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Research Article

The Formulation of Pacing (*Costus speciosus*) Extract Tablet By Using Avicel®PH 200 As Filler-Binder and Amylum as Disintegration Agent

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ABSTRACT

Pacing (*Costus speciosus*) is an herbaceous plant that is native to Indonesia and it can be used as a male contraceptive due to spermatogenesis inhibition. The purpose of this study is to find out the composition of optimum Avicel PH 200® as the filler-binder and amylum as the disintegration agent and to find out the variations on physical properties of the powder and tablet. Tablets of *Costus speciosus* extract (CS tablet) were produced by direct compression in 8 runs based on Simplex Lattice Design (SLD) from Design Expert 7.1.5. Evaluation on physical properties of powder included tapping index, water absorption, and moisture content, while evaluation on the physical properties of tablet included hardness, friability, and disintegration time. The results showed that the variation in the composition between Avicel® PH 200 as the filler-binder and amylum as the disintegration agent had a significant effect on the friability of CS tablet, in which the combination of both materials can increase the friability of the tablet. The optimum formula of CS tablet had a composition of Avicel® PH 200 by 462.5mg and amylum by 37.5mg contained in each tablet.

Keywords: tablet, Avicel® PH 200, amylum, *Costus speciosus*

INTRODUCTION

Pacing (*Costus speciosus*) is an herbaceous plant that is native to Indonesia. It can be used as an effective male contraceptive may be because it contains diosgenin which is capable of inhibiting spermatogenesis (Sari, 2016[a,b]). Sari *et al.* (2016[b]) reported that there is no significant obstruction of both physical symptoms as well as blood and urine biochemical parameters in the subchronic toxicity test conducted after the administration of CS extract for 90 days in the dose range of 275-1100 mg/kg of Body Weight (BW), therefore considered safe. In order to increase men's participation in the use of contraceptive, there is a need to develop male contraceptive from *Costus speciosus* herbaceous plant into an easy-to-use pharmaceutical preparation in the form of tablet. Tablet is preferred because it is stable in storage and easy to use.

The dried CS extract is hygroscopic and has a poor fluidity. It will be difficult to make a tablet dosage form without any filler used in the compression and the tablet will be friable ,thus, it cannot be stored for a long term period. In order to overcome these problems, an excipient is required to improve the fluidity of the powder and to cover the hygroscopic property of the extract. Avicel® PH 200 was used as a *filler-binder* in an average particle size of 180 μm (Guy, 2009) in order to improve the fluidity of the powder, so as to enable it to be compressed directly. The disintegration agent will help the break of the tablet after allowing water or gastric fluid into its constituent particles. Considering the importance of filler and disintegration agent, the optimization of CS herbal extract formula was conducted. The variation of composition of Avicel® PH 200 as *filler-binder* and amylum as disintegration agent with the Simplex Lattice Design (SLD) of Design Expert 7.1.5 was determined in this research.

The purpose of this study is to find out the optimum composition of Avicel®PH 200 as the filler-binder and amylum as the

disintegration agent related to physical properties of the powder and tablet of CS extract.

METHODOLOGY

Equipment and materials

Materials used are: dried CS extract (PT. Phytochemindo Reksa), Avicel® PH 200 (FMC Biopolymer), amylum (Bratachem), stearic magnesium (Bratachem), mannitol (Bratachem), aspartame (Bratachem), talcum (Bratachem) and aerosil (Brataco).

Research procedures

Formula CS tablet

The tablet was made in 8 runs with a variation in composition of Avicel® PH 200 and amylum (Table I). Avicel® PH 200 is used as filler binder and amylum is used as disintegration agent. The amount of Avicel® PH 200 in each tablet is 387.5-462.5mg (51.6-61.67% of tablet total weight). The amount of amylum in each tablet is 37.5-112.5 mg (5-15% of tablet total weight). Avicel can use as tablet filler binder in concentration at 20-90 % (Guy, 2009) and amylum can use as tablet disintegration agent in concentration at 3-25% of tablet total weight (Hausler, 2009).

Preparation of the powder

The CS extract was mixed by Avicel® PH 200 in a *cube mixer* for 5 min at the speed of 20rpm. The powder was added by amylum, stirred for 5min at the same speed. The powder was then added by mannitol, Mg stearic, and aerosil and was stirred for 5min at the same speed. The powder was then put into the oven for 1h at temperature 50°C until it became dried, and was then sieved with sieves no.12 and no.16.

Evaluation of physical properties of the powder

Powder was mixed each other and homogenized then measured its physical properties of the powder, included fluidity testing by tapping device, water absorption, and moisture content.

Tapping test

The powder was poured slowly to volumenometer glass until 100mL, noted as V_o. Then volumenometer glass was set on the tapping device and run in 4min. The volume after tapping process was noted as Vt. Calculation of tapping test was measured by equation 1.

$$\text{Tapping result (\%)} = \frac{Vo - Vt}{Vo} \times 100\% \quad \ldots\ldots\ldots (1)$$

Vo = initial volume; Vt = finish volume

Water absorption test

The powder was put on the wetting paper. The diminish of water weight which measured on the analytical balance was comparable with the amount of water which was absorped by the powder, showed by equation 2.

$$\text{Capacity of water absorption (\%)} = \frac{Wb}{Wa} \times 100\%$$

W_b= Weight of the water which was absorped by powder after 15min; W_a= Weigh of powder after testing

Moisture content measurement

Approximately 500mg dried powder was set on the moisture content tester and then the powder was measured its moisture content.

Evaluation of Physical Properties of CS Tablet

The powder was pressed using a tablet press machine and was adjusted to 750mg (CS) as the desired weight and pressure with a hardness range of 4-8kg. The tablet was then tested for its physical properties, including organoleptic, hardness, fragility and disintegration time.

Organoleptic Test

The organoleptic test for the tablet used body sensory, included: the shape, taste, smell, and color.

Hardness Test

Hardness tester was set to zero. The tablet was placed on the tip of the compressor at a perpendicular position to the machine.

Table I. The Composition of run of CS tablets with SLD

Materials	***Run* 1**	***Run* 2**	***Run* 3**	***Run* 4**	***Run* 5**	***Run* 6**	***Run* 7**	***Run* 8**
Costus speciosus Extract (mg)	210	210	210	210	210	210	210	210
Avicel® PH 200 (mg)	406.25	462.5	425	387.5	443.75	462.5	425	387.5
Amylum (mg)	93.75	37.5	75	112.5	56.25	37.5	75	112.5
Mg stearic (mg)	7.5	7,5	7.5	7.5	7.5	7.5	7.5	7.5
Mannitol (mg)	25	25	25	25	25	25	25	25
Aerosil (mg)	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Total Weight (mg)	750	750	750	750	750	750	750	750

Tabel II. The result of physical properties extract CS powder

Run	**Tapping index (%)**	**Water absorption (mg/mg)**	**Moisture content (%)**
1	15.33 ± 2.08	1.17 ± 0.25	4.2 ± 0.55
2	16.33 ± 1.33	1.70 ± 0.04	3.90 ± 0
3	18.50 ± 1.50	1.71 ± 0.02	4.85 ± 0
4	18.67 ± 0.58	1.45 ± 0.14	4.85 ± 0
5	16.00 ± 1.04	1.67 ± 0.12	1.67 ± 0.58
6	18.67 ± 0.58	1.64 ± 0.11	4.85 ± 0
7	19.17 ± 0.76	1.62 ± 0.03	4.85 ± 0
8	19.67 ± 0.58	1.61 ± 0.17	5.85 ± 0

The compressor was turned slowly until the tablet broke. The scale on the machine showed the hardness level of the tablet expressed in kg unit.

Friability test

A number of dust-free tablets were weighed and put into the abrasive tester. The machine was run at 25rpm for 4min. The tablets were removed and freed from dust once again, and were then weighed. The percentage of weight loss indicates the fragility of the tablet, calculated by the following equation (2).

$$K = \frac{W_0 - W_1}{W_0} \times 100\% \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (2)$$

W_0 = Initial weight of tablet; W_1 = Weight of tablet after the test

Test of disintegration time

About 5 tablets were put into a disintegration tester tube. The tube was put into a beaker glass containing 750mL of water at 37°C temperature. The tube was put up and down regularly at 30 times speed per minute. The time required from the start of the device until no part of the tablets are left on the screen wire was recorded as the breaking time of the tablets.

The determination of optimum formula using SLD and the evaluation of optimum formula of the tablet

The data obtained from the test of physical properties of the tablets, including the response of hardness, friability, and disintegration time of each run was processed using SLD and thereafter the optimum formula could be determined.

RESULTS AND DISCUSSION

The result of powder properties

The result of powder properties is shown in table II.

Tapping test

The powder from 8 runs have tapping index less than 20%. It means, the powder has the good fluidity.

Water absorption test

The table II shows that water absorption of the powder has variation in result, with the variation range 1.17±0.25-1.71±0.02 mg/mg.

Table III. The equation of powder properties from simplex lattice design

No.	Response	Equation
1.	Tapping index (%)	Y = 0.033(A)+0,0507(B)
2.	Water absorption (mg/mg)	Y= 3.821 x 10^{-3}(A)+8.244 x 10^{-3}(B)–2.155 x 10^{-5}(A)(B)
3.	Moisture content (%)	Y = 5.893 x 10^{-3}(A)+0.025(B)

Note: A: Avicel® PH 200 fraction; B: Amylum fraction

Table IV. The results of physical properties test of the CS tablet

Run	Hardness (kg)	Friablity (%)	Disintegration Time (minutes)
1	6.31 ± 0.64	1.69 ± 2.14	1.47 ± 0.35
2	5.60 ± 0.18	0.71 ± 0.16	1.16 ± 0.17
3	4.93 ± 0.22	1.17 ± 0.38	0.56 ± 0.22
4	5.01 ± 0.25	1.06 ± 0.20	0.56 ± 0.26
5	6.72 ± 0.23	0.10 ± 0.06	2.45 ± 0.38
6	5.15 ± 0.32	0.53 ± 0.18	1.21 ± 0.20
7	4.73 ± 0.36	0.52 ± 0.33	1.28 ± 0.38
8	4.56 ± 0.17	0.69 ± 0.33	1.11 ± 0.07
Standard	4-8 kg (Sulaiman, 2007)	≤1% (Allen and Ansel, 2014)	≤30min(Anonym, 2014)

Table V. The equation of tablet properties from simplex lattice design

No.	Response	Equation
1.	Hardness	Y = 0.012(A) + 3.776 x 10^{-3}(B)
2.	Friability	Y= 0.0226(A)-5.508(B)+0.019(A)(B)+1.795 x 10^{-5}(A)(B)(A-B)
3.	Disintegration time	Y=3.480 x 10^{-3}(A)-3.572 x 10^{-3}(B)

Note: A: Avicel® PH 200 fraction; B: Amylum fraction

Moisture content

Run 2, 3, 4, 6,7, and 8 have 0 standard deviation because they have the same results in three times of each run measurement. The powder has water content less than 10% in all runs. It means, the result fulfill the requirement from the rule BPOM number 12 year 2014 about quality requirement of traditional medicines. The rules explained that water content from solid dosage form of herbal medicine doesn't allow more than 10%.

The equation of powder properties from Simplex Lattice Design in Design Expert 7.15 (Table III).

Based on equation in tapping index response (Table III), both of Avicel® PH 200 and amylum can increase the tapping index. The particle size of amylum is smaller than Avicel® PH 200, so amylum has less fluidity which can increase the tapping index of the powder. In water absorption respons, the single Avicel® PH 200 and amylum can increase the water absorption, but the combination of them can result an interaction which decrease the water absorption ability of the powder. In the moisture content response, amylum can increase the moisture conten of the powder. It is caused amylum is a hygroscopic agent. Amylum is smaller than Avicel® PH 200 so it can bind the more water than Avicel® PH 200.

The result of physical properties CS tablet

All tablet have the younger brown color with white spot on the tablet surface. Tablet has a unique odor and little bitter taste. The result of physical properties CS tablet (Table IV) and the equation of Simplex Lattice Design in Design Expert 7.15 (Table V).

The result of the hardness test of the tablets for all run is in the range of 4-8kg, thus it can be stated that the produced tablets meet

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2.	Friability	$Y= 0.0226(A)-5.508(B)+0.019(A)(B)+1.795 \times 10^{-5}(A)(B)(A-B)$
3.	Disintegration time	$Y=3.480 \times 10^{-3}(A)-3.572 \times 10^{-3}(B)$

Note: A: Avicel® PH 200 fraction; B: Amylum fraction

Table VI. The criteria of the determination parameter of optimum formula for CS tablet

Response	Goal	Minimum Point	Maximum Point	Weight
Tapping Index (%)	In Range	1	20	None
Hardness (kg)	In Range	4	8	None
Friability (%)	In Range	0	1	None
Disintegration Time (minutes)	Minimize	0	30	+++++

Information: Maximize : The response value expected to close to maximum point; Minimize : The response value expected to close to minimum point

the requirements of hardness test. The results of the ANOVA analysis provide a non-significant model which means that the variation in the amount of the two components does not have any effect on the hardness of the tablets. The hardness response also cannot adequately provide the prediction value of optimum formula. But, based on equation (Table V), Avicel® PH 200 can increase the tablet hardness. Avicel® PH 200 as filler binder binds intermolecules the compounds. The more concentration of Avicel® PH 200 in tablet, the more increasing of tablet compactibility and hardness.

From table IV, the friability of the CS tablets from 1, 3, and 4 run does not meet the requirements because the percentage of friability is more than 1%. The results of the ANOVA analysis provide a significant model which means that the variation in the amount of two components has an effect on the friability of the tablets. The friability response

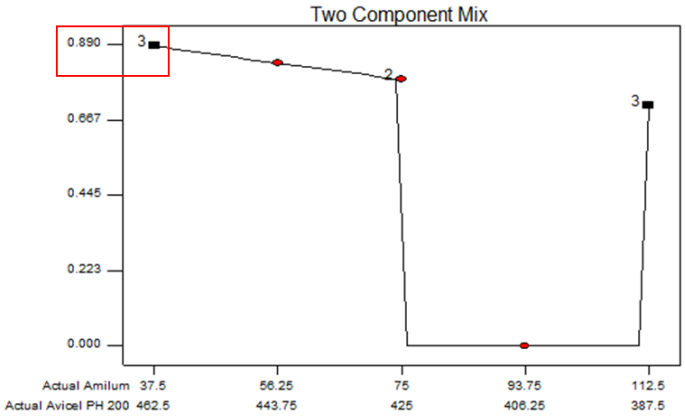

Figure 1. The optimum formula selected CS tablet from Contour Plot

Table VII. The comparison of the prediction response and experimental results of optimum formula

Response	**CS tablet**			
	Prediction result	**Test result**	**P value**	**Note**
Tapping Index (%)	17.13	19.83	0.004	significance
Hardness (kg)	5.68	6.35	0.001	significance
Friability (%)	0.62	0.52	0.118	nonsignificance
Disintegration Time (minutes)	1.48	1.2	0.006	significance

can adequately provide the prediction value of the optimum formula. Based on the result of SLD analysis (actual components), the cubic equation is generated (Table V). The Avicel® PH 200 in the friability profile of the tablet has a positive coefficient of 0.0226; which means that an increase in the amount of Avicel® PH 200 will also increase the friability of the tablet. Amylum has a smaller negative coefficient value of 5.508; which means that an increase in the amount of amylum will reduce the friability of the tablet. The combination of Avicel® PH 200 and amylum can increase the friability which is shown by positive coefficient value of 0.019 and positive 1.795×10^{-5}. This is presumably so because the composition of Avicel® PH 200 is more dominant such that although, the amylum itself can reduce the friability of the tablet, but the combination of both materials will still increase the friability of the tablet.

From Table IV, it can be seen that the disintegration time of the tablet shows the variations ranging from 0-3min. These results indicate that the disintegration time of the CS tablets of all runs meet the requirements according to the Regulation of Indonesian National Agency of Drug and Food Control Number 12 of 2014, regarding the quality requirements of traditional medicine which states that the disintegration time of any tablet preparations with herbal ingredients should not be more than 30min. The results of the equation from SLD (Table V) said that Avicel® PH 200 can longer the disintegration time of the tablet, opposite with amylum fraction. But, ANOVA analysis provide a non-significant model which means that the variation in the amount of the two components does not have any effect on the disintegration time of the tablet. The disintegration time response also cannot adequately give the prediction value of the optimum formula . For optimization in formulation process, there are some criterias from several properties of the powder and tablet (Table VI).

Table VI shows that each response has different weight. Each response is subjectively given the weight to determine the parameter priority and to obtain the tablet formula that meets the desired criteria. The determination of the goal is based on the expected response

value. The minimum and maximum points are set based on the terms specified by the references. If the requirements are not listed in the references, then the goal is determined using the highest and lowest actual values from the data.

Once the data are inputted, the SLD will recommend the most desirable formulas with the highest desirability value. The highest desirability value illustrates the proximity of the test results of the formula to the expected value in order to meet the requirements. The prediction formula is expected to have an optimum response. Based on the calculation, the highest desirability value is 0.890 with the amount of Avicel® PH 200 of 462.5mg per tablet and 37.5mg amylum per tablet. A good desirability value is the value close to 1. The optimum formula selected from the contour plot (Figure 1).

In the optimum formula, the amount of Avicel® PH 200 is 462.5mg per tablet and amylum is 37.5mg per tablet or the optimum formula is run II. The selection of run II as the optimum formula is assumed to be due to the significant response physical properties test of tablets and the non-significant Lack of Fit at run 1-8, which is only given by the friability response of the tablet. Thus, the software will recommend the optimum formula on the basis of consideration of the fragility value of the tablet. The selection of run 2 with the least amount of amylum as the optimum formula is based on the assumption that amylum does not have good compressibility. Thus, the increase in the amount of amylum is not followed by the good results of physical properties tests, both on powder and tablet. Then, it becomes the basis of the selection of run 2 as the optimum formula because it is considered adequate by the software regarding the least amount of amylum. After got the optimum formula, the next step is continued by comparing between prediction response and experimental results of the optimum formula (Table VII).

The response data of friability test results showed nonsignificant difference between the test and prediction results, while the other parameters differ significantly. The significant differences between prediction and test result on the tapping index, hardness, and disintegration time responses occur because there are many factors which can influence the test result : the personel, the machine, and the condition around the laboratory (humidity, temperature). However, the test results of these CS tablet data still meet the requirements.

CONCLUSION

The more Avicel® PH 200 concentration as filler binder in tablet makes the tablet more friable. The combination between Avicel® PH 200 as filler binder and amylum as disintegration agent can increase the friability of the tablet. The optimum formula of CS tablet had a composition of 462.5 mg Avicel® PH 200 and 37.5 mg amylum.

REFERENCES

Allen LV., Ansel HC., 2014, *Pharmaceutical Dosage Forms and Drug Delivery Systems*, 10th Ed., 272, Lippincott William & Wilkins, Baltimore.

Anonymus, 2014, Regulation of Indonesian National Agency of Drug and Food Control Number 12 of 2014 on *The requirements of Traditional Medicine Quality*, INADFC, Jakarta.

Guy A., 2009, Cellulose, Microcrystalline, dalam Rowe, R.C., Sheskey, P.J., dan Quinn, M.E., (Eds.), *Handbook of Pharmaceutical Excipients*, 6th Ed., 129-131, Pharmaceutical Press, London.

Hausler O., 2009, Cellulose, Microcrystalline, dalam Rowe, RC., Sheskey PJ., dan Quinn, M.E., (Eds.), *Handbook of Pharmaceutical Excipients*, 6th Ed., 129-131, Pharmaceutical Press, London.

Lukitaningsih E., 2009, The Exploration of Whitening and Sun Screening Compounds in Bengkoang Roots, *Disertasi,* Pharmazie und Lebensmittel Chemie Institüt, Würzburg University.

Nurrochmad A, Leviana F, Wulancarsari CG, Lukitaningsih E, 2010, Phytoestrogens of Pachyrhizus erosus prevent bone loss in an ovariectomized rat model of osteoporosis. *Int J Phytomed* **2**:363–372.

Sari IP., Nurrochmad A. Rahayu S, 2016[a], Evaluation of anti-fertility effect of aqueos extract of Costus speciosus

(Koen.) J.E.Smith rhizome in mice . IJPPS 8 (12):97-101

Sari IP., Nurrochmad A., 2016[b], Sub-acute toxicity study of ethanolic extract of pacing (*Costus speciosus*) in male mice. IJPCR 8(5)Suppl:440-444

Sulaiman, TNS., 2007, Teknologi dan Formulasi Sediaan Tablet, 151, Pustaka Laboratorium Teknologi Farmasi Fakultas Farmasi Universitas Gadjah Mada, Yogyakarta.