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Optimisation of SSG (Sodium Starch Glycolate) and Avicel PH 102 in the Formula of Orally Disintegrating Acetaminophen Tablets by Simplex Lattice Design Method

Oktaviani Himmayatin Nisaa[1]*, Tri Minarsih[1]

[1]Department of Pharmacy, Faculty of Medicine, Universitas Negeri Semarang, Semarang, Central Java, Indonesia

*Correspondence to: *himmayatinnisaa10@students.unnes.ac.id*

Abstract: **Background:** ODT acetaminophen tablets are an alternative drug therapy for patients who have difficulty in swallowing tablets or capsules. Additional ingredients that play an important role in the ODT tablet formula are disintegrants. The disintegrants used in this study were avicel ph 102 and SSG. The use of disintegrants can help increase the dissolution rate and accelerate the destruction time. Aim: The purpose of this study was to determine the optimum formula of ODT acetaminophen tablets and analyses the effect of SSG and avicel ph 102 on dissolution and disintegration time. **Material and Methods:** Determination of acetaminophen ODT tablet formula was carried out running in design expert software with the simplex lattice design method. Preparation of ODT acetaminophen tablets was carried out by direct felting. The evaluation of ODT acetaminophen tablets was IPC physical evaluation, determination of content, and dissolution. Determination of the optimum formula was done by simplex lattice design method. **Results:** The results showed that all ODT acetaminophen tablet formulas fulfilled all the requirements of the IPC test, physical evaluation, dissolution, and determination of levels according to the Pharmacopoeia VI edition standards. Formula 3 produced the fastest disintegration time of 3 minutes, but the dissolution rate of 100% was reached in the 15th minute. It is suspected that gel formation in the SSG swelling mechanism slowed down the dissolution rate. While formulas 1, 2, and 4 which have a longer disintegration time reached >80% dissolution in the 10th minute. **Conclusion:** The optimum formula results with the simplex lattice design method were SSG 8% and avicel ph 102 7%. Avicel ph 102 and SSG had the effect of accelerating the destruction time and slowing down the dissolution rate.

Keywords: acetaminophen, Avicel Ph 102, simplex lattice design, SSG

INTRODUCTION

Pediatric s is an age group of patients who are vulnerable to disease. According to the Kementerian Kesehatan Republik Indonesia (2014) the age group of pediatric patients is 0-18 years old. A medical disorder that pediatrics' patients often experience is pain. Pediatric patients can experience pain that causes impaired function in organs, depression, and decreased quality of life. According to research, based on observations in Rome hospitals there is a prevalence of pediatric patients experiencing mild to severe pain of 20% to 50%. (Marchetti et al., 2023) Based on the prevalence of pediatric patients experiencing pain in Indonesia of 15.26% (Nurafriani et al., 2019)

As many as 29% of pediatric patients experience chest pain, abdominal pain, head pain, and 10% of them experience postoperative pain. (Anderson et al., 2022) The administration of analgesic drugs can overcome pain problems in pediatric patients. Generally, analgesic drugs for pediatric patients are made in syrup preparations, but syrups have poor stability compared to tablet and capsule preparations. Research states that pediatric patients tend to have difficulty in swallowing tablets and capsules, which can reduce the level of patient compliance in increasing the effectiveness of therapy. (Canadell-Heredia et al., 2022) This led to the development of an ODT tablet formula (orally disintegrating tablets) that can improve drug acceptance in pediatric patients.

ODT tablets have good solubility characteristics in water as well as saliva in order to produce an eligible disintegration time. (Demirtürk et al., 2023) The advantages of ODT tablets are higher drug bioavailability and minimal first pass effect. (Parfati et al., 2018) Acetaminophen can be used as an active substance in the preparation of ODT tablets for analgesic medication of pediatric patients. Acetaminophen used for analgesic drugs in pediatric patients has been proven safe. (MIMS, 2023) Acetaminophen has high solubility in saliva. (Idkaidek et al., 2017) A dose of 120mg acetaminophen can be used for pediatrics. With this dose, it can be used for pediatric patients aged < 2 years. The dose of acetaminophen meets the ODT tablet dosage standard, which has an active substance dose of less than 400mg. (Alğin et al., 2014) The ODT acetaminophen tablets in the study were formulated with a weight of 450 mg, the weight met the standard ODT tablet weight of < 500 mg. (Khan et al., 2022) This study was conducted to manufacture ODT acetaminophen tablets with optimization of Avicel ph 102 and SSG (Sodium Starch Glycolate) materials using direct felt tablet molding method. The optimization method used in this study was simplex lattice design.

This study aims to determine the optimum formula of ODT acetaminophen tablets using the simplex lattice design method. This study also aims to analyze the effect of variation in concentration of SSG (sodium starch glycolate) and Avicel ph 102 on the disintegration time and dissolution release profile of ODT acetaminophen tablets

using simplex lattice design method.

METHODS

Materials

The materials used in this study were acetaminophen, Avicel ph 102, SSG, sorbitol, Mg stearate, talc, parchment paper, Whatman filter paper, KH_2PO_4, NaOH, and 96% ethanol p.a, and distilled water. Tools used in this study such as analytical balance, mortar, pestle, watch glass, beaker glass, stirring rod, volume pipette, rotary tablet press, UV spectrophotometer, type II paddle dissolution apparatus, friability tester, hardness tester, flowability tester, volumetric flask, measuring cup, dropper pipette, vial, benchtop pH meter, ruler, cube mixer, and micropipette.

Running Formula With Simplex Latice Design Method

The ODT acetaminophen formula was made with a standard dose of acetaminophen of 120mg (MIMS, 2022). The procedure of making ODT acetaminophen tablets was optimized with SSG as superdisintegrant and Avicel ph 102 as disintegrant with simplex lattice design method using design expert software. The running result formula of the optimization of avicel ph 102 and Sodium Starch Glycolate ingredients can be reviewed in table 1. The formula determined in the manufacture of ODT acetaminophen can be reviewed in table 2.

Table 1. Simplex lattice design optimization formula

Materials	F1 (%)	F2 (%)	F3 (%)	F4 (%)	Function
Avicel ph 102	7,25	7,75	7	8	Disintegran
SSG	7,75	7,25	8	7	Superdisintegran

Table 2. ODT Acetaminophen Tablet Formula

Materials	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	Function
Asetaminofen	120	120	120	120	Active substance
Avicel ph 102	32,625	34,875	31,5	36	Disintegrant
SSG	34,875	32,625	36	31,5	Superdisintegrant
sorbitol	240	240	240	240	Filler-binder, sweetener
Mg stearat	9	9	9	9	Lubricant
Talk	13,5	13,5	13,5	13,5	Glidant
Total	450 mg				

Preparation of Tablets

The stages in the preparation of ODT tablets are weighing acetaminophen, SSG, Avicel ph 102, sorbitol, Mg stearate, and talc. The weighed ingredients were put into a cube mixer. The powder was mixed for 10 minutes. The prepared powder mixture was subjected to IPC test.

Evaluation of Granules

Flow Time

The tool used in the flow properties IPC test is a flow tester or hollow cone. The stages of testing the flow properties are powder mixing results in the manufacture of ODT acetaminophen tablets weighed as much as 100 g, then poured into the funnel. After all the powder is poured, the funnel cover is opened. The flow properties of a powder are qualified if ≤ 10 seconds. (European Pharmacopoeia, 2019)

Angle of Repose

In testing the angle of repose using paper placed at the bottom of the flow tester when testing flow properties. The stages in the test are powder flowing through the funnel given a graph paper at the bottom of the funnel hole. In the pile of powder, the radius is measured with a height with the formula, $\tan \propto = \frac{h}{r}$.

Bulk and Tapped Density

The steps taken were that the powder was put into a 250 ml measuring cup, then weighed 100 grams of powder. The measuring cup containing the powder is placed on the density device, switch on the instrument and tapped for 500 taps, calculate the compressibility index and Hausner ratio. (European Pharmacopoeia, 2019)

Evaluation of Tablets

Organoleptic

In the organoleptical test, 20 tablets were taken and visually observed for color, shape, and taste.

Weight Uniformity Test

At the weight uniformity test stage, 20 tablets were taken, weighed each tablet with an analytical balance and calculated the average tablet weight. (Farmakope Indonesia, 2020) Tablets are declared eligible if no one tablet unit deviates less than ± 10% from the average weight and no one tablet unit deviates more than 20% from the average weight. (Farmakope Indonesia, 2020)

Size Uniformity

Stages in size uniformity testing are taken as many as 10 tablets, measuring the diameter and thickness of the tablet on each tablet with a caliper. Calculate the average tablet thickness and diameter. Tablets are declared to meet the size uniformity test if the average diameter is not more than 3 times the average tablet thickness and not less than 1 1/3 of the average tablet thickness. (Farmakope Indonesia, 2020)

Hardness Test

Stages in the hardness test are taken as many as 20 tablets, each tablet is measured for hardness using a hardness tester. The tablet is positioned vertically and the screw on the hardness tester is rotated until the tablet is destroyed and the scale is read. The data was recorded, and the average hardness of the tablets was calculated. Tablets have good hardness ranging from 4-8 kg. (Syukri, 2018)

Friability

Ten tablets were taken for friability testing. Tablets were discharged and weighed at initial weight. Tablets were put into the friability tester, turn on the instrument at 100 rpm for 4 minutes, weigh the final weight. Tablets have good friability if < 1%. (Syukri, 2018)

Disintegration Test

The disintegration tester tool was added with 900 ml of water in a beaker glass, then put 6 tablets in the basket, the temperature of the tool was 37oC. Tablets inserted into the disintegration tester were observed for 15 minutes. Disintegration time has acceptance criteria for uncoated tablets < 15 minutes. (Farmakope Indonesia, 2020)

Determination of Acetaminophen Level by UV Spectrophotometer

Preparation of 40 ppm standard solution

Acetaminophen standard powder was weighed as much as 2 mg, then put into a 50 ml measuring flask. The powder was dissolved with ethanol and stirred until homogeneous. Then 96% p.a ethanol was added until the limit mark.

Maximum Wavelength Determination

The standard solution was pipetted as much as 0.5 ml into a 10 ml measuring flask and added ethanol to the limit mark stirring until homogeneous, obtained a concentration of 2 ppm. The solution was put into a cuvette measured in the wavelength range of 200-400 nm.

Calibration curve

From the standard solution, concentration solutions of 2 ppm, 3 ppm, 4 ppm, 5 ppm, 6 ppm, and 7 ppm were made in a 10 ml volumetric flask. The series solution was put into the cuvette and read the absorbance at the maximum wavelength. In the measurement results, a standard curve is made where x as concentration (ppm) and y as absorbance on the equation line y = ax +b.

Level Determination

ODT asteminophen tablets were crushed and 2 mg ODT acetaminophen powder was dissolved with 96% ethanol p.a. The solution was filtered with Whatman filter paper no. 42. Then put into a 50 ml volumetric flask and added 96% ethanol p.a to the limit mark. Measure the absorbance of the solution at the maximum wavelength. The levels of active compounds of paracetamol drugs are qualified if they should not be less than 90% and should not be more than 110% of the amount stated on the etiquette. (Farmakope Indonesia, 2020)

In Vitro Dissolution Test

At the tablet dissolution test stage, 1 tablet was inserted into the chamber of a type 2 paddle dissolution device using 900 ml of phosphate-buffered saline ph 5.8 media at 37oC for 30 minutes using a speed of 50 rpm. The buffer solution used was KH_2PO_4 0.2M and NaOH 0.2M made in a volume of 1 liter. In the treatment of sampling the solution was taken 5 ml every 0 minutes, 5 minutes, 10 minutes, 15 minutes, 30 minutes. At 0 minutes, 5 minutes, 10 minutes, 15 minutes, 30 minutes, absorbance measurements were taken at a wavelength of 243 nm using UV spectrophotometry. The results of absorbance measurements, the standard curve equation was made with x as minutes and y as absorbance to get the value y = ax + b. Acetaminophen ODT tablets have good solubility if not less than 80% of the active substance for 30 minutes. (Farmakope Indonesia, 2020)

Data Analysis Technique

Determination of the factors of optimization used using 2 ingredients such as Avicel ph 102 as a binder and SSG as a superdisintegrant. Determination of the variation concentration of 2 factors using design expert software by

entering the minimum and maximum ranges on each component of the ingredients (avicel ph 102 and Sodium Starch Glycolate). The optimized ingredients were tested against the specified responses of disintegration time and dissolution to obtain the optimum formula. In the simplex lattice design method, data on the formula concentration range of Avicel ph 102 and SSG were entered into the design expert software to review the optimum formula to be used in the manufacture of ODT tablets. Based on the evaluation carried out, the data on crushing time and dissolution were entered into the response in design expert. The data results were run to determine the contour plot and optimum formula.

RESULT AND DISCUSSION

Evaluation of Granules

Flowability

Good flow properties have a flow time of <10 seconds. (European Pharmacopoeia, 2019) Based on the data in table 5, the four formulas fulfil the requirements of the flow properties test. The results of the flow properties test in this study using SSG and avicel ph 102 as a disintegrant produced flow properties that met the requirements. Avicel ph 102 has a non-shafted particle shape so that the interparticle bond is strong and the increased compactness of the powder mass can minimize the porosity of SSG. (Puspita et al., 2017) The concentration variation of SSG and avicel ph 102 is more optimal to improve the flow properties.

Table 3. Result of Flowability

Sample	Flowability (second)
F1	6,667 ± 0,471
F2	7,667 ± 0,471
F3	8,333 ± 0,943
F4	8,000 ± 0,816

Angle of Repose

The results of the stationary angle test in all formulas fulfil the requirements In formula 1 has an avicel concentration: SSG (Sodium Starch Glycolate) of 7.25: 7.75 produces a stationary angle with excellent criteria. This is influenced by the flow properties of the powder. (Cheiya et al., 2023) The results of the flow properties of formula 1 were 6.667 seconds, while formula 3 showed flow properties of 8.333 seconds. The flow properties of formula 3 are longer than formula 1 so that formula 3 produces a stationary angle with sufficient criteria and formula 1 produces a stationary angle with very good criteria. Formulas 2 and 4 produce a good degree of angle of silence. Based on the results of the stationary angle test, all formulas meet the requirements. The difference in the degree of stationary angle can be influenced by the hygroscopic nature of SSG. Formulas 1 and 2 produce a balanced concentration of SSG and Avicel ph 102, while in formula 4 the concentration of avicel ph 102 is higher than SSG so that the cohesion of avicel ph 102 can reduce the hygroscopic properties of SSG. (Kharisma et al., 2018)

Table 4. Result of Angle of Repose

Sample	Angle of Repose	Category
F1	28,5° ± 0,018	Excellent
F2	31° ± 0,079	Good
F3	37° ± 0,078	Fair
F4	31,5° ± 0,074	Good

Bulk and Tapped Density

In this study, the values of % compressibility index and Hausner ratio shown in table 7 of all formulas fulfil the requirements of the stationary angle test. The % compressibility index and Hausner ratio values of formulas 1 and 4 are in the good category. The smaller the % compressibility index, the better the flow properties of the powder. (Zulfa et al., 2019) Meanwhile, the compressibility index values of formulas 2 and 3 are included in the good enough category. This category shows that the powder fulfils the compressibility requirements. This is due to the low concentration of avicel ph 102 which can affect compressibility. The characteristics of avicel ph 102 have a large and uniform particle size so as to increase the bonding density of powder particles. (Peciar et al., 2016) While SSG has particle characteristics that easily expand causing particles to form weak interparticle bonds resulting in low powder density. (Anas et al., 2018)

Table 5. Result of Density

Sampel	% Compressibility Index	Hausner Ratio	Category
F1	14,957%	1,176	Good
F2	18,667%	1,230	Fair
F3	18,222%	1,223	Fair
F4	13,793%	1,16	Good

Evaluation of Tablets

Organoleptic

The organoleptic test conducted on all formulas produced tablets that were white in color, odorless, and tasted sweet.

Weight Uniformity Test

Tablets are declared eligible if no one tablet unit deviates ± 10% from the average weight and no one tablet unit deviates more than ± 20% from the average weight. The tablet weight in this test is 450 mg so that the acceptance limit in the weight uniformity test from ± 10% of the average weight is 405 mg to 495 mg, the maximum limit of deviation from ± 12% of the average weight is 360 mg - 540 mg. The results of the weight uniformity test which can be reviewed in table 8 show that formulas 1, 2, 3, and 4 are in the range of 443 mg - 454 mg so that the average weight does not deviate from the acceptance requirements. Thus, formulas 1 to 4 fulfil the requirements of the weight uniformity test in accordance with the pharmacopeial standard edition VI.

Table 6. Result of Weight Uniformity

Sample	Weight Uniformity
F1	450,417 mg ± 6,264
F2	453,750 mg ± 4,753
F3	443,367 mg ± 7,241
F4	454,133 mg ± 4,537

Size Uniformity

Tablets are declared to meet the size uniformity test if the average diameter is not more than 3 times the average tablet thickness and not less than 1 1/3 of the average tablet thickness. The size uniformity test results of formula 1 had a tablet diameter of 10.132 mm with a tablet thickness of 5.387; formula 2 had a tablet diameter of 10.154 mm with a tablet thickness of 5.341; formula 3 had a tablet diameter of 10.109 mm with a tablet thickness of 5.420; and formula 4 had a tablet diameter of 10.208 mm with a tablet thickness of 5.350. Thus, all formulas fulfil the requirements of the size uniformity test.

Table 7. Result of Size Uniformity

Sample	Size Uniformity	
	Diameter (mm)	Thickness (mm)
F1	10,132 ± 0,091	5,387 ± 0,900
F2	10,154 ± 0,077	5,341 ± 0,033
F3	10,109 ± 0,122	5,420 ± 0,109
F4	10,208 ± 0,131	5,350 ± 0,071

Hardness Test

Tablets have good hardness ranging from 4-8 kg 13. The hardness test results in table 8 show that formulas 1, 2, 3, and 4 are in the range of 5.157-6.297 kg. Thus, all formulas fulfil the hardness test requirements.

Table 8. Hardness

Sample	Hardness
F1	5,235 kg ± 1,077
F2	5,492 kg ± 0,972
F3	6,297 kg ± 0,954
F4	5,157 kg ± 0,789

Friability

Tablets have good friability if < 1% (Syukri, 2018). The friability test results in table 9 show that formulas 1, 2, 3, and 4 are in the range of 0.072-0.802%. Thus, all formulas fulfil the requirements of the friability test. Good compressibility properties in density evaluation can increase the binding force between strong tablet particles so as

to minimise tablet fragility 20. Variations in the concentration of SSG and avicel ph 102 minimise the brittleness of the tablets, this is influenced by SSG which can increase compressibility so that the tablet particle bond is strong.

Table 9. Result of Friability

Sample	% Friability
F1	0,802%
F2	0,733%
F3	0,299%
F4	0,072%

Disintegration Test

The disintegration time has acceptance criteria for uncoated tablets < 15 minutes. Based on the test results of this study with variations in the concentration of SSG and avicel ph 102, all formulas met the pharmacopoeia VI standard for the destruction time test.

Formula 3 has the fastest disintegration time which is caused by the high concentration of SSG as much as 8%, SSG has the ability to swell faster so that it can break down tablet particles easily. Based on research, an 8% SSG concentration can accelerate the destruction time so that the higher the SSG concentration, the faster the destruction time.

Formula 1 produced a crushing time of 5 minutes. Formulas 2 and 4 have the longest disintegration time of 8 minutes, this can be influenced by the content of avicel ph 102 with a higher concentration than SSG. Avicel ph 102 has disintegrant and binder characteristics so that it can increase the bond between strong tablet particles and slow down the disintegration time.

Table 10 Result of Disintegration

Sample	Disintegration (minutes)
F1	5
F2	8
F3	3
F4	8

Determination of Acetaminophen Level by UV Spectrophotometer

Preparation of standard solutions of 2 ppm, 4 ppm, and 6 ppm measured with a wavelength of 248 nm. From the measurement results of the standard solution, a standard curve was made, with the results of the linear regression equation y = 0.09976x + 0.08113 and the regression coefficient (r) = 0.99979.

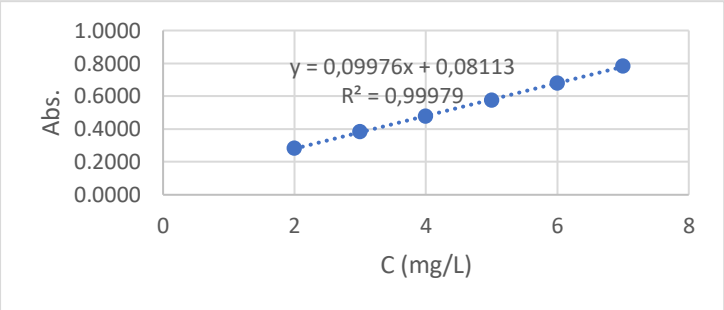

Figure 1. Standardised Curve

The active substance content of acetaminophen is qualified if it cannot be less than 90% and cannot be more than 110% of the amount stated on the etiquette. Previous research conducted using a combination of SSG, avicel ph 102, and mannitol met the requirements of the level determination test in all formulas. (Siswanto et al., 2024) Based on the results of the determination of the active substance content of ODT acetaminophen tablets using variations in the concentration of SSG and avicel ph 102 in table 4.13, the levels of formulas 1, 2, 3, and 4 were 94.0639% - 102.5405%, so that all formulas met the test requirements for the active substance content of acetaminophen.

Table 11. Result of % Level Acetaminophen ODT Tablet

Formula	% Levels
F1	94,0639
F2	100,5294
F3	102,5405
F4	101,5819

In Vitro Dissolution Test

The maximum wavelength measurement result was 244 nm, so the maximum wavelength result was used in the measurement of standard solutions and the preparation of standard curves. Standard solutions were made at 3 ppm, 4 ppm, 5 ppm, 6 ppm, 7 ppm, and 8 ppm. Then the absorbance of the standard solution was measured with a UV spectrophotometer. From the standard solution data, a standard curve of acetaminophen in phosphate buffer 5.8 was made and a linear regression equation y = 0.06905x - 0.00736 was obtained with a regression coefficient (r^2) = 0.99715.

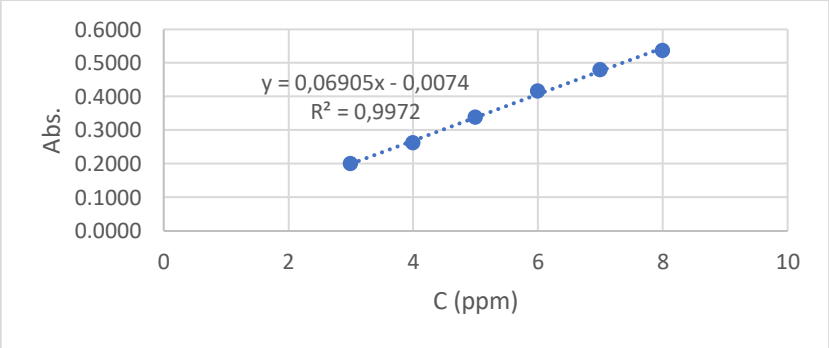

Figure 2. Standardised Curve

ODT acetaminophen tablets have good solubility if not less than 80% of the active substance for 30 minutes. The results of dissolution testing every minute can be reviewed in Figure 4.4. Formula 1 showed a dissolution result of 91.299% at minute 10. Formula 2 showed a dissolution result of 97.251% at minute 10. Formula 3 showed a dissolution result of 100.316% at minute 15. Formula 4 showed a dissolution result of 81.361% at minute 10. All formulas meet the dissolution test requirements. The active substance levels contained in all formulas met the requirements even though formula 3 experienced a slow release of active substances.

The slow release in formula 3 can be influenced by the high concentration of SSG, causing the tablets to expand and gel. This is in accordance with the characteristics of SSG, which has the ability to swell to break the tablet quickly and as a gelling agent. (Manzoor, 2021)

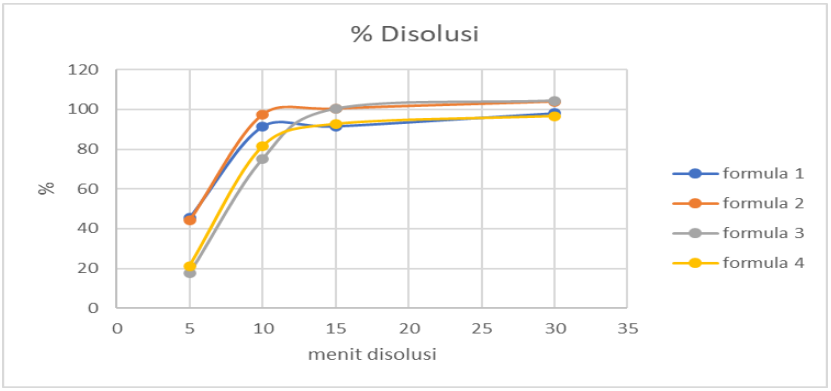

Figure 3. % Dissolution

Data Analysis Technique

Optimization of ODT acetaminophen tablet preparation using the simplex lattice design method with variations in the concentration of SSG and avicel ph 102 as disintegrants. The lower and upper limit values of the variations in the concentration of SSG and avicel ph 102 were measured from the concentration of these components as disintegrants. The lower and upper limit concentration range of SSG was 2-8% and avicel ph 102 was 5-15%.

Graphical analysis of the normal plot of residuals and contour plot of the crushed time response can be reviewed in Figure 4. Based on the normal plot of residual graph shows the normality of the distribution of data spread normally so that the data can be accepted. This is indicated from the scattered points approaching the linear line. The graph shows the highest crushing time response in the concentration of avicel ph 102 8% and SSG 7%, as well as in the concentration of avicel ph 102 7.25% and SSG 7.75% with a time of 8 minutes. While the lowest disintegration time response was found at avicel ph 102 concentration of 8% and SSG 7%

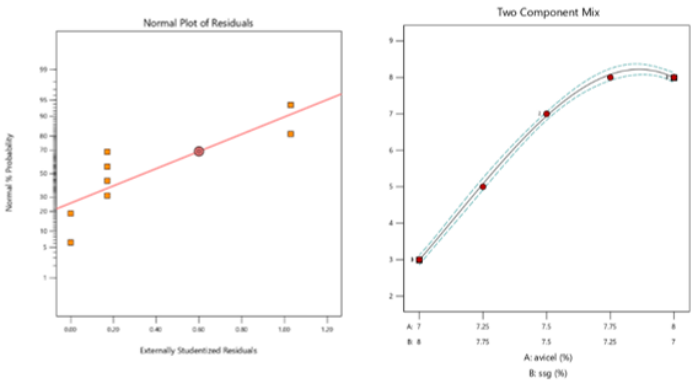

Figure 4. Graph of normal plot of residuals and countour plot disintegrantion

Graphical analysis of normal plot of residual and contour plot of dissolution response can be reviewed in Figure 4. Based on the normal plot of residual graph shows the normality of the distribution of data spread normally so that the data can be accepted. This is shown from the scattered points approaching the linear line. The graph shows the highest dissolution response in the concentration of avicel ph 102 7% and SSG 8% with 100% dissolution % data. While the lowest dissolution response is found in the concentration of avicel ph 8% and SSG 7%.

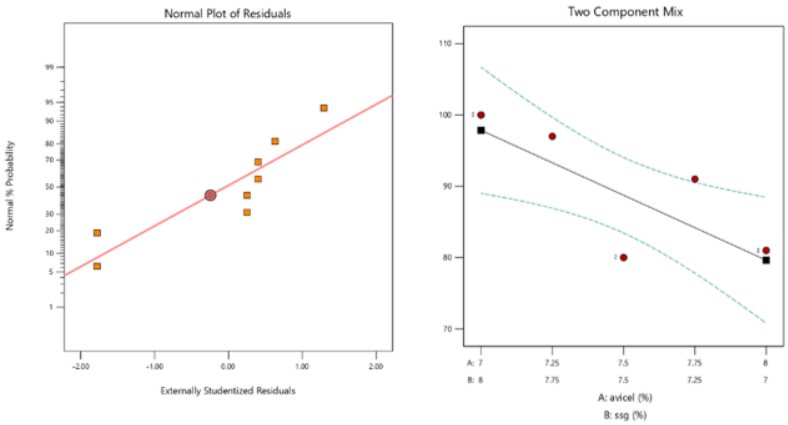

Figure 5. Graph of normal plot of residuals and contour plot dissolution

Based on the dissolution test response equation and the destruction time, it can be seen that each component gives a positive response to the dissolution response and destruction time. A positive response can mean that the higher the concentration of each component, the more positive influence it can have on dissolution and destruction time. The mechanism of avicel ph 102 as wicking and SSG as swelling provides an increase in the release of active substances to penetrate the tablet media. Avicel ph 102 is able to absorb water into the pores of the tablet quickly so that the tablet is easily destroyed. SSG accelerates the dissolution process and disintegration time through the development of tablet volume due to contact with water thus expanding the tablet surface.

Based on data analysis, the optimum formula composition obtained from the design expert software can be reviewed from table 4.17. The optimum formula is shown in the concentration of avicel components ph 102 7% and SSG 8% with a desirability value of 1. The maximum desirability value is 1 so that the closer to 1, the better the value [23]. The composition of the formula was chosen as the optimum formula because it produces physical properties of tablets that match the target criteria. The value is obtained based on mathematical model predictions so that it is considered to provide more optimum formula results. The target response results of the expected destruction time test were 2.990 minutes, and the target response of the expected dissolution test was 97.861%.

Table 12. The result of determining the optimum formula

Composition		Respond		Desirability
Avicel ph 102 (%)	SSG (%)	Disintegration (menit)	Dissolution (%)	
7%	8%	2,990 menit	97,861%	1,000 (selected)

CONCLUSION

The optimum formula resulting from running in the design expert software was obtained at a concentration of avicel ph 102 of 7% and SSG of 8% with a desirability value of 1. This combination produced an optimum formula with the results of IPC test parameters, physical evaluation, determination of levels, and dissolution that met the standards of Pharmacopoeia edition VI. The variation of SSG and avicel ph 102 can have an effect on increasing the crushing and dissolution time. In simple lattice design, the combination of the two materials gives a positive response to the response of the crushing and dissolution time test. A positive response can mean that the higher the concentration of each component, the more positive influence it can have on the crushing and dissolution time. This is in accordance with the mechanism of SSG as swelling and avicel ph 102 as wicking affecting the destruction and dissolution time. In the destruction time test, the higher the concentration of SSG, the faster the destruction time. While in the dissolution test, the higher the concentration of SSG, the slower the release of active substances.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest

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