Research Article

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ANTI-INFLAMMATION TABLET OF LEGUNDI (*VITEX TRIFOLIA* L.) ETHANOL EXTRACT WITH VARIATION OF SODIUM STARCH GLYCOLATE

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Received on: 19/08/15 Revised on: 19/09/15 Accepted on: 04/10/15

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DOI: 10.7897/2277-4343.07140

ABSTRACT

This article reports the formulation of tablets of ethanol extract Legundi as an adjuvant to anti-inflammatory drugs on breast cancer. Extraction was done by maceration method in 95% ethanol. Furthermore, the standardized extract which includes the calculation of yield, moisture content, ash content, TLC, and phytochemical screening. Tablet formulations prepared by wet granulation method in five variations of concentrations of Na-starch glycolate as a disintegrator. Fifth formula made have met the criteria of granules or tablets before felted mass of a good, include the levels of drying shrinkage (LOD), compressibility, flow rate and angle of rest. Fifth formula also has met the criteria for a good tablet includes uniformity of weights and measures, friability, and disintegration time. The results of this study indicate that the variation in concentrations of Na-starch glycolate as a disintegrator in the formula III is the most optimal concentration, i.e by 25 mg at the time were destroyed during the 12 minutes 36 seconds.

Keywords: Legundi, *Vitex trifolia* L., anti-inflammatory, tablet, Na-starch glycolate

INTRODUCTION

Indonesian society has long been treating diseases by utilizing plants around. This habit continued as hereditary, even up in the modern era as it was when the synthetic drugs emerging, modern society still use natural materials as a drug because of its superiority low side effects. Empirically, Legundi (*Vitex trifolia* L.) is widely used as a folk remedy for headache, flu, migraine, sore eyes, and so on[1,2]. In another study by Astuti[3] obtained the result that the plant Legundi empirically used as a remedy for stomach cramps, coughs, wounds, tonsillitis, and typhoid fever.
Benefits contained in Legundi plant has not been widely used by the general public, but further research showed that Legundi as an anti-inflammatory activity[4], anticarcinogenic in prostate cancer[5], lung and colon, stomach[6,7], and breast[8]. Haidara *et al*. (2006)[9] has conducted pharmacological studies that prove that casticin have anti-inflammatory, antitumor, cytotoxics, anti-asthmatic, analgesic, and casticin itself contained in the plant Legundi. Prabu and Kumuthakalavalli in their article mentions that *vitex trifolia* have medicinal use for diarrhoea, urticaria, cellulites, abscess, carbuncle, and eczema[10]. In 2013, we reported that the ethanol extract of *Vitex* sp. have anti-inflammatory effects in mice and is also efficacious against cell lines T47D[11].
From the literature study was done, so far there has been no research to develop Legundi into the form of pharmaceutical preparations, especially as anti-inflammatory drugs, therefore, based on the description of the background described above, this paper reporting research on the Formulation and Evaluation of anti-inflammatory tablets of extracts ethanol of *Vitex trifolia* L. as an adjuvant herbal remedy for inflammatory breast cancer with sodium starch glycolate variation as its disintegrator.

MATERIALS AND METHOD

Plant material

The plant material used in this study was Legundi (*Vitex trifolia* L.) fruits from the beach in Karawang, West Java, Indonesia which was then determined in Taxonomy Labortory, Department of Biology, Faculty of Mathematics and Natural Sciences, Universitas Padjadjaran, Indonesia.

Extraction

The maceration extraction method was used in this study. Legundi dried in the sun to be dried, mashed and then inserted into macerator and soaked in 95% ethanol for 3 days 2 nights with stirring every day. The extract obtained was then concentrated with rotary evaporator, and then evaporated over the water bath to get a thick extract with a constant weight. Subsequent extraction results include standardized phytochemical screening, moisture content, ash content, and thin layer chromatography.

Tablet Formulation

Tablet formulations in this study using wet granulation method[12] wherein the composition of the tablets can be seen in Table 1. As an active compound, Legundi ethanol extract was included in the inner-phase along with aerosil, disintegrator, emcompress, and Na-CMC where Na-CMC was added as a binder after mucilage made in advance. As the external phase Na-starch glycolate was added as a disintegrator with various concentrations together with Mg-stearate and Oleum Menthae. Furthermore, the results of the formulation were evaluated of its characteristics. Granule evaluation was conducted on the test Loss On Drying (LOD), compressibility test, and flow rate and angle of rest. While the evaluation was conducted on the test tablet weight uniformity and size, hardness, friability test, destroyed time test, and the qualitative assay. For qualitative assay, it was cconducted by thin layer chromatography or TLC. Tablets masshed and dissolved in the ethanol 95% to dilute, then spotted on a silica gel plate 254 and chromatographed with a suitable solvent (n-hexane: ethyl acetate, 2: 1).

Table 1: Formulation of Legundi ethanol extract tablet

Composition	Formula (mg)				
	I	II	III	IV	V
Legundi ethanol extract	300	300	300	300	300
Aerosil	80	80	80	80	80
Amprotab	80	80	80	80	80
Emcompress	154,35	154,35	154,35	154,35	154,35
Na-CMC	10,66	10,66	10,66	10,66	10,66
Na-Starch Glicolate	15	20	25	30	35
Mg-Stearat	1	1	1	1	1
Oleum Menthae	qs	qs	qs	qs	qs

RESULTS AND DISCUSSION

Extracted from Legundi fruits in 95% ethanol by maceration method, viscous extract obtained with a yield of 12.05%. 95% ethanol solvent chosen because it has the appropriate polarity to attract secondary metabolites mainly flavonoids found in plants Legundi.

Based on the screening done showed that Legundi contained polyphenol, flavonoids, steroids, monoterpenes and sesquiterpenes and quinones. The phytochemical screenings conducted has differences with the results reported by Thenmozhi *et al.* [13] which stated Legundi plant also contains tannins and saponins compounds. The content of possible differences caused by different sources of Legundi plant used.

From the examination of water content, the results showed that the ethanol extract Legundi used in this study contained a water content of 9.51%. Extract moisture content should not be more than 10% w/w because it can increase the risk of growth-mold and mildew. According to Thenmozhi *et al*. determination of the water content of the extract is useful to know the nature of the chemical compounds in natural materials, especially regarding their solubility in water.

In the determination of ash content, it was found that ash content of 9.64%. According to the Indonesian Pharmacopoeia[14], Legundi sample should not contain more than 11% w/w ash. The test aims to determine the ash content assay and inorganic compounds contained in crude samples.

Examination of the extract by thin layer chromatography method was also performed using a mobile phase of n-hexane and ethyl acetate in the ratio 2: 1, and 254 silica gel as the stationary phase. From the results obtained by thin layer chromatography resulted in a six spots were visible under UV light with a wavelength of 254 and 366 nm.

Tablet Formulation results

Anti-inflammatory tablets of Legundi ethanol extract made by wet granulation method. This method was chosen because the ethanol extract Legundi become active ingredient in this tablet is thermostable or resistant to heat. In addition, the wet granulation method also has several advantages, among others, can improve the flowability and compressibility of the powder as well as distribution and good uniformity of the active substance[15].

Granule evaluation done to see if the character granules to be used already meet all contingencies good granules in accordance with the terms specified. Evaluation was conducted on the granule drying shrinkage test, test-sibilitas kompre, and test flow rate and angle of rest.

Loss On Drying (LOD) results

Testing Loss On Drying (LOD) is a test that is done to determine the water content is still contained in the granules that have been dried in an oven for approximately 18-24 hours. The granules were tested for the granules which had not been added the outer phase. The results of the test Loss On Drying (LOD) can be seen in Table 2.

Drying shrinkage are still allowed is below 2%, because when the moisture content is too high will affect the physical appearance of the tablet caused by poor attachment of the mass flow rate and the granules on the punch and the die wall when the compression process takes place.

Table 2: Loss On Drying (LOD) test results

	Formula				
Drying shrinkage	I	II	III	IV	V
	1,08%	1,08%	1,5%	1,5%	1,5%

From the water content of all formulas test results it could be concluded that granules were eligible to be used in the tablet printing process.

Compressibility Test Results

Compressibility testing was carried out to determine the ability of compressible granules to be compressed into tablets. Results of testing granule compressibility and its flow properties based Carr index Carr found that all formulas have good compressibility range compressibility percentage ranged from 4.8% to 15.39% with good flow properties of powders[16].

Flow rate and rest angle tests

Testing flow rate and angle of print or granule mass break done to see how well

flow properties owned granules. Granule ability to flow very influential during the tablet printing process. From the tests, it obtained flow rates and test results break angle as shown in Table 3 with good and excellent results.

Table 3: Flowability and Rest angle of tablet legundi

Formula	Flowability (g/s)	Powder flow properties for flowability	Rest angle	Powder's flow properties for rest angle
I	6,977	good	20,20º	excellent
II	6,303	good	21,65º	excellent
III	8,197	good	19,12º	excellent
IV	13,27	excellent	10,357º	excellent
V	9,615	good	9,648º	excellent

Tablet evaluation
Evaluation was done to look at the quality tablet made. Good quality tablet dosage should be in accordance with the conditions that had been set.

Uniformity Test Results Weight and Size
The results of weight measurement and uniformity of size tablet can be seen in Table 4.

Table 4: Uniformity of tablet weight and size

Formula	Weight		Diamater		Thickness	
	Mean (mg)	SD	Mean (mg)	SD	Mean (mg)	SD
I	668,65	9,155240087	12,036	0,053946855	5,39	0,122474487
II	659,35	16,53473218	12,068	0,026925824	5,648	0,054760243
III	660,16	8,700349358	12,123	0,022028689	4,272	0,038058127
IV	658,55	10,08284108	12,019	0,023725403	5,227	0,095647379
V	662,035	10,63499066	12,604	0,025567249	5,025	0,063864577

From the results of measurements of the tablet weight uniformity, could be seen from the standard deviation of the data obtained tablet weight uniformity was very varied, but the results of weight measurement of 20 tablets of each formula had met the requirements of the Indonesian Pharmacopoeia IV[14] which states that if the weight is more than 300 mg tablet then not should be no more than two tablets whose weight deviates by 5% of the weight should be, and no single tablet that weighs deviate by 10% of the weight should be. Of testing uniformity resulting tablet size ranges tablet diameter ranging from 11.91 mm to 12.16 mm and a thickness range of tablets ranging from 4.17 mm to 5.75 mm.

Hardness Test Results
From the test results obtained tablet hardness range ranged between 62.5 to 85 newtons. Hardness of tablets made uniform attempted to minimize the possible influence of violence against friability and disintegration time of tablets.

Friability test results
Friability testing done to see tablet resistance against a wide range of mechanical shocks such as impact or dings that may occur during the process of manufacture, packing, to the distribution of tablets. Tablet friability test results can be seen in Table 5.

Table 5: Friability test results

Formula	Initial weight (g)	Finish weight (g)	Friability (%)
I	6,7544	6,7430	0,17
II	6,5430	6,5320	0,17
III	7,1411	7,1411	0
IV	6,8319	6,8319	0
V	6,6519	6,6308	0,32

From the results obtained, the fifth tablet friability formula has met the requirements set by USP[17] as the fifth tablet friability formula has an average weight loss of no more than 0.8%

Desintegration time test results
Tests conducted disintegration time to see how quickly the tablet can be broken and destroyed in the human body fluids. Speed destruction of the tablet is an important step before the tablet can be dissolved and absorbed by the body. Test results obtained tablet disintegration time can be seen in Table 6, and its relationship with the concentration of Na-starch glycolate disintegrator of each formula shown in Figure 1.

Table 6: Desintegration time

Formula	Desintegration time mean (second)	SD
I	895.3333	2.516611
II	777.3333	2.516611
III	756.3333	2.516611
IV	874.6667	0.57735
V	877.3333	1.527525

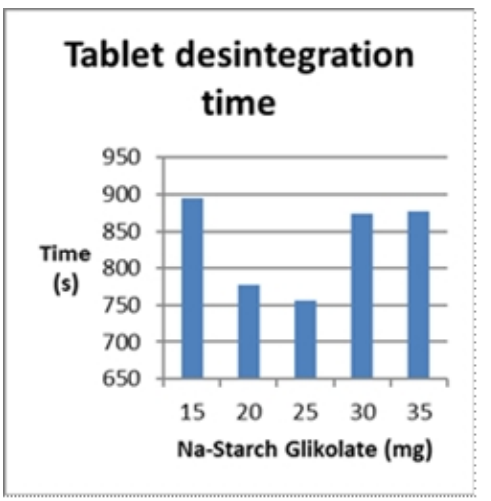
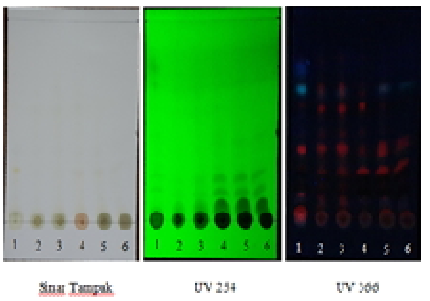


Figure 1: Effect of Na-Starch Glikolate on desintegration time

From the results obtained, the tablet disintegration time of the fifth formula had met the conditions set by the Indonesian Pharmacopoeia IV, the disintegration time of no more than 15 minutes (900 seconds), and the variation of the concentration of Na-starch glycolate influence on tablet disintegration time. Furthermore, the data were statistically processed using SPSS 2.0 software IBM stat with the method of one-way ANOVA and Tukey's test method to further see how changing the formula for tablet disintegration time. From the statistical data obtained it can be concluded that the tablet formula gives a significant influence on tablet disintegration time. And the results of further tests obtained results state that the formula contains 25 mg of Na-starch glycolate (formula III) had the fastest disintegration time compared with other formulas.

Qualitative Assay Test Results
Tablet qualitative assay was conducted to make sure the content of the extract compounds still present in the tablet and not damaged or lost during the process of formulation. From the test results obtained TLC chromatogram as shown in figure 2. It can be seen that the five formulas tablet has the same spot with the ethanol extract Legundi, with Rf 0.14; 0.24; 0.35; 0.44; 0.55; 0.64. This indicated that the compound contained in the ethanol

extract Legundi did not lost during the process of tablet formulation.



Note : **Sinar tampak = visible light**
Figure 2. TLC of tablet content test

Tablet obtained can be seen in Figure 1.

Figure 1. Tablet Legundi (*Vitex trifolia* L.)

CONCLUSION

Antiinflammatory tablet dosage of ethanol extract Legundi can be made by wet granulation method. Fifth formula made are qualified good tablet includes LOD, compressibility, flow rate, corner breaks, uniformity of weight and size, hardness, and disintegration time. From the results of research conducted, proved that the addition of Na-starch glycolate as a disintegrator does not always improve tablet disintegration time, but there are optimal levels. Of the five formulas are made, the formula III is the most optimal formula for increasing the disintegration time of tablets antiinflammatory Legundi ethanol extract.
As this study is an initial step in the manufacture of the preparation of the ethanol extract Legundi, so it is necessary to continue to phase comparisons with other dosage forms of ethanol extract Legundi to determine the dosage forms of the most effective and efficient in the use of ethanol extract Legundi as an anti-inflammatory herbal medicine.

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Cite this article as:

Resmi Mustarichie, Yoga Windhu Wardhana and Ryan Wahyudi. Anti-inflammation tablet of legundi (*Vitex trifolia* L.) ethanol extract with variation of sodium starch glycolate. Int. J. Res. Ayurveda Pharm. Jan – Feb 2016;7(Suppl 1):114-117 http://dx.doi.org/10.7897/2277-4343.07140

Source of support: Nil, Conflict of interest: None Declared