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Formulation and Pharmaceutical Quality Evaluation of Tablets Containing Extract of *Cinnamomum burmannii* BARK and *Colocasia esculenta* (L) Schott Leaves

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ABSTRACT

Cinnamon bark (*Cinnamomum burmannii*) is used traditionally and has an ingredient containing cinnamic acid compounds. *Colocasia esculenta* (L) Schott leaves contains of flavonoids, alkaloids, tannins, saponins, steroids, and terpenoids. Both of the plants C. esculenta and C. burmannii plants have the potential as anti-diabetics because they can lower blood glucose levels. This study aims to make combination tablets of *C. burmannii* bark and *C. esculenta* leaves extract with various concentrations of PVP K30 binder. This research made four formulas with the concentration of PVP K30, namely F1 (2%), F2 (3%), F3 (4%), and F4 (5%). Tablet preparations were prepared by the wet granulation method. Tablet analysis used flavonoids quercetin and cinnamic acid as markers. The results showed that the tablets were flat, round in shape, light green, had a slightly bitter taste, and had a distinctive aromatic odor. The differences in the concentration of PVP K30 binder 2-5% could affect the hardness, friability, disintegration time, and tablet dissolution ($p<0.05$). The tablet's hardness was 3.65-5.01 KP; friability was 0.705%, disintegration time was <15 minutes, and dissolution was 84.61% in 40 minutes. The levels of the flavonoid quercetin in the tablets were 4.21% and 8.03% cinnamic acid. A tablet combination of *C. burmannii* bark and *C. esculenta* leaves extract with a PVP K30 concentration of 5% (F4) has the best quality.

Keywords: Cinnamic acid, Diabetic, Dissolution, Flavonoids, Granulation

ABSTRAK

Kulit batang kayu manis *(Cinnamomum burmannii)* merupakan salah satu tanaman obat yang digunakan secara tradisional dan mengandung senyawa asam sinamat. Daun talas *(Colocasia esculenta (L) Schott*) mengandung flavonoid, alkaloid, tanin, saponin, steroid, dan terpenoid. Kedua ekstrak tumbuhan tersebut berpotensi sebagai antidiabetes karena dapat menurunkan kadar glukosa darah. Penelitian ini bertujuan untuk membuat tablet kombinasi ekstrak kulit batang kayu manis dan daun daun talas dengan berbagai konsentrasi pengikat PVP K30. Penelitian ini membuat empat formula dengan konsentrasi PVP K30 yaitu 2% (F1), 3% (F2), 4% (F3), dan 5% (F4). Proses pembuatan tablet menggunakan metode granulasi basah. Analisis tablet menggunakan flavonoid kuersetin dan asam sinamat sebagai penanda. Hasil penelitian menunjukkan bahwa tablet berbentuk pipih, bulat, berwarna hijau muda, memiliki rasa agak pahit, dan memiliki bau aromatik yang khas. Perbedaan konsentrasi pengikat PVP K30 2-5% dapat mempengaruhi kekerasan, kerapuhan, waktu hancur, dan disolusi tablet ($p<0,05$). Kekerasan tablet 3,65-5,01 KP; kerapuhan 0,705%, waktu hancur <15 menit, dan disolusi 84,61% dalam 40 menit. Kadar flavonoid kuersetin dalam tablet adalah 4,21% dan asam sinamat 8,03%. Tablet kombinasi ekstrak kulit batang kayu manis dan daun talas dengan konsentrasi PVP K30 5% (F4) memiliki kualitas terbaik.

Kata kunci: Asam sinamat, Diabetes, Disolusi, Flavonoid, Granulasi

INTRODUCTION

Cinnamon bark (*Cinnamomum burmannii*) contains flavonoids and cinnamic acid. The mechanism of cinnamic acid as an antihyperglycemic is by inhibiting the action of the α-glucosidase enzyme which plays a role in breaking down carbohydrates into blood glucose (Hanefeld, 2007), so that it can lower blood glucose levels (Reppi et al., 2016).Cinnamon bark at a dose of 7.56 mg/200 g weight of rats can reduce blood glucose levels according to research by (Alfisyahrin et al., 2014). According to Lestari & Prajuwita (2021) by giving cinnamon doses of 100 mg/Kg weight, rats can increase blood insulin levels in test animals.

The taro plant *(Colocasia esculenta* (L) Schott) contains one of the secondary metabolites, namely flavonoids which have the potential as an antidiabetic. The mechanism of flavonoid compounds for diabetes is through the activity of glucose transporters from the intestine and stimulating β-pancreatic cells so that they can release more insulin (Masaenah et al., 2019). According to research by Bisala et al., (2019), that taro leaf extract at a dose of 200 mg/Kg weight can be used as hypercholesterolemia-diabetes in male white rats.

Taro leaf extract will be combined with cinnamon bark extract and made into tablet preparations because this preparation is a practical, efficient, and ideal dosage form for oral drug administration. One of the binders to be used is PVP K30 because this material is compatible with a wide variety of pharmaceutical excipients, is non-toxic, and has a solubility in polar or non-polar solvents making it easier to choose a solvent in the manufacture of tablets using the wet granulation method in addition to in addition, PVP K30 can function in increasing the rate of dissolution and solubility of an active substance (Rowe et al., 2006).

METHOD

Tools and Materials

The tools used in this study were laboratory standard glassware (Pyrex®), tablet presses (Stokes®), dissolution tester (LID-6®), disintegration test (Erweka®), density tester (TDT-IH®), Flowmeter (Intralab Trading Mandirin®), Friability tester (Panjaya Teknik®), Grinder, Hardness tester (Erweka®), Moisture analyzer (Bacco BM035®), pH meter (Starter 5000®), Uv-Vis Spectrophotometry (Thermo®) , Stopwatch (Samsung®), Analytical balance (Afrindo®), Vacuum dryer (Ogawa®).

The materials used in this study were taro leaves and cinnamon bark (BIOFARMAKA IPB, Bogor), PVP K30 (BOAIPharm®), Avicel PH 102 (FMC®), Mg stearate (FACI®), Talc (Millio-Luing ®), Lactose, Aquades, Ethanol 96% (IndoClasica®), Cinnamic Acid, Sodium acetate, Aluminum chloride, Quercetin, Methanol PA and Tween 80 (Avantor®).

Manufacture of Simplicia Powder and Taro Leaf Extract and Cinnamon Bark

Taro leaves and cinnamon bark obtained from the Center for the Study of Biopharmaca, Bogor Agricultural University, were dried and then ground with a grinder and sieved through a 40-mesh sieve. The simplicia powder was macerated in 96% ethanol solvent with a ratio of 1:10 at room temperature (20- 25°C) for 6 hours. The maceration process was carried out for 3 days with shaking and stirring (Kemenkes RI, 2008). The entire filtrate obtained was poured in six, then added with Avicel PH 102 as much as 5% and tween 80 as much as 2% (w/w). The filtrate is dried with a vacuum dryer until a dry extract is obtained, then it is sieved with an N0.40 mesh sieve (Farida et al., 2019).

Manufacture of Tablet Preparations

Four formulas of taro leaf and cinnamon bark extract tablets were made with different concentrations of PVP K30 used as a binder. The extract has been added filler tween 80 and avicel PH 102.

Each tablet formula contains 220 mg (36.67%) dry extract of taro leaves equivalent to 160 mg of pure extract of taro leaves while 60 mg (10%) dry extract of cinnamon bark is equivalent to 30 mg of pure extract of cinnamon bark. Each batch of formula was made of 500 tablets with a weight per tablet of 600 mg/tablet. The combination tablet formula of taro leaf extract and cinnamon bark can be seen in Table 1.

The method used in the manufacture of tablets is the wet granulation method, using a binder solution, namely PVP K30 in 70% ethanol. The granule drying process uses an oven at a temperature of 40-50°C. Wet granule sieving with mesh sieve no. 8 and dry granules with mesh sieve no. 12.

Table 1. Tablet Formula Combination of Taro Leaf Extract and Cinnamon Bark

No.	Ingredients	Function	Formula (% w/w)			
			1	2	3	4
1	Taro leaf dry extract	Active ingredient	36,67	36,67	36,67	36,67
2	Cinnamon bark dry extract	Active ingredient	10	10	10	10
3	PVP K-30	Binder	2	3	4	5
4	Avicel PH 102	crusher	15	15	15	15
5	Magnesium stearate	Lubricant	1	1	1	1
6	Talk	Glidant	2	2	2	2
7	Laktosa ad	filler	100	100	100	100

RESULTS AND DISCUSSION

Simplicia and Extract Characterization

Observation of simplicia and extract characteristics included organoleptic tests, drying shrinkage, moisture content, and ash content. The results can be seen in table 2.

The drying shrinkage results of the simplicia obtained met the requirements, namely not more than 10%, while the results of the water content of the extract met the requirements of not more than 10% (Ministry of Health RI, 2008). The results of the simplicia ash content met the requirements, namely not more than 10% (taro leaf powder) and not more than 10.5% (cinnamon bark powder) (Ministry of Health RI, 2008). Meanwhile, the ash content of taro leaf extract and cinnamon bark meets the requirements, namely not more than 10% (Ministry of Health RI, 2008).

Testing Flavonoid Levels of Taro Leaf Extract and Cinnamon Bark

The flavonoid content of taro leaf extract and cinnamon bark was determined using the flavonoid quercetin marker, using UV-Vis spectrophotometry. the maximum wavelength obtained was 431.5 nm with an optimum incubation time of 20 minutes. The standard series was prepared using 100 ppm quercetin mother liquor, then a series curve was made with concentrations of 2,4,6,8 and 10 ppm, the linear regression results were obtained y = 0.0692x + 0.1262 with a correlation coefficient of r2 = 0.991. The average value of flavonoid levels obtained for taro leaf extract was 2.82% ± 0.0707, cinnamon bark extract 2.58% ± 0.0212, and a combination of taro leaf extract and cinnamon bark extract 4.70% ± 0 .0282. These results indicate that combining taro leaf extract and cinnamon bark can produce greater levels of flavonoids due to a synergistic effect when combining the two types of extracts (Caesar & Cech, 2019).

Testing Cinnamic Acid Levels of Cinnamon Bark Extract

Analysis of cinnamic acid compounds in cinnamon bark extract using UV-Vis spectrophotometry. The maximum wavelength results obtained were 270 nm with linear regression y = 0.132x – 0.0196 , R2 = 0.9924. The average yield of cinnamic acid levels in cinnamon bark extract was 8.90% ± 0.0212. The results obtained are different from the results of Rackmah's research (2018), namely 10.75%. The results of Alfiani's research (2016) obtained cinnamic acid levels in cinnamon bark extract of 151.362 mg/g.

Granule Evaluation

Determination of granule water content aims to determine the water content contained in the granule. The results of granule water content can be seen in Table 3. The results of the overall granule moisture content show that the results obtained meet the requirements in the range of 3-5% (Hadisoewignyo and Fudholi, 2013).

Determination of good flow rate or flow properties will facilitate the tablet printing process. The purpose of testing the granule compressibility index is to determine the properties of the material to form a stable and compact mass when pressure is applied. The Hausner ratio can be interpreted as compressed density to bulk density. The results of flow rate, angle of repose, compressibility index and Hausner's ratio can be seen in Table 4.

Table 2. Test Results for Simplicia and Extract Characteristics

No.	Sample type	Organoleptic	Drying shrinkage	Water content	Ash content
1	Simplicia of taro leaves	 rather coarse powder form, brownish-green color, characteristic aromatic odor, and slightly bitter taste	5,28% ± 0,3959	-	6,11 ± 3,02
2	Cinnamon bark simplicia	 slightly coarse powder form, brown color, characteristic aromatic odor, and slightly sweet taste	5,95% ± 0,2262.	-	4,48 ± 0,03
3	Taro leaf extract	 Powder form, brownish-black in color, characteristic aromatic odor and bitter taste.	-	3,77 ± 0,7990	5,05 ± 2,75
4	Cinnamon bark extract	 It is in the form of powder, brown in color, has a slightly sweet taste, and has a distinctive aromatic odor	-	3,85 ± 0,5091	3,04 ± 1,04

Table 3. Results of granule moisture content

No.	Formula	Formula Moisture content of granules (%) ± SD
1	1 (PVP K30 2%)	3,00 ±0,43
2	2 (PVP K30 3%)	3,43 ± 0,26
3	3 (PVP K30 4%)	3,20 ±0,45
4	4 (PVP K30 5%)	3,16 ± 0,40

Table 4. Results of flow rate, an angle of repose, compressibility index and Hausner's ratio

No.	Formula	Average Flow rate (g/s) ± SD	Mean Angle of repose (°) ± SD	Compressibility index (%) ± SD	Hausner ratio mean ± SD
1	1 (PVP K30 2%)	5,27 ± 0,88	30,13 ± 1,91	7,55 ± 4,6176	1,0755 ± 0,0461
2	2 (PVP K30 3%)	5,59 ± 1,34	28,36 ±1,28	9,50 ± 2,2000	1,1041 ± 0,022
3	3 (PVP K30 4%)	5,61 ± 0,62	29,84 ± 1,18	8,90 ± 0,8396	1,0890 ± 0,0083
4	4 (PVP K30 5%)	5,78 ± 0,40	30,26 ± 0,99	10,85 ± 1,3116	1,1085 ± 0,0131

All formulas show the results of an average flow rate of 4-10 (g/sec) and angle of repose with a range of 25-30° including the easy-flow category according to Patel, et al (2012). The results of the compressibility index of all formulas were included in the very good category according to Nurdianti et al (2018) with a range of 5-12% and the Hausner ratio with a range of 1.00-1.11 was included in the very good category (Singh & Kumar, 2012).

Evaluation of Tablet Quality

Organoleptic observations The combination of taro leaf extract and cinnamon bark tablets showed a round and flat shape on both sides. Uniform light green color with black spots. The tablet has a characteristic aromatic odor of taro leaves and cinnamon bark, and has a slightly bitter taste. A tablet combination of taro leaf extract and cinnamon bark can be seen in Figure 1.

Figure 1. Tablet combination of taro leaf extract and cinnamon bark

Weight uniformity testing is carried out to see the uniformity of preparations that enter the body so that the amount of active substance in the drug is precise and evenly distributed. The results of the tablet weight uniformity test can be seen in Table 5.

Table 5. Results of tablet weight uniformity test

No.	Formula	Range (mg)	Average (mg) ± SD	KV (%)
1	1 (PVP K30 2%)	593 - 608	602,10 ± 3,8784	0,6441
2	2 (PVP K30 3%)	597 - 612	604,70± 3,9749	0,6573
3	3 (PVP K30 4%)	601 - 638	610,50± 12,3395	2,0212
4	4 (PVP K30 5%)	600 - 616	605,15 ± 5,6872	0,9398

The results of the tablet weight uniformity test show that all formulas meet the requirements because they have a coefficient of variation (KV) value of <5% (Depkes RI, 2008).

The tablet hardness test reflects the strength or resistance of a tablet as a whole while the friability test aims to determine the degree of fragility of a tablet, because tablets must be resistant to friction and shock. Tablets that disintegrate in body fluids will guarantee the availability of the active substance in its molecular form. The hardness value is related to the friability and disintegration time of the tablet. Test data can be seen in Table 6.

Table 6. Results of tablet quality evaluation

No.	Formula	Hardness (kp)	Tablet friability (%)	Average disintegration time (minutes 'seconds")
1	1	$3{,}1715^{a}$	$0{,}955^{c}$	$12'14"^{a}$
2	2	$3{,}7490^{b}$	$0{,}840^{b}$	$13'03"^{b}$
3	3	$4{,}1200^{c}$	$0{,}760^{ab}$	$13'34"^{c}$
4	4	$4{,}2530^{c}$	$0{,}705^{a}$	$13'24"^{d}$

Note: The treatment with the same superscript means not significantly different, whereas if the superscripts are significantly different, there is a significant difference

In general, tablets can be said to be good, if they have a hardness between 4-8 kp (Parrott, 1970). The results of the tablet friability test showed that all formulas had a value of <1% and met the requirements according to Lachman & Lieberman (1994). The results of testing the disintegration time of the formula met the requirements according to the Depkes RI (1995), namely the disintegration time of tablets is less than 15 minutes for non-coated tablets.

Based on the results of statistical tests on tablet hardness, friability and disintegration time, sig <0.05 was obtained, indicating that the difference in PVP K30 concentration had a significant effect on all of these parameters. The highest hardness and lowest friability are indicated by formula 4 (5% PVP K30). The higher the tablet hardness value, the smaller the tablet friability value. These results are by research that the greater the amount of PVP K30 binder used, the smaller the fragility of the tablets (Putri & Husni, 2018).

The high hardness value causes the tablet disintegration time to be longer. This is because the greater the concentration of the PVP K30 binder used, the longer the disintegration time is due to the adhesion between granules which also affects the increase in tablet hardness (Putra, 2019).

Determination of Flavonoid and Cinnamic Acid Levels in Tablets

Determination of levels of flavonoids and cinnamic acid in tablets using UV-Vis spectrophotometry. Absorbance measurements were carried out at a wavelength of 431.5 nm for flavonoids and 270 nm for cinnamic acid. The results of the levels of Flavonoids and cinnamic acid tablets mixed with taro leaf extract and cinnamon bark can be seen in Table 7.

Tablet 7. Results of flavonoid and cinnamic acid levels mixed tablets of taro leaf extract and Cinnamon Bark

No.	Formula	Tablet Flavonoid Levels (%) ± SD	Cinnamic Acid Tablet Levels (%) ± SD
1	1 (PVP K30 2%)	3,81 ± 0,042	7,84± 0,014
2	2 (PVP K30 3%)	3,91 ± 0,007	7,86 ± 0,056
3	3 (PVP K30 4%)	4,09 ± 0,042	7,96± 0,056
4	4 (PVP K30 5%)	4,21 ± 0,042	8,03 ±0,028

Dissolution test

The dissolution test used a dissolution tester type 2 (paddle), using dissolution media with buffer pH 6.8 at a temperature of 37°C, rotating speed of 100 rpm and observing dissolution for 1 hour. Data on the average percentage of the active

substance released in the extract can be seen in Table 8.

Based on the average rate of dissolution and release of the active substance of all tablet formulas, it can be seen that the concentration value of the active substance increases over time up to 60 minutes. These results meet the requirements because they are not less than 80% at any given time (Departemen Kesehatan RI, 2015).

Table 8. Average release of extract active substances in dissolution medium

No.	Time (minutes)	Percentage of drug release (%) (mean)			
		F1	F2	F3	F4
1	5	34,04	32,50	35,42	35,55
2	10	44,76	44,07	36,22	46,21
3	20	51,58	54,28	49,66	64,27
4	30	60,09	67,71	69,36	75,01
5	40	74,52	73,74	80,08	84,61
6	50	81,28	84,79	93,92	92,93
7	**60**	**92,04** ^{a}	**97,49** ^{b}	**98,41** ^{b}	**98,01** ^{b}

Note: The treatment with the same superscript means not significantly different, whereas if the superscripts are significantly different, there is a significant difference

The results of statistical tests on the tablet dissolution test, obtained sig <0.05, so it can be concluded that the dissolution rates of all formulas were significantly different and the concentration of PVP k30 binder affected the release of the extract active substance. the greater the concentration of PVP k30 in the tablet, the faster the release of the active substance takes place (Sharma & Jain, 2010). The reason is that PVP K30 is a polymer that has good solubility in water so it can reduce particle size or form polymorphs that are more soluble it helps accelerate the rate of tablet dissolution (Sharma & Jain, 2010).

CONCLUSION

Combination tablets of taro leaf extract and cinnamon bark with PVP K30 binder concentration of 5% (formula 4) produced the best tablet quality based on parameters of hardness (4.25 kp), friability (0.705%), tablet disintegration time (13 minutes 24 seconds) and dissolution rate at 60 minutes (98.41%).

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REFERENCE

Alfisyahrin, M. N., Moerfiah, & Rustiani, E. (2014). Efektivitas Sediaan Tablet Ekstrak Kulit Kayu Manis (Cinnamomum burmannii) Sebagai Antidiabetes Pada Tikus Putih Jantan Galur Sprague Dawley Yang Diinduksi Aloksan. *Ejournal*.

Bisala, F. K., Ya'la, U. F., & T, D. (2019). Uji Efek Antidiabetes Ekstrak Etanol Daun Talas Pada Tikus Putih Jantan Hiperkolesterolemia-Diabetes. *Farmakologika Jurnal Farmasi*, *XVI*(1), 13–24.

Caesar, L. K., & Cech, N. B. (2019). Synergy and antagonism in natural product extracts: When 1 + 1 does not equal 2. *Natural Product Reports*, *36*(6), 869–888. https://doi.org/10.1039/c9np00011a

Departemen Kesehatan RI. (2015). *Farmakope Indonesia edisi V*.

Depkes RI. (1995). Farmakope Indonesia edisi IV. In *Departemen Kesehatan Republik Indonesia*.

Depkes RI. (2008). *Farmakope Herbal Indonesia Ed 1*. Depkes RI.

Farida, S., Aries Mana, T., Friska Dewi, T., Besar Penelitian dan Pengembangan Tanaman Obat dan Obat Tradisional Tawangmangu, B., Litbang Kesehatan, B., & Kesehatan, K. (2019). Karakteristik Mutu Kapsul Ramuan

Kebugaran Untuk Saintifikasi Jamu. *Jurnal Tumbuhan Obat Indonesia*, *12*(1), 25–32.

Hanefeld, M. (2007). Cardiovascular benefits and safety profile of acarbose therapy in prediabetes and established type 2 diabetes. *Cardiovascular Diabetology*, *6*, 1–10. https://doi.org/10.1186/1475-2840-6-20

Kemenkes RI. (2008). Fa Herbal. *Farmakope Herbal Indonesia Edisi 1*, *1*, 67–71.

Lachman, L., & Lieberman, H. A. (1994). *Teori dan Praktek Farmasi Industri Edisi Kedua*. UI Press.

Lestari, I., & Prajuwita, M. (2021). Penentuan Nilai SPF Kombinasi Ekstrak Daun Ketepeng dan Binahong Secara In Vitro. *Parapemikir : Jurnal Ilmiah Farmasi*, *10*(1), 1–10. https://doi.org/10.30591/pjif.v

Masaenah, E., Inawati, I., & Annisa, F. R. (2019). Aktivitas Ekstrak Etanol Buah Belimbing Wuluh (Averrhoa bilimbi L) Terhadap Penurunan Kadar Glukosa Darah Mencit Jantan (Mus musculus). *Jurnal Farmamedika (Pharmamedica Journal)*, *4*(2), 37–47. https://doi.org/10.47219/ath.v4i2.79

Parrott, E. L. (1970). *Pharmaceutical technology : fundamental pharmaceutics*. Burgess Publishing Company.

Putra, D. J. S. (2019). Penggunaan Polivinill Pirolidon (PVP) Sebagai Bahan Pengikat Pada Formulasi Tablet Ekstrak Daun Sirih (Piper betle L.). *Jurnal Farmasi Udayana*, 14. https://doi.org/10.24843/jfu.2019.v08.i01.p03

Putri, Y. K., & Husni, P. (2018). Artikel Tinjauan: Pengaruh Bahan Pengikat Terhadap Fisik Tablet. *Farmaka*, *16*(1), 33–39.

Reppi, N. B., Mambo, C., & Wuisan, J. (2016). Uji efek antibakteri ekstrak kulit kayu manis (Cinnamomum burmannii) terhadap Escherichia coli dan Streptococcus pyogenes. *Jurnal E-Biomedik*, *4*(1). https://doi.org/10.35790/ebm.4.1.2016.12204

Rowe, R. C., Sheskey, P. J., Owen, S. C., & American Pharmacists Association. (2006). *Handbook of pharmaceutical excipients*. 918.

Sharma, A., & Jain, C. P. (2010). Preparation and characterization of solid dispersions of carvedilol with PVP K30. *Research in Pharmaceutical Sciences*, *5*(1), 49–56.

Singh, I., & Kumar, P. (2012). Preformulation studies for direct compression suitability of cefuroxime axetil and paracetamol: A graphical representation using SeDeM diagram. *Acta Poloniae Pharmaceutica - Drug Research*, *69*(1), 87–93.