Formulation of Fast Disintegrating Tablet Paracetamol Employing Selected Super-disintegrant

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ABSTRACT

The objective of this research was to investigate paracetamol FDT formula with potato starch and xanthan gum or glycine or ac di sol combination that can produce the best tablet quality. The tablets were prepared by direct compression technique. Superdisintegrant such as Glycine, Ac di sol, Xanthan Gum, and Potato Starch Extract was optimized as 1-19% on the basis of least disintegration time. Binders such as HPMC were optimized along with optimized superdisintegrant concentration. 3.5% HPMC was selected as optimum binder concentration on the basis of least disintegration time. Granule parameters included in the analysis were flowability, angle of repose, Carr’s index, Hausner’s ratio, and loss on drying (LOD). Tablet parameters included in the analysis were hardness, friability, disintegration time, dissolution, wetting time, and absorption ratio. The result was analyzed by Design Expert 11.1.0.1 program to decide the combination of superdisintegrant that can provide the best tablet qualities. The result showed that potato starch 15.162% and xanthan gum 4.838%, potato starch 15.050% and glycine 4.950%, and potato starch 18.390% and ac di sol 1.610%. Combination of superdisintegrant that can provide the best tablet qualities. It was concluded that, by employing commonly available pharmaceutical excipients such as superdisintegrants, hydrophilic and swellable excipients and proper filler, a fast disintegrating tablet of Paracetamol in tablet dosage form, were formulated successfully with desired characteristics.

INTRODUCTION

Paracetamol is a para-aminophenol derivative which has an analgesic and antipyretic effect and is slightly anti-inflammatory. The efficacy of paracetamol is very commonly used to treat fever, headaches, and mild to moderate pain (Sweetman, 2009). Paracetamol is widely available in syrup preparations for use in children. Even though it has a dosage form that is easily consumed by children, if its use is not appropriate it can cause unwanted effects. To overcome this problem, there are now many studies on fast disintegrating tablets (FDT) that are suitable for pediatric patients. Practical and safe drug dosage forms, also easy to carry make the tablet popular with most patients. FDT can disintegrate in the mouth in less than a minute or even faster only with the help of a little water (Fu et al., 2004).
tame, KH, tol, glycine, sodium laurylsulfate, talc, HPMC, aspar-

Prima Rasa. Paracetamol, paracetamol p.a., mannitol, glycine, sodium lauryl sulfate, talc, HPMC, aspartame, KH2PO4, NaOH, liquid paraffin, and sunset yellow were purchased from Duta Jaya, Malang. Tisu lensa (Kimwipes), cotton fabric and filter paper.

Preparation of Potato Starch Extract

Potatoes were purchased from Pasar Mergan, Malang, East Java. Aquadest was purchased from Panadia Laboratory, Malang. H2O2 30% was purchased from Makmur Sejati, Malang. Potato starch reference standard (food grade) was purchased from Prima Rasa. Paracetamol, paracetamol p.a., mannitol, glycine, sodium lauryl sulfate, talc, HPMC, aspartame, KH2PO4, NaOH, liquid paraffin, and sunset yellow were purchased from Duta Jaya, Malang. Tisu lensa (Kimwipes), cotton fabric and filter paper.

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using the following formula, where $W_a$ and $W_b$ are respectively tablet weights before and after testing.

$$AR = \frac{W_b - W_a}{W_a}$$

**Analysis of Data**

Analysis of granule and tablet test results with the help of the Design Expert 11.1.0.1. application. Then there will be a comparison of the composition of superdisintegrants which can give the desired disintegration time. The composition is then made and tested for the quality of granules and tablets as stated above. The next test results will be compared with the results of calculations by the application.

**RESULTS AND DISCUSSION**

**Preparation of Potato Starch Extract**

Making potato starch extract involves a bleaching process using $6\% \text{ H}_2\text{O}_2$. It aims to improve the color of potato starch from gray to white so that it is expected not to interfere with the appearance of the tablet. About 1 kg of peeled and washed potatoes can produce 60 – 70 g of potato starch.

**Evaluation of Potato Starch Extract**

Potato starch has a bond between C–H, C–C, C–O atoms and the bonds between O–H atoms. The peak value obtained in the sample compared to the standard shows a similar result which can be seen in Figure 1, where in the sample shown in Figure 2 there is a peak with a wavelength of 700 cm$^{-1}$– 800 cm$^{-1}$ which illustrates the existence of a bond between C–O, peak at wavelength 2927,24 cm$^{-1}$ which describes the existence of a bond between C–H atoms, peak at wave 1373,22 cm$^{-1}$ which describes the presence of aromatic groups and peaks at a wavelength of 3380,98 cm$^{-1}$ which describes the existence of bonds between O–H atoms. The results of the peak interpretations obtained illustrate that the
Table 1: Composition of Super disintegrant

| Kode Formula | F₁ | F₂ | F₃ | F₄ | F₅ | F₆ | F₇ | F₈ |
|--------------|----|----|----|----|----|----|----|----|
| Glycine (%)  | 1  | 1  | 2  | 3  | 3  | 4  | 5  | 5  |
| Ac di sol (%)|    |    |    |    |    |    |    |    |
| Xanthan Gum (%)|    |    |    |    |    |    |    |    |
| Potato starch extract (%)| 19 | 19 | 18 | 17 | 17 | 16 | 15 | 15 |

Table 2: Formulation of Fast Disintegrating Paracetamol

| Materials               | F₁ (mg) | F₂ (mg) | F₃ (mg) | F₄ (mg) | F₅ (mg) | F₆ (mg) | F₇ (mg) | F₈ (mg) |
|-------------------------|---------|---------|---------|---------|---------|---------|---------|---------|
| Paracetamol (50%)       | 125     | 125     | 125     | 125     | 125     | 125     | 125     | 125     |
| Mannitol (19%)          | 47.5    | 47.5    | 47.5    | 47.5    | 47.5    | 47.5    | 47.5    | 47.5    |
| Potato starch extract    | 47.5    | 47.5    | 45      | 42.5    | 42.5    | 40      | 37.5    | 37.5    |
| Glycine Ac di sol (%)   | 2.5     | 2.5     | 5       | 7.5     | 7.5     | 10      | 12.5    | 12.5    |
| Xanthan Gum (%)         | 3.75    | 3.75    | 3.75    | 3.75    | 3.75    | 3.75    | 3.75    | 3.75    |
| Sodium lauryl sulfate (1,5%) | 8.75 | 8.75 | 8.75 | 8.75 | 8.75 | 8.75 | 8.75 | 8.75 |
| Talc (5%)               | 12.5    | 12.5    | 12.5    | 12.5    | 12.5    | 12.5    | 12.5    | 12.5    |
| HPMC (3.5%)             | 2.5     | 2.5     | 2.5     | 2.5     | 2.5     | 2.5     | 2.5     | 2.5     |
| Aspartame (1%)          | 250     | 250     | 250     | 250     | 250     | 250     | 250     | 250     |

Table 3: Flow ability and Angle of Repose Evaluation of Paracetamol FDT

| Formula Code | F₁ | F₂ | F₃ | F₄ | F₅ | F₆ | F₇ | F₈ |
|--------------|----|----|----|----|----|----|----|----|
| Flow rate (g/s) | 7.042 ± 33.562 ± | 8.525 ± 31.692 ± | 12.213 ± 32.082 ± | 0.056 ± 1.165 ± | 0.209 ± 1.849 ± | 0.748 ± 1.941 ± |
| Angle of repose (°) | 46.052 ± 36.240 ± | 42.210 ± 35.046 ± | 10.807 ± 29.150 ± | 0.152 ± 1.363 ± | 0.192 ± 1.207 ± | 0.074 ± 0.677 ± |
| Flow rate (g/s) | 6.495 ± 35.280 ± | 9.264 ± 31.234 ± | 9.677 ± 33.687 ± | 8.106 ± 8.377 ± | 0.375 ± 0.552 ± | 0.192 ± 1.207 ± |
| Angle of repose (°) | 35.260 ± 28.546 ± | 35.046 ± 27.552 ± | 21.351 ± 24.727 ± | 0.192 ± 1.207 ± | 0.192 ± 1.207 ± | 0.192 ± 1.207 ± |
| Flow rate (g/s) | 7.512 ± 31.109 ± | 9.749 ± 30.466 ± | 7.071 ± 29.150 ± | 12.5 ± 12.5 ± | 12.5 ± 12.5 ± | 12.5 ± 12.5 ± |
| Angle of repose (°) | 14.443 ± 1.363 ± | 0.349 ± 0.561 ± | 0.038 ± 0.947 ± | 0.038 ± 0.947 ± | 0.038 ± 0.947 ± | 0.038 ± 0.947 ± |
| Flow rate (g/s) | 7.775 ± 32.310 ± | 8.348 ± 32.861 ± | 6.448 ± 28.361 ± | 3.75 ± 3.75 ± | 3.75 ± 3.75 ± | 3.75 ± 3.75 ± |
| Angle of repose (°) | 1.363 ± 0.349 ± | 0.192 ± 0.349 ± | 0.038 ± 0.947 ± | 0.038 ± 0.947 ± | 0.038 ± 0.947 ± | 0.038 ± 0.947 ± |
| Flow rate (g/s) | 7.816 ± 34.725 ± | 8.482 ± 29.665 ± | 10.807 ± 32.996 ± | 12.5 ± 12.5 ± | 12.5 ± 12.5 ± | 12.5 ± 12.5 ± |
| Angle of repose (°) | 1.363 ± 0.192 ± | 1.207 ± 1.207 ± | 0.174 ± 0.677 ± | 0.174 ± 0.677 ± | 0.174 ± 0.677 ± | 0.174 ± 0.677 ± |
| Flow rate (g/s) | 7.674 ± 33.103 ± | 8.300 ± 29.376 ± | 6.987 ± 28.961 ± | 12.5 ± 12.5 ± | 12.5 ± 12.5 ± | 12.5 ± 12.5 ± |
| Angle of repose (°) | 2.322 ± 0.107 ± | 1.603 ± 1.603 ± | 0.036 ± 0.812 ± | 0.036 ± 0.812 ± | 0.036 ± 0.812 ± | 0.036 ± 0.812 ± |
| Flow rate (g/s) | 8.205 ± 36.078 ± | 8.384 ± 29.632 ± | 9.608 ± 30.810 ± | 12.5 ± 12.5 ± | 12.5 ± 12.5 ± | 12.5 ± 12.5 ± |
| Angle of repose (°) | 0.423 ± 0.221 ± | 0.633 ± 0.633 ± | 0.341 ± 3.203 ± | 0.341 ± 3.203 ± | 0.341 ± 3.203 ± | 0.341 ± 3.203 ± |
| Flow rate (g/s) | 6.870 ± 29.716 ± | 8.377 ± 29.351 ± | 5.938 ± 27.192 ± | 12.5 ± 12.5 ± | 12.5 ± 12.5 ± | 12.5 ± 12.5 ± |
| Angle of repose (°) | 2.776 ± 0.044 ± | 1.114 ± 0.031 ± | 0.785 ± 0.031 ± | 0.785 ± 0.031 ± | 0.785 ± 0.031 ± | 0.785 ± 0.031 ± |
### Table 4: True Density and Carr’s Index Evaluation of Paracetamol FDT

| Formula Code | Potato Starch and Xanthan Gum | Potato Starch and Glycine | Potato Starch and Ac DiSol | Carr’s Index (%) |
|--------------|-------------------------------|---------------------------|-----------------------------|------------------|
|              | True Density (g/ml) | Carr’s Index | True Density (g/ml) | Carr’s Index | True Density (g/ml) | Carr’s Index |
| F1           | 1.529 ± 0.042 | 13.184 ± 0.060 | 1.754 ± 0.074 | 18.972 ± 0.054 | 1.565 ± 0.019 | 14.647 ± 0.018 |
| F2           | 1.359 ± 0.087 | 14.647 ± 0.074 | 1.724 ± 0.074 | 17.461 ± 0.054 | 1.473 ± 0.039 | 15.568 ± 1.157 |
| F3           | 1.465 ± 0.019 | 13.790 ± 0.095 | 1.633 ± 0.074 | 16.761 ± 0.054 | 1.422 ± 0.012 | 13.237 ± 1.067 |
| F4           | 1.419 ± 0.059 | 15.608 ± 0.101 | 1.514 ± 0.074 | 16.658 ± 0.054 | 1.478 ± 0.017 | 13.790 ± 1.127 |
| F5           | 1.400 ± 0.096 | 15.568 ± 0.080 | 1.766 ± 0.095 | 14.126 ± 0.074 | 1.506 ± 0.030 | 15.538 ± 1.096 |
| F6           | 1.404 ± 0.107 | 15.538 ± 0.107 | 1.871 ± 0.075 | 13.946 ± 0.074 | 1.487 ± 0.044 | 15.211 ± 1.167 |
| F7           | 1.439 ± 0.044 | 13.237 ± 0.143 | 1.751 ± 0.100 | 14.524 ± 0.100 | 1.447 ± 0.022 | 13.184 ± 0.963 |
| F8           | 1.352 ± 0.016 | 15.211 ± 0.049 | 1.792 ± 0.064 | 16.463 ± 0.064 | 1.373 ± 0.037 | 15.608 ± 1.549 |

### Table 5: Ratio Hausner and Porosity Evaluation of Paracetamol FDT

| Formula Code | Potato Starch and Xanthan Gum | Potato Starch and Glycine | Potato Starch and Ac DiSol | Hausner’s Ratio | Porosity (%) | Hausner’s Ratio | Porosity (%) | Hausner’s Ratio | Porosity (%) |
|--------------|-------------------------------|---------------------------|-----------------------------|-----------------|--------------|-----------------|--------------|-----------------|--------------|
| F1           | 1.152 ± 0.013 | 72.710 ± 1.079 | 1.234 ± 0.022 | 79.374 ± 0.702 | 1.122 ± 0.013 | 76.407 ± 0.328 |
| F2           | 1.172 ± 0.014 | 71.792 ± 2.030 | 1.212 ± 0.014 | 78.273 ± 1.433 | 1.158 ± 0.014 | 74.676 ± 0.868 |
| F3           | 1.160 ± 0.015 | 71.738 ± 0.636 | 1.201 ± 0.011 | 77.923 ± 1.613 | 1.162 ± 0.025 | 72.048 ± 0.505 |
| F4           | 1.185 ± 0.022 | 70.595 ± 1.120 | 1.120 ± 0.012 | 74.502 ± 2.062 | 1.154 ± 0.018 | 75.380 ± 0.506 |
| F5           | 1.157 ± 0.016 | 69.269 ± 2.049 | 1.164 ± 0.012 | 78.114 ± 0.514 | 1.199 ± 0.015 | 74.624 ± 0.252 |
| F6           | 1.184 ± 0.015 | 70.995 ± 2.477 | 1.162 ± 0.011 | 78.677 ± 0.668 | 1.122 ± 0.026 | 74.283 ± 0.494 |
| F7           | 1.152 ± 0.002 | 69.291 ± 0.832 | 1.170 ± 0.015 | 76.738 ± 2.088 | 1.204 ± 0.028 | 70.787 ± 0.082 |
| F8           | 1.180 ± 0.016 | 69.866 ± 2.654 | 1.197 ± 0.009 | 79.192 ± 0.529 | 1.179 ± 0.047 | 72.149 ± 0.494 |
Table 6: Wetting Time and Absorption Ratio (AR) Evaluation of Paracetamol FDT

| Formula Code | Potato Starch and Xanthan Gum | Potato Starch and Glycine | Potato Starch and Ac Di Sol |
|--------------|--------------------------------|--------------------------|-----------------------------|
|              | Wetting time (hour) | AR (%) | Wetting time (second) | AR (%) | Wetting time (hour) | AR (%) |
| F1           | 10.037 ± 0.025     | 46.028 ± 3.435         | 16609.000 ± 3.837         | 7.257 ± 0.038 | 45.507 ± 0.163 |
| F2           | 13.897 ± 0.270     | 52.166 ± 4.862         | 15836.000 ± 1.699         | 7.247 ± 0.040 | 44.985 ± 0.366 |
| F3           | 10.030 ± 0.010     | 65.542 ± 5.272         | 8612.333 ± 6.857          | 6.557 ± 0.035 | 44.095 ± 0.573 |
| F4           | 10.180 ± 0.195     | 91.727 ± 8.176         | 4044.333 ± 2.979          | 6.323 ± 0.032 | 44.291 ± 0.225 |
| F5           | 14.273 ± 0.065     | 87.475 ± 3.770         | 3468.333 ± 3.620          | 6.360 ± 0.026 | 44.119 ± 0.967 |
| F6           | 10.200 ± 0.079     | 63.553 ± 5.190         | 1180.667 ± 2.096          | 6.123 ± 0.025 | 43.938 ± 0.673 |
| F7           | 10.083 ± 0.031     | 69.955 ± 3.527         | 92.000 ± 4.582            | 5.447 ± 0.015 | 43.069 ± 0.452 |
| F8           | 14.533 ± 0.060     | 64.268 ± 5.759         | 126.000 ± 7.937           | 5.557 ± 0.006 | 43.782 ± 0.979 |

Figure 5: Dissolution Rate Evaluation of Paracetamol FDT with Combination of Potato Starch with Ac Di Sol

Qualitative tests carried out showed similar results between the standard potato starch and samples and IR spectra showed that IR spectra were in accordance with the molecular structure of potato starch (Field et al., 2007).

Particle Size Distribution

The results of distribution of granule size does not represent bells which means that the distribution of granules is abnormal. The problems that occur can be due to the inconsistent granulation process where the addition of distilled water is not as much as one formulation with another formulation which causes the consistency of different granules which causes the size of the resulting granule to be different between each formulation. The size of the granule that is not homogeneous can have an impact on the flow of the granule which is not good or the physical appearance of the granule itself. Furthermore,
Flowability and Angle of Repose

The flow rate of granules with superdisintegrant combinations of potato starch with glycine, xanthan gum or potatoes can be shown in Table 3. Based on the results, the flow rate that met the requirements of ≥10 g/s was found in the combination of potato starch and ac di sol formula 5 (17% : 3%) and formula 1 (19%: 1%). This can be caused due to the nature of ac di sol as superdisintegrant which has properties as a towing moisture where when the amount of ac di sol increases, the flow rate will decrease (Rowe et al., 2009). The equation for the flow rate of granules generated from Design Expert 11.1.0.1 the model of extreme vertice design:

\[ Y = 7.14A + 8.14B \text{ (Xanthan Gum)} \]
\[ Y = 8.38A + 8.89B - 0.8903AB - 6.36AB \text{ (A - B)} + 11.81AB (A–B)^2 \text{ (Glycine)} \]
\[ Y = 11.91A + 9.79B - 19.07AB \text{ (Ac di sol)} \]

The angle of repose of combination of potato starch with glycine, Ac disol or xanthan gum is shown in Table 3. Combination of potato starch with glycine on F1 and F5 - F8, in combination of starch and ac di sol F3, F4, F6, and F8 and combinations of potato starch and xanthan gum on F8 follow good flow properties because they include a range of 25 – 30° (Nagar et al., 2011). Based on this, it is known that granules with 15% potato starch content provide a smaller stationary angle. Granules that have moderate flow properties can be caused by the size of the granule that is not evenly distributed and the bonding between large particles or poor cohesion results in large angles (Stamatopoulos et al., 2016). The following equation for the silent angle of the granule produced from Design Expert 11.1.0.1 is the model of extreme vertice design:

\[ Y = 33,32A + 36,13B - 11,94AB \text{ (Xanthan Gum)} \]
\[ Y = 29,54A + 31,58B \text{ (Glycine)} \]
\[ Y = 31,98A + 30,89B - 12,52AB \text{ (Acdisol)} \]

Bulk and Tapped Density

The bulk density of the combination of potato starch with xanthan gum is greater, namely F1 – F8 around 0.382 – 0.442 g/ml. Bulk density of potato starch with glycine F1 – F8 0.359 – 0.405 g/ml. While the bulk density of potato starch with ac di sol F1 – F8 is 0.193 – 0.423 g/ml. The tapped density of combination of potato starch with glycine, xanthan gum or ac di sol ranges between 0.420 – 0.508 g/ml.

True Density and Carr’s Index

The true density of granules with superdisintegrant combinations of potato starch and xanthan gum, glycine or ac di sol ranged from 1.352 – 1.766 g/ml for F1 to F8 as in Table 5. The Carr’s index value of a combination of potato starch with xanthan gum, Ac disol or glycine is shown in Table 4. The value of potato starch with xanthan gum combination or ac di sol follows a good flow characteristic of 12 – 16% (Qiu et al., 2016), whereas the Carr’s index of a combination of potato starch and glycine tends to have rather good flow properties. This can be caused by the high number of fines that have an impact on the magnitude of the tapped density of
the granule which in turn has an impact on increasing the Carr’s index (Medina and Kumar, 2006). The following equation for Carr’s index generated from Design Expert 11.1.0.1 models extreme vertex design:

\[ Y = 11.34A + 16.67B \text{(Ac di sol)} \]
\[ Y = 14.59A + 17.64B \text{(Glycine)} \]
\[ Y = 13.14A + 13.20B + 8.79AB - 9.08AB(A - B) \text{(Xanthan Gum)} \]

**Hausner’s Ratio and Porosity**
The test results of the hausner’s ratio value of a combination of potato starch with xanthan gum, glycine or ac di sol shown in Table 5. Hausner’s ratio of F1 – F8 ranged from 1.152 – 1.234. Granules have a value of less than 1.25, so it can be said to have a very good flow (Nagar et al., 2011). The Hausner’s ratio affects the flow of the powder in the printing process which is the better the flow, then the weight, content and size of the tablet will be uniform. The following equation for compressibility generated from Design Expert 11.1.0.1 models extreme vertex design:

\[ Y = 1.12A + 1.20B - 0.0665AB + 0.4323 AB(A - B) \text{(Ac di sol)} \]
\[ Y = 1.17A + 1.21B \text{(Glycine)} \]
\[ Y = 1.15A + 1.15B + 0.1211AB - 0.1280 AB(A - B) \text{(Xanthan Gum)} \]

The porosity value of a combination of potato starch with glycine, xanthan gum or ac di sol for F1-F8 ranged from 69.269 – 79.192%. The porosity value does not meet the requirements of conventional tablet porosity 37 – 40%. This is in accordance with the theory that FDT tends to have a high porosity level to support water absorption into the tablet. Therefore, the right pressurizing pressure of the tablet is needed so that it can compensate for high porosity but still can produce optimal FDT hardness and friability (Fu et al., 2004). The porosity of a tablet can later affect the disintegration time and fragility of a tablet (Panigrahi and Beheras, 2010). The following equation for compressibility generated from Design Expert 11.1.0.1 models extreme vertex design:

\[ Y = 76.21A + 70.59B + 3.09AB - 26.91AB(A - B) \text{(Ac di sol)} \]
\[ Y = 72.58A + 69.55B \text{(Xanthan Gum)} \]

**Loss on Drying (LOD) and Uniformity of Content**
The LOD value of the granules with a combination of potato starch and ac di sol, glycine or xanthan gum for F1-F8 0.061 – 0.138%. LOD are too low (less than 3%) will reduce the adhesion between particles and cause the tablet to become brittle, but when the moisture of the granule is more than 5%, it will cause granule attachment to the tablet punch machine that produces the tablet into capping/picking (Gohel, 2005). The following equation for compressibility generated from Design Expert 11.1.0.1 models extreme vertex design:

\[ Y = 0.0762A + 0.1095B + 0.00696AB \text{(Ac di sol)} \]
\[ Y = 0.0811A + 0.0671B - 0.1109AB - 0.1726AB(A - B) \text{(Glycine)} \]
\[ Y = 0.1324A + 0.1144B - 0.2760AB - 0.7627AB(A - B) \text{(Xanthan Gum)} \]

The measurement results of uniformity of content on granules with a combination of potato starch and glycine, xanthan gum or ac di sol from F1 to F8 containing an active ingredient of paracetamol around 115.710 – 134.744 mg. The granule can be said to meet the requirements of 90 – 110% (Banker, 1970).

**Uniformity of Weight and Thickness**
The uniformity of the weight shown a good result from all formulations of the combination of potato starch with xanthan gum, glycine, and ac di sol as a whole met the required weight range of ±15% by weight of 250 mg tablets. The range of values obtained for the whole formulation was 253.0 ± 0.002 mg – 258.80 ± 0.216 mg where the lowest weight value was owned by FDT tablets with a combination of potato starch with xanthan gum and the highest weight was owned by FDT tablets with a combination of potato starch and ac di sol. The uniformity of tablet size shown a good result from all formulations of combinations of potato starch with xanthan gum, glycine, and ac di sol as a whole met the requirements, namely the tablet diameter not less than 1 and not more than 3 times the thickness of the tablet.

**Content Uniformity**
The value of uniformity of the content of the entire formulation shows that all formulations have the required content of not less than 90% and no more than 120% of the active ingredient listed on the label. If the drug level does not meet the requirements, it means that the drug does not have a good therapeutic effect and is not suitable for consumption.

**Hardness and Friability**
The hardness of tablets from all formulations showed results that met the requirements of tablet hardness for FDT, with a range of hardness values of 3 – 5 kg / cm². The value of the hardness obtained from the whole formulation is 3.285 ± 0.135-5.109 ± 0.371. The hardness value of a tablet can affect
the disintegration time, wetting time, and absorption ratio of a tablet. The hardness of the tablet can be influenced by the nature of the material used, the amount of binding material, and the pressing method.

Based on the results of the analysis using the Design Expert program 11.1.0.1 the hardness value of the combination tablets of potato starch and xanthan gum is $Y = 3.39A + 3.55B + 3.98AB$, the glycine combination is obtained by the equation $Y = 4.52A + 4.54B + 0.1475AB - 3.13AB(A - B)$, and the combination ac di sol with the equation $Y = 3.61A + 4.32B$. The coefficient value of variable $A$ which positively illustrates that the single use of potato starch can increase the value of hardness, the coefficient value of variable $B$ which positively illustrates that the single use of xanthan gum, glycine, or ac di sol can increase the hardness value, coefficient value of variable $AB$ the positive value illustrates that the combination of superdisintegrants can increase the value of hardness and if the coefficient value of each variable is negative then the single use or combination of each component decreases the value of tablet hardness. The higher the value of hardness will cause the tablet to be more difficult to break.

Friability of all formulations as a whole has values ranging from 0.370 ± 0.020% -1.089 ± 0.097%. Some formulations show results that come out of the range of friability requirements which are less than 1%. Different friability values of each formulation can be caused by different moisture profiles of each formulation combination where moisture can affect the adhesion force of each particle which can affect the fragility of the tablet. Humidity levels that are poorly maintained can cause tablet hardness to decrease.

Based on the results of the analysis using the Design Expert program 11.1.0.1 the friability value of the combination tablets of potato starch and xanthan gum is obtained by the equation $Y = 0.7667A + 0.4139B + 0.8731AB$, the glycine combination is obtained equation $Y = 1.00A + 0.9607B + 0.3199AB + 0.0132AB(A - B) - 6.00AB(A - B)^2$, and the combination ac di sol with the equation $Y = 0.7650A + 0.9915B + 0.3758AB + 0.4941AB(AB)$. Friability of the tablet is higher then it shows that a tablet is more easily fragile and more quickly destroyed.

**Disintegration Time**

The disintegration time obtained from a combination formulation between potato starch with xanthan gum and ac di sol ranged from 14,178 ± 2,516 – 32,665 ± 0.926 minutes, in which the total disintegration time of the formulation contained a combination of potato starch and xanthan gum and ac di sol do not meet the requirements for disintegration time less than 60 seconds (Table 6). Whereas the disintegration time of the combination formulation between potato starch and glycine was ranged from 44,167 ± 4.355 -184.833 ± 2,994 second where there were several formulas which did not meet the requirements of disintegration time. Disintegration time that does not meet the requirements can be caused the tablet formulation uses a binder namely HPMC where HPMC can increase the hardness value of a tablet so that it retains stronger release from a drug, but on the other hand causes longer disintegration time by forming a polymer with viscosity consistency which is high enough on the surface of the tablet so that the liquid outside the tablet environment will be difficult to absorb so that the liquid cannot wet the core of the tablet containing superdisintegrant so that ultimately the super disintegrant cannot work optimally. HPMC is also a polymer with strong binding capacity so the use of HPMC which involves the addition of water activates the binding capacity and increases the strength of the polymer (Bhowmik et al., 2009). The disintegration time can be improved by the addition of mannitol which has a role in accelerating the tablet disintegration time. Mannitol closes existing pores with watersoluble polymers so that it can shorten the time of destruction of FDT. Addition of sodium lauryl sulfate can also help speed up the tablet's disintegration time. Sodium lauryl sulfate is a water-soluble surface-active agent so that it can support tablet disintegration (Parkash et al., 2011).

**Dissolution**

The dissolution percentage of tablets with a combination of potato starch and glycine content showed good results and met the requirements where the requirements for dissolved percentages of tablets were at least 80% dissolved in the number of active substances listed on the label in the 30th minute (Figure 3). Whereas for the combination formulation of potato starch with xanthan gum and ac di sol showed poor results which did not meet the requirements. Dissolution results that meet the requirements there are only one in eight formulations that exist either in combination formulations of potato starch with xanthan gum or with ac di sol (Figure 4). The low percentage of solutes can be caused by various factors including the type of excipients, the process of making granulations which causes the granules to have a form that is not evenly spread, thus affecting the rate of dissolution of tablets (Silva et al., 2018).

Based on the results of the analysis using the Design Expert program 11.1.0.1, the dissolution of the com-
Combination of potato starch and xanthan gum obtained the equation \( Y = 26.24A + 18.92B - 6.41AB - 29.11AB \), glycine combination obtained the equation \( Y = 2.53A + 4.02B + 2.15AB \), and the combination ac di sol with the equation \( Y = 81.20A + 11.43B \). The coefficient value of variable A which positively illustrates that the single use of potato starch can increase tablet dissolution, the coefficient value of variable B which positively illustrates that the single use of xanthan gum, glycine, or ac di sol can increase tablet dissolution, coefficient value of variable AB a positive value illustrates that a combination of superdisintegrants can increase tablet dissolution and if the coefficient value of each variable is negative then a single use or combination of each component decreases the dissolution value of the tablet. The higher the dissolution percentage value the better that indicates that the tablet dissolves faster and absorbs faster too (Figure 5).

**Wetting Time and Absorption Ratio (AR)**

The wetting time obtained from a combination formulation of potato starch with xanthan gum or ac on di sol was \( 5.447 \pm 0.015 - 32.655 \pm 0.926 \) hours, while the wetting time of the combination of potato starch and glycine was around \( 92.000 \pm 4.582 \) seconds to \( >16609.000 \) second. The absorption ratio obtained from the whole formulation ranged from \( 38.877 \pm 3.837 - 91.727 + 8.176 \) (Table 6). The wetting time and absorption ratio are related to one another where the longer the tablet takes to be wetted as a whole, the smaller the amount of solute in a given time. Long wetting time can prove if water penetration into the matrix is slow (Silva et al., 2018). Based on the results of the analysis using the Design Expert program 11.1.0.1, the wetting time of the combination tablets of potato starch and xanthan gum found the equation \( Y = 10.03A + 10.08B + 0.4000AB - 0.7840 \), the glycine combination obtained the equation \( Y = 163.74A + 15794.77B - 16729.57AB \), and the combination ac di sol with the equation \( Y = 7.26A + 5.45B - 0.0914AB - 2.52AB(AB) \). The coefficient value of variable A which positively illustrates that the single use of potato starch can increase wetting time, the coefficient value of variable B which positively illustrates that the single use of xanthan gum, glycine, or ac di sol can increase wetting time, coefficient value of The positive AB variable illustrates that the combination of superdisintegrants can increase wetting time and if the coefficient value of each variable is negative then the single use or combination of each component decreases the absorption ratio. The absorption ratio the higher the better the signal that the water absorption time is faster.

**Analysis of Data**

The results of the optimization obtained are as follows where the value of desirability from each combination of ingredients in a row for xanthan gum, glycine, and ac di sol is 0.513; 0.640; and 0.833. The optimum formula with combination of potato starch and xanthan gum is potato starch 15.162% dan xanthan gum 4.838% (Figure 6). The optimum formula with combination of potato starch and glycine is potato starch 18.39% dan ac di sol 1.61% (Figure 8).

**CONCLUSION**

The combination of potato starch and glycine as super disintegrant is recommended on FDT formulation. Glycine which has excellent wettability can promote entry of water so it supports potato starch to swelling and the tablet is disintegrated quickly.

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**Conflict of interest**

The authors declare no conflicts of interest.

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