BAB V

PENUTUP

A. Kesimpulan

Komponen *effervescent* dan HPMC K15M memberikan pengaruh terhadap *floating lag time* dan pelepasan obat. Komponen *effervescent* berperan lebih dominan terhadap penurunan *floating lag time*. Peningkatan HPMC K15M akan menurunkan jumlah obat yang dilepaskan. Interaksi HPMC K15M dan komponen *effervescent* akan meningkatkan kemampuan mengapung.

Berdasarkan pemeriksaan menggunakan *simplex lattice design* didapatkan formula optimum dengan proporsi HPMC K15M 108 mg dan komponen *effervescent* 32 mg. Persamaan *floating lag time*, jumlah obat yang dilepaskan serta *dissolution efficiency* menyatakan bahwa persamaan telah terverifikasi.

A. Saran

Perlu dilakukan study lanjutan mengenai pengaruh HPMC K15M dan komponen *effervescent* terhadap *floating lag time* dan pelepasan obat dengan rentang formula yang lebih lebar menggunakan metode *factorial design*.

DAFTAR PUSTAKA

Adibkia K, Sanaz H, Yousef J.2011. Drug release kinetics and physicochemical characteristic of drug delivery system. *University of Toronto* 8:891-903

Anonim. 1979. Farmakope Indonesia Edisi ke-III. Departemen Kesehatan RI. Hlm 7.

Anonim. 1995. Farmakope Indonesia. Edisi ke-IV. Departemen Kesehatan RI. Hlm 55, 515, 751, 771, 1083.

Amit K, Jain, Hatila Usmahankar. 2011. A review on floating drug delivery system. *International Journal Pharmaceutical and Research*.2: (1-6)

Amstrong NA, James KC.1986. *Pharmaceutical Experimental Design and Interpretation*. London: Taylor and Francis Ltd. Hlm 83-91.

Anggraini, Deni. 2011. Formulasi dan Uji in Vitro granul mukoadhesif salbutamol sulfat menggunakan kombinasi polimer carbopol 940P dan hidroksipropil selulosa[Skripsi]. Univesitas Andalas : Padang

Archiyanto, Achsar Indiwan. 2012. Optimasi Tablet Lepas Lambat Kaptropil dengan Matriks Methocel K15M dan Avicel pH 102 sebagai *Filler* secara *Simplex Lattice Design.* Surakarta : Universitas Setia Budi

Bolton S, Bon C. 2004. *Pharmaceutical Statistics : Practical and Clinical Applications* 4th Ed. New York : Marcel Dekker Inc. Hlm 265-270, 508-512.

Choiri S. 2014, Sulaiman TNS, Kuncahyo I. Optimation and accessing the Influence of xanthan gum, effervescent component, and hardness on floatation behavior and drug release of gasro-floating captropil tablet. *Indonesian J.Pharm*. Vol 25 No. 4 : 255-264.

Costa P, Lobo JMS. 2001. Modeling and comparison of dissolution profiles : review. *Eur. J. Pharm. Sci*. 13 : 123-133

Dantoriya Sanjay , Govid Bhandari, Suresh Chandra. 2013. The Recent Developments on Gastric Floating Drug Delivery System : On Review. *World Journal of Pharmaceutical Research*. Volume 2, Issue 6, 2034 -2062

Fudholi A. 2013. *Dissolusi dan pelepasan obat in vitro.* Yogyakarta : Pustaka Pelajar. Hlm 111-112, 142-145

Gandjar IG, Rohman A. 2009. Kimia Farmasi Analisis. Yogyakarta : Pustaka Pelajar. Hlm 466 – 497.

Gaur A, Shah H. P. 2010. Research article formulation, development, and evaluation of floating tablet of metformin hydrochloride using optimization of gas generating agent. *IJCPRR* Vol 1 ; Issue 3

Grassi M., Grassi G. 2005. Mathematical modeling controlled drug delivery : matrix system. *Current Drug Delivery*. 2:97-116

Jaimini M, Rana AC, Tanwar YS. 2007. Formulation and evaluation of famotidine floating tablets. *Cur. Drug. Del*. 4 : 51-55.

Kumar V, Shakti Dwivedi. Floating Drug Delivery System – A Concept of Gastroretentive Dosage Form. *IJRPBS*. Vol. 2 ; Issue 4

Lowman A, Peppas NA.1999. Encyclopedia of Controlled Drug Delivery. Vol 1. *Canada: A Whiley – Interscience Publicaton.* Hlm 405

Mahendar G, Jaya S. 2012. Formulation and evaluation of floating salbutamol sulphate. *International Research Journal of Pharmaceutical Applied Science.* 2:97-109

Moffat AC, Osselton MD, Widdop B. 2011. *Clarke's Analysis of Drug and Poison* 4th Ed. London : Pharmaceutical Press. 2038-2039

Narendra, C. Srinath, M.S. Babu, G. 2006. Optimization of Bilayer Floating Tablet Containing Metoprolol Tartrate as a Model Drug for Gastric Retention. *AAPS PharmSciTech*. 7(2): *Article* 34. DOI: 10.1208/pt070234.

Nodhochi A, Shaista R, Patel P, Kofi AA. 2012. The role of oral controlled release matrix tablets in drug delivery system. *BioImpact*. 2:175-187

Oktora, Lusia. 2010. Optimasi formula floating tablet kaptropil-sistem effervescent menggunakan desain factorial. *Indonesia J.Pharm*

Panjaitan, RD. 2011. Pengaruh konsentrasi natrium bikarbonat dan konsentrasi manitol terhdanadap mutu tablet effervescent rosella [Skripsi]. Universitas Sumatera Utara

Pratiwi, N R .2008. Karakteristik sediaan [Skripsi].FMIPA UI.Depok

Pratiwi, M. Hadiseowigyo L. 2010. Optimasi formula tablet lepas lambat kaptropil menggunakan metode design factorial. *Maj. Farm. Indonesia.* 21(4), 285-295.

Rashati D, Lusia O.R. 2009. Optimasi komposisi kitosan dan natrium bikarbonat pada formulasi tablet lepas lambat teofilin sistem mengapung menggunakan desain faktorial[Skripsi]. Jember : Fakultas Farmasi Universitas Negri Jember

Ravikumar KG, O.G Vinaya, U. Santhikrishna. Development of floating matrix tablets of salbutamol sulphate and study of drug release kinetics. *International Journal of Research in Pharmaceutical and Biomedical Sciences.* 2229-3701

Riyanti, Dwi. 2013. Formulasi tablet salbutamol sulfat sistem mukoadhesif menggunakan kombinasi polimer kitosan dan CMC Na sebagai matriks mukoadhesif[Skripsi]. Surakarta : Univeristas Setia Budi

Rowe RC, Sheskey PJ, Quinn ME. 2009. *Handbook of Pharmaceuticals Exipient* 9th Ed. London. Pharmaceutical Press. Hlm 129-135, 181-183, 581-585.

Shaha S.H, J. K Pattel, K. Pundharikaksudhu. 2009. An overview Gastroretentive Drug Delivery System. *Asian Journal of Pharmaceutical Sciences.* 4:65-80

Sinko JP. 2011. *Martin's Physical Pharmacy and Pharmaceutical Science*. Ed ke-5. Lippincott: Williams and Wilkins. Hlm 557

Siregar CJP, Wikarsa S. 2010.*Teknologi Farmasi Sediaan Tablet Dasar-Dasar Praktis,* Cetakan 2. Jakarta : EGC. Hlm 33-34, 417, 273, 257.

Sulaiman TNS, Syukri Y, Utami R. 2007. Profil pelepasan propranolol HCL dari tablet lepas lambat dengan sistem floating menggunakan matriks Methocel K15M. *Maj. Farm. Indonesia*. 18(1) : 48-55.

Sulaiman TNS, Fudholi A, Nugroho AK. 2011. Optimasi formula tablet gastroretentive ranitidine HCl dengan sistem floating. *Maj. Farm. Indonesia*. 22(2):106-114.

Tan HT, Rahardja. 1978. *Obat – Obat Penting edisi IV*. Jakarta: Departemen Kesehatan Republik Indonesia. Hal 637

Tiwari SB, Rajabi-Siahboomi A. 2008. Modulation of Drug Release From Hydrophilic Matrices. *Pharmaceutical Technology Europe*

LAMPIRAN

Lampiran 1. Sertifikat Analisis Salbutamol Sulfat

SUPRIYA LIFESCIENCE LTD.
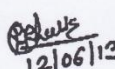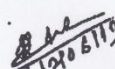(Formerly known as Supriya Chemicals)

CERTIFICATE OF ANALYSIS
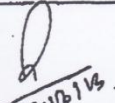
Name	:	Salbutamol Sulphate BP		
Batch No.	:	SLL/SS/0613030	A.R.Number	: SLL/QC/FP/13/0401
Batch Size	:	225.00 kgs	Dispatch Quantity	: 02 x 25 kg = 50 kg
Mian Ganring Date	:	April-2013	Expiry Date	: Mar-2018

Tests	Specification & Limits	Results
Description	White or almost white crystalline powder	White crystalline powder
Solubility	Freely soluble in water,very slightly soluble in ethanol(96%) and in methylene chloride	Freely soluble in water,very slightly soluble in ethanol(96%) and in methylene chloride
Identification		
A) UV Absorption	Specific absorbance at 276 nm, should be range within 55 to 64	Absorbance is 59
B) Infrared Absorption	The infra red absorption spectrum should be concordant with the reference spectrum of salbutamol sulphate.	The infra red absorption spectrum is concordant with the reference spectrum of salbutamol sulphate
C) TLC	The principal spot in the chromatogram obtained with the test solution should be similar in position, colour and size to the principal spot in the chromatogram obtained with the reference solution	The principal spot in the chromatogram obtained with the test solution is similar in position, colour and size to the principal spot in the chromatogram obtained with the reference solution
D) Colour Test	Orange-red colour develops	Orange-red colour develops
E) Sulfate Test	It give reaction of sulfate	It give reaction of sulfate
Appearance of solution	Solution should be clear and not more coloured than BY6	Solution is clear and not more coloured than BY6
Optical rotation	-0.10° to +0.10°	-0.0003°
Acidity or alkalinity	Not more than 0.4ml of 0.01M HCl required	0.20ml of 0.01M HCl is required
Related substances		
Impurity D	Not more than 0.3%	Not detected
Impurity F	Not more than 0.3%	Not detected
Impurity C	Not more than 0.2%	Not detected
Impurity N	Not more than 0.2%	Not detected
Impurity O	Not more than 0.3%	Not detected
Unspecified impurity	Not more than 0.10%	0.07%
Total Impurities	Not more than 0.9 %	0.07%
Boron	Not more than 50ppm	31 ppm
Loss on drying	Not more than 0.5%	0.12%
Sulphate Ash	Not more than 0.1%	0.05%
Assay (on dried basis)	98.0% to 101.0%	99.78%
Residual Solvents		
Methanol	Not more than 3000 ppm	999 ppm
Acetone	Not more than 5000 ppm	Not detected
Methylene Dichloride	Not more than 600 ppm	Not detected
Ethyl Acetate	Not more than 5000 ppm	Not detected

Date of Release : 12/06/2013

REMARKS: Salbutamol sulphate complies /-does-not-comply with respect to above mentioned test as per BP 2013 Specification

12/06/13

PREPARED BY

REVIEWED BY

APPROVED BY

Customer Name: Shinkea Drug Co. Ltd.

Ref.SOP.No.SOP/SLL/QC/065

SQC/F/108-02

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Tel : +91 22 40332727 / 66942507   Fax : +91 22 26860011
E-mail : supriya@supriyalifescience.com   Website : www.supriyalifescience.com
Factory : Plot No. A-5/2, Lote Parshuram Industrial Area, M.I.D.C., Tal. - Khed, Dist. - Ratnagiri, Pin : 415 722, Maharashtra, India.
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E-mail : factory@supriyalifescience.com

GOVT. RECOGNISED EXPORT HOUSE

Lampiran 2. Sertifikat Analisis HPMC K15M

DOW
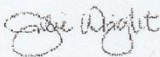
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Certificate 6392371      The Dow Chemical Company          Page    1
Date: 05.12.2013         Certificate of Analysis      Shipped: 05.12.2013
File Copy
DOW CHEMICAL PACIFIC LIMITED            Fax: COA ARCHIVE
SHANGHAI PUDONG AIRPORT
SHANGHAI                 SG 201202       CHINA
Cust P.O.: 7000033349 101241581 X                Dlvy Note: 72310223 20
Material:  METHOCEL* K15M Premium
           Hydroxypropyl Methylcellulose         Spec:   00053984-S
Batch:    2F28012N04    Mfgd:    28.06.2013   Retest Date:  27.06.2018
Ship from: THE DOW CHEMICAL COMPANY      BAY CITY     MI UNITED STATES
```

It is hereby certified the material indicated above has been manufactured in accordance with the FDA cGMPs, Kosher guidelines, was inspected and tested in accordance with the conditions and the requirements of current USP, EP and JP for Hypromellose as well as the current specific purity criteria for the food additive Hydroxypropyl Methyl Cellulose (E464) and unless agreed otherwise conforms in all respects to the specification relevant thereto.

Feature	Units	Results 2F28012N04	Limits Minimum	Maximum	Method
Apparent Viscosity Brookfield 2% in water, @ 20degC	mPa.s	17,867	13,275	24,780	Current USP/EP/JP
Loss on Drying	%	3.3	----	5.0	Current USP/EP/JP
Residue on Ignition	%	0.5	----	1.5	Current USP/JP
Ash, Sulfated	%	0.5	----	1.5	Current EP
pH, 2% in Water	-	6.1	5.0	8.0	Current USP/EP/JP
Assay, Methoxyl	%	22.7	19.0	24.0	Current USP/EP/JP
Assay, Hydroxypropoxy	%	10.2	7.0	12.0	Current USP/EP/JP
Appearance Opalescence		Passes			Current EP
Appearance solution color		Passes			Current EP

This Batch, based on audit testing and process control, is certified to be NMT 20 ppm heavy metals (as Pb) and also meets all specification requirements for harmonized identification tests, residual solvents and microbiological limits.
Batch (Lot) Number manufacture location (char 7-8): 2N = Midland, MI; ND = Bomlitz,Germany; 24 = Plaquemine, LA; 07 = Stade, Germany

Julie Wright, FORTEFIBER, METHOCEL Quality Systems Specialist
For inquiries please contact Customer Service at 1-800-232-2436 (USA).

* Trademark of The Dow Chemical Company

Lampiran 3. Data pengujian sifat fisik granul

a. Kandungan Lembab (%)

Replikasi	Kandungan Lembab (%)		
	Formula 1	Formula 2	Formula 3
I	5,30	4,60	5,80
II	4,80	4,40	5,30
III	5,00	5,40	6,00
Rata – rata	5,03	4,80	5,70
SD	0,25	0,53	0,29

b. Waktu alir (detik)

Replikasi	Waktu Alir (detik)		
	Formula 1	Formula 2	Formula 3
I	15,40	16,00	16,62
II	14,90	16,60	17,4
III	14,50	15,30	17,26
Rata – rata	14,93	15,96	16,27
SD	0,45	0,650	0,621

c. Sudut diam (^{o})

Replikasi	Sudut Diam (^{o})		
	Formula 1	Formula 2	Formula 3
I	27,69	29,16	29,9
II	27,36	29,88	25,05
III	30,52	29,50	28,61
Rata – rata	28,52	29,50	27,85
SD	1,74	0,36	2,51

Lampiran 4. Data Pengujian sifat fisik tablet

a. Keseragaman Bobot

Tablet	bobot tablet		
	Formula 1	Formula 2	Formula 3
1	203	203	198
2	204	204	204
3	203	190	203
4	202	204	203
5	203	203	198
6	203	202	202
7	204	203	204
8	204	203	201
9	195	203	200
10	203	195	204
11	202	204	202
12	201	204	203
13	202	205	203
14	204	203	203
15	198	202	204
16	202	201	203
17	202	202	204
18	202	204	203
19	204	201	205
20	200	202	204
Rata – rata	202,05	201,9	202,55
SD	2,23	3,47	1,93
CV	1,11	1,72	0,95

Perhitungan rentang keseragaman bobot

Formula	Kolom A		kolom B	
	minimal	Maksimal	minimal	Maksimal
1	186,89	217,20	171,74	232,18
2	186,75	217,04	171,61	232,18
3	187,35	217,74	172,16	232,93

Keterangan :

Kolom A : penyimpangan 7,5% bobot rata-rata tablet

Kolom B : penyimpangan 15% bobot rata-rata tablet

Perhitungan :

Rentang minimal penyimpangan kolom A :

$$= rata - rata\ bobot\ tablet\ F1 - \left(\frac{7,5}{100}\ x\ rata - rata\ bobot\ F1\right)$$

$$= 202,05 - \left(\frac{7,5}{100}\ x\ 202,05\right)$$

$$= 186,8963$$

Rentang maksimal penyimpangan kolom A :

$$= rata - rata\ bobot\ tablet\ F1 + \left(\frac{7,5}{100}\ x\ rata - rata\ bobot\ F1\right)$$

$$= 202,05 + \left(\frac{7,5}{100}\ x\ 202,05\right)$$

$$= 217,2038$$

b. Kekerasan Tablet

Replikasi	Kekerasan (Kg)		
	formula 1	formula 2	formula 3
I	9	7	9
II	8	7	7
III	9	9,5	8
IV	7,5	8	9,5
V	9	9	8
VI	10	8	9
Rata-rata	8,75	8,08	8,41
SD	0,88	0,66	0,91

c. Kerapuhan Tablet

Formula	Bobot awal	Bobot akhir	% kerapuhan	Rata – rata	SD
1	4.029	4.018	0.273		
1	4.05	4.039	0.272	0.239513	0.056816
1	4.025	4.018	0.174		
2	4.002	3.994	0.200		
2	4.11	4.103	0.170	0.173256	0.025303
2	4.012	4.006	0.150		
3	4.025	4.015	0.248		
3	4.003	3.995	0.200	0.207476	0.037741
3	4.02	4.013	0.174		

Perhitungan kerapuhan tablet

$$= \frac{bobot\ awal - bobot\ akhir\ tablet}{bobot\ awal\ tablet} x 100\%$$

d. *Floating lag time*

Replikasi	floating lag time		
	formula 1	formula 2	formula 3
I	12,00	8,63	4,87
II	19,23	10,59	4,23
III	12,00	6,00	4,65
Rata-rata	14,41	8,41	4,58
SD	4,17	2,30	0,33

e. Penetapan kadar

Formula 1

Replikasi	Serapan	Kadar (µg/ml)	Faktor pengenceran	kadar terukur (mg)
1	0,475	9,06	25	11,33
2	0,490	9,34	25	11,67
3	0,504	9,60	25	12,00
		Rata – rata		11,67
		SD		0,33

Formula 2

Replikasi	Serapan	Kadar (µg/ml)	Faktor pengenceran	kadar terukur (mg)
1	0,472	9,01	25	11,26
2	0,474	9,05	25	11,31
3	0,500	9,52	25	11,91
Rata – rata				11.48
SD				0.36

Formula 3

Replikasi	Serapan	Kadar (µg/ml)	Faktor pengenceran	kadar terukur (mg)
1	0,486	9,27	25	11,58
2	0,489	9,32	25	11,65
3	0,433	8,29	25	10,36
Rata – rata				11,20
SD				0,73

Kadar = (serapan + 0,0171)/0,0543

$$Kadar\ terukur = \frac{kadar}{1000} \: x \: faktor \: pembuatan \: x \: faktor \: pengenceran$$

$$Kadar\ terukur = \frac{kadar}{1000} x \: 50 \: ml \: x \: 25$$

f. Keseragaman kandungan

Formula 1

Keseragaman kandungan formula 1

Tablet	serapan	Kadar (ppm)	Jumlah (mg)	bobot (mg)	kandungan mg)	kandungan (%)
1	0,475	9,06	11,33	203	11,50	98,76
2	0,460	8,78	10,98	204	11,20	96,22
3	0,444	8,49	10,61	202	10,72	92,08
4	0,445	8,51	10,64	203	10,79	92,74
5	0,452	8,64	10,80	204	11,01	94,61
6	0,430	8,23	10,29	203	10,44	89,73
7	0,475	9,06	11,33	202	11,44	98,28
8	0,478	9,12	11,40	201	11,45	98,38
9	0,439	8,40	10,50	202	10,60	91,08
10	0,471	8,99	11,23	204	11,46	98,44
Rata – rata				202,80	11,06	95,03
Standart Deviasi				1,03	0,40	3,44
RSD				0,51	3,62	3,62

Formula 2

Formula	Absorbansi	Konsentrasi (ppm)	Jumlah (mg)	Recovery (%)
1	0,486	9,26	11,58	96,49
2	0,489	9,32	11,65	97,07
3	0,492	9,37	11,72	97,64
4	0,433	8,29	10,36	86,33
5	0,504	9,59	11,99	99,95
6	0,490	9,34	11,67	97,26
7	0,431	8,25	10,31	85,94
8	0,431	8,25	10,31	85,94
9	0,486	9,26	11,58	96,49
10	0,490	9,34	11,67	97,26
			Rata – rata	94,04
			SD	5.58

Formula 3

No	absorbansi	Konsentrasi (ppm)	Jumlah (mg)	Recovery (%)
1	0,439	8,40	10,50	87,48
2	0,452	8,64	10,80	89,97
3	0,472	9,01	11,26	93,81
4	0,474	9,04	11,30	94,19
5	0,502	9,56	11,95	99,56
6	0,445	8,51	10,64	88,63
7	0,437	8,36	10,45	87,09
8	0,432	8,27	10,34	86,13
9	0,456	8,71	10,89	90,74
10	0,500	9,52	11,90	99,18
Rata – Rata				91,68
SD				4,85

Perhitungan

$$\text{Konsentrasi} = \frac{\text{absorbansi} + 0{,}017}{0.0543}$$

$$= \frac{0{,}500 + 0{,}017}{0{,}0543} = 9{,}52$$

$$\text{Jumlah} = \frac{konsentrasi}{1000} \, x \, Faktor \, buat \, x \, faktor \, pengenceran$$

$$= \frac{9{,}52}{1000} \, x \, 50 \, x \, 25 = 11{,}90$$

$$\text{Recovery} = \frac{jumlah}{hasil \, penetapan \, kadar} \, x100$$

$$= \frac{11{,}90}{hasil \, penetapan \, kadar} \, x \, 100 = 99{,}18$$

Lampiran 5. Pembuatan kurva baku

5.1 Penentuan panjang gelombang maksimum

Peak (Threshold:0.001 Sensitivity:1)

ID	WL(nm)	ABS	ID	WL(nm)	ABS	ID	WL(nm)	ABS
1	295.0	0.228	2	244.0	0.834	3	214.5	0.477
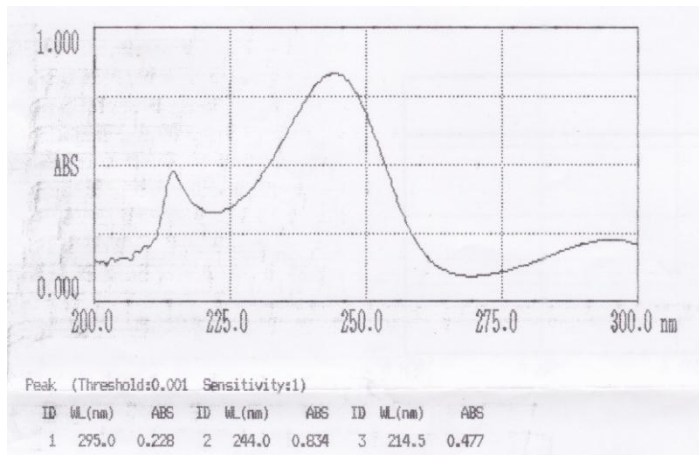
Panjang gelombang maksimum dilakukan dengan melakukan scanning larutan salbutamol sulfat 16µg/ml dan diperoleh panjang gelombang maksimum sebesar 244 nm dengan serapan sebesar 0,843.

5.2 Penentuan *operating time*
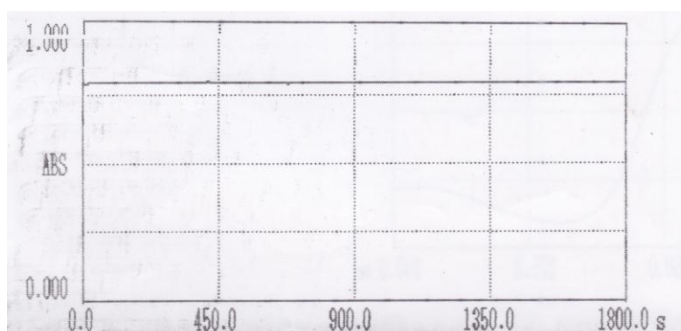
Data List (List Interval(s):60.0)

ID	TIME(s)	ABS	ID	TIME(s)	ABS	ID	TIME(s)	ABS
1	0.0	0.795	2	60.0	0.796	3	120.0	0.798
4	180.0	0.797	5	240.0	0.797	6	300.0	0.797
7	360.0	0.796	8	420.0	0.802	9	480.0	0.796
10	540.0	0.796	11	600.0	0.796	12	660.0	0.796
13	720.0	0.795	14	780.0	0.795	15	840.0	0.795
16	900.0	0.795	17	960.0	0.796	18	1020.0	0.796
19	1080.0	0.796	20	1140.0	0.796	21	1200.0	0.796
22	1260.0	0.796	23	1320.0	0.797	24	1380.0	0.796
25	1440.0	0.797	26	1500.0	0.797	27	1560.0	0.797
28	1620.0	0.797	29	1680.0	0.797	30	1740.0	0.797
31	1800.0	0.797						

Hasil pemeriksaan menunjukkan bahwa salbutamol sulfat memiliki serapan yang

stabil

5.3 Kurva kalibrasi

kadar (ppm)	absorbansi
4	0.198
6	0.307
8	0.419
10	0.537
12	0.629
14	0.742

Persamaan regresi linier

a = - 0,0171

b = 0,0543

r = 0,996

y = - 0,0171 + 0,0543x

keterangan :
y = serapan
x = kadar

5.4 Penentuan LOD dan LOQ

Kadar	abs	y'	$|y-y'|$	$|y-y'|^2$
4	0,198	0,2001	-0,0021	4,41E-06
6	0,307	0,3087	-0,0017	2,89E-06
8	0,419	0,4173	0,0017	2,89E-06
10	0,537	0,5259	0,0111	0,000123
12	0,629	0,6345	-0,0055	3,02E-05
14	0,742	0,7431	-0,0011	1,21E-06
Jumlah total ($\sum|y-y'|^2$)				0,000165

Nilai y' diperoleh dari subtitusi konsentrasi dalam persamaan y'= -0,01709

+0,05434x dengan x adalah konsentrasi dan y adalah absorbansi.

$$S_{x/y} = \sqrt{\frac{\sum|y-y'|2}{N-2}}$$

$$S_{x/y} = \sqrt{\frac{0,000165}{4}} = 0,00642$$

LOD $= 3,3x \frac{Sx/y}{b}$

LOD $= 3,3x \frac{0,009079}{0,0543}$

LOD $= 0.390159$

y $= -0,017 + (0,0543x\ 0,551768)$

y $= 0,004$

Serapan LOD adalah 0,004

LOQ $= 10\ x \frac{Sx/y}{b}$

LOQ $= 10\ x \frac{0,009079}{0,0543}$

LOQ $= 1.1823$

y $= -0,017 + (0,0543\ x\ 1,672025)$

y $= 0,047$

Serapan LOQ 0,047

5.5 Penentuan perolehan kembali (*recovery*)

Penim-bangan (mg)	Jumlah salbutamol (mg)	Serapan			Rata-rata	Kadar (µg/ml)	kadar terukur (mg)	*recovery* (%)
		Rep 1	Rep 2	Rep 3				
30	24,85	0,414	0,412	0,415	0,414	7,933	24,791	99,76
		0,410	0,412	0,411	0,411	7,884	24,637	99,14
		0,413	0,414	0,413	0,413	7,927	24,772	99,68
25	20,71	0,342	0,341	0,342	0,342	6,607	20,647	99,70
		0,340	0,340	0,339	0,340	6,567	20,523	99,09
		0,339	0,339	0,338	0,339	6,552	20,475	98,86
20	16,56	0,265	0,265	0,267	0,266	5,207	16,273	98,27
		0,263	0,264	0,266	0,264	5,183	16,197	97,81
		0,267	0,266	0,266	0,266	5,220	16,312	98,50
Rata – rata								98,98
Standart Deviasi								0,69
Simpangan baku relative (RSD)								0,70

Kadar = (rata-rata serapan + 0,0171)/0,0543

Kadar terukur $= \frac{kadar}{1000}$x faktor pembuatan x faktor pengenceran

$Recovery = \frac{kadar\ terukur}{penmabahan}$ x 100

Faktor pembuatan   = 25 ml

Faktor pengenceran   = 125 x

Lampiran 6. Hasil disolusi

6.1   Formula 1

Replikasi 1

Kadar adisi = 6,5764 (µg/ml)

Bobot tablet = 200 mg (kadar salbutamol = 11,67 mg)

Waktu (menit)	Serapan	Kadar sampel (µg/ml)	Kadar sampel - adisi (µg/ml)	Fp	Kadar (µg/ml)	Jumlah (mg)	Korek-si (mg)	Total koreksi (mg)	Terdi-solusi (mg)	Disolusi (%)
0	0	0	0	0	0	0	0	0	0	0
5	0,346	6,69	0,11	5	0,55	0,50	0,00	0,00	0,50	4,26
15	0,350	6,76	0,18	5	0,92	0,83	0,01	0,01	0,83	7,15
30	0,366	7,06	0,48	5	2,39	2,15	0,01	0,01	2,17	18,59
60	0,377	7,26	0,68	5	3,41	3,07	0,02	0,04	3,11	26,61
90	0,384	7,39	0,81	5	4,05	3,65	0,03	0,07	3,72	31,87
120	0,401	7,70	1,12	5	5,62	5,06	0,04	0,11	5,17	44,29
180	0,413	7,92	1,34	5	6,72	6,05	0,06	0,17	6,22	53,29
240	0,432	8,27	1,69	5	8,47	7,62	0,07	0,24	7,86	67,36
300	0,443	8,47	1,90	5	9,48	8,54	0,08	0,32	8,86	75,90
360	0,450	8,60	2,03	5	10,13	9,12	0,09	0,42	9,53	81,68

Kecepatan pelepasan = 0,025

Koefisisen korelasi = 0,982

Replikasi 2

Kadar adisi = 7,497 (µg/ml)

Bobot tablet = 201 (kadar salbutamol = 11,73)

Waktu (menit)	Serapan	Kadar sampel (µg/ml)	Kadar sampel - adisi (µg/ml)	fp	Kadar (µg/ml)	Jumlah (mg)	Koreksi (mg)	Total koreksi (mg)	Terdi-solusi (mg)	Disolusi (%)
0	0	0	0	0	0	0	0	0	0	0
5	0,397	7,63	0,13	5	0,65	0,58	0,00	0,00	0,58	4,95
15	0,403	7,74	0,24	5	1,20	1,08	0,01	0,01	1,08	9,25
30	0,420	8,05	0,55	5	2,76	2,49	0,01	0,02	2,51	21,36
60	0,429	8,22	0,72	5	3,59	3,23	0,03	0,05	3,28	27,96
90	0,440	8,42	0,92	5	4,61	4,14	0,04	0,08	4,23	36,03
120	0,452	8,64	1,14	5	5,71	5,14	0,05	0,13	5,27	44,90
180	0,144	2,97		2,5	7,42	6,68	0,06	0,19	6,86	58,49
240	0,164	3,34		2,5	8,34	7,50	0,07	0,26	7,76	66,18
300	0,195	3,91		2,5	9,77	8,79	0,08	0,34	9,13	77,85
360	0,197	3,94		2,5	9,86	8,87	0,10	0,44	9,31	79,39

Kecepatan pelepasan   = 0,025

Koefisien korelasi   = 0,973

Replikasi 3

Kadar adisi 9,004 (µg/ml)

Bobot tablet = 202 (kadar salbutamol 11.79)

Waktu (menit)	Serapan	Kadar sampel (µg/ml)	Kadar sampel - adisi (µg/ml)	fp	Kadar (µg/ml)	Jumlah (mg)	Koreksi (mg)	Total koreksi (mg)	Terdi-solusi (mg)	Disolusi (%)
0	0	0	0	0	0	0	0	0	0	0
5	0,480	9,15	0,11	5	0,55	0,50	0,01	0,01	0,50	4,27
15	0,485	9,25	0,20	5	1,01	0,91	0,01	0,02	0,93	7,87
30	0,496	9,45	0,41	5	2,03	1,82	0,02	0,04	1,86	15,78
60	0,512	9,74	0,70	5	3,50	3,15	0,04	0,07	3,22	27,32
90	0,517	9,84	0,79	5	3,96	3,56	0,04	0,11	3,67	31,17
120	0,524	9,97	0,92	5	4,61	4,14	0,05	0,16	4,30	36,48
180	0,144	2,97		2,5	7,42	6,68	0,07	0,23	6,91	58,58
240	0,169	3,43		2,5	8,57	7,,71	0,09	0,32	8,03	68,09
300	0,195	3,91		2,5	9,77	8,79	0,10	0,41	9,20	78,06
360	0,197	3,94		2,5	9,86	8,87	0,10	0,51	9,38	79,59

Kecepatan pelepasan = 0,026

Koefisien korelasi   = 0,979

6.2 Formula 2

Replikasi 1

Kadar adisi 6,5764 (µg/ml)

Bobot tablet = 203 (kadar salbutamol : 11,66mg)

Waktu (menit)	Serapan	Kadar sampel (µg/ml)	Kadar sampel - adisi (µg/ml)	fp	Kadar (µg/ml)	Jumlah (mg)	Koreksi (mg)	Total koreksi (mg)	Terdi-solusi (mg)	Disolusi (%)
0	0	0	0	0	0	0	0	0	0	0
5	0,342	6,61	0,04	5	0,18	0,17	0,00	0,00	0,17	1,42
15	0,355	6,85	0,28	5	1,38	1,24	0,00	0,00	1,25	10,68
30	0,363	7,00	0,42	5	2,12	1,91	0,01	0,02	1,92	16,48
60	0,379	7,29	0,72	5	3,59	3,23	0,02	0,04	3,27	28,04
90	0,398	7,64	1,07	5	5,34	4,81	0,04	0,07	4,88	41,85
120	0,405	7,77	1,20	5	5,99	5,39	0,05	0,13	5,51	47,28
180	0,420	8,05	1,47	5	7,37	6,63	0,06	0,19	6,82	58,46
240	0,427	8,18	1,60	5	8,01	7,21	0,07	0,26	7,47	64,06
300	0,447	8,55	1,97	5	9,85	8,87	0,08	0,34	9,21	78,96
360	0,450	8,60	2,03	5	10,13	9,12	0,10	0,44	9,55	81,94

Kecepatan pelepasan = 0,025

Koefisien korelasi   = 0,966

Replikasi 2

Kadar adisi 7,50 (µg/ml)

bobot tablet = 200 mg (kadar salbutamol : 11.49 mg)

Waktu (menit)	Serapan	Kadar sampel (µg/ml)	Kadar sampel - adisi (µg/ml)	fp	Kadar (µg/ml)	Jumlah (mg)	Koreksi (mg)	Total koreksi (mg)	Terdi-solusi (mg)	Disolusi (%)
0	0	0		0	0	0	0	0	0	0
5	0,392	7,53	0,03	5	0,17	0,15	0,00	0,00	0,15	1,33
15	0,403	7,74	0,24	5	1,18	1,06	0,00	0,00	1,07	9,28
30	0,419	8,03	0,53	5	2,66	2,39	0,01	0,01	2,40	20,93
60	0,434	8,31	0,81	5	4,04	3,63	0,03	0,04	3,67	31,98
90	0,441	8,44	0,94	5	4,68	4,21	0,04	0,08	4,29	37,38
120	0,450	8,60	1,10	5	5,51	4,96	0,05	0,13	5,09	44,28
180	0,134	2,78		2,5	6,96	6,26	0,06	0,18	6,44	56,08
240	0,159	3,24		2,5	8,11	7,30	0,07	0,25	7,55	65,70
300	0,197	3,94		2,5	9,86	8,87	0,08	0,33	9,20	80,11
360	0,199	3,98		2,5	9,95	8,95	0,10	0,43	9,39	81,69

Kecepatan pelepasan = 0,025001

Koefisien korelasi   = 0,970848

Replikasi 3

Kadar adisi 9,044 (µg/ml)

Bobot tablet = 200 mg (kadar salbutamol : 11.49)

Waktu (menit)	Serapan	Kadar sampel (µg/ml)	Kadar sampel - adisi (µg/ml)	fp	Kadar (µg/ml)	Jumlah (mg)	Koreksi (mg)	Total koreksi (mg)	Terdi-solusi (mg)	Disolusi (%)
0	0	0	0	0	0	0	0	0	0	0
5	0,480	9,15	0,11	5	0,55	0,50	0,00	0,00	0,50	4,34
15	0,491	9,36	0,31	5	1,57	1,41	0,01	0,01	1,42	12,32
30	0,496	9,45	0,41	5	2,03	1,82	0,02	0,02	1,85	16,06
60	0,513	9,76	0,72	5	3,59	3,23	0,02	0,04	3,27	28,50
90	0,524	9,97	0,92	5	4,61	4,14	0,04	0,08	4,22	36,74
120	0,538	10,22	1,18	5	5,89	5,30	0,05	0,12	5,43	47,24
180	0,142	2,93		2,5	7,33	6,59	0,06	0,18	6,77	58,96
240	0,169	3,43		2,5	8,57	7,71	0,07	0,26	7,97	69,34
300	0,196	3,92		2,5	9,81	8,83	0,09	0,34	9,17	79,82
360	0,211	4,20		2,5	10,50	9,45	0,10	0,44	9,89	86,08

Kecepatan pelepasan = 0,0261

Koefisien korelasi   = 0,9808

6.3 Formula 3

Replikasi 1
Kadar adisi = 6,5764 (µg/ml)
Bobot tablet = 201mg (kadar salbutamol : 11,25 mg)

Waktu (menit)	Serapan	Kadar sampel (µg/ml)	Kadar sampel - adisi (µg/ml)	fp	Kadar (µg/ml)	Jumlah (mg)	Koreksi (mg)	Total koreksi (mg)	Terdi-solusi (mg)	Disolusi (%)
0	0	0	0	0	0	0	0	0	0	0
5	0,346	6,69	0,11	5	0,55	0,50	0,00	0,00	0,50	4,42
15	0,352	6,80	0,22	5	1,11	0,99	0,01	0,01	1,00	8,89
30	0,364	7,02	0,44	5	2,21	1,99	0,01	0,02	2,01	17,83
60	0,385	7,41	0,83	5	4,14	3,73	0,02	0,04	3,77	33,49
90	0,393	7,55	0,98	5	4,88	4,39	0,04	0,08	4,47	39,76
120	0,401	7,70	1,12	5	5,62	5,06	0,05	0,13	5,18	46,08
180	0,425	8,14	1,57	5	7,83	7,04	0,06	0,19	7,23	64,26
240	0,436	8,34	1,77	5	8,84	7,96	0,08	0,26	8,22	73,06
300	0,445	8,51	1,93	5	9,67	8,70	0,09	0,35	9,05	80,48
360	0,455	8,69	2,12	5	10,59	9,53	0,10	0,45	9,98	88,70

Kecepatan pelepasan = 0,02636
Koefisien korelasi = 0,97295

Replikasi 2
Kadar adisi = 7,497 (µg/ml)
Bobot tablet 202 mg (kadar salbutamol : 11.31)

Waktu (menit)	Serapan	Kadar sampel (µg/ml)	Kadar sampel - adisi (µg/ml)	fp	Kadar (µg/ml)	Jumlah (mg)	Koreksi (mg)	Total koreksi (mg)	Terdi-solusi (mg)	Disolusi (%)
0	0	0	0	0	0	0	0	0	0	0
5	0,396	7,61	0,11	5	0,55	0,50	0,00	0,00	0,50	4,41
15	0,401	7,70	0,20	5	1,01	0,91	0,01	0,01	0,92	8,12
30	0,418	8,01	0,52	5	2,58	2,32	0,01	0,02	2,34	20,66
60	0,433	8,29	0,79	5	3,96	3,56	0,03	0,04	3,61	31,88
90	0,450	8,60	1,11	5	5,53	4,97	0,04	0,08	5,05	44,69
120	0,459	8,77	1,27	5	6,35	5,72	0,06	0,14	5,86	51,77
180	0,154	3,15		2,5	7,88	7,09	0,06	0,20	7,29	64,45
240	0,164	3,34		2,5	8,34	7,50	0,08	0,28	7,78	68,81
300	0,195	3,91		2,5	9,77	8,79	0,08	0,36	9,15	80,91
360	0,212	4,22		2,5	10,55	9,49	0,10	0,46	9,95	88,00

Kecepatan pelepasan = 0,02574
Koefisien korelasi = 0,96215

Replikasi 3

Kadar adisi = 9,044 (µg/ml)

Bobot tablet = 200 mg (kadar salbutamol 11,20)

Waktu (menit)	Serapan	Kadar sampel (µg/ml)	Kadar sampel - adisi (µg/ml)	fp	Kadar (µg/ml)	Jumlah (mg)	Koreksi (mg)	Total koreksi (mg)	Terdi-solusi (mg)	Disolusi (%)
0	0	0	0	0	0	0	0	0	0	0.00
5	0,480	9,15	0,11	5	0,55	0,50	0,00	0,00	0,50	4,45
15	0,485	9,25	0,20	5	1,01	0,91	0,01	0,01	0,92	8.20
30	0,496	9,45	0,41	5	2,03	1,82	0,01	0,02	1,84	16,43
60	0,512	9,74	0,70	5	3,50	3,15	0,02	0,04	3,19	28,45
90	0,523	9,95	0,90	5	4,51	4,06	0,04	0,07	4,13	36,90
120	0,532	10,11	1,07	5	5,34	4,81	0,05	0,12	4,92	43,96
180	0,145	2,99		2,5	7,46	6,72	0,05	0,17	6,89	61,49
240	0,169	3,43		2,5	8,57	7,71	0,07	0,24	7,96	71,03
300	0,196	3,92		2,5	9,81	8,83	0,09	0,33	9,16	81,78
360	0,216	4,29		2,5	10,73	9,66	0,10	0,43	10,09	90,06

Kecepatan pelepasan = 0,027059

Koefisien korelasi = 0,984425

Rata –rata terdisolusi

Waktu (menit)	Formula 1 (%)	formula 2 (%)	formula 3 (%)
0	0	0	0
5	4,50 ± 0,40	2,36 ± 1,71	4,42 ± 0,01
15	8,09 ± 1,07	10,76 ± 1,52	8,40 ± 0,42
30	18,58 ± 2,79	17,28 ± 2,70	18,31 ± 2,16
60	27,29 ± 0,67	29,50 ± 2,15	31,27 ± 2,58
90	33,02 ± 2,63	38,66 ± 2,78	40,45 ± 3,94
120	41,89 ± 4,70	46,27 ± 1,72	47,27 ± 4,04
180	56,79 ± 3,03	57,83 ± 1,54	63,40 ± 1,66
240	67,21 ± 0,96	66,37 ± 2,70	70,.97 ± 2,12
300	77,27 ± 1,19	79,63 ± 0,60	81,06 ± 0,67
360	80,22 ± 1,27	83,24 ± 2,47	88,92 ± 1,05

Keterangan :

Fp   = faktor pengenceran

Kadar sampel = kadar obat dalam sampel yang ditambah adisi (µg/ml)

Kadar sampel – adisi = selisih kadar sampel dan adisi (µg/ml)

Kadar   = kadar salbutamol dalam medium disolusi (µg/ml)

Jumlah   = banyaknya salbutamol dalam medium disolusi (mg/900 ml)

Koreksi   = jumlah salbutamol dalam cuplikan sampel (mg)

Total koreksi   = jumlah komulatif koreksi (mg)

Terdisolusi   = Jumlah obat yang terdisolusi (mg)

Disolusi   = prosentase jumlah obat yang terdisolusi (%)

Contoh Perhitungan Disolusi Obat

Diasumsikan absorbansi sampel adalah 0,480 dan absorbansi adisi adalah 0,471

$$\text{Kadar} = \frac{Absorbansi + 0,017}{0,054}$$

$$\text{Kadar sampel dan adisi} = \frac{0,480 + 0,0171}{0,0543} = 9,15 \text{ µg/ml}$$

$$\text{Kadar adisi} = \frac{0,471 + 0,017}{0,0543} = 9,04 \text{ µg/ml}$$

Kadar sampel = Kadar sampel adisi – kadar adisi

$$= 9,1 - 9,04 = 0,11 \text{ µg/ml}$$

Kadar salbutamol dalam medium disolusi = Kadar sampel x fp

$$= 0,11 \text{ x } 5 = 0,55 \text{ µg/ml}$$

Banyaknya salbutamol dalam medium disolusi = kadar dalam medium x 0,9

$$= 0,55 \text{ x } 0,9 = 0,50 \text{ mg}$$

$$\text{Koreksi} = \frac{jumlah\ pengambilan\ sampel}{volume\ medium\ disolusi} \text{x banyaknya obat yang terdisolusi sebelumnya}$$

$$= \frac{10\ ml}{900\ ml} \ x \ 0 = 0 \text{ mg}$$

Total Koreksi = koreksi pada sampling sebelumya + koreksi

$$= 0 + 0 = 0 \text{ mg}$$

Terdisolusi = jumlah obat yang terlarut + total koreksi

$$= 0,50 + 0,00 = 0,50 \text{ mg}$$

disolusi $\quad = \dfrac{Q}{Hasil\ penetapan\ kadar} x100$

$\qquad = \dfrac{0,50}{11,45} x100 = 4,41$

Perhitungan DE

Waktu	Formula 1		
	Replikasi 1	Replikasi 2	Replikasi 3
5	10,65	12,39	10,68
15	57,06	71,02	60,72
30	193,05	229,58	177,37
60	677,98	739,76	646,44
90	877,17	959,83	877,35
120	114,41	1214,06	1014,77
180	2927,49	3101,74	2851,74
240	3619,63	3740,16	3799,99
300	4297,81	4320,93	4384,36
360	4727,45	4717,19	4729,52
AUC total	18530,70	19106,66	18552,94
Luas total	36000	36000	36000
DE360	51,47	53,07	51,54

Waktu (menit)	Formula 2		
	Replikasi 1	Replikasi 2	Replikasi 3
5	3,56	3,34	10,84
15	60,50	53,09	83,26
30	203,70	226,57	212,83
60	667,78	793,54	668,37
90	1048,26	1040,29	978,63
120	1336,95	1224,78	1259,81
180	3172,12	3010,63	3186,19
240	3675,57	3653,37	3849,05
300	4290,84	4374,29	4474,77
360	4827,22	4853,96	4977,16
AUC TOTAL	19286,50	19233,85	19700,92
DE360	53,57	53,43	54,72

waktu (menit)	Formula 3		
	Replikasi 1	Replikasi 2	Replikasi 3
5	11,05	11,01	11,12
15	66,55	62,62	63,22
30	200,38	215,88	184,67
60	769,83	788,23	673,10
90	1098,74	1148,62	980,17
120	1287,57	1446,97	1212,88
180	3310,32	3486,82	3163,8
240	4119,65	3998,00	3975,48
300	4606,09	4491,65	4584,47
360	5075,33	5067,24	5155,36
AUC Total	20545,53	20717,05	20003,85
DE360	57,07	57,55	55,57

Rata – rata *dissolution efficiency*

Replikasi	*Dissolution efficiency* (%)		
	Formula 1	Formula 2	Formula 3
1	51,47	53,57	57,07
2	53,07	53,43	57,54
3	51,54	54,72	55,56
Rata-rata	52,03	53,91	56,73
SD	0,91	0,71	1,03

Lampiran 7. Hasil analisis kinetika dan pelepasan obat

Formula	orde nol		Orde satu	Higuchi		Korsmayer Peppas	
	K_0	R^2	R^2	K_H	R^2	N	R^2
I	0,218	0,960	0,734	4,816	0,993	0,697	0,991
II	0,221	0,949	0,634	4,923	0,998	0,781	0,966
III	0,234	0,950	0,707	5,224	0,997	0,721	0,990

Keterangan :

Orde nol   : plot antara waktu (menit) dengan jumlah obat yang terdisolusi (%).

Orde satu   : plot antara waktu (menit) dengan log jumlah obat yang terdisolusi (%)

Higuchi   : plot antara akar waktu (menit$^{1/2}$) dengan jumlah obat yang terdisolusi (%)

Korsmayer Peppas : plot regresi antara log waktu dengan log fraksi obat yang telepas

K_0 : Kecepatan pelepasan orde nol

R^2 : Koefiseien determinasi

K_H : Kecepatan pelepasan model Higuchi

N   : eksponensial difusi

Lampiran 8. Perhitungan farmakokinetik salbutamol sulfat

Parameter farmakokimia salbutamol adalah sebagai berikut :

waktu paruh ($t^1/_2$) 4 jam

konstanta kecepatan eliminasi (Kel) 0,17325/jam.

Dosis lazim salbutamol sulfat sebesar 6 - 16 mg;

Bioavailabilitas 50 % (berat badan diasumsikan 60 kg)

Cp 0,0179 mg/L (Moffat 2011) .

Volume distribusi salbutamol sulfat 156 L (Morgan 1986) maka :

Rate in (keceparan pelepasan obat dari sediaan) = *Rate out* (kecepatan hilangnya obat dari badan).

$$\textbf{Rate in = Kr = Cp x Vd x Kel}\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots(16)$$

$$= 0,0179 \text{ mg/L x } 156 \text{ L x } 0,17325/\text{jam}$$

$$= 0,484 \text{ mg/jam}$$

Jumlah salbutamol yang harus dilepaskan dari sediaan (R) dalam waktu 12 jam adalah :

$$\textbf{R} = \frac{Kr}{f}\textbf{x 12 jam}\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots(17)$$

$$= \frac{0,484 \text{ } mg/jam}{0,5} \text{ x 12 jam}$$

$$= 11,616 \text{ mg} \sim 12 \text{ mg}$$

Lampiran 9. Hasil pemerikasaan formula optimum

a. Pemerikasaan sifat fisik

Sifat fisik	Hasil
Waktu alir (detik)	$16,95 \pm 0,36$
Kelembaban (%)	$5,44 \pm 0,35$
Sudut diam (^{o})	$28,95 \pm 0,48$
Penetapan kadar (mg)	$11.30 \pm 0,04$
kekerasan (kg)	$8 \pm 0,54$
kerapuhan (%)	$0,230 \pm 0,3$
Floating lag time (detik)	$0,457 \pm 0,81$

b. Pelepasan obat

Replikasi 1
Kadar adisi = 5,25 (µg/ml)
Bobot tablet = 204 mg (kandungan salbutamol 11.54)

Waktu (menit)	Serapan	Kadar sampel (µg/ml)	Kadar sampel - adisi (µg/ml)	fp	Kadar (µg/ml)	Jumlah (mg)	Koreksi (mg)	Total koreksi (mg)	Terdi-solusi (mg)	Disolusi (%)
0	0	0	0	0	0	0	0	0	0	0
5	0,274	5,36	0,11	5	0,55	0,50	0,00	0,00	0,50	4,40
15	0,278	5,43	0,18	5	0,92	0,83	0,01	0,01	0,84	7,25
30	0,293	5,71	0,46	5	2,30	2,07	0,01	0,01	2,09	18,10
60	0,309	6,01	0,76	5	3,78	3,40	0,02	0,04	3,44	29,79
90	0,321	6,23	0,98	5	4,88	4,39	0,04	0,08	4,47	38,73
120	0,330	6,39	1,14	5	5,71	5,14	0,05	0,12	5,26	45,62
180	0,139	2,87		2,5	7,19	6,47	0,06	0,18	6,65	57,62
240	0,163	3,32		2,5	8,29	7,46	0,07	0,25	7,72	66,86
300	0,199	3,98		2,5	9,95	8,95	0,08	0,34	9,29	80,51
360	0,216	4,29		2,5	10,73	9,66	0,10	0,44	10,09	87,48

Kecepatan pelepasan = 0.026549082
Koefisien korelasi = 0.980348653

Replikasi 2
Kadar adisi = 5,25 (µg/ml)
Bobot tablet = 201 (kadar salbutamol = 11,37 mg)

Waktu (menit)	Serapan	Kadar sampel (µg/ml)	Kadar sampel - adisi (µg/ml)	fp	Kadar (µg/ml)	Jumlah (mg)	Koreksi (mg)	Total koreksi (mg)	Terdi-solusi (mg)	Disolusi (%)
0	0	0	0		0	0	0	0	0	0
5	0,275	5,38	0,13	5	0,65	0,58	0,00	0,00	0,58	5,12
15	0,280	5,47	0,22	5	1,11	1,00	0,01	0,01	1,00	8,82
30	0,291	5,67	0,42	5	2,12	1,91	0,01	0,02	1,93	16,94
60	0,308	5,99	0,74	5	3,69	3,32	0,02	0,04	3,36	29,51
90	0,317	6,15	0,90	5	4,51	4,06	0,04	0,08	4,14	36,40
120	0,329	6,37	1,12	5	5,62	5,06	0,05	0,12	5,18	45,54
180	0,145	2,99		2,5	7,46	6,72	0,06	0,18	6,89	60,63
240	0,169	3,43		2,5	8,57	7,71	0,07	0,25	7,96	70,03
300	0,194	3,89		2,5	9,72	8,75	0,09	0,34	9,08	79,90
360	0,210	4,18		2,5	10,46	9,41	0,10	0,43	9,84	86,58

Kecepatan pelepasan = 0.026245
Koefisien koerelasi = 0.980383

Replikasi 3
Kadar adisi = 5,25 (µg/ml)
Bobot tablet 204 mg (kandungan salbutamol 11,54)

Waktu (menit)	Serapan	Kadar sampel (µg/ml)	Kadar sampel - adisi (µg/ml)	fp	Kadar (µg/ml)	Jumlah (mg)	Koreksi (mg)	Total koreksi (mg)	Terdi-solusi (mg)	Disolusi (%)
0	0	0	0	0	0	0	0	0	0	0
5	0,271	5,31	0,06	5	0,28	0,25	0,00	0,00	0,25	2,17
15	0,279	5,45	0,20	5	1,02	0,91	0,00	0,00	0,92	7,94
30	0,291	5,67	0,42	5	2,12	1,91	0,01	0,01	1,92	16,65
60	0,312	6,06	0,81	5	4,05	3,65	0,02	0,03	3,68	31,91
90	0,321	6,23	0,98	5	4,88	4,39	0,04	0,07	4,47	38,73
120	0,332	6,43	1,18	5	5,90	5,31	0,05	0,12	5,43	47,05
180	0,141	2,91		2,5	7,28	6,55	0,06	0,18	6,73	58,35
240	0,160	3,26		2,5	8,15	7,34	0,07	0,26	7,59	65,80
300	0,194	3,89		2,5	9,72	8,75	0,08	0,34	9,08	78,72
360	0,217	4,31		2,5	10,78	9,70	0,10	0,43	10,13	87,82

Kecepatan pelepasan = 0.026448829
Koefisien korelasi = 0.974847865

C. Perhitungan DE_{360}

time	AUC Replikasi 1	Replikasi 2	Replikasi 3
5	11,01	12,81	5,43
15	58,25	69,71	50,57
30	190,10	193,19	184,16
60	718,33	696,76	728,39
90	1027,85	988,68	1059,57
120	1265,32	1229,09	1286,63
180	3097,33	3185,18	3161,96
240	3734,63	3919.97	3724,58
300	4421,19	4497,99	4335,62
360	5039,53	4994,49	4996,09
AUC total	19563,55	19787,85	19533,24
DE360 (%)	54,343	54.966	54,26

d. Analisis kinetika dan mekanisme pelepasan obat

Replikasi	Orde nol		orde satu	Higuchi		Korsmayer Peppas	
	K_0	R^2	R^2	K_H	R^2	n	R^2
1	0,230	0,960	0,713	5,094	0,997	0,728	0,985
2	0,231	0,961	0,746	5,094	0,997	0,690	0,994
3	0,229	0,950	0,636	5,103	0,997	0,829	0,972

Keterangan :

Orde nol   : plot antara waktu (menit) dengan jumlah obat yang terdisolusi (%).

Orde satu   : plot antara waktu (menit) dengan log jumlah obat yang terdisolusi (%)

Higuchi   : plot antara akar waktu ($menit^{1/2}$) dengan jumlah obat yang terdisolusi (%)

Korsmayer Peppas : plot regresi antara log waktu dengan log fraksi obat yang telepas

Lampiran 10. Hasil uji statistik

1. Waktu alir

Uji normalitas

One-Sample Kolmogorov-Smirnov Test

		waktualir
N		9
Normal Parameters[a,b]	Mean	15.9578
	Std. Deviation	1.01668
Most Extreme Differences	Absolute	.153
	Positive	.153
	Negative	-.122
Kolmogorov-Smirnov Z		.458
Asymp. Sig. (2-tailed)		.985

a. Test distribution is Normal.

b. Calculated from data.

Uji homogenitas varian

Test of Homogeneity of Variances

Waktualir

Levene Statistic	df1	df2	Sig.
.295	2	6	.754

Uji ANOVA

ANOVA

waktu alir

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	6.243	2	3.121	9.242	.015
Within Groups	2.026	6	.338		
Total	8.269	8			

L-LSD

Multiple Comparisons

waktualir

LSD

(I) formula	(J) formula	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
1	2	-1.03333	.47451	.072	-2.1944	.1277
	3	-2.04000*	.47451	.005	-3.2011	-.8789
2	1	1.03333	.47451	.072	-.1277	2.1944
	3	-1.00667	.47451	.078	-2.1677	.1544
3	1	2.04000*	.47451	.005	.8789	3.2011
	2	1.00667	.47451	.078	-.1544	2.1677

*. The mean difference is significant at the 0.05 level.

2. Kelembaban

Uji normalitas

One-Sample Kolmogorov-Smirnov Test

		kelembaban
N		9
Normal Parameters[a,b]	Mean	5.3444
	Std. Deviation	.38766
Most Extreme Differences	Absolute	.146
	Positive	.146
	Negative	-.121
Kolmogorov-Smirnov Z		.439
Asymp. Sig. (2-tailed)		.991

a. Test distribution is Normal.

b. Calculated from data.

Uji homogenitas varian

Test of Homogeneity of Variances

Kelembaban

Levene Statistic	df1	df2	Sig.
.038	2	6	.963

Uji ANOVA

ANOVA

Kelembaban

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	.862	2	.431	7.608	.023
Within Groups	.340	6	.057		
Total	1.202	8			

Uji LSD

Multiple Comparisons

Kelembaban

LSD

(I) formula	(J) formula	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
1	2	-.20000	.19437	.343	-.6756	.2756
	3	-.73333*	.19437	.009	-1.2089	-.2577
2	1	.20000	.19437	.343	-.2756	.6756
	3	-.53333*	.19437	.034	-1.0089	-.0577
3	1	.73333*	.19437	.009	.2577	1.2089
	2	.53333*	.19437	.034	.0577	1.0089

*. The mean difference is significant at the 0.05 level.

3. Sudut diam

Uji normalitas

One-Sample Kolmogorov-Smirnov Test

		sudut diam
N		9
Normal Parameters[a,b]	Mean	28.9444
	Std. Deviation	.98439
Most Extreme Differences	Absolute	.185
	Positive	.164
	Negative	-.185
Kolmogorov-Smirnov Z		.555
Asymp. Sig. (2-tailed)		.917

a. Test distribution is Normal.

b. Calculated from data.

Uji homogenitas varian

Test of Homogeneity of Variances

sudut diam

Levene Statistic	df1	df2	Sig.
2.532	2	6	.160

Uji ANOVA

ANOVA

sudut diam

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	4.762	2	2.381	4.778	.057
Within Groups	2.990	6	.498		
Total	7.752	8			

4. Kekerasan

Uji normalitas

One-Sample Kolmogorov-Smirnov Test

		kekerasan
N		18
Normal Parameters[a,b]	Mean	8.4167
	Std. Deviation	.92752
Most Extreme Differences	Absolute	.235
	Positive	.173
	Negative	-.235
Kolmogorov-Smirnov Z		.998
Asymp. Sig. (2-tailed)		.272

a. Test distribution is Normal.

b. Calculated from data.

Uji homogenitas varian

Test of Homogeneity of Variances

Kekerasan

Levene Statistic	df1	df2	Sig.
.083	2	15	.921

Uji ANOVA

ANOVA

Kekerasan

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	1.333	2	.667	.752	.488
Within Groups	13.292	15	.886		
Total	14.625	17			

5. **Kerapuhan**

   Uji normalitas

One-Sample Kolmogorov-Smirnov Test

		kerapuhan
N		9
Normal Parameters[a,b]	Mean	.20678
	Std. Deviation	.046308
Most Extreme Differences	Absolute	.225
	Positive	.225
	Negative	-.147
Kolmogorov-Smirnov Z		.675
Asymp. Sig. (2-tailed)		.753

a. Test distribution is Normal.

b. Calculated from data.

Uji homogenitas varian

Test of Homogeneity of Variances

kerapuhan

Levene Statistic	df1	df2	Sig.
1.891	2	6	.231

Uji ANOVA

ANOVA

kerapuhan

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	.007	2	.003	1.877	.233
Within Groups	.011	6	.002		
Total	.017	8			

6. Hasil uji statistik formula optimum
Floating lag time

Uji distribusi data

One-Sample Kolmogorov-Smirnov Test

		floating lag time
N		5
Normal Parameters[a,b]	Mean	4.5680
	Std. Deviation	.81558
Most Extreme Differences	Absolute	.227
	Positive	.227
	Negative	-.167
Kolmogorov-Smirnov Z		.507
Asymp. Sig. (2-tailed)		.959

a. Test distribution is Normal.

b. Calculated from data.

One sample t-test

One-Sample Test

	Test Value = 5.7					
					99% Confidence Interval of the Difference	
	t	df	Sig. (2-tailed)	Mean Difference	Lower	Upper
floating lag time	-3.104	4	.036	-1.13200	-2.8113	.5473

Q$_{60}$ (Jumlah obat yang terlepas pada menit ke 60)

Uji distribusi data

One-Sample Kolmogorov-Smirnov Test

		Q60
N		3
Normal Parameters[a,b]	Mean	30.4033
	Std. Deviation	1.31230
Most Extreme Differences	Absolute	.347
	Positive	.347
	Negative	-.248
Kolmogorov-Smirnov Z		.600
Asymp. Sig. (2-tailed)		.864

a. Test distribution is Normal.

b. Calculated from data.

One sample t-test

One-Sample Test

	Test Value = 29.83					
					99% Confidence Interval of the Difference	
	T	df	Sig. (2-tailed)	Mean Difference	Lower	Upper
Q60	.757	2	.528	.57333	-6.9463	8.0930

Q$_{360}$ (Jumlah Obat yang dilepaskan selama 360 menit)
Uji distribusi data

One-Sample Kolmogorov-Smirnov Test

		q360
N		3
Normal Parameters[a,b]	Mean	87.2933
	Std. Deviation	.64073
Most Extreme Differences	Absolute	.281
	Positive	.206
	Negative	-.281
Kolmogorov-Smirnov Z		.487
Asymp. Sig. (2-tailed)		.972

a. Test distribution is Normal.

b. Calculated from data.

One sample t-test

One-Sample Test

	Test Value = 85.16					
					99% Confidence Interval of the Difference	
	T	df	Sig. (2-tailed)	Mean Difference	Lower	Upper
q360	5.767	2	.029	2.13333	-1.5381	5.8048

DE$_{360}$ (Jumlah obat yang dilepaskan pada menit ke 360)

Uji distribusi data

One-Sample Kolmogorov-Smirnov Test

		DE360
N		3
Normal Parameters[a,b]	Mean	54.5223
	Std. Deviation	.38671
Most Extreme Differences	Absolute	.346
	Positive	.346
	Negative	-.248
Kolmogorov-Smirnov Z		.600
Asymp. Sig. (2-tailed)		.864

a. Test distribution is Normal.

b. Calculated from data.

One sample t-test

One-Sample Test

	Test Value = 54.77					
					99% Confidence Interval of the Difference	
	t	df	Sig. (2-tailed)	Mean Difference	Lower	Upper
DE360	-1.109	2	.383	-.24770	-2.4636	1.9682