

## Formulation of *Peperomia pellucida* (L) Kunth extract tablet by modified filler

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### Abstrak

**Latar belakang:** *Peperomia pelusida* telah banyak digunakan dalam pengobatan tradisional. Pada saat ini, bentuk-bentuk yang ada masih konvensional seperti jus dan infusum, karena itu, perlu dirumuskan lebih praktis dan berat seragam seperti bentuk tablet. Tujuan dari penelitian ini adalah untuk mendapatkan formula optimum pelusida tablet ekstrak *P. pellucida*.

**Metode:** *P. pelusida* ekstrak tablet yang diproduksi dengan variasi selulosa mikrokristalin (MCC) PH 101 - laktosa dengan metode granulasi basah dalam tiga formula, formula I (100% MCC PH 101), II (laktosa 100%), dan III (MCC PH 101: laktosa = 50%: 50%). Butiran dievaluasi karakteristik fisik termasuk laju aliran, penyerapan air, dan kompaktilitas untuk mendapatkan formula optimum dengan menggunakan desain simplex lattice dan jumlah respon. Formula yang digunakan untuk membuat tablet dan diuji karakteristik fisik (keseragaman bobot, kekerasan, dan kerapuhan dan waktu hancur).

**Hasil:** Laktosa secara signifikan dipengaruhi oleh laju alirannya, sedangkan MCC PH 101 - laktosa dengan metode granulasi basah dalam tiga formula, formula I (100% MCC PH 101) dipengaruhi penyerapan kompaktilitas dan air. Berdasarkan karakteristik fisik granul dan jumlah responsnya, kombinasi formula MCC PH 101 80% dan laktosa 20% dapat disimpulkan menjadi yang paling optimal untuk tablet filler. Formula tablet ini yang memiliki karakteristik fisik terbaik dengan berat  $620,84 \pm 1,04$  mg, kekerasan  $8,54 \pm 0,68$  kg, kerapuhan  $0,26\% \pm 0,04$  dan waktu hancur  $4,58 \pm 0,17$  menit.

**Kesimpulan:** Proporsi MCC PH 101 80% dan laktosa 20% merupakan formula optimum terbaik dan memenuhi persyaratan karakteristik fisik tablet. (*Health Science Indones 2013;1:32-6*)

**Key words:** formulasi, extract *P. pellucida*, optimal

### Abstract

**Background:** *Peperomia pellucida* has been widely used in traditional medicine. Recently, its existing forms are still conventional such as juice and infusum; therefore, it needs to be formulated more practically and in uniform weight such as tablet form. The objective of this research was to get the optimum formula of *P. pellucida* extract tablet.

**Methods:** *P. pellucida* extract tablets were produced with variation of microcrystalline cellulose (MCC) PH 101 – lactose by wet granulation method in three formulas, formula I (100% MCC PH 101), II (lactose 100%), and III (MCC PH 101: lactose = 50%: 50%). Granules were evaluated their physical characteristics including their flow rate, water absorption and compactibility to obtain the optimum formula by using simplex lattice design and total response. The optimum formula was used to make tablet and tested its physical characteristics (uniformity weight, hardness, and friability and disintegration time).

**Results:** Lactose significantly influenced by its flow rate, whereas MCC PH 101 influenced the compactibility and water absorption. Based on the granules physical characteristics and their total responses, the formula combination of MCC PH 101 80% and lactose 20% was concluded to be the most optimum one for tablet filler. This optimum formula tablet had the best physical characteristics with weight uniformity of  $620.84 \pm 1.04$  mg, hardness of  $8.54 \pm 0.68$  kg, friability of  $0.26\% \pm 0.04$  and disintegration time of  $4.58 \pm 0.17$  minutes.

**Conclusion:** The proportion MCC PH 101 80% and lactose of 20% obtained the best optimum formula and passed requirements of the tablet physical characteristics. (*Health Science Indones 2013;1:32-6*)

**Key words:** formulation, *P. pellucida* extract, optimize

In general, people use *P. pellucida* as a cure for abscess, boil acne, gout, and headaches, analgesic, antipyretic and rheumatic. In Indonesia a tropical country, many *P. pellucida* grow well in the garden, rocks and rice field so it makes easier cultivated for large scale.<sup>1</sup> Pharmacological test results of *P. pellucida* used as antipyretic in rabbit.<sup>2</sup> Phytochemical screening of *P. pellucida* contains alkaloids, flavonoids, cardenolides, saponins and tannins.<sup>3</sup>

People consume *P. pellucida* in term conventionally forms such as juice and *infusum* so that it needs to be developed more practical form. *P. pellucida* extract tablet is an alternative dosage form that can be developed the tablet dosage forms considering has several advantages such as practical, stable and more uniform dose weight.<sup>4</sup>

Methods of tablet produced can be done by direct compression and granulation.<sup>5</sup> Granulation is to prevent the mixture mass segregation, improve flow properties as well as compactibility.<sup>6</sup> Granulation methods can be divided into wet granulation and dry granulation. In wet granulation, liquid binders are added in the process. While the dry granulation binders are added in the powder form.<sup>7</sup>

Excipients usually used in the tablet produced such as filler, binder, disintegrant, and sweetener, coloring and flavoring agent when needed. The fillers has been used in this research are microcrystalline cellulose (MCC) PH 101, lactose or a mixture of both. MCC PH 101 is a filler material that has a good ability to expand so that causing a short disintegration time to tablets. The flow rate was inhibited by the formation of hydrogen bridges, but good compactibility, very stable, and easy to compress.<sup>8</sup> Lactose was the most excipients has been widely used because it does not react with almost any active ingredient, fast dried granules but low disintegrant. Lactose has a good of flow rate.<sup>9</sup> The combination of MCC PH 101 and lactose were selected in this research can be gotten benefit to covered weakness of both. This encourages the efforts of formulation for combination of MCC PH 101 and lactose to get the best mix formula of both so that good tablet physical characteristics can be maintained.

One of methods to get the optimized formula is simplex lattice design. This method is suitable for formula optimization procedure which the total number of different ingredients is constant. This procedure can be used to determine the relative proportions of the ingredients to make the best formulation of the variables or expected outcomes.

Based on this method it can determine coefficient equation  $Y = a (A) + b (B) + ab (A) (B)$  which can be used to determine the proportion of couple factors that produce the desired responses.<sup>10</sup> The objective of this research is to optimize the formulation of *P. pellucida* extract to be a good tablet dosage with variation proportion of MCC PH 101 and lactose.

## METHODS

*P. pellucida* extracts made by maceration method using ethanol 70% as solvent. The filtrate has been evaporated on the water bath until get dry extract. *P. pellucida* extract obtained, added with aerosil, MCC PH 101 and or lactose by the number of different proportion according formula, mix until homogeneous. A solution of gelatin 10% (gelatin dissolved in aquadestillata) was added and stirred to get a ready granulated mass. Mass granules sieved with siever no. 16, the results were dried in an oven with a temperature of 40°-50°C. After dried, the granules sieved again with siever no. 18, then added sodium starch glycolate and magnesium stearate mix until homogenous. The composition of *P. pellucida* extracts tablet formula can be seen in the following table:

Table 1. Formula of *P. pellucida* extract tablet

Composition	Formula (mg)		
	I	II	III
<i>P. pellucid</i> extract	200	200	200
Aerosil	20	20	20
Microcrystalline cellulose PH 101	320	0	160
Lactosa	0	320	160
Gelatin	20	20	20
Sodium starch glycolate	54	54	54
Magnesium stearate	6	6	6
Tablet weight	620	620	620

The three formulas are tested in physical characteristics included flow rate, water absorption and compactibility. Based on the physical characteristics test of the granules can be calculated coefficients a, b and ab on the simplex lattice design equation  $Y = a (A) + b (B) + ab (A) (B)$  with (A) as a proportion of MCC PH 101 and (B) as a proportion of lactose. The optimum formula was determined by the total responses of the test results of the physical characteristics of the granules.

Largest total response selected as the condition of each response optimum. For Physical characteristics of the granules we give score to the total amount

of score equal was 1. The flow rate score of 0.4; compactibility score of 0.3, as well as water absorption score 0.3. Every of the different responses it is necessary to look for the value of the normality of response assessment. Values for X min flow rate was 8 g/sec, and X max of 16 g/sec; compactibility values for X min was 3 kg and X max of 10 kg; X min values for water absorption was 70 mg/min and X max of 150 mg min. So it is able to calculate the response using the equation:<sup>10</sup>

$$R = [(x-xmin) / (xmax-xmin)] \times \text{weight of the physical properties of the granules}$$

Remarks:

X = response obtained from the calculation of the equation SLD,

Xmin = minimum response

Xmax = maximum response

After known the optimum formula then it is used to make tablet and tested its physical characteristics included uniformity weight, hardness, and friability and disintegration time.

### RESULTS

The test results of granules such as flow rate, compactibility and water absorption of the *P. pellucida* extract formula can be seen in table 2.

Table 2. Physical characteristics of *P. pellucida* extract granules

Granules physical characteristics	Formula		
	I	II	III
Flow rate (g/sec)	9.25±0.11	14.49±0.23	12.25±0.12
Compactibility (kg)	9.82±0.12	5.19±0.12	7.60±0.17
Water absorption (mg/min)	134.80±1.07	82.92±0.22	115.71±0.34

Lactose significantly influenced by its flow rate, whereas MCC PH 101 influenced the compactibility and water absorption.

Determination of the optimum formula can not be done just by looking at each one generated of granule physical characteristics; because of each granule has a contribution in determining the quality parameters tablet. Therefore the optimization is done based on the total response of granule physical characteristics. Based on the results of the formula optimization calculation is obtained that a formula containing MCC PH 101 and lactose in the ratio 80%: 20% have the greatest value of the total response (0.603)

Table 3. Responses value physical characteristics of granules

Proportion	Flow rate	Compactibility	Water absorption	Total
100% MCC PH 101	0.063	0.292	0.243	0.598
90% : 10%	0.096	0.274	0.233	0.602
80% : 20 %	0.127	0.255	0.221	0.603
70% : 30%	0.157	0.236	0.206	0.599
60% : 40%	0.186	0.217	0.190	0.592
50% : 50%	0.213	0.197	0.171	0.581
40% : 60%	0.238	0.177	0.151	0.566
30% : 70%	0.262	0.157	0.128	0.547
20% : 80%	0.284	0.136	0.104	0.524
10% : 90%	0.305	0.115	0.077	0.497
100% lactose	0.325	0.094	0.048	0.467

The test results of the physical characteristics of optimum formula of *P. pellucida* extracts tablet was shown in Table 3.

In table 3 shows that tablets are produced to passed the requirements of the physical characteristics of the tablet.

Table 4. Physical characteristics of optimum formula *P. pellucida* extract tablets

Tablet physical characteristics	Results	Requirements
Uniformity weight (mg)	620.84±1.04	589-651
Hardness (kg)	8.54±0.68	>4
Friability (%)	0.26±0.4	<1
Disintegration time (min)	4.58±0.17	<15

### DISCUSSION

The physical characteristics test of granules are meant to produce a profile of the physical characteristics of a mixture of equations and calculations based on simplex lattice design. This profile is used to determine the optimum formula seen of granules quality. The results of granules characteristics such as flow rate, compactibility and water absorption test is used to determine the optimum formula.

The flow rate of granules would influenced the tablet uniformity weight. The results of flow rate through the granules approach of simplex lattice design equation for flow properties by follow:

$$Y = 9.25 (A) 14.49 + (B) + 1.52 (A) (B)$$

The equation shows that lactose 100% has greater impact (coefficient = 14.49) to the flow rate than MCC PH 101 (coefficient = 9.03). Reduced levels of

lactose in the mix will decrease the speed response of flow rate. This can be caused by the density of lactose that is larger than MCC PH 101 and the flow rate of MCC PH 101 is inhibited by the hydrogen bridge.<sup>8,11</sup>

Granules compactibility test is intended to determine the ability of the material to form a compact mass after a given pressure. Compactibility of granules can be determined by testing the hardness tablet obtained using hardness tester. To compare each granule compactibility of granules per formula the volume and pressure of compression are controlled to be same for every formula because it will influenced of the tablet hardness.<sup>12</sup> the equation of compactibility profiles test:

$$Y = 9.82 (A) + 5.19 (B) + 0.38 (A) (B)$$

The equation shows that the MCC PH 101 (coefficient = 9.82) gives a greater influenced on compactibility than lactose (coefficient = 5.19). The combination MCC PH 101 and lactose will increase granules compactibility by adding proportion of MCC PH 101. Because of MCC PH 101 is able to provide inter-particle bonding that is stronger than lactose, so the granules are formed will provide better compactibility. The compactibility of granules will be influenced of tablet hardness.<sup>12</sup>

The water absorption test is an important parameter because it was directly related to the ability of tablet to release active ingredients. From the test results of the water absorption granules based approach simplex lattice design equation:

$$Y = 134.80 (A) + 82.92 (B) + 27.40 (A) (B)$$

The above equation shows that the MCC PH 101 (coefficient = 134.80) gives a greater influenced on water absorption than lactose (coefficient = 82.92). The combination of MCC PH 101 and lactose will increase granules water absorption by adding proportion of MCC PH 101. Granules absorption influenced on tablet disintegration time. The influenced factors of the penetration are dependent compression where the tablet porosity and water absorption ability of the material used. The disintegrant began to work through the development process, a chemical reaction or enzymatically after water got into tablet.<sup>4</sup>

Total response was calculated by summing the response of each of the physical properties of the granules. Based on the results of the optimization calculation formula, it is obtained that the formula containing MCC PH 101 and lactose in the ratio 80%: 20% had the greatest total value of the response

(0.603) in the proportion of mixed optimization MCC PH 101 and lactose is to consider the physical properties of the resulting granules, including flow rate, compactibility and absorption of water. Flow rate will affect the uniformity of weight, compactibility effect on tablet hardness and brittleness, while the absorption of water can affect tablet disintegration time. Physical properties of the granules are important to note that gives the parameters that will greatly affect whether or not tablets are produced.<sup>13</sup>

After obtaining the optimum formula, granules had been made. The composition of filler used MCC PH 101 and lactose in the ratio 80%: 20%, their equivalent with MCC PH 101 as much as 256 mg and 64 mg lactose. Besides as filler, MCC PH 101 can serve as a binder and a disintegrant of both the wet granulation method and direct compress. While lactose act as a filler, and also serves as binder.<sup>11</sup> the granules was obtained compress into tablets and physical characteristics tested such as uniformity weight, hardness, friability and disintegration time. Test data of tablets physical characteristics can be seen in Table 3.

The uniformity weight is a very important parameter in the quality of the tablet, as it affects the uniformity levels of the active substance. Tablets with an average weight of more than 300 mg, there should be no two tablets that deviate 5% of the weighted average rata.<sup>4</sup> The results of this study indicate that the tablets pass the requirements. This proves that the formula chosen above has a good flow rate.

Tablet hardness test performed to describe the endurance of tablets by pressure, shake, and erosion during the process of production, packaging, transport or distribution. The value of good tablet hardness at least was 4 kg in this research,<sup>4</sup> a tablet obtained amount of 8.54 kg, pass the requirement as good tablet. The proportion of MCC PH 101 is greater than lactose showed a good tablet characteristics.<sup>14</sup>

The friability describes tablet strength to be related with the bond strength of the particles on the edge or surface of the tablet. The tablet friability test results using friabilator obtained optimum formula is a good amount of 0.26%. The friability tablet was eligible if less than 1%.<sup>15</sup>

The disintegration time describes the time required by the tablet to disintegrate in the body fluids. The process of disintegration of the tablet was preceded by the absorption of water so that the tablet can be divided into parts. The results of tablet disintegration

time tested of optimum formula on *P. pellucida* extract obtained optimum results and pass requirements that is amount of 4.58 minutes less than 15 minutes for a uncoated tablet.<sup>4</sup> The good disintegration time was due the ability of an excellent filler to absorb water and expands, so it is resistance to the strength of the bond between the larger particles.<sup>14</sup> The consequently was the tablet will rapidly disintegrate.

In conclusion, proportion of MCC PH 101 80% and lactose 20% provide optimum results on the physical characteristics of granules and produce *P. pellucida* extract tablet that is pass requirements of the physical characteristics.

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