

BAB V

KESIMPULAN DAN SARAN

A. KESIMPULAN

Berdasarkan dari hasil penelitian yang telah dilakukan dapat diperoleh kesimpulan bahwa :

Pertama, loratadin dapat dibuat kristal sferis dengan menggunakan metode *spherical agglomeration*

Kedua, didapatkan karakteristik kristal sferis loratadin dengan metode *spherical agglomeration*

Ketiga, kristal sferis loratadin memiliki kelarutan lebih besar dibandingkan dengan loratadin murni

B. SARAN

Penelitian ini masih banyak kekurangan, maka perlu dilakukan penelitian lebih lanjut mengenai :

Pertama, sifat kristalinitas loratadin baik bentuk murni maupun kristal sferis dengan DSC

Kedua, pengujian terhadap sifat alir, porositas dan kompresibilitas kristal sferis loratadin

Ketiga, pembuatan kristal sferis loratadin dengan jenis polimer dan metode lainnya

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Lampiran 1. Certifict Of Analysis

S.No		TESTS	RESULT	SPECIFICATION
1.0	Description		White powder	White to off-white powder
2.0	Solubility		Complies	Freely soluble in acetone, in chloroform, in methanol and in toluene, Insoluble in water.
IDENTIFICATION				
3.0	A	By Infrared Spectrum (In Mineral oil)	Complies	The IR absorption spectrum of the preparation of the test specimen, exhibits maxima only at the same wavelengths as that of a similar preparation of the corresponding Lorastadine reference standard/working Standard.
	B	HPLC	Complies	The retention time of the major peak in the chromatogram of the assay preparation corresponds to that in the chromatogram of the standard preparation as obtained in the assay
4.0	Loss on drying (% w/w)		0.25	Not more than 0.5
5.0	Residue on ignition (% w/w)		0.06	Not more than 0.1
6.0 Organic Impurities Procedure 2 (by HPLC, %)				
		Lorastadine related compound A	Not detected	Not more than 0.1
		Lorastadine related compound B	Not detected	Not more than 0.1
		Lorastadine related compound C	Not detected	Not more than 0.1
		Hydroxy desacyl analog	Not detected	Not more than 0.1
		Hydroxy lorastadine	Not detected	Not more than 0.1
		*Dehydro Lorastadine isomer-B	0.08	Not more than 0.10
		*Iso Lorastadine-A	0.04	Not more than 0.10
		Any individual unknown impurity	Not detected	Not more than 0.10
		Total impurities	0.12	Not more than 0.3
7.0	Assay by HPLC (% w/w, on dried basis)		99.7	Not less than 98.5 and Not more than 101.0

	Prepared By	Checked By	Approved By
Signature	<i>D.V.S. Kishore</i>	<i>N. Shivavasa Raju</i>	<i>P.M. Krishna</i>
Name	D.V.S. Kishore	N. Shivavasa Raju	P.M. Krishna
Designation	Jr. Manager (QC)	Jr. Manager (QC)	Dy. Manager (QC)

Manufactured at: Vasudha Pharma Chem Ltd, Unit-E, Plot No. 79, Jewahar Nagar, Pharms City, Thimma village, Juvvabolu (M), Visakhapatnam District, Andhra Pradesh, India.

CQA/023001/09

EFFECTIVE DATE: 01/10/2011

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 78/A, VENGAL RAO NAGAR, HYDERABAD-38, INDIA
 PHONE: 91-40-2381 2046, 2371 1717, FAX: 91-40-2381 1576
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VASUDHA PHARMA CHEM. LTD

CERTIFICATE OF ANALYSIS

QUALITY ASSURANCE CELL

Name of the product	: LORATADINE USP	Analyzed on	: 27/02/2018
Batch Number	: BLRD/1802009	Expiry Date	: JAN 2023
Manufacturing Date	: FEB 2018	A.R.No	: BFP/180858
Quantity	: 131.60 Kg		

S.No	TESTS	RESULT	SPECIFICATION
8.0	Residual solvents/Organic volatile impurities (by GC with HSS,ppm)		
	Tetrahydrofuran	Not detected	Not more than 500
	Toluene	Not detected	Not more than 500
	Di-isopropyl ether	106	Not more than 500
	Triethylamine	Not detected	Not more than 50

REMARKS: The material Complies as per the USP40 specification.
 Note: **In-House impurities
 The two impurities 4, 8-dichloro-6, 11-dihydro-5H-benzo [5, 6] cyclohepta- [1, 2-b] pyridin-11- one/Dichloro-benzo cycloheptapyridinone and Ethyl 4(4,8-dichloro-5,6dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridine-11-ylidene) piperidine-1-carboxylate/4-chloro loratadine are not potential related compounds as per manufacturing process adopted Vasudha. However if tested it covers in any individual unknown impurities (i.e. not more than 0.10%)

	Prepared By	Checked By	Approved By
Signature	<i>D.V.S.Kishore</i>	<i>N.Srinivasa Raju</i>	<i>P.M.Krishna</i>
Name	D.V.S.Kishore	N.Srinivasa Raju	P.M.Krishna
Designation	Jr.Manager (QC)	Jr.Manager (QC)	Dy.Manager (QC)

Manufactured at: Vasudha Pharma Chem Ltd, Unit-II, Plot No. 79, Lenebatal Nethu Pharam City, Thamma village, Puzosada (M), Vijayapattanam District, Andhra Pradesh, India.

CQA/002/00500

EFFECTIVE DATE: 01/16/201

Lampiran 2. Penentuan panjang gelombang

No.	P/V	Wavelength	Abs.	Description
1	●	288.00	2.3029	
2	●	251.00	0.5798	
3	●	269.00	-1.1685	
4	●	247.00	-0.7334	

Lampiran 3. Penentuan *operating time***Kinetics Data Print Report**

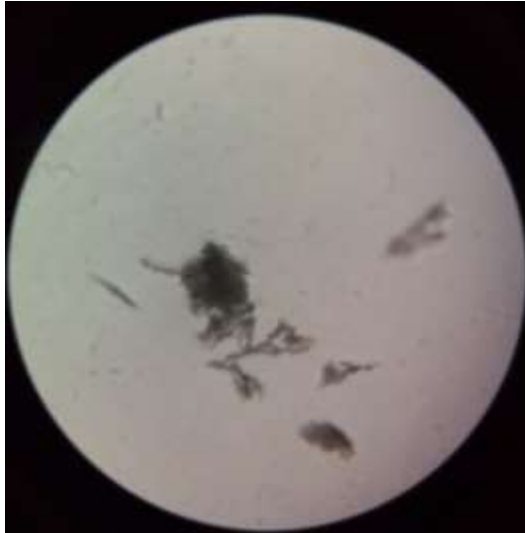
07/12/019 12:05 PM

Time (Minute)	Raw Data ---
0.00	0.579
1.00	0.579
2.00	0.578
3.00	0.578
4.00	0.579
5.00	0.580
6.00	0.580
7.00	0.580
8.00	0.580
9.00	0.582
10.00	0.582
11.00	0.582
12.00	0.582
13.00	0.582
14.00	0.582
15.00	0.582
16.00	0.582
17.00	0.582
18.00	0.582
19.00	0.582
20.00	0.582
21.00	0.582
22.00	0.583
23.00	0.582
24.00	0.582
25.00	0.582
26.00	0.582
27.00	0.582
28.00	0.583
29.00	0.582
30.00	0.582

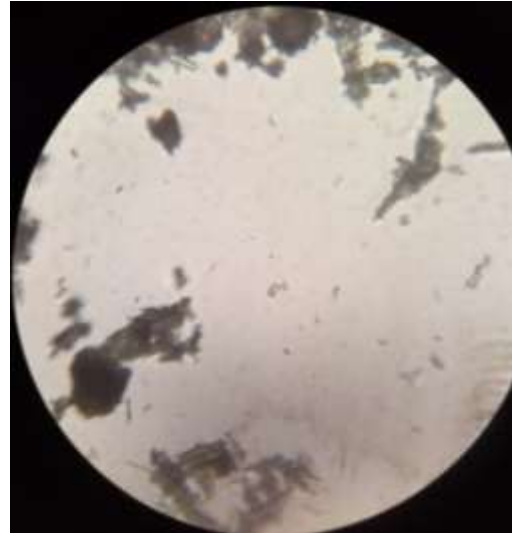
Lampiran 4. Serbuk loratadin dan serbuk kristal sferis



Kristal Sferis Loratadin

Lampiran 5. Hasil uji morfologi 3 formula

Formula 1
PVP 3 ml



Formula 2
PVP 5 ml



Formula 3
PVP 7 ml

Lampiran 6. Hasil uji morfologi mikrosko optik (perbesarab 100x)



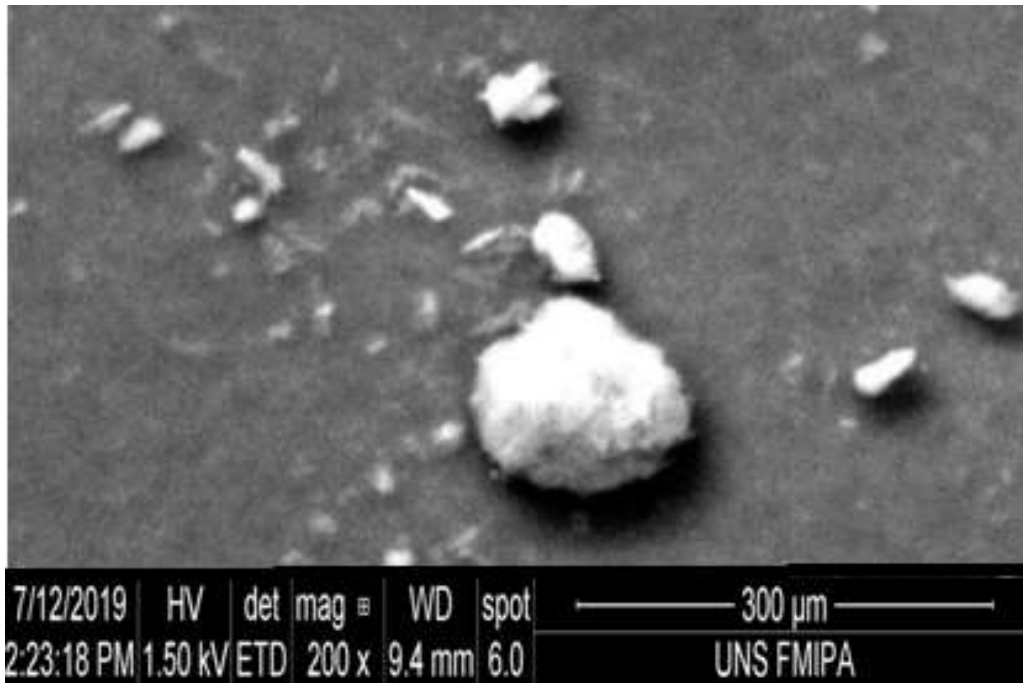
a. Loratadin murni



b. Kristal sferis loratain

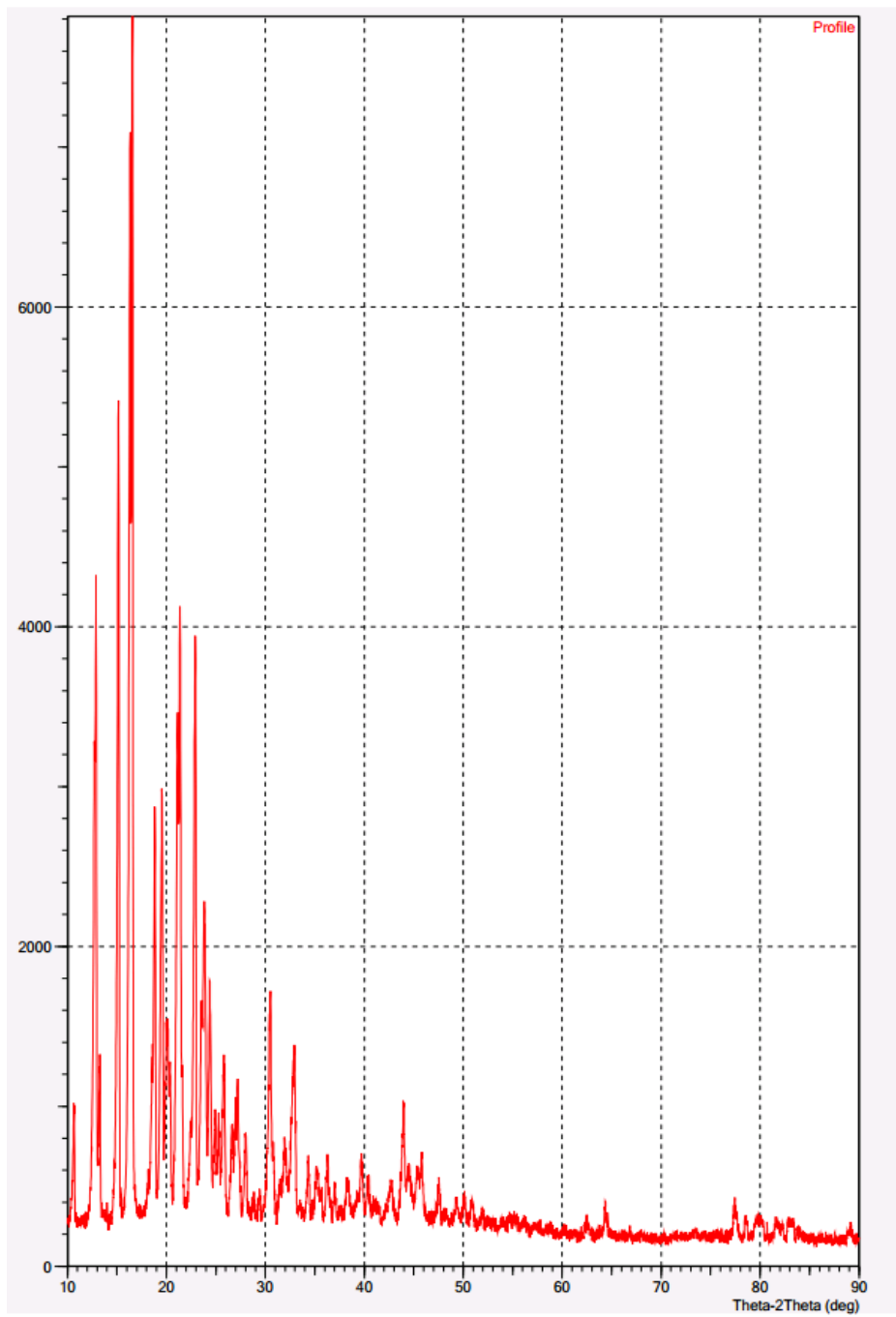
Lampiran 7. Hasil SEM (Scanning Electron Microscopy)

Perbesaran 200x

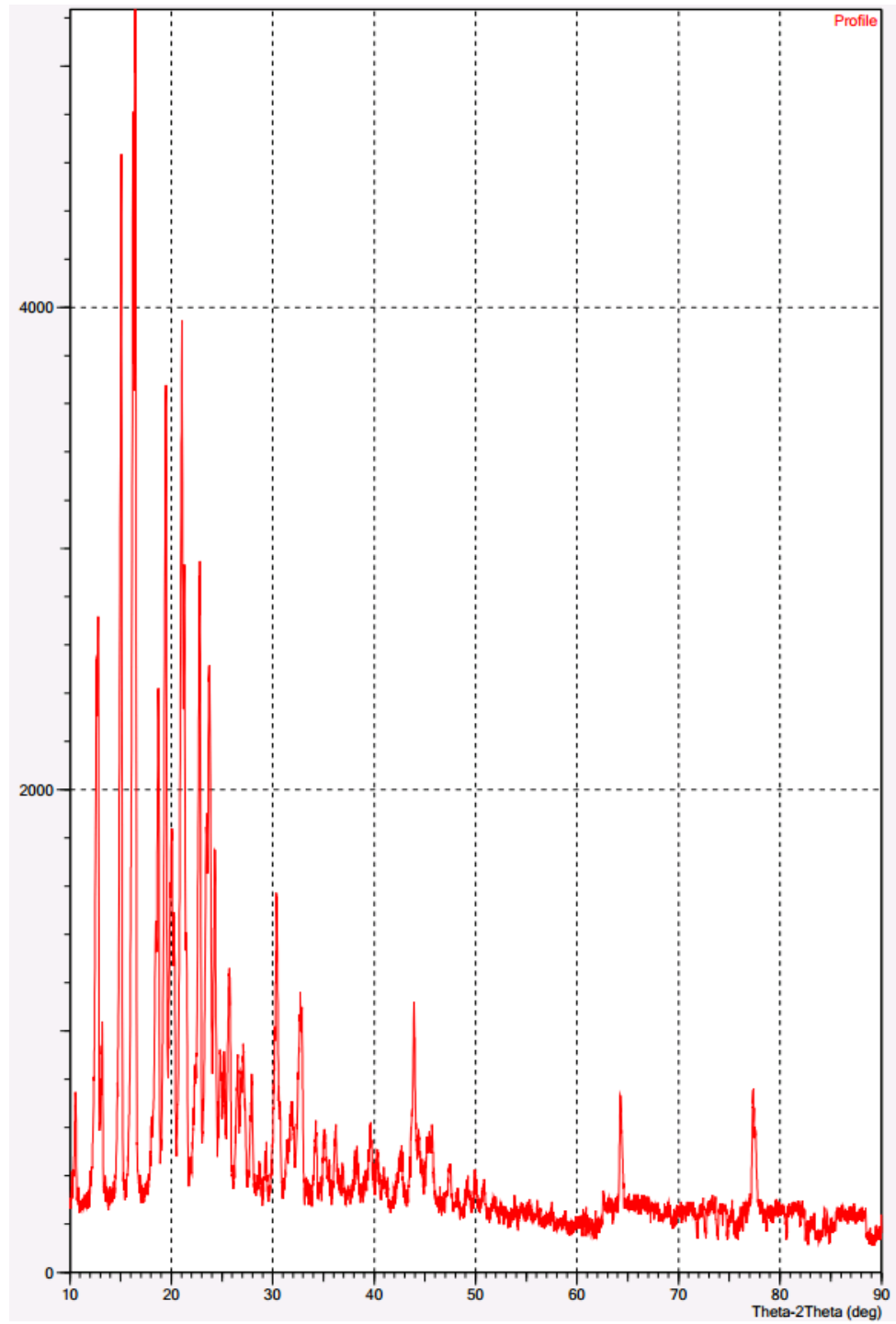


Lampiran 8. Difraktogram XRD (X-ray Diffraction)

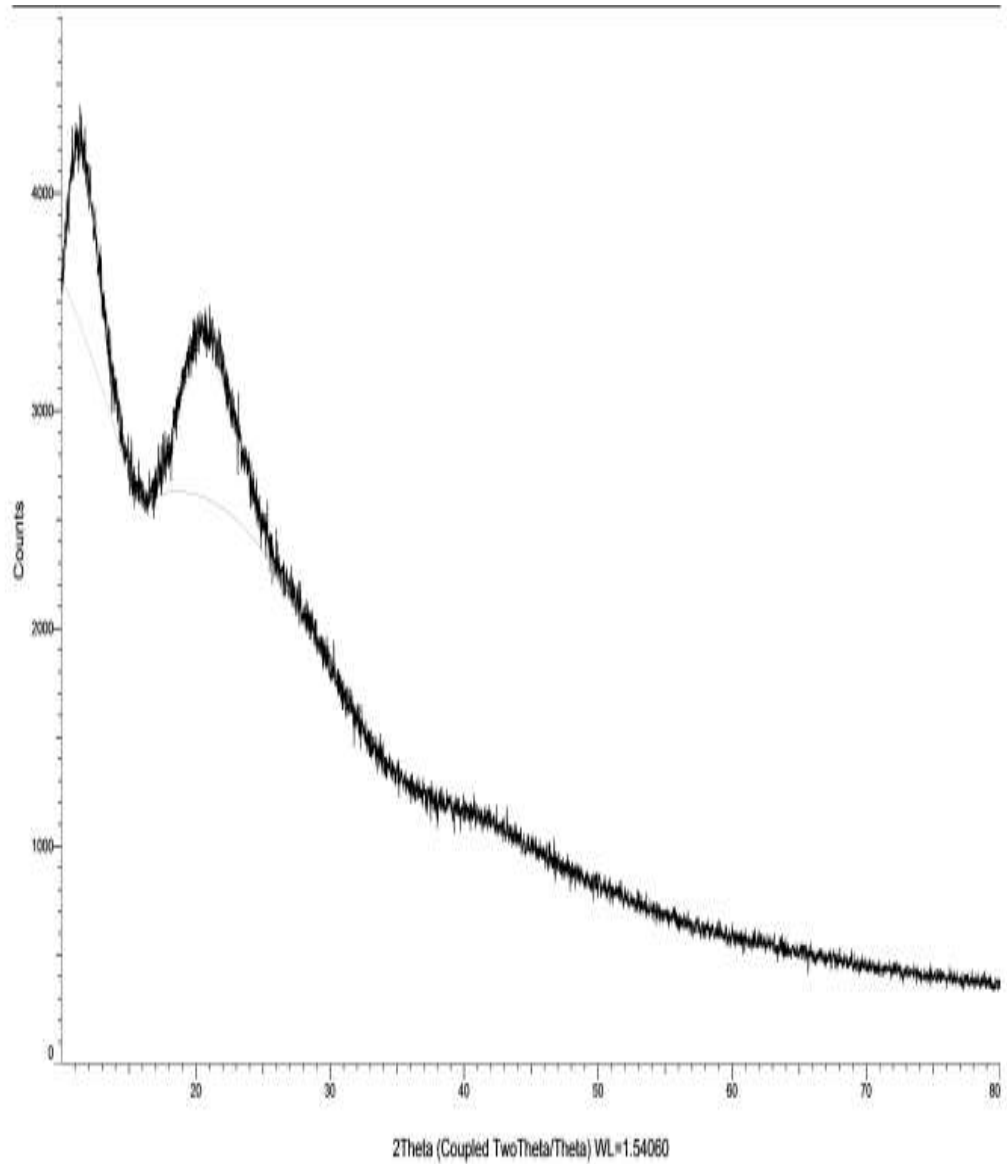
1. Loratadin Murni



2. Kristal Sferis Loratadin



3. PVP (Poyvinil Pirolidon)



Lampiran 9. Perhitungan rendemen kristal sferis loratadin

Rumus :

$$\% \text{ rendemen} = \frac{\text{Bobot kristal sferis loratadin}}{\text{Bobot loratadin murni}} \times 100 \%$$

Hasil Penimbangan :

$$\text{Kertas tikmbang} = 376,3 \text{ mg}$$

$$\text{Kertas saring} = 351,3 \text{ mg}$$

$$\text{Kertas timbang + loratadin murni} = 1351,3 \text{ mg}$$

$$\text{Kertas saring + kristal sferis} = 1273,4 \text{ mg}$$

Perhtitungan :

- Bobot loratadin murni

Kertas timbang + loratadin murni	= 1376,3 mg	
Kertas sisa	= 376,3 mg	-
Bobot loratadin murni	= 1000	mg

- Bobot kristal sferis

Kertas saring + kristal sferis	= 1273,4 mg	
Kertas sisa	= 351,3 mg	-
Bobot loratadin murni	= 922,1	mg

$$\% \text{ rendemen} = \frac{\text{Bobot kristal sferis loratadin}}{\text{Bobot loratadin murni}} \times 100 \%$$

$$= \frac{922,1}{1000} \times 100\%$$

$$= 92,21 \%$$

Lampiran 10. Pembuatan kurva kalibrasi loratadin

Konsentrasi (x)	Absorbansi (y)
4	0,296
6	0,379
8	0,465
10	0,569
12	0,652
14	0,744

Persamaan regresi linear antara konsentrasi (ppm) dan serapan diperoleh

$$a = 0,11083$$

$$b = 0,04519$$

$$r = 0,999570$$

Persamaan regresi linear

$$y = a + bx$$

$$y = 0,11083 + 0,04519x$$

Keterangan :

y = konsentrasi (ppm)

x = serapan

Lampiran 11. Perhitungan kurva kalibrasi

Medium dapar fosfat 6,8

Kertas timbang	= 270,5 mg
Kertas timbang + zat	= 280,5mg
Kertas timbang sisa	= 271,0 mg -
Zat Loratadin	= 9,5 mg

Konsentrasi larutan induk kurva kalibrasi medium dapar fosfat 6,8

$$9,5 \text{ mg} / 100 \text{ ml} = 95 \text{ mg} / 1000 \text{ ml}$$

$$= 95 \text{ ppm}$$

Penentuan panjang gelombang (dengan konsentrasi 10 ppm)

$$V1 \times C1 = V2 \times C2$$

$$V1 \times 95 \text{ ppm} = 10 \text{ ml} \times 10$$

$$C2 = 1,0 \text{ ml}$$

Perhitungan seri konsentrasi kurva kalibrasi medium dapar fosfat 6,8

- 4 ppm
 $V1 \times C1 = V2 \times C2$
 $V1 \times 95 \text{ ppm} = 10 \times 4 \text{ ppm}$
 $V1 = 0,42 \text{ ml}$
- 6 ppm
 $V1 \times C1 = V2 \times C2$
 $V1 \times 95 \text{ ppm} = 10 \times 6 \text{ ppm}$
 $V1 = 0,63 \text{ ml}$
- 8 ppm
 $V1 \times C1 = V2 \times C2$
 $V1 \times 95 \text{ ppm} = 10 \times 8 \text{ ppm}$
 $V1 = 0,84 \text{ ml}$
- 10 ppm
 $V1 \times C1 = V2 \times C2$
 $V1 \times 95 \text{ ppm} = 10 \times 10 \text{ ppm}$
 $V1 = 1,0 \text{ ml}$
- 12 ppm
 $V1 \times C1 = V2 \times C2$
 $V1 \times 95 \text{ ppm} = 10 \times 12 \text{ ppm}$
 $V1 = 1,2 \text{ ml}$
- 14 ppm
 $V1 \times C1 = V2 \times C2$
 $V1 \times 95 \text{ ppm} = 10 \times 14 \text{ ppm}$
 $V1 = 1,4 \text{ ml}$

Lampiran 12. Perhitungan LOD dan LOQ

Konsentrasi (x)	Absorbansi (y)	y'	y-y'	y-y' ²
4	0,296	0,29159	0,00441	0,00001
6	0,379	0,38197	-0,00297	0,000008
8	0,465	0,47235	-0,00735	0,00005
10	0,569	0,56273	0,00627	0,00003
12	0,652	0,65311	-0,00111	0,000001
14	0,744	0,74349	0,00051	0,0000002
Jumlah y-y' ²				0,0000992

Nilai y' diperoleh dari hasil persamaan $y = 0,11083 + 0,04519x$ dengan x adalah konsentrasi (ppm) dan y adalah serapan (y').

1. $y' = 0,11083 + 0,04519x$
 $= 0,11083 + 0,04519 \times 4 = 0,29159$
2. $y' = 0,11083 + 0,04519x$
 $= 0,11083 + 0,04519 \times 6 = 0,38197$
3. $y' = 0,11083 + 0,04519x$
 $= 0,11083 + 0,04519 \times 8 = 0,47235$
4. $y' = 0,11083 + 0,04519x$
 $= 0,11083 + 0,04519 \times 10 = 0,56273$
5. $y' = 0,11083 + 0,04519x$
 $= 0,11083 + 0,04519 \times 12 = 0,65311$
6. $y' = 0,11083 + 0,04519x$
 $= 0,11083 + 0,04519 \times 14 = 0,74349$

$$s_{x/y} = \sqrt{\frac{\sum |y - y'|^2}{n - 2}}$$

$s_{x/y}$ = simpangan baku residual

N = Jumlah data

$(\sum |y - y'|)^2 =$ Jumlah kuadrat total residual

$$= \sqrt{\frac{0,0000992}{6 - 2}} = 0,00497$$

- LOD = $3,3 \times \frac{Sx/y}{b}$
 $= 3,3 \times \frac{0,00497}{0,04519}$
 $= 0,36366$
- LOQ = $10 \times \frac{Sx/y}{b}$
 $= 10 \times \frac{0,00497}{0,04519}$
 $= 1,102$

Lampiran 13. Perhitungan presisi

Konsentrasi (ppm)	Absorbansi	Konsentrasi (ppm)
10	0,551	9,74043
10	0,554	9,91746
10	0,559	9,91746
10	0,564	10,02810
10	0,568	10,11662
10	0,569	10,13875
10	0,557	9,87320
10	0,553	9,78469
10	0,567	10,09449
10	0,558	9,89533
Rata-rata		9,95065
SD		0,13849
KV		1%

$$KV = \frac{SD}{rata-rata} \times 100\%$$

Lampiran 14. Perhitungan Akurasi

Konsentrasi (ppm)	Absorbansi	Konsentrasi	Recovery	Rata-rata
6	0,377	5,89002	98%	97%
6	0,379	5,93428	99%	
6	0,367	5,66873	94%	
8	0,467	7,88161	99%	99%
8	0,469	7,92587	99%	
8	0,471	7,97013	100%	
10	0,563	10,00597	100%	100%
10	0,558	9,89533	99%	
10	0,563	10,00597	100%	
Rata-rata				99%

Keterangan :

$$\% \text{recovery} = (\text{konsentrasi (ppm)} - \text{Absorbansi}) / \text{Konsentrasi} \times 100\%$$

Lampiran 15. Perhitungan kelarutan

- **Kristal sferis loratadin**

Penimbangan :

Kertas kosong	= 274,6 mg
Kertas + zat	= 326,1 mg
Kertas sisa	= <u>276,1 mg</u> -
Zat	= 50 mg

- **Obat murni loratadin**

Penimbangan :

Kertas kosong	= 268,6 mg
Kertas + zat	= 319,6 mg
Kertas sisa	= <u>269,6 mg</u> -
Zat	= 50 mg

- **Kelarutan kristal sferis loratadin dan loratadin murni**

No.	Obat	Absorbansi	Vol. Pembuatan	Fp	Kadar (ppm)	Kadar (mg)
1.	Kristal sferis loratadin	0,789	50	10	15,00708	7,50354
2.	Loratadin murni	0,434	50	10	7,15136	3,57568

$$\text{Kadar (ppm)} = y = a + bx$$

$$\text{Kadar (ppm)} = \frac{(\text{kadar (ppm)} \times \text{pengenceran}) \times \text{volume pembuatan}}{1000}$$

- **Perhitungan kadar**

- Kristal sferis loratadin

$$0,789 = 0,11083 + 0,04519x$$

$$X = \frac{0,789 - 0,11083}{0,04519} = 15,00708 \text{ ppm}$$

$$\text{Kadar (mg)} = \frac{15,00708 \times 10 \times 50}{1000} = 7,50354 \text{ mg}$$

- Loratadin murni

$$0,434 = 0,11083 + 0,04519x$$

$$X = \frac{0,434 - 0,11083}{0,04519} = 7,15136 \text{ ppm}$$

$$\text{Kadar (mg)} = \frac{7,15136 \times 10 \times 50}{1000} = 3,57568 \text{ mg}$$

Lampiran 16. Perhitungan PVP 1% (1 gram dalam 100 ml aquadest)

Kertas kosong	= 277,2 mg	
Kertas + zat	= 1279,2 mg	
Kertas sisa	= 279,2 mg	-
Zat	= 1000 mg ~ 1 gram	