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Formulation of Nano Curcuminoid Effervescent Tablet

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ABSTRACT

Traditional medicine has been used by Indonesian people for a long time. *Curcuma domestica*, one of the plants containing curcuminoid, is usually used as the component in traditional medicine. The oral curcuminoid has not only low level concentration in serum and tissues, but also fast metabolism and elimination due to its poor solubility of curcuminoid. Particle size in nano can be used to improve the solubility, therefore nano curcuminoid is studied in this reserach for this purpose. The nano curcuminoid was formulated in effervescent tablet. The aim of this study was to develop formula of effervescent tablet containing nano curcuminoid. The effervescent tablets were prepared by wet granulation method using non-aquoeus solvent. Evaluations of the tablets met the requirements of Indonesian Pharmacopoeia. The evaluation involved uniformity of weight, hardness, friability, disintegration test, pH, and hedonic test. The study results showed that formula containing nano curcuminoid 4,14%, PVP K30 5%, sucrose 0,61%, aspartame 6,25%, citric acid 45%, ethanol 0,22%, sodium bicarbonate 25%, PEG 6000 5% and orange powder flavour 9% was the best formula based on the physical evaluation and hedonic test.

Keywords: *Curcuma domestica*, curcuminoid, effervescent tablet.

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INTRODUCTION

Traditional medicine has been known and used by Indonesian people for a long time. One of the potential medicinal plants for health is *Curcuma* species [1,2]. *Curcuma domestica* is usually used as the component in traditional medicine. The main content of *Curcuma domestica* is curcuminoid [3]. As a traditional medicine, Curcuminoid is used as a hepatoprotector, gastroprotector, etc [3,4]. Curcuminoid is insoluble in water and diethyl ether, however, it is soluble in acetone, alcohol, acetic acid glacial and alkali hydroxide. Organoleptic of curcuminoid are yellow to orange powder and slightly bitter [3]. The oral curcuminoid has not only low level concentration in serum and tissues, but also fast metabolism and elimination due to its poor solubility so that it has a problem in bioavailability [5,6]. Delivery system based nanoparticle is an approach to solve the bioavailability problem [7,8,9,10]. Many benefits of curcuminoid in health make it potential to develop into effervescent tablet preparation. Effervescent tablet consist of acid and base phase which can be reacted in the existence of water and result carbon dioxide gas, that giving fresh effect [11]. Based on the background above, the study on formulation of nano curcuminoid effervescent tablet has been done. Evaluation of granules and tablets were done to get the best formula.

MATERIALS AND METHODS

Chemical materials:

Nano curcuminoid powder (PT. Phytocheminda Reksa), PVP K30, sucrose, mannitol, aspartame, citric acid, sodium bicarbonate, PEG 6000, orange flavour and ethanol 96%.

Instruments:

Dry cabinet (Krisbow), hygrometer (Corona), dehumidifier (Best Air), oven (Incubator Binder BD115), moisture analyzer (Mettler Toledo), mini drum roller (Erweka), tapped density (MK3), flowability tester (Copley BEP3), digimatic heightgauge (Mitutoyo), vibratory sieve shaker (Retsch), tableting machine (Kambert), friabilator (Sotax F2), disintegrator tester (Pharmatest PTZ Dist 3), hardness tester (J.Borals), pH meter (Schott Instrument Lab 850), and stirring hot plate cimarec (Thermo Scientific).

Methods:

Preparation of Granules:

Composition of effervescent tablet formulation is shown in Table 1. The effervescent tablets were prepared by wet granulation method using non-aqueous solvent (ethanol or isopropanol). Nano curcuminoid, sucrose, citric acid, aspartame and PVP K30 was mixed in mixing machine. Solvent was added slowly into the mixed material until it is wet enough. Mesh No. 8 was used to sieve the wet mixed material to get granules. The granules were dried into oven (60°C) until moisture content was $\leq 1\%$. Dried sodium bicarbonate (moisture content $\leq 1\%$) was mixed with the granules and then PEG 6000 and orange powder flavour was added slowly. All of the preparation process of the effervescent tablet was done at humidity $\leq 25\%$ [11].

Evaluation of Granules:

Moisture content, powder flow, angle of repose, bulk and tapped density, and compressibility index of the granules were evaluated to determine the granules which met the requirements of Indonesian Pharmacopoeia [11].

Preparation of Effervescent Tablet:

The final mixed material was compressed by tableting machine using suitable punch. Diameter of the tablet was 19 mm and 1500 mg in weight. The tableting process was done at humidity $\leq 25\%$ [11].

Evaluation of Effervescent Tablet:

The evaluations involved uniformity of weight, hardness, friability, disintegration test, pH, and hedonic test. The spesification of the test based on the requirements of Indonesian Pharmacopoeia [11].

Data Analysis

Data and statistic analysis were made by using analysis of varians (one way ANOVA). A value of $p < 0.05$ was considered significant statistically.

RESULTS AND DISCUSSION

Formulation and Preparation of The Effervescent Tablet

There were 7 formula of effervescent tablet with variation of the ingredients (Table 1). Nano curcuminoid was 480 nm in particle size. Weight of the effervescent tablets were range from 1500 to 2000 mg. All of the preparation process including granulation and preparation of the effervescent tablet was done at humidity $\leq 25\%$. The maximum humidity was needed to avoid the influence of humidity on product. High humidity can initiate reaction between acid and base phase so the humidity must be controlled [11].

Table 1: Formula of Effervescent Tablet

Ingredients	Formula						
	1	2	3	4	5	6	7
Nanocurcuminoid (%)	5.52	5.52	5.52	5.52	5.52	4.60	4.14
PVP K30 (%)	3.00	3.00	3.00	3.00	3.00	3.00	5.00
Sucrose (%)	21.48	17.98	-	16.48	10.98	0.40	0.61
Mannitol (%)	-	-	17.98	-	-	-	-
Aspartame (%)	-	3.50	3.50	5.00	5.50	7.00	6.25
Citric acid (%)	40.00	40.00	40.00	40.00	45.00	45.00	45.00
Ethanol 96% (%)	0.22	0.22	0.22	0.22	0.22	0.22	0.22
Sodium bicarbonate (%)	25.00	25.00	25.00	25.00	25.00	25.00	25.00
PEG 6000 (%)	5.00	5.00	5.00	5.00	5.00	5.00	5.00
Orange powder flavour (%)	-	-	-	-	-	10.00	9.00
Tablet weight (mg)	1500	1500	1500	1500	1500	1800	2000

Evaluation of Granules

The aim of granules evaluation on all formula was to determine the characteristic of the granules [11]. The evaluation results were compared with the requirement of Indonesian Pharmacopoeia. Moisture content of the granules was checked using automatic moisture analyzer type 1 at 70°C. The moisture content was $\leq 1\%$ (Figure 1). 100 gram granules was tested using flowability tester to determine the angle of repose and flow of the granules. Angle of repose of the granules was between 30-40°. Based on the index Carr table, the granules was good enough on its flow (Figure 2). The test result of bulk and tapped density of the granules were conducted to calculate compresibility index. The flow of the granules was good enough due to its compresibility index ≤ 23 . The compresibility index of the granules can be seen on Figure 1. All of the granules evaluation showed that the granules of all formula had good enough on its flow. Then, the granules was compressed on tableting machine using punch with 19 in diameter. Weight tablet was set in 1500-2000 mg.

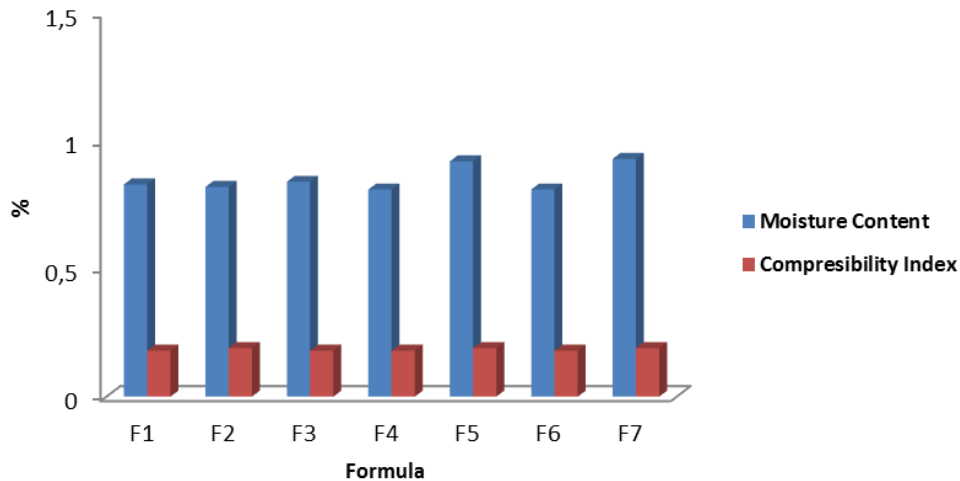


Figure 1: Moisture Content and Compressibility Index of granules (n = 3)

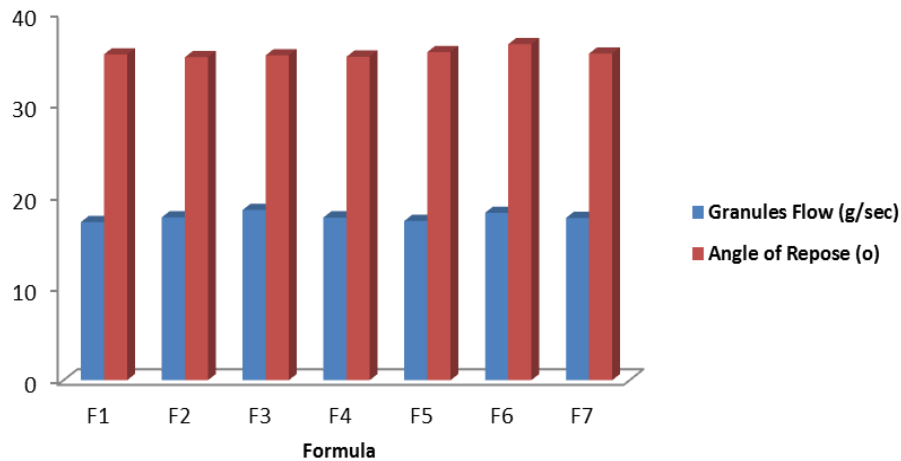


Figure 2: Granules Flow and Angle of Repose of granules (n = 3)

Evaluation of Effervescent Tablet

Uniformity of weight, hardness, friability, disintegration and pH were evaluated to determine the physical characteristic of the effervescent tablet (n=3). Figure 3 showed all of the effervescent tablet evaluations. Hedonic test (n=20) was done to know response of the responden on organoleptic of the effervescent tablet (texture, taste and odor) (Figure 4). Hedonic test was important to do because the nano curcuminoid effervescent tablet was potential to be commercial product.

Uniformity of tablet weight was not more than 5% and met the requirements of Indonesian Pharmacopoeia for tablet with average weight more than 300 mg. Hardness tester was used to check the hardness of the effervescent tablet. Pressure in Kg/cm² which needed to break the tablet could be seen on the instrument. The hardness of the tablets was 10.00-15.00 Kg/cm². The tablets were good in hardness.

Friability test was needed to evaluate the performance of the tablets on unstable condition while production process, packaging, transportation, etc [11]. Good tablet must have friability test result ≤ 1% after testing by the instrument (25 rpm, 4 minutes). Result of friability test was met the requirement.

Disintegration and pH of the effervescent tablet were checked by taking the tablets into 200 mL water [11]. The disintegration time of the effervescent tablets and pH of the solution was determined. All of the tablets with different formula disintegrated not more than 4 minutes while the requirement for effervescent

tablet disintegration ideally was approximately 5 minutes on room temperature. The pH solution of the effervescent tablet was 4.00-5.50.

Hedonic test was done using 20 responden. Each responden must drink the effervescent tablet diluted in 200 mL water. The responden gave their response about texture, taste and odor of the effervescent tablet. Hedonic test result can be seen in Figure 4.

The result of statistical analysis using one way ANOVA showed that data of granules (moisture content, powder flow, compresibility index) and tablet evaluations (uniformity of weight, hardness, friability, disintegration, pH) of all formula were not significantly different ($p < 0.05$), however, formula 7 resulted better tablet in hardness and friability than other tablets. Hedonic test showed that most of responden like the effervescent tablet with formula 7. Based on the physical evaluation and hedonic test, formula 7 was the best formula for nano curcuminoid effervescent tablet.

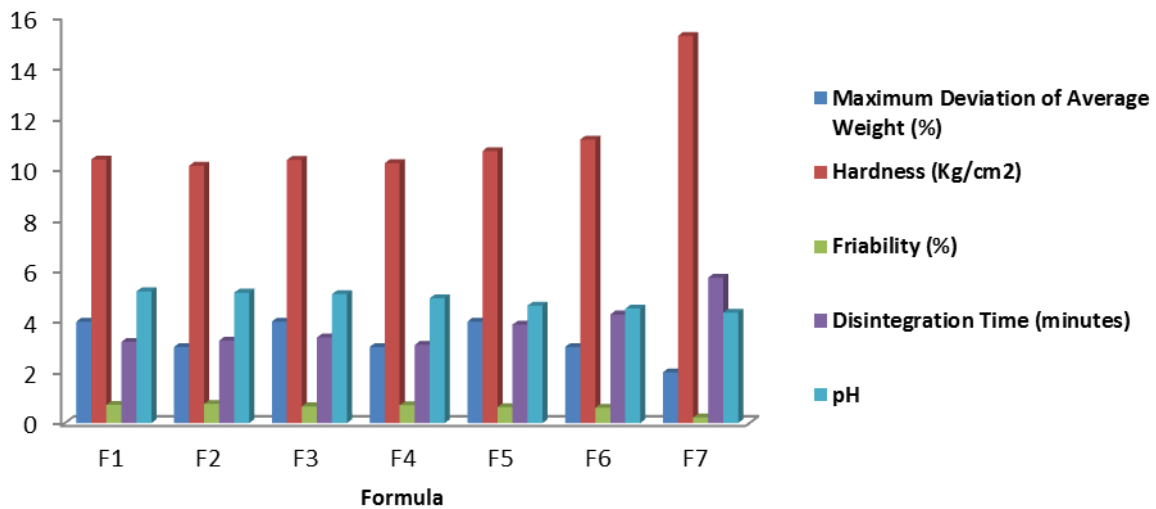


Figure 3: Average Weight, Hardness, Friability, Disintegration Time and pH of Tablet (n = 3)

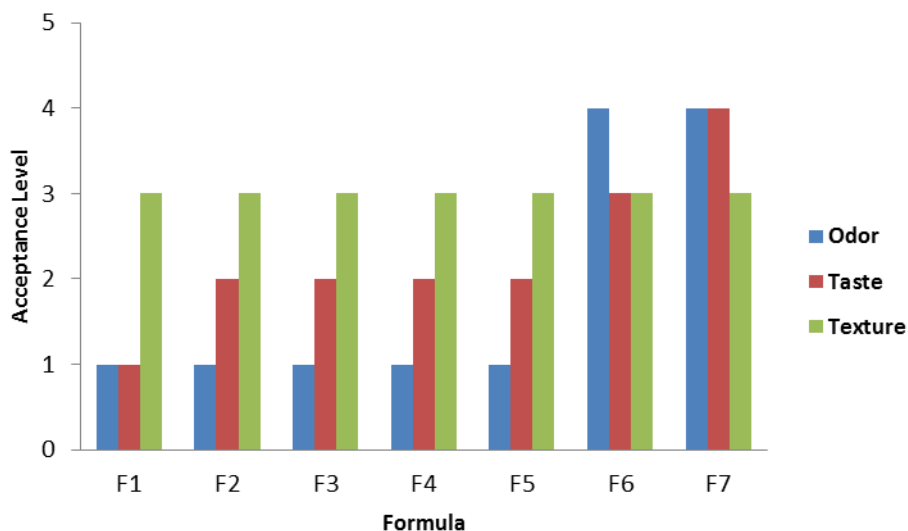


Figure 4: Hedonic Test (n = 20)

CONCLUSIONS

Based on the physical evaluation and hedonic test, it can be concluded that formula 7 containing nano curcuminoid 4.14%, PVP K30 5%, sucrose 0.61%, aspartame 6.25%, citric acid 45%, ethanol 0.22%, sodium bicarbonate 25%, PEG 6000 5% and orange powder flavour 9% was the best formula for preparation of nano curcuminoid effervescent tablet.

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