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Formulation and Stability Evaluation Nanoemulsion of Ethanol Extract of Parang Romang Leaf (Boehmeria Virgata)

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ABSTRACT: Parang romang (Boehmeria virgata) has an anti-cancer effect but has low biovailability orally. To increase the therapeutic effect, a new breakthrough is needed to make a nanoemulsion for the ethanol extract of parang romang leaves. Concentrated parang romang leaf extract was added to the selected mixture, the ratio of the surfactant (Tween20/80), olive oil and propylenglycol cosurfactant using the sonication method, the nanoemulsion was then evaluated for its stability including viscosity, pH, emulsion type, emulsion stability, droplet size and distribution particle. The results showed 14 formulas, with the best formula being formula 4 which has a viscosity of 66.7 cp, pH 5.5, w / o emulsion type, a nanoemulsion with stable pH and viscosity after freeze thaw cycle, a droplet size of 397.23 nm and distribution particle is 0,840.

Keyword : Nanoemulsion, Ethanol extract of parang romang leaves, Nanoemulsion stability

I. INTRODUCTION

The discovery of medicinal active substances is dominated by low solubility in water so that it provides low drug levels in the blood so that it does not achieve the desired therapeutic effect [1], one of the drugs used comes from plants, the active substances in plants have various kinds. one of the problems is the poor solubility in water, therefore it is necessary to do a new breakthrough in the manufacture of herbal formulations[2]. Many methods of developing drug delivery for modern medicines that aim to increase the therapeutic effect with specific targets in nano size have been widely used to improve the solubility of substances / drugs that are insoluble in water but the development of nano preparations in herbs is still rare. medicine in the form of nano is a nanoemulsion[1].

Nanoemulsion is a submicron size emulsion as a drug carrier to increase the bioavailability of therapeutic agents[3]. Nanoemulsion is the most advanced nanoparticle system for systemic active pharmaceutical delivery for controlled or continuous drug delivery and targeting[4]. Nanoemulsion is a thermodynamically stable isotropic system in which two immiscible liquids (water and oil) are mixed to form a single phase via a suitable surfactant[5]. The nanoemulsion globule size is in the 50-500 nm range and shows a narrow size distribution. One of the plants that has anti-cancer effects but has low bioavailability is parang romang (Boehmeria virgata)[6]. This study aims to make and to evaluate the nanoemulsion formulation of parang romang (Boehmeria virgata) in order to obtain herbal nanoemulsion which has high stability.

II. MATERIAL AND METHODS

Material

Tween 20 (Brataco), Tween 80 (Brataco), olive oil (Bertolli), Propylenglikol (Brataco) and aquadest (Brataco)

Method

Extraction

Parang romang leaves 800 gram extracted by maceration then concentrated with a rotary evaporator and water bath and obtained a thick extract.

Preparation of Formulation Nanoemulsion

Extract ethanol of parang romang leaves 15 mg add to 100 ml of the mixture of tween 20/80 surfactant, propylenglycol and olive oil which has been optimized with various comparisons to obtain 14 nanoemulsion formulations of parang romang leaf ethanol extract, The optimal formula on various formulas made can be seen in table 1. The response was homogeneity and clarity. Furthermore, the formula which remains homogeneous and clarity is chosen to be the best formulation that will be evaluated for stability

Viscosity test

The nanoemulsion viscosity can be measured by Brookfield viscometer.

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pH test
The pH of the formulation is measured with a pH meter.

Emulsion type
The nanoemulsion type test was performed by the dilution method. Test this done by dissolving the sample inward the water phase (1: 100) and the oil phase (1: 100). If the sample dissolves completely in aquadest, hence the type nanoemulsion is classified type oil in water (o/w), where as if the sample dissolves perfect in the oil phase, hence the type nanoemulsion is classified type water/oil (w/o).

Emusification time
Formula nanoemulsion (0.1 mL) was added to distilled water, AIF (artificial intestinal fluid), AGF (artificial gastrointestinal fluid to a final volume of 50 ml, homogenized by vortex. The emulsification time was observed.

Freeze-thaw cycle
Nanoemulsion formula stored at 25° C, 5 ° C and -20 ° C / 75% RH for 24 hours for 3 cycles. The nanoemulsion observed freeze-thaw cycle, The pH and viscosity.

Droplet size, Distribution particle
Droplet size and distribution particle is measured by particle size analyzer. 10 mL sample put into the cuvette and analyzed by particle size analyzer (PSA).

III. RESULT DAN DISCUSSION

Plant Extraction
The yield of the 800 kilogram of dried parang roman leaves , with a result of 5,31 %

Preparation of Formulation Nanoemulsion
Optimization of combination tween 20/80, propylenglycol and olive oil using the lattice design method obtained 14 formulas. The formula was stored for 24 hours and homogeneity was observed. The non-separating formula was selected as a nanoemulsion formula the requirements of the noemulsion. Result of the stability of the surfactant, cosurfactant and oil for 24 hours in optimization tween 20/80, propilen glikol and oil olive can be seen in table 1.

Tabel 1. Formula design and stability of the surfactant, cosurfactant and oil For 24 hours

No	Component of Nanoemulsion			Homogeneity	Clarity
	Oil (ml)	Surfactant(ml)	Co-Surfactant (ml)		
F1	3	67	30	√	√
F2	3,333326	66,33334	30,33333	√	X
F3	3,333326	65,33334	31,33333	√	X
F4	3	67	30	√	√
F5	3	66	31	√	X
F6	5	65	30	√	X
F7	4	65	31	√	X
F8	3	65	32	√	X
F9	3	65	32	√	X
F10	5	65	30	√	X
F11	3,666674	65,66666	30,66667	√	X
F12	4	66	30	√	X
F13	3	66	31	√	X
F14	4,333326	65,33334	30,33333	√	X

Viscosity Test
. The rheology properties play an important role in stability as viscosity is immediately affected by storage conditions[7]. Table 2. Viscosity of nanoemulsion extract ethanol parang romang leaves

pH Test
The pH affects the stability of the emulsions, the solubility and bioavailability of the drug through micro/nano emulsion at the site of permeation[7]. The pH nanoemulsian preparation can be seen in table 3.

Emulsion Type
The emulsion type nanoemulsian preparation can be seen in table 3.

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Emulsification time

The emulsification time is an important index for the assessment of the efficiency of nanoemulsi. The emulsification time nanoemulsian preparation can be seen in table 3.

Freeze-thaw cycle

Stability test do through freeze-thaw cycle method by observing the viscosity and pH. The observation result data shows that fluctuation occurred. The effect freeze-thaw cycle nanoemulsian preparation can be seen Fig 1.

Droplet size and distribution particle

The droplet size and distribution particle nanoemulsian preparation can be seen in figure 2.

Discussion

Based on the research results in table 1, combination of tween 20, olive oil with propylenglycol is able to produce a homogeneous and clarity mixture in a high ratio combination of Tween 20/80. This is because tween 20/80 as surfactan play an important role in reducing interface tension in phase[8]. The surfactant should capable of micro emulsification of the oily phase and should also possess the good solubilizing potential for the hydrophobic drug compounds[9]. increasing oil proportion resulted in a decrease in the clarity of emulsion[10].

Table 3. pH, emulsion type and emulsification time of Nanoemulsion

Formula	Viscosity	pH	Emulsion type	Emulsification time
F1	70,6	5.54	O/W	13
F2	183,3	5.23	O/W	14
F3	108,3	5.57	O/W	15
F4	66,7	5.85	O/W	13
F5	153,3	5.75	O/W	15
F6	150,0	5.65	O/W	16
F7	116,7	5.90	O/W	14
F8	100,9	6.01	O/W	15
F9	130,0	5.03	O/W	15
F10	115,5	5.89	O/W	14
F11	150,0	5.34	O/W	14
F12	125,0	6.06	O/W	15
F13	100,0	5.73	O/W	16
F14	128,9	5.50	O/W	17

The viscosity of the ethanol extract of parang romang leaf nanoemulsion formulas ranged from 66.7–183,3 mPa.sec, nanoemulsion preparations containing high concentrations of Tween 20/80, propylenglycol and olive oil had higher viscosities than preparations with a low concentration combination of Tween 20/80, propylenglycol and olive oil. This occurs because the higher amount of surfactant causes the bond between the surfactant and the oil and water phases are also more and result in greater resistance to flow. Low viscosity of systems shows that it is O/W type and high viscosity shows that it is water in oil type system[11] Ghareeb et al. has determined viscosity of nimodipine nanoemulsion formulations by using NDJ-digital viscometer (spindle no 1) ata 25^{o}C reported the viscosity of formulations in range 33,026-107.782 cP).

The result of pH of nanoemulsion were found to be in range 5,23-6,06. It was show all nanoemulsion acceptable in oral use. Chidi et al. measured the pH of the carvedilol nanoemulsion by pH meter digital and found pH in the range of 5.43 to 6.23 is suitable for oral administration.

The result of nanoemulsion type show all nanoemulsion are diluted with water w/o are not and thus they undergo phase inversion into o/w Nanoemulsion. A water soluble dye is solubilized within the aqueous phase of the w/o globule but is dispersible in the o/w globule. An oil soluble dye is solubilized within the oil phase of the o/w globule but is dispersible in the w/o globule[12]. The aqueous continuous phase was labelled with dye while the oily dispersed phase remained unlabelled therefore confirming the formed nanoemulsion as O/W type[11]

The result of emulsification time all formulas show in range 13-17 second. a good emusificatuion time is less than 1 minutes[13]. Tween 80 to lower the interfacial tension at o/w

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interface, as the presence of high concentration of surfactant will facilitate the self-emulsification process and eventually lead to rapid emulsification rate and cosurfactant would augment the reduction to the interfacial tension and also influence interfacial film curvature and hence spontaneity of emulsification process[10].

Physical stability during storage is of vital importance for the nanoemulsion[14]. formulas nanoemulsion were stable during the experiment for 3 different temperature namely room temperature (25^{o}C), Low temperature (5 ^{o}C) and high temperature (-20 ^{o}C). The pH and viscosity nanoemulsion were observed before and after freeze-thaw cycle. The result show increase pH and viscosity after freeze thaw cycle, One way ANOVA statistical analysis shows that the

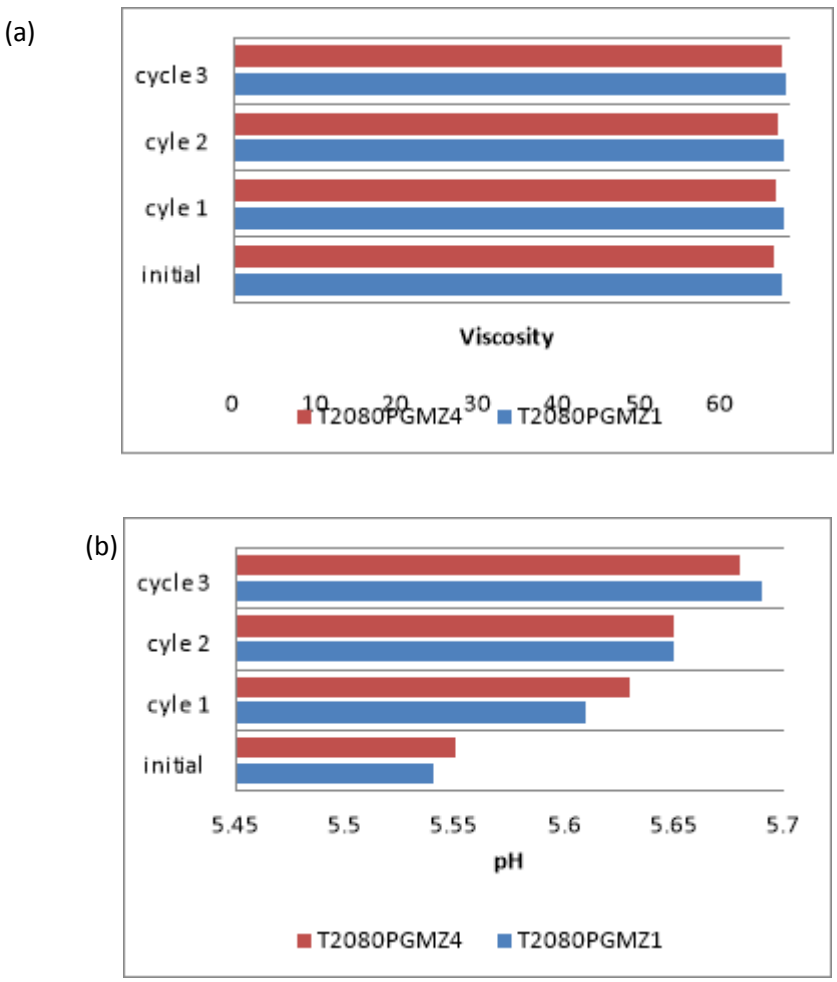

Fig 1. Effect of Freeze thaw cycle stability of nanoemulsian ethanol extract ethanol parang romang

pH and viscosity values of the two formulas before and after the frezze thaw cycle are not significantly different with a p-value> 0.05. One way ANOVA statistical analysis showed that the pH and viscosity values of the two formulas before and after the frezze thaw cycle were not significantly different with a p-value> 0.05. This shows that the nanoemulsion formula for the ethanol extract of parang romang leaves with a combination of the surfactant tween 20 and tween 80 produces a nanoemulsion with stable pH and viscosity.

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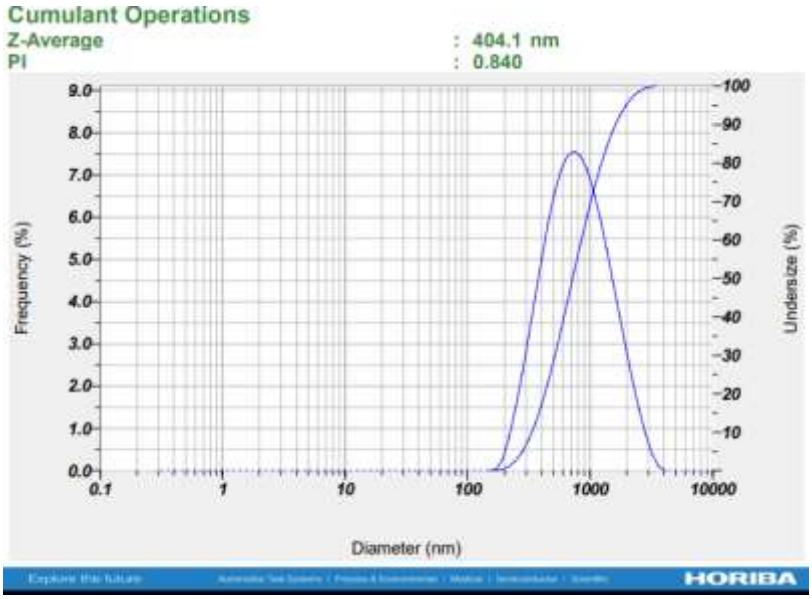

Figure 2. Particle size and distribution of nanoemulsion

In this study, show F4 nanoemulsion ethanol extract parang romang leaves droplet size is 404,1 nm and distribution particle is 0,840. it is indicate nanoemulsion droplet size and distribution particle accept. Nanoemulsion are transparant colloidal dispersion having the average dropletsize 20-500 nm. Polydispersity is the ratio of the standard deviation to mean droplet size, so it indicates the uniformity of droplet size within the formulation. The higher the polydispersity, the lower the uniformity of the droplet size in the formulation[9].

IV. CONCLUSION

Nanoemulsions ethanol extracts parang romag leaves prepared from mixed tween80-tween20, Propilenglikol and olive were successfully. The obtained nanoemulsions were viscosity 66.7 cp, pH 5.5, w / o emulsion type, a nanoemulsion with stable pH and viscosity after freeze thaw cycle, a droplet size of 397.23 nm and distribution particle is 0,840.

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