FORMULATION AND CHARACTERIZATION OF *ELEUTHERINE PALMIFOLIA* EXTRACT-LOADED SELF NANOEMULSIFYING DRUG DELIVERY SYSTEM USING MIGLYOL 812 AND VIRGIN COCONUT OIL (VCO) AS THE CARRIER OIL

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ABSTRACT

Background: *Eleutherine palmifolia* (*E. palmifolia*), also known as Dayak onion, is a native plant of Kalimantan, Indonesia, used to cure various diseases, and it has the disadvantage of low solubility. However, the application of self-nanoemulsifying drug delivery system (SNEDDS) increases the solubility and bioavailability. **Methods:** The formulation of SNEDDS *E. palmifolia* consists of oil, surfactant, and co-surfactant. The components of this formula are determined based on the optimization results. **Results:** The results of this study showed that there is no phase separation with SNEDDS because of the surfactant contents. Furthermore, it showed that two out of forty optimized designs were able to meet the predetermined specifications of formula A (miglyol 812: Tween 80: PEG 400) and E (miglyol 812: Tween 80: propylene glycol) at a ratio of 1:1:1 and 1:3:1 respectively. The characteristics of the optimal formulation showed transmittance value of > 90%; pH of 5,10-5,20; viscosity of 2,21-14,51 cP; emulsification time of < 120 second, and particle size of 24,71-136,77 nm. **Conclusion:** The optimal formula of SNEDDS *E. palmifolia,* for Formula A uses miglyol 812 as oil, Tween 80 as surfactants, and PEG 400 as co-surfactant at a component ratio of 1:1:1 (Formula A). Meanwhile, it uses 812 as oil, Tween 80 as surfactants, and propylene glycol as co-surfactant at a component ratio of 1:3:1 for Formula E.
Keywords: SNEEDS, self-nanoemulsifying, characterization, formulation, *Eleutherine palmifolia*

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INTRODUCTION

SNEDDS is an oil-based isotropic nanoparticle formulation containing surfactant and co-surfactants [1-3]. The solubility of natural ingredients, estimated at 40% as a new source of the drug, is only slightly soluble in water [4]. Low water solubility and permeability in penetrating through the absorption barrier may alter the bioavailability of a naturally occurring compound in the body [5]. Meanwhile, *Eleutherine palmifolia*, also known as Dayak onion, is an indigenous plant of Kalimantan, used to cure various types of diseases. The phytochemical constituent of Dayak onion, which functions as an anticancer is naphthoquinone, and it has bioactivity as an antioxidant [6]. In addition, it is a lipophilic compound with a logP value of 3.933 [7], which means that the solubility in water media is reduced. Therefore, it is necessary to develop SNEDDS to improve the bioavailability of naphthoquinone contained in *E. palmifolia* extract.

This study aims to assess the effect of the comparison of oils, surfactants, and co-surfactants in the SNEDDS formula of *E. palmifolia* extract using miglyol 812 and VCO as a carrier oil. In addition, the surfactants used were tween 80 and transcutol, while the co-surfactants used were PEG 400 and propylene glycol. The optimal formula was determined based on the homogeneity of the mixture of oil, surfactant, and co-surfactant, with a transmittance value> 90%. The characteristic formulas consist of emulsification time, pH, particle size, viscosity, and particle morphology. Therefore, this study is considered an optimization stage to obtain the optimal SNEDDS formula.

MATERIALS AND METHOD

MATERIAL

Miglyol 812 purchased from Sigma Aldrich, Tween 80 purchased from Merck, Transcutol gift from Gattefose. Virgin Coconut Oil (VCO) was purchased from Herbal Bagoes, PEG 400 and propylene glycol purchased from Merck.

METHOD

Table 1. Formulation ratio of *E.palmifolia* SNEDDS

Formula		Ratio	Miglyol 812	VCO	Tween 80	Transcutol	PEG 400	Propylene glycol
A		1:1:1	1	-	1	-	1	-
		1:2:1	1	-	2	-	1	-
		1:3:1	1	-	3	-	1	-
		1:4:1	1	-	4	-	1	-
		1:5:1	1	-	5	-	1	-
B		1:1:1	-	1	1	-	1	-
		1:2:1	-	1	2	-	1	-
		1:3:1	-	1	3	-	1	-
		1:4:1	-	1	4	-	1	-
		1:5:1	-	1	5	-	1	-
C		1:1:1	1	-	-	1	1	-
		1:2:1	1	-	-	2	1	-
		1:3:1	1	-	-	3	1	-
		1:4:1	1	-	-	4	1	-
		1:5:1	1	-	-	5	1	-
D		1:1:1	-	1	-	1	1	-
		1:2:1	-	1	-	2	1	-
		1:3:1	-	1	-	3	1	-
		1:4:1	-	1	-	4	1	-
		1:5:1	-	1	-	5	1	-
E		1:1:1	1	-	1	-	-	1
		1:2:1	1	-	2	-	-	1
		1:3:1	1	-	3	-	-	1
		1:4:1	1	-	4	-	-	1
		1:5:1	1	-	5	-	-	1
F		1:1:1	-	1	1	-	-	1
		1:2:1	-	1	2	-	-	1
		1:3:1	-	1	3	-	-	1
		1:4:1	-	1	4	-	-	1
		1:5:1	-	1	5	-	-	1
G		1:1:1	1	-	-	1	-	1
		1:2:1	1	-	-	2	-	1
		1:3:1	1	-	-	3	-	1
		1:4:1	1	-	-	4	-	1
		1:5:1	1	-	-	5	-	1
H		1:1:1	-	1	-	1	-	1
		1:2:1	-	1	-	2	-	1
		1:3:1	-	1	-	3	-	1
		1:4:1	-	1	-	4	-	1
		1:5:1	-	1	-	5	-	1

Optimization of oil: surfactant: co-surfactant at a ratio of 1:1:1, 1:2:1, 1:3:1, 1:4:1, 1:5:1. The component mixture produces a clear, transparent solution and no phase separation (homogeneous).

RESULTS

Table 2. Physical Characteristics and Transmitance (%) of *E. palmifolia* extract-Loaded SNEDDS

Formula		Physical characteristics	Transmittance (%)	Formula		Physical characteristic	Transmittance (%)
1	A (1:1:1)	+	99.57	21	E (1:1:1)	-	10.55
2	A (1:2:1)	+	99.88	22	E (1:2:1)	+	69.71
3	A (1:3:1)	+	94.98	23	E (1:3:1)	+	92.45
4	A (1:4:1)	+	96.17	24	E (1:4:1)	+	95.80
5	A (1:5:1)	+	96.95	25	E (1:5:1)	+	99.10
6	B (1:1:1)	-	97.06	26	F (1:1:1)	-	4.97
7	B (1:2:1)	-	66.06	27	F (1:2:1)	-	8.51
8	B (1:3:1)	-	87.75	28	F (1:3:1)	-	73.98
9	B (1:4:1)	-	71.05	29	F (1:4:1)	-	83.44
10	B (1:5:1)	-	86.40	30	F (1:5:1)	-	98.96
11	C (1:1:1)	-	97.92	31	G (1:1:1)	-	97.21
12	C (1:2:1)	-	95.71	32	G (1:2:1)	-	95.31
13	C (1:3:1)	-	85.32	33	G (1:3:1)	-	84.61
14	C (1:4:1)	-	89.68	34	G (1:4:1)	-	88.61
15	C (1:5:1)	-	86.69	35	G (1:5:1)	-	85.91
16	D (1:1:1)	-	97.54	36	H (1:1:1)	-	98.09
17	D (1:2:1)	-	66.67	37	H (1:2:1)	-	95.77
18	D (1:3:1)	-	88.46	38	H (1:3:1)	-	97.25
19	D (1:4:1)	-	71.54	39	H (1:4:1)	-	91.31
20	D (1:5:1)	-	87.02	40	H (1:5:1)	-	91.86

Note :
+ = Clear, transparent, no phase separation (homogeneous)
- = Clear, transparent, phase separation (not homogeneous)

The use of miglyol 812 and VCO at a ratio of 1:1:1, 1:2: 1, 1:3:1, 1:4:1, 1:5:1. Based on the optimization of the *E. palmifolia* SNEDDS formula, it is known that formulas that can be continued in the next stage are eight formulas out of 40 formulas. Formulas that, in small proportions, produce a clear, transparent mixture, and no phase separation and transmittance values> 90% are the basic parameters for choosing the best formula. Based on these considerations, the next step is to make *E. palmifolia* SNEDDS, and the following characteristic is formula A (miglyol 812: Tween 80: PEG 400) at a ratio of 1: 1: 1 and formula E (miglyol 812: Tween 80: propylene glycol) at a ratio 1: 3: 1.

Table 3. Result characterization of *E. palmifolia* extract-loaded SNEDDS

Selected SNEDDS formula		pH ± SD	Viscosity (Cp) ± SD	Emulsification Time (second) ± SD		Particles size (nm) ± SD	
				AIF	AGF	AIF	AGF
1	A (1:1:1)	5.20 ± 0,05	2.21 ± 0,77	69.00 ± 0,01	69.00 ± 0,05	74.02 ± 3.97	24.71 ± 0.93
23	E (1:3:1)	5.10 ± 0,10	14.51 ± 0,50	52.00 ± 0,03	49.00 ± 0,03	134.77 ± 2.83	75.86 ± 2.63

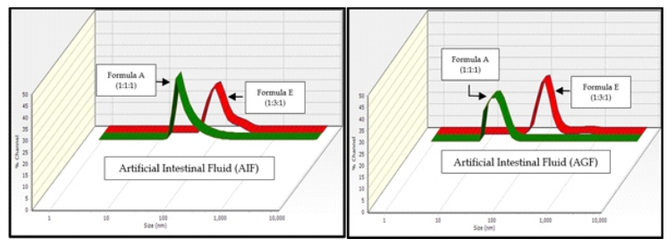

Figure 1. Diagram of the particle size distribution of *E. palmifolia* extract-loaded SNEDDS

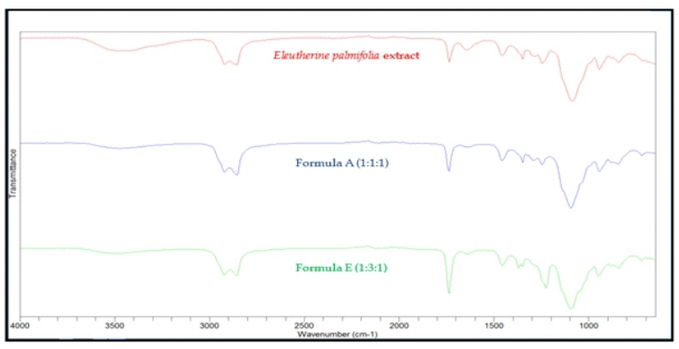

Figure 2. Infrared Spectrum of *E. palmifolia* ( ), Formula A 1:1:1 ( ), Formula E 1:3:1 ( )

CONCLUTION

The formulation of SNEDDS *E. palmifolia* consists of oil, surfactant, and co-surfactant. Forty designs that only two formulas that meet the characteristics of formula A (miglyol 812: tween 80: PEG 400) at a ratio of 1:1:1 and formula E (miglyol 812: Tween 80: propylene glycol) at a ratio of 1:3:1. The optimal formula of SNEDDS *E. palmifolia* uses miglyol oil 812, Tween 80 surfactants, and PEG 400 co-surfactant at a component ratio of 1:1:1 and with propylene glycol as co-surfactant at a component ratio of 1:3:1.

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