

FORMULATION DEVELOPMENT AND OPTIMIZATION OF TABLET CONTAINING COMBINATION OF SALAM (SYZYGIUM POLYANTHUM) AND SAMBILOTO (ANDROGRAPHIS PANICULATA) ETHANOLIC EXTRACTS

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FORMULATION DEVELOPMENT AND OPTIMIZATION OF TABLET CONTAINING COMBINATION OF SALAM (*SYZYGIUM POLYANTHUM*) AND SAMBILOTO (*ANDROGRAPHIS PANICULATA*) ETHANOLIC EXTRACTS

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ABSTRACT

Objective: The present study was aimed at finding the appropriate type of a binder and a disintegrant which can be used formulate tablets containing a combination of two ethanol extracts of *Syzygium polyanthum* leaves and *Andrographis paniculata* herbs, as well as to find their optimum concentrations which would produce the tablets with desired hardness and disintegration time.

Methods: Tablet manufacturing was done in two methods with the use of PVP K30 as a binder using the wet granulation method, and gelatin as a binder using the direct compression method. The design optimization used was the 2² full factorial designs with two factors and two levels, with the factors used being the binder concentration and the disintegrant.

Results: Tablets produced using gelatin as a binder had a hardness level similar to those using PVP K30 as a binder. However, their disintegration time was strongly affected by the choice of the binder. The result suggested that different binder (PVP K30 and gelatin) affected different disintegration time despite producing tablet hardness values that were almost identical.

Conclusion: The herbal tablet development of combined ethanolic extracts of *Syzygium polyanthum* and *Andrographis paniculata* herbs could be made using gelatin as a binder and croscopovidone as a disintegrating agent using the direct compression method. The optimal formula was obtained using gelatin 3.61% and croscopovidone 3.45%, which had theoretical results in the hardness of 6.50 kp, the friability of 0.35%, and the disintegration time of 12.76 min.

Keywords: *Syzygium polyanthum*, *Andrographis paniculata*, Gelatin, Croscopovidone, Optimization

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INTRODUCTION

The Indonesian-originated Salam leaves (*Syzygium polyanthum* folium) contain flavonoids, tannins, essential oils including sitral and eugenol, saponins, alkaloids, flavonoids, and polyphenols [1]. It has been characterized as having a function as an anti-inflammatory, antioxidant, antibacterial, and antifungal agent. Another plant that can be used in the therapy of inflammatory condition is the herb Sambiloto (*Andrographis paniculata* herbs). *Andrographis paniculata* contains resin, kalmeghin, andrographolide, diterpene, neo andrographolide, deoxy andrographolide, apigenin, flavonoids and phenols with the bitter taste. A previous study [2] suggested that the optimum dose for a 10:1 combination of water fractions of *Syzygium polyanthum* and *Andrographis paniculata*, respectively, as an anti-inflammatory agent is 250 mg. At this dose, the combination gave a better anti-inflammatory effect (45.68%) than that of ibuprofen at a dose of 36 mg/kg BB (40.63%). The ethanolic extract combination was selected as the active ingredients in this research with doses determined based on comparisons between total flavonoid levels of ethanol extracts and the water fractions.

Polyvinyl pyrrolidone (PVP K-30) is a binder which can be used in a dry state or in a solution [3], and has a high binding strength which is suitable for wet granulation method and direct compression. Gelatin is a natural binder polymer widely used in the tablet formulation process. Gelatin is generally dissolved beforehand in a solvent to be used in a wet granulation process, but gelatin can also be used in the form of good solid powder and granule for direct compression method, with a concentration of 0.1%-99.9% of tablet weight. Gelatin has been used for a variety of uses such as binders, fillers, even as disintegrants. The usual gelatin concentration user for the binder is approximately 5% [4]. The metabolism of gelatin in the body is assisted by the enzyme protease. This enzyme also plays a role in the disintegration of tablets [5].

Croscopovidone is one of the super disintegrants which does not form a complex with the active ingredient because it is a nonionic polymer. The disintegration of the tablet by croscopovidone is done through a combination mechanism of wicking, swelling, and deformation. Croscopovidone rapidly expands when it is in contact with the water without forming a gel, and it has a higher compression and disintegrating activity which is not affected by the pH of the medium [6]. Starch is a polysaccharide found in plants. Starch has many functions. One pharmaceutical use of starch is for tablet disintegration. In this study corn starch was used. It has the property of a white powder, tasteless, odorless and insoluble in water. Starch undergoes plastic deformation during compression, but this property depends on the size, size distribution, and particle shape. Starch is composed by two kinds of main components of the polymer of D-glucopyranose is 15-30% amylose (linear polymers), 70-85% amylopectin (branched polymer), and 5-10% of other material (protein and fat) [7]. Starch can serve as a disintegrating agent on the tablet by increasing the amount of water that goes into a tablet since starch powder has pores that cause capillary action. An increase in the amount of water that goes into the tablet causes the tablet to disintegrate into granules. The granules will then disintegrate into powders which will dissolve in bodily fluid and give their pharmacological effects [8].

The aim of this research was therefore to find an optimal concentration and specification of a binder and a disintegrant which were suitable for making tablet dosage form containing *Syzygium polyanthum* and *Andrographis paniculata* ethanolic extracts.

MATERIALS AND METHODS

Materials

The *Syzygium polyanthum* and *Andrographis paniculata* ethanolic extracts were obtained from PT. Javaplant, Solo. Chemicals used in

this research were purchased as follows: PVP K-30 and crospovidone were from PT. BASF Indonesia), lactose monohydrate was from Lepirino Foods, US. Talc and magnesium stearate were sourced from Peter Greven, Venlo, the Netherlands). AlCl₃, FeCl₃, hydrochloric acid, anhydrous acetic acid, sulfuric acid, chloroform, mayer reagents, dragendroff reagent, and quercetin were purchased from Sigma, Switzerland. Ethanol 96% distilled water were sourced locally from Surabaya, Indonesia.

Standardization of dry ethanolic extracts

Standardization of dry ethanol extracts was done with the determination of the organoleptic, determination of total ash, determination of water soluble ash, determination of acid insoluble ash, and lost on drying was performed according to standard parameters that fulfill the BPOM Indonesia and the Indonesian Materia Medika requirements.

Phytochemical screening

Phytochemical screening test for the *Syzygium polyanthum* and *Andrographis paniculata* ethanolic extracts included were standardized alkaloids, steroids or triterpenoids, flavonoids, tannins, saponins, and glycosides amounts.

Determination of total flavonoid content in the ethanolic extracts and the water fraction

Determination of total flavonoid content in the *Syzygium polyanthum* leaves and *Andrographis paniculata* ethanolic extracts and also in the water fraction is performed by a modification of the method by Humadi and Istudor [9]. The standard solution was prepared by weighing 25 mg quercetin in 25 ml of volumetric flask and dissolved in 15 ml of ethanol 96% and volume was made up with ethanol 96% (1000 µg/ml). The stock solution was further diluted with ethanol 96% to obtain working solution in the range 6.5–100 µg/ml. 1 ml of the each working solution was withdrawn and added a mixture of 3 ml of ethanol 96%, 0.2 ml of 10% AlCl₃, 0.2 ml of 1M sodium acetate, and 5.6 ml of distilled water. The absorbance of the solution was measured at 440.8 nm after incubation for 30 min at room temperature.

The ethanolic extract or the water fraction of *Syzygium polyanthum* leaves-*Andrographis paniculata* 10: 1 (1 g) was weighed accurately and dissolved in 25 ml of ethanol 96%, then hydrolyzed with 4N HCl (1:1) for 30 min. After that, 25 ml of distilled water was added. The flavonoids were extracted by using ethyl acetate. The extract solution was evaporated to remove the solvent. The residue was dissolved in ethanol 96% to made up 25 ml volume. 1 ml of the solution was withdrawn and added a mixture of 3 ml of ethanol

96%, 0.2 ml of 10% AlCl₃, 0.2 ml of 1M sodium acetate, and 5.6 ml of distilled water. The flavonoid was evaluated by spectrophotometer uv-vis 440.8 nm after incubation for 30 min at room temperature.

Preparation of tablet formulation development of *Syzygium polyanthum* leaves and *Andrographis paniculata* ethanolic extracts

Tablet manufacturing was done in two methods, wet granulation, and direct compression. The tablets weight was fixed to 700 mg. Wet granulation method of tablet was made by mixing dry extract (1 tablet contains 450 mg with the comparison between *Syzygium polyanthum* leaves, and *Andrographis paniculata* are 10: 1), lactose monohydrate, disintegrating agent (crospovidone or corn starch) and PVP K-30 solution to form a damp coherent mass which was screened through a sieve no 16 and was dried at 50 °C. The compositions of the batches are shown in table 1 (F1-8).

Direct compression method was used to prepare tablet with gelatin as a binder. Dry extracts were taken and then mixed with Pharmatose 80M, gelatin, and cornstarch. Magnesium stearate and talc were mixed and followed by compression of the blend. The compositions of the batches are shown in table 1 (F9-16).

Physical properties evaluation of powder

The physical properties of powder were evaluated by their bulk density, tapped density, Carr's index, and Hausner ratio.

Physical properties evaluation of tablets

Tablet hardness test was done by taking 20 tablets at random, and then placed one by one in the clamp on the hardness tester. Tablet hardness values can be seen on the screen. The terms of good tablet hardness were 4-8 kp.

Twenty tablets were cleaned from dust, weighed (W₁), and then put in friability tester, 4 min of rotating at 25 RPM, and then the whole tablet removed, cleaned of dust and reweighing (W₂). Loosing weight in percentage can be calculated by the formula in equation 1. Terms friability good is less than 0.8%.

$$\% \text{ Friability tablet} = (W_1 - W_2) / W_1 \times 100\% \dots \dots \dots (\text{Eq.1})$$

Tablet disintegration time was tested by inserting 6 tablets into the basket, and the basket fluctuates in the immersion fluid at a constant frequency rate between 29-32 cycles. If there was no parts of the tablets are left on the screen, except fragments of the coating agent, the tablet could be declared as disintegrated. Disintegration time for the uncoated tablet was no more than 15 min [13].

Table 1: Formulation of tablets

Formula	Ingredients in each tablet (700 mg per tablet)								
	Dry Extract of <i>Syzygium polyanthum</i> Leaves	Dry Extract of <i>Andrographis paniculata</i>	PVP K-30	Gelatin	Crospovidone	Corn Starch	Lactose Monohydrate	Mg. Stearate	Talc
F1	409.09	40.91	21	-	21	-	173	7	28
F2	409.09	40.91	35	-	21	-	159	7	28
F3	409.09	40.91	21	-	35	-	159	7	28
F4	409.09	40.91	35	-	35	-	145	7	28
F5	409.09	40.91	21	-	-	21	173	7	28
F6	409.09	40.91	35	-	-	21	159	7	28
F7	409.09	40.91	21	-	-	35	159	7	28
F8	409.09	40.91	35	-	-	35	145	7	28
F9	409.09	40.91	-	21	21	-	179	7	28
F10	409.09	40.91	-	35	21	-	159	7	28
F11	409.09	40.91	-	21	35	-	159	7	28
F12	409.09	40.91	-	35	35	-	145	7	28
F13	409.09	40.91	-	35	-	35	173	7	28
F14	409.09	40.91	-	35	-	21	159	7	28
F15	409.09	40.91	-	21	-	35	159	7	28
F16	409.09	40.91	-	21	-	21	145	7	28

Determination of total flavonoid content in the tablet

An accurately weighed amount of the powdered tablets (700 mg) was dissolved in 25 ml of ethanol 96%, and then hydrolyzed with 4N

HCl (1:1) for 30 min. After that, 25 ml of distilled water was added. The flavonoid was extracted by using ethyl acetate. The extract solution was evaporated to remove the solvent. The residue was dissolved in ethanol 96% to made up 25 ml volume. 1 ml of the

solution was withdrawn and added a mixture of 3 ml of ethanol 96%, 0.2 ml of 10% AlCl₃, 0.2 ml of 1M sodium acetate, and 5.6 ml of distilled water. The flavonoid was evaluated by spectrophotometer uv-vis at 440.8 nm after incubation for 30 min at room temperature.

RESULTS AND DISCUSSION

Standardization of *Syzygium polyanthum* and *Andrographis paniculata* ethanolic extracts

The dry ethanolic extract and the results of standardization of the *Syzygium polyanthum* and *Andrographis paniculata* are shown in fig. 1 and table 2.

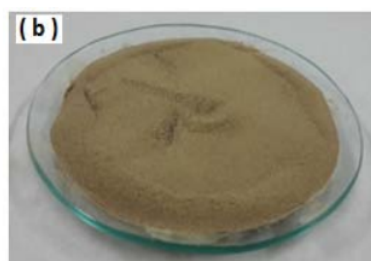
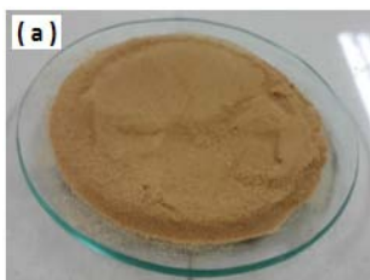


Fig. 1: Ethanolic extract of *Syzygium polyanthum* leaves (a) and ethanolic extract of *Andrographis paniculata* (b)

Phytochemical screening of *Syzygium polyanthum* and *Andrographis paniculata* ethanolic extract

Phytochemical screening was conducted to determine the qualitative secondary metabolite contents of *Syzygium polyanthum* and *Andrographis paniculata* ethanolic extract (table 3). The various phytochemical compounds detected are known to have beneficial importance in medicinal sciences. The flavonoids have been referred to as nature's biological response modifiers, because of their inherent ability to modify the body's reaction to allergies and virus and their antiallergic, anti-inflammatory, antimicrobial and anti-cancer activities [14].

Table 2: Standardization of *Syzygium polyanthum* leaves and *Andrographis paniculata* ethanolic extracts

Standardization parameters	Ethanol extract of <i>Syzygium polyanthum</i> Leaves	Requirement	Ethanol extract of <i>Andrographis paniculata</i>	Requirement
Organoleptic:		-		-
-Appearance	powder		powder	
-Color	light brown		greenish brown	
-Taste	chelates		very bitter	
-Odor	aromatic		specific	
Total ash content (%)	5.30±0.04	≤ 5.5%	9.66±0.05	≤ 10%
Water soluble ash content (%)	1.61±0.20		7.80±0.10	
Acid insoluble ash content (%)	2.12±0.10	≤ 1.8%	9.16±0.05	≤ 0.1%
Lost on drying (%)	5.73	<6%	5.23	≤ 6%

All values represent mean±SD, n=3, The standardization of dry extract shown to have a parameter that does not meet the requirements is acid insoluble ash this may be due to impurities in the extract.

Table 3: The qualitative analysis of *Syzygium polyanthum* leaves and *Andrographis paniculata* ethanolic extracts

Phytoconstituents	Ethanol extract of <i>Syzygium polyanthum</i> leaves	Other research [11-12]	Ethanol Extract of <i>Andrographis paniculata</i>	Other research [13]
Triterpenoid-Steroid	(+)	(+)	(+)	(+)
Flavonoid	(+)	(+)	(+)	(+)
Tannin	(+)	(+)	(+)	(+)
Glycoside	(-)	(-)	(-)	(-)
Alkaloid	(+)	(+)	(+)	(+)

Table 4: Total flavonoids content in the water fraction and the ethanolic extracts

Sample	Flavonoid total (%)	Comparison of ethanol extract and water fraction <i>Syzygium polyanthum</i> leaves- <i>Andrographis paniculata</i>
Ethanol Extract of <i>Syzygium polyanthum</i> Leaves- <i>Andrographis paniculata</i> (10:1)	0.175±0.011	1: 5.25
Water Fraction of <i>Syzygium polyanthum</i> Leaves- <i>Andrographis paniculata</i> (10:1)	0.916±0.011	

All values represent mean±SD, n=3

Determination of total flavonoid content in the ethanol extracts and the water fractions of *Syzygium polyanthum* leaves-*Andrographis paniculata*

The calibration curve was constructed by plotting absorbance against respective concentration of quercetin. The result shows an excellent correlation between absorbance and concentration within the concentration range 6.5–100 µg/ml. The correlation coefficient was greater than 0.995 (fig. 2).

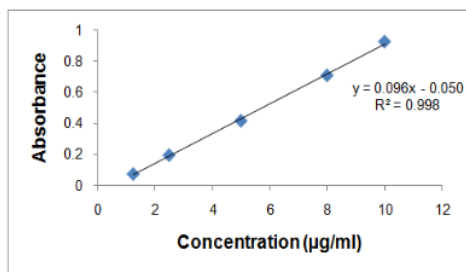


Fig. 2: Linear curve between quercetin absorbance versus concentration (µg/ml)

The physical properties of the powder and the tablet

The physical properties of the powder and the tablet are shown in table 5. F1, F2, F3, and F4 use PVP K30 as a binder and crospovidone as a disintegrant produce a granular material which has good flow properties indicated by the Carr's index and Hausner ratio which obtained. The tablet has good hardness with low friability. It is also found in F5, F6, F7, and F8 are using PVP K30 as a binder and corn starch as a disintegrant. The use of PVP K30 as a binder in the manufacture of tablets by wet granulation method will produce granules with good flow properties due to the fact that a solution of PVP K30 can spread well during granulation so as to form a bridge of liquid between the particles that will produce a good bonding resulting in excellent tablet hardening process. The use of PVP K30 as a binder produces tablets with good hardness and low friability, but it has a high disintegration time, which does not meet the requirements of the Indonesian Pharmacopoeia. The high disintegration time resulted from the strong bonds between the particles, and hence, they also produce high tablet hardness. Hygroscopic properties of PVP K30 are causing water in the air to be absorbed into the tablet which can reduce its ability of swell when

contact with a liquid medium, resulting in a longer tablet disintegration time.

Hendrati et al. (2011) used a water extract of *Syzygium polyanthum* Leaves-*Andrographis paniculata*, with a dose of 400 mg per tablet (*Syzygium polyanthum* Leaves: *Andrographis paniculata* = 2: 1), stating that the use of PVP K-30 4.45%, crospovidone 4.45% and a combination of Avicel and emcompress as a filler would produce a tablet with hardness of 6.6 kp, friability of 0.15%, and the disintegration time of 6.6 min [15]. In contrast to previous studies, in this research, the extract which used is ethanolic extract at a dose of 450 mg per tablet (*Syzygium polyanthum* Leaves: *Andrographis paniculata* = 10: 1) and the filler which used is lactose monohydrate. The use of ethanol in the extraction process produced more active substances which extracted, wherein flavonoids more easily soluble in ethanol. In this research, lactose monohydrate was used as a filler which it was easily soluble in water, so when the manufacture of tablets with wet granulation method, lactose monohydrate can be functioning as the self-binder, therefore increasing the disintegration time. This problem can be overcome by using gelatin as a binder and selected direct compression method in the manufacture of tablets. The reason to selected lactose monohydrate as filler was to increase the density of the extract that was known to have a small density.

The use of gelatin as a binder with crospovidone or corn starch as a disintegrant obtained granule with poorer flow properties compared to PVP K30 as a binder. This can be caused by a solution of gelatin in water, while at the same concentration with a solution of PVP K30, has a high viscosity. It needed a better mixing upon the addition of the binder to the powder mixture. The liquid binder can spread more evenly throughout the particle to form liquid bridges between particles that will generate strong granules and reduce the occurrence of fines which can worsen the flow properties of powders. Tablets produced using gelatin as a binder has a hardness that is no different from the tablet hardness that uses PVP K30 as a binder. This result suggests that the compressibility and compatibility of granules produced good enough to be compressed into a tablet because the bonding between the particles has good bond strength. Disintegration time of a tablet that use gelatin as a binder is faster than that using PVP K30, although both have a tablet hardness value that is nearly equal, an effect related to the porosity of the tablet, wherein the tablet which uses gelatin will have a porosity greater than a tablet that uses PVP K30 as a binder. Differences in values of bulk density and tapped density in granules that use gelatin as a binder is greater than granules using PVP K30, resulting in a tablet that is more porous, which can facilitate the entry of water in order to obtain disintegration time faster than the tablet using a PVP K30.

Table 5: Physical properties of the powder and the tablet

Formula	Bulk Density (g/ml)	Tapped density (g/ml)	Carr's Index (%)	Hausner ratio	Hardness (kp)	Friability (%)	Disintegration time (min)
F1	0.36±0.04	0.42±0.04	15.00±1.41	1.18±0.02	5.72±0.11	0.46±0.00	41.03±1.97
F2	0.35±0.03	0.41±0.03	15.50±0.71	1.19±0.01	6.16±0.09	0.39±0.05	48.85±0.14
F3	0.35±0.03	0.41±0.01	14.50±0.71	1.17±0.01	6.18±0.22	0.44±0.00	39.37±1.42
F4	0.33±0.00	0.39±0.00	15.75±0.35	1.19±0.01	7.21±0.03	0.39±0.00	42.77±0.08
F5	0.40±0.02	0.47±0.03	14.76±0.35	1.17±0.00	6.15±0.08	0.63±0.02	47.55±0.78
F6	0.37±0.01	0.44±0.01	14.75±0.35	1.17±0.01	7.02±0.35	0.52±0.14	44.96±1.68
F7	0.38±0.01	0.44±0.01	15.00±0.00	1.18±0.00	6.02±0.11	0.59±0.05	42.27±0.46
F8	0.37±0.00	0.44±0.01	15.49±0.69	1.18±0.01	6.67±0.10	0.48±0.11	45.08±0.01
F9	0.72±0.02	0.44±0.01	18.50±0.71	1.23±0.01	6.55±0.38	0.36±0.00	12.50±0.33
F10	0.72±0.01	0.57±0.00	18.50±0.71	1.23±0.01	7.03±0.31	0.33±0.13	13.54±0.06
F11	0.73±0.01	0.59±0.01	18.50±0.71	1.23±0.01	7.32±0.26	0.39±0.01	12.73±0.15
F12	0.72±0.00	0.59±0.00	18.00±1.41	1.22±0.02	6.96±0.23	0.32±0.04	13.68±0.21
F13	0.59±0.00	0.73±0.01	18.74±0.61	1.23±0.01	6.17±0.01	0.52±0.05	13.35±0.11
F14	0.59±0.01	0.73±0.01	18.62±0.80	1.23±0.01	6.24±0.01	0.56±0.01	13.54±0.06
F15	0.58±0.01	0.71±0.01	19.01±0.62	1.23±0.01	5.84±0.02	0.48±0.01	13.42±0.12
F16	0.59±0.01	0.72±0.01	18.18±0.18	1.22±0.00	5.72±0.05	0.40±0.04	13.58±0.25

All values represent mean±SD, n=3

Tablet disintegration time is strongly influenced by the binder used. The different binder (PVP K30 and gelatin) poses a very different disintegration time, despite producing tablet hardness value which is almost identical.

The use of PVP K30 as a binder with croscopovidone or corn starch as a disintegrant will produce a tablet with disintegration time nearly the same time as the tablet that uses gelatin as a binder. A tablet that uses gelatin as a binder gives a friability value higher than that which uses PVP K30 as a binder. This is due to the fact that gelatin usage as a binder produces granules with a higher content of fines which can lead to increased tablet friability. This research also conducted the optimization of the tablet formula which uses gelatin as a binder and as a disintegrant used croscopovidone and corn starch.

Optimization tablet is using 2^2 full factorial designs

Based on data from the tablet hardness, tablet friability, and the disintegration time can be obtained the polynomial equations that are shown in table 6.

Based on the polynomial equation depicted in table 6, it appears that the concentration of gelatin has a positive correlation to the tablet hardness response, which means that increasing the concentration of gelatin will increase the hardness of tablet on either combination, with the corn starch or with croscopovidone. On the response of friability, if gelatin is combined with croscopovidone, it reduces brittleness compared to when combined with corn starch which can increase friability. This is due to the nature of croscopovidone which is more compressible than the other super disintegrant, so it will form a tablet with a higher hardness and low friability. Based on the polynomial equations as in table 6 can be obtained contour plot as shown in fig. 3 and fig. 4.

In this research combination of gelatin as a binder and croscopovidone as a disintegrant was selected because it produces a tablet with a higher hardness and a low disintegration time. The determination of the optimum formula using design expert program and obtained contour plots of superimposed as shown in fig. 5. The lower and upper limits are determined to get the optimum area can be seen in table 7.

Table 6: Polynomial equations

Response	Gelatin-croscopovidone	Gelatin-corn starch
Hardness (kp)	$Y = 6.9625 + 0.0325X_A + 0.175X_B - 0.21X_AX_B$	$Y = 5.99 + 0.21X_A + 0.014X_B - 0.046X_{AB}$
Friability (%)	$Y = 0.35 - 0.023X_A + 5.10^{-3}X_B - 0.01X_AX_B$	$Y = 0.49 + 0.051X_A + 0.00875X_B - 0.031X_{AB}$
Disintegration tme (min)	$Y = 13.11 + 0.49875X_A + 0.091X_B - 0.021X_AX_B$	$Y = 13.47 - 0.026X_A - 0.089X_B - 0.00875X_{AB}$

Y is the response, X_A is the value of the level of concentration of gelatin, X_B is the value of the level of concentration of the disintegrant (croscopovidone/corn starch).

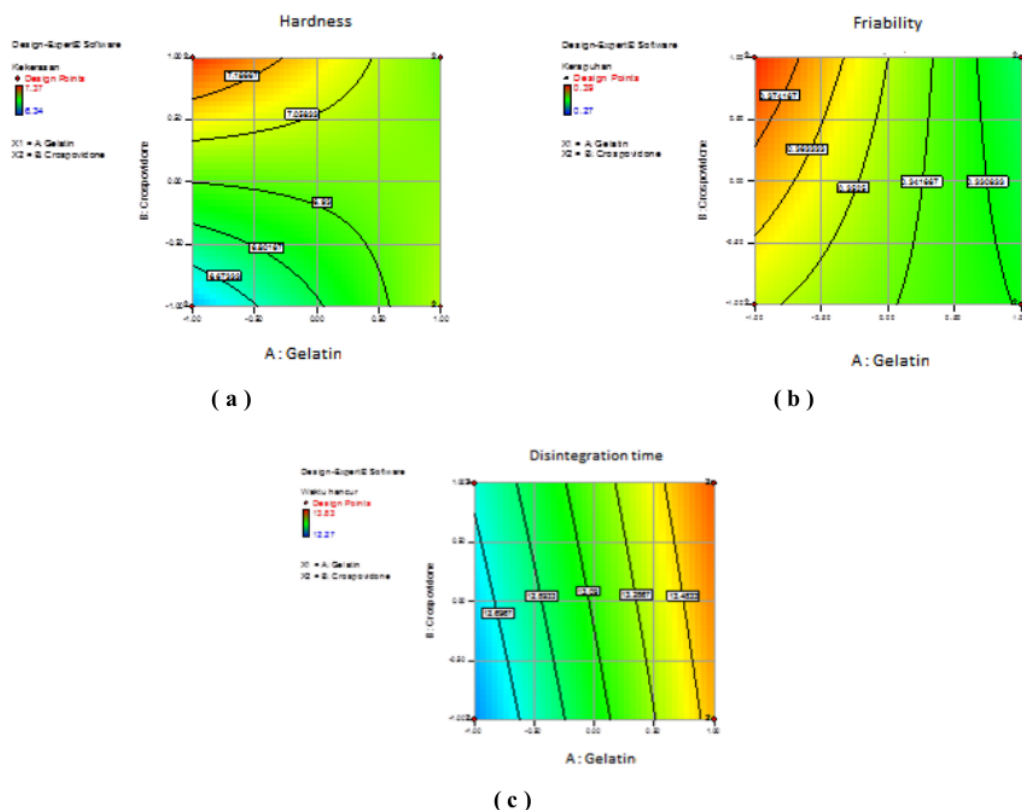


Fig. 3: Contour plot of hardness (a), friability (b), and disintegration time (c) of the tablet formulation development of *Syzygium polyanthum* and *Andrographis paniculata* ethanolic extract using gelatin as a binder and croscopovidone as a disintegrant

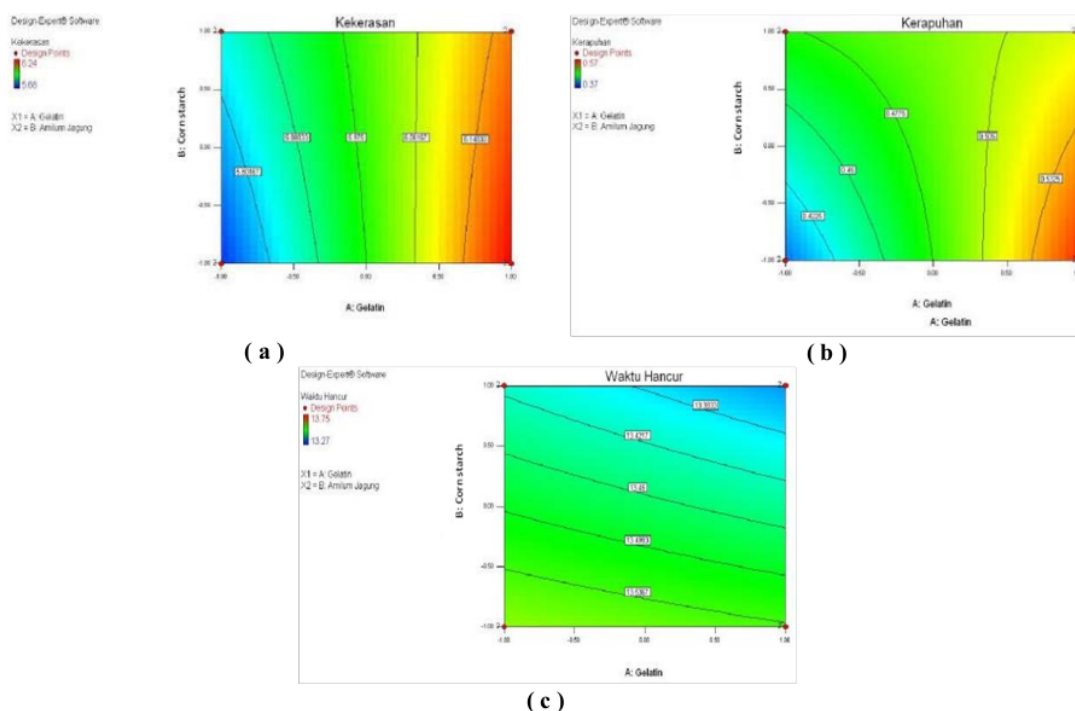


Fig. 4: Contour plot of hardness (a), friability (b), and disintegration time (c) of the tablet formulation development of *Syzygium polyanthum* leaves and *Andrographis paniculata* ethanolic extracts use gelatin as a binder and corn starch as a disintegrant

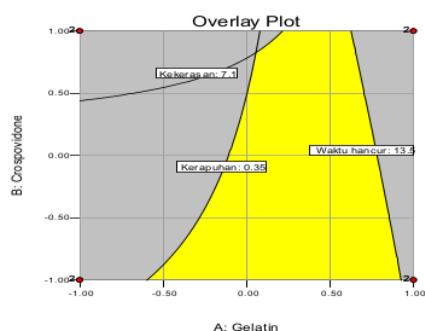


Fig. 5: Superimposed contour plot

Yellow areas depict regions predicted optimum tablet-ethanol extract of *Syzygium polyanthum* leaves-*Andrographis paniculata* with the desired response. One composition that is used as the optimum formula by using gelatin concentration of 3.61% and 3.45% crospovidone concentration.

Physical properties of granules and tablets on a optimum tablet formula

The test results theoretically and testing of hardness, friability, and disintegration time can be seen in table 8. Based on one test sample t-test, it was found that the test results in the hardness, the friability, and the disintegration time are not significantly different with theoretical results. It can be seen from the value of $-11.00 < t_{(0.025,1)} (12.706)$, the value of $t \text{ friability } (0.195) < t_{(0.025,1)} (12.706)$, and the disintegration time $t \text{ value } (-0.404) < t_{(0.025,1)} (12.706)$, which shows that a polynomial equation for a response of hardness, friability, and disintegration time is valid.

Table 7: The lower and upper limits to determined the optimum formula

Response	Lower limit	Upper limit
Hardness (kp)	6.0	7.0
Friability (%)	0.25	0.35
Disintegration time (min)	10	13

Table 8: Comparison between experiment and theoretical

Tablet properties	Theoretical	Experiment
Hardness (kp)	6.77	6.50±0.3
Friability (%)	0.35	0.35±0.02
Disintegration time (min)	12.85	12.76±0.32

All values represent mean±SD, n=3

Determination of total flavonoid content in the tablet

The maximum absorption wavelength used is 440.8 nm with a standard curve equation $Y = -0.049 + 9.610 \times 10^{-2}X$. The assay of total flavonoids in the tablet formulation development of *Syzygium polyanthum* and *Andrographis paniculata* ethanolic extract is 0.112% with 98.44% recovery.

CONCLUSION

The herbal tablet formulation development of *Syzygium polyanthum* and *Andrographis paniculata* ethanolic extract can be prepared using gelatin as a binder and croscopovidone as a disintegrant using the direct compression method. The optimum formula derived from the design optimization using 2^2 full factorial design is the use of gelatin (3.61%) and croscopovidone (3.45%), which will generate hardness of 6.50 kp, friability of 0.35%, and disintegration time of 12.76 min.

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CONFLICT OF INTERESTS

Declared none

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