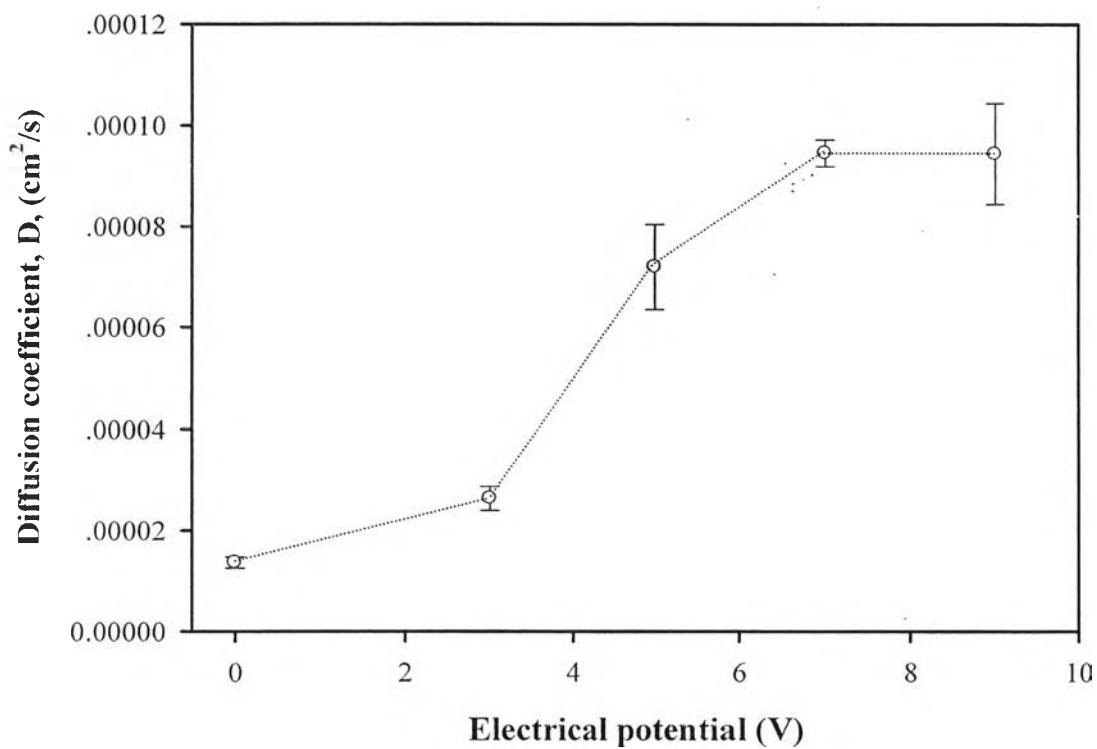
Figure Q4 Diffusion coefficient, D, of IN permeated from 200IN-10EG_DPNR1 versus electrical potentials.

Table Q1   The diffusion coefficients (D) of IN permeated from   the 200IN-10EG_DPNR1 with various electrical potentials, pH 7.4 at 37 °C

Sample	slope	M_∞(mg)	C_0(mg/cm^3)	D(cm^2/s)
0 V	0.312	5.097	4.49	1.24453E-05
	0.333	5.058	4.49	1.39609E-05
	0.313	5.498	4.49	1.45735E-05
Avg	**0.319**			**1.36599E-05**
SD	**0.012**			**1.09558E-06**
3 V	0.313	7.032	4.49	2.38404E-05
	0.345	6.994	4.49	2.86521E-05
	0.323	7.197	4.49	2.65934E-05
Avg	**0.327**			**2.6362E-05**
SD	**0.016**			**2.41419E-06**
5 V	0.435	8.417	4.49	6.59720E-05
	0.455	8.180	4.49	6.81704E-05
	0.476	8.552	4.49	8.15485E-05
Avg	**0.455**			**7.1897E-05**
SD	**0.021**			**8.43042E-06**
7 V	0.400	11.024	4.49	9.56896E-05
	0.408	10.569	4.49	9.15071E-05
	0.417	10.611	4.49	9.63499E-05
Avg	**0.408**			**9.45155E-05**
SD	**0.009**			**2.62624E-06**
9 V	0.333	12.515	4.49	8.54706E-05
	0.370	12.496	4.49	0.000105199
	0.375	1?.554	4.49	9.23834E-05
Avg	**0.359**			**9.4351E-05**
SD	**0.023**			**1.00104E-05**

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Table Q2 The absorbance intensity and amount of IN permeated from 200IN-10EG_DPNR1 under an absence of electrical potential (E = 0 V)

Time (h)	Absorbance			Amount of drug permeated (mg)				
	1	2	3	1	2	3	Avg	SD
0.0833	0.0357	0.0013	0.0512	0.2797	0.0102	0.4011	0.2303	0.2001
0.1667	0.0074	0.0038	0.0138	0.3376	0.0400	0.5092	0.2956	0.2374
0.25	0.0163	0.0121	0.0034	0.4653	0.1347	0.5359	0.3786	0.2141
0.3333	0.0032	0.0435	0.0367	0.4904	0.4755	0.8234	0.5964	0.1967
0.4167	0.0027	0.0037	0.0357	0.5116	0.5045	1.1030	0.7064	0.3435
0.5	0.0173	0.0257	0.0057	0.6471	0.7059	1.1477	0.8335	0.2736
0.6667	0.0099	0.0303	0.0099	0.7247	0.9432	1.2253	0.9644	0.2510
0.8333	0.0051	0.0030	0.0024	0.7646	0.9667	1.2441	0.9918	0.2407
1	0.0120	0.0085	0.0147	0.8586	1.0333	1.3592	1.0837	0.2541
1.25	0.0100	0.0127	0.0200	0.9370	1.1328	1.5159	1.1952	0.2945
1.5	0.0047	0.0041	0.0246	0.9738	1.1649	1.7086	1.2824	0.3813
1.75	0.0148	0.0120	0.0295	1.0897	1.2589	1.9397	1.4295	0.4499
2	0.0164	0.0061	0.0379	1.2182	1.3067	2.2366	1.5872	0.5642
2.5	0.0268	0.0285	0.0209	1.4282	1.5300	2.4004	1.7862	0.5343
3	0.0338	0.0103	0.0096	1.6929	1.6107	2.4756	1.9264	0.4774
3.5	0.0147	0.0201	0.0389	1.8081	1.7682	2.7803	2.1189	0.5732
4	0.0442	0.0239	0.0640	2.1544	1.9554	3.2817	2.4638	0.7153
5	0.0564	0.0850	0.0252	2.5962	2.6213	3.4791	2.8989	0.5027
6	0.0767	0.0574	0.0205	3.1971	3.0710	3.6397	3.3026	0.2987
7	0.1074	0.0526	0.0630	4.0385	3.4830	4.1333	3.8849	0.3513
8	0.0479	0.0437	0.0752	4.4137	3.8254	4.7224	4.3205	0.4557
12	0.0158	0.0348	0.0261	4.5375	4.0980	4.9269	4.5208	0.4147
16	0.0062	0.0203	0.0137	4.5861	4.2571	5.0342	4.6258	0.3901
20	0.0187	0.0167	0.0191	4.7326	4.3879	5.1838	4.7681	0.3992
24	0.0137	0.0226	0.0189	4.8399	4.5649	5.3319	4.9122	0.3886
28	0.0059	0.0299	0.0173	4.8861	4.7992	5.4674	5.0509	0.3633
32	0.0147	0.0088	0.0009	5.0013	4.8681	5.4745	5.1146	0.3187
40	0.0124	0.0251	0.0019	5.0984	5.0647	5.4894	5.2175	0.2360
48	0.0120	0.0227	0.0051	5.1924	5.2426	5.5293	5.3214	0.1818

Table Q3 The absorbance intensity and amount of IN permeated from 200IN-10EG_DPNR1 under an electrical potential (E = 3 V)

Time (h)	Absorbance			Amount of drug permeated (mg)				
	1	2	3	1	2	3	Avg	SD
0.0833	0.0699	0.0728	0.0246	0.5476	0.5703	0.1927	0.4369	0.2118
0.1667	0.0280	0.0234	0.0457	0.7670	0.7536	0.5507	0.6904	0.1212
0.25	0.0162	0.0279	0.0340	0.8939	0.9722	0.8171	0.8944	0.0776
0.3333	0.0166	0.0326	0.0144	1.0239	1.2276	0.9299	1.0605	0.1522
0.4167	0.0143	0.0001	0.0225	1.1359	1.2284	1.1062	1.1568	0.0637
0.5	0.0090	0.0161	0.0288	1.2065	1.3545	1.3318	1.2976	0.0797
0.6667	0.0190	0.0169	0.0210	1.3553	1.4869	1.4963	1.4462	0.0788
0.8333	0.0137	0.0025	0.0302	1.4626	1.5065	1.7329	1.5673	0.1450
1	0.0125	0.0249	0.0077	1.5606	1.7016	1.7932	1.6851	0.1172
1.25	0.0356	0.0104	0.0100	1.8394	1.7830	1.8716	1.8314	0.0448
1.5	0.0142	0.0215	0.0199	1.9507	1.9515	2.0275	1.9765	0.0441
1.75	0.0425	0.0143	0.0096	2.2836	2.0635	2.1027	2.1499	0.1174
2	0.0287	0.0416	0.0060	2.5085	2.3894	2.1497	2.3492	0.1828
2.5	0.0806	0.0371	0.0118	3.1399	2.6800	2.2421	2.6874	0.4489
3	0.0150	0.0793	0.0657	3.2574	3.3013	2.7568	3.1052	0.3025
3.5	0.0319	0.0991	0.0775	3.5073	4.0776	3.3640	3.6496	0.3775
4	0.0384	0.0500	0.0654	3.8082	4.4694	3.8763	4.0513	0.3637
5	0.0732	0.0602	0.0596	4.3816	4.9410	4.3432	4.5553	0.3346
6	0.0936	0.0608	0.0503	5.1149	5.4173	4.7373	5.0898	0.3407
7	0.0594	0.0326	0.0951	5.5802	5.6727	5.4823	5.5784	0.0952
8	0.0548	0.0512	0.0469	6.0095	6.0738	5.8497	5.9777	0.1154
12	0.0446	0.0265	0.0304	6.3589	6.2814	6.0879	6.2427	0.1396
16	0.0240	0.0133	0.0212	6.5470	6.3856	6.2540	6.3955	0.1467
20	0.0093	0.0202	0.0180	6.6198	6.5438	6.3950	6.5195	0.1144
24	0.0247	0.0208	0.0276	6.8133	6.7068	6.6112	6.7104	0.1011
28	0.0181	0.0103	0.0242	6.9551	6.7875	6.8008	6.8478	0.0932
32	0.0214	0.0185	0.0153	7.1228	6.9324	6.9206	6.9919	0.1135
40	0.0076	0.0079	0.0118	7.1823	6.9943	7.0131	7.0632	0.1036
48	0.0131	0.0077	0.0192	7.2849	7.0546	7.1635	7.1677	0.1152

Table Q4 The absorbance intensity and amount of IN permeated from 200IN-10EG_DPNR1 under an electrical potential (E = 5 V)

Time (h)	Absorbance			Amount of drug permeated (mg)				
	1	2	3	1	2	3	Avg	SD
0.0833	0.0607	0.0430	0.0505	0.4755	0.3369	0.3956	0.4027	0.0696
0.1667	0.0146	0.0203	0.0317	0.5899	0.4959	0.6440	0.5766	0.0749
0.25	0.0161	0.0466	0.0170	0.7160	0.8610	0.7771	0.7847	0.0728
0.3333	0.0155	0.0437	0.0276	0.8375	1.2033	0.9934	1.0114	0.1836
0.4167	0.0201	0.0220	0.0298	0.9949	1.3757	1.2268	1.1991	0.1919
0.5	0.0269	0.0255	0.0128	1.2057	1.5754	1.3271	1.3694	0.1885
0.6667	0.0344	0.0309	0.0316	1.4752	1.8175	1.5747	1.6224	0.1761
0.8333	0.0283	0.0190	0.0346	1.6969	1.9664	1.8457	1.8363	0.1350
1	0.0373	0.0462	0.0170	1.9891	2.3283	1.9789	2.0988	0.1989
1.25	0.0178	0.0479	0.0154	2.1285	2.7035	2.0995	2.3105	0.3407
1.5	0.0251	0.0266	0.0216	2.3252	2.9119	2.2688	2.5020	0.3562
1.75	0.0512	0.0277	0.0524	2.7263	3.1289	2.6793	2.8448	0.2472
2	0.0494	0.0226	0.0298	3.1133	3.3060	2.9127	3.1107	0.1966
2.5	0.0546	0.0381	0.0519	3.5410	3.6045	3.3193	3.4883	0.1497
3	0.0643	0.0344	0.0530	4.0447	3.8740	3.7345	3.8844	0.1554
3.5	0.0663	0.0325	0.0614	4.5641	4.1286	4.2155	4.3027	0.2305
4	0.0706	0.0536	0.0883	5.1172	4.5485	4.9073	4.8577	0.2876
5	0.0844	0.0518	0.1442	5.7784	4.9543	6.0370	5.5899	0.5654
6	0.0938	0.0749	0.0470	6.5133	5.5411	6.4052	6.1532	0.5328
7	0.0818	0.1039	0.0327	7.1541	6.3550	6.6613	6.7235	0.4031
8	0.0365	0.0468	0.0346	7.4400	6.7217	6.9324	7.0314	0.3693
12	0.0221	0.0299	0.0211	7.6132	6.9559	7.0977	7.2223	0.3459
16	0.0286	0.0352	0.0395	7.8372	7.2317	7.4071	7.4920	0.3116
20	0.0310	0.0299	0.0412	8.0801	7.4659	7.7299	7.7586	0.3081
24	0.0162	0.0202	0.0444	8.2070	7.6241	8.0777	7.9696	0.3061
28	0.0179	0.0289	0.0079	8.3472	7.8506	8.1398	8.1125	0.2495
32	0.0082	0.0155	0.0258	8.4115	7.9720	8.3419	8.2418	0.2362
40	0.0177	0.0350	0.0074	8.5501	8.2462	8.3999	8.3987	0.1520
48	0.0183	0.0097	0.0139	8.6935	8.3222	8.5088	8.5081	0.1857

Table Q5 The absorbance intensity and amount of IN permeated from 200IN-10EG_DPNR1 under an electrical potential (E = 7 V)

Time (h)	Absorbance			Amount of drug permeated (mg)				
	1	2	3	1	2	3	Avg	SD
0.0833	0.0475	0.0621	0.0459	0.3721	0.4865	0.3596	0.4061	0.0699
0.1667	0.0235	0.0338	0.0409	0.5562	0.7513	0.6800	0.6625	0.0987
0.25	0.0164	0.0379	0.0616	0.6847	1.0482	1.1626	0.9652	0.2495
0.3333	0.0169	0.0320	0.0915	0.8171	1.2989	1.8794	1.3318	0.5319
0.4167	0.0164	0.0539	0.0635	0.9456	1.7212	2.3769	1.6812	0.7165
0.5	0.0273	0.0290	0.0247	1.1594	1.9483	2.5704	1.8927	0.7071
0.6667	0.0291	0.0355	0.0222	1.3874	2.2265	2.7443	2.1194	0.6847
0.8333	0.0353	0.0479	0.0237	1.6640	2.6017	2.9300	2.3985	0.6570
1	0.0365	0.0585	0.0168	1.9499	3.0600	3.0616	2.6905	0.6414
1.25	0.0544	0.0444	0.0122	2.3761	3.4078	3.1571	2.9804	0.5381
1.5	0.0369	0.0389	0.0261	2.6652	3.7126	3.3616	3.2465	0.5331
1.75	0.0454	0.0384	0.0877	3.0208	4.0134	4.0487	3.6943	0.5835
2	0.0485	0.0583	0.0497	3.4008	4.4701	4.4380	4.1030	0.6083
2.5	0.0534	0.0426	0.0400	3.8191	4.8039	4.7514	4.4581	0.5540
3	0.0620	0.0763	0.1485	4.3048	5.4016	5.9147	5.2071	0.8224
3.5	0.0833	0.0590	0.0996	4.9574	5.8638	6.6950	5.8388	0.8691
4	0.0597	0.0664	0.0261	5.4251	6.3840	6.8995	6.2362	0.7482
5	0.1066	0.0583	0.1455	6.2602	6.8407	8.0394	7.0468	0.9073
6	0.1300	0.0683	0.0817	7.2787	7.3758	8.6794	7.7780	0.7822
7	0.1001	0.0799	0.0754	8.0629	8.0018	9.2701	8.4449	0.7153
8	0.0533	0.0564	0.0408	8.4804	8.4436	9.5897	8.8379	0.6513
12	0.0604	0.0369	0.0154	8.9536	8.7327	9.7104	9.1322	0.5127
16	0.0386	0.0374	0.0412	9.2560	9.0257	10.033	9.4383	0.5279
20	0.0514	0.0470	0.0199	9.6587	9.3939	10.189	9.7472	0.4049
24	0.0546	0.0348	0.0381	10.086	9.6665	10.488	10.080	0.4105
28	0.0191	0.0476	0.0294	10.236	10.039	10.718	10.331	0.3491
32	0.0296	0.0420	0.0272	10.468	10.368	10.931	10.589	0.3002
40	0.0219	0.0240	0.0091	10.640	10.557	11.002	10.733	0.2371
48	0.0109	0.0288	0.0176	10.725	10.782	11.140	10.882	0.2250

Table Q6 The absorbance intensity and amount of IN permeated from 200IN-10EG_DPNR1 under an electrical potential (E = 9 V)

Time	Absorbance			Amount of drug permeated (mg)				
(h)	1	2	3	1	2	3	Avg	SD
0.0833	0.0611	0.0724	0.0456	0.4787	0.5672	0.3572	0.4677	0.1054
0.1667	0.0597	0.0749	0.0412	0.9464	1.1540	0.6800	0.9268	0.2376
0.25	0.0273	0.0304	0.0396	1.1602	1.3921	0.9902	1.1809	0.2017
0.3333	0.0272	0.0324	0.0269	1.3733	1.6459	1.2010	1.4067	0.2244
0.4167	0.0212	0.0345	0.0337	1.5394	1.9162	1.4650	1.6402	0.2419
0.5	0.0264	0.0273	0.0445	1.7462	2.1301	1.8136	1.8966	0.2050
0.6667	0.0427	0.0170	0.0385	2.0807	2.2633	2.1152	2.1531	0.0970
0.8333	0.0328	0.0334	0.0353	2.3377	2.5249	2.3918	2.4181	0.0964
1	0.0366	0.0165	0.0496	2.6244	2.6542	2.7803	2.6863	0.0828
1.25	0.0431	0.0099	0.0759	2.9621	2.7318	3.3749	3.0229	0.3259
1.5	0.0469	0.0566	0.0667	3.3295	3.1752	3.8975	3.4674	0.3804
1.75	0.0542	0.0751	0.0666	3.7541	3.7635	4.4192	3.9789	0.3813
2	0.0570	0.1036	0.0732	4.2006	4.5751	4.9927	4.5895	0.3962
2.5	0.0688	0.0736	0.0823	4.7396	5.1517	5.6374	5.1763	0.4494
3	0.0899	0.1166	0.0940	5.4439	6.0652	6.3738	5.9610	0.4736
3.5	0.0509	0.1702	0.0720	5.8427	7.3985	6.9379	6.7264	0.7992
4	0.1355	0.1106	0.1384	6.9042	8.2650	8.0221	7.7304	0.7258
5	0.0800	0.1601	0.0742	7.5309	9.5192	8.6034	8.5512	0.9952
6	0.2078	0.1344	0.1152	9.1588	10.572	9.5059	9.7456	0.7365
7	0.1086	0.0715	0.0926	10.001	11.132	10.231	10.458	0.5946
8	0.0279	0.0426	0.0627	10.228	11.466	10.723	10.806	0.6231
12	0.0181	0.0125	0.0523	10.370	11.564	11.132	11.022	0.6045
16	0.0105	0.0310	0.0713	10.452	11.807	11.691	11.317	0.7508
20	0.0314	0.0243	0.0332	10.698	11.997	11.951	11.549	0.7369
24	0.0274	0.0264	0.0152	10.913	12.204	12.070	11.729	0.7099
28	0.0248	0.0174	0.0257	11.107	12.340	12.271	11.906	0.6929
32	0.0312	0.0085	0.0262	11.352	12.407	12.477	12.078	0.6303
40	0.0305	0.0080	0.0021	11.591	12.470	12.493	12.184	0.5144
48	0.0166	0.0181	0.0105	11.721	12.611	12.575	12.302	0.5042

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Proceedings:

1. Choowongapichat, S.; and Sirivat, A. (2015, April 21) Development of Natural Rubber Matrix using in Electrical Stimuli Transdermal Drug Delivery Application. Proceedings of the 6th Research Symposium on Petrochemical and Materials Technology and the 21st PPC Symposium on Petroleum, Petrochemicals, and Polymers, Bangkok, Thailand.

Presentations:

1. Choowongapichat, S.; and Sirivat, A. (2015, April 21) Development of Natural Rubber Matrix using in Electrical Stimuli Transdermal Drug Delivery Application. Paper presented at the 6th Research Symposium on Petrochemical and Materials Technology and the 21st PPC Symposium on Petroleum, Petrochemicals, and Polymers, Bangkok, Thailand.

2. Choowongapichat, S.; and Sirivat, A. (2015, May 20) Development of Natural Rubber Matrix using in Electrical Stimuli Transdermal Drug Delivery Application. Paper presented at the 4th International Symposium Frontiers in Polymer Science in Association with the Journal Polymer, Riva del Grada, Italy.