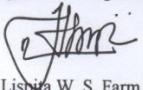
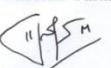


## LAMPIRAN

### Lampiran 1. Surat keterangan kesehatan hewan dan pengiriman ternak

 DARMA MITRA BAYA PRAJA	<p style="text-align: center;"><b>PEMERINTAH KABUPATEN SEMARANG</b>  <b>DINAS PERTANIAN, PERIKANAN DAN PANGAN</b>          Jl. Letjend Suprapto No. 9 B Telp (024) 6921811 Fax (024) 6924728          email: distanringan@gmail.com          UNGARAN - 50514</p> <hr/> <p style="text-align: center;"><b>SURAT KETERANGAN KESEHATAN HEWAN DAN PENGIRIMAN TERNAK</b></p> <hr/> <p style="text-align: center;">NOMOR : 524.3/ 2347 /2017          Nomor iSIKHNAS : 793257</p> <p>Yang bertanda tangan di bawah ini Kepala Bidang Kesehatan Hewan dan Kesehatan Masyarakat Veteriner Dinas Pertanian, Perikanan dan Pangan Kabupaten Semarang, menerangkan bahwa ternak yang akan di kirim dari Kabupaten Semarang ke Kota Semarang dengan perincian sebagai berikut:</p> <table border="1" style="width: 100%; border-collapse: collapse; text-align: center;"> <thead> <tr> <th>No</th> <th>Jenis Hewan</th> <th>Jenis Kelamin</th> <th>Umur</th> <th>Jumlah</th> <th>Vaksinasi</th> </tr> </thead> <tbody> <tr> <td>1.</td> <td>Tikus Putih (Rat) Galur Wistar</td> <td>Jantan</td> <td>2,5 bln</td> <td>35 ekor</td> <td></td> </tr> <tr> <td></td> <td></td> <td></td> <td></td> <td><b>Jumlah:</b></td> <td><b>35 ekor</b></td> </tr> </tbody> </table> <p>Nama Pengirim : NOVI MILASARI (ID.3374026610850003 Hp. 081357619689)          Alamat : Jombor RT.01/07 Desa Jetis Kec. Bandungan Kabupaten Semarang          Nama Penerima : DEWIN MARASMITA          Alamat : Kampus Wahid Hasyim Jl. Menoreh Tengah X/22 Sampangan Kec. Gajah Mungkur Kota Semarang Provinsi Jawa Tengah          Cara Pengiriman : Transportasi Darat</p> <p>Bawa lokasi asal ternak sampai saat ini tidak ada masalah lingkungan dan tidak sedang terjadi wabah penyakit hewan menular (PHM), pemilik ternak telah melakukan upaya-upaya pencegahan/pengendalian penyakit hewan menular seperti biosecurity/desinfeksi dll dan berdasarkan pemeriksaan fisik serta pemantauan dilapangan oleh Dokter Hewan Berwenang/Petugas di bawah penelia Dokter Hewan Berwenang, maka secara teknis dapat di simpulkan/dinyatakan bahwa ternak yang akan di kirim tidak menunjukkan gejala sakit dan dinyatakan sehat sehingga diijinkan untuk dikirim</p> <p style="text-align: right;">Ungaran, 21 Agustus 2017</p> <p style="text-align: right;">Kepala Dinas Pertanian,Perikanan dan Pangan Kabupaten Semarang Kepala Bidang Keswan dan Kesmat</p> <div style="text-align: center;">  <p style="font-size: small; margin-top: -10px;">PEMERINTAH KABUPATEN SEMARANG          DINAS PERTANIAN, PERIKANAN DAN PANGAN          BANTARAGUNG          NIP. 19600721/92032003          SEMARANG</p> </div>	No	Jenis Hewan	Jenis Kelamin	Umur	Jumlah	Vaksinasi	1.	Tikus Putih (Rat) Galur Wistar	Jantan	2,5 bln	35 ekor						<b>Jumlah:</b>	<b>35 ekor</b>
No	Jenis Hewan	Jenis Kelamin	Umur	Jumlah	Vaksinasi														
1.	Tikus Putih (Rat) Galur Wistar	Jantan	2,5 bln	35 ekor															
				<b>Jumlah:</b>	<b>35 ekor</b>														

**Lampiran 2.** Surat keterangan telah melakukan penelitian di Laboratorium Farmakologi dan Farmasi Klinik Fakultas Farmasi Universitas Wahid Hasyim Semarang

<b>REKAPITULASI PENGGUNAAN ALAT, BAHAN SERTA SEWA LABORATORIUM LAB. FARMAKOLOGI &amp; FARMASI KLINIK FAKULTAS FARMASI UNIVERSITAS WAHID HASYIM SEMARANG</b>		
<b>I. PENGGUNA</b>		
Nama	Fitria Dwi K (135010955) Ulfa Risalatul N (135010960) Dewin Marasmita (135010958) Yusrina Ulya (135010958)	
<b>II. PERINCIAN BIAYA</b>		
A. Penggunaan bahan		
B. Penggunaan alat		
1. HPLC	:.....jam x Rp. 150.000,- = Rp.	
2. Spektrofotometer UV/ Vis	:.... jam x Rp. 75.000,- = Rp.	
3. Disolution Tester	:..... x Rp. 25.000,- = Rp.	
4. CODA	:..... xRp. 25.000,- = Rp.	
C. Sewa Laboratorium		
1. Mahasiswa Fak. Farmasi UNWAHAS	:4 mhs w selama 6 bulan = Rp.	<b>900.000</b>
2. Mahasiswa atau Institusi di luar UNWAHAS	: ... bln x Rp. 250.000,- = Rp.	
<b>TOTAL BIAYA</b>		<b>900.000</b>
Semarang, 17 Februari 2017		
Mengetahui, Ka Bag. Farmakologi dan Farmasi Klinik	Yang Menerima, Laboran Farmakologi	
		
Ririn Lispita W, S. Farm., M.Si.Med., Apt	Dwi Meilani, A.Md	

**Lampiran 3.** Surat keterangan telah melakukan penelitian di Laboratorium

Farmasetika Fakultas Farmasi Universitas Wahid Hasyim Semarang



**UNIVERSITAS WAHID HASYIM  
FAKULTAS FARMASI  
BAGIAN FARMASETIKA**

Jl. Menoreh Tengah X / 22 Sampangan – Semarang 50236 Telp. (024) 8505680 – 8505681 fax. (024) 8505680

**SURAT KETERANGAN**  
No. 016/Lab. Farmasetika/C.05/UWH/III/2017

Assalamu'alaikum Wr. Wb.

Yang bertanda tangan dibawah ini, Kepala Bagian Farmasi Fisika & Farmasetika Fakultas Farmasi Universitas Wahid Hasyim Semarang menerangkan bahwa :

Nama	:	Dewin Marasmita
NIM	:	135010958
Fakultas	:	Farmasi

Telah melakukan formulasi di Laboratorium Farmasetika dalam rangka penelitian dengan judul :

“Efektivitas Antihipertensi Film Transdermal Diltiazem HCl dengan Peningkat Penetrasi Isopropil Miristat pada Tikus Jantan Galur Wistar.”

Demikian surat keterangan ini dibuat untuk dipergunakan semestinya.

Wassalamu'alaikum Wr. Wb.

Semarang, Maret 2017



**Lampiran 4. Sertifikat analisis diltiazem HCl**



Shijiazhuang Aopharm Medical Technology Co., Ltd.

TEL: 86-311-66600578  
FAX: 86-311-66600576

### Certificate of Analysis

Product	Diltiazem hydrochloride		
CAS	33286-22-5	Batch No.	20141107
Mfg. Date	2014-11-06	Quantity	25KG
Item	Specification		Results
Apperance	White Crystalline powder		Comforms
Identification (by HPLC)	Corresponds to the requirement of the reference standard		Conforms
Specific optical rotation	+110°-+116°		+115°
Assay (on dried)	98.5%-101.5%		99.6%
Melting range	210°C-215°C		213.0°C-213.6°C
Loss on drying	$\leq 0.5\%$		0.28%
Residue on ignition	$\leq 0.1\%$		0.04%
PH	4.3-5.3		5.0
Heavy metals	$\leq 20\text{ppm}$		Conforms
Related substances	Single impurity $\leq 0.5\%$		0.32%
	Total impurity $\leq 1.0\%$		0.56%
Conclusion	It conforms with the standard USP 32		

Check:Song Yun

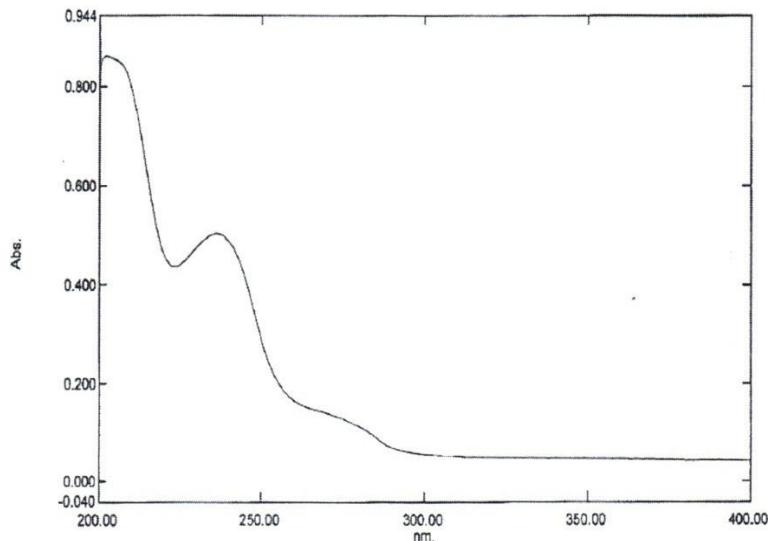
Inspector: Han Fei

**Lampiran 5.** Data panjang gelombang maksimal diltiazem HCl

## Spectrum Peak Pick Report

04/23/2015 12:44:30 PM

Data Set File\_130115\_155953\_123846 - RawData



[Measurement Properties]  
 Wavelength Range (nm.): 200.00 to 400.00  
 Scan Speed: Medium  
 Sampling Interval: 0.1  
 Auto Sampling Interval: Disabled  
 Scan Mode: Auto

No.	P/V	Wavelength	Abs.	Description
1	⊕	348.90	0.047	
2	⊕	340.00	0.048	
3	⊕	236.30	0.503	
4	⊕	202.30	0.862	
5	⊕	223.50	0.435	

[Instrument Properties]  
 Instrument Type: UV-1800 Series  
 Measuring Mode: Absorbance  
 Slit Width: 1.0 nm  
 Light Source Change Wavelength: 340.0 nm  
 S/R Exchange: Normal

[Attachment Properties]  
 Attachment: 6-Cell  
 Number of cells: 6

[Operation]  
 Threshold: 0.0010000  
 Points: 4  
 Interpolate: Disabled  
 Average: Disabled

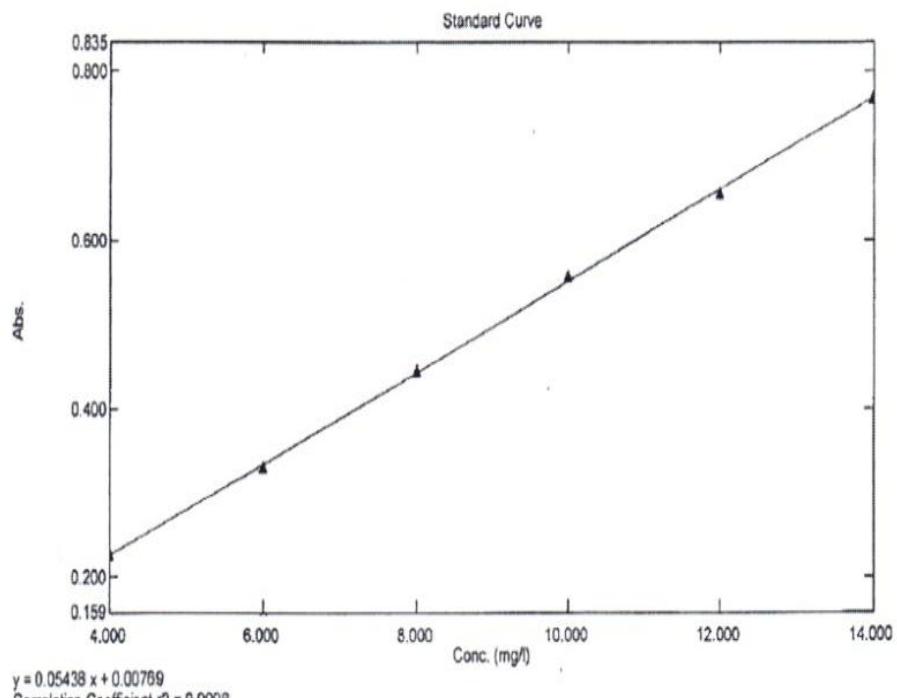
[Sample Preparation Properties]  
 Weight:  
 Volume:  
 Dilution:  
 Path Length:  
 Additional Information:

**Lampiran 6.** Data kurva baku

## Standard Table Report

05/24/2015 11:32:06 AM

File Name: C:\File\_150524\_100349.pho



Standard Table

	Sample ID	Type	Ex	Conc	WL236.3	Wgt.Factor	Comments
1	1	Standard		4.000	0.225	1.000	
2	2	Standard		6.000	0.331	1.000	
3	3	Standard		8.000	0.444	1.000	
4	4	Standard		10.000	0.558	1.000	
5	5	Standard		12.000	0.657	1.000	
6	6	Standard		14.000	0.768	1.000	
7							

**Lampiran 7.** Perhitungan pembuatan dapar fosfat pH 7,4

Mr KH<sub>2</sub>PO<sub>4</sub> = 136,0855 g/mol

Mr NaOH = 40 g/mol

a. Perhitungan KH<sub>2</sub>PO<sub>4</sub> yang ditimbang

$$M = \frac{\text{Berat}}{136,0855} \times 1000$$

$$0,2 = \frac{\text{Berat}}{136,0855} \times 1000$$

$$0,2 = \frac{136,0855}{136,0855} \times 62,5$$

$$0,2 = \frac{\text{Berat}}{136,0855} \times 1000$$

$$0,2 = \frac{136,0855}{136,0855} \times 62,5$$

Berat KH<sub>2</sub>PO<sub>4</sub> = 1,7 gram dilarutkan dalam 62,5 mL aquades

b. Perhitungan NaOH yang ditimbang

$$M = \frac{\text{Berat}}{\text{Mr}} \times \frac{1000}{P}$$

$$0,2 = \frac{\text{Berat}}{40} \times \frac{1000}{48,875}$$

$$0,2 = \frac{\text{Berat}}{40} \times \frac{1000}{48,875}$$

Berat NaOH = 0,38 gram dilarutkan dalam 48,875 mL aquades

- Kemudian KH<sub>2</sub>PO<sub>4</sub> dan NaOH dicukupkan hingga 250 mL

#### Lampiran 8. Perhitungan konversi dosis manusia ke tikus

1. Perhitungan konversi dosis

Dosis film transdermal untuk manusia = 25 mg.

Konversi dosis untuk manusia ke tikus = 0,018.

Dosis untuk tikus rata-rata bobot 200 g adalah

Dosis = dosis manusia x faktor konversi

$$= 25 \text{ mg} \times 0,018$$

$$= 0,45 \text{ mg/film untuk tikus bobot } 200 \text{ g}$$

Dibuat 120 film dalam 1 petri, jadi diltiazem HCl =  $120 \times 0,45 \text{ mg}$

$$= 54 \text{ mg/petri}$$

2. Perhitungan luas film

$$\begin{aligned} 1 \text{ petri} &= \pi \times r^2 &= 3,14 \times (4,5)^2 \\ &&= 63,585 \text{ cm}^2 \\ &&= 64 \text{ cm}^2 \end{aligned}$$

$$\text{Luas film} = 64 \text{ cm}^2 : 120 \text{ film} = 0,53 \text{ cm}$$

$$\text{Luas film} = s \times s$$

$$0,53 = s^2$$

$$\text{Sisi film} = 0,73 \text{ cm} \approx 0,7 \text{ cm}$$

**Lampiran 9.** Formula film transdermal diltiazem HCl

1. Formula awal film transdermal diltiazem HCl dalam 1 film (Laili, 2016)

Bahan	Formula		
	I	II	III
Diltiazem HCl (mg)	25	25	25
Polivinil alkohol (mg)	70	70	70
Etil selulosa (mg)	30	30	30
Isopropil miristat (mg)	15	20	25
Propilenglikol (mg)	25	20	15

2. Formula awal film transdermal diltiazem HCl dalam 1 petri (Laili, 2016)

Bahan	Formula		
	I	II	III
Diltiazem HCl (mg)	400	400	400
Polivinil alkohol (mg)	1120	1120	1120
Etil selulosa (mg)	480	480	480
Isopropil Miristat (mg)	240	320	400
Propilenglikol (mg)	400	320	240

3. Formula film transdermal diltiazem HCl setelah dikonversi ke tikus dalam 1 film

Bahan	Formula film transdermal		
	I (mg)	II (mg)	III (mg)
Diltiazem HCl (mg)	0,45	0,45	0,45
Polivinil alkohol (mg)	9,33	9,33	9,33
Etil sesulosa (mg)	4	4	4
Isopropil Miristat (mg)	2	2,67	3,34
Propilenglikol (mg)	3,34	2,67	2
Jumlah	19,12	19,12	19,12

- Jumlah formula PVA, EC, IPM, dan PG tiap film didapatkan dari formula awal 1 petri dibagi 120.
- Jika satuan diubah menjadi persen :

$$\begin{aligned}\% \text{ diltiazem HCl} &= 0,45 \text{ mg} : 19,12 \text{ mg} \times 100\% \\ &= 2,35 \% \text{ dst.}\end{aligned}$$

4. Formula film transdermal diltiazem HCl dalam 1 petri setelah diltiazem HCl dikonversi ke tikus

Bahan	Formula		
	I	II	III
Diltiazem HCl (mg)	54	54	54
Polivinil alkohol (mg)	1120	1120	1120
Etil sesulosa (mg)	480	480	480
Isopropil Miristat (mg)	240	320	400
Propilenglikol (mg)	400	320	240

Contoh perhitungannya (Formula I)

$$\text{Diltiazem HCl} = 0,45 \times 120 = 54 \text{ mg}$$

$$\text{Polivinil alkohol} = 9,33 \times 120 = 1120 \text{ mg}$$

$$\text{Etil selulosa} = 4 \times 120 = 480 \text{ mg}$$

$$\text{Isopropil Miristat} = 2 \times 120 = 240 \text{ mg}$$

$$\text{Propilenglikol} = 3,34 \times 120 = 400 \text{ mg}$$

- ❖ 120 (pemotongan jumlah film dalam 1 petri setelah dikonversi ke tikus)
- ❖ 16 (pemotongan jumlah film dalam 1 petri untuk manusia)
- ❖ Hanya diltiazem HCl yang dikonversi, agar tidak merubah formula dari penelitian yang sebelumnya (Laili, 2016)

**Lampiran 10.** Perhitungan kandungan zat aktif dalam film transdermal diltiazem

## HCl

Bobot teoritis tiap 1 petri film transdermal :

$$\text{Diltiazem HCl} = 0,054 \text{ g}$$

$$\text{PVA} = 1,120 \text{ g}$$

$$\text{EC} = 0,480 \text{ g}$$

$$\text{IPM} = 0,240 \text{ g}$$

$$\text{PG} = 0,400 \text{ g} +$$

$$2,294 \text{ g} : 120 \text{ film} = 0,01912 \text{ g} = 19,12 \text{ mg/film} = 19 \text{ mg} \\ = 19 \text{ mg} \times 5$$

$$= 95 \text{ mg/5 film}$$

Keterangan :

Angka 5 : repetisi saat uji kandungan zat aktif

### A. Formula 1

✓ Replikasi 1

- Kadar diltiazem HCl teoritis :

$$\text{Bobot 5 film} = 44,1 \text{ mg}$$

$$\text{RL } \rightarrow y = 0,05438 x + 0,00769$$

$$5 \text{ patch} = \frac{44,1 \text{ mg}}{95 \text{ mg}} = 0,464 \text{ mg}$$

$$0,464 \text{ mg} \times 2,25 \text{ mg} (0,45 \text{ mg dosis konversi} \times 5 \text{ film}) = 1,044 \text{ mg}$$

$$1,044 \text{ mg} : 5 = 0,21 \text{ mg/film}$$

- Kadar diltiazem HCl terukur :

$$\text{Absorbansi} = 0,225$$

$$Y = 0,05438 x + 0,00769$$

$$0,225 = 0,05438 x + 0,00769$$

$$x = 3,996 \mu\text{g/mL} \times 250 \text{ mL} (\text{Vol dapar fosfat pH 7,4})$$

$$= 999 \mu\text{g}$$

$$= 0,999 \text{ mg} : 5 = 0,200 \text{ mg}$$

- Persen kadar diltiazem HCl sebenarnya dari nilai teoritis (85%-115%)

% kadar Diltiazem HCl = kadar dtz terukur : kadar dtz teoritis x 100%

$$= 0,200 \text{ mg} : 0,209 \text{ mg} \times 100\%$$

$$= 0,957 \times 100\% = 95,7\%$$

✓ Replikasi 2

- Kadar diltiazem HCl teoritis :

Bobot 5 patch = 52,7 mg

$$\text{RL} \rightarrow y = 0,05438 x + 0,00769$$

$$5 \text{ patch} = 52,7 \text{ mg} = 0,5547 \times 2,25 \text{ mg} = 1,248 : 5 = 0,249 \text{ mg/film}$$

$$95 \text{ mg}$$

- Kadar diltiazem HCl terukur

Absorbansi = 0,286

$$Y = 0,05438 x + 0,00769$$

$$0,286 = 0,05438 x + 0,00769$$

$$x = 5,118 \mu\text{g/mL} \times 250 \text{ mL} = 1,279,5 \mu\text{g}$$

$$= 1,2795 \text{ mg} : 5 = 0,256 \text{ mg}$$

- Persen kadar diltiazem HCl sebenarnya, dari nilai teoritis (85%-115%)

% kadar Diltiazem HCl = kadar dtz terukur : kadar dtz teoritis x 100%

$$= 0,256 \text{ mg} : 0,249 \text{ mg} \times 100\%$$

$$= 1,0281 \times 100\%$$

$$= 102,81\%$$

✓ Replikasi 3

- Kadar diltiazem HCl teoritis :

Bobot 5 film = 61,8 mg

$$RL \rightarrow y = 0,05438 x + 0,00769$$

$$\begin{aligned} 5 \text{ patch} &= \underline{61,8 \text{ mg}} = 0,650 \times 2,25 \text{ mg} = 1,464 : 5 = 0,292 \text{ mg/film} \\ &\quad 95 \text{ mg} \end{aligned}$$

- Kadar diltiazem HCl terukur

Absorbansi = 0,313

$$Y = 0,05438 x + 0,00769$$

$$0,313 = 0,05438 x + 0,00769$$

$$\begin{aligned} x &= 5,614 \mu\text{g/mL} \times 250 \text{ mL} = 1.403,5 \mu\text{g} \\ &= 1,4035 \text{ mg} : 5 = 0,281 \text{ mg} \end{aligned}$$

- Persen kadar diltiazem HCl sebenarnya, dari nilai teoritis (85%-115%)

% kadar Diltiazem HCl = kadar dtz terukur : kadar dtz teoritis x 100%

$$\begin{aligned} &= 0,281 \text{ mg} : 0,292 \text{ mg} \times 100\% \\ &= 96,23 \% \end{aligned}$$

## B. Formula 2

- ✓ Replikasi 1

- Kadar diltiazem HCl teoritis :

Bobot 5 patch = 68,8 mg

$$RL \rightarrow y = 0,05438 x + 0,00769$$

$$\begin{aligned} 5 \text{ patch} &= \underline{68,8 \text{ mg}} = 0,724 \times 2,25 \text{ mg} = 1,63 : 5 = 0,33 \text{ mg/patch} \\ &\quad 95 \text{ mg} \end{aligned}$$

- Kadar diltiazem HCl terukur

Absorbansi = 0,329

$$Y = 0,05438 x + 0,00769$$

$$0,329 = 0,05438 x + 0,00769$$

$$x = 5,909 \mu\text{g/mL} \times 250 \text{ mL} = 1.477,25 \mu\text{g}$$

$$= 1,477 \text{ mg} : 5 = 0,295 \text{ mg}$$

- Persen kadar diltiazem HCl sebenarnya, dari nilai teoritis (85%-115%)  
 $\% \text{ kadar Diltiazem HCl} = \text{kadar dtz terukur} : \text{kadar dtz teoritis} \times 100\%$   
 $= 0,295 \text{ mg} : 0,33 \text{ mg} \times 100\%$   
 $= 89,39 \%$

✓ Replikasi 2

- Kadar diltiazem HCl teoritis :

$$\text{Bobot 5 patch} = 64,8 \text{ mg}$$

$$\text{RL} \rightarrow y = 0,05438 x + 0,00769$$

$$5 \text{ patch} = 64,8 \text{ mg} = 0,682 \times 2,25 \text{ mg} = 1,535 : 5 = 0,307 \text{ mg/patch}$$

$$95 \text{ mg}$$

- Kadar diltiazem HCl terukur

$$\text{Absorbansi} = 0,326$$

$$Y = 0,05438 x + 0,00769$$

$$0,326 = 0,05438 x + 0,00769$$

$$x = 5,853 \mu\text{g/mL} \times 250 \text{ mL} = 1.463,25 \mu\text{g}$$

$$= 1,46325 \text{ mg} : 5 = 0,293 \text{ mg}$$

- Persen kadar diltiazem HCl sebenarnya, dari nilai teoritis (85%-115%)  
 $\% \text{ kadar Diltiazem HCl} = \text{kadar dtz terukur} : \text{kadar dtz teoritis} \times 100\%$   
 $= 0,293 \text{ mg} : 0,307 \text{ mg} \times 100\%$   
 $= 95,44 \%$

✓ Replikasi 3

- Kadar diltiazem HCl teoritis :

Bobot 5 patch = 59,5mg

$$RL \rightarrow y = 0,05438 x + 0,00769$$

$$\begin{aligned} 5 \text{ patch} &= \frac{59,5\text{mg}}{95 \text{ mg}} = 0,626 \times 2,25 \text{ mg} = 1,408 : 5 = 0,281 \text{ mg/patch} \\ &= 0,281 \text{ mg/patch} \end{aligned}$$

- Kadar diltiazem HCl terukur

$$\text{Absorbansi} = 0,312$$

$$Y = 0,05438 x + 0,00769$$

$$0,312 = 0,05438 x + 0,00769$$

$$\begin{aligned} x &= 5,596 \mu\text{g/mL} \times 250 \text{ mL} = 1.399 \mu\text{g} \\ &= 1,399 \text{ mg} : 5 = 0,280 \text{ mg} \end{aligned}$$

- Persen kadar diltiazem HCl sebenarnya, dari nilai teoritis (85%-115%)

$$\% \text{ kadar Diltiazem HCl} = \text{kadar dtz terukur} : \text{kadar dtz teoritis} \times 100\%$$

$$\begin{aligned} &= 0,280 \text{ mg} : 0,281 \text{ mg} \times 100\% \\ &= 99,6 \% \end{aligned}$$

### C. Formula 3

- ✓ Replikasi 1

- Kadar diltiazem HCl teoritis :

Bobot 5 patch = 95,9 mg

$$RL \rightarrow y = 0,05438 x + 0,00769$$

$$\begin{aligned} 5 \text{ patch} &= \frac{95,9 \text{ mg}}{95 \text{ mg}} = 1,009 \times 2,25 \text{ mg} = 2,271 : 5 = 0,45 \text{ mg/patch} \\ &= 0,45 \text{ mg/patch} \end{aligned}$$

- Kadar diltiazem HCl terukur

$$\text{Absorbansi} = 0,473$$

$$Y = 0,05438 x + 0,00769$$

$$0,473 = 0,05438 x + 0,00769$$

$$x = 8,557 \mu\text{g/mL} \times 250 \text{ mL} = 2.139,25 \mu\text{g}$$

$$= 2,13925 \text{ mg} : 5 = 0,428 \text{ mg}$$

- Persen kadar diltiazem HCl sebenarnya, dari nilai teoritis (85%-115%)  
 $\% \text{ kadar Diltiazem HCl} = \text{kadar dtz terukur} : \text{kadar dtz teoritis} \times 100\%$   
 $= 0,428 \text{ mg} : 0,45 \text{ mg} \times 100\%$   
 $= 95,1 \%$

✓ Replikasi 2

- Kadar diltiazem HCl teoritis :

$$\text{Bobot 5 patch} = 94 \text{ mg}$$

$$\text{RL} \rightarrow y = 0,05438 x + 0,00769$$

$$\begin{array}{rcl} 5 \text{ patch} & = 94 \text{ mg} & = 0,99 x 2,25 \text{ mg} = 2,23 : 5 = 0,44 \text{ mg/patch} \\ & \hline & 95 \text{ mg} \end{array}$$

- Kadar diltiazem HCl terukur

$$\text{Absorbansi} = 0,460$$

$$Y = 0,05438 x + 0,00769$$

$$0,460 = 0,05438 x + 0,00769$$

$$x = 8,317 \mu\text{g/mL} \times 250 \text{ mL} = 2.079,25 \mu\text{g}$$

$$= 2,07925 \text{ mg} : 5 = 0,416 \text{ mg}$$

- Persen kadar diltiazem HCl sebenarnya, dari nilai teoritis (85%-115%)  
 $\% \text{ kadar Diltiazem HCl} = \text{kadar dtz terukur} : \text{kadar dtz teoritis} \times 100\%$   
 $= 0,416 \text{ mg} : 0,44 \text{ mg} \times 100\%$   
 $= 94,5\%$

✓ Replikasi 3

- Kadar diltiazem HCl teoritis :

$$\text{Bobot 5 patch} = 62,7 \text{ mg}$$

$$\text{RL} \rightarrow y = 0,05438 x + 0,00769$$

$$\begin{array}{rcl} 5 \text{ patch} & = 62,7 \text{ mg} & = 0,86 \times 2,25 \text{ mg} = 1,485 : 5 = 0,297 \text{ mg/patch} \\ & \hline & 95 \text{ mg} \end{array}$$

- Kadar diltiazem HCl terukur

$$\text{Absorbansi} = 0,378$$

$$Y = 0,05438 x + 0,00769$$

$$0,378 = 0,05438 x + 0,00769$$

$$x = 6,8097 \mu\text{g/mL} \times 250 \text{ mL} = 1,702,425 \mu\text{g}$$

$$= 1,702425 \text{ mg} : 5 = 0,340 \text{ mg}$$

- Persen kadar diltiazem HCl sebenarnya, dari nilai teoritis (85%-115%)

$$\% \text{ kadar Diltiazem HCl} = \text{kadar dtz terukur} : \text{kadar dtz teoritis} \times 100\%$$

$$= 0,340 \text{ mg} : 0,297 \text{ mg} \times 100\%$$

$$= 114,48 \%$$

**Lampiran 11.** Contoh perhitungan luas film yang harus dipotong sesuai berat badan tikus

#### 1. Formula I

Tikus BB 225 gram

$$\frac{\text{Kadar diltiazem HCl terukur (0,25 mg)}}{\text{Luas film (0,49 cm}^2\text{)}} = \frac{\text{Kadar diltiazem teori (0,45 mg)}}{\text{Luas film yang dipotong/x (cm}^2\text{)}}$$

$$\frac{0,25}{0,49 \text{ cm}^2} = \frac{0,45 \text{ mg}}{X (\text{cm}^2)}$$

$$X = 0,88 \text{ cm}^2$$

$$\text{Luas film yang dipotong/x} = 0,88 \text{ cm}$$

$$\frac{\text{Berat tikus 200 gram (g)}}{X} = \frac{\text{Berat tikus yang ditimbang (g)}}{\text{Luas film yang harus dipotong sesuai BB/Y (cm}^2\text{)}}$$

$$\frac{200 \text{ g}}{0,88 \text{ cm}^2} = \frac{225 \text{ g}}{Y}$$

$$Y = 0,99 \text{ cm}^2$$

$$\text{Sisi yang dipotong} = 0,99 \text{ cm}$$

## 2. Formula II

Tikus BB 218 gram

$$\frac{\text{Kadar diltiazem HCl terukur (0,31 mg)}}{\text{Luas film (0,49 cm}^2)} = \frac{\text{Kadar diltiazem teori (0,45 mg)}}{\text{Luas film yang dipotong/x (cm}^2)}$$

$$\frac{0,31}{0,49 \text{ cm}^2} = \frac{0,45 \text{ mg}}{X (\text{cm}^2)}$$

$$X = 0,71 \text{ cm}^2$$

$$\text{Luas film yang dipotong/x} = 0,71 \text{ cm}^2$$

$$\frac{\text{Berat tikus 200 gram (g)}}{X} = \frac{\text{Berat tikus yang ditimbang (g)}}{\text{Luas film yang harus dipotong sesuai BB/Y (cm}^2)}$$

$$\frac{200 \text{ g}}{0,71 \text{ cm}^2} = \frac{218 \text{ g}}{Y}$$

$$Y = 0,77 \text{ cm}^2$$

$$\text{Sisi yang dipotong} = 0,89 \text{ cm}$$

## 3. Formula III

Tikus BB 209 gram

$$\frac{\text{Kadar diltiazem HCl terukur (0,45 mg)}}{\text{Luas film (0,49 cm}^2)} = \frac{\text{Kadar diltiazem teori (0,45 mg)}}{\text{Luas film yang dipotong/x (cm}^2)}$$

$$\frac{0,45}{0,49 \text{ cm}^2} = \frac{0,45 \text{ mg}}{X (\text{cm}^2)}$$

$$X = 0,49 \text{ cm}^2$$

$$\text{Luas film yang dipotong/x} = 0,49 \text{ cm}^2$$

$$\frac{\text{Berat tikus 200 gram (g)}}{X} = \frac{\text{Berat tikus yang ditimbang (g)}}{\text{Luas film yang harus dipotong sesuai BB/Y (cm}^2)}$$

$$\frac{200 \text{ g}}{0,7 \text{ cm}^2} = \frac{209 \text{ g}}{Y}$$

$$Y = 0,73 \text{ cm}^2$$

$$\text{Sisi yang dipotong} = 0,85 \text{ cm}$$

**Lampiran 12.** Data hasil uji kandungan zat aktif diltiazem HCl

Formula	Rep	Abs	Kadar terukur (mg)	Kadar teoritis (mg)	% kadar sebenarnya, dari nilai teoritis 85%-115% (%)	Rata-rata % kadar sebenarnya,dari nilai teoritis 85%-115% (%)	± SEM
I (IPM 10,46%)	1	0,225	0,200	0,210	95,7	98,25	± 1,87
	2	0,286	0,256	0,249	102,81		
	3	0,313	0,281	0,292	96,23		
II (IPM 13,97%)	1	0,329	0,295	0,330	89,39	94,81	± 2,42
	2	0,326	0,293	0,307	95,44		
	3	0,312	0,280	0,281	99,6		
III (IPM 17,48%)	1	0,473	0,428	0,450	95,1	101,36	± 5,36
	2	0,460	0,416	0,440	94,5		
	3	0,378	0,340	0,297	114,48		

**Lampiran 13.** Data berat badan tikus

Kelompok perlakuan	Tikus	Bobot tikus (gram)
Kontrol Hipertensi (Induksi NaCl 3 gram/kgBB)	1	236
	2	228
	3	200
	4	222
	5	204
Kontrol Negatif (Induksi NaCl 3 gram/kgBB)	1	209
	2	240
	3	235
	4	215
	5	250
Uji FI (Induksi NaCl 3 gram/kgBB)	1	225
	2	235
	3	219
	4	227
	5	238
Uji FII (Induksi NaCl 3 gram/kgBB)	1	218
	2	234
	3	239
	4	215
	5	240
Uji FIII (Induksi NaCl 3 gram/kgBB)	1	229
	2	231
	3	222
	4	237
	5	217

Larutan stok NaCl 15% = 15 g/100mL  
 $= 15.000 \text{ mg}/100 \text{ mL}$   
 $= 150 \text{ mg/mL}$

NaCl dosis 3 g/KgBB

### 1. Kelompok hipertensi

Tikus 1 BB = 236 g

Dosis = 236 g x 3000 mg = 708 mg

1000 g

V.P = 708 mg x 1 mL : 150 mg = 4,72 mL

2. Kelompok kontrol negatif

Tikus 4 BB = 215 g

$$\text{Dosis} = \frac{215 \text{ g} \times 3000 \text{ mg}}{1000 \text{ mg}} = 645 \text{ mg}$$

$$\text{V.P} = \frac{645 \text{ mg} \times 1\text{mL}}{150 \text{ mg}} = 4,3 \text{ mL}$$

3. Kelompok formula 1

Tikus 1 BB = 225 g

$$\text{Dosis} = \frac{225 \text{ g} \times 3000 \text{ mg}}{1000 \text{ mg}} = 675 \text{ mg}$$

$$\text{V.P} = \frac{675 \text{ mg} \times 1\text{mL}}{150 \text{ mg}} = 4,5 \text{ mL}$$

4. Kelompok formula 2

Tikus 1 BB = 218 g

$$\text{Dosis} = \frac{218 \text{ g} \times 3000 \text{ mg}}{1000 \text{ mg}} = 654 \text{ mg}$$

$$\text{V.P} = 654 \text{ mg} \times 1\text{mL} : 150 = 4,36 \text{ mg}$$

5. Kelompok formula 3

Tikus 1 BB = 229 g

$$\text{Dosis} = \frac{229 \text{ g} \times 3000 \text{ mg}}{1000 \text{ mg}} = 687 \text{ mg}$$

$$\text{V.P} = 687 : 150 = 4,58 \text{ mL}$$

**Lampiran 14.** Data tekanan darah tikus sebelum dan setelah 14 hari induksi  
NaCl 3 gram/kgBB

Kelompok	Tikus	TDS (mmHg)		TDD (mmHg)	
		Minggu 0	Minggu 2	Minggu 0	Minggu 2
Normal (aquades)	1	102	106	73	71
	2	119	116	80	76
	3	112	112	77	75
	4	105	109	71	75
	5	109	103	74	67
	Rata-rata ± SEM	109,4 ± 2,9	109,2 ± 2,3	75 ± 1,6	72,8 ± 1,7
Kontrol Hipertensi (NaCl 3 gram/kgBB)	1	114	146	70	101
	2	117	145	76	107
	3	120	145	73	114
	4	108	143	74	114
	5	123	147	75	108
	Rata-rata ± SEM	116,4 ± 2,6	145,2* ± 0,7	73,6 ± 1,0	108,8* ± 2,4
Kontrol Negatif (NaCl 3 gram/kgBB)	1	105	144	98	111
	2	102	157	87	119
	3	94	151	100	114
	4	100	145	79	117
	5	112	144	81	107
	Rata-rata ± SEM	102,6 ± 3,0	148,2* ± 2,6	89 ± 4,3	113,6* ± 2,1
Uji FI (NaCl 3 gram/kgBB)	1	99	142	80	98
	2	105	156	92	108
	3	110	143	85	118
	4	95	151	92	119
	5	92	143	90	111
	Rata-rata ± SEM	100,2 ± 3,3	147* ± 2,8	87,8 ± 2,3	110,8* ± 3,8
Uji FII (NaCl 3 gram/kgBB)	1	115	161	79	93
	2	97	150	85	115
	3	108	146	90	119
	4	103	146	82	125
	5	100	157	93	132
	Rata-rata ± SEM	104,6 ± 3,2	150,5* ± 3,0	85,8 ± 2,6	116,8* ± 6,6
Uji FIII (NaCl 3 gram/kgBB)	1	111	153	94	109
	2	102	163	102	118
	3	109	147	83	116
	4	105	132	89	103
	5	99	140	92	98
	Rata-rata ± SEM	105,2 ± 3,2	147* ± 5,3	92 ± 3,1	108,8* ± 3,8

**Lampiran 15.** Contoh data hasil pengukuran tekanan darah pada alat CODA

<b>Session Summary - formula 3 tikus 1 awal</b>		11/23/2016 11:19:32 AM				
<b>Experiment Name</b>	Patch Diltiazem					
Key Researcher	Dewin					
Creation Date	9/22/2016 12:00:00 AM					
Comments	No comment					
<b>Session Name</b>	formula 3 tikus 1 awal					
Date	10/8/2016 09:02:57 AM					
Comments						
						
<b>Acclimation Cycles</b>						
<b>Rat1 (Ch 1)</b>						
<b>Accepted Cycles</b>						
Run	Diastolic	Systolic	Mean	Rate	Flow	Volume
1	92	157	113	512	9.58	39.24
2	102	151	118	558	8.26	24.61
3	101	148	116	0	8.12	23.58
Mean	98.333	152.000	115.667	356.667	8.653	29.143
Max	102	157	118	558	9.58	39.24
Min	92	148	113	0	8.12	23.58
SD	5.508	4.583	2.517	309.738	0.806	8.759
Var	30.333	21.000	6.333	95937.333	0.649	76.722
# Cycles	3					
<b>Rejected Cycles</b>						
Run	Diastolic	Systolic	Mean	Rate	Flow	Volume
1	103	179	128	0	5.57	27.15
2	116	159	130	0	8.13	22.83
Mean	109.500	169.000	129.000	0.000	6.850	24.990
Max	116	179	130	0	8.13	27.15
Min	103	159	128	0	5.57	22.83
SD	9.192	14.142	1.414	0.000	1.810	3.055
Var	84.500	200.000	2.000	0.000	3.277	9.331
# Cycles	2					

**Regular Cycles**

<u>Rat1 (Ch 1)</u>						
<u>Accepted Cycles</u>						
Run	Diastolic	Systolic	Mean	Rate	Flow	Volume
1	106	152	121	431	13.04	36.78
2	109	151	123	418	13.76	36.89
3	104	151	119	439	11.34	34.59
4	116	159	130	451	10.83	29.9
Mean	<b>108.750</b>	<b>153.250</b>	<b>123.250</b>	<b>434.750</b>	<b>12.243</b>	<b>34.540</b>
Max	<b>116</b>	<b>159</b>	<b>130</b>	<b>451</b>	<b>13.76</b>	<b>36.89</b>
Min	<b>104</b>	<b>151</b>	<b>119</b>	<b>418</b>	<b>10.83</b>	<b>29.9</b>
SD	<b>5.252</b>	<b>3.862</b>	<b>4.787</b>	<b>13.865</b>	<b>1.384</b>	<b>3.270</b>
Var	<b>27.583</b>	<b>14.917</b>	<b>22.917</b>	<b>192.250</b>	<b>1.916</b>	<b>10.691</b>
# Cycles						
4						

**Rejected Cycles**

Run	Diastolic	Systolic	Mean	Rate	Flow	Volume
1	205	209	206	0	11.94	2.27
Mean	<b>205.000</b>	<b>209.000</b>	<b>206.000</b>	<b>0.000</b>	<b>11.940</b>	<b>2.270</b>
Max	<b>205</b>	<b>209</b>	<b>206</b>	<b>0</b>	<b>11.94</b>	<b>2.27</b>
Min	<b>205</b>	<b>209</b>	<b>206</b>	<b>0</b>	<b>11.94</b>	<b>2.27</b>
SD						
Var						



**Lampiran 16.** Data tekanan darah sistolik sebelum dan setelah 1 jam pemberian sediaan uji

Kelompok Perlakuan	Tikus	TDS Sebelum Perlakuan (MmHg)	TDS Setelah Perlakuan (MmHg)
Kontrol Negatif (film tanpa obat diltiazem HCl)	1	144	139
	2	157	158
	3	151	144
	4	145	148
	5	144	148
	Rata-rata ± SEM	$148,2 \pm 2,2$	$147,4 \pm 3,1$
Formulasi I (film transdermal diltiazem HCl dengan IPM 10,46%)	1	142	140
	2	156	106
	3	143	135
	4	151	124
	5	143	138
	Rata-rata ± SEM	$147,0 \pm 2,8$	$128,6 \pm 6,9$
Formulasi II (film transdermal diltiazem HCl dengan IPM 13,97%)	1	161	137
	2	150	115
	3	146	135
	4	146	112
	5	157	128
	Rata-rata ± SEM	$150,5 \pm 3,0$	$125,4^* \pm 5,1$
Formulasi III (film transdermal diltiazem HCl dengan IPM 17,48%)	1	153	117
	2	163	108
	3	147	106
	4	132	107
	5	140	124
	Rata-rata ± SEM	$147 \pm 5,3$	$112,4^* \pm 3,5$

**Lampiran 17.** Data tekanan darah diastolik sebelum dan setelah 1 jam pemberian sediaan uji

Kelompok Perlakuan	Tikus	TDD Sebelum Perlakuan (MmHg)	TDD Setelah Perlakuan (MmHg)
Kontrol Negatif (film tanpa obat diltiazem HCl)	1	111	115
	2	119	115
	3	114	103
	4	117	117
	5	107	122
	Rata-rata ± SEM	113,6 ± 2,1	114,4 ± 3,1
Formulasi I (film transdermal diltiazem HCl dengan IPM 10,46%)	1	98	95
	2	108	69
	3	118	107
	4	119	103
	5	111	102
	Rata-rata ± SEM	110,8 ± 3,8	95,2 ± 6,8
Formulasi II (film transdermal diltiazem HCl dengan IPM 13,97%)	1	93	99
	2	115	94
	3	119	110
	4	125	88
	5	132	100
	Rata-rata ± SEM	116,8 ± 6,6	98,2 ± 3,6
Formulasi III (film transdermal diltiazem HCl dengan IPM 17,48%)	1	109	81
	2	118	75
	3	116	70
	4	103	75
	5	98	82
	Rata-rata ± SEM	108,8 ± 3,8	76,6* ± 2,2

**Lampiran 18.** Data penurunan tekanan darah sistolik

Kelompok Perlakuan	Tikus	TDS Sebelum Perlakuan (MmHg)	TDS Setelah Perlakuan (MmHg)	Penurunan Tekanan Darah (mmHg)
Formulasi II (film transdermal diltiazem HCl dengan IPM 13,97%)	1	161	137	24
	2	150	115	34
	3	146	135	11
	4	146	112	34
	5	157	128	29
	Rata-rata ± SEM	150,5 ± 3,0	125,4 ± 5,1	26,4 ± 3,8
Formulasi III (film transdermal diltiazem HCl dengan IPM 17,48%)	1	153	117	36
	2	163	108	55
	3	147	106	41
	4	132	107	25
	5	140	124	16
	Rata-rata ± SEM	147,0 ± 5,3	112,4 ± 3,5	34,6 ± 5,9

**Lampiran 19.** Data penurunan tekanan darah diastolik

Kelompok Perlakuan	Tikus	TDD Sebelum Perlakuan (MmHg)	TDD Setelah Perlakuan (MmHg)	Penurunan Tekanan Darah (mmHg)
Formulasi III (film transdermal diltiazem HCl dengan IPM 17,48%)	1	109	81	28
	2	118	75	43
	3	116	70	46
	4	103	75	28
	5	98	82	16
	Rata-rata ± SEM	108,8 ± 3,8	76,6 ± 2,2	32,2 ± 4,9

**Lampiran 20.** Hasil statistik tekanan darah sistolik sebelum dan setelah induksi tikus hipertensi

**a. Uji Normalitas**

		Tests of Normality					
Kelompok Perlakuan		Kolmogorov-Smirnov*			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
TDS	pre normal	.148	5	.200*	.974	5	.900
	post normal	.136	5	.200*	.990	5	.980
	pre kontrol hipertensi	.141	5	.200*	.979	5	.928
	post kontrol hipertensi	.246	5	.200*	.956	5	.777
	pre kontrol negatif	.158	5	.200*	.990	5	.980
	post kontrol negatif	.312	5	.125	.816	5	.108
	pre uji F1	.165	5	.200*	.962	5	.824
	post uji F1	.340	5	.059	.820	5	.116
	pre uji F2	.189	5	.200*	.960	5	.805
	post uji F2	.217	5	.200*	.876	5	.290
	pre uji F3	.180	5	.200*	.965	5	.843
	post uji F3	.122	5	.200*	.996	5	.996

a. Lilliefors Significance Correction

\*. This is a lower bound of the true significance.

**b. Uji T berpasangan kelompok normal (diberi aquades)**

Paired Samples Test

	Paired Differences						t	df	Sig. (2-tailed)			
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference								
				Lower	Upper							
Pair 1	TDS normal pre (diberi aquades) - TDS normal post (diberi aquades)	.20000	4.38178	1.95959	-5.24070	5.64070	.102	4	.924			

**c. Uji T berpasangan kelompok kontrol hipertensi (diberi NaCl 3 gram/kgBB)**

Paired Samples Test

	Paired Differences						t	df	Sig. (2-tailed)			
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference								
				Lower	Upper							
Pair 1	TDS kontrol hipertensi pre (diberi NaCl 3 gram/kgBB) - TDS kontrol hipertensi post (diberi NaCl 3 gram/kgBB)	-2.880E1	4.65833	2.08327	-34.58408	-23.01592	-13.824	4	.000			

**d. Uji T berpasangan kelompok kontrol negatif (diberi NaCl 3 gram/kgBB)**

Paired Samples Test											
	Paired Differences					t	df	Sig. (2-tailed)			
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference							
				Lower	Upper						
Pair 1 TDS kontrol negatif pre (diberi NaCl 3 gram/kgBB) - TDS kontrol negatif post (diberi NaCl 3 gram/kgBB)	-4.560E1	10.57355	4.72864	-58.72880	-32.47120	-9.643	4	.001			

**e. Uji T berpasangan kelompok uji FI (diberi NaCl 3 gram/kgBB)**

Paired Samples Test											
	Paired Differences					t	df	Sig. (2-tailed)			
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference							
				Lower	Upper						
Pair 1 TDS uji FI pre (diberi NaCl 3 gram/kgBB) - TDS uji FI post (diberi NaCl 3 gram/kgBB)	-4.680E1	9.01110	4.02989	-57.98876	-35.61124	-11.613	4	.000			

**f. Uji T berpasangan kelompok uji FII (diberi NaCl 3 gram/kgBB)**

Paired Samples Test											
	Paired Differences					t	df	Sig. (2-tailed)			
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference							
				Lower	Upper						
Pair 1 TDS uji FII pre (diberi NaCl 3 gram/kgBB) - TDS uji FII post (diberi NaCl 3 gram/kgBB)	-4.740E1	7.63544	3.41467	-56.88066	-37.91934	-13.881	4	.000			

**g. Uji T berpasangan kelompok uji FIII (diberi NaCl 3 gram/kgBB)**

Paired Samples Test											
	Paired Differences					t	df	Sig. (2-tailed)			
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference							
				Lower	Upper						
Pair 1 TDS uji FIII pre (diberi NaCl 3 gram/kgBB) - TDS uji FIII post (diberi NaCl 3 gram/kgBB)	-4.180E1	12.27599	5.48999	-57.04266	-26.55734	-7.614	4	.002			

**Lampiran 21.** Hasil statistik tekanan darah diastolik sebelum dan setelah induksi tikus hipertensi

**a. Uji Normalitas**

Tests of Normality						
Kelompok Perlakuan	Kolmogorov-Smirnov*			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
TDD pre normal (aquades)	.211	5	.200*	.965	5	.844
post normal (aquades)	.320	5	.103	.850	5	.194
pre kontrol hipertensi diberi induksi NaCl 3 gram/kgBB	.197	5	.200*	.943	5	.685
post kontrol hipertensi diberi NaCl 3 gram/kgBB	.230	5	.200*	.898	5	.400
pre kontrol negatif diberi NaCl 3 gram/kgBB	.225	5	.200*	.882	5	.317
post kontrol negatif diberi NaCl 3 gram/kgBB	.162	5	.200*	.974	5	.899
pre uji F1 diberi NaCl 3 gram/kgBB	.263	5	.200*	.859	5	.223
post uji F1 diberi NaCl 3 gram/kgBB	.201	5	.200*	.922	5	.541
pre uji F2 diberi NaCl 3 gram/kgBB	.169	5	.200*	.965	5	.843
post uji F2	.252	5	.200*	.920	5	.529
pre uji F3 diberi NaCl 3 gram/kgBB	.187	5	.200*	.987	5	.967
post uji F3 diberi NaCl 3 gram/kgBB	.202	5	.200*	.941	5	.675

a. Lilliefors Significance Correction

\*. This is a lower bound of the true significance.

**b. Uji T berpasangan kelompok normal (diberi aquades)**

	Paired Samples Test							
	Paired Differences				95% Confidence Interval of the Difference	t	df	Sig. (2-tailed)
	Mean	Std. Deviation	Std. Error Mean	Lower				
Pair 1 TDD normal pre (diberi aquades) - TDD normal post (diberi aquades)	2.20000	4.02492	1.80000	-2.79760	7.19760	1.222	4	.289

**c. Uji T berpasangan kelompok kontrol hipertensi (diberi NaCl 3 gram/kgBB)**

	Paired Samples Test							
	Paired Differences				95% Confidence Interval of the Difference	t	df	Sig. (2-tailed)
	Mean	Std. Deviation	Std. Error Mean	Lower				
Pair 1 TDD kontrol hipertensi pre (diberi NaCl 3 gram/kgBB) - TDD kontrol hipertensi post (diberi NaCl 3 gram/kgBB)	-3.520E1	4.91935	2.20000	-41.30818	-29.09182	-16.000	4	.000

**d. Uji T berpasangan kelompok kontrol negatif (diberi NaCl 3 gram/kgBB)**

Paired Samples Test											
	Paired Differences					t	df	Sig. (2-tailed)			
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference							
				Lower	Upper						
Pair 1 TDD kontrol negatif pre (diberi NaCl 3 gram/kgBB) - TDD kontrol negatif post (diberi NaCl 3 gram/kgBB)	-2.460E1	10.99091	4.91528	-38.24701	-10.95299	-5.005	4	.007			

#### e. Uji T berpasangan kelompok uji FI (diberi NaCl 3 gram/kgBB)

Paired Samples Test											
	Paired Differences					t	df	Sig. (2-tailed)			
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference							
				Lower	Upper						
Pair 1 TDD uji FI pre (diberi NaCl 3 gram/kgBB) - TDD uji FI post (diberi NaCl 3 gram/kgBB)	-2.300E1	6.96419	3.11448	-31.64719	-14.35281	-7.385	4	.002			

#### f. Uji T berpasangan kelompok uji FII (diberi NaCl 3 gram/kgBB)

Paired Samples Test											
	Paired Differences					t	df	Sig. (2-tailed)			
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference							
				Lower	Upper						
Pair 1 TDD uji FII pre (diberi NaCl 3 gram/kgBB) - TDD uji FII post (diberi NaCl 3 gram/kgBB)	-3.100E1	11.20268	5.00999	-44.90996	-17.09004	-6.188	4	.003			

#### g. Uji T berpasangan kelompok uji FIII (diberi NaCl 3 gram/kgBB)

Paired Samples Test											
	Paired Differences					t	df	Sig. (2-tailed)			
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference							
				Lower	Upper						
Pair 1 TDD uji FIII pre (diberi NaCl 3 gram/kgBB) - TDD uji FIII post (diberi NaCl 3 gram/kgBB)	-1.680E1	9.88433	4.42041	-29.07302	-4.52698	-3.801	4	.019			

**Lampiran 22.** Hasil statistik tekanan darah sistolik sebelum dan setelah 1 jam pemberian sediaan uji

### a. Uji Normalitas

		Tests of Normality					
Kelompok perlakuan		Kolmogorov-Smirnov <sup>a</sup>			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
TDS	pre kontrol negatif diberi film tanpa obat (ipm 10,52%)	.212	5	.200*	.936	5	.635
	post kontrol negatif diberi film tanpa obat (ipm 10,52%)	.266	5	.200*	.947	5	.713
	pre uji FI diberi film obat diltiazem HCl (IPM 10,52%)	.340	5	.059	.820	5	.116
	post uji FI diberi film obat diltiazem HCl (IPM 10,52%)	.275	5	.200*	.853	5	.204
	pre uji FII diberi film obat diltiazem HCl (IPM 14,03%)	.217	5	.200*	.876	5	.290
	post uji FII diberi film obat diltiazem HCl (IPM 14,03%)	.219	5	.200*	.882	5	.319
	pre uji FIII diberi film obat diltiazem HCl (IPM 17,54%)	.122	5	.200*	.996	5	.996
	post uji FIII diberi film obat diltiazem HCl (IPM 17,54%)	.313	5	.123	.843	5	.173

a. Lilliefors Significance Correction

\*. This is a lower bound of the true significance.

### b. Uji T berpasangan kelompok kontrol negatif (diberi film transdermal tanpa obat)

Paired Samples Test											
	Paired Differences					t	df	Sig. (2-tailed)			
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference							
				Lower	Upper						
Pair 1	TDS kontrol negatif sebelum diberi film tanpa obat (IPM 10,52%) - TDS kontrol negatif setelah 1 jam diberi film tanpa obat (IPM 10,52%)	-1.40000	6.58027	2.94279	-9.57049	6.77049	-476	.4	.659		

### c. Uji T berpasangan kelompok uji FI (diberi film transdermal diltiazem HCl IPM 10,52%)

Paired Samples Test											
	Paired Differences					t	df	Sig. (2-tailed)			
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference							
				Lower	Upper						
Pair 1	TDS FI sebelum diberi film transdermal diltiazem HCl (IPM 10,52%) - TDS FI setelah diberi film transdermal diltiazem HCl (IPM 10,52%)	1.8400E1	20.18167	9.02552	-6.65886	43.45886	2.039	.4	.111		

### d. Uji T berpasangan kelompok uji FII (diberi film transdermal diltiazem HCl IPM 14,03%)

Paired Samples Test											
	Paired Differences					t	df	Sig. (2-tailed)			
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference							
				Lower	Upper						
Pair 1 TDS FII sebelum diberi film transdermal diltiazem HCl (IPM 14,03%) - TDS FII setelah diberi film transdermal diltiazem HCl (IPM 14,03%)	2.6600E1	9.76217	4.36578	14.47866	38.72134	6.093	4	.004			

**e. Uji T berpasangan kelompok uji FIII (diberi film transdermal diltiazem HCl IPM 17,54%)**

Paired Samples Test											
	Paired Differences					t	df	Sig. (2-tailed)			
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference							
				Lower	Upper						
Pair 1 TDS FIII sebelum diberi film transdermal diltiazem HCl (IPM 17,54%) - TDS FIII setelah diberi film transdermal diltiazem HCl (IPM 17,54%)	3.4600E1	14.97665	6.69776	16.00403	53.19597	5.166	4	.007			

**Lampiran 23.** Hasil statistik tekanan darah diastolik sebelum dan setelah 1 jam pemberian sediaan uji

### a. Uji Normalitas

		Tests of Normality			Shapiro-Wilk		
		Statistic	df	Sig.			
TDD	pre kontrol negatif diberi film tanpa obat (ipm 10,52%)	.162	5	.200*	.974	5	.899
	post kontrol negatif diberi film tanpa obat (ipm 10,52%)	.334	5	.071	.881	5	.312
	pre uji FI diberi film obat diltiazem HCl (IPM 10,52%)	.201	5	.200*	.922	5	.541
	post uji FI diberi film obat diltiazem HCl (IPM 10,52%)	.295	5	.179	.792	5	.070
	pre uji FII diberi film obat diltiazem HCl (IPM 14,03%)	.252	5	.200*	.920	5	.529
	post uji FII diberi film obat diltiazem HCl (IPM 14,03%)	.212	5	.200*	.975	5	.908
	pre uji FIII diberi film obat diltiazem HCl (IPM 17,54%)	.202	5	.200*	.941	5	.675
	post uji FIII diberi film obat diltiazem HCl (IPM 17,54%)	.227	5	.200*	.914	5	.490

a. Lilliefors Significance Correction

\*. This is a lower bound of the true significance.

### b. Uji T berpasangan kelompok kontrol negatif (diberi film transdermal tanpa obat)

Paired Samples Test											
	Paired Differences					t	df	Sig. (2-tailed)			
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference							
				Lower	Upper						
Pair 1 TDD kontrol negatif sebelum diberi film tanpa obat (IPM 10,52%) - TDD kontrol negatif setelah 1 jam diberi film tanpa obat (IPM 10,52%)	-.80000	9.67988	4.32897	-12.81915	11.21915	-.185	4	.862			

### c. Uji T berpasangan kelompok uji FI (diberi film transdermal diltiazem HCl IPM 10,52%)

Paired Samples Test											
	Paired Differences					t	df	Sig. (2-tailed)			
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference							
				Lower	Upper						
Pair 1 TDD uji FI sebelum diberi film tanpa obat (IPM 10,52%) - TDD uji FI setelah 1 jam diberi film tanpa obat (IPM 10,52%)	1.5600E1	13.88524	6.20967	-1.64081	32.84081	2.512	4	.066			

### d. Uji T berpasangan kelompok uji FII (diberi film transdermal diltiazem HCl IPM 14,03%)

Paired Samples Test											
	Paired Differences					t	df	Sig. (2-tailed)			
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference							
				Lower	Upper						
Pair 1 TDD uji FII sebelum diberi film tanpa obat (IPM 14,03%) - TDD uji FII setelah 1 jam diberi film tanpa obat (IPM 14,03%)	1.8600E1	17.47284	7.81409	-3.09539	40.29539	2.380	4	.076			

**e. Uji T berpasangan kelompok uji FIII (diberi film transdermal diltiazem**

**HCl IPM 17,54%)**

Paired Samples Test											
	Paired Differences					t	df	Sig. (2-tailed)			
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference							
				Lower	Upper						
Pair 1 TDD uji FIII sebelum diberi film tanpa obat (IPM 14,03%) - TDD uji FIII setelah 1 jam diberi film tanpa obat (IPM 14,03%)	3.2200E1	12.29634	5.49909	16.93208	47.46792	5.856	4	.004			



**Lampiran 24.** Dokumentasi proses perlakuan pada tikus jantan galur wistar



Film transdermal diltiazem HCl



Induksi hipertensi



Pencukuran bulu abdomen tikus



Proses penempelan film transdermal diltiazem HCl





Perangkat alat CODA *non invasive blood pressure*



Hasil pembacaan tekanan darah dengan CODA