Test Report

Woorhi Mechatronics Co., Ltd.

In vitro skin absorption test

by using the 'MINI PIN' device

(Franz-diffusion cell)

Date: Jul./27/2018

Korea Dermatology Research Institute Co., Ltd.

TABLE OF CONTENTS

1.	Test Result Summary3
2.	Reliability Assurance on Test Result and Report4
3.	Purpose of Evaluation Test5
4.	Information on Test Material5
5.	Test summary6
6.	Test Method7
7.	Test Results12
	Discussion and Conclusions19
9.	References 20
	Testing Institution21
	10-1. Test Personnel21
	10-2. Research List of Test Institute21
	10-3. Equipment List of Test Institute22
11.	Raw data24

Summary of Test Result

TITLE	In vitro skin absorption test by using the 'MINI PIN' device						
INSTITUTE	KDRI Co., Ltd.	PERIOD	2018. 06	25 ~ 2018.	07. 27		
	Sample Form	- MINI PI - re:Face	N : device : liquid				
	Test Period	2018. 0 ~ 2018.		Number of test	Repeat 4 times per sample		
	Treatment	Franz diffusion cell & Human Skin					
TEST METHOD	Detail on Test Method	 Using a 9 mm Franz diffusion cell with a 5 mL receptor volume (FDC-6T, Logan Instruments, Somerset, NJ, USA). Sampling time point: 0.5, 1, 3, 6, 10hr Analysis by HPLC 					
TEST RESULT	The skin treated with 'MINI PIN' device for 60 seconds showed a relatively high diffusion coefficient for the marker substance (niacinamide) in the range of 0.5 to 10 hours compared to the untreated control skin, and skin permeability was approximately 4.78-fold greater than the control, thus promoting dermal penetration.						
Confirmation		Director of th	e Institute	Lee, Dong	jhwan (signature)		

2. Reliability Assurance on Test Result and Report

• TITLE In vitro skin absorption test by using the 'MINI PIN' device

• TEST No. KDRI-IV-2018-056

This efficacy test was performed according to self-test regulation of KDRI (Korea Dermatology Research Institute) and GCP (Good Clinical Practice) under supervision of a researcher in charge.

All test results obtained during the test period were recorded on this report without any omission, and the researcher in charge and head of the institute assure all contents in this report.



Jul./27/2018

Director of the Institute

Lee, Donghwan



3. Purpose of the Evaluation Test

This test was performed by using the 'MINI PIN' device and 're:FACE(2% niacinamide)' sample provided by Woorhi Mechatronics Co., Ltd., using the in vitro skin absorption test method for human skin. The purpose of this study is to obtain basic data for predicting the application, absorption and permeation pattern of marker substance in human skin.

4. Information on Test Material

A. Sample Name and the Origin

Device & Sample Name	Device characteristics & Raw Materials used in Manufacturing	Sample Code of KDRI	Note
MINI PIN	All-in-one micro-needle Device	IV-2018-056-D	-
re:Face	2% Niacinamide	IV-2018-056-L	-

B. Sample Storage Method

Should be stored at room temperature, avoid of direct UV radiation

C. Sample Storage and Disposal

The samples will be stored in the institute for 1 month after the test completion and then disposed accordingly.

5

5. Test Summary

A. Test Client

Woorhi Mechatronics Co., Ltd.

5th Floor, Woorhi Mecha building, 58 Sanbon-ro 48beon-gil, Gunpo-si, Gyeonggi-do, Republic of Korea

(Tel. 031-457-5032 / Fax. 031-457-5031)

B. Testing Institute

Korea Dermatology Research Institute Co., Ltd.

#702, No.81 Road, Yatap Street, Bundang-gu, Seongnam-City Gyeonggi-do, Korea

(Tel. +82-31-622-0311 / Fax. +82-31-622-0310)

C. Research Period

Jun. 25. 2018 ~ Jul. 27. 2018

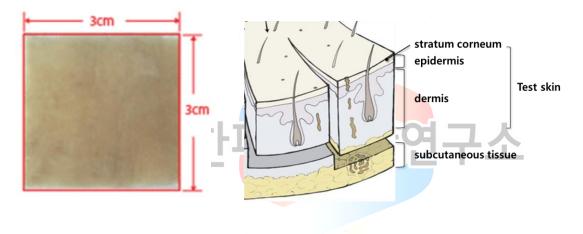
D. Test Period

Jun. 28. 2018 ~ Jul. 20. 2018

6. Test Method

A. Test Material Application Method

- (1) Human Full Skin, HansBiomed Corp, Republic of Korea
 - Skin No. RSK-17011U (Human Skin for percutaneous penetration research)
 - Back or thigh of human cadaver (age of 39, man)
 - Full thickness skin (<1mm)
 - Stored at -20°C.



1) Tewameter TM-300 (Corage+Khazaka, Germany)

A certain evaporation of water from the skin takes always place as part of the normal skin metabolism. As soon as the barrier function of the skin however is slightly damages, the water loss will increase. The Tewameter® probe measures the density gradient of the water evaporation from the skin indirectly by the two pairs of sensors (temperature and relative humidity) inside the hollow cylinder. A microprocessor analyses the values and expresses the evaporation rate in g/h/m2.

- 2) Franz diffusion cell (FDC-6T, Logan, USA)
- 3) High Performance Liquid Chromatography (Waters alliance e2695)
- 4) Niacinamide (99.0 %), Sigma-Aldrich

7

(2) Integrity of the skin structure (Suitability test)

In order to evaluate the suitability, the skin transdermal water loss was confirmed to be within the normal range of skin (less than 20), and the following results were obtained.

Table 1. Suitability test (TEWL)

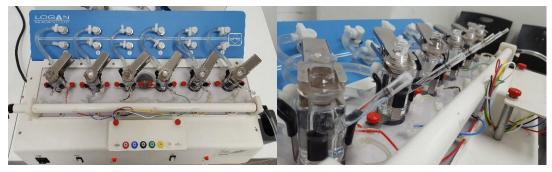
No.		Verification				
	1st	2nd	3rd	Mean	S.D.	
Skin #1	18.16	17.78	18.20	18.05	0.23	Υ
Skin #2	17.63	18.19	18.49	18.10	0.44	Υ
Skin #3	17.42	17.35	18.66	17.81	0.74	Y
Skin #4	16.32	18.63	17.84	17.60	1.17	Υ
Skin #5	18.45	17.64	18.75	18.28	0.57	Υ
Skin #6	18.63	19.78	19.45	19.29	0.59	Υ
Skin #7	17.45	16.58	18.90	17.64	1.17	Y
Skin #8	18.55	17.86	19.87	18.76	1.02	Υ

B. Test Procedure (Franz-diffusion cell test)

- (1) Determine the niacinamide content with the provided samples.
- (2) The temperature of the cell was maintained at 32 \pm 1 $^{\circ}$ C using a constant-temperature water bath.
- (3) The humidity of the equipment is maintained at 30-50%.



- (4) Human skin was washed with PBS (Phosphate Buffered Saline) for 30 minutes.
- (5) The skin of the test group is pretreated for 60 seconds using a 'MINI PIN' device provided by the client.
- (6) The skin was fixed between the donor and the receptor phase of stratum corneum side, facing upward into the donor compartment.
- (7) The sample 're: FACE(2% niacinamide)' 0.5ml was applied to skin surface (0.64 cm2) of the donor, and 5 mL of the receptor phase was withdrawn through the sampling port of the Franz diffusion cell at 0.5, 1, 3, 6, 10hr (5 time points).

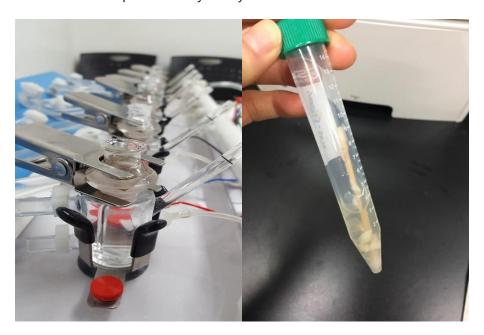


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Table 2. Sample application amount

	Details	Amount (niacinamide)
Test group	'MINI PIN' device + re:FACE(2% niacinamide)	15.7 mg/m² (10.017 mg)
Control group	re:FACE(2% niacinamide)	15.7 mg/m² (10.017 mg)

(8) The receptor phase was immediately replenished with an equal volume of fresh receptor phase. The withdrawn sample was analyzed by HPLC



(9) To determine the amount of niacinamide remaining in the skin, non-permeable samples were washed with phosphate-buffered saline (pH 7.4). After washing, the skin sample was cut into small pieces. Niacinamide in the skin was dissolved in phosphate-buffered saline (pH 7.4) using a sonicator. The amount of extracted niacinamide was determined using HPLC.

D. Analysis (HPLC)

- (1) Pretreatment of samples
- 0.1 ml of each sample and add to 1 ml of methanol, and disperse by sonication for 10 minutes
- add 8.9 ml of distilled water to the dispersion and sonicate for 10 minutes
- 1.5 ml of the dispersion is filtered and the content of niacinamide is analyzed by HPLC
- (2) Condition of HPLC analysis
- Instrument : Waters alliance e2695
- Detector: 2998 DAD Detector
- Column : Sunfire® C18 5µm 4.6x250mm
- Mobile phase : 0.05M Monopotassium phosphate buffer(pH7.0) : Methyl alcohol = (75 : 25)
- Flow rate : 1.0 ml/min
- Injection volume : 10 μl
- Wavelength: 263 nm
- Standard : Niacinamide (99.0 %), Sigma-Aldrich

7. Test Results

A. Standard Curve

Table 3. Concentration of Standard Curve

Concentration (ppm)	area (mV*s)	Note
0.1	1965	
0.5	6545	
1	12771	
3	37898	+100.01
15	190286	* LOQ: 0.1ppm
75	952642	
150	1906339	
500	6306977	

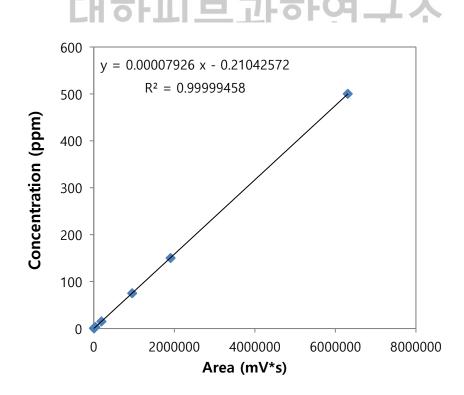
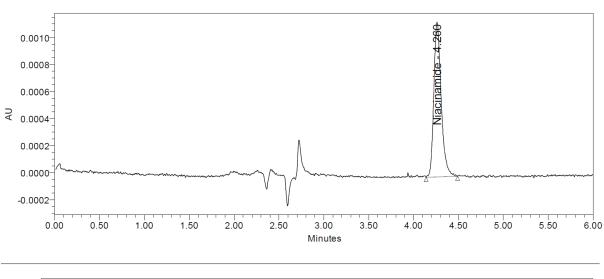
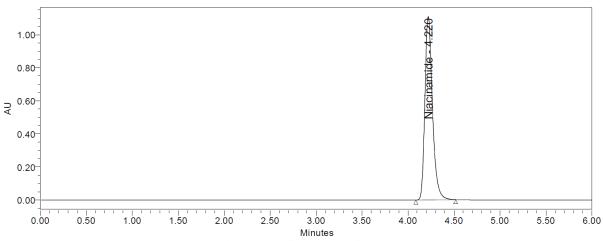


Fig 1. Niacinamide standard curve





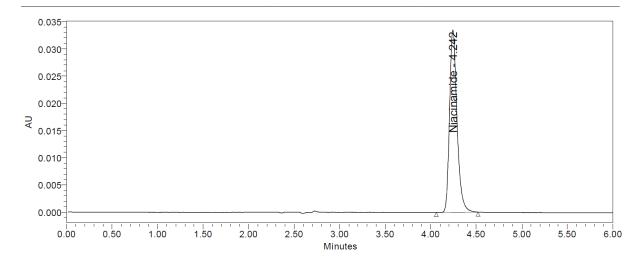


Fig 2. Chromatograms of niacinamide standard (0.5, 15, 500 ppm)

13

B. Determination of test substance content

Table 4. Determination of test substance content (niacinamide)

	Details	area (mV*s)	concentration (ppm)	Actual concentration (ppm)
Test group	'MINI PIN' device + re:FACE(2% niacinamide)	2530224	200.335	20034
Control group	re:FACE(2% niacinamide)	2530224	200.335	20034



C. Test results - Test group

This test was performed on human skin treated with 'MINI PIN' device for 60 seconds. After applying 're:FACE' containing about 2% of niacinamide as a marker substance.

As a result, it was confirmed that the percutaneous permeation of the marker substance continued for 10 hours. After 10 hours, about 4.78% of the niacinamide contained in the 're:FACE' of this test permeated the skin and the remaining amount absorbed to the skin was found to be 1.19% of the dose. In addition, the marker substance absorbed by the skin, the instrument and the marker substance remaining on the surface of the skin were recovered and the recovery rate was confirmed to be 103.57%.

Table 5. Results of niacinamide transdermal test in test group

Time	Drug concentration in receptor (µg/ml)	Transferred drug in receptor (µg)	Net transferred drug (μg)	Drug transferred (%, accumulation)	Transdermal diffusion rate (µg/s)	Flux (μg/s·cm²)	Diffusion coefficient (cm²/s)
0.5	0.85	4.26	4.26	0.04%	2.365E-03	0.0037	1.291E-08
1	4.10	20.52	20.95	0.21%	9.273E-03	0.0145	5.063E-08
3	24.69	123.43	125.90	1.26%	1.458E-02	0.0228	7.959E-08
6	54.09	270.46	285.28	2.85%	1.476E-02	0.0231	8.057E-08
10	92.81	464.03	478.85	4.78%	1.401E-02	0.0219	7.647E-08

Table 6. Results of niacinamide transdermal test in test group

	1st	2nd	3rd	4th	Mean	S.D.
Amount of permeation (μg)	498.174	459.632	497.756	459.846	478.852	22.071
Permeation rate	4.97%	4.59%	4.97%	4.59%	4.78%	0.22%
Amount of absorption (μg)	110.946	126.885	110.874	126.782	118.872	9.193
Absorption rate	1.11%	1.27%	1.11%	1.27%	1.19%	0.09%
Amount of recovery (μg)	10018.215	9665.278	9704.349	9719.302	9776.786	162.556
Recovery rate	106.10%	102.35%	102.96%	102.89%	103.57%	1.70%

15

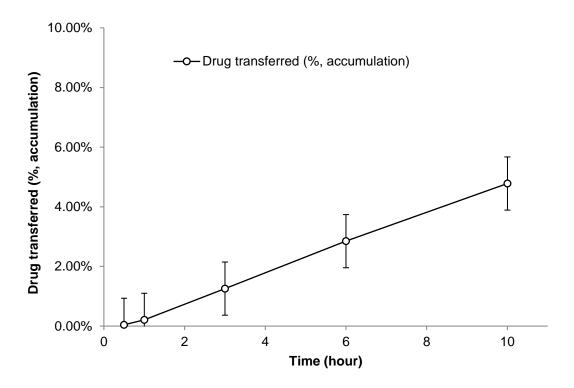


Fig 3. Results of transdermal permeability analysis of test group

D. Test results - Control group

This study was performed to examine the surface transdermal permeation pattern and the amount of skin absorption after applying 're:FACE' containing about 2% of niacinamide as a marker substance to human skin without 'MINI PIN' device treatment.

As a result, it was confirmed that the percutaneous permeation of the marker substance continued for 10 hours. After 10 hours, about 1.00% of the niacinamide contained in the 're:FACE' of this test permeated the skin and the remaining amount absorbed to the skin was found to be 0.96% of the dose. In addition, the marker substance absorbed by the skin, the instrument and the marker substance remaining on the surface of the skin were recovered and the recovery rate was confirmed to be 99.73%.

Table 7. Results of niacinamide transdermal test in control group

Time	Drug concentration in receptor (µg/ml)	Transferred drug in receptor (µg)	Net transferred drug (μg)	Drug transferred (%, accumulation)	Transdermal diffusion rate (µg/s)	Flux (μg/s·cm²)	Diffusion coefficient (cm²/s)
0.5	0.08	0.38	0.38	0.00%	2.138E-04	0.0003	1.084E-09
1	0.67	3.36	3.40	0.03%	1.674E-03	0.0026	8.488E-09
3	4.74	23.70	24.08	0.24%	2.872E-03	0.0045	1.456E-08
6	10.51	52.56	55.30	0.55%	2.891E-03	0.0045	1.466E-08
10	19.51	97.53	100.28	1.00%	3.024E-03	0.0047	1.533E-08

Table 8. Results of niacinamide transdermal test in control group

	1st	2nd	3rd	4th	Mean	S.D.
Amount of permeation (μg)	117.032	83.396	116.778	83.912	100.280	19.199
Permeation rate	1.17%	0.83%	1.17%	0.84%	1.00%	0.19%
Amount of absorption (μg)	106.264	85.853	106.073	85.907	96.024	11.714
Absorption rate	1.06%	0.86%	1.06%	0.86%	0.96%	0.12%
Amount of recovery (μg)	9692.171	9721.489	9703.576	10058.340	9793.894	176.710
Recovery rate	98.99%	98.74%	99.10%	102.11%	99.73%	1.59%

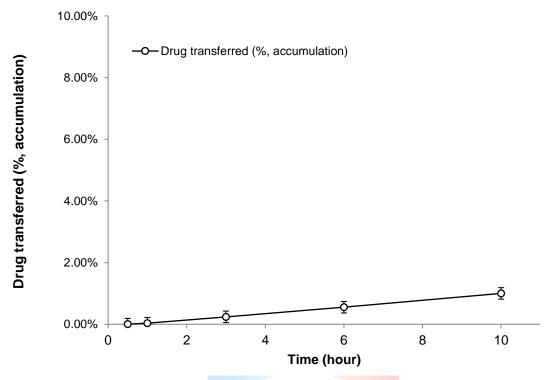


Fig 4. Results of transdermal permeability analysis of control group

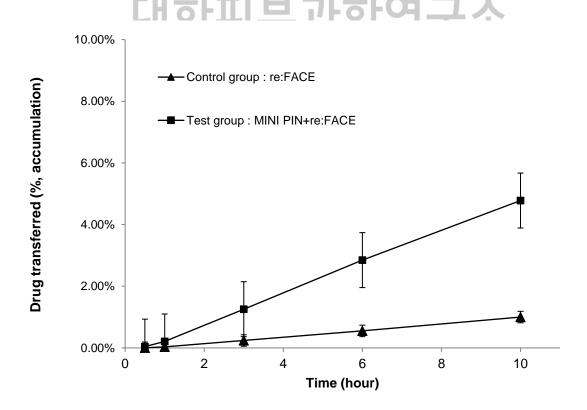


Fig 5. Comparison of transdermal permeability by group

8. Discussion and Conclusions

This test confirmed the effect of marker substance (niacinamide) on dermal absorption by using the "MINI PIN" device and 're:FACE(2% niacinamide)' provided by Woorhi Mechatronics Co., Ltd., using the in vitro skin absorption test method and M.H. Lee et al.

Results of this studies showed that with the test group(MINI PIN device + re:FACE 2% niacinamide), it was confirmed that the percutaneous permeation of the marker substance continued for 10 hours. After 10 hours, about 4.78% of the niacinamide contained in the 're:FACE' of this test permeated the skin and the remaining amount absorbed to the skin was found to be 1.19% of the dose. In addition, the marker substance absorbed by the skin, the instrument and the marker substance remaining on the surface of the skin were recovered and the recovery rate was confirmed to be 103.57%.

Results of this studies showed that with the control group(re:FACE 2% niacinamide), it was confirmed that the percutaneous permeation of the marker substance continued for 10 hours. After 10 hours, about 1.00% of the niacinamide contained in the 're:FACE' of this test permeated the skin and the remaining amount absorbed to the skin was found to be 0.96% of the dose. In addition, the marker substance absorbed by the skin, the instrument and the marker substance remaining on the surface of the skin were recovered and the recovery rate was confirmed to be 99.73%.

Overall, the skin treated with 'MINI PIN' device for 60 seconds showed a relatively high diffusion coefficient for the marker substance (niacinamide) in the range of 0.5 to 10 hours compared to the untreated control skin, and skin permeability was approximately 4.78-fold greater than the control, thus promoting dermal penetration.

9. References

- Diembeck W, Beck H, Benech-Kieffer F, Courtellemont P, Dupuis J, Lovell W, Paye M, Spengler J, Steiling W (1999). Test Guidelines for In Vitro Assessment of Dermal Absorption and Percutaneous Penetration of Cosmetic Ingredients. Fd Chem Tox, 37, 191-205.
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- 3) Jewell, C., Heylings JR., Clowes, HM. And Williams, FM. (2000). Percutaneous absorption and metabolism of dinitrochlorobenzene in vitro. Arch Toxicol, 74: 356-365.
- 4) J.M. Moolman (2010). Formulation, in vitro release and transdermal diffusion of azelaic acid with topical Niacinamide. North-West University, Master's thesis.
- 5) OECD (2004). Test Guideline 428: Skin absorption: in vitro Method. OECD, Paris.
- 6) OECD (2004). Test Guideline 427: Skin absorption: in vivo Method. OECD, Paris.
- 7) OECD (2004). Guidance Document for the Conduct of Skin Absorption Studies. OECD, Paris.
- 8) Yossi Tal, Ari Ayalon, Agnesa Sharaev, Zoya Kazir, Vera Brekhman, Tamar Lotan (2014). Continuous Drug Release by Sea Anemone Nematostella vectensis Stinging Microcapsules. Mar. Drugs, 12, 734-745.
- Guideline for in vitro Skin Absorption method. Korea Food & Drug Administration (2010. 2.
 18).

10. Testing Institution

10-1. Test Personnel

A. Researcher in Charge

Korea Dermatology Research Institute, Dermatology Specialist, Lee, Donghwan

B. Research Members

Korea Dermatology Research Institute, Li, Zhengri

10-2. Research List of Test Institute

- a. Evaluation and research on sun screen effect of cosmetic
- b. Evaluation and research on skin wrinkles improvement effect of cosmetic
- c. Evaluation and research on skin whitening effect of cosmetic
- d. Evaluation and research on safety of cosmetic
- e. Evaluation and research on other efficiencies of cosmetic
- f. Evaluation and research on percutaneous absorption of effective substance
- g. Sample analysis, effective substance extraction and research
- h. Development and research on vehicle formulation
- i. Development and research on other cosmetic related technologies

10-3. Equipment List of Test Institute

- a. Multiport solar simulator 601-150W
- b. Multiport solar simulator 601 V2.5 300W
- c. ERYTHEMA UV & UVA INTENSITY METER MODEL 3D-600 V2.0
- d. PMA2100 Data Logging Meter Package
- e. Biologically weighted UV sensor with LLG adaptor(SUV)
- f. Biologically weighted UV sensor with 8mm square adaptor for LLG with homogenizer
- g. UVA sensor with LLG adaptor
- h. UVA sensor with 8mm square adaptor for LLG with homogenizer
- i. The Mexameter® MX-18
- j. The Sebumeter® SM-815
- k. Visioscan® VC 98
- I. Sebufix® F 16 & Corneofix® F-20
- m. Skin-Visiometer® SV-600
- n. Corneometer® CM-825
- o. Cutometer® MPA-580
- p. Glossymeter® GL-200
- q. Tewameter® TM-300
- r. Ultrascan UC-22® cutis
- s. Chromameter CR-400®
- t. Vapometer®
- u. FLIR T-420
- v. ANTERA 3DTM
- w. Janus Facial Image Analysis System
- x. Polarized Dermoscopy Dermlite-II pro camera kit
- y. Digital Camera system DSLT, Macro Lens, Macro flash
- z. Constant Temperature and Humidity System
- aa. Electronic balance GF-4000, AF-220E
- bb. FDC-6 Diffusion Cell Drive Console
- cc. PCR-C1000
- dd. Clean bench
- ee. Chemi-doc

ff. SDS page electrophoresis

gg. Incubator

hh. Protein transfer

ii. D-code system

jj. Anareobic chamber

kk. Centrifuge

II. Polarized Micro-scope c image analyzer

mm. Skin-pH-meter® PH 905



11. RAW data

. KAW dat 현구 : MIN	VI PIN+리페이	 へ				
<u> </u>	1 1 1 1 1 1 1 1 1 1		ea		average	Stdev
0.5	14331	12766	13732	12752	13395	774
1	60511	48659	60017	48573	54440	6728
3	341981	286156	341600	286661	314100	31976
6	718869	651297	718181	652114	685115	38581
10	1218833	1128501	1217925	1129002	1173565	51748
Skin	282609	322828	282429	322570	302609	23198
회수량	5	5	5	5		
세척액	2530592	2441534	2451393	2455166	2469671	41018
세척액량	50	50	50	50		
	1		eceptor samp		average	Stdev
0.5	0.925	0.801	0.878	0.800	0.851	0.061
1	4.586	3.646	4.547	3.639	4.104	0.533
3	26.895	22.470	26.865	22.510	24.685	2.534
6	56.767	51.411	56.713	51.476	54.092	3.058
10	96.394	89.235	96.322	89.274	92.806	4.102
	<u> </u>		in receptor (average	Stdev
0.5	4.627	4.007	4.390	4.001	4.256	
1	\$	18.231	§			0.307
3	22.928		22.733	18.197	20.522 123.426	2.666
	134.475	112.351	134.324	112.552	-	12.672
6	283.836	257.057	283.563	257.381	270.459	15.290
10	481.971	446.173	481.612	446.371	464.032	20.508
Skin			ed drug (μg)		average	Stdev
0.5	4.627	4.007	4.390	4.001	4.256	0.307
1	23.391	18.632	23.172	18.598	20.948	2.696
3	137.231	114.575	137.036	114.772	125.903	12.968
6	300.039	270.516	299.708	270.856	285.279	16.852
10	498.174	459.632	497.756	459.846	478.852	22.071
	Drug	transferred	(%, accumulat	ion)	average	Stdev
0.5	0.046%	0.040%	0.044%	0.040%	0.042%	0.0039
1	0.234%	0.186%	0.231%	0.186%	0.209%	0.0279
3	1.370%	1.144%	1.368%	1.146%	1.257%	0.1299
6	2.995%	2.701%	2.992%	2.704%	2.848%	0.1689
10	4.973%	4.589%		4.591%	4.781%	0.2209
	Trai	nsdermal diff	usion rate (μο	g/s)	average	Stdev
0.5	2.571E-03	2.226E-03	2.439E-03	2.223E-03	2.365E-03	1.705E-0
1	1.042E-02	8.125E-03	1.043E-02	8.109E-03	9.273E-03	1.335E-0
3	1.581E-02	1.333E-02	1.581E-02	1.336E-02	1.458E-02	1.427E-0
6	1.507E-02	1.444E-02	1.506E-02	1.445E-02	1.476E-02	3.597E-0
10	1.432E-02	1.369E-02	1.431E-02	1.369E-02	1.401E-02	3.612E-0
		Flux (μ			average	Stdev
0.5	4.017E-03	3.478E-03		3.474E-03	3.695E-03	2.664E-0
1	1.629E-02	1.270E-02	1.630E-02	1.267E-02	1.449E-02	2.086E-0
3	2.470E-02	2.082E-02	2.471E-02	2.087E-02	2.278E-02	2.229E-0
6	2.355E-02	2.256E-02	2.353E-02	2.258E-02	2.306E-02	5.621E-0
10	2.238E-02	2.139E-02	2.237E-02		2.188E-02	5.644E-0
			ficient (cm²/s			
0 F	t	1.215E-08	1.331E-08		average	Stdev
0.5	1.403E-08		(1.291E-08	9.308E-1
1	5.691E-08	4.436E-08	5.697E-08	4.427E-08	5.063E-08	7.289E-0
3	8.632E-08	7.275E-08	8.634E-08	7.293E-08	7.959E-08	7.790E-0
6	8.230E-08	7.883E-08	8.223E-08	7.890E-08	8.057E-08	1.964E-0
10	7.820E-08	7.476E-08	7.815E-08	7.476E-08	7.647E-08	1.972E-0
Skin 두께	Donor 농도	Skin 면적	Receptor 용량	Donor 투입량	시료채취량	
0.07	20034	0.64	5	10017	0.5	
구 분	1차	2차	3차	4차	평균	표준편차
투과량	498.174	459.632	497.756	459.846	478.852	22.071
	4.97%	4.59%	4.97%	4.59%	4.78%	0.229
투과율						
	110.946	126.885	110.874	126.782	118.872	9.193
투과율			110.874 1.11%	126.782 1.27%	118.872 1.19%	
투과율 [부흡수량	110.946	126.885				9.193 0.099 162.556

24

조군 : 리퍼	11 41					
		ar	ea		average	Stdev
0.5	4117	3208	4194	2985	3626	619
1	13615	8712	13682	8526	11134	2905
3	78999	45509	79066	46304	62470	19128
6	174108	95922	173698	97386	135279	44604
10	289090	208146	288429	209409	248769	46181
Skin	270796	219291	270314	219427	244957	29559
회수량	5	5	5	5		
세척액	2448320	2455718	2451198	2540717	2473988	44590
게 ㅋ ㅋ 네척액량	50	50	50	50	2473300	77330
"778	LL.		in receptor (L	0)/050000	Stdev
				·	average	0.049
0.5	0.116	0.044	0.122	0.026	0.077	
1	0.869	0.480	0.874	0.465	0.672	0.23
3	6.051	3.397	6.056	3.460	4.741	1.51
6	13.589	7.392	13.557	7.508	10.512	3.53
10	22.703	16.287	22.650	16.387	19.507	3.66
	Trar		in receptor (,	average	Stdev
0.5	0.579	0.219	0.610	0.131	0.385	0.24
1	4.343	2.400	4.370	2.327	3.360	1.15
3	30.255	16.983	30.282	17.298	23.705	7.58
6	67.947	36.962	67.784	37.542	52.559	17.67
10	113.514	81.436	113.252	81.937	97.535	18.30
Skin	ļ		ed drug (μg)		average	Stdev
0.5	0.579	0.219	0.610	0.131	0.385	0.24
1	4.401	2.422	4.431	2.340	3.399	1.17
3	30.747	17.245		17.544		7.72
	<u> </u>		30.780		24.079	
6	71.465	38.922	71.311	39.518	55.304	18.57
10	117.032	83.396	116.778	83.912	100.280	19.19
			(%, accumulat		average	Stdev
0.5	0.006%	0.002%	0.006%	0.001%	0.004%	0.002
1	0.044%	0.024%	0.044%	0.023%	0.034%	0.012
3	0.307%	0.172%	0.307%	0.175%	0.240%	0.077
6	0.713%	0.389%	0.712%	0.395%	0.552%	0.185
10	1.168%	0.833%	1.166%	0.838%	1.001%	0.192
	Trar	sdermal diff	usion rate (μο	g/s)	average	Stdev
0.5	3.219E-04	1.218E-04	3.389E-04	7.268E-05	2.138E-04	1.363E-0
1	2.123E-03	1.224E-03	2.123E-03	1.227E-03	1.674E-03	5.182E-0
3	3.659E-03	2.059E-03	3.660E-03	2.112E-03	2.872E-03	9.091E-0
6	3.770E-03	2.007E-03	3.753E-03		2.891E-03	
	3.770E-03	ノ いいノトーいう	: ろノラストーロス:	2.U35E-U36		
10	2 42 45 02		9			
	3.424E-03	2.625E-03	3.413E-03	2.634E-03	3.024E-03	4.555E-0
		2.625E-03 Flux (μ	3.413E-03 g/s·cm²)	2.634E-03	3.024E-03 average	4.555E-0 Stdev
0.5	5.030E-04	2.625E-03 Flux (μ 1.903E-04	3.413E-03 g/s·cm²) 5.295E-04	2.634E-03 1.136E-04	3.024E-03 average 3.341E-04	4.555E-0 Stdev 2.129E-0
1	5.030E-04 3.318E-03	2.625E-03 Flux (µ; 1.903E-04 1.912E-03	3.413E-03 g/s·cm²) 5.295E-04 3.317E-03	2.634E-03 1.136E-04 1.918E-03	3.024E-03 average 3.341E-04 2.616E-03	4.555E-0 Stdev 2.129E-0 8.096E-0
	5.030E-04	2.625E-03 Flux (μ 1.903E-04	3.413E-03 g/s·cm²) 5.295E-04	2.634E-03 1.136E-04	3.024E-03 average 3.341E-04	4.555E-0 Stdev 2.129E-0 8.096E-0
1	5.030E-04 3.318E-03	2.625E-03 Flux (µ; 1.903E-04 1.912E-03	3.413E-03 g/s·cm²) 5.295E-04 3.317E-03	2.634E-03 1.136E-04 1.918E-03	3.024E-03 average 3.341E-04 2.616E-03	4.555E-0 Stdev 2.129E-0 8.096E-0 1.420E-0
1 3	5.030E-04 3.318E-03 5.717E-03	2.625E-03 Flux (µq 1.903E-04 1.912E-03 3.217E-03	3.413E-03 g/s-cm²) 5.295E-04 3.317E-03 5.718E-03	2.634E-03 1.136E-04 1.918E-03 3.299E-03 3.179E-03	3.024E-03 average 3.341E-04 2.616E-03 4.488E-03	4.555E-(Stdev 2.129E-(8.096E-(1.420E-(1.570E-(
1 3 6	5.030E-04 3.318E-03 5.717E-03 5.891E-03 5.350E-03	2.625E-03 Flux (µq 1.903E-04 1.912E-03 3.217E-03 3.136E-03 4.102E-03	3.413E-03 g/s-cm²) 5.295E-04 3.317E-03 5.718E-03 5.864E-03	2.634E-03 1.136E-04 1.918E-03 3.299E-03 3.179E-03 4.115E-03	3.024E-03 average 3.341E-04 2.616E-03 4.488E-03 4.517E-03 4.725E-03	4.555E-(Stdev 2.129E-(8.096E-(1.420E-(1.570E-(
1 3 6	5.030E-04 3.318E-03 5.717E-03 5.891E-03 5.350E-03	2.625E-03 Flux (µq 1.903E-04 1.912E-03 3.217E-03 3.136E-03 4.102E-03 iffusion coef	3.413E-03 g/s-cm²) 5.295E-04 3.317E-03 5.718E-03 5.864E-03 5.332E-03 ficient (cm²/s	2.634E-03 1.136E-04 1.918E-03 3.299E-03 3.179E-03 4.115E-03	3.024E-03 average 3.341E-04 2.616E-03 4.488E-03 4.517E-03 4.725E-03 average	4.555E-(Stdev 2.129E-(8.096E-(1.420E-(1.570E-(7.118E-(Stdev
1 3 6 10	5.030E-04 3.318E-03 5.717E-03 5.891E-03 5.350E-03 D 1.632E-09	2.625E-03 Flux (µq 1.903E-04 1.912E-03 3.217E-03 3.136E-03 4.102E-03 iffusion coef 6.174E-10	3.413E-03 g/s-cm²) 5.295E-04 3.317E-03 5.718E-03 5.864E-03 5.332E-03 ficient (cm²/s	2.634E-03 1.136E-04 1.918E-03 3.299E-03 3.179E-03 4.115E-03) 3.685E-10	3.024E-03 average 3.341E-04 2.616E-03 4.488E-03 4.517E-03 4.725E-03 average 1.084E-09	4.555E-(Stdev 2.129E-(8.096E-(1.420E-(1.570E-(7.118E-(Stdev 6.909E-1
1 3 6 10 0.5	5.030E-04 3.318E-03 5.717E-03 5.891E-03 5.350E-03 D 1.632E-09 1.076E-08	2.625E-03 Flux (µq 1.903E-04 1.912E-03 3.217E-03 3.136E-03 4.102E-03 iffusion coef 6.174E-10 6.205E-09	3.413E-03 g/s·cm²) 5.295E-04 3.317E-03 5.718E-03 5.864E-03 5.332E-03 ficient (cm²/s 1.718E-09 1.076E-08	2.634E-03 1.136E-04 1.918E-03 3.299E-03 3.179E-03 4.115E-03) 3.685E-10 6.222E-09	3.024E-03 average 3.341E-04 2.616E-03 4.488E-03 4.517E-03 4.725E-03 average 1.084E-09 8.488E-09	4.555E-(Stdev 2.129E-(8.096E-(1.420E-(1.570E-(7.118E-(Stdev 6.909E-1 2.627E-(
1 3 6 10 0.5 1 3	5.030E-04 3.318E-03 5.717E-03 5.891E-03 5.350E-03 0 1.632E-09 1.076E-08 1.855E-08	2.625E-03 Flux (µq 1.903E-04 1.912E-03 3.217E-03 3.136E-03 4.102E-03 iffusion coef 6.174E-10 6.205E-09 1.044E-08	3.413E-03 g/s·cm²) 5.295E-04 3.317E-03 5.718E-03 5.864E-03 5.332E-03 ficient (cm²/s 1.718E-09 1.076E-08 1.855E-08	2.634E-03 1.136E-04 1.918E-03 3.299E-03 3.179E-03 4.115E-03) 3.685E-10 6.222E-09 1.071E-08	3.024E-03 average 3.341E-04 2.616E-03 4.488E-03 4.517E-03 4.725E-03 average 1.084E-09 8.488E-09 1.456E-08	4.555E-0 Stdev 2.129E-0 8.096E-0 1.420E-0 1.570E-0 7.118E-0 Stdev 6.909E-1 2.627E-0 4.609E-0
1 3 6 10 0.5 1 3 6	5.030E-04 3.318E-03 5.717E-03 5.891E-03 5.350E-03 1.632E-09 1.076E-08 1.855E-08 1.911E-08	2.625E-03 Flux (µq 1.903E-04 1.912E-03 3.217E-03 3.136E-03 4.102E-03 iffusion coef 6.174E-10 6.205E-09 1.044E-08 1.018E-08	3.413E-03 g/s-cm²) 5.295E-04 3.317E-03 5.718E-03 5.864E-03 5.332E-03 ficient (cm²/s 1.718E-09 1.076E-08 1.855E-08 1.903E-08	2.634E-03 1.136E-04 1.918E-03 3.299E-03 3.179E-03 4.115E-03) 3.685E-10 6.222E-09 1.071E-08 1.031E-08	3.024E-03 average 3.341E-04 2.616E-03 4.488E-03 4.517E-03 4.725E-03 average 1.084E-09 8.488E-09 1.456E-08 1.466E-08	4.555E-C Stdev 2.129E-C 8.096E-C 1.420E-C 7.118E-C Stdev 6.909E-1 2.627E-C 4.609E-C 5.095E-C
1 3 6 10 0.5 1 3 6	5.030E-04 3.318E-03 5.717E-03 5.891E-03 5.350E-03 1.632E-09 1.076E-08 1.855E-08 1.911E-08 1.736E-08	2.625E-03 Flux (µq 1.903E-04 1.912E-03 3.217E-03 3.136E-03 4.102E-03 iffusion coef 6.174E-10 6.205E-09 1.044E-08 1.018E-08 1.331E-08	3.413E-03 g/s-cm²) 5.295E-04 3.317E-03 5.718E-03 5.864E-03 5.332E-03 ficient (cm²/s 1.718E-09 1.076E-08 1.855E-08 1.903E-08 1.730E-08	2.634E-03 1.136E-04 1.918E-03 3.299E-03 3.179E-03 4.115E-03) 3.685E-10 6.222E-09 1.071E-08 1.031E-08 1.335E-08	3.024E-03 average 3.341E-04 2.616E-03 4.488E-03 4.517E-03 4.725E-03 average 1.084E-09 8.488E-09 1.456E-08 1.466E-08 1.533E-08	4.555E-C Stdev 2.129E-C 8.096E-C 1.420E-C 7.118E-C Stdev 6.909E-C 4.609E-C 5.095E-C
1 3 6 10 0.5 1 3 6 10 Skin 두께	5.030E-04 3.318E-03 5.717E-03 5.891E-03 5.350E-03 1.632E-09 1.076E-08 1.855E-08 1.911E-08 1.736E-08 Donor 등도	2.625E-03 Flux (μ 1.903E-04 1.912E-03 3.217E-03 3.136E-03 4.102E-03 iffusion coef 6.174E-10 6.205E-09 1.044E-08 1.018E-08 1.331E-08 Skin 면적	3.413E-03 g/s-cm²) 5.295E-04 3.317E-03 5.718E-03 5.864E-03 5.332E-03 ficient (cm²/s 1.718E-09 1.076E-08 1.855E-08 1.903E-08 1.730E-08 Receptor 용량	2.634E-03 1.136E-04 1.918E-03 3.299E-03 3.179E-03 4.115E-03) 3.685E-10 6.222E-09 1.071E-08 1.031E-08 1.335E-08 Donor 투입량	3.024E-03 average 3.341E-04 2.616E-03 4.488E-03 4.517E-03 4.725E-03 average 1.084E-09 8.488E-09 1.456E-08 1.466E-08 1.533E-08 시료채취량	4.555E-C Stdev 2.129E-C 8.096E-C 1.420E-C 7.118E-C Stdev 6.909E-1 2.627E-C 4.609E-C 5.095E-C
1 3 6 10 0.5 1 3 6	5.030E-04 3.318E-03 5.717E-03 5.891E-03 5.350E-03 1.632E-09 1.076E-08 1.855E-08 1.911E-08 1.736E-08	2.625E-03 Flux (µq 1.903E-04 1.912E-03 3.217E-03 3.136E-03 4.102E-03 iffusion coef 6.174E-10 6.205E-09 1.044E-08 1.018E-08 1.331E-08	3.413E-03 g/s-cm²) 5.295E-04 3.317E-03 5.718E-03 5.864E-03 5.332E-03 ficient (cm²/s 1.718E-09 1.076E-08 1.855E-08 1.903E-08 1.730E-08	2.634E-03 1.136E-04 1.918E-03 3.299E-03 3.179E-03 4.115E-03) 3.685E-10 6.222E-09 1.071E-08 1.031E-08 1.335E-08	3.024E-03 average 3.341E-04 2.616E-03 4.488E-03 4.517E-03 4.725E-03 average 1.084E-09 8.488E-09 1.456E-08 1.466E-08 1.533E-08	4.555E-C Stdev 2.129E-C 8.096E-C 1.420E-C 7.118E-C Stdev 6.909E-1 2.627E-C 4.609E-C 5.095E-C
1 3 6 10 0.5 1 3 6 10 Skin 두께	5.030E-04 3.318E-03 5.717E-03 5.891E-03 5.350E-03 1.632E-09 1.076E-08 1.855E-08 1.911E-08 1.736E-08 Donor 答도 20034	2.625E-03 Flux (μ 1.903E-04 1.912E-03 3.217E-03 3.136E-03 4.102E-03 iffusion coef 6.174E-10 6.205E-09 1.044E-08 1.018E-08 1.331E-08 Skin 면적 0.64	3.413E-03 g/s·cm²) 5.295E-04 3.317E-03 5.718E-03 5.864E-03 5.332E-03 ficient (cm²/s 1.718E-09 1.076E-08 1.855E-08 1.903E-08 1.730E-08 Receptor 용량	2.634E-03 1.136E-04 1.918E-03 3.299E-03 3.179E-03 4.115E-03) 3.685E-10 6.222E-09 1.071E-08 1.031E-08 1.335E-08 Donor 투입량 10017	3.024E-03 average 3.341E-04 2.616E-03 4.488E-03 4.517E-03 4.725E-03 average 1.084E-09 8.488E-09 1.456E-08 1.533E-08 시료채취량 0.5	4.555E-6 Stdev 2.129E-6 8.096E-6 1.420E-6 7.118E-6 Stdev 6.909E-7 2.627E-6 4.609E-6 2.309E-6
1 3 6 10 0.5 1 3 6 10 kin 두께 0.065	5.030E-04 3.318E-03 5.717E-03 5.891E-03 5.350E-03 1.632E-09 1.076E-08 1.855E-08 1.911E-08 1.736E-08 Donor 등도 20034	2.625E-03 Flux (μ 1.903E-04 1.912E-03 3.217E-03 3.136E-03 4.102E-03 iffusion coef 6.174E-10 6.205E-09 1.044E-08 1.018E-08 1.331E-08 Skin 면적 0.64	3.413E-03 g/s-cm²) 5.295E-04 3.317E-03 5.718E-03 5.864E-03 5.332E-03 ficient (cm²/s 1.718E-09 1.076E-08 1.855E-08 1.903E-08 1.730E-08 Receptor 용량	1.136E-04 1.918E-03 3.299E-03 3.179E-03 4.115E-03) 3.685E-10 6.222E-09 1.071E-08 1.031E-08 1.335E-08 Donor 투입량 10017	3.024E-03 average 3.341E-04 2.616E-03 4.488E-03 4.517E-03 4.725E-03 average 1.084E-09 8.488E-09 1.456E-08 1.466E-08 1.533E-08 시료채취량	4.555E-6 Stdev 2.129E-6 8.096E-6 1.420E-6 7.118E-6 Stdev 6.909E-7 2.627E-6 4.609E-6 2.309E-6
1 3 6 10 0.5 1 3 6 10 Skin 두께	5.030E-04 3.318E-03 5.717E-03 5.891E-03 5.350E-03 1.632E-09 1.076E-08 1.855E-08 1.911E-08 1.736E-08 Donor 答도 20034	2.625E-03 Flux (μ 1.903E-04 1.912E-03 3.217E-03 3.136E-03 4.102E-03 iffusion coef 6.174E-10 6.205E-09 1.044E-08 1.018E-08 1.331E-08 Skin 면적 0.64	3.413E-03 g/s·cm²) 5.295E-04 3.317E-03 5.718E-03 5.864E-03 5.332E-03 ficient (cm²/s 1.718E-09 1.076E-08 1.855E-08 1.903E-08 1.730E-08 Receptor 용량	2.634E-03 1.136E-04 1.918E-03 3.299E-03 3.179E-03 4.115E-03) 3.685E-10 6.222E-09 1.071E-08 1.031E-08 1.335E-08 Donor 투입량 10017	3.024E-03 average 3.341E-04 2.616E-03 4.488E-03 4.517E-03 4.725E-03 average 1.084E-09 8.488E-09 1.456E-08 1.466E-08 1.533E-08 시료채취량 0.5	4.555E-C Stdev 2.129E-C 8.096E-C 1.420E-C 1.570E-C 7.118E-C Stdev 6.909E-1 2.627E-C 4.609E-C 2.309E-C
1 3 6 10 0.5 1 3 6 10 kin 두께 0.065	5.030E-04 3.318E-03 5.717E-03 5.891E-03 5.350E-03 1.632E-09 1.076E-08 1.855E-08 1.911E-08 1.736E-08 Donor 등도 20034	2.625E-03 Flux (μ 1.903E-04 1.912E-03 3.217E-03 3.136E-03 4.102E-03 iffusion coef 6.174E-10 6.205E-09 1.044E-08 1.018E-08 1.331E-08 Skin 면적 0.64	3,413E-03 g/s-cm²) 5.295E-04 3.317E-03 5.718E-03 5.864E-03 5.332E-03 ficient (cm²/s 1.718E-09 1.076E-08 1.855E-08 1.903E-08 1.730E-08 Receptor 용량 5	1.136E-04 1.918E-03 3.299E-03 3.179E-03 4.115E-03) 3.685E-10 6.222E-09 1.071E-08 1.031E-08 1.335E-08 Donor 투입량 10017	3.024E-03 average 3.341E-04 2.616E-03 4.488E-03 4.517E-03 4.725E-03 average 1.084E-09 8.488E-09 1.456E-08 1.533E-08 시료채취량 0.5	4.555E-C Stdev 2.129E-C 8.096E-C 1.420E-C 7.118E-C Stdev 6.909E-C 4.609E-C 2.309E-C 2.309E-C
1 3 6 10 0.5 1 3 6 10 Skin 두께 0.065 구 분 투과량	5.030E-04 3.318E-03 5.717E-03 5.891E-03 5.350E-03 1.632E-09 1.076E-08 1.855E-08 1.911E-08 1.736E-08 Donor 答도 20034	2.625E-03 Flux (μ 1.903E-04 1.912E-03 3.217E-03 3.136E-03 4.102E-03 iffusion coef 6.174E-10 6.205E-09 1.044E-08 1.018E-08 1.331E-08 Skin 면적 0.64 2차 83.396	3.413E-03 g/s·cm²) 5.295E-04 3.317E-03 5.718E-03 5.864E-03 5.332E-03 ficient (cm²/s 1.718E-09 1.076E-08 1.855E-08 1.903E-08 1.730E-08 Receptor 용량 5	2.634E-03 1.136E-04 1.918E-03 3.299E-03 3.179E-03 4.115E-03) 3.685E-10 6.222E-09 1.071E-08 1.031E-08 1.335E-08 Donor 투입량 10017	3.024E-03 average 3.341E-04 2.616E-03 4.488E-03 4.517E-03 4.725E-03 average 1.084E-09 8.488E-09 1.456E-08 1.533E-08 시료채취량 0.5	4.555E-0 Stdev 2.129E-0 8.096E-0 1.420E-0 1.570E-0 7.118E-0 Stdev 6.909E-1 2.627E-0 4.609E-0 2.309E-0 エを型
1 3 6 10 0.5 1 3 6 10 Skin 두께 0.065 구 분 투과량	5.030E-04 3.318E-03 5.717E-03 5.891E-03 5.350E-03 1.632E-09 1.076E-08 1.855E-08 1.911E-08 1.736E-08 Donor 法도 20034 1차 117.032 1.17%	2.625E-03 Flux (μ 1.903E-04 1.912E-03 3.217E-03 3.136E-03 4.102E-03 iffusion coef 6.174E-10 6.205E-09 1.044E-08 1.018E-08 1.331E-08 Skin 면적 0.64 2차 83.396 0.83%	3.413E-03 g/s·cm²) 5.295E-04 3.317E-03 5.718E-03 5.864E-03 5.332E-03 ficient (cm²/s 1.718E-09 1.076E-08 1.855E-08 1.903E-08 1.730E-08 Receptor 용량 5	2.634E-03 1.136E-04 1.918E-03 3.299E-03 3.179E-03 4.115E-03) 3.685E-10 6.222E-09 1.071E-08 1.031E-08 1.335E-08 Donor 투입량 10017 4차 83.912 0.84%	3.024E-03 average 3.341E-04 2.616E-03 4.488E-03 4.517E-03 4.725E-03 average 1.084E-09 8.488E-09 1.456E-08 1.466E-08 1.533E-08 시료채취량 0.5	4.555E-0 Stdev 2.129E-0 8.096E-0 1.420E-0 1.570E-0 7.118E-0 Stdev 6.909E-1 2.627E-0 4.609E-0 2.309E-0
1 3 6 10 0.5 1 3 6 10 Skin 두께 0.065 구 분 투과량 투과율 부흡수량	5.030E-04 3.318E-03 5.717E-03 5.891E-03 5.350E-03 1.632E-09 1.076E-08 1.855E-08 1.911E-08 1.736E-08 Donor 法도 20034 1차 117.032 1.17% 106.264	2.625E-03 Flux (μ 1.903E-04 1.912E-03 3.217E-03 3.136E-03 4.102E-03 iffusion coef 6.174E-10 6.205E-09 1.044E-08 1.018E-08 1.331E-08 Skin 면적 0.64 2차 83.396 0.83% 85.853	3.413E-03 g/s·cm²) 5.295E-04 3.317E-03 5.718E-03 5.864E-03 5.332E-03 ficient (cm²/s 1.718E-09 1.076E-08 1.855E-08 1.903E-08 1.730E-08 Receptor 용량 5 3차 116.778 1.17% 106.073	2.634E-03 1.136E-04 1.918E-03 3.299E-03 3.179E-03 4.115E-03) 3.685E-10 6.222E-09 1.071E-08 1.031E-08 1.335E-08 Donor 투입량 10017 4차 83.912 0.84% 85.907	3.024E-03 average 3.341E-04 2.616E-03 4.488E-03 4.517E-03 4.725E-03 average 1.084E-09 8.488E-09 1.456E-08 1.466E-08 1.533E-08 ALE MAPE 0.5 BE 100.280 1.00% 96.024	2.129E-0 8.096E-0 1.420E-0 1.570E-0 7.118E-0

25