

# Publikasi 1

*by* Iyan 1

---

**Submission date:** 23-Nov-2017 01:41PM (UTC+0700)

**Submission ID:** 884419759

**File name:** 3-Vol.-6-Issue-5-May-2015-IJPSR-RA-4920-Paper-3\_1.pdf (674.62K)

**Word count:** 3993

**Character count:** 20252



Received on 24 September, 2014; received in revised form, 16 November, 2014; accepted, 27 January, 2015; published 01 May, 2015

## A FORMULA OPTIMIZATION OF NIFEDIPINE TABLET COMBINATION WITH FLOATING MUCOADHESIVE SYSTEM IN A SIMPLEX LATTICE DESIGN

Endang Diyah Ikasari<sup>1\*</sup>, Achmad Fudholi<sup>2</sup>, Sudibyo Martono<sup>2</sup> and Marchaban<sup>2</sup>

<sup>1</sup>Yayasan Pharmasi College of Pharmacy<sup>1</sup>, Semarang 50193, Indonesia  
<sup>2</sup>Faculty of Pharmacy<sup>2</sup>, Gadjah Mada University, Yogyakarta, Indonesia

### Keywords:

Nifedipine, gas generating, Carbopol 934P, gelatin, floating mucoadhesive

### Correspondence to Author:

Endang Diyah Ikasari

Yayasan Pharmasi College of Pharmacy, Semarang - 50193, Indonesia

E-mail: eri\_ung@yahoo.co.id


**ABSTRACT:** Nifedipine has poor dissolution characteristics due to its poor wettability and dispersibility in body fluids, floating mucoadhesive system in a Simplex Lattice Design were combined in an attempt to prolong its gastric residence time. This research was aimed to find an optimum formula, through finding effects of adding polymers (Carbopol 934P, gelatin) concentration and optimum gas generating, to be combined with its Nifedipine spray-dry release with PVP K-30. Nifedipine was produced by a spray-dried method with the 30% drugloads using PVP K-30. All performed dispersions were characterized by using Scanning Electron Microscopy (SEM), X-ray Powder Diffractometry (XRPD), Differential Scanning Calorimetry (DSC) and in-vitro drug release. The 5% and 15% concentration of Carbopol 934P, gelatin, and (citric acid:Na<sub>2</sub>CO<sub>3</sub>) were used. Based on the Design Expert Optimization program, the optimum formula of Nifedipine tablets was obtained that it consisted of 12.02% Carbopol 934P, 5% gelatin, and 7.98% gas generating which resulting the physical characteristics of 3.00% moisture content, 10.51 g/sec flow-rate, 4.51 kg/cm<sup>2</sup> hardness, 0.48% fragility, 58.10% DE, 100.20 sec Floating Lag Time (FLT), and 0.1011 N mucoadhesive power.

**INTRODUCTION:** Nifedipine is a calcium channel blocker, which belongs to dihydropyridine derivatives. It exhibits poor dissolution characteristics due to its poor wet ability and dispersibility in body fluids. Therefore, a number of attempts, such as decreasing particle size, the use of wetting agents, co-precipitation, and preparation of solid dispersion, have been made to modify the dissolution characteristics to improve the absorption rate<sup>1</sup>. Amorphous solid dispersions can be used to improve dissolution rate of poorly soluble drugs.

This product consisting of a hydrophilic carrier which the drug is dispersed molecularly or as very small particles<sup>2,3</sup>.

In a previous study, a fully amorphous solid dispersion using PVP K-30 was prepared as hydrophilic carriers for Nifedipine. Spray dried and melted fusion methods are commonly used to evaporate a solvent<sup>4</sup>.

Nifedipine (dimethyl 1,4-dihydro-2,6-dimethyl-4-(o-nitrophenyl)-3,5-pyridinadicarboxylate) inhibits Ca<sup>2+</sup> infiltrate to cardiac muscle cells and arterial smooth muscle cells. This drugs commonly used to treat hypertension and angina pectoris. Nifedipine dose in retard tablet is 10-40 mg given 2 times daily. This drug has short half-life (2 hours). Hence, formulation in sustained release can reduce frequency of drug administration that would

QUICK RESPONSE CODE	DOI: 10.13040/IJPSR.0975-8232.6(5).1837-44
	Article can be accessed online on: www.ijpsr.com
DOI link: <a href="http://dx.doi.org/10.13040/IJPSR.0975-8232.6(5).1837-44">http://dx.doi.org/10.13040/IJPSR.0975-8232.6(5).1837-44</a>	

increase both patient compliance and treatment's effectivity<sup>5</sup>.

There are many methods for make sustained release dosage form. One of them is Gastroretentive Drug Delivery System (GRDDS) which keep this dosage form survive at the gastro fluids. GRDDS used to control drug delivery, especially for drugs which has narrow therapeutic window and good absorption in gastro membrane. Things would increase gastro lag time include bioadhesive (attached in the membrane's surface), increase the size of molecule drugs to prevent drugs across pylorus membrane, and density control which known as floating system<sup>6</sup>.

Floating mucoadhesive drug delivery system is defined as method for drug delivery which has low density, floating and attaching capability in the gastro membrane for a long time. This combination consist of effervescent components (sodium bicarbonate and citric acid) and polymers (Carbopol 934P and gelatin) that can extend lag time of Nifedipine tablets in the gastro membrane. Based on these descriptions, obtaining an optimum formula out of the physical characteristics and dissolution profile of floating mucoadhesive Nifedipine tablets, the Simplex Lattice Design can be used<sup>7</sup>.

## MATERIALS AND METHODS:

### Materials:

The materials used were technical grade (etanol 96%, acidum hydrochloridum), pharmaceutical grade (Nifedipine (Italy), Carbopol 934P (Hongkong), acidum citricum (China), sodium bicarbonate (Germany), polyvinylpyrrolidon K-30 (China), lactosum (New Zealand), Mg stearate, Avicel PH 102, NaCl), and analytical grade (sodium perchlorate, sodium acetate).

The instruments used were digital and analytical scales, mortir and stamper, sieve no. 18 and 20, dissolution apparatus type II paddle (Electrolab TDT-08L), tablet machine, spectrophotometer UV-

Vis mini 1240 (Shimadzu), moisturemeter (G-Won Hitect Co.LTD, RRC), flow rate tester (Stainless Steel), mucoadhesive tester, Stakes monsato hardness tester, and friability tester.

### Production of Solid Dispersion (SD):

Production of solid dispersion was done using 30% drug loads by PVP K-30 with spray dryer inlet at temperature 90<sup>0</sup>C, exhaust temperature 60<sup>0</sup>C, and pump speed 4. This solid dispersion products were analyzed by Scanning Electron Microscopy (Jeol JSM T300), Diffractometer (Philip PW 1800, Gadj. Mada University, Yogyakarta, Indonesia) with copper anode (Cu K $\alpha$  radiation,  $\lambda = 0.15405$  nm, 40 kV, 40 mA), FT-IR spectrophotometer (IR-Prestigo 21), Differential Scanning Calorimeter (ASTM D 3418, BPPT, Serpong, Jakarta, Indonesia), and in-vitro drug release using USP dissolution apparatus type II (Veego).

### Production of Tablets:

Granules were done by mixing Nifedipine solid dispersion and sodium citricum. Gelatin and Carbopol 934P are mixed, then this mixture adding by first mixture. Sodium bicarbonate and Avicel PH 102 was mixed by second mixture which followed by moisture content and flow rate test. Each formula were identified their physical characteristics with six replicates (Table 1). This granules were compressed the tablet machine to produce 200 mg/ tablet. Tablets were tested for weight variation, drug content, hardness, friability, floating lag time, total floating time, dissolution profile, and mucoadhesive power.

**RESULT AND DISCUSSION:** The Nifedipine solid dispersion (SD) was formed in granules yellow colour (Fig. 1) and has free flowing (22.80g/sec  $\pm$  0.28), moisture content (3.90%  $\pm$  0.11), and melting point (173.05<sup>0</sup>C  $\pm$  3,06). Nifedipine solid dispersion have been changed into amorphous form (Fig. 2) which no crystal form after confirmed using X-Ray Powder Diffractometry (XRPD), shown in Fig. 3.

TABLE 1. FORMULA OF FLOATING MUADHESIEVE NIFEDIPINE TABLETS

No	Material	Formula	Formula	Formula	Formula	Formula	Formula	Formula
		I	II	III	IV	V	VI	VII
1	Nifedipin SD (mg)	133,3	133,3	133,3	133,3	133,3	133,3	133,3
2	Acidum citricum (mg)	4,32	4,32	12,96	4,32	8,64	8,64	7,14
3	Sodium bicarbonate (mg)	5,68	5,68	17,04	5,68	11,36	11,36	9,46
4	Gelatin (mg)	10	30	10	20	10	20	16,67

5	Carbopol 934P (mg)	30	10	10	20	20	10	16,67
6	Magnesium stearat (mg)	8	8	8	8	8	8	8
7	Talc (mg)	0,5	0,5	0,5	0,5	0,5	0,5	0,5
8	Avicel PH 102 (mg)	8,2	8,2	8,2	8,2	8,2	8,2	8,2

Note:

- Formula I : Carbopol 934P 15%: Gelatin 5%: gas generating 5%
- Formula II : Carbopol 934P 5%: Gelatin 15%: gas generating 5%
- Formula III : Carbopol 934P 5%: Gelatin 5%: gas generating 15%
- Formula IV : Carbopol 934P 10%: Gelatin 10%: gas generating 5%
- Formula V : Carbopol 934P 10%: Gelatin 5%: gas generating 10%
- Formula VI : Carbopol 934P 5%: Gelatin 10%: gas generating 10%
- Formula VII : Carbopol 934P 8,33%: Gelatin 8,33%: gas generating 8,33%



FIG. 1 NIFEDIPINE SOLID DISPERSION WITH PVP K-30

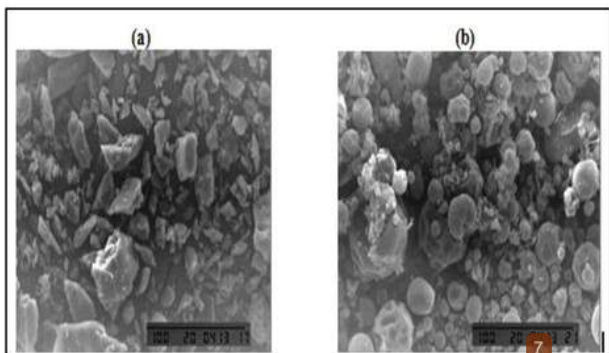


FIG. 2: (a) SEM NIFEDIPINE; (b) SEM NIFEDIPINE SOLID DISPERSION WITH PVP K-30

**FT-IR Studies:**

FT-IR used to describe interaction between Nifedipine and PVP K-30 based on their functional group spectrum at solid dispersion. The data showed no interaction between Nifedipine and PVP K-30, which is -OH group, C=O group and nitro group appear at 3400-2400 cm<sup>-1</sup>, 1820-1600 cm<sup>-1</sup>, and 1600-1500 cm<sup>-1</sup>, respectively. Analyze by IR resulted there is no new functional group or known as finger print because of their physical interaction (Table 2.). The solid dispersion Nifedipine in PVP K-30 or their physical mixture has same functional group with pure Nifedipine, but there is a little intensity difference for its functional group

although this interaction do not destroy the structure of pure Nifedipine (Fig. 4).

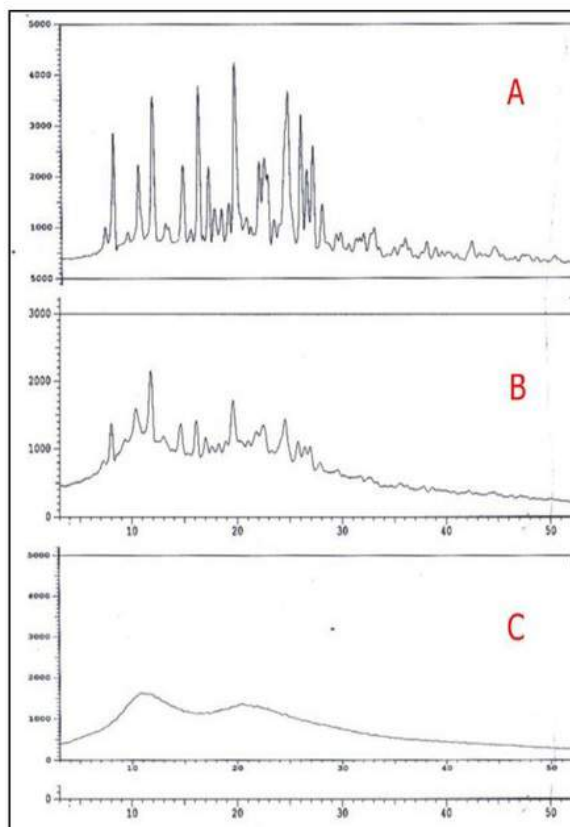


FIG.3. (a) XRPD NIFEDIPINE; (b) XRPD PHYSICAL MIXTURE OF 30% NIFEDIPINE IN PVP K-30; (c) XRPD NIFEDIPINE SOLID DISPERSION.

TABLE 2: FT-IR ANALYSIS

Formula	Wavenumber (cm <sup>-1</sup> )		
	-OH	C=O	Nitro
Nifedipine SD	3417.86	1681.93	1527.62
Physical mixture	3448.72	1681.93	1651.07
Pure Nifedipin	3332.99	1681.93	1527.62

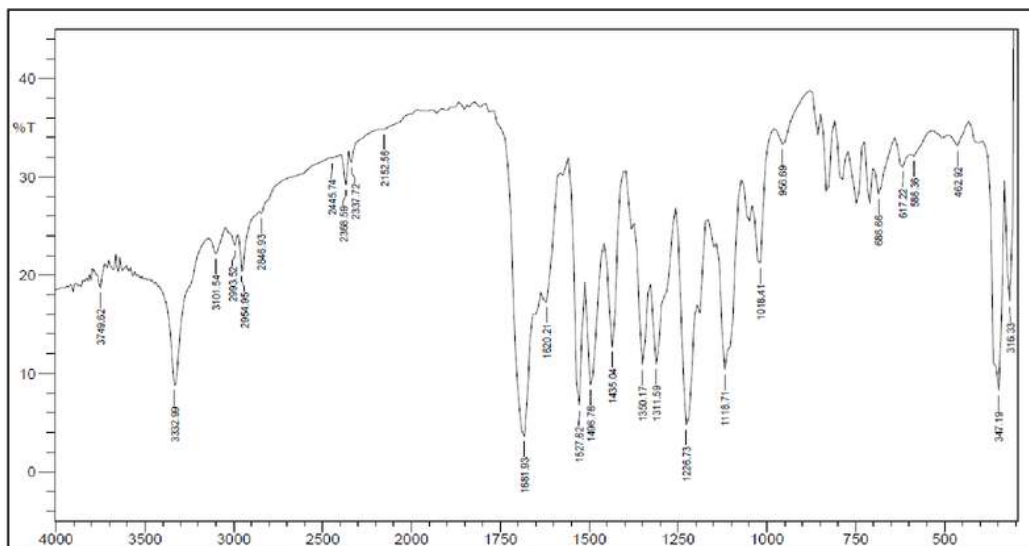


FIG.4: FT-IR SPECTRA OF PURE NIFEDIPINE

**Differential Scanning Calorimetry (DSC):**

DSC test were subjected to examine the form of solid dispersion molecules. Each sample which is pure Nifedipine, solid dispersion, and physical mixture were evaluated by DSC. Nifedipine melting point was 174.94°C and *T<sub>g</sub>*s of PVP K-30 was 173°C. While increasing the concentration of

Nifedipine in PVP K-30 result decreasing *T<sub>g</sub>* (133.04°C). This studies conclude that Nifedipine solid dispersion has amorphous form.

**In-Vitro Drug Release:**

Nifedipine SD can improve dissolution better than physical mixture and its pure form, which described in Table 3.

TABLE 3. CONCENTRATION OF NIFEDIPINE (%)

Formula	% Nifedipine					
	10 min	20 min	30 min	40 min	50 min	60 min
Nifedipine SD	17.27±2.45	22.58±0.71	30.91±2.96	33.84±1.76	34.54±2.04	36.74±1.32
Physical mixture	13.75±2.25	26.34±3.44	35.42±1.32	39.64±1.32	43.63±1.90	44.69±1.38
Pure Nifedipine	10.25±4.01	24.95±0.34	30.15±1.61	34.91±2.19	37.53±1.60	40.16±1.06

**Testing of Physical Characteristics Granules Flow Rate:**

Based on Table 4. resulting that increase the concentration of gas generating and Carbopol 934P, decrease the flow rate because of high moisture content of granules. However, high concentration of gelatin can be able to improve this flow rate. Gelatin has binder capacity which be able to produce better granules. All formula fulfill the specification of granules flow rate which more than 10 g/sec<sup>7</sup>.

**Moisture Content (MC):**

Table 4. indicated that the more concentration of gas generating and Carbopol 934P result the more moisture content there form because of their high hygroscopics. All formula fulfill the specification

of granules moisture content which average of 2-4%<sup>7</sup>.

TABLE 4: RESULT OF PHYSICAL CHARACTERISTICS GRANULES

Formulation Code	Flow Rate* (g/detik)	Moisture Content* (%)
I	10,78±0,19	2,27±0,15
II	12,40±0,98	2,10±0,17
III	10,66±0,32	3,47±0,17
IV	10,78±0,29	2,57±0,08
V	10,64±0,37	3,88±0,20
VI	10,63±0,36	3,27±0,08
VII	12,02±0,63	2,90±0,09

Note:  
\* Mean ± SD; n= 6

**Physical Characteristics Test of Floating Mucoadhesive Nifedipine Tablets:**

**TABEL 5: RESULT OF PHYSICAL CHARACTERISTICS OF FLOATING MUCOADHESIEVE NIFEDIPINE TABLETS**

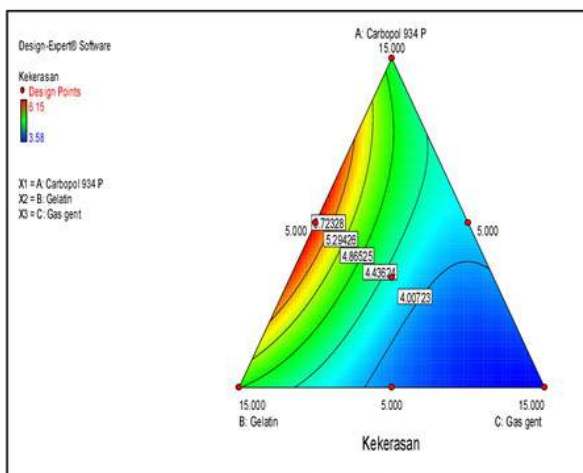
Physical Characteristics	Formulation Code						
	F I	F II	F III	F IV	F V	F VI	F VII
Weight variation* (mg)	195,21±3,73	194,57±2,93	202,69±3,61	198,60±3,78	198±3,59	199,93±3,50	204,68±3,08
CV (%)	1,91	1,50	1,78	1,91	1,81	1,75	1,52
Hardness* (kg/cm <sup>2</sup> )	4,65 ± 0,82	4,89 ± 0,87	3,58 ± 0,68	6,15 ± 1,45	4,16 ± 0,60	3,88 ± 0,41	4,32 ± 0,44
Friability* (%)	0,42 ± 0,14	0,35 ± 0,17	0,86 ± 0,03	0,19 ± 0,06	0,57 ± 0,07	0,60 ± 0,04	0,48 ± 0,05
Floating lag time* (second)	332,79 ± 3,07	232,14 ± 2,52	124,20 ± 3,33	12,20 ± 3,65	6,00 ± 1,89	4,70 ± 0,92	5,74 ± 1,53
Total Floating Time (hours)	>24	>24	>24	>24	>24	>24	>24
Drug content* (%)	103,36 ± 2,27	102,71±1,51	102,75±1,14	101,44±2,16	101,14±1,27	101,60 ± 0,85	101,03 ± 0,67
CV (%)	2,19	1,47	1,11	2,13	1,26	0,84	0,66
Dissolution Rate* C <sub>360</sub> (%)	49,82 ± 3,96	53,86 ± 2,20	64,06 ± 0,70	46,43 ± 3,68	61,87 ± 1,36	61,02 ± 2,69	45,98 ± 1,63
Mucoadhesive Power* (N)	0,1431± 8,46x10 <sup>-3</sup>	0,0996± 3,52x10 <sup>-3</sup>	0,0262± 1,21x10 <sup>-3</sup>	0,2125± 0,06	0,0763± 8,84x10 <sup>-4</sup>	0,0567± 9,74x10 <sup>-4</sup>	0,1226± 1,11x10 <sup>-3</sup>

Note:

\* Mean ± SD; n= 6

**Hardness:**

Carbopol 934P, gelatin, and gas generating in single form improve the hardness of Nifedipine tablets. Interaction between Carbopol 934P and gelatin increase the hardness of Nifedipine tablets, but interaction of gelatin and gas generating, also three components give negative alteration because they reduce the hardness of Nifedipine tablets (Table 6).

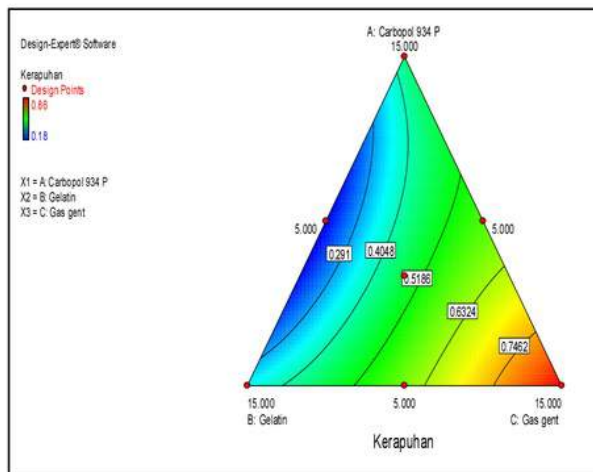


**FIG.5: THREE DIMENSIONAL CONTOUR PLOT FOR HARDNESS**

**Friability:**

Carbopol 934P, gelatin, dan gas generating in single form increase less friability. Interaction

between gelatin and Carbopol 934P give positive alteration which decrease the friability of Nifedipine tablets, however interaction between three components make the improving of friability due to decreasing of hardness tablets (Table 6).



**FIG. 6: THREE DIMENSIONAL CONTOUR PLOT FOR FRIABILITY**

**Drug content:**

Assay of Nifedipine in floating mucoadhesive tablets using spectrophotometry UV at 238 nm. Standar curve equation was obtained  $y = 0,0594x - 0,0002$  ( $r = 0,9999$ ). This studies resulted that all formula fulfill the specification of Nifedipine which described in Table 6.

**Floating Lag Time (FLT):**

FLT was used to examine the floating time for each tablets formula in HCl pH 1,2 medium test. Table 7. showed that three components (gelatin, Carbopol 934P, and gas generating) be able to improve FLT with coefficient rate of 332.79, 232.14, and 124.20, respectively. There are no similar data for each formula because of the different component's concentration. Formula IV, V, and VI fulfill the requirements which less than 2 minutes.

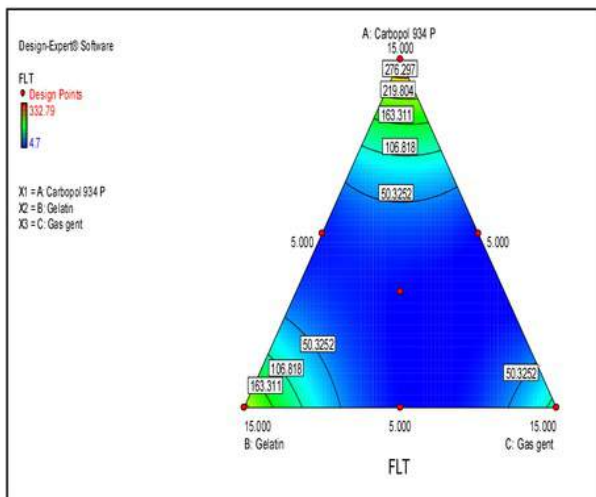


FIG.7: THREE DIMENSIONAL CONTOUR PLOT FOR FLOATING LAG TIME

**Mucoadhesive Power:**

Mucoadhesive power of Nifedipine tablets were tested for explain the capability of tablet's attached at gastro membrane<sup>8</sup>. Mucoadhesive mechanism consisting of two steps. First steps through contact between bioadhesive polymer (Carbopol 934P) and mucous due to wetting and swelling at the surface of bioadhesive membrane. Second steps was done by penetration of bioadhesive polymer into hole of membrane surface. This binding mechanism was reinforced by chemical interaction. Bioadhesive polymer which contain carboxylate

group in acidic medium would perform the unity between pure acid and protein mucin by hydrogen binding.

Based on equation (Table 6.) concluded that each components would able to increase the bioadhesive power of Nifedipine tablets with coefficient rate of 0.14, 0.10, and 0.026, respectively. Interaction between two components (gelatin dan Carbopol 934P) also give positive alteration by coefficient rate of 0, 36. Carbopol 934P significantly improving bioadhesive power but reduce the release of Nifedipine<sup>9</sup>.

This polymer has high swelling and mucoadhesive power which make the Nifedipine tablets survive at gastro membrane. The best of mucoadhesive power was obtained from Formula IV which use 10% Carbopol 934P and gelatin 10% whereas Formula VI has the lowest bioadhesive power because low concentration of gelatin and Carbopol 934P.

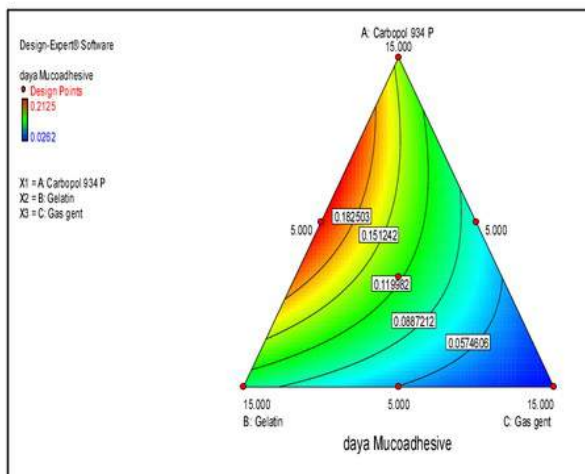


FIG.8: THREE DIMENSIONAL CONTOUR PLOT FOR MUCOADHESIVE POWER

TABEL 6: DESIGN EXPERT EQUATIONS

Response	Equations
Flow Rate	$Y=10,78 Xa + 12,40 Xb + 10,66 Xc - 3,26 Xab - 0,34 Xac - 3,63 Xbc + 41,60 Xabc$
MC	$Y=2,27 Xa + 2,10 Xb + 3,47 Xc + 1,54 Xab + 4,04 Xac + 1,94Xbc - 14,82 Xabc$
Hardness	$Y=4,65 Xa + 4,88 Xb + 3,58 Xc + 5,54 Xab + 0,18 Xac - 1,40 Xbc - 14,04 Xabc$
Friability	$Y=0,45 Xa+0,35 Xb + 0,86 Xc - 0,88 Xab - 0,34 Xac - 0,02 Xbc + 1,74 Xabc$
Dissolution Rate	$Y=53,84 Xa + 54,24 Xb + 67,09 Xc - 27,92 Xab + 20,66 Xac + 21,14 Xbc - 233,61 Xabc$
Floating Lag Time	$Y=322,79 Xa + 232,14 Xb + 124,20 Xc - 1081,07 Xab - 889,98 Xac - 693,88 Xbc + 1947,59 Xabc$
Mucoadhesive Power	$Y=0,14 Xa+0,10 Xb + 0,026 Xc + 0,36 Xab - 0,033 Xac - 0,025 Xbc - 0,026 Xabc$

**Optimization Tehnique:**

Optimum formula must requirements the specification of the test. Physical characteristics of granules consisting of moisture content and flow rate, whereas we variation, drug content, hardness, friability, floating lag time, total floating time, mucoadhesieve power, and dissolution profile were used as physical characteristics of tablets. The parameters of hardness, friability, mucoadhesieve power, and dissolution profile were used to determine the optimum formula from floating mucoadhesieve Nifedipine tablets.

The optimum formula was obtained from superimposed contour plot which is collected from the contour plot. Fig. 9 discovered that yellow area explain the prediction of optimum formula floating mucoadhesieve Nifedipine tablets. Based on Design Expert has been chosen one point which described the optimum formula consisting of 12,02% Carbopol 934P, 5% Gelatin, and 7.98% gas generating with their result prediction are flow rate 10,70 g/sec, hardness 4,56 kg/cm<sup>2</sup>, friability 0,50%, Floating Lag Time (FLT) 100.23 sec, mucoadhesieve power 0.1011 N, and dissolution (C<sub>360</sub>) 57,07%.

**Determination of The Optimum Formula:**

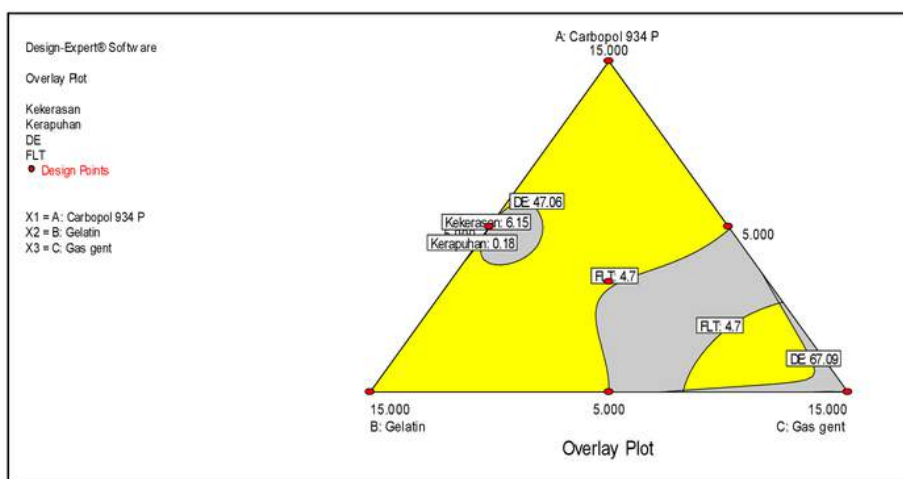


FIG. 9. SUPERIMPOSED CONTOUR PLOT OF FLOATING MUCOADHESIEVE NIFEDIPINE TABLETS

TABLE 7: T-TEST BETWEEN DESIGN EXPERT AND TRIAL RESULT

Parameters	Trial Result	Theoretical (Design Expert)	Significant
Moisture Content (%)	3,00	3,01	>0.05
Flow rate	10,51	10,70	>0.05
Hardness (Kg/cm <sup>2</sup> )	4,51	4,56	>0.05
Friability (%)	0,48	0,50	>0.05
Floating lag time (sec)	100,20	100,23	>0.05
Dissolution rate (C <sub>360</sub> ) (%)	58,10	57,07	>0.05
Mucoadhesieve power (N)	0,1011	0,1011	>0.05

Table 7. showed that T-test between Design Expert and trial result has p > 0.05 which indicated that the procedure optimization is valid.

**CONCLUSION:** In the present study, an attempt to formulate floating mucoadhesieve Nifedipine tablets using Carbopol 934P, gelatin, and gas generating was made by optimization tehnique. Using Simple Lattice Design, the effect of interaction of independent variabels Carbopol 934P, gelatin, and gas generating on dependent

moisture content, flow rate, hardness, friability, floating lag time, dissolution rate, and mucoadhesieve power were studied and optimized. The optimum formula of floating mucoadhesieve Nifedipine tablets had the approximated percentage drug release which met the required rate of drug release for a period of 24 hours through the gastro membrane. From the results, it can be concluded that floating mucoadhesieve Nifedipine tablets can be successfully formulate as treatment for hypertension.

**ACKNOWLEDGEMENTS:** The authors thank to Technology Pharmacy Research Laboratory, Faculty of Pharmacy, Gadjah Mada University, Yogyakarta, for providing all the facilities to carry out this work.

**REFERENCES:**

1. Cai T, Zhu L, Yu L: Crystallization of Organic Glasses. Effects of Polymer Additives on Bulk and Surface Crystal Growth in Amorphous Nifedipine. *Pharm Res* 2011; 28(9): 1515-1522.
2. Srinarong P, Kouwen S, Visser MR, Hinrichs WLLJ, Frijlink HW: Effect of Drug-Carrier Interaction on The Dissolution Behavior of Solid Dispersion Tablets. *Pharmaceutical Development and Technology* 2009; 10(1): 1-9.
3. Philo LMS, Shah S, Badarinath AV, Gopinath C: Formulation and Evaluation of Octreotide Acetate Loaded PLGA Microspheres. *International Journal of Pharmacy and Pharmaceutical Science* 2013; 5(3): 625-621.

4. Marsac PJ, Konno H, and Taylor LS: A Comparison of the Physical Stability of Amorphous Felodipine and Nifedipine System. *Pharm Res* 2006; 23(10): 2306-2316.
5. Sreekumar SK, Palanichamy S, Sekharan TR, Thirupathi AT: Formulation and Evaluation Studies of Floating Matrix Tablets of Nifedipine. *International Journal of Pharm and Biomed Sciences* 2010; 6(2): 12-15.
6. Omray LK: Design of Gastro Retentive Drug Delivery System of Diltiazem Hydrochloride. *International Journal of Pharm Science and Research* 2014; 5(2): 16-19.
7. Baumgartner S, Kristel J, Vreer F, Vodopivec P, Zorko B: Optimization of Floating Matrix Tablet and Evaluation of their Gastric Residence Time. *J Int Pharm* 2000; 195: 125-133.
8. Varshosaz J, Dehghan Z: Development and Characterization of Buccoadhesive Nifedipine tablets. *European Journal of Pharmaceutics and Biopharmaceutics* 2002; 54: 135-141.
9. Gohel MC, Mehta PR, Dave RK, Bariya NH: A More Relevant Dissolution Method For Evaluation of Floating Drug Delivery System. *Dissolution Technologies* 2004; Vol. 11(4): 22-26.

**How to cite this article:**

Ikasari ED, Fudholi A, Martono S and Marchand J: A Formula Optimization of Nifedipine Tablet Combination with Floating mucoadhesive system in a Simplex Lattice Design. *Int J Pharm Sci Res* 2015; 6(5): 1837-44. doi: 10.13040/IJPSR.0975-8232.6(5).1837-44.

All © 2013 are reserved by International Journal of Pharmaceutical Sciences and Research. This Journal licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 3.0 Unported License.

This article can be downloaded to ANDROID OS based mobile. Scan QR Code using Code/Bar Scanner from your mobile. (Scanners are available on Google Playstore)

# Publikasi 1

## ORIGINALITY REPORT

19%

SIMILARITY INDEX

18%

INTERNET SOURCES

10%

PUBLICATIONS

11%

STUDENT PAPERS

## PRIMARY SOURCES

1	<a href="http://ijpsr.com">ijpsr.com</a> Internet Source	8%
2	Submitted to Kyungsung University Student Paper	2%
3	<a href="http://www.japer.in">www.japer.in</a> Internet Source	1%
4	Emara, L. H., R. M. Badr, and A. Abd Elbary. "Improving the Dissolution and Bioavailability of Nifedipine Using Solid Dispersions and Solubilizers", Drug Development and Industrial Pharmacy, 2002. Publication	1%
5	<a href="http://link.springer.com">link.springer.com</a> Internet Source	1%
6	<a href="http://lrd.yahooapis.com">lrd.yahooapis.com</a> Internet Source	1%
7	Walter da Silva Júnior, Jonas Pinheiro, Danielle de Menezes, Natan e Silva et al. "Development, Physicochemical Characterization and In Vitro	1%

# Anti-Inflammatory Activity of Solid Dispersions of $\alpha,\beta$ Amyrin Isolated from Protium Oilresin", *Molecules*, 2017

Publication

---

8	<a href="http://gnu.inflibnet.ac.in">gnu.inflibnet.ac.in</a> Internet Source	1%
9	Srinarong, Parinda, Bao T. Pham, Maru Holen, Afke van der Plas, Reinout C.A. Schellekens, Wouter L.J. Hinrichs, and Henderik W. Frijlink. "Preparation and physicochemical evaluation of a new tacrolimus tablet formulation for sublingual administration", <i>Drug Development and Industrial Pharmacy</i> , 2012. Publication	1%
10	<a href="http://www.aapspharmscitech.org">www.aapspharmscitech.org</a> Internet Source	1%
11	Srinarong, Parinda, Sander Kouwen, Marinella R. Visser, Wouter L. J. Hinrichs, and Henderik W. Frijlink. "Effect of drug-carrier interaction on the dissolution behavior of solid dispersion tablets", <i>Pharmaceutical Development and Technology</i> , 2010. Publication	1%
12	<a href="http://doaj.org">doaj.org</a> Internet Source	<1%
13	Submitted to University of Sunderland Student Paper	<1%

---

---

14	<a href="http://earthjournals.org">earthjournals.org</a> Internet Source	<1%
15	Submitted to University of Auckland Student Paper	<1%
16	<a href="http://academicjournals.org">academicjournals.org</a> Internet Source	<1%
17	<a href="http://www.bibliotecadigital.ufmg.br">www.bibliotecadigital.ufmg.br</a> Internet Source	<1%
18	Siripuram, Praneeth Kumar, Suresh Bandari, Raju Jukanti, and Prabhakar Reddy Veerareddy. "Formulation and Characterization of Floating Gelucire Matrices of Metoprolol Succinate", Dissolution Technologies, 2010. Publication	<1%
19	<a href="http://www.arjournals.org">www.arjournals.org</a> Internet Source	<1%
20	<a href="http://wjpps.com">wjpps.com</a> Internet Source	<1%
21	<a href="http://umu.diva-portal.org">umu.diva-portal.org</a> Internet Source	<1%
22	<a href="http://www.infona.pl">www.infona.pl</a> Internet Source	<1%
23	<a href="http://arjournals.org">arjournals.org</a> Internet Source	<1%

---

24 [www.coriolis-pharma.com](http://www.coriolis-pharma.com) <1%

Internet Source

25 [farmacia.ugr.es](http://farmacia.ugr.es) <1%

Internet Source

26 [www.ijppsjournal.com](http://www.ijppsjournal.com) <1%

Internet Source

27 [www.coursehero.com](http://www.coursehero.com) <1%

Internet Source

Exclude quotes Off

Exclude matches Off

Exclude bibliography Off