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Original Article

THE ANTI-INFLAMMATORY TABLET FORMULATION OF COLEUS (*PLECTRANTHUS SCUTELLARIODES*) LEAVES EXTRACT USING KOLLICOAT®PROTECT COATING

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ABSTRACT

Objective: The purpose of this study was to find the concentration of weight gain on the use of Kollicoat®Protect to produce coleus leaf extract film-coated tablets with good physical properties.

Methods: Coleus extract was obtained by maceration using 70% ethanol. Tablet cores were prepared using the wet granulation method, then evaluated (uniformity of weight, size, hardness, friability, and disintegration time). Coated tablets were made in four variations of polymer weight gain, i.e. 5, 6, 7, and 8%. To determine the effect of the weight gain concentration of Kollicoat®Protect an evaluation of the coated tablets was carried out, i.e. the uniformity of weight, size, hardness, disintegration time, and physical appearance of the film-coated tablets.

Results: The four variations (Film Coated Tablet, FCT 5, 6, 7, and 8%) in weight gain of film-coated tablets showed the physical appearance results per the applicable requirements. However, the physical observation test at room temperature showed the instability of the film-coated tablet. The qualitative analysis of thin-layer chromatography showed that the productive substances in the extracts, tablet cores, and film-coated tablets were still contained even though they had undergone several formulation stages.

Conclusion: Film-coated tablets met the standards of the Indonesian Pharmacopoeia and the United States Pharmacopeia. After two weeks, there was slight instability in film-coated tablets at room temperature storage. The extract, tablet core, and film-coated tablet contain flavonoids.

Keywords: Coleus leaves, Film-Coated Tablet, Flavonoids, Kollicoat® Protect

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INTRODUCTION

At this time, medicinal plants or natural medicinal materials are not new. One of the plants used by the community as medicine is coleus (*Plectranthus scutellarioides* (L.) R. Br.) or iler in Indonesia. The efficacy of this plant is to treat haemorrhoid, fever, intestinal worms, diabetes, late menstruation, vaginal discharge, complicated bowel movements, and digestive disorders [1].

In the study that has been done, coleus leaves contain quercetin. Quercetin is a flavonoid aglycone and belongs to the flavonol group. These compounds have anti-inflammatory properties by inhibiting the production of prostaglandins through their inhibition of COX-2 activity [2, 3].

Film-coated tablets are compression tablets coated with a thin film of polymer that is soluble or insoluble in water or forms a layer covering the tablet [4]. One of the polymers used for coating is Kollicoat®Protect. Kollicoat®Protect is a polymer consisting of a mixture of Kollicoat IR (polyethylene glycol and polyvinyl alcohol in a ratio of 25: 75) and polyvinyl alcohol [5]. Previously, a study on film-coated tablets of coleus leaf extract had been carried out, but the results of the tablet brittleness at room temperature did not meet the requirements. So, this study reported the effect of polymer on the stability and physical properties of coleus leaf extract film-coated tablet.

MATERIALS AND METHODS

Plant material

The plant material was coleus (*P. scutellarioides*) leaves simplicia from Lembang, West Java. This plant was identified by the Laboratory of Plant Taxonomy, Department of Biology, Faculty of Mathematics and Natural Sciences, Universitas Padjadjaran.

Chemical material

Ethanol (E. Merck), n-hexane (E. Merck), ethyl acetate (E. Merck), ammonia (E. Merck), chloroform (E. Merck, hydrochloric acid (E. Merck), ferric chloride (E. Merck), gelatin(E. Merck), magnesium powder (E. Merck), amyl alcohol (E. Merck), ether (E. Merck), vanillin (E. Merck), sulfuric acid (E. Merck), and potassium hydroxide (E. Merck) was pro analytical grade and purchased from Merck (Germany). Starch, Aerosil, Ac-di-sol (Nandasan, India), Kollicoat@Protect (BASF, Germany), PVP (Dalian Sinobio Chemistry Co.), talcum, titanium dioxide (Triiso), and Avicel PH 101 (Du Pont) were pharmaceutical grade.

Table 1: Formula for coleus leaf tablet cores

Composition	%	Weight (g)
Coleus leaf extract	56	307.725
Aerosil	18	98.835
Amylum	12	65.934
Avicel PH 101	6	32.967
PVP	2	10.989
Ac-Di-Sol (inner phase)	2	10.989
Talcum	2	10.989
Ac-Di-Sol (outer phase)	2	10.989

Methods

The dried coleus leaves were ground, then weighed and macerated using 70% ethanol for 3 times 24 h. Every day, the solvent was changed with the fresh one. The liquid extract was evaporated using a rotary evaporator at 40 °C to obtain a concentrated extract. Phytochemical screening was carried out to determine the secondary metabolite groups in the dried leaves and extract. Tablet cores were made using the wet granulation method. Table 1 showed the composition of the tablet cores, which carried out by wet granulation. Evaluation of granules include loss on drying, bulk and tapped density, compressibility, flow rate, and repose angle. The granule evaluation was according to the compendial method, i.e. the Indonesian Pharmacopoeia [6, 7]. Then, the tablet cores were molded and coated using Kollicoat®Protect coating, then evaluated. The composition of the coating suspension was shown in table 2. The evaluation consisted of weight uniformity, size uniformity, hardness, friability, and

disintegration time. The tablet evaluation was according to the compendial method, i.e. the Indonesian Pharmacopoeia [6, 7]. The last step was the qualitative analysis with thin-layer chromatography (TLC) to analyze the presence of the extracts.

Table 2: Formula for coating suspension

Composition	Composition (%)
Kollicoat®Protect	11
Talcum	5.5
Titanium dioxide	3.5
Distilled water	80

RESULTS

Table 3: Results of phytochemical screening

Secondary metabolite	Dried leaves	Extract
Alkaloids	-	-
Polyphenols	+	+
Tannins	-	-
Flavonoids	+	+
Mono-and sesquiterpenes	+	+
Steroids and terpenoids	+/+	+/+
Quinones	+	+
Saponins	+	+

Note: (+) detected; (-) not detected; the data were obtained from 3 trials

Table 4: The results of the evaluation of the granule (n = 3)

Mass evaluation print	Results
Loss on drying (%)	1.48±0.006
Bulk density (g/ml)	0.64±0.016
Tapped density (g/ml)	0.74±0.014
Compressibility (%)	13.50±2.18
Flow rate (g/sec)	13.81±1.850
Repose angle (°)	22.07±1.070

Table 5: The results of the evaluation of tablet core (n = 3)

Evaluation of tablet core	Results
Tablet weight (mg)	659.64±14.36
Tablet diameter (mm)	12.13±0.062
Tablet thickness (mm)	5.11±0.053
Hardness (N)	104.38±0.01732
Friability (%)	0.1±0.001
Disintegration time (min)	10.53±0.02886

Table 6: The results of evaluation of coating suspension (n = 3)

Parameter	Results
Viscosity	388.5±0.404 mPa. s
Surface tension	60.63±0.416 dyne/cm

Table 7: The results of evaluation of film-coated tablets (n = 3)

Evaluation	Weight Gain			
	5%	6%	7%	8%
Tablet weight (mg)	695.24±15.79	718.08±10.95	735.32±10.51	751.75±10.32
Tablet diameter (mm)	12.17±0.025	12.21±0.016	12.23±0.024	12.25±0.039
Tablet thickness (mm)	5.24±0.073	5.31±0.062	5.37±0.024	5.46±0.064
Disintegration time (min)	13.30±0.5	13.58±0.4	14.38±0.4	15.10±0.3

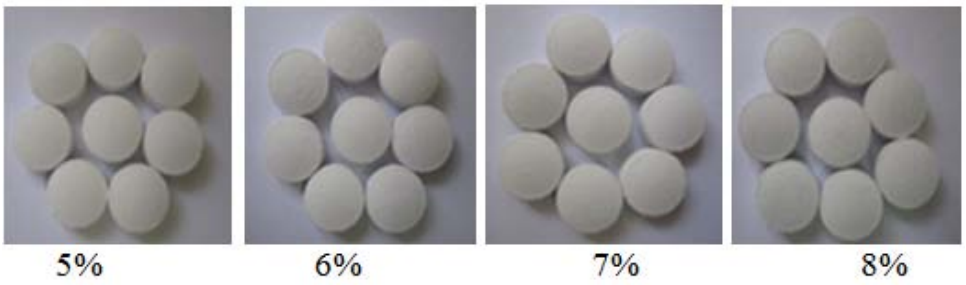

Fig. 1: Observation day 0

Table 8: TLC results of coleus leaf extract, tablet cores, and the film-coated tablet

Spot no.	Rf value	Observation					
		Extract	TC	FCT 5%	FCT 6%	FCT 7%	FCT 8%
1	0.17	Brown	Brown	Brown	Brown	Brown	Brown
2	0.36	Gray	Gray	Gray	Gray	Gray	Gray
3	0.42	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow
4	0.70	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow
5	0.88	Green	Green	Green	Green	Green	Green

Note: TC = tablet core, FCT = film-coated tablet

DISCUSSION

Phytochemical screening was carried out to determine the secondary metabolites of dried leaves and extract (table 3). This result was the same as Levita *et al.* [8], but slightly different from Fakhriati *et al.* [9], who reported there was no saponins, monoterpenes, and sesquiterpenes. Su *et al.* [10] found that terpenoids were detected in coleus Philippines. The difference in phytochemical screening results was most likely due to plant origin and the difference in the growth location [11].

In wet granulation process, the formula for 825 tablets was weighed. The number of tablets were calculated from the extract obtained and the amount required for the evaluation of granules and tablets. Table 1

showed the composition of the designed tablet cores and carried out by wet granulation. Tablet production by wet granulation method was the most common method in pharmaceutical practice [4, 12-13]. In general, the required extract and excipients are granulated before tableting, meaning that the powder particles are converted into granules. Granules were formed by bonding the powder with an adhesive. This technique required a solution, suspension, or slurry containing a binder usually added to the powder mixture.

Granule was free-flowing particles with regular shape and contain coleus leaf extract as active ingredient. The granule flow is the key requirement for the manufacturing process due to determine similar weight filling of granules in tablet manufacturing [14]. Table 4 shown the results of granule evaluation were met the requirement of a good granule [4, 12].

Loss on drying met the requirement. Too dry granules would lose their binding power and tend to form capping and lamination. In contrast, too-wet granules would cause peeling and sticking because of the adhesion of the tablet material to the punch and die walls during the molding process [12, 13]. The compressibility value was 13.5%, showed the powder flow was good according to the Carr's index [14, 15]. The measurement of the repose angle was carried out to determine the nature of the adhesion or cohesion of the granules, that would affect the flow properties of the granule. Repose angle of 22.07°, showed the excellent flow property [15, 16]. This value showed that granule was effortless to flow and will make uniform shape of tablet core. The flow rate value showed the excellent flow properties (13.81 g/sec) [17, 18]. This value indicated that the granule will flow freely when loading into the machine to produce tablet core.

The granules were molded into tablet core and the results of tablet core evaluation shown in table 5. Tablet cores have a uniform shape with hardness and disintegration time which met the requirements of good tablet cores [6, 19, 20].

The uniform weight of tablet cores had weight that met the requirements of the Indonesian Pharmacopoeia. The requirement was tablets with average weight was more than 300 mg; there was no tablet whose weight deviated more than 5% and there was no single tablet whose weight deviated more than 10% of the average weight planned tablet average [6, 21]. The range of tablet core was 633.13-699.77 mg. The size of the tablet core met the requirements of the Indonesian Pharmacopoeia [6]. Furthermore, the diameter of the tablet core was not more than three times and not less than four-thirds of the thickness of each tablet [6, 22, 23]. The tablet hardness test was conducted to measure the compactness of the pressure, i.e. the resistance of a tablet to the force acting until the tablet is broken. Tablets must be hard enough to withstand shattering during handling or manufacture, packaging, and transportation. A good tablet core hardness value was more than 70 N [24, 25]. The tablet friability indicated the tablet's resistance to surface erosion and shock. The results (0.1±0.001%) met the requirements of United State Pharmacopoeia. The average weight loss was not more than 0.8% [26, 27]. According to the Indonesian Pharmacopoeia, the required time to disintegrate uncoated tablets in a suitable medium, unless otherwise stated, was not more than 15 min [6, 28, 29]. The results met the requirement, i.e. 10.53±0.02886 min.

Kollicoat®Protect is a ready-to-use moisture barrier system for use in combination with pigments. Coating method used to minimize the risks for oxidative degradation of active ingredients and cover the unpleasant appearance and bitter taste [30, 31]. The coating suspension of the Kollicoat®Protect polymer showed a low viscosity value. In Europe Pharmacopoeia [32], this polymer has a value of less than 450 cp. The viscosity of the coating suspension was related to the spraying process (table 6). If the viscosity value were too high, it would inhibit the spraying of the suspension on the tablet core [33, 34]. Surface tension is related to the adhesion and cohesion properties of the coating suspension [35, 36].

The coating efficiency was affected by variables of tablet core, coating pan, and coating environment [21]. Film-coated tablets were compressed tablets coated with a thin, colored, or not coated water-soluble polymer material that disintegrates rapidly in the gastrointestinal tract [4]. Tablets were coated for various reasons, such as protecting the active ingredient from air, humidity, or light, masking unpleasant tastes and odors, improve appearance, and regulating the site of drug release in the gastrointestinal tract [12]. In coating, films on tablets usually contain various materials, such as polymers (film formation), plasticizers, surfactants, dyes, sweeteners/flavors/fragrances, polishes, and solvents [13]. The increase of the concentration of coating suspension were in line with the increase the weight, diameter, thickness, and disintegration time of film-coated tablets (table 7). The observation of film-coated tablets on day 0 shown in fig. 1. Tablets have a uniform shape but different on weight, diameter, and thickness, depend on the concentration of coating suspension. After 14 d, there were no changes in tablets. It means tablets were stable in room temperature. The film-coated tablets were complied with the requirements of the Indonesian Pharmacopoeia [6].

The physical appearance was conducted by storing the film-coated tablets at room temperature (23°-25 °C) with RH 73-80% for two weeks. At day 0, the film-coated tablets were white in color and odorless (fig. 1). After two weeks, there were change in physical appearance. Film-coated tablets with a weight gain of 5% showed a color change from white to brownish. As for the film-coated tablets with a weight gain of 6%, the color of the coated tablets becomes off-white. In film-coated tablets with 7% and 8%, there were no change from the original color, i.e. white. This showed that the weight gain of 5 and 6% were incapable to protect the tablet cores, because of the thinness of the film layer or uncoated tablet core. All tablets stored at room temperature in the open state resulted in soft tablets due to the presence of water trapped in the coated tablet due to the drying factor at the time of the incomplete coating. This made the tablet core became soften. However, the water content in the tablet core did not affect the polymer coating because there was no breakage of the coating layer.

TLC was carried out using a silica gel GF254 with butanol: acetic acid: water (4:1:5) as mobile phase and vanillin sulfate solution as the spot developer. This TLC condition was specific for flavonoid. Qualitative tests on the extracts, tablet cores, and film-coated tablets showed there was flavonoids (table 8).

CONCLUSION

Film-coated tablets met the standards of the Indonesian Pharmacopoeia and the United States Pharmacopeia. It was found Kollicoat®@Protect to produce coleus leaf extract film-coated tablets with good physical properties. After two weeks, there was slight instability in film-coated tablets at room temperature storage. The extract, tablet core, and film-coated tablet contain flavonoids.

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AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICTS OF INTERESTS

There is no conflict of interest between the authors.

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