

FORMULATION AND PHYSICAL CHARACTERISTICS OF DETAM II SOYBEAN (*GLYCINE MAX* (L.) MERR) TABLET WITH VARIOUS CONCENTRATION OF SILICON DIOXIDE AND MAGNESIUM STEARATE

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ABSTRACT

Objective: This research was conducted to obtain several formulation and evaluate the physical characteristics of the soybean *Glycine max* (L.) Merr Detam II variety tablets.

Methods: Detam II varieties of soybean (*G. max* (L.) Merr.) were cleaned and grinded into 30 mesh-sized powder. Weighed soybean powder and internal phase of excipients (based on the formula) mixed by a Y-cone mixer until homogeneous, and then continue with dry granulation process. Granules formed, then sieved into 16 mesh size, and then, the characteristics examined. Dried granules then mixed with magnesium stearate and silicon dioxide using a drum mixer and compressed into tablets. Physical characteristics of tablets measured at 0, 4, 7, 14, 21, and 28 days.

Results: Evaluation was done for particle size distribution, moisture content (MC), flow properties, weight uniformity, friability, hardness, and disintegration time. Dry granulation was the best method to improve the characteristics of soybean powder with poor compressibility, poor flowability, and hygroscopic. Flow properties of the granules became better for Formula II and III by adding the concentration of silicon dioxide. The formulas also showed the good uniformity of weight, size, MC, friability, and disintegration time. Reducing the lubricant until 0, 5% of the formula made differences in friability, hardness, and disintegration time better than another formula.

Conclusion: The result of this research indicates that differences in silicon dioxide and magnesium stearate composition of the formula can affect the physical characteristics of soybean (*G. max* (L.) Merr.) tablets.

Keywords: Soybean (*G. max* (L.) Merr.), Detam II variety, Tablet, Dry granulation, Silicon dioxide, Magnesium stearate.

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INTRODUCTION

Free radicals are reactive and oxidize other molecules nearby such as proteins, DNA, lipids, and others. Free radicals can be inhibited by the presence of antioxidants. Antioxidants are substances that protect cells from free radical damage. Antioxidants interact and stabilize free radicals. Antioxidants are molecules that prevent the oxidation of other molecules. The human body has been able to produce an antioxidant commonly called endogenous antioxidant, but endogenous antioxidant alone is not enough and needed antioxidants from outside called exogenous antioxidants [1,2].

There are two sources of exogenous antioxidants, synthetic antioxidants, and natural antioxidants. One of the natural antioxidants is isoflavones or flavonoid derived from plant secondary metabolites [3,4]. Plants are rich in phenolic compounds and flavonoids which have been reported to exert multiple biological effects, such as antioxidant activities, free radical scavenging abilities, anti-inflammatory, and anticarcinogenic [5]. Flavonoids are a class of secondary metabolites which are found mainly in nuts and seeds, and one of them is the soybean plant [6].

Soybean (*Glycine max*) has become a source of important nutrients since ancient times. Soybeans are easily processed and manufactured into various kinds of food. Soybean (*G. max* (L.) Merr) Ijen varieties used with Vitamin C as a comparison reported to reduce levels of lead in the blood and liver of male mice [7]. Depend on soybean seeds color, it is divided into two types, yellow and black soybean. Black soybeans have almost same potential of nutrients and result than yellow soybeans and even have a higher functional properties [8].

Flavonoid content of black soybean is 6 times higher than yellow soybeans (total flavonoid content of yellow and black soybean is 0.41 and 2.57 mg equivalent to catechins/gram, respectively), and the antioxidant activity is 15 times higher (DPPH scavenging capacity of yellow and black soybeans is 1.40 and 17.58 mol equivalent per gram, respectively) [9].

Tablet was a dosage form made as a result of black soybean isoflavone optimization. Usually for the natural compound, included soybean has a high amount of moisture content (MC) that affects the flowability become poor, so the formulation will be the key to build the quality of the tablets. Granulation process was done by dry granulation technique to improve the flowability. Granulation is a technique used in the preparation of tablets, in which it involves particles enlargement by agglomeration [10].

Good flow properties needed, and the powder should be easily flows into the die first. [11]. The improvement also developed by changing the composition of glidant and disintegrant of the formula.

MATERIALS AND METHODS

Materials

The plant material used in this study is the soybean (*G. max* (L.) Merr.) Detam II varieties, certified taken from UPBS (Seed Resources Management Unit) Balitkabi (Research Institute for Legumes and Tuber), Malang, East Java in August 2016.

Chemicals used in this study are sodium starch glycolate (SSG) (Primojel®), polyvinylpyrrolidone (PVP) K-30 p.g, lactose anhydrous

p.g, silicon dioxide (Cab-O-Sil®), magnesium stearate p.g, and cellulose powder (Vitacel®).

Research tools

The tools used in this study were oven, blender, Retsch vibrator (D-42 759 Haan/Germany), a digital type analytical balance, drum mixer, tapping machine type PT TD200, MC tester, stative, single punch tablet machine (Yung Chuan Industrial Co., Ltd; Taiwan), disintegration time test equipment (disintegration tester, Erweka type of QC-21), Monsanto hardness tester instruments friability tester (rolling and impact durability tester, Erweka type TA 100/TA 200), Oscillating granulator, a standard funnel, stopwatch, pipette drops, and vial.

Methods

Preparation of (*G. max* (L.) Merr.) Detam II varieties powder

Soybean (*G. max* (L.) Merr.) Detam II varieties were cleaned and then dried directed to the air. Dry soybeans were grinded and homogenized using 30 mesh-sized Sieve into a fine powder. The powder was then stored in an eksikator.

Preparation of (*G. max* (L.) Merr.) Detam II varieties granules

Soybean and cellulose powder was weighed in the required amount, and then, mixed with a Y-cone mixer until homogeneous. Each anhydrous lactose, PVP K30, Plasdone S 630, and SSG were weighed based on the formula, and then, mixed until homogeneous. The amount of the excipient based on the formula in Table 1. The mixture then compressed into slug and sieved with 16 mesh Oscillating granulator into granules. Physical characteristics of granules were then examined.

Preparation of (*G. max* (L.) Merr.) Detam II varieties tablets

Dried granules were mixed with magnesium stearate and silicon dioxide using a drum mixer for 3 min. After the flowability was examined, granules then compressed into tablets. Tablet results had 13 mm diameter and 650 mg tablet weight. Physical characteristics of tablets were measured at time interval of 0, 4, 7, 14, 21, and 28 days.

Granules evaluation

MC

MC value could be expressed by the measurement of dry granules weight and terms good for that 3–5% MC. The MC was calculated with the following formula:

$$MC = \frac{W_a - W_b}{W_b} \times 100\%$$

Where W_a means wet granule weight and W_b is the weight of dry granule.

The particle size distribution

Siever was prepared from the biggest to the smallest pan in size range by placing the container below the others. The Retsch sieve then placed on the vibrator. After vibrated, then each pan weighed and documented. The target of this examination was obtain good particle distribution of granules and 10–20% fines.

Compressibility

Real density value determined by weighed amount of powder, then poured into a measuring glass until readable volume obtained (V_0). Weighed amount of granules putted on volumometer and tapped, and constant volume obtained recorded as V_1 . Good compressibility range was 5–25%.

Flowability

Some granules inserted into the funnel which is closed in the bottom. After the funnel opened, the time required for the granules pass through the funnel and the angle of repose recorded. Maximum flow time of 100

g granule was 10 s, and the angle of repose must be inside the range of 25–40° based on Table 2.

Tablet evaluation

Weight uniformity

Weight uniformity test done by weighing 10 tablets one by one, and the average weight of each tablet calculated. The tablet acceptance value should not be greater than or equal to 15% based on the Indonesian Pharmacopoeia V [12].

Hardness

The hardness of the tablet was measured using a Monsanto hardness tester with 20 samples. Each tablet was placed one by one then rotated slowly and precisely until the tablet broke and showed the hardness value on the scale. Hardness requirement generally at least 4 kg.

Friability

Friability was measured using a friability tester. Samples taken as many as 10 tablets were randomly assigned to tablets with a weight above 650 mg. Tablet cleaned one by one and weighed using the analytical balance. The tablet is then inserted into the testing device with a rotation speed of 25 rpm for 4 min. Then, the tablet removed and cleaned from dust. The tablets were weighed and the friability calculated using the following equation:

$$\% \text{ Friability} = \frac{W_a - W_b}{W_a} \times 100\%$$

Where W_a is tablet weight before rotated and W_b is the final tablet weight.

Disintegration time

Each tablet was inserted in the basket, and then, the friability tester was started at medium temperature $37 \pm 2^\circ\text{C}$. Disintegration time required for testing six tablets should not be ≥ 15 min.

RESULT AND DISCUSSION

Identification of soybean seed powder (*G. max* (L.) Merr) Detam II varieties

The organoleptic results of soybean (*G. max* (L.) Merr) powder Detam II varieties were a yellow with black spots coarse powder, slightly sweet, and have a distinctive odor of soybeans. 1 kg of crushed soybeans resulted 950 g soy powder and manufactured into tablets. Organoleptic results of the product shown in Figure 1. MC of the powders was also identified to determine the initial water content in soybean powder, and the amount obtained was 6.11%.

Granules evaluation

Particle size distribution

Particle size distribution showed that all of the formulas had the amount of fines below the requirements of 10–20% [13], but they have a normal size distribution with the major fraction is in the 300–600 μm shown in Figure 2. particle size. The example of the particle size distribution curve was shown in Fig. 2 for Formula 1 until 3.

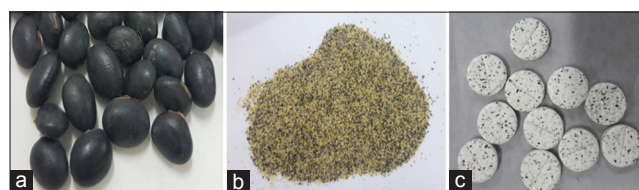


Fig. 1: (a) Soybean (*Glycine max* L. Merr) Detam II varieties seed, (b) soybean (*G. max* L. Merr) Detam II varieties powder, (c) soybean (*G. max* L. Merr) Detam II varieties tablet

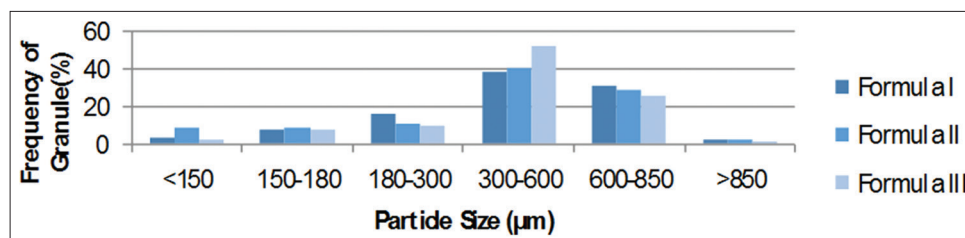


Fig. 2: Particle size distribution curve

Table 1: Formula Detam II varieties soybean tablet

Material	Function	Formula				
		I	II	III	VI	VII
Detam II black soybean powder	Active substance	200 mg	200 mg	200 mg	200 mg	200 mg
SSG	Disintegrant (%)	4	4	4	4	4
Magnesium stearate	Lubricants (%)	2	2	2	0.5	1
Polyvinylpyrrolidone (PVP K30)	Internal phase binder (%)	2	2	2	2	2
	External phase binder (%)	2	2	2	2	2
Silicon dioxide	Glidant (%)	0.1	0.5	1	1	1

SSG: Sodium starch glycolate

Table 2: Relationship of flow property and angle of repose

Flow property	Angle of repose (°)
Excellent	25–30
Good	31–35
Fair - aid not needed	36–40
Passable - may hang up	41–45
Poor - must agitate, vibrate	46–55
Very poor	56–65
Very, very poor	>66

Table 5: Compressibility of granules

Formula	% Compressibility	Requirement of compressibility of 5–25%
I	38.20	Did not meet the requirement
II	31.46	Did not meet the requirement
III	36.04	Did not meet the requirement
IV	33.85	Did not meet the requirement
V	38.19	Did not meet the requirement

Table 3: MC of soybean seeds (*G. max* (L.) Merr) Detam II varieties

Wb average (g)	Wa average (g)	% MC
4.753	5.062	6.11

MC: Moisture content, *G. max*: *Glycine max*

Table 6: Flowability of granules

Formula	T (s)	Angle of repose (°)
I	11.3	41.30
II	8.57	38.44
III	7.50	34.56
IV	9.57	34.77
V	9.50	36.24

Table 4: MC of granules

Formula	% MC
I	3.06
II	2.51
III	3.21
IV	2.56
V	3.13

MC: Moisture content

MC

The granules are taken as much as 5 g (replication 3 times for each formula) and tested moist content. Obtained results for the three formulas meet the requirements, which shown in Table 3 and Table 4. Under the terms, good moist content was between 3% and 5% [14].

Compressibility

All of the formula did not meet the requirement shown in Table 5 [15]. This condition could be due to lack of the amount of fines, so the small particles did not fill cavities between particles. Based on the compressibility value, it can caused the dense of tablet form became less.

Flowability

Flowability of 100 g granules was good shown in Table 6, and most of all formula could flow not more than 10 s. The value of the angle of repose must be between 25° and 40° to show good flowability [15]. Formulas I, II, and III determined the improvement of glidant composition in the formula.

Formula III has better flowability than Formulas I and II. It can be caused due to the amount of silicon dioxide as glidant. Glidant amount in formula I as much as 0.1% is too small to help the poor flowability of Detam II varieties soybean granule in the formula.

Tablet evaluation

Organoleptic tablet soybean seeds (*G. max* (L.) Merr) varieties Detam II

The organoleptic test results of the soybean tablet obtained that the tablets are round white with black spots with a slightly sweet taste and a distinctive smell of soybeans.

Tablet weight uniformity

The uniformity test result of 10 unit tablets must be lower than 15%. Tablets from all of the formulas met the requirements

Table 7: Tablet weight uniformity

Formula	The average weight \pm SD (g)	Requirements value (%)	Uniformity of weight value admission requirements \leq 15% (Depkes RI, 2014)
I	0.6504 \pm 0.0133	0.03	Meet the requirements
II	0.6494 \pm 0.0103	0.02	Meet the requirements
III	0.6501 \pm 0.0183	0.04	Meet the requirements
IV	0.6480 \pm 0.0124	0.03	Meet the requirements
V	0.6434 \pm 0.0081	0.02	Meet the requirements

SD: Standard deviation

Table 8: Tablet hardness

Days	Formula	The average of hardness \pm SD (kg)	Requirements of tablet hardness at least 4 kg (Troy, 2006)
0	I	1.35 \pm 0.34	Did not meet the requirement
	II	1.25 \pm 0.35	Did not meet the requirement
	III	1.6 \pm 0.32	Did not meet the requirement
	IV	4.12 \pm 0.10	Meet the requirement
	V	2.90 \pm 0.87	Did not meet the requirement
4	I	1.35 \pm 0.24	Did not meet the requirement
	II	1.05 \pm 0.16	Did not meet the requirement
	III	1 \pm 0.00	Did not meet the requirement
	IV	3.92 \pm 0.09	Did not meet the requirement
	V	2.45 \pm 0.50	Did not meet the requirement
7	I	1.3 \pm 0.35	Did not meet the requirement
	II	1.4 \pm 0.35	Did not meet the requirement
	III	1 \pm 0.00	Did not meet the requirement
	IV	2.15 \pm 0.53	Did not meet the requirement
	V	2.00 \pm 0.47	Did not meet the requirement
14	I	1.25 \pm 0.26	Did not meet the requirement
	II	0.875 \pm 0.21	Did not meet the requirement
	III	0.675 \pm 0.24	Did not meet the requirement
	IV	1.83 \pm 0.21	Did not meet the requirement
	V	1.58 \pm 0.44	Did not meet the requirement
21	I	1.45 \pm 0.37	Did not meet the requirement
	II	1.4 \pm 0.32	Did not meet the requirement
	III	1.3 \pm 0.48	Did not meet the requirement
	IV	2.15 \pm 0.24	Did not meet the requirement
	V	1.80 \pm 0.35	Did not meet the requirement
28	I	0.75 \pm 0.24	Did not meet the requirement
	II	1 \pm 0.00	Did not meet the requirement
	III	0.575 \pm 0.12	Did not meet the requirement
	IV	1.98 \pm 0.18	Did not meet the requirement
	V	1.35 \pm 0.27	Did not meet the requirement

SD: Standard deviation

shown in Table 7. Fair flowability helped the granule to enter the compression dies even there was a deviation also from target weight of 0.650 g.

Tablet hardness

Hardness of tablet was examined for all formulas with several intervals of sampling time and the result shown in Table 8. Hardness of tablet decreased time by time when it placed inside the climatic chamber with controlled condition in 40°C temperature and 75% RH. The formulation could not cover the hygroscopic properties of the active compound determined from decreasing value of tablet hardness.

Tablet friability

The requirement of maximum friability value was 1%. Friability of Formulas I and II did not meet the requirement on 14, 21, and 28 days, while the Formulas III and V did not meet the requirements since 7 and 4 days, respectively (shown in Table 9). High humidity can lead to break the particle bond, increased porosity, and affected changes in friability. It shown from hardness and friability data that improving the magnesium stearate amount as lubricant also gave the anti-bonding effect between particles. Finally it reduce the hardness and improve the friability of the tablets.

Disintegration time

Disintegration time of all formulas met the requirement which is <15 min. The result in Table 10 showed that higher hydrophobic excipients added in the external phase of the formula affect the disintegration time. The disintegration of tablets needed longer time resulted by improvement of hydrophobic external phase composition. Faster disintegration time could aid the absorption of drugs in the body.

CONCLUSION

Formulation of Detam II variety soybean tablets with several concentration of silicon dioxide and magnesium stearate was done in this research. Evaluation obtained some data about particle size distribution, MC, flow properties, weight uniformity, friability, hardness, and disintegration time. Soybean powder had poor compressibility, poor flowability, and hygroscopic properties, so dry granulation method was chosen to get tablet dosage form. Flow properties of the granules became better for Formulas II and III by adding the concentration of silicon dioxide as glidant. The formulas also showed a good uniformity of weight, size, MC, friability, and disintegration time. On the other hand, reducing the lubricant composition until 0.5% of the formula made differences in friability,

Table 9: Tablet friability

Days	Formula	Average friability \pm SD (%)	Friability requirements should not be >1% (USP 37 NF 32, 2014)
0	I	0.40 \pm 0.22	Meet the requirements
	II	0.43 \pm 0.42	Meet the requirements
	III	0.54 \pm 0.19	Meet the requirements
	IV	0.10 \pm 0.02	Meet the requirements
	V	0.27 \pm 0.02	Meet the requirements
4	I	0.25 \pm 0.08	Meet the requirements
	II	0.22 \pm 0.12	Meet the requirements
	III	0.67 \pm 0.09	Meet the requirements
	IV	0.51 \pm 0.03	Meet the requirements
	V	1.93 \pm 0.28	Did not meet the requirements
7	I	0.44 \pm 0.11	Meet the requirements
	II	0.86 \pm 0.34	Meet the requirements
	III	3.24 \pm 0.95	Did not meet the requirements
	IV	0.25 \pm 0.08	Meet the requirements
	V	1.47 \pm 0.58	Did not meet the requirements
14	I	1.34 \pm 0.25	Did not meet the requirements
	II	1.46 \pm 0.44	Did not meet the requirements
	III	4.51 \pm 1.90	Did not meet the requirements
	IV	0.26 \pm 0.07	Meet the requirements
	V	1.47 \pm 0.06	Did not meet the requirements
21	I	4.89 \pm 0.34	Did not meet the requirements
	II	3.39 \pm 0.48	Did not meet the requirements
	III	5.22 \pm 0.62	Did not meet the requirements
	IV	0.15 \pm 0.02	Meet the requirements
	V	2.04 \pm 0.37	Did not meet the requirements
28	I	2.85 \pm 0.61	Did not meet the requirements
	II	2.89 \pm 0.93	Did not meet the requirements
	III	4.29 \pm 0.55	Did not meet the requirements
	IV	0.56 \pm 0.26	Meet the requirements
	V	3.18 \pm 0.42	Did not meet the requirements

Table 10: Disintegration time

Days	Formula	Average disintegration time (minutes)	Requirement of disintegration time <15 min (USP 37 NF 32, 2014)
0	I	7'28"	Meet the requirements
	II	5'59"	Meet the requirements
	III	9'07"	Meet the requirements
	IV	5'15"	Meet the requirements
	V	5'35"	Meet the requirements
4	I	7'52"	Meet the requirements
	II	5'21"	Meet the requirements
	III	4'48"	Meet the requirements
	IV	4'55"	Meet the requirements
	V	4'03"	Meet the requirements
7	I	5'05"	Meet the requirements
	II	4'31"	Meet the requirements
	III	3'46"	Meet the requirements
	IV	4'50"	Meet the requirements
	V	4'58"	Meet the requirements
14	I	6'01"	Meet the requirements
	II	5'09"	Meet the requirements
	III	4'35"	Meet the requirements
	IV	3'58"	Meet the requirements
	V	4'09"	Meet the requirements
21	I	5'34"	Meet the requirements
	II	4'48"	Meet the requirements
	III	6'51"	Meet the requirements
	IV	5'04"	Meet the requirements
	V	6'04"	Meet the requirements
28	I	6'23"	Meet the requirements
	II	5'27"	Meet the requirements
	III	7'41"	Meet the requirements
	IV	6'38"	Meet the requirements
	V	6'05"	Meet the requirements

hardness, and disintegration time better than another formula. Too much lubrication affected the antibonding effect that increases the friability and reduces the crushing strength of the tablet. The other

important problem of soybean powder that must be solved was the hygroscopic characteristic that reduces the physical characteristics of tablets. Formulation of Detam II varieties soybean tablet must

be consider about the amount of adsorbent and humidity value of production room.

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