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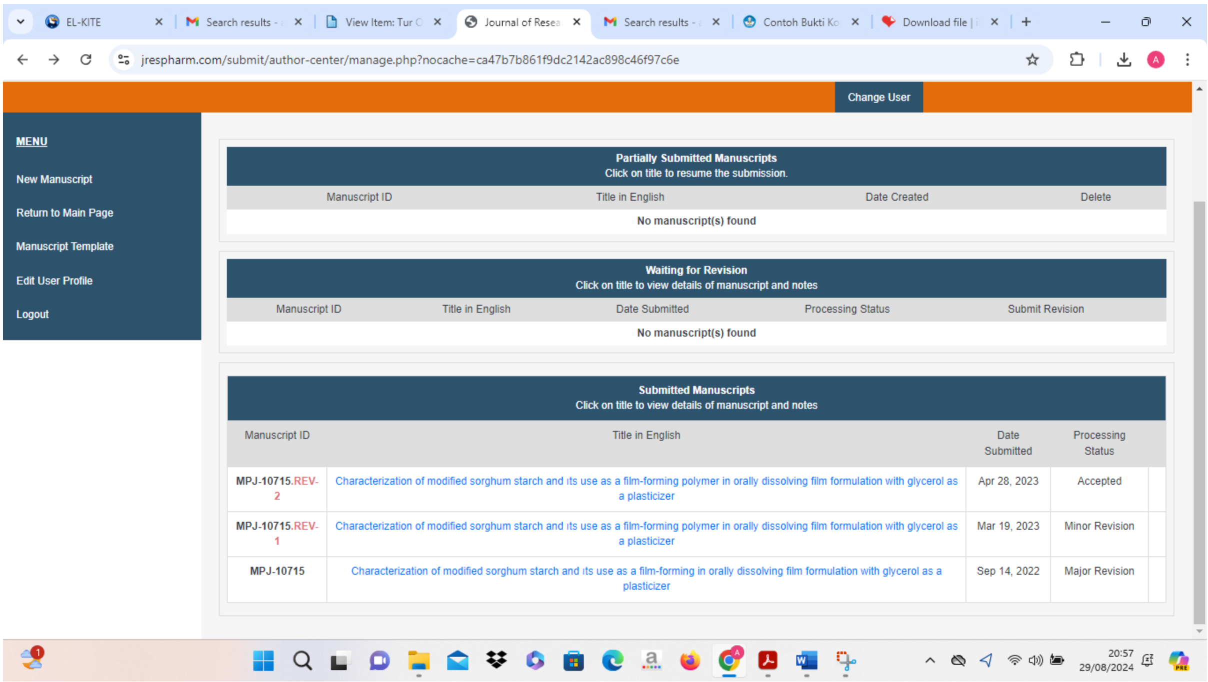

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Characterization of modified sorghum starch and ıts use as a film-forming in orally dissolving film composition with glycerol as a plasticizer

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ABSTRACT: Film-forming polymers and plasticizers are the components of Orally dissolving film (ODF) compositions that have the most influence on the physical properties of the film preparations. Modification of sorghum starch produces maltodextrin (MDX)-sorghum, which can be used as a film-forming polymer, and glycerol can be used as a plasticizer in ODF compositions. This research aims to determine the optimal concentrations of MDX-sorghum and glycerol for producing ODF compositions using the response surface method (RSM) with a central composite design (CCD). Hydrolysis of sorghum starch yielded MDX-sorghum, characterized by yield value, dextrose equivalent (DE) value, solubility, swelling power, and FTIR analysis. The CCD design included a 2-6% and 3-10% concentration range for MDX-sorghum and glycerol, respectively, as parameters in the optimization process. The test response was evaluated using tensile strength, elongation, and disintegration time tests, so 14 experimental designs were obtained. The modification of sorghum starch yields a light brown MDX-sorghum powder with desirable properties. Optimization of MDX-sorghum and glycerol concentrations yielded an optimal formula with a tensile value of 1.81 MPa with an error percentage of 0.33%, an elongation of 104% with an error percentage of 0.33%, and a disintegration time of 82.95 seconds with an error percentage of 0.06%. By modifying sorghum starch to make MDX-sorghum, the starch's properties can be enhanced and used as a film-forming. The optimal MDX-Sorghum and glycerol concentrations for the production of ODF are 3.56 % and 10 %, respectively.

KEYWORDS: Sorghum strach, modified, film-forming, glycerol, response surface methodology.

1. INTRODUCTION

Sorghum starch is a film-forming polymer with hydrophilic properties used in manufacturing orally dissolving film (ODF) preparations [1]. Sorghum starch is a natural biopolymer that is easily accessible and contains 72–75% carbohydrates, 20–30% amylose, and 70–80% amylopectin, which can be used as film-forming components [2,3]. However, there are several drawbacks to natural sorghum starch: it is sticky, hard, brittle, not transparent, and not resistant to acid treatment. In a study by Putri et al. (3), using single sorghum starch resulted in a less elastic film preparation. This problem can be overcome by modifying sorghum starch through a partial hydrolysis process so that its characteristics resemble those of maltodextrin (MDX) (4). MDX is obtained from starch that has been enzymatically modified by partial hydrolysis. As a result, MDX has a dextrose equivalent (DE) value of less than 20. Moreover, MDX has good film-forming solubility and adhesive characteristics, allowing it to produce elastic films [5,6].

The film-forming polymer influenced the film preparation's elasticity; plasticizers can also increase film's elasticity [7]. Glycerol is one of the plasticizers that can be used in the manufacture of ODF preparations. Glycerol is a plasticizer that is easily soluble in water (hydrophilic), has a low molecular weight so that it can reduce the intermolecular forces along the polymer chain, and has the advantage of increasing the viscosity of the solution, reducing the brittleness and increasing the strength of ODF preparations [8]. Glycerol, as a plasticizer, produced edible films with improved characteristics compared with sorbitol and polyethylene glycol [9]. Research conducted by Walfathiyyah et al. (2017) showed that adding of glycerol resulted in a more

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elastic edible film [10]. The optimal concentrations of glycerol and MDX-sorghum can be analyzed using the response surface methodology (RSM).

RSM can be used to design several formulas with varying concentrations of MDX-sorghum and glycerol. The RSM can reduce the number of materials used because it does not require a trial formula stage, which would require considerable research [11]. Furthermore, this method can describe the interaction among variables toward the response [11,12]. Several models can be used in RSM. The experimental design in this study used the central composite design (CCD) model. CCD is a fractional factorial design often used in RSM as it can speed up several experimental designs [13]. The independent variable was the concentration of MDX-sorghum as a film-forming agent and glycerol as a plasticizer, and the dependent variables (response) were the value of tensile strength, percentage elongation, and disintegration time. MDX-sorghum and glycerol as components in the manufacture of films are expected to produce films with characteristics that meet the requirements so that they can be used as alternative pharmaceutical preparations for the cetirizine. Therefore, it is necessary to optimize the concentrations of MDX-sorghum and glycerol to obtain an ODF compositions with the best physical properties so that it can be used as a reference in the development of natural excipients in the pharmaceutical field.

2. RESULTS AND DISCUSSION

2.1. Characteristics of MDX-Sorghum

The characteristics of sorghum starch and MDX-sorghum are shown in Table 1. Based on the results, the DE value of MDX-sorghum met the requirements (i.e., <20). In each sugar chain undergoing hydrolysis, there was one reducing sugar group; as the number of simple sugar groups increased, the number of reducing sugar groups and the value of DE also increased. In the swelling power and solubility studies, the swelling ability and solubility of MDX-sorghum more significant than that of sorghum starch. This was due to the hydrolysis reaction performed by the amylase enzyme on sorghum starch by breaking the glycosidic bond in starch molecules into simple sugars, such as glucose and dextrin, so that the three parameters increased [5,6].

Table 1. Characteristics of sorghum starch and modified sorghum starch

No	Inspection	Sorghum Starch	MDX-Sorghum
1	Organoleptic:		
	Form	Powder	Powder
	Texture	Fine/smooth	Fine/smooth
	Aroma	Typical Sorghum	Brown sugar
	Flavour	Slightly Sweet	Slightly Sweet
	Colour	Light brown	Dark brown
2	Dextrose Equivalent	0.84	6.22
3	Swelling Power	2.44	2.87
4	Solubility	12.52%	52.9%
5	Yield Value	72.58%	86.71%

Sorghum starch and modified sorghum starch were analyzed by evaluating the spectrum's shape, namely the specific peaks indicating the type of functional group by a starch compound. The analysis results using FTIR are shown in Figure 1 and 2. The peak for the O-H group was in the range of 3,400–2,400 cm^{-1}. The results of the sorghum starch group were around 3,270.7 cm^{-1}, while the O-H functional group was obtained at a modified sorghum starch peak of 3,287.0 cm^{-1}, and the C-H functional group was obtained at the peak of 2,924.1 cm^{-1} in the range of 3,850.0–2,850.0 cm^{-1}, indicating no change in peak between the two samples. However, the C-O-C functional group obtained 1,149.9 cm of sorghum starch and a peak shift of 1,148.0 cm^{-1}, which indicated a change in the modified starch. This treatment aimed to determine the results of the transfer between the functional groups on the two spectra, whereby the difference between the transmittance in the O-H and C-O-H functional groups could be observed. This was due to the breakdown of -1,4 glycosidic bonds by the amylase enzyme on the inside of the polysaccharide chain so that the starch could be modified into MDX [14].

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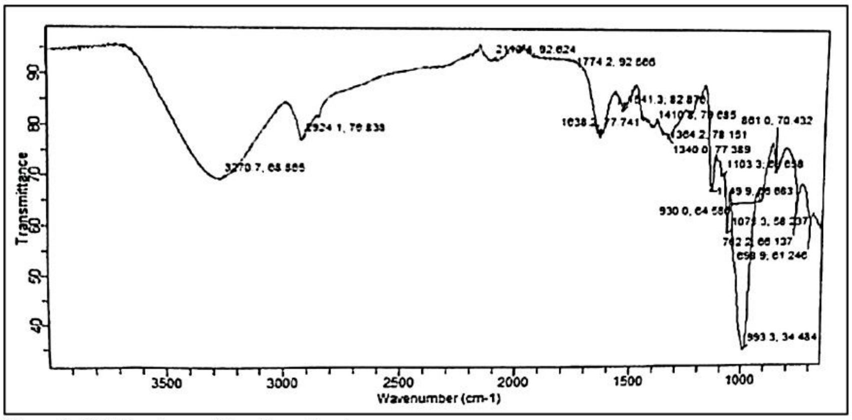

Figure 1. FTIR Spectrum of Sorghum Starch

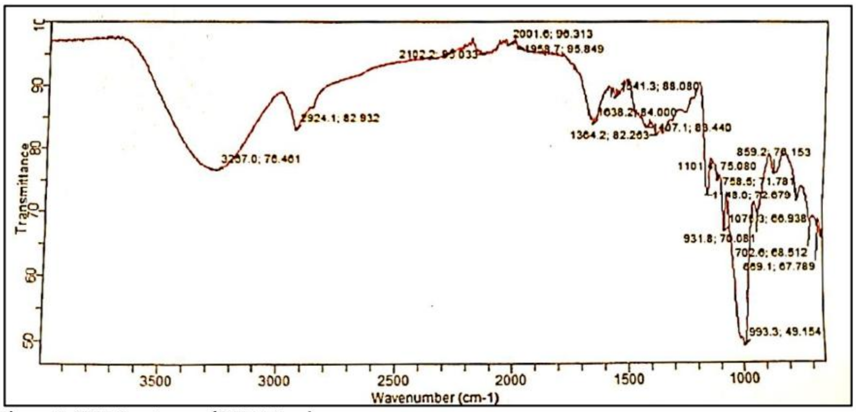

Figure 2. FTIR Spectrum of MDX-Sorghum

2.2. Evaluation of ODF Preparations

The results of the evaluation of ODF preparations are shown in Table 2. Based on the evaluation, all ODF formulas meet the requirements of a 'good' film. The film preparation was considered good if it had a tensile strength value of 1.02 – 10.2 Mpa [15], elongation > 70% [16], and disintegration time < 3 minutes [17].

Table 2. Evaluation of ODF Preparations

Run	Factor		Response		
	A: MDX-Sorghum Concentration (%)	B: Glycerol Concentration (%)	Y_1: Tensile Strength (MPa)	Y_2: Elongation (%)	Y_3: Disintegration Time (sec)
1.	4.00	6.50	1.98	86.26	152
2.	4.00	3.00	2.47	66.74	181
3.	4.00	10.00	1.52	101.68	75
4.	4.00	6.50	1.92	89.44	155
5.	5.41	8.97	1.32	103.96	85
6.	4.00	6.50	1.67	91.94	160
7.	2.59	8.97	1.48	97.72	112
8.	4.00	6.50	1.95	86.58	158
9.	6.00	6.50	1.61	99.16	90
10.	4.00	6.50	1.98	93.18	150

11.	4.00	6.50	1.91	84.84	159
12.	2.59	4.03	1.87	61.41	191
13.	2.00	6.50	2.05	72.41	176
14.	5.41	4.03	1.58	78.56	166

2.3. Data Analysis Using RSM

The combination of MDX-Sorghum as a film-forming agent and glycerol as a plasticizer affects the tensile strength, elongation, and disintegration time, as shown in Figure 3. The color on the graph represents the tensile strength (a), elongation percentage (b), and disintegration time (c). The color positioned bottom has the lowest response value, while the above color has the highest response value. The number of color changes along the curve indicates the influence of film-forming and plasticizing concentrations. The combination of factors (A and B) affects the response related to the number of colors on the curve [14,18]. According to the observed results, the disintegration time is the response most affected by factors concentration.

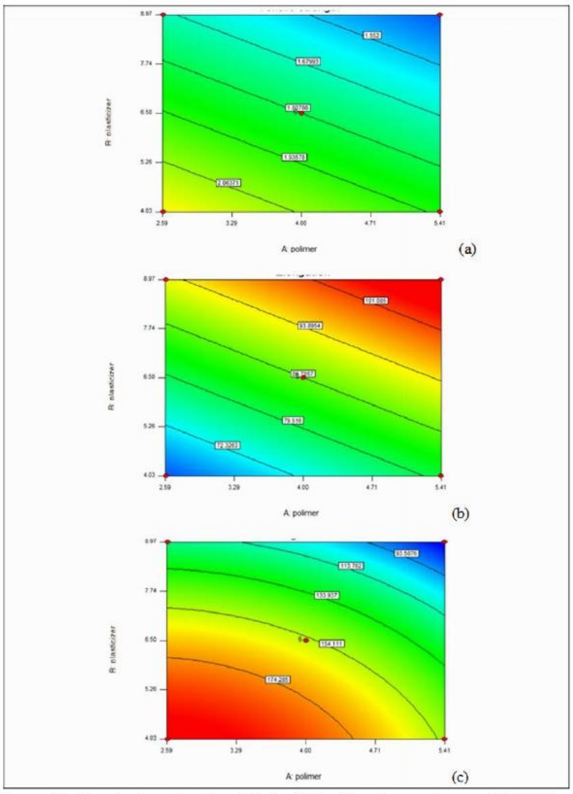

Figure 3. Graph showing the effect of film-forming polymer (MDX-Sorghum) concentration and plasticizer (glycerol) concentration on tensile strength value (a), percentage of elongation (b), and disintegration time (c)

2.3.1. Tensile Strength

The results of the tensile strength data analysis indicated that factors influenced the tensile strength. In the 14 formulas, tensile strength results ranged from of 1.32 to 2.47 MPa. The results met the requirements for good tensile strength, namely 1.02–10.20 MPa [9]. Based on the analysis results (Table 3), the suggested analytical model was a linear model based on the sum of the squares of the tensile strength response model sequence. The linear model with an R-squared value of 0.56 showed that the polymer concentration factor and the plasticizer concentration influenced the diversity of tensile strength responses. The adjusted R-squared value of 0.5613 served as a generalization of the population's R-Squared due to the existence of the population estimation element (11). Based on the data in Table 3, the model equation for the tensile strength response was: $Y_1 = +1.81 -0.13*A -0.25*B$.

The equation shows that the polymer value (A) was -0.13 and the plasticizer value (B) was -0.25, indicating an increase in the tensile strength response (Y_1) that was influenced by a decrease in the polymer concentration and a decrease in plasticizer concentration. The higher the concentrations of polymer and plasticizer, the lower the tensile strength. This occurs because plasticizers can reduce the strong intermolecular attraction between the polysaccharide chains in MDX-sorghum and promote hydrogen formation between the plasticizer and polysaccharide molecules, thereby reducing the tensile strength of the film by weakening the hydrogen bonds between the polymers and plasticizers. This reduces film's tensile strength by weakening the hydrogen bonds between polysaccharide chains [19].

2.3.2. *Elongation*

Elongation percent data indicated the influence of factors on the elongation results. In the 14 formulas, the elongation results were 61.41–10.96%. Therefore, based on the analysis results (Table 3), the suggested analytical model was a linear model based on the sum of the squares of the order of the elongation response model. Furthermore, it was emphasized by the results of the lack-of-fit test, which obtained the correct model and was suggested to be used in the elongation response as a linear model. This linear model had a P value (Prob>F) of 0.2747, which indicated the model's fit to the elongation response. Based on the data in Table 3, the model equation for the elongation response was: $Y_2 = +86.71 +7.67*A +13.90*B$.

Based on the equation, the polymer value (A) was +7.67, and the plasticizer value (B) was +13.90, indicating an increase in elongation response (Y_2) influenced by an increase in polymer concentration and plasticizer concentration. The higher the concentration of polymer and plasticizer, the more likely the elongation is to increase. This occurs because the glycerol molecules in the polymer matrix disrupt the polymer structure through hydrogen bonds and transform it into an irregular flexible structure, a process that can be considered as restructuring (rearrangement) of the polymer matrix, with increased resistance (resistance) towards received pressures which in turn increase the stretchability (elongation) of the film [19].

Table 3. Analysis of ODF Cetirizin HCl Tensile Strength, Percent Elongation, and Disintegration Time Using CCD

Factors		Y_1	Y_2	Y_3
A	Coefficient	-0.13	7.67	-21.75
	ρ-value	0.1031	0.0002**	0.0003**
B	Coefficient	-0.25	13.90	-38.78
	ρ-value	0.0070**	0.0001**	0.0001**
A B	Coefficient	-	-	-0.50
	ρ-value	-	-	0.9238
A^2	Coefficient	-	-	-9.37
	ρ-value	-	-	0.0364*
B^2	Coefficient	-	-	-11.87
	ρ-value	-	-	0.0130*
Analytical model		Linier	Linier	Quadratic
Intercept		1.81	86.71	155.68
Degree of freedom		2	2	5
Sum of squares		0.64	2012.01	17342.43
Mean of squares		0.32	1006.00	3468.49
F-value		7.04	62.85	33.80
ρ-value		0.0108	0.0001	0.0001
R-Squared		0.5613	0.9195	0.9548

* ρ-value < 0.05
** ρ-value < 0.01

2.3.4. *Disintegration Time*

The results of the disintegration time test indicated that the film could be destroyed within 75–191 seconds. Based on the analysis results in Table 3, the suggested analytical model was a quadratic model grounded on the sum of the squares of the sequence of the disintegration time response models. This was confirmed by the results of the analysis of variance using the suggested model, namely the quadratic model.

Furthermore, the P value (prob>F) of 0.0001 was smaller than 0.05, indicating a significant model to determine the interaction of responses to variables in the disintegration time response. Based on Table 3, the model equations for the disintegration time response were: $Y_3 = +155.68-21.75*A-38.78*B-0.50*A*B-9.37*A^2-11.87*B^2$.

Based on the equation, the polymer value (A) was -21.75, and the plasticizer value (B) was -38.78, indicating an increase in the disintegration time response (Y3) that was influenced by a decrease in polymer concentration and a decrease in plasticizer concentration. The higher the concentrations of polymer and plasticizer, the faster the disintegration time. This occurs due to the increase in polymer concentration. The shorter disintegration time is caused by MDX, which has a high solubility in water, which aids water penetration into the film structure [24]. Therefore, when the concentrations of polymer and plasticizer are high, the disintegration time is low. This result is in line with a study by Sri et al. (2018), which found that increasing the amount of MDX would make the film disintegrate more rapidly [21]. The plasticizer can increase the intermolecular space of the film, and the increased intermolecular space can provide space for water to move in and allow the film to disintegrate faster [9].

2.4. ODF Preparation Optimal Formula

Based on our experiments, the recommended model to observe the effect of the use of MDX-sorghum and glycerol on the tensile strength and elongation responses was a linear model. In contrast, the suggested model for the disintegration time response was a quadratic model. The optimal ODF formula was verified by reproducing the formula by the RSM recommendations, and testing was performed for tensile strength, elongation, and disintegration time. From the results listed in Table 4, the recommended optimal concentrations of MDX-sorghum and glycerol were 3.56% and 10%, respectively, with a predicted tensile strength value of 1.495 MPa, percent elongation of 104%, and disintegration time of 83 seconds. The prediction results were validated by producing an ODF with the optimal formula, which was then evaluated.

Table 4. Results of Optimal Oral Dissolving Film (ODF) Formula on Response

No	Polymer (%)	Plasticizer (%)	Tensile Strength (MPa)	Elongation (%)	Disintegration Time (sec)	Desirability
1.	3.56	10.00	1.495	104.0	83	0.807
2.	3.55	10.00	1.497	103.9	83	0.806
3.	3.53	10.00	1.499	103.8	83	0.804

The validation of the RSM prediction results is presented in Table 5. The results indicated no significant difference (percentage error < 0,05%) between the results obtained and the RSM predictions. Therefore, the ODF preparation met the requirements for good film-forming characteristics. The literature shows that using polymers and plasticizers affects the characteristics of ODF. A high plasticizer concentration would result in low tensile strength, short disintegration time, and a high elongation value [22].

Table 5. Optimal ODF Evaluation Results

No	Response	RSM Prediction	Observation Results	Percentage Error (%)
1	Tensile Strength (MPa)	1.495	1.50	0.33
2	Elongation (%)	104	104.26	0.25
3	Disintegration Time (second)	83	82.95	0.06

3. CONCLUSION

The modified sorghum starch resulted in MDX-sorghum with enhanced solubility and swelling power. At a concentration of 2-6%, MDX-sorghum can be used as a film-forming polymer with the required tensile strength, elongation (%), and disintegration time. Based on the CCD analysis, the optimal concentrations of MDX-sorghum and glycerol were 4.00% and 6.50%, with a tensile strength response of 1.81 MPa, 86.71% elongation, and a disintegration period of 156 seconds. On the foundation of the obtained data, it can be stated that sorghum starch modification can increase sorghum's use as a pharmaceutical excipient.

4. MATERIALS AND METHODS

4.1. MDX-Sorghum Production

In the production of MDX-sorghum, the sorghum was modified by dissolving sorghum starch (Timurasa, Indonesia) using aquadest to a concentration of 24% (w/v), with the pH of the solution adjusted using HCl (Merck, Germany) and NaOH (Merck, Germany) to pH 6. Then, anhydrous CaCl2 (Merck, Germany) and 0.5% (v/v) amylase enzymes (Hench Biotechnology, China) were added. The solution was stirred at 87ºC for 90 minutes. After the stirring was complete, the inactivation process began by adding HCl until the pH reached 4. The solution was then cooled to a temperature of 60ºC and neutralized using 0.1 M NaOH to pH 6. The solution was then placed into an oven at 50ºC in a tin in a thin layer. After drying, the powder was removed, mashed with a blender, and sieved. The MDX-sorghum characterization was then performed [2,5].

4.2. MDX-Sorghum Characterisation

4.2.1. Yield value

The resulting MDX-sorghum was weighed entirely, and the yield value was calculated using Equation [23,24]:

$$Yield\ (\%) = \frac{MDX - sorghum\ weight\ obtained}{weight\ of\ sorghum\ starch\ used}\ x\ 100$$

4.2.2. Dextrose Equivalent Value

The DE value started by finding the Fehling factor value by dissolving 2.5 g of glucose with distilled water up to 1,000 mL, then removing 15 mL and adding 5 mL each of Fehling's solutions A and B. The mixture was boiled and titrated in a boiling state with glucose solution until it became reddish-brown. The amount of titrant required was recorded, and the Fehling factor was calculated using Equation [5,24]:

$$FF = \frac{titrant\ volume\ mL\ x\ glucose\ weight\ (g)}{1{,}000}$$

The DE value was then determined by making a solution of MDX-sorghum with a concentration of 10 g/200 mL from the results of the previous dextrin manufacture on a dry starch basis; then, a burette was added. Next, we added 5 mL each of Fehling's solutions A and B and 15 mL of glucose solution to a total of 50 mL of distilled water. The solution was boiled and titrated with MDX-sorghum solution until a reddish-brown colour was obtained. Finally, the required titrant was recorded, and the DE value was calculated using Equation [5,24]:

$$DE = FF\ x\ \frac{100}{starch\ concentration\ \left(\frac{g}{mL}\right) x\ titrant\ volume\ (mL)}$$

4.2.3. Solubility

A total of 0.5 g of sample was weighed (b) and dissolved with 10 mL of distilled water, then vortexed for 30 seconds. Next, the solution was centrifuged at 3,000 rpm for 15 minutes. Next, we placed 5 mL of the solution in an oven at 105°C for 5 hours to be evaporated. The product was then weighed and recorded as weight a. Finally, the solubility (%) of the sample was calculated using Equation [23,25]:

$$Solubility\ (\%) = \frac{a}{b}\ x\ 2\ x\ 100$$

4.2.4. Swelling Power

A total of 0.1 g of MDX-sorghum (b) was heated in 10 mL of distilled water in a water bath at 60°C for 30 minutes with constant mixing. Samples were centrifuged at 1,600 rpm for 15 minutes. The part that was deposited was weighed (a) and swelling power was calculated using Equation [23,25]:

$$Swelling\ Power = \frac{a}{b}$$

4.2.5. Infra-Red Fourier Transform (FTIR) Analysis

MDX-sorghum was ground and 2 g was weighed. The sample was added to 200 g of KBr and mixed until homogeneous. It was then placed into a pellet mold and analyzed for the MDX-sorghum functional group using FTIR (Agilent cary 630). The sample was scanned 64 times at 2 cm^{1} above the wave number region of 4,000–400 cm^{1} [26,27].

4.3. Production of ODF Cetirizine HCl

ODF was produced using the solvent casting method (see Table 6 for composition). First, citric acid and sucrose were dissolved using distilled water to become mass A. MDX-sorghum was then dispersed in hot water and was stirred until it expanded, forming mass B. Hydroxypropyl Methyl Cellulose (HPMC) (Luxchem, Indonesia) was dispersed in hot water and was stirred until it expanded, forming mass C. Mass B and mass C were mixed, and glycerol was added and stirred until homogeneous. Then, cetirizine HCl (Kimia Farma, Indonesia) and mass A were added and stirred until homogeneous. The remaining water was added until a volume of 100 mL was reached and was stirred until homogeneous. The mixture was poured and leveled on the mold, then dried in the oven at 50°C for 24 hours. The formed film was then released from the mold and cut to a size of 2 × 2 cm^2 [3].

Table 6. ODF cetirizine HCl composition based on CCD

Run	Batch	Composition						
		Cetirizine HCl (mg)	MDX-Sorghum* (%)	Glycerol* (%)	Sucrose (%)	Citric Acid (%)	HPMC (%)	Aquadest ad (mL)
1.	F1	1,500	4.00	6.50	4	4	4	100
2.	F2	1,500	4.00	3.00	4	4	4	100
3.	F3	1,500	4.00	10.00	4	4	4	100
4.	F4	1,500	4.00	6.50	4	4	4	100
5.	F5	1,500	5.41	8.97	4	4	4	100
6.	F6	1,500	4.00	6.50	4	4	4	100
7.	F7	1,500	2.59	8.97	4	4	4	100
8.	F8	1,500	4.00	6.50	4	4	4	100
9.	F9	1,500	6.00	6.50	4	4	4	100
10.	F10	1,500	4.00	6.50	4	4	4	100
11.	F11	1,500	4.00	6.50	4	4	4	100
12.	F12	1,500	2.59	4.03	4	4	4	100
13.	F13	1,500	2.00	6.50	4	4	4	100
14.	F14	1,500	5.41	4.03	4	4	4	100

*CCD-RSM Concentration Design Results

4.4. Evaluation of ODF Preparation and Cetirizine HCl

4.4.1. Tensile Strength and Elongation Test

Tensile strength and elongation percentage tests were performed using the universal testing machine located at the Centre for Advanced Materials Science and Technology (Pusat Sains dan Teknologi Bahan Maju-PSTBM), Batan, Serpong, South Tangerang.

4.4.2. Disintegration Time Test

A film was placed in a petri dish containing 2 mL of distilled water. The time required for the film to completely disintegrate is recorded as the disintegration time [28].

4.5. Data Analysis

Response data in the form of tensile strength test results, elongation, and disintegration times were entered into the CCD-RSM (Design Expert 7.1.5, trial version) response column and were analyzed to obtain the optimal concentration of MDX-sorghum and glycerol for producing ODF preparations that best met the requirements. The level and limits of the response variables in data analysis using CCD are within range, where the requirements for a good ODF include tensile strength values between 1.02-10.2 MPa [15], elongation more than 70 % [16] , and disintegration time less than 3 minutes [17].

4.6. Production and Evaluation of the Optimal ODF Formula

The optimal formula obtained from CCD-RSM analysis was produced and evaluated. The results of the tensile strength, percentage elongation, and disintegration time tests were then compared with the predicted RSM data.

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Conflict of interest statement: The authors declare that this article has no actual, potential, or perceived conflict of interest.

REFERENCES

[1] Sharma D, Kaur D, Verma S, Singh D, Singh M, Singh G. Fast Dissolving Oral Films Technology : A Recent Trend For An Innovative Oral Drug Delivery Systeml International J. Int J Drug Deliv. 2015;7(2):60–75. [CrossRef]

[2] Haryani K, Retnowati DS, Handayani NA, Dewi WM, Pamularsih SA. Modifikasi Pati Sorgum menjadi Maltodekstrin secara Enzimatik Dengan Menggunakan Enzim Alfa Amilase dan Gluko Amilase. J Teknol Pangan. 2022;6(1):8–12. [CrossRef]

[3] Putri DA, Setiawan A, Anggraini PD. Physical properties of edible sorgum starch film added with carboxymethyl cellulose. J Phys Sci. 2018;29:185–94. [CrossRef]

[4] Borges AF, Silva C, Coelho JFJ, Simões S. Oral films: Current status and future perspectives. J Control Release. 2015;206(2015):1–19. [CrossRef]

[5] GI P, MK B, VN E, DM S, AO O. Effect of pH and temperature on the activities of alpha-amylase in cassava starch liquefaction. African J Food Sci Technol. 2018;09(02):37–42. [CrossRef]

[6] Shah KA, Gao B, Kamal R, Razzaq A, Qi S, Zhu Q-N, et al. Development and Characterizations of Pullulan and Maltodextrin-Based Oral Fast-Dissolving Films Employing a Box–Behnken Experimental Design. Materials (Basel). 2022;15(10):3591. [CrossRef]

[7] Caicedo C, Díaz-Cruz CA, Jiménez-Regalado EJ, Aguirre-Loredo RY. Effect of Plasticizer Content on Mechanical and Water Vapor Permeability of Maize Starch/PVOH/Chitosan Composite Films. Materials (Basel). 2022;15(4). [CrossRef]

[8] Rowe RC, Sheskey PJ, Quinn ME, editors. Handbook of pharmaceutical excipient. 6th ed. Pharmaceutical Press and the American Pharmacists Association; 2009.

[9] Fahrullah F, Radiati LE, Purwadi P, Rosyidi D. The Effect of Different Plasticizers on the Characteristics of Whey Composite Edible Film. J Ilmu dan Teknol Has Ternak. 2020;15(1):31–7. [CrossRef]

[10] Walfathiyyah A, Kusuma AP, Cahya FN, Qusyairi N, Wahyuningtyas D. Optimization of Plasticizer Glycerol in Edible Film Based Water Hyacinth (Eichornia crossipes) Starch. 5th ICRIEMS Proc. 2018;1–10. [CrossRef]

[11] Ahmad A, Lajis MA, Yusuf NK, Ab Rahim SN. Statistical optimization by the response surface methodology of direct recycled aluminum-alumina metal matrix composite (MMC-AlR) employing the metal forming process. Processes. 2020;8(7). [CrossRef]

[12] Almajed A, Srirama D, Moghal AAB. Response Surface Method Analysis of Chemically Stabilized Fiber-Reinforced Soil. Materials (Basel). 2021;14(6):1535. [CrossRef]

[13] Bhattacharya S. Central Composite Design for Response Surface Methodology and Its Application in Pharmacy. In: Kayaroganam P, editor. Response Surface Methodology in Engineering Science. IntechOpen; 2021. [CrossRef]

[14] Pathan RR, Siddiqui A. Preparation, Optimization, and Evaluation of Pellets Containing Mesalamine With Natural Gums For Colon Drug Delivery System. Fabad J Pharm Sci. 2022 Mar 1;47(1):35–56. [CrossRef]

[15] Setiani W, Sudiarti T, Rahmidar, L. Preparasi dan Karakterisasi Edible Film dari Poliblend Pati Sukun - Kitosan. Valensi. 2013;3(2):100-109. [CrossRef]

[16] Sulastri E, Yuyun Y, Heriani N, Khumaidi A. Application of chitosan shells meti (batissa violacea L. Von Lamarck, 1818) as edible film. Curr Res Nutr Food Sci. 2019;7(1):253–64. [CrossRef]

[17] Panraksa P, Tipduangta P, Jantanasakulwong K, Jantrawut P. Formulation of Orally Disintegrating Films as an Amorphous Solid Solution of a Poorly Water-Soluble Drug. Membranes (Basel). 2020 Nov 27;10(12):376. [CrossRef]

[18] Nurmiah S, Syarief R, Sukarno S, Peranginangin R, Nurmata B. Aplikasi Response Surface Methodology Pada Optimalisasi Kondisi Proses Pengolahan Alkali Treated Cottonii (ATC). J Pascapanen dan Bioteknol Kelaut dan Perikan. 2013;8(1):9. [CrossRef]

[19] Afifah N, Sholichah E, Indrianti N, Darmajana DA. Pengaruh Kombinasi Plasticizer terhadap Karakteristik Edible Film dari Karagenan dan Lilin Lebah. Biopropal Ind. 2018;9(No 1):49–60. [CrossRef]

[20] Mahmood SZ, Sabry HS, Yousif NZ, Salman ZD. Optimization and Evaluation of Chlorpheniramine Maleate Oral Strip for Pediatric Use. Asian J Pharm Clin Res. 2018;11(12):548. [CrossRef]

[21] Sri SJ, Krishna KSM, Kusuma D, Shankar CU. Formulation and in-Vitro Evaluation of Benazepril Mouth Dissolving Films. Indo Am J Pharm Sci. 2018;5(1):552–60. [CrossRef]

[22] Shah U, Naqash F, Gani A, Masoodi FA. Art and Science behind Modified Starch Edible Films and Coatings: A Review. Compr Rev Food Sci Food Saf. 2016;15(3):568–80. [CrossRef]

[23] Shrestha B, Dhungana PK, Dhital S, Adhikari B. Evaluation of Modified Sorghum Starches and Biodegradable Films. J Food Sci Technol Nepal. 2018;10:11–7. [CrossRef]

[24] Zusfahair Z, Riana Ningsih D. Pembuatan dekstrin dari pati ubi kayu menggunakan katalis amilase hasil fraksinasi dari Azospirillum sp. JG3. Molekul. 2012;7(1):9. [CrossRef]

[25] Kusumayanti H, Handayani NA, Santosa H. Swelling Power and Water Solubility of Cassava and Sweet Potatoes Flour. Procedia Environ Sci. 2015;23(164–7. [CrossRef]

[26.] Torrenegra ME, Solano R, Herrera A, León G, Pajaro A. Fourier Transform Infrared Spectroscopy (FTIR) Analysis of Biodegradable Films Based On Modified Colombian Starches of Cassava and Yam. Int J PharmTech Res. 2018;11(11):368–76. [CrossRef]

[27] Topal GR, Kiymaci ME, Özkan Y. Preparation and in Vitro Characterization of Vancomycin Loaded Plga Nanoparticles for the Treatment of Enterococcus Faecalis Infections. Ankara Univ Eczac Fak Derg. 2022 Mar 25;46(2):350–63. [CrossRef]

[28] Irfan M, Rabel S, Bukhtar Q, Qadir MI, Jabeen F, Khan A. Orally disintegrating films: A modern expansion in drug delivery system. Saudi Pharm J. 2016;24(5):537–46. [CrossRef]

2. Bukti Konfirmasi Review dan Hasil Review Pertama (25 Februari 2023)

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Dear Other Anisa Amalia,

The Editors have now assessed the reviewer response and have concluded that, in its present form, the manuscript is not yet ready for publication in the Journal. Below you will find the relevant review comments and editorial notes. Acceptance of the paper is contingent upon effectively revising the work by taking these comments into serious consideration, and by responding or rebutting them in detail. We ask you to submit your revision through the online system within 30 days. The web site is located at https://www.jrespharm.com.
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Suggestions

1.Reviewer Comments
Work is presented well. Few changes are suggested as given in track changes.

2.Reviewer Comments
The manuscript entitled "Characterization of modified sorghum starch and its use as a film-forming in orally dissolving film formulation with glycerol as a plasticizer" was about an oral dissolving film formulation that contains a modified sorghum starch. Authors modified sorghum starch to eliminate its undesired properties (such as stickiness and brittleness) and used it as a pharmaceutical excipient. There are serious inconsistencies between Tables 4-5, the abstract, and the conclusion sections in the manuscript. These inconsistencies cause confusion and must be corrected. In addition, the quality of the figures should be improved. Particularly, it is hard to read the numbers in Figures 1 and 2. There are also several misspelled words and grammar errors. In conclusion, I believe the manuscript may only be suitable for publication after a revision. Details are specified in the word document.

3.Reviewer Comments
My comments and corrections have been made on the attached file.

Reviewer 1

Comment File	Show Comment File (https://www.jrespharm.com/submit/uploads/rev_com/MPJ-10715-14503-rev-file-10715-mpj-10715-3-modified-sorghum-starch-jrp-review-comments.docx)

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Reviewer 3

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Manuscript Information

Manuscript ID:	**MPJ-10715**
Title in English:	Characterization of modified sorghum starch and ıts use as a film-forming in orally dissolving film formulation with glycerol as a plasticizer
Small Title in English:	No information entered
Authors:	Anisa Amalia[1], Nining Nining[1], Muhammad Dandi[2]
Institutions:	[1]Faculty of Pharmacy and Science, Universitas Muhammadiyah Prof. DR. HAMKA, Department of Pharmaceutics, East Jakarta/DKI Jakarta, Indonesia [2]Faculty of Pharmacy and Science, Universitas Muhammadiyah Prof. DR. HAMKA, Department of Pharmacy, East Jakarta/DKI Jakarta, Indonesia
Keywords in English:	Sorghum strach ; modified ; film-forming ; glycerol ; response surface methodology
Manuscript Type:	Research article
Processing Status:	Major Revision

Abstract in English

Film-forming polymers and plasticizers are the components of Orally dissolving film (ODF) compositions that have the most influence on the physical properties of the film preparations. Modification of sorghum starch produces maltodextrin (MDX)-sorghum, which can be used as a film-forming polymer, and glycerol can be used as a plasticizer in ODF preparations. This study aims to determine the optimal concentrations of MDX-sorghum and glycerol for producing ODF compositio using the central composite design (CCD) in response surface methodology (RSM). Hydrolysis of sorghum starch yielded MDX-sorghum, characterized by yield value, dextrose equivalent (DE) value, solubility, swelling power, and FTIR analysis. The CCD design included a 2-6% and 3-10% concentration range for MDX-sorghum and glycerol, respectively, as parameters in the optimization process. The test response was evaluated using tensile strength, elongation, and disintegration time tests, so 14 experimental designs were obtained. The modification of sorghum starch yields a light brown MDX-sorghum powder with desirable properties. Optimization of MDX-sorghum and glycerol concentrations yielded an optimal formula with a tensile value of 1.81 MPa with an error percentage of 0.33%, an elongation of 104% with an error percentage of 0.33%, and a disintegration time of 82.95 seconds with an error percentage of 0.06%. By modifying sorghum starch to make MDX-sorghum, the starch's properties can be enhanced and used as a film-forming. The optimal MDX-Sorghum and glycerol concentrations for the production of ODF are 3.56 % and 10 %, respectively.

Manuscript Files

File Name	File Size	Date Created	Category	Description
MPJ-10715-2-cover-letter-jrp.pdf (../pdf-files/out/10715-MPJ-10715-2-cover-letter-jrp.pdf)	14 KB	Sep 14, 2022	Cover letter	None
MPJ-10715-3-modified-sorghum-starch-jrp-template.pdf (../pdf-files/out/10715-MPJ-10715-3-modified-sorghum-starch-jrp-template.pdf)	1305 KB	Sep 14, 2022	Main Document	None
MPJ-10715-1-jrp-checklist.pdf (../pdf-files/in/10715-MPJ-10715-1-jrp-checklist.pdf)	241 KB	Sep 14, 2022	Author Checklist Form	None
MPJ-10715-4-modified-sorghum-starch-jrp-template.pdf (../pdf-files/out/10715-MPJ-10715-4-modified-sorghum-starch-jrp-template.pdf)	0 KB	Sep 14, 2022	Main Document	None
MPJ-10715-1-jrp-copyright-form-integrated.pdf (../pdf-files/out/10715-MPJ-10715-1-jrp-copyright-form-integrated.pdf)	85 KB	Sep 14, 2022	Copyright Transfer Form	None
MPJ-10715-6-figure-1.jpg (../pdf-files/in/10715-MPJ-10715-6-figure-1.jpg)	98 KB	Sep 14, 2022	Figure	None
MPJ-10715-5-figure-1.jpg (../pdf-files/in/10715-MPJ-10715-5-figure-1.jpg)	0 KB	Sep 14, 2022	Figure	None

MPJ-10715-9-figure-2.jpg (../pdf-files/in/10715-MPJ-10715-9-figure-2.jpg)	89 KB	Sep 14, 2022	Figure	None
MPJ-10715-9-figure-3.jpg (../pdf-files/in/10715-MPJ-10715-9-figure-3.jpg)	103 KB	Sep 14, 2022	Figure	None

Score Sheet

1. Reviewer

Does the content and value of the work justify publication in Marmara Pharmaceutical Journal ?	Yes
Does the title of the manuscript reflect the contents of the study ?	Yes
Are the keywords sufficient and appropriate ?	Yes
Is the summary concise and informative?	Yes
Is the text divided appropriately according to the article type ?	Yes
Is the language adequate?	Yes
Are the nomenclature and scientific terminology correct?	Yes
Are the references complete and recent?	Yes
Are the figures tables and graphics necessary ?	Yes
Are the figures tables and graphics clear ?	Yes

Is the introduction part	sufficiently developed
Are the experimental procedures sound?	Yes
Is the results and discussion part	sufficiently developed
Is conclusion sufficient and correlated with the results ?	Yes
Is the information about the approval of ETHICAL COMMISSION presented ?	Not applicable

2. Reviewer

Does the content and value of the work justify publication in Marmara Pharmaceutical Journal ?	After revision
Does the title of the manuscript reflect the contents of the study ?	Yes
Are the keywords sufficient and appropriate ?	Yes
Is the summary concise and informative?	Yes
Is the text divided appropriately according to the article type ?	Yes
Is the language adequate?	Yes

Are the nomenclature and scientific terminology correct?	Yes
Are the references complete and recent?	Yes
Are the figures tables and graphics necessary ?	Yes
Are the figures tables and graphics clear ?	No
Is the introduction part	sufficiently developed
Are the experimental procedures sound?	Yes
Is the results and discussion part	sufficiently developed
Is conclusion sufficient and correlated with the results ?	No
Is the information about the approval of ETHICAL COMMISSION presented ?	Not applicable

3. Reviewer

Does the content and value of the work justify publication in Marmara Pharmaceutical Journal ?	Yes
Does the title of the manuscript reflect the contents of the study ?	Yes
Are the keywords sufficient and	Yes

appropriate ?	
Is the summary concise and informative?	Yes
Is the text divided appropriately according to the article type ?	Yes
Is the language adequate?	No
Are the nomenclature and scientific terminology correct?	Yes
Are the references complete and recent?	No
Are the figures tables and graphics necessary ?	Yes
Are the figures tables and graphics clear ?	No
Is the introduction part	sufficiently developed
Are the experimental procedures sound?	Yes
Is the results and discussion part	sufficiently developed
Is conclusion sufficient and correlated with the results ?	No
Is the information about the approval of ETHICAL COMMISSION presented ?	Not applicable

3. Respon kepada Reviewer dan Artikel yang Diresubmit (19 Maret 2023)

RESPONSE TO REVIEWERS

OF THE JOURNAL OF RESEARCH IN PHARMACY

MANUSCRIPT ID: MPJ-10715

Reviewer: 1

Comments to the Author

Work is presented well. Few changes are suggested as given in track changes.

Response:

Thank you for your correction suggestion. We apologized for the mistakes in our writing. We have enhanced the writing and added the reasons for selecting cetirizine HCl and the advantages of establishing the ODF formula as an alternative method of delivering cetirizine HCl. The bibliography has been rewritten and a DOI hyperlink has been included.

Reviewer: 2

The manuscript entitled "Characterization of modified sorghum starch and its use as a film-forming in orally dissolving film formulation with glycerol as a plasticizer" was about an oral dissolving film formulation that contains a modified sorghum starch. Authors modified sorghum starch to eliminate its undesired properties (such as stickiness and brittleness) and used it as a pharmaceutical excipient. There are serious inconsistencies between Tables 4-5, the abstract, and the conclusion sections in the manuscript. These inconsistencies cause confusion and must be corrected. In addition, the quality of the figures should be improved. Particularly, it is hard to read the numbers in Figures 1 and 2. There are also several misspelled words and grammar errors. In conclusion, I believe the manuscript may only be suitable for publication after a revision. Details are specified in the word document.

Response:

Thank you for your improvement suggestion. We apologise for the mistakes in our writing. We have reviewed and updated the results stated in the abstract, conclusions, and tables 4 and 5. The resolution of figures 1-3 has been enhanced. We have corrected and rechecked for writing and grammar issues utilising a language editing service.

Reviewer: 3

My comments and corrections have been made on the attached file

<u>Response:</u>

Please accept our apologies for our writing errors and thank you for your improvement recommendations. The required amount of material has been incorporated into the methodology. The reason there are four identical formulas is because, according to the CCD model, it takes five to six repetitions of concentration to estimate the test error, and we have included this to the methodology section (4.3). The writing of the library has been enhanced, and a DOI hyperlink has been included. The image resolution has been enhanced.

Journal of Research in Pharmacy

Research Article

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Characterization of modified sorghum starch and ~~i~~its use as a film-forming polymer~~agent~~ in orally dissolving film formulations with glycerol as a plasticizer

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[1] Department of Pharmaceutics, Faculty of Pharmacy and Science, Universitas Muhammadiyah Prof. DR. HAMKA, Jakarta, Indonesia.

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Received: 0 Month 201X / Revised: 0 Month 201X / Accepted: 0 Month 201X

ABSTRACT: Film-forming polymers and plasticizers are ~~the~~ components of ~~O~~orally dissolving film (ODF) compositions that have the ~~most~~greatest influence on the physical properties of the film preparations. Modification of sorghum starch produces maltodextrin (MDX)-sorghum~~,~~ which can be used as a film-forming polymer, and glycerol can be used as a plasticizer in ODF preparations. This study aims to determine the optimal concentrations of MDX-sorghum and glycerol ~~for~~to produce~~ing~~ ODF compositions using the central composite design (CCD) in response surface methodology (RSM). Hydrolysis of sorghum starch yielded MDX-sorghum, characterized by yield value, dextrose equivalent (DE) value, solubility, swelling power~~,~~ and FTIR analysis. The CCD ~~design~~ included a concentration range of 2-6% and 3-10% ~~concentration range~~ for MDX-sorghum and glycerol, respectively, as parameters in the optimization process, so 14 experimental designs were obtained. The test response was evaluated using tensile strength, elongation~~,~~ and disintegration time tests~~, so 14 experimental designs were obtained~~. The modification of sorghum starch yields a light brown MDX-sorghum powder with desirable properties. Optimization of MDX-sorghum and glycerol concentrations yielded an optimal formulation with a tensile value of 1.50~~81~~ MPa with an error percentage of 0.33%, ~~an~~ elongation of 104.26% with an error percentage of 0.25~~33~~%, and ~~a~~ disintegration time of 82.95 seconds with an error percentage of 0.06%. By modifying sorghum starch into MDX-sorghum, the starch's ability to dissolve and swell can be improved, allowing it to be used as a film-forming polymer. ~~By modifying sorghum starch to make MDX-sorghum, the starch's properties can be enhanced and used as a film-forming.~~ The optimal MDX-Sorghum and glycerol concentrations for the production of ODF are ~~3.56~~3.56 % and 10.00~~10~~ %, respectively.

KEYWORDS: Sorghum strach, modified, film-forming, glycerol, response surface methodology.

Commented [G$1]: not grammatically correct.

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1. INTRODUCTION

Sorghum starch is a film-forming polymer with hydrophilic properties used in the manufactur~~ing of~~e of orally dissolving film (ODF) preparations ([1]) ~~[1]~~. Sorghum starch is a natural biopolymer that is easily accessible and contains 72–75% carbohydrates, 20–30% amylose, and 70–80% amylopectin, which can be used as film-forming components [2,3]. However, natural sorghum starch has several disadvantages: ~~there are several drawbacks to natural sorghum starch:~~ it is sticky, hard, brittle, not transparent, and not resistant to acid treatment. In a study by Putri et al. [(3]), using only~~single~~ sorghum starch resulted in a less elastic film preparation. This problem can be overcome by modifying sorghum starch through a partial hydrolysis process so that its characteristics resemble those of maltodextrin (MDX) ([4]). MDX is obtained from starch that has been enzymatically modified by partial hydrolysis. As a result, MDX has a dextrose equivalent (DE) value of less than 20. Moreover, MDX has good film-forming, solubility, and adhesive characteristics, allowing it to produce elastic films [5,6].

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Commented [G$5]: What is "film-forming solubility" ?

The film-forming polymer influence~~d~~s the film preparation's elasticity; plasticizers can also increase film's elasticity [7]. Glycerol is one of the plasticizers that can be used in the manufacture of ODF preparations. Glycerol is a plasticizer that is easily soluble in water (hydrophilic), has a low molecular weight and thus helps to reduce ~~to help bring down the~~ intermolecular tensions along the polymer chain, and provides~~has~~ the

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advantages of increasing the viscosity of the solution, reducing brittleness, and increasing the strength of ODF preparations [8]. Glycerol, as a plasticizer, produced edible films with improved characteristics compared with sorbitol and polyethylene glycol [9]. A ~~R~~research conducted by Walfathiyyah et al. (2017) showed that adding of glycerol resulted in a more elastic edible film [10]. The optimal concentrations of glycerol and MDX-sorghum can be analyzed using the response surface methodology (RSM).

RSM can be used to design several formulations with varying concentrations of MDX-sorghum and glycerol. The RSM can reduce the number of materials used because it does not require a trial formulation stage, which would require considerable research [11]. Furthermore, this method can describe the interaction among variables toward the response [11,12]. Several models can be used in RSM. The experimental design in this study used the central composite design (CCD) model. CCD is a fractional factorial design often used in RSM as it can speed up several experimental designs [13]. The concentration of MDX-sorghum~~,~~ which functions as a film-forming agent~~,~~ and glycerol~~,~~ which functions as a plasticizer~~,~~ were the independent factors, while the dependent variables (response) were ~~the value of~~ tensile strength, ~~percentage~~ elongation~~,~~ and disintegration time. MDX-sorghum and glycerol as components in the manufacture of films are expected to produce films with characteristics that meet the requirements so that they can be used as alternative pharmaceutical preparations containing ~~for the~~ cetirizine HCl. Cetirizine HCl is available in tablet dosage forms. However, the disadvantage of tablet preparations is that pediatric and geriatric patients and patients with throat disorders have difficulty swallowing tablets, resulting in decreased patient compliance. Therefore, alternative preparations are required to make it easier for these patients to consume cetirizine, such as oral dissolving film (ODF) preparations that dissolve rapidly in the mouth ~~(~~[14,15]~~)~~. Hence, it is necessary to optimize the concentrations of MDX-sorghum and glycerol to produce ODF preparation with optimal physical properties. The research findings can serve as a reference for developing natural excipients. ~~Therefore, it is necessary to optimize the concentrations of MDX-sorghum and glycerol to obtain an ODF preparations with the best physical properties so that it can be used as a reference in the development of natural excipients in the pharmaceutical field.~~

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2. RESULTS AND DISCUSSION

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2.1. Characteristics of MDX-Sorghum

The characteristics of sorghum starch and MDX-sorghum are shown in Table 1. Based on the results, the DE value of MDX-sorghum met the requirements (i.e., < 20). Low DE maltodextrin (< 20) had better elasticity and viscosity than high DE maltodextrin ~~(~~[16]~~)~~. In each sugar chain undergoing hydrolysis, there was one reducing sugar group; as the number of simple sugar groups increased, the number of reducing sugar groups and the value of DE also increased. In solubility and swelling power studies, MDX-sorghum demonstrated more solubility and swelling ability than sorghum starch. This was due to the hydrolysis reaction performed by the amylase enzyme on sorghum starch by breaking the glycosidic bond in starch molecules into simple sugars, such as glucose and dextrin, so that the two~~hree~~ parameters increased [5,6].

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Sorghum starch and modified sorghum starch were analyzed by evaluating the spectrum's shape, namely the specific peaks indicating the type of functional group in~~by~~ a starch compound. The FTIR analysis results ~~using FTIR~~ are shown in Figure 1 and 2. The O–H group's peak is between 3,400 and 2,100 cm^{-1}. At approximately 3,270.7 cm^{-1}, the yield of sorghum starch groups was measured, whereas the O-H functional group was identified at the peak of modified sorghum starch at 3,287.0 cm^{-1}. The C-H functional group was discovered at the peak of 2,924.1 cm^{-1} within the range of 3,850.0–2,924.1 cm^{-1}, with no variation in peak positions between samples. With a wavelength of 1,149.9 cm^{-1} and a peak transition of 1,148.0 cm^{-1}, the C-O-C functional group was found in sorghum starch, showing a change in the modified starch. This test is intended to identify transfer results between functional groups in two spectra, allowing for the observation of transmission differences between O-H and C-O-C functional groups. The amylase enzyme breaks the -1,4 glycosidic link in the polysaccharide chain for starch to be turned into MDX ~~(~~[17]~~)~~. ~~The peak for the O-H group was in the range of 3,400–2,400 cm^{-1}. The results of the sorghum starch group were around 3,270.7 cm^{-1}, while the O-H functional group was obtained at a modified sorghum starch peak of 3,287.0 cm^{-1}, and the C-H functional group was obtained at the peak of 2,924.1 cm^{-1} in the range of 3,850.0–2,850.0 cm^{-1}, indicating no change in peak between the two samples. However, the C-O-C functional group obtained 1,149.9 cm^{-1} of sorghum starch and a peak shift of 1,148.0 cm^{-1}, which indicated a change in the modified starch. This treatment aimed to determine the results of the transfer between the functional groups on the two spectra, whereby the difference between the transmittance in the O-H and C-O-H functional groups could be observed.~~

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~~This was due to the breakdown of -1,4 glycosidic bonds by the amylase enzyme on the inside of the polysaccharide chain so that the starch could be modified into MDX [14].~~

2.2. Evaluation of ODF Preparations

Table 2 ~~2~~ presents the results of the evaluation of ODF preparations. Based on the evaluation, all ODF formulations meet the requirements of a 'good' film. The film preparation was considered good if it had a tensile strength value of 1.02 – 10.20 Mp~~pa~~ ([18]) ~~[15]~~, elongation > 70% ([19]) ~~[16]~~, and disintegration time < 3 minutes ([20]) ~~[17]~~.

2.3. Data Analysis Using RSM

The combination of MDX-Sorghum as a film-forming agent and glycerol as a plasticizer affects the tensile strength, elongation, and disintegration time, as illustrated in Figure 3. The color on the graph represents the tensile strength (a), elongation ~~percentage~~ (b), and disintegration time (c). The color positioned bottom has the lowest response value, while the above color has the highest response value. The number of color changes along the curve indicates the influence of the concentrations film-forming agent (A) and plasticizer (B)~~ing concentrations~~. The combination of factors (A and B) affects the response related to the number of colors on the curve [14,18]. According to the observed results, the disintegration time is the response most affected by the concentration of the factors ~~concentration.~~

2.3.1. Tensile Strength

The results of the tensile strength data analysis indicated that the factors influenced the tensile strength. In the 14 formulations, tensile strength results ranged from of 1.32 to 2.47 MPa. The results met the requirements for good tensile strength, namely 1.02–10.20 MPa ([9,18]) ~~[9]~~. Based on the analysis results (Table 3), the suggested analytical model was a linear model based on the sum of the squares of the tensile strength response model sequence. The linear model with an R-squared value of 0.56 showed that the polymer concentration and the plasticizer concentration influenced the ~~diversity of~~ tensile strength responses. The adjusted R-squared value of 0.56~~13~~ served as a generalization of the population's R-Squared due to the existence of the population estimation element ([21]). ~~[11].~~ The model equation for the tensile strength response was $Y_1 = +1.81 - 0.13*A - 0.25*B$ based on the results in Table 3.

The equation shows that the coefficients of the polymer ~~value~~ concentration (A) ~~was -0.13~~ and the plasticizer concentration ~~value~~ (B) ~~was~~ were -0.13 and -0.25, respectively. It indicates~~ing~~ that a decrease in polymer and/or plasticizer concentration results in an increase in tensile strength response (Y_1) ~~an increase in the tensile strength response (Y_1) that was influenced by a decrease in the polymer concentration and a decrease in plasticizer concentration~~. The tensile strength decreases as the polymer and/or plasticizer content increases. This is because MDX-sorghum has a low molecular weight, making the polymer network less intense and decreasing the film's mechanical properties ([22]). ~~The higher the concentrations of polymer and/or plasticizer, the lower the tensile strength. This is because.~~ ~~t~~The plasticizer can reduce the strong intermolecular attraction in the polysaccharide chain of MDX-sorghum and promote hydrogen formation between the plasticizer and polysaccharide molecule, thereby weakening the hydrogen bonds in the polymer and decreasing the tensile strength of the film ([23]). ~~[19].~~

2.3.2. Elongation

Elongation ~~percent~~ data indicated the influence of factors on the elongation results. In the 14 formulations, the elongation results were between 61.41–103.96%. Consequently, a linear model based on the sum of squares ~~of the order~~ of the elongation response was suggested based on the analysis results (Table 3). In addition, the findings of the lack-of-fit test indicated that a linear model should be applied to the elongation response in order to produce the correct model. This linear model fitted the elongation response with a ~~P~~ p value (~~P~~prob>F) of 0.2747, indicating its validity ([11,13)]. $Y_2 = +86.71 + 7.67*A + 13.90*B$ was the model equation for the elongation response depending on the data in Table 3.

Based on the equation, coefficients of the the polymer ~~value~~ concentration (A) ~~was +7.67,~~ and the plasticizer ~~value~~ concentration (B) ~~was~~were +7.67 and +13.90, respectively. It indicates~~ing~~ that an increase in polymer and/or plasticizer concentration results in an increase in tensile strength response (Y_1)~~an increase in elongation response (Y_2) influenced by an increase in polymer concentration and plasticizer concentration.~~ The higher the concentration of polymer and/or plasticizer, the more likely the elongation is to increase. This occurs because the glycerol molecules in the polymer matrix disrupt the polymer structure through hydrogen

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bonds and transform it into an irregular flexible structure, a process that can be considered as restructuring (rearrangement) of the polymer matrix, with increased resistance ~~(resistance)~~ towards received pressures which in turn increase the stretchability (elongation) of the film ~~(~~[23]~~)~~. This is also because maltodextrin cannot create a strong network with other polymers that make ODF ~~(~~[22]~~)~~. ~~[19].~~

2.3.4. Disintegration Time

Based on results of the disintegration time test, the film could disintegrate within 75–191 seconds. According to the results of the study described in Table 3, the suggested analytical model was a quadratic model based on the sum of the squares of the sequence of the disintegration time response models. The findings of the analysis of variance using the suggested quadratic model confirmed this. Furthermore, the p value (prob>F) of 0.0001 was smaller than 0.05, indicating a significant model to determine the interaction of responses to variables in the disintegration time response ~~(~~[11,13]~~)~~. Based on Table 3, the model equations for the disintegration time response were: $Y_3 = +155.68-21.75*A-38.78*B-0.50*A*B-9.37*A^2-11.87*B^2$.

~~According to the results of the study described in Table 3, the suggested analytical model was a quadratic model based on the sum of the squares of the sequence of the disintegration time response models. The findings of the analysis of variance using the suggested quadratic model, a quadratic model, confirmed this. Furthermore, the Pp value (prob>F) of 0.0001 was smaller than 0.05, indicating a significant model to determine the interaction of responses to variables in the disintegration time response. Based on Table 3, the model equations for the disintegration time response were: Y3 = +155.68-21.75*A-38.78*B-0.50*A*B-9.37*A2-11.87*B2.~~

Based on the equation, the polymer ~~value~~ concentration (A) ~~was -21.75,~~ and the plasticizer ~~value~~ concentration (B) ~~was~~were -21.75 and -38.78, respectively. It indicat~~ing~~es that a decrease in polymer and/or plasticizer concentration results an increase in the disintegration time response (Y3) ~~that was influenced by a decrease in polymer concentration and a decrease in plasticizer concentration~~. The higher the concentrations of polymer and/or plasticizer, the faster the disintegration ~~time~~. This occurs due to the increase in polymer concentration. ~~The shorter disintegration time is caused by~~ MDX, which has a high solubility in water~~,~~ ~~which~~and aids water penetration into the film structure, provides a shorter disintegration time ~~(~~[24,25]~~)~~ ~~[24]~~. Therefore, when the concentrations of polymer and plasticizer are high, the disintegration time is ~~low~~short. This result is in line with a study by Sri et al. (2018), which found that increasing the amount of MDX ~~would make~~ made the film disintegrate more rapidly ~~(~~[26]~~)~~ ~~[21]~~. The plasticizer can increase the intermolecular gap of the film, and the enhanced intermolecular gap can allow water to migrate and accelerate the film's disintegration [9].

2.4. ODF Preparation Optimal Formulation

Based on our experiments, the recommended model to observe the effect of the use of MDX-sorghum and glycerol on the tensile strength and elongation responses was a linear model. In contrast, the suggested model for the disintegration time response was a quadratic model. The optimal ODF formulation was verified by reproducing the formulation by the RSM recommendations, and testing was performed for tensile strength, elongation, and disintegration time. From the results listed in Table 4, the recommended optimal concentrations of MDX-sorghum and glycerol were 3.56% and 10%, respectively, with a predicted tensile strength value of 1.495 MPa, percent elongation of 104%, and disintegration time of 83 seconds. The prediction results were validated by producing an ODF with the optimal formulation, which was then evaluated.

The validation of the RSM prediction results is presented in Table 5. The results indicated no significant difference (percentage error < 0,05%) between the results obtained and the RSM predictions. Therefore, the ODF preparation met the requirements for good film-forming characteristics. The literature shows that using polymers and plasticizers affects the characteristics of ODF. A high plasticizer concentration would result in low tensile strength, short disintegration time, and a high elongation value ~~(~~[25]~~)~~ ~~[22]~~.

3. CONCLUSION

The modified sorghum starch resulted in MDX-sorghum with enhanced solubility and swelling power. At a concentration of 2-6%, MDX-sorghum can be used as a film-forming polymer with the required tensile strength, elongation (%), and disintegration time. Based on the CCD analysis, the optimal concentrations of MDX-sorghum and glycerol were 3.56~~4.00~~% and 10.00~~6.50~~% respectively, with a tensile strength response of 1.50~~81~~ MPa, 104,26~~86.71~~% elongation, and a disintegration time~~period~~ of 82,95~~156~~ seconds. On the foundation

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of the obtained data, it can be stated that sorghum starch modification can increase the use of sorghum~~'s use~~ as a pharmaceutical excipient.

4. MATERIALS AND METHODS

4.1. MDX-Sorghum Production

In the production of MDX-sorghum, the sorghum was modified by dissolving sorghum starch (Timurasa, Indonesia) using distilled water ~~aquadest~~ to a concentration of 24% (w/v)~~, with t~~The pH of the solution was adjusted to 6 using HCl (Merck, Germany) and NaOH (Merck, Germany) ~~to pH 6~~. Then, 100 ppm anhydrous $CaCl_2$ (Merck, Germany) and 0.5% (v/v) amylase enzymes (Hench Biotechnology, China) were added. The solution was stirred at 87°C for 90 minutes. After the stirring was complete, the inactivation process began by adding HCl until the pH reached to 4. The solution was then cooled to ~~a temperature of~~ 60°C and neutralized using 0.1 M NaOH until the pH reached to ~~pH~~ 6. The solution was then placed into an oven at 50°C ~~in a tin~~ in a thin layer. After drying, the powder was ~~removed,~~ mashed with a blender, and sieved through a 100-mesh sieve.. The MDX-sorghum characterization was then performed [2,5].

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4.2. MDX-Sorghum Characterizsation

4.2.1. Yield value

The resulting MDX-sorghum was weighed entirely, and the yield value was calculated using the following ~~E~~equation ([27,28]) ~~[23,24]~~:

$$Yield\ (\%) = \frac{MDX - sorghum\ weight\ obtained}{weight\ of\ sorghum\ starch\ used}\ x\ 100$$

4.2.2. Dextrose Equivalent (DE) Value

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In order to calculate the DE value, firstly, the Fehling Factor value was calculated.~~The DE value started by finding the Fehling factor value by dissolving~~ 2.5 g of glucose was dissolved in~~with~~ distilled and the volume was made up~~water up to~~ 1,000 mL with distilled water.~~,~~ T~~t~~hen ~~removing~~ 15 mL of the solution was removed and add~~ed~~ing 5 mL each of Fehling's solutions A and B. The mixture was boiled. ~~and~~ While boiling, it was titrated ~~in a boiling state~~ with glucose solution until it turned~~became~~ reddish-brown. The amount of titrant required was recorded, and the Fehling ~~f~~Factor was calculated using the following ~~E~~equation ([5,28]): ~~[5,24]~~:

$$FF = \frac{titrant\ volume\ mL\ x\ glucose\ weight\ (g)}{1{,}000}$$

The DE value was then calculated by preparing ~~a~~ 10 g/200 mL solution of MDX-sorghum and ~~inserting~~ taking it into the burette. Then, 5 mL each of Fehling's solutions A and B, as well as 15 mL of glucose solution, were added to 50 mL of distilled water. The solution was heated and titrated with ~~a~~the solution of MDX-sorghum until a reddish brown colour was obtained. The required titrant ~~is~~was then recorded, and the DE value ~~is~~was calculated using the following ~~E~~equation ([5,28]) ~~[5,24]~~:

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$$DE = FF\ x\ \frac{100}{starch\ concentration\ \left(\frac{g}{mL}\right) x\ titrant\ volume\ (mL)}$$

4.2.3. Solubility

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A total of 0.5 g of the sample was weighted (b) then dissolved in 10 mL of distilled water and ~~before being~~ vortexed for 30 seconds. The solution was then centrifuged for 15 minutes at 3000 rpm. ~~In addition~~After that, 5 mL of the ~~solution~~ supernatant was separated and dried~~evaporated~~ in an oven at 105 °C~~. until~~ for 5 hours. The product was~~is~~ then weighed and the result was~~is~~ recorded as weight (a). The solubility (%) of the sample was~~is~~ then calculated using the following ~~E~~equation ([27,29]) ~~[23,25]~~:

$$Solubility\ (\%) = \frac{a}{b}\ x\ 2\ x\ 100$$

4.2.4. Swelling Power

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A total of 0.1 g of MDX-sorghum (b) was mixed with 10 mL of distilled water and heated at 60°C with steady stirring for 30 minutes in a water bath. The samples were centrifuged at 1,600 rpm for 15 minutes. The precipitate was weighted (a) and the swelling strength was calculated using the following ~~utilizing~~ ~~E~~equation ~~(~~[27]~~)~~ ~~[23,25]~~:

$$Swelling\ Power = \frac{a}{b}$$

4.2.5. Infra-Red Fourier Transform (FTIR) Analysis

MDX-sorghum was milled~~ground~~ and 2 g of the sample was weighed. The sample was added to 200 g of KBr and mixed until homogeneous. It was then placed into a pellet mold and analyzed for the MDX-sorghum functional group using FTIR (Agilent cary 630). The sample was scanned 64 times at resolution 2 cm^{-1} above the ~~wave number region~~spectral range of 4,000–400 cm^{-1} ~~(~~[30,31]~~)~~. ~~[26,27].~~

4.3. Production of ODF Cetirizine HCl

The CCD method in RSM was used to optimize the MDX-sorghum and glycerol concentrations. Because of the lack of fit tests, the CCD technique required five to six repetitions of the center point to estimate the pure error. Hence, Table 2 offers six formulas with the same concentrations of MDX-sorghum and glycerol. ODF was produced using the solvent casting method ~~(see Table 6 for composition)~~. First, citric acid (4 g) and sucrose (4 g) were dissolved using distilled water ~~to become~~ (mass A). MDX-sorghum was then added~~dispersed~~ in hot water and was stirred until it dispersed~~expanded, forming~~ (mass B). In hot water, 4 g of Hydroxypropyl Methyl Cellulose (HPMC) (Luxchem, Indonesia) was mixed and dispersed ~~and mixed~~ (mass C). Mass C was mixed with mass B and glycerol until it was homogeneous. Then, mass A and cetirizine HCl (Kimia Farma, Indonesia) were added and mixed until it was homogeneous. The ~~remaining~~ distilled water was added until the volume of the mixture reached to 100 mL and it was agitated until homogeneous. The mixture was poured and placed on the mold, before ~~being~~ heat~~ed~~ing ~~for 24 hours~~ at 50°C for 24 hours. The ~~created~~ obtained film ~~is~~was then removed from the mold and sliced to a 2 × 2 cm^2 size [3].

4.4. Evaluation of ODF Preparation and Cetirizine HCl

4.4.1. Tensile Strength and Elongation Test

Tensile strength and elongation ~~percentage~~ tests were performed using the universal testing machine located at the Centre for Advanced Materials Science and Technology (Pusat Sains dan Teknologi Bahan Maju-PSTBM), Batan, Serpong, South Tangerang.

4.4.2. Disintegration Time Test

A film was placed in a petri dish containing 2 mL of distilled water. The time required for the film to completely disintegrate ~~is~~was recorded as the disintegration time ~~(~~[32]~~)~~ ~~[28]~~.

4.5. Data Analysis

Response data in the form of tensile strength ~~test results~~, elongation~~,~~ and disintegration times were entered into the CCD-RSM (Design Expert 7.1.5, trial version) response column and were analyzed to obtain the optimal concentration of MDX-sorghum and glycerol for producing ODF preparations that best met the requirements. The level and limits of the response variables in data analysis using CCD are within range, where the requirements for a good ODF include tensile strength values between 1.02-10.2 MPa [15], elongation percentage more than 70 % [16] , and disintegration time less than 3 minutes. The optimum MDX-sorghum and glycerol concentration was determined from the formula with the highest desirability value. ~~(~~[16,18]~~)~~ ~~[17]~~.

4.6. Production and Evaluation of the Optimal ODF Formulation

The optimal formulation obtained from CCD-RSM analysis was produced and evaluated. The results of the tensile strength, ~~percentage~~ elongation~~,~~ and disintegration time tests were then compared with the predicted RSM data.

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Conflict of interest statement: The authors declare that this article has no actual, potential~~,~~ or perceived conflict of interest.

REFERENCES

[1. Zhu F. Structure, physicochemical properties, modifications, and uses of sorghum starch. Compr Rev Food Sci Food Saf. 2014;13(4):597–610. [Crossref]

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2. Haryani K, Retnowati DS, Handayani NA, Dewi WM, Pamularsih SA. Modifikasi Pati Sorgum menjadi Maltodekstrin secara Enzimatik Dengan Menggunakan Enzim Alfa Amilase dan Gluko Amilase. J Teknol Pangan. 2022;6(1):8–12. [Crossref]

3. Putri DA, Setiawan A, Anggraini PD. Physical properties of edible sorgum starch film added with carboxymethyl cellulose. J Phys Sci. 2018;29:185–94. [Crossref]

4. Borges AF, Silva C, Coelho JFJ, Simões S. Oral films: Current status and future perspectives. J Control Release [Internet]. 2015 May;206(March):1–19. [Crossref] ~~Available from: http://dx.doi.org/10.1016/j.jconrel.2015.03.006~~

5. GI P, MK B, VN E, DM S, AO O. Effect of pH and temperature on the activities of alpha-amylase in cassava starch liquefaction. African J Food Sci Technol ~~[Internet]~~. 2018;09(02):37–42. [Crossref] ~~Available from: https://www.interesjournals.org/articles/effect-of-ph-and-temperature-on-the-activities-of-alphaamylase-in-cassava-starch-liquefaction.pdf~~

6. Shah KA, Gao B, Kamal R, Razzaq A, Qi S, Zhu Q-N, et al. Development and Characterizations of Pullulan and Maltodextrin-Based Oral Fast-Dissolving Films Employing a Box–Behnken Experimental Design. Materials (Basel) ~~[Internet]~~. 2022 May 18;15(10):3591. [Crossref]~~Available from: https://www.mdpi.com/1996-1944/15/10/3591~~

7. Caicedo C, Díaz-Cruz CA, Jiménez-Regalado EJ, Aguirre-Loredo RY. Effect of Plasticizer Content on Mechanical and Water Vapor Permeability of Maize Starch/PVOH/Chitosan Composite Films. Materials (Basel). 2022;15(4):1274. [Crossref]

8. Rowe RC, Sheskey PJ, Quinn ME, editors. Handbook of Pharmaceutical Excipient. Sixth Edit. Pharmaceutical Press and the American Pharmacists Association; 2009.

9. Fahrullah F, Radiati LE, Purwadi P, Rosyidi D. The Effect of Different Plasticizers on the Characteristics of Whey Composite Edible Film. J Ilmu dan Teknol Has Ternak ~~[Internet]~~. 2020 Mar 1;15(1):31–7. [Crossref]~~Available from: https://jitek.ub.ac.id/index.php/jitek/article/view/388~~

10. Walfathiyyah A, Kusuma AP, Cahya FN, Qusyairi N, Wahyuningtyas D. Optimization of Plasticizer Glycerol in Edible Film Based Water Hyacinth (Eichornia crossipes) Starch. 5th ICRIEMS Proceedings. 2018. [Google Scholar]

11. Ahmad A, Lajis MA, Yusuf NK, Ab Rahim SN. Statistical optimization by the response surface methodology of direct recycled aluminum-alumina metal matrix composite (MMC-AlR) employing the metal forming process. Processes. 2020;8(7):805. [Crossref]

12. Almajed A, Srirama D, Moghal AAB. Response Surface Method Analysis of Chemically Stabilized Fiber-Reinforced Soil. Materials (Basel) ~~[Internet]~~. 2021 Mar 21;14(6):1535. [Crossref]~~Available from: https://www.mdpi.com/1996-1944/14/6/1535~~

13. Bhattacharya S. Central Composite Design for Response Surface Methodology and Its Application in Pharmacy. In: Kayaroganam P, editor. Response Surface Methodology in Engineering Science. IntechOpen; 2021. [Google Scholar]

14. Bhattarai M, Gupta AK. Fast Dissolving Oral Films: A Novel Trend to Oral Drug Delivery. Sunsari Tech Coll J. 2015;2(1):58–68. [Crossref]

15. Sharma D, Kaur D, Verma S, Singh D, Singh M, Singh G. Fast Dissolving Oral Films Technology : A Recent Trend For An Innovative Oral Drug Delivery SystemI International J. Int J Drug Deliv. 2015;7(2):60–75. [Google Scholar]

16. Siemons I, Politiek RGA, Boom RM, van der Sman RGM, Schutyser MAI. Dextrose equivalence of maltodextrins determines particle morphology development during single sessile droplet drying. Food Res Int ~~[Internet]~~. 2020;131:108988. [Crossref]~~Available from: https://doi.org/10.1016/j.foodres.2020.108988~~

17. Pathan RR, Siddiqul A. Preparation, Optimization, and Evaluation of Pellets Containing Mesalamine With Natural Gums For Colon Drug Delivery System. Fabad J Pharm Sci ~~[Internet]~~. 2022 Mar 1;47(1):35–56. [Crossref]~~Available from: https://dergipark.org.tr/en/doi/10.55262/fabadeczacilik.1078778~~

18. Sari DI, Fitriana Mi, Mulyadi RR, Hidayati L. Karakterisasi dan Uji Stabilitas Fisik Sediaan Edible Film Ekstrak Etanol Kulit Batang Kasturi (Mangifera casturi Kosterm) Berbasis Gelatin. Pros Semin Kefarmasian dan Present Ilm. 2017;8–17. [Google Scholar]

19. Sulastri E, Yuyun Y, Heriani N, Khumaidi A. Application of chitosan shells meti (batissa violacea L. Von Lamarck, 1818) as edible film. Curr Res Nutr Food Sci. 2019;7(1):253–64. [Crossref]

20. Panraksa P, Tipduangta P, Jantanasakulwong K, Jantrawut P. Formulation of Orally Disintegrating Films as an Amorphous Solid Solution of a Poorly Water-Soluble Drug. Membranes (Basel) ~~[Internet]~~. 2020 Nov 27;10(12):376. [Crossref]~~Available from: https://www.mdpi.com/2077-0375/10/12/376~~

21. Nurmiah S, Syarief R, Sukarno S, Peranginangin R, Nurmata B. Aplikasi Response Surface Methodology Pada Optimalisasi Kondisi Proses Pengolahan Alkali Treated Cottonii (ATC). J Pascapanen dan Bioteknol Kelautan dan Perikanan. 2013;8(1):9–22. [Crossref]

22. Wongphan P, Harnkarnsujarit N. Characterization of starch, agar and maltodextrin blends for controlled dissolution of edible films. Int J Biol Macromol [Internet]. 2020;156:80–93. [Crossref] ~~Available from: https://doi.org/10.1016/j.ijbiomac.2020.04.056~~

23. Afifah et al. "Pengaruh Kombinasi Plasticizer terhadap Karakteristik Edible Film dari Karagenan dan Lilin Lebah." Biopropal Ind. 2018;9(No 1):49–60. [Google Scholar]

24. Mahmood SZ, Sabry HS, Yousif NZ, Salman ZD. Optimization and Evaluation of Chlorpheniramine Maleate Oral Strip for Pediatric Use. Asian J Pharm Clin Res ~~[Internet]~~. 2018 Dec 7;11(12):548. [Crossref] ~~Available from: https://innovareacademics.in/journals/index.php/ajpcr/article/view/28985~~

25. Shah U, Naqash F, Gani A, Masoodi FA. Art and Science behind Modified Starch Edible Films and Coatings: A Review. Compr Rev Food Sci Food Saf. 2016;15(3):568–80. [Crossref]

26. Sri SJ, Krishna KSM, Kusuma D, Shankar CU. Formulation and in-Vitro Evaluation of Benazepril Mouth Dissolving Films. Indo Am J Pharm Sci. 2018;5(1):552–60. [Crossref]

27. Shrestha B, Dhungana PK, Dhital S, Adhikari B. Evaluation of Modified Sorghum Starches and Biodegradable Films. J Food Sci Technol Nepal ~~[Internet]~~. 2018 Jun 30;10:11–7. [Crossref]Available from: ~~https://www.nepjol.info/index.php/JFSTN/article/view/14800~~

28. Zusfahair Z, Riana Ningsih D. Pembuatan dekstrin dari pati ubi kayu menggunakan katalis amilase hasil fraksinasi dari Azospirillum sp. JG3. Molekul ~~[Internet]~~. 2012 May 1;7(1):9–19. [Crossref]~~Available from: http://ojs.jmolekul.com/ojs/index.php/jm/article/view/102~~

29. Kusumayanti H, Handayani NA, Santosa H. Swelling Power and Water Solubility of Cassava and Sweet Potatoes Flour. Procedia Environ Sci ~~[Internet]~~. 2015;23(Ictcred 2014):164–7. [Crossref]~~Available from: http://dx.doi.org/10.1016/j.proenv.2015.01.025~~

30. Torrenegra M, Solano R, Herrera A, León G, Pajaro A. Fourier Transform Infrared Spectroscopy (FTIR) Analysis of Biodegradable Films Based On Modified Colombian Starches of Cassava and Yam. Int J PharmTech Res.

2018;11(4):368–76. [Crossref]

31. Topal GR, Kiymaci ME, Özkan Y. Preparation and in Vitro Characterization of Vancomycin Loaded Plga Nanoparticles for the Treatment of Enterococcus Faecalis Infections. Ankara Univ Eczac Fak Derg ~~[Internet]~~. 2022 Mar 25;46(2):350–63. [Crossref]~~Available from: https://dergipark.org.tr/en/doi/10.33483/jfpau.1073081~~

32. Irfan M, Rabel S, Bukhtar Q, Qadir MI, Jabeen F, Khan A. Orally disintegrating films: A modern expansion in drug delivery system. Saudia Pharm J ~~[Internet]~~. 2016;24(5):537–46. [Crossref]~~Available from: http://dx.doi.org/10.1016/j.jsps.2015.02.024~~

~~1. Zhu F. Structure, physicochemical properties, modifications, and uses of sorghum starch. Compr Rev Food Sci Food Saf. 2014;13(4):597–610.~~

~~2. Haryani K, Retnowati DS, Handayani NA, Dewi WM, Pamularsih SA. Modifikasi Pati Sorgum menjadi Maltodekstrin secara Enzimatik Dengan Menggunakan Enzim Alfa Amilase dan Gluko Amilase. J Teknol Pangan. 2022;6(1):8–12.~~

~~3. Putri DA, Setiawan A, Anggraini PD. Physical properties of edible sorgum starch film added with carboxymethyl cellulose. J Phys Sci. 2018;29:185–94.~~

~~4. Borges AF, Silva C, Coelho JFJ, Simões S. Oral films: Current status and future perspectives. J Control Release [Internet]. 2015 May;206(March):1–19. Available from: http://dx.doi.org/10.1016/j.jconrel.2015.03.006~~

~~5. GI P, MK B, VN E, DM S, AO O. Effect of pH and temperature on the activities of alpha-amylase in cassava starch liquefaction. African J Food Sci Technol [Internet]. 2018;09(02):37–42. Available from: https://www.interesjournals.org/articles/effect-of-ph-and-temperature-on-the-activities-of-alphaamylase-in-cassava-starch-liquefaction.pdf~~

~~6. Shah KA, Gao B, Kamal R, Razzaq A, Qi S, Zhu Q-N, et al. Development and Characterizations of Pullulan and Maltodextrin-Based Oral Fast-Dissolving Films Employing a Box–Behnken Experimental Design. Materials (Basel) [Internet]. 2022 May 18;15(10):3591. Available from: https://www.mdpi.com/1996-1944/15/10/3591~~

~~7. Caicedo C, Díaz-Cruz CA, Jiménez-Regalado EJ, Aguirre-Loredo RY. Effect of Plasticizer Content on Mechanical and Water Vapor Permeability of Maize Starch/PVOH/Chitosan Composite Films. Materials (Basel). 2022;15(4).~~

~~8. Rowe RC, Sheskey PJ, Quinn ME, editors. Handbook of Pharmaceutical Excipient. Sixth Edit. Pharmaceutical Press and the American Pharmacists Association; 2009.~~

~~9. Fahrullah F, Radiati LE, Purwadi P, Rosyidi D. The Effect of Different Plasticizers on the Characteristics of Whey Composite Edible Film. J Ilmu dan Teknol Has Ternak [Internet]. 2020 Mar 1;15(1):31–7. Available from: https://jitek.ub.ac.id/index.php/jitek/article/view/388~~

~~10. Walfathiyyah A, Kusuma AP, Cahya FN, Qusyairi N, Wahyuningtyas D. Optimization of Plasticizer Glycerol in Edible Film Based Water Hyacinth (Eichornia crossipes) Starch. 5th ICRIEMS Proc. 2018;1–10.~~

~~11. Ahmad A, Lajis MA, Yusuf NK, Ab Rahim SN. Statistical optimization by the response surface methodology of direct recycled aluminum-alumina metal matrix composite (MMC-AlR) employing the metal forming process. Processes. 2020;8(7).~~

~~12. Almajed A, Srirama D, Moghal AAB. Response Surface Method Analysis of Chemically Stabilized Fiber-Reinforced Soil. Materials (Basel) [Internet]. 2021 Mar 21;14(6):1535. Available from: https://www.mdpi.com/1996-1944/14/6/1535~~

~~13. Bhattacharya S. Central Composite Design for Response Surface Methodology and Its Application in Pharmacy. In: Kayaroganam P, editor. Response Surface Methodology in Engineering Science. IntechOpen; 2021.~~

~~14. Bhattarai M, Gupta AK. Review Article FAST DISSOLVING ORAL FILMS : A NOVEL TREND TO ORAL DRUG DELIVERY. Sunsari Tech Coll J. 2015;2(1):58–68.~~

~~15. Sharma D, Kaur D, Verma S, Singh D, Singh M, Singh G. Fast Dissolving Oral Films Technology : A Recent~~

~~Trend For An Innovative Oral Drug Delivery Systeml International J. Int J Drug Deliv. 2015;7(2):60–75.~~

16. ~~Siemons I, Politiek RGA, Boom RM, van der Sman RGM, Schutyser MAI. Dextrose equivalence of maltodextrins determines particle morphology development during single sessile droplet drying. Food Res Int [Internet]. 2020;131(January):108988. Available from: https://doi.org/10.1016/j.foodres.2020.108988~~

17. ~~Pathan RR, Siddiqui A. Preparation, Optimization, and Evaluation of Pellets Containing Mesalamine With Natural Gums For Colon Drug Delivery System. Fabad J Pharm Sci [Internet]. 2022 Mar 1;47(1):35–56. Available from: https://dergipark.org.tr/en/doi/10.55262/fabadeczacilik.1078778~~

18. ~~Sari DI, Fitriana Mi, Mulyadi RR, Hidayati L. Karakterisasi dan Uji Stabilitas Fisik Sediaan Edible Film Ekstrak Etanol Kulit Batang Kasturi (Mangifera casturi Kosterm) Berbasis Gelatin. Pros Semin Kefarmasian dan Present Ilm. 2017;8–17.~~

19. ~~Sulastri E, Yuyun Y, Heriani N, Khumaidi A. Application of chitosan shells meti (batissa violacea L. Von Lamarck, 1818) as edible film. Curr Res Nutr Food Sci. 2019;7(1):253–64.~~

20. ~~Panraksa P, Tipduangta P, Jantanasakulwong K, Jantrawut P. Formulation of Orally Disintegrating Films as an Amorphous Solid Solution of a Poorly Water-Soluble Drug. Membranes (Basel) [Internet]. 2020 Nov 27;10(12):376. Available from: https://www.mdpi.com/2077-0375/10/12/376~~

21. ~~Nurmiah S, Syarief R, Sukarno S, Peranginangin R, Nurmata B. Aplikasi Response Surface Methodology Pada Optimalisasi Kondisi Proses Pengolahan Alkali Treated Cottonii (ATC). J Pascapanen dan Bioteknol Kelaut dan Perikan. 2013;8(1):9.~~

22. ~~Wongphan P, Harnkarnsujarit N. Characterization of starch, agar and maltodextrin blends for controlled dissolution of edible films. Int J Biol Macromol [Internet]. 2020;156:80–93. Available from: https://doi.org/10.1016/j.ijbiomac.2020.04.056~~

23. ~~Afifah et al. "Pengaruh Kombinasi Plasticizer terhadap Karakteristik Edible Film dari Karagenan dan Lilin Lebah." Biopropal Ind. 2018;9(No 1):49–60.~~

24. ~~Mahmood SZ, Sabry HS, Yousif NZ, Salman ZD. Optimization and Evaluation of Chlorpheniramine Maleate Oral Strip for Pediatric Use. Asian J Pharm Clin Res [Internet]. 2018 Dec 7;11(12):548. Available from: https://innovareacademics.in/journals/index.php/ajpcr/article/view/28985~~

25. ~~Sri SJ, Krishna KSM, Kusuma D, Shankar CU. Formulation and in-Vitro Evaluation of Benazepril Mouth Dissolving Films. Indo Am J Pharm Sci. 2018;5(1):552–60.~~

26. ~~Shah U, Naqash F, Gani A, Masoodi FA. Art and Science behind Modified Starch Edible Films and Coatings: A Review. Compr Rev Food Sci Food Saf. 2016;15(3):568–80.~~

27. ~~Shrestha B, Dhungana PK, Dhital S, Adhikari B. Evaluation of Modified Sorghum Starches and Biodegradable Films. J Food Sci Technol Nepal [Internet]. 2018 Jun 30;10:11–7. Available from: https://www.nepjol.info/index.php/JFSTN/article/view/14800~~

28. ~~Zusfahair Z, Riana Ningsih D. Pembuatan dekstrin dari pati ubi kayu menggunakan katalis amilase hasil fraksinasi dari Azospirillum sp. JG3. Molekul [Internet]. 2012 May 1;7(1):9. Available from: http://ojs.jmolekul.com/ojs/index.php/jm/article/view/102~~

29. ~~Kusumayanti H, Handayani NA, Santosa H. Swelling Power and Water Solubility of Cassava and Sweet Potatoes Flour. Procedia Environ Sci [Internet]. 2015;23(Ictcred 2014):164–7. Available from: http://dx.doi.org/10.1016/j.proenv.2015.01.025~~

30. ~~Torrenegra M, Solano R, Herrera A, León G, Pajaro A. Fourier Transform Infrared Spectroscopy (FTIR) Analysis of Biodegradable Films Based On Modified Colombian Starches of Cassava and Yam. Int J PharmTech Res. 2018;11(4):368–76.~~

31. ~~Topal GR, Kiymaci ME, Özkan Y. Preparation and in Vitro Characterization of Vancomycin Loaded Plga Nanoparticles for the Treatment of Enterococcus Faecalis Infections. Ankara Univ Eczac Fak Derg [Internet].~~

~~2022 Mar 25;46(2):350–63. Available from: https://dergipark.org.tr/en/doi/10.33483/jfpau.1073081~~

~~32. Irfan M, Rabel S, Bukhtar Q, Qadir MI, Jabeen F, Khan A. Orally disintegrating films: A modern expansion in drug delivery system. Saudi Pharm J [Internet]. 2016;24(5):537–46. Available from: http://dx.doi.org/10.1016/j.jsps.2015.02.024~~

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Commented [G$24]: DOI numbers were not input as a hyperlinks.

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Table 1. Characteristics of sorghum starch and modified sorghum starch

No	Inspection	Sorghum Starch	MDX-Sorghum
1	Organoleptic:		
	Form	Powder	Powder
	Texture	Fine/smooth	Fine/smooth
	Aroma	Typical Sorghum	Brown sugar
	Flavour	Slightly Sweet	Slightly Sweet
	Colour	Light brown	Dark brown
2	Dextrose Equivalent	0.84	6.22
3	Swelling Power	2.44	2.87
4	Solubility	12.52%	52.9%
5	Yield Value	~~72.58%~~	86.71%

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Table 2. Evaluation of ODF Preparations

Run	A: MDX-Sorghum Concentration (%)	B: Glycerol Concentration (%)	Y_1: Tensile Strength (MPa)	Y_2: Elongation (%)	Y_3: Disintegration Time (sec)
	Factor		Response		
1.	4.00	6.50	1.98	86.26	152
2.	4.00	3.00	2.47	66.74	181
3.	4.00	10.00	1.52	101.68	75
4.	4.00	6.50	1.92	89.44	155
5.	5.41	8.97	1.32	103.96	85
6.	4.00	6.50	1.67	91.94	160
7.	2.59	8.97	1.48	97.72	112
8.	4.00	6.50	1.95	86.58	158
9.	6.00	6.50	1.61	99.16	90
10.	4.00	6.50	1.98	93.18	150
11.	4.00	6.50	1.91	84.84	159
12.	2.59	4.03	1.87	61.41	191
13.	2.00	6.50	2.05	72.41	176
14.	5.41	4.03	1.58	78.56	166

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Commented [GŞ25]: What is the difference between the yellow highlighted formulations?

Commented [AA26R25]: is included in the methodology (4.3)

Table 3. Analysis of ODF Cetirizin HCl Tensile Strength, ~~Percent~~ Elongation, and Disintegration Time Using CCD

Factors		Y_1 Tensile Strength (MPa)	Y_2 Elongation (%)	Y_3 Disintegration Time (sec)
A (MDX-Sorghum Concentration (%))	Coefficient	-0.13	7.67	-21.75
	ρ-value	0.1031	0.0002**	0.0003**
B (Glycerol Concentration (%))	Coefficient	-0.25	13.90	-38.78
	ρ-value	0.0070**	0.0001**	0.0001**
A B	Coefficient	-	-	-0.50
	ρ-value	-	-	0.9238
A^2	Coefficient	-	-	-9.37
	ρ-value	-	-	0.0364*
B^2	Coefficient	-	-	-11.87
	ρ-value	-	-	0.0130*
Analytical model		Liniear	Liniear	Quadratic
Intercept		1.81	86.71	155.68
Degree of freedom		2	2	5
Sum of squares		0.64	2012.01	17342.43
Mean of squares		0.32	1006.00	3468.49
F-value		7.04	62.85	33.80
ρ-value		0.0108	0.0001	0.0001
R-Squared		0.5613	0.9195	0.9548

* ρ-value < 0.05
** ρ-value < 0.01

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Table 4. Results of Optimal Oral Dissolving Film (ODF) Formulation on Response

No	Polymer (%)	Plasticizer (%)	Tensile Strength (MPa)	Elongation (%)	Disintegration Time (sec)	Desirability
1.	3.56	10.00	1.495	104.0	83	0.807
2.	3.55	10.00	1.497	103.9	83	0.806
3.	3.53	10.00	1.499	103.8	83	0.804

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Table 5. Optimal ODF Evaluation Results

No	Response	RSM Prediction	Observation Results	Percentage Error (%)
1	Tensile Strength (MPa)	1.495	1.50	0.33
2	Elongation (%)	104	104.26	0.25
3	Disintegration Time (second)	83	82.95	0.06

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Table 6. ODF cetirizine HCl composition based on CCD

Run	Batch	Composition						
		Cetirizine HCl (mg)	MDX-Sorghum* (%)	Glycerol* (%)	Sucrose (%)	Citric Acid (%)	HPMC (%)	Distilled Water~~Aquadest~~ ad (mL)
1.	F1	1,500	4.00	6.50	4	4	4	100
2.	F2	1,500	4.00	3.00	4	4	4	100
3.	F3	1,500	4.00	10.00	4	4	4	100
4.	F4	1,500	4.00	6.50	4	4	4	100
5.	F5	1,500	5.41	8.97	4	4	4	100
6.	F6	1,500	4.00	6.50	4	4	4	100
7.	F7	1,500	2.59	8.97	4	4	4	100
8.	F8	1,500	4.00	6.50	4	4	4	100
9.	F9	1,500	6.00	6.50	4	4	4	100
10.	F10	1,500	4.00	6.50	4	4	4	100
11.	F11	1,500	4.00	6.50	4	4	4	100
12.	F12	1,500	2.59	4.03	4	4	4	100
13.	F13	1,500	2.00	6.50	4	4	4	100
14.	F14	1,500	5.41	4.03	4	4	4	100

*CCD-RSM Concentration Design Results

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Commented [GŞ27]: Have the batches F1, F4, F6, F8, F10 and F11 the same composition?

Commented [AA28R27]: The formula is the same, and point 4.3 of the methodology additionally includes an explanation.

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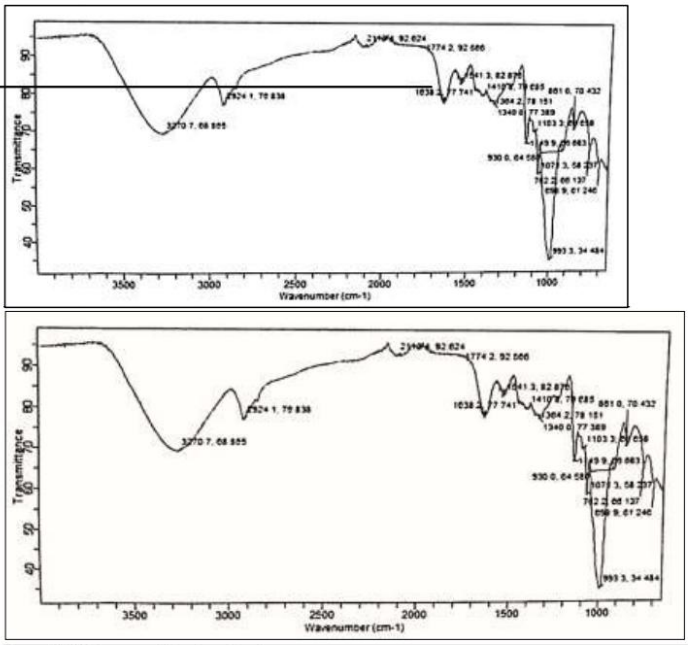

Figure 1. FTIR Spectrum of Sorghum Starch

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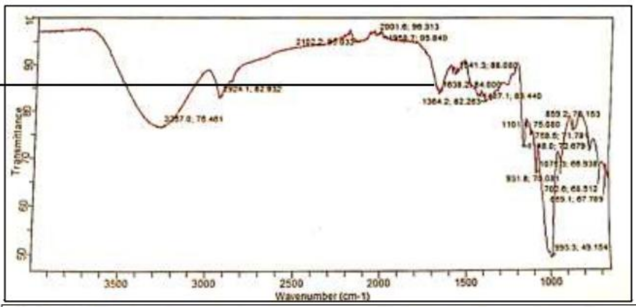

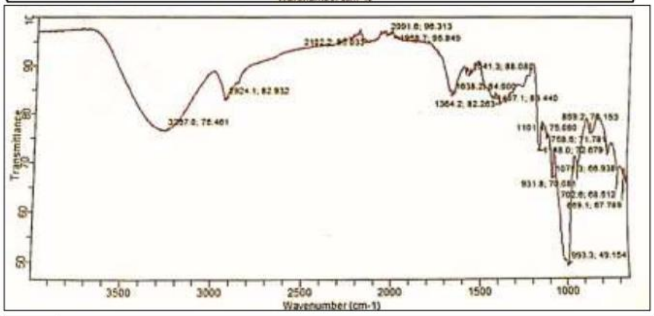

Figure 2. FTIR Spectrum of MDX-Sorghum

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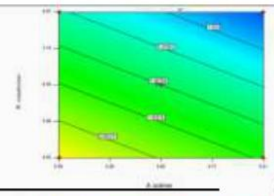
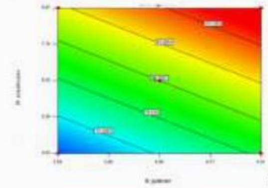
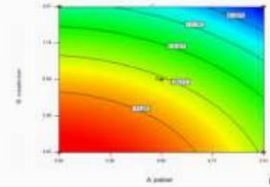

(a)


(b)


(c)

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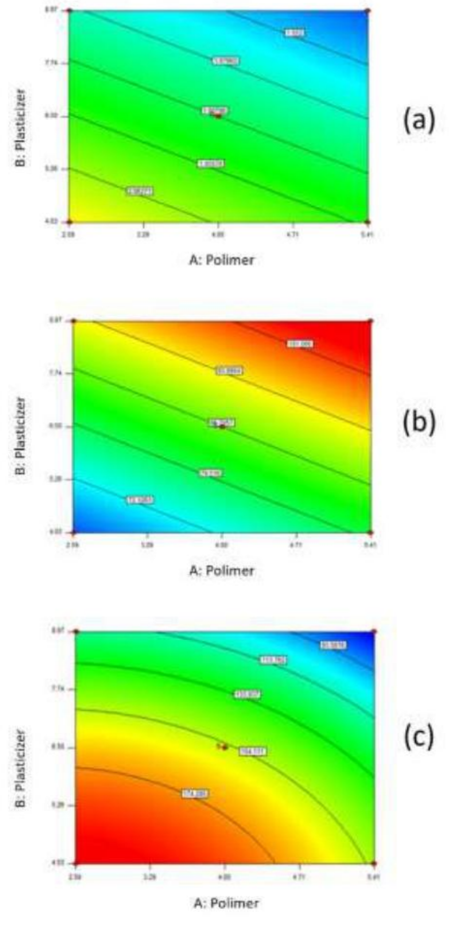

Figure 3. Graph showing the effect of film-forming polymer (MDX-Sorghum) concentration and plasticizer (glycerol) concentration on tensile strength value (a), ~~percentage of~~ elongation (b), and disintegration time (c)

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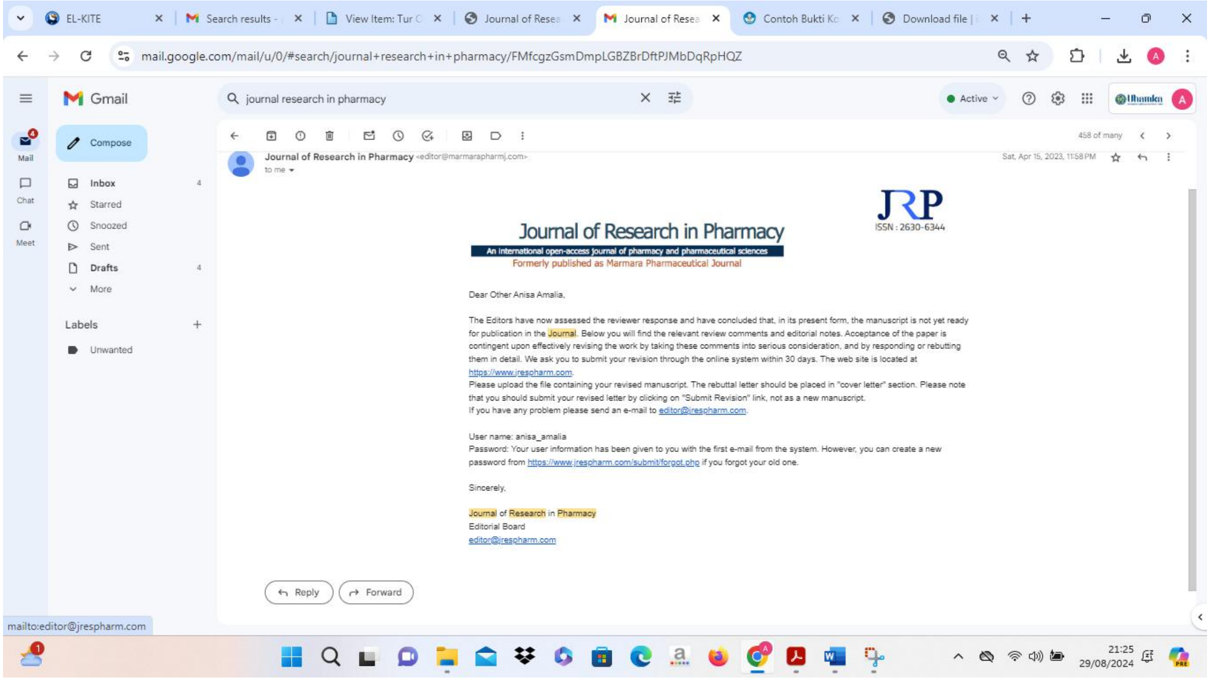
4. Bukti Konfirmasi Review dan Hasil Review Kedua (15 April 2023)

Second revision: Minor revision (15 April 2023)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The Editors have now assessed the reviewer response and have concluded that, in its present form, the manuscript is not yet ready for publication in the Journal. Below you will find the relevant review comments and editorial notes. Acceptance of the paper is contingent upon effectively revising the work by taking these comments into serious consideration, and by responding or rebutting them in detail. We ask you to submit your revision through the online system within 30 days. The web site is located at https://www.jrespharm.com.
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Suggestions

1.Reviewer Comments
Thank you for your all corrections. I have just fixed a few punctuation marks.
I think it is appropriate to publish it as it is. Please find the attached file.

2.Reviewer Comments
The revised manuscript is much better than the original one. One typo I can see after the revision is some decimal points written with a comma (,) instead of a period (.) in the conclusion section. I have no further queries or comments for the authors. I believe the manuscript is now suitable for publication after the correction stated above.

Reviewer 1

Comment File	Show Comment File (https://www.jrespharm.com/submit/uploads/rev_com/MPJ-12582-15608-rev-file-12582-mpj-12582-8-rev-01-second-revision.docx)

Manuscript Information

Manuscript ID:	**MPJ-10715.REV-1**
Title in English:	Characterization of modified sorghum starch and ıts use as a film-forming polymer in orally dissolving film formulation with glycerol as a plasticizer
Small Title in English:	No information entered
Authors:	Anisa Amalia[1], Nining Nining[1], Muhammad Dandi[2]
Institutions:	[1]Faculty of Pharmacy and Science, Universitas Muhammadiyah Prof. DR. HAMKA, Department of Pharmaceutics, East Jakarta/DKI Jakarta, Indonesia [2]Faculty of Pharmacy and Science, Universitas Muhammadiyah Prof. DR. HAMKA, Department of Pharmacy, East Jakarta/DKI Jakarta, Indonesia
Keywords in English:	Sorghum strach ; modified ; film-forming ; glycerol ; response surface methodology
Manuscript Type:	Research article
Processing Status:	Minor Revision

Manuscript Files

File Name	File Size	Date Created	Category	Description
MPJ-10715-2-cover-letter-jrp.pdf (../pdf-files/out/12582-MPJ-10715-2-cover-letter-jrp.pdf)	14 KB	Sep 14, 2022	Cover letter	None

MPJ-10715-3-modified-sorghum-starch-jrp-template.pdf (../pdf-files/out/12582-MPJ-10715-3-modified-sorghum-starch-jrp-template.pdf)	1305 KB	Sep 14, 2022	Main Document	None
MPJ-10715-1-jrp-checklist.pdf (../pdf-files/in/12582-MPJ-10715-1-jrp-checklist.pdf)	241 KB	Sep 14, 2022	Author Checklist Form	None
MPJ-10715-1-jrp-copyright-form-integrated.pdf (../pdf-files/out/12582-MPJ-10715-1-jrp-copyright-form-integrated.pdf)	85 KB	Sep 14, 2022	Copyright Transfer Form	None
MPJ-10715-6-figure-1.jpg (../pdf-files/in/12582-MPJ-10715-6-figure-1.jpg)	98 KB	Sep 14, 2022	Figure	None
MPJ-10715-9-figure-2.jpg (../pdf-files/in/12582-MPJ-10715-9-figure-2.jpg)	89 KB	Sep 14, 2022	Figure	None
MPJ-10715-9-figure-3.jpg (../pdf-files/in/12582-MPJ-10715-9-figure-3.jpg)	103 KB	Sep 14, 2022	Figure	None
MPJ-12582-8-rev-01-mpj-10715-14923-rev-file-10715-mpj-10715-3-modified-sorghum-starch-jrp-template.rev-1.pdf (../pdf-files/out/12582-MPJ-12582-8-rev-01-mpj-10715-14923-rev-file-10715-mpj-10715-3-modified-sorghum-starch-jrp-template.rev-1.pdf)	1859 KB	Mar 19, 2023	Main Document	None
MPJ-12582-5-response-to-reviewers.rev-1.pdf (../pdf-files/out/12582-MPJ-12582-5-response-to-reviewers.rev-1.pdf)	34 KB	Mar 19, 2023	Response to Reviewers	None
MPJ-12582-7-a.-figure-1-600-dpi-.rev-1.jpg (../pdf-files/in/12582-MPJ-12582-7-a.-figure-1-600-dpi-.rev-1.jpg)	3624 KB	Mar 19, 2023	Figure	None
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Are the keywords sufficient and appropriate ?	Yes
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Is the language adequate?	Yes
Are the nomenclature and scientific terminology correct?	Yes
Are the references complete and recent?	Yes
Are the figures tables and graphics necessary ?	Yes
Are the figures tables and graphics clear ?	Yes
Is the introduction part	sufficiently developed
Are the experimental procedures sound?	Yes
Is the results and discussion part	sufficiently developed
Is conclusion sufficient and correlated with the results ?	Yes
Is the information about the approval of ETHICAL COMMISSION presented ?	Not applicable

2. Reviewer

Does the content and value of the work justify publication in Marmara Pharmaceutical Journal ?	Yes
Does the title of the manuscript reflect the contents of the study ?	Yes
Are the keywords sufficient and appropriate ?	Yes
Is the summary concise and informative?	Yes
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Is the results and discussion part	sufficiently developed
Is conclusion sufficient and correlated with the results ?	Yes
Is the information about the approval of ETHICAL COMMISSION presented ?	Not applicable

5. Respon kepada Reviewer dan Artikel yang Diresubmit (28 April 2023)

RESPONSE TO REVIEWERS

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MANUSCRIPT ID: MPJ-10715

Reviewer: 1

Comments to the Author

Thank you for your all corrections. I have just fixed a few punctuation marks.

I think it is appropriate to publish it as it is. Please find the attached file.

Response:

Thanks for the guidance and suggestions. We rewrote the paragraph because we were unable to include citations in its sentences.

Reviewer: 2

The revised manuscript is much better than the original one. One typo I can see after the revision is some decimal points written with a comma (,) instead of a period (.) in the conclusion section. I have no further queries or comments for the authors. I believe the manuscript is now suitable for publication after the correction stated above.

Response:

Thanks for the guidance and suggestions. We have fixed the typing mistake

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Characterization of modified sorghum starch and ~~I~~its use as a film-forming polymer~~agent~~ in orally dissolving film formulations with glycerol as a plasticizer

Anisa AMALIA[1*], Nining NINING[1], Muhammad DANDI[2]

[1] Department of Pharmaceutics, Faculty of Pharmacy and Science, Universitas Muhammadiyah Prof. DR. HAMKA, Jakarta, Indonesia.

[2] Department of Pharmacy, Faculty of Pharmacy and Science, Universitas Muhammadiyah Prof. DR. HAMKA, Jakarta, Indonesia

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ABSTRACT: Film-forming polymers and plasticizers are ~~the~~ components of ~~O~~orally dissolving film (ODF) compositions that have the ~~most~~greatest influence on the physical properties of the film preparations. Modification of sorghum starch produces maltodextrin (MDX)-sorghum~~,~~ which can be used as a film-forming polymer, and glycerol can be used as a plasticizer in ODF preparations. This study aims to determine the optimal concentrations of MDX-sorghum and glycerol ~~for~~to produce~~ing~~ ODF compositions using the central composite design (CCD) in response surface methodology (RSM). Hydrolysis of sorghum starch yielded MDX-sorghum, characterized by yield value, dextrose equivalent (DE) value, solubility, swelling power~~,~~ and FTIR analysis. The CCD ~~design~~ included a concentration range of 2-6% and 3-10% ~~concentration range~~ for MDX-sorghum and glycerol, respectively, as parameters in the optimization process. So that 14 experimental designs were obtained. The test response was evaluated using tensile strength, elongation~~,~~ and disintegration time tests~~, so 14 experimental designs were obtained~~. The modification of sorghum starch yields a light brown MDX-sorghum powder with desirable properties. Optimization of MDX-sorghum and glycerol concentrations yielded an optimal formulation with a tensile value of 1.50~~81~~ MPa with an error percentage of 0.33%, ~~an~~ elongation of 10~~4~~.26% with an error percentage of 0.25~~33~~%, and ~~a~~ disintegration time of 82.95 seconds with an error percentage of 0.06%. By modifying sorghum starch into MDX-sorghum, the starch's ability to dissolve and swell can be improved, allowing it to be used as a film-forming polymer.~~By modifying sorghum starch to make MDX-sorghum, the starch's properties can be enhanced and used as a film-forming~~ The optimal MDX-~~s~~Sorghum and glycerol concentrations for the production of ODF are ~~3.56~~3.56 % and 10.00~~10~~ %, respectively.

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KEYWORDS: Sorghum strach, modified, film-forming, glycerol, response surface methodology.

1. INTRODUCTION

Sorghum starch is a film-forming polymer with hydrophilic properties used in the manufactur~~ing~~e of orally dissolving film (ODF) preparations ~~(~~[1]~~)~~ ~~[1]~~. Sorghum starch is a natural biopolymer that is easily accessible and contains 72–75% carbohydrates, 20–30% amylose, and 70–80% amylopectin, which can be used as film-forming components [2,3]. However, natural sorghum starch has several disadvantages:~~there are several drawbacks to natural sorghum starch:~~ it is sticky, hard, brittle, not transparent, and not resistant to acid treatment. In a study by Putri et al. [~~(~~3]~~)~~, using only~~single~~ sorghum starch resulted in a less elastic film preparation. This problem can be overcome by modifying sorghum starch through a partial hydrolysis process so that its characteristics resemble those of maltodextrin (MDX) ~~(~~[4]~~)~~. MDX is obtained from starch that has been enzymatically modified by partial hydrolysis. As a result, MDX has a dextrose equivalent (DE) value of less than 20. Moreover, MDX has good film-forming~~, solubility~~ and adhesi~~ve~~on properties as well as good solubility~~characteristics~~, allowing it to produce elastic films [5,6].

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The film-forming polymer influence~~d~~s the film preparation's elasticity; plasticizers can also increase film's elasticity [7]. Glycerol is one of the plasticizers that can be used in the manufacture of ODF preparations. Glycerol is a plasticizer that is easily soluble in water (hydrophilic), has a low molecular weight and thus helps to reduce ~~to help bring down the~~ intermolecular tensions along the polymer chain, and provides~~has~~ the

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advantages of increasing the viscosity of the solution, reducing brittleness, and increasing the strength of ODF preparations [8]. Glycerol, as a plasticizer, produced edible films with improved characteristics compared with sorbitol and polyethylene glycol [9]. A ~~R~~research conducted by Walfathiyyah et al. (2017) showed that adding of glycerol resulted in a more elastic edible film [10]. The optimal concentrations of glycerol and MDX-sorghum can be analyzed using the response surface methodology (RSM).

RSM can be used to design several formulations with varying concentrations of MDX-sorghum and glycerol. The RSM can reduce the number of materials used because it does not require a trial formulation stage, which would require considerable research [11]. Furthermore, this method can describe the interaction among variables toward the response [11,12]. Several models can be used in RSM. The experimental design in this study used the central composite design (CCD) model. CCD is a fractional factorial design often used in RSM as it can speed up several experimental designs [13]. The concentration of MDX-sorghum, which functions as a film-forming agent, and glycerol, which functions as a plasticizer, were the independent factors, while the dependent variables (response) were ~~the value of~~ tensile strength, ~~percentage~~ elongation, and disintegration time. MDX-sorghum and glycerol as components in the manufacture of films are expected to produce films with characteristics that meet the requirements so that they can be used as alternative pharmaceutical preparations containing ~~for the~~ cetirizine HCl. Cetirizine HCl is available in tablet dosage forms. However, the disadvantage of tablet preparations is that pediatric and geriatric patients and patients with throat disorders have difficulty swallowing tablets, resulting in decreased patient compliance. Therefore, alternative preparations are required to make it easier for these patients to consume cetirizine, such as oral dissolving film (ODF) preparations that dissolve rapidly in the mouth ([14,15]). Hence, it is necessary to optimize the concentrations of MDX-sorghum and glycerol to produce ODF preparation with optimal physical properties. The research findings can serve as a reference for developing natural excipients.

~~Therefore, it is necessary to optimize the concentrations of MDX-sorghum and glycerol to obtain an ODF preparations with the best physical properties so that it can be used as a reference in the development of natural excipients in the pharmaceutical field.~~

2. RESULTS AND DISCUSSION

2.1. Characteristics of MDX-Sorghum

The characteristics of sorghum starch and MDX-sorghum are shown in Table 1. Based on the results, the DE value of MDX-sorghum met the requirements (i.e., < 20). Low DE maltodextrin (< 20) had better elasticity and viscosity than high DE maltodextrin ([16]). In each sugar chain undergoing hydrolysis, there was one reducing sugar group; as the number of simple sugar groups increased, the number of reducing sugar groups and the value of DE also increased. In solubility and swelling power studies, MDX-sorghum demonstrated more solubility and swelling ability than sorghum starch. This was due to the hydrolysis reaction performed by the amylase enzyme on sorghum starch by breaking the glycosidic bond in starch molecules into simple sugars, such as glucose and dextrin, so that the two~~hree~~ parameters increased [5,6].

Sorghum starch and modified sorghum starch were analyzed by evaluating the spectrum's shape, namely the specific peaks indicating the type of functional group in~~by~~ a starch compound. The FTIR analysis results ~~using FTIR~~ are shown in Figure 1 and 2. The O–H group's peak is between 3,400 and 2,100 cm^{-1}. At approximately 3,270.7 cm^{-1}, the yield of sorghum starch groups was measured, whereas the O-H functional group was identified at the peak of modified sorghum starch at 3,287.0 cm^{-1}. The C-H functional group was discovered at the peak of 2,924.1 cm^{-1} within the range of 3,850.0–2,924.1 cm^{-1}, with no variation in peak positions between samples. With a wavelength of 1,149.9 cm^{-1} and a peak transition of 1,148.0 cm^{-1}, the C-O-C functional group was found in sorghum starch, showing a change in the modified starch. This test is intended to identify transfer results between functional groups in two spectra, allowing for the observation of transmission differences between O-H and C-O-C functional groups. The amylase enzyme breaks the -1,4 glycosidic link in the polysaccharide chain for starch to be turned into MDX ([17]). ~~The peak for the O-H group was in the range of 3,400–2,400 cm⁻¹. The results of the sorghum starch group were around 3,270.7 cm⁻¹, while the O-H functional group was obtained at a modified sorghum starch peak of 3,287.0 cm⁻¹, and the C-H functional group was obtained at the peak of 2,924.1 cm⁻¹ in the range of 3,850.0–2,850.0 cm⁻¹, indicating no change in peak between the two samples. However, the C-O-C functional group obtained 1,149.9 cm⁻¹ of sorghum starch and a peak shift of 1,148.0 cm⁻¹, which indicated a change in the modified starch. This treatment aimed to determine the results of the transfer between the functional groups on the two spectra,~~

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~~whereby the difference between the transmittance in the O-H and C-O-H functional groups could be observed. This was due to the breakdown of -1,4 glycosidic bonds by the amylase enzyme on the inside of the polysaccharide chain so that the starch could be modified into MDX [14].~~

2.2. Evaluation of ODF Preparations

Table 2 ~~2~~ presents the results of the evaluation of ODF preparations. Based on the evaluation, all ODF formulations meet the requirements of a 'good' film. The film preparation was considered good if it had a tensile strength value of 1.02 – 10.20 Mpa ~~pa~~ ([18]) ~~[15]~~, elongation > 70% ([19]) ~~[16]~~, and disintegration time < 3 minutes ([20]) ~~[17]~~.

2.3. Data Analysis Using RSM

The combination of MDX-Sorghum as a film-forming agent and glycerol as a plasticizer affects the tensile strength, elongation, and disintegration time, as illustrated in Figure 3. The color on the graph represents the tensile strength (a), elongation ~~percentage~~ (b), and disintegration time (c). The color positioned bottom has the lowest response value, while the above color has the highest response value. The number of color changes along the curve indicates the influence of the concentrations film-forming agent (A) and plasticizer (B) ~~ing concentrations~~. The combination of factors (A and B) affects the response related to the number of colors on the curve [14,18]. According to the observed results, the disintegration time is the response most affected by the concentration of the factors ~~concentration.~~

2.3.1. Tensile Strength

The results of the tensile strength data analysis indicated that the factors influenced the tensile strength. In the 14 formulations, tensile strength results ranged from of 1.32 to 2.47 MPa. The results met the requirements for good tensile strength, namely 1.02–10.20 MPa ([9,18]) ~~[9]~~. Based on the analysis results (Table 3), the suggested analytical model was a linear model based on the sum of the squares of the tensile strength response model sequence. The linear model with an R-squared value of 0.56 showed that the polymer concentration and the plasticizer concentration influenced the ~~diversity of~~ tensile strength responses. The adjusted R-squared value of 0.56 ~~13~~ served as a generalization of the population's R-Squared due to the existence of the population estimation element ([21]). ~~[11]~~. The model equation for the tensile strength response was Y_1 = +1.81 -0.13*A -0.25*B based on the results in Table 3.

The equation shows that the coefficients of the polymer ~~value~~ concentration (A) ~~was -0.13~~ and the plasticizer concentration ~~value~~ (B) ~~was~~ were -0.13 and -0.25, respectively. It indicates ~~ing~~ that a decrease in polymer and/or plasticizer concentration results in an increase in tensile strength response (Y_1) ~~an increase in the tensile strength response (Y_1) that was influenced by a decrease in the polymer concentration and a decrease in plasticizer concentration~~. The tensile strength decreases as the polymer and/or plasticizer content increases. This is because MDX-sorghum has a low molecular weight, making the polymer network less intense and decreasing the film's mechanical properties ([22]). ~~The higher the concentrations of polymer and/or plasticizer, the lower the tensile strength. This is because, t~~The plasticizer can reduce the strong intermolecular attraction in the polysaccharide chain of MDX-sorghum and promote hydrogen formation between the plasticizer and polysaccharide molecule, thereby weakening the hydrogen bonds in the polymer and decreasing the tensile strength of the film ([23]). ~~[19]~~.

2.3.2. Elongation

Elongation ~~percent~~ data indicated the influence of factors on the elongation results. In the 14 formulations, the elongation results were between 61.41–103.96%. Consequently, a linear model based on the sum of squares ~~of the order~~ of the elongation response was suggested based on the analysis results (Table 3). In addition, the findings of the lack-of-fit test indicated that a linear model should be applied to the elongation response in order to produce the correct model. This linear model fitted the elongation response with a ~~P~~ p value (~~P~~prob>F) of 0.2747, indicating its validity ([11,13]). Y_2 = +86.71 +7.67*A +13.90*B was the model equation for the elongation response depending on the data in Table 3.

Based on the equation, coefficients of the the polymer ~~value~~ concentration (A) ~~was +7.67,~~ and the plasticizer ~~value~~ concentration (B) ~~was~~were +7.67 and +13.90, respectively. It indicates ~~ing~~ that an increase in polymer and/or plasticizer concentration results in an increase in tensile strength response (Y_1) ~~an increase in elongation response (Y_2) influenced by an increase in polymer concentration and plasticizer concentration.~~ The higher the concentration of polymer and/or plasticizer, the more likely the elongation is to increase. This

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occurs because the glycerol molecules in the polymer matrix disrupt the polymer structure through hydrogen bonds and transform it into an irregular flexible structure, a process that can be considered as restructuring (rearrangement) of the polymer matrix, with increased resistance ~~(resistance)~~ towards received pressures which in turn increase the stretchability (elongation) of the film ~~(~~[23]~~)~~. This is also because maltodextrin can not create a strong network with other polymers that make ODF ~~(~~[22]~~)~~. ~~[19].~~

2.3.4. Disintegration Time

Based on results of the disintegration time test, the film could disintegrate within 75–191 seconds. According to the results of the study described in Table 3, the suggested analytical model was a quadratic model based on the sum of the squares of the sequence of the disintegration time response models. The findings of the analysis of variance using the suggested quadratic model confirmed this. Furthermore, the p value (prob>F) of 0.0001 was smaller than 0.05, indicating a significant model to determine the interaction of responses to variables in the disintegration time response ~~(~~[11,13]~~)~~. Based on Table 3, the model equations for the disintegration time response were: $Y_3 = +155.68-21.75*A-38.78*B-0.50*A*B-9.37*A^2-11.87*B^2$.
~~According to the results of the study described in Table 3, the suggested analytical model was a quadratic model based on the sum of the squares of the sequence of the disintegration time response models. The findings of the analysis of variance using the suggested~~ quadratic ~~model, a quadratic model, confirmed this. Furthermore, the Pp value (prob>F) of 0.0001 was smaller than 0.05, indicating a significant model to determine the interaction of responses to variables in the disintegration time response. Based on Table 3, the model equations for the disintegration time response were: $Y_3 = +155.68-21.75*A-38.78*B-0.50*A*B-9.37*A^2-11.87*B^2$.~~

Based on the equation, the polymer ~~value~~ concentration (A) ~~was -21.75~~, and the plasticizer ~~value~~ concentration (B) ~~was~~were -21.75 and -38.78, respectively. It indicat~~ing~~es that a decrease in polymer and/or plasticizer concentration results an increase in the disintegration time response (Y3) ~~that was influenced by a decrease in polymer concentration and a decrease in plasticizer concentration~~. The higher the concentrations of polymer and/or plasticizer, the faster the disintegration ~~time~~. This occurs due to the increase in polymer concentration. ~~The shorter disintegration time is caused by~~ MDX, which has a high solubility in water~~,~~ ~~which~~and aids water penetration into the film structure, provides a shorter disintegration time ~~(~~[24,25]~~)~~ ~~[24]~~. Therefore, when the concentrations of polymer and plasticizer are high, the disintegration time is ~~low~~short. This result is in line with a study by Sri et al. (2018), which found that increasing the amount of MDX ~~would make~~ made the film disintegrate more rapidly ~~(~~[26]~~)~~ ~~[21]~~. The plasticizer can increase the intermolecular gap of the film, and the enhanced intermolecular gap can allow water to migrate and accelerate the film's disintegration [9].

2.4. ODF Preparation Optimal Formulation

Based on our experiments, the recommended model to observe the effect of the use of MDX-sorghum and glycerol on the tensile strength and elongation responses was a linear model. In contrast, the suggested model for the disintegration time response was a quadratic model. The optimal ODF formulation was verified by reproducing the formulation by the RSM recommendations, and testing was performed for tensile strength, elongation, and disintegration time. From the results listed in Table 4, the recommended optimal concentrations of MDX-sorghum and glycerol were 3.56% and 10%, respectively, with a predicted tensile strength value of 1.495 MPa, percent elongation of 104%, and disintegration time of 83 seconds. The prediction results were validated by producing an ODF with the optimal formulation, which was then evaluated.

The validation of the RSM prediction results is presented in Table 5. The results indicated no significant difference (percentage error < 0,05%) between the results obtained and the RSM predictions. Therefore, the ODF preparation met the requirements for good film-forming characteristics. The literature shows that using polymers and plasticizers affects the characteristics of ODF. A high plasticizer concentration would result in low tensile strength, short disintegration time, and a high elongation value ~~(~~[25]~~)~~ ~~[22]~~.

3. CONCLUSION

The modified sorghum starch resulted in MDX-sorghum with enhanced solubility and swelling power. At a concentration of 2-6%, MDX-sorghum can be used as a film-forming polymer with the required tensile strength, elongation (%), and disintegration time. Based on the CCD analysis, the optimal concentrations of MDX-sorghum and glycerol were 3.56~~4.00~~% and 10.00~~6.50~~% respectively, with a tensile strength response of 1.50~~81~~ MPa, 104.26~~86.71~~% elongation, and a disintegration time~~period~~ of 82.95~~156~~ seconds. On the foundation

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of the obtained data, it can be stated that sorghum starch modification can increase the use of sorghum~~'s use~~ as a pharmaceutical excipient.

4. MATERIALS AND METHODS

4.1. MDX-Sorghum Production

In the production of MDX-sorghum, the sorghum was modified by dissolving sorghum starch (Timurasa, Indonesia) using distilled water ~~aquadest~~ to a concentration of 24% (w/v)~~, with t~~The pH of the solution was adjusted to 6 using HCl (Merck, Germany) and NaOH (Merck, Germany) ~~to pH 6~~. Then, 100 ppm anhydrous $CaCl_2$ (Merck, Germany) and 0.5% (v/v) amylase enzymes (Hench Biotechnology, China) were added. The solution was stirred at 87°C for 90 minutes. After the stirring was complete, the inactivation process began by adding HCl until the pH reached to 4. The solution was then cooled to ~~a temperature of~~ 60°C and neutralized using 0.1 M NaOH until the pH reached to ~~pH~~ 6. The solution was then placed into an oven at 50°C ~~in a tin~~ in a thin layer. After drying, the powder was ~~removed,~~ mashed with a blender, and sieved through a 100-mesh sieve~~.~~. The MDX-sorghum characterization was then performed [2,5].

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4.2. MDX-Sorghum Characteriz~~s~~ation

4.2.1. Yield value

The resulting MDX-sorghum was weighed entirely, and the yield value was calculated using the following ~~E~~equation ([27,28]) ~~[23,24]~~:

$$Yield\ (\%) = \frac{MDX - sorghum\ weight\ obtained}{weight\ of\ sorghum\ starch\ used}\ x\ 100$$

4.2.2. Dextrose Equivalent (DE) Value

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In order to calculate the DE value, firstly, the Fehling Factor value was calculated.~~The DE value started by finding the Fehling factor value by dissolving~~ 2.5 g of glucose was dissolved in~~with~~ distilled water and the volume was made up~~water up to~~ 1,000 mL with distilled water.~~,~~ T~~t~~hen ~~removing~~ 15 mL of the solution was removed and added~~ing~~ 5 mL each of Fehling's solutions A and B. The mixture was boiled. ~~and~~ While boiling, it was titrated ~~in a boiling state~~ with glucose solution until it turned~~became~~ reddish-brown. The amount of titrant required was recorded, and the Fehling ~~f~~Factor was calculated using the following ~~E~~equation ([5,28]): ~~[5,24]:~~

$$FF = \frac{titrant\ volume\ mL\ x\ glucose\ weight\ (g)}{1,000}$$

The DE value was then calculated by preparing ~~a~~ 10 g/200 mL solution of MDX-sorghum and ~~inserting~~ taking it into the burette. Then, 5 mL each of Fehling's solutions A and B, as well as 15 mL of glucose solution, were added to 50 mL of distilled water. The solution was heated and titrated with ~~a~~the solution of MDX-sorghum until a reddish brown colour was obtained. The required titrant ~~is~~was then recorded, and the DE value ~~is~~was calculated using the following ~~E~~equation ([5,28]) ~~[5,24]~~:

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$$DE = FF\ x\ \frac{100}{starch\ concentration\ \left(\frac{g}{mL}\right) x\ titrant\ volume\ (mL)}$$

4.2.3. Solubility

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A total of 0.5 g of the sample was weighted (b) then dissolved in 10 mL of distilled water and ~~before being~~ vortexed for 30 seconds. The solution was then centrifuged for 15 minutes at 3000 rpm. ~~In addition~~After that, 5 mL of the ~~solution~~ supernatant was separated and dried~~evaporated~~ in an oven at 105 °C~~.~~ ~~until~~ for 5 hours. The product was~~is~~ then weighed and the result was~~is~~ recorded as weight (a). The solubility (%) of the sample was~~is~~ then calculated using the following ~~E~~equation ([27,29]) ~~[23,25]~~:

$$Solubility\ (\%) = \frac{a}{b}\ x\ 2\ x\ 100$$

4.2.4. Swelling Power

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A total of 0.1 g of MDX-sorghum (b) was mixed with 10 mL of distilled water and heated at 60°C with steady stirring for 30 minutes in a water bath. The samples were centrifuged at 1,600 rpm for 15 minutes. The precipitate was weighted (a) and the swelling strength was calculated using the following ~~utilizing~~ ~~E~~equation ~~(~~[27]~~)~~ ~~[23,25]~~:

$$Swelling\ Power = \frac{a}{b}$$

4.2.5. Infra-Red Fourier Transform (FTIR) Analysis

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MDX-sorghum was milled~~ground~~ and 2 g of the sample was weighed. The sample was added to 200 g of KBr and mixed until homogeneous. It was then placed into a pellet mold and analyzed for the MDX-sorghum functional group using FTIR (Agilent cary 630). The sample was scanned 64 times at resolution 2 cm^{-1} above the ~~wave number region~~spectral range of 4,000–400 cm^{-1} ~~(~~[30,31]~~)~~.

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~~[26,27].~~

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4.3. Production of ODF Cetirizine HCl

The CCD method in RSM was used to optimize the MDX-sorghum and glycerol concentrations. Because of the lack of fit tests, the CCD technique required five to six repetitions of the center point to estimate the pure error. Hence, Table 2 offers six formulas with the same concentrations of MDX-sorghum and glycerol. ODF was produced using the solvent casting method ~~(see Table 6 for composition)~~. First, citric acid (4 g) and sucrose (4 g) were dissolved using distilled water ~~to become~~ (mass A). MDX-sorghum was then added~~dispersed~~ in hot water and was stirred until it dispersed~~expanded, forming~~ (mass B). In hot water, 4 g of Hydroxypropyl Methyl Cellulose (HPMC) (Luxchem, Indonesia) was mixed and dispersed ~~and mixed~~ (mass C). Mass C was mixed with mass B and glycerol until it was homogeneous. Then, mass A and cetirizine HCl (Kimia Farma, Indonesia) were added and mixed until it was homogeneous. The ~~remaining~~ distilled water was added until the volume of the mixture reached to 100 mL and it was agitated until homogeneous. The mixture was poured and placed on the mold, before ~~being~~ heat~~ing~~ed ~~for 24 hours~~ at 50°C for 24 hours. The ~~created~~ -obtained film ~~is~~was then removed from the mold and sliced to a -2 × 2 cm^2 size [3].

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4.4. Evaluation of ODF Preparation and Cetirizine HCl

4.4.1. Tensile Strength and Elongation Test

Tensile strength and elongation ~~percentage~~ tests were performed using the universal testing machine located at the Centre for Advanced Materials Science and Technology (Pusat Sains dan Teknologi Bahan Maju-PSTBM), Batan, Serpong, South Tangerang.

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4.4.2. Disintegration Time Test

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A film was placed in a petri dish containing 2 mL of distilled water. The time required for the film to completely disintegrate ~~is~~was recorded as the disintegration time ~~(~~[32]~~)~~ ~~[28]~~.

4.5. Data Analysis

Response data in the form of tensile strength ~~test results~~, elongation~~,~~ and disintegration times were entered into the CCD-RSM (Design Expert 7.1.5, trial version) response column and were analyzed to obtain the optimal concentration of MDX-sorghum and glycerol for producing ODF preparations that best met the requirements. The level and limits of the response variables in data analysis using CCD are within range, where the requirements for a good ODF include tensile strength values between 1.02-10.2 MPa [15], elongation percentage more than 70 % [16] , and disintegration time less than 3 minutes. The optimum MDX-sorghum and glycerol concentration was determined from the formula with the highest desirability value. ~~(~~[16,18]~~)~~ ~~[17]~~.

4.6. Production and Evaluation of the Optimal ODF Formulation

The optimal formulation obtained from CCD-RSM analysis was produced and evaluated. The results of the tensile strength, ~~percentage~~ elongation, and disintegration time tests were then compared with the predicted RSM data.

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Conflict of interest statement: The authors declare that this article has no actual, potential, or perceived conflict of interest.

REFERENCES

[1. Zhu F. Structure, physicochemical properties, modifications, and uses of sorghum starch. Compr Rev Food Sci Food Saf. 2014;13(4):597–610. [Crossref]

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2. Haryani K, Retnowati DS, Handayani NA, Dewi WM, Pamularsih SA. Modifikasi Pati Sorgum menjadi Maltodekstrin secara Enzimatik Dengan Menggunakan Enzim Alfa Amilase dan Gluko Amilase. J Teknol Pangan. 2022;6(1):8–12. [Crossref]

3. Putri DA, Setiawan A, Anggraini PD. Physical properties of edible sorgum starch film added with carboxymethyl cellulose. J Phys Sci. 2018;29:185–94. [Crossref]

4. Borges AF, Silva C, Coelho JFJ, Simões S. Oral films: Current status and future perspectives. J Control Release [Internet]. 2015 May;206(March):1–19. [Crossref] ~~Available from: http://dx.doi.org/10.1016/j.jconrel.2015.03.006~~

5. GI P, MK B, VN E, DM S, AO O. Effect of pH and temperature on the activities of alpha-amylase in cassava starch liquefaction. African J Food Sci Technol ~~[Internet]~~. 2018;09(02):37–42. [Crossref] ~~Available from: https://www.interesjournals.org/articles/effect-of-ph-and-temperature-on-the-activities-of-alphaamylase-in-cassava-starch-liquefaction.pdf~~

6. Shah KA, Gao B, Kamal R, Razzaq A, Qi S, Zhu Q-N, et al. Development and Characterizations of Pullulan and Maltodextrin-Based Oral Fast-Dissolving Films Employing a Box–Behnken Experimental Design. Materials (Basel) ~~[Internet]~~. 2022 May 18;15(10):3591. [Crossref]~~Available from: https://www.mdpi.com/1996-1944/15/10/3591~~

7. Caicedo C, Díaz-Cruz CA, Jiménez-Regalado EJ, Aguirre-Loredo RY. Effect of Plasticizer Content on Mechanical and Water Vapor Permeability of Maize Starch/PVOH/Chitosan Composite Films. Materials (Basel). 2022;15(4):1274. [Crossref]

8. Rowe RC, Sheskey PJ, Quinn ME, editors. Handbook of Pharmaceutical Excipient. Sixth Edit. Pharmaceutical Press and the American Pharmacists Association; 2009.

9. Fahrullah F, Radiati LE, Purwadi P, Rosyidi D. The Effect of Different Plasticizers on the Characteristics of Whey Composite Edible Film. J Ilmu dan Teknol Has Ternak ~~[Internet]~~. 2020 Mar 1;15(1):31–7. [Crossref]~~Available from: https://jitek.ub.ac.id/index.php/jitek/article/view/388~~

10. Walfathiyyah A, Kusuma AP, Cahya FN, Qusyairi N, Wahyuningtyas D. Optimization of Plasticizer Glycerol in Edible Film Based Water Hyacinth (Eichornia crossipes) Starch. 5th ICRIEMS Proceedings. 2018. [Google Scholar]

11. Ahmad A, Lajis MA, Yusuf NK, Ab Rahim SN. Statistical optimization by the response surface methodology of direct recycled aluminum-alumina metal matrix composite (MMC-AlR) employing the metal forming process. Processes. 2020;8(7):805. [Crossref]

12. Almajed A, Srirama D, Moghal AAB. Response Surface Method Analysis of Chemically Stabilized Fiber-Reinforced Soil. Materials (Basel) ~~[Internet]~~. 2021 Mar 21;14(6):1535. [Crossref]~~Available from:~~

~~https://www.mdpi.com/1996-1944/14/6/1535~~

13. Bhattacharya S. Central Composite Design for Response Surface Methodology and Its Application in Pharmacy. In: Kayaroganam P, editor. Response Surface Methodology in Engineering Science. IntechOpen; 2021. [Google Scholar]

14. Bhattarai M, Gupta AK. Fast Dissolving Oral Films: A Novel Trend to Oral Drug Delivery. Sunsari Tech Coll J. 2015;2(1):58–68. [Crossref]

15. Sharma D, Kaur D, Verma S, Singh D, Singh M, Singh G. Fast Dissolving Oral Films Technology : A Recent Trend For An Innovative Oral Drug Delivery SystemI International J. Int J Drug Deliv. 2015;7(2):60–75. [Google Scholar]

16. Siemons I, Politiek RGA, Boom RM, van der Sman RGM, Schutyser MAI. Dextrose equivalence of maltodextrins determines particle morphology development during single sessile droplet drying. Food Res Int ~~[Internet]~~. 2020;131:108988. [Crossref]~~Available from: https://doi.org/10.1016/j.foodres.2020.108988~~

17. Pathan RR, Siddiqul A. Preparation, Optimization, and Evaluation of Pellets Containing Mesalamine With Natural Gums For Colon Drug Delivery System. Fabad J Pharm Sci ~~[Internet]~~. 2022 Mar 1;47(1):35–56. [Crossref]~~Available from: https://dergipark.org.tr/en/doi/10.55262/fabadeczacilik.1078778~~

18. Sari DI, Fitriana Mi, Mulyadi RR, Hidayati L. Karakterisasi dan Uji Stabilitas Fisik Sediaan Edible Film Ekstrak Etanol Kulit Batang Kasturi (Mangifera casturi Kosterm) Berbasis Gelatin. Pros Semin Kefarmasian dan Present Ilm. 2017;8–17. [Google Scholar]

19. Sulastri E, Yuyun Y, Heriani N, Khumaidi A. Application of chitosan shells meti (batissa violacea L. Von Lamarck, 1818) as edible film. Curr Res Nutr Food Sci. 2019;7(1):253–64. [Crossref]

20. Panraksa P, Tipduangta P, Jantanasakulwong K, Jantrawut P. Formulation of Orally Disintegrating Films as an Amorphous Solid Solution of a Poorly Water-Soluble Drug. Membranes (Basel) ~~[Internet]~~. 2020 Nov 27;10(12):376. [Crossref]~~Available from: https://www.mdpi.com/2077-0375/10/12/376~~

21. Nurmiah S, Syarief R, Sukarno S, Peranginangin R, Nurmata B. Aplikasi Response Surface Methodology Pada Optimalisasi Kondisi Proses Pengolahan Alkali Treated Cottonii (ATC). J Pascapanen dan Bioteknol Kelautan dan Perikanan. 2013;8(1):9–22. [Crossref]

22. Wongphan P, Harnkarnsujarit N. Characterization of starch, agar and maltodextrin blends for controlled dissolution of edible films. Int J Biol Macromol [Internet]. 2020;156:80–93. [Crossref] ~~Available from: https://doi.org/10.1016/j.ijbiomac.2020.04.056~~

23. Afifah et al. "Pengaruh Kombinasi Plasticizer terhadap Karakteristik Edible Film dari Karagenan dan Lilin Lebah." Biopropal Ind. 2018;9(No 1):49–60. [Google Scholar]

24. Mahmood SZ, Sabry HS, Yousif NZ, Salman ZD. Optimization and Evaluation of Chlorpheniramine Maleate Oral Strip for Pediatric Use. Asian J Pharm Clin Res ~~[Internet]~~. 2018 Dec 7;11(12):548. [Crossref] ~~Available from: https://innovareacademics.in/journals/index.php/ajpcr/article/view/28985~~

25. Shah U, Naqash F, Gani A, Masoodi FA. Art and Science behind Modified Starch Edible Films and Coatings: A Review. Compr Rev Food Sci Food Saf. 2016;15(3):568–80. [Crossref]

26. Sri SJ, Krishna KSM, Kusuma D, Shankar CU. Formulation and in-Vitro Evaluation of Benazepril Mouth Dissolving Films. Indo Am J Pharm Sci. 2018;5(1):552–60. [Crossref]

27. Shrestha B, Dhungana PK, Dhital S, Adhikari B. Evaluation of Modified Sorghum Starches and Biodegradable Films. J Food Sci Technol Nepal ~~[Internet]~~. 2018 Jun 30;10:11–7. [Crossref]Available from: ~~https://www.nepjol.info/index.php/JFSTN/article/view/14800~~

28. Zusfahair Z, Riana Ningsih D. Pembuatan dekstrin dari pati ubi kayu menggunakan katalis amilase hasil fraksinasi dari Azospirillum sp. JG3. Molekul ~~[Internet]~~. 2012 May 1;7(1):9–19. [Crossref]~~Available from: http://ojs.jmolekul.com/ojs/index.php/jm/article/view/102~~

29. Kusumayanti H, Handayani NA, Santosa H. Swelling Power and Water Solubility of Cassava and Sweet Potatoes Flour. Procedia Environ Sci ~~[Internet]~~. 2015;23(Ictcred 2014):164–7. [Crossref]~~Available from: http://dx.doi.org/10.1016/j.proenv.2015.01.025~~

30. Torrenegra M, Solano R, Herrera A, León G, Pajaro A. Fourier Transform Infrared Spectroscopy (FTIR) Analysis of Biodegradable Films Based On Modified Colombian Starches of Cassava and Yam. Int J PharmTech Res. 2018;11(4):368–76. [Crossref]

31. Topal GR, Kiymaci ME, Özkan Y. Preparation and in Vitro Characterization of Vancomycin Loaded Plga Nanoparticles for the Treatment of Enterococcus Faecalis Infections. Ankara Univ Eczac Fak Derg ~~[Internet]~~. 2022 Mar 25;46(2):350–63. [Crossref]~~Available from: https://dergipark.org.tr/en/doi/10.33483/jfpau.1073081~~

32. Irfan M, Rabel S, Bukhtar Q, Qadir MI, Jabeen F, Khan A. Orally disintegrating films: A modern expansion in drug delivery system. Saudia Pharm J ~~[Internet]~~. 2016;24(5):537–46. [Crossref]~~Available from: http://dx.doi.org/10.1016/j.jsps.2015.02.024~~

~~1. Zhu F. Structure, physicochemical properties, modifications, and uses of sorghum starch. Compr Rev Food Sci Food Saf. 2014;13(4):597–610.~~

~~2. Haryani K, Retnowati DS, Handayani NA, Dewi WM, Pamularsih SA. Modifikasi Pati Sorgum menjadi Maltodekstrin secara Enzimatik Dengan Menggunakan Enzim Alfa Amilase dan Gluko Amilase. J Teknol Pangan. 2022;6(1):8–12.~~

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~~12. Almajed A, Srirama D, Moghal AAB. Response Surface Method Analysis of Chemically Stabilized Fiber-Reinforced Soil. Materials (Basel) [Internet]. 2021 Mar 21;14(6):1535. Available from: https://www.mdpi.com/1996-1944/14/6/1535~~

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Table 1. Characteristics of sorghum starch and modified sorghum starch

No	Inspection	Sorghum Starch	MDX-Sorghum
1	Organoleptic:		
	Form	Powder	Powder
	Texture	Fine/smooth	Fine/smooth
	Aroma	Typical Sorghum	Brown sugar
	Flavour	Slightly Sweet	Slightly Sweet
	Colour	Light brown	Dark brown
2	Dextrose Equivalent	0.84	6.22
3	Swelling Power	2.44	2.87
4	Solubility	12.52%	52.9%
5	Yield Value	~~72.58%~~	86.71%

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Table 2. Evaluation of ODF Preparations

Run	Factor		Response		
	A: MDX-Sorghum Concentration (%)	B: Glycerol Concentration (%)	Y_1: Tensile Strength (MPa)	Y_2: Elongation (%)	Y_3: Disintegration Time (sec)
1.	4.00	6.50	1.98	86.26	152
2.	4.00	3.00	2.47	66.74	181
3.	4.00	10.00	1.52	101.68	75
4.	4.00	6.50	1.92	89.44	155
5.	5.41	8.97	1.32	103.96	85
6.	4.00	6.50	1.67	91.94	160
7.	2.59	8.97	1.48	97.72	112
8.	4.00	6.50	1.95	86.58	158
9.	6.00	6.50	1.61	99.16	90
10.	4.00	6.50	1.98	93.18	150
11.	4.00	6.50	1.91	84.84	159
12.	2.59	4.03	1.87	61.41	191
13.	2.00	6.50	2.05	72.41	176
14.	5.41	4.03	1.58	78.56	166

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Table 3. Analysis of ODF Cetirizin HCl Tensile Strength, ~~Percent~~ Elongation, and Disintegration Time Using CCD

Factors		Y_1 Tensile Strength (MPa)	Y_2 Elongation (%)	Y_3 Disintegration Time (sec)
A (MDX-Sorghum Concentration (%))	Coefficient	-0.13	7.67	-21.75
	ρ-value	0.1031	0.0002**	0.0003**
B (Glycerol Concentration (%))	Coefficient	-0.25	13.90	-38.78
	ρ-value	0.0070**	0.0001**	0.0001**
A. B	Coefficient	-	-	-0.50
	ρ-value	-	-	0.9238
A^2	Coefficient	-	-	-9.37
	ρ-value	-	-	0.0364*
B^2	Coefficient	-	-	-11.87
	ρ-value	-	-	0.0130*
Analytical model		Liniear	Liniear	Quadratic
Intercept		1.81	86.71	155.68
Degree of freedom		2	2	5
Sum of squares		0.64	2012.01	17342.43
Mean of squares		0.32	1006.00	3468.49
F-value		7.04	62.85	33.80
ρ-value		0.0108	0.0001	0.0001
R-Squared		0.5613	0.9195	0.9548

* ρ-value < 0.05
** ρ-value < 0.01

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Table 4. Results of Optimal Oral Dissolving Film (ODF) Formulation on Response

No	Polymer (%)	Plasticizer (%)	Tensile Strength (MPa)	Elongation (%)	Disintegration Time (sec)	Desirability
1.	3.56	10.00	1.495	104.0	83	0.807
2.	3.55	10.00	1.497	103.9	83	0.806
3.	3.53	10.00	1.499	103.8	83	0.804

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Table 5. Optimal ODF Evaluation Results

No	Response	RSM Prediction	Observation Results	Percentage Error (%)
1	Tensile Strength (MPa)	1.495	1.50	0.33
2	Elongation (%)	104	104.26	0.25
3	Disintegration Time (second)	83	82.95	0.06

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Table 6. ODF cetirizine HCl composition based on CCD

Run	Batch	Composition						
		Cetirizine HCl (mg)	MDX-Sorghum* (%)	Glycerol* (%)	Sucrose (%)	Citric Acid (%)	HPMC (%)	Distilled Water~~Aquadest~~ ad (mL)
1.	F1	1,500	4.00	6.50	4	4	4	100
2.	F2	1,500	4.00	3.00	4	4	4	100
3.	F3	1,500	4.00	10.00	4	4	4	100
4.	F4	1,500	4.00	6.50	4	4	4	100
5.	F5	1,500	5.41	8.97	4	4	4	100
6.	F6	1,500	4.00	6.50	4	4	4	100
7.	F7	1,500	2.59	8.97	4	4	4	100
8.	F8	1,500	4.00	6.50	4	4	4	100
9.	F9	1,500	6.00	6.50	4	4	4	100
10.	F10	1,500	4.00	6.50	4	4	4	100
11.	F11	1,500	4.00	6.50	4	4	4	100
12.	F12	1,500	2.59	4.03	4	4	4	100
13.	F13	1,500	2.00	6.50	4	4	4	100
14.	F14	1,500	5.41	4.03	4	4	4	100

*CCD-RSM Concentration Design Results

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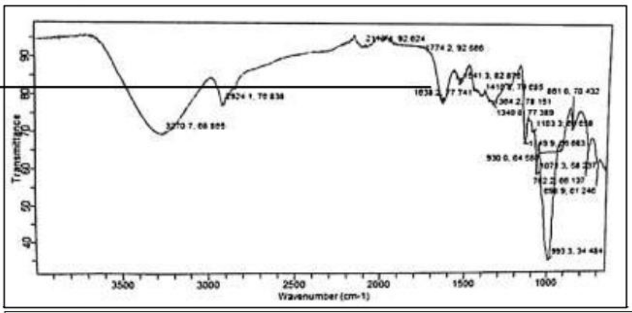

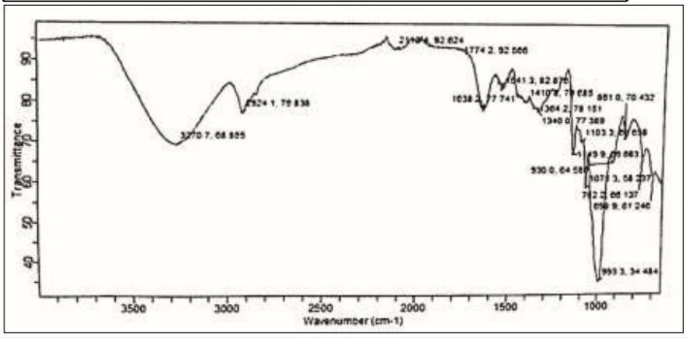

Figure 1. FTIR Spectrum of Sorghum Starch

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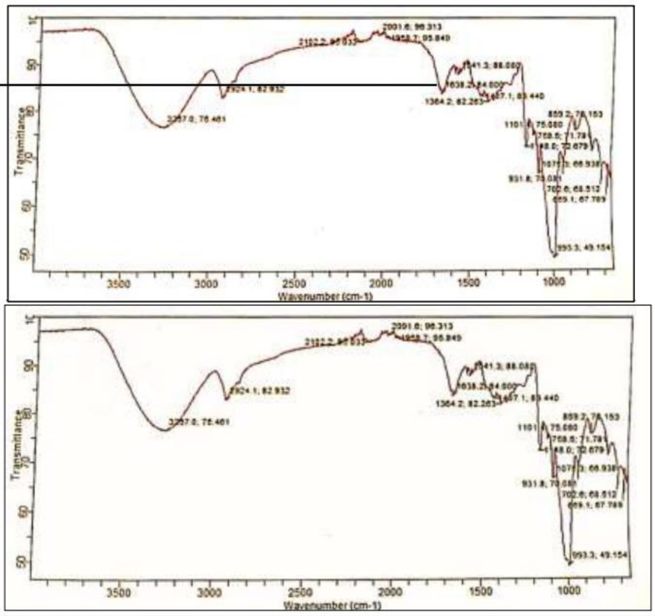

Figure 2. FTIR Spectrum of MDX-Sorghum

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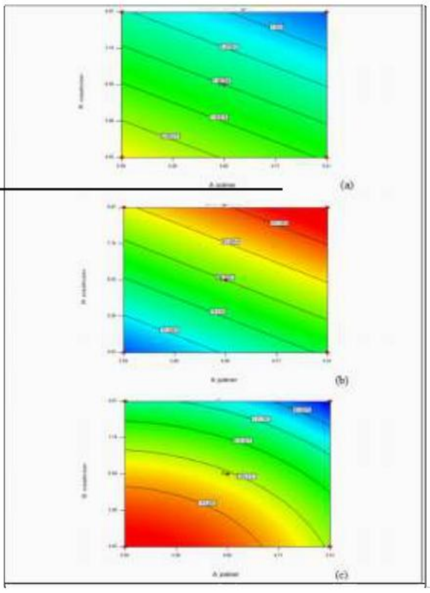

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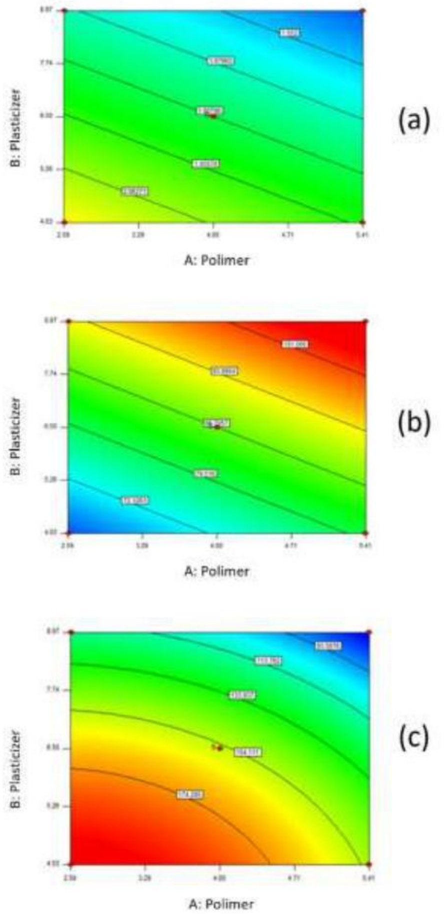

Figure 3. Graph showing the effect of film-forming polymer (MDX-Sorghum) concentration and plasticizer (glycerol) concentration on tensile strength value (a), ~~percentage of~~ elongation (b), and disintegration time (c)

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I am pleased to inform you that your manuscript entitled as "Characterization of modified sorghum starch and ıts use as a film-forming polymer in orally dissolving film formulation with glycerol as a plasticizer" has been accepted for publication in an upcoming issue of Journal of Research in Pharmacy . We will send the proof of your article for your approval prior to publication. You can reach the final information about your manuscript at online manuscript center (https://www.jrespharm.com).

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I am pleased to inform you that our reviewers has been accepted and recommended your manuscript for publication.
Your manuscript will be published in SEPTEMBER 2023. Your PDF proof will be enabled in AUGUST 2023.
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Kindest regards
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Title in English: Characterization of modified sorghum starch and ıts use as a film-forming polymer in orally dissolving film formulation with glycerol as a plasticizer

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Abstract in English

: Film-forming polymers and plasticizers are components of orally dissolving film (ODF) compositions that have the greatest influence on the physical properties of the film preparations. Modification of sorghum starch produces maltodextrin (MDX)-sorghum which can be used as a film-forming polymer, and glycerol can be used as a plasticizer in ODF preparations. This study aims to determine the optimal concentrations of MDX-sorghum and glycerol to produce ODF compositions using the central composite design (CCD) in response surface methodology (RSM). Hydrolysis of sorghum starch yielded MDX-sorghum, characterized by yield value, dextrose equivalent (DE) value, solubility, swelling power and FTIR analysis. The CCD included a concentration range of 2-6% and 3-10% for MDX-sorghum and glycerol, respectively, as parameters in the optimization process, so 14 experimental designs were obtained. The test response was evaluated using tensile strength, elongation and disintegration time tests. The modification of sorghum starch yields a light brown MDX-sorghum powder with desirable properties. Optimization of MDX-sorghum and glycerol concentrations yielded an optimal formulation with a tensile value of 1.50 MPa with an error percentage of 0.33%, elongation of 104.26% with an error percentage of 0.25%, and disintegration time of 82.95 seconds with an error percentage of 0.06%. By modifying sorghum starch into MDX-sorghum, the starch's ability to dissolve and swell can be improved, allowing it to be used as a film-forming polymer. The optimal MDX-Sorghum and glycerol concentrations for the production of ODF are 3.56% and 10.00 %, respectively.

Manuscript Files

File Name	File Size	Date Created	Category	Description
MPJ-10715-2-cover-letter-jrp.pdf (../pdf-files/out/12976-MPJ-10715-2-cover-letter-jrp.pdf)	14 KB	Sep 14, 2022	Cover letter	None
MPJ-10715-3-modified-sorghum-starch-jrp-template.pdf (../pdf-files/out/12976-MPJ-10715-3-modified-sorghum-starch-jrp-template.pdf)	1305 KB	Sep 14, 2022	Main Document	None
MPJ-10715-1-jrp-checklist.pdf (../pdf-files/in/12976-MPJ-10715-1-jrp-checklist.pdf)	241 KB	Sep 14, 2022	Author Checklist Form	None
MPJ-10715-1-jrp-copyright-form-integrated.pdf (../pdf-files/out/12976-MPJ-10715-1-jrp-copyright-form-integrated.pdf)	85 KB	Sep 14, 2022	Copyright Transfer Form	None
MPJ-10715-6-figure-1.jpg (../pdf-files/in/12976-MPJ-10715-6-figure-1.jpg)	98 KB	Sep 14, 2022	Figure	None

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MPJ-12582-8-rev-01-mpj-10715-14923-rev-file-10715-mpj-10715-3-modified-sorghum-starch-jrp-template.rev-1.pdf (../pdf-files/out/12976-MPJ-12582-8-rev-01-mpj-10715-14923-rev-file-10715-mpj-10715-3-modified-sorghum-starch-jrp-template.rev-1.pdf)	1859 KB	Mar 19, 2023	Main Document	None
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MPJ-12976-2-response-to-reviewers-second-revision-.rev-2.pdf (../pdf-files/out/12976-MPJ-12976-2-response-to-reviewers-second-revision-.rev-2.pdf)	33 KB	Apr 28, 2023	Response to Reviewers	None

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