

BAB V

KESIMPULAN DAN SARAN

A. Kesimpulan

Dari hasil penelitian dapat disimpulkan bahwa:

1. Kombinasi matriks mukoadhesif PVP dan xanthan gum berpengaruh terhadap peningkatan kekerasan, perbaikan waktu alir dan kerapuhan, serta memperlambat pelepasan sediaan tablet lepas lambat tramadol HCl dan dapat diketahui sifat mutu fisik serta pola pelepasannya yaitu secara difusi dan mengikuti kinetika orde nol.
2. Kombinasi matriks mukoadhesif PVP dan xanthan gum dapat menghasilkan formula optimum tablet lepas lambat tramadol HCl secara *Simplex Lattice Design* dengan proporsi PVP 55,031% dan xanthan gum 44,969%.

B. Saran

1. Perlu dilakukan penelitian lebih lanjut tentang pembuatan tablet lepas lambat dengan metode dan kombinasi matriks mukoadhesif lainnya.
2. Perlu dilakukan penelitian lebih lanjut tentang pembuatan tablet lepas lambat kombinasi matriks mukoadhesif dengan penambahan bahan pengikat.

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N

Lampiran 1. Sertifikat analisis tramadol HCl

 **PT IFARS PHARMACEUTICAL LABORATORIES**
Jl. Raya Solo - Sragen km 14,9 Karanganyar - Solo 57762 Telp. (0271) 8200888 (Hunting), 827724, 656220
INDONESIA Fax. (0271) 656230

Nomor : IF/III/2013/21.009/027
Lamp. : 1 lembar
Hal : Bahan baku Tramadol HCl


Surakarta, 07 Maret 2013

Kepada Yth. :
Dekan Fakultas Farmasi
Universitas Setia Budi
Jl. Let. Jend. Sutoyo
Solo 57127

Dengan hormat,
Bersama ini kami kirimkan sampel bahan baku Tramadol HCl sebanyak 20 g (Dua Puluh gram) beserta foto copy Certificate of Analysis untuk mahasiswa sebagaimana tercantum dalam surat saudara nomor: 647.28/FF.0/A/SPM/II/2013 pada tanggal 28 Februari 2013

Demikian agar dapat diterima dan diteruskan kepada mahasiswa yang bersangkutan.

Hormat kami,
PT IFARS Pharmaceutical Laboratories
Penanggung Jawab Produksi


PT IFARS
PHARMACEUTICAL LABORATORIES
SURAKARTA - INDONESIA

Dra. Agustini, Apt.
19690821/STRA-UNAIR/1995/224652

Cadila Healthcare Limited

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Zydus

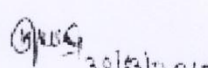
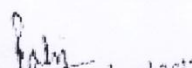

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API Division

CERTIFICATE OF ANALYSIS

Product Name	: TRAMADOL HYDROCHLORIDE BP	A.R.No	: QTLM/120150-11
Material Code	: 4000327	Specification No	: FPS/TLM/01-02
Batch Number	: TLM1BMA01B	Supplied Quantity	: 50.00 Kg
Batch Quantity	: 452.00 Kg	Sample Date	: 25/03/2012
Mfg Date	: MAR-2012	Release Date	: 26/03/2012
Expiry Date	: FEB-2017		
Storage Condition	: Store in tightly closed containers, protected from light, at temperature below 25°C		
Customer Name	: AADIVIGNESH CHEM PRIVATE LIMITED (181-271)		

TESTS	SPECIFICATIONS	OBSERVATIONS
Characters	White, crystalline powder	White crystalline powder
Solubility	Freely soluble in water and in methanol, very slightly soluble in acetone.	Complies
Identification	A. Melting point: 180°C to 184°C	181.0°C
	B. By IR: The infrared absorption spectrum of the test substance is concordant with the working standard spectrum of Tramadol Hydrochloride.	Complies
	C. TLC: The principal spot in the chromatogram obtained with test solution (b) is similar in position and size to the principal spot in the chromatogram obtained with reference solution (a).	Complies
	D. Chloride test: Should complying with the reaction for chloride.	Complies
Appearance of solution	Solution S is clear and colourless.	Complies
Acidity	Not more than 0.4 ml. of 0.01 M sodium hydroxide is required to change the colour of the indicator to yellow.	Complies
Optical rotation	-0.10° to +0.10°, determined on solution S.	-0.0022°

Sign / Date	 30/03/2012 Prepared by (QC)	 30/03/2012 Checked by (QC)	 30/03/2012 Approved by (QA)
Name	Kamlesh Kumbhane	Dr. Sanket Patel	Dilip sharma
Designation	Chemist	Officer	Sr. Manager

Page 1 of 2

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


(API Division)

CERTIFICATE OF ANALYSIS

Product Name	: TRAMADOL HYDROCHLORIDE BP		
Material Code	: 4000327	A.R.No	: QTLM/120150-11
Batch Number	: TLMBMA01B	Specification No	: FPS/TLMA/01-02
Batch Quantity	: 452.00 Kg	Supplied Quantity	: 50.00 Kg
Mfg Date	: MAR-2012	Sample Date	: 25/03/2012
Expiry Date	: FEB-2017	Release Date	: 26/03/2012
Storage Condition	: Store in tightly closed containers, protected from light, at temperature below 25°C		
Customer Name	: AADIVIGNESH CHEM PRIVATE LIMITED (181-271)		

TESTS	SPECIFICATIONS	OBSERVATIONS
Impurity E by TLC	Any spot corresponding to impurity E is not more intense and not greater than the spot in the chromatogram obtained with reference solution (b) (0.2%)	Complies
Related Substances by HPLC	Impurity A : Not more than 0.2 % Impurity C : Not more than 0.1% Any other impurity : Not more than 0.1 % Total impurities : Not more than 0.4 %	Not detected Not detected 0.03% 0.03%
Heavy metals	Not more than 20ppm	Less than 20 ppm
Water content	Not more than 0.5%w/w	0.12%w/w
Sulphated ash	Not more than 0.1%w/w	0.04%w/w
Assay by Potentiometrically	Not less than 99.0%w/w and not more than 101.0% w/w on anhydrous basis	99.8%w/w
Residual Solvent by HS - GC	Acetone : Not more than 3000ppm Isopropyl alcohol : Not more than 2000ppm Toluene : Not more than 500ppm Tetrahydrofuran : Not more than 400ppm Methanol : Not more than 3000ppm	959 ppm 1094 ppm 68 ppm Not detected Not detected

Remark: The product complies as per above specifications.

Sign / Date	 20/03/2012	 20/03/2012	 20/03/2012
Name	Kamlesh Kumbhakar	Dr. Sanket Patel	Dilip Sharma
Designation	Chemist	Officer	Sr. Manager

Page 2 of 2

Lampiran 2. Waktu alir granul

Formula I

Bobot (gram)	Waktu (detik)	Bobot (gram)	Waktu (detik)
	3		6
50,0032	3,7	100,0062	7,4
	3,3		6,6
Rata-rata			6,67
SD			0,70

Formula II

Bobot (gram)	Waktu (detik)	Bobot (gram)	Waktu (detik)
	4,2		8,4
50,0100	3,9	100,0200	7,8
	4,05		8,1
Rata-rata			8,1
SD			0,30

Formula III

Bobot (gram)	Waktu (detik)	Bobot (gram)	Waktu (detik)
	3,8		7,6
50,0020	4,35	100,0040	8,7
	4,75		9,5
Rata-rata			8,6
SD			0,95

Kontrol

Bobot (gram)	Waktu (detik)	Bobot (gram)	Waktu (detik)
	3,05		6,1
50,0093	3	100,0186	6
	3,2		6,4
Rata-rata			6,1
SD			0,21

Lampiran 3. Sudut diam granul

$$\text{Rumus sudut diam} = \tan \alpha = \frac{\text{jari-jari}}{\text{tinggi}}$$

Formula I

Jari-jari (cm)	Tinggi (cm)	Sudut diam (°)
3,400	1,365	21,87
3,173	1,360	23,20
3,200	1,375	23,25
Rata-rata		22,77
SD		0,78

Formula II

Jari-jari (cm)	Tinggi (cm)	Sudut diam (°)
3,125	1,105	19,47
3,250	1,175	19,88
3,462	1,250	19,85
Rata-rata		19,73
SD		0,23

Formula III

Jari-jari (cm)	Tinggi (cm)	Sudut diam (°)
3,300	1,400	22,99
3,362	1,275	20,77
3,287	1,325	21,95
Rata-rata		21,90
SD		1,11

Kontrol

Jari-jari (cm)	Tinggi (cm)	Sudut diam (°)
3,187	1,160	19,99
3,062	1,025	18,51
3,250	1,375	22,93
Rata-rata		20,48
SD		2,15

Lampiran 4. Keseragaman bobot

Tablet	Bobot tabletb(mg)			
	Formula I	Formula II	Formula III	Kontrol
1	248,1	239,9	254,7	247,1
2	251,1	242	253	247
3	249,2	235,2	254,3	237
4	247,8	242,5	251,9	243,2
5	243,8	256,1	252,3	242,1
6	247,6	244,7	253,7	239
7	253,5	239,6	254,4	238
8	251,9	241,1	251,5	243,1
9	244,8	244,1	254,8	243,1
10	250	244,3	255,5	244,2
11	247,1	245,7	255,2	243
12	249	239,8	255	348,1
13	243,9	240,2	254,9	242,3
14	241,8	237,9	245,2	245,1
15	252	231,1	251,5	246,2
16	245,7	250,8	253,6	249
17	247,5	230,6	256	245,3
18	251,7	242,4	251,3	243
19	245,8	243,6	253,5	244,1
20	242,1	235,9	252,9	238
Bobot rata	247,25	241,35	252,80	243,3
SD	3,52	5,87	2,38	3,36
CV	1,42%	2,43%	0,94%	0,01%

Hasil perhitungan rentang keseragaman bobot:

Formula	Kolom A	Kolom B
I	228,71 - 265,79	210,16 – 284,34
II	223,25 – 259,45	205,14 – 277,55
III	233,84 – 271,76	214,88 – 290,72
Kontrol	225,05 – 261,55	206,805 - 279,79

Keterangan:

Kolom A : penyimpangan 7,5% dari bobot rata-ratanya

Kolom B : penyimpangan 15% dari bobot rata-ratanya

Lampiran 5. Kekerasan tablet

Replikasi	Formula I	Formula II	Formula III	Kontrol
1	10,5	11	14,6	6,3
2	10	11,5	14,3	6,8
3	10,3	11,2	15	6,5
Rata-rata	10,27	11,23	14,63	6,53
SD	0,25	0,25	0,35	0,25

Lampiran 6. Kerapuhan tablet

$$\% \text{ kerapuhan} = \frac{\text{bobot awal} - \text{bobot akhir}}{\text{bobot awal}} \times 100\%$$

Formula	Bobot awal	Bobot akhir	% kerapuhan
I	4,9072	4,8810	0,53
II	4,7594	4,7491	0,22
III	5,1476	5,1423	0,10
Kontrol	4,7594	4,7143	0,95

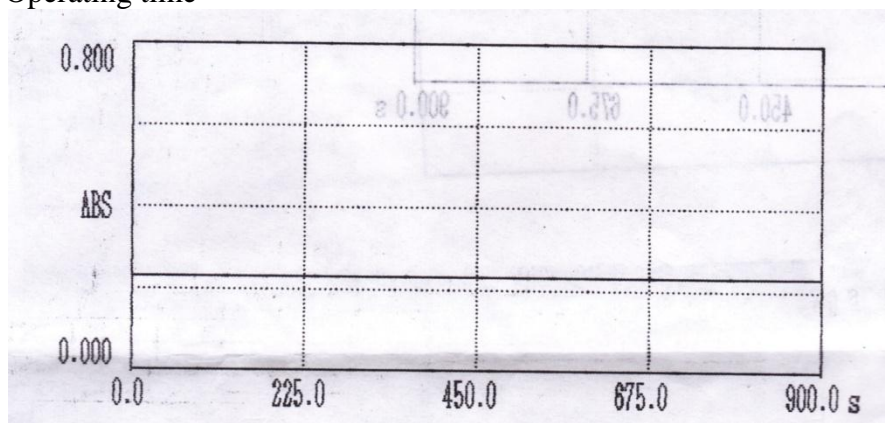
Lampiran 7. Penentuan panjang gelombang, operating time pembuatan kurva baku

❖ Penentuan panjang gelombang maksimum

Panjang gelombang (nm)	Absorbansi
200	2,041
210	1,068
220	0,954
230	0,325
240	0,026
250	0,04
260	0,117
270	0,230
280	0,149
290	-0,007
300	-0,011

Panjang gelombang maksimum tramadol HCl adalah 270 nm.

❖ Operating time



Data List (List Interval(s):10.0)

ID	TIME(s)	ABS	ID	TIME(s)	ABS	ID	TIME(s)	ABS
1	0.0	0.231	2	10.0	0.231	3	20.0	0.231
4	30.0	0.231	5	40.0	0.232	6	50.0	0.232
7	60.0	0.232	8	70.0	0.232	9	80.0	0.232
10	90.0	0.232	11	100.0	0.231	12	110.0	0.232
13	120.0	0.232	14	130.0	0.232	15	140.0	0.232
16	150.0	0.232	17	160.0	0.232	18	170.0	0.232
19	180.0	0.232	20	190.0	0.232	21	200.0	0.232
22	210.0	0.232	23	220.0	0.232	24	230.0	0.232
25	240.0	0.232	26	250.0	0.232	27	260.0	0.232
28	270.0	0.231	29	280.0	0.231	30	290.0	0.231
31	300.0	0.231	32	310.0	0.231	33	320.0	0.231
34	330.0	0.231	35	340.0	0.232	36	350.0	0.232
37	360.0	0.232	38	370.0	0.231	39	380.0	0.232
40	390.0	0.232	41	400.0	0.232	42	410.0	0.232
43	420.0	0.232	44	430.0	0.232	45	440.0	0.231
46	450.0	0.231	47	460.0	0.231	48	470.0	0.232
49	480.0	0.232	50	490.0	0.232	51	500.0	0.231
52	510.0	0.232	53	520.0	0.231	54	530.0	0.231
55	540.0	0.232	56	550.0	0.231	57	560.0	0.232
58	570.0	0.232	59	580.0	0.232	60	590.0	0.232
61	600.0	0.232	62	610.0	0.232	63	620.0	0.231
64	630.0	0.232	65	640.0	0.232	66	650.0	0.231
67	660.0	0.232	68	670.0	0.231	69	680.0	0.232
70	690.0	0.232	71	700.0	0.231	72	710.0	0.232
73	720.0	0.231	74	730.0	0.232	75	740.0	0.232
76	750.0	0.231	77	760.0	0.232	78	770.0	0.232
79	780.0	0.231	80	790.0	0.232	81	800.0	0.232
82	810.0	0.231	83	820.0	0.232	84	830.0	0.232
85	840.0	0.232	86	850.0	0.231	87	860.0	0.231
88	870.0	0.232	89	880.0	0.231	90	890.0	0.232
91	900.0	0.231						

❖ Penentuan kurva baku

Konsentrasi (ppm)	Absorbansi
40	0,24
60	0,325
80	0,454
100	0,589
120	0,674

Data regresi linier:

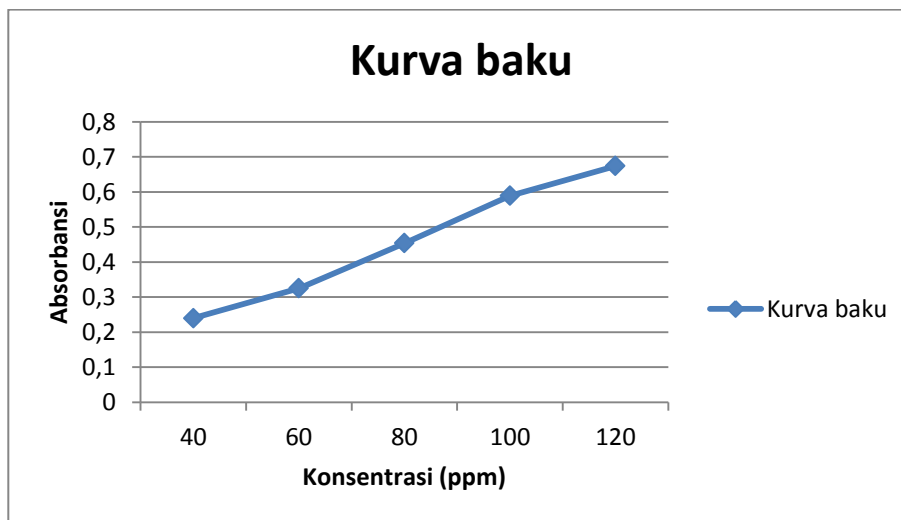
$$A = 3,6 \times 10^{-3}$$

$$B = 5,66 \times 10^{-3}$$

$$r = 0,996542$$

Persamaan regresi linier:

$$Y = 3,6 \times 10^{-3} + 5,66 \times 10^{-3} X$$

**Lampiran 8. Perhitungan kadar tramadol HCl**

Rumus kadar tramadol HCl : $\frac{\text{kadar (mg/ml)} \times \text{volum media disolusi} \times f_x}{\text{dosis tramadol HCl dalam 1 tablet}} \times 100\%$

Volum media disolusi : 1000 ml

Dosis tramadol HCl 1 tablet : 100 mg

Fx : faktor pengenceran

Formula I Replikasi 1

Waktu (menit)	Absorbansi	Kadar (mg/ml)	Kadar dalam 1000 ml	fx	Kadar (%)
5	0,036	0,00572438	5,72438	1	5,72
10	0,052	0,00855124	8,55124	1	8,55
15	0,083	0,01402827	14,02827	1	14,03
30	0,128	0,02197879	21,97879	1	21,98
60	0,208	0,03611307	36,11307	1	36,11
90	0,25	0,04353357	43,53357	1	43,53
120	0,294	0,05130742	51,30742	1	51,31
150	0,35	0,06120141	61,20141	1	61,2
180	0,377	0,06597	65,97	1	65,97
210	0,391	0,06844533	68,44533	1	68,45
240	0,416	0,07286219	72,86219	1	72,86
270	0,448	0,0785159	78,5159	1	78,52
300	0,453	0,07939929	79,39929	1	79,4
330	0,461	0,08081272	80,81272	1	80,81
360	0,473	0,08293286	82,93286	1	82,93

Formula I Replikasi 2

Waktu (menit)	Absorbansi	Kadar (mg/ml)	Kadar dalam 1000 ml	fx	Kadar (%)
5	0,033	0,00519435	5,19435	1	5,19
10	0,037	0,01226148	12,26148	1	12,26
15	0,106	0,01809187	18,09187	1	18,09
30	0,142	0,02445229	24,45229	1	24,45
60	0,282	0,04918728	49,18728	1	49,19
90	0,319	0,05572438	55,72438	1	55,72
120	0,343	0,05996466	59,96466	1	59,96
150	0,372	0,06508834	65,08834	1	65,09
180	0,409	0,07162544	71,62544	1	71,63
210	0,443	0,07763251	77,63251	1	77,63
240	0,46	0,08063604	80,63604	1	80,64
270	0,467	0,08187279	81,87279	1	81,87
300	0,469	0,08222615	82,22615	1	82,23
330	0,472	0,08275618	82,75618	1	82,76
360	0,476	0,08346289	83,46289	1	83,46

Formula I Replikasi 3

Waktu (menit)	Absorbansi	Kadar (mg/ml)	Kadar dalam 1000 ml	fx	Kadar (%)
5	0,052	0,00855124	8,55124	1	8,55
10	0,069	0,01153477	11,53477	1	11,53
15	0,079	0,01332155	13,32155	1	13,32
30	0,13	0,02233216	22,33216	1	22,33
60	0,201	0,03487633	34,87633	1	34,88
90	0,253	0,0440636	44,0636	1	44,06
120	0,28	0,04883392	48,83392	1	48,83
150	0,321	0,05607774	56,07774	1	56,08
180	0,369	0,0645583	64,5583	1	64,56
210	0,381	0,06667845	66,67845	1	66,68
240	0,397	0,0695053	69,5053	1	69,51
270	0,425	0,07445229	74,45229	1	74,45
300	0,434	0,0760424	76,0424	1	76,04
330	0,442	0,07745583	77,45583	1	77,46
360	0,445	0,07798586	77,98586	1	77,99

Rata-rata Kadar Formula I

R1	R2	R3	Rata-rata
5,72	5,19	8,55	6,49
8,55	12,26	11,53	10,78
14,03	18,09	13,32	15,15
21,98	24,45	22,33	22,92
36,11	49,19	34,88	40,06
43,53	55,72	44,06	47,77
51,31	59,96	48,83	53,36
61,20	65,09	56,08	60,79
65,97	71,63	64,56	67,4
68,45	77,63	66,68	70,92
72,86	80,64	69,51	74,37
78,52	81,87	74,45	78,28
79,40	82,23	76,04	79,22
80,81	82,76	77,46	80,34
82,93	83,46	77,99	81,46

Formulasi II Replikasi 1

Waktu (menit)	Absorbansi	Kadar (mg/ml)	Kadar dalam 1000 ml	fx	Kadar (%)
5	0,04	0,00643109	6,43109	1	6,43
10	0,053	0,00872791	8,72791	1	8,73
15	0,063	0,01049469	10,49469	1	10,49
30	0,096	0,01632508	16,32508	1	16,33
60	0,159	0,02745583	27,45583	1	27,46
90	0,21	0,03646643	36,46643	1	36,47
120	0,24	0,04176678	41,76678	1	41,77
150	0,262	0,04565371	45,65371	1	45,65
180	0,31	0,05413428	54,13428	1	54,13
210	0,313	0,05466431	54,66431	1	54,66
240	0,351	0,06137809	61,37809	1	61,38
270	0,364	0,06367491	63,67491	1	63,67
300	0,381	0,06667845	66,67845	1	66,68
330	0,393	0,06879859	68,79859	1	68,8
360	0,393	0,06879859	68,79859	1	68,8

Formulasi II Replikasi 2

Waktu (menit)	Absorbansi	Kadar (mg/ml)	Kadar dalam 1000 ml	fx	Kadar (%)
5	0,046	0,00749117	7,49117	1	7,49
10	0,052	0,00855124	8,55124	1	8,55
15	0,065	0,01084806	10,84806	1	10,85
30	0,094	0,01597173	15,97173	1	15,97
60	0,157	0,02710247	27,10247	1	27,1
90	0,198	0,03434628	34,34628	1	34,35
120	0,229	0,03982332	39,82332	1	39,82
150	0,245	0,04265018	42,65018	1	42,65
180	0,285	0,04971731	49,71731	1	49,72
210	0,292	0,05095406	50,95406	1	50,95
240	0,312	0,05448763	54,48763	1	54,49
270	0,332	0,0580212	58,0212	1	58,02
300	0,338	0,05908127	59,08127	1	59,08
330	0,349	0,06102473	61,02473	1	61,02
360	0,36	0,0629682	62,9682	1	62,97

Formula II Replikasi 3

Waktu (menit)	Absorbansi	Kadar (mg/ml)	Kadar dalam 1000 ml	fx	Kadar (%)
5	0,03	0,00466431	4,66431	1	4,66
10	0,061	0,01014134	10,14134	1	10,14
15	0,08	0,01349823	13,49823	1	13,5
30	0,1	0,0170318	17,0318	1	17,03
60	0,153	0,02639576	26,39576	1	26,4
90	0,175	0,03028269	30,28269	1	30,28
120	0,211	0,03664311	36,64311	1	36,64
150	0,247	0,04300353	43,00353	1	43
180	0,262	0,04565371	45,65371	1	45,65
210	0,294	0,05130742	51,30742	1	51,31
240	0,307	0,05360424	53,60424	1	53,61
270	0,327	0,05713781	57,13781	1	57,14
300	0,338	0,05908127	59,08127	1	59,08
330	0,347	0,06067138	60,67138	1	60,67
360	0,36	0,06296819	62,96819	1	62,97

Rata-rata Kadar Formula II

R1	R2	R3	Rata-rata
6,43	7,49	4,66	6,19
8,73	8,55	10,14	9,14
10,49	10,85	13,50	11,61
16,33	15,97	17,03	16,44
27,46	27,10	26,40	26,99
36,47	34,35	30,28	33,70
41,77	39,82	36,64	39,41
45,65	42,65	43,00	43,77
54,13	49,72	45,65	49,83
54,66	50,95	51,31	52,31
61,38	54,49	53,61	56,49
63,67	58,02	57,14	59,61
66,68	59,08	59,08	61,61
68,80	61,02	60,67	63,50
68,80	62,97	62,97	64,91

Formula III Replikasi 1

Waktu (menit)	Absorbansi	Kadar (mg/ml)	Kadar dalam 1000 ml	fx	Kadar (%)
5	0,051	0,00837456	8,37456	1	8,37
10	0,068	0,01137809	11,37809	1	11,38
15	0,096	0,01632509	16,32509	1	16,33
30	0,139	0,02392226	23,92226	1	23,93
60	0,198	0,03434629	34,34629	1	34,35
90	0,242	0,04212014	42,12014	1	42,12
120	0,29	0,05060071	50,60071	1	50,6
150	0,298	0,05201413	52,01413	1	52,01
180	0,334	0,05837456	58,37456	1	58,37
210	0,362	0,06332155	63,32155	1	63,32
240	0,371	0,06491166	64,91166	1	64,91
270	0,382	0,06685512	66,85512	1	66,86
300	0,387	0,06773852	67,73852	1	67,74
330	0,408	0,07144876	71,44876	1	71,45
360	0,409	0,07162544	71,62544	1	71,63

Formula III Replikasi 2

Waktu (menit)	Absorbansi	Kadar (mg/ml)	Kadar dalam 1000 ml	fx	Kadar (%)
5	0,032	0,00501767	5,01767	1	5,02
10	0,056	0,00925795	9,25795	1	9,26
15	0,081	0,01367491	13,67491	1	13,67
30	0,125	0,02144876	21,44876	1	21,45
60	0,187	0,03240283	32,40283	1	32,4
90	0,232	0,04035336	40,35336	1	40,35
120	0,264	0,04600707	46,00707	1	46,01
150	0,281	0,0490106	49,0106	1	49,01
180	0,325	0,05878445	58,78445	1	58,78
210	0,343	0,05996466	59,96466	1	59,96
240	0,364	0,06367491	63,67491	1	63,67
270	0,377	0,06597173	65,97173	1	65,97
300	0,396	0,06932862	69,32862	1	69,33
330	0,408	0,07144876	71,44876	1	71,45
360	0,407	0,07127208	71,27208	1	71,27

Formula III Replikasi 3

Waktu (menit)	Absorbansi	Kadar (mg/ml)	Kadar dalam 1000 ml	fx	Kadar (%)
5	0,025	0,00378092	3,78092	1	3,78
10	0,045	0,00731449	7,31449	1	7,31
15	0,067	0,01120141	11,20141	1	11,2
30	0,105	0,01791519	17,91519	1	17,92
60	0,158	0,02727915	27,27915	1	27,28
90	0,205	0,03558304	35,58304	1	35,58
120	0,229	0,03982332	39,82332	1	39,82
150	0,258	0,04621908	46,21908	1	46,22
180	0,283	0,04936396	49,36396	1	49,36
210	0,304	0,0530742	53,0742	1	53,07
240	0,322	0,05625442	56,25442	1	56,25
270	0,338	0,05908127	59,08127	1	59,08
300	0,346	0,06049469	60,49469	1	60,49
330	0,356	0,06226148	62,26148	1	62,26
360	0,369	0,0645583	64,5583	1	64,56

Rata-rata Kadar Formula III

R1	R2	R3	Rata-rata
8,37	5,02	3,78	8,78
11,38	9,26	7,31	61,73
16,33	13,67	11,20	13,73
23,93	21,45	17,92	21,10
34,35	32,4	27,28	31,34
42,12	40,35	35,58	39,35
50,60	46,01	39,82	45,48
52,01	49,01	46,22	49,08
58,37	58,78	49,36	55,50
63,32	59,96	53,07	58,78
64,91	63,67	56,25	61,73
66,86	65,97	59,08	63,97
67,74	69,33	60,49	65,85
71,45	71,45	62,26	68,39
71,63	71,27	64,56	69,06

Kontrol Replikasi 1

Waktu (menit)	Absorbansi	Kadar (mg/ml)	Kadar dalam 1000 ml	fx	Kadar (%)
5	0,393	0,068798587	68,79858657	1	68,80
10	0,436	0,07639576	76,39575972	1	76,40
15	0,456	0,079929329	79,92932862	1	79,93
30	0,479	0,083992933	83,99293286	1	83,99
60	0,503	0,088233216	88,23321555	1	88,23
90	0,514	0,090176678	90,17667845	1	90,18
120	0,605	0,106254417	106,254417	1	106,25
150	0,507	0,088939929	88,93992933	1	88,94
180	0,488	0,085583039	85,58303887	1	85,58
210	0,49	0,085936396	85,93639576	1	85,94
240	0,498	0,087349823	87,34982332	1	87,35
270	0,489	0,085759717	85,75971731	1	85,76
300	0,476	0,083462898	83,46289753	1	83,46
330	0,489	0,085759717	85,75971731	1	85,76
360	0,475	0,083286219	83,28621908	1	83,29

Kontrol Replikasi 2

Waktu (menit)	Absorbansi	Kadar (mg/ml)	Kadar dalam 1000 ml	fx	Kadar (%)
5	0,248	0,043180212	43,18021201	1	43,18
10	0,34	0,059434629	59,43462898	1	59,43
15	0,383	0,067031802	67,03180212	1	67,03
30	0,427	0,074805654	74,80565371	1	74,81
60	0,476	0,083462898	83,46289753	1	83,46
90	0,507	0,088939929	88,93992933	1	88,94
120	0,51	0,089469965	89,46996466	1	89,47
150	0,499	0,087526502	87,52650177	1	87,53
180	0,487	0,08540636	85,40636042	1	85,41
210	0,49	0,085936396	85,93639576	1	85,94
240	0,487	0,08540636	85,40636042	1	85,41
270	0,484	0,084876325	84,87632509	1	84,88
300	0,474	0,083109541	83,10954064	1	83,11
330	0,478	0,083816254	83,81625442	1	83,82
360	0,474	0,083109541	83,10954064	1	83,11

Kontrol Replikasi 3

Waktu (menit)	Absorbansi	Kadar (mg/ml)	Kadar dalam 1000 ml	fx	Kadar (%)
5	0,352	0,06155477	61,55477032	1	61,55
10	0,379	0,066325088	66,32508834	1	66,33
15	0,413	0,072332155	72,33215548	1	72,33
30	0,458	0,080282686	80,28268551	1	80,28
60	0,471	0,082579505	82,5795053	1	82,58
90	0,487	0,08540636	85,40636042	1	85,41
120	0,485	0,085053004	85,05300353	1	85,05
150	0,476	0,083462898	83,46289753	1	83,46
180	0,47	0,082402827	82,40282686	1	82,40
210	0,465	0,081519435	81,51943463	1	81,52
240	0,461	0,080812721	80,81272085	1	80,81
270	0,458	0,080282686	80,28268551	1	80,28
300	0,451	0,079045936	79,0459364	1	79,05
330	0,448	0,078515901	78,51590106	1	78,52
360	0,446	0,078162544	78,16254417	1	78,16

Rata-rata Kadar Kontrol

R1	R2	R3	Rata-rata
68,80	43,18	61,55	57,84
76,40	59,43	66,33	67,39
79,93	67,03	72,33	73,10
83,99	74,81	80,28	79,69
88,23	83,46	82,58	84,76
90,18	88,94	85,41	88,18
106,25	89,47	85,05	93,59
88,94	87,53	83,46	86,64
85,58	85,41	82,40	84,46
85,94	85,94	81,52	84,47
87,35	85,41	80,81	84,52
85,76	84,88	80,28	83,64
83,46	83,11	79,05	81,87
85,75	83,82	78,52	82,70
83,29	83,11	78,16	81,52

Persamaan regresi linier waktu vs kadar

Formula	Persamaan regresi linier	r
Formula I	$Y = 19,519 + 0,209X$	0,94315
Formula II	$Y = 13,435 + 0,166X$	0,96775
Formula III	$Y = 16,337 + 0,174X$	0,95170
Kontrol	$Y = 75,836 + 0,032X$	0,45113

Lampiran 9. Analisa kinetika pelepasan tramadol HCl

a. Analisa kinetika orde nol

Waktu (menit)	% Pelepasan			
	Formula I	Formula II	Formula III	Kontrol
5	6,49	6,19	5,72	57,84
10	10,78	9,14	9,32	67,39
15	15,15	11,61	13,73	73,1
30	22,92	16,44	21,10	79,69
60	40,06	26,99	31,34	84,76
90	47,77	33,70	39,35	88,18
120	53,36	39,41	45,48	93,59
150	60,79	43,77	49,08	86,64
180	67,40	49,83	55,5	84,46
210	70,92	52,31	58,78	84,47
240	74,37	56,49	61,73	84,52
270	78,28	59,61	63,97	83,64
300	79,22	61,61	65,85	81,87
330	80,34	63,50	68,39	82,70
360	81,46	64,91	69,06	81,52

Persamaan regresi linier waktu vs % pelepasan

Formula	Persamaan regresi linier	R
Formula I	$Y = 19,519 + 0,209X$	0,94315
Formula II	$Y = 13,435 + 0,166X$	0,96775
Formula III	$Y = 16,337 + 0,174X$	0,95170
Kontrol	$Y = 75,836 + 0,032X$	0,45113

b. Analisa kinetika orde satu

Waktu (menit)	Log % pelepasan			
	Formula I	Formula II	Formula III	Kontrol
5	0,81	0,79	0,76	1,76
10	1,03	0,96	0,97	1,83
15	1,18	1,06	1,14	1,86
30	1,36	1,22	1,32	1,90
60	1,6	1,43	1,5	1,93
90	1,68	1,53	1,59	1,95
120	1,73	1,6	1,66	1,97
150	1,78	1,64	1,69	1,94
180	1,83	1,7	1,74	1,93
210	1,85	1,72	1,77	1,93
240	1,87	1,75	1,79	1,93
270	1,89	1,78	1,81	1,92
300	1,9	1,79	1,82	1,91
330	1,9	1,8	1,83	1,92
360	1,91	1,81	1,84	1,91

Persamaan regresi linier waktu vs Log % pelepasan

Formula	Persamaan regresi linier	R
Formula I	$Y = 1,236 + 0,002X$	0,83833
Formula II	$Y = 1,123 + 0,002X$	0,87791
Formula III	$Y = 1,173 + 0,002X$	0,84641
Kontrol	$Y = 1,875 + 0,001X$	0,46195

c. Analisa kinetika model Higuchi

Akar Waktu	% pelepasan			
	Formula I	Formula II	Formula III	Kontrol
2,24	6,49	6,19	5,72	57,84
3,16	10,78	9,14	9,32	67,39
3,87	15,15	11,61	13,73	73,10
5,48	22,92	16,44	21,1	79,69
7,75	40,06	26,99	31,34	84,76
9,49	47,77	33,70	39,35	88,18
10,95	53,36	39,41	45,48	93,59
12,25	60,79	43,77	49,08	86,64
13,42	67,40	49,83	55,50	84,46
14,49	70,92	52,31	58,78	84,47
15,49	74,37	56,49	61,73	84,52
16,43	78,28	59,61	63,97	83,64
17,32	79,22	61,61	65,85	81,87
18,17	80,34	63,50	68,39	82,70
18,97	81,46	64,91	69,06	81,52

Persamaan regresi linier akar waktu vs % pelepasan

Formula	Persamaan regresi linier	R
Formula I	$Y = -0,874 + 4,755X$	0,99019
Formula II	$Y = -1,988 + 3,689X$	0,99786
Formula III	$Y = -0,409 + 3,922X$	0,99391
Kontrol	$Y = 70,305 + 0,943X$	0,60956

d. Mekanisme pelepasan Power Law

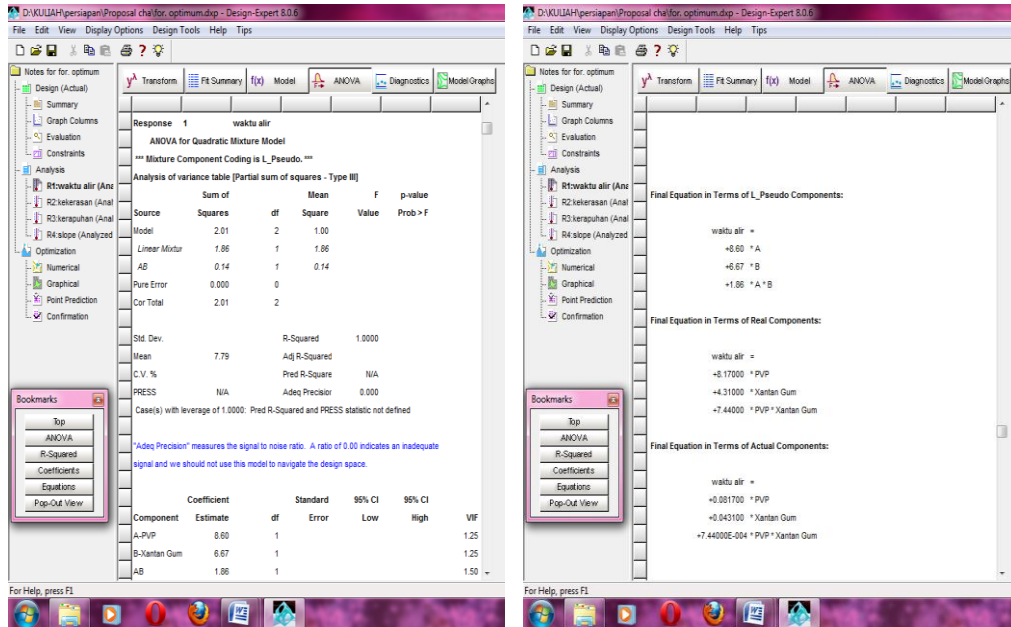
Log Waktu	Log % pelepasan			
	Formula I	Formula II	Formula III	Kontrol
0,70	0,81	0,79	0,76	1,76
1,00	1,03	0,96	0,97	1,83
1,18	1,18	1,06	1,14	1,86
1,48	1,36	1,22	1,32	1,90
1,78	1,6	1,43	1,5	1,93
1,95	1,68	1,53	1,59	1,95
2,08	1,73	1,6	1,66	1,97
2,18	1,78	1,64	1,69	1,94
2,26	1,83	1,7	1,74	1,93
2,32	1,85	1,72	1,77	1,93
2,38	1,87	1,75	1,79	1,93
2,43	1,89	1,78	1,81	1,92
2,48	1,9	1,79	1,82	1,91
2,52	1,9	1,8	1,83	1,92
2,56	1,91	1,81	1,84	1,91

Persamaan regresi linier log waktu vs log % pelepasan

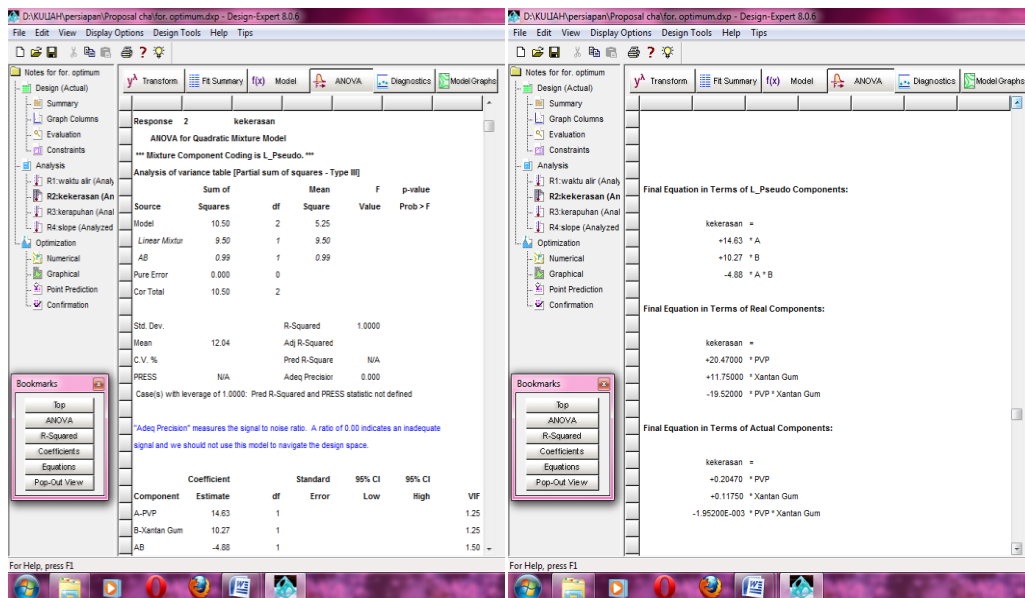
Formula	Persamaan regresi linier	R
Formula I	$Y = 0,466 + 0,592X$	0,99195
Formula II	$Y = 0,402 + 0,565X$	0,99841
Formula III	$Y = 0,430 + 0,573X$	0,99349
Kontrol	$Y = 1,769 + 0,070X$	0,79273

Lampiran 10. Penentuan formula optimum

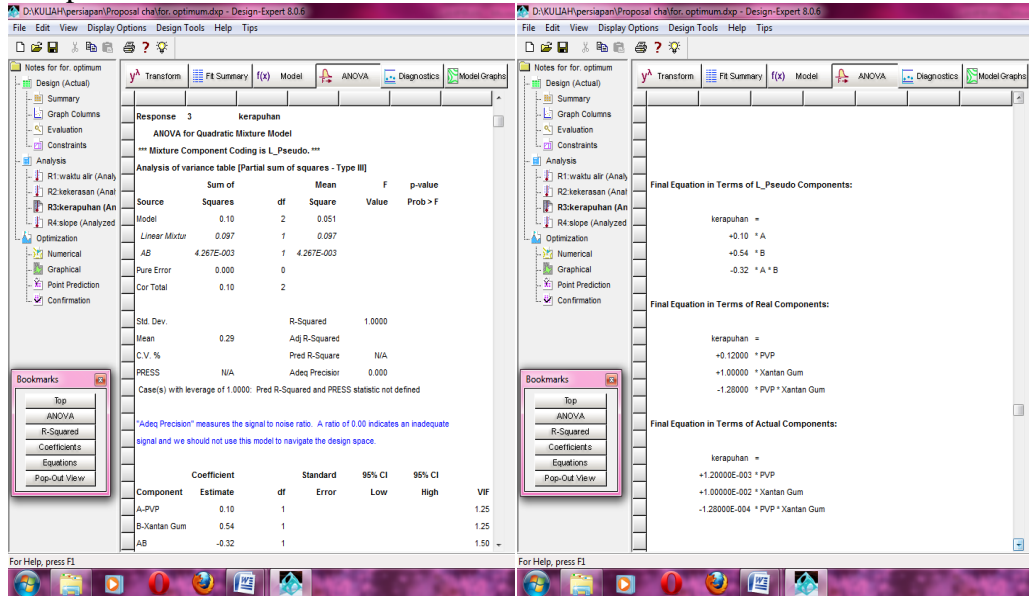
a. Waktu alir



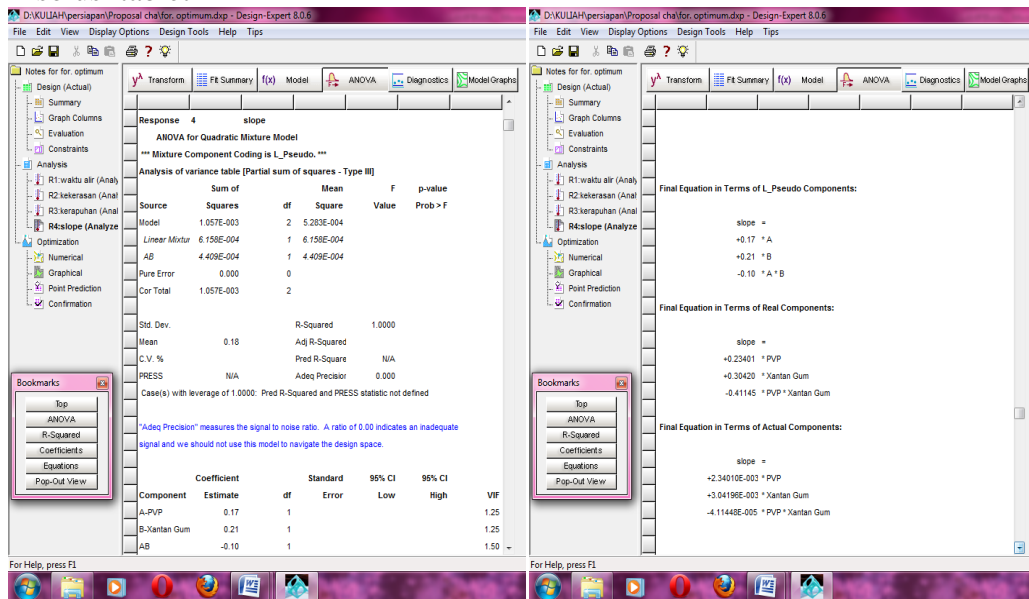
b. Kekerasan tablet



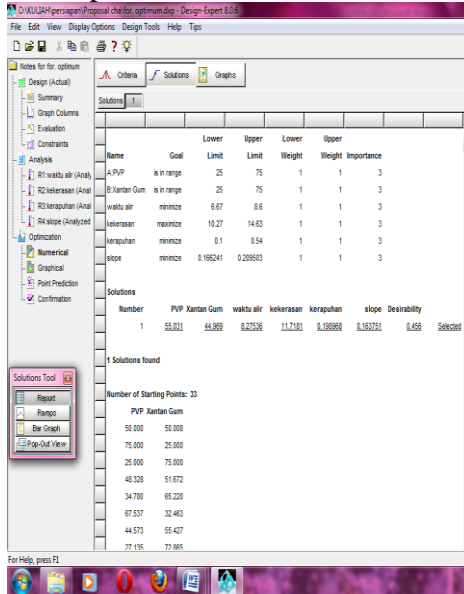
c. Kerapuhan tablet



d. Disolusi tablet



e. Titik optimum



Lampiran 11. Uji sifat fisik granul dan tablet formula optimum

a. Kandungan lembab

Bobot awal (g)	Bobot akhir (g)	Kandungan lembab (%)
2,00	1,860	7
2,00	1,867	6,6
2,00	1,854	7,3
Rat-rata		6,97
SD		0,35

b. Daya serap

Bobot awal (g)	Bobot akhir (g)	Daya serap (g/menit)	Daya serap (mg/menit)
1,0058	1,0169	0,00074	0,74
1,0087	1,0196	0,00073	0,73
1,0076	1,0189	0,00075	0,75
Rata-rata		0,00074	0,74
SD		0,00001	0,01

c. Waktu alir

Bobot granul (g)	Waktu (detik)	Bobot (gram)	Waktu (detik)
	4,25		8,5
50,00	36	100,0072	8,4
	3,7		7,4

Rata-rata	8,1
SD	0,61

d. Sudut diam

$$\text{Rumus sudut diam} = \tan \alpha = \frac{\text{jari-jari}}{\text{tinggi}}$$

Jari-jari (cm)	Tinggi (cm)	Sudut diam ($^{\circ}$)
3,3875	1,600	25,28
3,3250	1,425	23,20
3,2875	1,405	23,14
Rata-rata		23,87
SD		1,22

e. Kekerasan tablet

Replikasi	Kekerasan (kg)
1	11,5
2	12
3	11,3
Rata-rata	11,6
SD	0,36

f. Keseragaman bobot

Tablet	Bobot tablet (mg)
1	254
2	251
3	254
4	255
5	253
6	254
7	252
8	255
9	256
10	256
11	254
12	251
13	255
14	252
15	254
16	253
17	257
18	256
19	255
20	253
Rata-rata	254

SD	1,69
CV	0,66

g. Kerapuhan tablet

$$\% \text{ kerapuhan} = \frac{\text{bobot awal} - \text{bobot akhir}}{\text{bobot awal}} \times 100\%$$

Bobot awal (g)	Bobot akhir (g)	% kerapuhan
4,8553	4,8477	0,16
5,1063	5,0955	0,21
4,9678	4,9588	0,18
Rata-rata		0,18
SD		0,03

h. Swelling

$$\text{Swelling index} = \frac{\text{bobot akhir} - \text{bobot awal}}{\text{bobot awal}}$$

Bobot awal: 252,9

Bobot akhir: 716,4

$$\text{Swelling index} = \frac{716,4 - 252,9}{252,9} = 1,83$$

i. Disolusi

Replikasi 1

Waktu (menit)	Absorbansi	Kadar (mg/ml)	Kadar dalam 1000 ml	fx	Kadar (%)
5	0,058	0,009611307	9,61130742	1	9,61
10	0,07	0,011731449	11,73144876	1	11,73
15	0,081	0,013674912	13,67491166	1	13,67
30	0,124	0,021272085	21,27208481	1	21,27
60	0,189	0,032756184	32,75618375	1	32,76
90	0,223	0,038763251	38,76325088	1	38,76
120	0,268	0,046713781	46,71378092	1	46,71
150	0,28	0,048833922	48,83392226	1	48,83
180	0,281	0,049010601	49,01060071	1	49,01
210	0,303	0,052897527	52,8975265	1	52,9
240	0,321	0,056077739	56,07773852	1	56,08
270	0,354	0,061908127	61,90812721	1	61,91
300	0,368	0,064381625	64,38162544	1	64,38
330	0,381	0,066678445	66,67844523	1	66,68
360	0,396	0,069328622	69,32862191	1	69,33

Replikasi 2

Waktu (menit)	Absorbansi	Kadar (mg/ml)	Kadar dalam 1000 ml	fx	Kadar (%)
5	0,057	0,009434629	9,434628975	1	9,43
10	0,074	0,012438163	12,43816254	1	12,44
15	0,084	0,014204947	14,204947	1	14,2
30	0,124	0,021272085	21,27208481	1	21,27
60	0,185	0,03204947	32,04946996	1	32,05
90	0,235	0,040883392	40,88339223	1	40,88
120	0,278	0,048480565	48,48056537	1	48,48
150	0,307	0,05360424	53,60424028	1	53,6
180	0,308	0,053780919	53,78091873	1	53,78
210	0,314	0,054840989	54,8409894	1	54,85
240	0,336	0,058727915	58,72791519	1	58,73
270	0,359	0,062791519	62,79151943	1	62,79
300	0,374	0,065441696	65,44169611	1	65,44
330	0,389	0,068091873	68,09187279	1	68,09
360	0,393	0,068798587	68,79858657	1	68,8

Replikasi 3

Waktu (menit)	Absorbansi	Kadar (mg/ml)	Kadar dalam 1000 ml	fx	Kadar (%)
5	0,056	0,009257951	9,25795053	1	9,26
10	0,069	0,01155477	11,55477032	1	11,55
15	0,081	0,013674912	13,67491166	1	13,67
30	0,131	0,022508834	22,50883392	1	22,51
60	0,179	0,030989399	30,98939929	1	30,99
90	0,24	0,041766784	41,76678445	1	41,77
120	0,271	0,047243816	47,24381625	1	47,24
150	0,29	0,050600707	50,60070671	1	50,6
180	0,296	0,051660777	51,66077739	1	51,66
210	0,299	0,052190813	52,19081272	1	52,19
240	0,324	0,056607774	56,60777385	1	56,61
270	0,348	0,060848057	60,84805654	1	60,85
300	0,367	0,064204947	64,204947	1	64,2
330	0,382	0,066855124	66,85512367	1	66,86
360	0,387	0,067738516	67,7385159	1	67,74

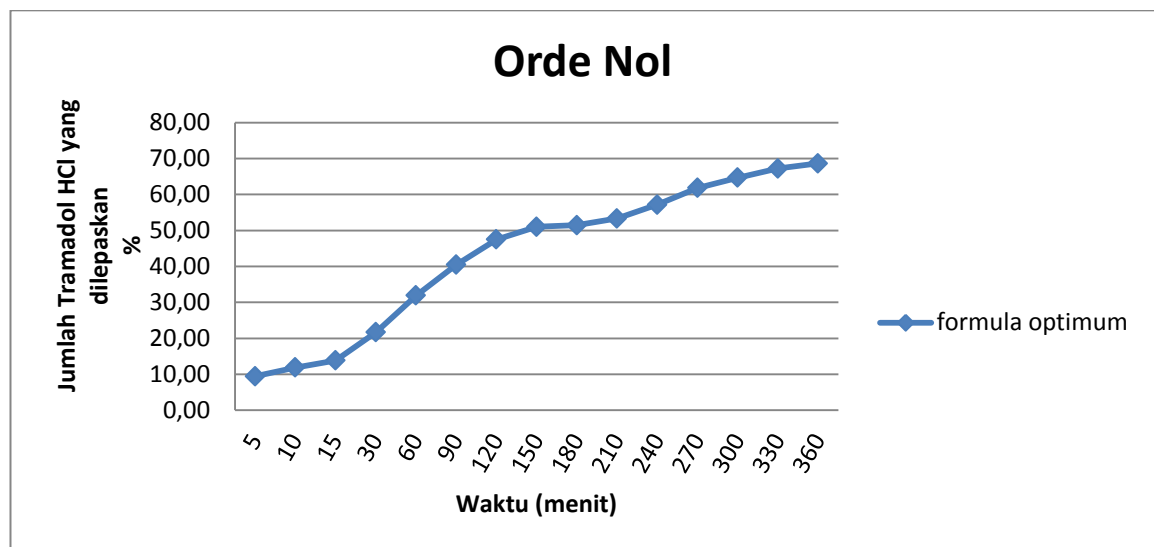
Rata-rata kadar formula optimum

Waktu (menit)	Replikasi 1	Replikasi 2	Replikasi 3	Rata-rata
5	9,61	9,43	9,26	9,43
10	11,73	12,44	11,55	11,91
15	13,67	14,2	13,67	13,85
30	21,27	21,27	22,51	21,68
60	32,76	32,05	30,99	31,93
90	38,76	40,88	41,77	40,47
120	46,71	48,48	47,24	47,48
150	48,83	53,6	50,6	51,01
180	49,01	53,78	51,66	51,48
210	52,9	54,85	52,19	53,31
240	56,08	58,73	56,61	57,14
270	61,91	62,79	60,85	61,85
300	64,38	65,44	64,2	64,67
330	66,68	68,09	66,86	67,21
360	69,33	68,8	67,74	68,62

Lampiran 12. Analisa kinetika pelepasan tramadol HCl formula optimum

a. Analisa kinetika orde nol

Waktu (menit)	% pelepasan
5	9,43
10	11,91
15	13,85
30	21,68
60	31,93
90	40,47
120	47,48
150	51,01
180	51,48
210	53,31
240	57,14
270	61,85
300	64,67
330	67,21
360	68,62



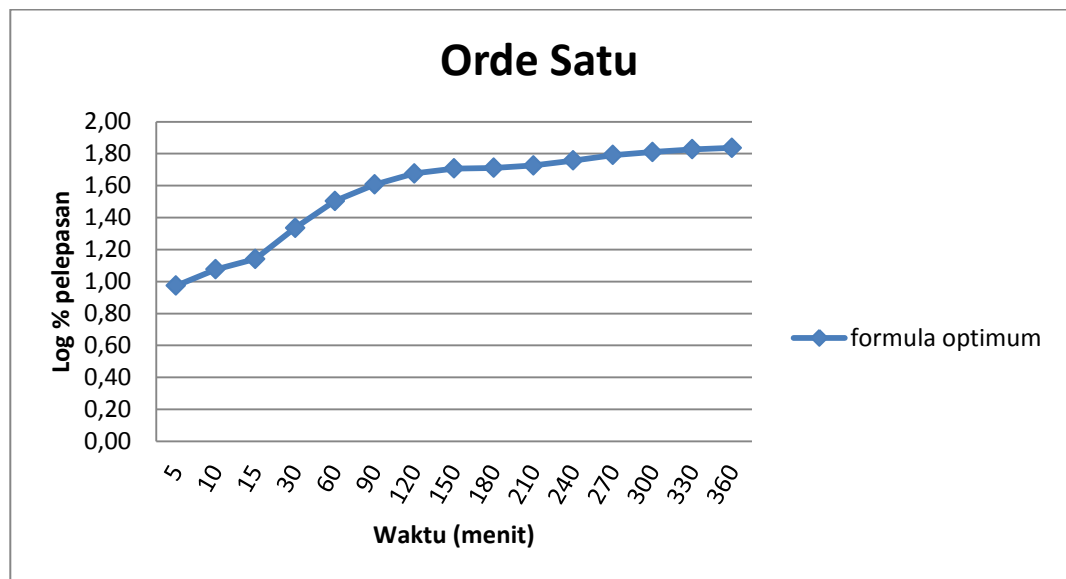
Persamaan regresi linier waktu vs % pelepasan:

$$Y = 17,946 + 0,162X$$

$$R = 0,95349$$

b. Analisa kinetika orde satu

Waktu (menit)	log % pelepasan
5	0,97
10	1,08
15	1,14
30	1,34
60	1,50
90	1,61
120	1,68
150	1,71
180	1,71
210	1,73
240	1,76
270	1,79
300	1,81
330	1,83
360	1,84



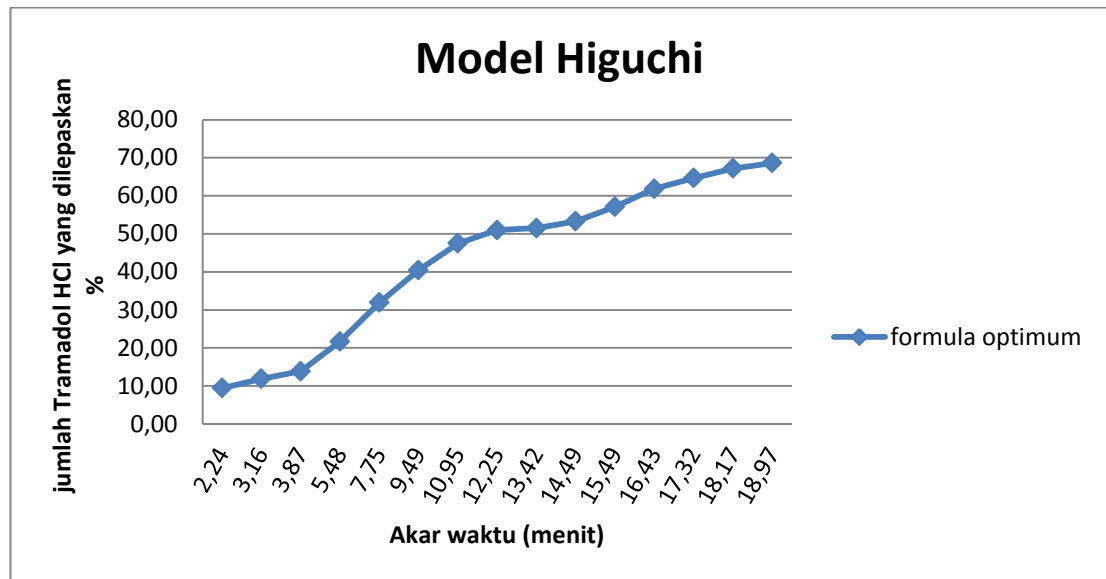
Persamaan regresi linier waktu vs log % pelepasan:

$$Y = 1,238 + 0,002X$$

$$R = 0,87141$$

c. Analisa kinetika model Higuchi

Akar Waktu	% pelepasan
2,24	9,43
3,16	11,91
3,87	13,85
5,48	21,68
7,75	31,93
9,49	40,47
10,95	47,48
12,25	51,01
13,42	51,48
14,49	53,31
15,49	57,14
16,43	61,85
17,32	64,67
18,17	67,21
18,97	68,62



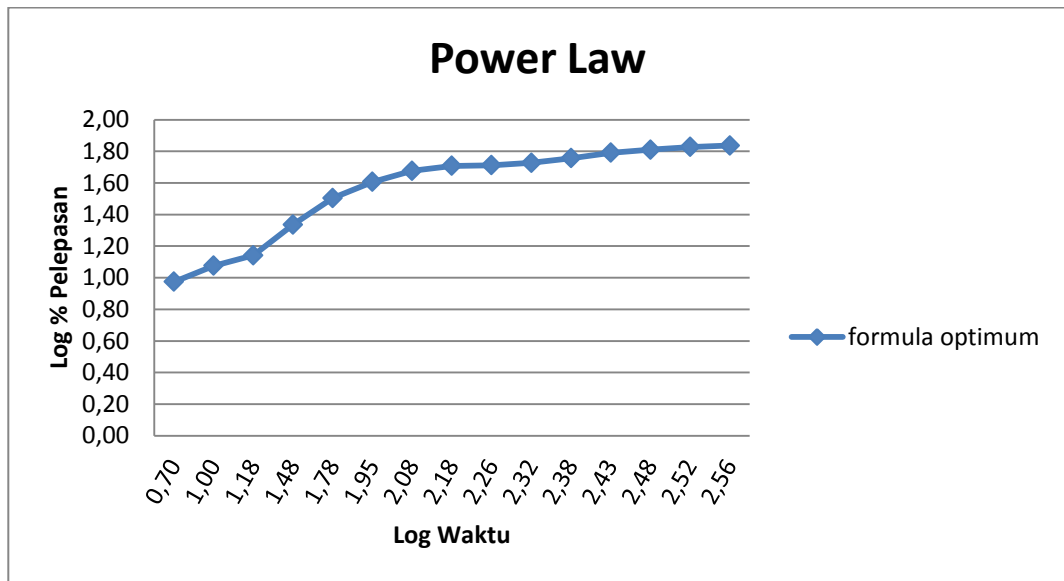
Persamaan regresi linier akar waktu vs % pelepasan:

$$Y = 2,560 + 3,621X$$

$$R = 0,99282$$

d. Mekanisme pelepasan Power Law

Log waktu	Log % pelepasan
0,70	0,97
1,00	1,08
1,18	1,14
1,48	1,34
1,78	1,50
1,95	1,61
2,08	1,68
2,18	1,71
2,26	1,71
2,32	1,73
2,38	1,76
2,43	1,79
2,48	1,81
2,52	1,83
2,56	1,84



Persamaan regresi linier log waktu vs log % pelepasan:

$$Y = 0,613 + 0,488X$$

$$R = 0,99556$$

Lampiran 13. Analisa statistika uji t

a. Waktu alir

Descriptives

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
waktu alir	6	7,40	8,50	8,1900	,39714
Valid N (listwise)	6				

NPar Tests

One-Sample Kolmogorov-Smirnov Test

		waktu alir
N		6
Normal Parameters ^{a,b}	Mean	8,1900
	Std. Deviation	,39714
Most Extreme Differences	Absolute	,423
	Positive	,218
	Negative	-,423
Kolmogorov-Smirnov Z		1,036
Asymp. Sig. (2-tailed)		,233

a. Test distribution is Normal.

b. Calculated from data.

T-Test

Group Statistics

waktu alir		N	Mean	Std. Deviation	Std. Error Mean
waktu	prediksi	3	8,2800	,00000	,00000
alir	percobaan	3	8,1000	,60828	,35119

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
waktu alir	Equal variances assumed	15,077	,018	,513	4	,635	,18000	,35119	- ,79506	1,15506
	Equal variances not assumed			,513	2,000	,659	,18000	,35119	- 1,33104	1,69104

b. Kekerasan
Descriptives

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
kekerasan tablet	6	11,30	12,00	11,6600	,23732
Valid N (listwise)	6				

NPar Tests**One-Sample Kolmogorov-Smirnov Test**

		kekerasan tablet
N		6
Normal Parameters ^{a,b}	Mean	11,6600
	Std. Deviation	,23732
Most Extreme Differences	Absolute	,266
	Positive	,234
	Negative	-,266
Kolmogorov-Smirnov Z		,653
Asymp. Sig. (2-tailed)		,788

a. Test distribution is Normal.

b. Calculated from data.

T-Test**Group Statistics**

kekerasan tablet		N	Mean	Std. Deviation	Std. Error Mean
kekerasan di prediksi		3	11,7200	,00000	,00000
tablet me percobaan nsi on1		3	11,6000	,36056	,20817

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
kekerasan tablet	Equal variances assumed	9,143	,039	,576	4	,595	,12000	,20817	-,45796	,69796
	Equal variances not assumed			,576	2,000	,623	,12000	,20817	-,77567	1,01567

c. Kerapuhan
Descriptives

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
kerapuhan tablet	6	,16	,21	,1915	,01826
Valid N (listwise)	6				

NPar Tests**One-Sample Kolmogorov-Smirnov Test**

		kerapuhan tablet
N		6
Normal Parameters ^{a,b}	Mean	,1915
	Std. Deviation	,01826
Most Extreme Differences	Absolute	,325
	Positive	,155
	Negative	-,325
Kolmogorov-Smirnov Z		,797
Asymp. Sig. (2-tailed)		,549

a. Test distribution is Normal.

b. Calculated from data.

T-Test**Group Statistics**

kerapuhan tablet		N	Mean	Std. Deviation	Std. Error Mean
kerapuhan tablet	dim prediksi	3	,1997	,00060	,00035
	ens percobaan	3	,1833	,02517	,01453
	ion				
	1				

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
kerapuhan tablet	Equal variances assumed	5,647	,076	1,123	4	,324	,01632	,01453	-,02403	,05667
	Equal variances not assumed			1,123	2,002	,378	,01632	,01453	-,04615	,07879

d. Disolusi
Descriptives

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
disolusi tablet Valid N (listwise)	6	,159172	,163859	,16265175	,001914040

NPar Tests**One-Sample Kolmogorov-Smirnov Test**

		disolusi tablet
N		6
Normal Parameters ^{a,b}	Mean	,16265175
	Std. Deviation	,001914040
Most Extreme Differences	Absolute	,385
	Positive	,264
	Negative	-,385
Kolmogorov-Smirnov Z		,943
Asymp. Sig. (2-tailed)		,337

a. Test distribution is Normal.

b. Calculated from data.

T-Test**Group Statistics**

disolusi tablet		N	Mean	Std. Deviation	Std. Error Mean
disolusi	d prediksi	3	,16375700	,000000000	,000000000
tablet	i percobaan	3	,16154650	,002343959	,001353285
	m				
	e				
	n				
	s				
	i				
	o				
	n				
	l				

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
disolusi tablet	Equal variances assumed	4,329	,106	1,633	4	,178	,002210500	,001353285	-,001546823	,005967823
	Equal variances not assumed			1,633	2,000	,244	,002210500	,001353285	-,003612217	,008033217

Lampiran 14. Foto granul dan tablet



Granul formula I



Granul Formula II



Granul formula III



Granul kontrol



Tablet formula I



Tablet formula II



Tablet formula III



Tablet kontrol



Granul formula optimum



Tablet formula optimum

Lampiran 15. Foto alat-alat



Friabilator tester



Hardnes tester



Disolusi tester



Alat uji kekuatan mukoadhesif



Moisture balance



Spectrophotometer UV-VIS