BAB V
KESIMPULAN DAN SARAN

A. Kesimpulan

Pertama, Konsentrasi kitosan – natrium tripolifosfat mempengaruhi karakteristik nanopartikel asiklovir meliputi ukuran partikel, indeks polidispersitas, zeta potensial, dan efisiensi penjerapan obat yang dapat meningkatkan kualitas sistem penghantaran obat menuju target. Konsentrasi kitosan yang terlalu tinggi membuat zat aktif terjerap banyak namun tidak dalam matriks yang kompak. Konsentrasi penaut silang natrium tripolifosfat yang terlalu tinggi membuat partikel teraglomerasi bebas. Keseimbangan konsentrasi kitosan-natrium tripolifosfat sangat mempengaruhi karakteristik nanopartikel.

Kedua, Konsentrasi optimum dari polimer kitosan – penaut silang natrium tripolifosfat adalah kitosan 0,237% dan natrium tripolifosfat 0,167% dengan zat aktif asiklovir 0,5% yang memiliki karakteristik naopartikel yang baik sehingga akan menghasilkan sediaan nanogel asiklovir dengan penghantaran obat yang optimum menuju target terapi.

Ketiga, faktor yang mempengaruhi karakteristik nanopartikel kitosan-natrium tripolifosfat meliputi faktor instrinsik dan ekstrinsik. Faktor intrinsik meliputi sifat fisika kimia bahan, jenis pelarut, proporsi bahan, dan kondisi sediaan. Faktor ektrinsik meliputi proses pembuatan, metode yang digunakan, dan peneliti.

B. Saran

Perlu dilakukan penelitian selanjutnya untuk mengetahui stabilitas karakteristik nanopartikel dalam sediaan nanotopikal asiklovir. Perlu dilakukan uji penetrasi difusi pada membran kulit dan hewan uji untuk mengathui efek fisiologis dan efek toksiksitas sebelum dikembangkan dalam skala pabrikasi.

DAFTAR PUSTAKA

A. Nanda, J. Khanam, K.S. Das, Optimization of Preparation Method for Ketoprofen-Loaded Microspheres Consisting Polymeric Blends using Simplex Lattice Mixture Design. Materials Science & Engineering C.

Agnihotri, SA.. Mallikarjuna NN, Aminabhavi TM. 2014. *Journal of Controlled Release.* 5 (28): 93-100.

Anief M. 1997. Ilmu Meracik Obat. Yogyakarta: Gadjah Mada University Press

Ansel HC. 1989. Pengantar Bentuk Sediaan Farmasi Edisi Keempat. Jakarta: UI Press.

Aranaz, I, Harris R, Heras A. 2010, Chitosan Amphiphilic Derivatives. Chemistry and Applications, J. Curr. Org. Chem. 7(10):308-330.

Astika DN. 2015. Pengaruh Penambahan Surfaktan Tween 80 terhadap Sifat Mutu Fisik Stabilitas Mikroemulsi Ketoprofen. Jember: Fakultas Farmasi Universitas Jember.

Bahrami Gh, Mirzaeei Sh, Kiani A. 2005. Determination of acyclovir in human serum by high performance liquid chromatography using liquid-liquid extraction and its application in pharmacokinetic studies. J. Chromatogr. B, 816 (2):327-331.

Barry, W. 1983. Dermatological Formulations, Percutaneous Absorbtion. Ney York: Marcel Dekker Inc

Bhumkar DR, VB Pokharkar, 2006. Studies on Effect of pH on Cross-Linking of Chitosan With Sodium Tripolyphosphate. A technical note. AAPS PharmSciTech 7(2):50-61.

Bolton, S. 1997, Pharmaceutical statistical: practical and clinical aplication, dalam Mariani, V. 2010, 'Optimasi formula tablet ekstrak daun sambung nyawa (*Gynura procumbens* (lour.) merr.) dengan kombinasi bahan pengikat amilum manihot dan bahan penghancur starch1500 dengan metode *factorial design*', *Skripsi*, S.Farm., Fakultas Farmasi, Universitas Muhammadiyah Surakarta, Surakarta, Indonesia.

Buzea C, Pacheo Blandino I.I, Robbie K. 2007. Nanomaterials and nanoparticles. Sources and toxicity, Biointerphases. 2(4):17-22

Chan CC, Herman L, Lee YC, Zhang XM. 2004. Analitical Method Validation and Instrument Performance Verification. New Jersey: Inc Publication

Clegg. 1995. Bahan-bahan Pembentuk Gel. Gellingagentsfile.pdf. Diakses 10 Oktober 2019.

De Campos M, Sanchez A, Alonso MJ. Chitosan nanoparticles: A new vehicle for the improvement of the delivery of drugs to the ocular surface. Application to cyclosporin A. Int J Pharm 2001;224:159-68.

Delie, F. and Blanco, M.J. 2005. Polymeric Particulate to Improve Oral Bioavailabiliti of Peptide Drugs. Molecules, 10 : 65-75.

Departemen Kesehatan Republik Indonesia. Farmakope Indonesia. Edisi IV. Jakarta : Depkes RI; 1995

Dustgani, A.; Vasheghani-Farahani, E.; Imani, M. Determination of the Optimum Conditions for Production of Chitosan Nanoparticles. Iran. J. Polym. Sci. Technol., 2007, 20, 457-464.

Ganiswarna G . Sulistia, 1995, Farmakologi dan Terapi Edisi IV. Jakarta: Fakultas Kedokteran Universitas Indonesia.

Garg AD, Aggarwal S, Garg, A. K.Sigla. 2002. Spreading of Semisolid Formulation. An Update. Pharmaceutical Tecnology 4(78):84-102.

Gold D, Corey L. Acyclovir Prophylaxis for Herpes Simplex Virus Infection. Antimicrob Agents Chemother 1987; 31:361-367.

Grassi, Mario. 2007. Understanding drug Realese and Absorpstion Mechanisms . London: Taylor & Francis Group.

Gupta, R. B. & Kompella, U. B., 2006, Nanoparticle Technology for Drug Delivery (Drugs and the Pharmaceutical Science), Chapter I: Fundamentals of Drug Nanoparticles, 1-17, Taylor & Francis Group, New York.

Haneefa K.P.M., Easo S., Hafsa P. V, Mohanta G.P. and Nayar C., 2013, Emulgel: An Advanced Review, Journal Of Pharmaceutical Sciences and Research, 5 (12), 254–258.

Harmita. 2004. Petunjuk Pelaksanaan Validasi Metode dan Cara Perhitungannya. Majalah Ilmu Kefarmasian 1(3):23-34

Istiantoro, Yati H, Gan Vincent HS. 2007. Penisilin, Sefalosporin dan Antibiotik Betalaktam lainnya. Farmakologi dan Terapi. Edisi 5. Jakarta: Bagian Farmakologi Fakultas Kedokteran Universitas Indonesia

Jonassen H. 2014. Polysaccharide Based Nanoparticles for Drug Delivery Applications Thesis School of Pharmacy. Faculty of Matematics and Natural Sciences Oslo: University of Oslo.

Kafshgari MH, Khorram M, Khodadoost M, Khavari S. 2011. Reinforcement of chitosan nanoparticles obtained by an ionic cross-linking process. Iran. Polymer J 20(5):445-456

Kaur, Simar Preet; Rekha Rao; Afzal Hussain; Sarita Khatkar. Preparation and Characterization of Rivastigmine Loaded Chitosan Nanoparticles. *Jounal of Pharmaceutical Science and Research* 3, no.5 (2011): h. 1227-1232.

Ko JA, Park HJ, Hwang SJ, Park JB, Lee JS. 2002. Preparation and Characterization of Chitosan Microparticles Intended for Controlled Drug Delivery. Int J Pharm. 249(2):165-174

Kumar MNVR. 2000, A Review of Chitin and Chitosan Applications. React Funct Polym 46(31): 1-27.

Kuncari ES, Iskandarsyah, Praptiwi. 2014. Evaluasi, Uji Stabilitas Fisik Dan Sineresis Sediaan Gel yang Mengandung Minoksidil, Apigenin dan Perasan Herba Seledri (Apium Graveolens L.). Bulletin Penelitian Kesehatan. 42(4):213-222.

Lachman L, Lieberman A, Kanig JL. 1986. The Theory and Practice of Industrial Pharmacy 2 nd edition. Philadelphia: Lea and Febiger.

Lachman L, Lieberman, Herbert A. 2008. Pharmaceutical Dosage Form : Tablets. New York: Pharmaceutical Press

Lachman L. 1994. Teori dan praktek farmasi industry Eedisi 3. Jakarta: UI Press.

Lieberman HA, Ringer MM, Banker GS. 1996. Pharmaceutical Dosage Form, Second edition. New York.: Marcel Decker Inc.

Martien R, Adhyatmika, Irianto, Iramie DK, Farida, V, Sari, Dian Purwita. 2012. Perkembangan Teknologi Nanopartikel Sebagai Sistem Penghantaran Obat. Majalah Farmasetik 8(1):243-258.

Martien R, Loretz B, Bernkop SA. 2006. Oral Gene Delivery: Design of polymeric carrier systems shielding toward intestinal enzymatic attack, Biopolymers. Mater. Sci. Eng 83(57):327 – 336.

Martin A, Swarbick J A Cammarata. 1993. Farmasi Fisik 2. Edisi III. Jakarta: UI Press.

Martin A., Swarbrick J. dan Cammarata, 1993, Farmasi Fisik: Dasar-dasar Farmasi Fisik dalam Ilmu Farmasetik, edisi 3., UI Press, Jakarta.

Mason, T.J., Paniwnyk, L. & Lorimer, J.P. 1996, The uses of ultrasound in food technology, *Ultrasonics Sonochemistry*, **3**: 253 − 260.

Mohanraj VJ dan Chen Y. Nanoparticles-a review. Tropical Journal of Pharmaceutical Research 2006; 561-573.

Mohanraj, V.J. and Y. Chen. 2006. Nanoparticles : A Review. Tropical Journal of Pharmaceutical Research, 5 :1.

Mulhaquddin. 2014. Validation Method. Dipresentasikan pada Diklat Validasi Metode, Baristand Industri Ambon 10 - 13 Juni 2014.

Murdock, R.C., Braydich-Stole, L., Schrand, A.M., Schlager, J.J., Hussain, S.M. 2008. Characterization of Nanoparticle Dispersion in Solution Prior to In Vitro Exposure using Dynamic Light Scattering Tehnique. Toxicol, Sci, 101 : 239-253.

Mycek MJ, Harvey RA, Champe PC. 2001. Farmakologi. Ulasan Bergambar 2nd ed. H. Hartanto. Jakarta: Widya Medika

N.A. Armstrong, James, 1996. Pharmaceutical Experimental Design and Interpretation, Taylor and Francis, hal. 205-222.

Niyogi, P., N.J. Raju, P.G. Reddy, & B.G. Rao, 2012, Formulation and Evaluation of Antiinflamatory Activity of Solanum pubscens Wild Extracts Gel on Albino Wistar Rats, International Journal of Pharmacy, 2(3), 484-490

Park, K., Yeo, Y., Swarbrick, J. 2007. Microencapsulation Technology in: Encyclopedia of Pharmaceutical Technology 3rd Edition. New York: Informa Healthcare USA, Inc., p. 2315- 2325.

Patravale, V.B., Date, A.A., Kulkarni, R.M. 2004. Nanosuspensions: a promising drug delivery strategy. J Pharm Pharmacol, 56(7) : 827-40.

Primadiati, R., 2001, Kecantikan, Kosmetika & Estetika, Jakarta : PT. Gramedia Pustaka Utama.

Raton, F.L Boca and C.K Smoley, 1993, Everything Added to Food in the United States. http://en.wikipedia.org/wiki/Gellingagent. di akses pada tanggal 24 Oktober 2019.

Rauhatun N, Iis W. 2013. Preparasi Nanopartikel Kitosan-TPP/ Ekstrak Etanol Daging Buah Mahkota Dewa (Phaleriamacrocarpa (Scheff) Boerl) dengan Metode Gelasi Ionik. Yogyakarta: Jurnal Farmasi Sains dan Komunitas. 11(1): 7-12.

Rawat M, Singh D, Saraf S. 2006. Nanocarriers: Promising Vehicle for Bioactive drugs. Biol Pharm Bull. 29(9):1790-1798

Reddy, P. Dwarakanadha; D. Swarnalatha. Recent Advances in Novel Drug Delivery Systems. *International Journal of PharmTech Research* 2, no. 3 (Juli-September 2010): h. 2025-2027

S. D. Prajapati, D.L. Patel, 2016 . Floating Matrix Tablets of Domperidone: Formulation And Optimization using Simplex Lattice Design. Thai J. Pharm. Sci., vol. 33, hal. 113-122. 2009.

Sa'adah, Eva, dan Ari Surya Winata. 2010. Validasi metode pengujian logam tembaga pada produk air minum dalam kemasan secara spektrofotometri serapan atom nyala. BIOPROPAL INDUSTRI 01 (02) : 31–37.

Sainah. 2013, 'Optimasi formula suspensi siprofloksasin dengan kombinasi *Pulvis Gummi Arabici* (PGA) dan carbopol 934 menggunakan metode desain faktorial', *Skripsi*, S.Farm., Program Studi Farmasi, Fakultas Kedokteran, Universitas Tanjungpura, Pontianak, Indonesia.

Sakkinen M. Biopharmaceutical evaluation of microcrystalline chitosan as release rate controlling hydrophilic polymer in granules for gastroretentive drug

delivery. Academic Dissertation Faculty of Science of the University of Helsinki, 2003.

Sayuti, Nutrisia Aquariushinta, (2015), *Formulasi dan Uji Stabilitas Fisik Sediaan Gel Ekstrak Daun Ketepeng Cina (Cassia alata* L.), Politeknik Kesehatan Kemenkes Surakarta, Surakarta

Setiawati A, Nafrialdi. 2007. Farmakologi dan Terapi Edisi V. Jakarta: Departeman Farmakologi dan Terapeutik Fakultas Kedokteran Universitas Indonesia.

Sharma N., Mishra S., Sharma S., Deshpande R.D. and Sharma R.K., 2013, Preparation and Optimization of Nanoemulsions for targeting Drug Delivery, Int. J. Drug Dev. & Res., 5 (4), 37–48.

Spruance SL, Rea TL, Thoming C, Tucker R, Saltzman R, Boon R. Penciclovir Cream for the Treatment of Herpes Simplex Labialis. A Randomized, Multicenter, Double-Blind, Placebo- Controlled Trial. Topical Penciclovir Collaborative Study Group. JAMA 1997; 277:1374-1379.

Swarbrick J. (ed).. Encyclopedia of pharmaceutical technology (3rd ed., vol. 4). New York: Informa Healthcare USA Inc., 2007.

Sweetman SC. 2009. Martindale The Complete Drug Reference Thirty Sixth Edition. New York : Pharmaceutical Press

Tiyaboonchai, W. 2003. Chitosan nanoparticles: Apromising system for drug delivery. Naresuan University Journal 11(3):51–66.

Tranggono RI, Latifah F. 2007. Buku Pegangan Ilmu Pengetahuan Kosmetik. Jakarta: Gramedia Pustaka Utama.

Verma S., Singh A.K. and Mukerjee A., 2016, Formulation and Evaluation of Ketoconazole, World Journal of Pharmacy and Pharmaceutical Science, 5 (2), 899–911.

Veronica E.F. dan Dwiastuti R., 2013, Optimasi Humektan Propilenglikol dan Gelling Agent Carbopol 940 dalam Sediaan Gel Penyembuh Luka Ekstrak Daun Petai Cina (Leucaena leucocephala (Lam.) de Wit.) : Aplikasi Desain Faktorial, Fakultas Farmasi, Universitas Sanata Dharma, Yogyakarta.

Voigt R., 1984, Buku Pelajaran Teknologi Sediaan Farmasi, Edisi 5. Soendani, N.,, Gadjah Mada University Press, Yogyakarta.

Voigt. 1984. Buku Ajar Teknologi Farmasi. Yogyakarta: UGM Press

Walters Kenneth A. 2002. Dermatological and Transdermal Formulation. New York: Marcel Dekker Inc.

Wu Y, Yang, Wang C, Hu J, Fu S. 2005. Chitosan nanoparticle as a novel delivery system for ammonium glycyrrhizinate, International Journal of Pharmaceutics. 295(42):235-245

Wyatt E, Sutter SH, Drake LA. 2001. Dermatology Pharmacology. The Pharmacological Basis of Therapeutics 7(68):1801-1803.

Yu HL, Kiran S, Kurt ML, Jyuhn HJ, Fwu LM, Han WY, dan Hsing WS. 2008. Multi-ion-crosslinked nanopar-ticles with pH-responsive characteristics for oral delivery of protein drugs. Journal of Controlled Release :132 ; 141-149.

Zats, J.L & Gregory, P.K., 1996, Gel, in Liebermen, H.A., Rieger, M.M., Banker, G.S., Pharmaceutical Dosage Forms: Disperse Systems, 2, 400 - 403, 405 – 415, Marcel Dekker Inc, New York.

L A M P I R A N

Lampiran 1. Certificate Of Analysis

Certificate of Analysis
CHITOSAN [Powder]

- Product Name : CHITOSAN . [Shrimp Shell]
- Raw Material : Black tiger
- Use : Food Grade dan Medical Grade

- The date of manufacture : 10 , MARET 2019
- Expiry Date : 10 , MARET 2021

- Analysis Date : 11 , MARET 2019

Items	Specification	Results	Method
Appearance	White Or Yellow	Pale Yellow	
Odor	Odorless	Complies	
Solution	99 % Min.	99 % UP	6 % Soln. in HCl 1.0 %
Moisture Content	12.0 % Max.	8.5 %	Infrared Moisture meter
Ash Content	1.0 % Max.	0.5 %	Ashing Method
Protein Content	1.0 % Max.	0.5 %	Lowry method
De-Acetylation (DAC)	70 % Min.	87,5 %	PVSK
Viscosity	50 cps Max.	20 cps	0.5 % Soln. in Acid
Transparency	30 Cm Min.	39 Cm	Transparency meter (JIS K)
pH (5 % dispersion)	6.5 ~ 7.5	7,1	pH meter
As	0.2 ppm Max.	Complies	ICP
Pb	1.0 ppm Max.	Complies	ICP
E-Coli	Negative	Negative	Flat Disk method
Salmonella	Negative	Negative	Flat Disk method
Particale size	Crushed	100 mesh	Mesh Method

- **Chitosan Berat Molekul : 50,000 – 80,000 M / W**

HACCP CERTIFIED

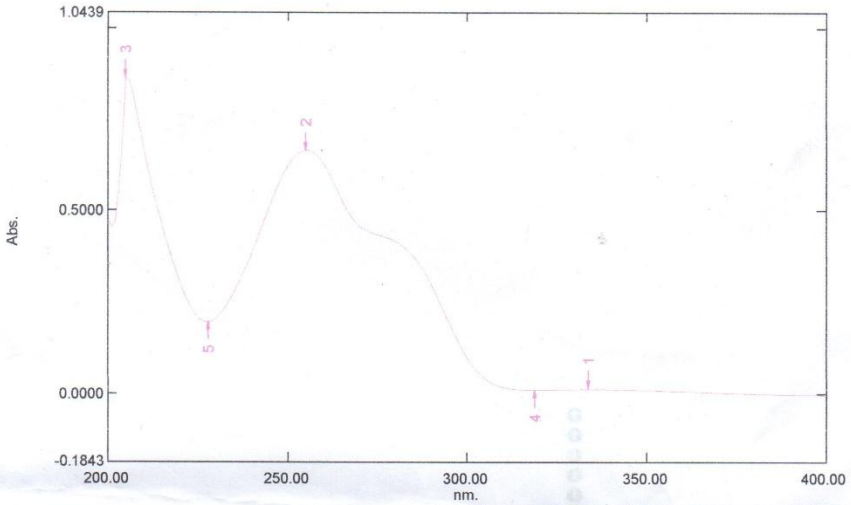
Ref No. : 24/PPI/HACCP/PK/1/10

Lampiran 2. Panjang Gelombang Maksimal

Spectrum Peak Pick Report

06/15/2020 11:37:46 AM

Data Set: File_200615_111611 - RawData



No.	P/V	Wavelength	Abs.	Description
1	↑	334.00	0.0119	
2	↑	255.00	0.6663	
3	↑	205.00	0.8637	
4	↓	319.00	0.0099	
5	↓	228.00	0.1956	

[Measurement Properties]
Wavelength Range (nm.): 200.00 to 400.00
Scan Speed: Medium
Sampling Interval: 1.0
Auto Sampling Interval: Disabled
Scan Mode: Single

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

[Attachment Properties]
Attachment: None

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

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

Lampiran 3. Operating Time Asiklovir

Kinetics Data Print Report

06/15/2020 12:20:35 PM

Time (Minute)	RawData ...
0.000	0.623
1.000	0.624
2.000	0.624
3.000	0.624
4.000	0.624
5.000	0.625
6.000	0.625
7.000	0.624
8.000	0.624
9.000	0.624
10.000	0.624
11.000	0.624
12.000	0.624
13.000	0.624
14.000	0.625
15.000	0.625
16.000	0.624
17.000	0.624
18.000	0.624
19.000	0.624
20.000	0.624
21.000	0.624
22.000	0.624
23.000	0.625
24.000	0.625
25.000	0.624
26.000	0.624
27.000	0.624
28.000	0.624
29.000	0.624
30.000	0.624

Lampiran 4. Kurva Linieritas

No	Konsentrasi	ABS	y'	y-y'
1	1,92	0,123	0,11653571	0,006
2	3,84	0,229	0,23721429	-0,008
3	5,76	0,355	0,35789286	-0,003
4	7,68	0,483	0,47857143	0,004
5	9,60	0,594	0,59925	-0,005
6	11,52	0,731	0,71992857	0,011
7	13,44	0,835	0,84060714	-0,006

A	-0,00414286
B	0,062853423
r	0,999609299

Lampiran 5. Presisi

No	Konsentrasi	ABS	Konsentrasi (X)
1	7,68	0,483	7,750458716
2	7,68	0,477	7,65499852
3	7,68	0,481	7,71863865
4	7,68	0,477	7,65499852
5	7,68	0,476	7,639088488
6	7,68	0,475	7,623178455
7	7,68	0,473	7,59135839
8	7,68	0,474	7,607268423
9	7,68	0,476	7,639088488
10	7,68	0,474	7,607268423
		Rata-Rata	7,648634507
		Standart Deviasi	0,050423621
		Coofisien Variasi	0,66%

Lampiran 6. Akurasi

pipet	Konsentrasi	ABS	Nilai X	Akurasi	Rata-Rata	Rata-rata akhir
1.5 ml	3,84	0,239	3,868	101%	100,19%	99,38%
1.5 ml	3,84	0,234	3,789	99%		
1.5 ml	3,84	0,240	3,884	101%		
2 ml	7,68	0,467	7,496	98%	98,43%	
2 ml	7,68	0,470	7,544	98%		
2 ml	7,68	0,476	7,639	99%		
5 ml	9,60	0,599	9,596	100%	99,52%	
5 ml	9,60	0,592	9,485	99%		
5 ml	9,60	0,598	9,580	100%		

Lampiran 7. LOD & LOD

No	Konsentrasi	ABS	y'	y-y'	(y-y')^2
1	1,92	0,123	0,1165	0,006	0,00004
2	3,84	0,229	0,2372	-0,008	0,00007
3	5,76	0,355	0,3579	-0,003	0,00001
4	7,68	0,483	0,4786	0,004	0,00002
5	9,60	0,594	0,5993	-0,005	0,00003
6	11,52	0,731	0,7199	0,011	0,00012
7	13,44	0,835	0,8406	-0,006	0,00003
				∑	0,00032
	a	-0,00414		Y/N-2	0,00008
	b	0,06285		Sy/x	0,008928
	r	0,999609299		LOD	0,468736
				LOQ	1,420414
				Vx0	1,8%