

The Effect of Pregelatinized Taro Starch (*Colocasia Esculenta* (L.) Schott) Temperature as Filler on Thiamine Hydrochloride Tablet

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Abstract

Citation: Lestari PM, Widayanti A, Afifah H. The Effect of Pregelatinized Taro Starch (*Colocasia Esculenta* (L.) Schott) Temperature as Filler on Thiamine Hydrochloride Tablet. Open Access Maced J Med Sci. 2019 Nov 30; 7(22):3827-3832.
https://doi.org/10.3889/oamjms.2019.513

Keywords: Pregelatinized taro starch; Filler; Thiamine Hydrochloride

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Received: 25-Sep-2019; **Revised:** 17-Oct-2019; **Accepted:** 18-Oct-2019; **Online first:** 14-Nov-2019

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Funding: This research did not receive any financial support

Competing Interests: The authors have declared that no competing interests exist

BACKGROUND: Pregelatinizing is processed to modify structure of starch by heating a certain temperature. Increasing of temperature causes the starch to absorb water and swell quickly in order to obtain a larger particle size. Larger particle size will improve the flowability and compressibility of the granules. Pregelatinized taro starch is used as diluent tablets with wet granulation method.

AIM: The objective research was to determine the effect of increasing pregelatinized taro starch temperature as diluent on compressibility and comprimability granule of thiamine hydrochloride compression.

METHODS: Pregelatinized taro starch is made by heating the suspension of starch at 50°C, 60°C and 70°C for 10 minutes and then dried. Pregelatinized taro starch is used as a filler of Thiamine Hydrochloride tablets which made by wet granulation method. Test wereperformed for each formula such as quality tests of granules and tablets physical properties and assay.

RESULT: Granule compressibility evaluation results show that the formula 1, 2, and 3 qualified with compressibility value is 7.9941 respectively; 6.9929; and 5.9950%. From the results of the one-way ANOVA analysis of the compressibility obtained sig. 0,000 less than 0.05, then there is a significant difference between formula one with the other formulas.

CONCLUSION: It shows the difference in temperature affect the compressibility pregelatinized taro starch. The higher the temperature of pregelatinized taro starch, produces tablets with low compressibility.

Introduction

Excipients are pharmaceutical additives, the inactive ingredients used to make up a medication. They include dyes, flavors, binders, emollients, fillers, lubricants, preservatives, and many more classifications. Common excipients used as fillers include starch [1], [2]. The filler material is the material used in the manufacture of tablets that are intended for weight, tablet size as required, to assist in making tablets, and to improve the quality of tablet preparations [3].

To provide satisfactory performance in a tablet dosage form, a diluent should be [4]: 1. Inert so as not to cause pharmacological activity of its own; 2. Compatible with the drug substance and other

excipients used in the formulation; 3. Non-hygroscopic so the formulation does not absorb significant amounts of moisture from its surroundings; and 4. Compactable and of similar particle size to the active ingredient.

Starch is one of the most abundant natural carbohydrates stored in plants. It is found in many different plant organs including seeds, fruits, tubers and roots, functioned as a source of energy. Although starch is idespread, abundantly available, cheap, degradable, pollution-free and renewable, it has many short falls, i.e., insoluble in cold water, easy to dehydration, low emulsifying power and unstable in acid, due to which commercial application is limited.3 A survey of the literature shows that the usefulness of starches from various botanical sources as pharmaceutical excipients [4]. Starches are widely

available and have been very useful in tablet production due to their inertness, cheapness and utilization as fillers, binders, disintegrants and glidants [5].

However, the use of starch is limited by its poor functional properties of flow, compressibility and compatibility. Several modifications have been shown to improve these functional properties [6]. Modified starches, also called starch derivatives, are prepared by physically, enzymatically or chemically treating native starch, thereby changing the properties of the starch. The different types of modifications include heat gelatinization, enzymatic hydrolysis, acid hydrolysis and other various forms of chemical modifications [7].

Pregelatinization is a process of changing the structure of starch both physically and chemically, by heating the starch suspension at a temperature of 62-72°C [8]. The temperature at which gelatinization of a starch occurs. The *gelatinization temperature* is dependent upon such factors as starch concentration, pH of the suspension, rate of heating, the presence of certain salts, and the specific procedure being followed. Under well-defined conditions, starches can be classified using gelatinization temperature as a means for differentiation. The properties of the starch granule are dependent upon the arrangement of the bonds which link glucose units to one-another within the starch molecule itself [9].

The starch used for making pregelatinized starch is taro starch (*Colocasia esculenta* (L.) Schott). Taro has abundant productivity, but the utilization of taro has not been explored to its full potential. Utilization of taro in rural communities is limited to frying or steaming. The community does not know much about the advantages of taro which have bioactive compounds that can be used as functional food [10]. Carbohydrate levels found in taro tubers were 88.03%. Carbohydrates consist of fraction of starch and crude fiber. Both of these fractions are important parts that can be used as bioactive components of taro [11].

The increasing use of heat causes the hydrogen bond between amylose and amylopectin to weaken so that the starch granule absorbs water and expands rapidly to obtain a larger particle size. Larger particle size will improve the flow and compressibility properties of granules. Partial pregelatinized starch is usually used for tablet formulations as fillers with concentrations of 5-75%, binders with a concentration of 5-20% and crushers with concentrations of 5-10%. Pregelatinization is made by heating the starch suspension containing water not less than 42% by weight of starch at a temperature of 62-72°C [8].

At this temperature difference whether it will affect the compressibility and compatibility of the thiamine hydrochloride tablet formulation produced. Compressibility and compatibility affect the manufacturing process of tablets, the smaller the

percentage of compressibility, the easier the print mass is compressed, while the compatibility is powder or granules to be compressed into tablets. In this study 3 formulas were used with a temperature increase of pregelatinized taro starch (*Colocasia esculenta* (L.) Schott) ie 50, 60 and 70°C.

Material and Methods

Material

Oven (Mettler), single punch tablet machine, friability tester (Guoming CS-2), desintegration tester (BJ-2), hardness tester (Min hua YD-3), tapped density tester, granule flow tester, analytic scale (Ohaus), multilevel sieve, stopwatch, UV-Vis spectrophotometer (Shimadzu UV-1601), volumetric flask, volume pipette, waterbath (Eyela OSB-2100), crucible, desiccator and other glassware.

Thiamine hydrochloride, taro starch, PVP, talc, magnesium stearate, primojel, and aquadest, iodine solution, HCl solution, ethanol.

Examining the characteristics of taro starch

The examination included organoleptic, organoleptic analysis was carried out by observing the shape, color, and odor. Iodine reaction, loss on drying and residual annealing.

Pregelatinized taro starch

Taro starch was weighed approximately 500 grams, then suspended in water in a ratio of 1: 4 (500 grams of starch in 2.0 liters of water). Then the suspension is heated over the waterbath at a predetermined temperature, ie 50, 60, and 70°C for 10 minutes, until it produces thick starch or starch suspension. After obtaining starch suspension from each temperature, the suspension was dried with a dryer used, ie oven at $\pm 50^\circ\text{C}$ for 48 hours. The results obtained are smoothed using mortar and stamper to become fine powder. After that the powder is sieved with a mesh 30 sieve. The aggregated taro amyllum is stored in a dry and clean container [12]. Furthermore, the aggregated taro starch was tested for flow time and angle of repose.

Formulation of Thiamine Hydrochloride Tablets

Thiamine hydrochloride tablets are prepared by wet granulation method. Each formula is prepared with a segregated taro starch at different temperatures. The formula can be seen from Table 1.

Table 1: Formula of Thiamine Hydrochloride tablets

| Material | Formula (%) | | |
|---------------------------------------|-------------|-----|-----|
| | F1 | F2 | F3 |
| Thiamine Hydrochloride | 25 | 25 | 25 |
| PVP | 3 | 3 | 3 |
| Primogel | 5 | 5 | 5 |
| Talc | 1 | 1 | 1 |
| Mg stearate | 0.5 | 0.5 | 0.5 |
| Pregelatinized taro starch at 50°C ad | 100 | - | - |
| Pregelatinized taro starch at 60°C ad | - | 100 | - |
| Pregelatinized taro starch at 70°C ad | - | - | 100 |

Tablets are made with wet granulation method. After the raw material is weighed, the inner phase is mixed, namely thiamine hydrochloride and pregelatinized taro starch. Then the binder is made by dissolving PVP with 96% alcohol until it dissolves. Then the binding in several phases in many parts can create a mass that can be clenched and can be broken but not destructive. The wet mass that has been homogeneous is sieved with sieve No. 16, then dried at a temperature of 50-60°C, then sieved with sieve No. 20. Then enter the outer phase, namely primojel, mg stearate, and talc into a dry granule, mix until homogeneous. evaluation include granule flow, angle of repose, particle size distribution, compressibility, compatibility and compactibility and granule loss on drying. The granule is pressed into a tablet. The tablets produced were evaluated in the form of Organoleptic test, size uniformity, weight uniformity, hardness, friability, disintegration time, assay and uniformity.

Results

The used taro starch was obtained from Indonesian Spice and Medicinal Crops Research Institute (ISMCRI).

Table 2: Characteristics of Taro starch

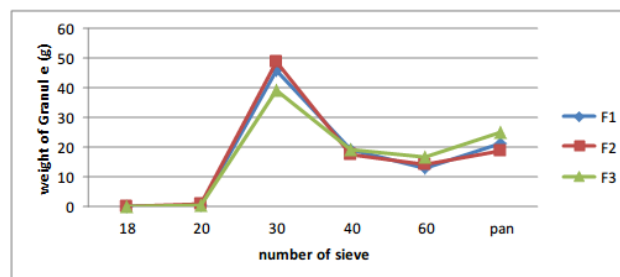
| No. | Evaluation | Result | Standard |
|-----|--|--|-------------|
| | Organoleptic: | | |
| 1. | a. Shape b. Odor c. Taste d. Colour | a. powder b. Odorless c. Tasteless d. Beige | - |
| 2. | Loss on drying | 9.42% | < 15% [13] |
| 3. | Sisapemijaran | 0.43% | < 0.6% [13] |
| 4. | Iodine reaction | + (dark blue) | dark blue |

The evaluation of taro starch was carried out to test the characteristics of taro starch in accordance with the literature.

Table 3: The evaluation result of granule

| Evaluation | F1 | F2 | F3 | Standart |
|------------------------------|--------|--------|--------|----------------|
| Loss in drying (%) | 5.1157 | 5.0331 | 5.1314 | 2-4% [14] |
| Granule flow tester (second) | 7.3 | 8.1 | 7.3 | ≤ 5 detik [14] |
| Angle of repose (°) | 31.42 | 30.09 | 28.49 | 25-45° [14] |
| Compressibility (%) | 7.9941 | 6.9929 | 5.9950 | < 20% [14] |

The evaluations carried out included organoleptic, chemical reactions, drying losses and residual spawning.

**Figure 1: Granule size distribution**

Discussion

Organoleptic tests were carried out to determine the shape, color, taste and aroma of taro starch using the five senses. The results obtained from taro starch have the form of powder, creamy, tasteless and odorless.

Table 4: The evaluation result of Compatibility

| Punch drop on (mm) | Hardness (kg) | | | Compactibility |
|--------------------|---------------|------|------|-------------------|
| | F1 | F2 | F3 | |
| 0 | - | - | - | - |
| 1 | - | - | - | - |
| 2 | 0 | 0 | 0 | - |
| 3 | 0.02 | 0.04 | 0.07 | - |
| 4 | 0.02 | 0.05 | 0.05 | - |
| 5 | 0.13 | 0.15 | 0.13 | - |
| 6 | 0.21 | 1.72 | 1.85 | - |
| 7 | 5.75 | 6.18 | 6.22 | Compact and shiny |

In the qualitative test of the identification of starch, Taro starch which has been suspended into water and then heated to form a colloidal solution which is then cooled shows a dark blue color change if reacted with iodine, this color change is reversible which blue color will disappear when reheated. This reaction shows positive powder containing starch.

Table 5: The evaluation result of tablets

| Evaluation | F1 | F2 | F3 | Standart |
|--------------------------|--------|--------|--------|--|
| Diameters (cm) | 0.80 | 0.80 | 0.80 | 11 / 3 thick tablets < diameter < 3 times the thickness of the tablet [13] |
| Thickness (cm) | 0.22 | 0.31 | 0.31 | - |
| Hardness (kg) | 4.96 | 6.02 | 4.35 | 4-8 kg [15] |
| Friability (%) | 0.2904 | 0.2168 | 0.3763 | ≤ 1% [13] |
| Disintegration (minute) | 6.39 | 5.30 | 5.49 | < 15 menit [13] |
| uniformity (% deviation) | 2.4149 | 1.5277 | 1.5192 | 7.5-15% [13] |
| assay (%) | 98.28 | 98.68 | 100.77 | 90-110% [13] |
| uniformity (RSD) | 1.90 | 1.85 | 3.08 | ≤ 6% [13] |

Loss on drying (LOD) test is carried out to determine the amount of part of the substance that evaporates. The results of the LOD test is 9.42%. The value meets the starch LOD requirements according to the Indonesian Pharmacopoeia, which is not more than 15% [13]. The remaining test results of the annealing are 0.43%, according to the standard that the remaining spawning permitted based on the Indonesian pharmacopoeia is not more than 0.6% stated on manihot starch.

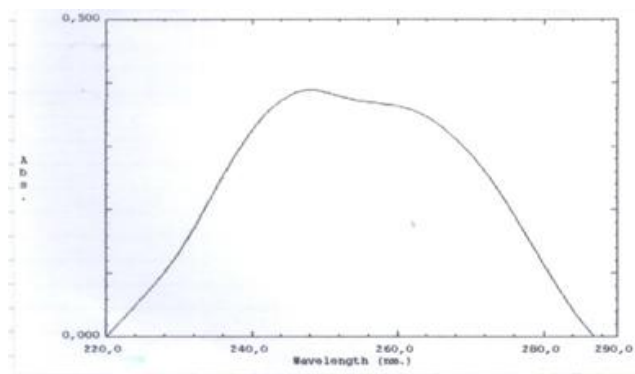


Figure 2: Wavelength Thiamine Hydrochloride Curva

Preparation of pregelatinized taro starch is carried out first in orientation to the ratio of taro starch and water, namely 1: 1, 1: 2, 1: 3, and 1: 4 with pregelatinization temperatures of 50, 60, 70, and 80°C above water bath for 10 minutes, which then filtered and dried in an oven at 50°C for 48 hours. Then the aggregated starch formed is crushed and sieved with 30 sieves. The orientation results at 80°C in all comparisons have formed a gel. So that this temperature cannot be used. So, the temperature used in this study is the temperature of 50, 60, 70°C in the ratio of taro starch and water is 1: 4. A ratio of 1: 4 was chosen because it produced more amount of pregelatinized taro starch.

Evaluations carried out included the flow properties of pregelatinized taro starch compared to the flow properties of taro starch. The results of taro starch and pregelatinized taro starch did not have good flow properties. Because when tested, the powder of starch starch and pregelatinized taro starch does not flow (compressed) and the angle of repose cannot be measured because the fall of the powder spreads irregularly.

The evaluated taro starch is then modified to pregelatinized taro starch which will be used as a filler for thiamine hydrochloride tablets with wet granulation method. The composition of the tested tablet formula contained the same levels of active substances and excipients, but the difference lies in the pregelatinizing temperature used from each formula, namely 50, 60, and 70°C with the aim to determine the effect of the increasing pregelatinizing temperature of taro starch.

In this study wet granulation method was used because wet granulation is the widest method in making tablets, producing more homogeneous granules and almost all types of active substances can be processed by wet granulation methods. The process of making granules begins by weighing thiamine hydrochloride and pregelatinized taro starch until homogeneous as the inner phase. PVP binder was dissolved in 96% ethanol as much as 5 ml until the dissolved PVP was complete and then added to the inner phase and added to aquadest until a banana breaking mass was formed which then carried

out wet sifting by passing the tablet mass at sieve no. 16, This sifting aims to reduce the particle size so that the ingredients can be evenly mixed during granulation with the desired particle size distribution. Then drying is done which aims to remove the binding solvent that has been added before so as to produce dry granules. Furthermore, it was dried in an oven at 50°C for 18-24 hours to remove the solvents used in the formation of lumps and to reduce moisture. After drying, the granules are sifted back with screen number 20. The size is then sieved again with 20 sieves. The sieve used depends on the diameter of the punch to be used. The outer phase to be used is primojel, mg stearate, and talc added to the dry granule then stirred until homogeneous and granulate evaluation.

Granule evaluation includes granule flow tester, angle of repose, particle size distribution, compressibility, compatibility and compactibility. This evaluation is important because the properties of granules can affect the tablets produced. Generally, good granule properties can produce good tablets.

The results of the evaluation of loss on drying (LOD) do not meet the requirements. The LOD of granular drying is 2-4%. This happens because the resulting granule contains a lot of water. The High value of LOD can interfere with the granule flow, while drying losses that are too small can make the granule crisp or brittle.

The results of the evaluation of the flow rate of thiamine hydrochloride tablet granules from the three formulas did not meet the requirements of less than 5 seconds. This is related to the condition of moist granules. Then an evaluation of the stationary angle is carried out. The smaller the angle that is formed, the better the flow properties. Judging from the stationary angle produced, the flow properties of the three formulas are still good because they are less than 45° [3] properties are also determined by the compressibility value. Compressibility is an important stage in making tablets. The smaller the percentage of compressibility, the better the flow properties and the easier the granules are compressed into tablets. All formulas have a compressibility percentage that meets the requirements, but granule formula 3 has a good compressibility percentage, which is 5,995 from other formula granules. The terms of the compressibility percentage with very good grades are < 15%. Flow properties are very important because they relate to the uniformity of filling mold space which will affect uniformity of weight and will ultimately affect the uniformity of the active substance content [14].

The particle distribution test is intended to determine the particle size and particle dispersion. The size and dispersion of the particles need to be known because this can affect the flowing properties of the powder which can affect the average weight of the tablet, variations in tablet weight, granule crispness, and granular flowability. The test results of

particle size distribution of all granule formulas scattered on no mesh sieve 30. A good size distribution of curves follows the normal curve of the bell-shaped particle size distribution, where the number of large particles and small particles is equal and the number of particles is the most. The test results show that the particle size distribution of the third formula granule does not follow the normal curve because the number of granules left behind is more stored than in the no mesh 60 sieve.

The next granule test is the test of compatibility. Tests are carried out to determine the ability of the powder to be printed into a tablet. From the granulability comparability test data on all formulas have good compatibility because the 2 mm punch reduction has been formed into a tablet with a hardness of 0 kg ($F = 2$), but at the maximum emphasis on tablet hardness in formula 3 is higher than formula 1 and 2, namely amounting to 6.22 kg. This is probably due to the fact that granules in formula 3 have a high bulk density, because the higher the bulk density, the higher the hardness of the tablet. And the upper punch drop can only be done up to 7 mm. At 7 mm punch decrease visually seen the physical shape of the tablet is compact and shiny.

Organoleptic evaluation of tablets is important to control tablet appearance uniformity, consumer acceptance, and to monitor the correct manufacturing process. Evaluation is done by observing the shape, color, odor and taste. The evaluation results showed that all three tablet formulas did not have organoleptic differences. This implies that the effect of temperature in making this pregelatinized starch does not affect the organoleptic of the tablet. In evaluating tablet size uniformity, the evaluation results obtained show that all three formulas meet the requirements of Indonesian Pharmacopoeia.

Tablet hardness is affected by the pressure applied during the printing process and the nature of the material being compressed. In general, the greater the pressure, the tablet produced will be harder and harder, although granular properties can also affect tablet hardness. The hardness of the tablet greatly affects the fragility and disintegration time of the tablet, the higher the hardness of the tablet, the longer the time of destruction. Tablet hardness obtained from formula 1 to 3 is 4.96; 6.02; 4.35 kg., Formulas 1 to 3 meet the tablet requirements of 4-8 kg [15].

The test of friability and disintegration time of the tablet useful to determine tablet resistance to shocks that occur during the manufacturing process, packing, transportation, to use by consumers. The greater the percentage friability value, the greater the value of the lost tablet life. The evaluation results of the fragility test of the three formulas met the requirements, which is less than 1% [3]. While the tablet crush test determines whether the tablet can be destroyed in a certain time when placed in a liquid medium in certain experimental conditions [16].

According to the Indonesian Pharmacopoeia the requirements for time-out tests for tablets are not coated not more than 15 minutes (900 seconds).

Based on the results of uniformity of weight, no more than 2 tablets deviate greater than 7.5% and none deviate greater than 15%, so it can be stated that all four formulas meet the requirements for weight uniformity in the Indonesian Pharmacopoeia III edition. The uniformity of the weight of the tablet depends on the flow rate of the granule from the hopper to the mold space.

In the assay determination test in each formula so that obtained thiamine HCl levels in formula 1 = 98.28%; formula 2 = 98.68%; and formula 3 = 100.77%. The calculation of the level determination was carried out with the linear regression value made with 2% HCl media in accordance with what was stated in the Indonesian Pharmacopoeia. Followed by testing the uniformity of thiamine hydrochloride tablet content, the results obtained show that all tablets of each formula meet the requirements of Indonesian Pharmacopoeia, namely the relative standard deviation of thiamine hydrochloride is less than 6%. The level of thiamine hydrochloride per tablet is within the range of Indonesian Pharmacopoeia requirements, ie not less than 90.0% and not more than 110% of the amount stated on the label. The content uniformity obtained from the three formulas ranged from 100.7041-104.1134%. The variation in the level of active substances in the tablet is influenced by several factors, including mixing factors that are less homogeneous and the flow properties of the powder from hopper to die.

Furthermore, data from the evaluation of compressibility is analyzed by data. Statistical analysis uses one-way ANOVA and is followed by the Honestly Significant Differences (Tukey HSD) test. In testing the normality and homogeneity of compressibility data obtained sig value greater than 0.05, the data is normally distributed and homogeneous, so that the analysis can be continued with one-way analysis of variance (ANOVA). From the results of one-way ANOVA analysis on compressibility obtained sig values. 0,000 is less than 0.05. This shows that there are significant differences between formulas so that it must be continued with the Tukey test. Based on the results of ANOVA testing showed that the pregelatinizing temperature difference affects compressibility. The data then continued with Tukey testing with a 95% confidence level or significance $\alpha = 0.05$. The Tukey test was conducted to see more clearly the meaningful differences in each formula. The test results on compressibility in formulas 1, 2 and 3 showed that there was an effect of increasing the pregelatination temperature on the compressibility of thiamine hydrochloride tablets.

In conclusion, based on the results of the research that has been done, it can be concluded that

an increase in the temperature of pregelatinized taro starch can reduce the compressibility of thiamine hydrochloride tablet formulations. The higher the temperature of pregelatinized taro starch used, the lower the compressibility, so that it can be seen that at a temperature of 50-70°C it indicates that there is a decrease in compressibility. The effect of this temperature can accelerate the formation process of pregelatinized starch. From the three formulas shows that the compressibility value meets the requirements of each is 7.9941; 6,9929; and 5.9950%. While the value of the comparability of each formula has a value of $F = 2$, meaning that the value of the compatibility is formed at a decrease in the upper punch by 2 mm.

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