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*Article*

# The Effect of Coating Material Variations on Sugar-Coated Tablets *Curcuma Zanthorrhiza* Roxb. Extract Using The Simplex Lattice Design Method

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**Abstract:** Javanese turmeric (*Curcuma xanthorrhiza*, Roxb.) contains curcuminoids, taste of herbal medicine can be disguised, so researchers want to make sugar-coated tablets. The aim of this study was to formulate sugar-coated tablets using HPMC and PVA as gelling agents, which are essential for controlling the drug release of ethanolic extract of Javanese turmeric using Simplex Lattice Design (SLD). Javanese turmeric (*Curcuma xanthorrhiza*, Roxb.) was extracted by remaceration using ethanol 70%, then made into tablets using the wet granulation method. Tablets are coated by combination of HPMC and PVA which have been formulated with LSD (5 formulas). The determination of the optimum region for the curcuma extract coated tablet formulation was analyzed using Design Expert. The physical properties used were friability, hardness, and disintegration time. Formula optimum with tablet friability was chosen to be minimized within the range <1 with value 0,762; hardness was chosen in range 4 – 8 with value 7,7; then disintegration time less than 30 minutes with value 24,932. The optimum composition of HPMC and PVA in a coated preparation that can produce optimal physical properties for coated tablets of ethanol extract of Javanese turmeric (*Curcuma xanthorrhiza*, Roxb.) is HPMC 30 and PVA 20 with a desirability of 0.864.

**Keywords:** curcumin; extract; tablet; coated.

## 1. Introduction

Javanese turmeric (*Curcuma xanthorrhiza, Roxb.*) is one of the plants that grows widely and is often used by Indonesian people as a traditional medicine. The main active ingredient in turmeric utilized as medicine is curcuminoid, whose function is to enhance immune power or restore imbalances in the immune system (Immunomodulator) [1]. An immunomodulator is a pharmaceutical substance that helps restore imbalances in the immune system. Its mechanism is to restore the function of a compromised immune system (*immunorestoration*) and boost the body's immune system [2].

A tablet is a solid dosage form technology that has different sizes, shapes, and thicknesses depending on the desired drug dose, and contains one or more active ingredients and other excipients such as fillers, sweeteners, binders, disintegrants, and lubricants [3]. A coated tablet is a tablet covered with a mixture of various substances such as resins, gums, gelatin, fillers, sugar, plasticizers, polyols, colorants, and flavor enhancers on the active ingredients. The substances are usually applied as a solution or suspension containing a volatile carrier [4]. Tablet coating is useful in protecting the drug substance by acting as a barrier against moisture and air, masking the unpleasant taste of the drug substance, and improving the tablet's appearance. The thickness and color of the coating can vary depending on the addition of coloring agents to the sugar coating.

The mechanism of a sugar-coated tablet is very simple. After ingestion, the sugar layer of the tablet will dissolve in the water in the stomach. The protected contents of the tablet can then be slowly released into the intestine so that the medicine can work optimally. Sugar-coated tablets can help protect the tablet contents from harmful environments, such as the acidic environment of the stomach, so that the quality of the drug is maintained until it reaches the intestine where the drug will be absorbed. Furthermore, sugar-coated tablets can also help increase drug effectiveness by slowly releasing the tablet contents into the intestine so that the drug can provide an optimal effect. In practice, sugar-coated tablets are often used for drugs with slow absorption or drugs that need to be released gradually. Therefore, the use of sugar-coated tablets is highly recommended to maintain the quality and effectiveness of the drug. The objective of this research is to formulate a sugar-coated tablet using HPMC and PVA as coating agents and gelling agents, which are important for controlling the release of the turmeric ethanol extract drug.

The combination of HPMC and PVA is expected to provide an ideal sustained release dosage profile and meet the physical requirements of a dosage form capable of maintaining drug release over a certain period through analysis using the Simplex Lattice Design (SLD). This method supports formulation and minimizes *trial and error* by reading the analysis into ANOVA to check the validity of the resulting equation to obtain the formulation parameters along with their predictions.

## 2. Materials and Methods

This research utilizes javanese turmeric rhizome extract (sourced from Kendal Regency, Central Java) as the primary active ingredient containing curcuminoid, which will be formulated into a sustained-release sugar-coated tablet. The selection of coating agents is focused on a combination of HPMC and PVA, which function as gelling agents to control drug release. Other supporting excipients include Lactose, Avicel, PVP, Mg. Stearate, Talc, Aerosil, Sucrose, PEG 6000, $CaCO_3$, $TiO_2$, and Coloring Agents.

The formulation and optimization process is conducted scientifically using the Simplex Lattice Design (SLD) approach, followed by ANOVA analysis to validate the equation and predict dosage parameters, thus minimizing trial and error. The final tablet product is compressed using a tablet compression machine and coated with a coating machine. Dosage evaluation is carried out using bulk-tapped density and flowmeter for powder characteristics, as well as physical quality testing of the core and coated tablets using a hardness tester, friability tester, and caliper. The sustained-release performance will be specifically tested with a dissolution tester, and the assay of the released curcuminoid will be performed using a UV-Vis Spectrophotometer.

## 3. Results

### *3.1. Turmeric Extract Tablets*

#### *3.1.1. Curcuma xanthorrhiza, Roxb. Extract*

The extract preparation process started with the raw material preparation *Curcuma xanthorrhiza, Roxb* rhizomes were washed, cut, and dried, and then powdered using a blender. This powder was sieved through a 20 mesh sieve to achieve the optimal fineness grade. The extraction technique used was repeated maceration: one kilogram of powder was soaked in 7 liters of 70% ethanol for 5 days (the first maceration) followed by re-soaking the residue for 1 day (the second maceration), while being stirred and protected from light. All the resulting liquid (*macerate*) was then collected. The final step was the concentration of the macerate over a water bath to evaporate the ethanol until a viscous extract was obtained that was ready to be used for tablet formulation.

The results of the yield of ethanol extract of *Curcuma xanthorrhiza, Roxb* in this study can be seen in the table below.

**Table 1.** Ethanol Extract Yield Results

| Powder (gram) | Result (gram) | Yield (%) |
|---|---|---|
| 1000 | 500,012 | 50,012 |

The yield calculation was performed to determine the amount of extract obtained from the fresh simplisia (crude drug) that was used. The result obtained from the yield calculation approached 50%. This yield result suggests an influence of the solvent used, which was 70% ethanol, on the obtained yield. Several factors that can affect the yield result include the size of the simplisia, the type of solvent, the polarity level of the solvent, and the duration of maceration.

*3.1.2. Tablet Formulation*

After the viscous extract was obtained, aerosil was added to the extract, and the active ingredient was mixed homogeneously with Lactose. The formulation of tablets can be seen in the table 2.

**Table 2.** Formulation of Turmeric Extract Tablet

| Materials | Concentration (mg) |
|---|---|
| Extract | 110,00 |
| Lactose | 88,50 |
| PVP | 16,25 |
| Avicel PH 102 | 48,75 |
| Mg. Stearate | 3,25 |
| Talc | 3,25 |
| Aerosil | 55,00 |

This mixture was then wetted with PVP until a good granule mass was formed. The wet granule mass was sieved with a No. 12 mesh sieve, then it was dried at a temperature of 40◦C - 60◦C for 18 hours. The dry granules were sieved again with a No. 14 mesh sieve. Subsequently, Avicel and Mg. Stearate were added and mixed until homogeneous. This dry granule mixture was then tested for its flow properties, and was subsequently compressed into tablets. Finally, the resulting core tablets were tested for their specification characteristics.

*3.1.3. Evaluation of Granules*

The granule flow rate test was performed by slowly pouring 100 grams of granules through the edge of a funnel that had its outlet initially closed. The time required for all 100 grams of the granules to flow out of the funnel was recorded. A critical criterion for tableting success was established: if the time taken for the 100 grams of granules to flow out of the funnel exceeded 10 seconds, it was concluded that difficulties would be encountered during the tableting process [5]. The result was 9 seconds for this granules, then granules were molded into tablets. From this formula, 100 tablets were obtained which will be used further for evaluation.

**Table 3.** The Result of Granules Evaluation

| Evaluation | Result |
|---|---|
| Flow Time | 9 seconds |
| Angle of Repose | 30◦ |
| Compressibility | 12% |

The formulation of the turmeric extract sugar-coated tablet was designed with the aim of protecting the drug substance by acting as a barrier against moisture and air, masking the unpleasant taste and odor of the drug substance, and improving the tablet's appearance. The combination of materials used, HPMC and PVA, is expected to be able to protect the drug substance and improve the moisture stability of the turmeric extract tablets. The formula can be seen on table below.

**Table 4.** Formulation of Coating Material Tablets

| Materials | F1 | F2 | F3 | F4 | F5 |
|---|---|---|---|---|---|
| Sucrose (g) | 60 | 60 | 60 | 60 | 60 |
| HPMC (g) | 30 | 20 | 27,5 | 22,5 | 25 |
| PVA(g) | 20 | 30 | 22,5 | 27,5 | 25 |
| PEG 6000(g) | 4,5 | 4,5 | 4,5 | 4,5 | 4,5 |
| CaCO3 (g) | 22,5 | 22,5 | 22,5 | 22,5 | 22,5 |
| TiO2 (g) | 1,5 | 1,5 | 1,5 | 1,5 | 1,5 |
| Carmine (g) | qs | qs | qs | qs | qs |
| Aqusadest (mL) | ad 150 | ad 150 | ad 150 | ad 150 | ad 150 |

Sucrose was dissolved in a portion of water by heating (mixture 1), then a certain amount of PVA was added little by little into a beaker glass containing a portion of water while stirring using a homogenizer at low speed for 15 minutes (mixture 2). In a separate place, a suspension was made from other additives, namely talc, titanium dioxide, polyethylene glycol 6000, dye and water using a homogenizer for 20 minutes (mixture 3). Suspensions (2) and (3) were added to mixture (1) and stirred again for 5 minutes at low speed (do the same thing with HPMC) [6]. A total of 30 core tablets were placed in a coating pan and the coating solution of each concentration was sprayed. The coating pan was subjected to a flow of hot air at a temperature of 50◦C – 70◦C. After the spraying process was complete, the tablets were left in the rotating coating pan until cooled, while the drying process continued using a dryer.

This research was conducted to determine the effect of the HPMC and PVA combination on the hardness, friability, and disintegration time of the turmeric extract tablets through sugar coating, and to determine the optimum formulation.

*3.2. Evaluation of Tablets*

*3.2.1. Friability of Tablets*

The tablet friability test aims to determine the tablet's resistance to friction and impact during handling and distribution. Based on the test results, the average tablet friability value was 0.8587% with a standard deviation of 0.0972. According to the Indonesian Pharmacopoeia, edition VI, the maximum limit for tablet friability is ≤ 1% [7]. Thus, the tested tablets still met the established standards, indicating good mechanical quality.

The data results were analyzed using the Simplex Lattice Design method from the Design Expert software version 13 trial, the response equation from the tablet friability test was obtained as follows:

$$Y = 0{,}7917\ (A) + 0{,}9798\ (B), \quad (1)$$

Y : Friability Tablets (%)
A : HPMC (mg)
B : PVA (mg)

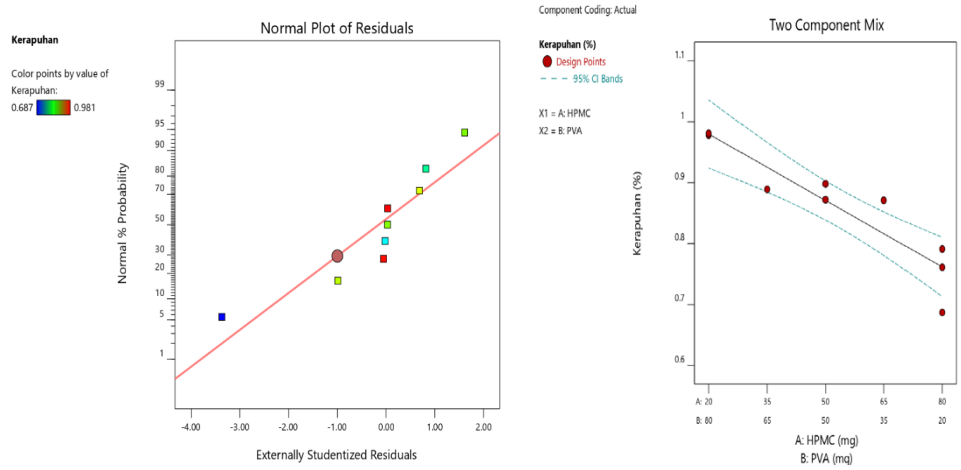


**Figure 1.** Two Component Friability Test

The tablet friability test profile shows that higher HPMC concentrations increase friability, while higher PVA concentrations decrease friability in coated tablets. PVA components are more effective in reducing friability than HPMC. This is because PVA can form better granules, resulting in tablets that disintegrate faster and do not harden during storage [8].

*3.2.2. Hardness of Tablets*

Hardness tests were conducted to determine the tablet's resistance to mechanical stress during production, storage, and use. The test results showed that tablet hardness varied within the range of 4–7.8 kg. The good tablet should have a hardness in the range of 4–8 kg to prevent it from crumbling during handling but still dissolve well [9]. Some samples showed higher standard deviations, indicating inter-batch variations that need to be controlled in the production process.

The data results were analyzed using the Simplex Lattice Design method from the Design Expert software version 13 trial, the response equation from the tablet hardness test was obtained as follows:

$$Y = 7{,}73\ (A) + 4{,}20\ (B) + 3{,}73\ (AB) - 4{,}09\ (AB(A\text{-}B)) - 41{,}96\ (AB(A\text{-}B)^2), \quad (2)$$

Y : Hardness Tablets (kg)
A : HPMC (mg)
B : PVA (mg)
AB : HPMC + PVA (mg)

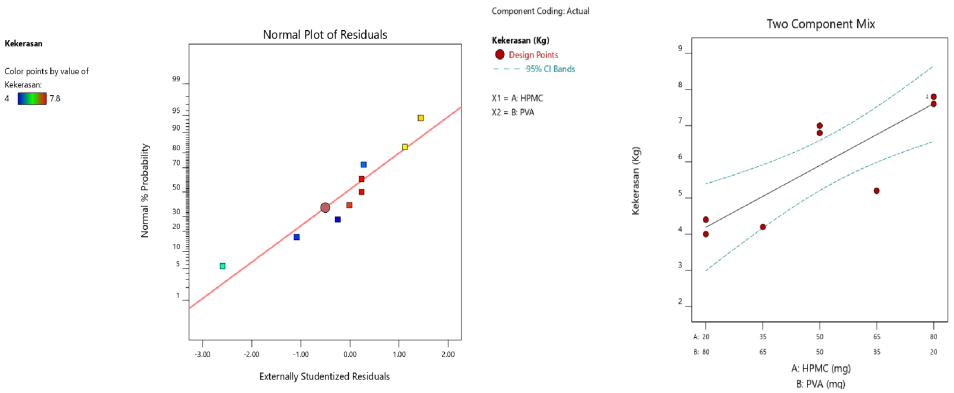


**Figure 2.** Two Component Hardness Test

*3.2.3. Disintegration Time*

Tablet disintegration time is crucial for ensuring the release of active ingredients in the body. Based on test results, the average tablet disintegration time ranged from 25 to 30 minutes, with a standard deviation of 0 to 2.04. According to the Indonesian Pharmacopoeia VI, coated tablets must disintegrate within ≤ 30 minutes in aqueous media [7]. These results indicate that the tablets still meet disintegration time requirements, but there are some variations between batches that require attention.

The data results were analyzed using the Simplex Lattice Design method from the Design Expert software version 13 trial, the response equation from the disintegration time test was obtained as follows:

$$Y = 24{,}93\ (A) + 30{,}01\ (B) + 7{,}38\ (AB), \quad (3)$$

Y : Disintegration Time (minutes)
A : HPMC (mg)
B : PVA (mg)
AB : HPMC + PVA (mg)

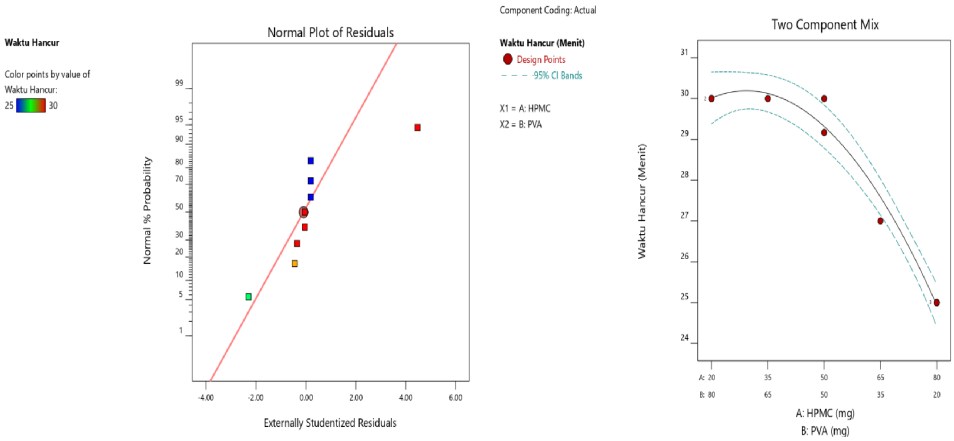


**Figure 3.** Two Component Disintegration Time Test

*3.3. Data Analysis*

*3.3.1. Optimization of sugar-coated tablets*

Formula optimization using SLD with the help of Design Expert software version 13 trial numerically by entering optimization parameter data as shown in the table below.

**Table 5.** Optimization Parameter

| Parameter | Criteria | Information | Importance |
|---|---|---|---|
| Friabilty (%) | 500,012 | Minimum | +++ |
| Hardness (kg) | 4 - 8 | In Range | +++ |
| Disintegration Time (minutes) | <30 | Minumum | +++ |

## 4. Discussion

In this study, the SLD equation model from Design Expert was used. The model was validated using the normal plot of residual and Two Component methods. Analysis of the normal curve plot of residual showed that the data was normally distributed. The measurement results of 9 formulas with 4 replications showed that the tablet friability test was evenly distributed approaching the normal line. If the distribution of the friability test approaches the normal line, it means that the experimental results are getting closer to the software's prediction results.

For the response based on the results of the ANOVA analysis, the results show that the model created has a p-value <0.05, namely 0.0004 with a linear mixture model where if this value is greater than 0.05, it can be concluded that this model is significant, meaning that both factors, namely HPMC and PVA, provide a significant interaction on tablet friability. Meanwhile, for the lack of fit analysis value, the p-value is 0.4188, which means this model is not significant against pure error, meaning there is no difference between the observation data and the predicted data from the model created. Tablet fragility based on data from the analysis results obtained in equation 1 from Simplex Lattice Design, it was found that factor B, namely PVA (0.9798), had the dominant influence on tablet fragility, then factor A, namely HPMC (0.7917).

The measurement results of 9 formulas with 4 replications show that the tablet hardness test is evenly distributed approaching the normal line. If the distribution of the hardness test approaches the normal line, it means that the experimental results are getting closer to the software's prediction results. For the response based on the results of the analysis with ANOVA, the results show that the model created has a p-value > 0.05, namely 0.00026 with a linear mixture model where if this value is greater than 0.05, it can be concluded that this model is significant, meaning that both factors, namely HPMC and PVA, provide a significant interaction on tablet hardness.

Meanwhile, for the value lack of fit analysis obtained a p-value of 0.0011, which means that this model is significant for pure error, meaning that there is a difference between the observation data and the predicted data from the model created. Tablet hardness based on data from the analysis results obtained in equation 1 from Simplex Lattice Design, it was found that factor A, namely HPMC (7.73), had the dominant influence on tablet hardness, then factor B, namely PVC (4.20), and finally the combination of HPMC and PVA (3.73).

The measurement results of 9 formulas with 4 replications show that the tablet disintegration time test is evenly distributed approaching the normal line. If the distribution of the tablet disintegration time test approaches the normal line, it means that the experimental results are getting closer to the software's prediction results. For the response based on the results of the analysis with ANOVA, the results show that the model created has a p-value <0.05, namely 0.0001 with a linear mixture model where if this value is less than 0.05, it can be concluded that this model is significant, meaning that both factors, namely HPMC and PVA, provide a significant interaction on the tablet disintegration time. Meanwhile, for the lack of fit analysis value, the p-value is 0.1622, which means that the model is not significant for pure error, meaning there is no difference between the observation data and the predicted data from the model created.

Tablet disintegration time test based on data from the analysis results obtained in equation 3 of Simplex Lattice Design showed that factor B, namely PVA (30.01), had a dominant influence on tablet disintegration time, then factor A (HPMC), and factor AB (HPMC + PVA). This is due to differences in the polymers used where PVA is a polymer that has better swelling power compared to HPMC as a polymer in the manufacture of coated tablet preparations so that PVA is able to release drugs faster than HPMC [10]. Films from PVA polymers experience faster development than films from HPMC polymers. This is due to the nature of PVA which is more hydrophilic than HPMC.

## 5. Conclusions

The optimum composition of HPMC and PVA in a coated preparation that can produce optimal physical properties for coated tablets of ethanol extract of Javanese turmeric (Curcuma xanthorrhiza, Roxb.) is HPMC 30 and PVA 20 with a desirability of 0.864.

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