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Red Ginger oleoresin nanoemulsion characteristics by ultrasonication

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Abstracts

Red ginger is a biopharmaceutical plant that is used as herbal medicine. The use of red ginger in the food industry is mainly in an emulsion form, but that is unstable and hydrophobic. The ultrasonication technique could change the emulsion into a nanoemulsion to minimize these disadvantages. This research aimed to determine the effect of ultrasonication on red ginger oleoresin nanoemulsion characteristics. The study used a completely randomized design of 4 treatments based on sonication time (0, 30, 60, and 90 minutes). The study was analyzed by ANOVA Tukey's test at $P \leq 0.05$, it showed that ultrasonication affected the characteristics of red ginger oleoresin nanoemulsion. The best result shows that in 90 minutes mixed time with transparent yellow colour. It is soluble in acetone, methanol, ethanol, and aquadest solvents. The best particle size is 572.43±8.72 nm, and antioxidant activity is (IC_{50}) 16.34 ±1.33 ppm.

Keywords: nanoemulsion; oleoresin; red ginger; sonication time; ultrasonication

1. Introduction

People prefer to use traditional medicines such as herbs and biopharmaceuticals for prevention and health care. It is supported by the Circular Letter of the Ministry of Health of the Republic of Indonesia, Directorate General of Health Services Number: HK.02.02/IV.2243/2020 concerning the use of traditional medicines for health maintenance, disease prevention, and health care [1].

Red ginger is a biopharmaceutical plant that is used as herbal medicine. Red ginger contains gingerol and shogaol, which function as immunomodulators. Red ginger has anti-inflammatory and antioxidant effects that can relieve symptoms of inflammation in the lungs due to the Coronavirus [2].

One processed red ginger product is oleoresin, consisting of resin and essential oils. The resin consists of active compounds in the form of phenols such as gingerol, shogaol, and zingerone, giving it a spicy taste and as a natural antioxidant. Meanwhile, essential oils are volatile compounds that give ginger flavour characteristics [3].

Oleoresin is used in the food, agriculture, pharmaceutical, and cosmetic industries as emulsions. However, emulsions have the disadvantage that they are unstable. The environment quickly affects emulsions, such as temperature, heat, and light [3]. Emulsions are hydrophobic, difficult to dissolve in water, difficult to disperse, speed, low absorption and reduce their ability as a flavouring agent [4].

An alternative to overcome the weakness of red ginger oleoresin emulsion is to process it into the nanoemulsion [5]. Nanoemulsion combine of oil, water, and surfactant phases with nanoparticle sizes of 1-1000 nm [6]. Nanoemulsions increase the solubility, the bioavailability of active ingredients, absorbability and improve organoleptic properties. It made the active substance more stable [4].

Nanoemulsification manufacturing techniques are divided into two. It is a High Energy Emulsification (HEE) and Low Energy Emulsification (LEE). HEE includes high-pressure homogenization, micro-fluidification, and ultrasonication. LEE includes spontaneous emulsification, solvent evaporation and phase reversal [7].

Ultrasonication is one of the methods of producing nanoemulsions by utilizing ultrasonic waves. Ultrasonic waves have a frequency between 20-40 kHz [8]. The physical effect of high-intensity ultrasonication is emulsification. The application of ultrasonic waves produces waves in the interface (interfacial), which result in the movement of the oil phase into the liquid phase in the form of droplets, causing an increase in pressure in the liquid, resulting in the breakdown of oil droplets into smaller sizes and dispersed in the liquid phase [9].

Until now, research on the use of ultrasonication in the manufacturing of red ginger oleoresin nanoemulsions is still limited. There are several studies on the method of making ginger nanoemulsions. It is HEE and LEE, as described above. The manufacture of nanoemulsions with HEE usually uses an ultra turrax homogenizer, as reported by Harmi [10] and Noor et al. [11]. While the LEE method was reported by Cahyani [12] and Faradisa [13] using spontaneous emulsification. Redha, et al. [14] using EIP emulsification (Emulsion Phase Inversion).

Therefore, this research focused on ultrasonication's effect on the characteristics of red ginger oleoresin nanoemulsions, including particle size, solubility, and antioxidant activity. So red ginger oleoresin nanoemulsion can be a raw material in producing of herbal medicines, herbs, and supplements. It is also functional food with better and more efficient characteristics than red ginger oleoresin, which has not been in the form of nanoemulsion.

2. Experiments Procedure

Materials

The tools used in this research are analytical balance (Radwag-AS220.R2®), oven (Memmert ®), hammer mill, incubator (Memmert ®), hotplate magnetic stirrer (Chimarec+®), vacuum rotary evaporator (B-ONE®), ultrasonicator type bath (Branson 5800®), buret (Iwaki-pyrex®), erlenmeyer (Iwaki-pyrex®), beaker glass (Iwaki-pyrex®), measuring pipette (Iwaki-pyrex®), measuring cup (Iwaki-pyrex®), measuring flask (Iwaki-pyrex®), test tube (Iwaki-pyrex®), micro pipette (Dragon Lab®), Spectrophotometer UV-Vis Single Beam (K-LAB®), and Particle Size Analyzer (Horiba SZ-100®).

The materials used in this research are red ginger (10-12 months) from Adirejo-Jabung-East Lampung (the species is *Zingiber officinale* var. *rubrum*), aquadest, ethanol 96% (Merck®), Tween 80 (Merck®), hexane (Merck®), acetone (Merck®), methanol (Merck®), DPPH (Himedia®), and filter paper (Whatman®).

Research Design

The study used a one-factor, Completely Randomized Design (CRD) of 4 treatments based on sonication time. It is N0 (without sonication time), N30 (30 minutes), N60 (60 minutes), and N90 (90 minutes) with three replications. The research stages were: sample preparation, extraction of red ginger rhizome, red ginger oleoresin nanoemulsion, and characterization of red ginger oleoresin nanoemulsion.

Sample Preparation

The red ginger was cleaned of soil and dirt and then washed, sliced with a thickness of ± 1-3 mm, and dried using an oven for 48 hours at 50 ^{0}C until a moisture content of 12% was obtained. Dried ginger was ground using a hammer mill and sieved using a 50-mesh sieve [15].

Red Ginger Rhizome Extraction

The extraction method uses graded maceration, modified with a ratio of powder and solvent, namely 1:3 (w/v) [16]. The Red ginger powder used 100 grams and ethanol solvent 96% 300 mL. Then soak for 24 hours at room temperature with stirring every 6 hours, then filter to obtain the dregs and filtrate. Maceration was carried out in stages three times. Next, filtrate 1, filtrate 2, and filtrate 3 were mixed. The extraction results were separated from the solvent using a rotary evaporator at 50 ^{0}C for 60 minutes to obtain red ginger oleoresin.

Ginger Oleoresin Nanoemulsion

The production of nanoemulsions using a modified ultrasonication [17][18]. Red ginger oleoresin (oil phase) was dissolved in 96% ethanol (co-surfactant) at a concentration of 50% (50 mL ginger oleoresin in 100 mL ethanol). Then added Tween 80 (surfactant) by 10% of the oil phase, as much as 5 mL, then added distilled water (water phase) which was dripped with a burette slowly at a speed of 5 ml/minute until a volume of 500 mL was obtained accompanied by stirring at a speed of 750 rpm. Then the water phases were added. They have stirred again with a magnetic stirrer for 60 minutes at a speed of 1500 rpm at a temperature of 30 ^{0}C. The mixture was placed in a bath-type ultrasonicator of 40 kHz and 30 ^{0}C at the predetermined time. Then the results of the process were filtered with 0.45 micron filter paper, and the solvent was separated using a rotary evaporator at a temperature of 50 ^{0}C for 30 minutes.

Characterization of Red Ginger Oleoresin Nanoemulsion

The Particle Size

The Particle size of red ginger oleoresin nanoemulsion was analyzed using Particle Size Analyzer (PSA) [19]. The testing process uses the principle of Dynamic Light Scattering (DLS).

The Solubility

The red ginger oleoresin nanoemulsion solubility test was carried out by mixing the nanoemulsion with organic solvent (1:1) in a 10 ml container. It is a measuring cup of various polarity levels, namely hexane, acetone, ethanol, methanol, and aquadest. The volume of each organic solvent phase is measured before mixing. Then the solubility value increased the organic phase volume [20].

The Antioxidant Activity

DPPH method is testing of antioxidant activity. Antioxidant activity is expressed in IC_{50} value or concentration capable of reducing 50% of DPPH free radicals. The test was carried out by making a 50 ppm DPPH solution. A red ginger oleoresin nanoemulsion made in solution with five concentration series. It is 200 ppm, 400 ppm, 600 ppm, 800 ppm, and 1000 ppm from each research sample. The percentage of antioxidant inhibition was determined by reacting the test solution and DPPH solution in a ratio of 1:1 and then incubating for 30 minutes at 37 ^{0}C. Next, the absorbance was measured using a spectrophotometer at 517 nm. The percentage of antioxidant inhibition calculated from the absorbance value obtained from the test was included in the percent inhibition formula. The IC_{50} value is expressed as Ln x in the regression equation y = ax + b from the curve of percent antioxidant inhibition as ordinate and Ln concentration as abscissa. “Y” is the value of 50, “a”, and “b” is obtained from the regression equation [21].

Statistical Analysis

The data obtained from the research results were processed with variance to determine the effect of treatment on the parameters tested using the analysis of variance (ANOVA) at $p \leq 0.05$. Further tests were carried out using the Tukey test to determine which treatments differed.

3. Result and Discussion

Red Ginger Oleoresin Nanoemulsion

Red ginger oleoresin nanoemulsion is yellow with different levels of clarity. In the treatment, N0 was slightly cloudy yellow, N30 and N60 were cloudy yellows, and N90 was clear/transparent yellow (Figure 1). These results are under research by Noor et al. [11], that the ginger nanoemulsion was cloudy yellow to transparent yellow.

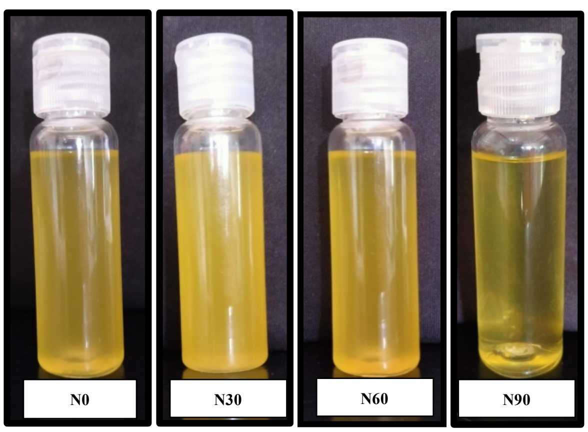

Figure 1 Red Ginger Oleoresin Nanoemulsion. N0 (without sonication time), N30 (30 minutes of sonication time), N60 (60 minutes of sonication time), and N90 (90 minutes of sonication time)

Ultrasonication affects the clarity level of red ginger oleoresin nanoemulsion. The longer the sonication time, the more transparent the colour of the nanoemulsion. It is in line with the research of Redha et al. [22] that nanoemulsion's clarity level is influenced by particle size. The smaller the particle size, the easier it is to disperse so that the colour will be more explicit and transparent.

The Particle Size

The particle size of red ginger oleoresin nanoemulsion is presented in Table 1. Based on the analysis of variance, the particle size of the red ginger nanoemulsion in each treatment showed significant differences. All treatments in this study fit into the nanoparticle size range. At N0 the particle size is 727.53 ± 15.61 nm. In contrast, at N30 the particle size has increased, meaning that at the time of sonication of 30 minutes, the ultrasonic waves have been unable to break the chemical bonds, resulting in particle clumping [23]. At N60, a size reduction begins to occur, which means that at 60 minutes of sonication, it can destroy chemical bonds so that the size gets smaller. The smallest particle size obtained from the ultrasonication treatment of N90 is 572.43±8.72 nm. The sonication time affects the particle size. The longer the sonication time, the smaller the particle size [24]. It is due to the longer duration of the power of ultrasonic radiation, which can separate agglomerated particles and break them into smaller sizes [25].

Table 1 Particle size of red ginger oleoresin nanoemulsion

Treatment	Particle size (nm)
N0	727,53±15,61b
N30	891,80±22,50a
N60	882,40±2,71a
N90	572,43±8,72c

Note: The average value followed by a different letter indicates that there is a significant difference in the 5% Tukey test ($P \leq 0.05$)

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The Solubility

The solubility of red ginger oleoresin nanoemulsion in various solvents is shown in Table 2. The solubility of red ginger oleoresin nanoemulsion showed a significant difference at $P \leq 0.05$ using the Tukey test. However, acetone, methanol, ethanol, and aquadest solvents were not significantly different. Although statistically not significantly different, the solubility, especially in acetone and methanol, the longer the sonication time, the higher the solubility. Red ginger oleoresin nanoemulsion was insoluble in hexane, soluble in acetone, methanol, ethanol, and aquadest. These results are consistent with the research by Jusnita and Syurya [20] that red ginger oleoresin cannot be dissolved in hexane because hexane is non-polar. One of the active compounds in red ginger nanoemulsion is a phenolic compound that tends to be polar, so that it will dissolve in semi-polar solvents (acetone) and polar solvents (methanol, ethanol, and aquadest) [26]. The compatibility of the solute and solvent properties largely determines the solubility of a substance in a solvent. The nature of like dissolves likes, among others, due to its polarity [17].

Table 2 The Solubility of red ginger oleoresin nanoemulsion in various solvents

Treatment	The solubility (%)				
	Hexane	Acetone	Methanol	Ethanol 96%	Aquadest
N0	0,00±0,00b	80,00±14,14a	73,33±14,14a	100,00±0,00a	100,00±0,00a
N30	0,00±0,00b	80,00±14,14a	75,00±17,67a	100,00±0,00a	100,00±0,00a
N60	0,00±0,00b	81,67±10,61a	76,67±14,14a	100,00±0,00a	100,00±0,00a
N90	0,00±0,00b	83,33±3,53a	100,00±0,00a	100,00±0,00a	100,00±0,00a

Note: The average value followed by a different letter indicates that there is a significant difference in the 5% Tukey test ($P \leq 0.05$)

The Antioxidant Activity

The IC_{50} values obtained from the red ginger oleoresin nanoemulsion research showed significantly different results. In the N0 treatment, the IC_{50} value of 50.56±1.47 ppm was included in the category of vigorous antioxidant activity. In the N30 treatment, the IC_{50} value was 36, 13±1.47 ppm, in N60 the IC_{50} value was 30.44±2.78 ppm, and in N90 the IC_{50} value was 16.34±1.33 ppm (Figure 2). The IC_{50} values of N30, N60, and N90 were less than 50 ppm, which means that the antioxidant activity in the treatment was potent. The IC_{50} value of the red ginger oleoresin nanoemulsion is higher than the red ginger extract in [27] research, which is 57.14 ppm.

The longer the sonication time, the smaller the IC_{50} value, which means the antioxidant activity is getting stronger. Sholihah et al. [28] research show that sonication time affects the IC_{50} value.

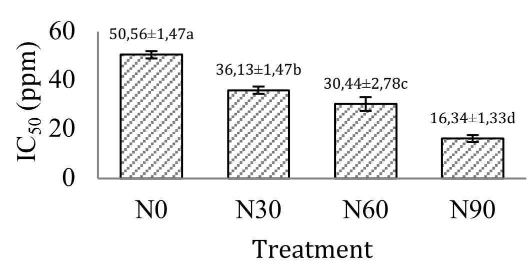

Figure 2 Histogram of antioxidant activity (IC_{50}) of red ginger oleoresin nanoemulsion

The longer the sonication time, the ultrasonicator will emit heat, causing the IC_{50} value to decrease. It means the antioxidant activity is getting stronger. According to Dzakwan and Priyanto [29] ultrasonication can reduce the particle size to the nanometer scale, thereby increasing the specific surface area, particle solubility, the concentration of bioactive components, and antioxidant activity.

4. Conclusion

Ultrasonication affects the characteristics of red ginger oleoresin nanoemulsion. The longer sonication time. The colour of the nanoemulsion becomes transparent yellow. The particle size gets smaller. It dissolves in polar and semi-polar solvents and the antioxidant activity increase.

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